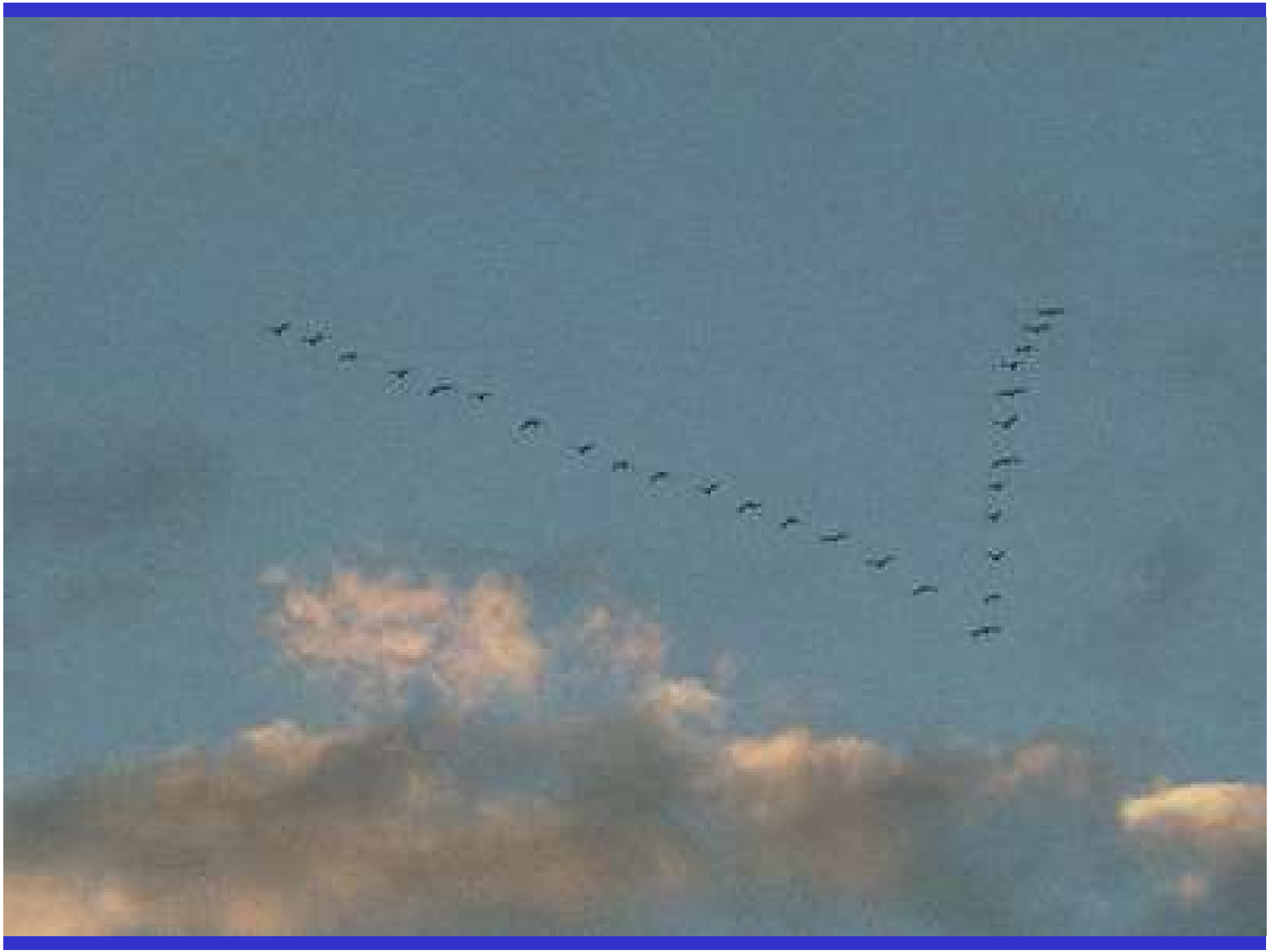
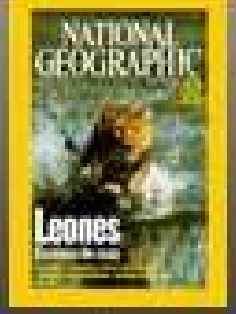


CONVIVENCIA MORTAL

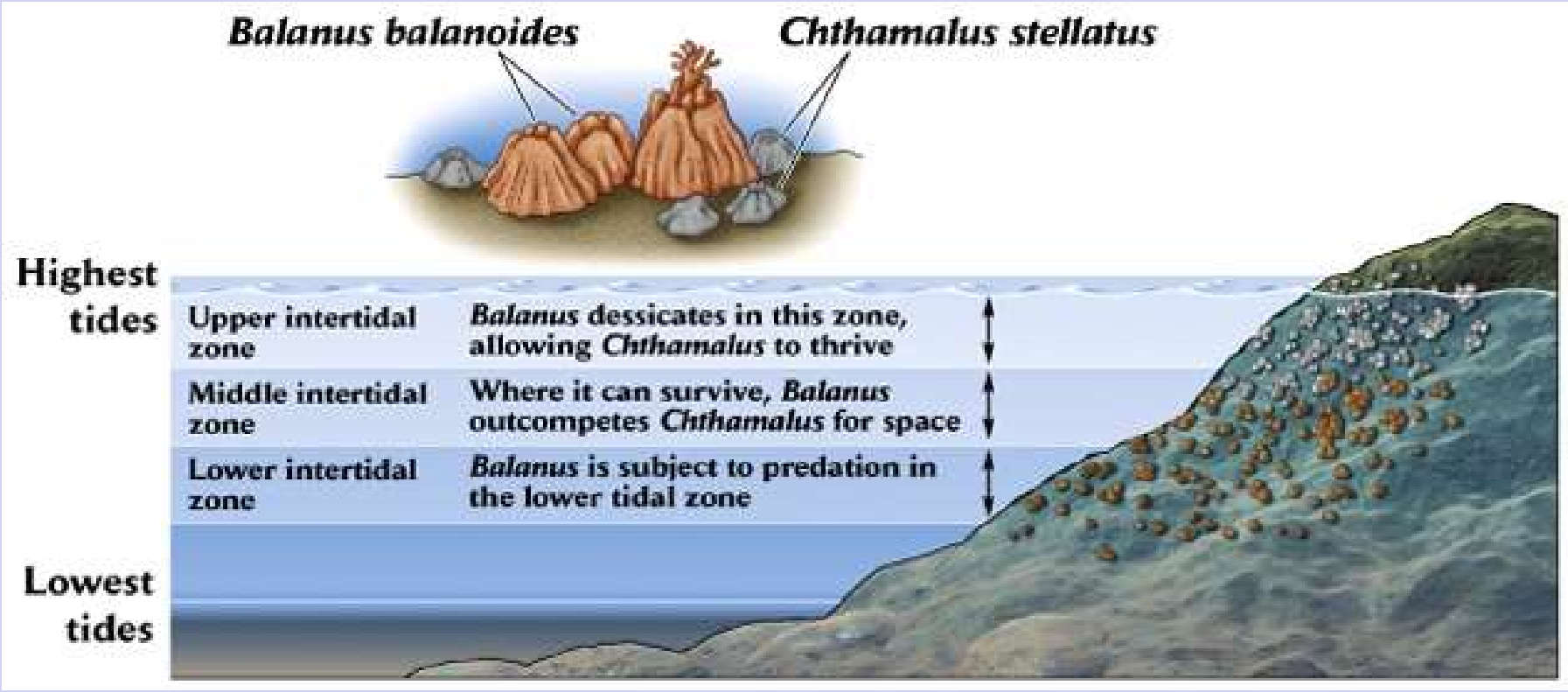
NATIONAL GEOGRAPHIC
ESPAÑA

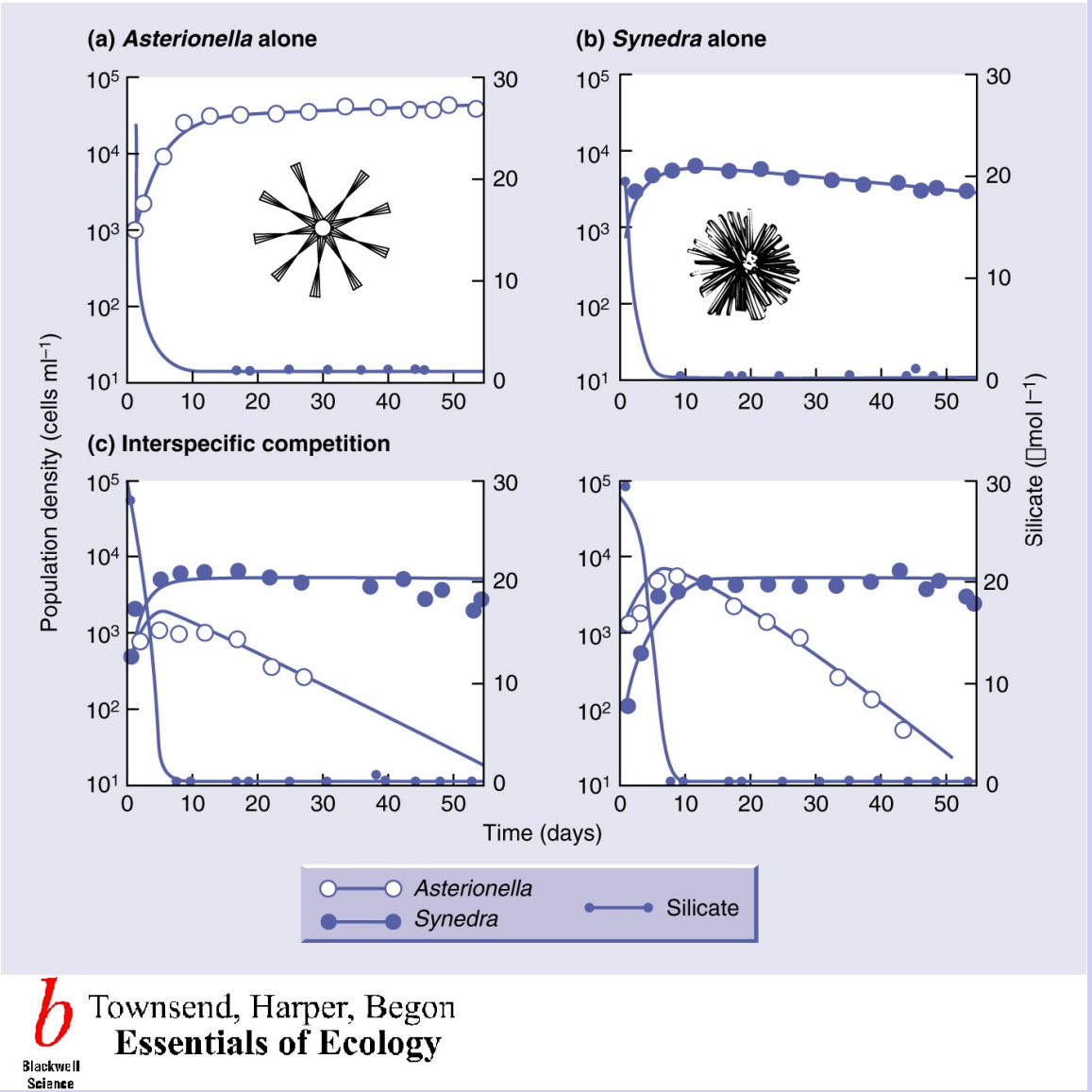


septiembre 2006

Factores por los que se puede entablar competencia entre plantas de igual o distinta especie

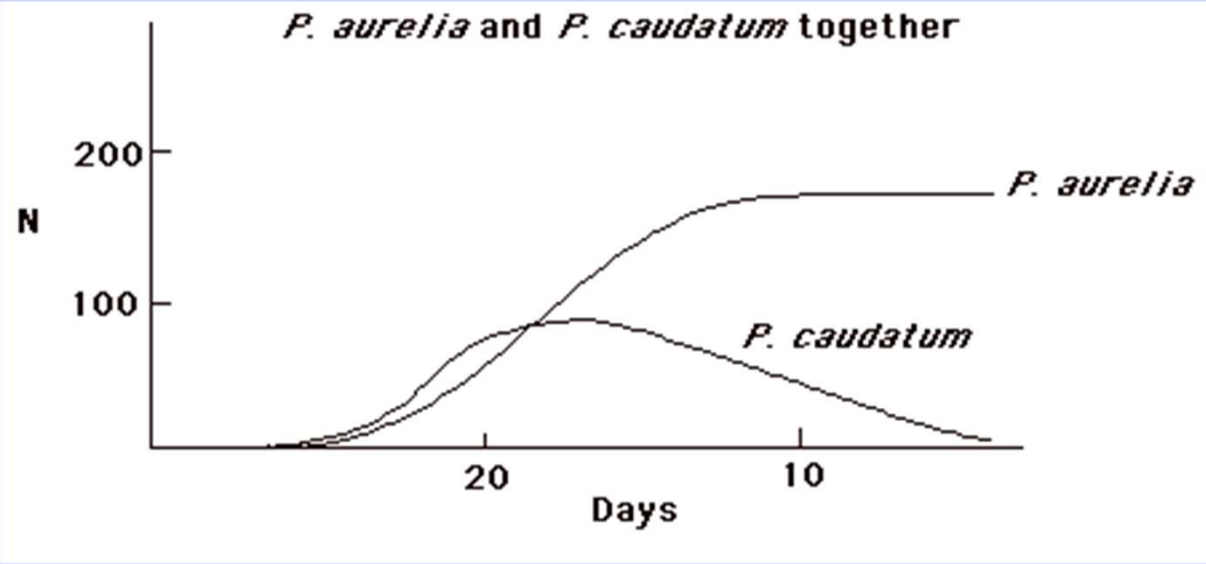
La competencia es una interacción entre individuos, provocada por la necesidad común de un recurso limitado, y que conduce a la reducción de la supervivencia, el crecimiento y/o la reproducción de por lo menos algunos de los individuos competidores implicados.

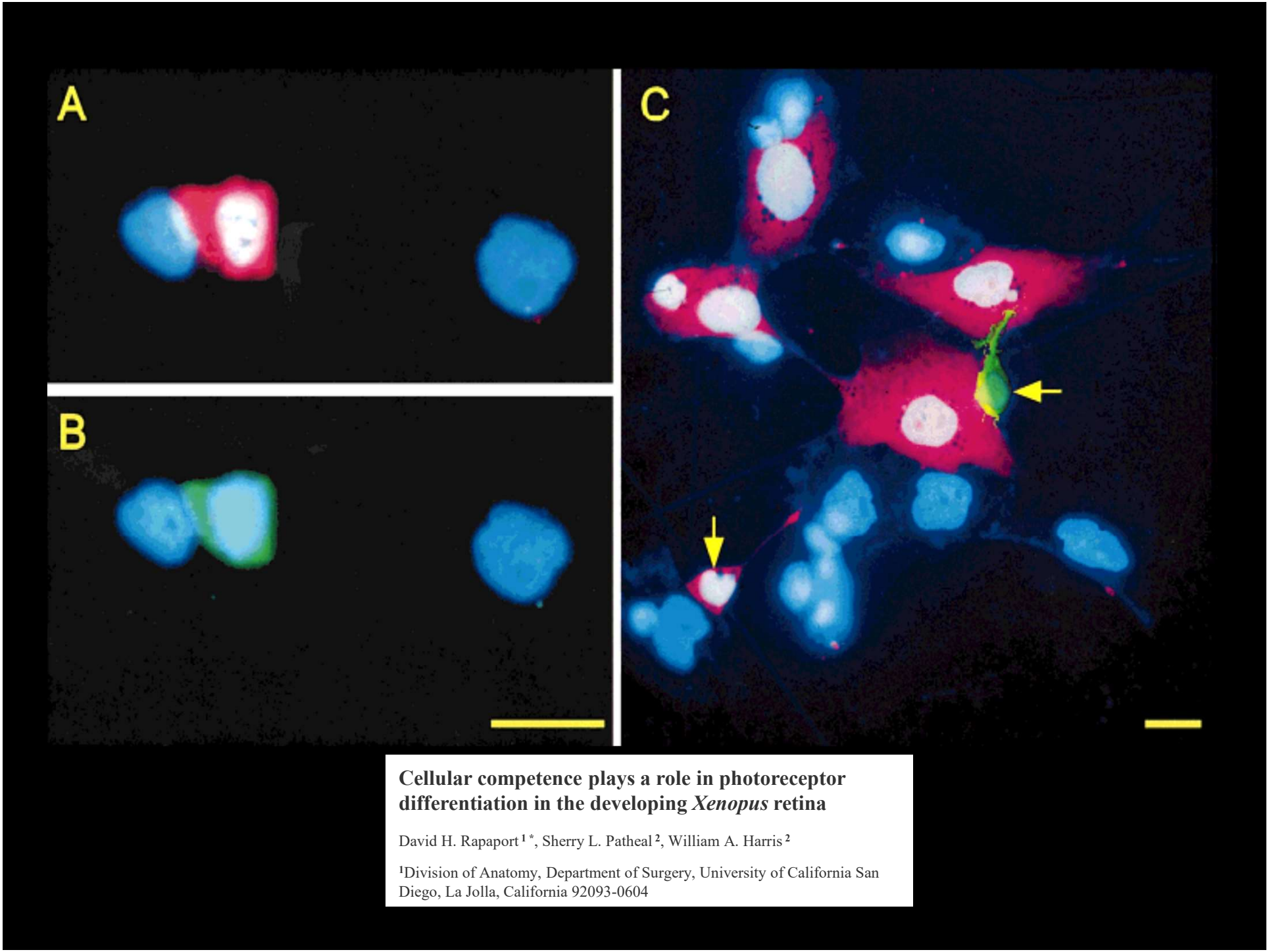

Balanus balanoides
Chthamalus stellatus
Highest tides
Upper intertidal zone
Balanus dessicates in this zone, allowing Chthamalus to thrive
Middle intertidal zone
Where it can survive, Balanus outcompetes Chthamalus for space
Lower intertidal zone
Balanus is subject to predation in the lower tidal zone
Lowest tides


(a) Asterionella alone
(b) Synedra alone
(c) Interspecific competition
Population density (cells ml⁻¹)
Silicate (□mol l⁻¹)
Time (days)
Asterionella
Synedra
Silicate
Townsend, Harper, Begon
Essentials of Ecology
Blackwell Science

DIATOMEAS

COMPETENCIA EN PARAMECIOS

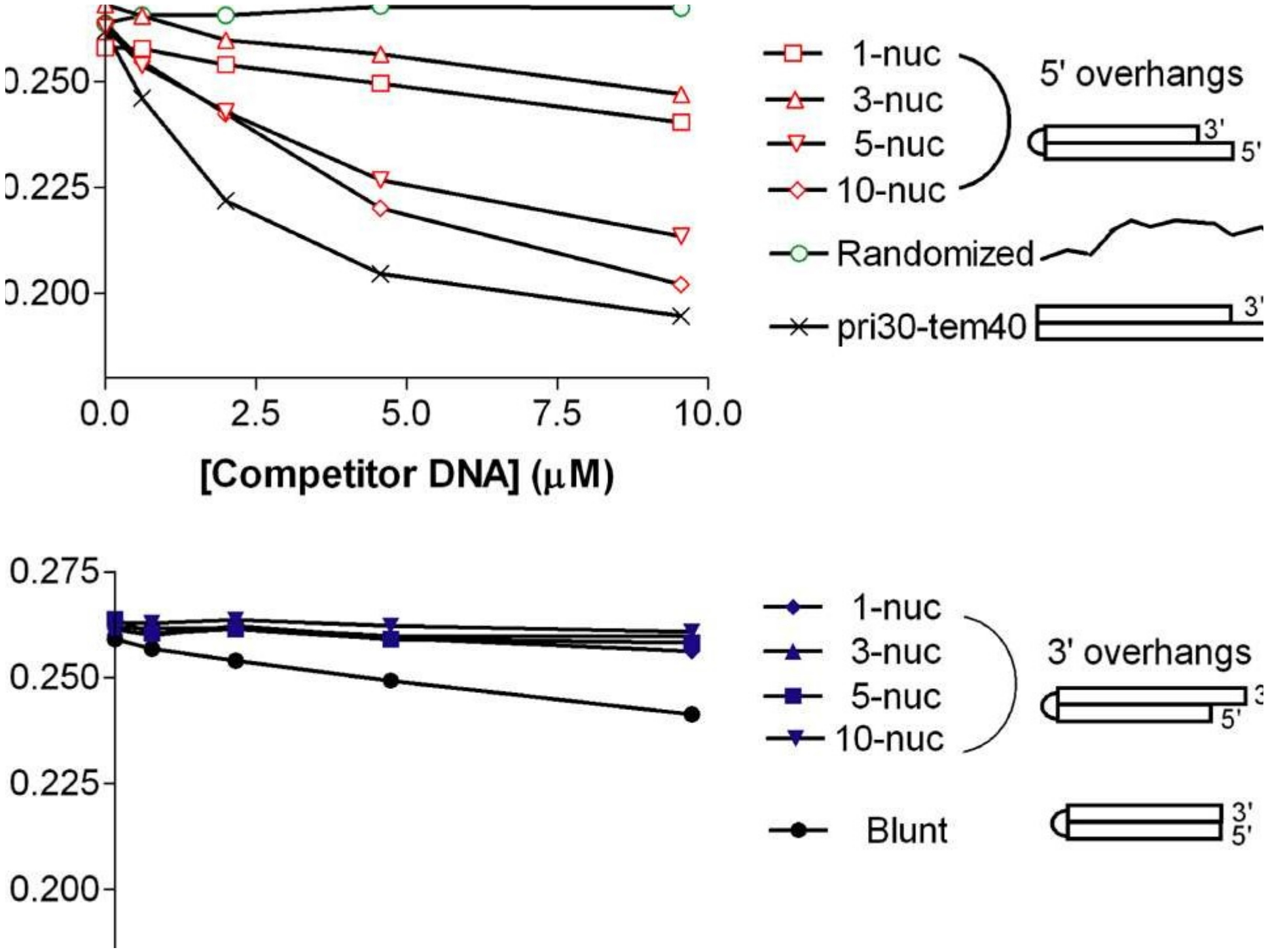


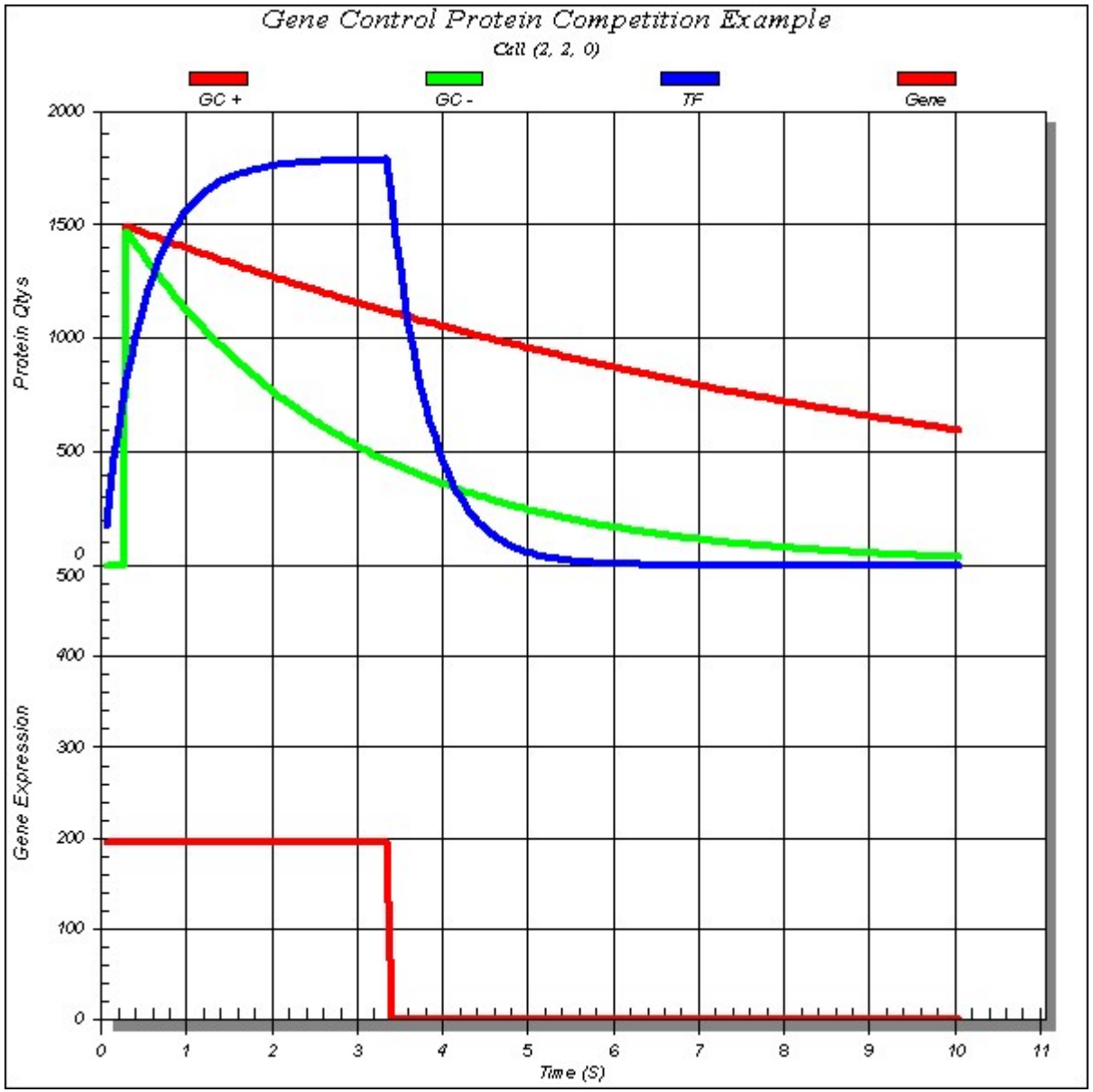


Cellular competence plays a role in photoreceptor differentiation in the developing *Xenopus* retina

David H. Rapaport [1] *, Sherry L. Patheal [2], William A. Harris [2]

[1]Division of Anatomy, Department of Surgery, University of California San Diego, La Jolla, California 92093-0604


0.250
0.225
0.200
0.0
2.5
5.0
7.5
10.0
[Competitor DNA] (μM)
1-nuc
3-nuc
5-nuc
10-nuc
5' overhangs
3'
5'
Randomized
pri30-tem40
3'
0.275
0.250
0.225
0.200
1-nuc
3-nuc
5-nuc
10-nuc
3' overhangs
3'
5'
Blunt
3'
5'


Gene Control Protein Competition Example
Call (2, 2, 0)
GC +
GC -
TF
Gene
Protein Qtys
2000
1500
1000
500
0
500
400
300
200
100
0
Gene Expression
0
1
2
3
4
5
6
7
8
9
10
11
Time (S)

Synergy and discounting of cooperation in social dilemmas

Christoph Hauert , Franziska Michorb, Martin A. Nowakb and Michael Doebeli

aDepartments of Zoology and Mathematics, University of British Columbia, 6270 University Boulevard, Vancouver BC, Canada V6T 1Z4
bProgram for Evolutionary Dynamics, Department of Organismic and Evolutionary Biology, Department of Mathematics, Harvard University, One Brattle Square, Cambridge MA 02138, USA
cHarvard Society of Fellows, 78 Mt. Auburn Street, Cambridge MA 02138, USA

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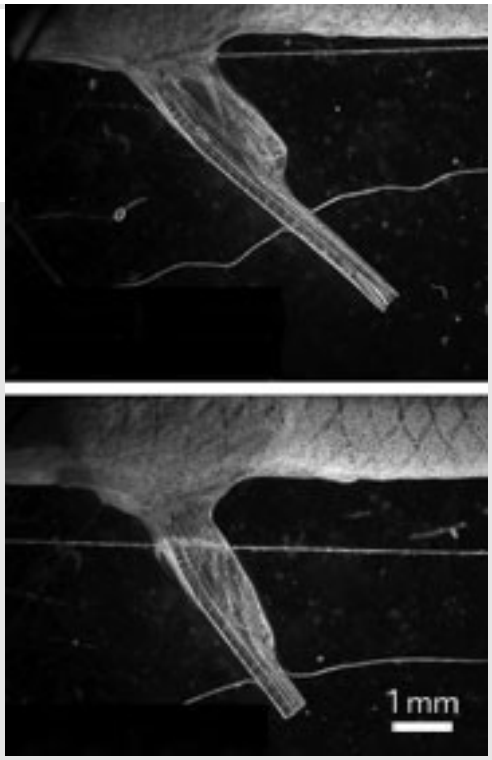
Abstract

The emergence and maintenance of cooperation by natural selection is an enduring conundrum in evolutionary biology, which has been studied using a variety of game theoretical models inspired by different biological situations. The most widely studied games are the Prisoner's Dilemma, the Snowdrift game and by-product mutualism for pairwise interactions, as well as Public Goods games in larger groups of interacting individuals.

***Nature* 461**, 451 (24 September 2009)

Evolutionary biology: Well endowed



BIOLOGY LETTERS/THE ROYAL SOCIETY 2009
Biol. Lett. doi:10.1098/rsbl.2009.0637 (2009)

The wide variation in male genitalia size in animals is thought to have evolved mostly in response to selection pressures that come into play during or after copulation and increase the male's share of paternity.

But it seems that females of the mosquito-fish *Gambusia holbrooki* choose mates before copulation on the basis of the size of their genitalia — and for them, bigger is better. Andrew Kahn and his team at the Australian National University in Canberra tested female preference for males that had had their genitalia considerably reduced in size by surgery (pictured, bottom) compared with those with only a minor reduction (pictured, top). They found that females spent, on average, around one-and-a-half times longer associating with the better-endowed males.

We're Still Evolving--And We May Be Shrinking

By Michael Torrice
*Science*NOW Daily News
22 October 2009

A subset of women in Framingham, Massachusetts, is evolving at the same rate as the average animal and plant, and will become shorter and heavier over successive generations. That means that natural selection continues to exert its influence over humans, researchers argue in a new study, one of the more ambitious to assess evolution's impact on modern humans.

Soon after Darwin published his theory of evolution, Lawson Tait, a surgeon, wrote that the law of natural selection does not apply to people because medicine keeps adverse traits in the gene pool. Some doctors still think this today, says Yale University evolutionary biologist Stephen Stearns, but they're wrong. Natural selection continues to exert its pressure through our reproductive success: the more children we have, the more our traits spread through the population.

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www.csic.es/prensa

Madrid, miércoles 28 de abril de 2010

Prueban la teoría darwinista en la población de gaviotas del vertedero de Mallorca

- **Un equipo del CSIC aprovechó el uso de aves de cetrería para controlar la población de gaviotas en el lugar y poder comprobar el aforismo 'sobrevive el más apto'**

- **Los halcones y busardos cazaban ejemplares jóvenes, con patologías internas, sobrepeso o deformaciones corporales**

De todos los descubrimientos que se atribuyen al naturalista Charles Darwin, uno de los más citados se resume en el aforismo "sobrevive el más apto". Aunque aceptada por la comunidad investigadora, existen escasas evidencias científicas que prueben esta hipótesis, dado que resulta complicado determinar en qué estado se hallan, por ejemplo, las presas de un depredador. Investigadores del Consejo Superior de Investigaciones Científicas (CSIC) han aprovechado los trabajos para reducir la población de gaviotas en el vertedero de Mallorca, donde se emplearon aves de cetrería, para aportar pruebas empíricas a los planteamientos darwinistas.

Business Insights

Brand New Research:

The Medical Device Outlook in Emerging Markets

Nature Group and Business Insights would like to announce the release of this brand new research report- **The Medical Device Outlook in Emerging Markets**.

The emerging economies of Brazil, Russia, India, and China (BRIC) have become lucrative, high-growth markets for medical devices.

The emerging economies are not only growing due to increased adoption of medical devices owing to increased health awareness, but these nations are also lucrative investment regions for multinational medical device companies to offshore business operations and production.

The report provides detailed analysis of the healthcare environment in various emerging nations; including each emerging nation's medical device market size; evolving healthcare regulations; growth opportunities unique to each country with respect to the medical device market; business-related trends and opportunities unique to each country

MARKET OUTLOOK REPORTS

BRAND NEW RESEARCH-

The Hepatitis Market Outlook to 2015

The HIV/AIDS Market Outlook to 2015

The Genitourinary Market Outlook to 2015

The Market Outlook for Neurodegenerative Diseases

(on p.2) and send to **+44 (0)161 238 4141**

De aquí, que como se producen más individuos de los que es posible que sobrevivan, tiene que haber forzosamente en todos los casos una lucha por la existencia / ... / Es la doctrina de Malthus aplicada con multiplicada fuerza al conjunto de los reinos animal y vegetal; porque en este caso, no hay aumento artificial de alimento y limitación prudente de matrimonios.

“Sobre el origen de las especies...”
(p.78)

Cuando vemos que han ocurrido indudablemente variaciones útiles para el hombre, no podemos creer improbable que ocurran en el curso de muchas generaciones sucesivas, otras variaciones útiles de algún modo a cada ser en la batalla grande y compleja de la vida. Y si ocurren, ¿podemos dudar (recordando que nacen muchos más individuos que los que es posible que vivan) que los individuos que tengan alguna ventaja sobre los demás, por pequeña que sea, tendrán la mejores probabilidades de sobrevivir y reproducir su especie?. Por otra parte, podemos estar seguros de que cualquier variación en el más pequeño grado perjudicial, sería rígidamente destruida. Esta conservación de las variaciones y diferencias individuales favorables, y la destrucción de aquellas que son nocivas, es lo que he llamado "selección natural" o "supervivencia de los más aptos. "

"Sobre el origen de las especies..." (p. 94)

He hablado hasta aquí como si las variaciones, tan comunes y multiformes en los seres orgánicos en estado de domesticidad y no tan comunes en los silvestres, fueran debidas a la casualidad. Innecesario es decir que este término es completamente inexacto y que sólo sirve para reconocer paladinamente nuestra ignorancia de la causa de cada variación particular **"Sobre el origen de las especies…" (Pág. 149)**.

"Estas leyes, tomadas en un sentido más amplio, son crecimiento con reproducción; herencia que casi va implícita en la reproducción; variabilidad, resultado de la acción directa e indirecta de las condiciones de vida y del uso y desuso; aumento en una proporción tan alta, que conduce a una lucha por la existencia, y como consecuencia, a la selección natural, la cual trae consigo la divergencia de carácter y la extinción de las formas menos mejoradas Así, es consecuencia directa de la guerra de la naturaleza, de la escasez y la muerte, el objeto más elevado que somos capaces de concebir, a saber; la producción de los animales superiores"

Recapitulación

"Lo que se puede alegar, se puede sintetizar de ésta manera: que la "selección natural" es incapaz de explicar las etapas incipientes de las estructuras útiles; que no armoniza con la coexistencia de estructuras muy similares de diverso origen; que hay fundamentos para pensar que las diferencias específicas se pueden desarrollar súbita y no gradualmente; que la opinión de que las especies tienen límites definidos, aunque muy diferentes para su variabilidad todavía es sostenible; que ciertas formas fósiles de transición todavía están ausentes, cuando cabría esperar que estuviesen presentes/ ... /que hay muchos fenómenos notables de las formas orgánicas sobre los cuales la "selección natural no arroja la menor luz".
(Mivart,1871).


nature
SELFISH
DNA

El planteamiento de este libro es que nosotros, al igual que todos los demás animales, somos máquinas creadas por nuestros genes. De la misma manera que los prósperos gangsters de Chicago, nuestros genes han sobrevivido, en algunos casos durante millones de años, en un mundo altamente competitivo. Esto nos autoriza a suponer ciertas cualidades en nuestros genes . Argumentaré que una cualidad predominante que podemos esperar que se encuentre en un gen próspero será el egoísmo despiadado. Esta cualidad egoísta en el gen dará, normalmente, origen al egoísmo en el comportamiento humano. **Richard Dawkins (1975)** ***El gen egoísta***

Darwinismo: la "Teoría mínima según la cuál la evolución es guiada, adaptativamente, en direcciones que no son al azar, por la supervivencia que tampoco es al azar, de pequeños cambios hereditarios al azar" (Dawkins, A Devil's Chaplain).

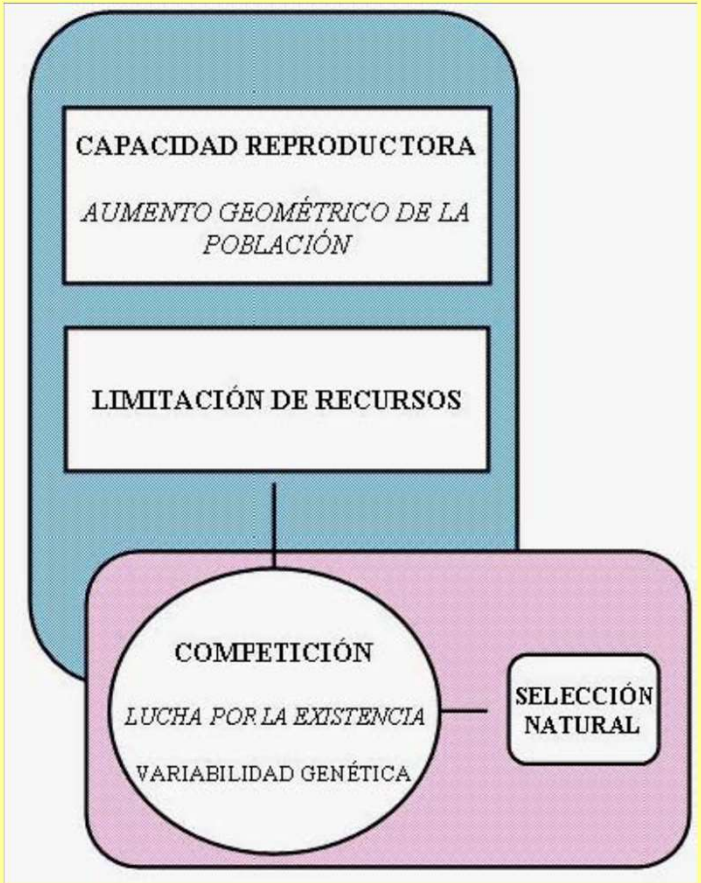
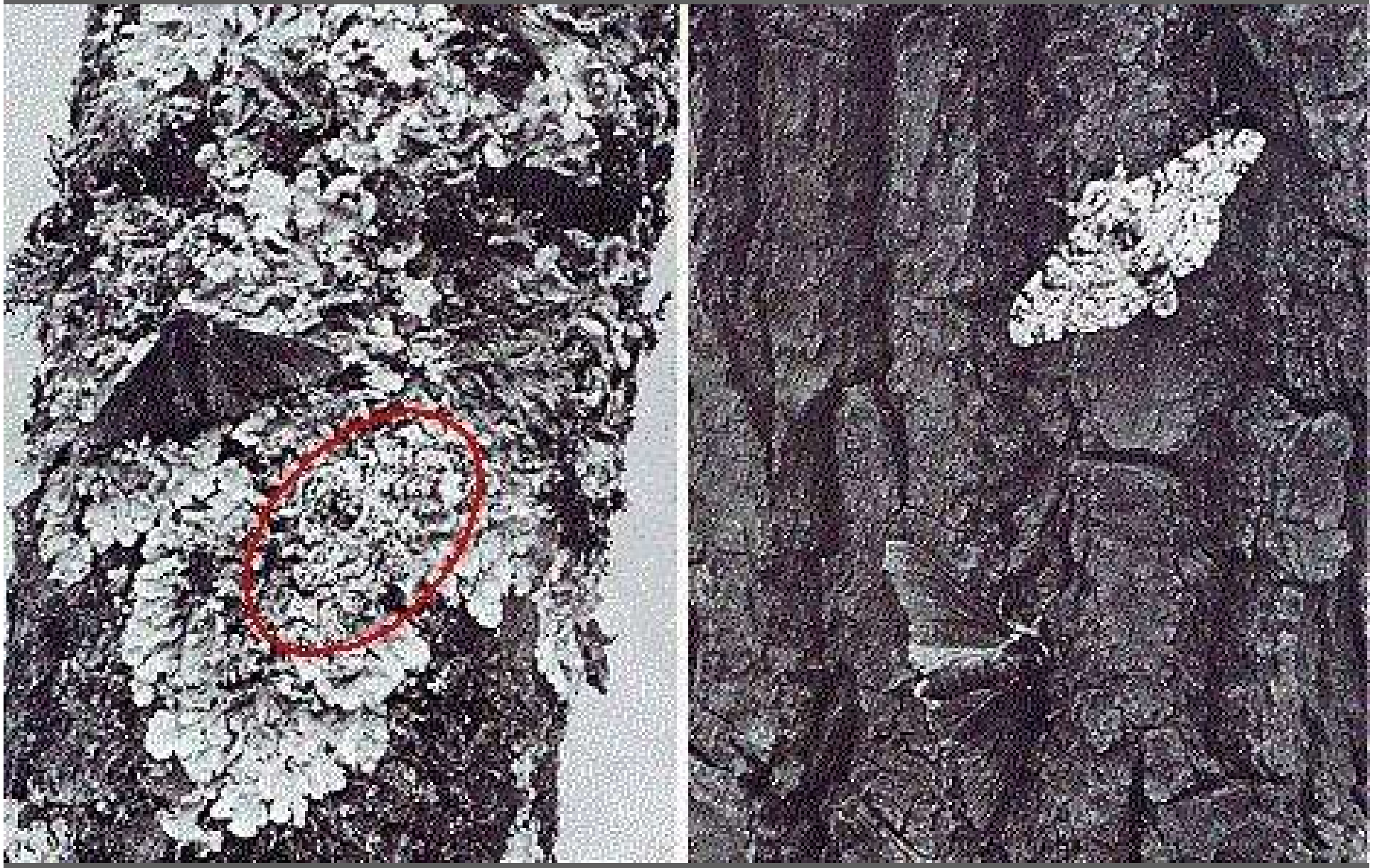


Fig. 8.- Esquema del mecanismo de la selección natural. En el marco superior interactúan la capacidad reproductora (o aumento geométrico de la población) con la limitación de recursos: las dos primeras premisas del razonamiento darwiniano. Esta interacción conduce a la competición (o lucha por la existencia) que en conjunción con la variabilidad genética, la otra premisa de Darwin, hace posible la selección natural (marco inferior) (tomado de Fontdevila y Moya 2003).

Evolution

Evolution is the change in gene frequency in a population. Over long periods of time these changes will result in new species.

genicas de las poblaciones, o sea los factores de evolucion, son la mutacion, la deriva genética, la migración y la selección natural.



Biston betularia: Where do 99.9% of the peppered moths rest by day according to all the known data - or where do they not rest?

Wolf-Ekkehard Lönnig (2003)

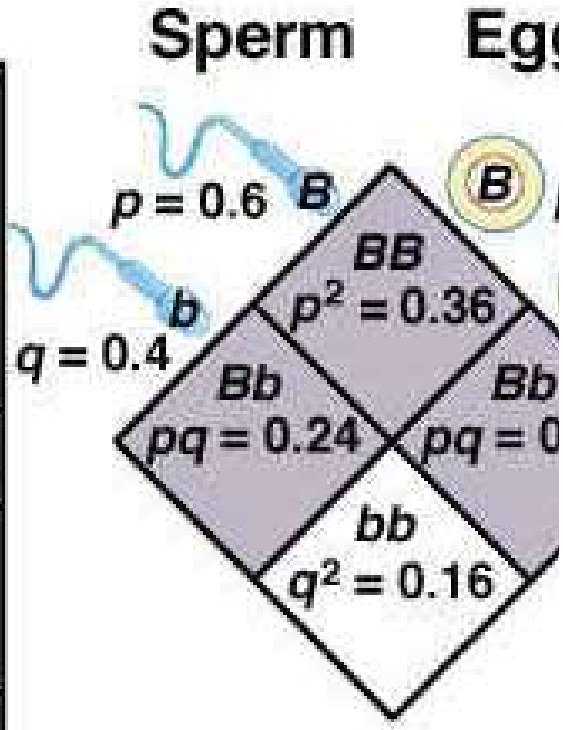
An extensive documentation of facts is presented below showing that the peppered moth (*Biston betularia*) does not normally rest in exposed positions on tree trunks (except in perhaps less than 0.1% of the cases). 99.9% of the moths rest in unexposed positions mostly high up in the canopies. Thus, the biological and evolutionary textbooks have, in fact, to be revised on the issue of the peppered moth.

"De acuerdo con De Vries (y también con otros genéticos de principios del sigloXX, como el inglés William Bateson) hay dos tipos de variaciones en los organismos: un tipo consiste en la variación "ordinaria" observada entre los individuos de una especie: por ejemplo, variación en el color de los ojos o las flores, o variación en el tamaño. Este tipo de variación no tiene consecuencias últimas en la evolución, porque, según De Vries, "no puede traspasar los límites de la especie, incluso bajo las condiciones de la más fuerte y continua selección". El otro tipo consiste en las variaciones que surgen por "mutación genética"; esto es, alteraciones espontáneas de los genes que ocasionan grandes modificaciones de los organismos y que pueden dar origen a nuevas especies: "Una nueva especie se origina de repente, es producida a partir de una especie preexistente sin ninguna preparación visible y sin transición".

F. J. Ayala "La teoría de la evolución"(1999)

Hardy-Weinberg Equilibrium

Phenotypes			
Genotypes	*BB*	*Bb*	*bb*
Frequency of genotype in population	0.36	0.48	0.16
Frequency of gametes	0.36 + 0.24 = 0.6*B*	0.24 + 0.16 = 0.4*b*	



LEY HARDY-WEINBERG

El equilibrio de Hardy-Weinberg, es también conocido como equilibrio panmíctico, fue estudiado a principios del siglo 20 por diferentes autores, pero fueron Hardy, un matemático y Weinberg, un físico quienes lo establecieron.

El equilibrio de Hardy-Weinberg es un modelo teórico para genética de poblaciones. El concepto de equilibrio en el modelo de Hardy-Weinberg se basa en las siguientes hipótesis.

Supondremos que:

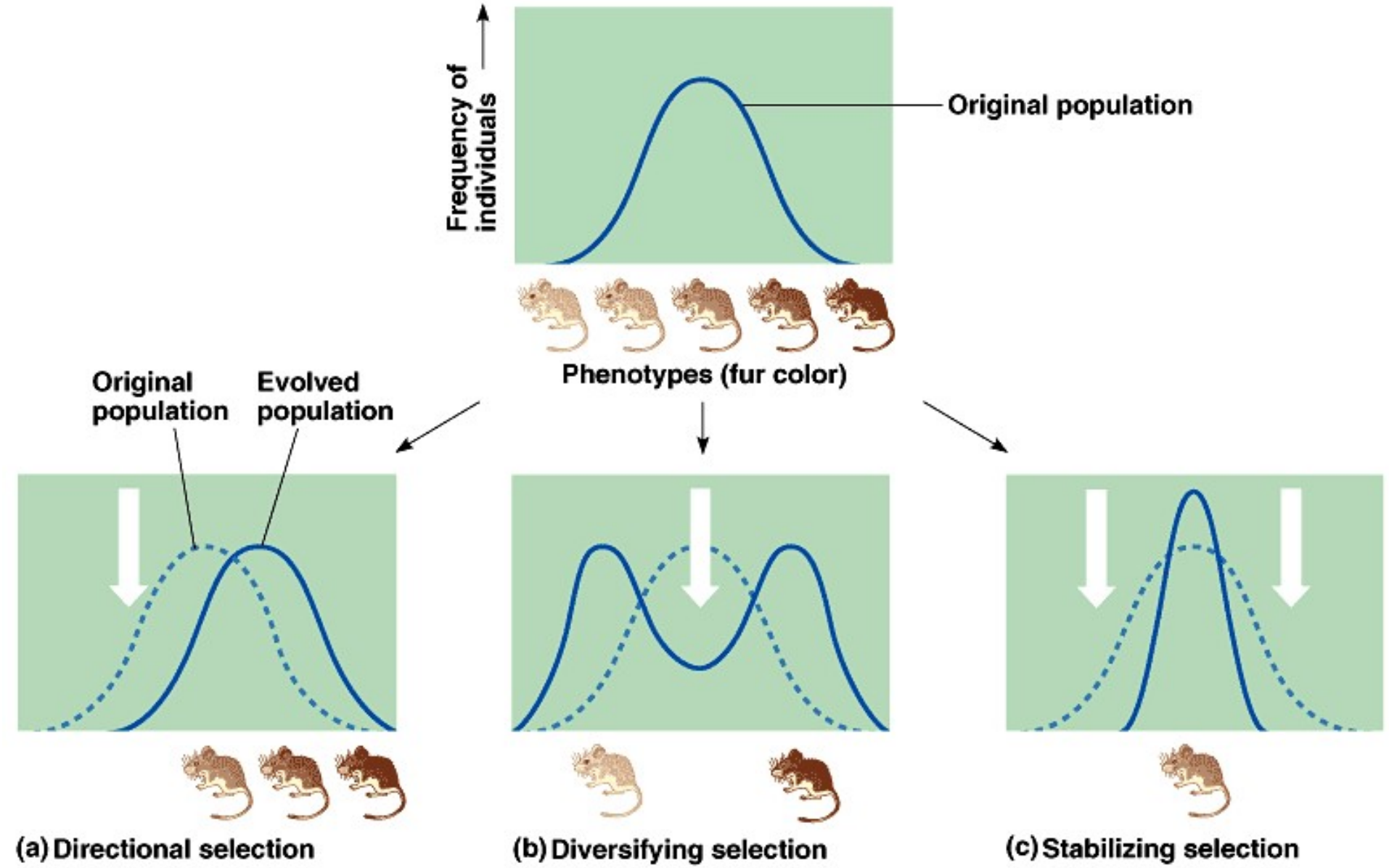
- **Existe panmixia, es decir, que, en cada caso, la probabilidad de aparear con un individuo de tipo X es igual a la frecuencia de X en la población.**
- **Las generaciones son discretas, esto es, que los adultos se reproducen una vez y desaparecen .**
- **El acervo alélico es igual en ambos sexos.**

Además, mantendremos las suposiciones planteadas al principio:

- **La población tiene tamaño (censo) infinito $\Rightarrow$ No hay deriva genética.**
- **No existen fuerzas sistemáticas de cambio de las frecuencias génicas: Migración, mutación o selección.**

Los matemáticos demostraron convincentemente que, incluso mutaciones con ventajas relativamente pequeñas, eran favorecidas por la selección, y sus hallazgos ayudaron a superar varias objeciones a la Selección Natural.

MAYR, E. 1997. *The establishment of evolutionary biology as a discrete biological discipline*. BioEssays, 19 (3): 263-266.



Estos descubrimientos (?) teóricos, sin embargo, tuvieron inicialmente un impacto limitado entre los biólogos contemporáneos, porque fueron formulados en ecuaciones y lenguaje matemáticos que la mayoría de los evolucionistas no podían entender; también debido a que estos descubrimientos, (?) casi exclusivamente teóricos, tenían poca corroboración empírica, y, por último, a causa de que los problemas resueltos habían dejado de lado muchas otras materias de gran interés, como el proceso de especiación.

F. J. Ayala (1999), *La teoría de la evolución.*

El rango de una mutación génica puede ir, pues, de inapreciable a letal /.../ las mutaciones nuevas tienen mayor posibilidad de ser perjudiciales que beneficiosas para los organismos. Una nueva mutación es posible que haya sido precedida de una mutación idéntica en la historia previa de una especie. Si esa mutación previa no existe en la población, lo más probable es que no sea beneficiosa para el organismo y, por ello, será eliminada de nuevo/.../ El proceso de mutación cambia las frecuencias génicas muy lentamente debido a que las tasas de mutación son bajas /.../ Si en un momento dado la frecuencia del alelo A es 0,10, en la generación siguiente se habrá reducido a 0,0999999, un cambio evidentemente pequeñísimo /.../ Por otra parte, las mutaciones son reversibles: el alelo B puede también convertirse en alelo A /.../ Aunque las tasas de mutación son bajas si se considera un gen individualmente, el hecho de que haya muchos genes en cada individuo y muchos individuos en cada especie hace que el número total de mutaciones sea elevado.

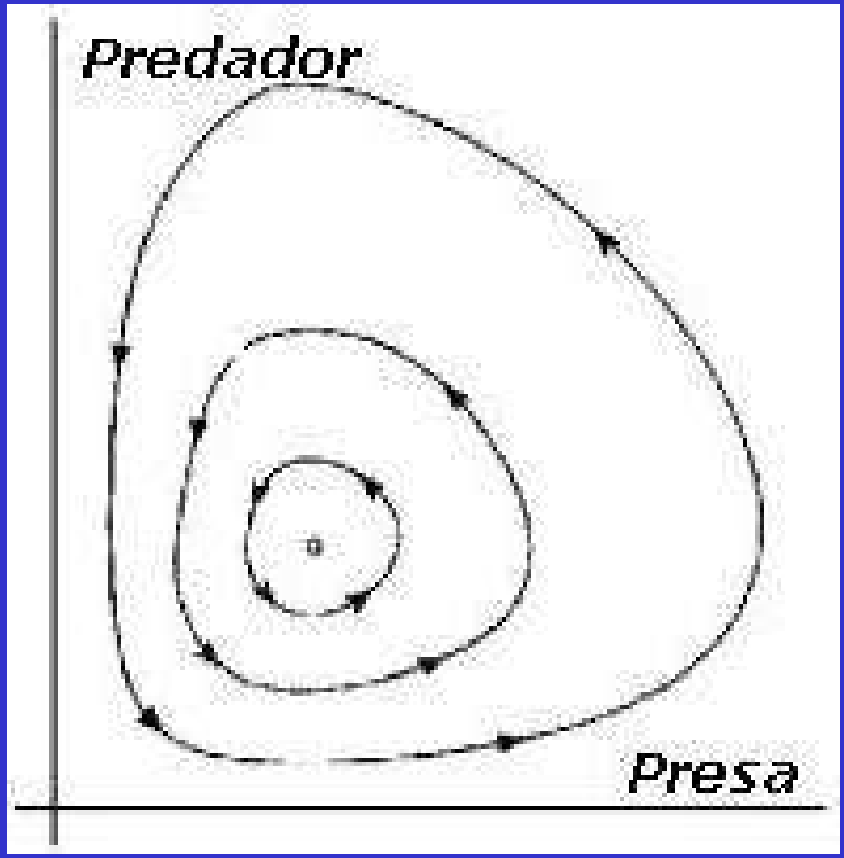
F. J. Ayala (2001), “Senderos de la evolución humana”

Usted puede buscar a Darwin para una respuesta pero buscará en vano. Darwin estudió leves variaciones en características externas, sugiriendo cómo esas variaciones pueden ser favorecidas por circunstancias externas, y extrapoló el proceso al árbol completo de la vida. Pero, seguramente, hay cuestiones mas profundas para preguntarse que por qué las polillas tienen alas mas negras o mas blancas, o por qué las orquídeas tienen pétalos de esta u otra forma. ¿Por qué las polillas tienen alas y por qué las orquídeas tienen pétalos? ¿Qué creó esas estructuras por primera vez?.

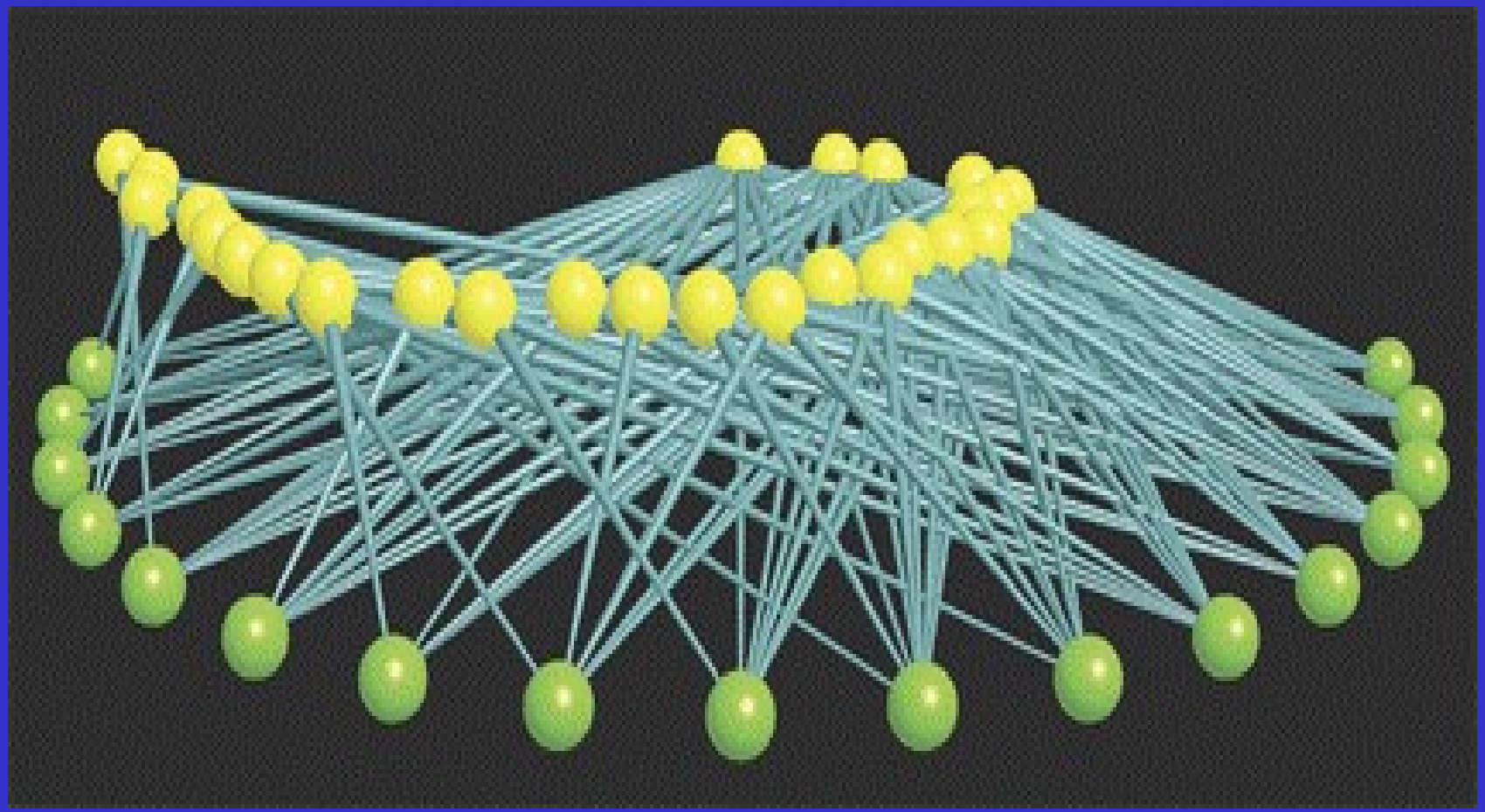
La victoria del Darwinismo ha sido tan completa que es un shock darse cuenta de cuan vacía es realmente la visión Darwiniana de la vida. **GEE, H. (2000) Nature**

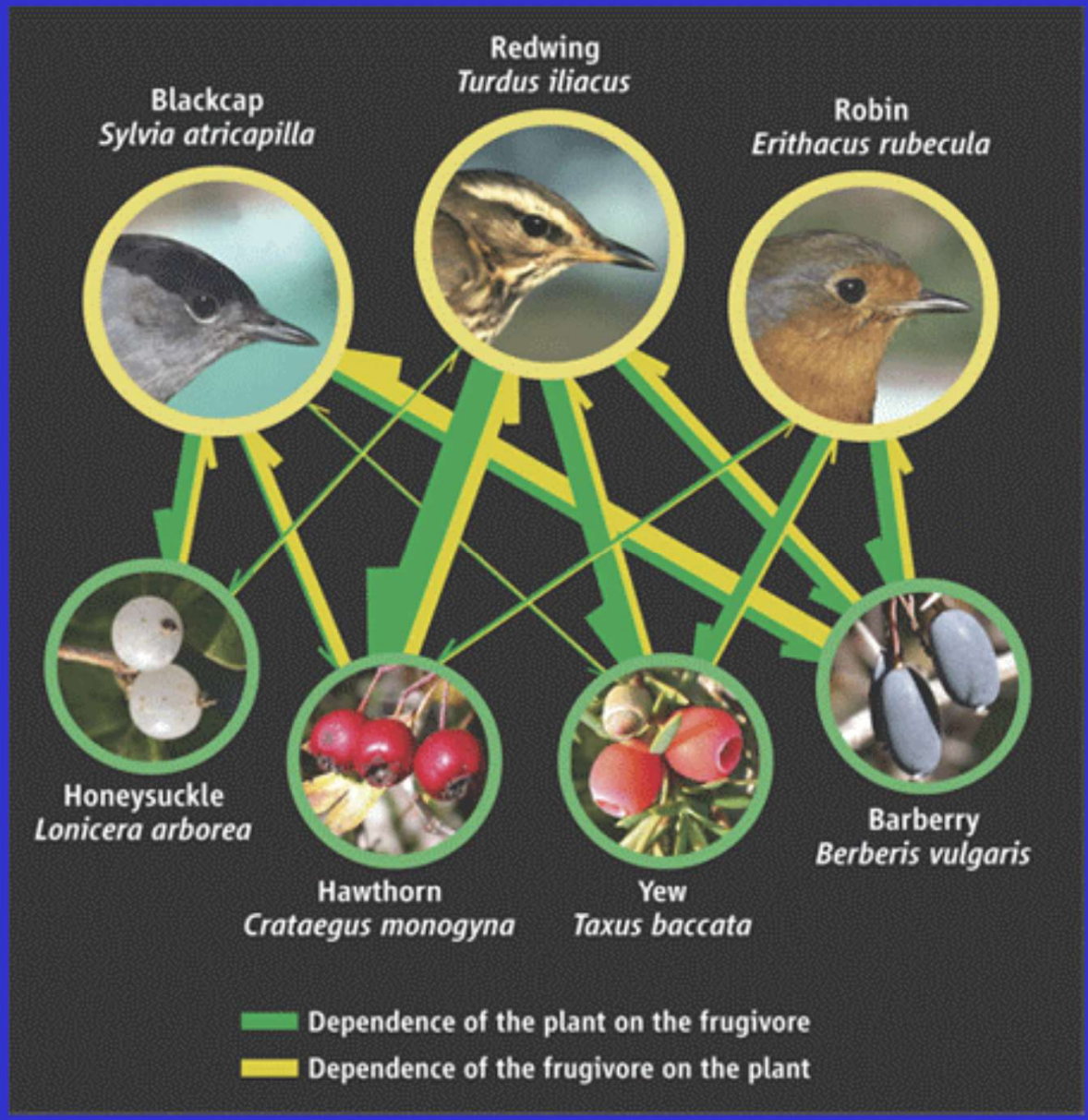
El hecho de que una teoría tan vaga, tan insuficientemente demostrable, tan ajena a los criterios que suelen aplicarse en las ciencias empíricas, se haya convertido en un dogma no es explicable, si no es con argumentos sociológicos.
Ludwing Von Bertalanffy (1901-1972)

LOTKA-VOLTERRA



Interrelaciones Ecosistema




Redwing
Turdus iliacus
Blackcap
Sylvia atricapilla
Robin
Erithacus rubecula
Honeysuckle
Lonicera arborea
Hawthorn
Crataegus monogyna
Yew
Taxus baccata
Barberry
Berberis vulgaris
Dependence of the plant on the frugivore
Dependence of the frugivore on the plant

Nature **396**, 69-72 (5 November 1998) | doi:10.1038/23932; Received 28 July 1998; Accepted 10 September 1998

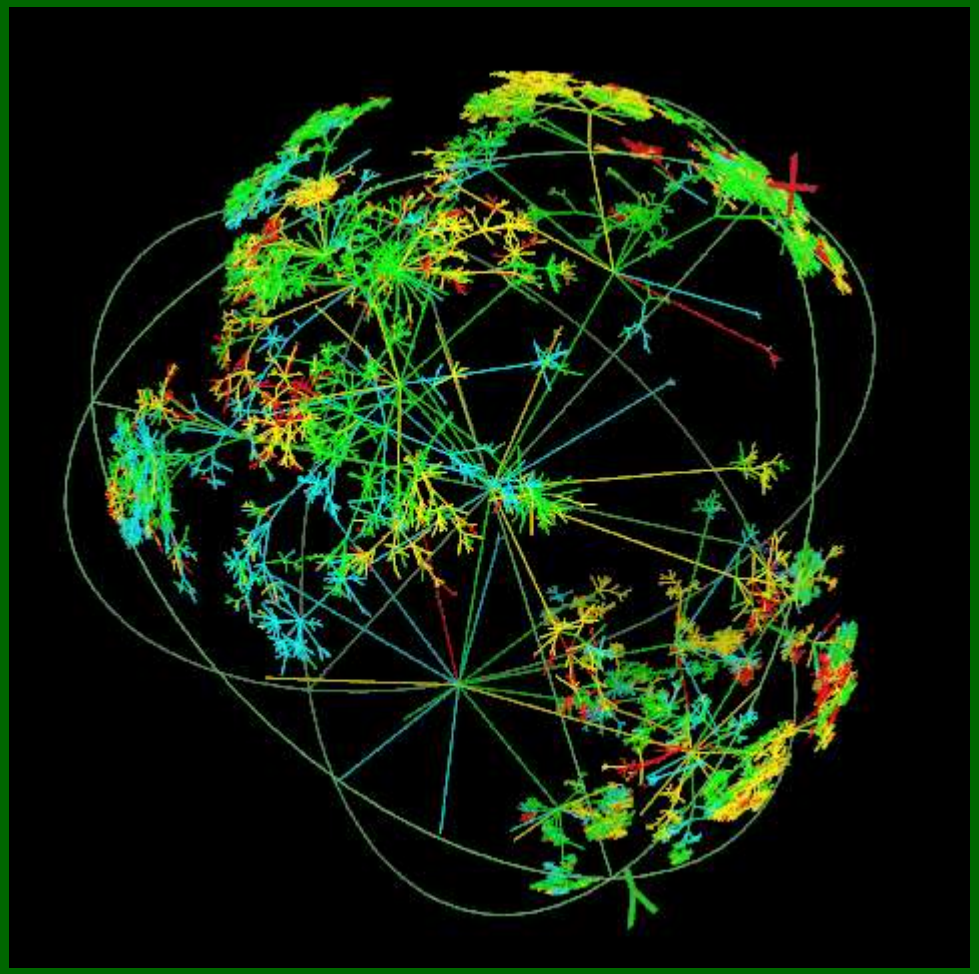
Mycorrhizal fungal diversity determines plant biodiversity, ecosystem variability and productivity

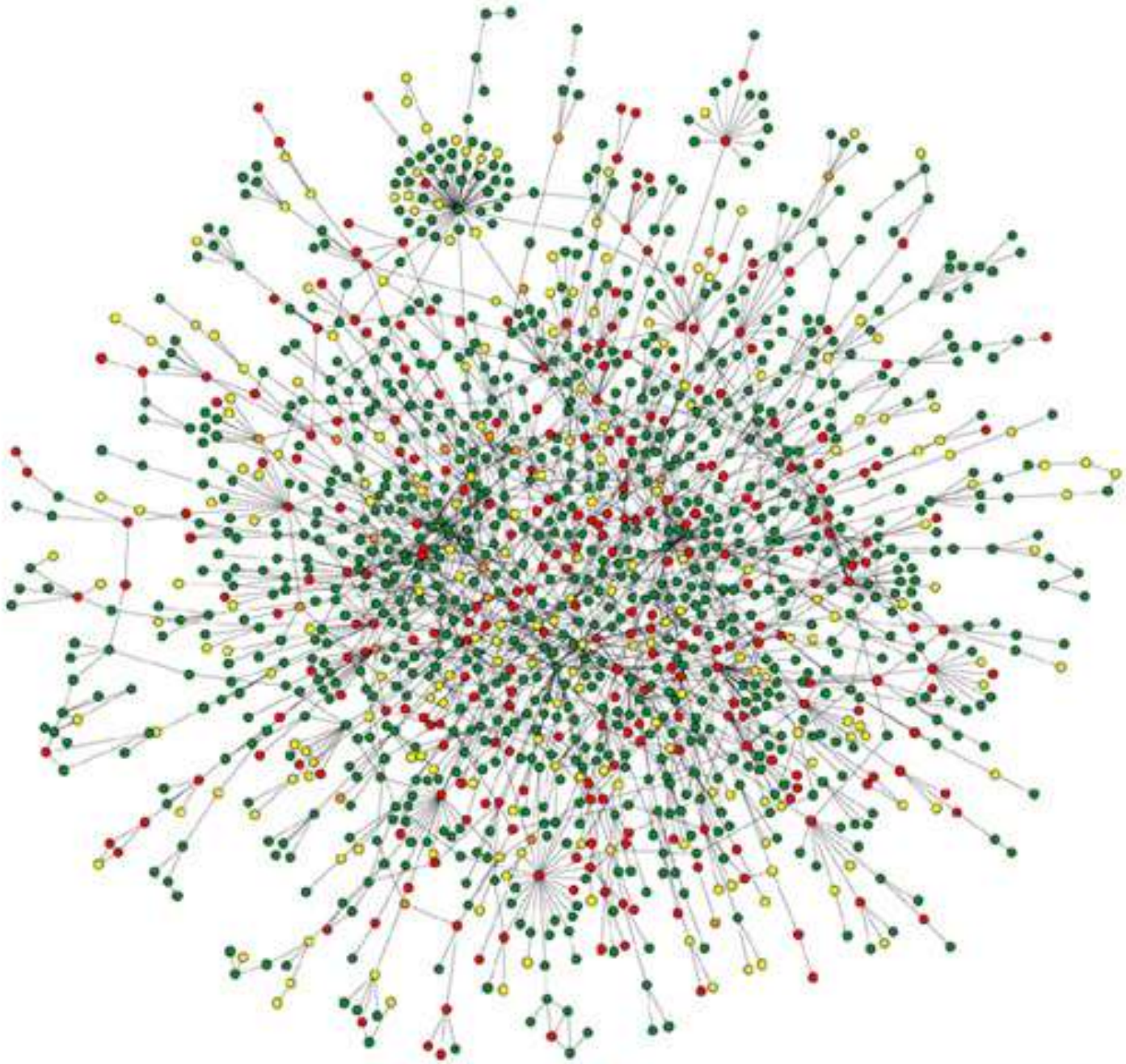
Marcel G. A. van der Heijden[1,2], John N. Klironomos[2,3], Margot Ursic[3], Peter Moutoglis[4], Ruth Streitwolf-Engel[1], Thomas Boller[1], Andres Wiemken[1] & Ian R. Sanders[1]

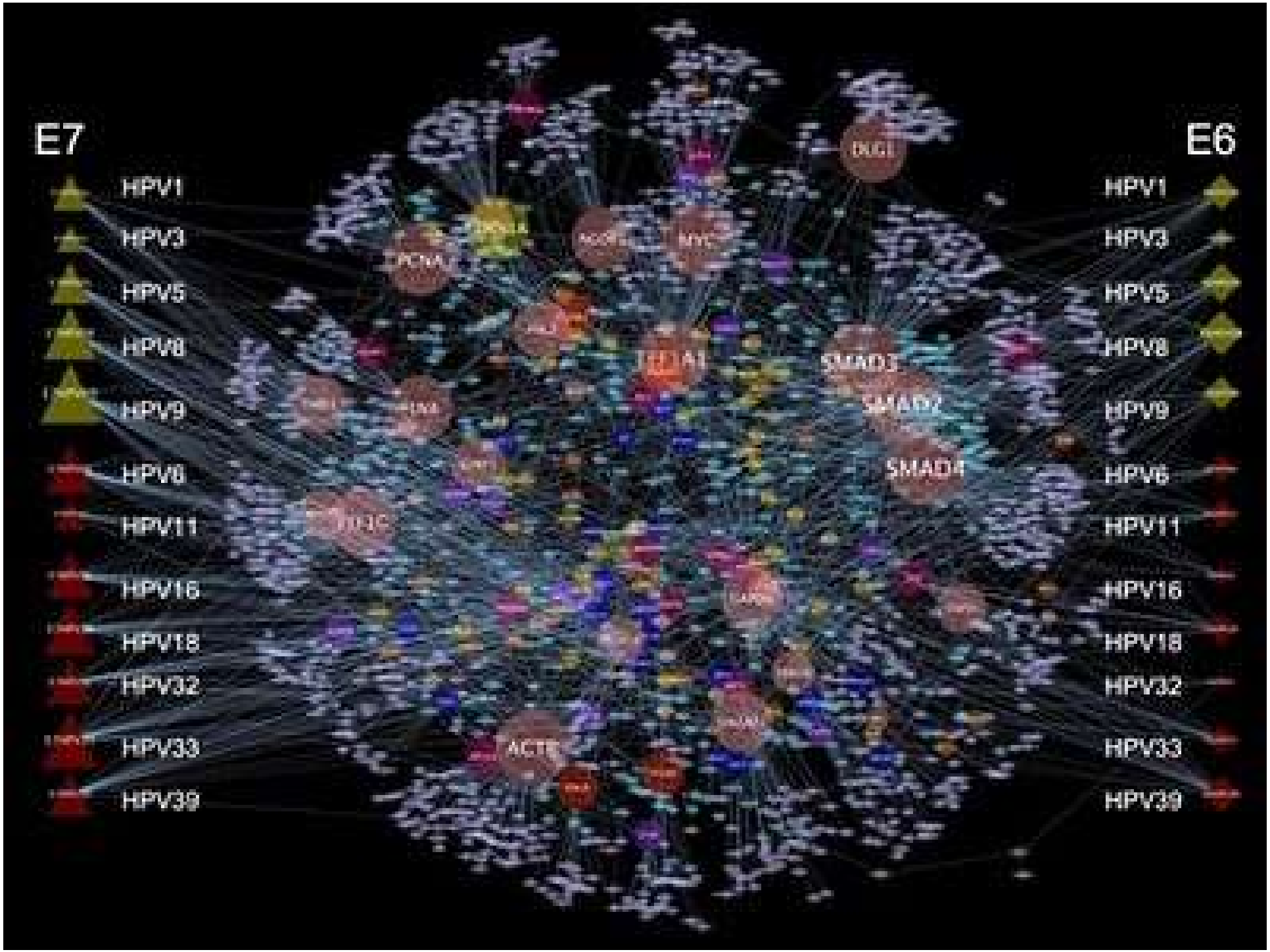
Abstract

The functioning and stability of terrestrial ecosystems are determined by plant biodiversity and species composition[1, 2, 3, 4, 5]. However, the ecological mechanisms by which plant biodiversity and species composition are regulated and maintained are not well understood. These mechanisms need to be identified to ensure successful management for conservation and restoration of diverse natural ecosystems. Here we show, by using two independent, but complementary, ecological experiments, that below-ground diversity of arbuscular mycorrhizal fungi (AMF) is a major factor contributing to the maintenance of plant biodiversity and to ecosystem functioning. At low AMF diversity, the plant species composition and overall structure of microcosms that simulate European calcareous grassland fluctuate greatly when the AMF taxa that are present are changed. Plant biodiversity, nutrient capture and productivity in macrocosms that simulate North American old-fields increase significantly with increasing AMF-species richness. These results emphasize the need to protect AMF and to consider these fungi in future management practices in order to maintain diverse ecosystems. Our results also show that microbial interactions can drive ecosystem functions such as plant biodiversity, productivity and variability.

SISTEMAS COMPLEJOS




Nature Reviews | Genetics


E7
E6
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HPV6
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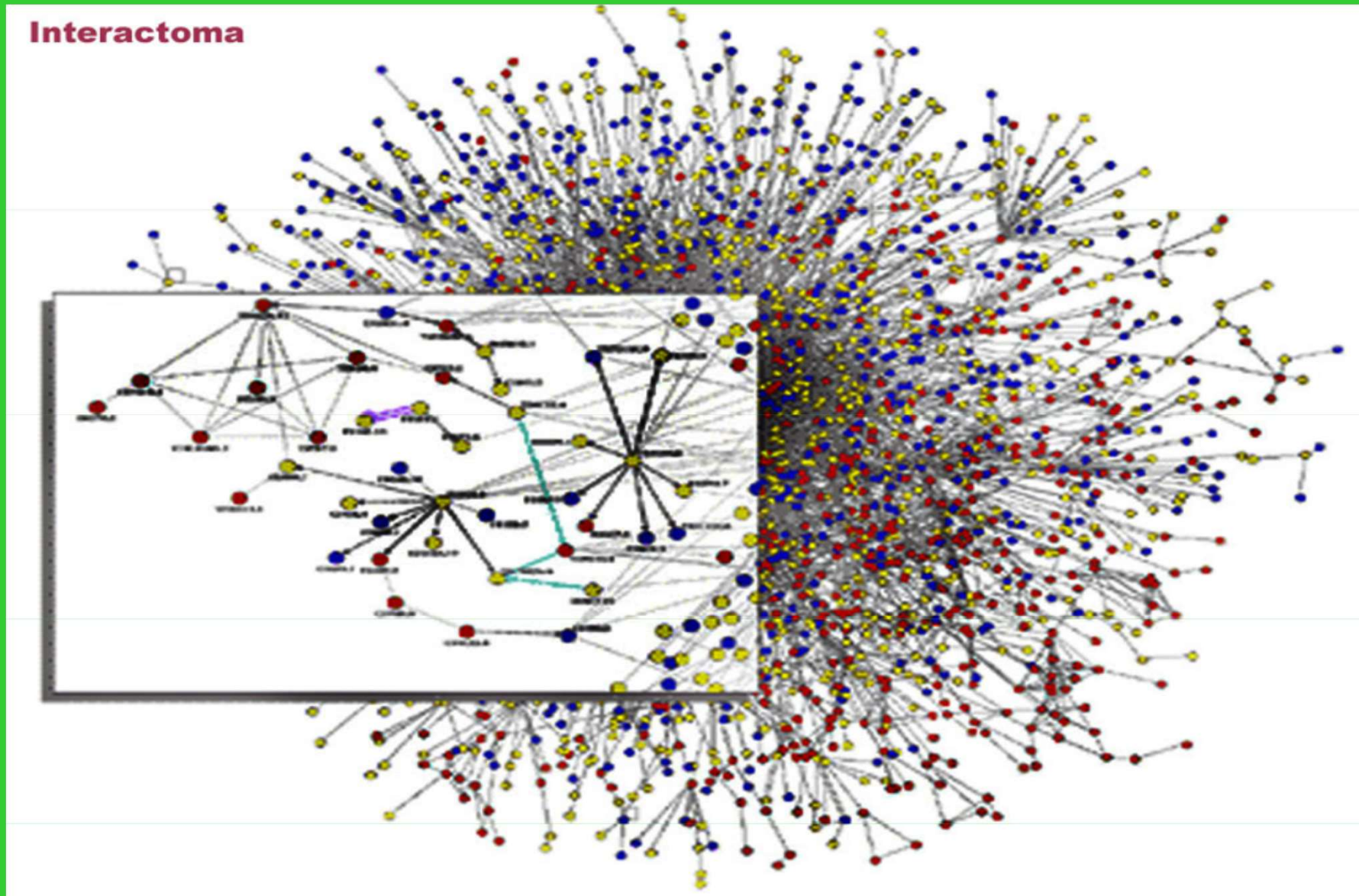
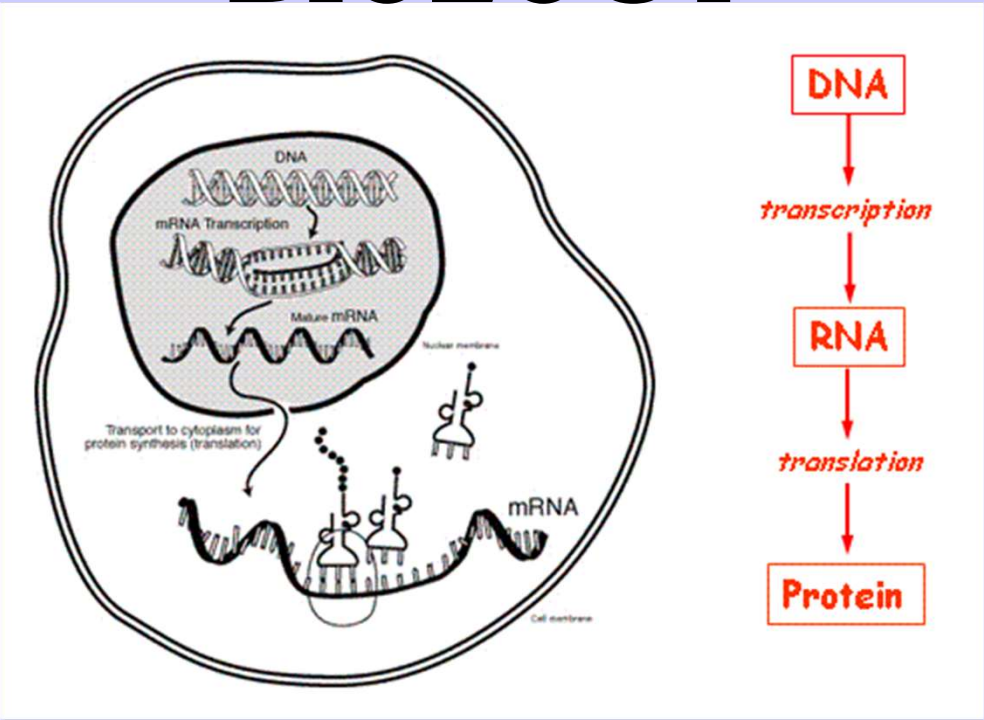
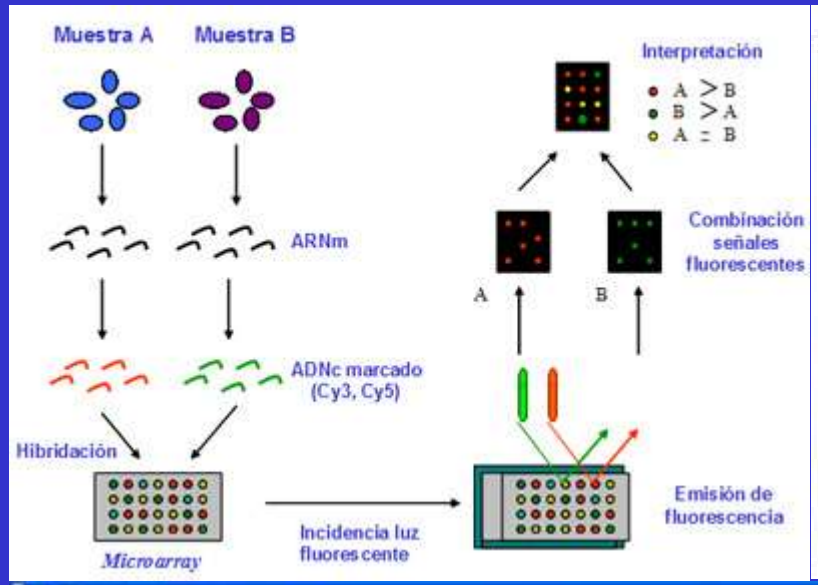
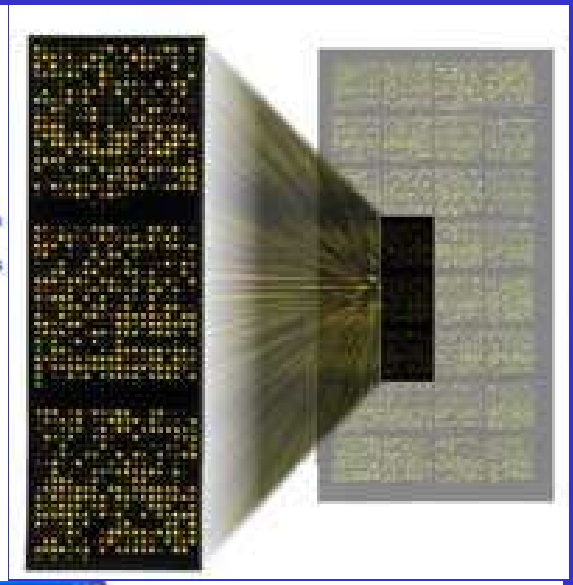
SMAD4
ACTB

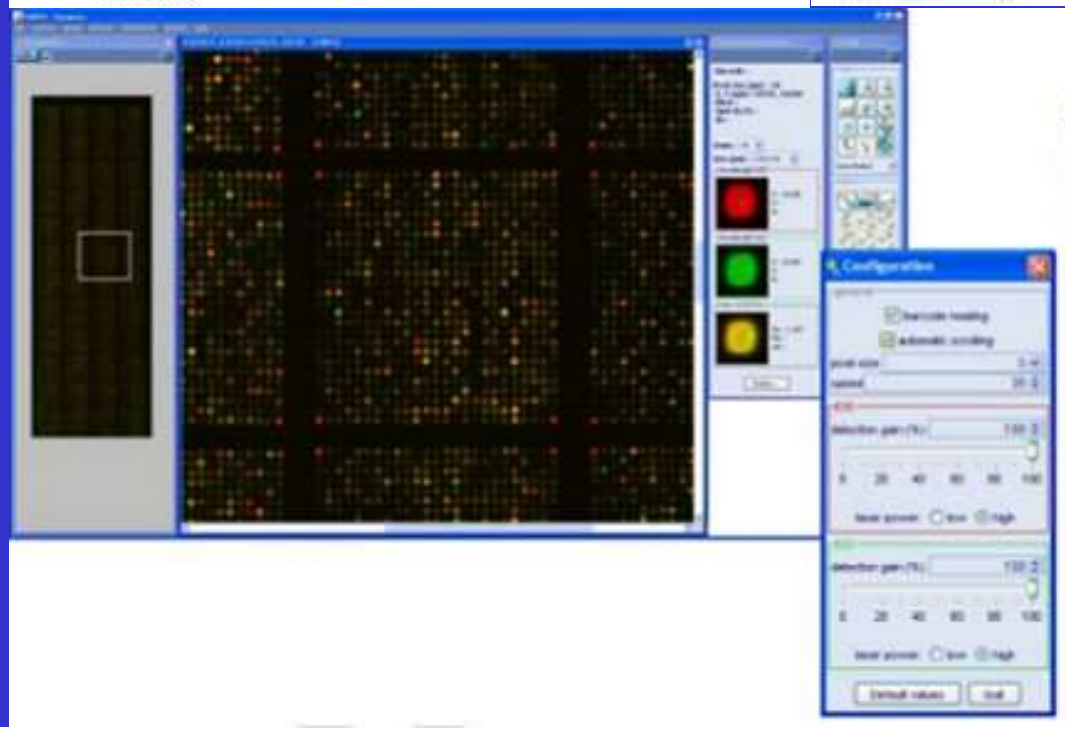

Interactoma

CENTRAL DOGMA OF BIOLOGY




Muestra A
Muestra B
ARNm
ADNc marcado
(Cy3, Cy5)
Hibridación
Microarray
Incidencia luz
fluorescente
Emisión de
fluorescencia
A
B
Combinación
señales
fluorescentes
Interpretación
A > B
B > A
A = B





INTRO TO ISB AND SYSTEMS BIOLOGY

- SYSTEMS BIOLOGY -- THE 21ST CENTURY SCIENCE
- PREDICTIVE PREVENTIVE PERSONALIZED AND PARTICIPATORY
- WHY SYSTEMS MATTER
- USING MODEL ORGANISMS
- DISEASE
- TOUR ISB

SYSTEMS BIOLOGY -- THE 21ST CENTURY SCIENCE

"Organisms function in an integrated manner-- our senses, our muscles, our metabolism and our minds work together seamlessly. But biologists have historically studied organisms part by part and celebrated the modern ability to study them molecule by molecule, gene by gene. ISB is devoted to a new science, a critical science of the future that seeks to understand the integration of the pieces to form biological systems."

David Baltimore
Nobel Laureate
President
California Institute of Technology
Pasadena, California

Systems Biology: the 21st Century Science

Systems biology is the study of an organism, viewed as an *integrated* and *interacting network* of genes, proteins and biochemical reactions which give rise to life. Instead of analyzing individual components or aspects of the organism, such as sugar metabolism or a cell nucleus, systems biologists focus on all the components and the interactions among them, all as part of one system. These interactions are ultimately responsible for an organism´s form and functions. For example, the immune system is not the result of a single mechanism or gene. Rather the interactions of numerous genes, proteins, mechanisms and the organism´s external environment, produce immune responses to fight infections and diseases.

Systems biology emerged as the result of the genetics "catalog" provided by the Human Genome project, and a growing understanding of how genes and their resulting proteins give rise to biological form and function. The study of systems biology has been aided by the ease with

As scientists have developed the tools and technologies which allow them to delve deeper into the foundations of biological activity — genes and proteins — they have learned that these components almost never work alone. They interact with each other and with other molecules in highly structured but incredibly complex ways, similar to the complex interactions among the countless computers on the Internet. Systems biology seeks to understand these complex interactions, as these are the keys to understanding life.

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Aravinda Chakravarti is a professor at the McKusick-Nathans Institute of Genetic Medicine at the Johns Hopkins University of Medicine, Baltimore, MD. E-mail: aravinda@jhmi.edu.

Genomics Is Not Enough

NEXT WEEK, THE INTERNATIONAL CONGRESS OF HUMAN GENETICS CONVENES IN MONTREAL, WHERE genomic science, its technologies, genetic disease, and personalized medicine will be discussed. Translating current knowledge into medical practice is an important goal for the public who support medical research, and for the scientists and clinicians who articulate the critical research needs of our time. However, despite innumerable successful gene discoveries through genomics, a major impediment is our lack of knowledge of how these genes affect the fundamental biological mechanisms that are dysregulated in disease. If genomic medicine is to prosper, we need to turn our attention to this gaping hole.

Advances in biomedical research have raised high expectations for translating research into medical applications, including individualizing treatment and prevention. The concept of individualized medicine is not new to genetics. The identification of numerous inborn errors of metabolism and the discovery of their associated enzyme deficiencies paved the way for their specific genetic diagnosis and treatment. However, understanding their biological mechanisms was key. For example, severe mental retardation can arise from the effects of systemic phenylalanine accumulation on the brain, a condition called phenylketonuria. It was determining the underlying cause as a recessive genetic defect in the liver enzyme phenylalanine hydroxylase that led to individualized treatment and public health screening of newborns for the disorder.

Today, genomics technologies can routinely scan the human genome for genetic alterations in any disorder. More than 2000 single-gene Mendelian diseases have been elucidated in this way. Finding the genetic changes that cause the remaining 2000 Mendelian diseases appears within reach. But despite many efforts, attaining a similar understanding of common, chronic, complex diseases has been disappointing. Here, to bring major medical benefit, biomedical research must move beyond simple gene discovery by mapping, sequencing, or genome-wide association studies to focus on understanding human disease mechanisms. We need to answer not only which DNA variants in which genes lead to disease, but how they do so.

The lessons from genome biology are quite clear. Genes and their products almost never act alone, but in networks with other genes and proteins and in context of the environment. The corollary to this is that compromising the activity of one gene need not cripple an entire network. This is consistent with the observations that most traits involve multiple genes, common complex disorders arise from an accumulation of genetic defects in many genes, and Mendelian diseases are rare. Moreover, variation in the regulatory machinery of genes is much more frequent than that in the structure of gene products. Genome biology now needs to move to cell biology and physiology (systems biology) to understand how genetic perturbations lead to downstream dysregulation of proteins, their networks, and cells in disease.

Our evolving knowledge of genetic variation complicates this understanding. Each individual is genomically unique, with the DNA variation in our genomes serving as markers of our ancestries. Are each individual's biology and disease also unique? Or does the extensive sequence diversity in any disease coalesce into a smaller set of common functional deficiencies? By focusing on a mechanistic understanding of disease, genomic science has much to offer and can provide concrete suggestions about when medical treatment needs to be individualized and when made universal. These answers will themselves evolve as the science evolves. Consider the simple example of blood typing for everyday transfusions. This is individualized treatment that ignores widespread differences in type frequency between different populations because the focus of treatment is the individual, not the group. Recent research offers the future possibility of enzymatic treatment of any blood type to make it the universal type O, thus making a once successful individualized treatment universal. As this example shows, for genomic medicine there is no time with a more acute need for science than now.

Aravinda Chakravarti

10.1126/science.1214458

Published by AAAS

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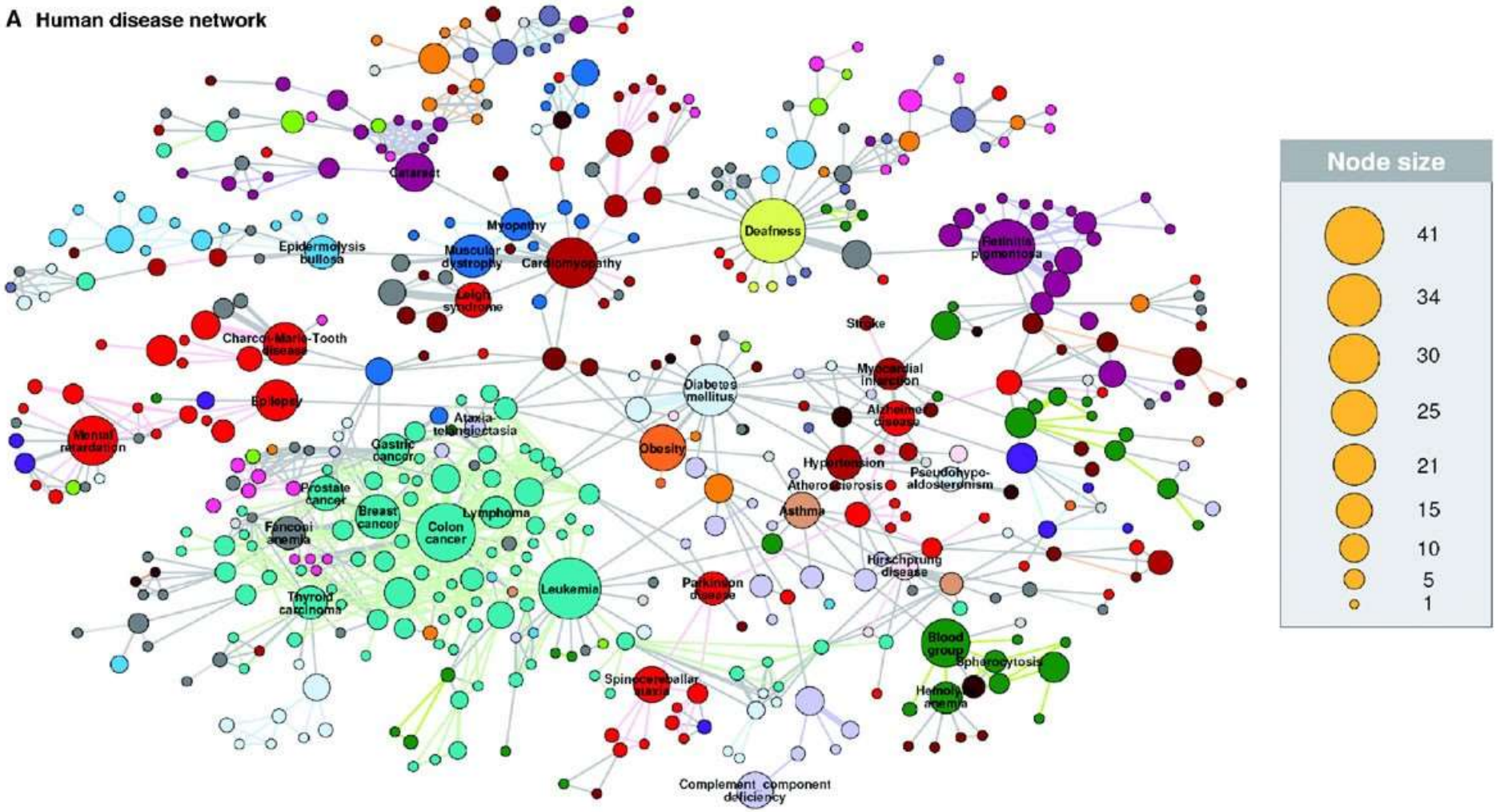
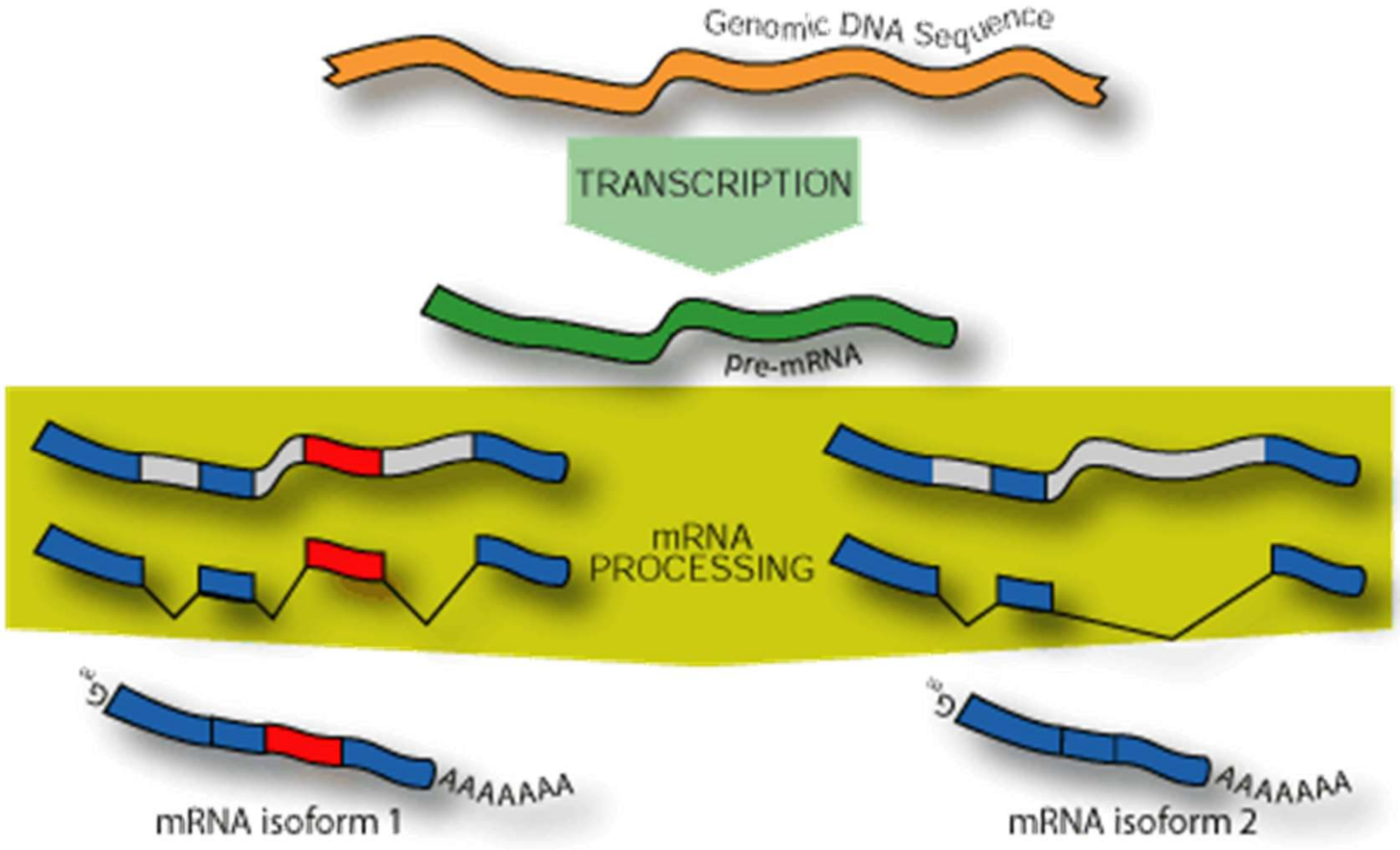


Figure 4 (**A**) Human disease network. Each node corresponds to a specific disorder colored by class (22 classes, shown in the key to (**B**)). The size of each node is proportional to the number of genes contributing to the disorder. Edges between disorders in the same disorder class are colored with the same (lighter) color, and edges connecting different disorder classes are colored gray, with the thickness of the edge proportional to the number of genes shared by the disorders connected by it. (B) Disease gene network. Each node is a single gene, and any two genes are connected if implicated in the same disorder. In this network map, the size of each node is proportional to the number of specific disorders in which the gene is implicated. (Reproduced with permission from the National Academies Press; Goh *et al*, in press.)

Los genes, piedra angular del desarrollo y funcionamiento de los organismos, no pueden explicar por sí solos qué hace a las vacas vacas y maíz al maíz. Los mismos genes se han manifestado en organismos tan diferentes como, digamos, ratón y medusa. Es más, nuevos hallazgos de una variedad de investigadores han puesto en claro que es el exquisito control por el genoma de la actividad de cada gen –y no los genes per se- lo que más importa.

Pennisi, E. (2004) Science



Alternative splicing increases mRNA diversity

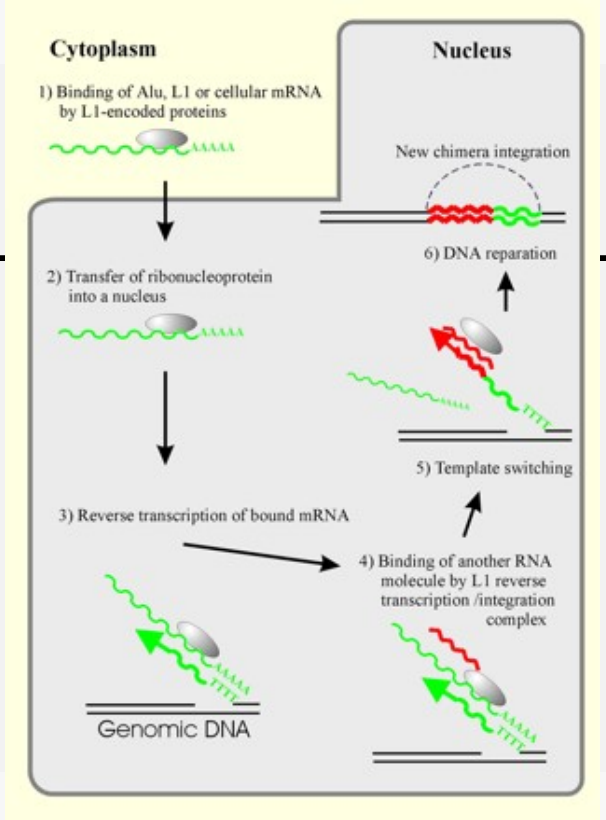
Alternative splicing is the process whereby a single genetic locus can be transcribed and processed to generate multiple, distinct isoforms[1-3]. Recent reports have shown that more than one third of all human genes may be affected by alternative splicing[4-9]. The presence, absence, abundance and activity of splicing factors can effect which regions of the pre-mRNA will be included in the mature mRNA. How alternative splicing (or splicing in general) is regulated remains poorly understood.

Nucleic Acids Res. 2003 Aug 1;31(15):4385-90.

The human genome contains many types of chimeric retrogenes generated through in vivo RNA recombination.

Buzdin A, Gogvadze E, Kovalskaya E, Volchkov P, Ustyugova S, Illarionova A, Fushan A, Vinogradova T, Sverdlov E.

Abstract:

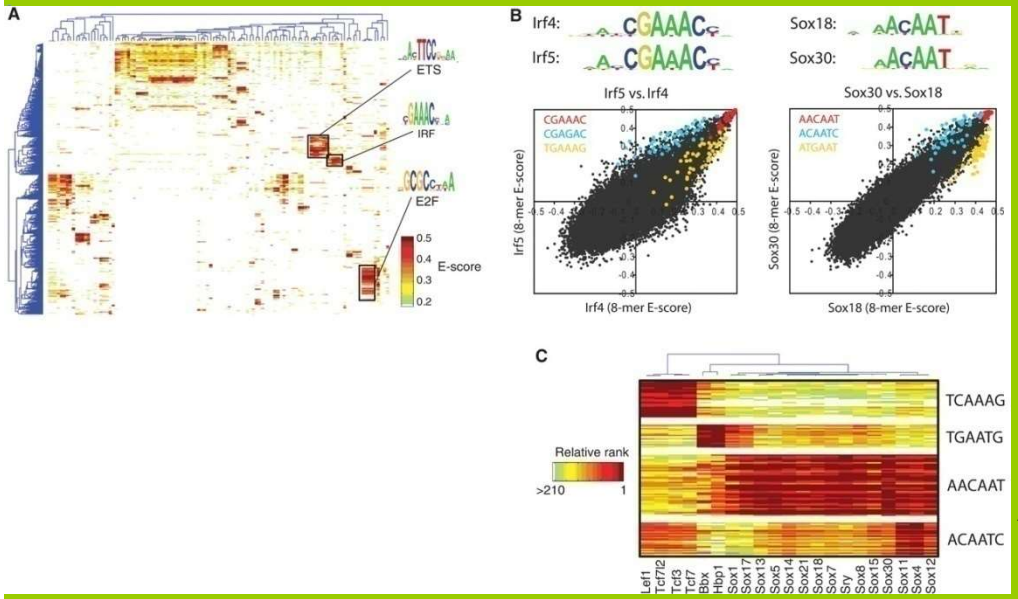


L1 retrotransposons play an important role in mammalian genome shaping. In particular, they can transduce their 3'-flanking regions to new genomic loci or produce pseudogenes or retrotranscripts through reverse transcription of different kinds of cellular RNAs. Recently, we found in the human genome an unusual family of chimeric retrotranscripts composed of full-sized copies of U6 small nuclear RNAs fused at their 3' termini with 5'-truncated, 3'-poly(A)-tailed L1s. The chimeras were flanked by 11-21 bp long direct repeats, and contained near their 5' ends T2A4 hexanucleotide motifs, preferably recognized by L1 nicking endonuclease. These features suggest that the chimeras were formed using the L1 integration machinery.
These findings suggest that RNA-RNA recombination during L1 reverse transcription followed by the integration of the recombinants into the host genome is a general event in genome evolution.

Science 26 June 2009:
Vol. 324. no. 5935, pp. 1720 - 1723
DOI: 10.1126/science.1162327

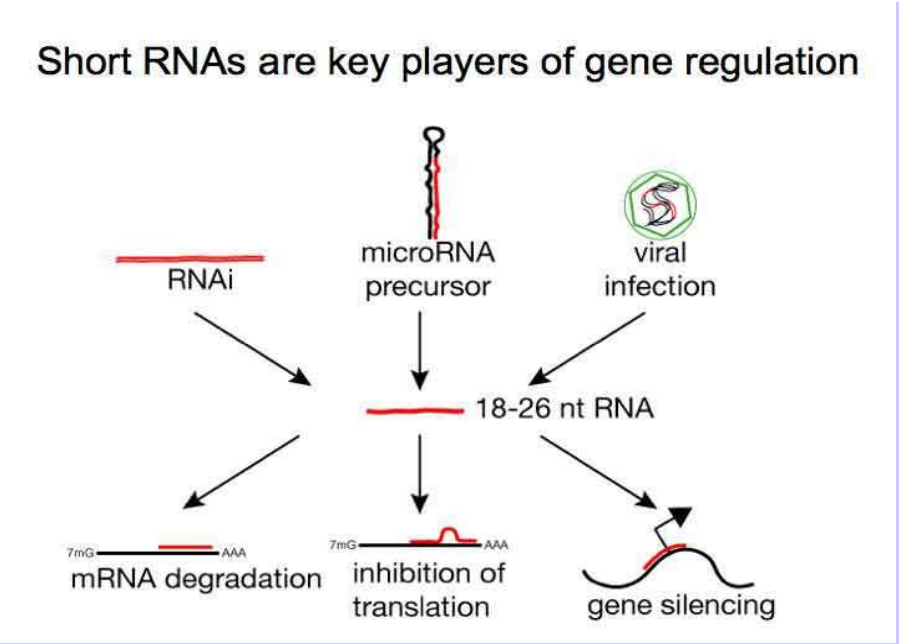
Diversity and Complexity in DNA Recognition by Transcription Factors

Gwenael Badis,[1,*] Michael F. Berger,[2,3,*] Anthony A. Philippakis,[2,3,4,*] Shaheynoor Talukder,[1,5,*] Andrew R. Gehrke,[2,*] Savina A. Jaeger,[2,*] Esther T. Chan,[5,*] Genita Metzler,[6] Anastasia Vedenko,[7] Xiaoyu Chen,[1] Hanna Kuznetsov,[6] Chi-Fong Wang,[8] David Coburn,[1] Daniel E. Newburger,[2] Quaid Morris,[1,5,9,10] Timothy R. Hughes,[1,5,10,]



Sequence preferences of DNA binding proteins are a primary mechanism by which cells interpret the genome. Despite the central importance of these proteins in physiology, development, and evolution, comprehensive DNA binding specificities have been determined experimentally for only a few proteins. Here, we used microarrays containing all 10–base pair sequences to examine the binding specificities of 104 distinct mouse DNA binding proteins representing 22 structural classes. Our results reveal a complex landscape of binding, with virtually every protein analyzed possessing unique preferences. Roughly half of the proteins each recognized multiple distinctly different sequence motifs, challenging our molecular understanding of how proteins interact with their DNA binding sites. This complexity in DNA recognition may be important in gene regulation and in the evolution of transcriptional regulatory networks.

Los genes tienen muchas formas alternativas y un mismo gen puede dar lugar a proteínas distintas dependiendo de cómo se combinen las distintas regiones. Estas regiones del genoma analizadas están muy interconectadas unas con otras, mientras que la idea que tenían hasta el momento los científicos era que los genes estaban claramente delimitados. En el genoma, todo un conjunto de instrucciones dictan cómo son las características de los seres vivos. Los científicos no sabemos muy bien cómo leer esas instrucciones y qué regiones del genoma son las que realmente codifican esas instrucciones. /.../ La mayor parte del genoma tiene actividad, es decir, no está "silencioso", lo que echa por tierra la idea de que una gran parte del ADN sería algo así como "basura", sin función alguna. (Guigo, R., 2007. PROYECTO ENCODE)



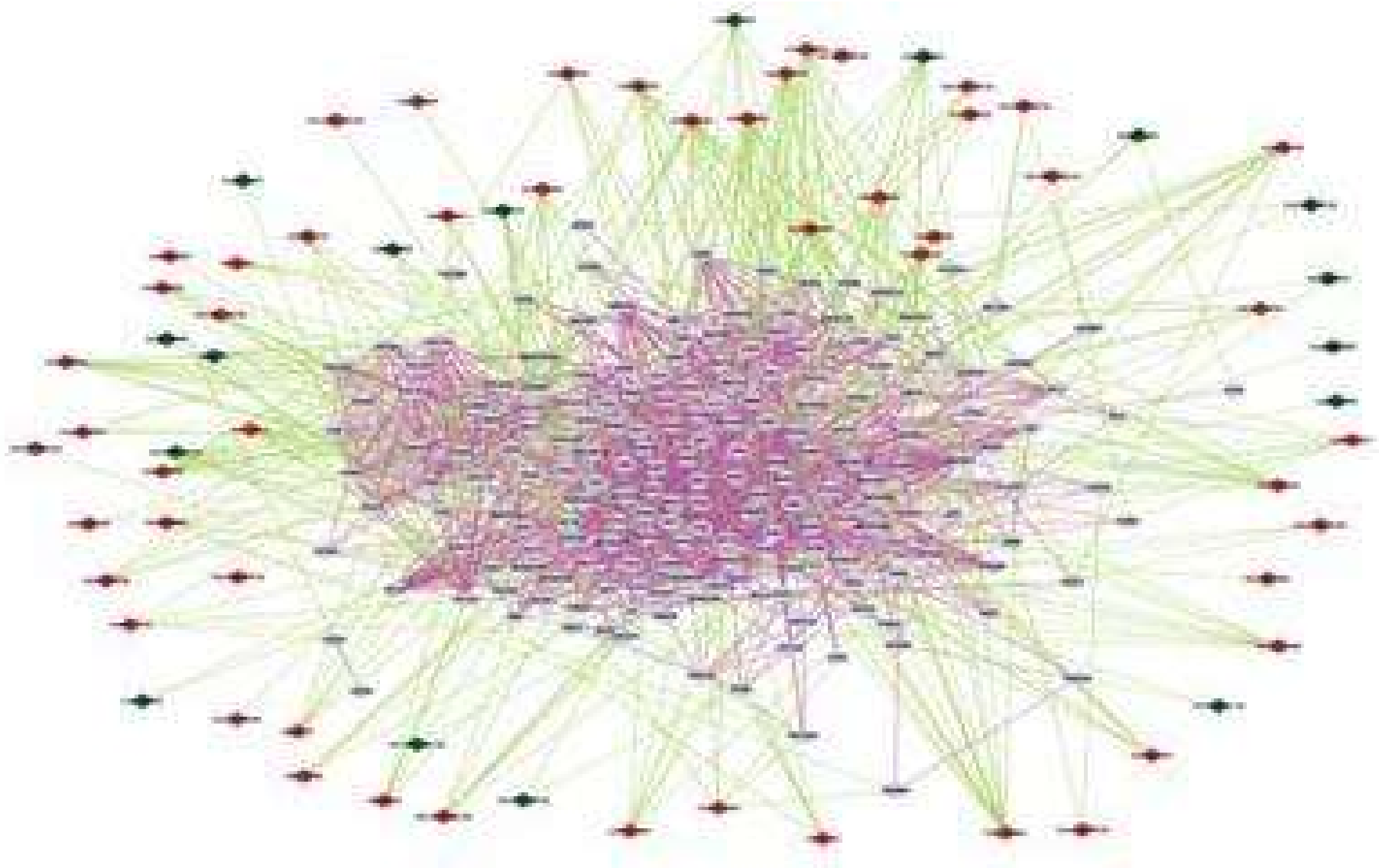
Nature Reviews Genetics **5**, 316 -323 (2004); doi:10.1038/nrg1321

RNA REGULATION: A NEW GENETICS?

John S. Mattick

Abstract

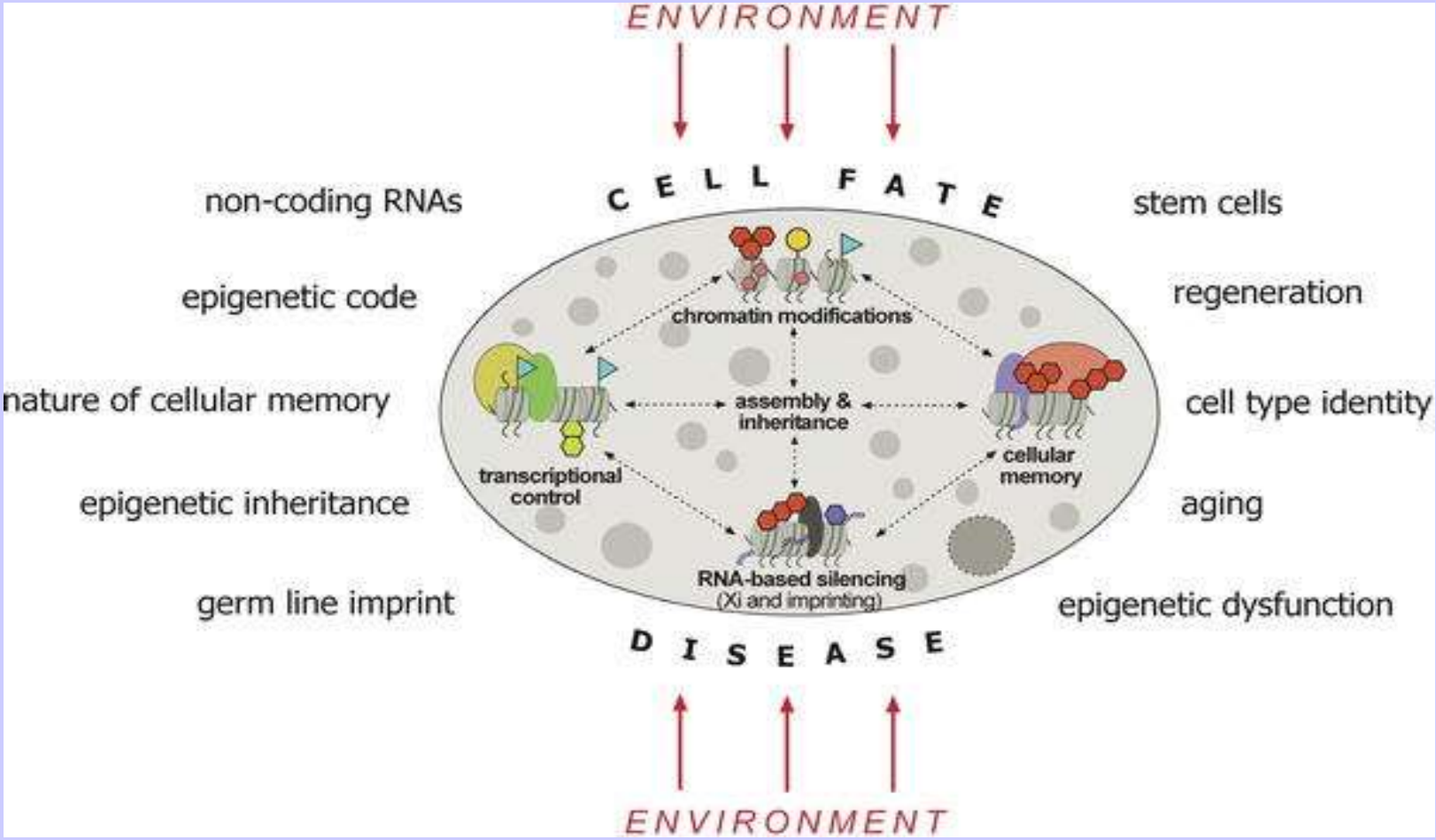
Do non-coding RNAs that are derived from the introns and exons of protein-coding and non-protein-coding genes represent a fundamental advance in the genetic operating system of higher organisms? Recent evidence from comparative genomics and molecular genetics indicates that this might be the case. If so, there will be profound consequences for our understanding of the genetics of these organisms, and in particular how the trajectories of differentiation and development and the differences among individuals and species are genomically programmed. But how might this hypothesis be tested?



microRNA and its target gene network

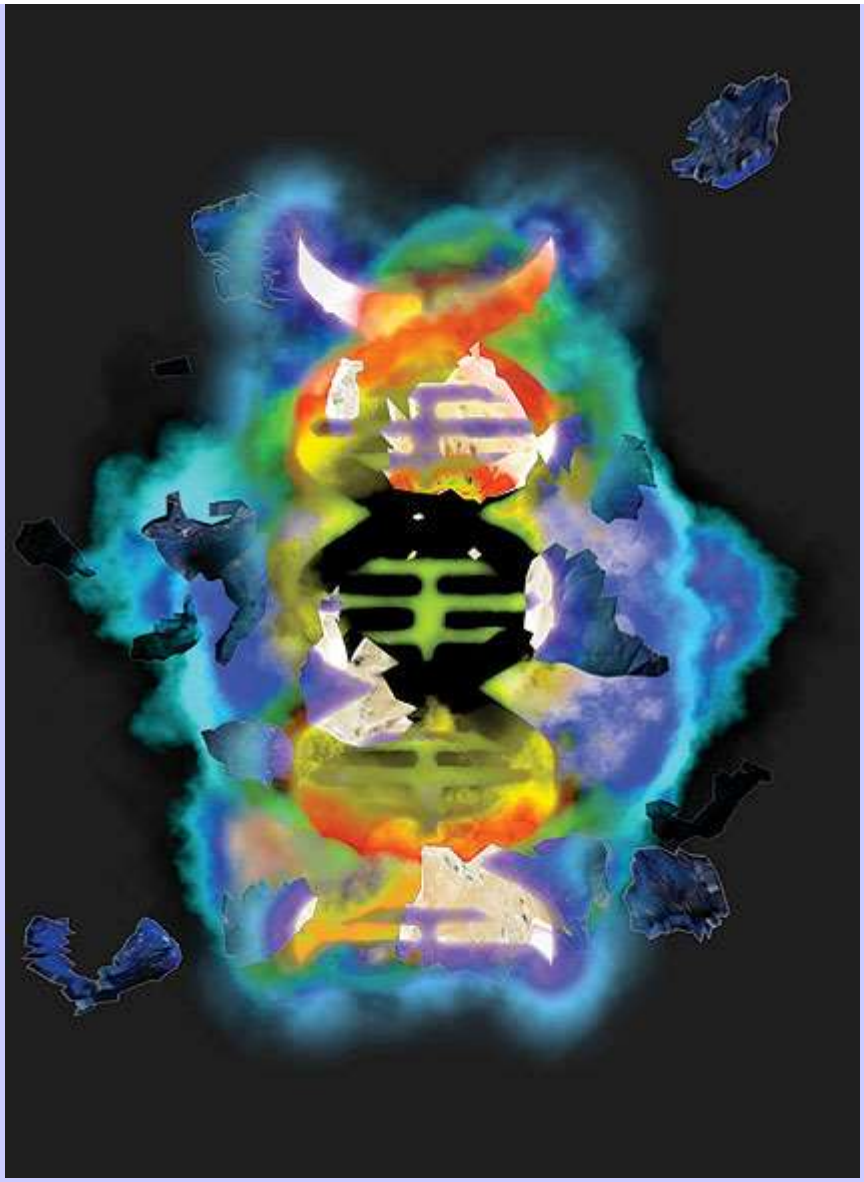
Nature **434**, 505-509 (24 March 2005) | doi: 10.1038/nature03380

Genome-wide non-mendelian inheritance of extra-genomic information in *Arabidopsis*

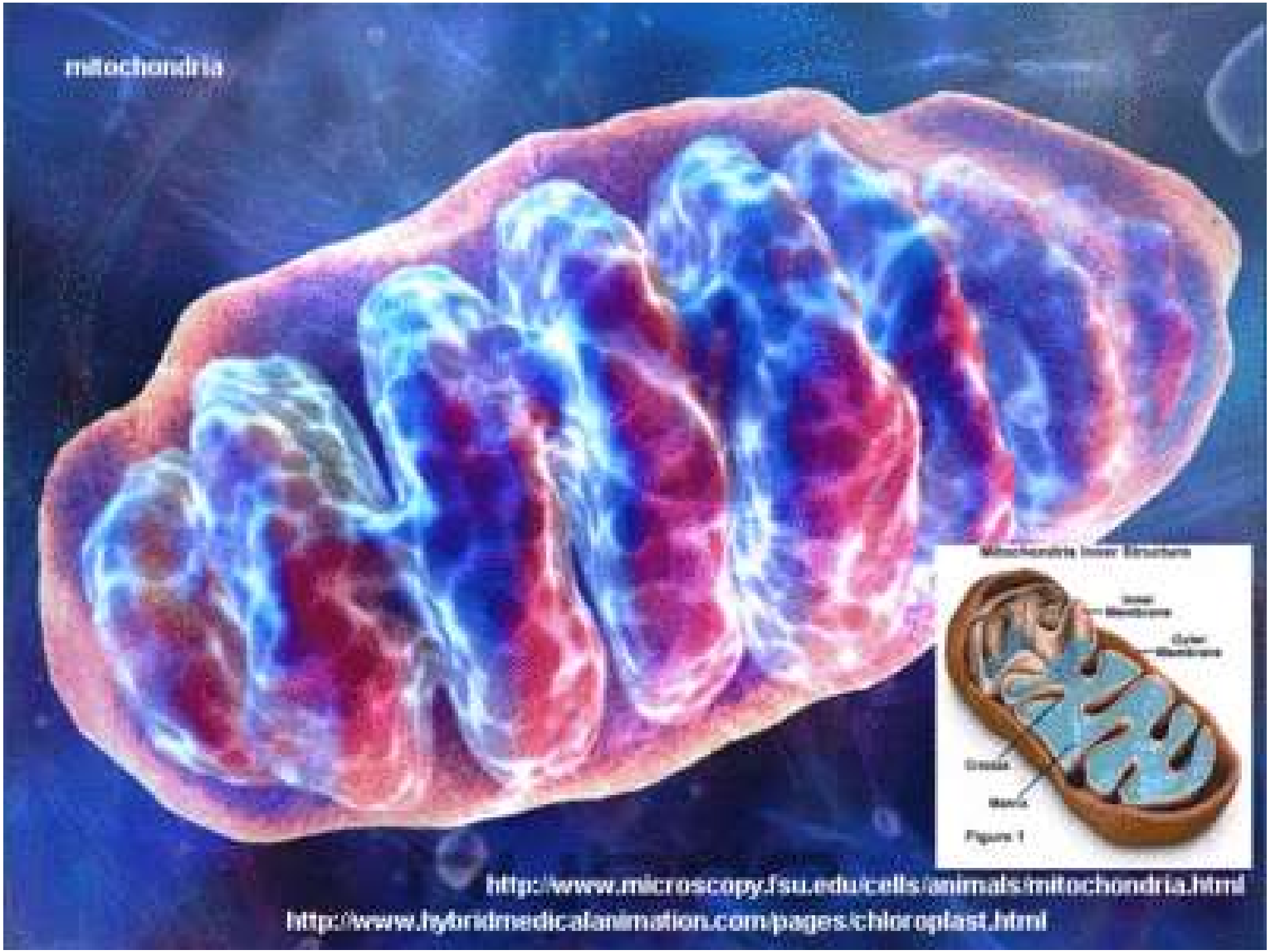


The Impact of Epigenetic Gene Control

Diverse biochemical modifications of DNA and histones, such as DNA methylation (indicated by small hexagons), histone methylation (large hexagons), acetylation (triangles), and phosphorylation (circles), occur in response to the environment and modulate chromatin structure. The organization of chromatin controls the access of many proteins, including transcription factors (ovals), to the DNA template and thus regulates gene expression. This epigenetic gene control has an impact on a variety of biological processes, with implications for agriculture and human biology and disease, including our understanding of stem cells, cancer, and aging.



The more expert scientists become in molecular genetics, the less easy it is to be sure about what, if anything, a gene actually is. (Nature 5,25,06)


mitochondria
http://www.microscopyu.su.edu/cells/animals/mitochondria.html
http://www.hybridmedicalanimation.com/pages/chloroplast.html

Current Biology, Volume 16, Issue 14, R551-R560, 25 July 2006
doi:10.1016/j.cub.2006.06.054

Mitochondria: More Than Just a Powerhouse

Heidi M. McBride [1], Margaret Neuspiel[2] and Sylwia Wasiak

Summary

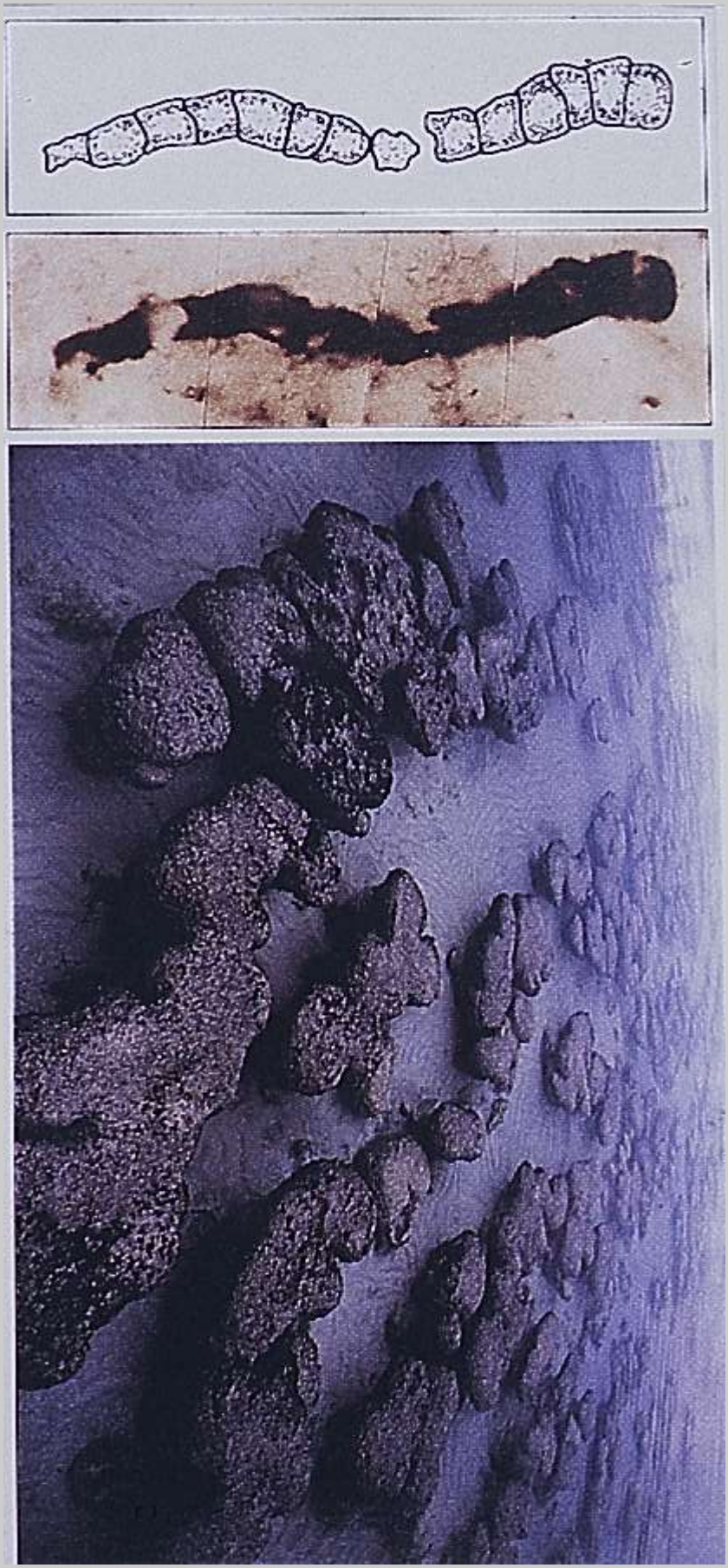
Pioneering biochemical studies have long forged the concept that the mitochondria are the energy powerhouse of the cell

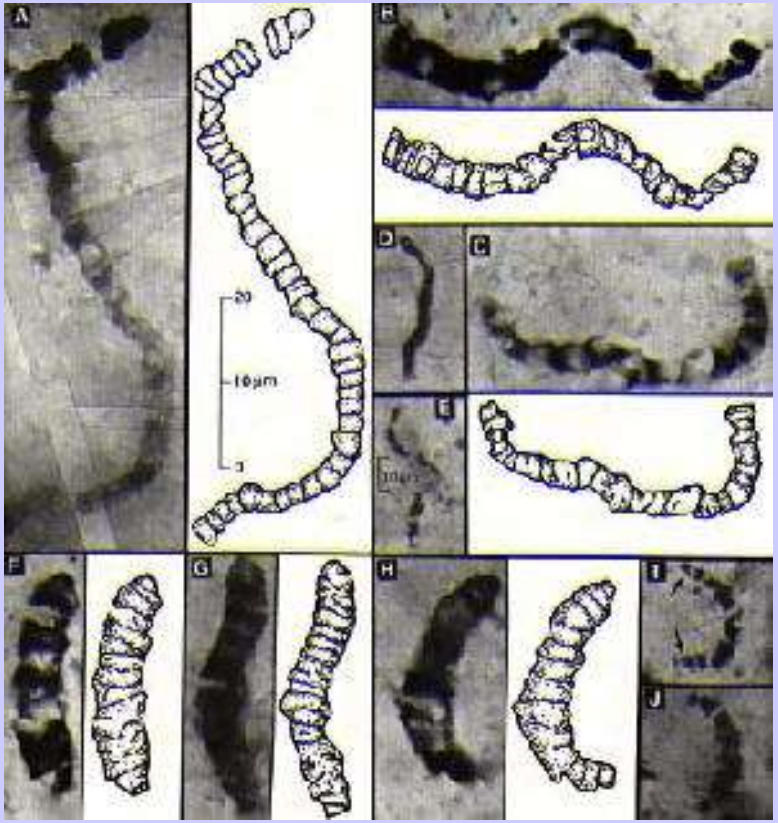
. These studies, combined with the unique evolutionary origin of the mitochondria, led the way to decades of research focusing on the organelle as an essential, yet independent, functional component of the cell. Recently, however, our conceptual view of this isolated organelle has been profoundly altered with the discovery that mitochondria function within an integrated reticulum that is continually remodeled by both fusion and fission events. The identification of a number of proteins that regulate these activities is beginning to provide mechanistic details of mitochondrial membrane remodeling. However, the broader question remains regarding the underlying purpose of mitochondrial dynamics and the translation of these morphological transitions into altered functional output. One hypothesis has been that mitochondrial respiration and metabolism may be spatially and temporally regulated by the architecture and positioning of the organelle. Recent evidence supports and expands this idea by demonstrating that mitochondria are an integral part of multiple cell signaling cascades. Interestingly, proteins such as GTPases, kinases and phosphatases are involved in bi-directional communication between the mitochondrial reticulum and the rest of the cell. These proteins link mitochondrial function and dynamics to the regulation of metabolism, cell-cycle control, development, antiviral responses and cell death. In this review we will highlight the emerging evidence that provides molecular definition to mitochondria as a central platform in the execution of diverse cellular events.

El **silogismo** es una forma de razonamiento deductivo que consta de dos proposiciones como premisas y otra como conclusión, siendo la última una inferencia necesariamente deductiva de las otras dos. Fue formulado por primera vez por Aristóteles, en su obra lógica recopilada como *El Organon* de sus libros conocidos como *Primeros Analíticos,* (en griego *Proto Analytika*, en latín –idioma en el que se reconoció la obra en Europa Occidental-, *Analytica Priora*).

La Biología carece de un marco teórico para describir este tipo de situación /.../ los biólogos van a tener que construir una nueva biología. Desde que en los años sesenta se descifró el código genético, la biología molecular ha sido una ciencia cualitativa, dedicada a investigar y clasificar las moléculas de la célula como los zoólogos victorianos catalogaban las especies. El genoma humano marca la culminación de ese esfuerzo. Ahora se necesitan modelos y teorías que ayuden a lograr que la inmensa fortuna de datos que se han amasado cobre sentido.

Ball, P. (2001) Nature





Archaeoscillatoriopsis maxima (cianobacteria)
Primaevifilum attenuatum (cianobacteria)
Archaeoscillatoriopsis grandis (cianobacteria)
Primaevifilum laticellulosum(cianobacteria)
Primaevifilum conicoterminatum (cianobacteria)figuras F,G y H
Archaeoscillatoriopsis disciformis (cianobacteria)
Primaevifilum amoenum (bacteria ? cianobacteria), figura A
Primaevifilum delicatulum (bacteria ? cianobacteria)
Primaevifilum minutum (bacteria)
Eoleptonema apex (bacteria)
Archaeotrichion septatum (bacteria)

APEX CHERT


10 µm

Published online: 7 June 2006; | doi:10.1038/news060605-7

Complex ecosystems arrived early

Diversity of oldest fossils could mean extraterrestrial life is more likely.

Michael Hopkin

The variety of different markings on the stromatolites suggests that many different types of microbe were living there, the team report in this week's *Nature* . And if life could diversify so soon, the researchers speculate, then maybe it could also have flourished on hostile worlds such as Mars.

The 3.4-billion-year-old rocks show the dappled hallmarks of ancient life.

ASTROBIO

Asteroid Provides Clues to Earth's Oceans

Summary: The first-ever discovery of ice and organic molecules on an asteroid may hold clues to the origins of Earth's oceans and life 4 billion years ago. Researchers detected a thin layer of water ice and organic molecules on the surface of a large asteroid orbiting between Mars and Jupiter.

Nature **464**, 1320-1321 (29 April 2010) | doi:10.1038/nature09029; Received 21 September 2009; Accepted 24 February 2010

Water ice and organics on the surface of the asteroid 24 Themis

Humberto Campins[1], Kelsey Hargrove[1], Noemi Pinilla-Alonso[2], Ellen S. Howell[3], Michael S. Kelley[4], Javier Licandro[5,6], T. Mothé-Diniz[7], Y. Fernández[1] & Julie Ziffer[8]

Abstract

It has been suggested[1, 2, 3] that Earth's current supply of water was delivered by asteroids, some time after the collision that produced the Moon (which would have vaporized any of the pre-existing water). So far, no measurements of water ice on asteroids[4, 5] have been made, but its presence has been inferred from the comet-like activity of several small asteroids, including two members of the Themis dynamical family[6]. Here we report infrared spectra of the asteroid 24 Themis which show that ice and organic compounds are not only present on its surface but also prevalent. Infrared spectral differences between it and other asteroids make 24 Themis unique so far, and our identification of ice and organics agrees with independent results[7] that rule out other compounds as possible sources of the observed spectral structure. The widespread presence of surface ice on 24 Themis is somewhat unexpected because of the relatively short lifetime of exposed ice at this distance (~3.2 au) from the Sun. Nevertheless, there are several plausible sources, such as a subsurface reservoir that brings water to the surface through 'impact gardening' and/or sublimation.

Nature. 1999 Jun 10;399(6736):541-8.

nature

Marine viruses and their biogeochemical and ecological effects.

- Fuhrman JA.

Department of Biological Sciences, Wrigley Institute for Environmental Studies, University of Southern California, Los Angeles 90089-0371, USA. fuhrman@usc.edu

Viruses are the most common biological agents in the sea, typically numbering ten billion per litre. They probably infect all organisms, can undergo rapid decay and replenishment, and influence many biogeochemical and ecological processes, including nutrient cycling, system respiration, particle size-distributions and sinking rates, bacterial and algal biodiversity and species distributions, algal bloom control, dimethyl sulphide formation and genetic transfer. Newly developed fluorescence and molecular techniques leave the field poised to make significant advances towards evaluating and quantifying such effects

PNAS | **August 8, 2006** | vol. 103 | no. 32 | **12115-12120**
OPEN ACCESS ARTICLE

BIOLOGICAL SCIENCES / MICROBIOLOGY

Microbial diversity in the deep sea and the underexplored "rare biosphere"

Mitchell L. Sogin[*], Hilary G. Morrison[*], Julie A. Huber[*], David Mark Welch[*], Susan M. Huse[*], Phillip R. Neal[*], Jesus M. Arrieta, and Gerhard J. Herndl

Table 1. Environmental DNA samples used for sequence tag analyses (collected from North Atlantic Deep Water and Axial Seamount, Ju de Fuca Ridge)

Site	Lat °N, Long °W	Depth, m	Temperature, °C	Cells per ml of water
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Journal of Cosmology, 2009, Vol 1,
pages 1-56
Cosmology 2009
Peer Reviewed - With Open Peer

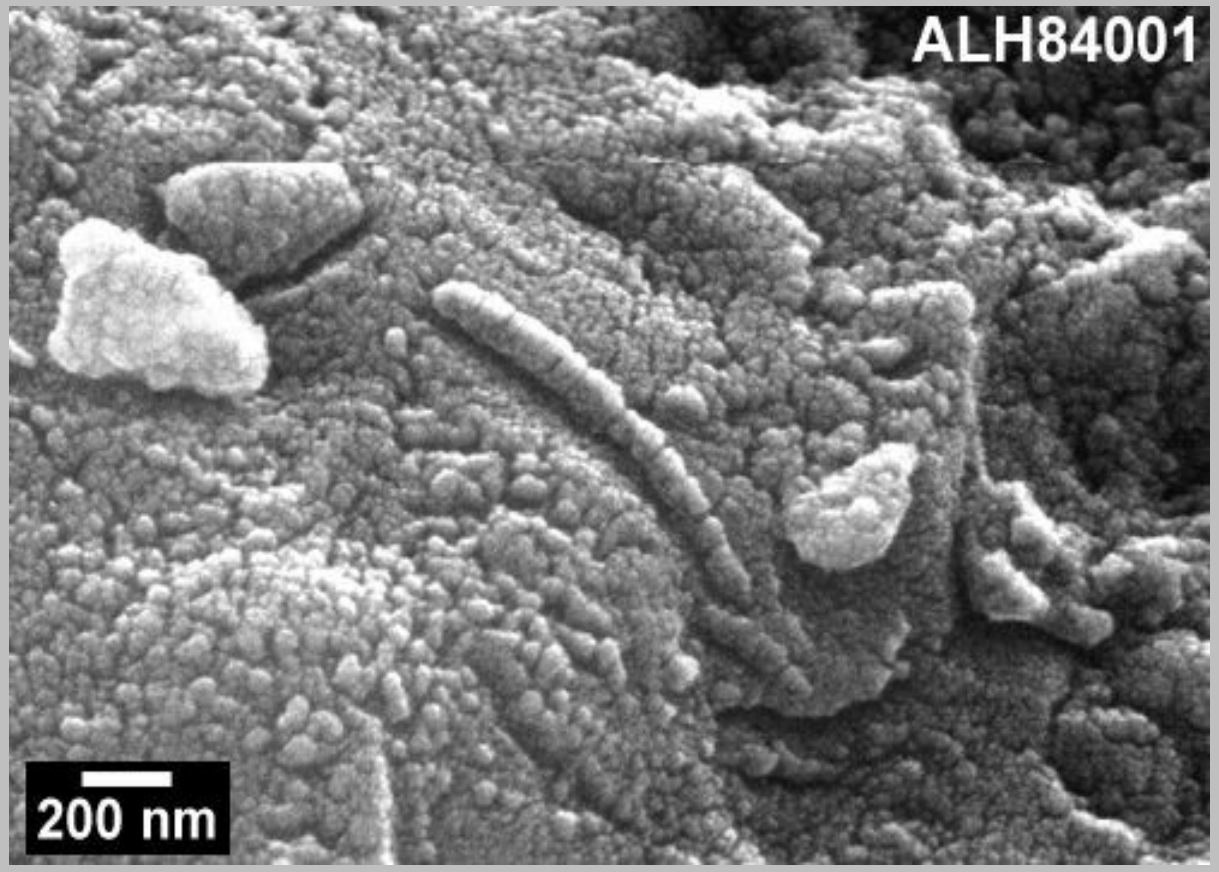
Life on Earth
Came From Other Planets

by Rhawn Joseph, Ph.D.*
Emeritus, Brain Research Laboratory, Northern California

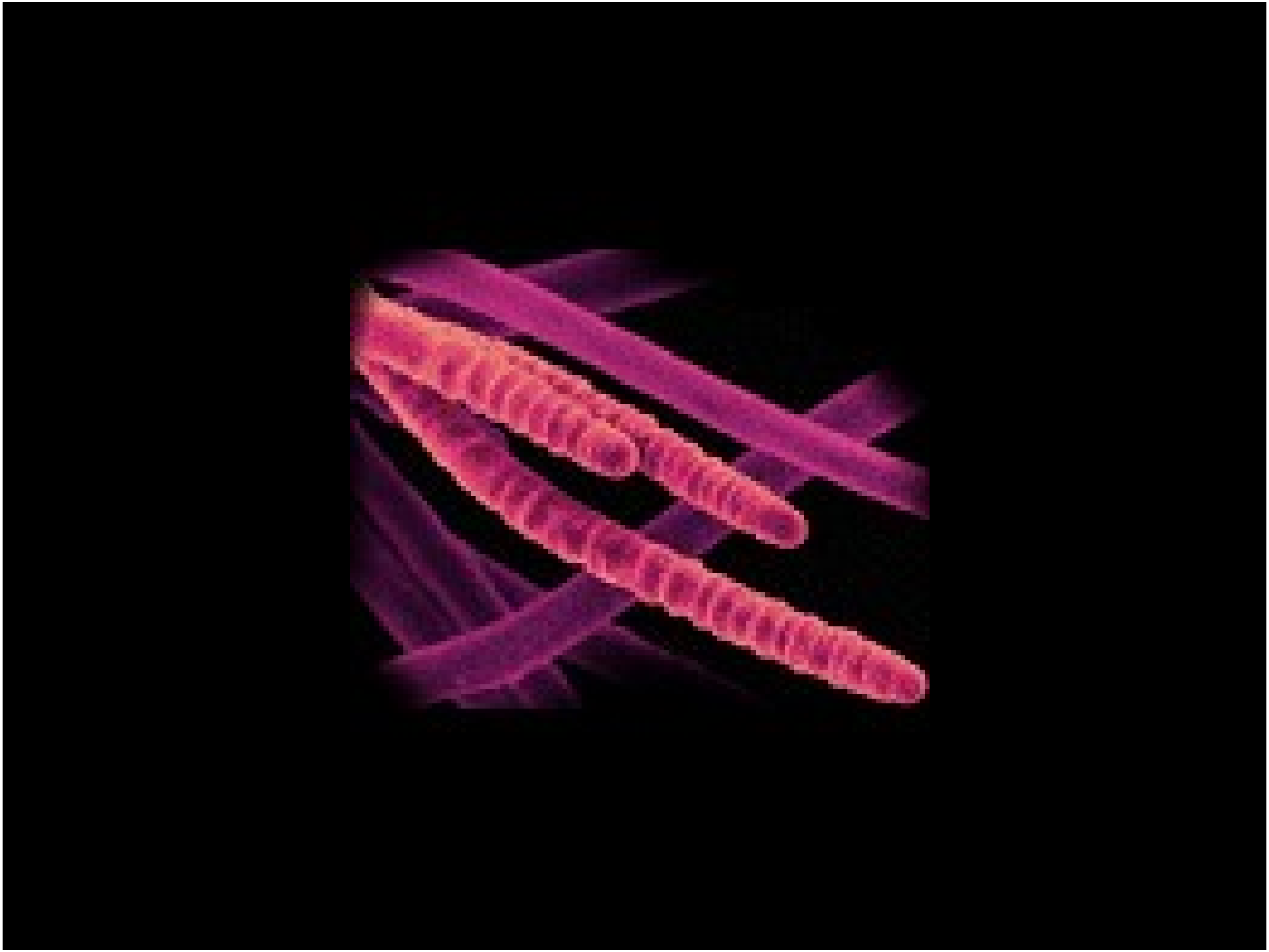
ABSTRACT

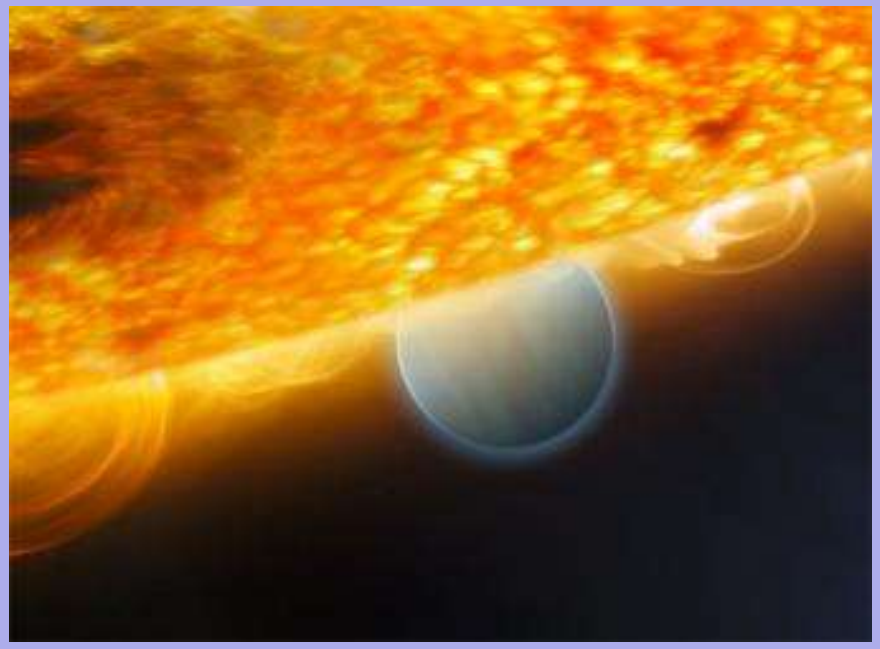
A comprehensive theory based on a review of scientific findings published in prestigious scientific journals, is presented to explain how life on Earth came from other planets. Life appeared a few hundred million years after the Earth's creation during a period of heavy bombardment. Life on Mars may have appeared near the same time. Microbes are adapted for surviving the hazards of space, including ejection from and landing upon a planet. Microbial fossils have been discovered in fifteen carbonaceous chondrites, most impacted by supernova. The Sun and Earth were created from a nebular cloud and protoplanetary disc, the remnants of an exploding star and its planets which may have harbored life. When the parent star became a red giant, its solar winds blew away planetary atmospheres along with airborne microbes, which were deposited in a growing nebular cloud. Because the red giant lost 40% to 80% of its mass and its gravitational influences were reduced, its planets increased orbital distances or were ejected prior to supernova and may not have been atomized. The inner layers of a nebular cloud and protoplanetary disk protects against radiation and extreme cold enabling spores to survive. Microbes may have also survived within planetary debris which bombarded the Earth. As only life can produce life, then life on Earth also came from life which may have originated on planets which orbited the parent star.

Key Words: Panspermia; Origin of life; Abiogenesis, Supernova; Meteors, microfossils



Reproduced from NASA website.





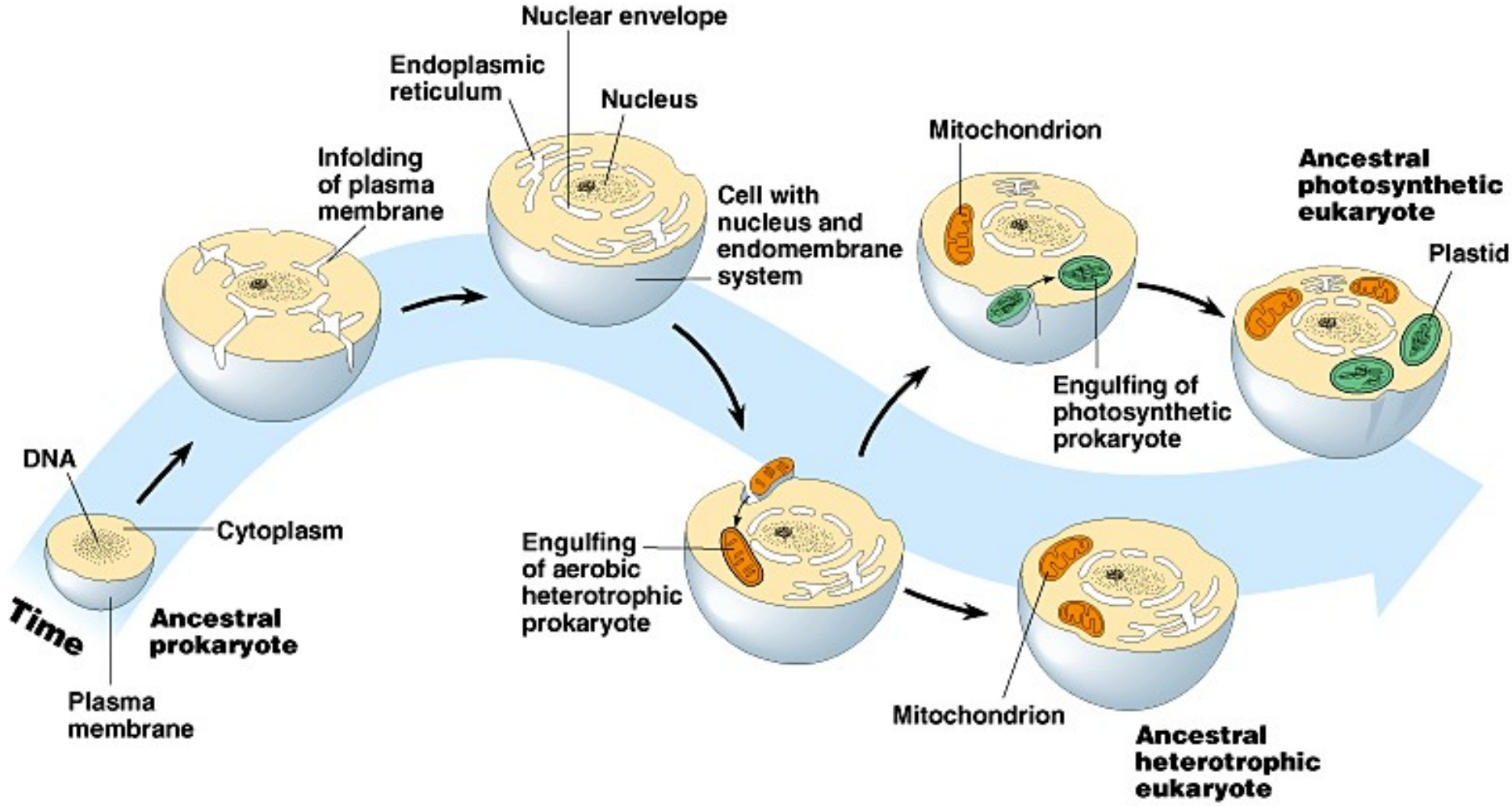
El 'Hubble' descubre dióxido de carbono en un planeta extrasolar

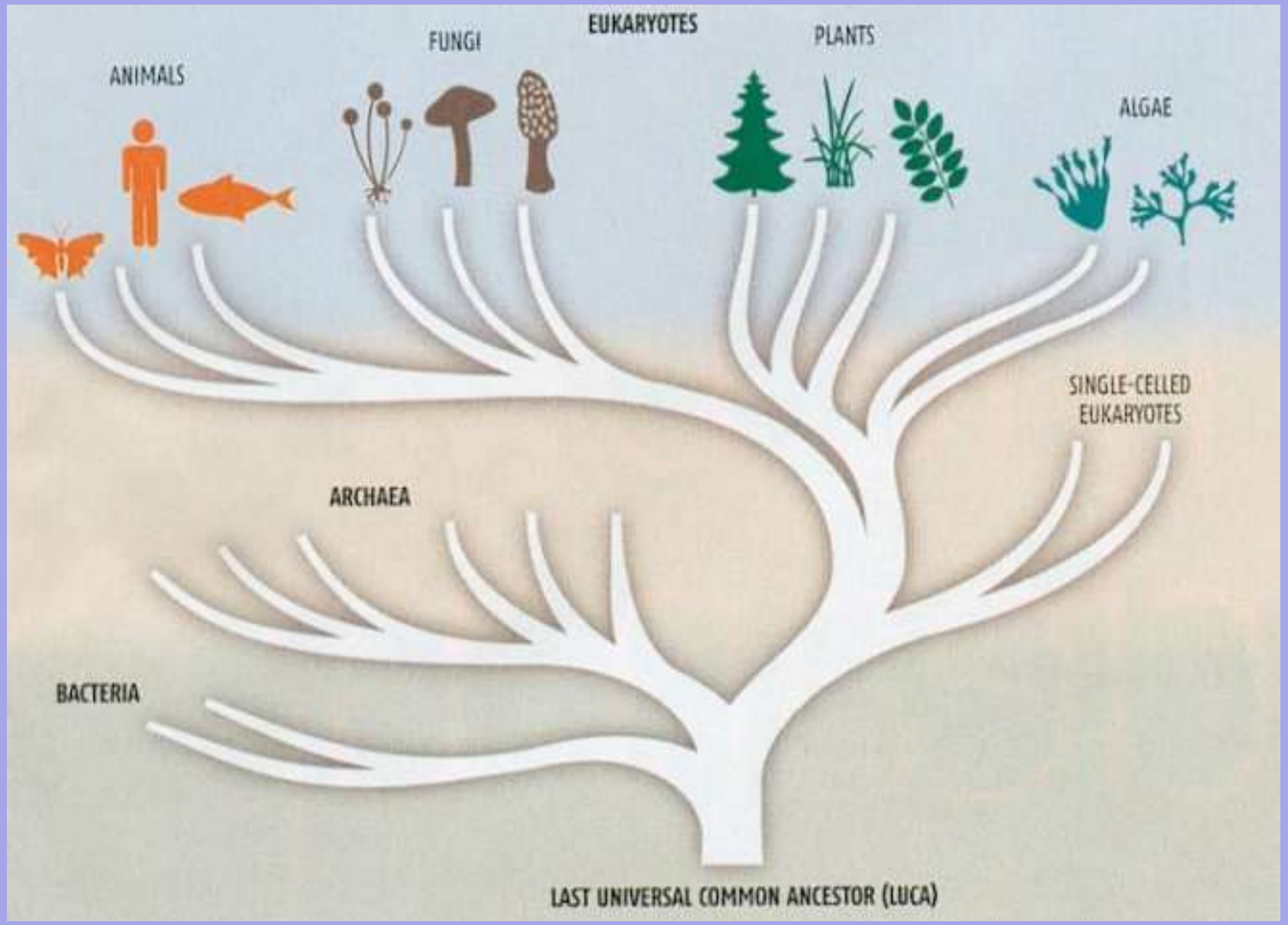
El hallazgo del telescopio espacial de la NASA supone un paso importante en la búsqueda de rastros químicos de vida extraterrestre

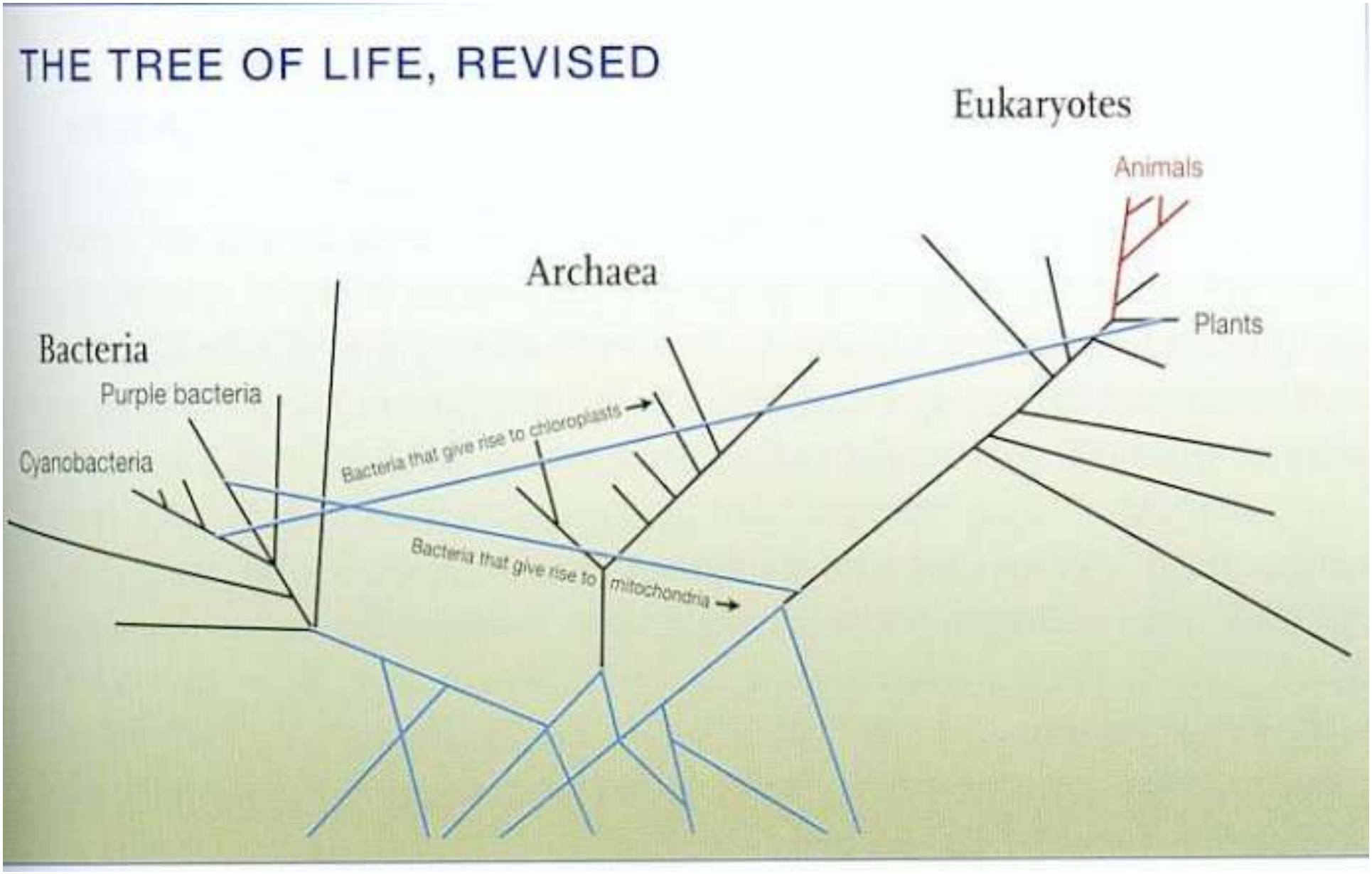
ELPAÍS.com - Madrid - 10/12/2008

Introduction to the Cyanobacteria
Architects of earth's atmosphere

The oxygen atmosphere that we depend on was generated by numerous cyanobacteria during the Archaean and Proterozoic Eras. Before that time, the atmosphere had a very different chemistry, unsuitable for life as we know it today.




EUKARYOTES
ANIMALS
FUNGI
PLANTS
ALGAE
SINGLE-CELLED EUKARYOTES
ARCHAEA
BACTERIA
LAST UNIVERSAL COMMON ANCESTOR (LUCA)


THE TREE OF LIFE, REVISED
Eukaryotes
Animals
Plants
Archaea
Bacteria
Purple bacteria
Cyanobacteria
Bacteria that give rise to chloroplasts
Bacteria that give rise to mitochondria

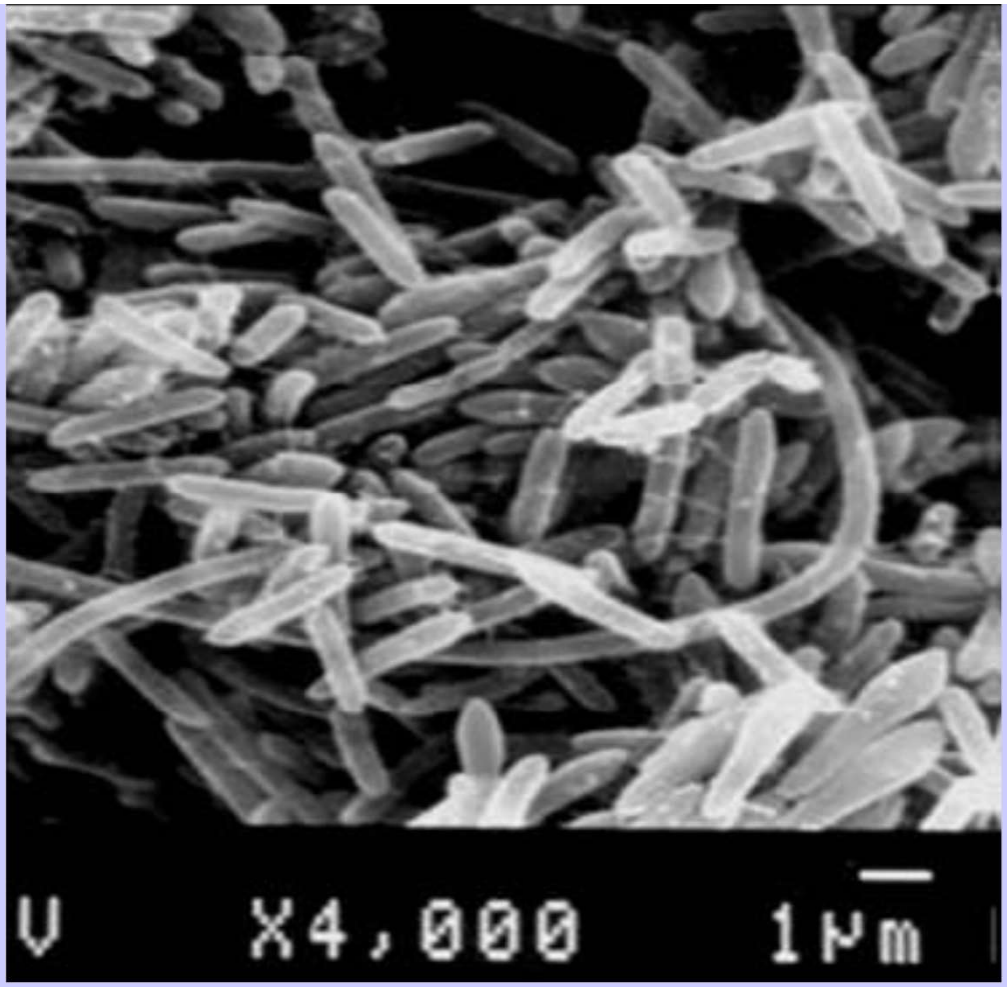
Bacteria Harnessing Complexity

By

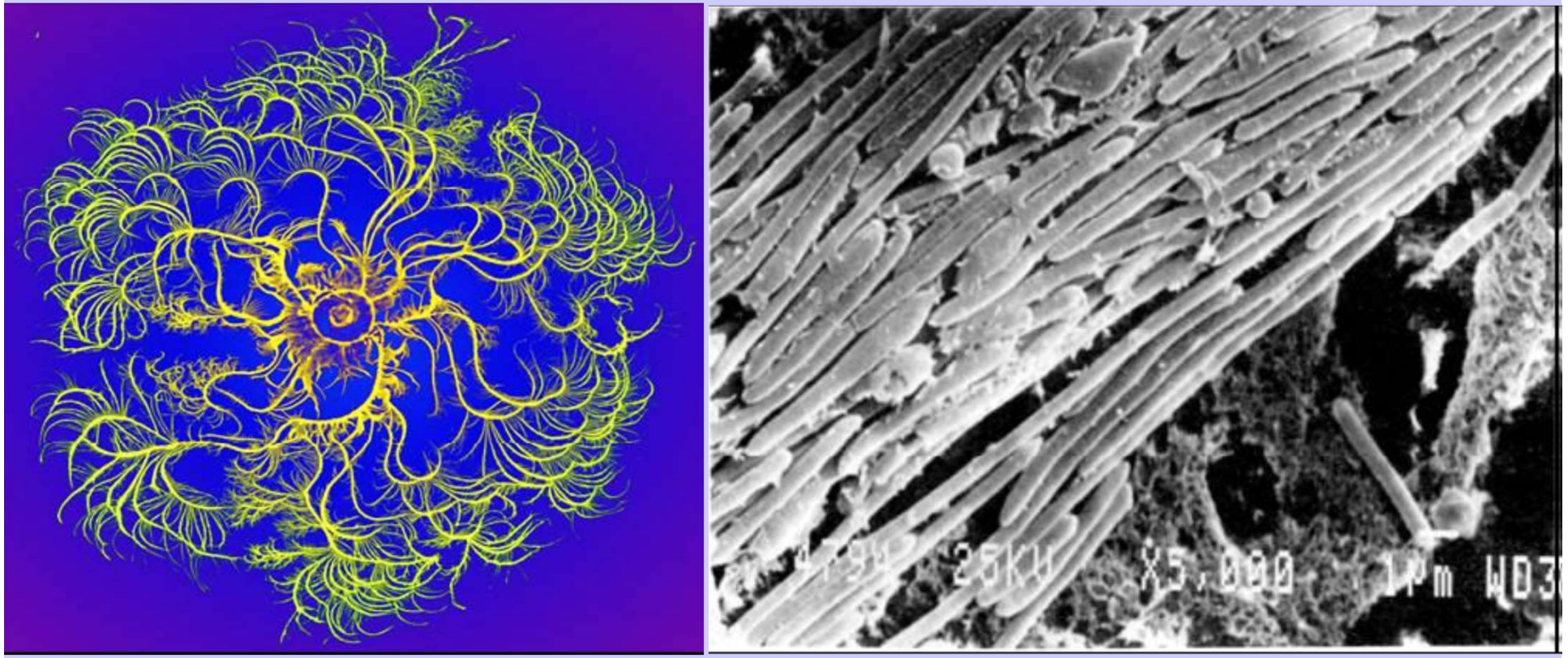
Eshel Ben Jacob, Yakir Aharonov and Yoash Shapira
School of Physics and Astronomy
Raymond & Beverly Sackler Faculty of Exact Sciences
The Maguy-Glass Chair in Physics of Complex Systems
Tel Aviv University, 69978 Tel Aviv Israel

Abstract

The study of bacterial colonies - groups of bacteria grown from a single or few similar cells - is a crucial step towards understanding biofilms, which are composed of many different bacterial colonies. In this article, we review some of the exciting discoveries about the cooperative behavior of bacteria in colonies, which might shed new light on biocomplexity in general and biofilms in particular. The review is aimed at researchers from different disciplines - microbiology, biology, chemistry, physics, mathematics, and computer science. We start with the realization that, under natural growth conditions, bacteria can selforganize into hierarchically structured colonies, 109-1012 bacteria each. To that end, they developed and utilize a great variety of biochemical communication agents, such as simple molecules, polymers, peptides, complex proteins, genetic material, and also "cassettes of genetic information" like plasmids and viruses.

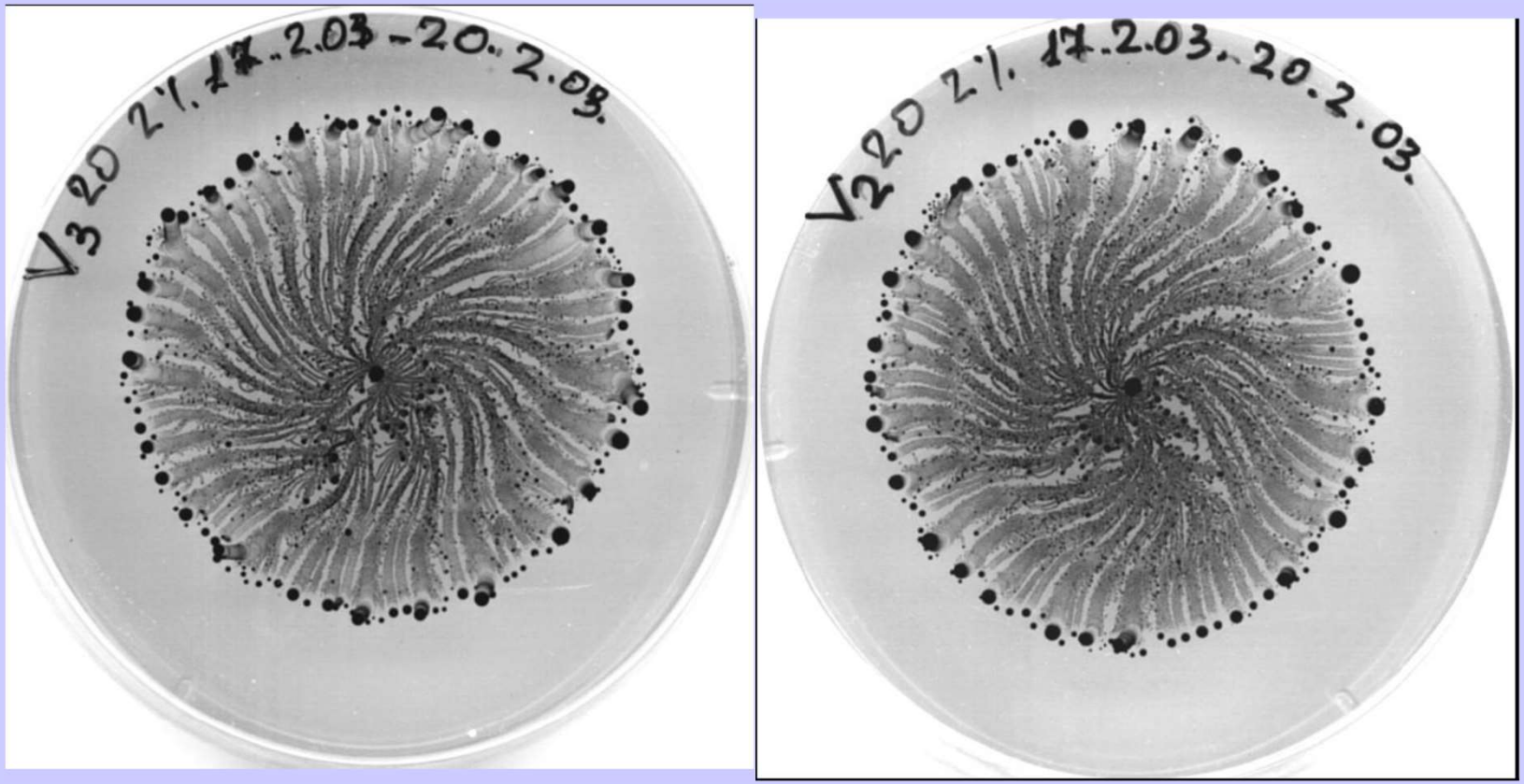


A scanning electron microscope picture. Note the versatility in the individual bacteria. It is now understood that it is not arbitrary but collectively regulated to afford the colony elevated group flexibility.

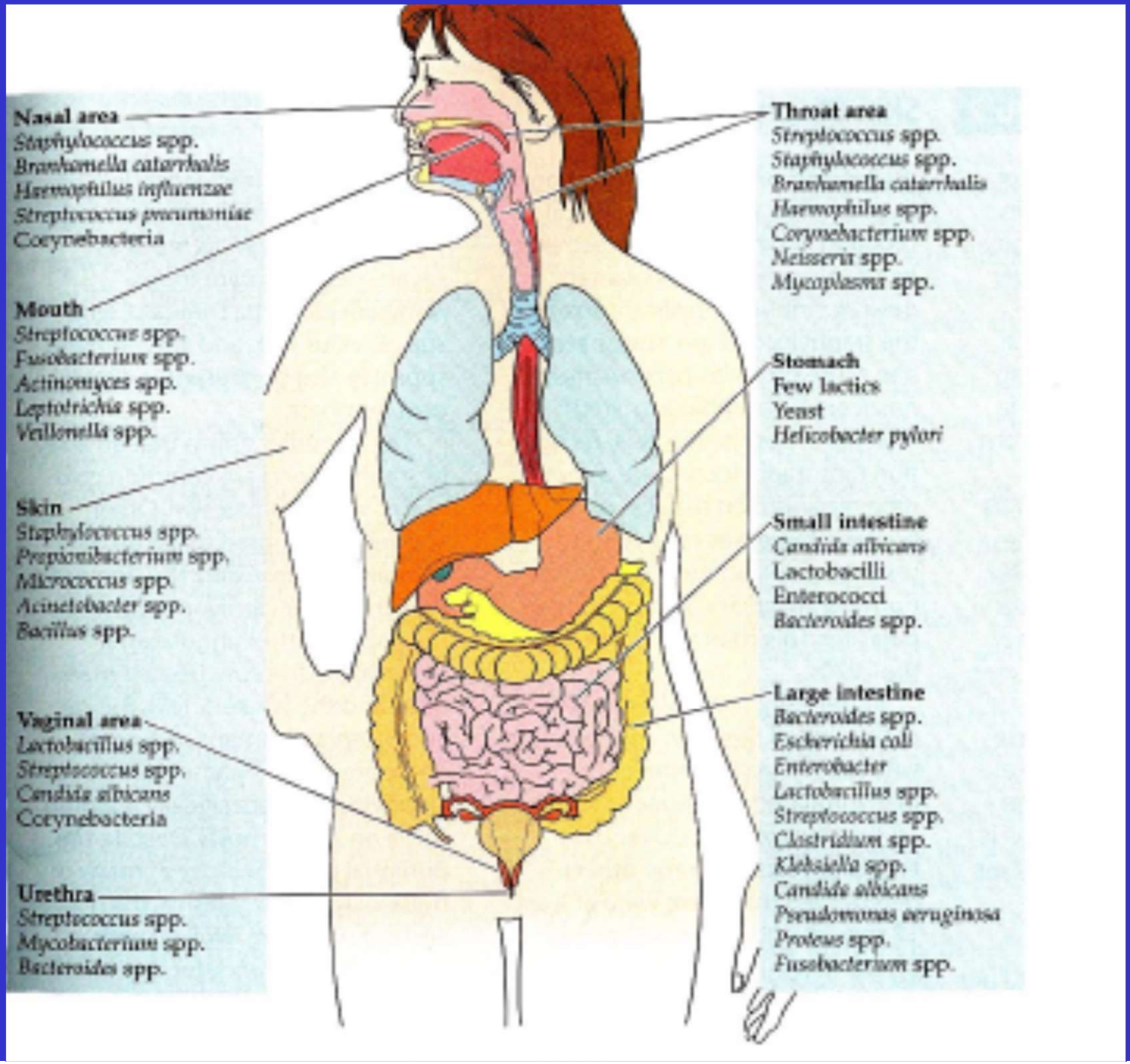


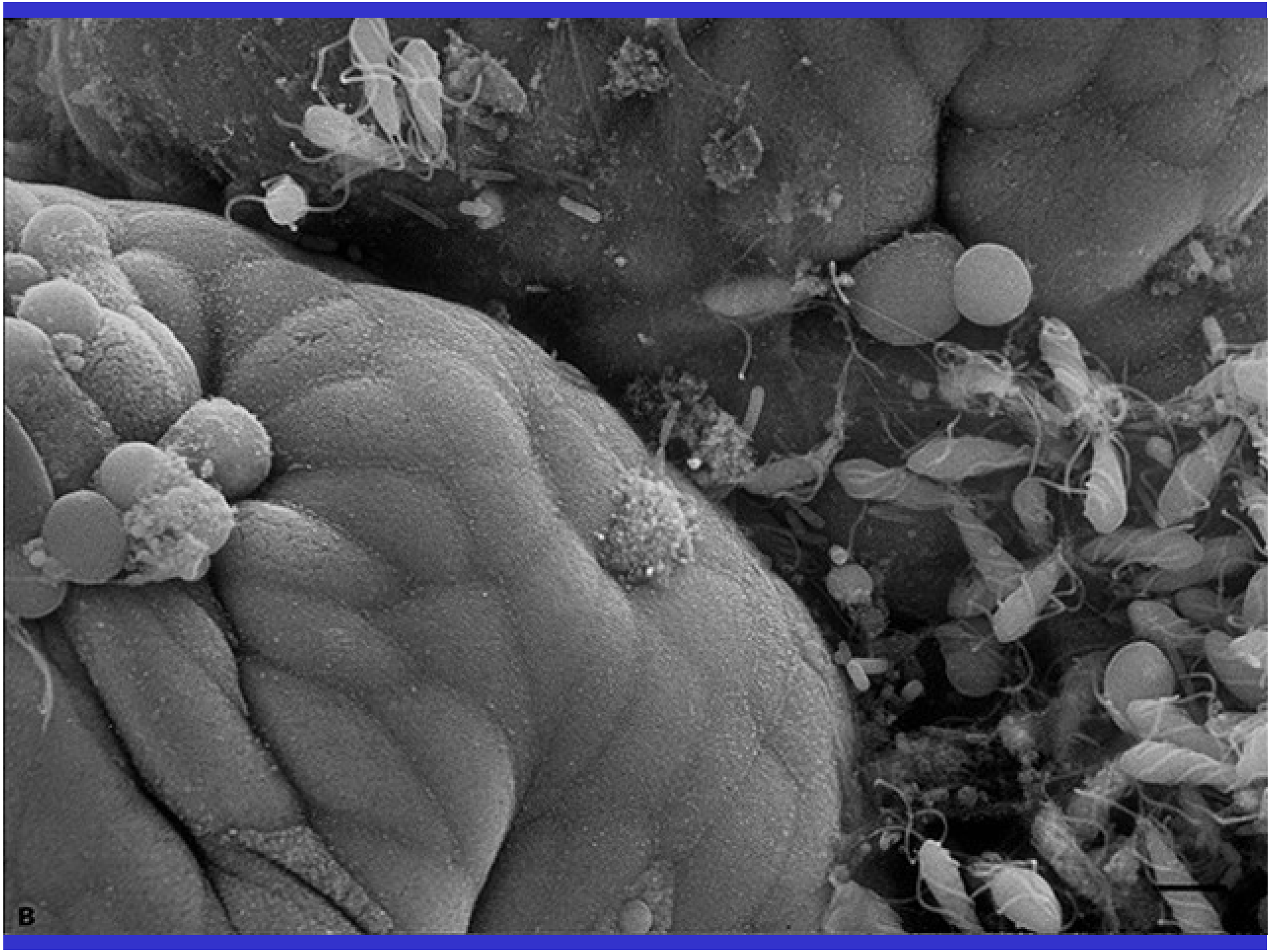
The chiral morphotype. The engineering skills of the *P. dendritiformis* bacteria are manifested during growth on softer substrates, in the formation of curly branches like in the colony shown in (a). This special geometrical organization allows faster expansion while also using patches of food left behind as the branches twist inward. To bring this about, the bacteria suppress cell division and become elongated, as observed via scanning electron microscope (b). Optical microscope observations during colony development

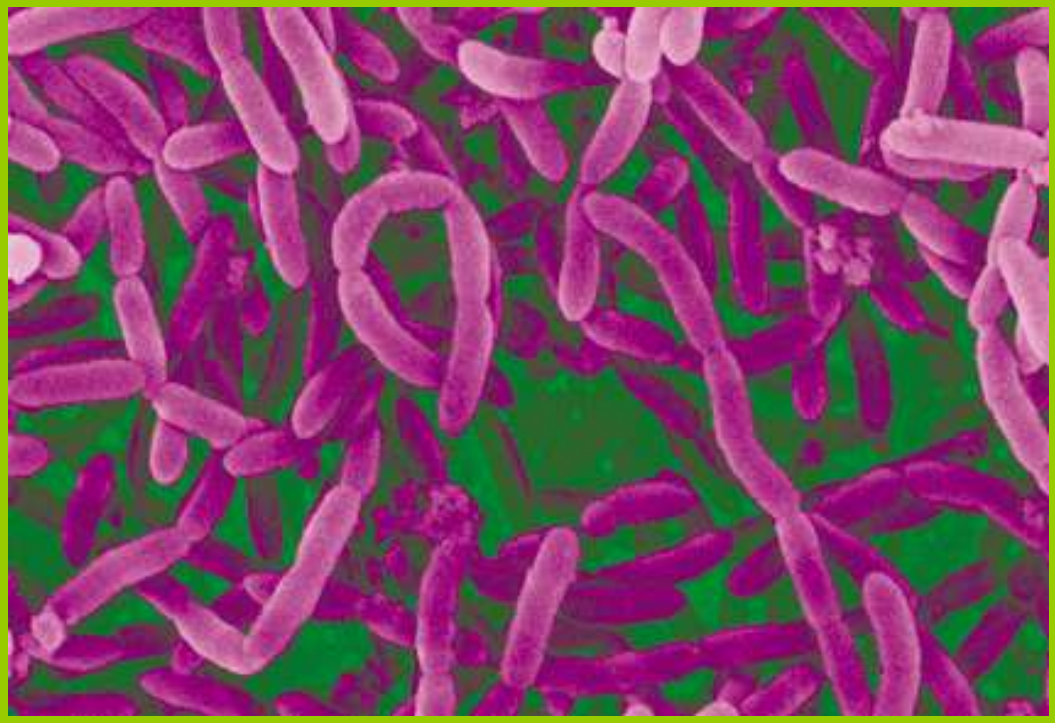
Morphotype transitions. (a) A spontaneous B -> C morphotype transition. (b) An example of a stress induced morphotype transition when a colony of branching morphotype bacteria encounters a fungi (the bright spot).



Reproducible complexity. The two pictures show two colonies started from bacteria taken from the same mother colony. It is an illustration of the level of reproducibility that can be achieved when a strict growth protocol is followed.


Nasal area
Staphylococcus spp.
Branhamella catarrhalis
Haemophilus influenzae
Streptococcus pneumoniae
Corynebacteria
Mouth
Streptococcus spp.
Fusobacterium spp.
Actinomyces spp.
Leptotrichia spp.
Veillonella spp.
Skin
Staphylococcus spp.
Propionibacterium spp.
Micrococcus spp.
Acinetobacter spp.
Bacillus spp.
Vaginal area
Lactobacillus spp.
Streptococcus spp.
Candida albicans
Corynebacteria
Urethra
Streptococcus spp.
Mycobacterium spp.
Bacteroides spp.
Throat area
Streptococcus spp.
Staphylococcus spp.
Branhamella catarrhalis
Haemophilus spp.
Corynebacterium spp.
Neisseria spp.
Mycoplasma spp.
Stomach
Few lactics
Yeast
Helicobacter pylori
Small intestine
Candida albicans
Lactobacilli
Enterococci
Bacteroides spp.
Large intestine
Bacteroides spp.
Escherichia coli
Enterobacter
Lactobacillus spp.
Streptococcus spp.
Clostridium spp.
Klebsiella spp.
Candida albicans
Pseudomonas aeruginosa
Proteus spp.
Fusobacterium spp.


B

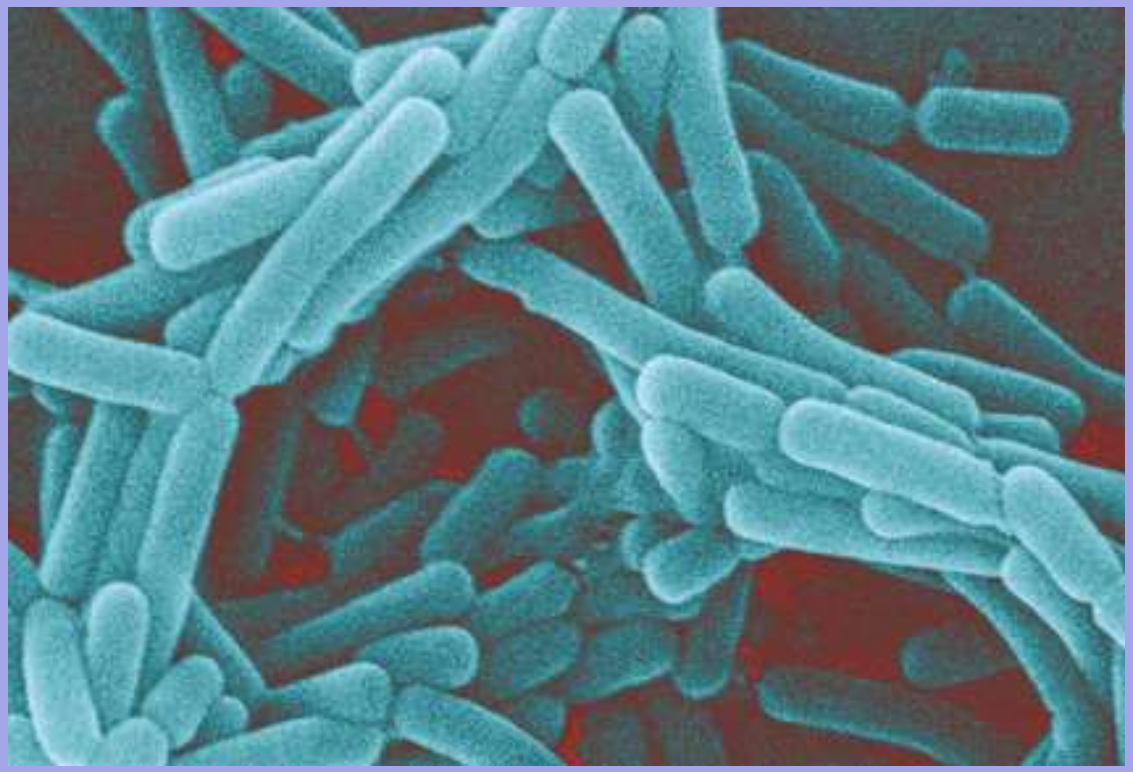


BIFIDOBACTERIUM

BACTERIAS

Son ubicuas, encontrándose en todo hábitat de la tierra, creciendo en el suelo, en manantiales calientes y ácidos, en desechos radioactivos, en las profundidades del mar y de la corteza terrestre. Algunas bacterias pueden incluso sobrevivir en las condiciones extremas del espacio exterior. Se estima que hay en torno a 40 millones de células bacterianas en un gramo de tierra y un millón de células bacterianas en un mililitro de agua dulce. En total, se calcula que hay aproximadamente 5×10e30 bacterias en el Mundo.

En el tracto digestivo proliferan unas mil especies bacterianas. Sintetizan vitaminas tales como ácido fólico, vitamina K y biotina. También fermentan los carbohidratos de complejos indigeribles y convierten las proteínas de la leche en ácido láctico (por ejemplo, *Lactobacillus*). *Streptococcus mitis* que fueron llevadas a la Luna por accidente en la Surveyor 3 en 1967, pudieron ser revividas sin dificultad cuando llegaron de vuelta a la Tierra tres años después



LACTOBACILLUS

Nature 464, 908-912 (8 April 2010) | doi:10.1038/nature08937; Received 9 November 2009; Accepted 19 February 2010

Transfer of carbohydrate-active enzymes from marine bacteria to Japanese gut microbiota

Jan-Hendrik Hehemann 1,2,3 , Gaëlle Correc 1,2 , Tristan Barbeyron 1,2 , William Helbert 1,2 , Mirjam Czjzek 1,2 & Gurvan Michel 1,2

Abstract

Gut microbes supply the human body with energy from dietary polysaccharides through carbohydrate active enzymes, or CAZymes [1], which are absent in the human genome. Here we characterize the first porphyranases from a member of the marine Bacteroidetes, Zobellia galactanivorans, active on the sulphated polysaccharide porphyran from marine red algae of the genus Porphyra. Furthermore, we show that genes coding for these porphyranases, agarases and associated proteins have been transferred to the gut bacterium Bacteroides plebeius isolated from Japanese individuals [5]. Our comparative gut metagenome analyses show that porphyranases and agarases are frequent in the Japanese population [6] and that they are absent in metagenome data [7] from North American individuals. Seaweeds make an important contribution to the daily diet in Japan (14.2 g per person per day) [8] , and Porphyra spp. (nori) is the most important nutritional seaweed, traditionally used to prepare sushi [9, 10] .

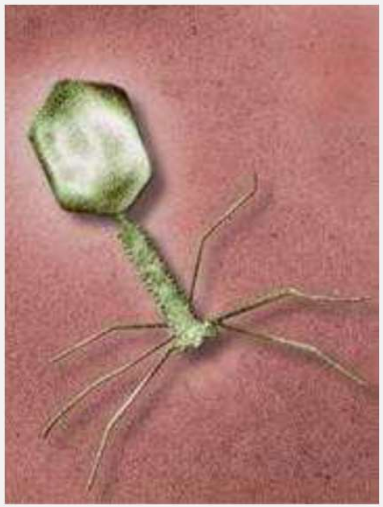
This indicates that seaweeds with associated marine bacteria may have been the route by which these novel CAZymes were acquired in human gut bacteria, and that contact with non-sterile food may be a general factor in CAZyme diversity in human gut microbes.

Science 29 May 2009:
Vol. 324. no. 5931, pp. 1136 - 1137
DOI: 10.1126/science.324_1136

Gut Reactions

Elizabeth Pennisi

The flora tended to be species-specific. Pandas from the two zoos had quite similar communities, despite the geographic separation, for example. Diet also seems to have an effect: The herbivore communities tended to be more similar to each other than to communities in carnivores, and the human microbial repertoire fell squarely in line with that of other omnivore primates. "Ruth showed that there are different signatures for different types of diets," says Bryan White, a microbiologist at the University of Illinois, Urbana-Champaign. When she built a family tree to see how the microbial communities were related, the branching pattern mirrored the family trees of the animals providing the samples. The flora of brown bears and polar bears were closely related and distantly related to that of their second cousin the dog, for example. "The ancestral bear microbial community of the gut has been passed along, and you can see it," Ley explains.



Published online 14 July 2010 | Nature | doi:10.1038/news.2010.353
News

The gut's 'friendly' viruses revealed

DNA sequencing reveals a new world of bacterial viruses in our intestines.

Amy Maxmen

In the gut, viruses that normally prey on bacteria seem to live in harmony them.*DR. HAROLD FISHER, VISUALS UNLIMITED /SCIENCE PHOTO LIBRARY*

More than 80% of the viral genetic sequences found, which included sequences characteristic of both animal and bacterial viruses, have never been reported previously. "This is a largely unexplored world," says Jeffrey Gordon at Washington University in St Louis, Missouri, and an author on the paper, which is published in *Nature* today1. "We are truly distinct lifeforms — sums of microbial and human parts."

More than 10 trillion bacteria normally inhabit the gastrointestinal tract, where they synthesize essential amino acids and vitamins, produce anti-inflammatory factors and help break down starches, sugars and proteins that people could not otherwise digest. Within and among these bacteria live bacterial viruses, or bacteriophages, which affect bacterial numbers and behaviour as they either prey on bacteria or coexist with them, shuttling genes from one bacterium to another.

This microscopic dynamic ecosystem affects our lives in ways we still do not fully understand. Indeed, the rise in the incidence of food allergies in Western societies has led to hypotheses that extreme hygiene disrupts the ability of microbes to colonize human guts, resulting in a lack of tolerance to usually harmless foods.

"This is a wonderful study," says David Relman, a microbiologist at Stanford University in California, who is involved with the US National Institute of Health's Human Microbiome Project. "It could be that viruses are the real drivers of the system because of their ability to modify the bacteria that then modify the human host," he says. "So this study is in some ways looking into the genesis of the human body by seeing what viruses within it are up to."

Science 29 May 2009:
Vol. 324. no. 5931, pp. 1190 - 1192
DOI: 10.1126/science.1171700

Topographical and Temporal Diversity of the Human Skin Microbiome

Elizabeth A. Grice,[1] Heidi H. Kong,[2] Sean Conlan,[1] Clayton B. Deming,[1] Joie Davis,[3] Alice C. Young,[4] NISC Comparative Sequencing Program,[4,] Gerard G. Bouffard,[4,5] Robert W. Blakesley,[4,5] Patrick R. Murray,[6] Eric D. Green,[4,5] Maria L. Turner,[2] Julia A. Segre[1,]

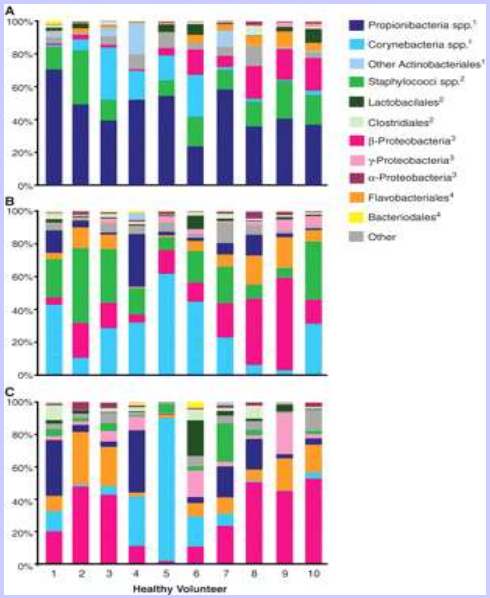


Fig. 1 The 20 skin sites and associated microbiota are representative of three microenvironments: (**A**) sebaceous, (**B**) moist, and (**C**) dry. The relative abundance of the most abundant bacterial groups associated with each microenvironment is depicted for each healthy volunteer. Superscripts indicate phylum: 1, Actinobacteria; 2, Firmicutes; 3, Proteobacteria; 4, Bacteroidetes.

Human skin is a large, heterogeneous organ that protects the body from pathogens while sustaining microorganisms that influence human health and disease. Our analysis of 16*S* ribosomal RNA gene sequences obtained from 20 distinct skin sites of healthy humans revealed that physiologically comparable sites harbor similar bacterial communities. The complexity and stability of the microbial community are dependent on the specific characteristics of the skin site. This topographical and temporal survey provides a baseline for studies that examine the role of bacterial communities in disease states and the microbial interdependencies required to maintain healthy skin.

PNAS | **August 8, 2006** | vol. 103 | no. 32 | **12115-12120**
OPEN ACCESS ARTICLE

BIOLOGICAL SCIENCES / MICROBIOLOGY

Microbial diversity in the deep sea and the underexplored "rare biosphere"

Mitchell L. Sogin[*], Hilary G. Morrison[*], Julie A. Huber[*], David Mark Welch[*], Susan M. Huse[*], Phillip R. Neal[*], Jesus M. Arrieta, and Gerhard J. Herndl

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Nature
Published online: 25 January 2006; | doi:10.1038/439384a

Genomics: Discovery in the dirt

Soil microbes are notoriously hard to culture, so how can we make the ground yield its secrets? Virginia Gewin finds that genetic sequencing — of samples not species — may be the answer.

Virginia Gewin

Leonardo da Vinci once remarked that "We know more about the movement of celestial bodies than about the soil underfoot." You could argue that his insight still holds true the best part of 500 years later. But new genomic technologies mean that the microscopic bodies that enliven soil may be about to get the attention they deserve — if not as individuals, then as communities.

Twice as much carbon is stored in Earth's soil as exists in the plants that grow from it and the animals that depend on them. It is the soil's microbes that are responsible for recycling this carbon, and other nutrients. Living in the fractal jumble of weathered rock, mineral particles and decaying organic matter are a cast of thousands, some say millions, of species. These soil organisms occupy an endless foam of tiny niches; they purify water, detoxify harmful substances and recycle waste products. They restore carbon dioxide to the air and make the atmosphere's nitrogen available to plants. Without them, continents would be deserts — home to little more than lichen, and not much of that.

TheScientist
MAGAZINE OF THE LIFE SCIENCES

6 comments

Comment on this news story

By Vanessa Schipani

Atlas of the atmosphere

The air is teeming with microbes, and scientists are finally starting to understand how they influence everything from meteorology to epidemiology

[Published 1st December 2010 03:21 PM GMT]

Every cubic meter of air holds up to 100 million microorganisms, but the diversity and behavior of these microbes remains masked to microbiologists — until recently, that is.

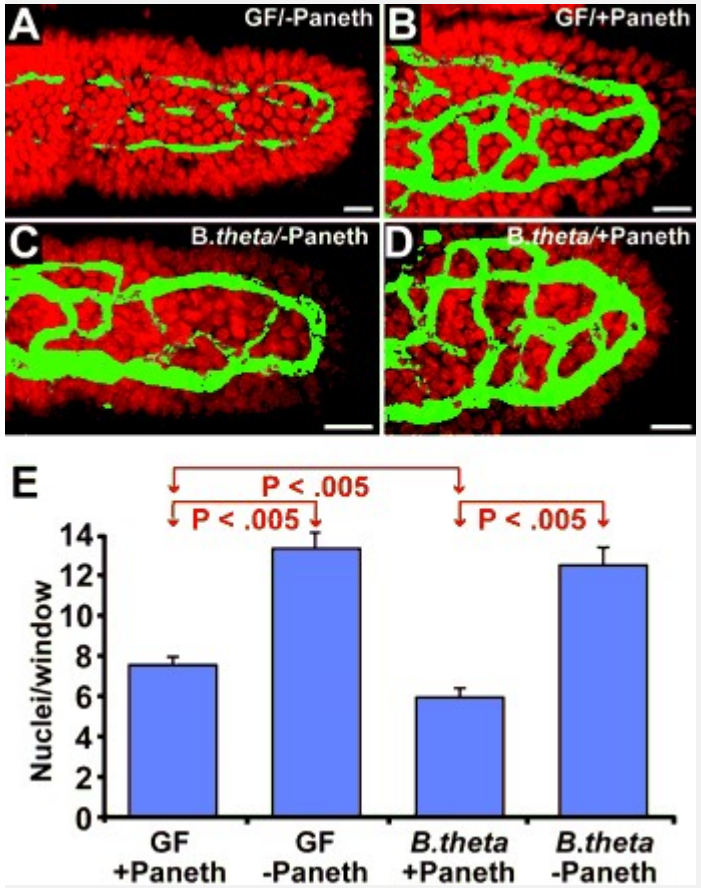
Thanks to next-generation sequencing techniques, scientists are finally uncovering the details of the biodiversity and biogeography

The News

- The rhythm of biology
- XMRV doesn't cause chronic fatigue
- Arsenic-based life debate continues
- What lab mice are made of
- News in a nutshell
- Deep-Earth devil worms
- Pick your frog poison
- Top 7 in microbiology
- How influenza drives asthma
- Monkey mind control
- Controlling chaos
- News in a nutshell
- An autism brain signature?
- Top 7 in genetics and genomics
- Flies alter lice evolution
- More Entries...

"Just seven or ten years ago we didn't realize bacteria existed in clouds," said Anne-Marie Delort, professor of microbiology and organic chemistry at Université Blaise Pascal in France. Now researchers know microbes act as a surface for the condensation of water vapor in the atmosphere, thus forming clouds. Recent research publish in *Science* shows microbes also play the same role during snowflake formation and other types of precipitation. The next step, Delort said, is to uncover their metabolic activity in clouds and influence on atmospheric processes. If they are metabolically active, she added, microbes could not only be acting as cloud condensers, but affecting the carbon and nitrogen cycles as well.

PNAS | **November 26, 2002** | vol. 99 | no. 24 | **15451-15455**

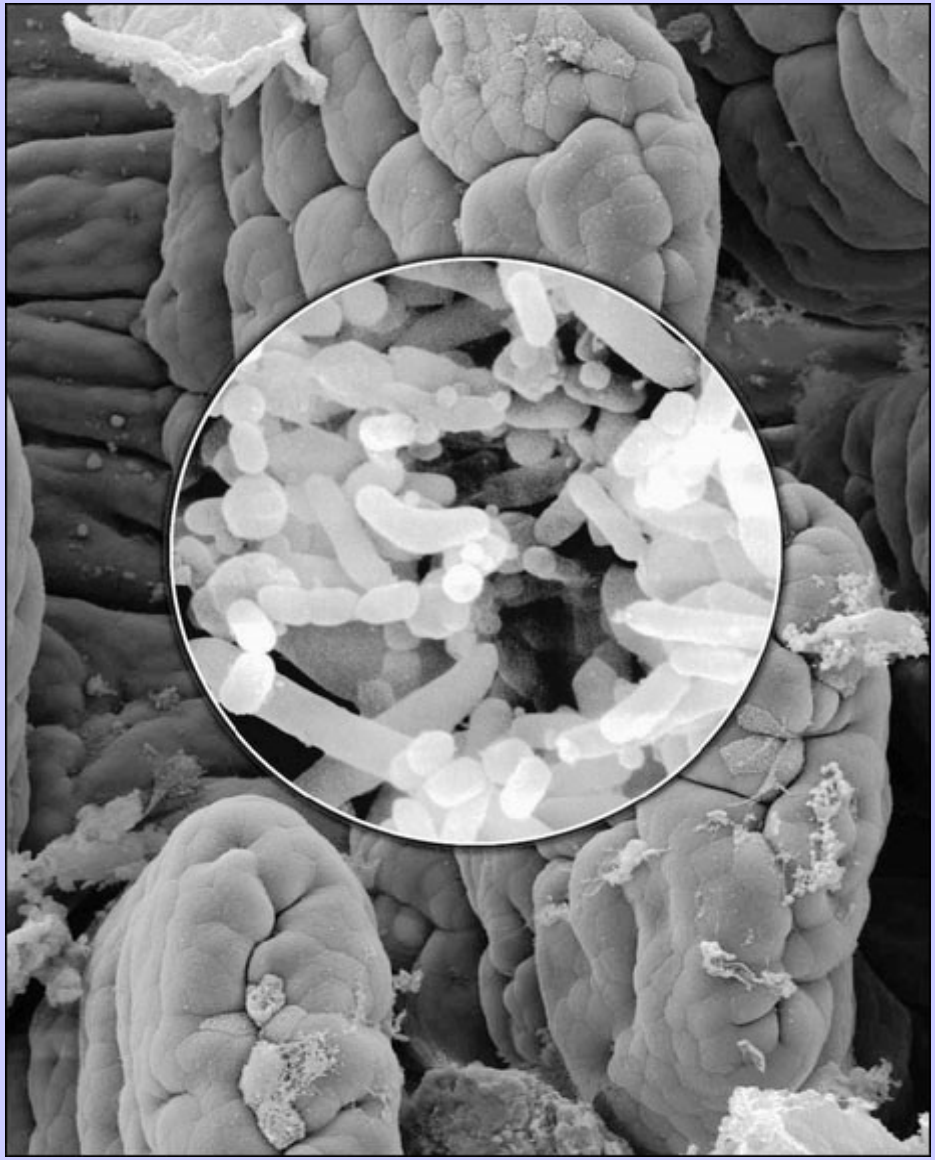


Developmental Biology

Developmental regulation of intestinal angiogenesis by indigenous microbes via Paneth cells

Thaddeus S. Stappenbeck, Lora V. Hooper, and Jeffrey I. Gordon *
Department of Molecular Biology and Pharmacology, Washington University School of Medicine, St. Louis, MO 63110
Contributed by Jeffrey I. Gordon and approved October 7, 2002

The adult mouse intestine contains an intricate vascular network. The factors that control development of this network are poorly understood. Quantitative three-dimensional imaging studies revealed that a plexus of branched interconnected vessels developed in small intestinal villi during the period of postnatal development that coincides with assembly of a complex society of indigenous gut microorganisms .



Scanning electron microscope images of *B. thetaiotaomicron*, a prominent human gut bacterium, and the intestine.

MACHOS TRANSFORMADOS EN HEMBRAS

Primer proceso

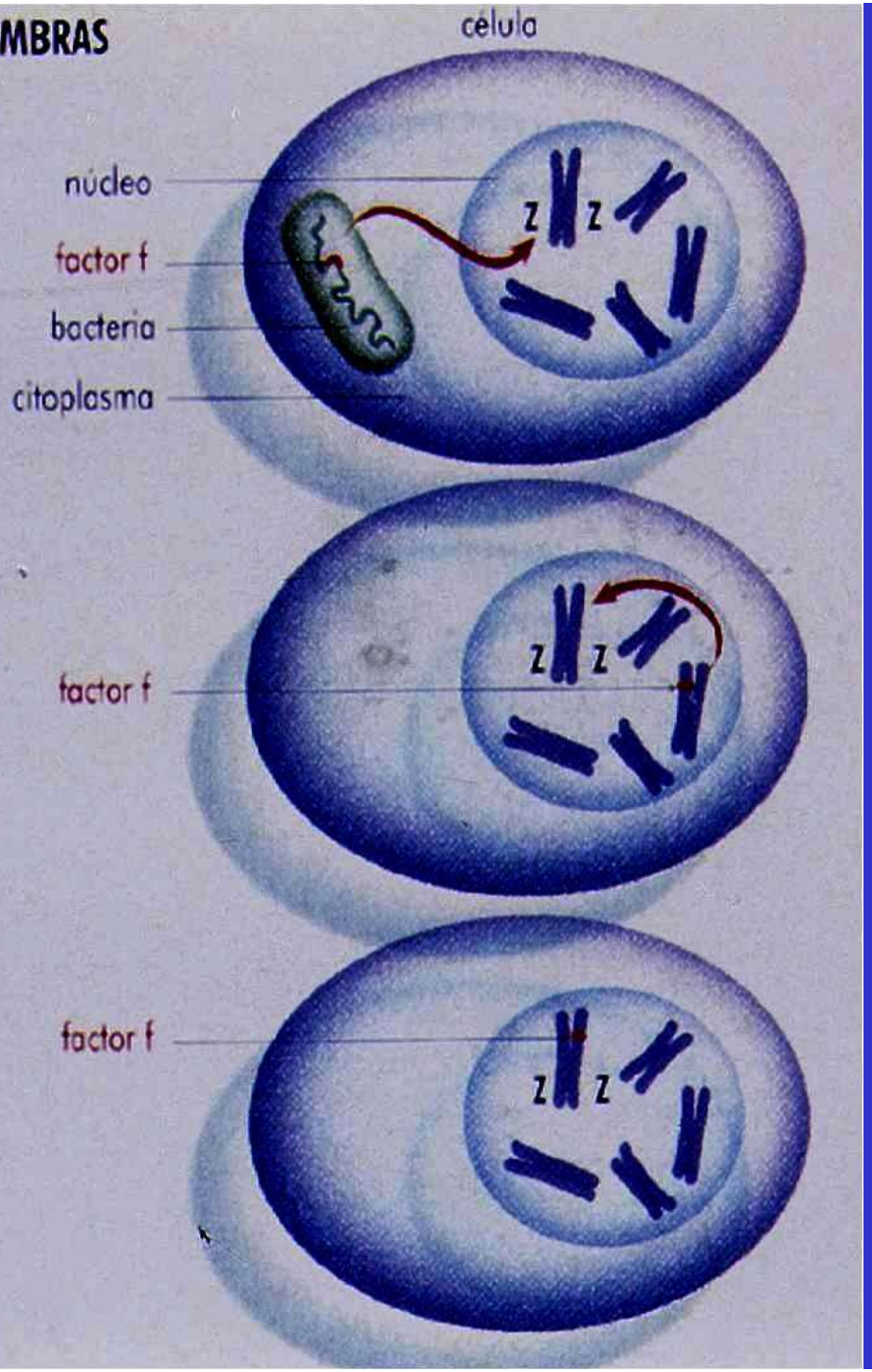
La bacteria está en el citoplasma. El factor f presente en su genoma inhibe el funcionamiento de los cromosomas masculinos ZZ.

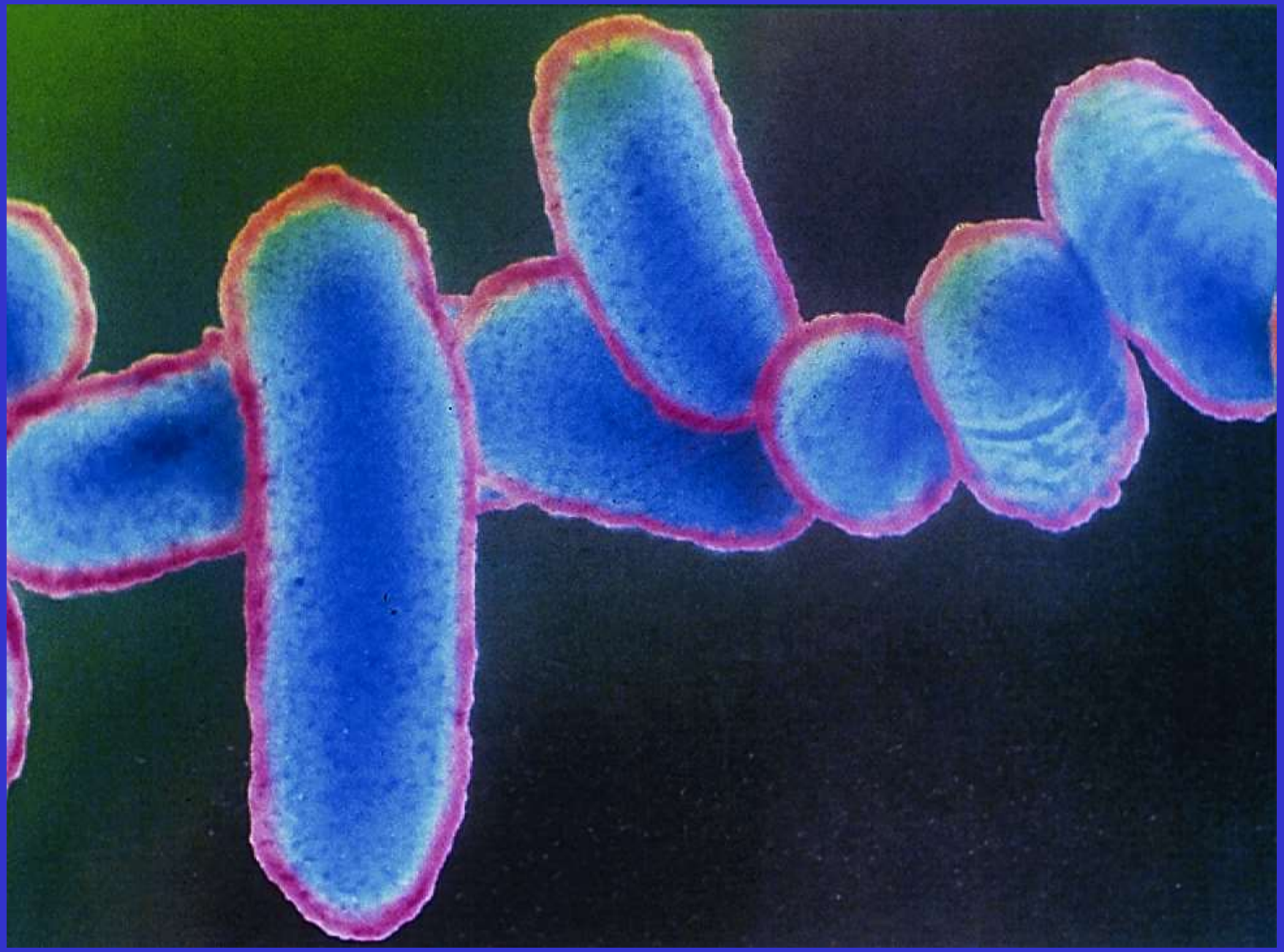
Segundo proceso

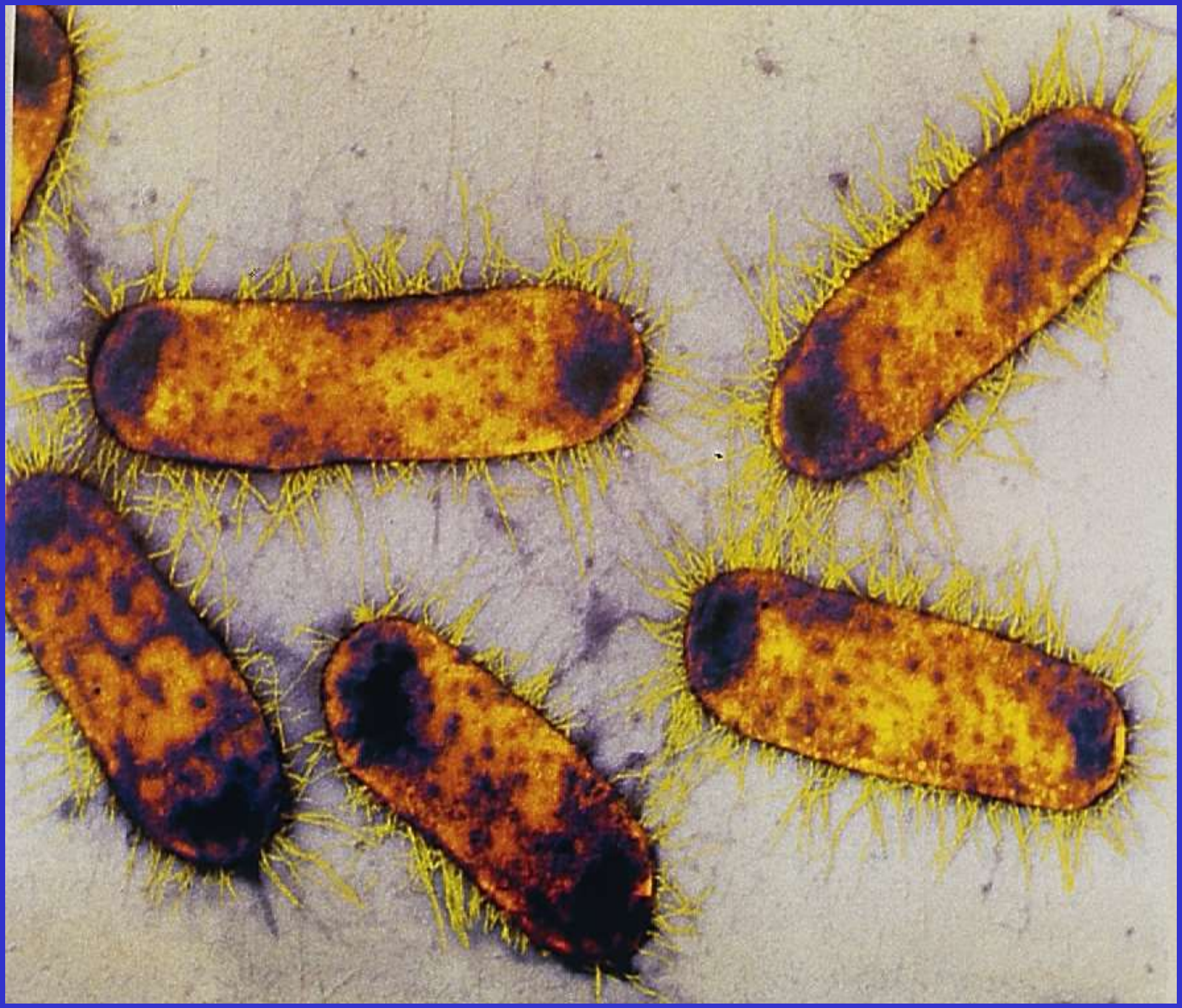
La bacteria ya no está en el citoplasma, pero el factor f ha penetrado en el núcleo. Convertido en «gen saltador» (transposón), inhibe el funcionamiento de los cromosomas masculinos ZZ desde el genoma mismo de la cochinilla.

Tercer proceso

El factor f se ha integrado definitivamente en uno de los cromosomas sexuales masculinos, transformándolo en cromosoma femenino.





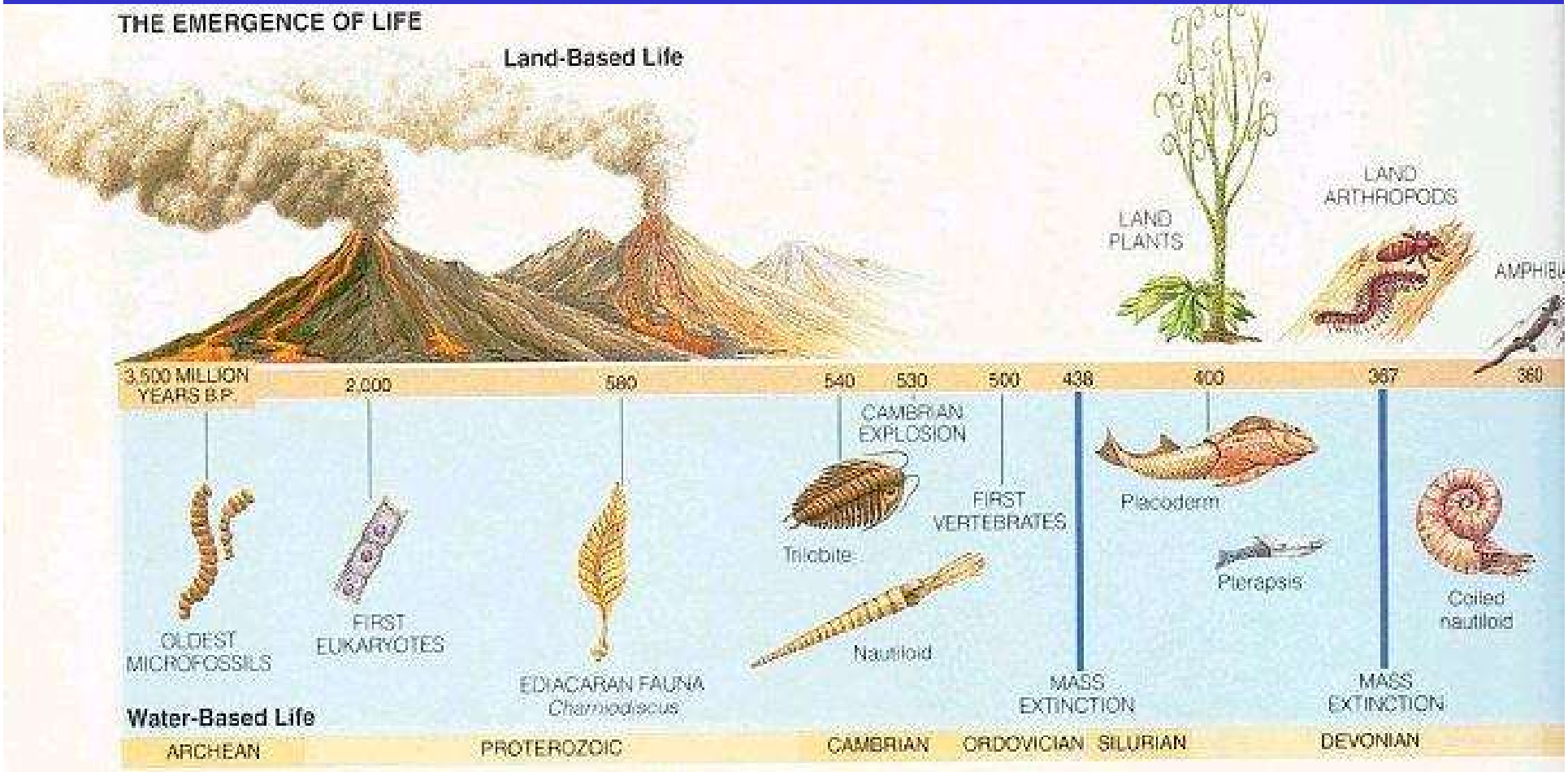


BIOLOGICAL SCIENCES / MICROBIOLOGY

How to become a uropathogen: Comparative genomic analysis of extraintestinal pathogenic *Escherichia coli* strains

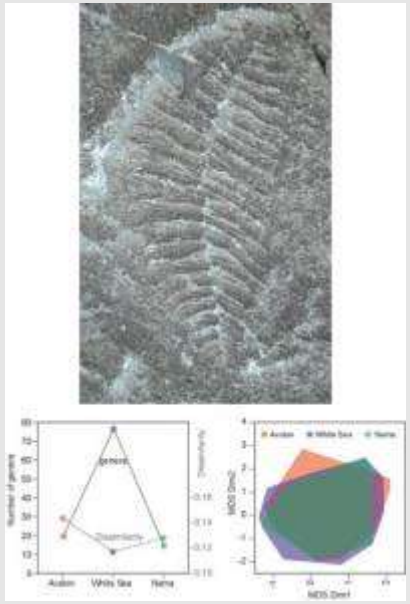
Elzbieta Brzuszkiewicz*„ Holger Brüggemann*„ Heiko Liesegang*, Melanie Emmerth, Tobias Ölschläger, Gábor Nagy, Kaj Albermann¶, Christian Wagner¶, Carmen Buchrieser, Levente Emdy, Gerhard Gottschalk*, Jörg Hacker, and Ulrich Dobrindt,||

Uropathogenic *Escherichia coli* (UPEC) strain 536 (O6:K15:H31) is one of the model organisms of extraintestinal pathogenic *E. coli* (ExPEC). To analyze this strain's genetic basis of urovirulence, we sequenced the entire genome and compared the data with the genome sequence of UPEC strain CFT073 (O6:K2:H1) and to the available genomes of nonpathogenic *E. coli* strain MG1655 (K-12) and enterohemorrhagic *E. coli*. The genome of strain 536 is 292 kb smaller than that of strain CFT073. Genomic differences between both UPEC are mainly restricted to large pathogenicity islands, parts of which are unique to strain 536 or CFT073. Genome comparison underlines that repeated insertions and deletions in certain parts of the genome contribute to genome evolution.

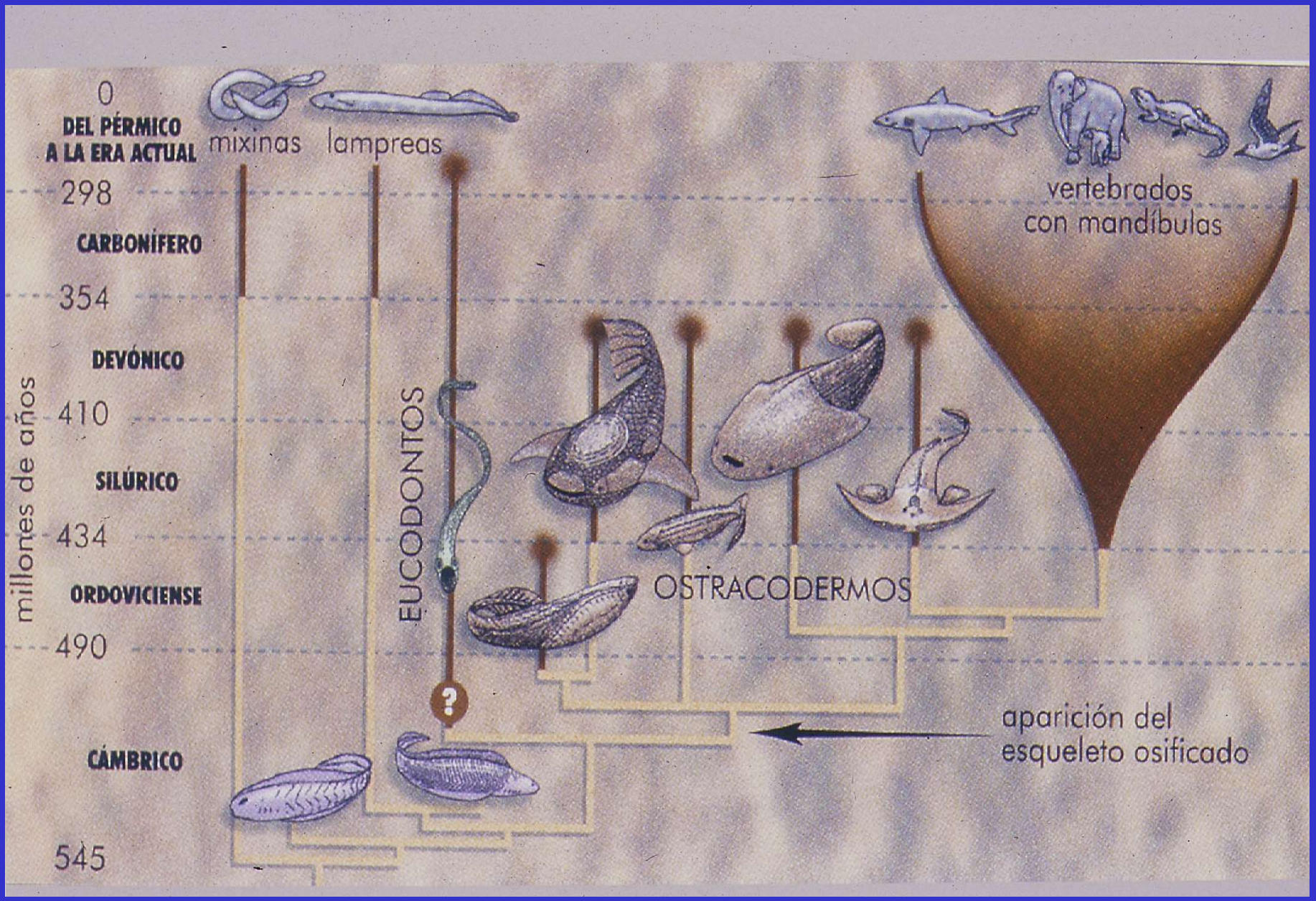

THE EMERGENCE OF LIFE
Land-Based Life
LAND PLANTS
LAND ARTHROPODS
AMPHIBI
3,500 MILLION YEARS B.P.
2,000
580
540
530
500
438
400
367
360
CAMBRIAN EXPLOSION
OLDEST MICROFOSSILS
FIRST EUKARYOTES
EDIACARAN FAUNA
Charnodiscus
Trilobite
FIRST VERTEBRATES
Nautiloid
Placoderm
Pterapsis
Coiled nautiloid
MASS EXTINCTION
MASS EXTINCTION
Water-Based Life
ARCHEAN
PROTEROZOIC
CAMBRIAN
ORDOVICIAN
SILURIAN
DEVONIAN

Explosión de Vida Anterior a la del Cámbrico

11 de Febrero de 2008.



Los científicos saben desde hace algún tiempo que la mayoría de los principales grupos de animales complejos entraron por vez primera en el registro fósil durante la Explosión Cámbrica, un evento evolutivo aparentemente rápido que ocurrió hace 542 millones de años. Ahora paleontólogos del Instituto Tecnológico de Virginia, utilizando rigurosos métodos analíticos, han identificado otro evento evolutivo explosivo que se produjo aproximadamente 33 millones de años antes en formas macroscópicas de vida no relacionadas con los animales del Cámbrico. A este evento anterior se le ha llamado la "Explosión de Avalon".


0
DEL PÉRMICO A LA ERA ACTUAL
298
CARBONÍFERO
354
DEVÓNICO
410
SILÚRICO
434
ORDOVICIENSE
490
CÁMBRICO
545
millones de años
mixinas
lampreas
EUCODONTOS
?
OSTRACODERMOS
vertebrados con mandíbulas
aparición del esqueleto osificado

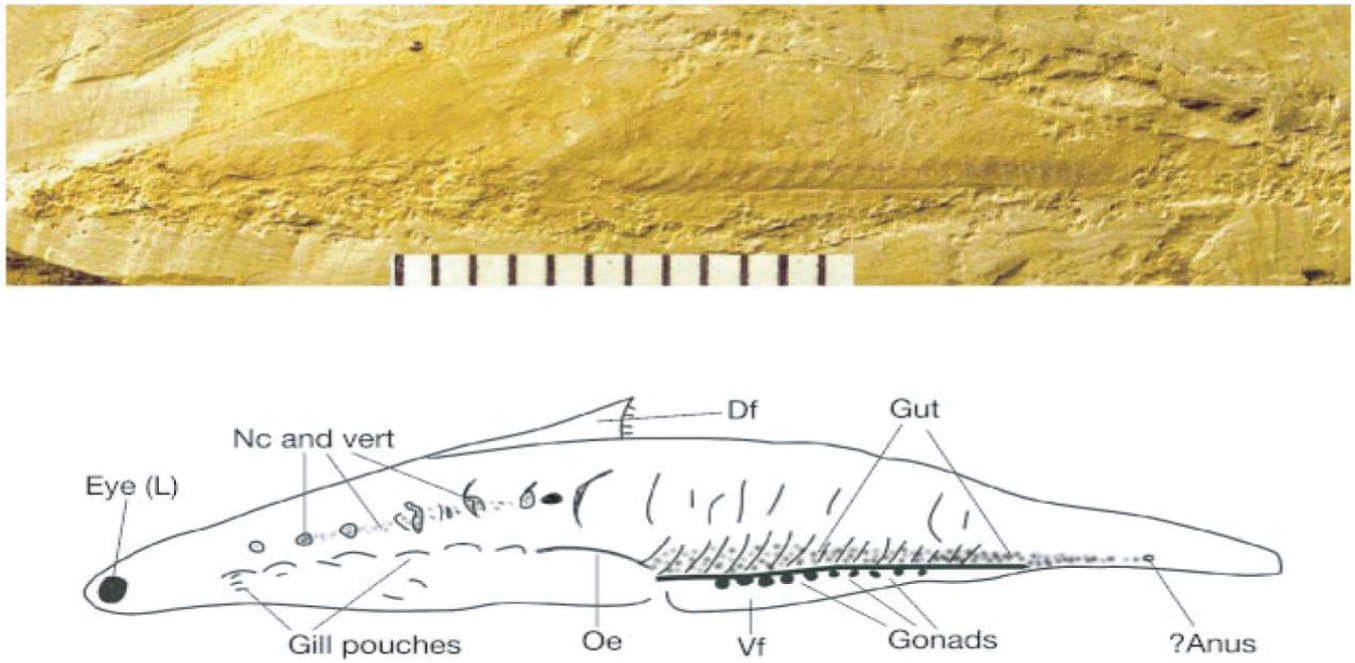
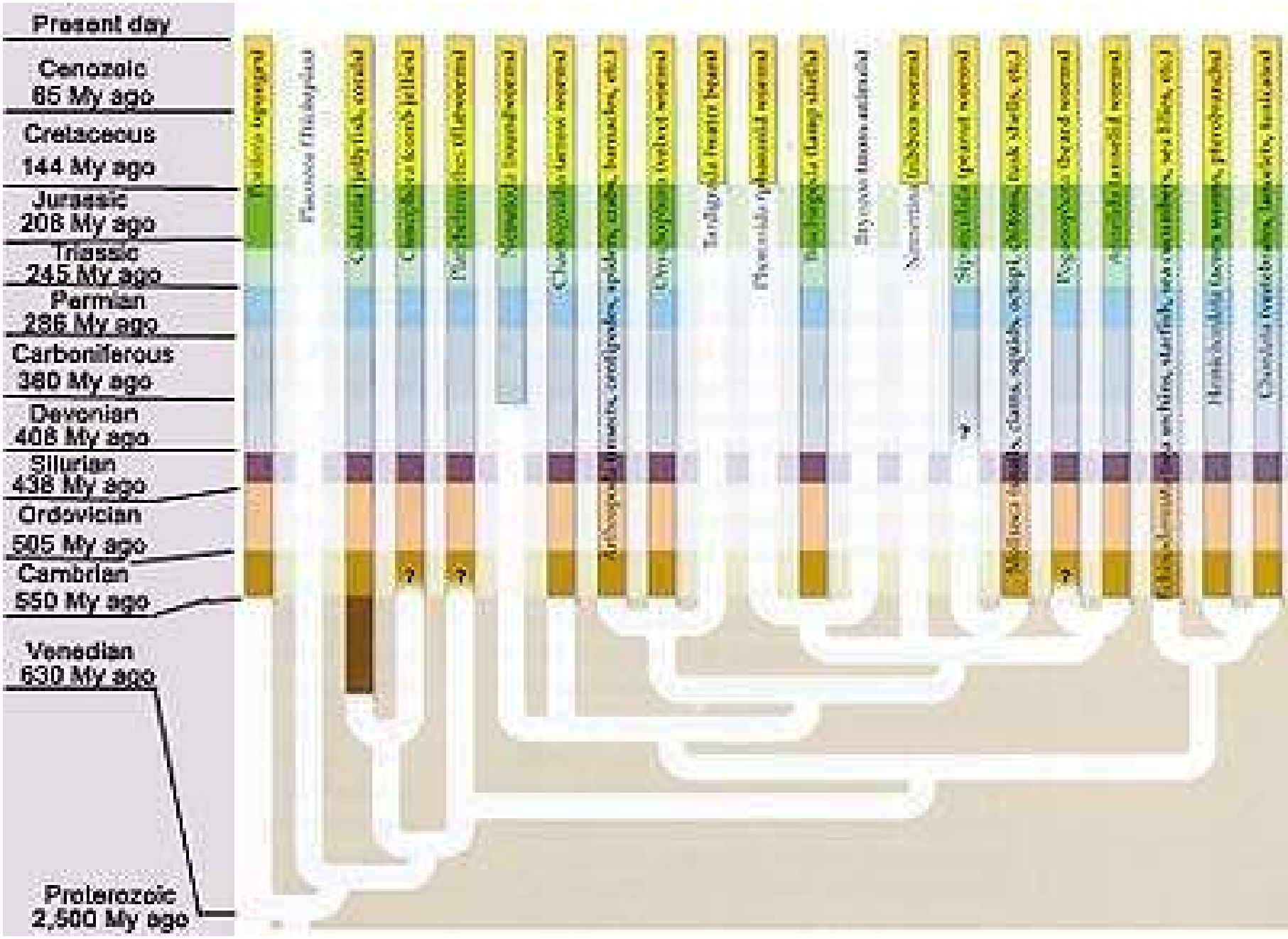
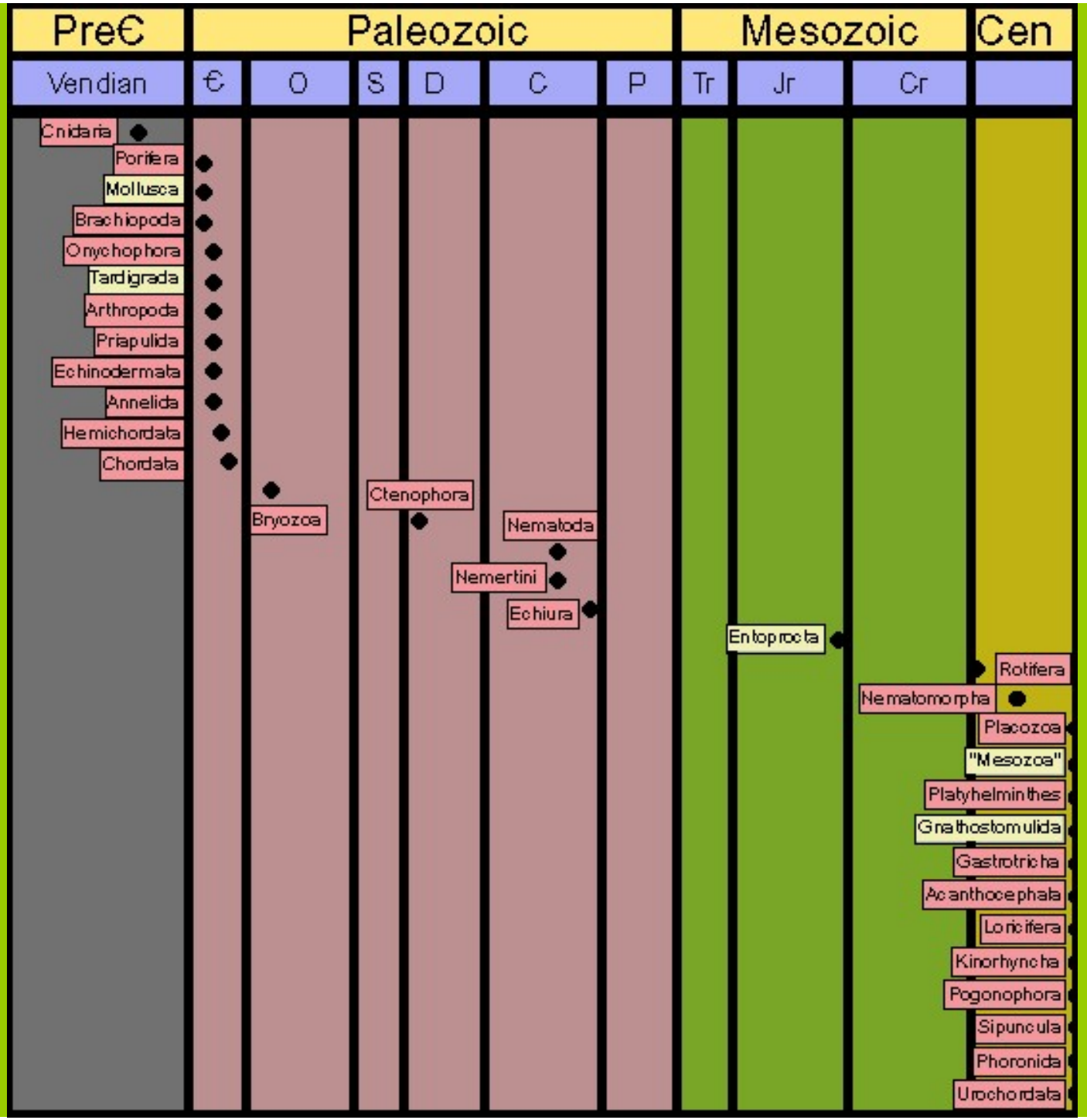


FIGURE 10.18. Early Cambrian jawless fish *Haikouichthys ercaicunensis* from Haikou, Kunming, Yunnan in southern China. The anterior end is to the *left*. This organism has a small lobate extension to the head including eyes, possible nasal sacs, and otic capsules, and a notochord with separate vertebral elements. These features indicate well-advanced vertebrate evolution by the Early Cambrian. Nc and vert, notochord with vertebral elements; Df, dorsal fin; Oe, esophagus; Vf, ventral fin fold. The divisions in the scale are mm.

10.18, reprinted from Shu D.G. et al., *Nature* **421:** 526–529, © 2003 Macmillan, www.nature.com


Present day
Cenozoic
65 My ago
Cretaceous
144 My ago
Jurassic
208 My ago
Triassic
245 My ago
Permian
286 My ago
Carboniferous
360 My ago
Devonian
408 My ago
Silurian
438 My ago
Ordovician
505 My ago
Cambrian
550 My ago
Venedian
630 My ago
Proterozoic
2,500 My ago


PreЄ
Paleozoic
Mesozoic
Cen
Vendian
Є
O
S
D
C
P
Tr
Jr
Cr
Cnidaria
Porifera
Mollusca
Brachiopoda
Onychophora
Tardigrada
Arthropoda
Priapulida
Echinodermata
Annelida
Hemichordata
Chordata
Bryozoa
Ctenophora
Nematoda
Nemertini
Echiura
Entoprocta
Rotifera
Nematomorpha
Placozoa
"Mesozoa"
Platyhelminthes
Gnathostomulida
Gastrotricha
Acanthocephala
Loricifera
Kinorhyncha
Pogonophora
Sipuncula
Phoronida
Urochordata

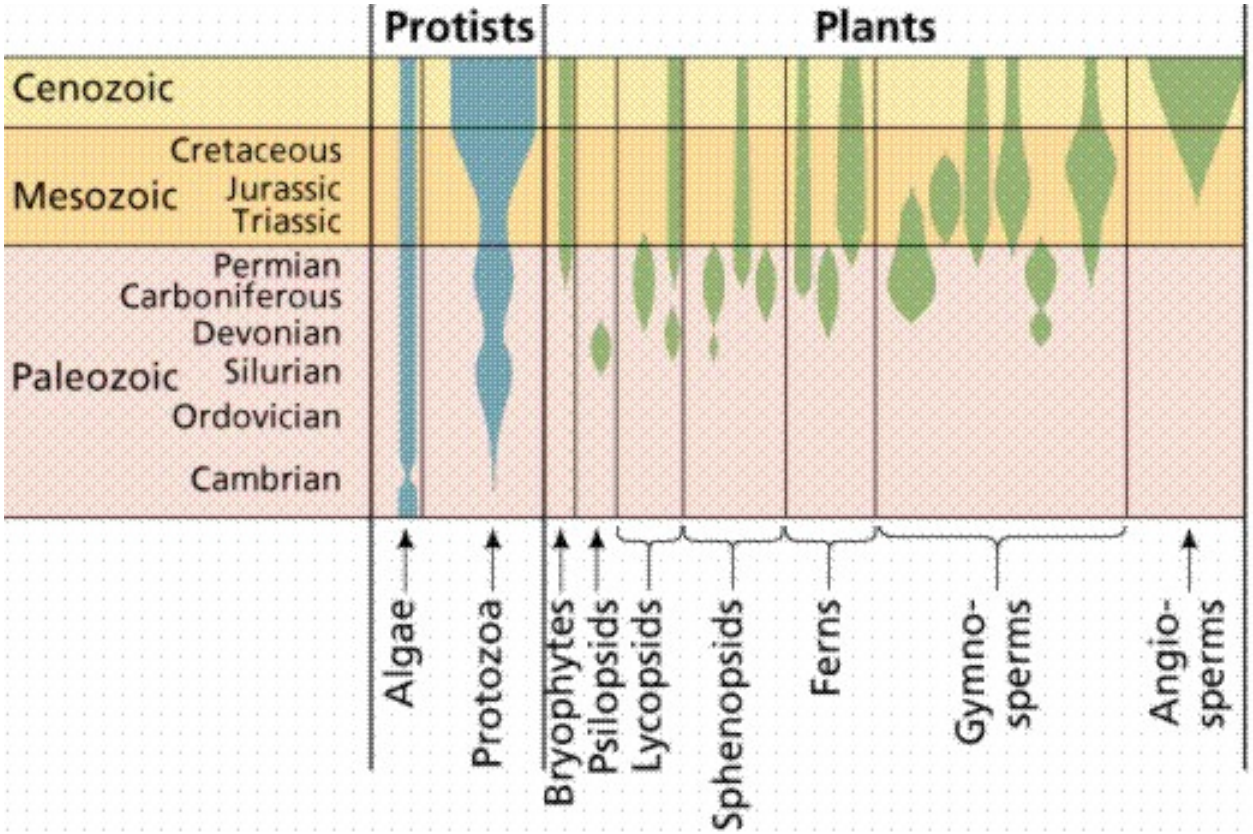
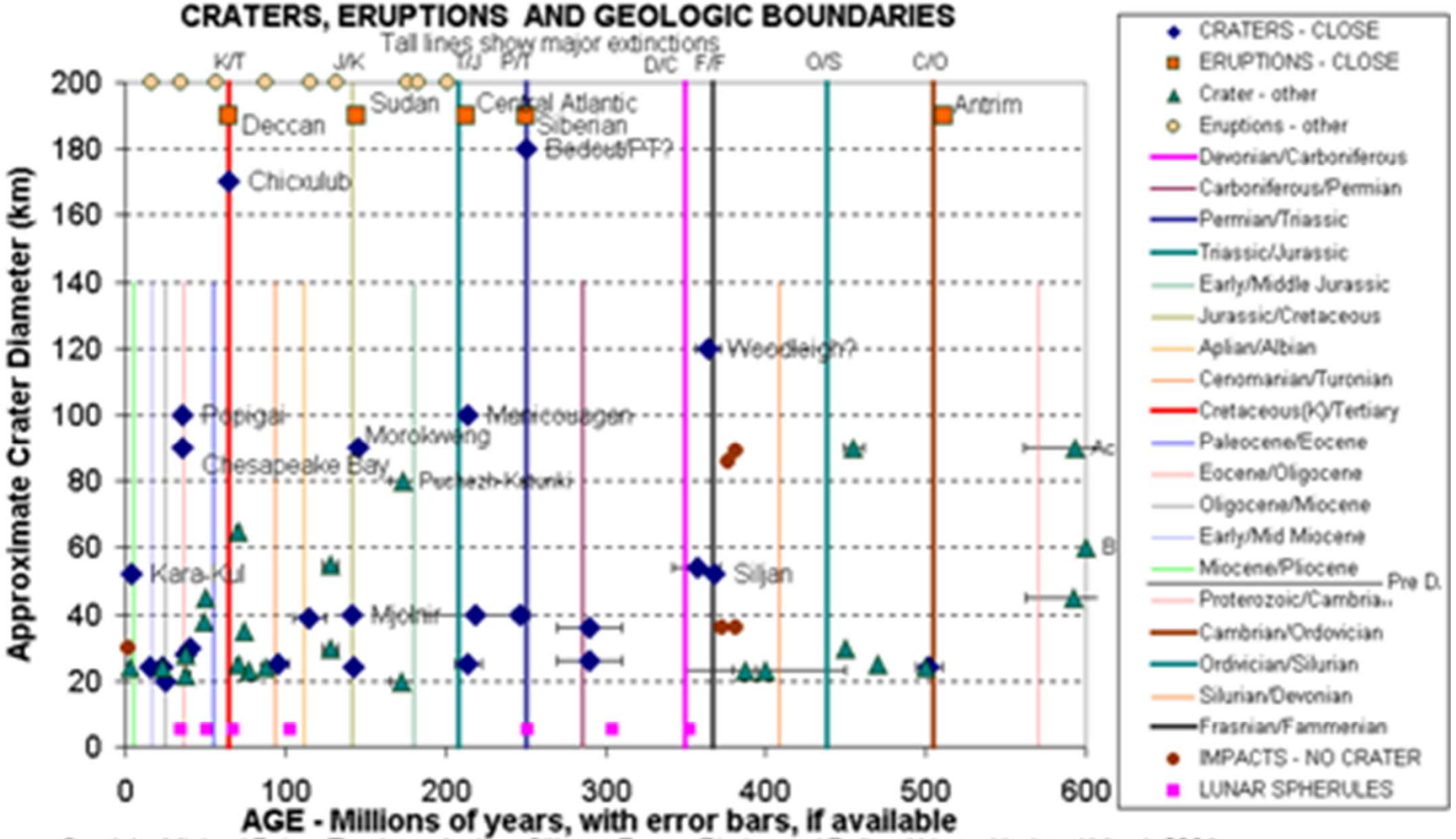

Protists
Plants
Cenozoic
Mesozoic
Cretaceous
Jurassic
Triassic
Paleozoic
Permian
Carboniferous
Devonian
Silurian
Ordovician
Cambrian
Algae
Protozoa
Bryophytes
Psilopsids
Lycopsids
Sphenopsids
Ferns
Gymno-
sperms
Angio-
sperms

Table 25.1 Mass extinctions and other major extinction events[a]

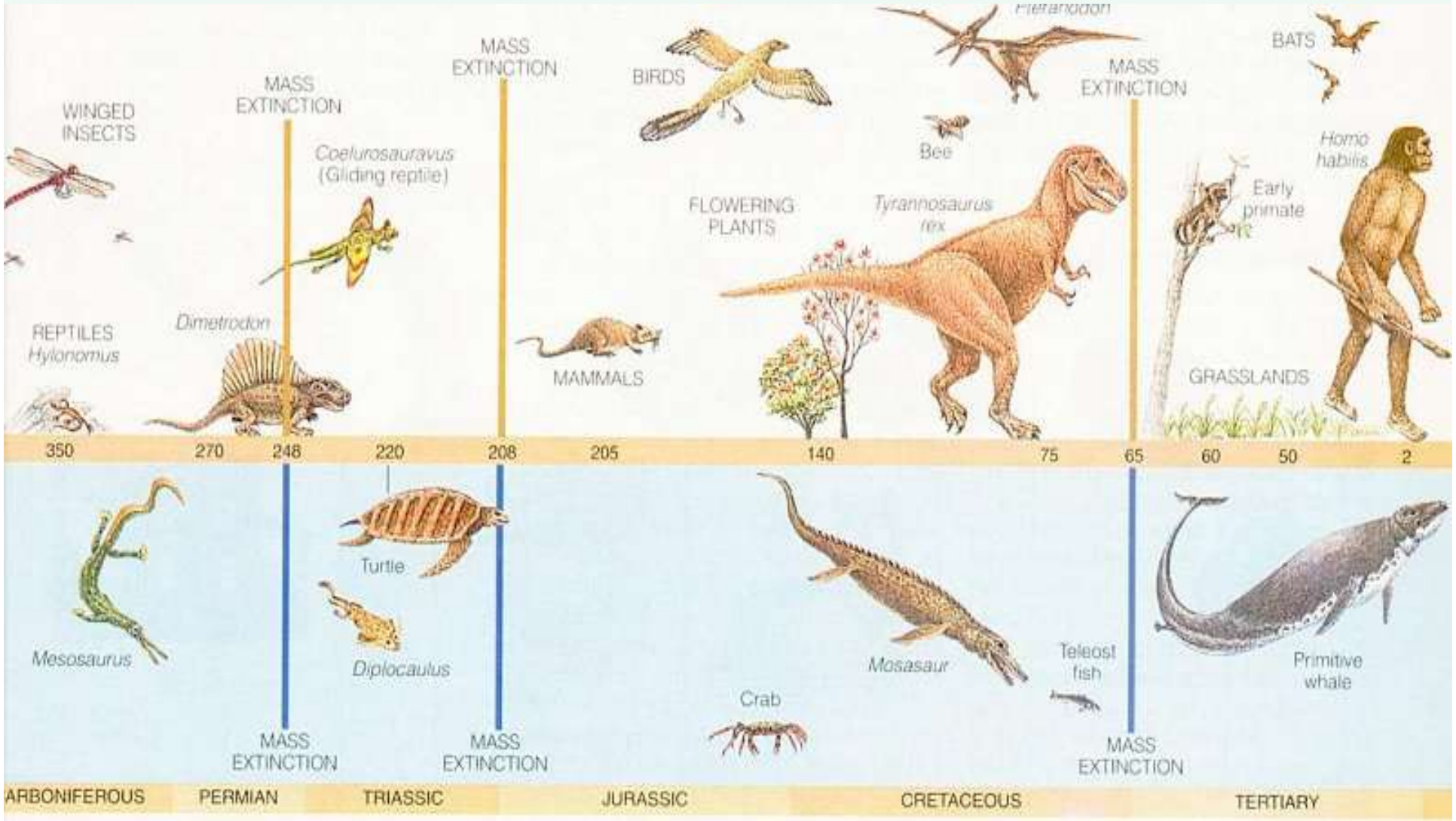
EXTINCTION EVENT	AGE ($\times 10^6$ YEARS)	FAMILIES (%)[a]	GENERA (%)[a]	SPECIES (%)[a]
Late Eocene	35.4	—	15	35 ± 8
End-Cretaceous	65.0	16	47	76 ± 5
Early Late Cretaceous (Cenomanian)	90.4	—	26	53 ± 7
End-Jurassic	145.6	—	21	45 ± 7.5
Early Jurassic (Pliensbachian)	187.0	—	26	53 ± 7
End-Triassic	208.0	22	53	80 ± 4
End-Permian	245.0	51	82	95 ± 2
Late Devonian	367.0	22	57	83 ± 4
End-Ordovician	439.0	26	60	85 ± 3

Source: After Jablonski (1991, 1995).

[a]Percentages of families, genera, and species of skeletonized marine invertebrates that became extinct during the five major mass extinctions (uppercase) and several lesser extinction events (lowercase) during the Phanerozoic. Values for genera were calculated directly from fossil data; those for species are estimated from statistical analyses of the numbers of species per genus.

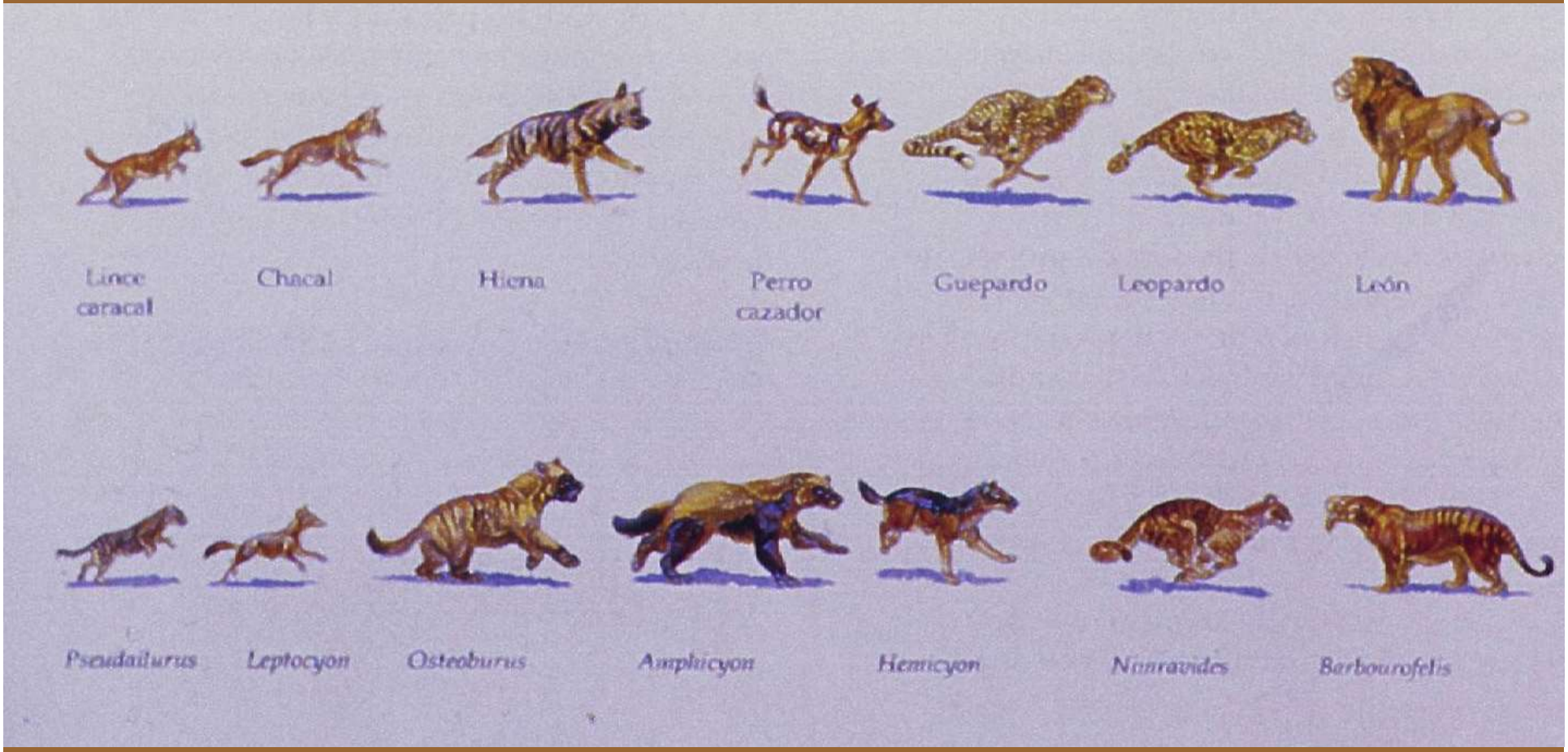


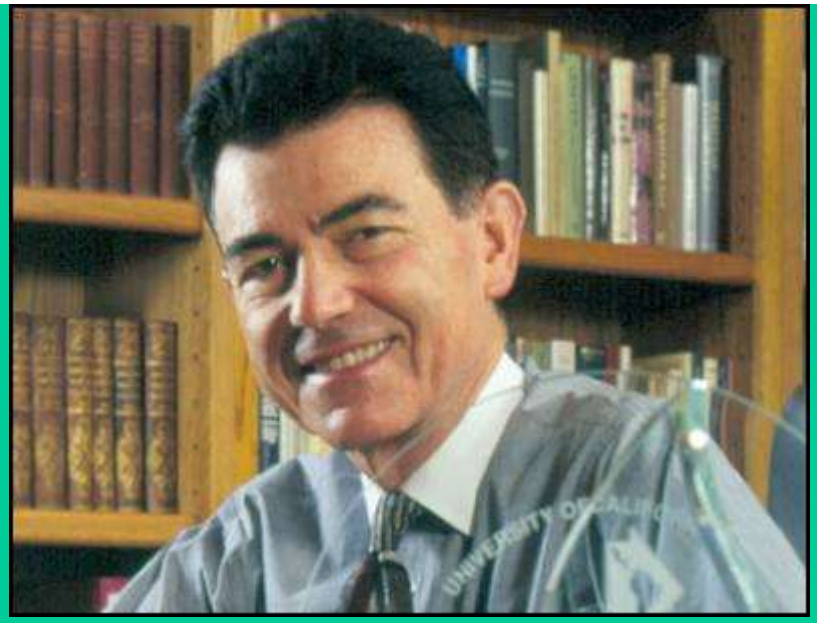
Graph by Michael Paine. Thanks to Andrew Glikson, Franco Pirajno and Dallas Abbott. Updated March 2001


WINGED INSECTS
MASS EXTINCTION
Coelurosauravus (Gliding reptile)
MASS EXTINCTION
BIRDS
Pteranodon
BATS
Bee
MASS EXTINCTION
Homo habilis
Early primate
FLOWERING PLANTS
Tyrannosaurus rex
REPTILES Hylonomus
Dimetrodon
MAMMALS
GRASSLANDS
350
270
248
220
208
205
140
75
65
60
50
2
Mesosaurus
Turtle
Diplocaulus
Mosasaur
Teleost fish
Primitive whale
Crab
MASS EXTINCTION
MASS EXTINCTION
MASS EXTINCTION
ARBONIFEROUS
PERMIAN
TRIASSIC
JURASSIC
CRETACEOUS
TERTIARY

Según la teoría de Darwin, la evolución tiene lugar exclusivamente por la vía de pequeña y continua formación y modificación de especies. /.../ Nuestra experiencia, obtenida de la observación del material fósil, contradice directamente esta interpretación. Nosotros encontramos que la estructura organizadora de una Familia o un Orden no surge como el resultado de modificaciones continuas en una larga cadena de especies, sino mas bien por medio de una repentina y discontinua remodelación del complejo tipo de Familia a Familia, de Orden a Orden, de Clase a Clase. Los caracteres que cuentan para las distinciones entre especies son completamente diferentes de los que distinguen un tipo de otro.

Schindewolf, O. 1993.


Lince caracal
Chacal
Hiena
Perro cazador
Guepardo
Leopardo
León
Pseudailurus
Leptocyon
Osteoburus
Amphicyon
Hemicyon
Nimravides
Barbourofelis



Los origenes evolutivos de los taxones superiores son poco conocidos.
La posibilidad de que las brechas tengan como causa la extinción de intermedios se convierte cada vez en más inverosímil.
La mayor parte de de los órdenes, clases y filos aparecen de repente y normalmente con todos los caracteres que las distinguen.
Estamos obligados a concluir que la mayor parte de los taxones realmente nuevos que aparecen repentinamente debieron de hecho de originarse repentinamente.
***"La evolución en acción"** FJ Ayala y JW Valentine (1983)*

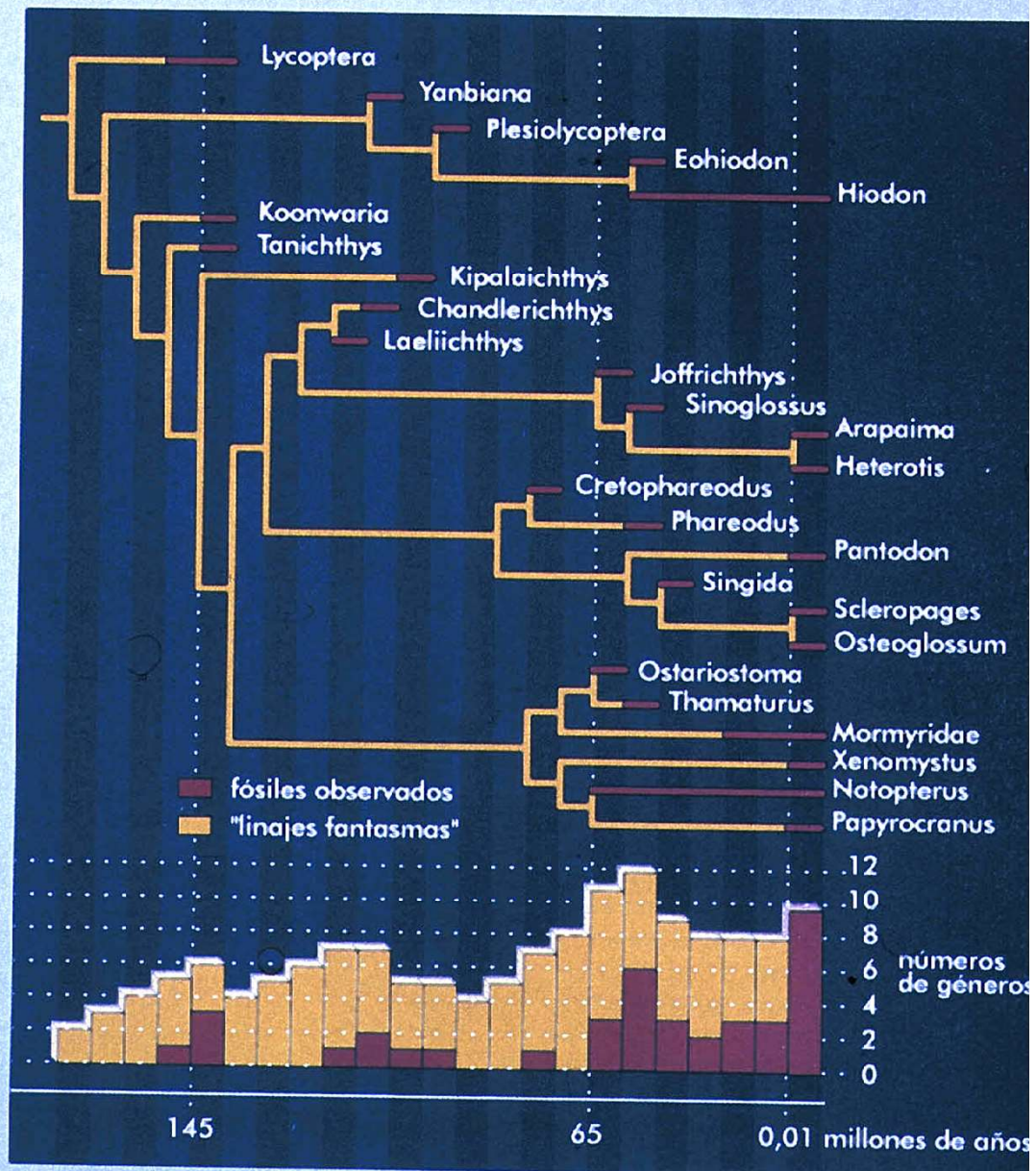
«Charles Darwin completa la revolución copernicana, que había dejado fuera el origen de los seres vivos. Copérnico, Galileo y Newton habían explicado los fenómenos naturales como resultado de procesos naturales. Darwin hace lo mismo respecto a los seres vivos. Todo se puede explicar por la selección natural.

La evolución consiste en la transformación gradual de unos organismos ya existentes en otros.

F.J. Ayala, ***'Darwin y el diseño inteligente. Creacionismo, cristianismo y evolución'*** *(Alianza Editorial, 2007)*

Figura 2. La enumeración de los linajes fantasmas (en naranja), además de los fósiles conocidos (en rojo), incrementa fuertemente la diversidad de los géneros del grupo de los osteoglosomorfos, peces teleósteos, en los últimos 160 millones de años (abajo, un osteogloso actual).

La existencia de linajes fantasmas se deduce del análisis filogenético. Por ejemplo, el género Papyrocranus (en la parte inferior del gráfico) tiene un ancestro común con el género *Notopterus*, del que se conocen fósiles de periodo más antiguos. Por tanto, el Papyrocranus ya existía en la misma época que el *Notopterus* y su ancestro común vivió en durante el periodo precedente a su aparición, aunque no se tiene ningún fósil. La noción de crisis biológica para este grupo, por ejemplo la crisis Cretácico-Terciario hace 65 millones de años, se ha relativizado.



Heredity (2010) 105, 113 121

www.nature.com/hdy

REVIEW

Epigenomic plasticity within populations: its evolutionary significance and potential

LJ Johnson and PJ Tricker
School of Biological Sciences, University of Reading, Reading, UK

Epigenetics has progressed rapidly from an obscure quirk of heredity into a data-heavy 'omic' science. Our understanding of the molecular mechanisms of epigenomic regulation, and the extent of its importance in nature, are far from complete, but in spite of such drawbacks, population-level studies are extremely valuable: epigenomic regulation is involved in several processes central to evolutionary biology including phenotypic plasticity, evolvability and the mediation of intragenomic conflicts. The first studies of epigenomic variation within populations suggest high levels of phenotypically relevant variation, with the patterns of epigenetic regulation varying between individuals and genome regions as well as with environment. Epigenetic mechanisms appear to function primarily as genome defences, but result in the maintenance of plasticity together with a degree of buffering of developmental programmes; periodic breakdown of epigenetic buffering could potentially cause variation in rates of phenotypic evolution.
Heredity (2010) **105,** 113–121; doi:10.1038/hdy.2010.25; published online 24 March 2010

Keywords: epigenetics; population genomics; canalisation; capacitance

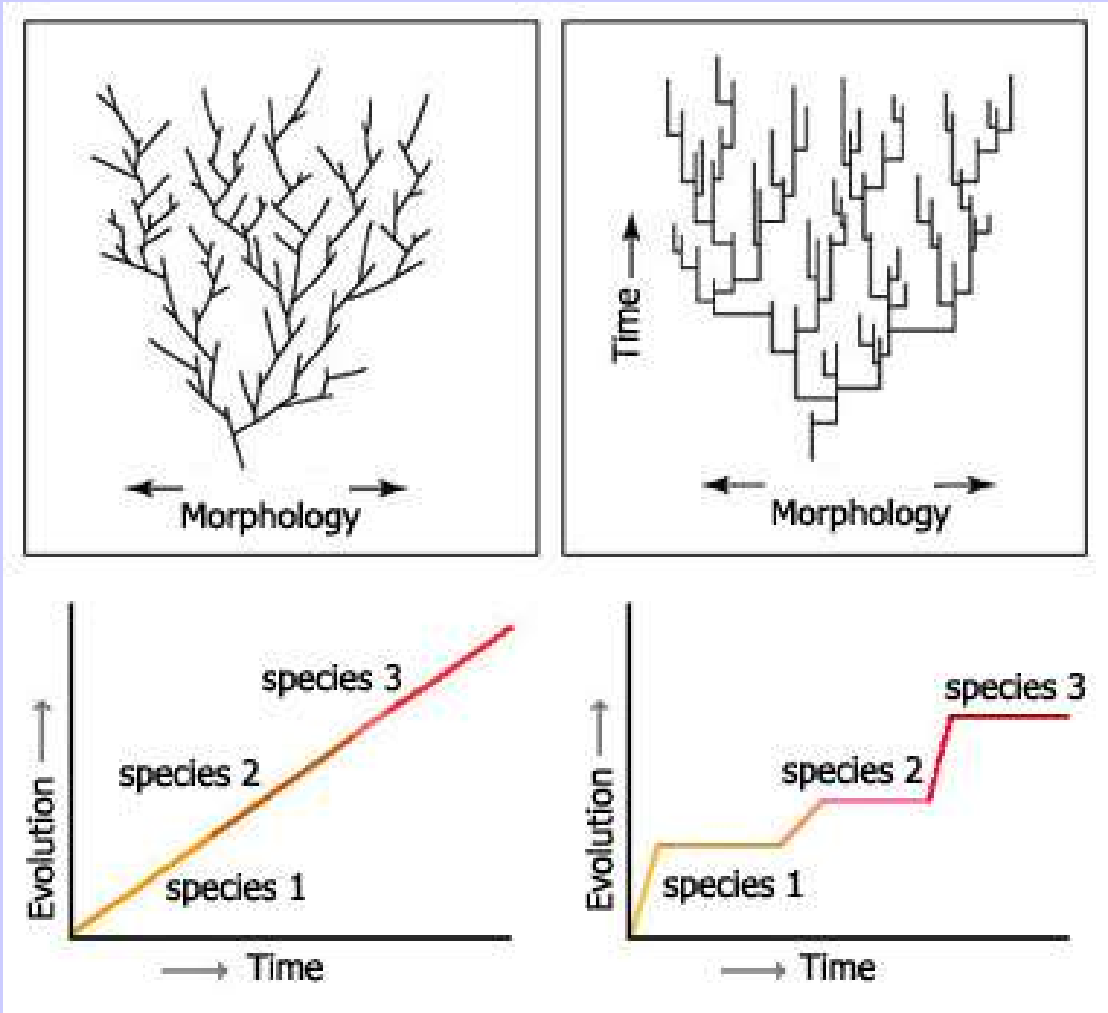
EQUILIBRIO PUNTUADO

ELDREDGE, N. & GOULD, S. J. 1972

Models in Paleobiology. T. J. M. Schopf (Ed.) W. M. Freeman

1º.-La **estasis**: la mayoría de las especies no exhibe cambio direccional alguno durante su estancia sobre la tierra. Aparecen en el registro fósil con una apariencia muy similar a cuando desaparecen. El cambio morfológico es generalmente limitado y no direccional.

2º.-La **aparición repentina**: en cualquier área local de una especie, que no surge gradualmente por la transformación paulatina de sus antecesores, sino que aparece plenamente formada, y establecida en el registro fósil.



Two ways of representing evolution by gradualism versus evolution by punctuated equilibria. In the case of gradualism (left), the diagonal lines indicate that morphological changes occur bit by bit over time. In the case of punctuated equilibria (right), the step-like patterns represent rapid morphological changes followed by long periods when the species evolves very little.

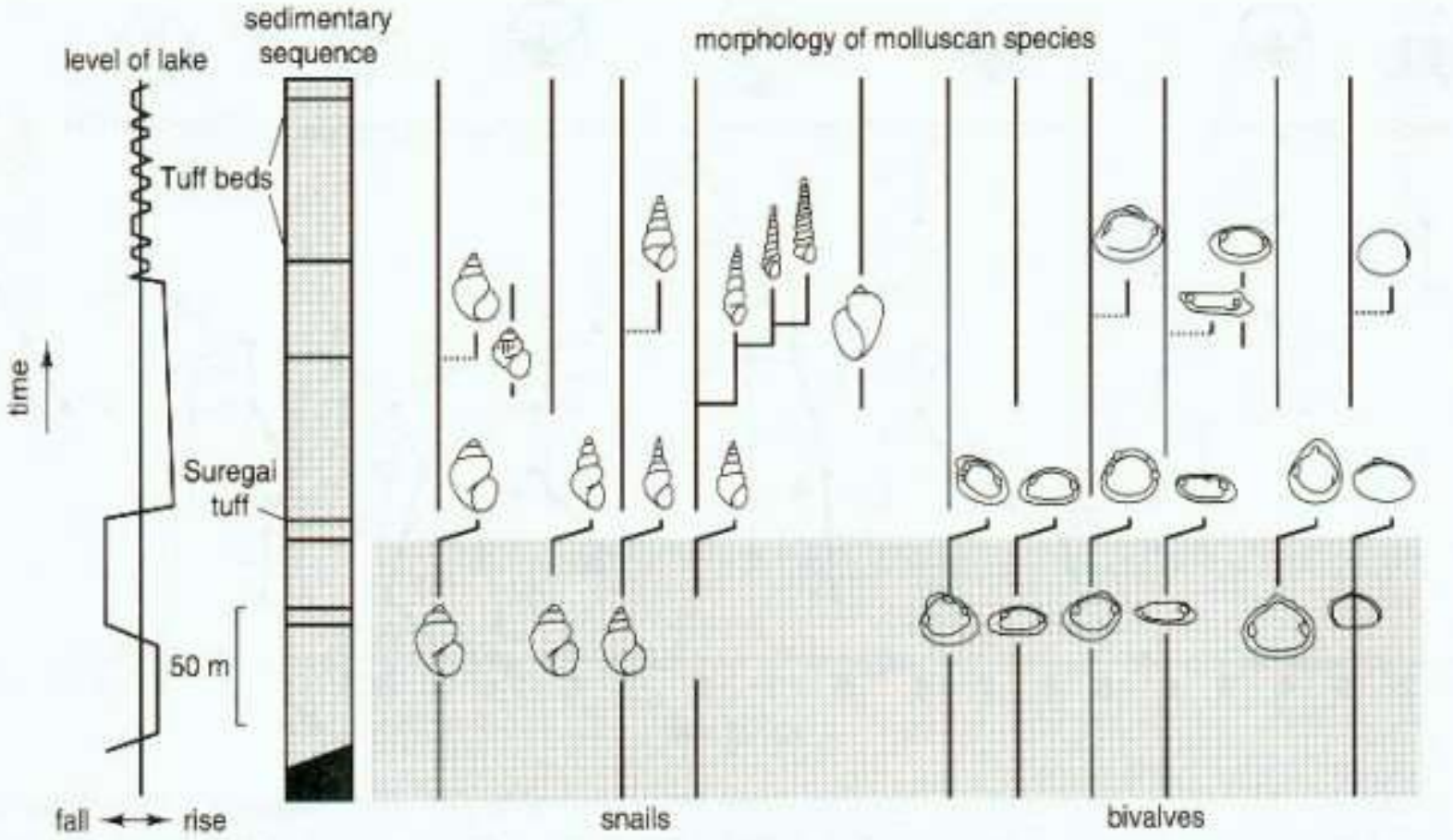


Fig. 4. Stasis in Pliocene molluscs. Ten evolving lineages of gastropods and bivalves in sediments of Lake Turkana, plotted through the past 4 million years. At times of major changes in lake level (shown on the left-hand scale), there appears to be a flurry of speciation events in most lineages: shell shape and size change. However, after the physical environmental crisis, shell form reverts to the pre-crisis morphology. It seems likely that the changes are ecophenotypic changes, non-evolutionary shifts in morphology in response to stress. More important is the demonstration of long-term stasis of all ten lineages, for over 3 million years. Based on the work of P. G. Williamson.

Published online 9 December 2009 | Nature | doi:10.1038/news.2009.1134
News

New species evolve in bursts

Red Queen hypothesis of gradual evolution undermined.

Kerri Smith

Alice and the Red Queen had to run as fast as they could to stay in the same place - just like evolving species, according to the eponymous hypothesis.*Through the Looking Glass/John Tenniel*

This contradicts a widely accepted theory of how speciation occurs: that species are continually changing to keep pace with their environment, and that new species emerge as these changes accrue. Known as the 'Red Queen' hypothesis, it is named after the character in Lewis Carroll's book *Through the Looking-Glass, and What Alice Found There* who tells a surprised Alice: "Here, you see, it takes all the running you can do, to keep in the same place."

But Mark Pagel and his team at the University of Reading, UK, challenge this idea. In a paper published today in *Nature*, they compared four models of speciation — one of which was the Red Queen hypothesis — to see which best explains the rate of speciation in more than 100 species groups from the animal and plant kingdoms, including bumblebees, turtles, foxes and roses.

They looked at the lengths of branches in thousands of species' evolutionary trees contained within these groups to estimate the time periods between speciation events.

"What we've shown is that speciation is about happy accidents — rare events that happen in the environment that cause a species to speciate," says Pagel. These events could include a mountain range being thrust up or a shift in climate, he says.

The team's findings might stir things up in the world of evolutionary biology. "It really goes against the grain because most of us have this Darwinian view of speciation," says Pagel. "What we're saying is that to think about natural selection as the cause of speciation is perhaps wrong."

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Science 10
February 2006:
Vol. 311. no. 5762,
pp. 796 - 800
DOI:
10.1126/science.111
3832

REVIEW

Gene Regulatory Networks and the Evolution of Animal Body Plans

Eric H. Davidson[1] and Douglas H. Erwin[2]

Development of the animal body plan is controlled by large gene regulatory networks (GRNs), and hence evolution of body plans must depend upon change in the architecture of developmental GRNs. However, these networks are composed of diverse components that evolve at different rates and in different ways. Because of the hierarchical organization of developmental GRNs, some kinds of change affect terminal properties of the body plan such as occur in speciation, whereas others affect major aspects of body plan morphology. A notable feature of the paleontological record of animal evolution is the establishment by the Early "Cambrian of virtually all phylum-level body plans. We identify a class of GRN component, the kernels" of the network, which, because of their developmental role and their particular internal structure, are most impervious to change. Conservation of phyletic body plans may have been due to the retention since pre-Cambrian time of GRN kernels, which underlie development of major body parts.

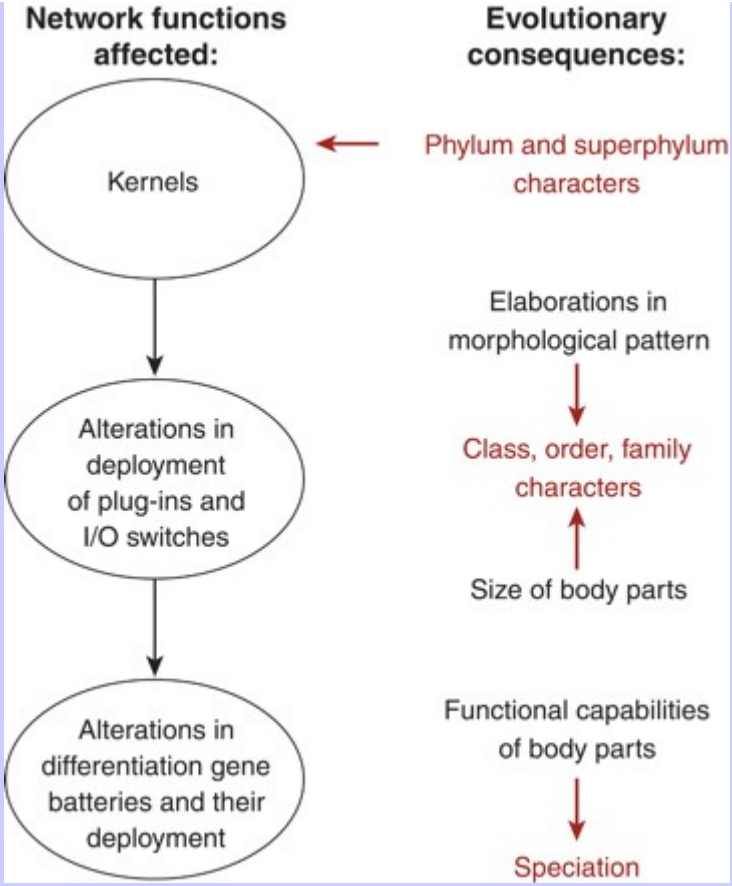
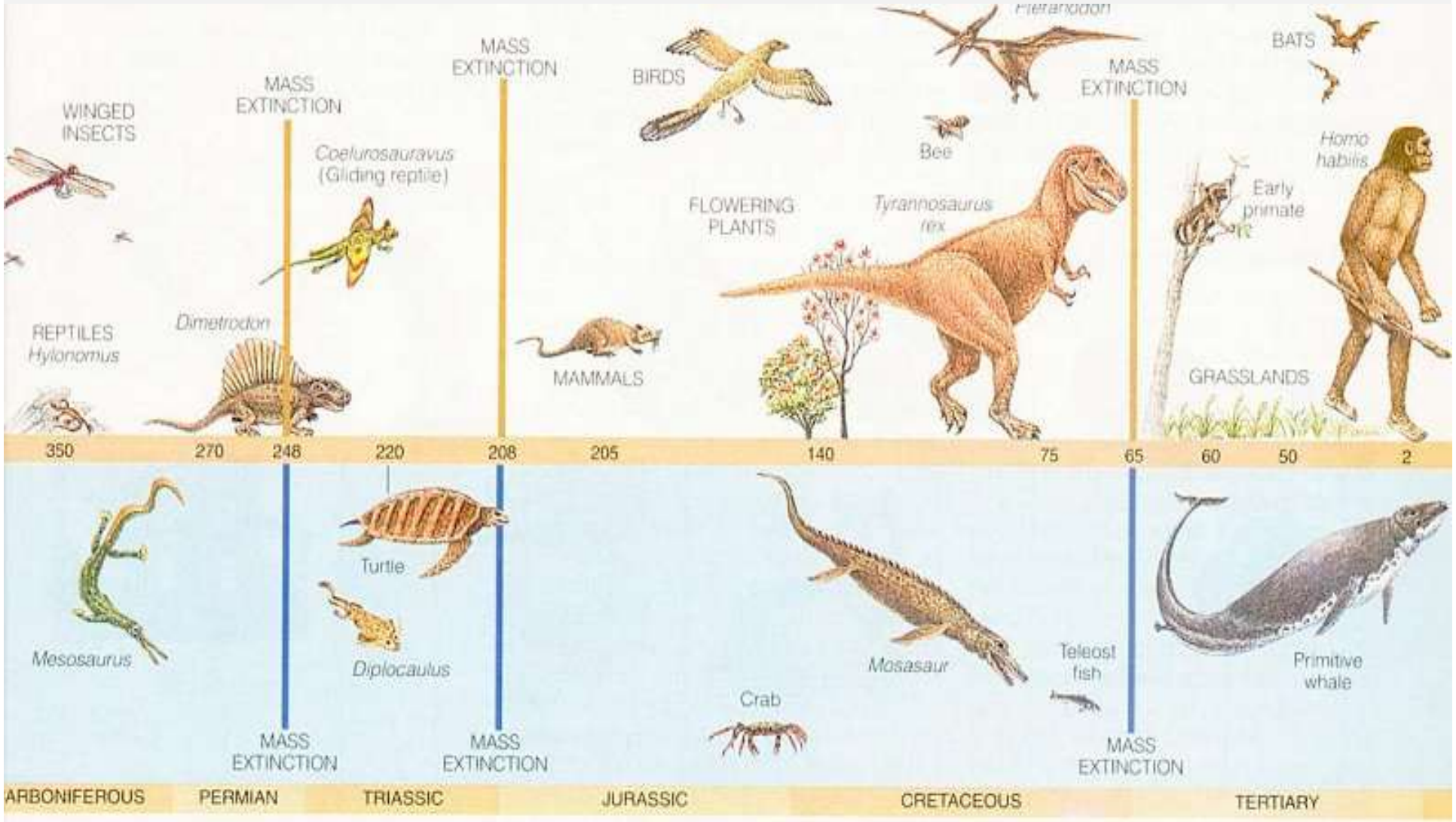
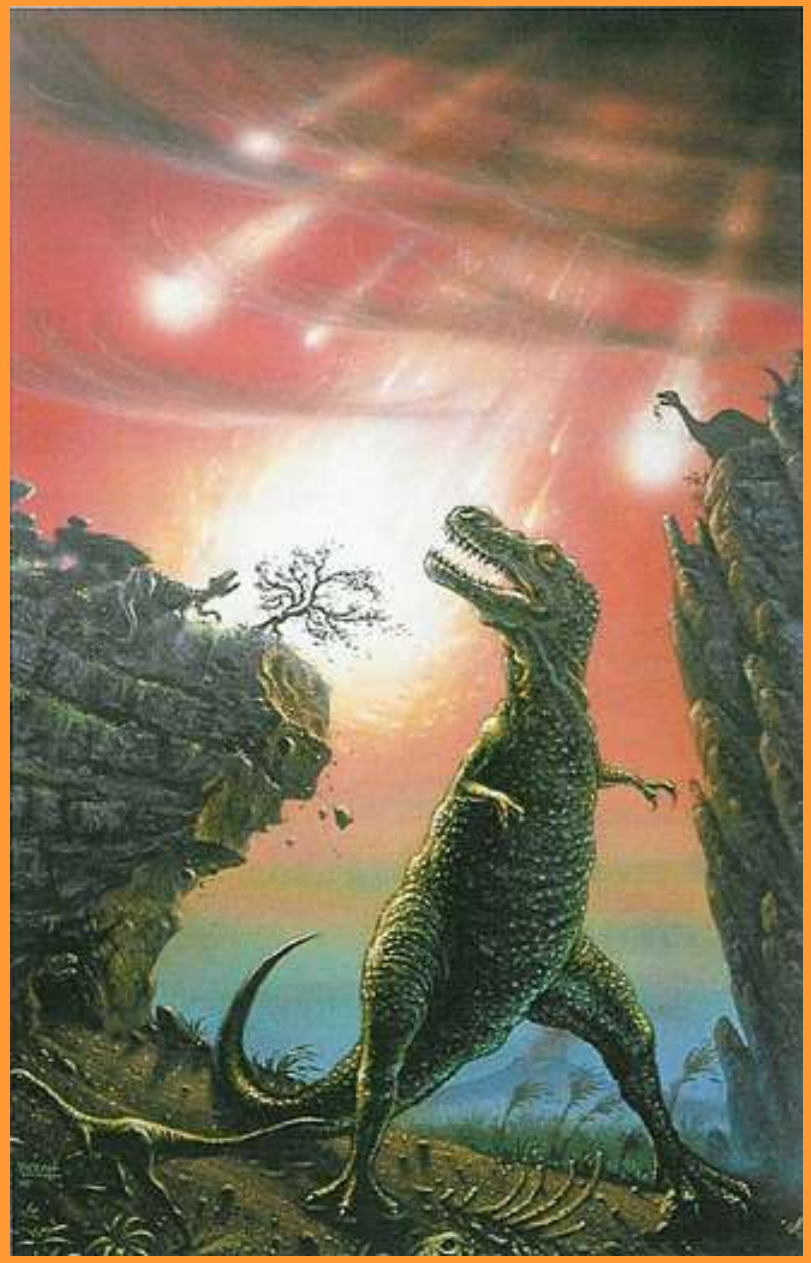


Fig. 3. Diverse kinds of change in GRNs and their diverse evolutionary consequences. The left column shows changes in network components; the right column shows evolutionary consequences expected, which differ in their taxonomic level (red).

“El mas asombroso acontecimiento en la historia de la vida sobre la Tierra, es el cambio que ocurrió del Mesozoico, edad de los reptiles, a la edad de los mamíferos. Parece como si el telón hubiese caído repentinamente sobre un escenario en el que todos los papeles habían sido desempeñados por los reptiles, especialmente los dinosaurios, en un número enorme y con una variedad sorprendente, y se hubiese vuelto a levantar inmediatamente para poner de manifiesto idéntica escenografía, pero con un reparto enteramente distinto".
(Simpson et al., 57).


WINGED INSECTS
MASS EXTINCTION
Coelurosauravus (Gliding reptile)
MASS EXTINCTION
BIRDS
Pteranodon
BATS
Bee
MASS EXTINCTION
Homo habilis
Early primate
FLOWERING PLANTS
Tyrannosaurus rex
REPTILES
Hylonomus
Dimetrodon
MAMMALS
GRASSLANDS
350
270
248
220
208
205
140
75
65
60
50
2
Mesosaurus
Turtle
Diplocaulus
Mosasaur
Teleost fish
Primitive whale
Crab
MASS EXTINCTION
MASS EXTINCTION
MASS EXTINCTION
ARBONIFEROUS
PERMIAN
TRIASSIC
JURASSIC
CRETACEOUS
TERTIARY



A finales de los 90, el paleontólogo indio Sankar Chatterjee encontró otra cicatriz en la corteza terrestre: el cráter "Shiva", una estructura en el fondo del océano Índico, al oeste de Bombay. Su edad, 65 millones de años. Por lo tanto, su origen coincide con la extinción masiva del Cretácico-Terciario. Tiene una longitud de unos 600 km y una anchura de unos 400 km, si bien su aspecto ha cambiado mucho desde su formación debido a la expansión del fondo oceánico. Dadas estas dimensiones, debió ser causado por un asteroide o cometa de unos 40 km de diámetro... Cuatro veces mayor de lo estimado para el de Chicxulub. La cicatriz de Shiva es uno de los pilares de una teoría que sostiene que la causa de la extinción del Cretácico-Terciario no fue un solo impacto, sino la fragmentación de un asteroide masivo, cuyos trozos golpearon la Tierra en diferentes lugares.

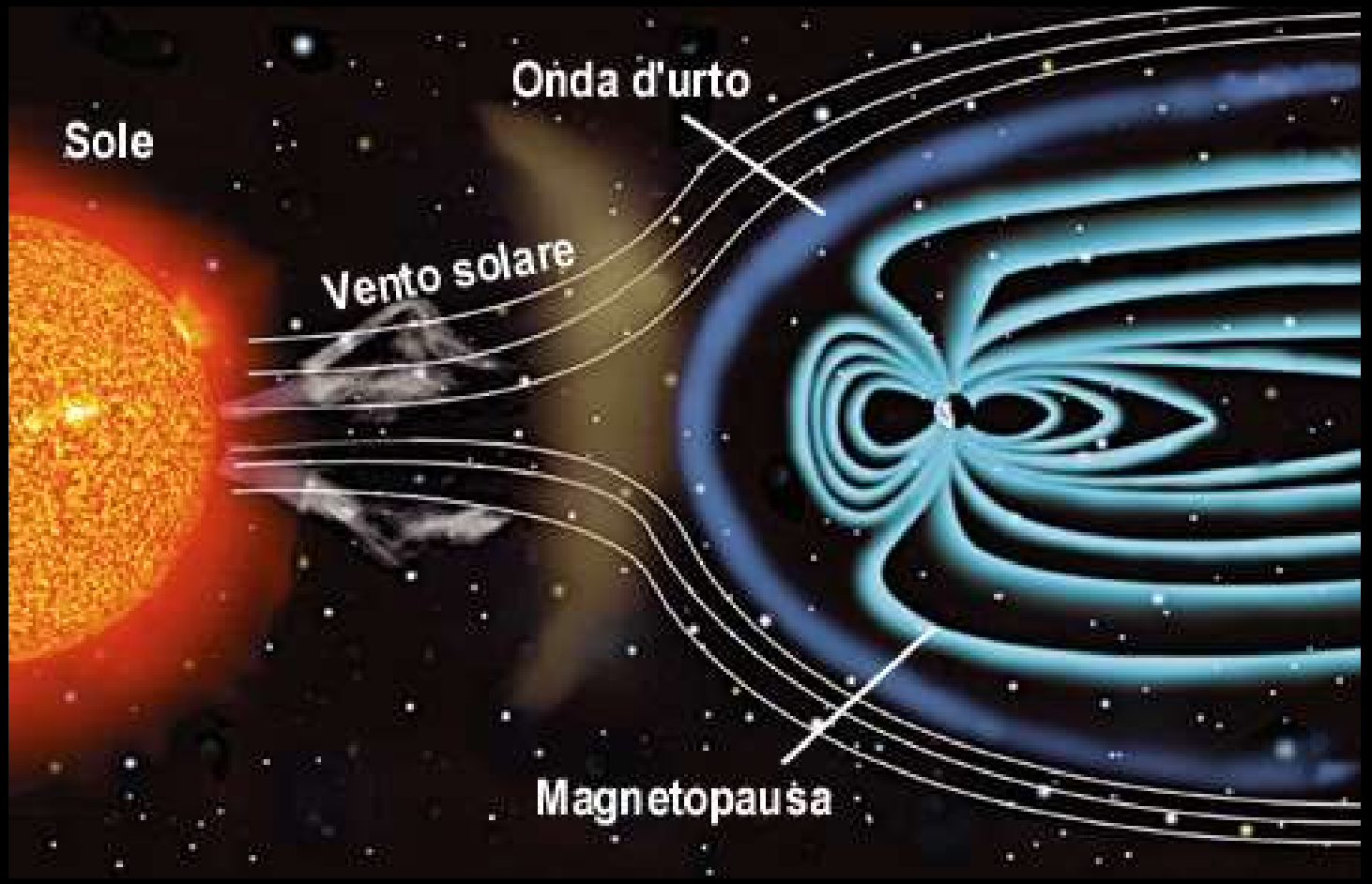
Asteroid strike into ocean could deplete ozone layer

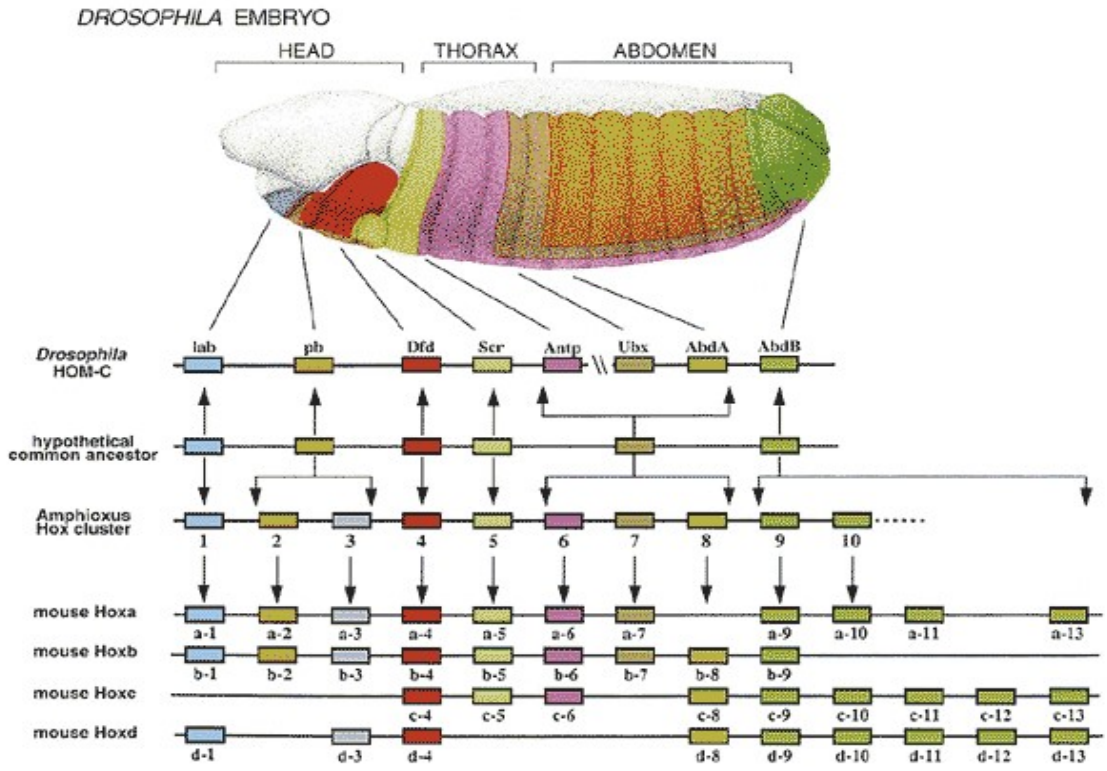
October 27, 2010 by Lin Edwards

Image credit: NASA

(PhysOrg.com) -- Scientists in Texas say if a medium-sized asteroid were to crash into the ocean the ozone layer could be depleted, allowing high levels of ultraviolet radiation to reach the surface.

Dr. Elisabetta Pierazzo and colleagues from the Planetary Science Institute in Tucson ran computer simulations that revealed if an asteroid 500 m to 1 km in diameter were to hit the Pacific Ocean it would eject enough water vapor and sea salt high enough into the atmosphere to affect the protective ozone layer. The results of the simulations showed the 1 km asteroid could affect an area over 1000 km in diameter, and vast quantities of water and vapor would be ejected up to 160 km high. The scientists say the water vapor would contain chlorine and bromine from the vaporized sea salts, and this would result in significant global depletion of the ozone layer by destroying it faster than it is created naturally. Pierazzo said such an asteroid would produce “an ozone hole that will engulf the entire Earth,” and produce a huge spike in ultraviolet (UV) radiation with levels higher than anywhere on the surface today.


Onda d'urto
Sole
Vento solare
Magnetopausa


DROSOPHILA EMBRYO
HEAD
THORAX
ABDOMEN
Drosophila HOM-C
lab
pb
Dfd
Scr
Antp
Ubx
AbdA
AbdB
hypothetical common ancestor
Amphioxus Hox cluster
1
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4
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mouse Hoxa
a-1
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a-3
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mouse Hoxb
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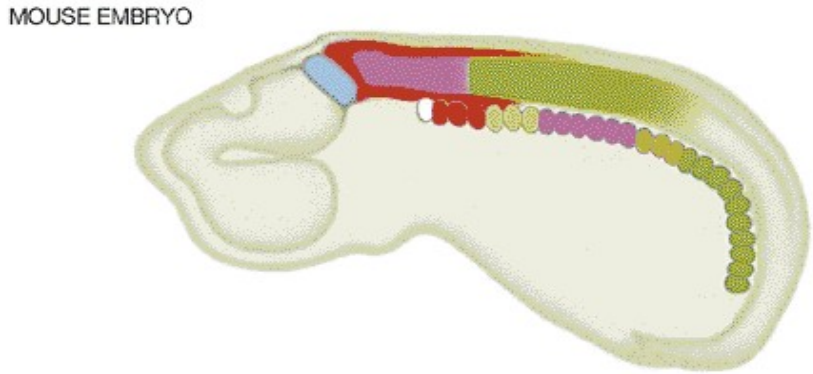
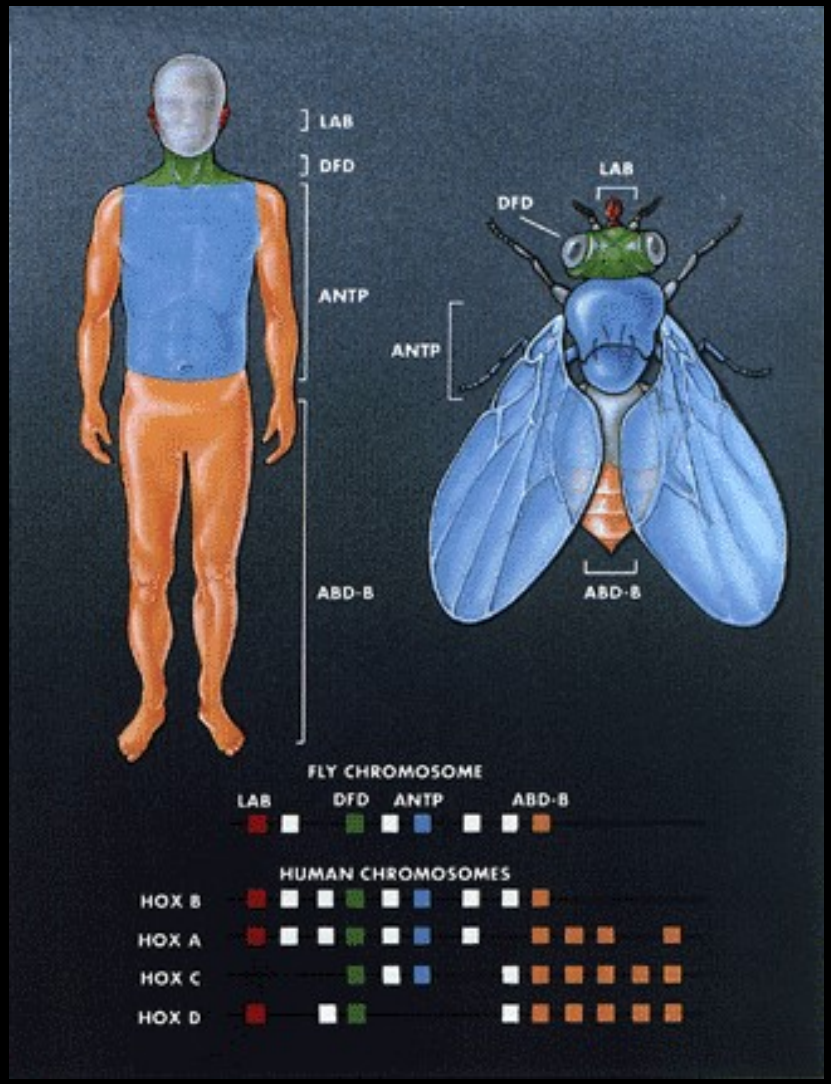
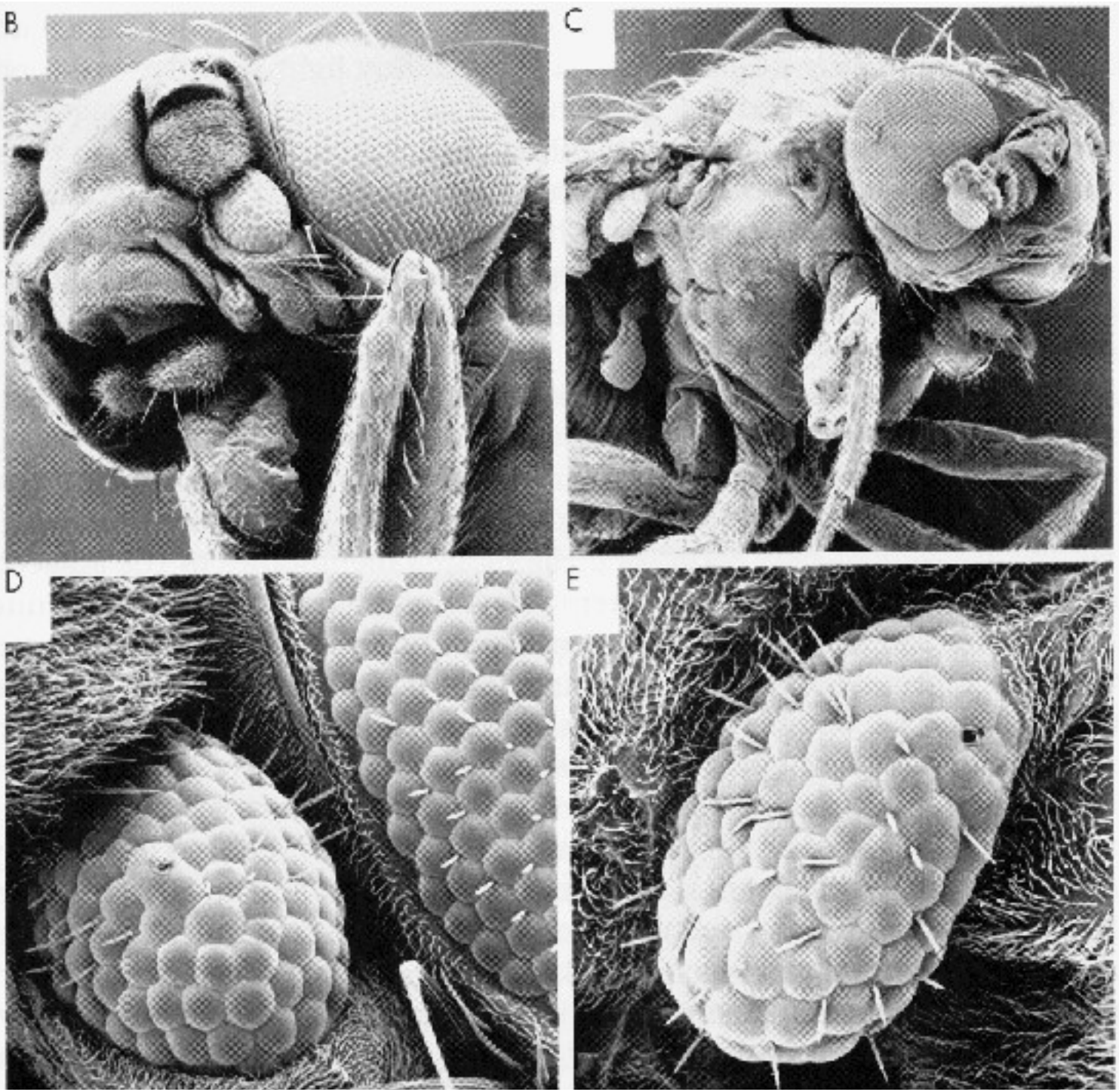
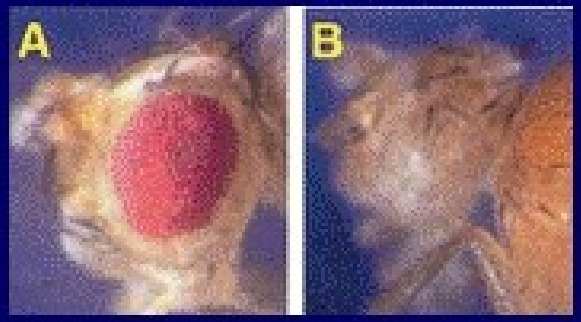

MOUSE EMBRYO


LAB
DFD
ANTP
ABD-B
LAB
DFD
ANTP
ABD-B
FLY CHROMOSOME
LAB
DFD
ANTP
ABD-B
HUMAN CHROMOSOMES
HOX B
HOX A
HOX C
HOX D


B
C
D
E

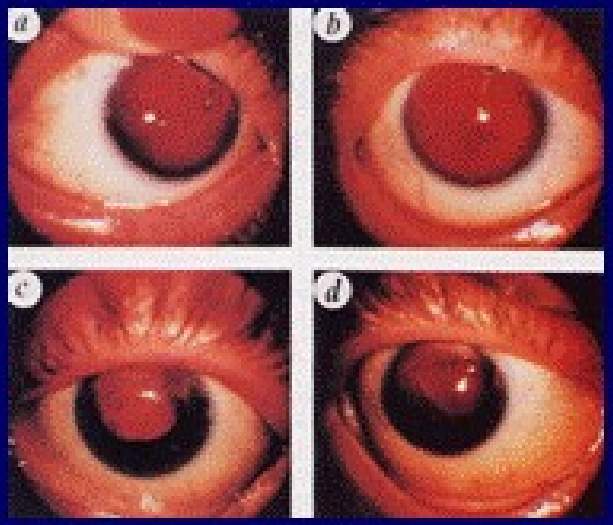
Model organisms - Pax6 mutants



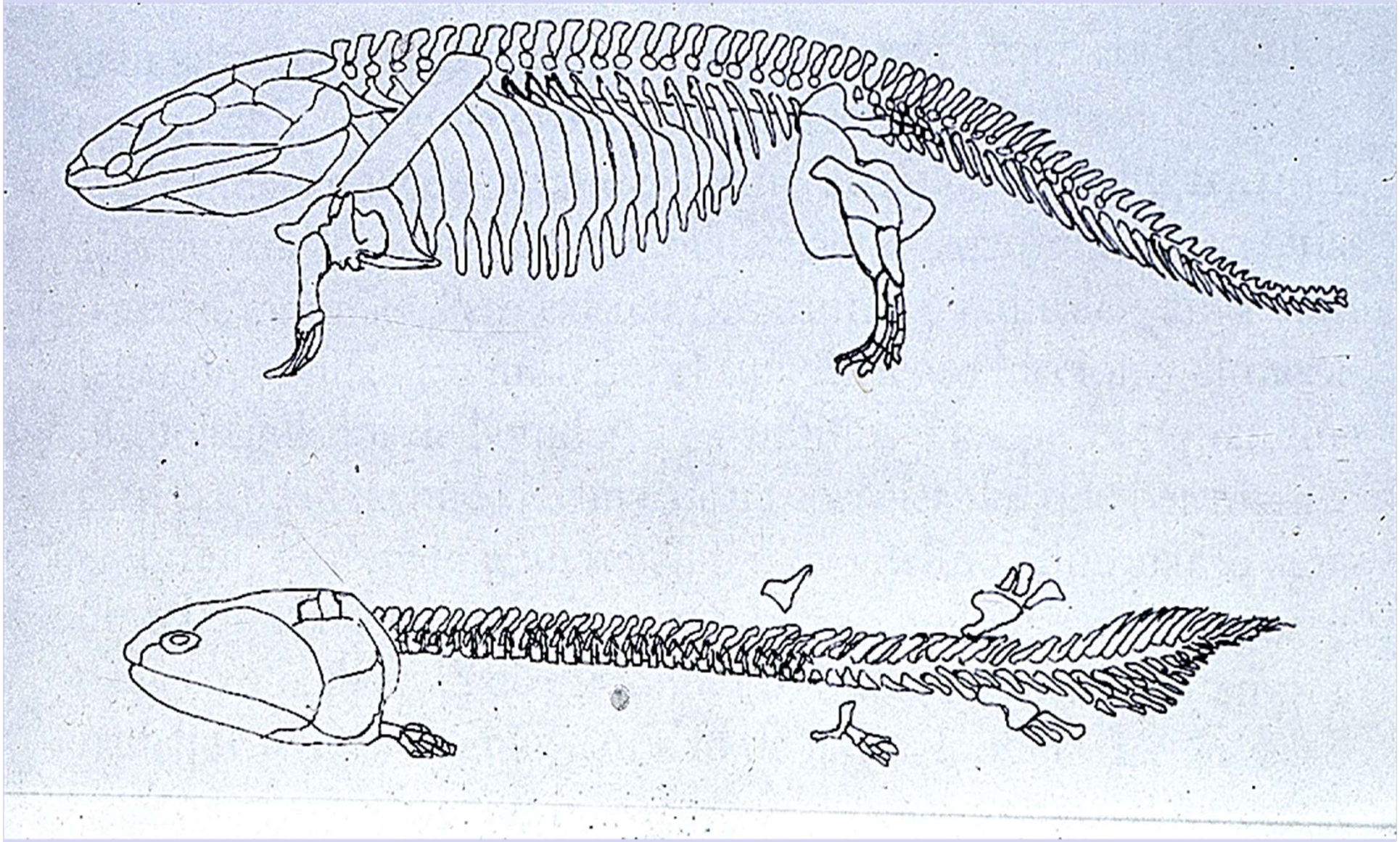
Drosophila mutant

Prezo et al,2001

Mouse mutant



Glaser et al. Nat Genet 7: 463-471 (1994)



Nature 390, 29 (6 November 1997) | doi:10.1038/36234

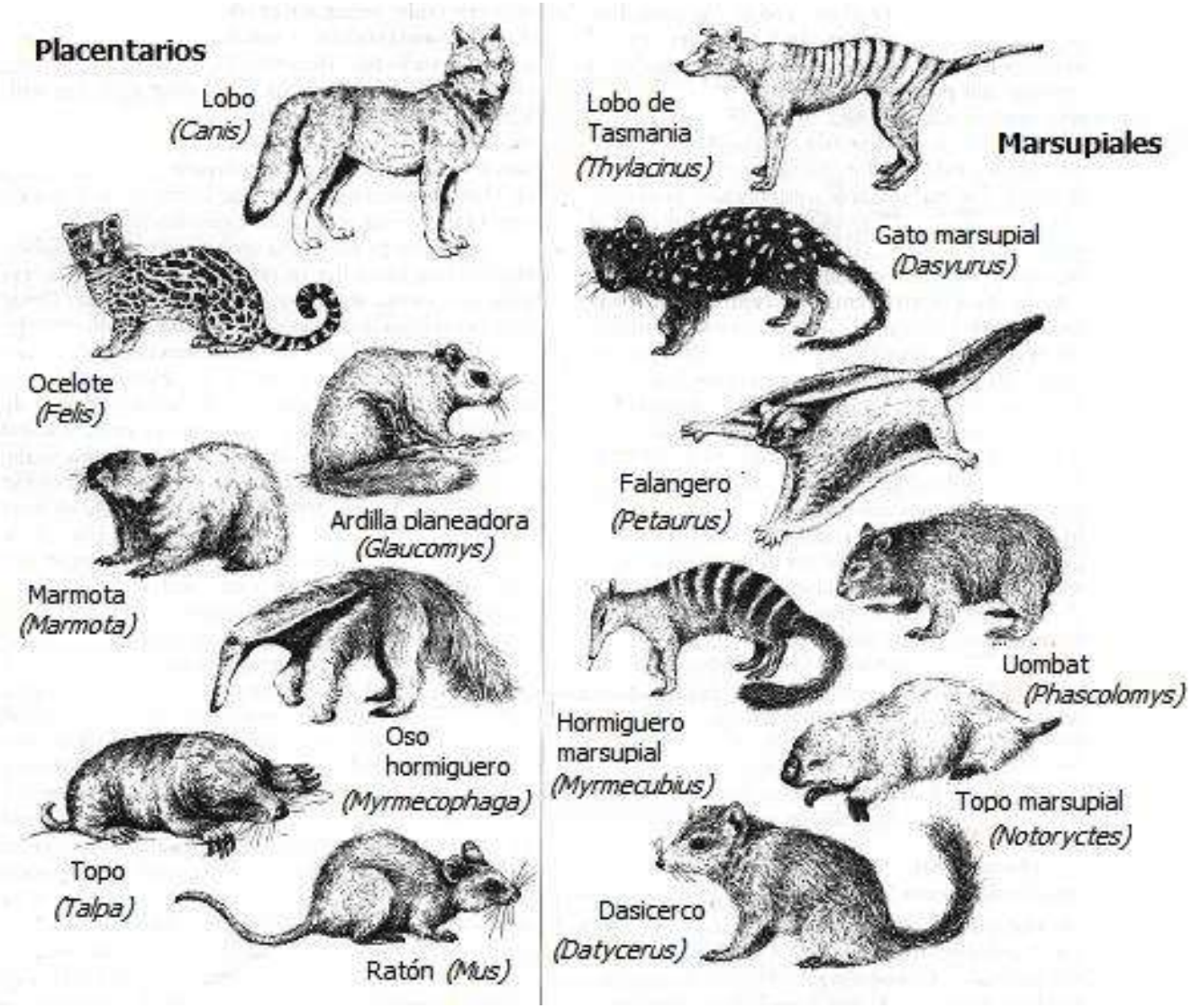
Of fingers, toes and penises

Takashi Kondo , József Zákány , Jeffrey W. Innis & Denis Duboule

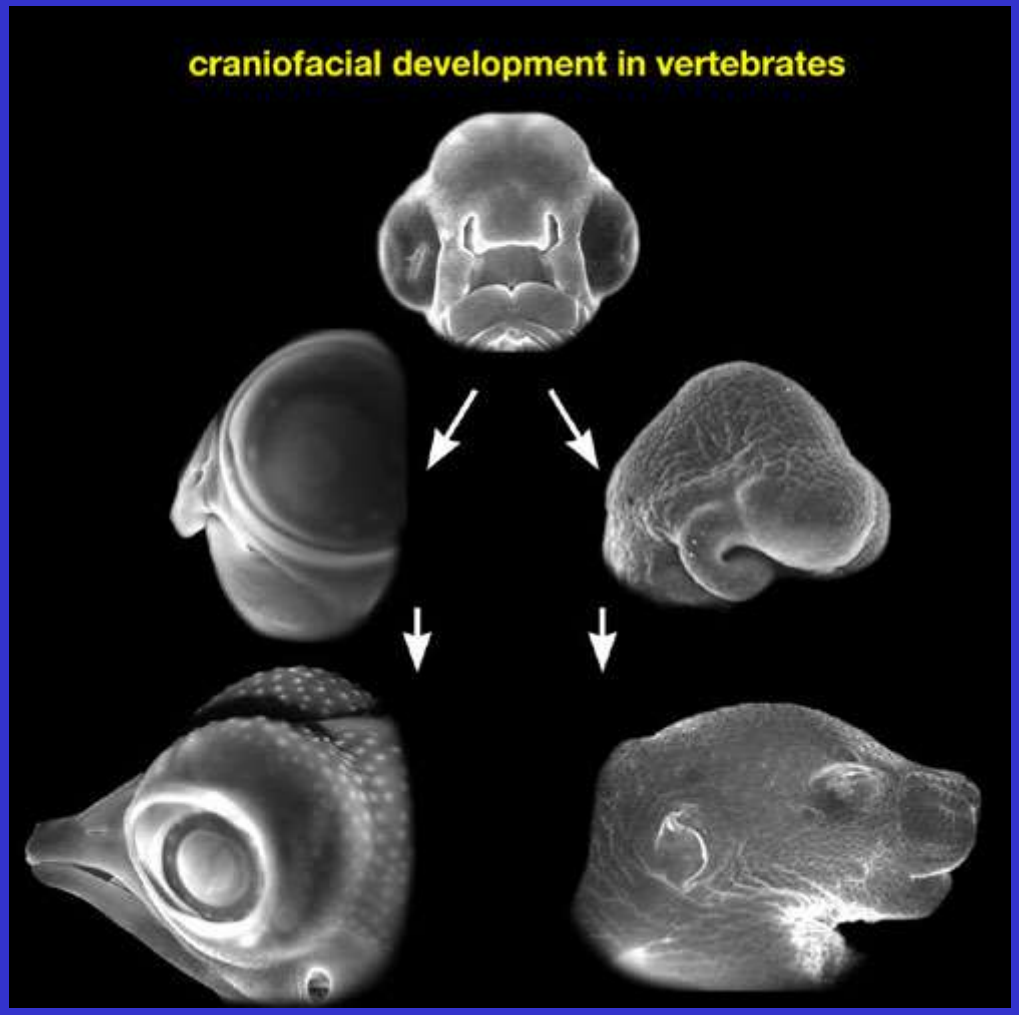
Abstract

Vertebrate Hox genes are essential for limb development. The posteriormost Hoxd and Hoxa genes are required for growth and patterning of digits and are also strongly expressed in the genital bud, which gives rise to the urogenital system, including the penis. Here, we show that removal of posterior Hox gene function results in a concomitant loss of digits and genital bud-derivatives, illustrating that similar developmental mechanisms are at work in these different buds.

http://www.nature.com/nature/journal/v390/n6655/full/390029a0.html

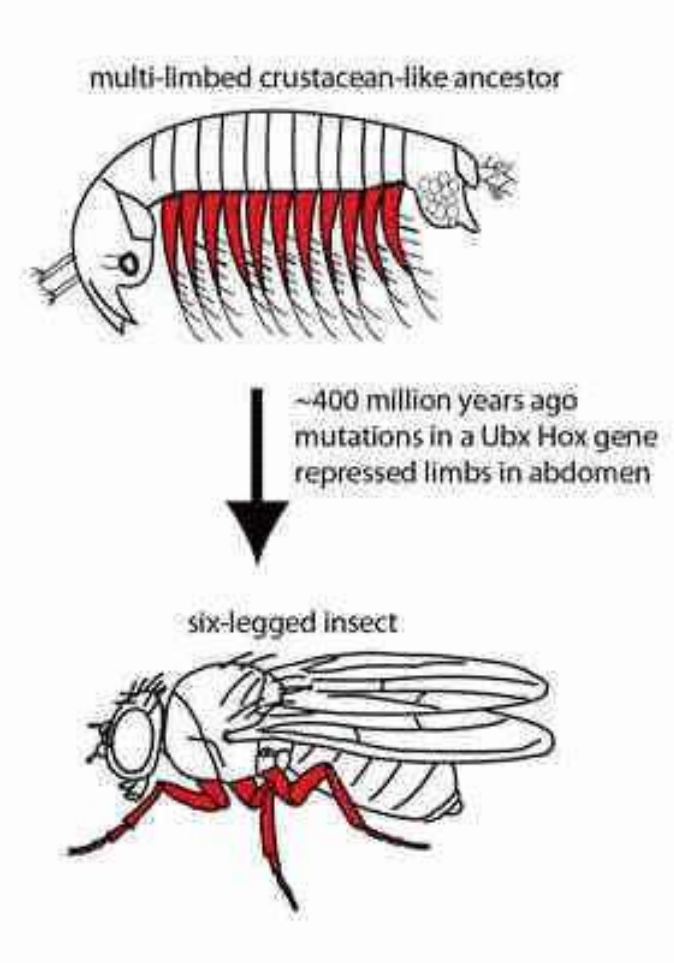

Placentarios
Lobo
(Canis)
Ocelote
(Felis)
Ardilla planeadora
(Glaucomys)
Marmota
(Marmota)
Oso
hormiguero
(Myrmecophaga)
Topo
(Talpa)
Ratón (Mus)
Lobo de
Tasmania
(Thylacinus)
Marsupiales
Gato marsupial
(Dasyurus)
Falangero
(Petaurus)
Uombat
(Phascolomys)
Hormiguero
marsupial
(Myrmecubius)
Topo marsupial
(Notoryctes)
Dasicerco
(Datycerus)

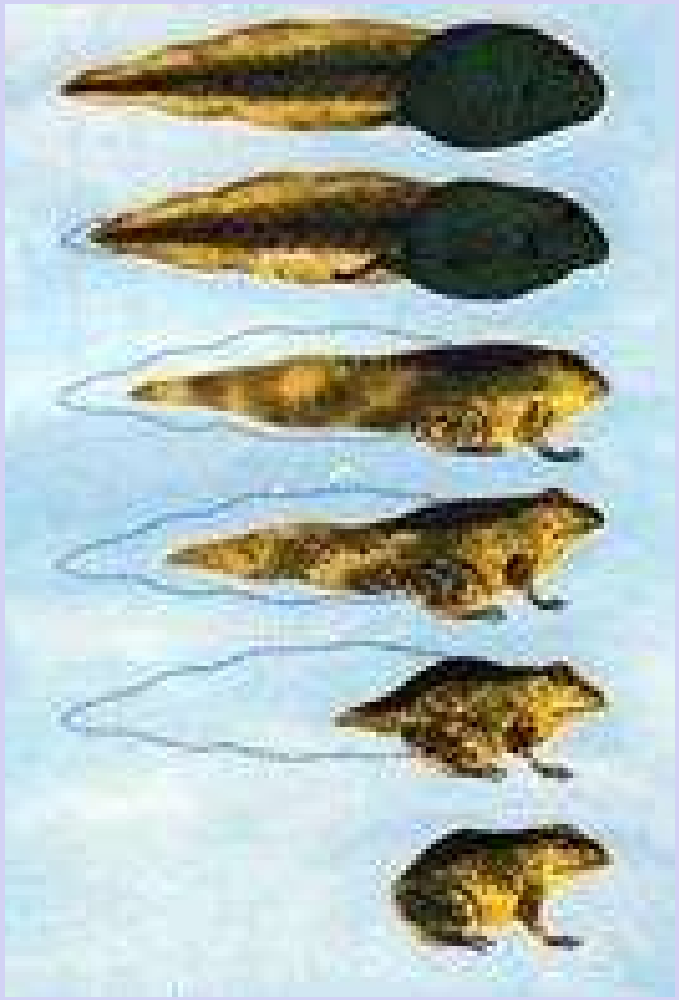

Ichthyosaurs
Ichthyosaurus
Shonisaurus
Euthinosaurus
Mixosaurus
Ophthalmosaurids
Cymbospondylus
Temnodontosaurus
Cymbospondylus

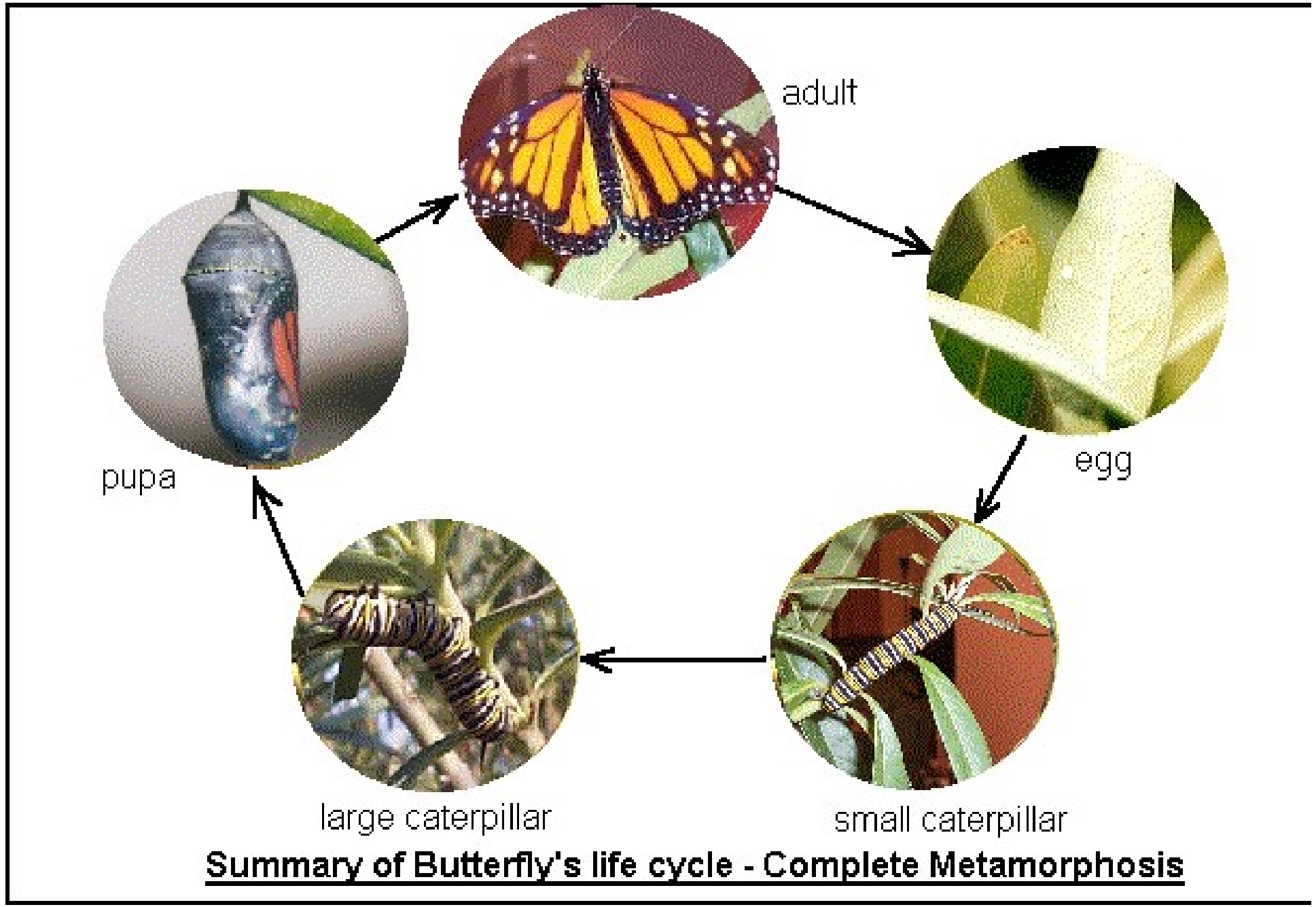

craniofacial development in vertebrates

Hox protein mutation and macroevolution of the insect body plan

Matthew Ronshaugen, Nadine McGinnis & William McGinnis
Section of Cell and Developmental Biology, University of California —San Diego,







Summary of Butterfly's life cycle - Complete Metamorphosis

Loss and recovery of wings in stick insects

MICHAEL F. WHITING, SVEN BRADLER & TAYLOR MAXWELL

Nature **421,** 264–267 (2003); doi:10.1038/nature01313

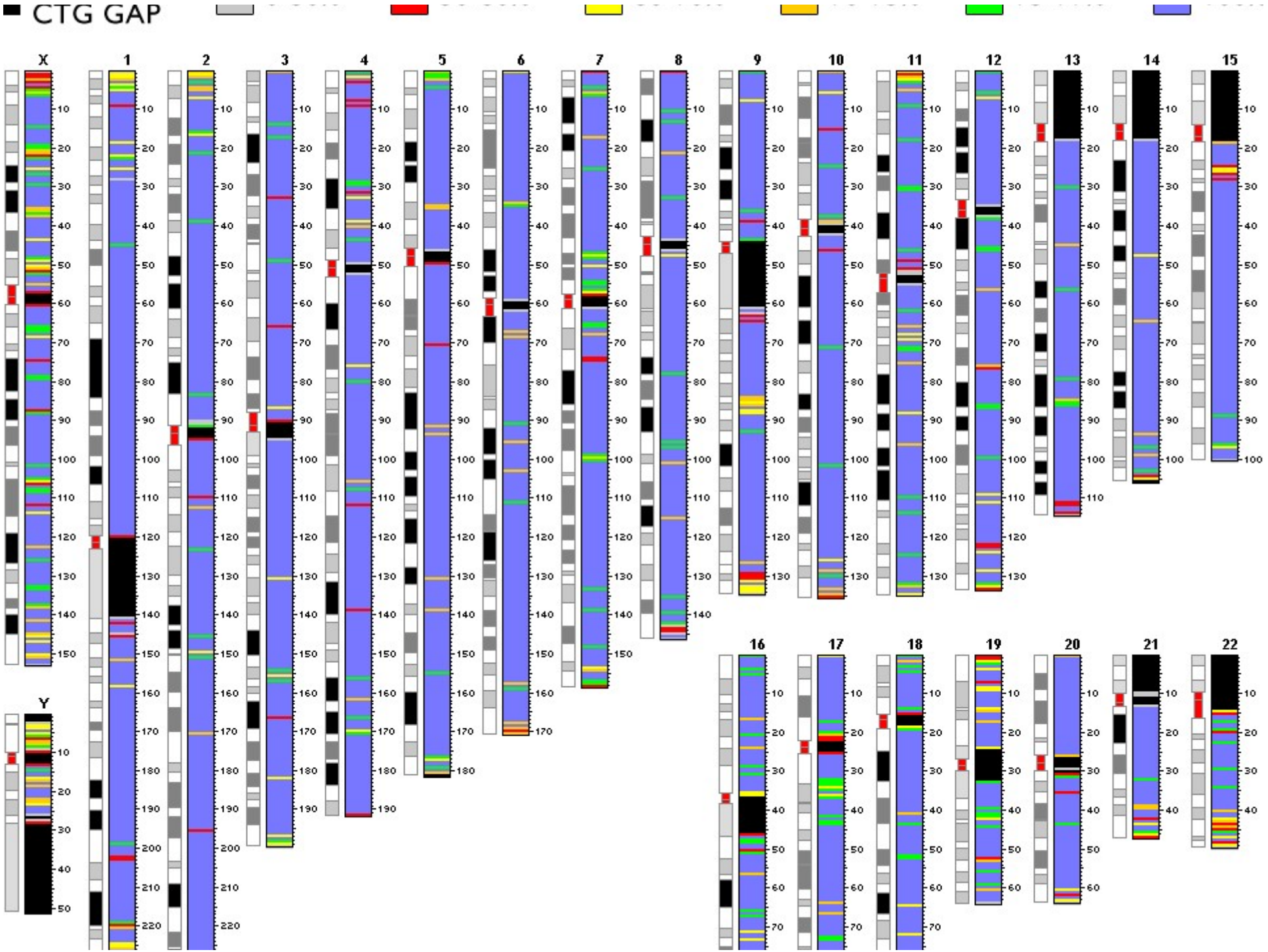
DNA evidence shows that wings were lost in the primitive ancestor of stick insects, then subsequently reacquired at least four times during stick insect evolution. Loss of wings is common in insect evolution but this is the first series of 're-evolution' events to be recognized. This challenges two common assumptions — that wings evolved just the once in insects and that once a lineage loses its wings, its descendants would remain flightless.

Repeats are often described as 'junk' and dismissed as uninteresting. However, they actually represent an extraordinary trove of information about biological processes. The repeats constitute a rich palaeontological record, holding crucial clues about evolutionary events and forces. As passive markers, they provide assays for studying processes of mutation and selection. It is possible to recognize cohorts of repeats 'born' at the same time and to follow their fates in different regions of the genome or in different species. As active agents, repeats have reshaped the genome by causing ectopic rearrangements, creating entirely new genes, modifying and reshuffling existing genes, and modulating overall GC content. They also shed light on chromosome structure and dynamics, and provide tools for medical genetic and population genetic studies.

The human is the first repeat-rich genome to be sequenced, and so we investigated what information could be gleaned from this majority component of the human genome. Although some of the general observations about repeats were suggested by previous studies, the draft genome sequence provides the first comprehensive view, allowing some questions to be resolved and new mysteries to emerge.

Transposon-derived repeats

Most human repeat sequence is derived from transposable elements[142, 143]. We can currently recognize about 45% of the genome as belonging to this class. Much of the remaining 'unique' DNA must also be derived from ancient transposable element copies that have diverged too far to be recognized as such. To describe our analyses of interspersed repeats, it is necessary briefly to review the relevant features of human transposable elements.


CTG GAP
X
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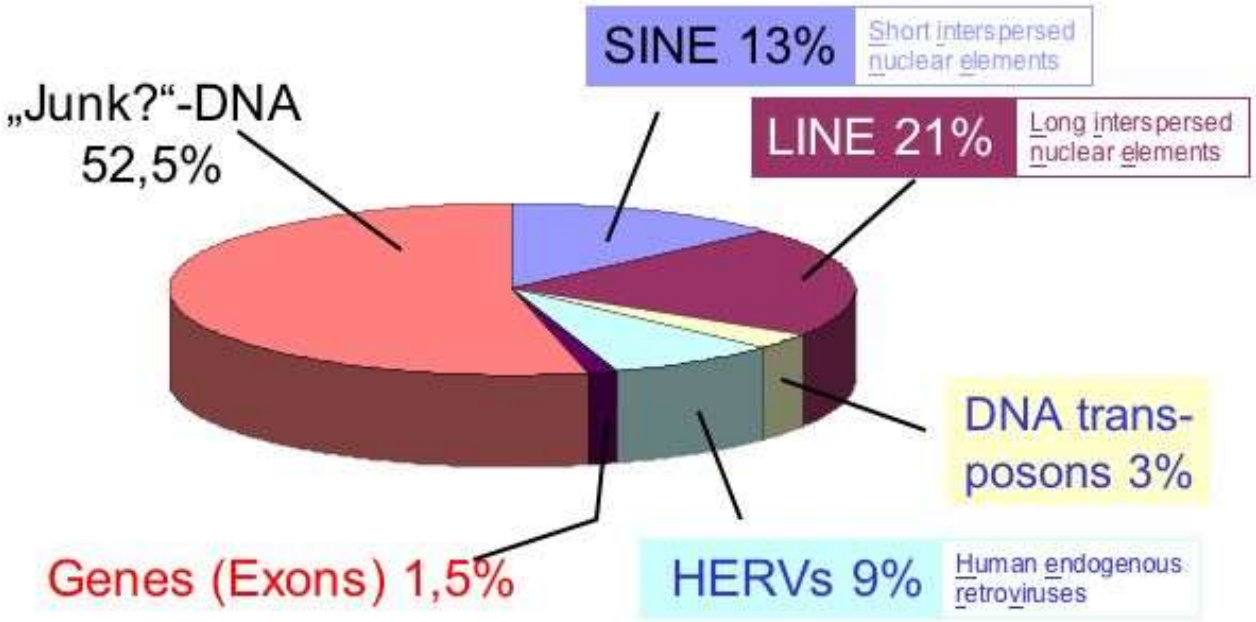
Composition of the human genome



Coding sequences of functioning human genes derived entirely from mobile element sequences

Roy J. Britten*

California Institute of Technology, 101 Dahlia Avenue, Corona del Mar, CA 92625

Contributed by Roy J. Britten, September 20, 2004

Among all of the many examples of mobile elements or "parasitic sequences" that affect the function of the human genome, this paper describes several examples of functioning genes whose sequences have been almost completely derived from mobile elements. There are many examples where the synthetic coding sequences of observed mRNA sequences are made up of mobile element sequences, to an extent of 80% or more of the length of the coding sequences. In the examples described here, the genes have named functions, and some of these functions have been studied. It appears that each of the functioning genes was originally formed from mobile elements and that in some process of molecular evolution a coding sequence was derived that could be translated into a protein that is of some importance to human biology. In one case (AD7C), the coding sequence is 99% made up of a cluster of *Alu* sequences. In another example, the gene BNIP3 coding sequence is 97% made up of sequences from an apparent human endogenous retrovirus. The Syncytin gene coding sequence appears to be made from an endogenous retrovirus envelope gene.

Mobile elements form the majority of the human genome, but that is unimportant compared to all of the functional effects these "parasites" have had on our evolution. Insertions have influenced the regulation of transcription of some genes and the termination of transcription. Hundreds of examples have been recognized where individual exons have sequences that are similar or identical to fragments of mobile element (ME) sequences (1, 2). In many of these cases a single exon is involved, and its transcription yields a variant mRNA (3). The suggestion is that MEs are a source of variation as a result of the insertion of fragments of sequence into functioning genes. Here, I am using MEs (*sensu lento*) to represent any repeated sequence present in many copies in the genome. Smit (4) has made a list of 19 examples of human genes "probably derived from transposable elements."

have been theoretical proposals (10) of the evolutionary role of variety and change in these relationships, particularly in the control of gene expression. There is direct evidence for the evolutionarily significant role of mobile elements/repeats (11–13) and evidence for strong associations and functions including the regulation of transcription. The cases described in this paper add to this earlier evidence in that, in these cases, nearly the entire coding sequences of genes have apparently been derived from ME sequences.

A survey is in process to determine the fraction of the coding sequences recognized at present in available genomes that are derived from ME sequences. The early results turned up the AD7C or neural thread protein gene, which sparked interest because it is apparently derived entirely from a cluster of *Alu* repeated sequences. The investigators pointed out that the coding sequence contained regions of sequence similarity to four *Alu* sequences (14). Table 1 describes this and several other cases.

Methods

A collection of coding sequences was made from the NCBI file seq_gene.md. These were examined by REPEATMASKER, and those that were reported to be almost completely similar in sequence to mobile elements were set aside for further study. The examples examined in the first part of this paper were selected from this list on the basis of their known function. Some of the remainder of them are shown in Table 4.

Results and Discussion

AD7C. AD7C is a neuronal thread protein gene. It encodes a 41-kDa membrane spanning phosphoprotein that is useful in the diagnosis of early Alzheimer's disease (14, 15). The coding sequence is 1,128 nt long and REPEATMASKER shows that it consists of fragments of five (or four, see below) *Alu* sequences. All of the matches are with the reverse complements of the *Alu*

Other Transcript Coding Sequences Apparently Derived from ME.

Table 4 is a list of 49 examples of observed transcripts for which the coding sequences have been determined by computer programs, and these cds are made up from MEs at least to the extent of 80%. This collection was made by running REPEATMASKER against the NCBI collection of gene transcripts in February of 2004, but when checks were made in early March, all of the transcripts so marked had been removed from the collection. It seems likely that someone decided they were junk, which in a sense may be true, but from the point of view of this article they may be considered potentially useful and should be further examined.

Quantitative Biology
Date: Thu, 15 Jan 2004 00:39:29 GMT

Increasing biological complexity is positively correlated with the relative genome-wide expansion of non-protein-coding DNA sequences

Authors: **R.J. Taft, J.S. Mattick**

Prior to the current genomic era it was suggested that the number of protein-coding genes that an organism made use of was a valid measure of its complexity. It is now clear, however, that major incongruities exist and that there is only a weak relationship between biological complexity and the number of protein coding genes. For example, using the protein-coding gene number as a basis for evaluating biological complexity would make urochordates and insects less complex than nematodes, and humans less complex than rice.

Results: We analyzed the ratio of noncoding to total genomic DNA (ncDNA/tgDNA) for 85 sequenced species and found that this ratio correlates well with increasing biological complexity. The ncDNA/tgDNA ratio is generally contained within the bandwidth of 0.05-0.24 for prokaryotes, but rises to 0.26-0.52 in unicellular eukaryotes, and to 0.62-0.985 for developmentally complex multicellular organisms. Significantly, prokaryotic species display a non-uniform species distribution approaching the mean of 0.1177 ncDNA/tgDNA ($p=1.58 \times 10^{-13}$), and a nonlinear ncDNA/tgDNA relationship to genome size ($r=0.15$). Importantly, the ncDNA/tgDNA ratio corrects for ploidy, and is not substantially affected by variable loads of repetitive sequences. Conclusions: We suggest that the observed noncoding DNA increases and compositional patterns are primarily a function of increased information content. It is therefore possible that introns, intergenic sequences, repeat elements, and genomic DNA previously regarded as genetically inert may be far more important to the evolution and functional repertoire of complex organisms than has been previously appreciated.

Annals of the New York Academy of Sciences 981:154-188 (2002)

On the Roles of Repetitive DNA Elements in the Context of a Unified Genomic-Epigenetic System

RICHARD v. STERNBERG
Department of Systematic Biology, National Museum of Natural History, Smithsonian Institution.

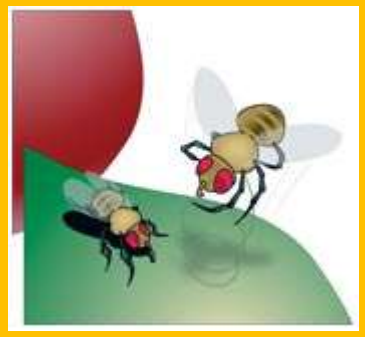
Repetitive DNA sequences comprise a substantial portion of most eukaryotic and some prokaryotic chromosomes. Despite nearly forty years of research, the functions of various sequence families as a whole and their monomer units remain largely unknown. The inability to map specific functional roles onto many repetitive DNA elements (REs), coupled with the taxon-specificity of sequence families, have led many to speculate that these genomic components are "selfish" replicators generating genomic "junk." The purpose of this paper is to critically examine the selfishness, evolutionary effects, and functionality of REs. First, a brief overview of the range of ideas pertaining to RE function is presented. Second, the argument is presented that the selfish DNA "hypothesis" is actually a narrative scheme, that it serves to protect neo-Darwinian assumptions from criticism, and that this story is untestable and therefore not a hypothesis. Third, attempts to synthesize the selfish DNA concept with complex systems models of the genome and RE functionality are critiqued. Fourth, the supposed connection between RE-induced mutations and macroevolutionary events are stated to be at variance with empirical evidence and theoretical considerations. Hypotheses that base phylogenetic transitions in repetitive sequence changes thus remain speculative. Fifth and finally, the case is made for viewing REs as integrally functional components of chromosomes, genomes, and cells. It is argued throughout that a new conceptual framework is needed for understanding the roles of repetitive DNA in genomic/epigenetic systems, and that neo-Darwinian "narratives" have been the primary obstacle to elucidating the effects of these enigmatic components of chromosomes

Genetics: Junk DNA as an evolutionary force

Christian Biémont[1] and Cristina Vieira[1]

Abstract

Transposable elements were long dismissed as useless, but they are emerging as major players in evolution. Their interactions with the genome and the environment affect how genes are translated into physical traits



Nature Reviews Genetics 7, 740-741 (October 2006) | doi:10.1038/nrg1975

Evolution: Jump-starting speciation

Louisa Flintoft

In the process of speciation, when two new species go their separate evolutionary ways, a critical step is reproductive isolation. This happens when groups of individuals acquire differences that prevent them from successfully interbreeding. At the genetic level, the most widely considered cause of this isolation is a change in the function of a key gene in one of the diverging groups, rendering the two populations sexually incompatible. A recent study now provides evidence for an alternative route to speciation in which the jumping of a gene that is essential for fertility to a new location in the genome is the cause.

BioEssays
Volume 31 Issue 7, Pages 715 - 726

Transposable elements and an epigenetic basis for punctuated equilibria

David W. Zeh [1]*, Jeanne A. Zeh [1], Yoichi Ishida [2]

[1]Department of Biology and Program in Ecology, Evolution and Conservation Biology, University of Nevada, Reno, USA
[2]Department of History and Philosophy of Science, University of Pittsburgh, 1017 Cathedral of Learning, Pittsburgh, USA

ABSTRACT

Evolution is frequently concentrated in bursts of rapid morphological change and speciation followed by long-term stasis. We propose that this pattern of punctuated equilibria results from an evolutionary tug-of-war between host genomes and transposable elements (TEs) mediated through the epigenome. According to this hypothesis, epigenetic regulatory mechanisms (RNA interference, DNA methylation and histone modifications) maintain stasis by suppressing TE mobilization. However, physiological stress, induced by climate change or invasion of new habitats, disrupts epigenetic regulation and unleashes TEs. With their capacity to drive non-adaptive host evolution, mobilized TEs can restructure the genome and displace populations from adaptive peaks, thus providing an escape from stasis and generating genetic innovations required for rapid diversification.

Nature Genetics **31**, 200 - 204 (2002)
Published online: 28 May 2002; | doi:10.1038/ng884

Extensive genomic duplication during early chordate evolution

Aoife McLysaght1, 2, Karsten Hokamp1, 2 & Kenneth H. Wolfe1, 2

Opinions on the hypothesis1 that ancient genome duplications contributed to the vertebrate genome range from strong skepticism2, 3, 4 to strong credence5, 6, 7. Previous studies concentrated on small numbers of gene families or chromosomal regions that might not have been representative of the whole genome4, 5, or used subjective methods to identify paralogous genes and regions5, 8. Here we report a systematic and objective analysis of the draft human genome sequence to identify paralogous chromosomal regions (paralogons) formed during chordate evolution and to estimate the ages of duplicate genes. We found that the human genome contains many more paralogons than would be expected by chance. Molecular clock analysis of all protein families in humans that have orthologs in the fly and nematode indicated that a burst of gene duplication activity took place in the period 350−650 Myr ago and that many of the duplicate genes formed at this time are located within paralogons. Our results support the contention that many of the gene families in vertebrates were formed or expanded by large-scale DNA duplications in an early chordate. Considering the incompleteness of the sequence data and the antiquity of the event, the results are compatible with at least one round of polyploidy.

Cytogenetic and Genome Research

Retrotransposable Elements and Gene Evolution

Impact of transposable elements on the evolution of mammalian gene regulation

P. Medstrand[a], L.N. van de Lagemaat[b], C.A. Dunn[b], J.-R. Landry[b], D. Svenback[a], D.L. Mager[b]

[a]Department of Cell and Molecular Biology, Biomedical Centre, Lund University, Lund (Sweden);
[b]Terry Fox Laboratory, BC Cancer Agency, and Department of Medical Genetics, University of British Columbia, Vancouver, British Columbia (Canada)

Abstract.
Transposable elements (TEs) are present in all organisms and nearly half of the human and mouse genome is derived from ancient transpositions. This fact alone suggests that TEs have played a major role in genome organization and evolution. Studies undertaken over the last two decades or so clearly show that TEs of various kinds have played an important role in organism evolution. Here we review the impact TEs have on the evolution of gene regulation and gene function with an emphasis on humans.

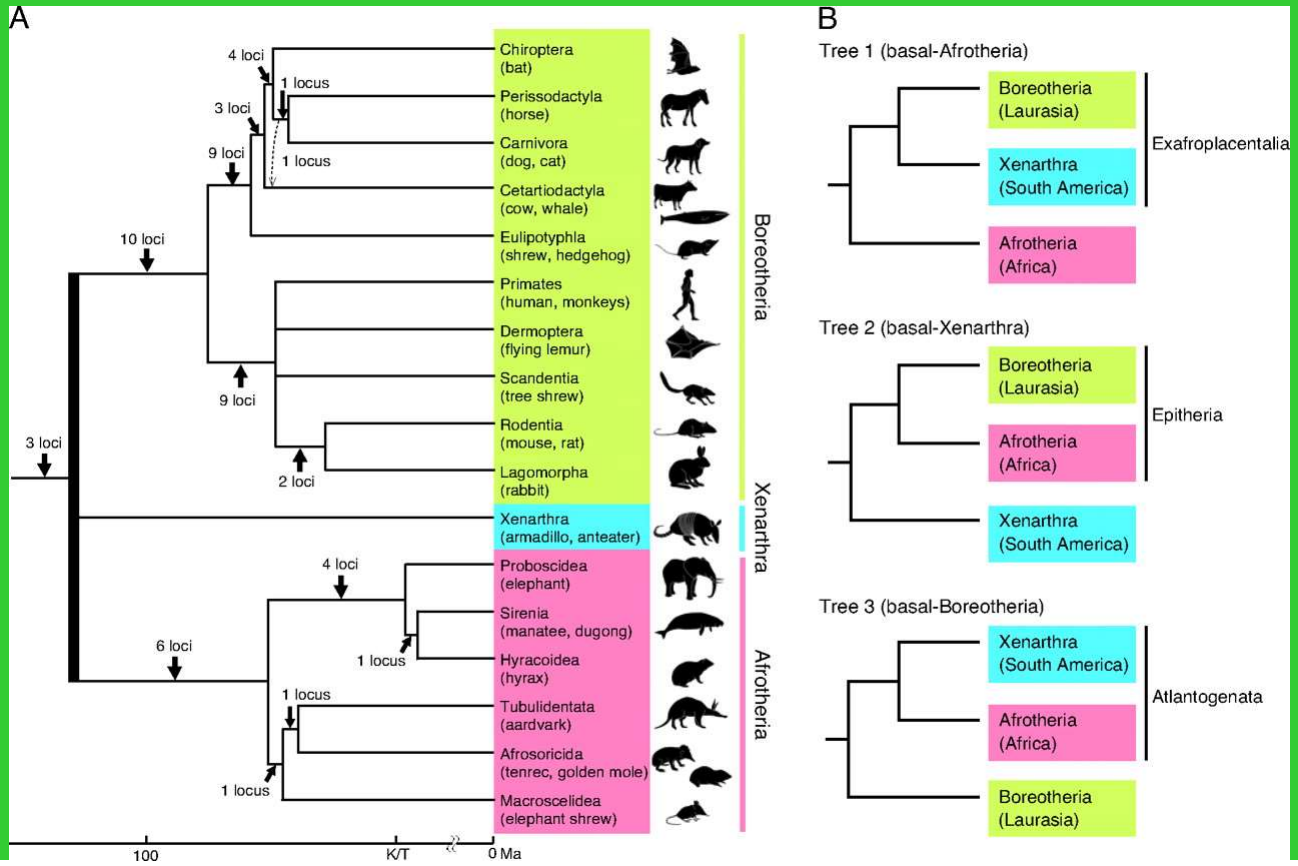
PNAS **March 31, 2009** vol. 106 no. 13 **5235-5240**

Retroposon analysis and recent geological data suggest near-simultaneous divergence of the three superorders of mammals

Hidenori Nishiharaa,
Shigenori Maruyamab and
Norihiro Okadaa,1

Abstract

As a consequence of recent developments in molecular phylogenomics, all extant orders of placental mammals have been grouped into 3 lineages: Afrotheria, Xenarthra, and Boreotheria, which originated in Africa, South America, and Laurasia, respectively. Despite this advancement, the order of divergence of these 3 lineages remains unresolved. Here, we performed extensive retroposon analysis with mammalian genomic data. Surprisingly, we identified a similar number of informative retroposon loci that support each of 3 possible phylogenetic hypotheses: the basal position for Afrotheria (22 loci), Xenarthra (25 loci), and Boreotheria (21 loci). This result indicates that the divergence of the placental common ancestor into the 3 lineages occurred nearly simultaneously.



TREE-1256; No. of Pages 10
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Promiscuous DNA: horizontal transfer of transposable elements and why it matters for eukaryotic evolution

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Horizontal transfer is thepassage of genetic material between genomes by means other than parent-to-off- spring inheritance. Although the transfer of genes is thought to be crucial in prokaryotic evolution, few instances of horizontal gene transfer have been reported in multicellular eukaryotes; instead, most cases involve transposable elements. With over 200 cases now documented, it is possible to assess the importance of horizontal transfer for the evolution of transposable elements and their host genomes. We review criteria for detecting horizontal transfers and examine recent examples of the phenomenon, shedding light on its mechanistic underpinnings, including the role of host– parasite interactions. We argue that the introduction of transposable elements by horizontal transfer in eukaryotic genomes has been a major force propelling genomic variation and biological innovation.

Gene
Volume 365, 3 January 2006, Pages 104-110

Transposable elements as a significant source of transcription regulating signals

Bartley G. Thornburg[a, 1], Valer Gotea[a, b, 1] and Wojciech Makałowski[a, b],

Abstract

Transposable elements (TEs) are major components of eukaryotic genomes, contributing about 50% to the size of mammalian genomes. TEs serve as recombination hot spots and may acquire specific cellular functions, such as controlling protein translation and gene transcription. The latter is the subject of the analysis presented. We scanned TE sequences located in promoter regions of all annotated genes in the human genome for their content in potential transcription regulating signals. All investigated signals are likely to be over-represented in at least one TE class, which shows that TEs have an important potential to contribute to pre-transcriptional gene regulation, especially by moving transcriptional signals within the genome and thus potentially leading to new gene expression patterns. We also found that some TE classes are more likely than others to carry transcription regulating signals, which can explain why they have different retention rates in regions neighboring genes.

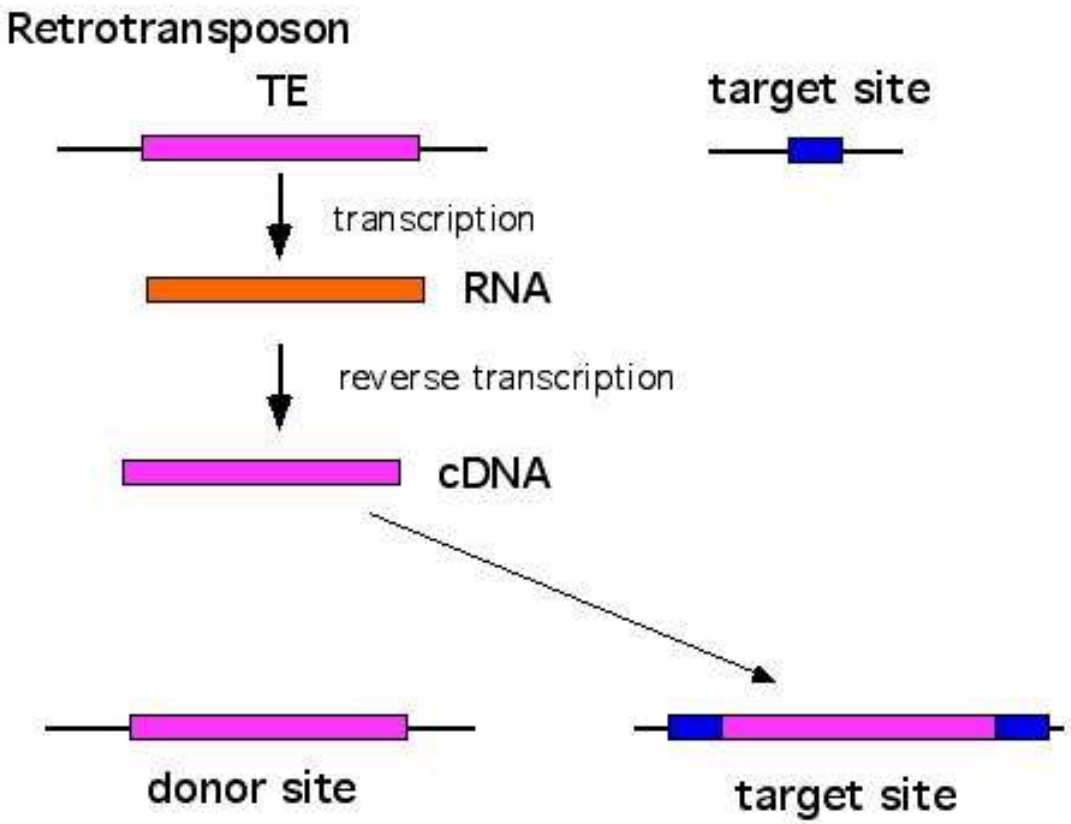
Stress activation and genomic impact of Tnt1 retrotransposons in Solanaceae

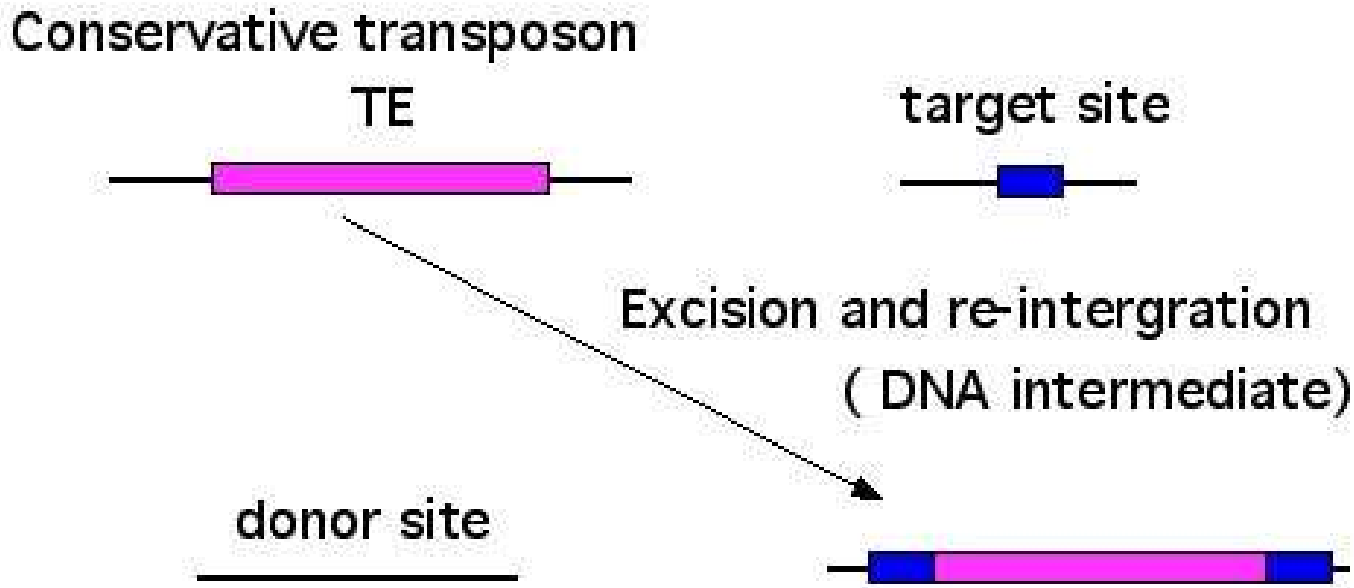
M.-A. Grandbastien[a], C. Audeon[a], E. Bonnivard[a], J.M. Casacuberta[b], B. Chalhoub[a], A.-P.P. Costa[a,c], Q.H. Le[a], D. Melayah[a], M. Petit[a], C. Poncet[a], S.M. Tam[a], M.-A. Van Sluys[c], C. Mhiri[a]

Cytogenetic and Genome Research 2005;110:229-241 (DOI: 10.1159/000084957)

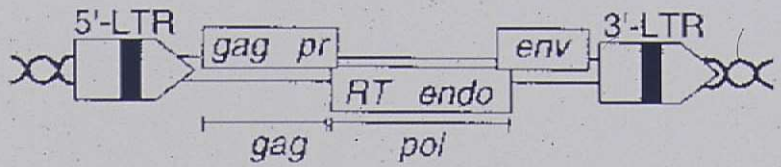
Abstract.

Tnt1 elements are a superfamily of LTR-retrotransposons distributed in the Solanaceae plant family and represent good model systems for studying regulatory and evolutionary controls established between hosts and transposable elements. Tnt1 retrotransposons tightly control their activation, by restricting expression to specific conditions. The Tnt1A element, originally discovered in tobacco, is expressed in response to stress, and its activation by microbial factors is followed by amplification, demonstrating that factors of pathogen origin can generate genetic diversity in plants. The Tnt1A promoter has the potential to be activated by various biotic and abiotic stimuli but a number of these are specifically repressed in tobacco and are revealed only when the LTR promoter is placed in a heterologous context


Retrotransposon
TE
target site
transcription
RNA
reverse transcription
cDNA
donor site
target site


Conservative transposon
TE
target site
Excision and re-intergration
(DNA intermediate)
donor site

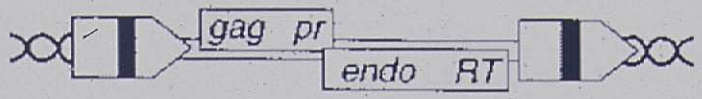
Retroviruses



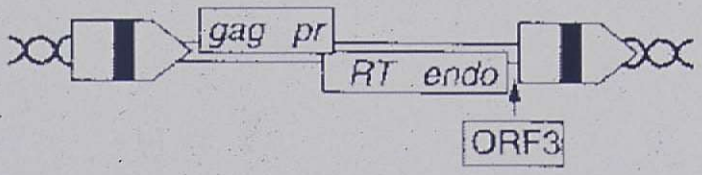
Retrotransposons

Subclass I: LTR retrotransposons

Superfamily *Ty1/copia*

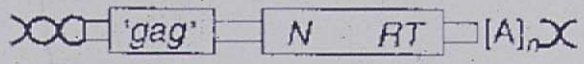


Superfamily *Ty3/gypsy*

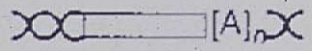


Subclass II: Non-LTR retrotransposons

Superfamily LINEs



Superfamily SINEs



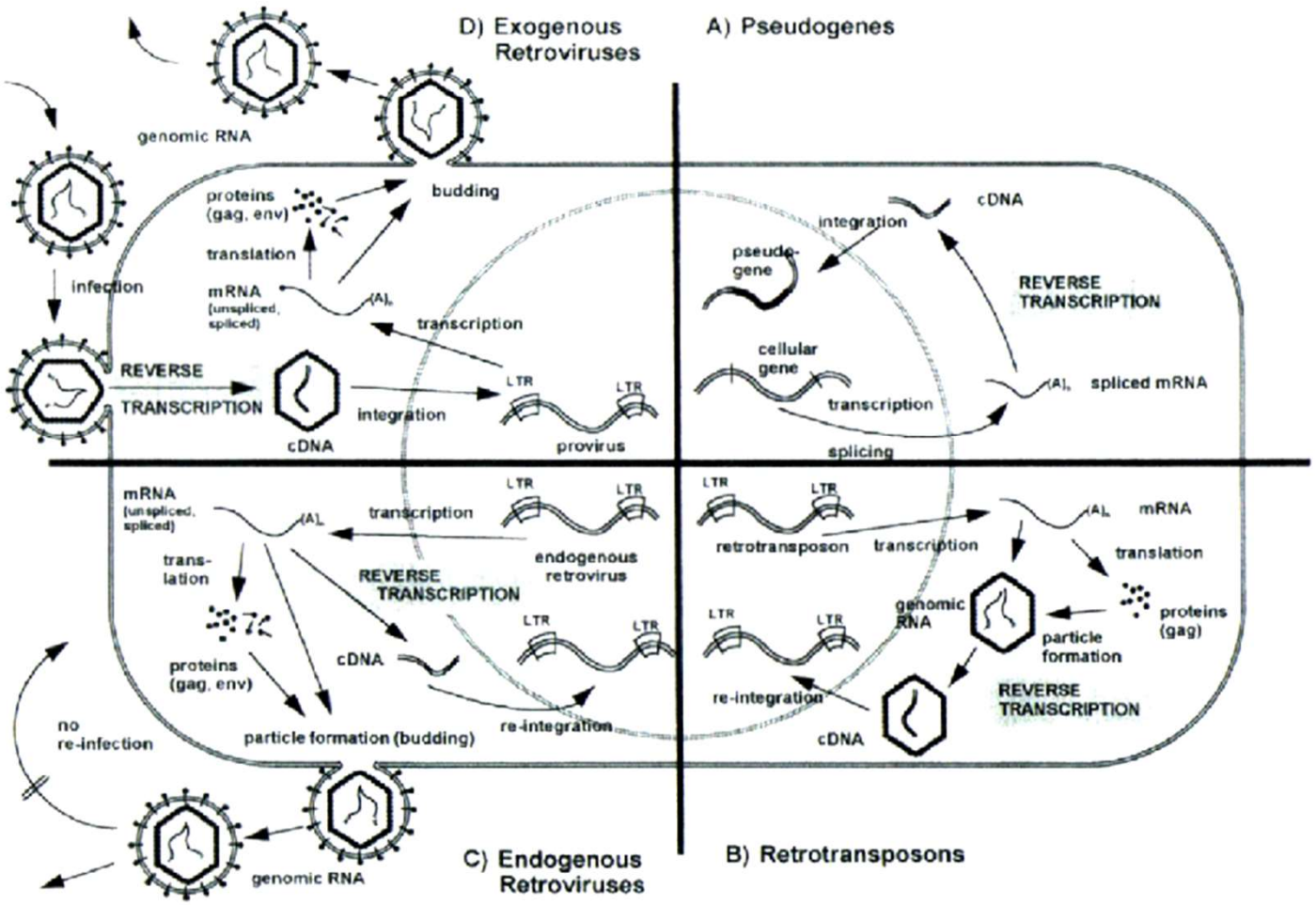


FIG. 2. Life cycles of retroelements. (*A*) Generation of pseudogenes. (*B*) Transposition of retrotransposons. (*C*) Expression and amplification of ERVs. (*D*) Replication cycle of exogenous retroviruses.

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GLOSARIO

Virus: entidad acelular infecciosa que, aunque puede sobrevivir extracelularmente, es un parásito absoluto porque solamente es capaz de replicarse en el seno de células vivas específicas, pero sin generar energía ni ninguna actividad metabólica. Los componentes permanentes de los virus son ácido nucleico (ADN o ARN, de una o de dos cadenas) envuelto por una cubierta proteica llamada cápside.

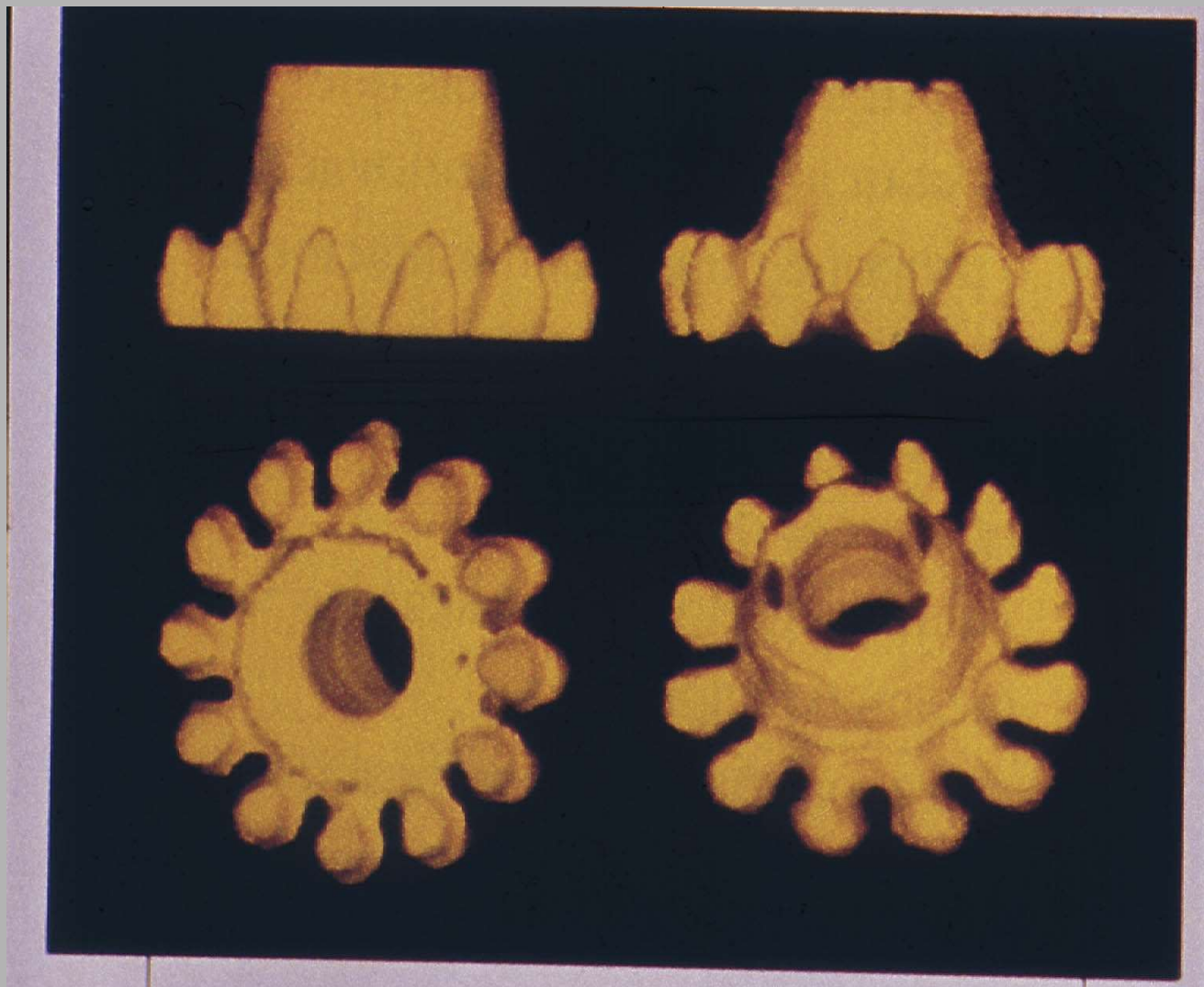
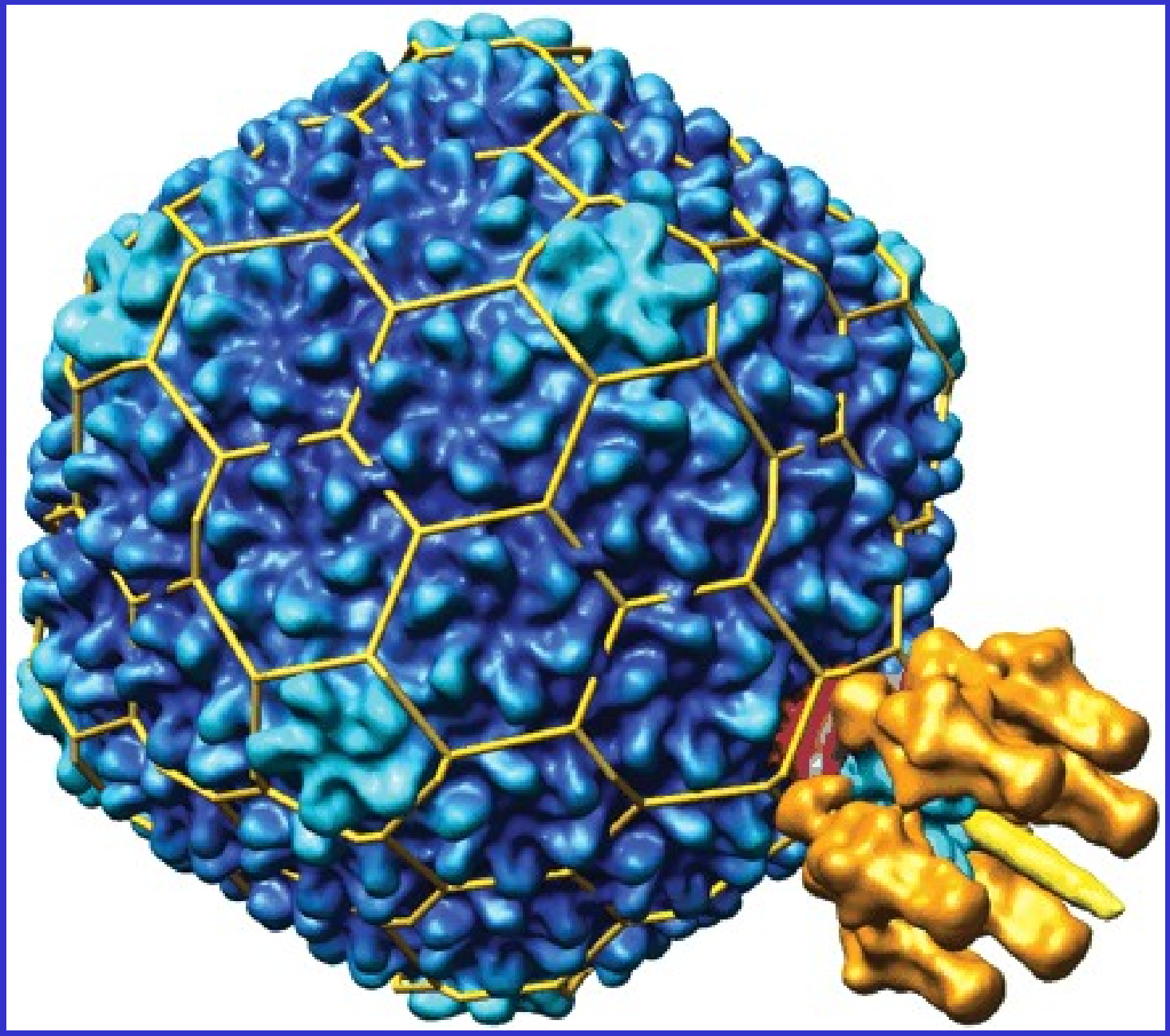
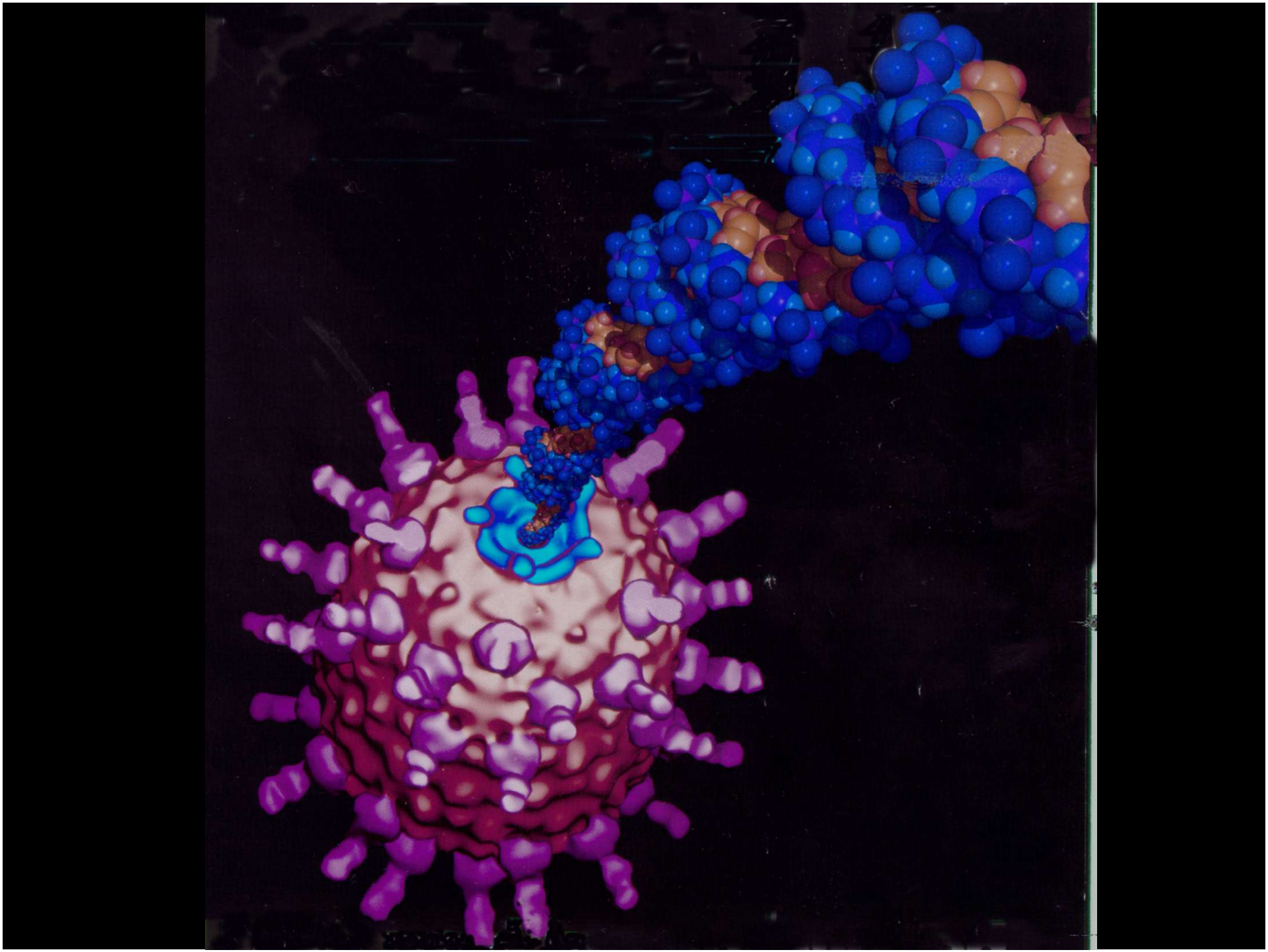


Imagen tridimencional del bacteriófago Ø29, obtenida por microscopía de fuerza atómica (Foto José Carrascosa.)





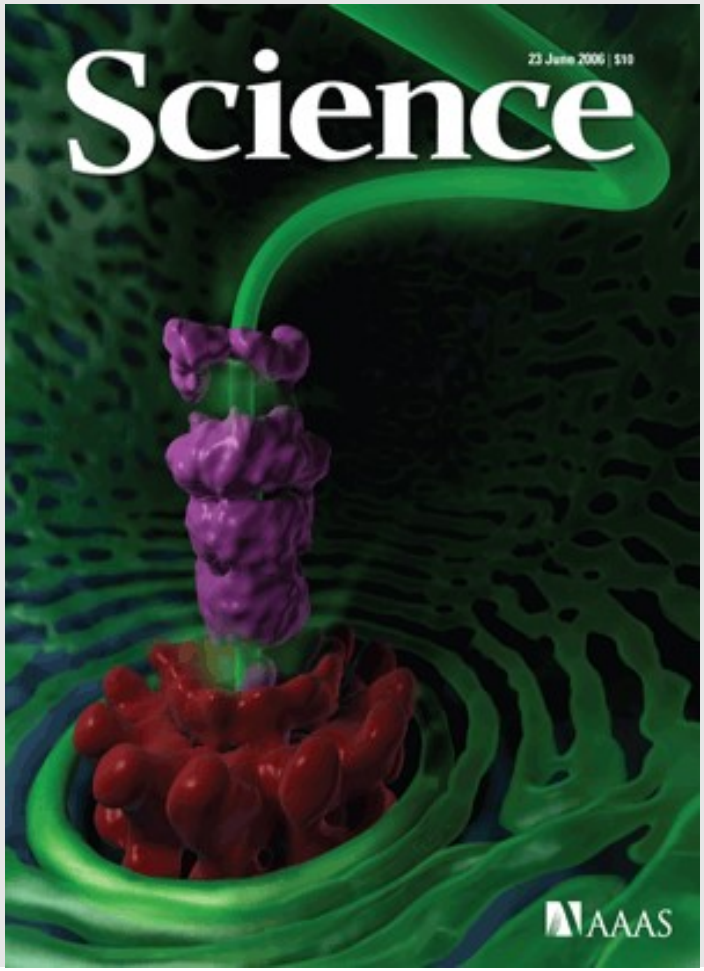
SMITH, D.E. et al., 2001. ***The bacteriophage ϕ 29 portal motor can package DNA against a large internal force.*** **Nature, vol 413: 748-751.**

"El bacteriófago ϕ 29 empaqueta su doble cadena de ADN de 6,6 micrómetros de longitud en una cápsida de 45x54 nanómetros, por medio de un complejo portal que hidroliza ATP. Este proceso es remarcable, porque han de ser superadas energías entrópicas, electrostáticas y de plegamiento para empaquetar el ADN hasta un estado de densidad casi cristalina"

"Este motor puede trabajar contra fuerzas de 55 piconewtons en media, convirtiéndole en uno de los más potentes motores moleculares reportados hasta la fecha"/ .../"Nuestros datos sugieren que ésta fuerza debe estar disponible para iniciar la eyección de ADN de la cápsida durante la infección".

COVER The pressure-sensing mechanism of bacteriophage P22 that signals when the phage head is full, viewed from the interior. The portal complex (red) is hypothesized to change conformation when the virus is full of DNA (green), which signals the packaging motors to stop. Such a sensor may serve as a drug target in human viruses. See page 1791.

Image: G. Johnson and G. Lander



J Theor Biol. 2006 Nov 7;243(1):54-63.

Sex and the eukaryotic cell cycle is consistent with a viral ancestry for the eukaryotic nucleus.

Bell PJ.

Macquarie University, Biological Sciences, Talavera Road, North Ryde, Sydney NSW 2109, Australia.
pbell@rna.bio.mq.edu.au

The origin of the eukaryotic cell cycle, including mitosis, meiosis, and sex are as yet unresolved aspects of the evolution of the eukaryotes. The wide phylogenetic distribution of both mitosis and meiosis suggest that these processes are integrally related to the origin of the earliest eukaryotic cells. According to the viral eukaryogenesis (VE) hypothesis, the eukaryotes are a composite of three phylogenetically unrelated organisms: a viral lysogen that evolved into the nucleus, an archaeal cell that evolved into the eukaryotic cytoplasm, and an alpha-proteobacterium that evolved into the mitochondria. In the extended VE hypothesis presented here, the eukaryotic cell cycle arises as a consequence of the derivation of the nucleus from a lysogenic DNA virus.

Biosemiotics, Volume 1, Number 2. 1875-1342. 2008

The Viral Origins of Telomeres and Telomerases and their Important Role in Eukaryogenesis and Genome Maintenance

Guenther Witzany

Abstract

Whereas telomeres protect terminal ends of linear chromosomes, telomerases identify natural chromosome ends, which differ from broken DNA and replicate telomeres. Although telomeres play a crucial role in the linear chromosome organization of eukaryotic cells, their molecular syntax most probably descended from an ancient retroviral competence. This indicates an early retroviral colonization of large double-stranded DNA viruses, which are putative ancestors of the eukaryotic nucleus. This contribution demonstrates an advantage of the biosemiotic approach towards our evolutionary understanding of telomeres, telomerases, other reverse transcriptases and mobile elements. Their role in genetic/genomic content organization and maintenance is no longer viewed as an object of randomly derived alterations (mutations) but as a highly sophisticated hierarchy of regulatory networks organized and coordinated by natural genome-editing competences of viruses.

Virology
Volume 297, Issue 2,
5 June 2002, Pages 220-225

Developmental Expression of HERV-R (ERV3) and HERV-K in Human Tissue

Ann-Catrin Andersson[a, 1], Patrick J. W. Venables[b], Ralf R. Tönjes[c], Jürgen Scherer[c], Lars Eriksson[a] and Erik Larsson[a]

Abstract

The human endogenous retroviruses (HERVs), ERV3 (HERV-R) and HERV-K, are both known to be transcriptionally active in human placenta. In the case of ERV3 there is also indirect evidence for its participation in cellular differentiation. In this study we examined the expression of ERV3 (HERV-R) and HERV-K in human normal fetal tissues by *in situ* hybridization. The highest level of ERV3 *env* expression was detected in primitive adrenal cortex. Elevated levels of expression were also found in the following developing tissues: kidneys (tubules), tongue, heart, liver, and central nervous system. Tissue-specific expression was found for HERV-K *rec* (former *cORF*) but not for *pol/int* transcripts. The highest *rec* expression was found in placenta and levels slightly higher than sense control were found in the rest of the tissues examined. *Pol/Int* was not possible to quantitate. It appears that ERV3 is expressed in an organ-specific way during embryogenesis and might suggest a possible role in the development and differentiation of human tissues.

J Virol. 2005 January; 79(1): 341–352.

Comprehensive Analysis of Human Endogenous Retrovirus Transcriptional Activity in Human Tissues with a Retrovirus-Specific Microarray

Wolfgang Seifarth,1*† Oliver Frank,1† Udo Zeilfelder,1 Birgit Spiess,1 Alex D. Greenwood,2,3 Rüdiger Hehlmann,1 and Christine Leib-Mösch1,2

ABSTRACT

In the present study, we have investigated the transcriptional activity of representative members of 20 HERV families in 19 different normal human tissues. Qualitative evaluation of chip hybridization signals and quantitative analysis by real-time RT-PCR revealed distinct HERV activity in the human tissues under investigation, suggesting that HERV elements are active in human cells in a tissue-specific manner. Most active members of HERV families were found in mRNA prepared from skin, thyroid gland, placenta, and tissues of reproductive organs. In contrast, only few active HERVs were detectable in muscle cells. Human tissues that lack HERV transcription could not be found, confirming that human endogenous retroviruses are permanent components of the human transcriptome. Distinct activity patterns may reflect the characteristics of the regulatory machinery in these cells, e.g., cell type-dependent occurrence of transcriptional regulatory factors.

Trends in Genetics

Volume 22, Issue 2 , February 2006, Pages 90-95

Bacteriophage origins of mitochondrial replication and transcription proteins

Timothy E. Shutt and Michael W. Gray

Program in Evolutionary Biology, Canadian Institute for Advanced Research, Department of Biochemistry and Molecular Biology, Dalhousie University, Sir Charles Tupper Medical Building, 5850 College Street, Halifax, NS, Canada, B3H 1X5

Available online 20 December 2005.

Mounting evidence suggests that key components of the mitochondrial transcription and replication apparatus are derived from the T-odd lineage of bacteriophage rather than from an α-Proteobacterium, as the endosymbiont hypothesis would predict. We propose that several mitochondrial replication genes were acquired together from an ancestor of T-odd phage early in the evolution of the eukaryotic cell, at the time of the mitochondrial endosymbiosis. We further propose that at a later stage the single-subunit RNA polymerase, originally acquired for mitochondrial DNA replication, was co-opted to serve in mitochondrial transcription.

Nature **432**, 995-1001 (23 December 2004) | doi: 10.1038/nature03157

Transposition of *hAT* elements links transposable elements and V(D)J recombination

Liqin Zhou , Rupak Mitra , Peter W. Atkinson , Alison Burgess Hickman , Fred Dyda and Nancy L. Craig1

Abstract

Transposons are DNA sequences that encode functions that promote their movement to new locations in the genome. If unregulated, such movement could potentially insert additional DNA into genes, thereby disrupting gene expression and compromising an organism's viability. Transposable elements are classified by their transposition mechanisms and by the transposases that mediate their movement. The mechanism of movement of the eukaryotic *hAT* superfamily elements was previously unknown, but the divergent sequence of *hAT* transposases from other elements suggested that these elements might use a distinct mechanism. Here we have analysed transposition of the insect *hAT* element *Hermesin vitro*. Like other transposons, *Hermes* excises from DNA via double-strand breaks between the donor-site DNA and the transposon ends, and the newly exposed transposon ends join to the target DNA. Interestingly, the ends of the donor double-strand breaks form hairpin intermediates, as observed during V(D)J recombination, the process which underlies the combinatorial formation of antigen receptor genes. Significant similarities exist in the catalytic amino acids of *Hermes* transposase, the V(D)J recombinase RAG, and retroviral integrase superfamily transposases, thereby linking the movement of transposable elements and V(D)J recombination.

Science, Vol 304, Issue 5671, 734-736 , 30 April 2004

Identification of Virus-Encoded MicroRNAs

Sébastien Pfeffer,[1] Mihaela Zavolan,[2] Friedrich A. Grässer,[3] Minchen Chien,[4] James J. Russo,[4] Jingyue Ju,[4] Bino John,[5] Anton J. Enright,[5] Debora Marks,[4] Chris Sander,[5] Thomas Tuschl[1]

RNA silencing processes are guided by small RNAs that are derived from double-stranded RNA. To probe for function of RNA silencing during infection of human cells by a DNA virus, we recorded the small RNA profile of cells infected by Epstein-Barr virus (EBV). We show that EBV expresses several microRNA (miRNA) genes. Given that miRNAs function in RNA silencing pathways either by targeting messenger RNAs for degradation or by repressing translation, we identified viral regulators of host and/or viral gene expression.

J Mol Biol. 2001 Apr 6;307(4):1011-21

The prion protein has DNA strand transfer properties similar to retroviral nucleocapsid protein.

Gaius C, Auxilien S, **Pechoux C**, Dormont D, Swietnicki W, Morillas M, Surewicz W, Nandi P.

LaboRetro, Unite de Virologie Humaine INSERM-ENS #412, ENS de Lyon, 46 Allee d'Italie, Lyon, 69 364, France.

The transmissible spongiform encephalopathies are fatal neurodegenerative diseases that are associated with the accumulation of a protease-resistant form of the cellular prion protein (PrP). Although PrP is highly conserved and widely expressed in vertebrates, its function remains a matter of speculation. Indeed PrP null mice develop normally and are healthy. Recent results show that PrP binds to nucleic acids in vitro and is found associated with retroviral particles. Furthermore, in mice the scrapie infectious process appears to be accelerated by MuLV replication. Our results show that the human prion protein (huPrP) functionally resembles NCp7 of HIV-1.

Proceedings of the National Academy of Sciences, Vol 87, 409-413, Copyright © 1990 by National Academy of Sciences

ARTICLE

Identification of a Viral Gene Encoding a Ubiquitin-Like Protein

LA Guarino

The baculovirus Autographa californica nuclear polyhedrosis virus (AcMNPV, which is representative of the MNPV subtype in which the virions may contain many nucleocapsids within a single viral envelope) encodes a protein, v-ubi, that has 76% identity with the eukaryotic protein ubiquitin. Transcriptional mapping indicated that the gene for v-ubi was transcribed during the late phase of viral infection. Two transcriptional start sites potentially encoding v-ubi were identified. Both sites were contained within a sequence motif common to baculovirus late genes. A recombinant virus, AcUbi-ßGal, encoding a ubiquitin-ß-galactosidase fusion protein was constructed to monitor the temporal regulation of v-ubi gene during viral infection. The fusion protein was expressed maximally at 14-18 hr postinfection, consistent with its classification as a late protein. The amount of ubiquitin-ß-galactosidase fusion protein that accumulated in AcUbi-ßGal-infected cells by 48 hr postinfection was
14% of the level of ß-galactosidase that was synthesized under control of the polyhedrin promoter. Transcriptional analysis confirmed that synthesis of the fusion protein was directed by the v-ubi gene promoter.

J Gen Virol 85 (2004), 2741-2754; DOI 10.1099/vir.0.80320-0

Review article

Glycosyltransferases encoded by viruses

Nicolas Markine-Goriaynoff1, Laurent Gillet1, James L. Van Etten2, Haralambos Korres3, Naresh Verma3 and Alain Vanderplasschen1
1 Immunology-Vaccinology (B43b), Department of Infectious and Parasitic Diseases, Faculty of Veterinary Medicine, University of Liège, B-4000 Liège, Belgium
2 Department of Plant Pathology and Nebraska Center for Virology, University of Nebraska, Lincoln, NE 68583-0722, USA
3 School of Biochemistry & Molecular Biology, Faculty of Science, Australian National University, Canberra, ACT 0200, Australia

ABSTRACT

Studies of cellular biology in recent decades have highlighted the crucial roles of glycans in numerous important biological processes, raising the concept of glycomics that is now considered as important as genomics, transcriptomics and proteomics. For millions of years, viruses have been co-evolving with their hosts. Consequently, during this co-evolution process, viruses have acquired mechanisms to mimic, hijack or sabotage host processes that favour their replication, including mechanisms to modify the glycome. The importance of the glycome in the regulation of host–virus interactions has recently led to a new concept called ‘glycovirology’. One fascinating aspect of glycovirology is the study of how viruses affect the glycome. Viruses reach that goal either by regulating expression of host glycosyltransferases or by expressing their own glycosyltransferases. This review describes all virally encoded glycosyltransferases and discusses their established or putative functions. The description of these enzymes illustrates several intriguing aspects of virology and provides further support for the importance of glycomics in biological processes.

Molecular Biology and Evolution: Vol. 20, No. 6, pp. 979–987.

Genome-Wide Survey for Genes Horizontally Transferred from Cellular Organisms to Baculoviruses

Austin L. Hughes,[a, c] and Robert Friedman[a, b]

ABSTRACT

The phylogeny of 13 viral species in the genera *Granulovirus* and *Nucleopolyhedrovirus* (family Baculoviridae) was reconstructed on the basis of 22 conserved protein families shared by all species, and a comprehensive homology search and phylogenetic analysis of the complete genomes of these viruses was used to test for horizontal gene transfer from cellular organisms. Statistically significant evidence of horizontal transfer was found in the case of six protein families (DNA ligase, ribonucleotide reductase 1, SNF2 global transactivator, inhibitor of apoptosis, chitinase, and UDP-glucosyltransferase). Three of these families are known to play key roles in the infection of insect hosts by these viruses. There was evidence that two of these (inhibitor of apoptosis and UDP-glucosyltransferase) were derived from the insect host. By contrast, the gene encoding chitinase in these viruses was evidently derived from a group of bacteria (the gamma subdivision of proteobacteria), which use chitinase to break down fungal chitins.

PNAS **October 28, 2003** vol. 100 no. 22 **12841-12846**

An endogenous retroviral long terminal repeat is the dominant promoter for human β1,3-galactosyltransferase 5 in the colon

Catherine A. Dunn*,†, Patrik Medstrand‡, and Dixie L. Mager*,†,§

Abstract

LTRs of endogenous retroviruses are known to affect expression of several human genes, typically as a relatively minor alternative promoter. Here, we report that an endogenous retrovirus LTR acts as one of at least two alternative promoters for the human β1,3-galactosyltransferase 5 gene, involved in type 1 Lewis antigen synthesis, and show that the LTR promoter is most active in the gastrointestinal tract and mammary gland. Indeed, the LTR is the dominant promoter in the colon, indicating that this ancient retroviral element has a major impact on gene expression.

PNAS | **September 26, 2006** | vol. 103 | no. 39 | **14390-14395**

BIOLOGICAL SCIENCES / DEVELOPMENTAL BIOLOGY

Endogenous retroviruses regulate periimplantation placental growth and differentiation.

Kathrin A. Dunlap*, Massimo Palmarini, Mariana Varela, Robert C. Burghardt, Kanako Hayashi*, Jennifer L. Farmer*, and Thomas E. Spencer*, *Center for Animal Biotechnology and Genomics, Department of Animal Science, and Image Analysis Laboratory, Department of Veterinary Integrative Biosciences, Texas A&M University, College Station, TX 77843; and Institute of Comparative Medicine, University of Glasgow Veterinary School, Glasgow G61 1QH, United Kingdom

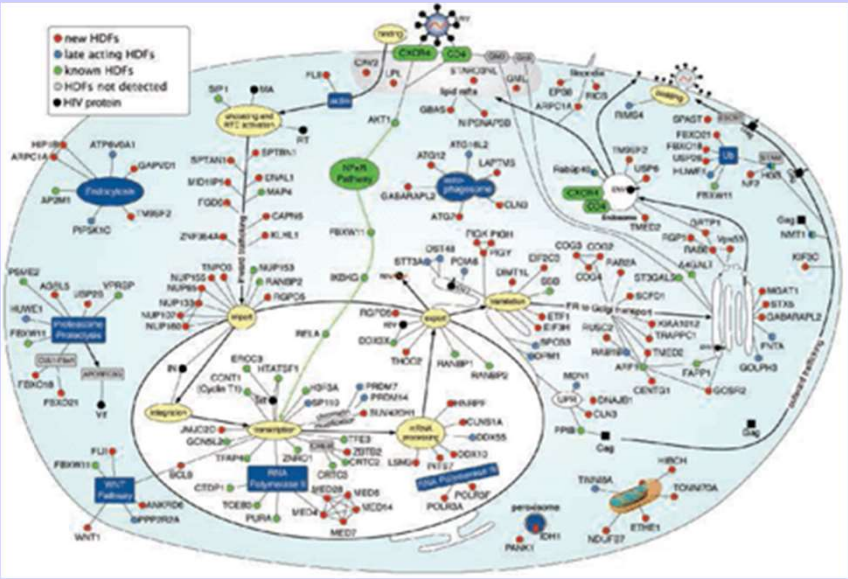
Edited by George E. Seidel, Jr., Colorado State University, Fort Collins, CO, and approved August 8, 2006 (received for review May 10, 2006)

Endogenous retroviruses (ERVs) are fixed and abundant in the genomes of vertebrates. Circumstantial evidence suggests that ERVs play a role in mammalian reproduction, particularly placental morphogenesis, because intact ERV envelope genes were found to be expressed in the syncytiotrophoblasts of human and mouse placenta and to elicit fusion of cells *in vitro*.

Science 11 January 2008:
Vol. 319. no. 5860, pp. 143 - 144
DOI:
10.1126/science.319.5860.143

VIROLOGY:
HIV Gets By With a Lot of Help From Human Host

Jon Cohen



Complex relationship. HIV (*top*, purple) relies on more than 200 human proteins to infect immune cells, enter the nucleus, integrate itself into the chromosomes, and then make copies of itself.
CREDIT: A. L. BRASS *ET AL.*, *SCIENCE*

HIV is ridiculously simple yet astonishingly complex. The virus contains a mere 9000 bases of RNA--one-millionth the amount of genetic material in a human cell--and a paltry suite of nine genes that code for a measly 15 proteins. Yet this virus can relentlessly nibble at immune cells until the entire system collapses, opening the door for a vast array of illnesses and, ultimately, death. For HIV to do its damage, however, it must repeatedly infect new cells and copy itself, a feat that requires help from its human host.

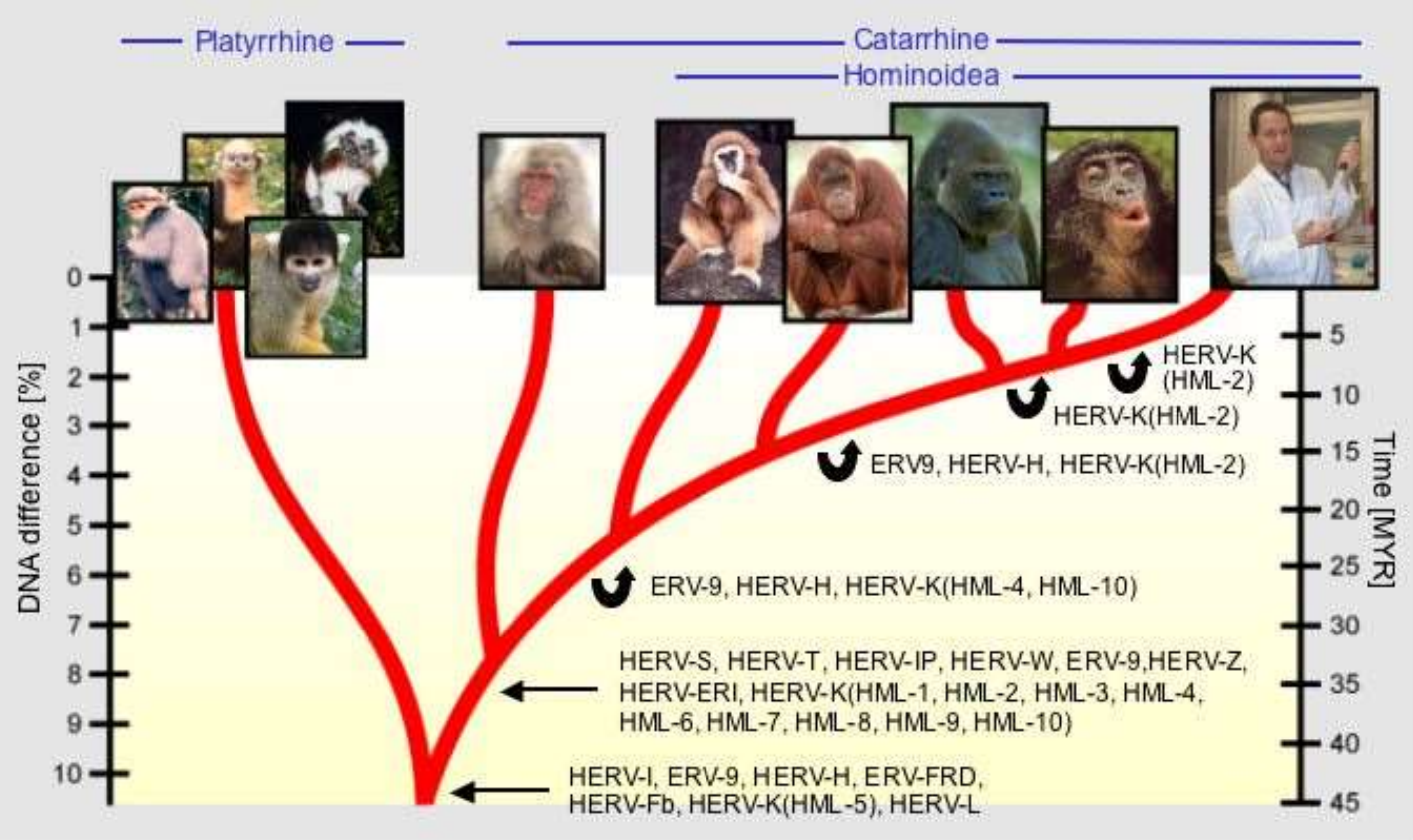
Nature Genetics **29**, 487 - 489 (2001)
Published online: 12 November 2001; | doi:10.1038/ng775

Evidence for genomic rearrangements mediated by human endogenous retroviruses during primate evolution

Jennifer F. Hughes & John M. Coffin
Department of Molecular Biology and Microbiology and Program in Genetics, Tufts University School of Medicine, 136 Harrison Avenue, Boston, Massachusetts 02111, USA.

Human endogenous retroviruses (HERVs), which are remnants of past retroviral infections of the germline cells of our ancestors , make up as much as 8% of the human genome and may even outnumber genes . Most HERVs seem to have entered the genome between 10 and 50 million years ago, and they comprise over 200 distinct groups and subgroups . Although repeated sequence elements such as HERVs have the potential to lead to chromosomal rearrangement through homologous recombination between distant loci, evidence for the generality of this process is lacking. To gain insight into the expansion of these elements in the genome during the course of primate evolution, we have identified 23 new members of the HERV-K (HML-2) group, which is thought to contain the most recently active members. Here we show, by phylogenetic and sequence analysis, that at least 16% of these elements have undergone apparent rearrangements that may have resulted in large-scale deletions, duplications and chromosome reshuffling during the evolution of the human genome.

Integration and expansion of HERVs in primates



Acta Biotheoretica (2006) 54:235_253
DOI: 10.1007/s10441-007-9000-7

NATURAL GENOME-EDITING COMPETENCES OF VIRUSES

Günther Witzany

Received 4 October 2006; Accepted 22 December 2006

ABSTRACT

It is becoming increasingly evident that the driving forces of evolutionary novelty are not randomly derived chance mutations of the genetic text, but a precise genome editing by omnipresent viral agents. These competences integrate the whole toolbox of natural genetic engineering, replication, transcription, translation, genomic imprinting, genomic creativity, enzymatic inventions and all types of genetic repair patterns. Even the non-coding, repetitive DNA sequences which were interpreted as being ancient remnants of former evolutionary stages are now recognized as being of viral descent and crucial for higherorder regulatory and constitutional functions of protein structural vocabulary.

Mobile DNA 2010, **1:**4doi:10.1186/1759-8753-1-4

Mobile DNA and evolution in the 21st century

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Introduction: summary of the argument

The review assumes that readers of this journal are familiar with the actions of mobile DNA and other genome restructuring functions. It will try to integrate that familiarity into the historical development of evolutionary concepts and incorporate recent discoveries from genome sequencing. Just as our knowledge of mobile DNA has introduced new ways of thinking about hereditary change, the results of sequence analysis have documented several types of genome alterations at key places in evolutionary history, alterations which are notable because they happened within a single generation and affected multiple cellular and organismal characters at the same time: horizontal transfers of large DNA segments, cell fusions and symbioses, and whole genome doublings (WGDs). These rapid multi-character changes are fundamentally different from the slowly accumulating small random variations postulated in Darwinian and neo-Darwinian theory.

Annual Review of Genetics
Vol. 36: 389-410 (Volume publication date December 2002)
(doi:10.1146/annurev.genet.36.040202.092802)

CHROMOSOME REARRANGEMENTS AND TRANSPOSABLE ELEMENTS

Wolf-Ekkehard Lönnig and Heinz Saedler
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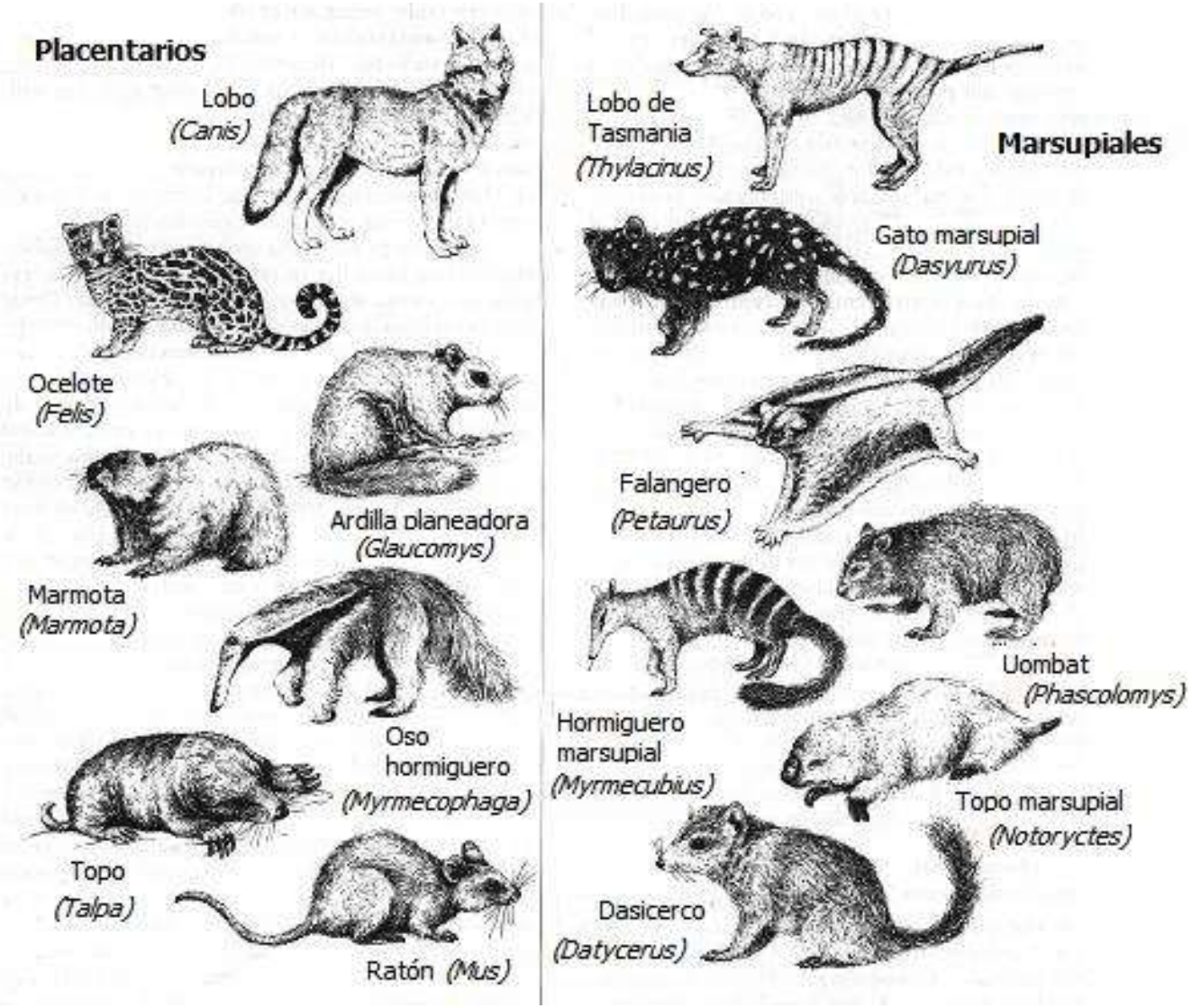
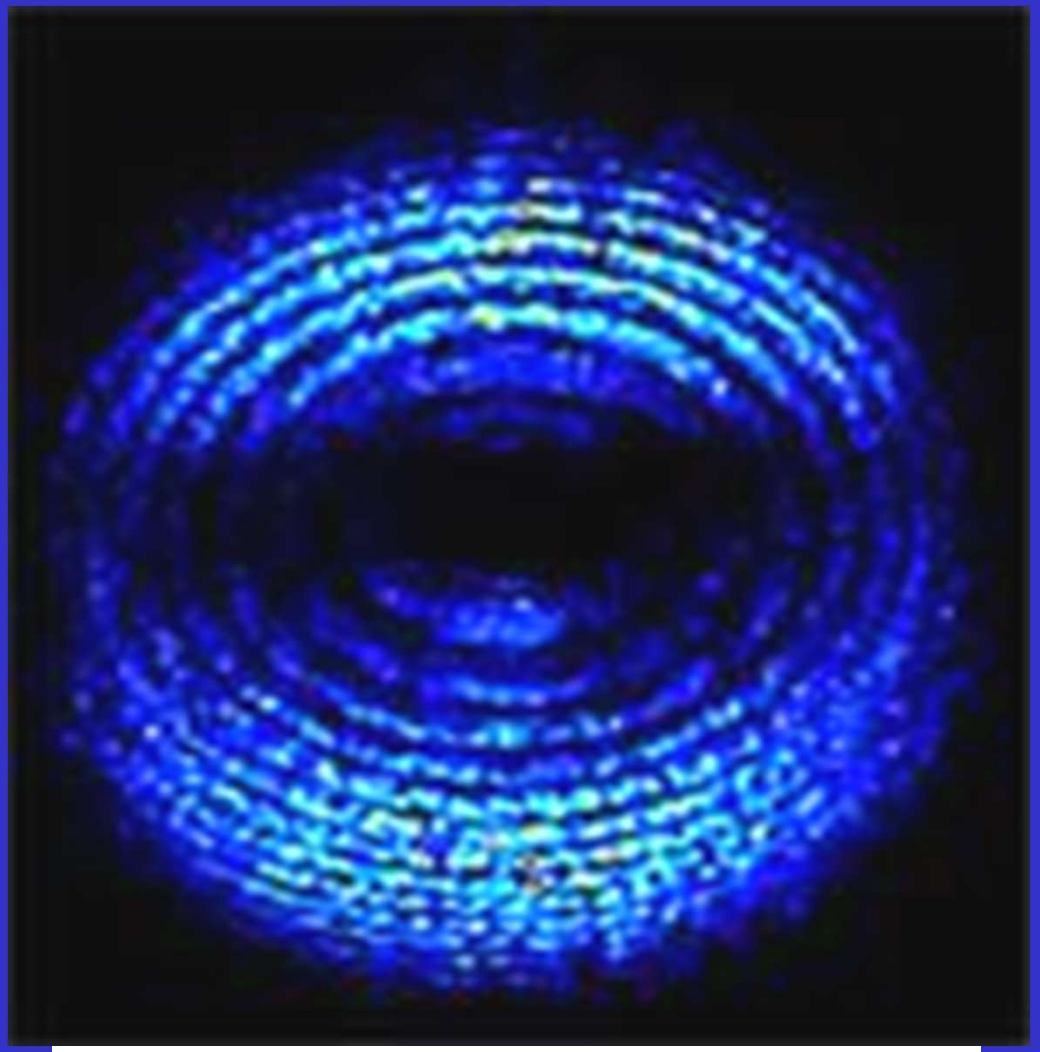
e-mail: loennig@mpiz-koeln.mpg.de

There has been limited corroboration to date for McClintock's vision of gene regulation by transposable elements (TEs), although her proposition on the origin of species by TE-induced complex chromosome reorganizations in combination with gene mutations, i.e., the involvement of both factors in relatively sudden formations of species in many plant and animal genera, has been more promising. Moreover, resolution is in sight for several seemingly contradictory phenomena such as the endless reshuffling of chromosome structures and gene sequences versus synteny and the constancy of living fossils (or stasis in general). Recent wide-ranging investigations have confirmed and enlarged the number of earlier cases of TE target site selection (hot spots for TE integration), implying preestablished rather than accidental chromosome rearrangements for nonhomologous recombination of host DNA. The possibility of a partly predetermined generation of biodiversity and new species is discussed. The views of several leading transposon experts on the rather abrupt origin of new species have not been synthesized into the macroevolutionary theory of the punctuated equilibrium school of paleontology inferred from thoroughly consistent features of the fossil record.


Placentarios
Lobo
(Canis)
Ocelote
(Felis)
Ardilla planeadora
(Glaucomys)
Marmota
(Marmota)
Oso
hormiguero
(Myrmecophaga)
Topo
(Talpa)
Ratón (Mus)
Lobo de
Tasmania
(Thylacinus)
Marsupiales
Gato marsupial
(Dasyurus)
Falangero
(Petaurus)
Uombat
(Phascolomys)
Hormiguero
marsupial
(Myrmecubius)
Topo marsupial
(Notoryctes)
Dasicerco
(Datycerus)

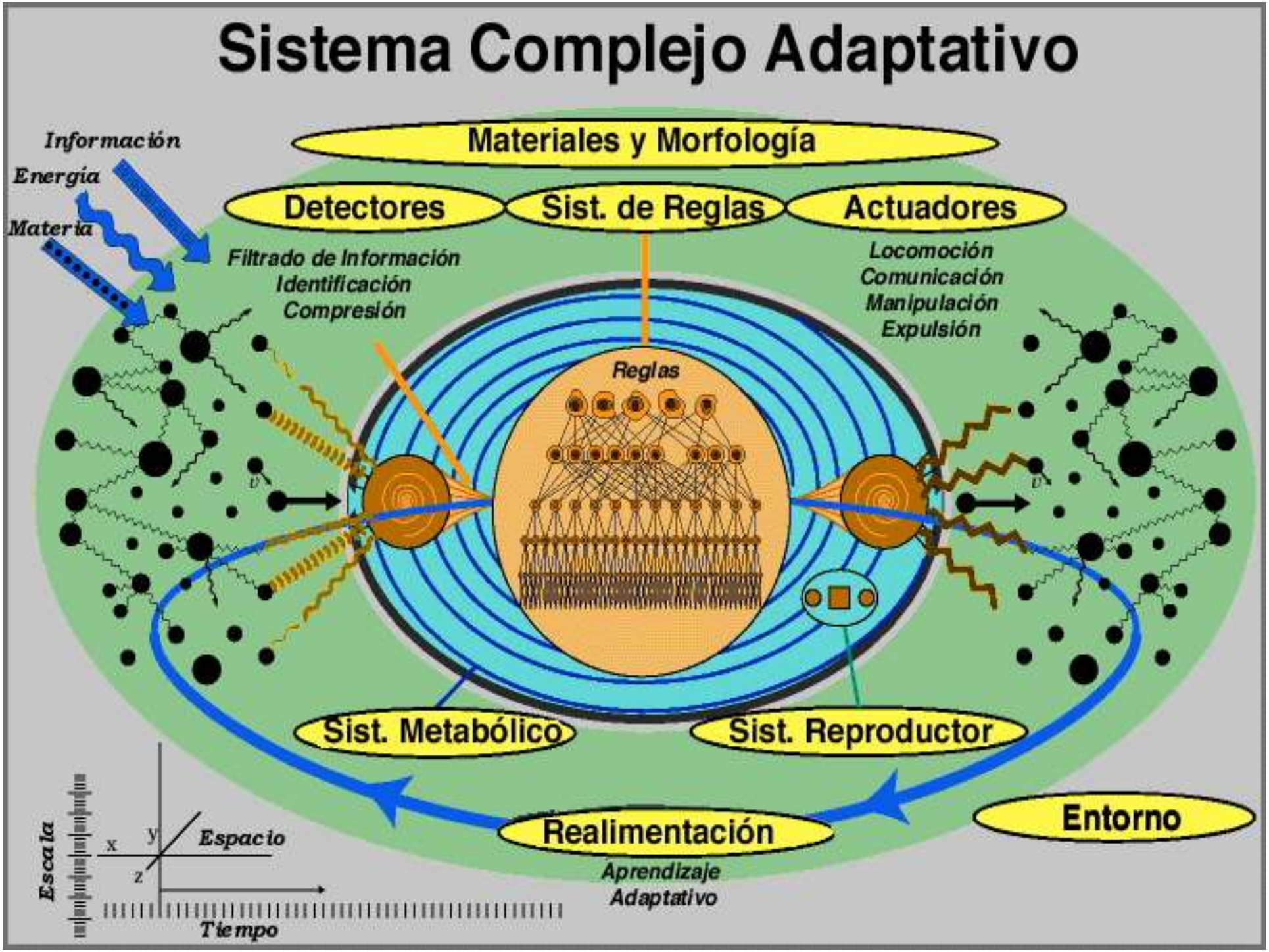
Según la teoría de Darwin, la evolución tiene lugar exclusivamente por la vía de pequeña y continua formación y modificación de especies. /.../ Nuestra experiencia, obtenida de la observación del material fósil, contradice directamente esta interpretación. Nosotros encontramos que la estructura organizadora de una Familia o un Orden no surge como el resultado de modificaciones continuas en una larga cadena de especies, sino mas bien por medio de una repentina y discontinua remodelación del complejo tipo de Familia a Familia, de Orden a Orden, de Clase a Clase. Los caracteres que cuentan para las distinciones entre especies son completamente diferentes de los que distinguen un tipo de otro.

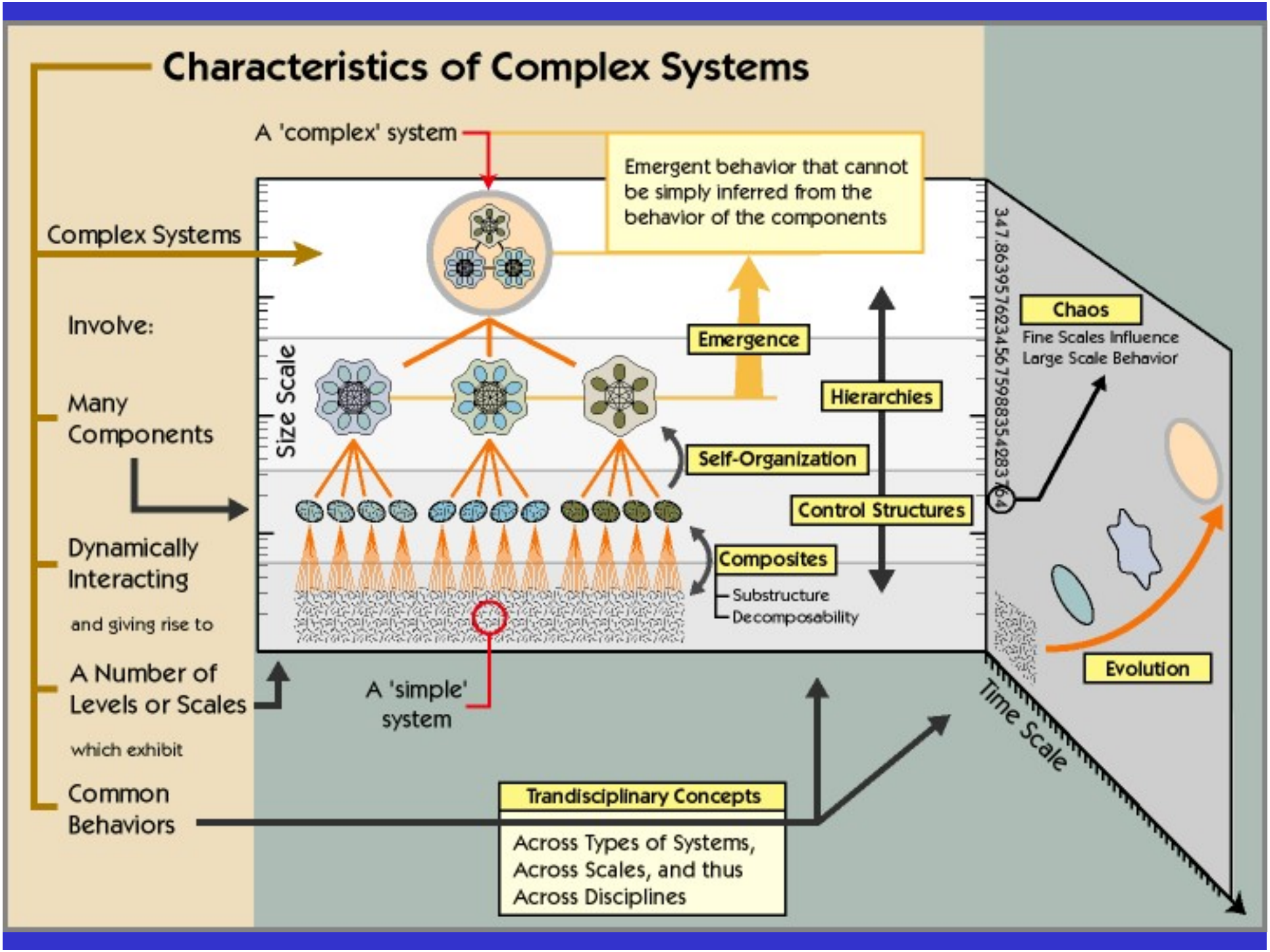
Schindewolf, O. 1993.



Primera fotografía de un electrón (estados cuánticos)

Sistema Complejo Adaptativo




Characteristics of Complex Systems
A 'complex' system
Emergent behavior that cannot be simply inferred from the behavior of the components
Complex Systems
Involve:
Many Components
Dynamically Interacting
and giving rise to
A Number of Levels or Scales
which exhibit
Common Behaviors
Size Scale
Emergence
Hierarchies
Self-Organization
Control Structures
Composites
Substructure
Decomposability
A 'simple' system
Chaos
Fine Scales Influence Large Scale Behavior
Evolution
Time Scale
Trandisciplinary Concepts
Across Types of Systems, Across Scales, and thus Across Disciplines

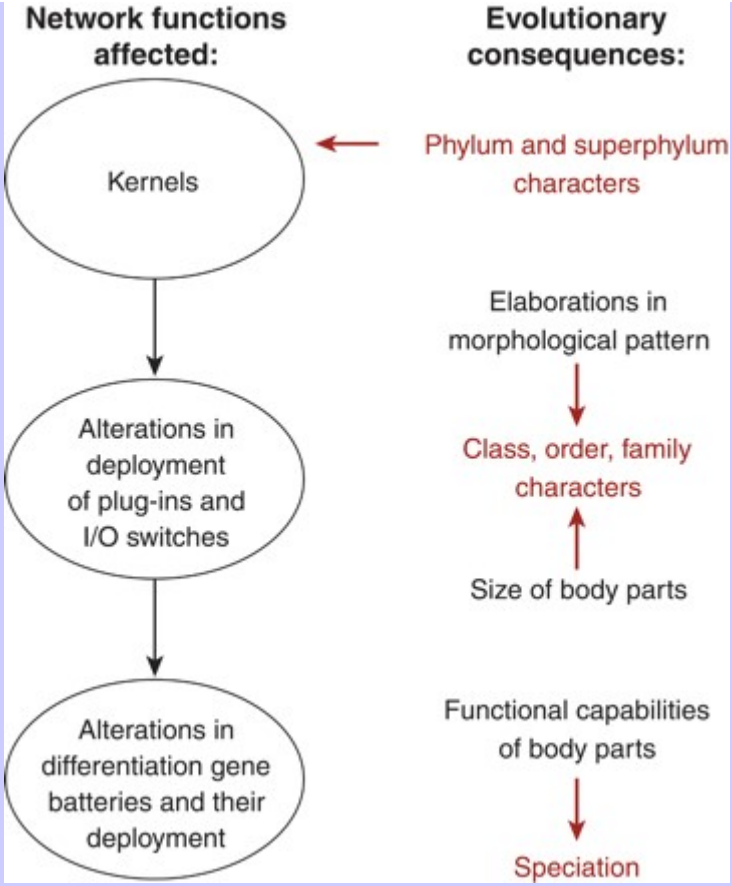
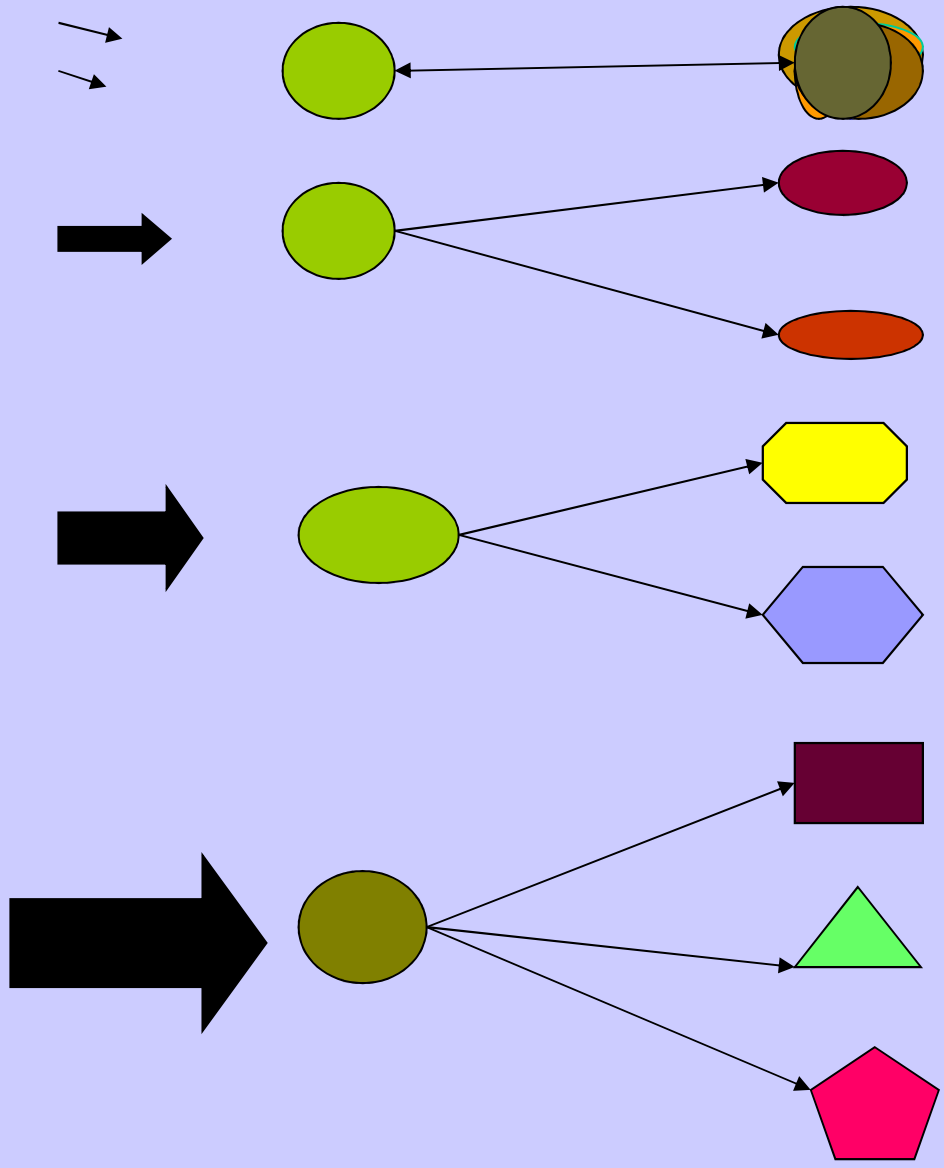


Fig. 3. Diverse kinds of change in GRNs and their diverse evolutionary consequences. The left column shows changes in network components; the right column shows evolutionary consequences expected, which differ in their taxonomic level (red).



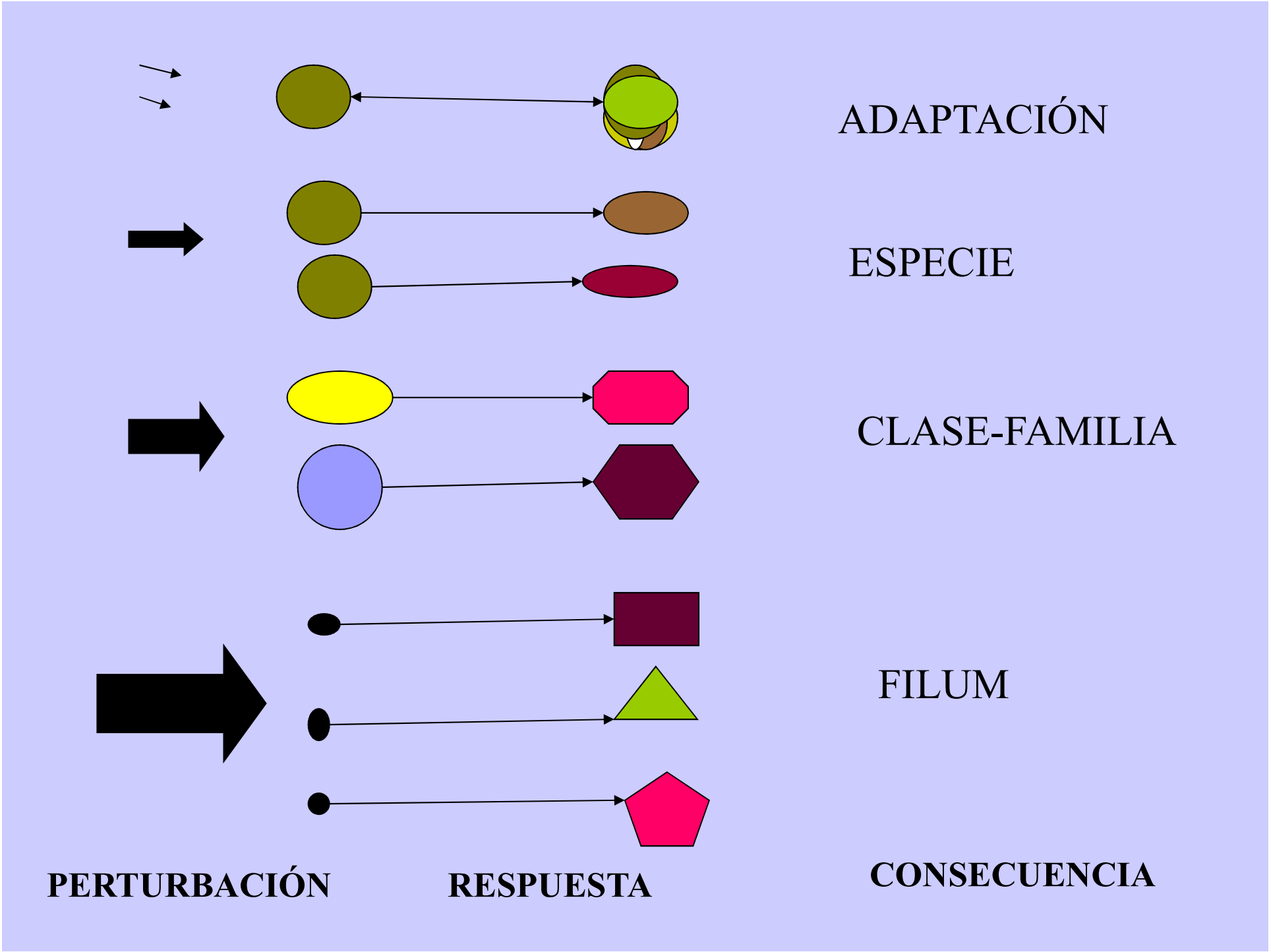
ADAPTACIÓN

ESPECIE

CLASE-FAMILIA

FILUM

PERTURBACIÓN **RESPUESTA** **CONSECUENCIA**


ADAPTACIÓN
ESPECIE
CLASE-FAMILIA
FILUM
PERTURBACIÓN
RESPUESTA
CONSECUENCIA

El Motor de la Coevolución entre Plantas e Insectos: Los Virus.

Almudena Zaragoza

"Nuestra apreciación de lo importante y de lo accesorio, de lo grande y lo pequeño, asiéntase en un falso juicio, en un verdadero error antropomórfico. En la Naturaleza no hay superior ni inferior ni cosas accesorias y principales."

Santiago Ramón y Cajal

Introducción.

El término "coevolución" se utiliza cuando hay una relación estrecha entre los ciclos biológicos de dos especies distintas. La explicación clásica de este proceso implica una adaptación mutua de ambas especies de forma gradual. Es decir, cada una de las especies a lo largo de la Evolución cambiaría algún rasgo de su fenotipo y la otra especie se adaptaría a este cambio, todo ello de forma azarosa, de manera que al final una especie no podría vivir sin la otra, ya que sus ciclos de vida estarían ligados. El ejemplo más conocido de coevolución lo encontramos en los insectos y las plantas, por ejemplo en las orquídeas y los polinizadores: las estructuras florales de las orquídeas tienen la misma la morfología del insecto que las poliniza y se alimenta de su néctar. Pero esta explicación clásica nos deja muchas preguntas sin contestar ¿cómo una planta puede desarrollar la morfología "exacta" de su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mongabay.com


Limonera. Gonepteryx Rhamni Macho
fotomaf.com 2006


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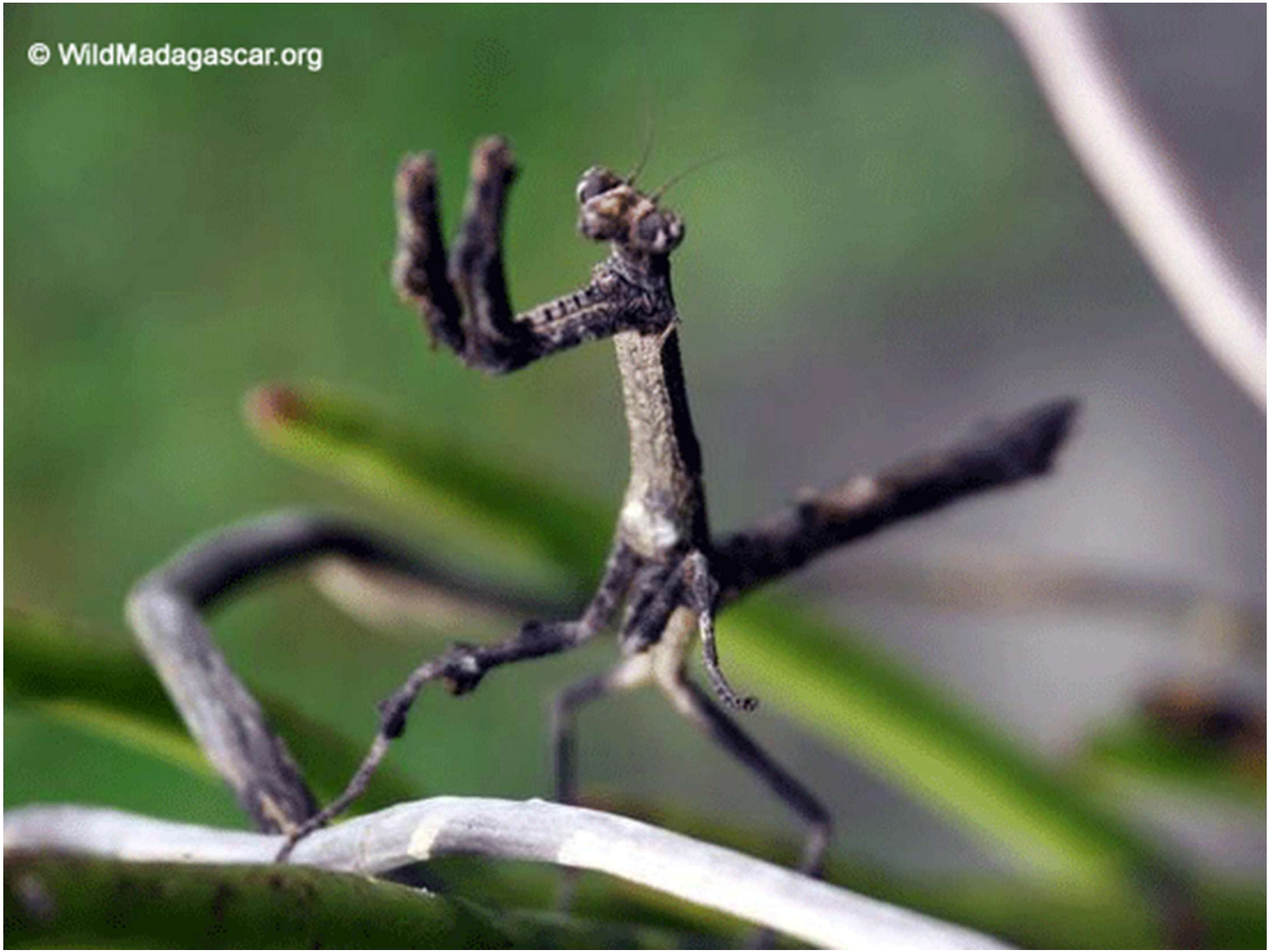
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PNAS | **November 13, 2007** | vol. 104 | no. 46 | **17959-17964**

A protein key to plant virus transmission at the tip of the insect vector stylet

Marilyne Uzest*, Daniel Gargani*, Martin Drucker*, Eugénie Hébrard, Elisa Garzo, Thierry Candresse, Alberto Fereres, and Stéphane Blanc*,

Abstract

Hundreds of species of plant viruses, many of them economically important, are transmitted by noncirculative vector transmission (acquisition by attachment of virions to vector mouthparts and inoculation by subsequent release), but virus receptors within the vector remain elusive. Here we report evidence for the existence, precise location, and chemical nature of the first receptor for a noncirculative virus, cauliflower mosaic virus, in its insect vector. Electron microscopy revealed virus-like particles in a previously undescribed anatomical zone at the extreme tip of the aphid maxillary stylets. A novel *in vitro* interaction assay characterized binding of cauliflower mosaic virus protein P2 (which mediates virus–vector interaction) to dissected aphid stylets. A P2-GFP fusion exclusively labeled a tiny cuticular domain located in the bottom-bed of the common food/salivary duct. No binding to stylets of a non-vector species was observed, and a point mutation abolishing P2 transmission activity correlated with impaired stylet binding. The novel receptor appears to be a nonglycosylated protein deeply embedded in the chitin matrix. Insight into such insect receptor molecules will begin to open the major black box of this scientific field and might lead to new strategies to combat viral spread.

Cell Research , (20 September 2011) | doi:10.1038/cr.2011.158

Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA

Lin Zhang, Dongxia Hou, Xi Chen, Donghai Li, Lingyun Zhu, Yujing Zhang, Jing Li, Zhen Bian, Xiangying Liang, Xing Cai, Yuan Yin, Cheng Wang, Tianfu Zhang, Dihan Zhu, Dianmu Zhang, Jie Xu, Qun Chen, Yi Ba, Jing Liu, Qiang Wang, Jianqun Chen, Jin Wang, Meng Wang, Qipeng Zhang, Junfeng Zhang, Ke Zen and Chen-Yu Zhang

Abstract

Our previous studies have demonstrated that stable microRNAs (miRNAs) in mammalian serum and plasma are actively secreted from tissues and cells and can serve as a novel class of biomarkers for diseases, and act as signaling molecules in intercellular communication. Here, we report the surprising finding that exogenous plant miRNAs are present in the sera and tissues of various animals and that these exogenous plant miRNAs are primarily acquired orally, through food intake. MIR168a is abundant in rice and is one of the most highly enriched exogenous plant miRNAs in the sera of Chinese subjects. Functional studies in vitro and in vivo demonstrated that MIR168a could bind to the human/mouse low-density lipoprotein receptor adapter protein 1 (LDLRAP1) mRNA, inhibit LDLRAP1 expression in liver, and consequently decrease LDL removal from mouse plasma. These findings demonstrate that exogenous plant miRNAs in food can regulate the expression of target genes in mammals.

Nature **445**, 369 (25 January 2007) | doi:10.1038/445369a; Published online 24 January 2007
Connections

Biology's next revolution

Nigel Goldenfeld and Carl Woese

The emerging picture of microbes as gene-swapping collectives demands a revision of such concepts as organism, species and evolution itself.

The place to start is horizontal gene transfer (HGT), the non-genealogical transfer of genetic material from one organism to another — such as from one bacterium to another or from viruses to bacteria.

Equally exciting is the realization that viruses have a fundamental role in the biosphere, in both immediate and long-term evolutionary senses. Recent work suggests that viruses are an important repository and memory of a community's genetic information, contributing to the system's evolutionary dynamics and stability.

…Thus, we regard as regrettable the conventional concatenation of Darwin's name with evolution, because other modalities must also be considered.

Bacteria, viruses alter evolution's speed

HOUSTON, Jan. 29 (UPI) -- A U.S. study suggests the speed of evolution has increased over time due to the activity of bacteria and viruses.

It's long been a mystery why the speed and complexity of evolution appear to increase with time. For example, the fossil record indicates single-celled life first appeared about 3.5 billion years ago, and it then took about 2.5 billion more years for multi-cellular life to evolve. That leaves 1 billion years or so for the evolution of the diverse menagerie of plants, mammals, insects, birds and other species that populate the Earth.

But recent research by Rice University scientists suggests an answer. The scientists say the speed of evolution has increased because bacteria and viruses constantly exchange transposable chunks of DNA between species, thus making it possible for life forms to evolve faster than they would if they relied only on sexual selection or random genetic mutations.

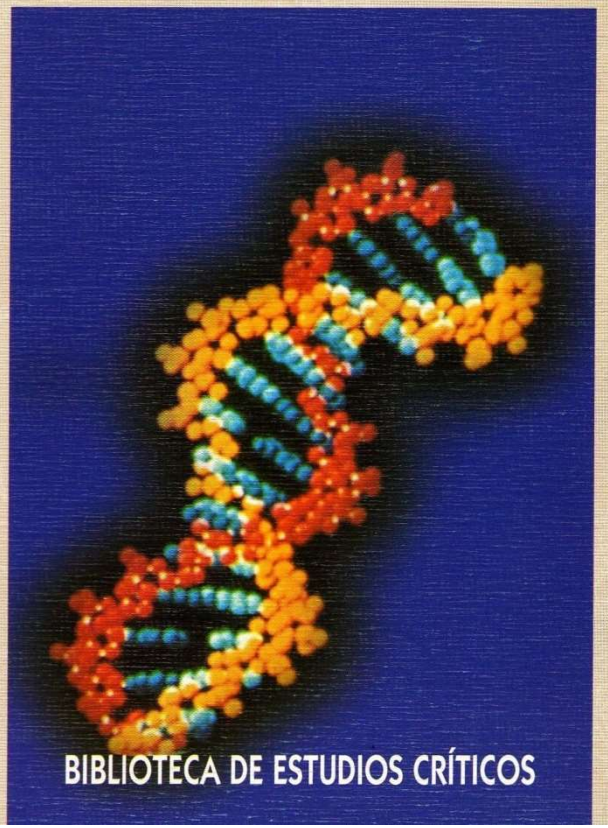
"We have developed the first exact solution of a mathematical model of evolution that accounts for this cross-species genetic exchange," said Professor Michael Deem.

The research appears in the Jan. 29 issue of Physical Review Letters.

LAMARCK
Y LOS MENSAJEROS

La función de los virus en la Evolución

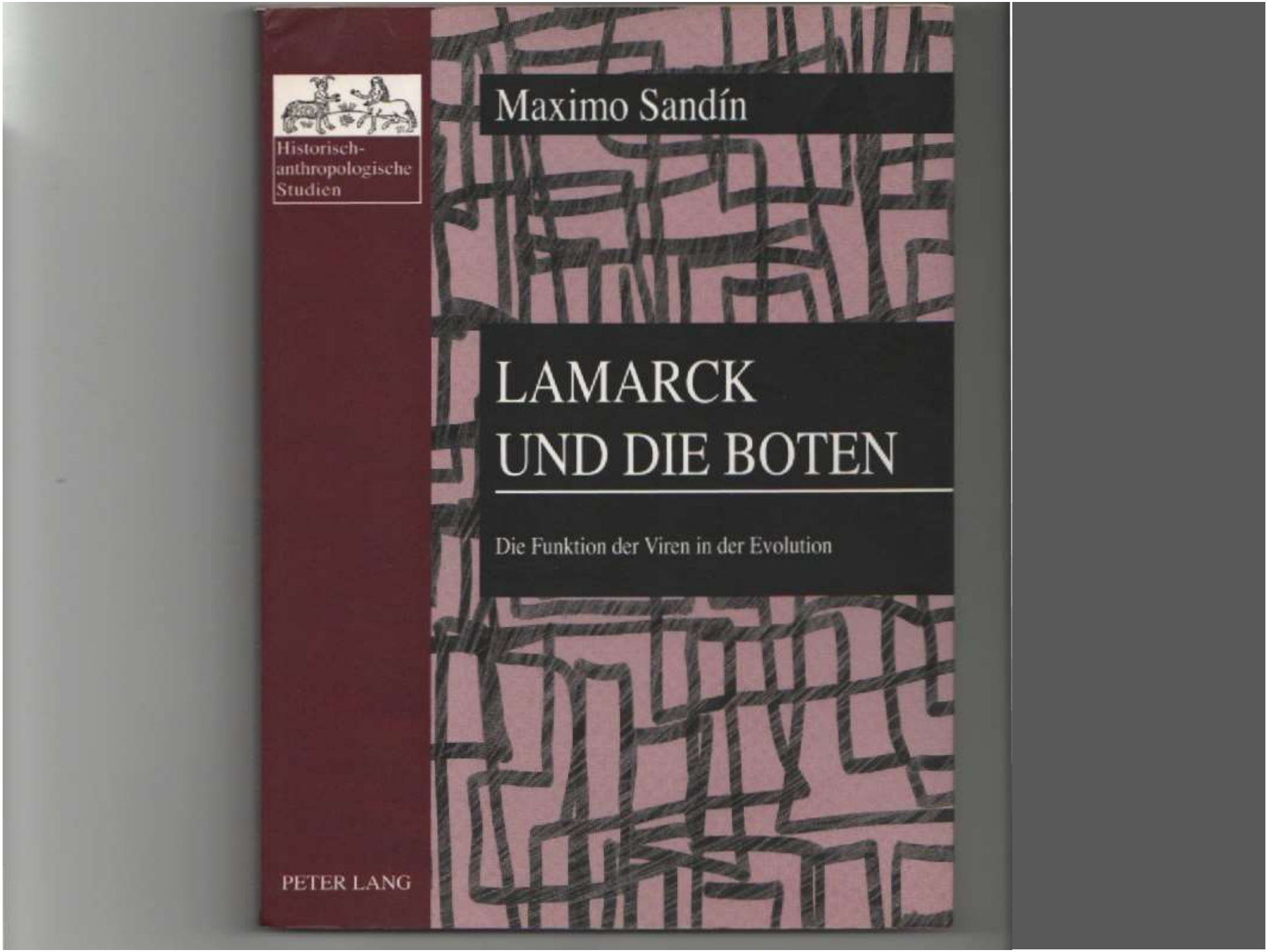
MÁXIMO SANDÍN



EDICIONES ISTMO

BIBLIOTECA DE ESTUDIOS CRÍTICOS

Este modelo se podría sintetizar de esta forma: el origen y evolución de la vida sería un proceso de integración de sistemas complejos que se autoorganizarían en otros sistemas de nivel mayor. Las unidades básicas serían las bacterias que cuentan con todos los procesos y mecanismos fundamentales de la vida celular, cuyos componentes parecen haberse conservado con muy pocos cambios a lo largo del proceso evolutivo. Los virus, mediante su mecanismo de integración cromosómica, serían los que, bien individualmente, bien mediante combinaciones entre ellos, introducirían las nuevas secuencias responsables del control embrionario de la aparición de nuevos tejidos y órganos, así como de la regulación de su funcionamiento.


Historisch-anthropologische Studien
Maximo Sandín
LAMARCK UND DIE BOTEN
Die Funktion der Viren in der Evolution
PETER LANG

Nature. 1999 Jun 10;399(6736):541-8.

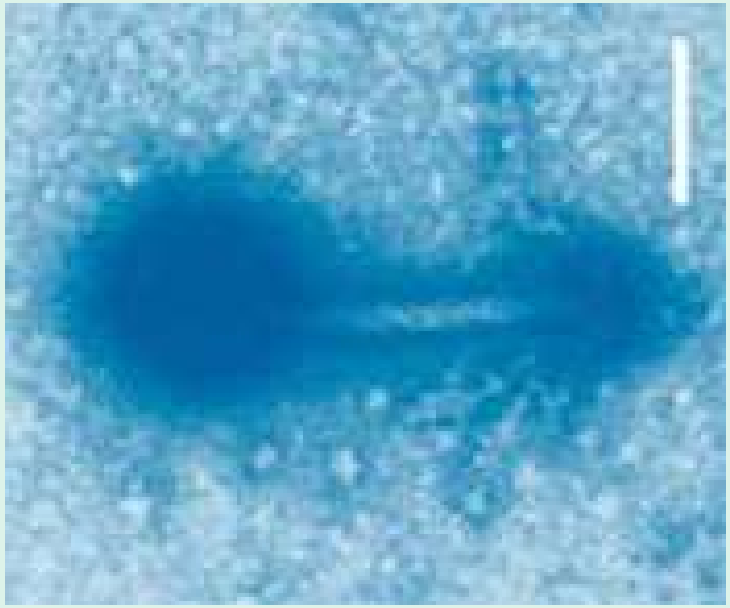
nature

Marine viruses and their biogeochemical and ecological effects.

- **Fuhrman JA**.

Department of Biological Sciences, Wrigley Institute for Environmental Studies, University of Southern California, Los Angeles 90089-0371, USA. fuhrman@usc.edu

Viruses are the most common biological agents in the sea, typically numbering ten billion per litre. They probably infect all organisms, can undergo rapid decay and replenishment, and influence many biogeochemical and ecological processes, including nutrient cycling, system respiration, particle size-distributions and sinking rates, bacterial and algal biodiversity and species distributions, algal bloom control, dimethyl sulphide formation and genetic transfer. Newly developed fluorescence and molecular techniques leave the field poised to make significant advances towards evaluating and quantifying such effects

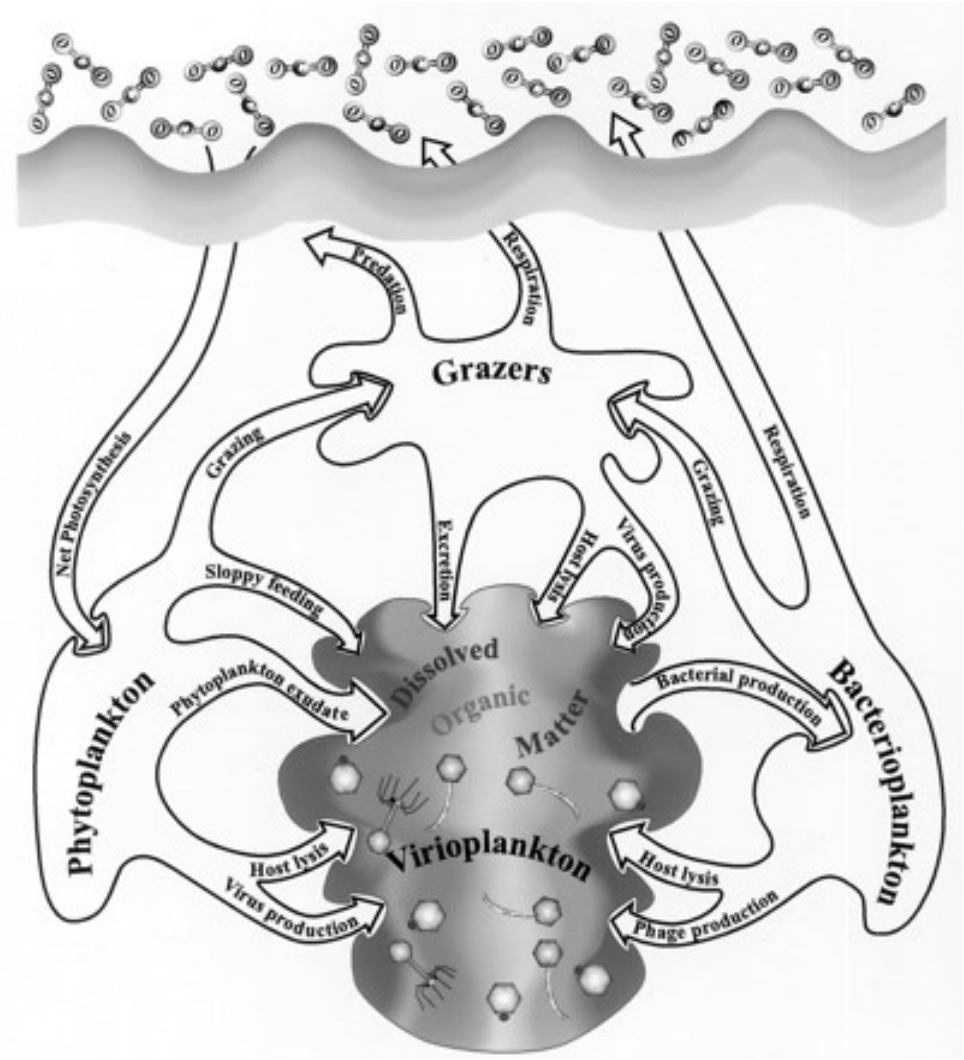


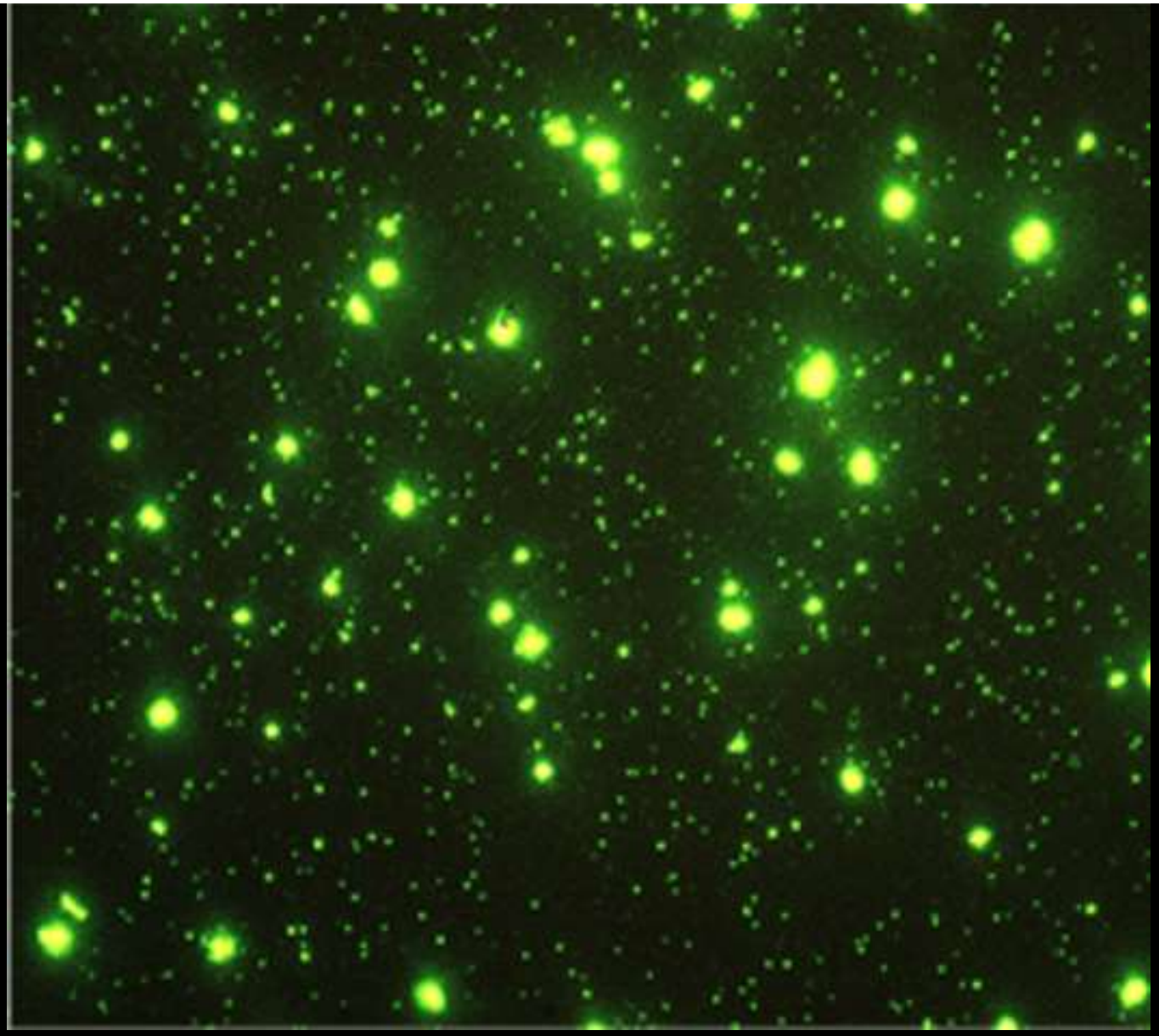
Nature **424**, 741 (14 August 2003) | doi: 10.1038/424741a

Marine ecosystems: Bacterial photosynthesis genes in a virus

Nicholas H. Mann[1], Annabel Cook[1], Andrew Millard[1], Shaun Bailey[1] and Martha Clokie[1].

Cyanobacteria contribute to the overall photosynthetic production of oxygen in the oceans, but they are susceptible to infection by viruses and also to photo-inhibition when sunlight is too intense. Here we show that the genomic sequence of one such virus, a bacteriophage known as S-PM2, encodes the D1 and D2 proteins that are key components of one of the photosynthetic reaction centres (photosystem II, PSII), which are crucial sites of damage in photo-inhibition. The presence of this virus, and others like it, in the ocean may ensure that photo-inhibition is prevented in infected cells, allowing photosynthesis to continue and therefore provide the energy needed by the virus for its replication.


Predation
Respiration
Grazers
Net Photosynthesis
Grazing
Excretion
Host lysis
Virus production
Grazing
Respiration
Sloppy feeding
Phytoplankton exudate
Dissolved
Organic
Matter
Bacterial production
Phytoplankton
Bacterioplankton
Virioplankton
Host lysis
Virus production
Host lysis
Phage production



Viruses (small green dots) and bacteria (larger green dots) from a sea water sample. The sample is stained with SYBR Green, a fluorescent stain that binds to DNA. More DNA means more of the reagent attached

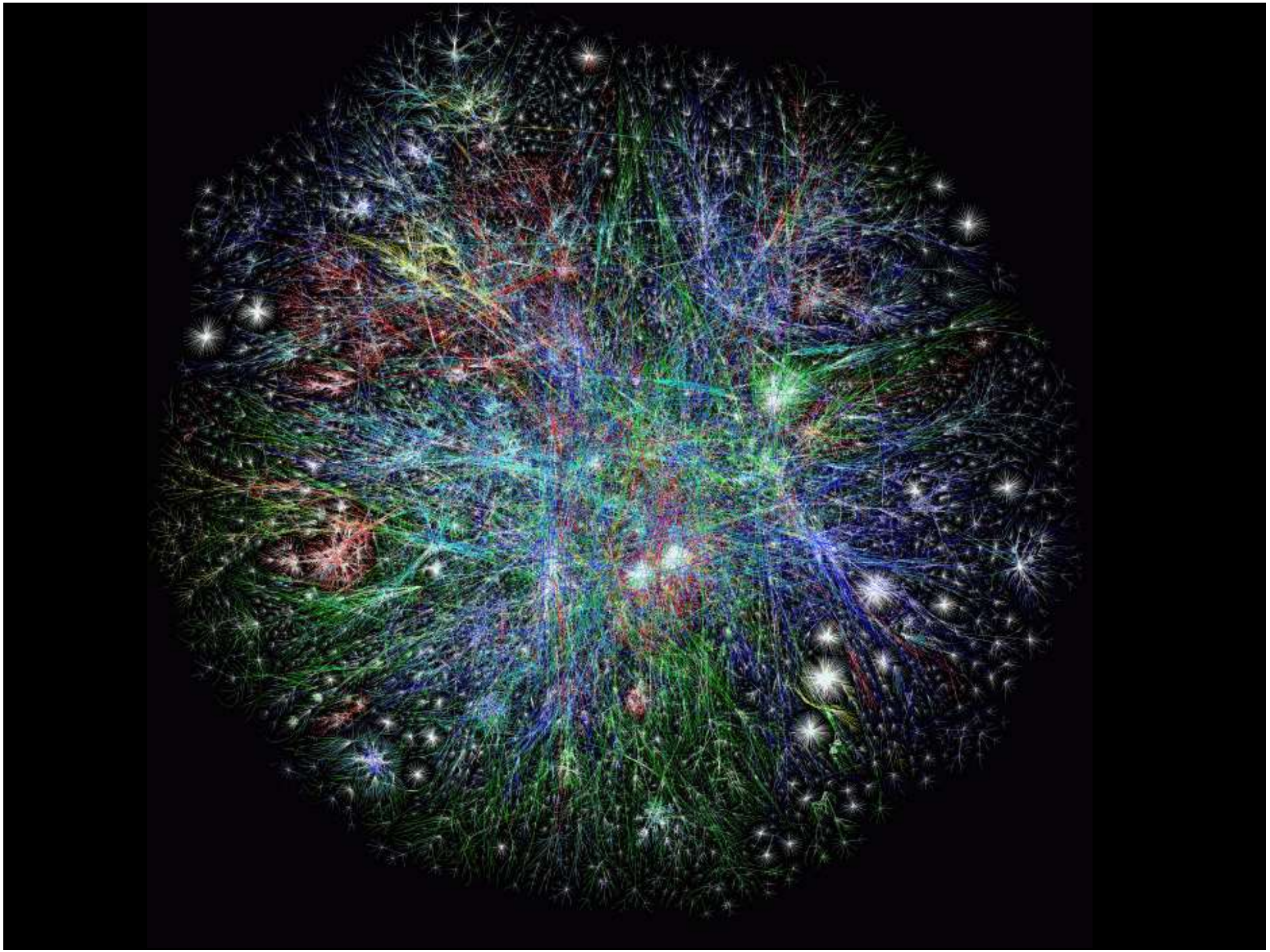
Applied and Environmental Microbiology, November 2003, p. 6628-6633, Vol. 69, No. 11
0099-2240/03/$08.00+0 DOI: 10.1128/AEM.69.11.6628-6633.2003

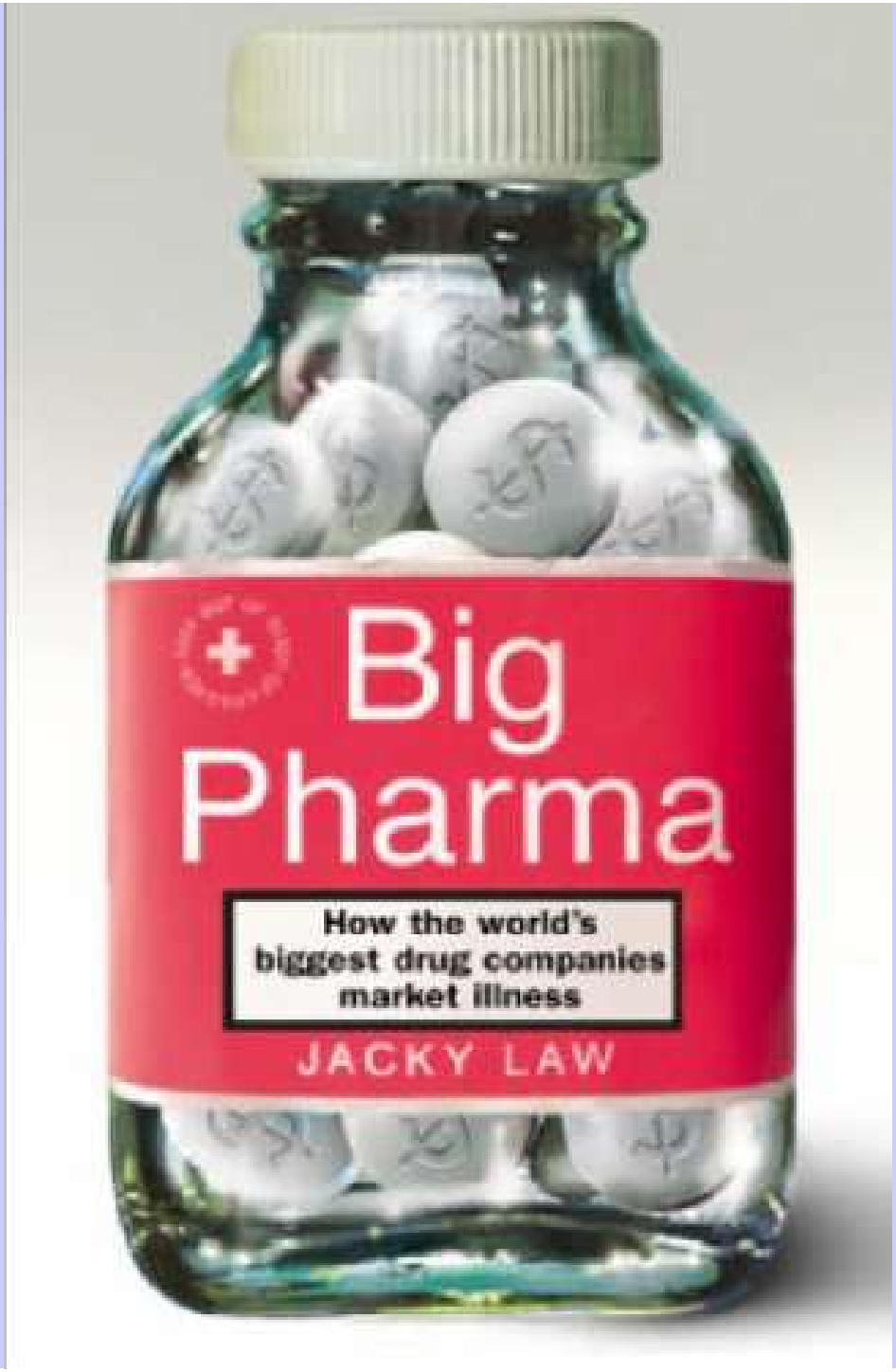
Sampling Natural Viral Communities from Soil for Culture-Independent Analyses

Kurt E. Williamson,[1] K. Eric Wommack,[1] and Mark Radosevich[2]
Department of Plant and Soil Sciences, University of Delaware, Newark, Delaware 19716,[1] Department of Biosystems Engineering and Environmental Science, University of Tennessee, Knoxville, Tennessee 37996[2]
Received 3 April 2003/ Accepted 12 August 2003

ABSTRACT

An essential first step in investigations of viruses in soil is the evaluation of viral recovery methods suitable for subsequent culture-independent analyses. In this study, four elution buffers (10% beef extract, 250 mM glycine buffer, 10 mM sodium pyrophosphate, and 1% potassium citrate) and three enumeration techniques (plaque assay, epifluorescence microscopy [EFM], and transmission electron microscopy [TEM]) were compared to determine the best method of extracting autochthonous bacteriophages from two Delaware agricultural soils. Beef extract and glycine buffer were the most effective in eluting viable phages inoculated into soils (up to 29% recovery); however, extraction efficiency varied significantly with phage strain. Potassium citrate eluted the highest numbers of virus-like particles from both soils based on enumerations by EFM (mean, 5.3×10^8 g of dry soil^{-1}), but specific soil-eluant combinations posed significant problems to enumeration by EFM. Observations of virus-like particles under TEM gave confidence that the particles were, in fact, phages, but TEM enumerations yielded measurements of phage abundance (mean, 1.5×10^8 g of dry soil^{-1}) that were about five times lower. Clearly, the measurement of phage abundance in soils varies with both the extraction and enumeration methodology; thus, it is important to assess multiple extraction and enumeration approaches prior to undertaking ecological studies of phages in a particular soil.




Big
Pharma
How the world's biggest drug companies market illness
JACKY LAW

Guerra de patentes en el fondo marino

Los científicos se lanzan a registrar organismos de los océanos para desarrollar aplicaciones médicas o energéticas - Pero la apropiación de elementos de la naturaleza es vista como una nueva biopiratería

MÓNICA LÓPEZ FERRADO 20/10/2009

Actualmente, no está permitido patentar organismos vivos. Sin embargo, ahora, las nuevas tecnologías de secuenciación, han hecho accesible la caja negra de estos bichos: su ADN. El funcionamiento de un gen o varios puede convertirse en el engranaje de bacterias artificiales al servicio de la humanidad, puestas a trabajar para crear energía o tratar enfermedades. Y eso sí que puede patentarse.

Visto este potencial, cada vez son más las expediciones científicas y comerciales (o ambas a la vez) que se adentran en los ecosistemas acuáticos del planeta a la pesca de nuevos genomas. De hecho, en los últimos seis años se han registrado más de la mitad de las patentes relacionadas con recursos genéticos marinos.

Un método busca nuevos usos a viejos fármacos

Un estudio publicado hoy en *Nature* presenta una estrategia para identificar efectos "fuera de indicación" de fármacos ya conocidos

A. I. - MADRID - 02/11/2009 08:00

La mayoría de los fármacos se diseña para actuar contra una proteína específica, pero la experiencia clínica demuestra que, en muchas ocasiones, no son más las afectadas. Cuando el medicamentos interactúa con otras proteínas corporales pueden desarrollarse efectos secundarios indeseables o que, casi por azar, se traten patologías distintas a la pretendida.

Un estudio publicado en *Nature* presenta una estrategia para identificar efectos "fuera de indicación" de fármacos ya conocidos con el objeto de evitar la primera de estas consecuencias y sacar provecho de la segunda. El equipo dirigido por el investigador de la Universidad de California en San Francisco (UCSF) Brian Shoichet estudió 3.665 medicamentos aprobados para su comercialización o para el uso de la agencia que regula los fármacos en EEUU, la FDA

Pruebas realizadas

Mediante un programa específico, observaron el efecto de los principios activos **no sólo frente a las moléculas a las que pretendían dirigirse** sino también frente a las que eran objetivo del resto de medicamentos estudiados. En total, más de 1.400 dianas terapéuticas.

Los fármacos que resultaron interactuar con proteínas distintas a sus objetivos originales **fueron probados después en ratones de laboratorio**, aunque no todos se confirmaron en la segunda prueba. Pese a ello, el sistema demostró un valor predictivo que podría perfeccionarse y aplicarse de forma rutinaria a nuevos fármacos e incluso a los ya comercializados.

De hecho, mediante su estrategia, lograron identificar 364 dianas adicionales para 158 medicamentos.

EL AVANCE DE LA RESISTENCIA

Las bacterias **GRAM NEGATIVAS** y **GRAM POSITIVAS** se distinguen según su reacción diferente a una técnica de coloración preparada por el danés Christian Gram. Las bacterias Gram- tienen una doble membrana.

TMP/SMX: Trimetoprima sulfametoxazol.

APARECEN CASOS DE RESISTENCIA BACTERIANA ANTE UN NUMERO CRECIENTE DE ANTIBIOTICOS

años: 1940 · 1950 · 1960 · 1970 · 1980 · 1990 · 2000

GRAM⁻ NEGATIVAS

Enterobacterias (*K. pneumoniae*)
Esta familia está compuesta de varios géneros: Escherichia, Klebsiella, Enterobacter, Salmonella, etc. Causan neumonías, septicemias, infecciones urinarias y úlceras, así como disentería. *E. coli* es en algunos países la causa principal de infecciones hospitalarias

β-lactaminas
TMP/SMX*
gentamicina
doramfenicol, tetraciclina
ampicilina

Haemophilus (*H. influenzae*)
Neumonías infantiles, sinusitis, meningitis y otitis

TMP/SMX*
doramfenicol
gentamicina
β-lactaminas

Pseudomonas (*P. fluorescens*)
Neumonías e infecciones urinarias

fluoroquinonas
aminoácidos
carbapenem, imipenem
gentamicina

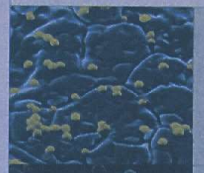
Campylobacter (*C. jejuni*)
Diarreas

fluoroquinonas
tetraciclina

Neisseiria (*N. meningitidis*)
Gonorreas y meningitis

fluoroquinonas
tetraciclina
gentamicina
ampicilina
sulfamidas

GRAM⁺ POSITIVAS



Estafilococo (*S. aureus*)
Neumonías, infecciones urinarias y meningitis

vancomicina
rifampicina
fluoroquinonas
aminoácidos
meticilina
doramfenicol
eritromicina
penicilina

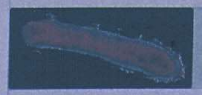
Enterococo (*E. faecalis*)
Meningitis, endocarditis, infecciones urinarias y neonatales

glicopéptidos
gentamicina
β-lactaminas

Estreptococo (*S. pneumoniae*)
Neumonías, meningitis y otitis

penicilina
eritromicina
TMP/SMX*
cefalosporinas
tetraciclina

MICOBACTERIAS



Mycobacterium (*M. tuberculosis*)
Tuberculosis

rifampicina
isoniacida
estreptomicina

Esta tabla presenta de manera no exhaustiva el momento a partir del cual se han constatado casos de resistencia. Se han clasificado por géneros bacterianos (en las enterobacterias, por familias) y por tipo de antibióticos. Los nombres latinos entre paréntesis corresponden a las bacterias fotografiadas. (Fotos Karl Lounsbery, Brain, Barry Rowsett, Olivier Meckes/Cosmos, Mycobacterium, etc.)

La resistencia plantea problemas en clínica

Ciertas cepas son resistentes a todos los tratamientos

La vacuna contra el cáncer de útero llega hoy a las farmacias al precio de 464,58 euros

El ministro de Sanidad, Bernat Soria, recomienda esperar hasta enero, cuando el tratamiento empezará a repartirse por los servicios públicos

EFE

Gardasil, la vacuna contra el papiloma humano.
AFP

La primera vacuna de prevención del cáncer de cuello de útero y otras enfermedades genitales, causadas por el virus del papiloma humano, está disponible en las farmacias desde hoy a un precio de 464,58 euros por las tres dosis necesarias.

La vacuna, comercializada por Sanofi Pasteur MSD con el nombre de Gardasil, protege contra cuatro clases de virus del papiloma humano (VPH), dos causantes del cáncer de cuello de útero y otras dos que provocan enfermedades genitales como las verrugas.

Sólo estas cuatro cepas del VPH causan entre el 70 y el 75% de las infecciones que degeneran en cáncer de cuello de útero, de modo que las mujeres que nunca se hayan infectado con este virus y que se vacunen estarán inmunizadas contra la mayoría de las infecciones genitales que causa el VPH.

La vacunación completa consiste en tres dosis separadas (vía inyecciones intramusculares) que deberán administrarse en un plazo de entre seis meses y un año (la segunda dosis dos meses después de la primera, y la tercera y última, a partir del sexto mes

"Habría que vacunar al 100% de la población contra el papilomavirus"

MARCO EVERS / JOHANN GROLLE 26/10/2008

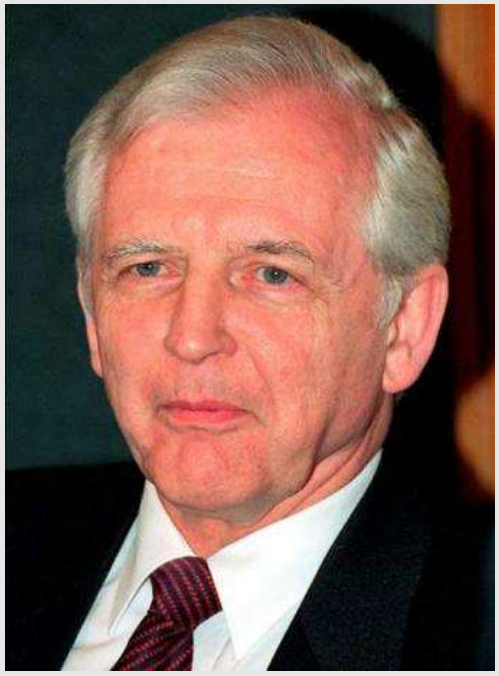
El eminente científico alemán, de 72 años, habla del papel que desempeñan los virus en el desarrollo del cáncer y relaciona el consumo abundante de carne de vacuno casi cruda como un importante factor de riesgo

El virólogo alemán Harald zur Hausen, de 72 años, reciente premio Nobel de Medicina, habla en esta entrevista de los virus como factores desencadenantes del cáncer, de las nuevas terapias antitumorales y de sus motivos para preferir los bistecs muy hechos.

Los premios Nobel, bajo sospecha

Dos de los miembros del jurado tienen fuertes vínculos con una farmacéutica beneficiada por el galardón de Medicina de este año

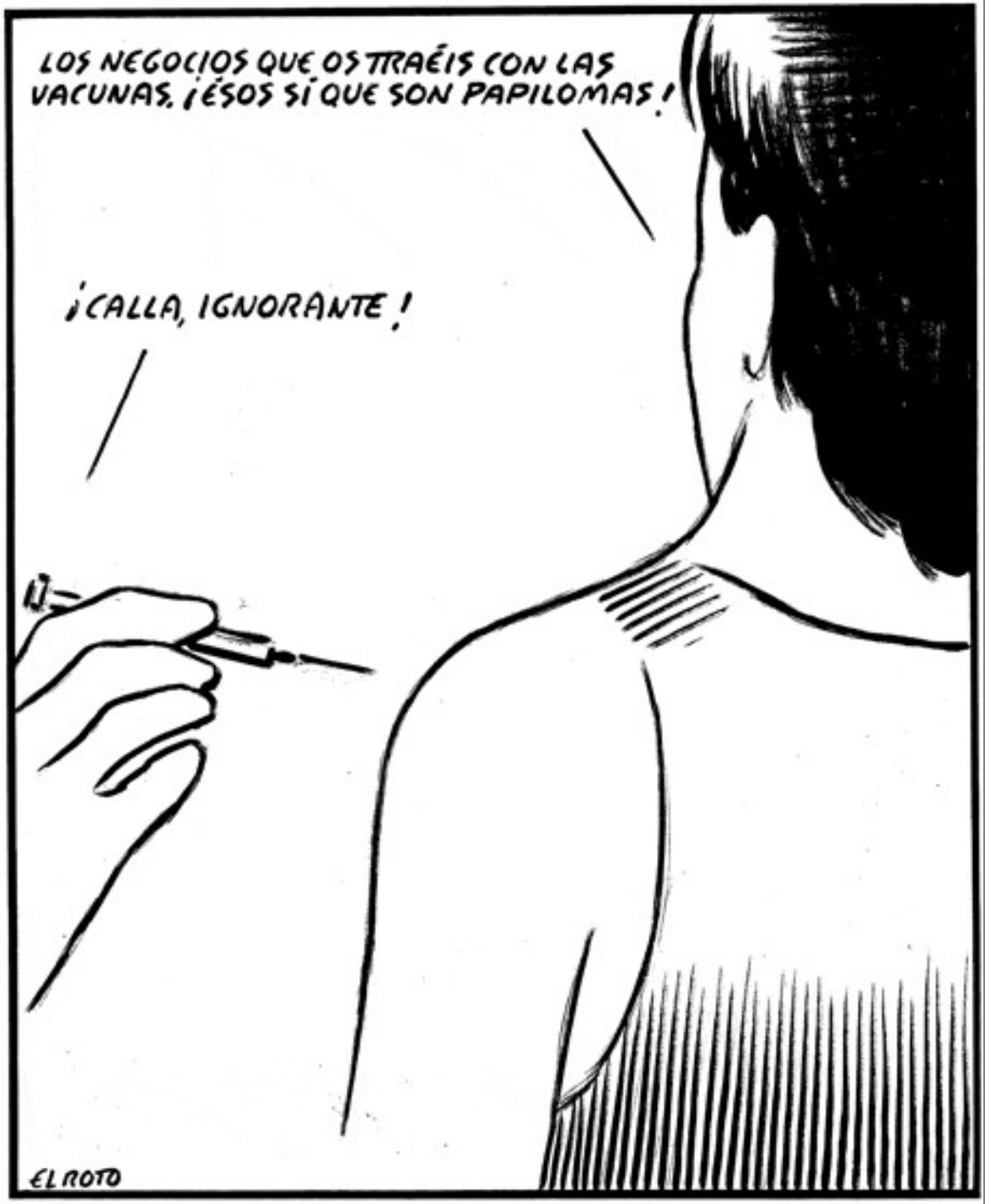
EFE - Londres - 19/12/2008

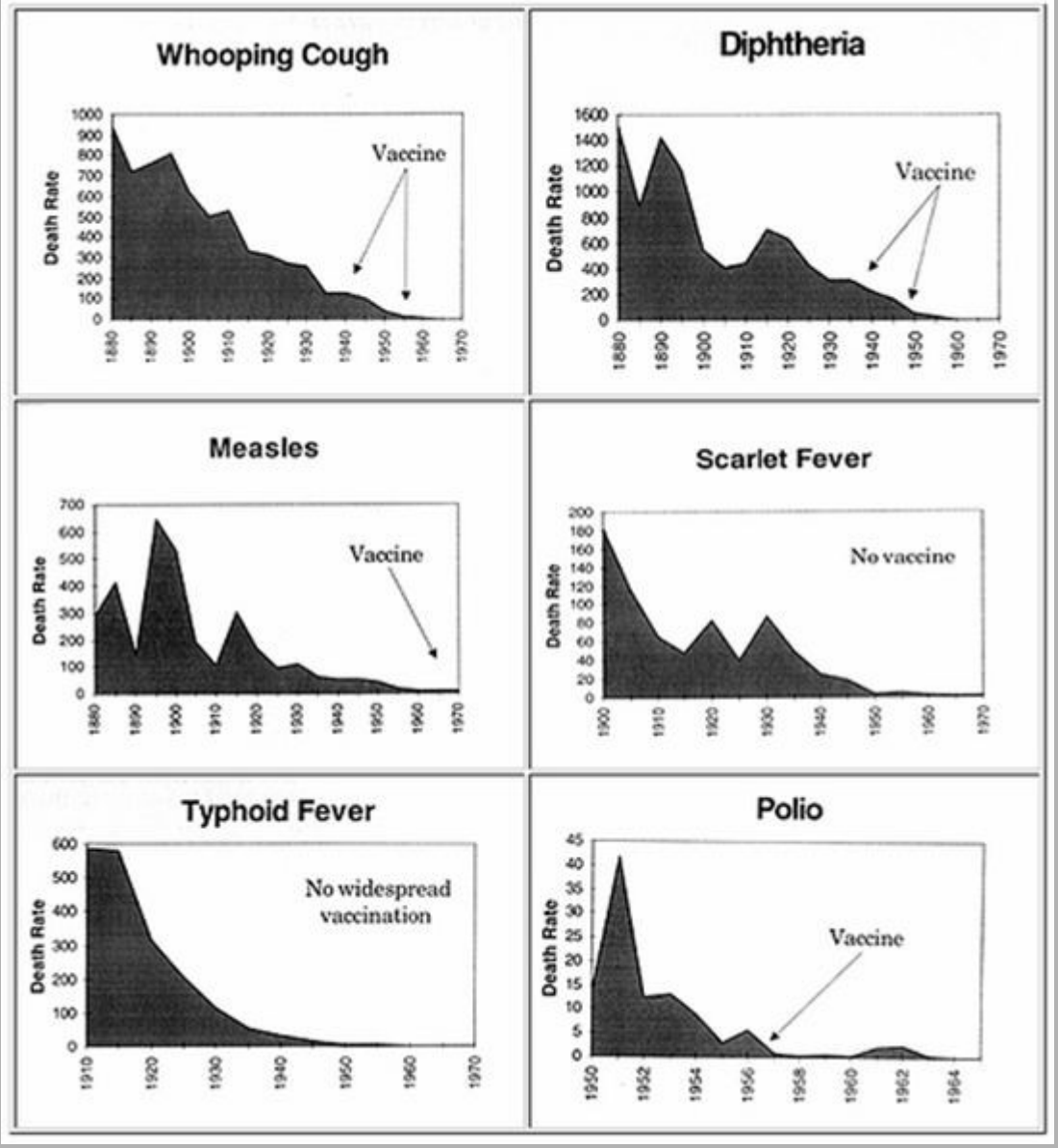


La integridad del jurado que concede los premios Nobel está en tela de juicio tras la revelación de que dos de sus miembros están estrechamente vinculados al consejo de dirección de una empresa farmacéutica beneficiada por el galardón de Medicina 2008.

PAPILOMAVIRUS: URGE DETENER LAS VACUNACIONES

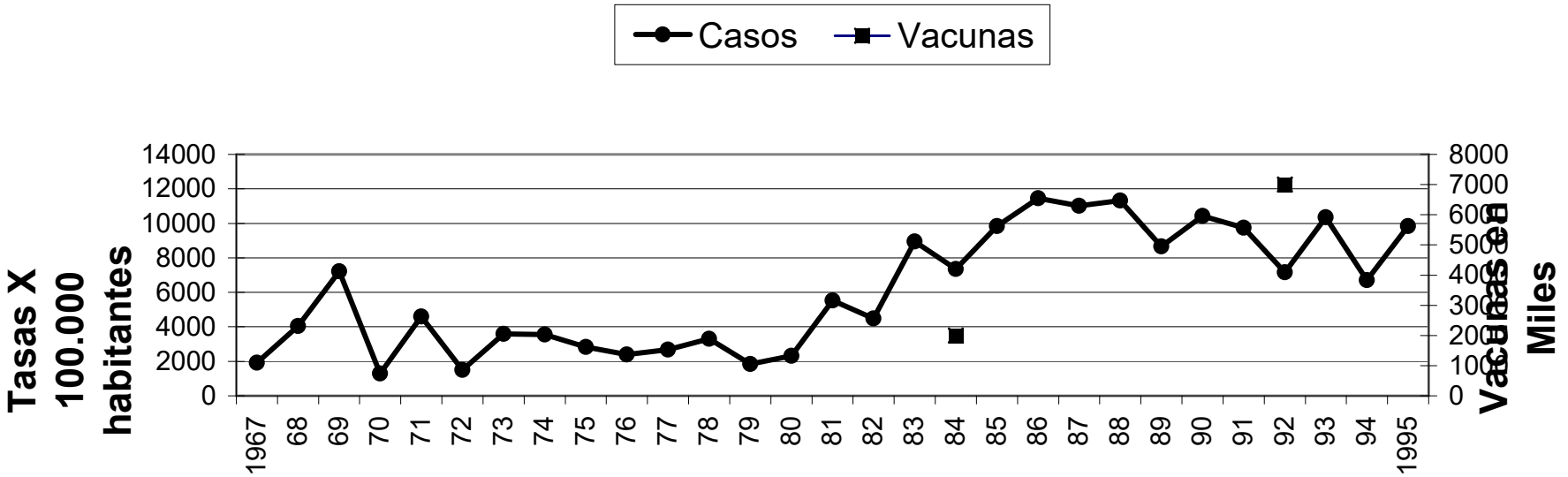
El alineamiento de las secuencias del papilomavirus (HPV 16) con las del genoma humano (NCBI y Ensembl) pone de manifiesto la presencia del gen E6 (considerado protooncogénico) y de las secuencias que codifican para la proteína L1 (cápsida) en el cromosoma 2 y secuencias virales dispersas en los cromosomas 1, 5 y 12. Pero, independientemente del verdadero papel de las secuencias virales en los genomas, los datos puramente empíricos nos muestran que los papilomavirus están presentes en distintos epitelios desde la más temprana infancia (22,23,24), que su ubicuidad y diversidad sugiere, desde el punto de vista convencional, "una naturaleza comensalista" (25) y que son extremadamente abundantes en la piel humana y de toda clase de animales saludables (26,27).


LOS NEGOCIOS QUE OS TRAÉIS CON LAS VACUNAS. ¡ÉSOS SÍ QUE SON PAPILOMAS!
¡CALLA, IGNORANTE!
EL ROTO



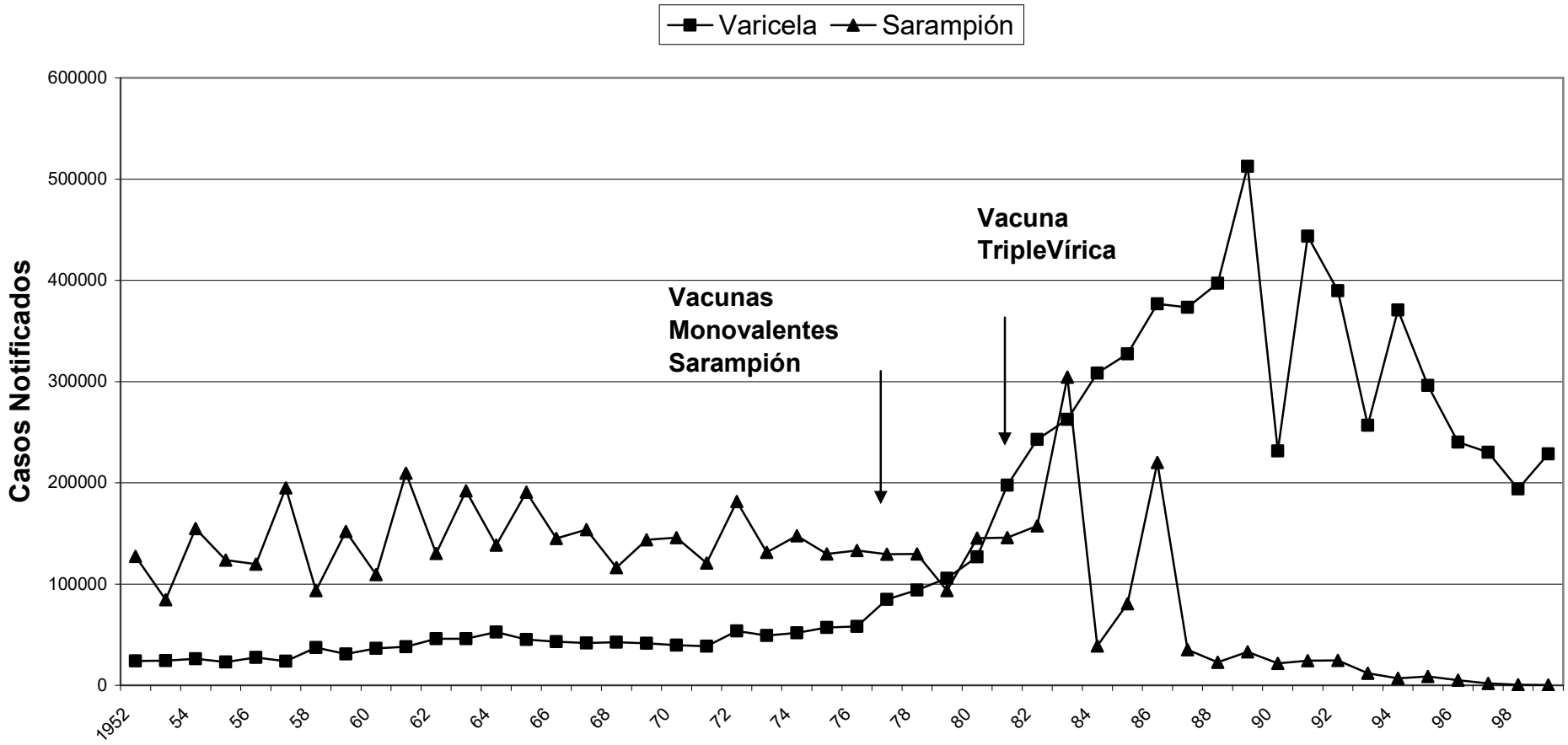
La Dr. Viera Scheibner, quien ha estudiado casi 100.000 páginas de investigaciones sobre vacunación durante años junto su marido, muestra la caída pre-vacunación con múltiples tablas.

ESPAÑA
Morbilidad Gripe y Coberturas Vacunales
1967-1995



Fuente: Elaboración propia. Datos del Centro Nacional de Epidemiología

Varicela y Sarampión
Morbilidad 1952-1999



Fuente: Elaboración propia. Datos del Anuario Estadístico de España

eMedicine
Vaccinia

Author: Jennifer J Lee, MD, Resident Physician, Department of Dermatology, University of Texas Southwestern at Austin
Coauthor(s): Dayna Diven, MD, Clinical Professor, Department of Dermatology, University of Texas Medical Branch School of Medicine; **Tasneem A Poonawalla, MD,** Staff Physician, Department of Internal Medicine, University of Texas Medical Branch School of Medicine; **Howard L Kaufman, MD,** Chief, Division of Surgical Oncology, Columbia University; **Ken Flanagan,** Department of Microbiology and Immunology, Albert Einstein

Introduction

Background

Vaccination with vaccinia virus has been directly responsible for the successful eradication of smallpox (variola). Although the exact origins of vaccinia virus are uncertain, vaccinia may represent a hybrid of the variola and cowpox viruses.

Inoculation with vaccina virus produces a localized skin infection. In immunocompromised persons, vaccinia may disseminate and cause severe disease. However, adverse reactions have become increasingly rare since routine childhood immunization for smallpox in the general population was officially discontinued in the United States in 1972. Nonetheless, because news of this did not reach all health care providers and since supplies of the vaccine remained throughout the country, the vaccine continued to be administered for a few years following the official stop date.

During 2003, because of the concern for biological warfare, the United States government recommended that all first responders be vaccinated with the vaccinia virus. However, vaccination of first responders was halted upon the occurrence of vaccination-related complications, including a previously unrecognized complication, cardiomyopathy. Certain military recruits continue to receive vaccinia vaccine owing to the concern for bioterrorism. Laboratory personnel working with vaccinia and others for whom the benefits outweigh the risks of vaccination may also receive vaccinations.

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ISIS Report 07/10/09

Flu Vaccines and the Risk of Cancer

Flu vaccines are increasingly manufactured in cell lines that are actually or potentially oncogenic, and FDA guidelines allow high levels of contamination and no spot checks are carried out

Dr. Sherri J Tenpenny

Much concern has been generated over the new swine flu H1N1 vaccines that are being rushed to market. Clinical trials have been short – less than three weeks – and there is also the possibility of adding toxic oil-in-water adjuvants at the last minute to stretch the vaccine supply (see [1] Fast-tracked Swine Flu Vaccine under Fire, *ISiS* 43). Those are not the only concerns. The new manufacturing process for flu shots, called cell-line technologies, are little understood and have the potential for serious, long term consequences.

Biologicals. 2009 Mar 17. [Epub ahead of print] Links

Proposed algorithm to investigate latent and occult viruses in vaccine cell substrates by chemical induction.

Khan AS, Ma W, Ma Y, Kumar A, Williams DK, Muller J, Ma H, Galvin TA.

Laboratory of Retrovirus Research, Center for Biologics, Evaluation and Research, U.S. Food and Drug Administration, 8800 Rockville Pike HFM-454, Building 29B, Room 4NN10, Bethesda, MD 20892, USA.

The recent urgency to develop new vaccines for emerging and re-emerging diseases, such as pandemic influenza, has necessitated the use of cell substrates not previously used in the manufacture of licensed vaccines. A major safety concern in the use of novel cell substrates is the presence of potential adventitious agents, such as latent and occult viruses, that may not be detected by currently used conventional assays. In cases where the novel cell substrate is known to be tumorigenic, there are additional safety issues related to tumorigenicity of intact cells and oncogenicity of residual cellular DNA. We have developed a strategy for evaluating vaccine cell substrates for the presence of latent/occult viruses, including endogenous retroviruses, latent RNA viruses and oncogenic DNA viruses, by optimizing conditions for chemical induction of viruses and using a combination of broad and specific assays to enable detection of known and novel viruses.

J Virol. 2005 January; 79(1): 341–352.

Comprehensive Analysis of Human Endogenous Retrovirus Transcriptional Activity in Human Tissues with a Retrovirus-Specific Microarray

Wolfgang Seifarth,1*† Oliver Frank,1† Udo Zeilfelder,1 Birgit Spiess,1 Alex D. Greenwood,2,3 Rüdiger Hehlmann,1 and Christine Leib-Mösch1,2

ABSTRACT

In the present study, we have investigated the transcriptional activity of representative members of 20 HERV families in 19 different normal human tissues. Qualitative evaluation of chip hybridization signals and quantitative analysis by real-time RT-PCR revealed distinct HERV activity in the human tissues under investigation, suggesting that HERV elements are active in human cells in a tissue-specific manner. Most active members of HERV families were found in mRNA prepared from skin, thyroid gland, placenta, and tissues of reproductive organs. In contrast, only few active HERVs were detectable in muscle cells. Human tissues that lack HERV transcription could not be found, confirming that human endogenous retroviruses are permanent components of the human transcriptome. Distinct activity patterns may reflect the characteristics of the regulatory machinery in these cells, e.g., cell type-dependent occurrence of transcriptional regulatory factors.

Vaccine Manufacture :
Egg-Based Vaccine Production

Currently commercialized seasonal influenza vaccines rely upon the supply of embryonated chicken eggs as the substrate for virus propagation. Seed virus strains bearing the recommended hemagglutinin

Virology
Volume 297, Issue 2,
5 June 2002, Pages 220-225

Developmental Expression of HERV-R (ERV3) and HERV-K in Human Tissue

Ann-Catrin Andersson[a, 1], Patrick J. W. Venables[b], Ralf R. Tönjes[c], Jürgen Scherer[c], Lars Eriksson[a] and Erik Larsson[a]

Abstract

The human endogenous retroviruses (HERVs), ERV3 (HERV-R) and HERV-K, are both known to be transcriptionally active in human placenta. In the case of ERV3 there is also indirect evidence for its participation in cellular differentiation. In this study we examined the expression of ERV3 (HERV-R) and HERV-K in human normal fetal tissues by *in situ* hybridization. The highest level of ERV3 *env* expression was detected in primitive adrenal cortex. Elevated levels of expression were also found in the following developing tissues: kidneys (tubules), tongue, heart, liver, and central nervous system. Tissue-specific expression was found for HERV-K *rec* (former *cORF*) but not for *pol/int* transcripts. The highest *rec* expression was found in placenta and levels slightly higher than sense control were found in the rest of the tissues examined. *Pol/Int* was not possible to quantitate. It appears that ERV3 is expressed in an organ-specific way during embryogenesis and might suggest a possible role in the development and differentiation of human tissues.

J Virol. 2003 January; 77(2): 1105–1111.

Identification and Characterization of Avian Retroviruses in Chicken Embryo-Derived Yellow Fever Vaccines: Investigation of Transmission to Vaccine Recipients

Althaf I. Hussain,1 Jeffrey A. Johnson,1 Marcos da Silva Freire,2 and Walid Heneine1*

All currently licensed yellow fever (YF) vaccines are propagated in chicken embryos. Recent studies of chick cell-derived measles and mumps vaccines show evidence of two types of retrovirus particles, the endogenous avian retrovirus (EAV) and the endogenous avian leukosis virus (ALV-E), which originate from the chicken embryonic fibroblast substrates. In this study, we investigated substrate-derived avian retrovirus contamination in YF vaccines currently produced by three manufacturers (YF-vax [Connaught Laboratories], Stamaril [Aventis], and YF-FIOCRUZ [FIOCRUZ-Bio-Manguinhos]). Testing for reverse transcriptase (RT) activity was not possible because of assay inhibition. However, Western blot analysis of virus pellets with anti-ALV RT antiserum detected three distinct RT proteins in all vaccines, indicating that more than one source is responsible for the RTs present in the vaccines.

Riesgos de las Vacunas Genéticamente Modificadas

26-09-05, *Por Lim Li Ching **

El uso de vacunas genéticamente modificadas (vacunas GM) han incrementado tanto en el campo de la medicina humana como veterinaria, así como en acuacultura. Sin embargo, algunos tipos de vacunas GM que se están desarrollando al momento poseen potenciales impactos ecológicos y ambientales.

La ingeniería genética crea efectos impredecibles ya que no es posible controlar que el vector transgénico se coloque en un sitio específico del genoma de los organismos huésped. Esto significa que si se lleva a cabo una modificación genética con idéntico procedimiento, usando los mismos organismos y bajo las mismas condiciones experimentales, el resultado puede dar dos organismos genéticamente modificados (OGM) muy diferentes, dependiendo de dónde se insertaron los transgenes. Tampoco se puede controlar los patrones de la expresión génica de los genes insertados en el OGM, ni si los transgenes insertados o sus partes se mueven dentro del genoma huésped. No es posible saber tampoco si la secuencia del ADN transferido, terminan de alguna manera incorporándose al medio ambiente.

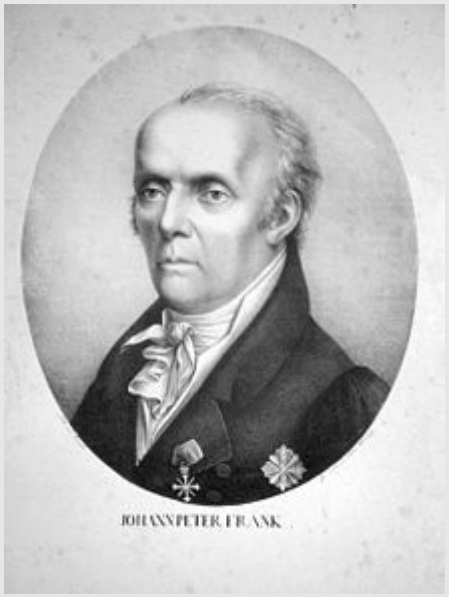
Confirman la relación entre el mercurio presente en vacunas infantiles y un aumento del riesgo de autismo

El Defensor del Paciente considera que este tipo de preparados "deberían ser retirados de inmediato del mercado"

21 de junio de 2003

Un grupo de investigadores de "The Genetic Centers of America" (Maryland, EE.UU.) ha confirmado la relación entre el mercurio que se encuentra presente en vacunas infantiles contra la difteria, el tétanos y la pertussis acelular, con un incremento del riesgo de desarrollar trastornos neuronales y autismo, según un estudio publicado en el último número de "Experimental biology and medicine", revista de la Sociedad Americana de Biología Experimental.

El componente supuestamente responsable de estos trastornos es el timerosal y los expertos aseguran que su estudio supone "la primera evidencia epidemiológica" del riesgo asociado a este derivado del mercurio.

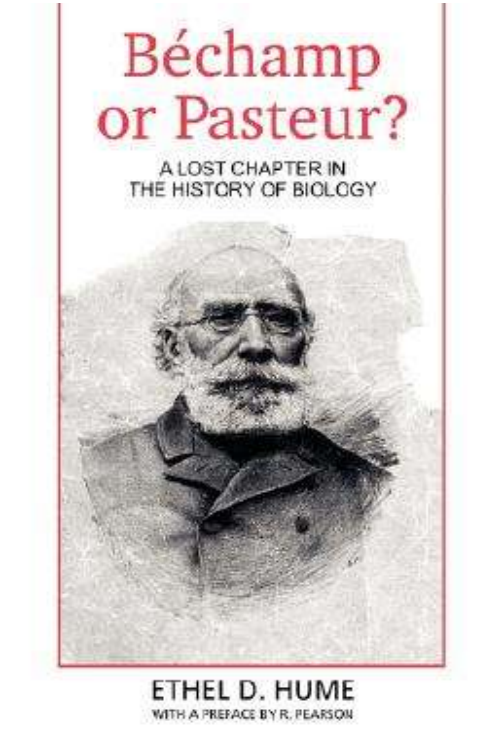


Johann Peter Frank (1745–1821)

En Europa, desde la publicación en 1790 de la obra del médico vienés J.P. Frank, titulada *La miseria del pueblo, madre de enfermedades*, otros higienistas como Turner Thackrah, Arnold, Chadwick, Villermé o Virchow contribuyeron con sus estudios a refundar la higiene, que entonces formaba parte junto con la medicina legal de la llamada medicina pública, como ciencia profiláctica y disciplina médica independiente de aquellas, dotándola de un cuerpo doctrinario propio que la situó en primera línea de la lucha por la erradicación de enfermedades como el la fiebre amarilla o el cólera-morbo, afecciones que se desarrollaban con más frecuencia en el medio urbano y que afectaban a la mayor parte de la población, especialmente aquella conformada por las clases más bajas, trabajadores, obreros y sus familias, cuyas insalubres condiciones de vida y de trabajo se convertían en focos de enfermedad permanentes.

Louis Pasteur (1822-1895)
Químico.

Expuso la "teoría germinal de las enfermedades infecciosas", según la cual toda enfermedad infecciosa tiene su causa (etiología) en un germen con capacidad para propagarse entre las personas. Esta sencilla idea representa el inicio de la medicina científica, al demostrar que la enfermedad es el *efecto* visible (signos y síntomas) de una *causa* que puede ser buscada y eliminada mediante un tratamiento específico. En el caso de las enfermedades infecciosas, se debe buscar el germen causante de cada enfermedad para hallar un modo de combatirlo. Por sus trabajos es considerado el pionero de la microbiología moderna, que inicia así la llamada "Edad de Oro de la Microbiología".



"Nothing is lost, nothing is created ... all is transformed. Nothing is the prey of death. All is the prey of life." -- Antoine Bechamp

Las bacterias encontradas en el hombre y animales no causan la enfermedad. Ellos tienen la misma función que las encontradas en la tierra, o en el alcantarillado, o en otra parte en la naturaleza; ellos están allí parar reconstruir el tejido muerto o los tejidos enfermos, para reciclar los desperdicios, y se sabe bien que ellos no quieren o no pueden atacar los tejidos saludables. Ellos son parte importante y necesaria de la vida humana como aquellos encontrados en otra parte en la naturaleza, y está en la realidad así como indemne si nosotros vivimos correctamente, como Bechamp tan claramente mostró.

Florence Nightingale (1820-1910)

Enfermera

”Las enfermedades no son individuos organizados en clases, como los gatos y perros, sino estados que crecen unos de otros. ¿No estamos viviendo en un continuo error al considerar las enfermedades como hacemos ahora, como entidades separadas que deben existir como los gatos y perros, en lugar de verlas como condiciones, como una condición sucia y una limpia, y siempre bajo nuestro control, o más bien como reacciones de naturaleza suave, contra las que nos hemos puesto nosotros?/.../ “Desde entonces he visto con mis propios ojos y olido con mi propia nariz la viruela que crece de los primeros especimenes, o en los cuartos cerrados o en espacios apiñados donde por alguna posibilidad no pudo haber sido 'cogida', pero debe de haber empezado. He visto empezar las enfermedades, crecer, y pasar. Ahora, los perros no terminan en gatos.”

La doctrina de la enfermedad específica es el gran refugio de las mentes débiles, incultas, e inestables, como ahora es regla en la profesión médica. No hay ninguna enfermedad específica; ¡hay condiciones de enfermedad específicas".

Tamiflu ®

Tamiflu (fosfato de oseltamivir 75mg) es un antivírico para el tratamiento y prevención de la gripe (A y B) en adultos y adolescentes a partir de los 13 años, y niños mayores de 1 año.
La gripe es una infección causada por el virus de la gripe.Los sintomas de la gripe empiezan con fiebre, moqueo o congestion nasal, dolores de cabeza, dolores musculares.
Tamiflu es un inhibidor de la enzima neuramidasa, por lo que previene que el virus de la gripe se disemine dentro del cuerpo, y por tanto ayuda a aliviar o a prevenir que aparezcan los síntomas de la infección del virus de la gripe.
Para el tratamiento de la gripe tome 1 cápsula tan pronto como empiecen los síntomas y luego 1 cápsula dos veces al día durante 5 días.
Laboratotio **Tamiflu**: ROCHE
www.tamiflu.com

Tamiflu 75mg 10 cápsulas 31.56€
Tamiflu 12mg/ml 30ml 31.56€

Journal of Neurochemistry
Volume 58 Issue 1, Pages 78 - 82
Published Online: 5 Oct 2006

Neuraminidase Activities in Oligodendroglial Cells of the Rat Brain

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KEYWORDS
Neuraminidase • Oligodendroglial cells • Myelin • Gangliosides • Myelination

ABSTRACT

Abstract: Neuraminidase activities in oligodendroglial cells were characterized using rats of different ages. Rat oligodendroglial cells had intrinsic neuraminidase activities directed toward GM3 and *N*-acetylneuramin(2–3)lactitol (NL). Developmental profiles of the neuraminidase activities toward the two substrates in oligodendroglial cells were different from each other. The neuraminidase activity toward GM3 increased rapidly with the onset of active myelination and, after 26 days of development, reached the adult level which was about 18 times higher than that in myelin. At the adult age, oligodendroglial cells had the highest neuraminidase activity toward GM3 among the individual brain cell types examined. The activity of NL-neuraminidase showed a less remarkable developmental profile, with a peak value at 26 days. The UDP-galactose:ceramide galactosyltransferase activity in oligodendroglial cells increased during the period of active myelination and, afterward, returned to the basal level. The enrichment and unique developmental profile in oligodendroglial cells of the neuraminidase activity toward GM3 suggest that this enzyme may play an important role in the formation and maintenance of the myelin sheath.

Alta tasa de efectos secundarios en niños que recibieron Tamiflu contra la gripe A

Actualizado jueves 30/07/2009 21:40 (CET)

EFE

LONDRES.- El 53% de los niños de tres escuelas londinenses que fueron tratados con Tamiflu como medida preventiva frente a la gripe A sufrieron uno o más efectos secundarios, principalmente náuseas y pesadillas, según un informe oficial difundido este jueves por las autoridades sanitarias británicas.

El estudio, elaborado por la Agencia de Protección de la Salud (HPA) del Reino Unido, analiza los datos correspondientes a 103 niños, a 85 de los cuales se les administró este fármaco **por profilaxis** después de que un compañero contrajera la gripe A.

De estos 85 niños, 45 experimentaron uno o varios efectos secundarios, siendo las náuseas el más habitual, seguido de **dolores de estómago, vómitos, calambres** y problemas de sueño.

El 18% de los que recibieron el tratamiento experimentó también "efectos secundarios neuropsiquiátricos", como mala concentración, incapacidad para pensar con claridad, insomnio, mareos, confusión, pesadillas y "comportamientos extraños", según lo definió la HPA.

Schizophr Res. 2010 May;118(1-3):224-31. Epub 2010 Feb 13.

Neuroanatomic and cognitive abnormalities related to herpes simplex virus type 1 in schizophrenia.

Schretlen DJ, Vannorsdall TD, Winicki JM, Mushtaq Y, Hikida T, Sawa A, Yolken RH, Dickerson FB, Cascella NG.

Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States. dschret@jhmi.edu

Abstract

Herpes simplex virus 1 (HSV-1) tends to replicate in the temporal cortex and can damage the limbic system. The presence of serum antibodies to HSV-1 is associated with cognitive impairment in adults with schizophrenia, suggesting that cerebral gray matter abnormalities might distinguish patient subgroups defined by HSV-1 exposure. We assessed 43 adult outpatients with schizophrenia. The assessment included clinical interviews, neurocognitive testing, anatomic brain magnetic resonance imaging and measures of serum IgG antibodies specific to herpes simplex viruses 1 and 2. We then compared 25 patients who tested positive for antibodies to HSV-1 with 15 who were seronegative for both HSV-1 and HSV-2. The seropositive patients performed significantly worse than the seronegative patients on four neuropsychological measures of psychomotor speed, executive functioning, and explicit verbal memory.

El 'virus' de la esquizofrenia

No es la primera vez que un estudio relaciona un virus con la esquizofrenia. "Estamos descubriendo qué parte del deterioro cognitivo que suele atribuirse sólo a la esquizofrenia podría ser en realidad una combinación de la patología y la exposición previa al virus del herpes simple 1 (VHS-1), que se reproduce en el cerebro", asegura a ELMUNDO.es David Schretlen, del Departamento de Psiquiatría de la Universidad Johns Hopkins (EE.UU.) y autor principal de una nueva investigación que vuelve a mostrar un vínculo entre las infecciones y esta patología mental.

FUENTE | El Mundo Digital 15/06/2010

Al parecer, y tal y como publica *'Schizophrenia Research'*, la exposición al virus común que "causa el herpes labial puede ser parcialmente responsable de la disminución de las regiones del cerebro y la pérdida de capacidad de concentración, memoria, coordinación de movimientos y destreza ampliamente observado en los pacientes con esquizofrenia", afirman los científicos.

"La mayor contribución de nuestro estudio es que demuestra una implicación de los factores ambientales a la expresión de la esquizofrenia. Si bien la infección por VHS-1 no puede aumentar la probabilidad de desarrollar la patología, sí puede interactuar con los genes que hacen susceptible a una persona de desarrollarla, de tal manera que altera la estructura y función del cerebro en los esquizofrénicos", añade.

Estos hallazgos podrían derivar en nuevas formas de tratamiento o de prevención del deterioro cognitivo "que normalmente acompaña a la enfermedad, incluida la terapia con fármacos antivirales", explican los autores.

La Comisión Europea desvela nuevos proyectos de investigación para combatir la gripe

El proyecto GRIPE-PHARM se aprovecharán los avances recientes en la comprensión detallada de la estructura y función de la polimerasa viral, la máquina de replicación del virus, para desarrollar nuevos fármacos candidatos que inhiben la replicación viral en las células infectadas. FLU-PHARM ofrecerá nuevas oportunidades para tratar la gripe estacional y pandémica, incluida la que circula origen porcino H1N1 y H5N1 de alta patogenicidad (aviar). Por lo tanto, puede tener un enorme impacto en la salud pública en todo el mundo y el bienestar, así como en la competitividad del sector farmacéutico europeo

Duración: 42 meses

Previstos contribución de la UE: € 6,000,000

Coordinator: Stephen Cusack, European Molecular Biology Laboratory (France) cusack@embl.fr Coordinador: Stephen Cusack, European Molecular Biology Laboratory (Francia) cusack@embl.fr 14 socios de 7 países: Alemania, Austria, Francia, España, Eslovaquia, Bélgica, Suecia

eMedicine
Vaccinia

Author: Jennifer J Lee, MD, Resident Physician, Department of Dermatology, University of Texas Southwestern at Austin
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Introduction

Background

Vaccination with vaccinia virus has been directly responsible for the successful eradication of smallpox (variola). Although the exact origins of vaccinia virus are uncertain, vaccinia may represent a hybrid of the variola and cowpox viruses.

Inoculation with vaccina virus produces a localized skin infection. In immunocompromised persons, vaccinia may disseminate and cause severe disease. However, adverse reactions have become increasingly rare since routine childhood immunization for smallpox in the general population was officially discontinued in the United States in 1972. Nonetheless, because news of this did not reach all health care providers and since supplies of the vaccine remained throughout the country, the vaccine continued to be administered for a few years following the official stop date.

During 2003, because of the concern for biological warfare, the United States government recommended that all first responders be vaccinated with the vaccinia virus. However, vaccination of first responders was halted upon the occurrence of vaccination-related complications, including a previously unrecognized complication, cardiomyopathy. Certain military recruits continue to receive vaccinia vaccine owing to the concern for bioterrorism. Laboratory personnel working with vaccinia and others for whom the benefits outweigh the risks of vaccination may also receive vaccinations.

Nature **437**, 794-795 (6 October 2005) | doi:10.1038/437794a; Published online 5 October 2005

Special ReportThe 1918 flu virus is resurrected

Abstract

The recreation of one of the deadliest diseases known could help us to prevent another pandemic. Or it might trigger one, say critics. Andreas von Bubnoff investigates whether the benefits outweigh the risks.

It is thought to have killed 50 million people, and yet scientists have brought it back to life. In this issue of *Nature*, scientists publish an analysis of the full genome sequence of the 1918 human influenza virus. And in this week's *Science*, researchers describe how they used that sequence to recreate the virus and study its effects in mice.

Some scientists have already hailed the work as giving unprecedented insight into the virus. But others have raised concerns that the dangers of resurrecting the virus are just too great. One biosecurity expert told *Nature* that the risk that the recreated strain might escape is so high, it is almost a certainty. And the publication of the full genome sequence gives any rogue nation or bioterrorist group all the information they need to make their own version of the virus.

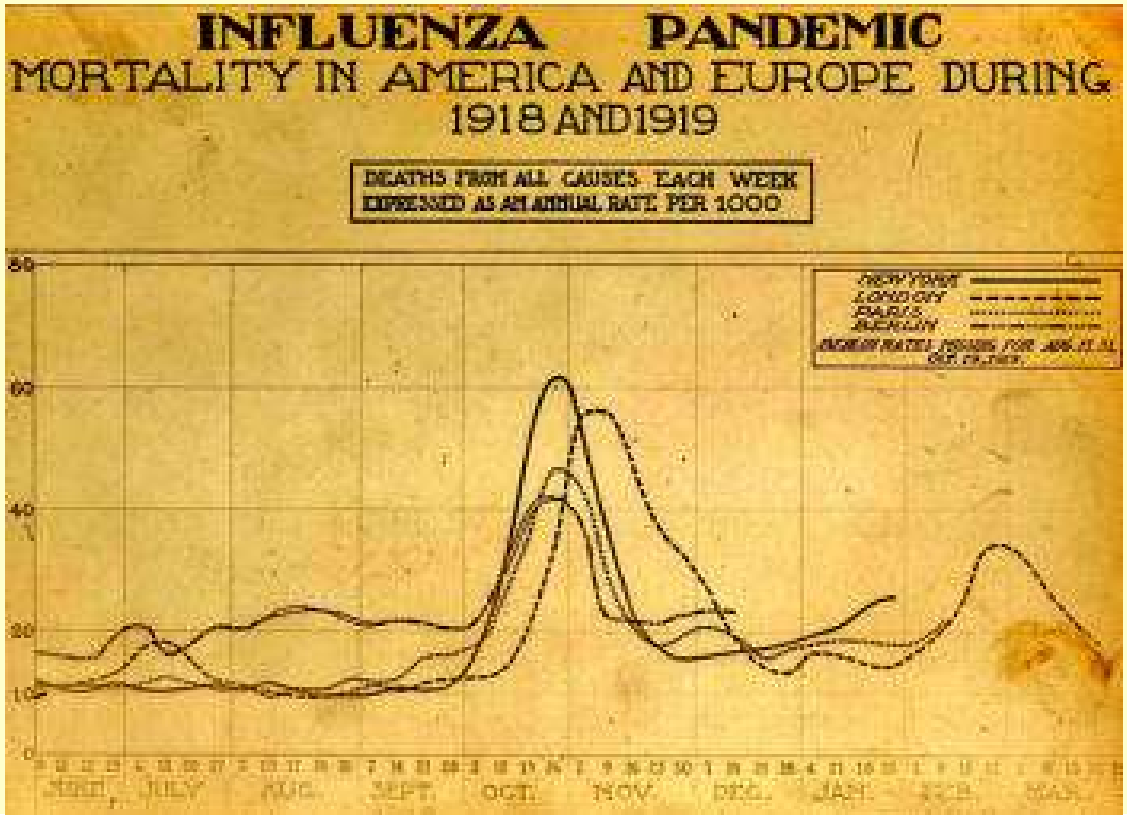
Jeffery Taubenberger of the Armed Forces Institute of Pathology in Rockville, Maryland, is the lead author of the sequencing study. He says the work was necessary and the risks were low. The paper on page 889 gives details of the final three genes; the sequences of the rest have already been published.

THE 1918 INFLUENZA EPIDEMIC WAS A VACCINE-CAUSED DISEASE

http://www.drcarley.com/

E. McBean (Vaccination The Silent Killer p28)

Very few people realize that the worst epidemic ever to hit America, the Spanish Influenza of 1918 was the after effect of the massive nation-wide vaccine campaign. If we check back in history to that 1918 flu period, we will see that it suddenly struck just after the end of World War I when our soldiers were returning home from overseas. That was the first war in which all the known vaccines were forced on all the servicemen.



Journal of Virology, May 2009, p. 4287-4296, Vol. 83, No. 9
0022-538X/09/$08.00+0 doi:10.1128/JVI.02399-08

Experimental Infection of Pigs with the Human 1918 Pandemic Influenza Virus

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Received 19 November 2008/ Accepted 6 February 2009

Swine influenza was first recognized as a disease entity during the 1918 "Spanish flu" pandemic. The aim of this work was to determine the virulence of a plasmid-derived human 1918 pandemic H1N1 influenza virus (reconstructed 1918, or 1918/rec, virus) in swine using a plasmid-derived A/swine/Iowa/15/1930 H1N1 virus (1930/rec virus), representing the first isolated influenza virus, as a reference. Four-week-old piglets were inoculated intratracheally with either the 1930/rec or the 1918/rec virus or intranasally with the 1918/rec virus.

Science 10 July 2009:
Vol. 325. no. 5937, pp. 197 - 201
DOI: 10.1126/science.1176225

Antigenic and Genetic Characteristics of Swine-Origin 2009 A(H1N1) Influenza Viruses Circulating in Humans

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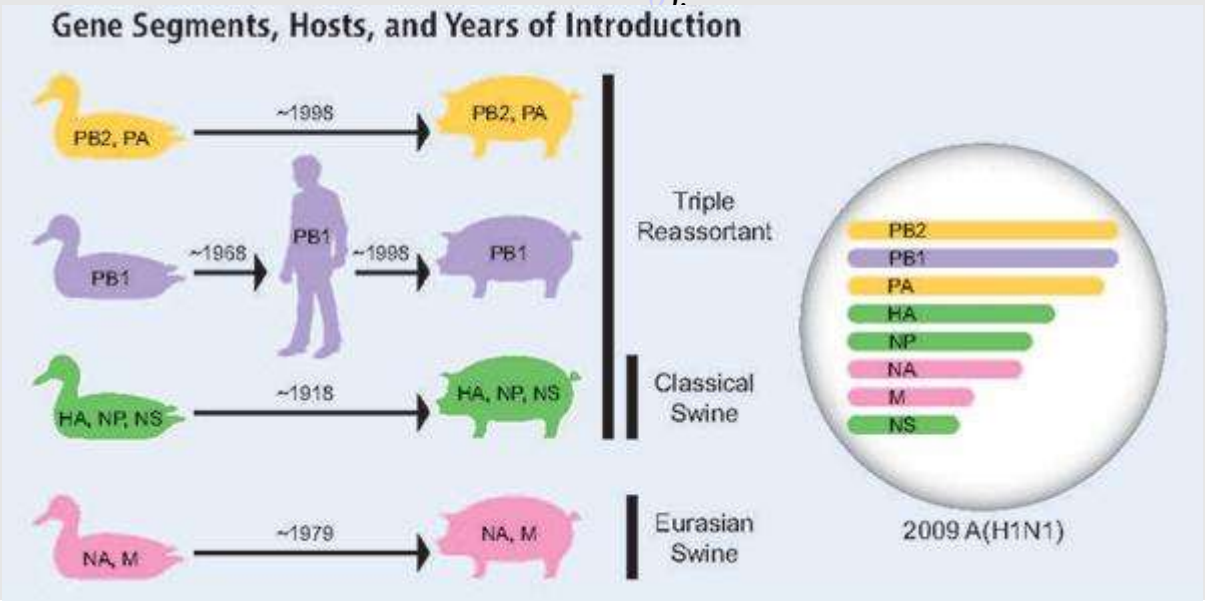
Influenza pandemics occur when an influenza virus with a hemagglutinin (*HA*), against which there is little or no existing immunity, emerges in the human population and efficiently transmits from human to human. The genomes of the last three pandemic influenza viruses (1918 H1N1, 1957 H2N2, and 1968 H3N2) all originated in whole or in part from nonhuman reservoirs, and the *HA* genes of all of the pandemic viruses ultimately originated from avian influenza viruses.

† A(H1N1) influenza viruses were first isolated from swine in 1930 (1). They have been shown to be antigenically highly similar to a recently reconstructed human 1918 A(H1N1) virus (2) and likely share a common ancestor (3, 4). From 1930 to the late 1990s, these "classical swine influenza" viruses circulated in swine and remained relatively antigenically stable (5, 6).



ISIS Report 27/07/09

Fast-tracked Swine Flu Vaccine under Fire

The vaccines far more deadly than the swine flu; mass vaccinations a recipe for disaster Dr. Mae-Wan Ho *and* Prof. Joe Cummins

This report has been submitted to Sir Liam Donaldson, Chief Medical Officer of the UK, and to the US Food and Drugs Administration

A swine flu outbreak occurred in Mexico and the United States in April 2009 and spread rapidly around the world by human-to human transmission. The new type A H1N1 influenza virus is unlike any that had been previously isolated [1, 2], judging from the first data released in May. It is a messy combination of sequences from bird, human and swine flu virus lineages from North America and Eurasia. A senior virologist based in Canberra, Australia, told the press he thought that the virus could have been created in the laboratory and released by accident [3]. Some even suggest it was made intentionally as a bioweapon [4], while others blame the intensive livestock industry and extensive trafficking of love animals over long distances, which provide plenty of opportunity for generating exotic recombinants [5]. But what worries the public most is the mass vaccination programmes governments are putting in place to combat the emerging pandemic, which could well be worse than the pandemic itself.

TORONTO SUN

Baxter: Product contained live bird flu virus

By HELEN BRANSWELL, THE CANADIAN PRESS

Last Updated: 27th February 2009, 3:26pm

The company that released contaminated flu virus material from a plant in Austria confirmed Friday that the experimental product contained live H5N1 avian flu viruses.

And an official of the World Health Organization's European operation said the body is closely monitoring the investigation into the events that took place at Baxter International's research facility in Orth-Donau, Austria.

"At this juncture we are confident in saying that public health and occupational risk is minimal at present," medical officer Roberta Andraghetti said from Copenhagen, Denmark.

"But what remains unanswered are the circumstances surrounding the incident in the Baxter facility in Orth-Donau."

The contaminated product, a mix of H3N2 seasonal flu viruses and unlabelled H5N1 viruses, was supplied to an Austrian research company. The Austrian firm, Avir Green Hills Biotechnology, then sent portions of it to sub-contractors in the Czech Republic, Slovenia and Germany.

The contamination incident, which is being investigated by the four European countries, came to light when the subcontractor in the Czech Republic inoculated ferrets with the product and they died. Ferrets shouldn't die from exposure to human H3N2 flu viruses.

Public health authorities concerned about what has been described as a "serious error" on Baxter's part have assumed the death of the ferrets meant the H5N1 virus in the product was live. But the company, Baxter International Inc., has been parsimonious about the amount of information it has released about the event.

ENTREVISTA: JEFFREY L. STURCHIO Director del Consejo Mundial de la Salud

"En la gripe, todavía no nos ha llegado la prueba decisiva"

MALEN RUIZ DE ELVIRA - Madrid - 03/11/2009

Jeffrey L. Sturchio es desde hace pocas semanas el nuevo presidente y director ejecutivo del Consejo Mundial de la Salud (Global Health Council), la mayor alianza de organizaciones y profesionales dedicados a la salud pública en los países en desarrollo. Hace menos de un año era vicepresidente de la multinacional farmacéutica Merck.

Pregunta. ¿Está preparado el mundo para la nueva gripe?
Respuesta. Hemos tenido mucha suerte con la alarma hace un par de años por la gripe aviar, que es de alta mortalidad pero difícil de transmitir, y lo que tenemos ahora es una gripe que se transmite muy fácilmente pero causa pocas víctimas mortales. El problema será cuando tengamos una gripe fácil de transmitir y de alta mortalidad y por eso es tan importante que los países estén preparados. La gripe aviar hizo que se elevara el nivel de percepción de los gobiernos. Además, la industria de las vacunas ha hecho un gran esfuerzo para tenerlas, y existen programas de colaboración para hacer llegar la inmunización a los países en desarrollo, pero aún no nos ha llegado la prueba decisiva.

Science 2 December 2011:
Vol. 334 no. 6060 pp. 1192-1193
DOI: 10.1126/science.334.6060.1192

•NEWS & ANALYSIS

INFECTIOUS DISEASES

Controversial Studies Give a Deadly Flu Virus Wings

•Martin Enserink

ROTTERDAM, NETHERLANDS—Locked up in the bowels of a medical faculty building here and accessible to only a handful of scientists lies a humanmade flu virus that scientists say could change world history if it were ever set free.

The virus is an H5N1 avian influenza strain that has been genetically altered and is now easily transmissible between ferrets, the animals that most closely mimic the human response to flu. Flu researchers believe it's likely that the pathogen, if it emerged in nature or were released, would trigger an infl uenza pandemic, quite possibly with many millions of deaths.

In an office on the 17th floor, virologist Ron Fouchier of Erasmus Medical Center calmly concedes that his team has created what is “probably one of the most dangerous viruses you can make.” But he says the research, which has been submitted for publication, promises major public health benefits. Knowing exactly what could turn H5N1 into a virus with pandemic potential is useful because scientists can look out for such changes in the wild and prepare countermeasures.

Descubren una variante del virus de la gripe aviar contagiosa y mortal para el ser humano

Investigadores holandeses han descubierto cómo se puede desarrollar una variante del virus H5N1 de la llamada "gripe aviar" para que sea contagiosa y mortal para el ser humano, pero el hecho ha abierto un debate sobre si se debería publicar el resultado de sus investigaciones por miedo a que pudieran ser utilizadas por grupos terroristas como una terrible arma biológica.

FUENTE | ABC Periódico Electrónico S.A. 28/11/2011

Según publicaba el diario holandés "Volkskrant", el Instituto Nacional de Salud norteamericano (NIH) encargó a algunos laboratorios de distintos países una investigación sobre la posibilidad de que el virus H5N1 pudiera mutar hasta una variante capaz de transmitirse de las aves al ser humano. Ron Fouchier, profesor de virología en Centro Médico Erasmus de Roterdam, anunció el pasado mes de septiembre en una conferencia sobre la gripe en Malta que ha conseguido una variante altamente contagiosa de este virus que es común en las aves pero que en su estado conocido no suele traspasar la barrera biológica hasta los humanos. En todo el mundo han muerto hasta ahora unas 500 personas a causa de este virus, uno de ellos un veterinario holandés que estaba en contacto directo con pájaros.

Cuando logra infectar a personas, la tasa de mortalidad del virus es muy alta y aunque muchos científicos consideraban que las posibilidades de una epidemia de H5N1 son muy remotas, el profesor Fouchier asegura que unas pocas mutaciones en el ADN viral, que también pueden producirse de forma natural, lo convertirían en una variante altamente contagiosa.

Comienza la campaña de vacunación contra la gripe

Más de un millón de personas se vacunarán en los centros de salud de la Comunidad hasta el próximo 30 de noviembre en la campaña de vacunación conjunta contra la gripe estacional y el neumococo.

La **Comunidad de Madrid pone en marcha este lunes la campaña de vacunación conjunta contra la gripe estacional y el neumococo** en los centros de salud, que finalizará el próximo 30 de noviembre. La previsión de vacunación contra la gripe estacional es de más de un millón de personas, las personas que se vacunarán son las mismas que años anteriores: **un 69% de personas mayores**; y cerca de 500.000 personas menores de 64 años pertenecientes a los grupos de riesgo. Y las razones para no hacerlo también son comunes a los años anteriores, como la falta de efectividad.

La **inversión de la campaña antigripal** asciende a 4.636.859 euros y el coste de la vacuna antineumocócica es de 905.242. Se han adquirido **70.000 dosis de vacunas** frente a la gripe virosómicas para personas con factores de riesgo, como son enfermos crónicos: cardiovasculares, pulmonares, diabéticos e inmunodeprimidos; y las **embarazadas,** y 581.000 dosis de una vacuna destinada a los mayores de 64 años, altamente protectora en **personas de edad avanzada**, que puedan tener problemas crónicos de salud y bajas defensas.

Composición de la vacuna para la compaña 2011

Los virus de la gripe evolucionan constantemente, con rápidos cambios en sus características antigénicas. **La vacuna contiene tres cepas;** entre los principales tipos de virus que circulan por todo el mundo se incluye un tipo A (H1N1), un tipo A (H3N2) y un tipo B. Su composición se modifica cada año incluyendo un subtipo de cada una de estas categorías para garantizar la protección frente a las cepas prevalentes en cada temporada.

La pérdida de confianza en los laboratorios -y sobre todo en sus vacunas- que impulsaron una **pandemia inexistente** como la de la **Gripe A** ha debido ser tal que alguien se ha visto obligado a crear un *spot* publicitario de hora y media de duración bajo el título de ***Contagio***. Lo ofrecen en los cines dirigido por un director de reconocida solvencia **Steven Soderbergh** y con un elenco de actores de relumbrón que se han prestado a un juego macabro: **Matt Damon**, **Gwyneth Paltrow**, **Lawrence Fishburne**, **Kate Winslett**, **Marion Cotillard**, **Jude Law**.

'Contagio', el nuevo film de Steven Soderbergh, ha llamado la atención de la comunidad sanitaria por la verosimilitud con que refleja las distintas reacciones sociales ante una **supuesta epidemia mundial**. Uno de los personajes principales, interpretado por Jude Law, muestra a un **bloguero independiente y antisistema** que pretende socavar la credibilidad de las autoridades sanitarias con el fin de**promocionar un remedio homeopático**.

PNAS | **September 26, 2006** | vol. 103 | no. 39 | **14390-14395**

BIOLOGICAL SCIENCES / DEVELOPMENTAL BIOLOGY

Endogenous retroviruses regulate periimplantation placental growth and differentiation.

Kathrin A. Dunlap*, Massimo Palmarini, Mariana Varela, Robert C. Burghardt, Kanako Hayashi*, Jennifer L. Farmer*, and Thomas E. Spencer*, *Center for Animal Biotechnology and Genomics, Department of Animal Science, and Image Analysis Laboratory, Department of Veterinary Integrative Biosciences, Texas A&M University, College Station, TX 77843; and Institute of Comparative Medicine, University of Glasgow Veterinary School, Glasgow G61 1QH, United Kingdom

Edited by George E. Seidel, Jr., Colorado State University, Fort Collins, CO, and approved August 8, 2006 (received for review May 10, 2006)

Endogenous retroviruses (ERVs) are fixed and abundant in the genomes of vertebrates. Circumstantial evidence suggests that ERVs play a role in mammalian reproduction, particularly placental morphogenesis, because intact ERV envelope genes were found to be expressed in the syncytiotrophoblasts of human and mouse placenta and to elicit fusion of cells *in vitro*.

Bioessays. 1998 Apr;20(4):307-16.

Placental endogenous retrovirus (ERV): structural, functional, and evolutionary significance.

• Harris JR.
Institute of Zoology, University of Mainz, Germany.
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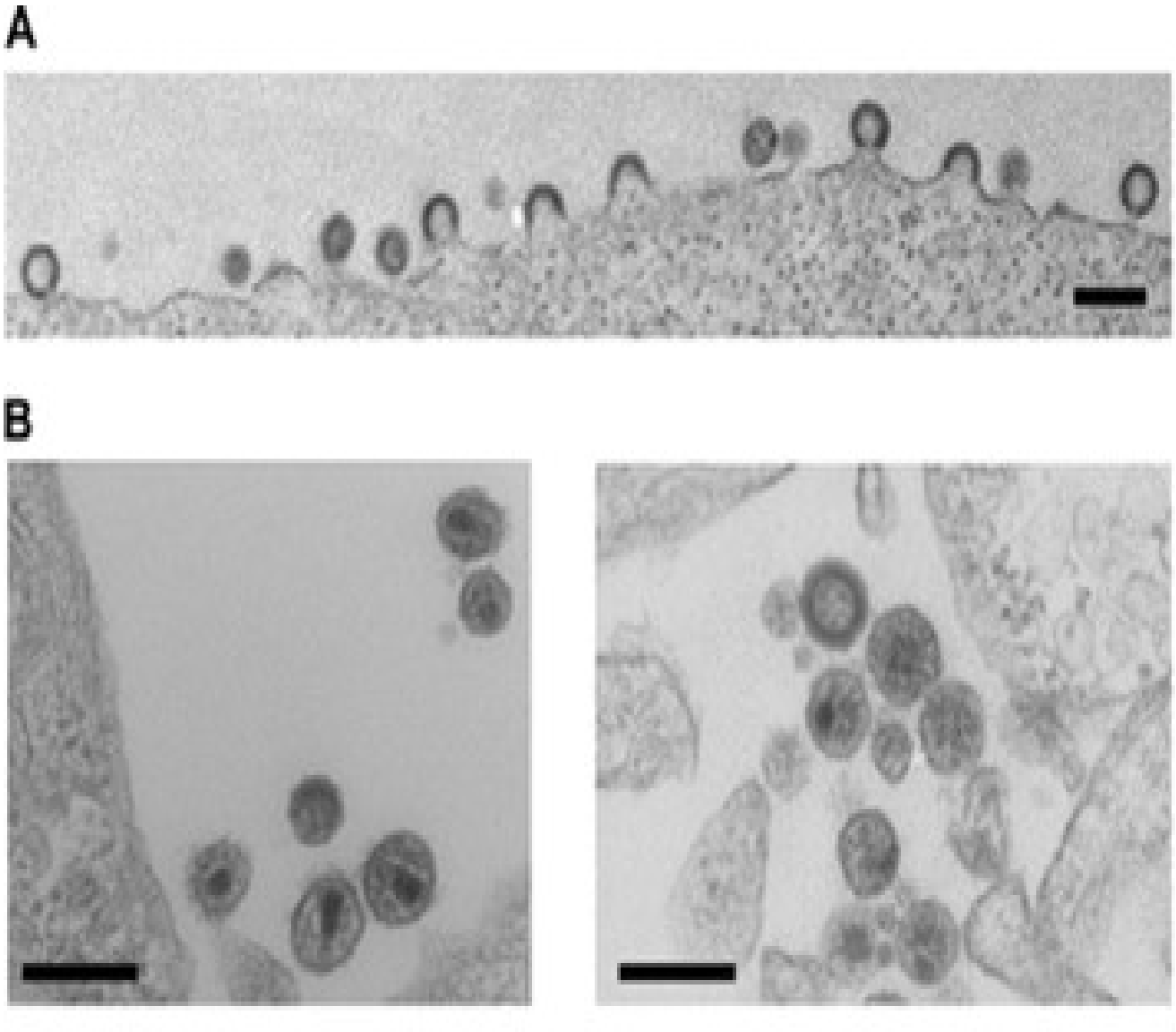
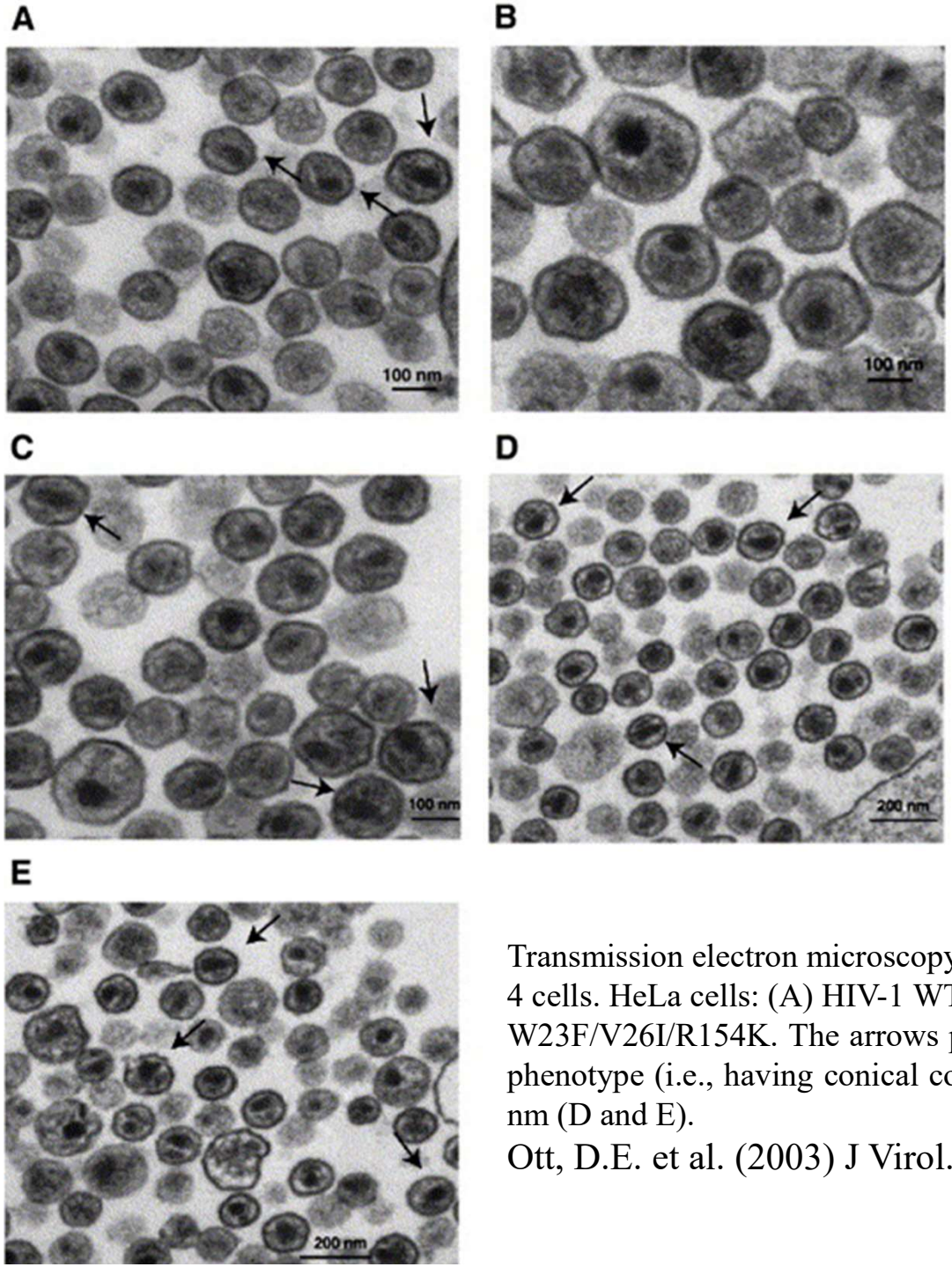
That endogenous retrovirus (ERV) is present within the placenta of humans and other mammals has been known for the past 25 years, but the significance of this observation is still not fully understood. Much molecular biological data have emerged in recent years to support the earlier electron microscopic data on the presence of placental ERV. The evidence for ERV in animal and human placental tissue is presented, then integrated with data on the presence of ERV in a range of other tissues, in particular teratocarcinoma cells. Placental invasiveness and maternal immunosuppression are then discussed in relation to metalloproteinase secretion, the immunosuppressive potential of retroviruses, and placental growth factors, while the evidence for a functional link between placental protooncogenes and trophoblast malignancy is reviewed. Finally, placental development, structure, and life span are discussed within an evolutionary context. The hypothesis that one or more ancient trophoblastic ERVs could have played a role in the evolution and divergence of all placental mammals is evaluated.



Ultrastructure of budding sites and released particles. A, representative section of a plasma membrane region of HeLaP4 cells transfected with wild-type pNL4-3 showing budding sites and immature virions. These structures appeared similar for wild-type HIV-1 and all mutant constructs. B, representative sections depicting normal mature virions released from wild-type pNL4-3 transfected cells (left panel) and aberrant HIV-1 structures released from variant L211S transfected cells (right panel). Similar phenotypes were observed for the other assembly-competent (N183A, E187A) and assembly-incompetent (Y169A, L211A) variants, respectively.

Waheed, A.A., y col. (2008) J Virol.

82:9776-9781



Transmission electron microscopy of WT and mutant virions produced in HeLa and MT-4 cells. HeLa cells: (A) HIV-1 WT; (B) W23F. MT-4 cells: (C) WT; (D) W23F/V26I; (E) W23F/V26I/R154K. The arrows point to representative particles in the field with a WT phenotype (i.e., having conical cones). The scale bars are 100 nm (A, B, and C) or 200 nm (D and E).

Ott, D.E. et al. (2003) J Virol. 2003 77:5547-5556

Nature Medicine **3**, 37 - 41 (1997)
doi:10.1038/nm0197-37

A new transmissible AIDS-like disease in mice induced by alloimmune stimuli

Victor S. Ter-Grigorov[1,2,3], Oleg Krifuks[1], Eugenia Liubashevsky[1], Abraham Nyska[1], Zeev Trainin[1] & Vladimir Toder[2]

The search for a suitable and reliable animal model for human AIDS that is easy to use on a large scale continues. Here we describe a new condition in mice that closely resembles human AIDS, namely, chronic lymphoproliferation with dramatic depletion of CD4-positive cells, progressive impairment of the immune responses, and Kaposi's sarcoma-like tumors or terminal B-lymphomas. The AIDS-like disease was primarily induced by mating BALB/c female mice to C57BL/6 males during a 1-year period (7−10 allogeneic pregnancies) followed by immunization with paternal lymphocytes. The disease is sexually and vertically transmissible, transferrable by cell-free plasma and is associated with autoimmune reactions to major histocompatibility complex antigens and CD4 cells. We hope that this becomes a model for studying the mechanisms of AIDS immunopathogenesis and immune-based treatment approaches.

Bioessays. 1998 Apr;20(4):307-16.

Placental endogenous retrovirus (ERV): structural, functional, and evolutionary significance.

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That endogenous retrovirus (ERV) is present within the placenta of humans and other mammals has been known for the past 25 years, but the significance of this observation is still not fully understood. Much molecular biological data have emerged in recent years to support the earlier electron microscopic data on the presence of placental ERV. The evidence for ERV in animal and human placental tissue is presented, then integrated with data on the presence of ERV in a range of other tissues, in particular teratocarcinoma cells. Placental invasiveness and maternal immunosuppression are then discussed in relation to metalloproteinase secretion, the immunosuppressive potential of retroviruses, and placental growth factors, while the evidence for a functional link between placental protooncogenes and trophoblast malignancy is reviewed. Finally, placental development, structure, and life span are discussed within an evolutionary context. The hypothesis that one or more ancient trophoblastic ERVs could have played a role in the evolution and divergence of all placental mammals is evaluated.

El VIH se originó en un tipo de chimpancés que habita en Camerún, según un estudio

ELPAIS.es - Sociedad - 25-05-2006

EFE - Washington

Aunque la leyenda urbana más extendida sitúa el nacimiento del Virus de Inmunodeficiencia Humana (VIH) en un laboratorio, la comunidad científica hace tiempo que acordó que fueron monos africanos los causantes del mal. Ahora, un equipo internacional de científicos ha confirmado que el virus que causa el sida se originó en chimpancés que viven en el África Central, según un informe que hoy publica en la revista *Science*.El grupo, integrado por investigadores de EE UU, Francia, Reino Unido y Camerún, explica que pruebas genéticas extraídas de material fecal de esos chimpancés en las selvas de Camerún han determinado que el virus, identificado como VIH-1, surgió de ese tipo de primates, una subespecie llamada *Pan troglogdytes troglodytes* que vive en las selvas del sur de Camerún. Una forma de otro virus de inmunodeficiencia llamado VIS (por Virus de Inmunodeficiencia Simia), que es el pariente más cercano del VIH, había sido hallado solamente en chimpancés cautivos. No existe una variante del VIS que haya infectado hasta ahora a seres humanos.

Monkey meat riddled with SIV

HIV's ancestor common in African bushmeat.

25 March 2002

TOM CLARKE

The boom in bushmeat is bringing more people into contact with SIV.

© Ecoscene/Karl Ammann

More than one-fifth of the monkey meat sold in the markets of Cameroon is infected with HIV's ancestor, SIV, the first thorough survey of bushmeat reveals[1].

The level and variety of simian immunodeficiency virus (SIV) strains found highlights the risk of new HIV-like viruses entering humans via bushmeat, claim the researchers."It happened before, so why shouldn't it happen again?" asks Martine Peeters, a virologist at the Research Institute for Development in Montpellier, France who led the research team. She suspects the situation in Cameroon is typical of tropical Africa.The traditional bushmeat trade has boomed as roads have penetrated the jungles. Urban growth has boosted demand for rare delicacies, bringing more people into contact with SIV. "The risk now is much higher than 40 or 50 years ago," says Peeters.

www.sciencemag.org SCIENCE VOL 288 9 JUNE 2000

Timing the Ancestor of the HIV-1 Pandemic Strains

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HIV-1 sequences were analyzed to estimate the timing of the ancestral sequence of the main group of HIV-1, the strains responsible for the AIDS pandemic. Using parallel supercomputers and assuming a constant rate of evolution, we applied maximum-likelihood phylogenetic methods to unprecedented amounts of data for this calculation. We validated our approach by correctly estimating the timing of two historically documented points. Using a comprehensive full-length envelope sequence alignment, we estimated the date of the last common ancestor of the main group of HIV-1 to be 1931 (1915Ð41). Analysis of a gag gene alignment, subregions of envelope including additional sequences, and a method that relaxed the assumption of a strict molecular clock also supported these results.

Nuclear DNA does not reconcile ‘rocks’ and ‘clocks’ in Neoaves: a comment on Ericson et al.

Biol. Lett. (2007) 3, 257–259
doi:10.1098/rsbl.2006.0611
Published online 27 March 2007

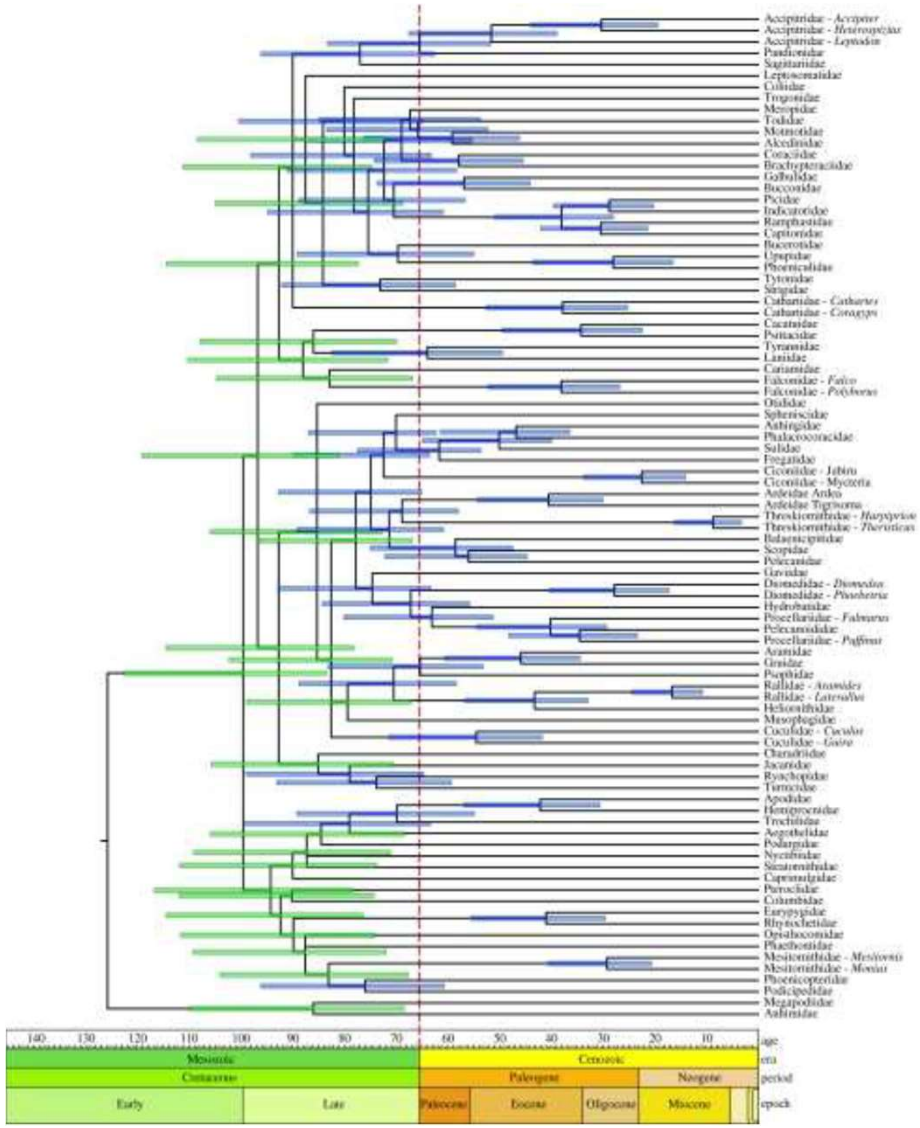


Figure 1. Chronogram for Neoaves estimated using a Bayesian modelling of rate evolution. The dashed vertical red line marks the K–T boundary. Error bars represent posterior probability (0.95) credible intervals (root node 104–154 Myr).
An unambiguous ancient diversification of Neoaves is indicated by 24 credible intervals restricted to the Cretaceous (green bars).

THE ORIGIN OF AIDS by Matt Ridley

Wednesday, 14 June 2000

Prospect
(UK), June 2000, pp. 31-35; reprinted as "The true origin of AIDS" in *Mail and Guardian* (Johannesburg), 7-13 July 2000, pp. 22-23, 31.

Most scientists believe that Aids was "naturally" transferred from primates to human beings via a hunter who ate a chimpanzee. But a competing theory claims that Aids was caused in the 1950s when thousands of Africans were given a live polio vaccine derived from chimp kidneys. The stakes are getting higher.

Dr. Hilary Koprowski is the creator of the live polio vaccine, the developer of the rabies vaccine, and the first researcher to advance the diagnostic and therapeutic use of monoclonal antibodies.

Una vacuna experimental contra el sida se aplicará a 3.000 personas en Suráfrica

Los voluntarios deben ser activos sexualmente, tener entre 18 y 35 años y, en el caso de las mujeres, no estar embarazada

ELPAIS.com / EFE - *Madrid / Johannesburgo* - 08/02/2007

La primera prueba a gran escala de una vacuna experimental contra el sida se llevará a cabo en Suráfrica, el país africano más azotado por la enfermedad, en el que 3.000 hombres y mujeres no infectados con el virus VIH y activos sexualmente serán sometidos a un tratamiento médico durante cuatro años. Hasta entonces no se sabrán si los resultados son un éxito en la lucha contra la pandemia o un nuevo y sonoro fracaso.

La vacuna del sida confirma su eficacia

La presentación detallada de los resultados de la primera fórmula que frena el VIH corrobora que la protección es modesta pero real. Aún se desconoce por qué ha funcionado

ÁNGEL NAVARRETE
AINHOA IRIBERRI - PARÍS - 21/10/2009 00:00

...Dos años después del sonado fracaso del estudio clínico STEP (el último de una inmunización contra el VIH que había llegado a fase III), nadie pensaba que el único ensayo en la misma fase que se mantenía en todo el mundo algunos, incluso, habían llegado a solicitar su cancelación anticipada fuera a dar buenas noticias en la lucha contra el sida.

… cuando los principales investigadores del estudio, algunos vestidos con el imponente uniforme del Ejército estadounidense, se disponían a dar los datos. Los investigadores y la prensa esperaban que los responsables del estudio despejaran **algunas dudas sobre la eficacia de la vacuna**, que habían sido puestas de manifiesto la semana pasada por algunos investigadores citados en el blog de la revista *Science* .

… por primera vez, la combinación de dos vacunas antiVIH ha evitado que un 31,2% de los inmunizados eludan al virus *ineludible* casi por definición.

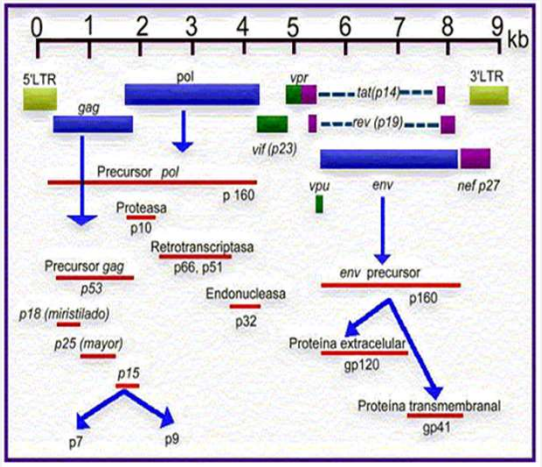
…Pero el hecho es que, cuando se cuenta con estos siete infectados, **el porcentaje de eficacia baja a 26,4% y deja de ser estadísticamente significativo**.

…Según Esteban, lo más importante de lo que se presentó ayer en París no son estas diferencias porcentuales. **"Por fin hay un sentimiento de optimismo, no de pesimismo como en anteriores conferencias"**

…Pero **siguen existiendo grandes incógnitas sobre por qué ha funcionado la combinación de estas dos vacunas** que, por separado, no habían demostrado ser eficaces. Por ejemplo, por qué la presencia del virus entre los infectados vacunados y los que no habían recibido la inmunización era similar, algo muy sorprendente.

…Sin embargo, una vacuna desarrollada por el laboratorio Merck lo hizo y con ella se diseñó un estudio en fase III. Un año antes de lo previsto, se suspendió porque se descubrió que la vacuna no sólo no protegía del sida, sino que lo favorecía. Después de este fracaso, la comunidad científica pensó que ninguna otra vacuna iba a funcionar.

Mediante el motor de búsqueda BLAST (*Basic Local Alignment Search Tool*) y seleccionando las funciones blastp (que compara una secuencia de aminoácidos con todas las proteínas que codifica el genoma humano) o tblastn (compara una secuencia de aminoácidos con una secuencia nucleotídica traducida a aminoácidos en las 6 pautas de lecturas posibles de las dos cadenas de ADN) se intentaron identificar algunas de las proteínas más significativas del VIH en el genoma humano.



Para la proteína **Env**: encuentra identidad para una extensión del 45% de la proteína, y la identidad es del 88% con una secuencia que está anotada como Env de un retrovirus endógeno tipo HERV-K

- Para la proteína **Gag**: encuentra identidad para una extensión del 46% de la proteína, y la identidad es del 33% con una secuencia que está anotada como Gag de un retrovirus endógeno tipo HERV-K.
- Para la proteína **Pol**: encuentra identidad para una extensión del 83% de la proteína, y la identidad es del 29% con una secuencia que está anotada como Pol de un retrovirus endógeno tipo HERV-K
- Para la **retrotranscriptasa**: encuentra identidad para una extensión del 65% de la proteína, y la identidad es del 35% con una secuencia que está anotada como transcriptasa inversa de un retrovirus endógeno tipo HERV-K

II

HIV-1/SIVcpz Complete Genomes

Alignment of HIV-1/SIVcpz Genomes

This year again many new full-length viral sequences have become available, originating from diverse geographic origins and representing the spectrum of known HIV variation. We have decided to publish only full length HIV-1/CPZ sequences in our printed nucleotide alignment section, as this set is now becoming an adequate representation of the overall diversity of the virus.

As of March 2002 there were 344 complete or nearly complete (defined as greater than 8,000 consecutive basepairs of sequence) HIV-1 genomes in the database. Of these, some were not included in the printed alignment, as they are very closely related to a sequence already included in the alignment, and our intent is to print a hardcopy alignment representative of global diversity. The complete alignment including all sequences is available at our web site.

http://hiv-web.lanl.gov/ALIGN_CURRENT/ALIGN-INDEX.html

One hundred twenty-two HIV-1 sequences plus viral strains isolated from chimpanzees comprise the printed alignment. In phylogenetic analyses, the CPZ sequences are the simian-derived viruses most similar to HIV-1; in fact HIV-1 M, N and O group sequences are roughly as distant from one another as they are from the CPZ sequences (see Figure 1 in Section III page 468of this compendium).

The sequences in this section are identified by their common name preceded by the HIV subtype designations and country of origin. The primary sequence reference, country of origin, database accession number, and brief notes describing the isolate and sequence, with some additional relevant references, can be found in Table 2, page 286. The sequences that have been found to be recombinants with portions of the genetic sequences associated with different subtypes are indicated by listing all of the subtypes in the prefix to the name. For example, the prefix AG simply indicates that some regions of the sequence are subtype A-like, others G-like. The subtypes are organized alphabetically and not meant to reflect the proportion of either subtype in the mosaic genome.

This alignment was generated by using the HMMER Hidden Markov Model sequence alignment software developed by Sean Eddy.

http://genome.wustl.edu/eddy/hmmer.html

An iterative process was used involving alignment of the genomes using HMMER, followed by hand-editing (using the programs MASE and BioEdit).

http://www.mbio.ncsu.edu/RNaseP/info/programs/BIOEDIT/bio-edit.html

One hundred twenty-two HIV-1 sequences plus viral strains isolated from chimpanzees comprise the printed alignment. In phylogenetic analyses, the CPZ sequences are the simian-derived viruses most similar to HIV-1; in fact HIV-1 M, N and O group sequences are roughly as distant from one another as they are from the CPZ sequences (see Figure 1 in Section III page 468of this compendium).

giri

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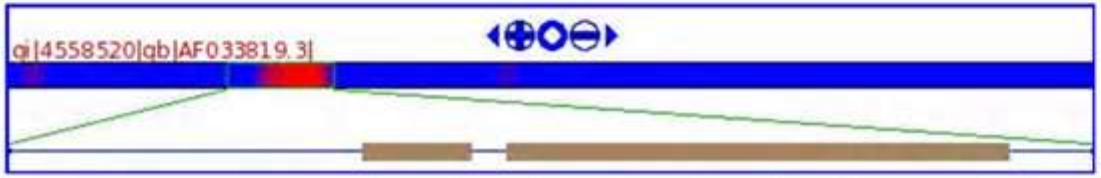
Map of Hits

SVG viewer is required to view graphical representation of the map as Scalable Vector Graphics (SVG plot).

gi|4558520|gb|AF033819.3| (SVG Plot; Alignments; Masked)



Name	From	To	Name	From	To	Class	Dir	Sim	Pos	Score
gi|4558520|gb|AF033819.3|	182	215	MacERV4_int	1	32	ERV/ERV2	d	0.8788	0.8788	233
gi|4558520|gb|AF033819.3|	2140	2233	HERV-K14CI	2891	2993	LTR	d	0.6875	0.6875	201
gi|4558520|gb|AF033819.3|	2264	2689	HERV-K14I	2772	3189	LTR	d	0.6715	0.6715	443
gi|4558520|gb|AF033819.3|	4193	4231	MacERV4_int	5078	5116	ERV/ERV2	d	0.8462	0.8462	243

Masked Sequence

```
>gi|4558520|gb|AF033819.3|
GGTCTCTCTGGTTAGACCAGATCTGAGCCTGGGAGCTCTCTGGCTAACTAGGGAACCCACTGCTTAAGCC
TCAATAAAGCTTGCCTTGAGTGCTTCAAGTAGTGTGTGCCCGTCTGTTGTGTGACTCTGGTAACTAGAGA
TCCCTCAGACCCTTTTAGTCAGTGTGGAAAATCTCTAGCAGXXXXXXXXXXXXXXXXXXXXXXXXXXXX
XXXXXAACCAGAGGAGCTCTCTCGACGCAGGACTCGGCTTGCTGAAGCGCGCACGGCAAGAGGCGAGGGG
CGGCGACTGGTGAGTACGCCAAAAATTTTGACTAGCGGAGGCTAGAAGGAGAGAGATGGGTGCGAGAGCG
TCAGTATTAAGCGGGGGAGAATTAGATCGATGGGAAAAAATTCGGTTAAGGCCAGGGGGAAAGAAAAAAT
ATAAATTAAAACATATAGTATGGGCAAGCAGGGAGCTAGAACGATTCGCAGTTAATCCTGGCCTGTTAGA
AACATCAGAAGGCTGTAGACAAATACTGGGACAGCTACAACCATCCCTTCAGACAGGATCAGAAGAACTT
AGATCATTATATAATACAGTAGCAACCCTCTATTGTGTGCATCAAAGGATAGAGATAAAAGACACCAAGG
AAGCTTTAGACAAGATAGAGGAAGAGCAAAACAAAAGTAAGAAAAAAGCACAGCAAGCAGCAGCTGACAC
AGGACACAGCAATCAGGTCAGCCAAAATTACCCTATAGTGCAGAACATCCAGGGGCAAATGGTACATCAG
GCCATATCACCTAGAACTTTAAATGCATGGGTAAAAGTAGTAGAAGAGAAGGCTTTCAGCCCAGAAGTGA
TACCCATGTTTTCAGCATTATCAGAAGGAGCCACCCCACAAGATTTAAACACCATGCTAAACACAGTGGG
GGGACATCAAGCAGCCATGCAAATGTTAAAAGAGACCATCAATGAGGAAGCTGCAGAATGGGATAGAGTG
CATCCAGTGCATGCAGGGCCTATTGCACCAGGCCAGATGAGAGAACCAAGGGGAAGTGACATAGCAGGAA
```

PLoS Pathog 6(7): e1001030. doi:10.1371/journal.ppat.1001030

Unexpected Inheritance: Multiple Integrations of Ancient Bornavirus and Ebolavirus/Marburgvirus Sequences in Vertebrate Genomes

Abstract

Vertebrate genomes contain numerous copies of retroviral sequences, acquired over the course of evolution. Until recently they were thought to be the only type of RNA viruses to be so represented, because integration of a DNA copy of their genome is required for their replication. In this study, an extensive sequence comparison was conducted in which 5,666 viral genes from all known non-retroviral families with single-stranded RNA genomes were matched against the germline genomes of 48 vertebrate species, to determine if such viruses could also contribute to the vertebrate genetic heritage. In 19 of the tested vertebrate species, we discovered as many as 80 high-confidence examples of genomic DNA sequences that appear to be derived, as long ago as 40 million years, from ancestral members of 4 currently circulating virus families with single strand RNA genomes. Surprisingly, almost all of the sequences are related to only two families in the Order *Mononegavirales*: the Bornaviruses and the Filoviruses, which cause lethal neurological disease and hemorrhagic fevers, respectively. The integrations represent genes that encode viral nucleocapsid, RNA-dependent-RNA-polymerase, matrix and, possibly, glycoproteins. Integrations are generally limited to one or very few copies of a related viral gene per species, suggesting that once the initial germline integration was obtained (or selected), later integrations failed or provided little advantage to the host. Clearly, the sources of genetic information in vertebrate genomes are much more diverse than previously suspected.

Specie	Scaffold or Chromosome	Virus	Integrated gene	Location within present-day virus protein	Viral protein length	BLAST hit, E-value and percent identity[1]	Label	Significant large ORFs (length and position)
Human (*Homo Sapiens*)	chr10	Bornavirus	N	28–349	370aa	2E-65/41%	hsEBLN-1	366aa (full protein)
Squirrel (*Spermophilus Tridecemlineatus*)	scaffold113120	Bornavirus	N	40–368	370aa	1E-155/77%	stEBLN	203aa (residues 170–370)
Microbat (*Myotis Lucifugus*)	scaffold144630	Reston Ebolavirus	VP35	74–329	329aa	5E-23/30%	mlEEL35	281aa (residues 52–329)
Tarsier (*Tarsius Syrichta*)	scaffold521	Reston Ebolavirus	VP35	138–329	329aa	5E-16/34%	tsEEL35	131aa (residues 137–261)
Grey Mouse Lemur (*Microcebus Murinus*)	scaffold5488	Bornavirus	M	1–123	142aa	4E-13/45%	mmEBLM	93aa (residues TSS-102)
Medaka (*Oryzias Latipes*)	scaffold1213	Bornavirus	M	15–138	142aa	5E-07/33%	olEBLM	69aa (residues TSS-71)
Microbat (*Myotis Lucifugus*)	scaffold114379	Bornavirus	L	189–1066	1608aa	3E-96/42%	mlEBLL-1B	149aa
Microbat (*Myotis Lucifugus*)	scaffold131047	Lake Victoria Marburgvirus	N	63–437	695aa	2E-36/32%	mlEELN-1	158aa (residues 72–228) and 164aa (residues 228–391)
Opossum (Monodelphis Domestica)	chr2	Reston Ebolavirus	NP	175–409	739aa	4E-39/46%	mdEELN	no significant ORF found
Wallaby (*Macropus Eugenii*)	scaffold117569	Sudan Ebolavirus	NP	22–312	738aa	1E-28/33%	meEELN-S	>218aa likely (incomplete scaffold)
Opossum (Monodelphis Domestica)	chr3	Lake Victoria Marburgvirus	L	605–1354	2331aa	5E-72/	mdEELL	no significant ORF found
Zebrafish (*Danio Rerio*)	chr25	Midway Virus	L	238–962	1935aa	8E-027/21%	drEMLL-3	761aa (residues TSS-756)
								180aa (residues 792–971)

[1]Only the top BLAST E-value and average percent identity are shown when BLAST alignment returns multiple gene fragments. Please refer to supplementary data (Tables S1, S2, S3, S4, S5, S6 and S7) for a complete list of integrations and individual BLAST hits.

doi:10.1371/journal.ppat.1001030.t002

Table 2. Selected endogenous viral sequences found in vertebrate genomes.

Un ensayo de terapia genética expone por error al virus del sida a enfermos de cáncer

Dos hospitales de Estados Unidos pudieron infectar a más de 20 niños y adolescentes

EL PAÍS, **Madrid**

La terapia genética vuelve a colocarse bajo sospecha. Dos docenas de menores enfermos de cáncer se han visto expuestos por error al virus del sida, en un experimento genético para curarles de sus tumores en dos hospitales de Estados Unidos. Según el diario *The Washington Post*, los investigadores federales lo descubrieron el pasado diciembre, pero no lo hicieron público hasta el pasado jueves. Los pacientes se habían sometido voluntariamente al experimento. Ya hay constancia de al menos nueve muertes más en Estados Unidos en programas de este tipo de terapia.

Los datos todavía no son definitivos, porque la Agencia de Alimentos y Fármacos de Estados Unidos (Food and Drug Administration, FDA) debe aún determinar si realmente hubo contaminación con los virus del sida y de la hepatitis C, pero el caso viene a sumarse a recientes denuncias sobre graves fallos de notificación en ensayos de terapia genética.

Según fuentes oficiales, en la actualidad sobrevive un puñado de la veintena larga de pacientes sometidos al experimento. Todos los fallecimientos, se informa, se han debido a los cánceres que padecían, puesto que se encontraban en fase terminal.

Pero, pese a la denuncia, el

EL PAÍS, jueves 30 de septiembre de 1999

Muere un voluntario tras recibir un tratamiento genético experimental

Médicos de Filadelfia intentaban curarle una dolencia hereditaria

EL PAÍS, Madrid

La terapia genética no se ha apuntado todavía ningún éxito, pero es probable que ya cuente con su primera víctima. Jesse Gelsinger, un hombre de 18 años que padecía una enfermedad hereditaria y se había prestado voluntariamente a recibir un tratamiento genético experimental, murió el pasado día 17 tras ser inoculado con virus modificados por un equipo científico de la Universidad de Pensilvania en Filadelfia (EE UU).

Los científicos tienen puestas grandes esperanzas en la terapia genética, es decir, en la posibilidad de corregir cualquier enfermedad hereditaria mediante la introducción en el paciente (generalmente mediante un virus modificado) de versiones correctas del gen erróneo que provoca la dolgún éstos, los procedimientos experimentales necesitan madurar mucho más en los laboratorios de investigación básica antes de dar el salto a los ensayos clínicos con pacientes humanos.

La enfermedad de Gelsinger (llamada deficiencia de la ornitina transcarbamilasa) se debía a ningún daño. Sin embargo, las dosis de virus que recibió Gelsinger eran mayores que las de los demás. Los virus modificados fueron administrados directamente al hígado a través de los vasos sanguíneos que irrigan ese órgano. Al día siguiente, el hígado del paciente empezó a fallar

Jesse Gelsinger died after receiving experimental gene therapy for an inherited liver disease

Gene Therapy: Is Death an Acceptable Risk?

By Brandon Keim

08.30.07

Jolee Mohr, 36, died during a clinical trial using gene therapy to treat rheumatoid arthritis. The photograph was taken on July 1, the day before she received the injection.

Photo: Courtesy of the Mohr family

A 36-year-old woman with rheumatoid arthritis died in July, while participating in a gene-therapy clinical trial. Some experts say she shouldn't have received such an unpredictable, potentially dangerous treatment in the first place.

Jolee Mohr was married, the mother of a 5-year-old daughter, and worked at the Secretary of State's office in her hometown of Springfield, Illinois. By all accounts she was able to lead a full and active life, with existing drugs keeping her disease under control.

Médicos de EE UU piden que no se informe de las muertes por terapia génica

TWP, **Washington**

Un prestigioso científico y una compañía farmacéutica han pedido a la Administración de EE UU que se mantenga en secreto la información sobre las muertes o las enfermedades de pacientes que se encuentren en tratamiento con terapia génica. La solicitud ha desatado inmediatamente la polémica en un campo científico que se ha enorgullecido siempre de su transparencia.

Ronald Crystal, un genetista de Nueva York, informó con todo detalle a los Institutos Nacionales de la Salud (INH) de la muerte de uno de sus pacientes sometido a terapia génica y de su conclusión de que el fallecimiento no había sido causado por el tratamiento. El médico pidió a los INH que su notificación se mantuviera "confidencial y no parte de la información pública" que tradicionalmente ofrece este organismo federal. En el mismo sentido, la compañía farmacéutica Schering-Plough solicitó que los efectos secundarios de la terapia fueran también materia reservada.

dos del Gobierno han admitido que las leyes que obligan a los investigadores a hacer públicos sus resultados son imperfectas y, por lo tanto, pueden ser mejoradas. Los defensores de la confidencialidad de los datos alegan que todo aquello que puede ser patentado —caso de una terapia génica—es algo que la compañía que lo desarrolla tiene derecho a mantener en secreto. Los detractores ponen un límite: la notificación de los fallecimientos.

Estas revelaciones se producen en medio de un creciente interés público sobre la seguridad de la terapia génica, un campo experimental que busca corregir enfermedades hereditarias o trata algunos tipos de tumores. En respuesta a esta preocupación, en los comienzos del desarrollo de este campo médico se creó un comité especial, al que deben ser notificadas todas las investigaciones relacionadas con tratamientos genéticos.

En opinión de Amy Patterson, miembro de este comité, la terapia génica "es una nueva

Last chance to stop and think on risks of xenotransplants

US regulations are soon to be released allowing trials of animal-to-human transplants. Some feel this is premature, arguing that the risks of creating human diseases remain uncertain, and more preclinical research is needed.

Prospects that the transplant of animal organs, tissues and cells into humans will become a practical proposition are looking increasingly promising, as progress is made towards overcoming the formidable barriers of cross-species rejection. Few doubt that xenotransplantation could eventually bring important medical benefits. But there is still heated debate about the circumstances under which it should be allowed to cross the Rubicon from animal studies into the clinic — if at all.

The dilemma is that, when one tests animal-to-human transplants, one is also carrying out another, unwanted, experiment — testing the remote but real danger that animal viruses might jump to humans and cause man-made pandemics. This concern has come to the fore over the past year just as earlier concerns about animal welfare and the ethics of xenotransplantation have faded (see *Nature* **382**, 197 & **380**, 6; 1996).

Optimism that breeding disease-free animals might overcome viral risks has been dealt a blow recently by the discovery that pigs, the current donor of choice, harbour endogenous retroviruses (PERV) that can infect human cells *in vitro*. Multiple copies of PERV are integrated in the pig genome which suggests that breeding 'clean' pigs will be extremely difficult, if not impossible.

The discovery was made independently by virologists Robin Weiss, at the Institute of Cancer Research in London (see *Nature* **389**, 581; 1997), and David Onions, at the University of Glasgow. It has already prompted the US Food and Drug Administration (FDA) to call a moratorium on porcine transplants until trials can build in adequate tests to screen for the viruses in donor organs, and to monitor for them in the recipients afterwards.

Weiss and Onions' work makes it "painfully evident" that the understanding of the risks is still evolving, said Mary Pendergast, the then senior adviser to the commissioner of the FDA, at a meeting of the agency's advisory sub-committee on xenotransplantation last month. This made development of regulations "difficult," she added.

Regulation of xenotransplantation in the United States is at a turning point with the imminent release of guidelines that will give the go-ahead to clinical trials. The guidelines are expected to be published soon after a public meeting organized in Washington this week by US Public Health Service (PHS) agencies, including the FDA, the National Institutes of Health, and the Centers for Disease Control and Prevention (CDC).

US pre-eminence in medical research means that the guidelines will inevitably influence the development of xenotransplantation internationally (see box, page 322). Moreover, as infectious diseases do not respect national borders, US actions may have consequences for the rest of the world.

The new guidelines will be more stringent than a draft version put out for consultation in 1996. They will give the FDA oversight of all trials, instead of leaving this to local institutional review boards as originally proposed. The creation of a federal xenotransplantation advisory committee along the lines of the Recombinant DNA Advisory Committee is also being explored.

This tougher tone has been welcomed by many, including the American Society of Transplant Physicians (ASTP), which had criticized the earlier guidelines for failing to provide sufficient public health safeguards. The society said the proposal to leave oversight to institutional review boards was a recipe for disaster, arguing that the boards had a narrow view of the issues that could be detrimental to broader public concerns.

Trials might open Pandora's box

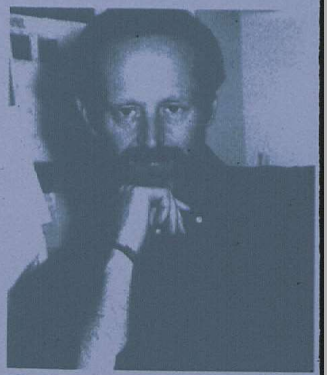
The emphasis on the risk of xenozoonosis — the transmission of animal diseases to humans via organ transplants or blood — is relatively recent. Louisa Chapman, an expert on xenotransplantation at CDC, recalls that when the issue was first raised at CDC in 1993 her first thought was "why would we spend taxpayers' money on that, as it's only once in a blue moon that someone puts a baboon or liver heart into someone, they die within 72 hours and that is the end of the story?".

Past transplants of animals' organs into humans have been so rare and unsuccessful as to have never been considered a serious public health issue. But, as the prospect that the techniques may become a clinical reality moves closer, many fear that, as the number of organ recipients grows, so too will the risk to the human population. "We are at the cusp of a possible explosion of xenotransplantation efforts," says Pendergast.

Commercial interest is already strong. The Swiss company, Novartis, the main corporate player in xenotransplantation, is prepared to invest up to US$1 billion in the technology in the near term. And the market may be worth up to $6 billion in 2010, estimates Peter Laing, an analyst at Société Générale Strausse Turnbull in London, who predicts that Novartis could account for more than half.

But there is a broad consensus that substantial preclinical research is needed before xenotransplantation is likely to succeed in the clinic, and that more time is needed to study the nature of the risks. And some scientists are worried that the proposed regulations may herald a premature and dangerous acceleration of clinical applications.

What is mainly fuelling this momentum is the shortage of human donor solid organs, such as hearts, kidneys, lungs and livers. But the numbers of patients involved at present is relatively small in public health terms (although a reliable source of organs could greatly expand use of transplants). Most scientists also believe that, whereas success in implanting animal cells may be within reach, the ability to transplant solid animal organs is many years away (see page 324), despite claims to the contrary by some biotech-



Allan: 'precautionary principle' must be followed.

This briefing has been written by Declan Butler, European correspondent for *Nature*, with additional reporting by Meredith Wadman in Washington, Sally Lehrman in San Francisco and Quirin Schiermeier in Munich.

On other pages | Moratoriums on clinical research: p321 | Clear need for international regulations: p322 |

Habría que modificar, al menos, unos diez genes porcinos

¿HUMANIZAR A LOS CERDOS?

ANNETTE MILLET

Las más arcaicas de nuestras defensas inmunitarias impiden al cuerpo aceptar el trasplante de un órgano de cerdo, ya que provocan el rechazo, llamado sobreagudo, del trasplante. ¿Cómo evitarlo? Varias estrategias de ingeniería genética pretenden «humanizar» a los animales. ¿Serán eficaces en clínica? Todavía no puede afirmarse. Pero sí se sabe lo que tienen en común: aumentar el riesgo de transmisión de algún virus porcino al hombre.

ANNETTE MILLET es periodista de *La Recherche*.

En 1906, Mathieu Jaboulay trasplanta en el pliegue del codo de una enferma afectada de insuficiencia renal un riñón de cerdo sacrificado recientemente. ¿Qué observa, según toda verosimilitud, este cirujano de Lyon? Una vez terminadas las suturas vasculares, el órgano, irrigado por la sangre del receptor, empieza por tomar color rosáceo. El riñón es capaz incluso de producir

Xenotransplantation:

How Bad Science and Big Business Put the World at Risk from Viral Pandemics

by Mae-Wan Ho and Joe Cummins

Summary

Xenotransplantation - the transplant of animal organs into human beings - is a multi-billion dollar business venture built on the anticipated sale of patented techniques and organs, as well as drugs to overcome organ-rejection (1). It has received strong criticism and opposition from scientists warning of the risks of new viruses crossing from animal organs to human subjects and from there to infect the population at large. But regulators are adopting a permissive attitude for clinical trials to go ahead. Scientific reports of virus crossing from pig to human cells (2) and of viral infections in humans subjects transplanted with baboon livers (3) are being ignored or dismissed, while inconclusive, widely faulted papers are taken as evidence that no viruses are found in xenotransplant patients (4).

This audit exposes the shoddy science that puts the world at risk of viral pandemics for the sake of corporate profit, and concludes that xenotranplantation should not be allowed to continue in any form.

Un estudio halla nuevas conexiones entre el virus del herpes labial y el Alzheimer

Un grupo de científicos de la Universidad de Mancherster cree que los antivirales empleados contra las erupciones cutáneas podrían combatir la enfermedad neurodegenerativa

ELPAÍS.com / EFE - Madrid / Londres - 07/12/2008

Un equipo de científicos de la Universidad inglesa de Manchester ha establecido una conexión entre el virus del herpes labial y el Alzheimer, lo que podría desembocar en nuevos tratamientos contra la enfermedad neurodegenerativa.

HealthLink
MEDICAL COLLEGE OF WISCONSIN

Bacteria, Viruses Can Cause Infectious Arthritis

Most people are familiar with osteoarthritis – the common "wear and tear" arthritis that occurs over years of musculoskeletal stress and injury, and the source of many of the aches and pains we attribute to aging. Another well-known ailment is rheumatoid arthritis, an autoimmune disease that usually affects several joints in the body at once. But there are actually about 100 types of arthritis and related disorders, many of which are caused by bacteria or viruses.

Rheumatology

- Oxford Journals
- Medicine
- Rheumatology
- Volume 32, Number 12
- Pp. 1044-1048

- **VIRUS-LIKE PARTICLES IN SYNOVIAL FLUIDS FROM PATIENTS WITH RHEUMATOID ARTHRITIS**

- **G. STRANSKY, J. VERNON, W. K. AICHER, L. W. MORELAND, R. E. GAY** and **S. GAY**
- Division of Clinical Immunology and Rheumatology, The University of Alabama at Birmingham Birmingham, Alabama, USA

- Based on the elevated expression of oncogenes in proliferating transformed-appearing synoviocytes we searched for the possible involvement of a viral agent in the pathogenesis of RA. We report the detection of virus-like particles with retro viral C type morphology in SF, which lack the typical morphologic as well as immunohistochemical features of the human T-lymphotropic and immunodeficiency viruses.

Science 9 October 2009:
Vol. 326. no. 5950, p. 215

VIROLOGY:

Chronic Fatigue and Prostate Cancer: A Retroviral Connection?

Sam Kean

A new study published online by *Science* links chronic fatigue syndrome to a possibly contagious rodent retrovirus, XMRV, which has also been implicated in an aggressive form of prostate cancer. Related work by the authors also suggests CFS might best be treated with AIDS drugs. Even the lead author, Judy Mikovits, says she understands why linking CFS to both a retrovirus and prostate cancer has already drawn skepticism.

Identificado un virus relacionado con el síndrome de fatiga crónica

Los científicos creen que el patógeno se transmite por vía sexual

EL PAÍS - Madrid - 09/10/2009

El trabajo, sin embargo, es muy preliminar. Se trata de una relación estadística (se ha hallado el virus en un 67% de las personas con fatiga crónica, frente a sólo un 4% en quienes no lo tienen). Los investigadores del Whittemore Peterson Institute de Nevada admiten que no han sido capaces de describir el posible proceso entre el patógeno y la enfermedad.

El XMVR es un retrovirus. Esto quiere decir que tiene la capacidad de ocultar su código genético integrándolo en el de las células que infecta (como hace el VIH que causa el sida, por ejemplo). Los médicos ya le habían echado el ojo, pero por otra causa: también se asocia con el cáncer de próstata.

Este tipo de microorganismo necesita un contacto estrecho antes de transmitirse de una persona infectada a otra sana. Por eso parece que la vía sexual es la más probable.

Volume 361:1067-1074 September 10, 2009 Number 11

The NEW ENGLAND JOURNAL of MEDICINE

Asymptomatic Reactivation of JC Virus in Patients Treated with Natalizumab

Yiping Chen, M.D., Ph.D., Evelyn Bord, B.S., Troy Tompkins, B.S., Janice Miller, B.S., Chen S. Tan, M.D., R. Philip Kinkel, M.D., Marion C. Stein, M.D., Raphael P. Viscidi, M.D., Long H. Ngo, Ph.D., and Igor J. Koralnik, M.D.

ABSTRACT

Background Progressive multifocal leukoencephalopathy (PML) occurs in a fraction of patients with multiple sclerosis who were treated with natalizumab. Most adults who are infected with the JC virus, the etiologic agent in PML, do not have symptoms. We sought to determine whether exposure to natalizumab causes subclinical reactivation and neurotropic transformation of JC virus.

Una infección empaña la efectividad de un fármaco para la esclerosis múltiple

Un estudio publicado en 'The New England Journal of Medicine' confirma que las personas con esclerosis múltiple tratadas con natalizumab tienen un mayor riesgo de desarrollar una enfermedad cerebral grave. El fármaco ejerce su acción terapéutica al evitar que un tipo de células del sistema inmune, los linfocitos T, ataquen la vaina aislante que recubre las células nerviosas (mielina).

FUENTE | El Mundo Digital 14/09/2009

Sin embargo, este beneficio se convierte en un arma de doble filo, ya que también impide que los linfocitos ejerzan su acción defensiva normal frente a un virus muy peligroso, denominado JC.

Hasta un 90% de la población tiene el patógeno, pero éste permanece 'dormido' en los riñones de los individuos sanos y solamente se reactiva en quienes se encuentran inmunodeprimidos, como los pacientes con sida.

Cuando el virus JC se 'despierta', como ya ha ocurrido en 14 de los 20.000 individuos tratados en todo el mundo con natalizumab, desencadena una Leucoencefalopatía Multifocal Progresiva (LMP). Se trata de un trastorno muy destructivo que puede provocar ceguera, demencia o parálisis. No tiene cura y la mitad de quienes lo padecen muere un año después del diagnóstico.

Aunque el trabajo que acaba de ver la luz refuerza la certeza de que el medicamento merma las defensas frente a este mortífero enemigo, también supone un punto de partida para el despliegue de estrategias para reducir el riesgo.

S. Ramón y Cajal

Investigador de la génesis del cáncer

Santiago Ramón y Cajal. /G. PASCUAL

"El 20% de los cánceres humanos está causado por virus"

J. Virol., 10 1995, 6408-6416, Vol 69, No. 10

Retrovirus-like particles released from the human breast cancer cell line T47-D display type B- and C-related endogenous retroviral sequences

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The human mammary carcinoma cell line T47-D releases retrovirus-like particles of type B morphology in a steroid-dependent manner (I. Keydar, T. Ohno, R. Nayak, R. Sweet, F. Simoni, F. Weiss, S. Karby, R. Mesa-Tejada, and S. Spiegelman, Proc. Natl. Acad. Sci. USA 81:4188-4192, 1984). Furthermore, reverse transcriptase (RT) activity is found to be associated with particle preparations. Using a set of degenerate primers derived from a conserved region of retroviral pol genes, we repeatedly amplified three different retroviral sequences (MLN, FRD, and FTD) from purified T47-D particles in several RT-PCR experiments. Screening of a human genomic library and Southern blot analysis revealed that these sequences are of endogenous origin.

Nature **256**, 670 - 672 (21 August 1975); doi:10.1038/256670a0

Genetic relationship of a primate RNA tumour virus genome to genes in normal mice

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HUEBNER and Todaro[1] and Temin[2] proposed that the genomes of RNA tumour viruses originate from genes in DNA of normal cells. Subsequently, a class of RNA tumour viruses (endogenous or class 1 viruses) was discovered and shown by molecular hybridisation to contain RNA genetically related or identical to genes in normal cells[3–8]. Both the biological and hybridisation data leave little doubt that normal cells carry genes capable of giving rise to class 1 RNA tumour viruses (see refs 7 and 8 for reviews). A second class of RNA tumour viruses is more distantly related to cell genes (exogenous or class 2 viruses, see refs 7 and 8). Mouse and chicken class 2 viruses, however, are genetically related to class 1 viruses from the same species[7–12] and the genome of one class 2 mouse RNA tumour virus (Rauscher leukaemia virus) consists primarily of RNA sequences that are related distantly to genes in normal mice but not to genes found in several other animals[13]. Indirect evidence has indicated that primate RNA tumour viruses and certain mouse RNA tumour viruses are unusually closely related[10,11,14,15], suggesting that the viruses have a common origin, for example, in genes of mice. We report here that a primate RNA tumour virus isolated originally from a woolly monkey sarcoma and passaged in marmosets does contain a genome that by molecular hybridisation criteria is related to genes found in mice. The data further indicate that a small portion of the primate RNA tumour virus genome is related to genes of normal primates.

. Cross-species comparison reveals shared features between tumorigenesis and organogenesis

Main Category: Cancer / Oncology News
Article Date: 20 Mar 2004

A new study, published in the March 15th issue of Genes & Development, provides critical new insight into the shared mechanisms of normal organ development and solid tumor formation.

By studying the cerebellum (the structure in the brain largely responsible for coordinating motor activities) Drs. Alvin Kho, Isaac Kohane, David Rowitch, and colleagues at The Children's Hospital and Dana-Farber Cancer Institute in Boston have developed a novel method for comparing the genetic changes associated with normal development in mice with that of the most common malignancy of the pediatric nervous system, medulloblastoma.

'With information derived from the Human Genome Project we now have the ability to easily compare and identify meaningful patterns of gene expression between species such as mouse and human,' said Kho, a postdoctoral fellow and the paper's lead author. Such cross-species comparison provides a powerful new tool for understanding the genetic changes associated with human tumor development.

In a developing organ, the pattern of gene expression changes as the individual cells commit to their own specialized functions. By analyzing the changing patterns of expression of more than 2000 genes in the developing cerebellum in mice and comparing these to genes expressed in human medulloblastomas, the investigators were able to characterize the malignant cells from a developmental perspective.

Una científica española halla el nexo entre las causas del cáncer

El trabajo es uno de los más importantes realizados en España en su especialidad

JAVIER SAMPEDRO - Madrid

EL PAÍS - Sociedad - 26-01-2006

María Domínguez acaba de descubrir el nexo. Es la primera vez en 20 años que un trabajo íntegramente español merece el artículo principal de *Nature*. Típicamente, las únicas autoras en plantilla son Domínguez y su ayudante técnica.

"Muchos tumores humanos tienen mutaciones en genes de comunicación celular como *Notch*", explica la investigadora, "pero sabemos que eso no basta para producir cáncer en modelos como el ratón, el pez cebra o la mosca". Los 200 genes *del cáncer*, que existen en todos los animales, no están ahí para causar cáncer, naturalmente. Son parte de la maquinaria esencial del desarrollo embrionario.

"Las ideas falsas, es decir, inadecuadas y confusas, se suceden unas a otras con la misma necesidad que las verdaderas, es decir claras y distintas".

Baruch Spinoza (Ética demostrada según el orden geométrico, 1675)