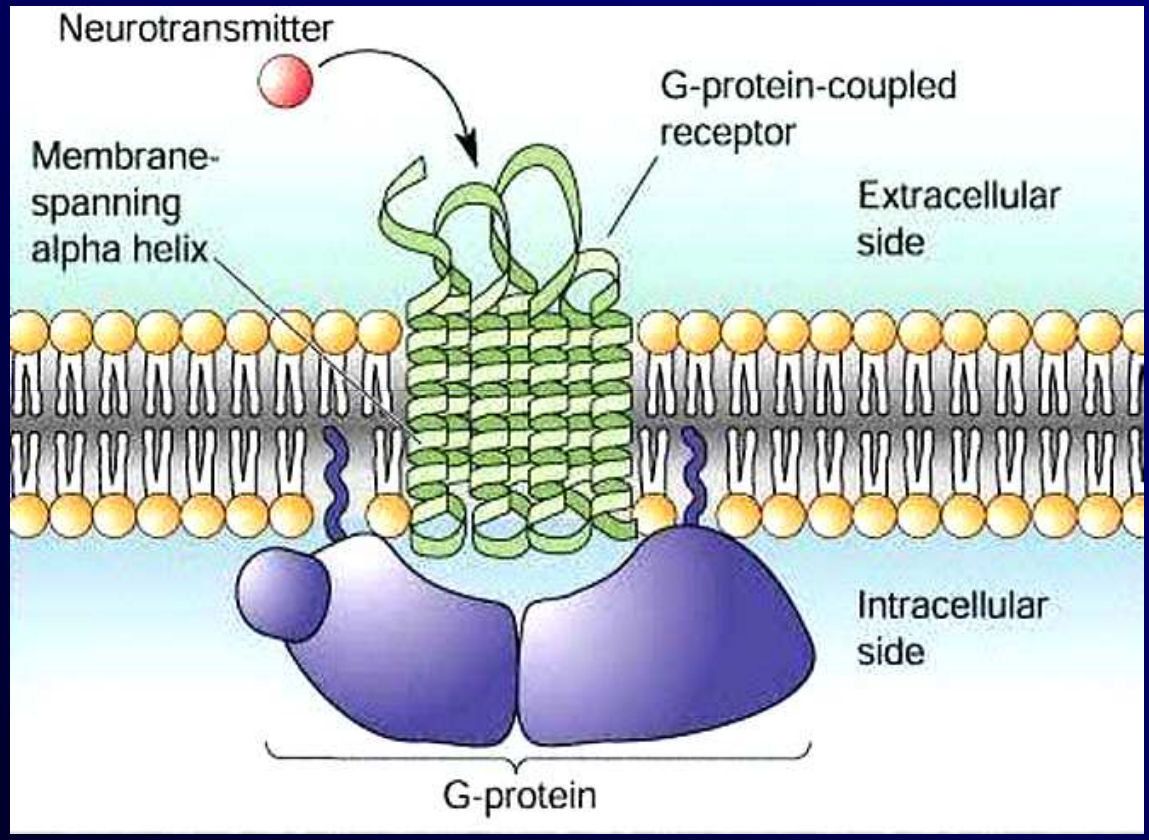
THE SCIENCE OF SIN AND SALVATION

ROBERT MELASHENKO MD

LECTURE FIVE

IN THE GARDEN

REVIEW


Neurotransmitter
G-protein-coupled receptor
Membrane-spanning alpha helix
Extracellular side
Intracellular side
G-protein

G protein-coupled receptors are found only in eukaryotes, including yeast, and animals. The ligands that bind and activate these receptors include light-sensitive compounds, odors, pheromones, hormones, and neurotransmitters, and vary in size from small molecules to peptides to large proteins. G protein-coupled receptors are involved in many diseases, and are also the target of approximately 40% of all modern medicinal drugs.

(From Wikipedia web page)

Mol. Cells *30*, 77-87, July 31, 2010
DOI/10.1007/s10059-010-0091-2

Communication

Molecules and Cells

Functional Impact of Transposable Elements Using Bioinformatic Analysis and a Comparative Genomic Approach

Dae-Soo Kim[1,4], Jae-Won Huh[1,4], Young-Hyun Kim[1,2,4], Sang-Je Park[1,3], and Kyu-Tae Chang[1,*]

Table 2. Functional analysis of coding regions modified by the insertion of transposable elements in the human genome

Gene	Repeat family	Database		InterPro ID	Discription
		Pfam	SMART		
ADAM15	MIR_Mars	PF08516	SM00608	IPR006586	ADAM, cysteine-rich
ADAM28	L1M4	PF01421		IPR001590	Peptidase M12B, ADAM/reprolysin
ADAR	L4	PF00035	SM00552	IPR001159	Double-stranded RNA binding
ADARB1	AluJb	PF02137	SM00552	IPR002466	Adenosine deaminase/editase
ADRA1A	AluSc	PF00001		IPR000276	Rhodopsin-like GPCR superfamily
OGG1	MLT1K	PF00730	SM00478	IPR003265	HhH-GPD
OPN4	MIRb	PF00001		IPR000276	Rhodopsin-like GPCR superfamily
SYNE1	L3_Mars	PF00435	SM00150	IPR002017	Spectrin repeat
TBXA2R	AluSg/x	PF00001		IPR000276	Rhodopsin-like GPCR superfamily
TIPRL	AluY	PF04176		IPR007303	TIP41-like protein

THE GARDEN STORY

WHAT WAS THE ACTUAL TEMPTATION?

WHAT WAS THE ADVERSARY TRYING TO ACHIEVE?

THE STORY

“And the Lord commanded the man, saying, Of every tree of the garden thou mayest freely eat: But of the tree of the knowledge of good and evil, thou shalt not eat of it: for in the day that thou eatest thereof thou shalt surely die (dying thou shalt die)”.

(Genesis 2:16,17 KJV)

“And the serpent said unto the woman, Ye shall not surely die: For God doth know that in the day ye eat thereof, your eyes will be opened, and ye shall be as gods, knowing good from evil.”

(Genesis 3: 4,5 KJV)

ONE OF THE TWO IS LYING……BUT WHICH ONE?

What was the Adversary asking Eve to do?

Rely on her own sensory input as the ultimate reality instead of God's word.

To doubt God had her best interest in mind when He forbade eating the fruit from Tree of Knowledge of Good and Evil (TKGE). Implied in the following questions:

Is God not the Creator of the whole world and this garden?

Has God been only loving and good in all His dealings with you and Adam?

Has any of the fruit from other Garden trees ever had any ill effects?

Questions Cont.:

Is it logical then, that a life-giving God would create a tree whose fruit had the power to cause your death and put it in Garden right next to the Tree of Life where you can't miss it?

Given the fact that everything in God's creation has been for your benefit, would it not be logical to assume that the fruit from the TKGE would also be beneficial--not harmful-- if eaten?

Would you like to see evidence supporting this assertion?

I am providing this as we speak as I have already partaken of the fruit—and, as can be readily seen, not only have I no untoward effects, I have actually entered a higher state of existence.

Questions cont.:

Since we are both created beings, if the fruit has given me greater intelligence (ability to verbally communicate), what wonderful things might it do for you? (Pantheism)

Anyway, If obedience is the purpose of this "test" would God, who created all life, use a harsh tactic that results in death?

WHAT HAD THE DEVIL CONVIENENTLY LEFT OUT OF THIS DISCUSSION?

HIMSELF

What was the Adversary's goal?

1. Disbelief?
2. Believe a lie?
3. Disobedience?

Yes—but all three were a "means to an end"—not the goal itself!

NOTE: ADAM WAS NOT DECEIVED!

And Adam was not deceived, but the woman being deceived was in the transgression.

(1 Timothy 2:14 AKJV)

And it was not Adam who was deceived; it was the woman who was deceived and broke God's law.

(1 Timothy 2:14 GNB)

In order to be deceived, one must first disbelieve God and then believe a lie—Adam did neither.

What was the Deceiver's goal?

For God does know that in the day **you eat** thereof, then your eyes shall be opened, and you shall be as gods, knowing good and evil.

And when the woman saw that the tree was good for food, and that it was pleasant to the eyes, and a tree to be desired to make one wise (to give insight, to teach), she took of the fruit thereof, **and did eat**, and gave also to her husband with her; and he did eat. (Genesis 3:5-6 AKJV)

All three players in this drama completely agree that **"eating of the fruit"** is key to what comes next.

"Wise"—to give insight, to teach, to have comprehension..

The only way that this could happen instantaneously (if it could at all) would be through a change in the information system of Eve--because **apparently** the snake (who had already eaten of the fruit) had developed vocal cords and the CNS circuitry to control them—and this could **only** happen via an addition to his information system.

The temptation's final purpose then, was not just to deceive her about God's character, it was to get Eve to agree to change her information system—for that is what <u>apparently</u> had happened to the snake.

Does sin have a physical basis? Or is it just a state of mind?

1. How is it transferred? Through heredity—MGE's in genome. **(Physical)**

Why, as by one man sin entered into the world, and death by sin; and so death passed on all men, for that all have sinned:

(Romans 5:12 AKJV)

2. What are its consequences? The First Death (MGE's) and the Second Death (MGE's?)—**(Physical)**

For the wages of sin is death; but the gift of God is eternal life through Jesus Christ our Lord.

(Romans 6:23 AKJV)

Does sin have a physical basis? Cont.:

3. Is there something that can reverse the "death"? Yes, eating the fruit of the Tree of Life. **(Physical)**

And the LORD God said, Behold, the man is become as one of us, to know good and evil: and now, lest he put forth his hand, and take also of the tree of life, and eat, and live for ever:

(Genesis 3:22 AKJV)

HOW COULD MGE's GET INTO ADAM AND EVE'S GENOME IN THE FIRST PLACE?

1. God and the Devil made an agreement that should the pair eat of the forbidden fruit, God would remove them from the Garden allowing the Devil to carry out his purposes.

2. The MGE's were in the fruit of the TKGE.

Two Trees

Tree of Life

According to Genesis 3:22, something in the fruit is biologically active.

In Revelation 22:2, it states, “and the leaves of the tree were for the healing of the nations;” indicating biologically active ingredients in the leaves.

Tree of the Knowledge of Good and Evil

Could something biologically active also be present in this fruit as well??

Mol Gen Genomics (2003) 270: 362–368
DOI 10.1007/s00438-003-0930-3

ORIGINAL PAPER

A. Forsman · D. Ushameckis · A. Bindra · Z. Yun
J. Blomberg

Uptake of amplifiable fragments of retrotransposon DNA from the human alimentary tract

Received: 30 April 2003 / Accepted: 13 September 2003 / Published

Abstract Few attempts have been made to study the transfer of DNA from ingested food across the intestinal barrier. A low uptake of ingested DNA has been observed in mice, cattle and poultry. There have been no reports on humans so far. Maintenance of species barriers, protection against retrotransposons, optimisation of oral DNA vaccines and the fate of genetically modified foodstuffs are issues where this topic is of importance. We therefore used the high-copy-number rabbit retrotransposon RERV-H, and rabbit mitochondrial DNA, to study the transfer of DNA from ingested rabbit meat into the bloodstream of two human volunteers. A quantitative PCR was used to measure RERV-H levels in food and in the blood. Amplification with the primers selected results in the generation of a 250-bp fragment of RERV-H. Transfer across the intestinal epithelium could be demonstrated in both subjects. Levels of the fragment in the bloodstream peaked at 1–3 h after ingestion of the experimental meal. One hour after a meal of rabbit meat containing 10^{14} copies of RERV-H DNA, a maximum concentration of 200 copies of RERV-H DNA per ml of peripheral blood was observed, which corresponds to the uptake of approximately 10^6 RERV-H DNA copies in 1 h. RERV-H DNA was detected in both cellular and plasma compartments. Both rabbit retrotransposon and mitochondrial DNA was taken up from the human alimentary tract. The size of the fragments detected is similar to that of SINE retrotransposons (approximately 300 bp). The fate and functionality of alimentary DNA in humans will require further study.

against them, similar to the immune system. Yet, transposons are ubiquitous, and are sometimes transmitted horizontally. Thus, the defence mechanisms cannot be perfect. The relative ease with which mammalian cells in culture can take up, integrate and express exogenous, non-self, DNA by transfection (see e.g. Graham and van der Eb 1973a, 1973b) shows that cellular defences against foreign DNA have their limitations. However, transfected transgenes are often silenced after a few months, demonstrating that cells can in fact limit the effects of foreign DNA (Doerfler 1991, 1992).

accumulated over the last 20 years which shows that phylogeny inferred from sequence similarity is generally monophyletic, i.e. a given species gives rise to new species via Mendelian (vertical) transfer of characters between generations, with the more or less gradual accumulation of mutations (Bushman 2001). Barriers to cross-species fertilisation and inter-species graft rejection are examples of how species are kept intact. However, occasionally inter-species barriers may break down. Then genetic information can be transmitted to a different species by so-called lateral or horizontal gene transfer (Bushman 2001). Mobile genetic elements can propagate in genomes as parasitic sequences or "selfish DNA". Occasionally, these are transmitted between species. Although such transfers are relatively common on an evolutionary timescale, they are probably very rare during the lifetime of an individual. The deleterious effects which they, or any foreign DNA, can have on the host imply that organisms have evolved defence systems against them, similar to the immune system. Yet, transposons are ubiquitous, and are sometimes trans-

Mol Gen Genomics (2003) 270: 201–215
DOI 10.1007/s00438-003-0907-2

ORIGINAL PAPER

M. Palka-Santini · B. Schwarz-Herzke · M. Hösel
D. Renz · S. Auerochs · H. Brondke · W. Doerfler

The gastrointestinal tract as the portal of ent macromolecules: fate of DNA and proteins

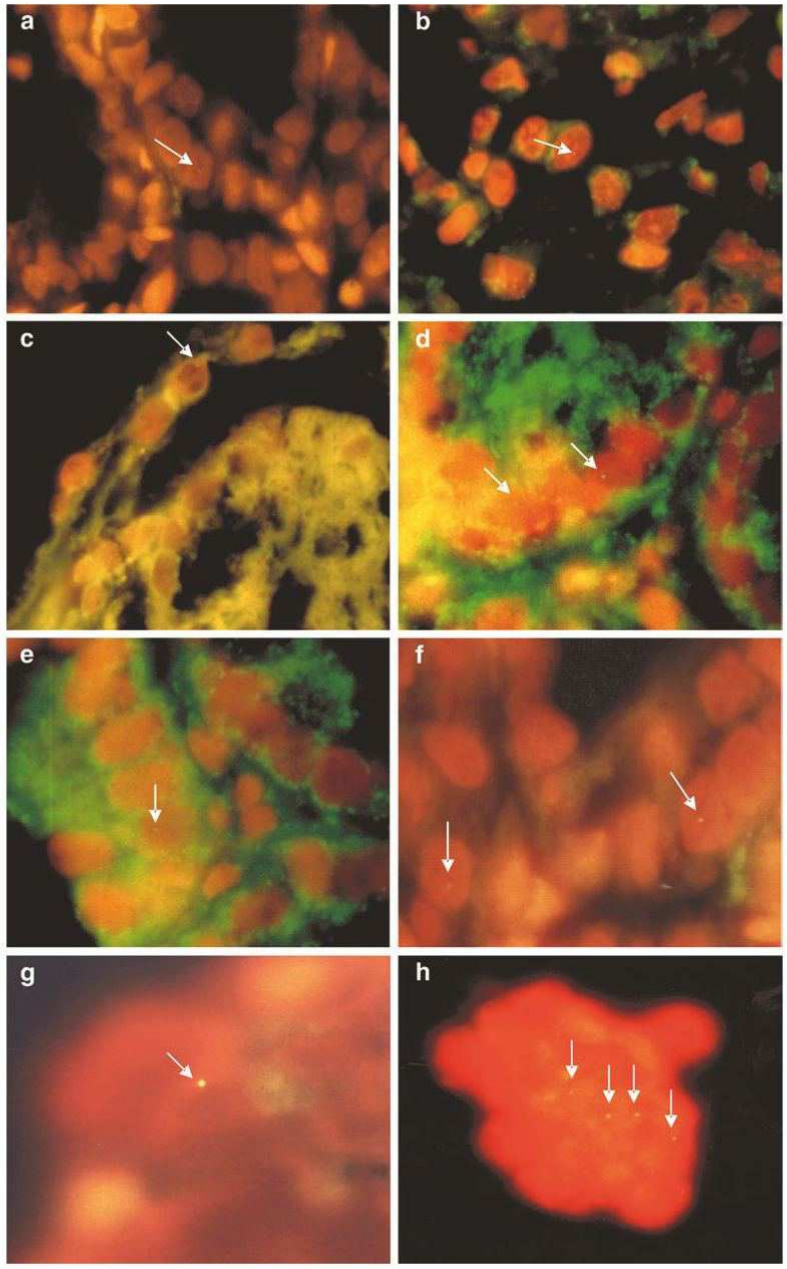
Received: 24 April 2003 / Accepted: 24 July 2003 / Published online: 23 August 2003

Abstract The gastrointestinal tract (GIT) of mammals is the main portal of entry for foreign DNA and proteins. We have documented the fate of orally administered DNA or protein in the GIT of the mouse. The gene for the Green Fluorescent Protein (GFP) (4.7 kb) and the genomes of bacteriophage M13 (7.25 kb) and adenovirus type 2 (Ad2; 35.9 kb) were used as test DNAs. Persistence of these DNAs in the GIT was monitored by Southern hybridization and fluorescent in situ hybridization (FISH) or by PCR. For studies on proteins, recombinant glutathione-S-transferase was fed to mice. Survival of the protein in the GIT was then assessed by Western blotting. Depending on feeding schedules and food regimens, but irrespective of mouse strain or DNA length, fragments of the GFP gene or other DNAs were detectable for up to 18 h after feeding by Southern blot analysis. The GFP DNA could be visualized by FISH in cecal epithelia. A high fiber diet reduced the time required for food to pass through the GIT, and foreign DNA was cleared more rapidly. A high fat diet or complexing of the foreign DNA with protamine or lipofectin did not extend DNA persistence times. Undegraded GST protein was detected only in foregut contents up t post feeding, tracts of the highly recom to intact forei studies on ca pathogenicity

Keywords Pe gastrointestin (GFP) · Soutl Glutathionine

Introduction

The gastroint entry for fo lining forms t and proteins In previous i digestive trac



It is concluded that the state of filling of the GIT prior to feeding the test DNA noticeably affects the transit time and the extent of digestion of naked foreign DNA molecules subsequently introduced into the intestinal system.

Interesting evidence which supports that MGE's were fruit born, and not introduced later outside the Garden, can be found in what transpired soon after the pair ate the fruit:

And the eyes of them both were opened, and they knew that they were naked; and they sewed fig leaves together, and made themselves aprons. (This happened before the pair were confronted by God and still in the Garden.)

(Genesis 3:7 AKJV)

And the man said, The woman whom you gave to be with me, she gave me of the tree, and I did eat. (This occurred while still in the Garden)

(Genesis 3:12 AKJV)

THE THREE “CURSES”?

'ârar

BDB Definition:

1) to curse

Hebrew 'arar means "to bind (with a spell), hem in with obstacles, render powerless to resist."

GOD RESPONDS TO THE SERPENT

And the LORD God said to the serpent, Because you have done this, you are cursed above all cattle, and above every beast of the field; on your belly shall you go, and dust shall you eat all the days of your life:

And I will put enmity between you and the woman, and between your seed and her seed; it shall bruise your head, and you shall bruise his heel.

(Genesis 3:14-15 AKJV)

Vol 464|4 March 2010|doi:10.1038/nature08789 nature

LETTERS

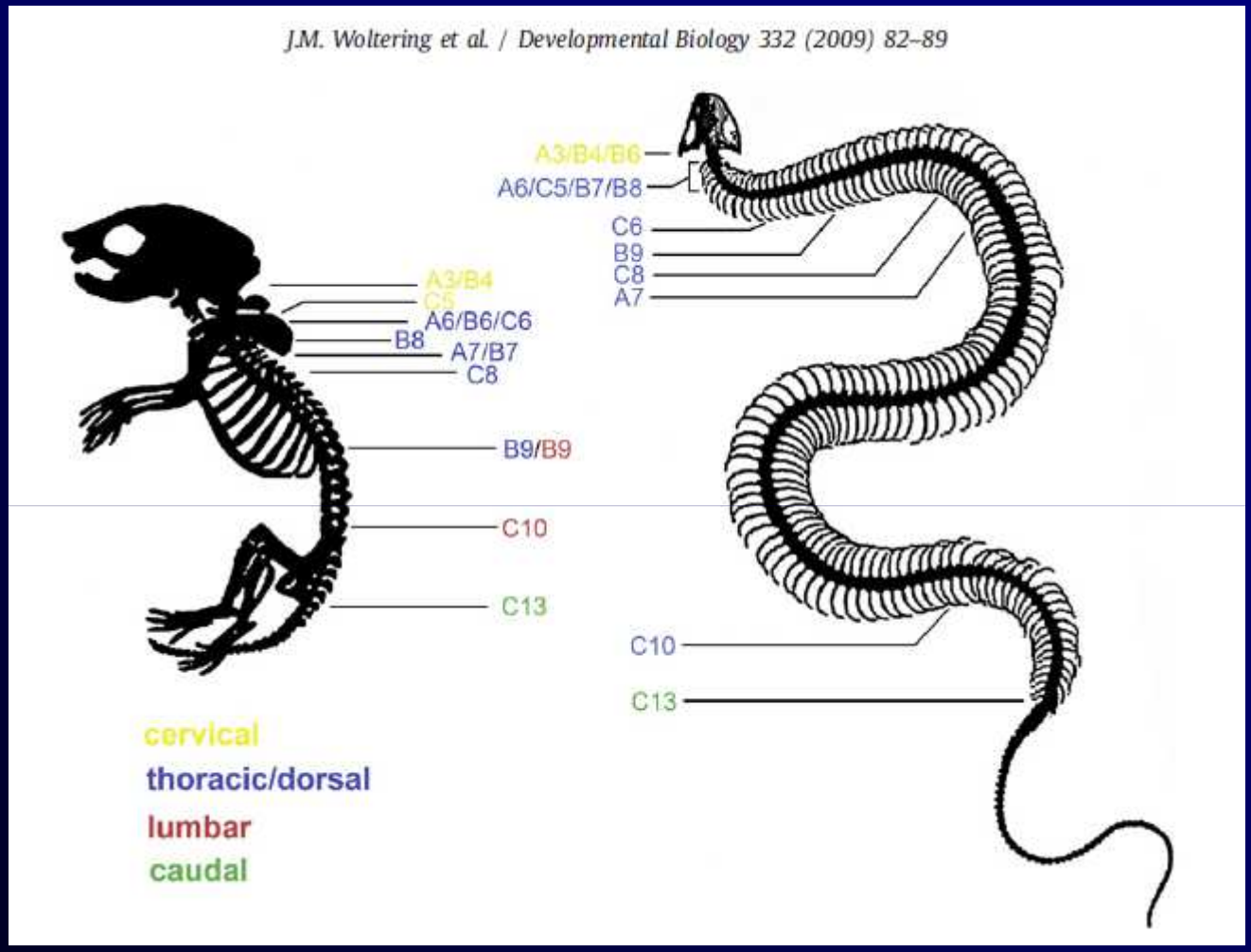
Changes in *Hox* genes' structure and function during the evolution of the squamate body plan

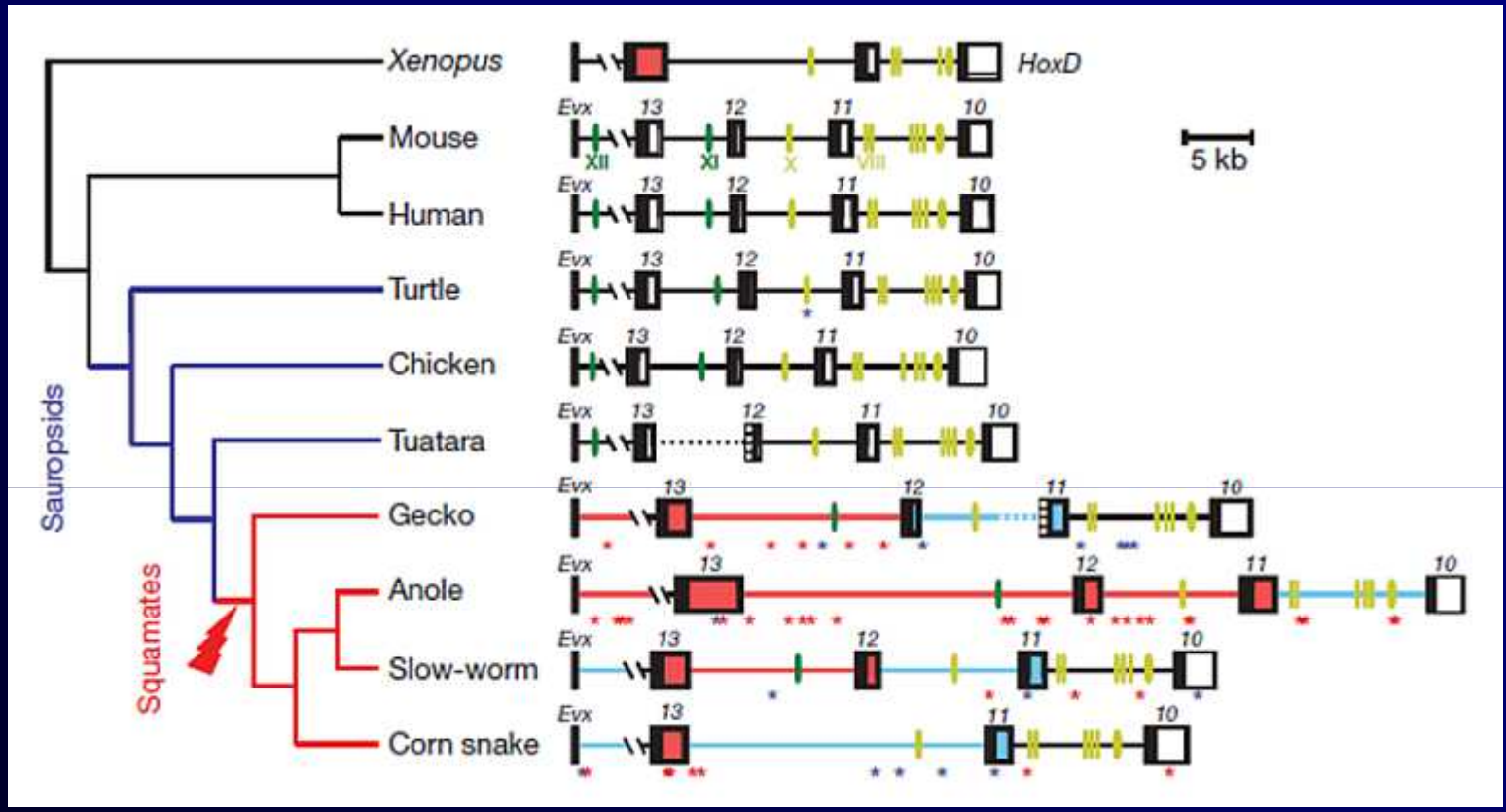
Nicolas Di-Poï[1], Juan I. Montoya-Burgos[1], Hilary Miller[2], Olivier Pourquié[3,4]†, Michel C. Milinkovitch[1] & Denis Duboule[1,5]

Hox genes are central to the specification of structures along the anterior–posterior body axis[1,2], and modifications in their expression have paralleled the emergence of diversity in vertebrate body plans[3,4]. Here we describe the genomic organization of *Hox* clusters in different reptiles and show that squamates have accumulated unusually large numbers of transposable elements at these loci[5], reflecting extensive genomic rearrangements of coding and non-coding regulatory regions. Comparative expression ana-

number. The predominant type of interspersed repeats found in anole *Hox* clusters consists of Penelope-like retrotransposons (PLEs)[5], whereas repeats in other Squamata species are more degenerated and include short (SINE) and long (LINE) non-LTR retrotransposons, as well as DNA transposons (Fig. 1 and Supplementary Fig. 1). This atypical structure for *Hox* gene clusters suggests that a strong constraint was lost within this order of animals, permitting repeats to invade loci that are otherwise resistant. In turn, such repeats may have impacted significantly on both the rearrangement of coding and non-coding regulatory *Hox* regions and the direct regulation of *Hox* gene transcription in Squamata, for example through epigenetic modifications around their insertion sites[17].

NATURE| Vol 464|4 March 2010


J.M. Woltering et al. / Developmental Biology 332 (2009) 82–89
A3/B4/B6
A6/C5/B7/B8
C6
B9
C8
A7
A3/B4
C5
A6/B6/C6
B8
A7/B7
C8
B9/B9
C10
C13
C10
C13
cervical
thoracic/dorsal
lumbar
caudal

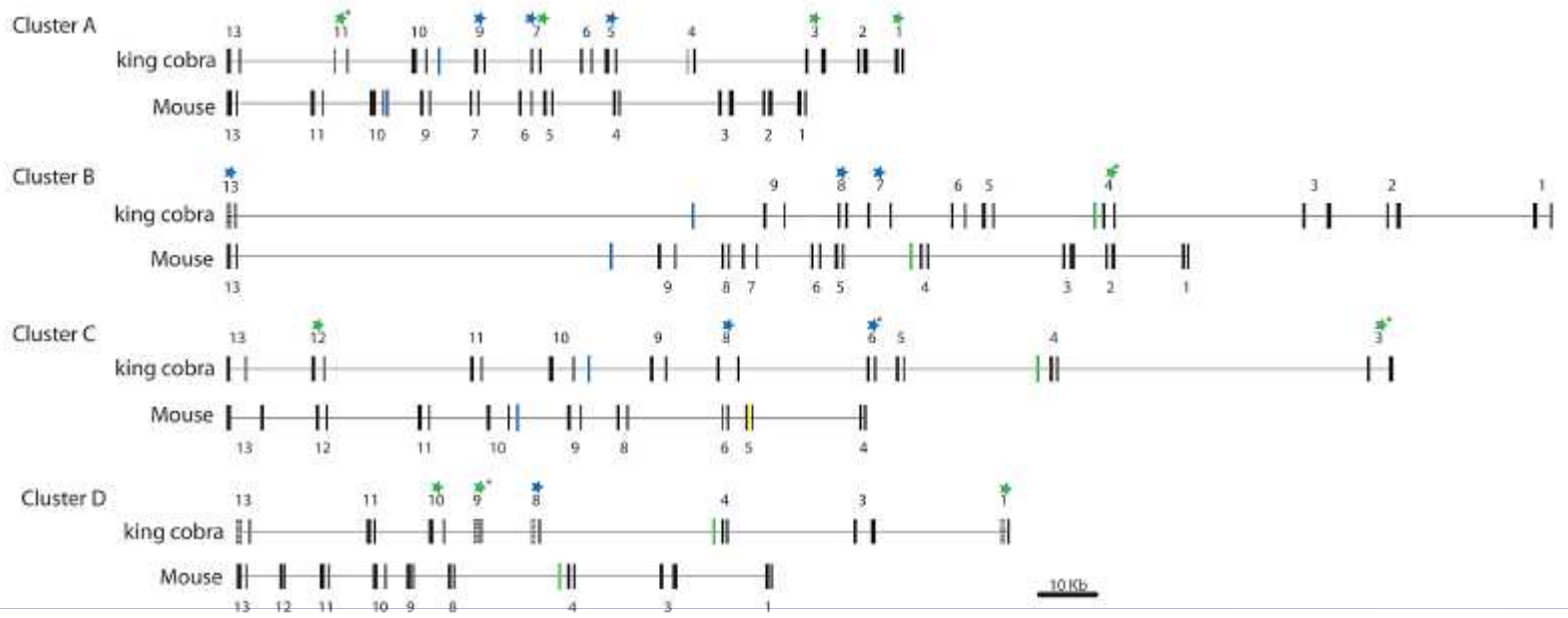


Transposable elements are indicated with asterisks of different colors (blue for DNA transposons; red for retrotransposons).

NATURE| Vol 464|4 March 2010

genes, in the absence of genomic information. Here we describe how structural and regulatory adaptations in this gene family may have accompanied the transition towards such a body plan and suggest that the unexpected invasion of all Squamata *Hox* clusters by transposons might have facilitated such adaptations.

NATURE| Vol 464|4 March 2010



10 (see File S1 for details). Asterisks denote targets in the king cobra, which are not predicted for mouse or human. The king cobra *Hox* genes, as in other vertebrates, were found clustered at four distinct genomic loci, but the gene clusters are substantially larger than in mammals, with a 10 to 40 percent increase in size for the *HoxA* and *HoxD* clusters, respectively. This expansion in size was mainly due to the presence of repeated elements, a peculiarity that seems to be a genomic synapomorphy of the squamate reptiles, as similar observations have been described in the corn snake and *Anolis* lizard and not been reported in other vertebrate taxa. In

Current Genomics, 2012, *13*, 289-299

From Lizard to Snake; Behind the Evolution of an Extreme Body Plan

Joost M. Woltering*

University of Geneva, Department of Genetics and Evolution, 30 quai Ernest Ansermet, 1211 CH, Genève, Switzerland

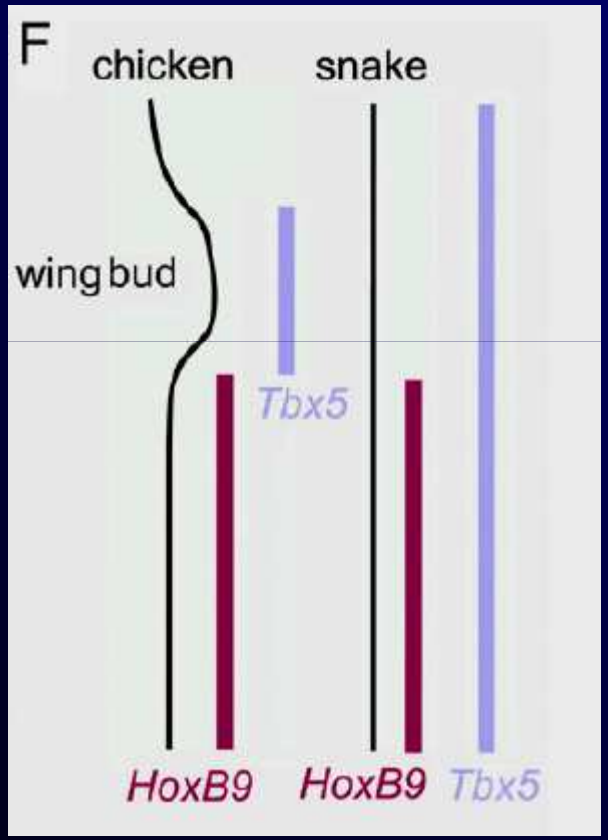
Abstract: The elongated, snake-like skeleton, as it has convergently evolved in numerous reptilian and amphibian lineages, is from a developmental biologist's point of view amongst the most fascinating anatomical peculiarities in the animal kingdom. This type of body plan is characterized by a greatly increased number of vertebrae, a reduction of skeletal regionalization along the primary body axis and loss of the limbs. Recent studies conducted on both mouse and snakes now hint at how changes inside the gene regulatory circuitries of the *Hox* genes and the somitogenesis clock likely underlie these striking departures from standard tetrapod morphology, suggesting scenarios by which snakes and other elongated species may have evolved from more ordinarily bodied ancestors.

unclear in the snake. Interestingly, the accumulation of transposable elements within the *squamate Hox* clusters [41,5], absent from their mammalian counterparts, may have caused the disruption of regulatory modules.

Evolution of Developmental Control Mechanisms

Axial patterning in snakes and caecilians: Evidence for an alternative interpretation of the *Hox* code

Joost M. Woltering [a,*], Freek J. Vonk [b], Hendrik Müller [c,1], Nabila Bardine [a,d], Ioana L. Tuduce [d], Merijn A.G. de Bakker [b], Walter Knöchel [d], I. Ovidiu Sirbu [d], Antony J. Durston [a], Michael K. Richardson [b]



No limb buds are present in corn snakes however, and neither is any molecular trace of a discrete forelimb domain.

Developmental Biology 332 (2009) 82–89

Cell

Leading Edge
Review

Evolution of Gene Regulatory Networks Controlling Body Plan Development

Isabelle S. Peter[1,*] and Eric H. Davidson[1,*]
[1]Division of Biology 156-29, California Institute of Technology, Pasadena, CA 91125, USA

contexts. Because *cis*-regulatory modules may be carried around by transposing mobile elements, and because the transposition of mobile elements is the most rapid type of large-scale genomic sequence change in animal genomes, this is likely to be a major mechanism of GRN evolution. In human, mouse, and

(Garza et al., 1991; Ostertag and Kazazian, 2001), and it is clear that there have been great bursts of mobile element insertion in the evolutionary history of many animal lineages including our own (e.g., Ohshima et al., 2003; Ostertag and Kazazian, 2001).

the Tbx5 gene, deeply embedded in the vertebrate heart formation GRN, turns out to be regulated differently during heart formation in reptiles than in birds and mammals,…(p 976)

Cell 144, March 18, 2011

Historical view of Genesis 3:15:

You and this woman will hate each other; your descendants and hers will always be enemies. One of hers will strike you on the head, and you will strike him on the heel." (Genesis 3:15 CEV)

The Adversary does not have any “descendants”, all of the “descendants” come from the woman and Adam (who is not even mentioned here…why?).

Genomic view:

And I will put enmity between thee and the woman, and between thy seed (Genetic Material) and her seed (Genetic Material); it shall bruise thy head, and thou shalt bruise his heel.

(Gen 3:15 KJV)

G4690 - Strong's Number - Greek

sperma	H319	acharit - after part, end
sperma	H1121	ben - son, grandson, child
sperma	H1320	basar - flesh
sperma	H2233	zera - seed, sowing, semen virile
sperma	H5209	nin - offspring, posterity
sperma	H5220	nekhed - progeny, posterity

Genomic imprinting: **Mother maintains methylation marks**

Wendy Dean* and Anne Ferguson-Smith†

A DNA methyltransferase has been identified that plays a role in maintaining the methylation status of imprinted genes. Interestingly, although expressed in the unfertilised egg, this enzyme functions only during one round of replication in the eight-cell embryo.

Addresses: *Developmental Genetics Programme, The Babraham Institute, Cambridge CB2 4AT, UK. †Department of Anatomy, University of Cambridge, Downing Street, Cambridge CB2 3DY, UK.

Current Biology 2001, 11:R527–R530

0960-9822/01/$ – see front matter

inherited chromosomes are progressively demethylated over several rounds of cell division — 'passive demethylation' [7,10], consistent with the absence of DNA methyltransferases responsible for replication-mediated 'maintenance' methylation. After implantation, there is a wave of *de novo* methylation and subsequent maintenance methylation restores methylation profiles to the levels usually described for somatic cells [13].

To date, three functional DNA methyltransferases have been identified in the mouse: Dnmt1, Dnmt3A and Dnmt3B (reviewed in [1]). Mice which do not express these genes die by mid-gestation [5,14]. Dnmt3A and

Leading Edge
Review

Cell

Mighty Piwis Defend the Germline against Genome Intruders

Kathryn A. O'Donnell[1,2] and Jef D. Boeke[1,2,*]
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[2]The High Throughput Biology Center
The Johns Hopkins University School of Medicine, 733 N. Broadway, Baltimore, MD 21205, USA
*Correspondence: jboeke@bs.jhmi.edu
DOI 10.1016/j.cell.2007.03.028

In recent years, Piwi proteins were recognized as having potential anti-mobile element activity.

Cell *129, April 6, 2007*

Cell

Review

Small RNAs as Guardians of the Genome

Colin D. Malone[1,2] and Gregory J. Hannon[1,2,*]
[1]Watson School of Biological Sciences
[2]Howard Hughes Medical Institute
Cold Spring Harbor Laboratory, 1 Bungtown Road, Cold Spring Harbor, NY 11724, USA
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DOI 10.1016/j.cell.2009.01.045

Early clues to the nature of the maternal factor came from observations that Piwi proteins are essential for transposon silencing in the context of several models of hybrid dysgenesis (Reiss et al., 2004; Sarot et al., 2004). Moreover, both Piwi and Aub are maternally deposited and accumulate in the pole plasm, the specialized cytoplasm at the posterior end of the developing embryo that will give rise to the future germline.

Cell 136, 656–668, February 20, 2009

Small RNAs as Guardians of the Genome:

Small RNAs present in maternal germ cells are also faithfully transmitted to progeny (Blumenstiel and Hartl, 2005); however, since the sperm discards most of its cytoplasm postmeiotically, similar species are likely not paternally inherited. This gave rise to clear differences in the embryonic content of piRNAs, depending upon whether an element was maternally or paternally inherited, and these differences correlated perfectly with the ability of progeny to silence the dysgenesis-inducing transposon (Brennecke et al., 2008). These studies demonstrated that differences in the inheritance of maternal small RNA populations underlie hybrid dysgenesis. They also highlighted the broader conclusion that maternally inherited small RNAs are required to prime resistance pathways at each generation in order to effectively silence at least some elements, and the presence of sequences within a piRNA cluster corresponding to a particular element may not alone be sufficient to achieve effective silencing in the absence of maternal small RNAs (Brennecke et al., 2008).

Cell 136, 656–668, February 20, 2009

Thank your Mother:

Defense of Genome Comes from Mother

GOD RESPONDS TO EVE

To the woman he said, I will greatly multiply your sorrow and your conception; in sorrow you shall bring forth children; and your desire shall be to your husband, and he shall rule over you.

(Genesis 3:16 AKJV)

To the woman he said, "I will greatly increase your pains in childbearing; with pain you will give birth to children. Your desire will be for your husband, and he will rule over you."

(Genesis 3:16 NIV)

Pregnancy and Birth

Transposon-mediated rewiring of gene regulatory networks contributed to the evolution of pregnancy in mammals

Vincent J Lynch, Robert D Leclerc, Gemma May & Günter P Wagner

A fundamental challenge in biology is explaining the origin of novel phenotypic characters such as new cell types[1–4]; the molecular mechanisms that give rise to novelties are unclear[5–7]. We explored the gene regulatory landscape of mammalian endometrial cells using comparative RNA-Seq and found that 1,532 genes were recruited into endometrial expression in placental mammals, indicating that the evolution of pregnancy was associated with a large-scale rewiring of the gene regulatory network. About 13% of recruited genes are within 200 kb of a Eutherian-specific transposable element (MER20). These transposons have the epigenetic signatures of enhancers, insulators and repressors, directly bind transcription factors essential for pregnancy and coordinately regulate gene expression in response to progesterone and cAMP. We conclude that the transposable element, MER20, contributed to the origin of a novel gene regulatory network dedicated to pregnancy in placental mammals, particularly by recruiting the cAMP signaling pathway into endometrial stromal cells.

Nature Genetics 25 September 2011

There is a broad consensus that many of the genetic changes underlying the evolution of morphology occur by the stepwise modification of individual pre-existing *cis*-regulatory element modules[5,6,29]. However, it is questionable whether the origin of complex novelties—such as the origin of new cell types, which involves the recruitment of hundreds of genes—can be achieved by these small-scale changes[7,29]. Our findings indicate that the gene regulatory network of ESCs was rewired in placental mammals during the evolution of pregnancy, a reorganization partly mediated by the transposable element MER20. Furthermore, MER20s coopted specific signaling pathways essential for implantation and pregnancy into ESCs by acting as cell type–specific regulatory elements. These findings strongly support the existence of transposon-mediated gene regulatory innovation at the network level, a mechanism of gene regulation first suggested more than forty years ago by McClintock[30] and Britten and Davidson[31]. Our data and those of other recent studies[13,14,32] show that transposable elements are potent agents of gene regulatory network evolution and add to an increasing body of evidence indicating that the evolution of novel characters involves genetic mechanisms that are distinct from those involved in the modification of existing characters[23,33–35].

Nature Genetics 25 September 2011

J. Mamm. Ova Res. Vol. 30 (1), 16–23, 2013

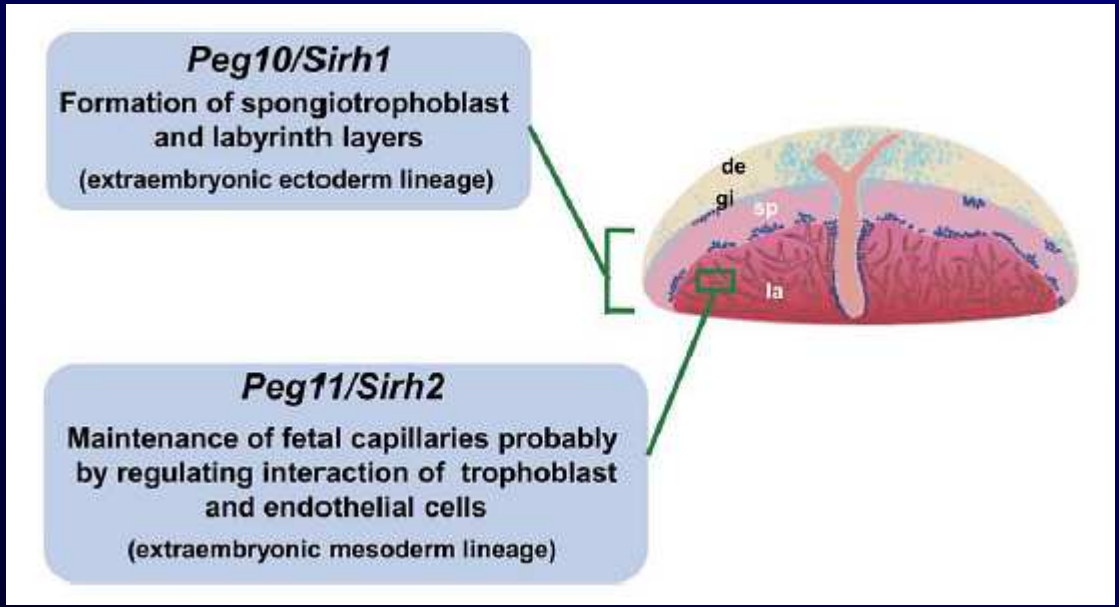
—Mini Review—

The Evolution of the Placenta and Viviparity is Related to LTR Retrotransposon-derived Genes in Mammals

Tomoko Kaneko-Ishino[1] and Fumitoshi Ishino[2*]

[1]*School of Health Sciences, Tokai University, Kanagawa 259-1193, Japan*
[2]*Medical Research Institute, Tokyo Medical and Dental University, Tokyo 113-8510, Japan*

Two LTR Retrotransposon-derived Genes, *PEG10* and *PEG11/RTL1,* Play an Essential Role in Mammalian Development



Reproductive Sciences

Review: Human Endogenous Retroviruses and the Placenta

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Up to 8% of the human genome is of retroviral origin. These stably integrated retroviral sequences that characterize the human endogenous retrovirus (HERV) arose from retroviral infections that occurred more than 25 million years ago. The host and the retrovirus have subsequently coevolved as retrovirally derived genetic material is propagated in a Mendelian fashion. Although most HERV sequences are silenced, several have been described that are functional. The effects of some HERV-derived products are linked to human disease; others appear essential to human organ function. The human placenta, unique in its active expression of retroviral sequences that are not expressed in other tissues, may hold the key to an improved understanding of the functional significance of HERVs. In this review, we discuss the contribution of retroelements, particularly HERVs, to placental function and dysfunction. We describe fusogenic and immunosuppressive HERV activities and emphasize epigenetic regulation of retroelement expression.

Key Words: Human endogenous retrovirus • placenta • immunosuppression • fusion • transposon.
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Retroviruses and the Placenta

Minireview

David Haig

Placental Contagion

The close apposition of uterine and placental tissues creates a site for viral transmission from mother to fetus. By this path, a heterozygous ERV in the mother could potentially colonize all of a mother's offspring, not just the 50% that inherit the ERV by Mendelian means. For this to be an effective route of ongoing contagion, viruses transmitted from mother to placenta must sometimes re-infect somatic or germ cells of the fetus (or mother) before the placenta is discarded at delivery. Retroviruses are known to use this route: HIV-1 can be transmitted from mother to fetus across the placenta [26] and endogenous Jaagsiekte Sheep Retro-

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Bottom Line?

BIRTH = INFECTION

Behold, I was shaped in iniquity; and in sin did my mother conceive me.

(Psalms 51:5 AKJV)

Surely I was sinful at birth, sinful from the time my mother conceived me.

(Psalms 51:5 NIV)

The missing link

Viruses revise evolutionary theory

Philip Hunter

genome. Similarly to the bacterial ancestors of mitochondria and chloroplasts, endogenous retroviruses have introduced fundamental functions, such as the ability to form syncytia: cellular conglomerates that contain multiple nuclei.

Syncytia underpin several crucial structural and functional roles in vertebrates, especially mammals. In vertebrates, skeletal muscles develop through the fusion of myocite cells into long fibres. Similarly, fibre

PAIN RECEPTORS ARE ALL G-COUPLED PROTEINS, AND THEY WERE ALL MODIFIED BY MGE's.

GOD RESPONDS TO ADAM

And to Adam he said, Because you have listened to the voice of your wife, and have eaten of the tree, of which I commanded you, saying, You shall not eat of it: cursed is the ground for your sake; in sorrow shall you eat of it all the days of your life;

Thorns also and thistles shall it bring forth to you; and you shall eat the herb of the field;

In the sweat of your face shall you eat bread, till you return to the ground; for out of it were you taken: for dust you are, and to dust shall you return (first death).

(Genesis 3:17-19 AKJV)

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ANNALS OF BOTANY
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INVITED REVIEW

The more the better? The role of polyploidy in facilitating plant invasions

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example, in *Oxalis pes-caprae*. We have shown that polyploidy might be an important factor in species invasion success and suggest that ploidy must be considered in any general model that seeks to explain why some species are more successful than others as invaders.

TABLE 1. *Differences in ploidal level of invasive species between native and introduced ranges*

Species	Family	Native range	Introduced range	Reference(s)
Pre-introduction processes and founder effects				
Pre-adaptation of polyploid cytotype				
*Centaurea stoebe** (syn. *C. maculosa*)	Asteraceae	Eurasia, **2x**, 4x	North America, 2x, **4x**	Treier *et al.* (2009)
Lythrum salicaria	Lythraceae	Europe/Asia, 2x, (3x), 4x, 6x	North America, 4x	Kubátová *et al.* (2008)
Rubus alceifolius	Rosaceae	Asia, (3x), **4x**	Indian Ocean islands, 4x	Amsellem *et al.* (2001)
Senecio inaequidens	Asteraceae	South Africa, 2x, 4x	Europe, 4x	Lafuma *et al.* (2003)
Solidago gigantea	Asteraceae	North America, 2x, (3x), **4x**, (5x), 6x	Europe/eastern Asia, 2x, **4x**	Schlaepfer *et al.* (2008); Hull-Sanders *et al.* (2009)
Strong founder effects				
Brachypodium distachyon	Poaceae	Eurasia, 2x, 4x	North America, 4x	Bakker *et al.* (2009)
Butomus umbellatus	Butomaceae	Europe, 2x, **3x**	North America, **2x**, 3x	Kliber and Eckart (2005)
Post-introduction processes and 'evolution of invasiveness'				
High ploidy polymorphism coupled with shifts in reproductive mode				
Hieracium pilosella	Asteraceae	Europe, **4x**, 5x, 6x	New Zealand, 4x, **5x**, 6x	Trewick *et al.* (2004)
*Oxalis pes-caprae**	Oxalidaceae	South Africa, 2x, **4x**, (5x)	Mediterranean and temperate ecosystems, 4x, **5x**	Castro *et al.* (2007)
Allopolyploidization				
*Fallopia japonica**	Polygonaceae	Eastern Asia, 4x, 6x, 8x, 10x	Europe, **8x**	Bailey *et al.* (2007)
F. sachalinensis		Eastern Asia, 4x, 12x	Europe, USA, **4x**, 6x, 8x	
F. × bohemica		Eastern Asia, 6x	Europe, 4x, **6x**, 8x	
Phragmites australis	Poaceae	Cosmopolitan, 3x–22x	North America, 3x, **4x**, 6x, 8x	Hansen *et al.* (2007); Saltonstal (2007)
Spartina maritima	Poaceae	Europe, 6x	–	Ainouche *et al.* (2009)
S. alterniflora		Eastern America, 6x	Europe, 6x	
S. × townsendii		Europe, 6x	–	
*S. anglica**		–	Europe, 12x	

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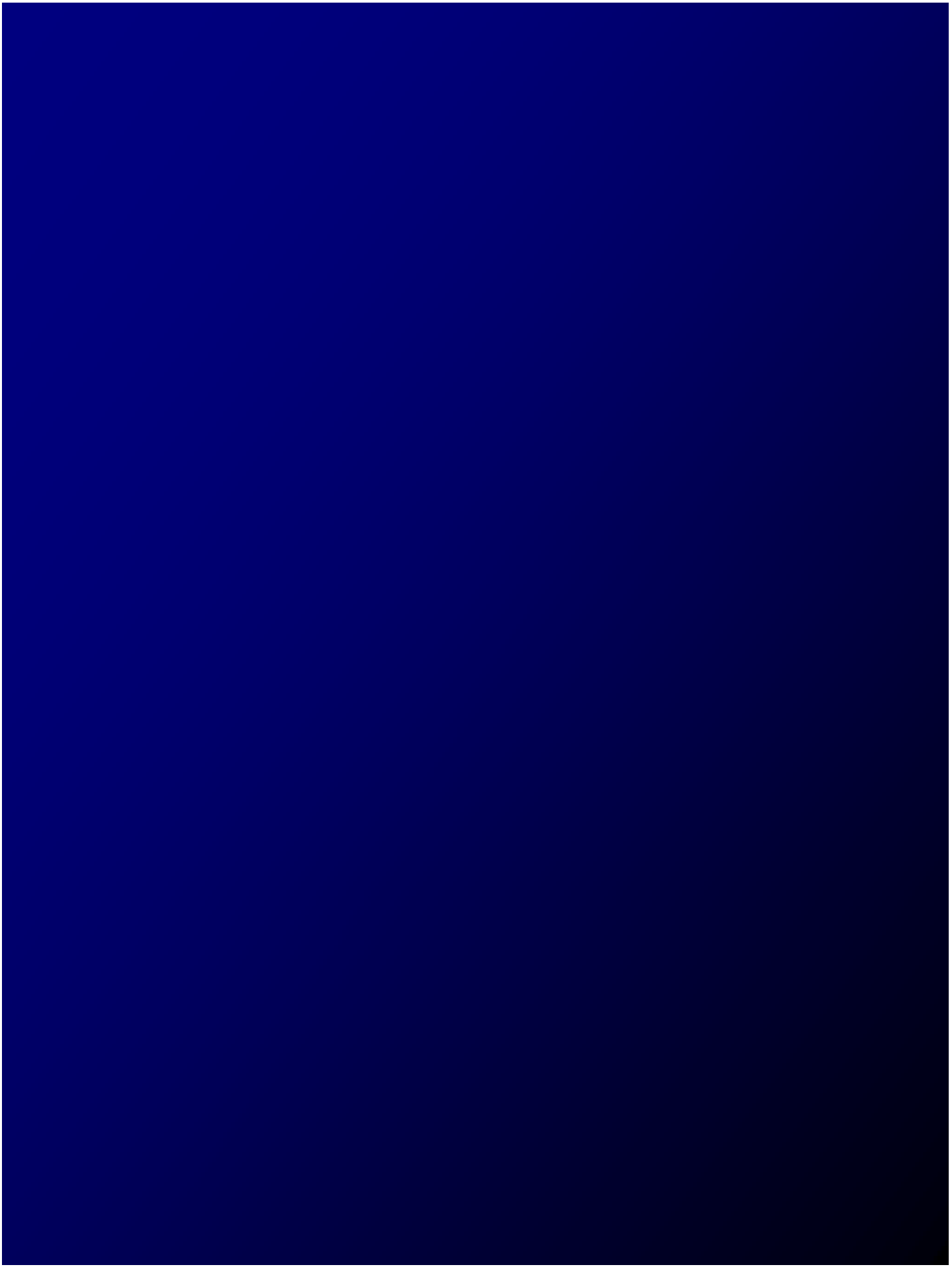
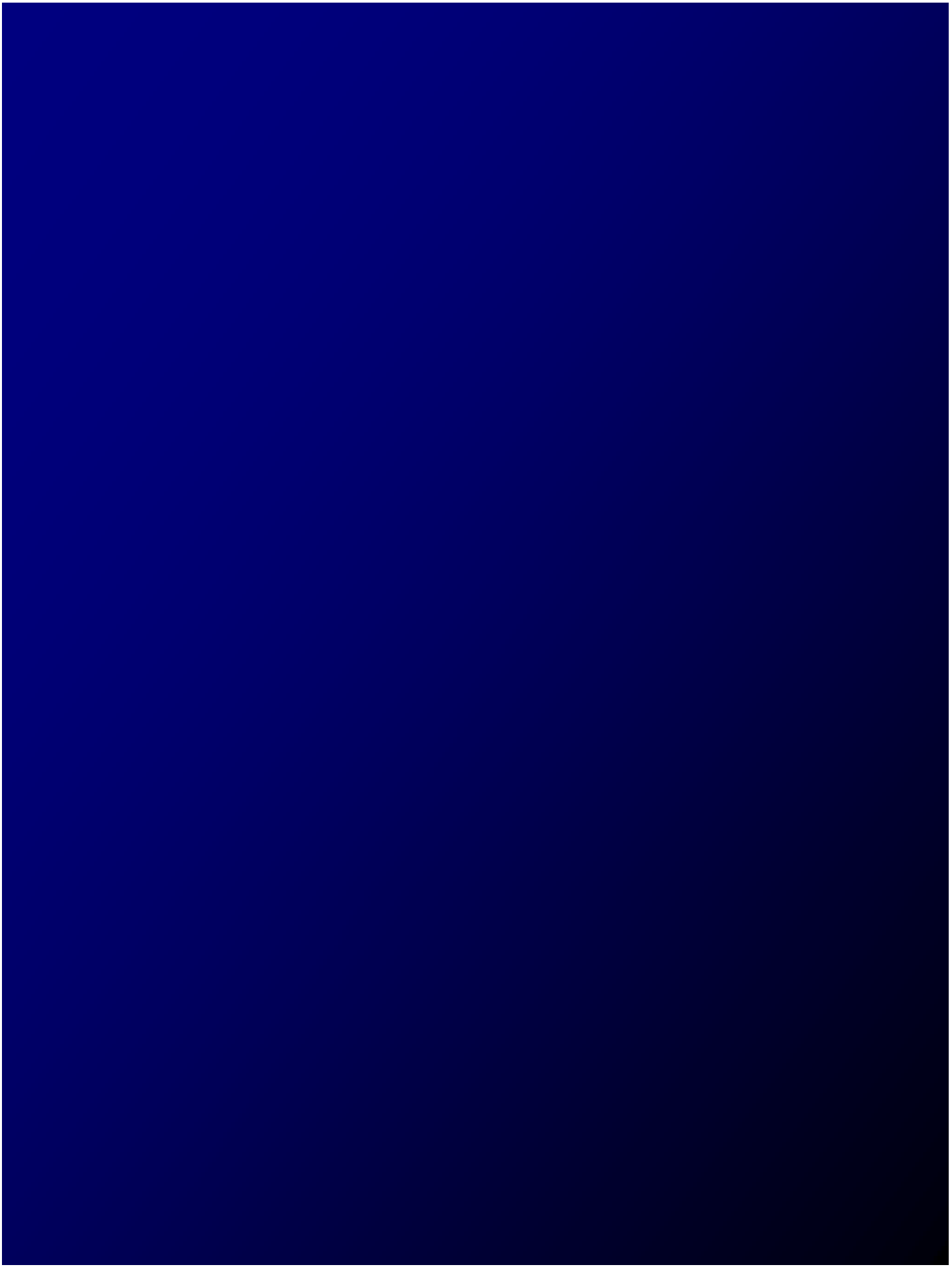
“First death” already discussed in Lecture 3.

E.G. White

There was nothing poisonous in the fruit of the tree of knowledge itself, nothing that would cause death in partaking of it. The tree had been placed in the garden to test their loyalty to God.

{ST, February 13, 1896 par. 6}





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