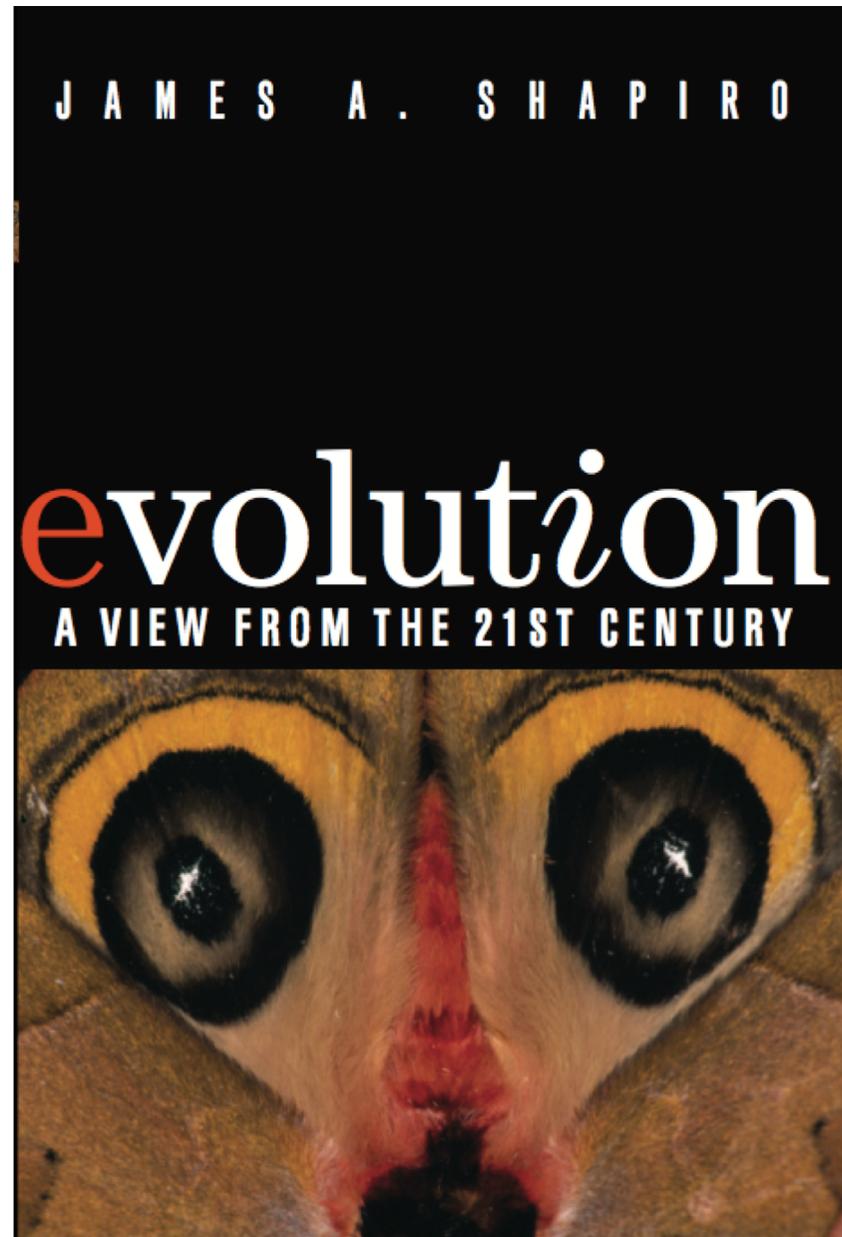


# How Should We Think About Evolution in the Age of Genomics?

James A. Shapiro  
September 17, 2018



## Prevailing 20<sup>th</sup> Century Assumptions (ca. 1968)

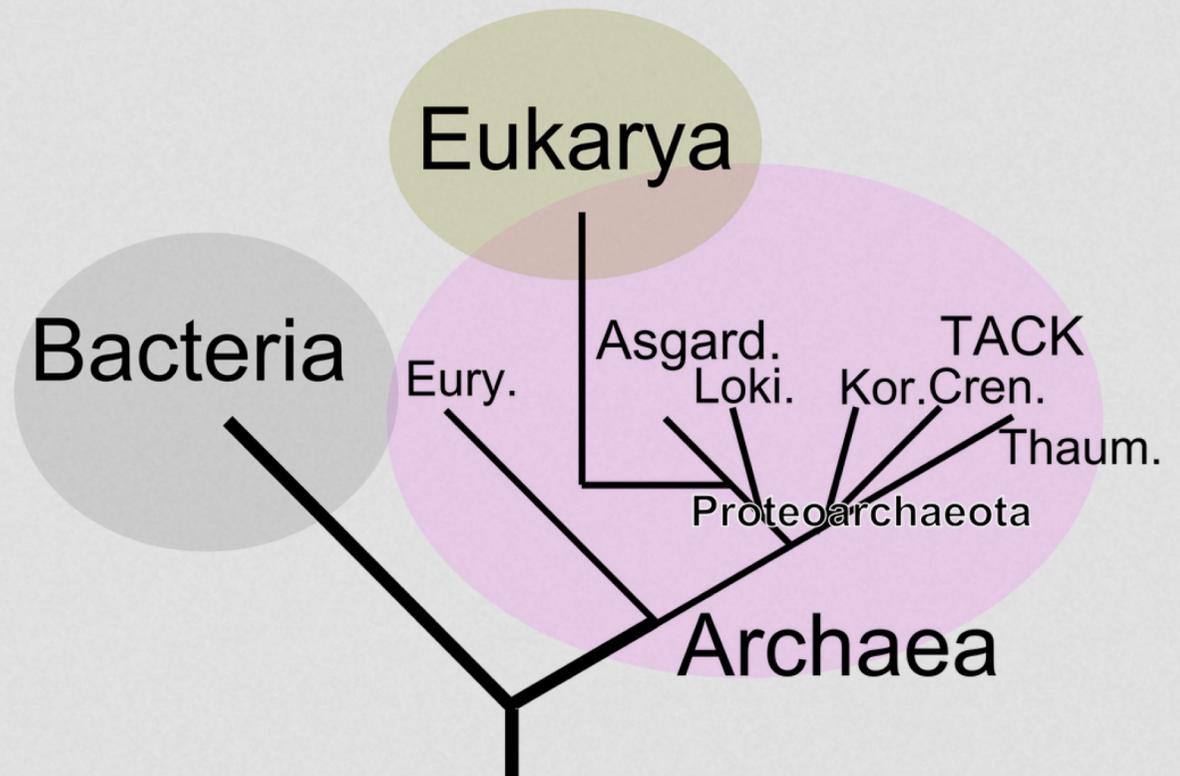
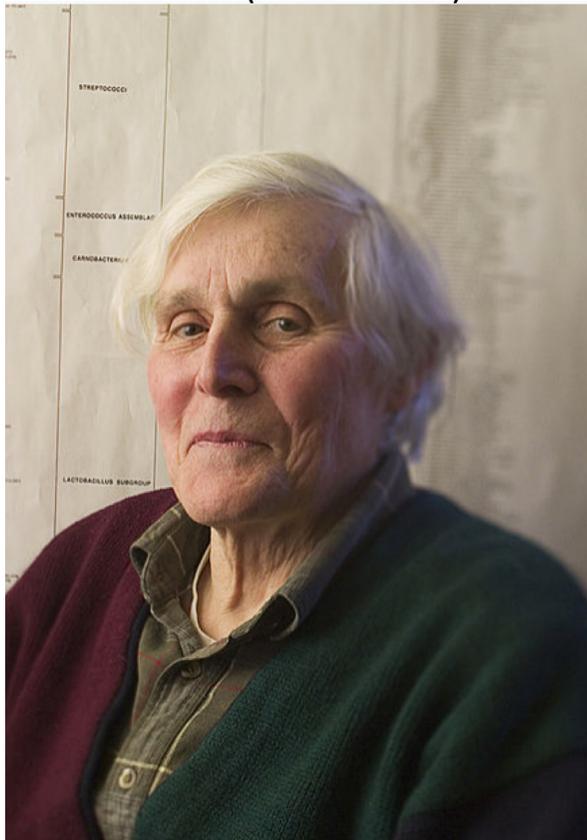
- Reproductively isolated organismal genomes
- All hereditary change takes place within the species' genome
- No transmission of life-history information to the germline
  - Weismann doctrine
  - Central Dogma (molecular Weismannism)
- Random, accidental genome change leading to numerous small selective advantages and slow gradual evolution

# Some Underlying Themes Learned From Genomics

- Evolutionary Cell and Genome Changes Result From Active Processes - Basic Systems Thinking Tells Us that Organisms With Tools to Accelerate their Evolution Will Prevail Over Organisms that Depend on Random Changes
- Sequencing Teaches Us that Basic Eukaryotic Cell Types Evolved by Cell Fusions, Not by Accumulating Gradual Changes (Symbiogenesis)
- Evolutionary Change is Rapid and Connected to Biological Interactions
- Natural Genetic Engineering Capabilities Exist in All Cells
- The Idea of “Junk DNA” is a Myth that has been Debunked by Learning About Functionalities of So-called “Non-coding” DNAs and RNAs
- Viruses are Far More than Parasites and Act as Horizontal DNA Transfer Vectors and as Mobile Genetic Elements that Format Transcriptional Networks

# Three, not Two, Kinds of Living Cells (1977)

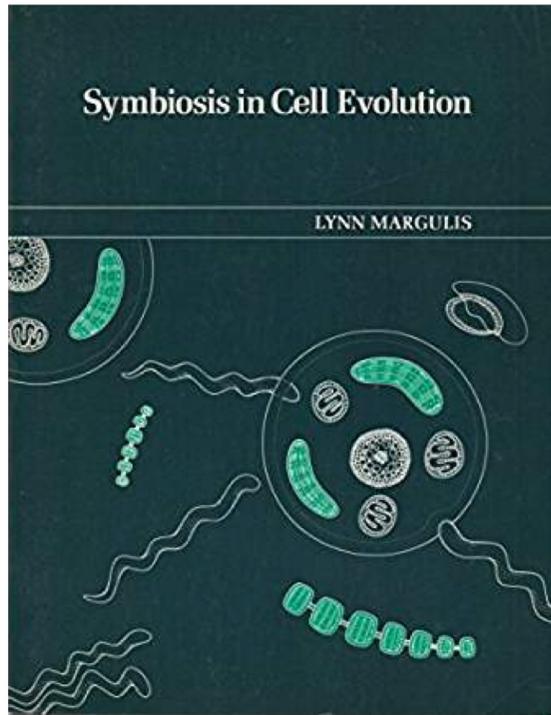
Carl Woese (1928 –2012)



Woese, Carl R.; George E. Fox (1977). "[Phylogenetic structure of the prokaryotic domain: the primary kingdoms](#)". *Proceedings of the National Academy of Sciences of the United States of America*. **74** (11): 5088–5090.

# Biomath: One + One = One

Lynn Margulis (1938-2011) Cell Mergers in Reproduction and Evolution

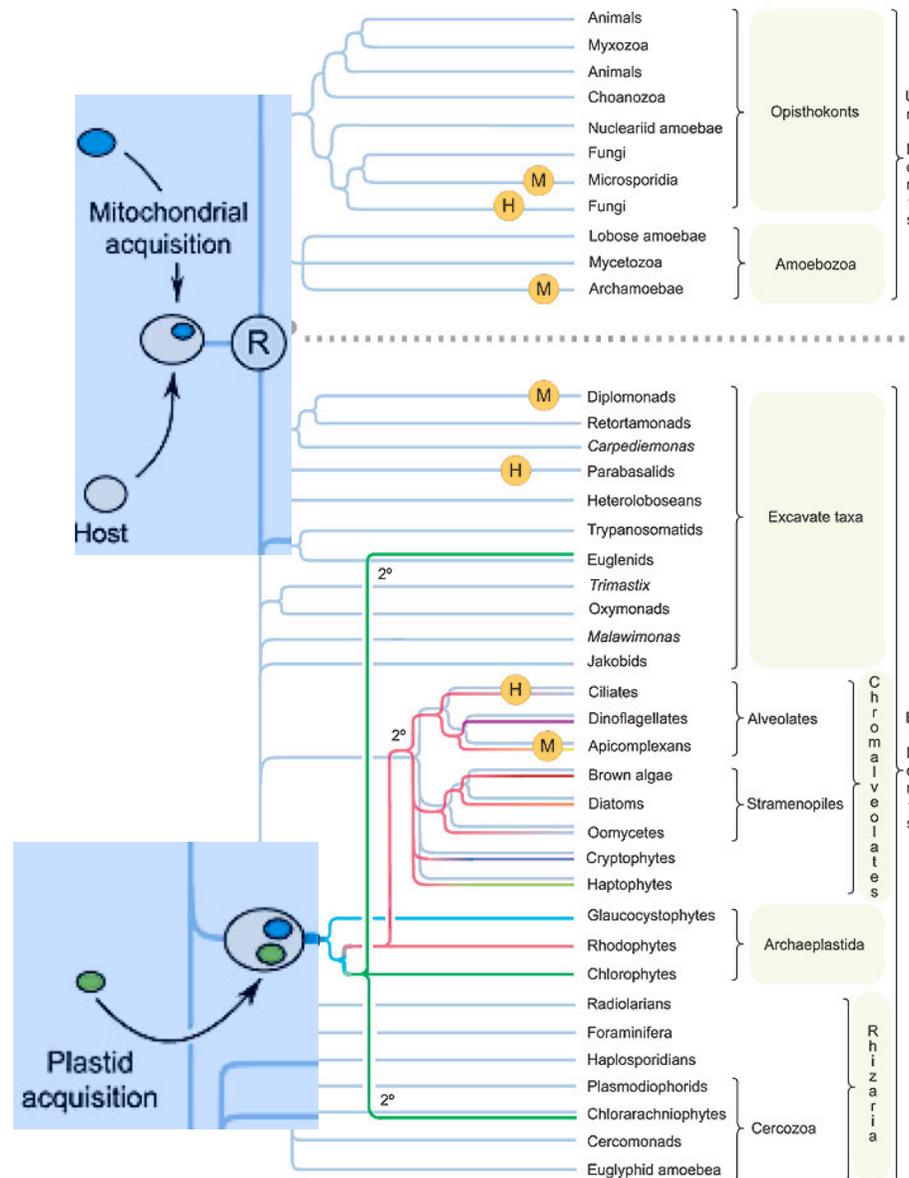


## SYMBIOTIC EARTH Screenings

Margulis, L. (1971). "Symbiosis and evolution." *Sci Am* **225**(2): 48-57.  
<http://www.ncbi.nlm.nih.gov/pubmed/5089455>.

Please join us at a screening of *Symbiotic Earth: How Lynn Margulis rocked the boat and started a scientific revolution*. Spread the word and invite your friends, colleagues, and students to participate in honoring Lynn Margulis and her symbiotic world view.

# Evolutionary genome writing by cell fusions – symbiogenetic origins of the eukaryotic cell and descendant photosynthetic taxa



T. M. Embley and W. Martin. 2006. [Eukaryotic evolution, changes and challenges](#). Nature 440, 623-630.

# Timeline of Planetary and Cell Evolution – Two-Way Organism-Ecosphere Feedback

- ≥3.8 GYA – Prokaryotic cells (*Bacteria*, *Archaea*), H<sub>2</sub>-rich atmosphere, anaerobic metabolism by chemosynthesis
- ca. 3.4 GYA – Photosynthetic bacteria; *Cyanobacteria* oxygenic photosynthesis
- ca. 2.5 GYA – **Great Oxygenation Event**, aerobic metabolism evolves in *Bacteria*
- ca. 2.5-1.6 GYA – First Eukaryotic fossils descended from **symbiogenetic** merger of anaerobic *Archaea* with aerobic *α-Proteobacterium* relative

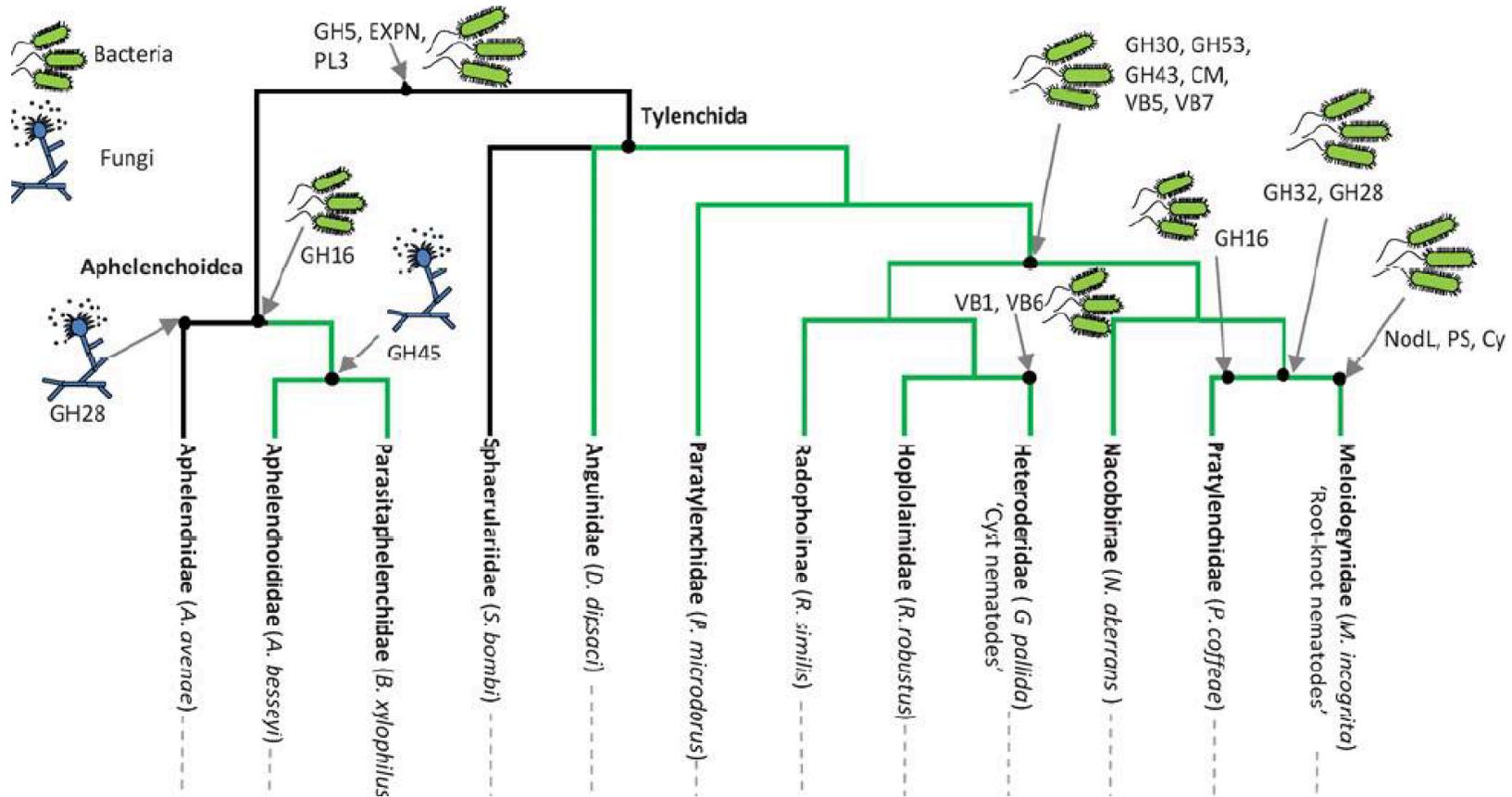
# Ubiquitous Horizontal DNA Sequence Mobility

- Among prokaryotes (transformation, conjugation, transduction): antibiotic resistance, virulence, metabolism; plasmids, integrons, ICEs
- From prokaryotes and fungi to multicellular eukaryotes: biosynthetic, metabolic and degradative capabilities
- From eukaryotes to bacteria: eukaryotic regulatory domains in “effector” proteins injected during host infection, human LINE retrotransposons in bacterial genomes
- Among eukaryotes: organelle genomes between plants; metabolic functions and mobile DNA elements between plants and animals
- Viral and endosymbiont DNA integrations into host genomes: DNA and RNA virus insertions in plants and animals, cancer integrations, endosymbiont (e.g. *Wolbachia*) genomes in invertebrate host genomes
- Amoeba-Megavirus DNA sequence “melting pot”: Megaviruses infect amoebae, which are hosts to bacteria that also infect plant and animal cells; Megavirus genomes contain sequences from all three cell kingdoms
- Environmental sequences: Metagenomic evidence revealing massive coding sequence reservoirs in environmental virus and extracellular particles

# Acquiring Adaptive Innovations Through Horizontal DNA Transfers Rather Than Reinventing the Wheel

- Hundreds of *eubacteria-archaea* DNA transfers in the independent evolution of four distinct mesophilic *archaeal* taxa from thermophilic ancestors (Lopez-Garcia, P., Y. Zivanovic, et al. (2015). "Bacterial gene import and mesophilic adaptation in *archaea*." Nat Rev Microbiol **13**(7): 447-456.)
- 128 distinct DNA transfers from *eubacteria*, *archaea*, and viruses encoding activities involved in xylem formation, plant defense, nitrogen recycling, and biosynthesis of starch, polyamines, hormones and glutathione into the nuclear genome of a primitive land plant (the moss *Physcomitrella patens*) (Yue, J., X. Hu, et al. (2012). "Widespread impact of horizontal gene transfer on plant colonization of land." Nat Commun **3**: 1152.)
- Dozens of DNA transfers from *eubacteria* and fungi conferring the ability to digest phytopolymers to distinct taxa of plant parasitic nematodes (Haegeman, A., J. T. Jones, et al. (2011). "Horizontal gene transfer in nematodes: a catalyst for plant parasitism?" Mol Plant Microbe Interact **24**(8): 879-887.)

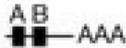
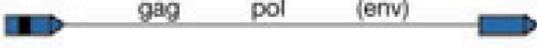
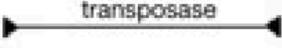
# Evolutionary genome writing by horizontal transfer – nematode plant parasitism



[Haegeman A, Jones JT, Danchin EG. Horizontal gene transfer in nematodes: a catalyst for plant parasitism? Mol Plant Microbe Interact. 2011 Aug;24\(8\):879-87](#)

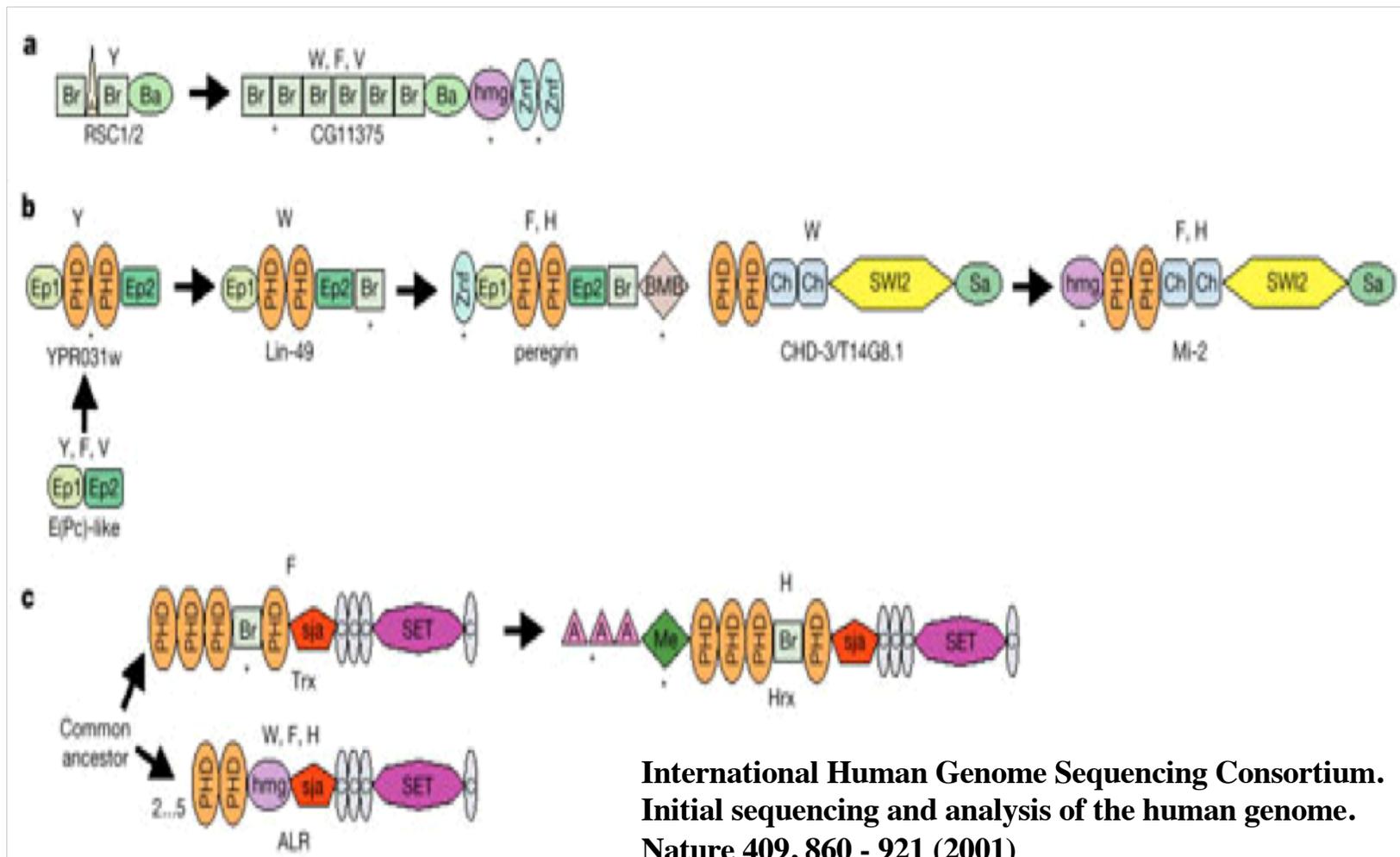
# Evolutionary time: Genome writing by natural genetic engineering – massive amplification of dispersed repetitive mobile DNA elements

Classes of interspersed repeat in the human genome

|                          |                |  | Length      | Copy number | Fraction of genome |
|--------------------------|----------------|--|-------------|-------------|--------------------|
| LINEs                    | Autonomous     |    | 6–8 kb      | 850,000     | 21%                |
|                          | Non-autonomous |   | 100–300 bp  |             |                    |
| Retrovirus-like elements | Autonomous     |    | 6–11 kb     | 450,000     | 8%                 |
|                          | Non-autonomous |   | 1.5–3 kb    |             |                    |
| DNA transposon fossils   | Autonomous     |  | 2–3 kb      | 300,000     | 3%                 |
|                          | Non-autonomous |  | 80–3,000 bp |             |                    |

International Human Genome Sequencing Consortium. Initial sequencing and analysis of the human genome. *Nature* 409, 860 - 921 (2001)

# Genome writing by natural genetic engineering – Protein evolution by domain rearrangements

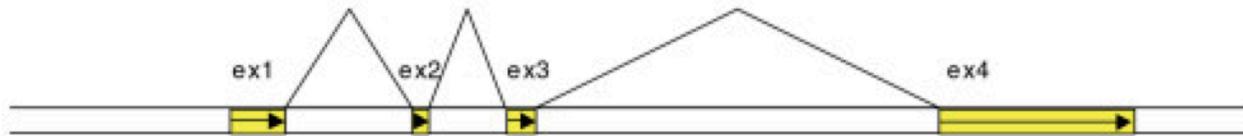


# Origins of Novel Protein Functionalities

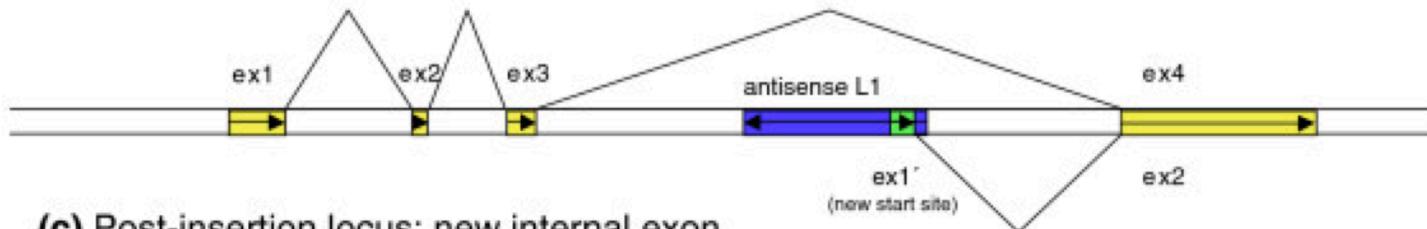
- Duplication, modification and rearrangement of existing protein domains
- Role of mobile DNA in exon and intron origination
- Synthesis of novel exons and introns by reverse transcription and integration of processed RNA molecules

# Evolutionary time: Genome writing by natural genetic engineering –mobile element inserts for new exons

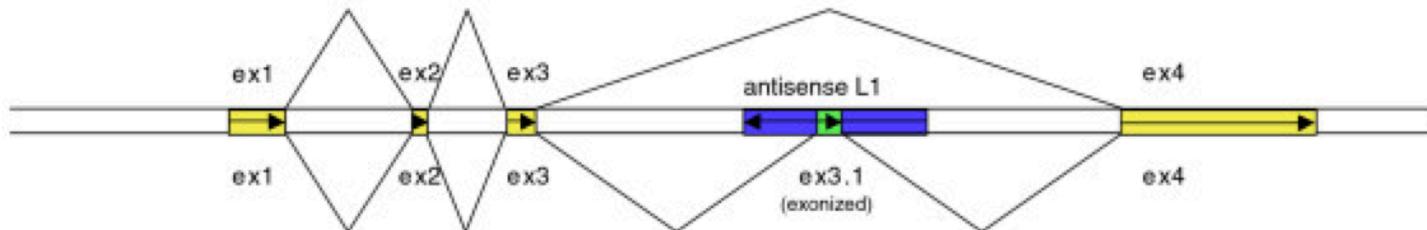
(a) Pre-insertion locus



(b) Post-insertion locus: new start site for transcription



(c) Post-insertion locus: new internal exon



[Burns KH, Boeke JD. Great exaptations. J Biol. 2008;7\(2\):5. doi: 10.1186/jbiol66. http://www.ncbi.nlm.nih.gov/pubmed/18279541](#)

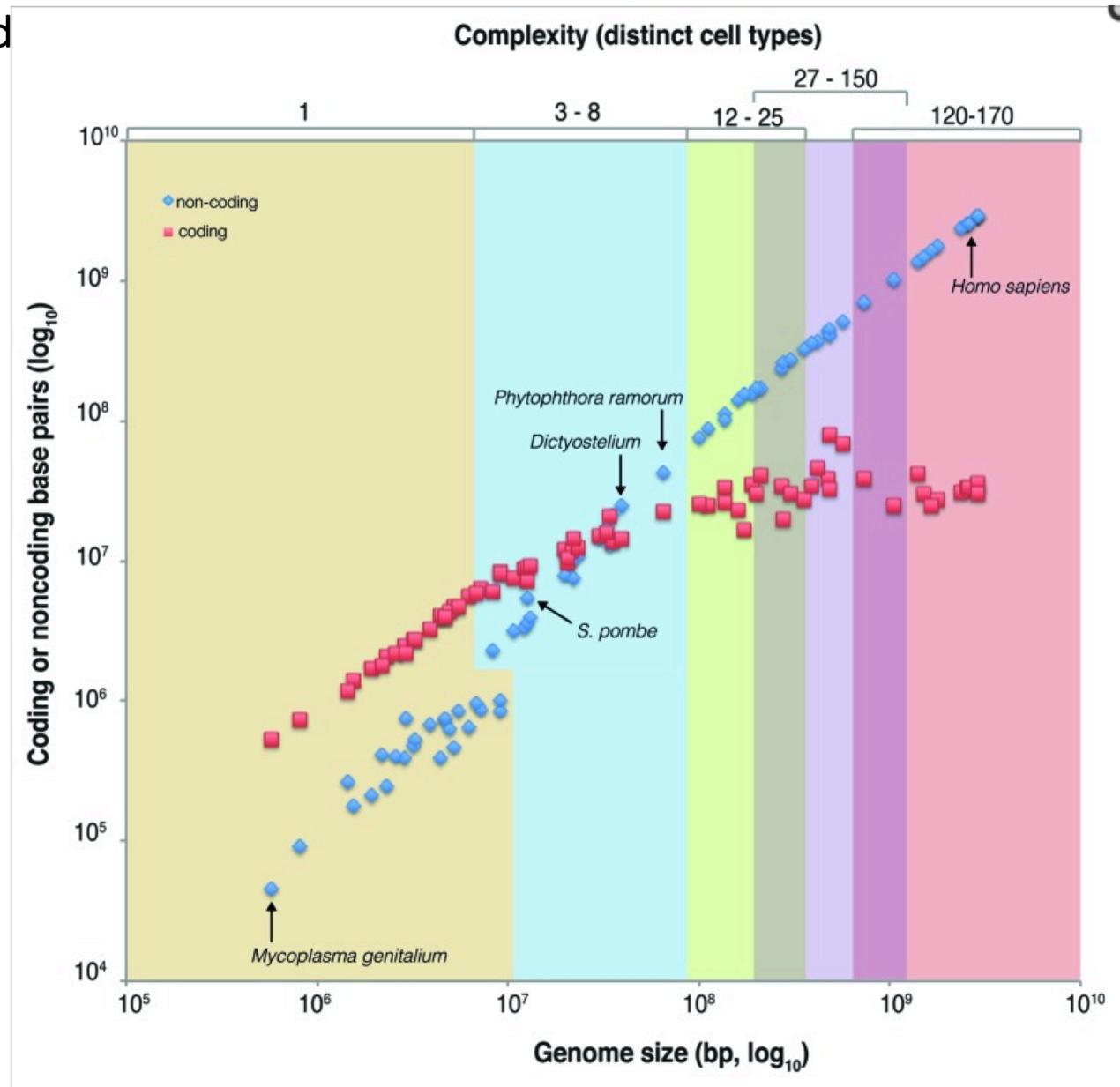
## Functionality of so-called “non-coding” DNA

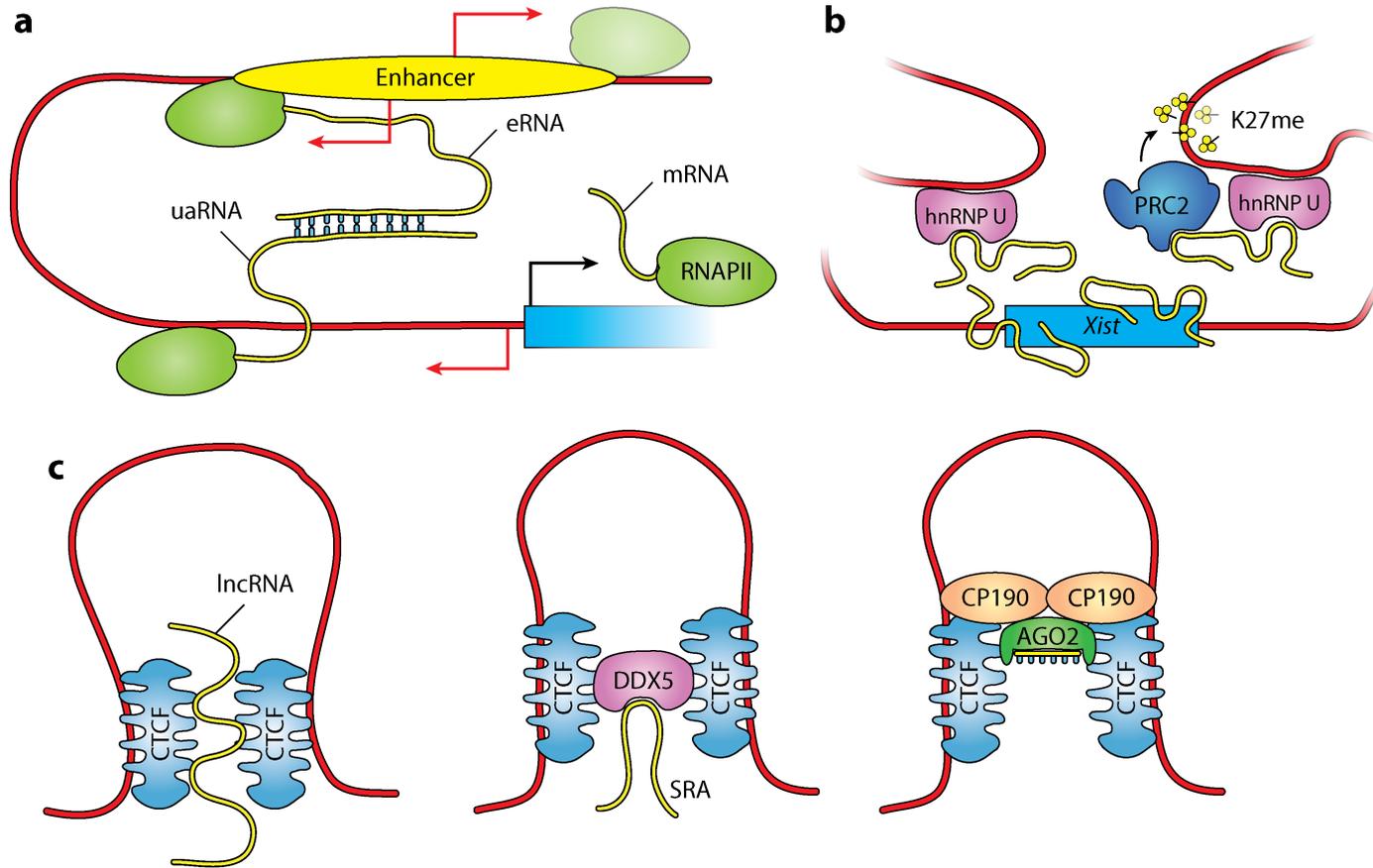
“...using data from a total of 1,627 prokaryotic and 153 eukaryotic complete and annotated genomes, show that the proportion of ncDNA per haploid genome is significantly positively correlated with a previously published proxy of biological complexity, the number of distinct cell types... the vast majority of ncDNA in animals is transcribed. This includes more than 60 human loci previously considered “gene deserts,” many of which are expressed tissue-specifically and associated with previously reported GWAS SNPs.”

[Liu G<sup>1</sup>](#), [Mattick JS](#), [Taft RJ](#).

**A meta-analysis of the genomic and transcriptomic composition of complex life.**

[Cell Cycle](#). 2013 Jul 1;12(13):2061-72.





 Bonasio R, Shiekhattar R. 2014.  
Annu. Rev. Genet. 48:433–55

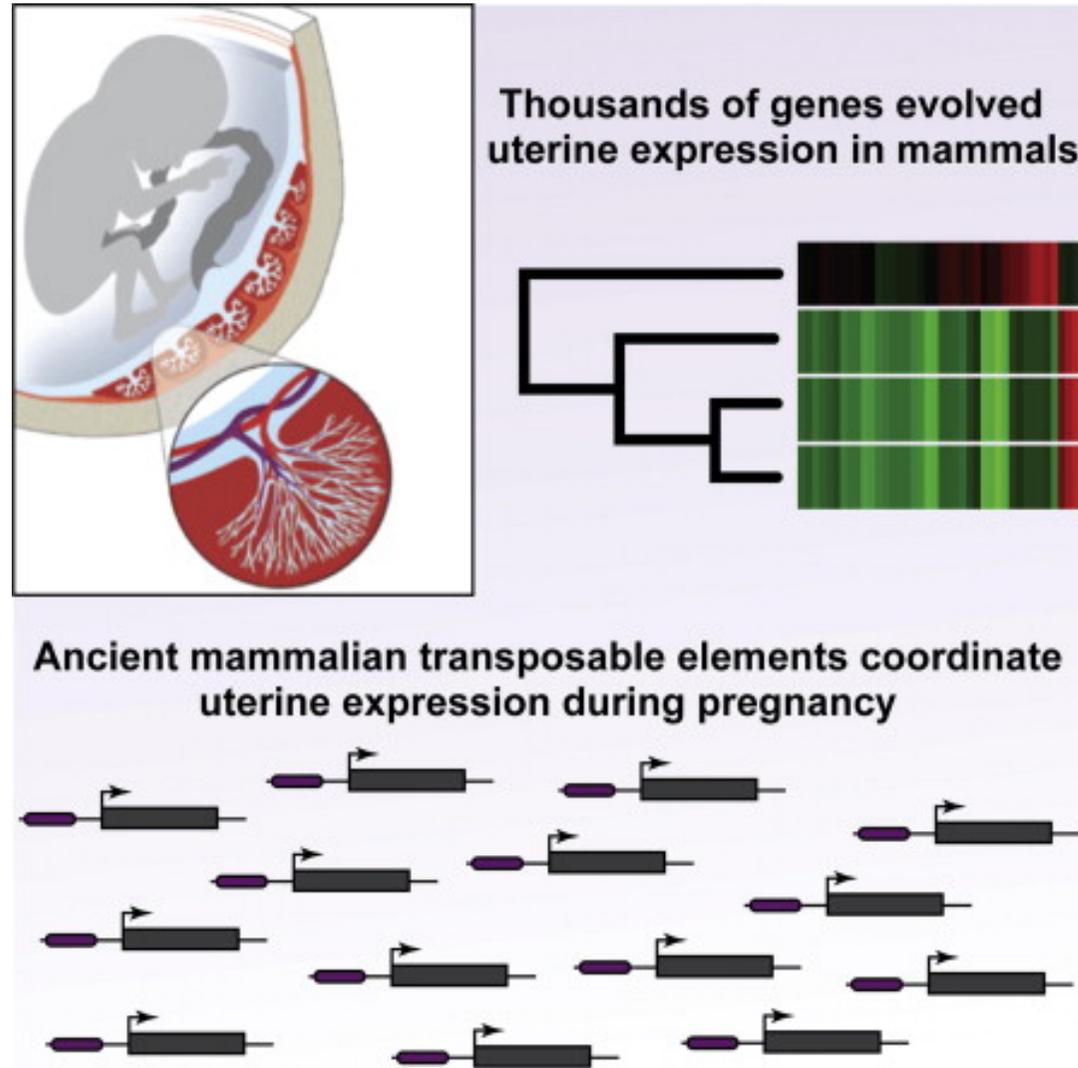
**Bonasio & Shickattar. 2014. Regulation of Transcription by Long Noncoding RNAs. Annual Review of Genetics 48: 433-455.**

| Organism   | lncRNA Regulated Function(s)  |
|------------|---|
| Plants     | Flower development and timing   |
| Tomato     | Fruit ripening  |
| Drosophila | Sex determination   |
| Tetrapods  | Spermatogenesis, synaptic transmission, placenta development  |
| Mouse      | lncRNA EVF2; forebrain development  |
| Mouse      | lncRNA FENDRR; heart and body wall development  |
| Mouse      | Male germline development   |
| Rat        | Synaptic connectivity in adult brain development  |
| Human      | lncRNA ROR; p53 repressor in DNA damage response; acts as microRNA sponge in transcription factor control |
| Human      | lncRNA APTR; cell cycle regulation  |
| Human      | lncRNA ROR; stem cell pluripotency; sequences from $\geq 12$ mobile elements, including HERVH             |
| Human      | Innate and adaptive immune responses  |
| Human      | lncRNA TINCR regulates epidermal differentiation  |
| Human      | Neurodevelopment and brain function   |

Shapiro, J. A. (2017). "Living Organisms Author Their Read-Write Genomes in Evolution." Biology (Basel) 6(4).  
<http://www.ncbi.nlm.nih.gov/pubmed/29211049>.

# DNA Transposons and Uterine Evolution

Vincent J. Lynch , Mauris C. Nnamani ,, et al. 2015.  
**Ancient Transposable Elements Transformed the Uterine Regulatory Landscape and Transcriptome during the Evolution of Mammalian Pregnancy.** Cell Reports, Volume 10, Issue 4, 2015, 551 - 561



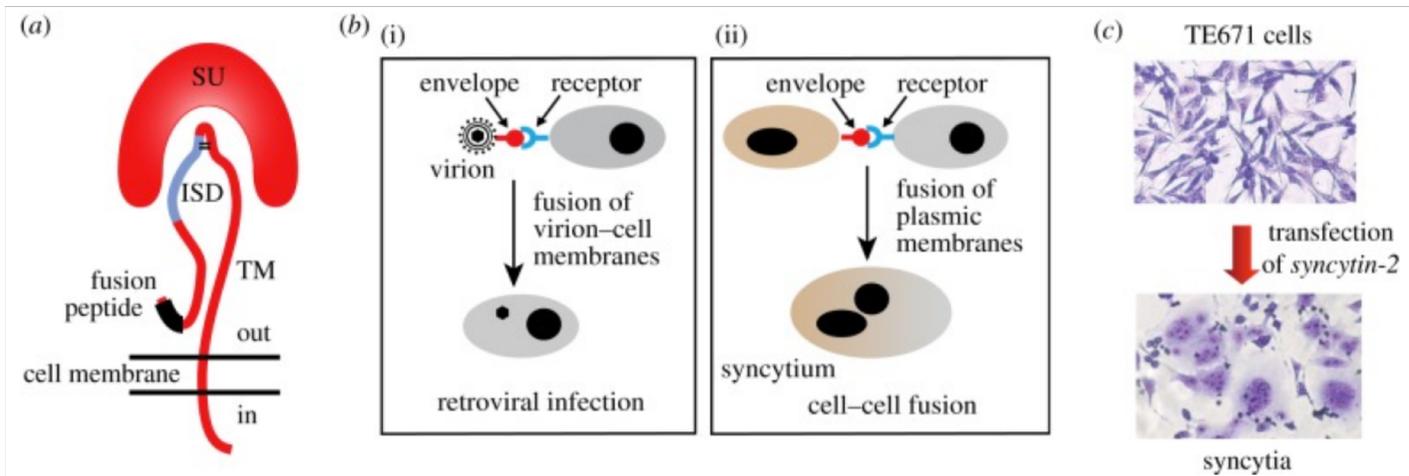
# Mammalian Reproduction Network Wiring by Mobile DNA – Both Sides of the Fetal-Maternal Interface

## UTERUS

- Eutherian-specific DNA transposon MER20 elements as enhancers for progesterone- and cAMP-stimulated expression of 200 uterine functions (Lynch et al, 2011).
- MER20-MER39 transposons provide Prolactin promoter (Emera & Wagner, 2012).
- 1,721 uterine-expressed Progesterone Receptor binding sites found within Mammalian- or Eutherian-specific transposable elements (Lynch et al., 2015).

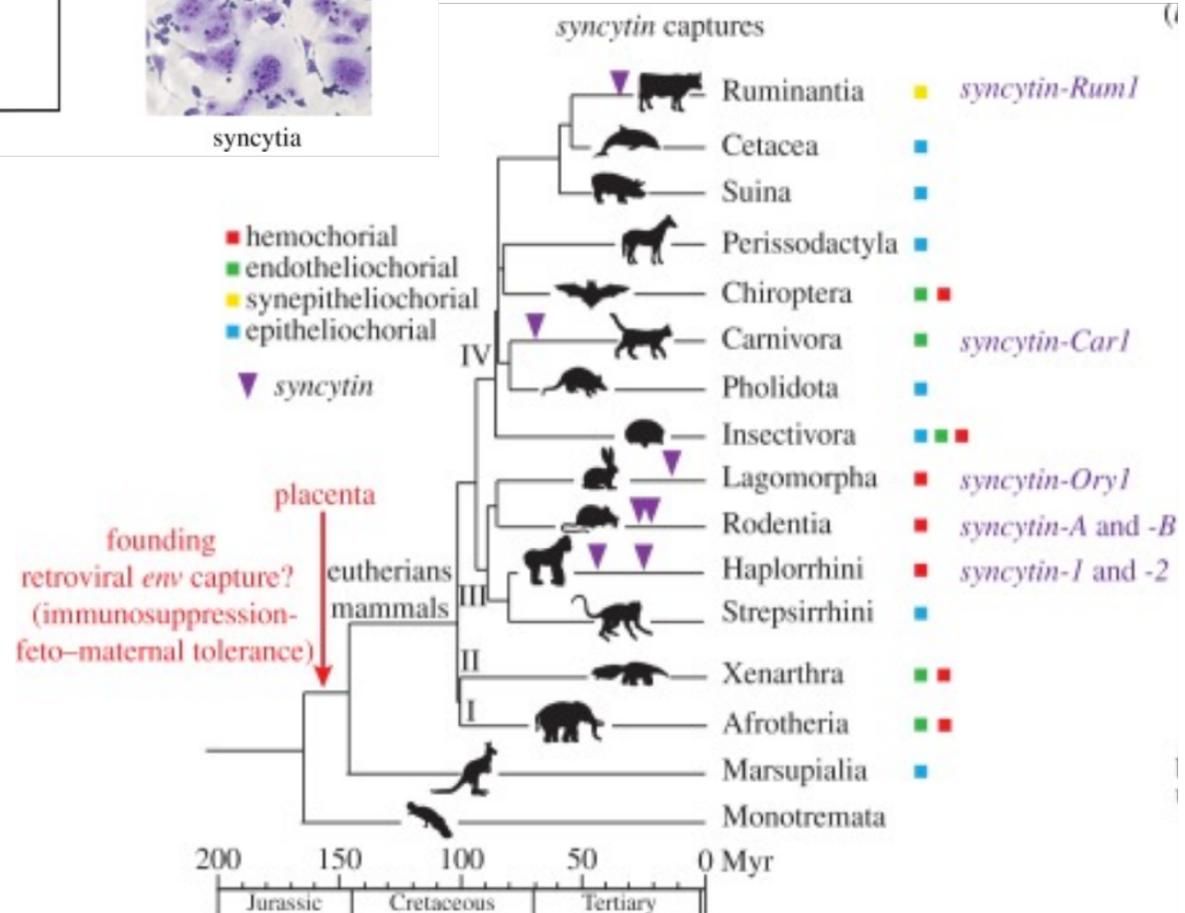
## PLACENTA

- Endogenous retroviruses (ERVs) provide Promoters for Human Placental-Specific Transcripts (Macaulay et al, 2011) as well as Syncytin coding sequences.
- HERV family MER41 contributes hundreds of human-specific enhancers for development of placental trophoblast stem cells (Chuong et al., 2013).
- MERV family RLTR13D5 contributes hundreds of mouse-specific enhancers for development of placental trophoblast stem cells (Chuong et al., 2013).



## Repeated Independent Exaptation of Different Retroviral Env Proteins as Syncytins in Distinct Mammalian Orders

Lavialle, C., G. Cornelis, et al. (2013). "Paleovirology of 'syncytins', retroviral env genes exapted for a role in placentation." *Philos Trans R Soc Lond B Biol Sci* **368**(1626): 20120507.  
<http://www.ncbi.nlm.nih.gov/pubmed/23938756>.



Phenotypic changes after interspecific hybridization (and rapid speciation with whole genome doubling)

**G. Ledyard Stebbins.**  
**Cataclysmic Evolution.**  
Scientific American 184, 54-59 (April 1951)

# Cataclysmic Evolution

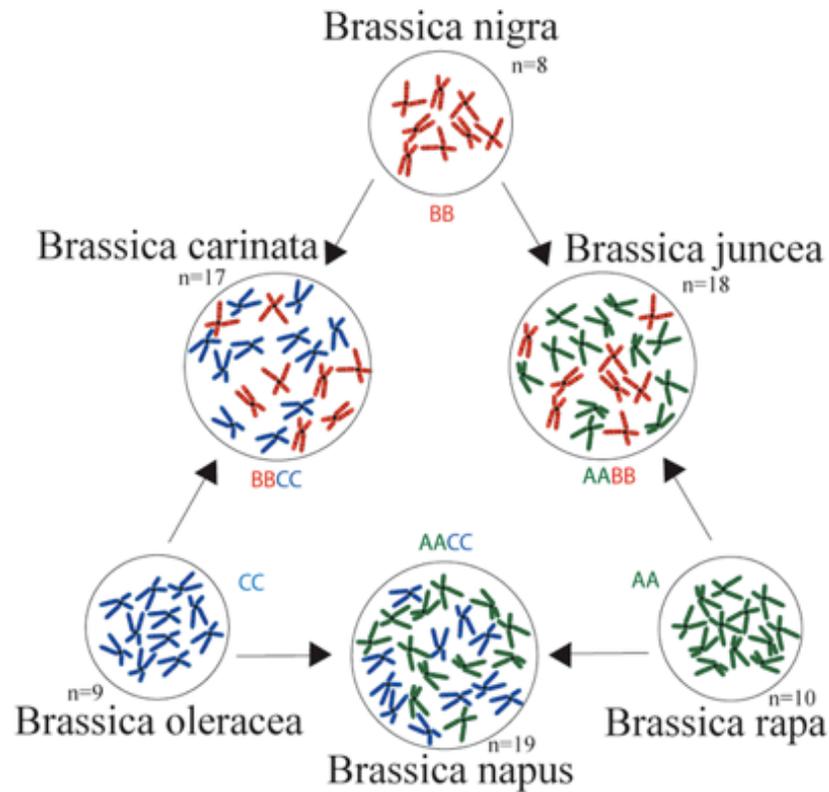
*Many plants (e.g., wheat, cotton, tobacco) evolved suddenly by a process involving the doubling of chromosomes. The same process is artificially induced to create useful new species*

by G. Ledyard Stebbins, Jr.



**TWO GRASSES**, blue wild rye (*left*) and squirrel-tail grass (*right*), were crossed to produce a hybrid (*center*). The hybrid was sterile, but when its chromosomes had been doubled with colchicine, it became fertile.

# GL Stebbins and interspecific hybridization



Nigra = black mustard

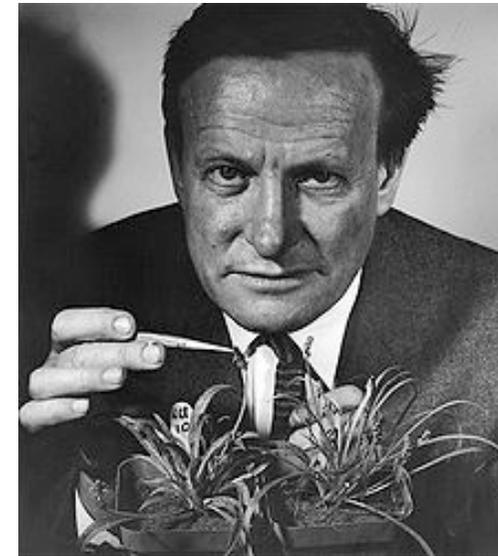
Juncea = mustard greens

Rapa = mizuna (turnip mustard)

Napus = rapeseed (canola)

Oleracea = wild cabbage

Carinata = Ethiopian mustard



G. L. Stebbins, Jr. **Cataclysmic Evolution**. *Scientific American* April 1951, Volume 184 No 4 pp54 –59.

[www.answers.com/topic/g-ledyard-stebbins](http://www.answers.com/topic/g-ledyard-stebbins)

# Examples of Speciation and Adaptive Radiations by Interspecific Hybridization

- **Fungi:** *Saccharomyces* species (Greig et al., 2002; Muller & McCusker, 2009; Sipiczki, 2008)
- **Plants** (Soltis & Soltis, 2009):
  - *Pinus densata* (Mao, 2011)
  - *Primula* (Guggisberg, 2008)
  - Sunflowers (Ungerer, 1998)
  - Irises (Arnold, 1991)
  - *Orchidaceae* (Vega, 2013)
  - *Brassica napus* (Albertin, 2007; Chalhoub, 2014)
  - *Arabidopsis* (Schmickl, 2011)
  - *Nicotiana* (Kelly, 2010; Fuentes, 2014)
  - Potatoes (Pendinen, 2008)
  - Wheats (Stebbins, 1951; Ozkan, 2001, 2003; Qi et al., 2012)
  - Cultivated oats, cotton and sugar cane (Stebbins, 1951; Li, 2015)
  - *Triticale* (Hulse & Spurgeon, 1974)
- **Animals** (Dowling & Secor, 1997; Schwenk, 2008):
  - Tephritid fruitflies (Schwarz, 2007)
  - Swallowtail Butterflies (Kunte, 2011)
  - *Heliconus* butterflies (Mallet, 2007; Pardo-Diaz, 2012, Heliconus Genome Consortium, 2012)
  - Army ants (Kronauer, 2011)
  - Sculpins (*Cottus* sp., *Teleostei*) (Renaut, 2011)
  - Sailfin silversides (*Teleostei*) (Herder, 2006)
  - **E. Africa Cichlids** (Keller, 2013; Brawand, 2014; Selz, 2014; Svensson, 2016)
  - Sparrows (Hermansen, 2011)
  - Audubon's warbler (Jacobsen, 2011)
  - **Galapagos finches** (Grant & Grant, 2014 etc. ; Lamichhaney, 2015; Palmer, 2015 )
  - Clymene dolphin (Amaral, 2014)
  - Bats (*Noctilio*) (Khan, 2014)
  - Cats (*Felidae*) (Li, 2016)

**Pennisi, E. (2016). "Shaking up the Tree of Life." Science 354(6314): 817-821.**

# Genomic Consequences of Interspecific Hybridization

- Epigenetic changes affecting mobile DNA elements and other natural genetic engineering activities
- Massive and repeated patterns of repeat amplifications and chromosome rearrangements
- Whole genome duplications followed by selective loss of duplicated regions (“Allopolyploidy”) : “All data stress allopolyploidization as a shock associated with drastic genome reorganization” in plant hybrids

Parisod, C., et al., *Impact of transposable elements on the organization and function of allopolyploid genomes*. *New Phytol*, 2010. **186**(1): p. 37-45.

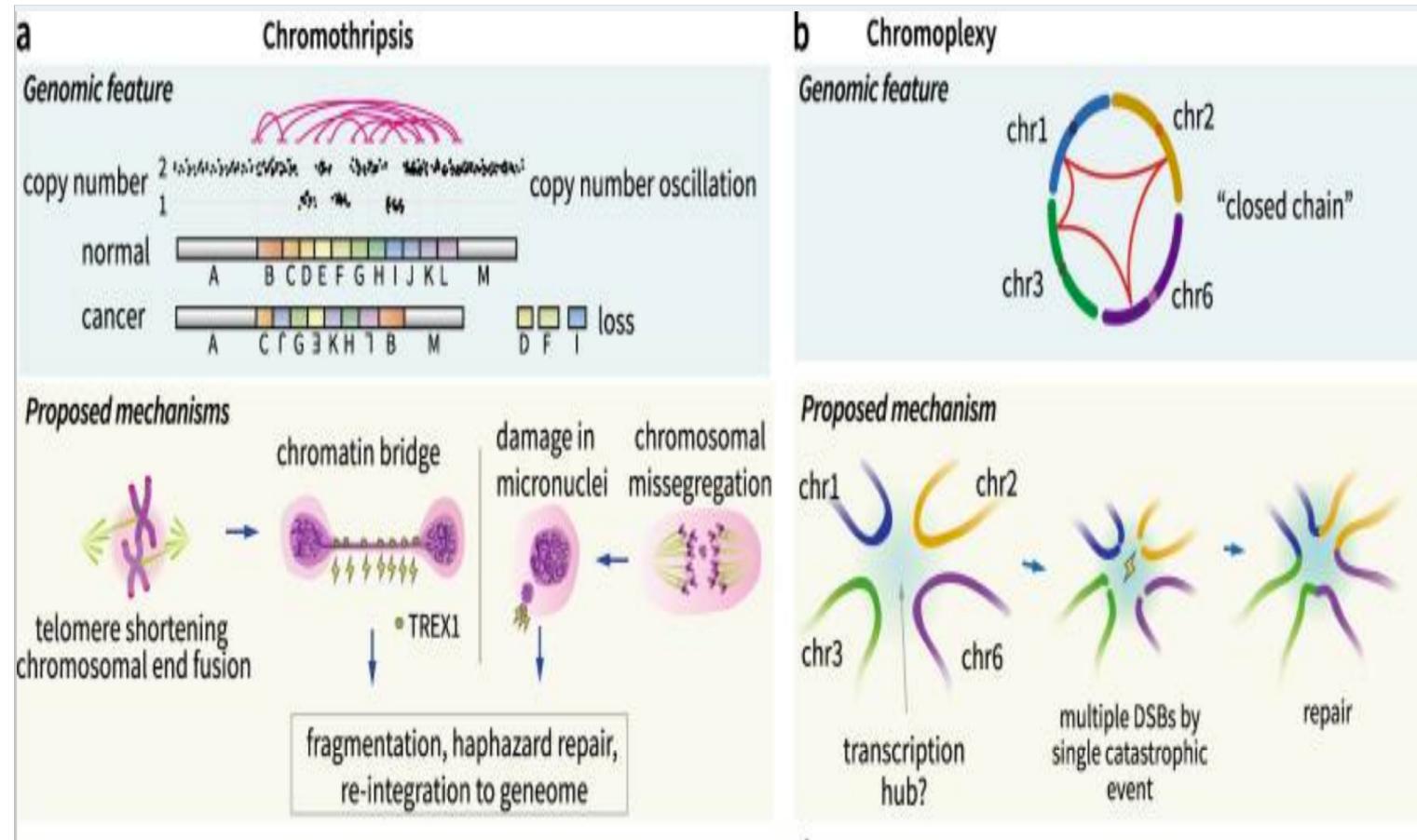
# The Special Impacts of Interspecific Hybridization on Evolutionary Innovation

- The initiating event involves the entire genomes of each parent species – so all organismal traits are affected in a single evolutionary episode.
- Since interspecific hybridization serves as a major stimulus to genome variability (“genome shock”), including chromosome rearrangements and activation of mobile DNA elements, hybrid organisms have a markedly elevated potential for generating novel DNA sequence configurations that were not present in the genome of either parent species.

# Genome Changes in Tumors (and Healthy Germlines)

- NB - duration for complex genome changes in tumor evolution < 1 human or animal lifespan

- Chromothripsis
- Chromoplexy
- Kataegis (deaminases)
- Duplications,
- Deletions,
- genome doublings,
- circular cDNAs,
- etc.



Yi, K. and Y. S. Ju (2018). "Patterns and mechanisms of structural variations in human cancer." Exp Mol Med **50**(8): 98.  
<http://www.ncbi.nlm.nih.gov/pubmed/30089796>.

# Importance of Biotic Interactions in Stimulating Genome Change

- Nutritional challenges as agents of quantitative and qualitative mutability changes
  - Starvation-induced hypermutability in *E. coli*, *A. baumannii*
  - Starvation-induced genome restructuring in *S. cerevisiae*
  - Distinct nutritional stress-specific mutation spectra in *E. coli*
- Biomolecules as activators of genome variability (genotoxins, antibiotics, alcohols, pheromones/signaling molecules)
- Infectious agents as genome change vectors (viruses, gene transfer agents (GTAs), extracellular vesicles (EVs), etc.)
- Interspecific mating, hybrid dysgenesis as evolutionary triggers (allopolyploid hypermutability in yeast, plants and animals, mobile element derepression when introduced in paternal chromosomes)
- Infection and symbiosis as evolutionary triggers
  - For host: *Wolbachia*-induced mating incompatibilities, bacterial pathogens producing genotoxins and inducing tumors, genital viral and bacterial pathogens inducing germline changes?
  - For infectious agent: *P. aeruginosa* hypermutability in cystic fibrosis lungs, IS elements modifying *Sinorhizobium* host-range in soybean root nodules

# Some Experimental Evolution Questions

- Is most or all of eukaryotic taxonomic origination triggered by interspecific hybridization?
- How important are infectious agents in evolutionary change?
- To what extent do sensory inputs bias genome changes?

# Novel Experimental Evolution Methods Based on Interactive Genome Model

- Testing role of mixed populations on efficiency of genome innovation
  - Sibling species (interspecific hybridization potential)
  - Competitors (*e.g.*, mixed microbial, plant populations)
- Testing effect of infectious agents on efficiency of genome innovation for characters unrelated to infection (*e.g.*, photosynthesis)
  - Viruses (endogenous, external)
  - Microbial symbionts, parasites and pathogens
- Testing influence of external conditions on mutational outcomes (prior growth history, stresses and sensory inputs from physical and biological environment)