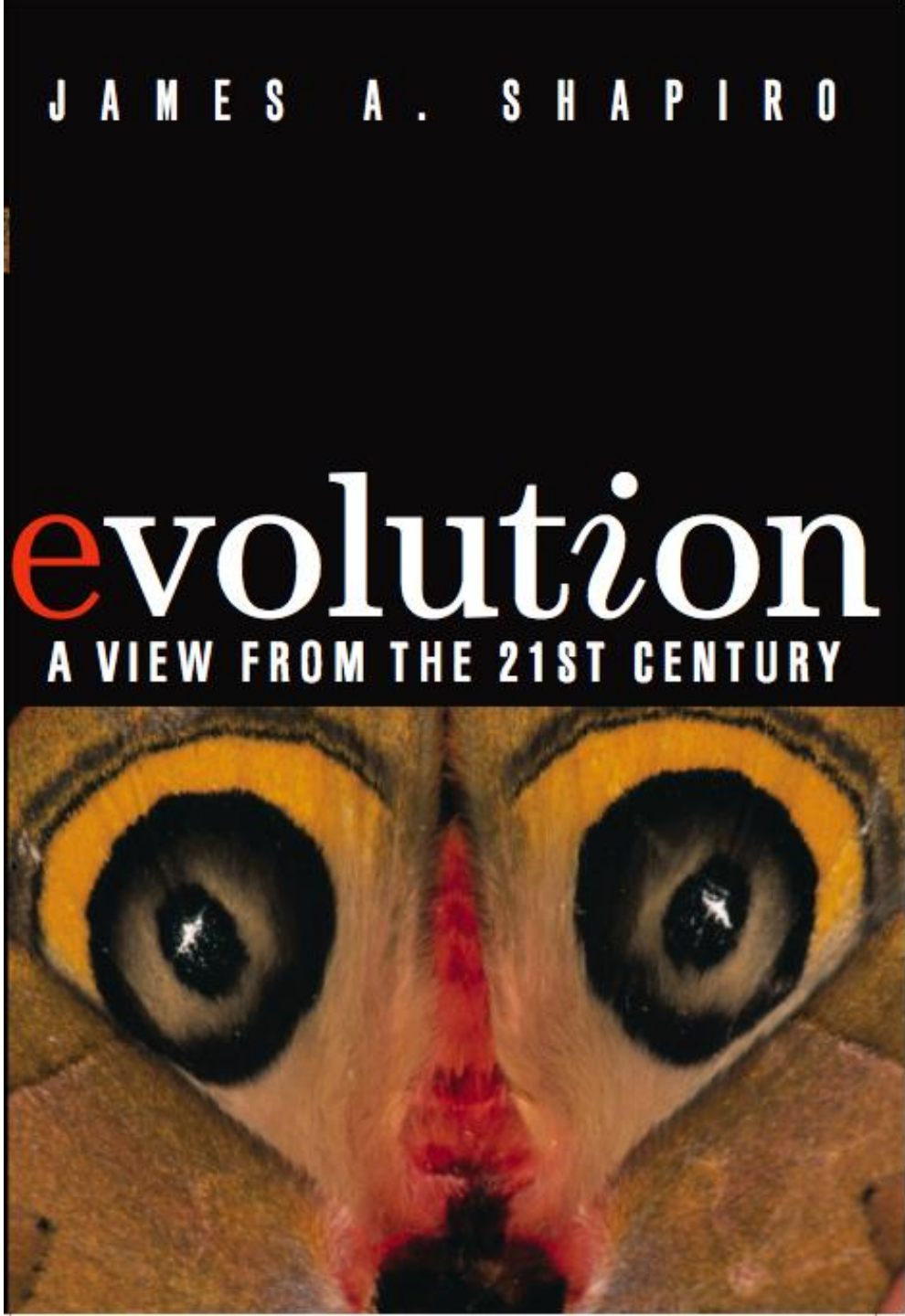
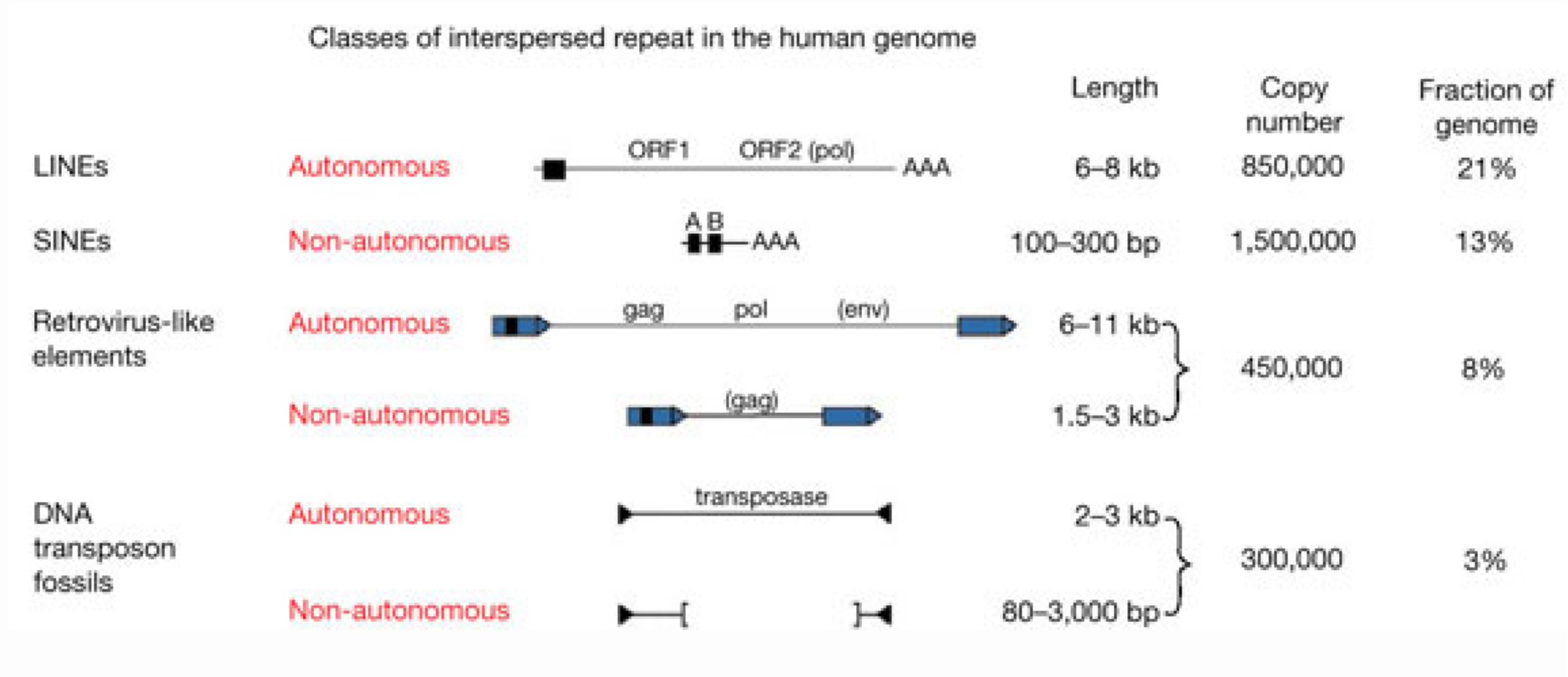
Retroviruses and the RW Genome – Active Roles in Evolution of Immunity and Pregnancy

Retroviruses 2015
Chicago, June 8, 2015
James A. Shapiro
University of Chicago
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Evolutionary time: Genome writing by natural genetic engineering – dispersed mobile elements



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

Conventional Wisdom About Mobile DNA

"However, as much as two-thirds or more of the human genome is derived from repetitive sequences. Most of these are retrotransposon sequences that were active in the distant evolutionary past and are now present as fossils that litter our genomes. But this image belies the damage that can be wreaked by evolutionarily recent transposable elements."

Vera Gorbunova, Jef D. Boeke, Stephen L. Helfand, John M. Sedivy. Human Genomics: **Sleeping dogs of the genome.** *Science 5 December 2014. 346 pp. 1187-1188 DOI: 10.1126/science.aaa3177*

Evolutionary time: Genome innovations by mobile elements

- Alter genome expression by inserting control signals for transcription and epigenetic modification
- Rewire dispersed genome regulatory networks by related insertions at multiple sites
- Facilitate rapid protein evolution by mobilizing functional domains to form proteins with new combinations
- Generate novel protein-coding information (new domains) by “exonization” of DNA from inserted mobile elements

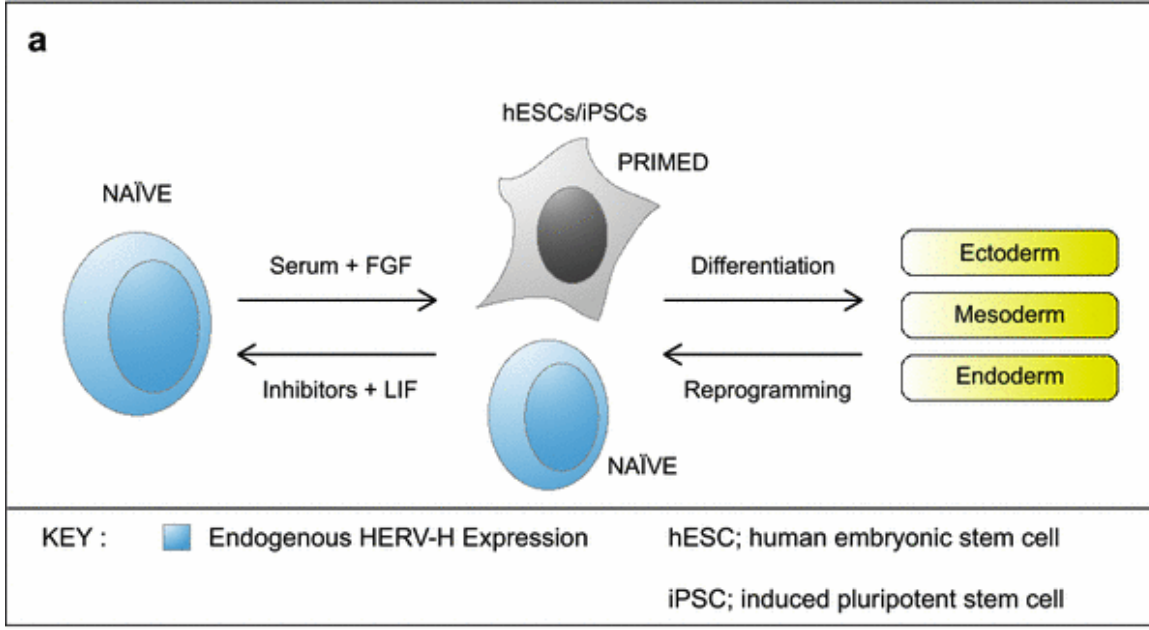
“Our data revealed >280,000 mobile element exaptations common to mammalian genomes covering ~7 Mb…, a considerable expansion from the ~10,000 previously recognized cases. Of the ~1.1 million constrained elements that arose during the 90 million years between the divergence from marsupials and the eutherian radiation, we can trace >19% to mobile element exaptations.”

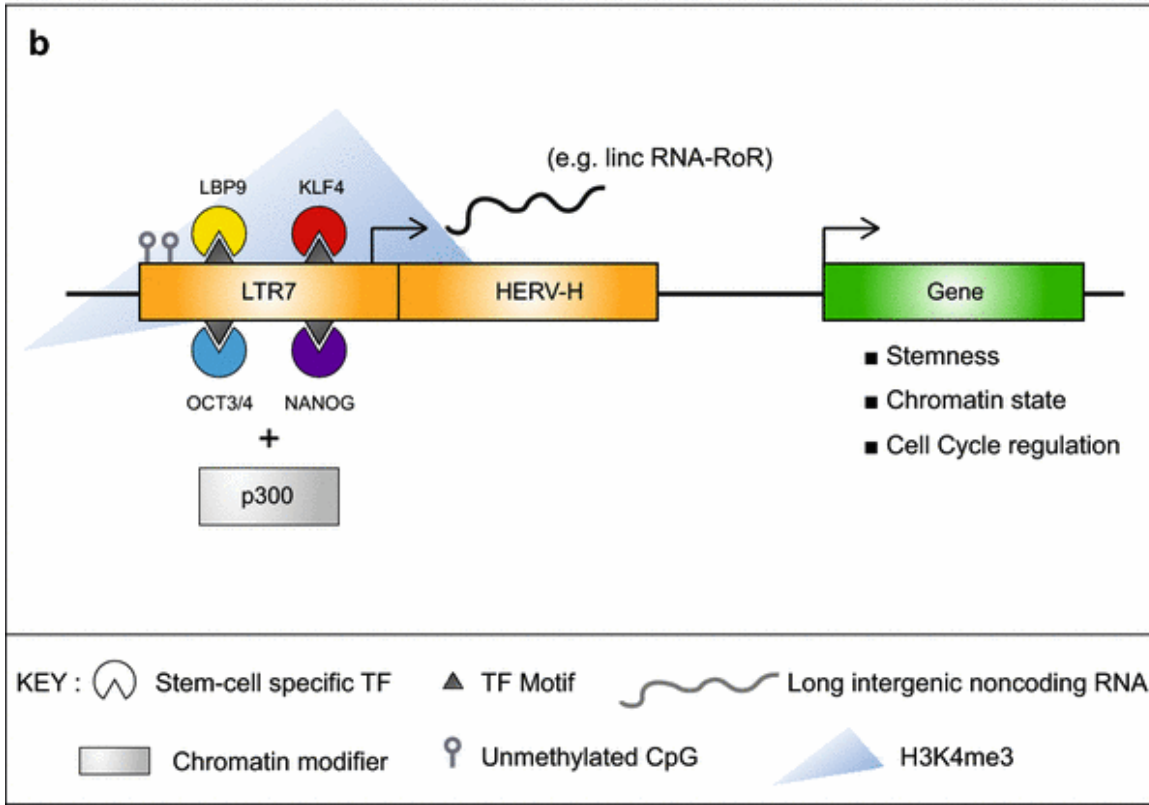
Lindblad-Toh, K., M. Garber, et al. (2011). "**A high-resolution map of human evolutionary constraint using 29 mammals**." Nature **478**(7370): 476-482.

The Majority of Primate-Specific Regulatory Sequences Are Derived from Transposable Elements. Pierre-Étienne Jacques, Justin Jeyakani, Guillaume Bourque, 2013. PLOS Genetics DOI: 10.1371/journal.pgen.1003504

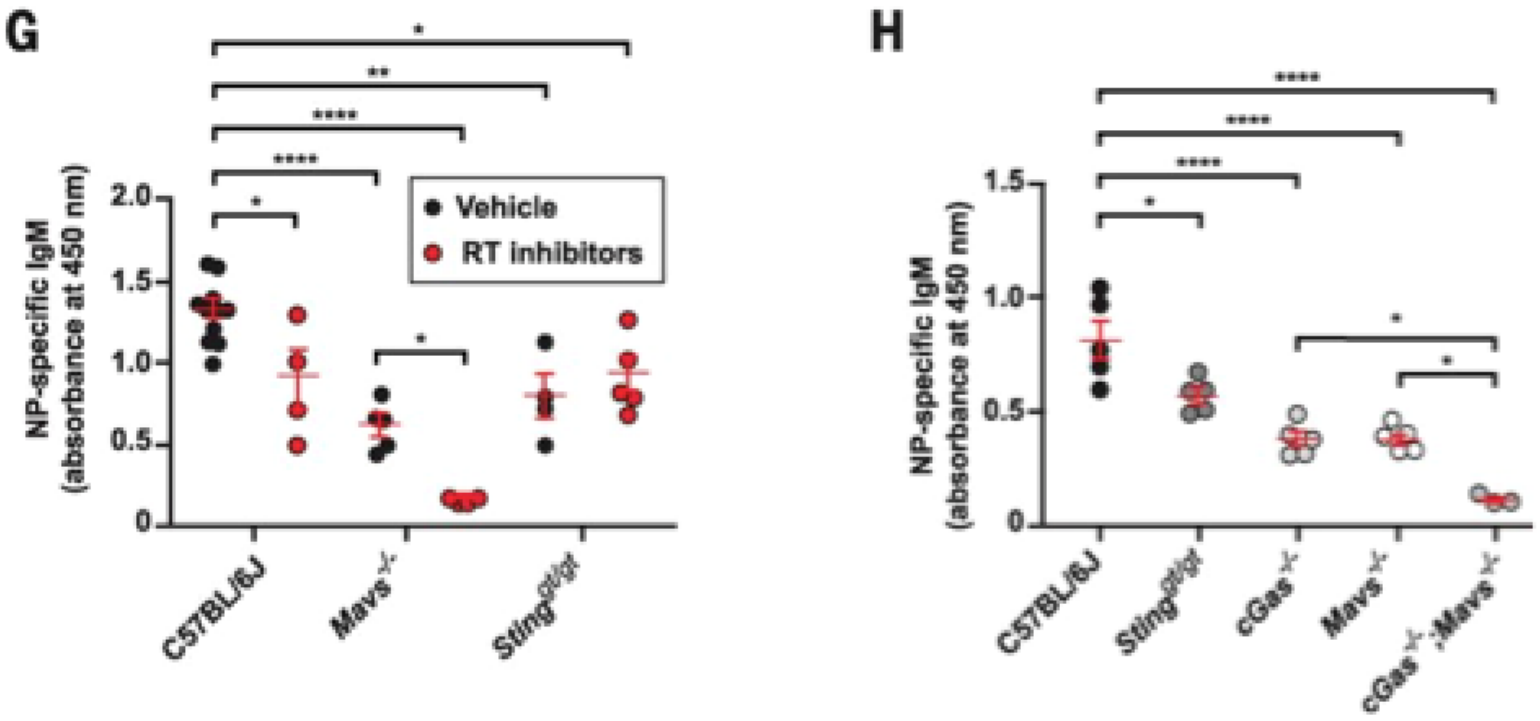
HERV-H activity overlaps with ground state pluripotency. **a** HERV-H expression is thought to define naïve-like stem cells. **b** Mechanism of HERV-H regulation of stem cell gene expression.

Robbez-Masson and Rowe. **Retrotransposons shape species-specific embryonic stem cell gene expression.** *Retrovirology* 2015 **12**:45 doi:10.1186/s12977-015-0173-5





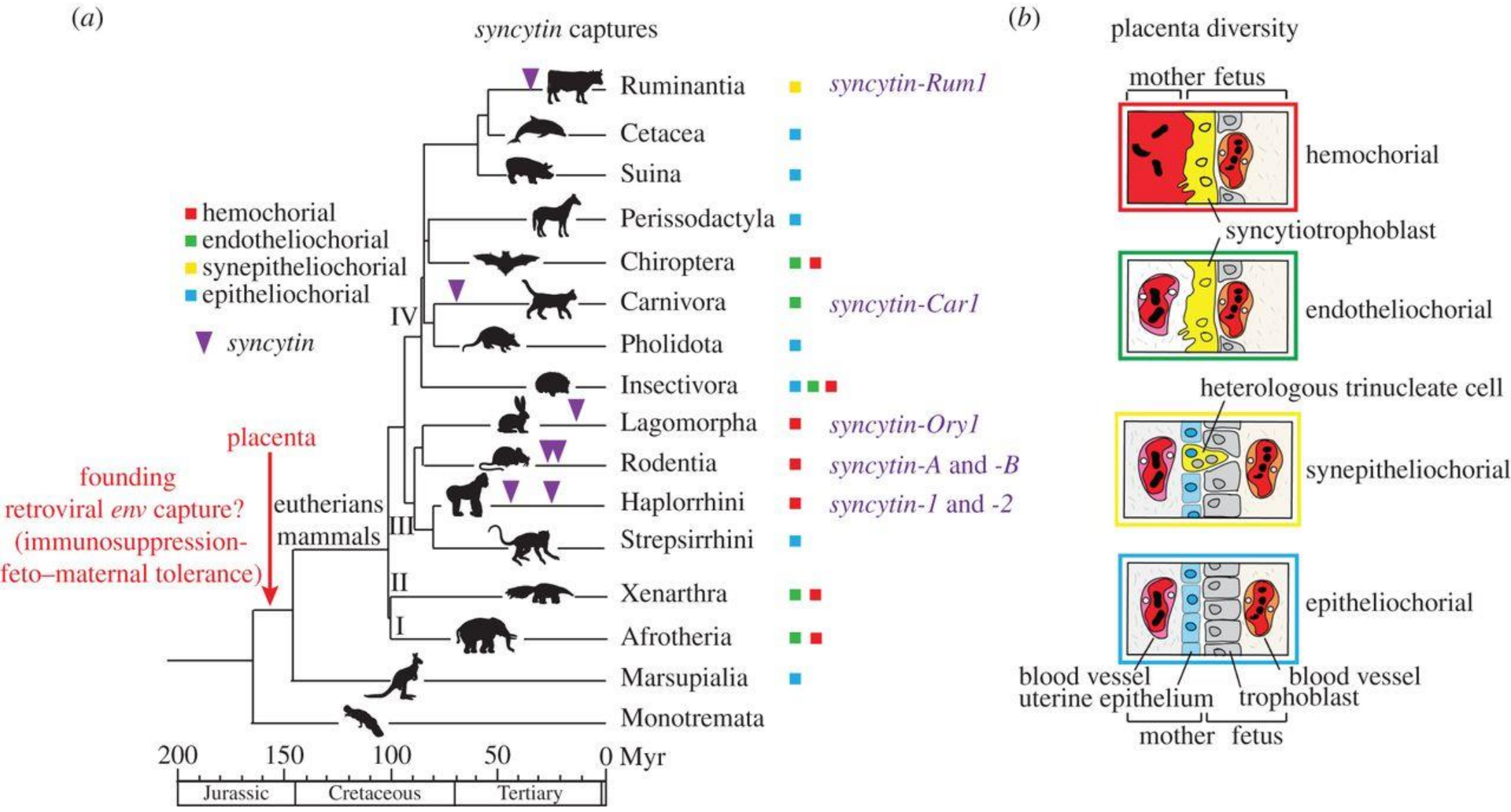
TI-2 antigen immunization induces expression of ERV mRNA and cDNA that is detected by cytosolic sensors in antigen-specific B cells.



Ming Zeng et al. MAVS [mitochondrial antiviral signaling protein]**, cGAS [**cGMP-AMP synthase, involved in DS RNA sensing]**, and endogenous retroviruses in T-independent B cell responses.**
Science 2014;346:1486-1492

Published by AAAS

Multiple syncytin gene captures and diversity of placental structures in eutherian mammals.

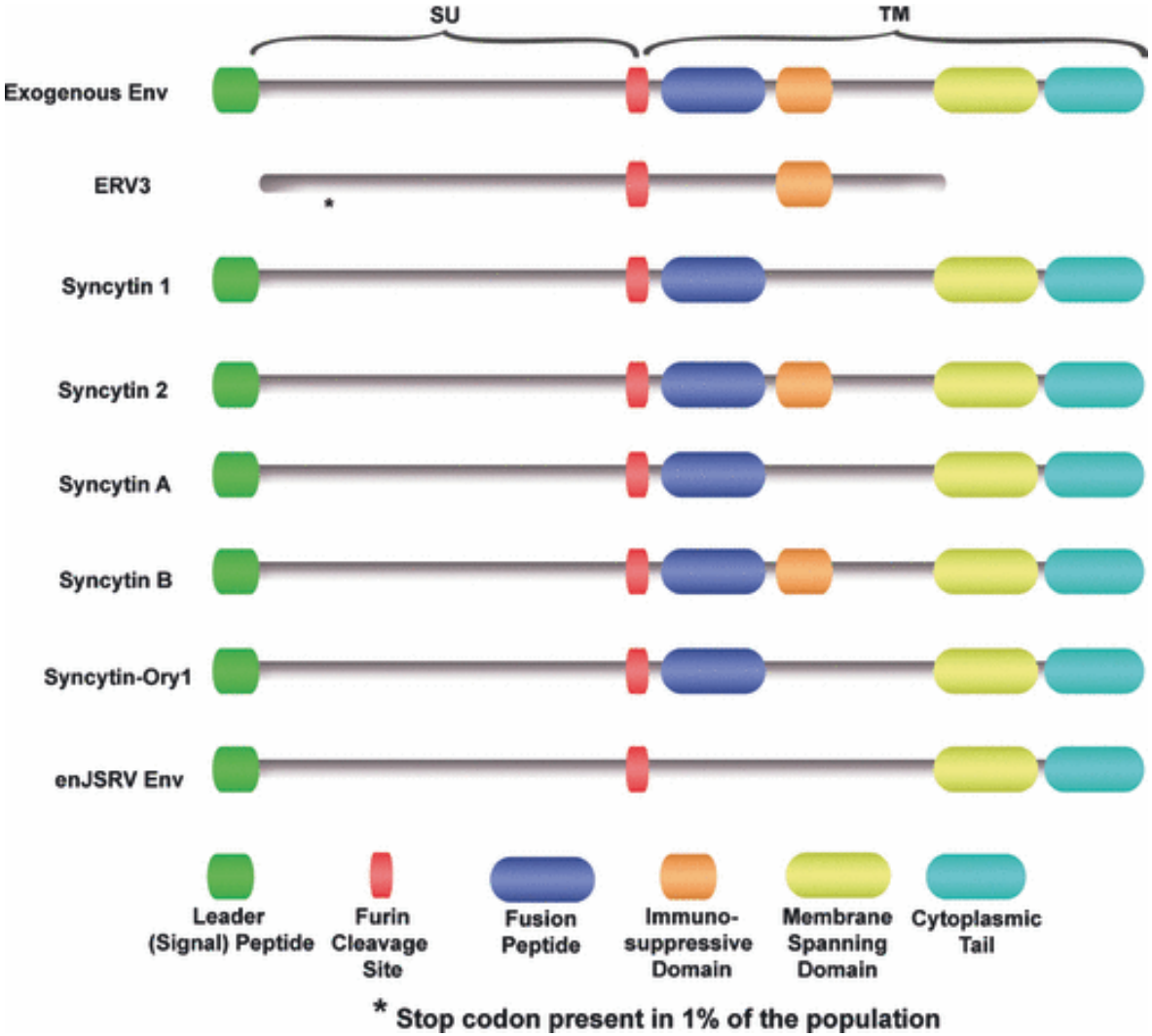


Lavialle C et al. 2013 Paleovirology of 'syncytins', retroviral env genes exapted for a role in placentation. Phil. Trans. R. Soc. B;368:20120507

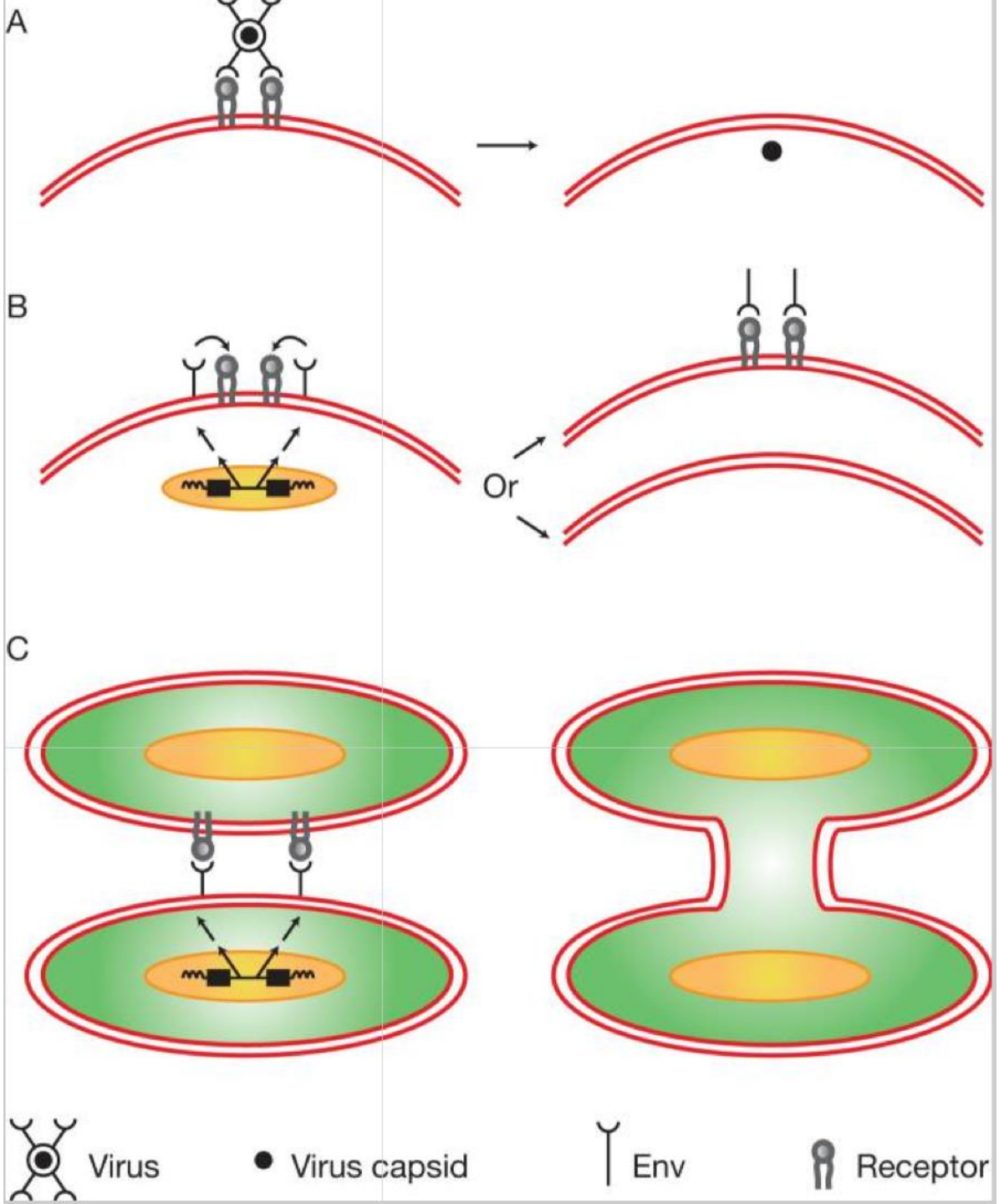
©2013 by The Royal Society

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

Endogenous Retroviruses in Trophoblast and Placental Development: Syncytin Evolution from ERV Envelope Protein



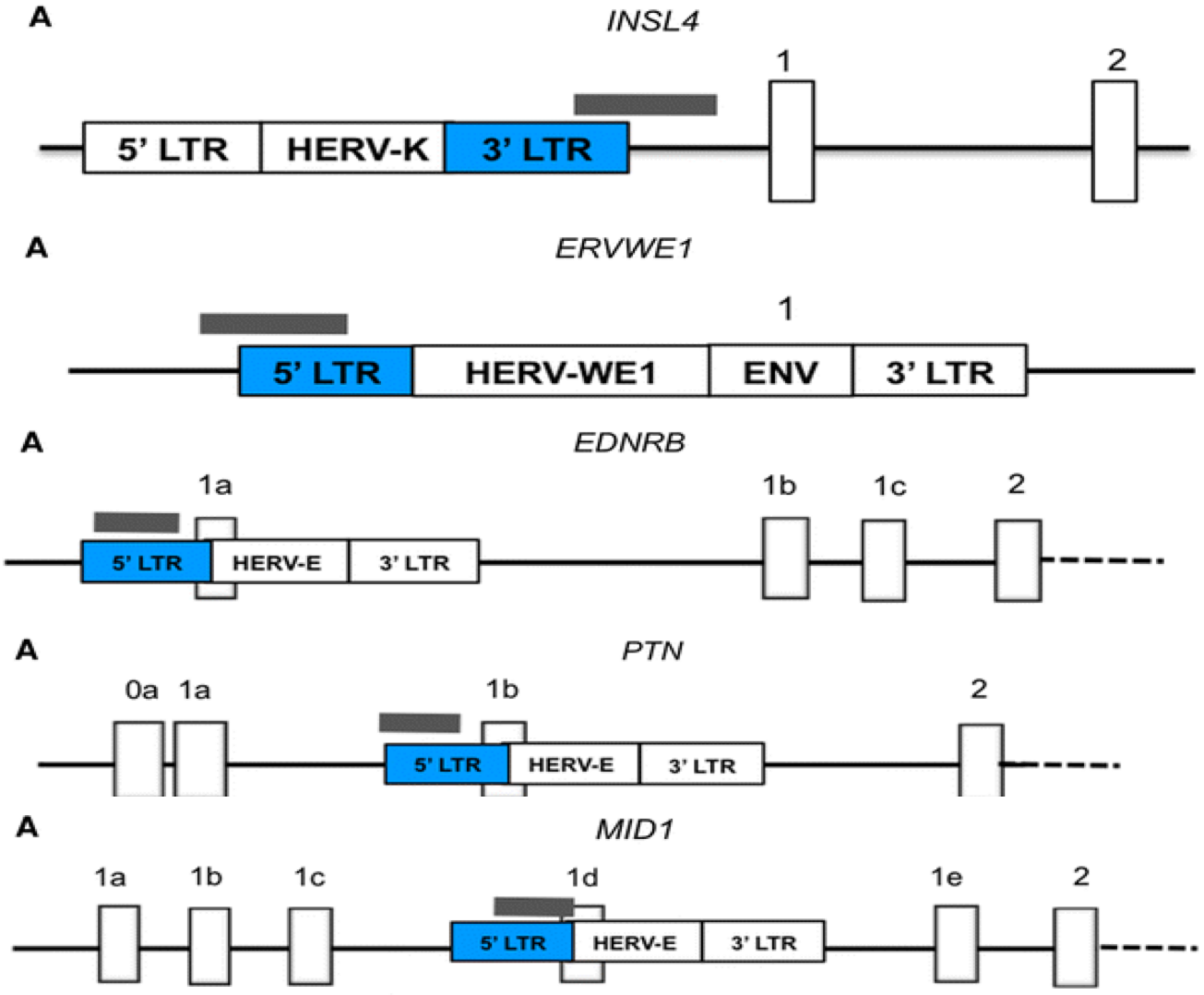
Sarah G. Black et al. **Endogenous Retroviruses in Trophoblast Differentiation and Placental Development. American Journal of Reproductive Immunology**. Vol 64 (4), pages 255-264, 2010 DOI: 10.1111/j.1600-0897.2010.00860. http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0897.2010.00860.x/full#f2



Proviral protein provides placental function

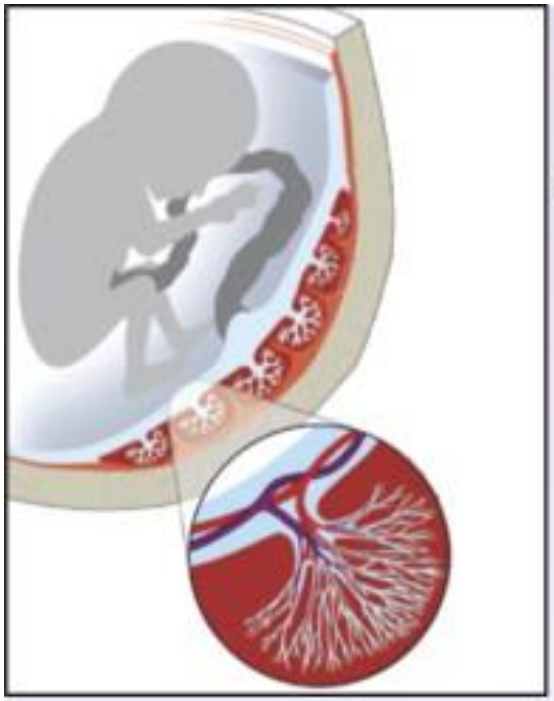
Stoye, J. P. (2009). "Proviral protein provides placental function." Proc Natl Acad Sci U S A 106(29): 11827-11828. http://www.ncbi.nlm.nih.gov/pubmed/19617545.

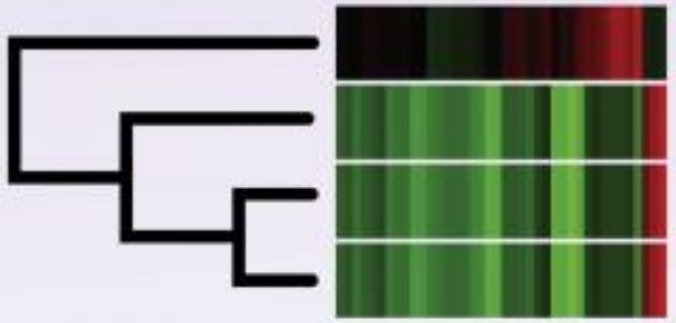
ERVs as Promoters for Human Placental-Specific Transcripts and Sites for Epigenetic Regulation

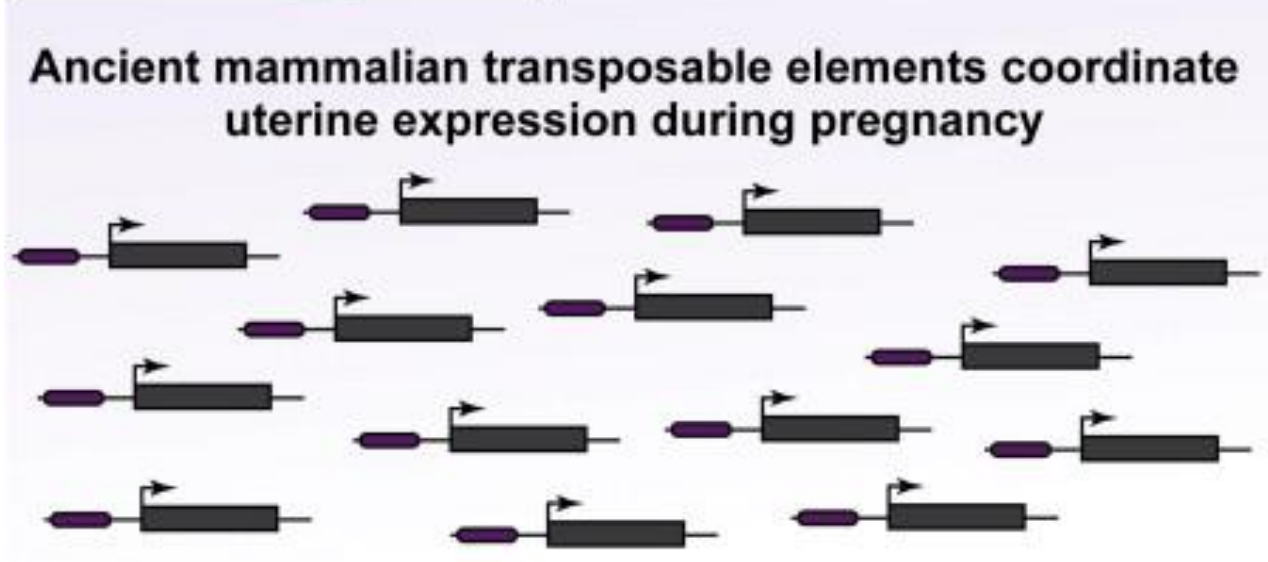


Macaulay EC, Weeks RJ, Andrews S, Morison IM. Hypomethylation of functional retrotransposon-derived genes in the human placenta. Mamm Genome. 2011 Dec;22(11-12):722-35.

DNA Transposons and Uterine Evolution







Vincent J. Lynch , Mauris C. Nnamani ,, et al. **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

Take-Home Lesson

Genomes and their host organisms can do more -- and are more likely to persist -- when they have mobile DNA than when they don’t.