Rethinking the (Im)Possible in Evolution, or Biological Plausibility Is Not What You Thought It Was

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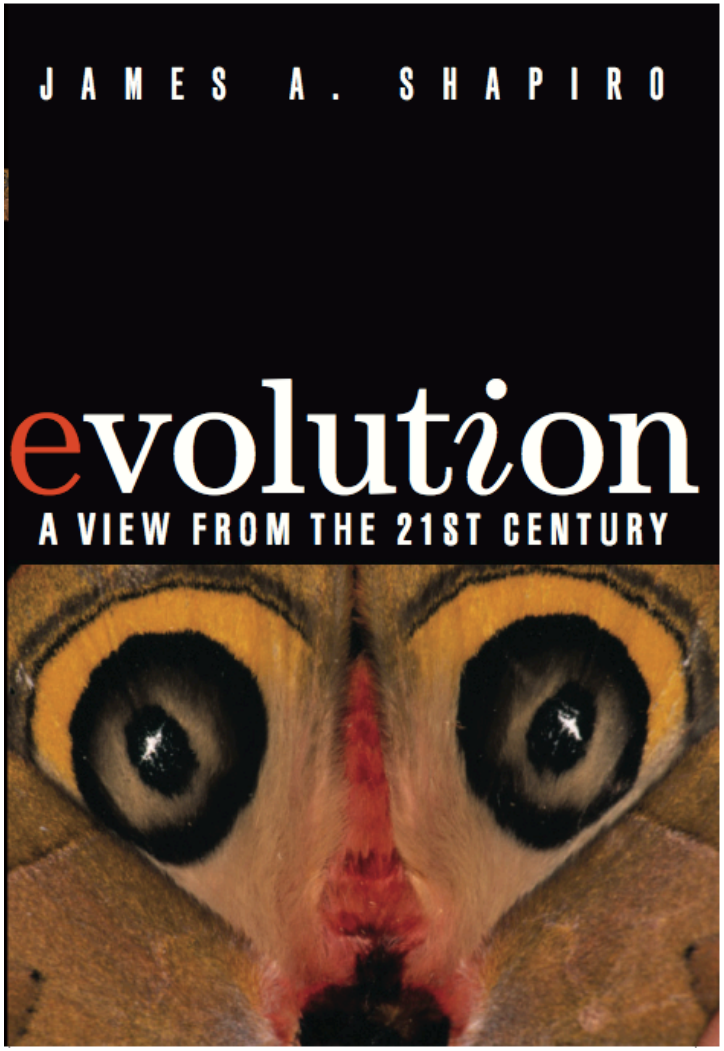


Objectives

- Inform computer scientists that biological evolution is an active cell process involving multiple DNA restructuring operators working on a RW genomic storage system;
- Demonstrate the roles of regulation, targeting and feedback possible in DNA restructuring;
- Provide models for *in silico* evolution operators so that their roles in the evolutionary process can be tested empirically;
- Identify computer scientists interested in modeling the ***innovative*** aspects of *in silico* evolution (not just the ***optimizing*** aspects).

Philosophical Assumptions about Organization and Evolution of Living Cells

- Random, gradual nature of evolutionary variation: "If it could be demonstrated that any complex organ existed, which could not possibly have been formed by numerous, successive, slight modifications, my theory would absolutely break down. But I can find out no such case" (*Origin of Species*, Chapter 6; "accretive evolution" in Richard Watson terminology).
- The blind watchmaker versus the operation of an engineering process (*i.e.* excluding functional goals and design principles).
- Mechanism vs. Vitalism debate in 19th/20th Centuries (purely hardwired explanations of life versus the need for some information-processing "vital force" to control growth and reproduction).

Seven Widely Accepted Propositions about Heredity & Variation Inconsistent with Empirical Observations

1. “All heredity transmission occurs from parent to progeny;”
2. “Mutations are the result of inevitable replication errors;”
3. “Mutations occur at constant low probabilities over time” (= there are "mutation rates");
4. “Virus infection cannot induce genetic changes giving heritable resistance” (Luria-Delbrück experiment);
5. “Mutations cannot be targeted within the genome;”
6. “Spontaneous hereditary changes are localized and limited to those of small effect” (Darwin quote);
7. “Cells cannot integrate DNA change with biologically useful adaptive needs.”

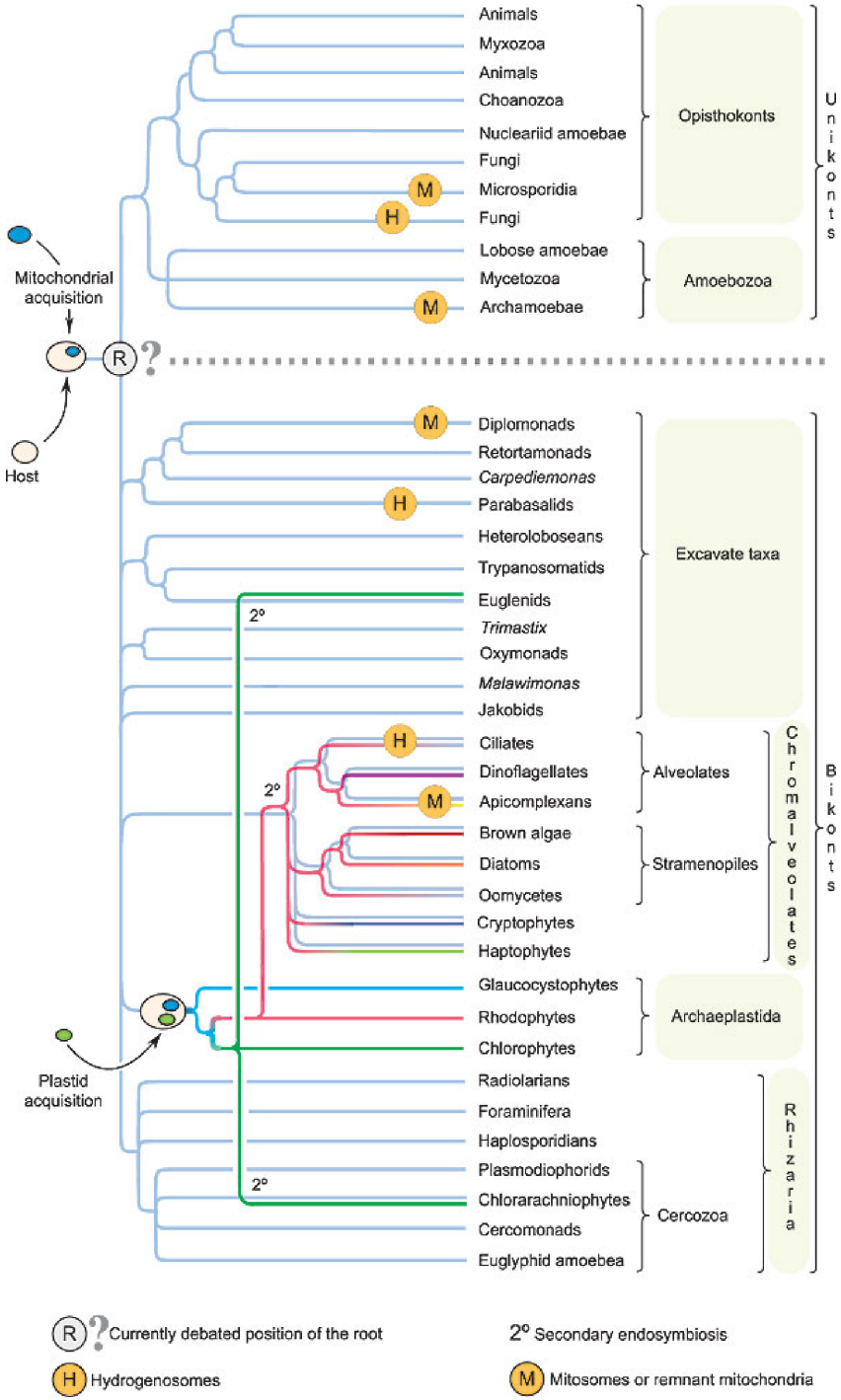
“All heredity transmission occurs from parent to progeny”

Counterfactuals:

- Virus infection (all taxa)
- Uptake of DNA from the environment (prokaryotes, animal cells in culture, plant protoplasts)
- Horizontal cell-cell transfer of DNA (between prokaryotes, bacteria to plants, endosymbiotic insects to animal hosts, “genomic islands”)
- Symbiogenesis (mitochondria, plastids, secondary and tertiary algal symbioses, mycorrhiza, photosynthetic animals)

==> genomes can evolve by acquisition of external DNA (“module acquisition”)

Symbiogenesis at key points in eukaryotic evolution



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

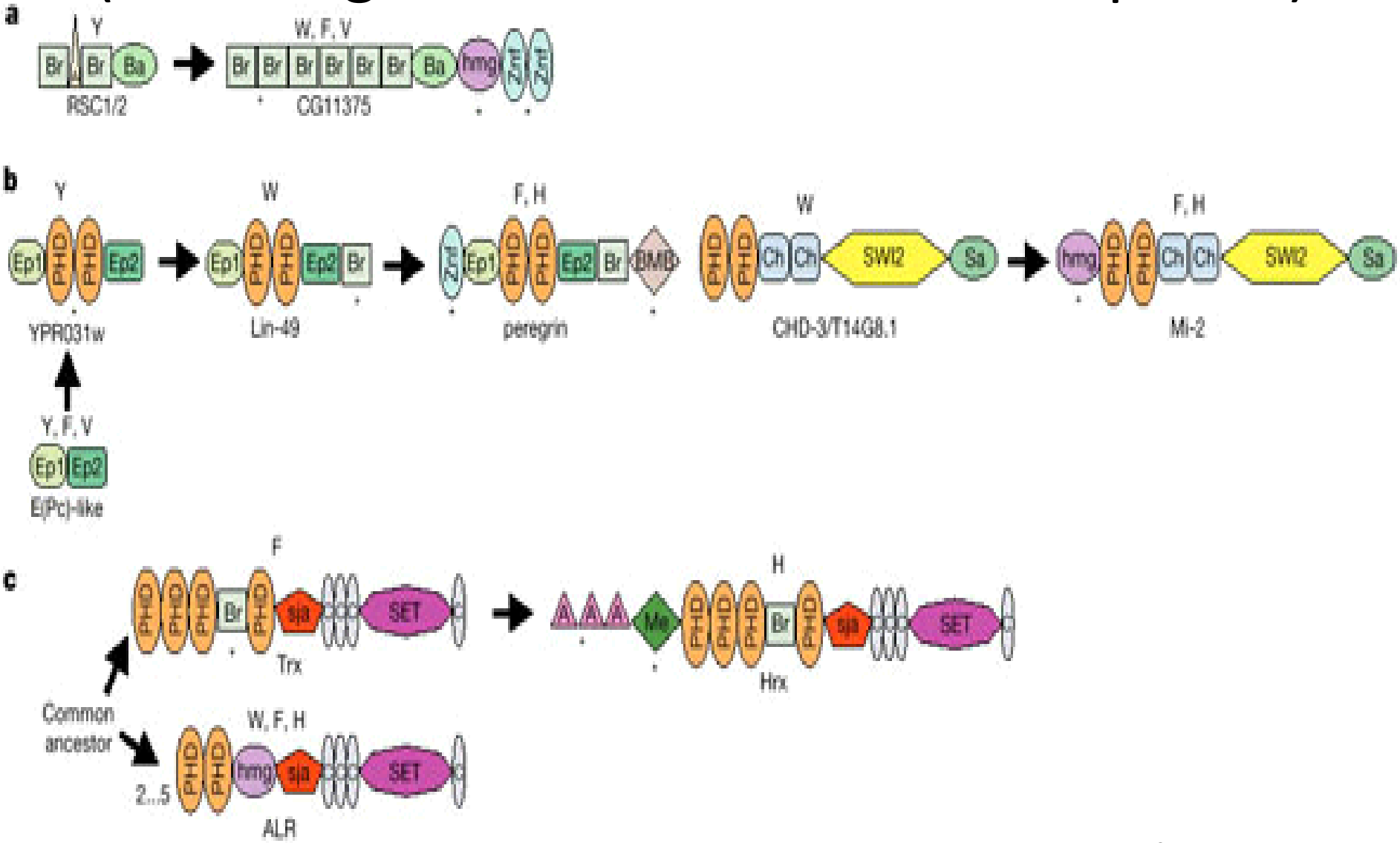
“Mutations are the result of inevitable replication errors” (*i.e.* genome = ROM storage)

Counterfactuals:

- Polymerase proofreading to remove replication errors
- Mismatch repair proofreading to remove replication errors
- Elimination of specific classes of mutation by loss of trans-lesion (“mutator”) polymerases
- Incorporation of reverse-transcribed RNA into genome
- Mutations resulting from mobile genetic elements (often most common source of spontaneous mutations = “module acquisition”)
- Duplications and other amplifications (Ohno, 1970)
- Coding sequence & chromosome rearrangements

==> genome = RW memory system

Domain accretion in chromatin proteins ("building blocks" or "divide & conquer"?)



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

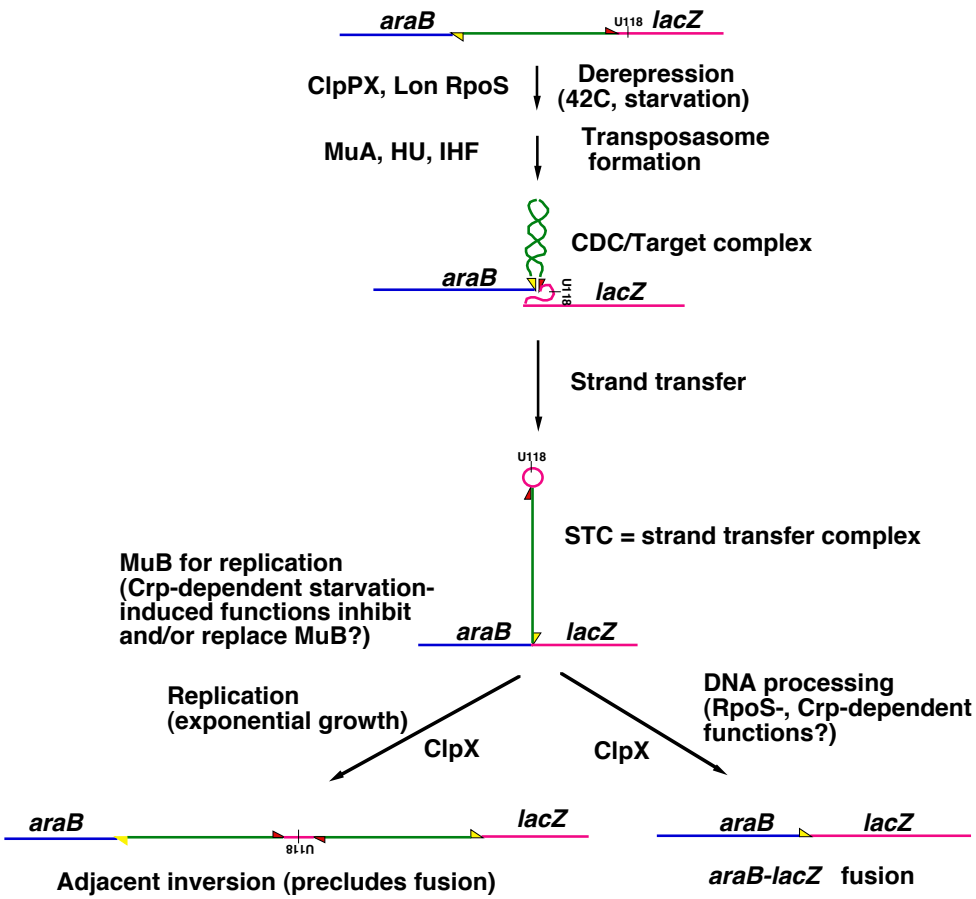
“Mutations occur at constant low probabilities over time” (*i.e.* there are ‘mutation rates’)

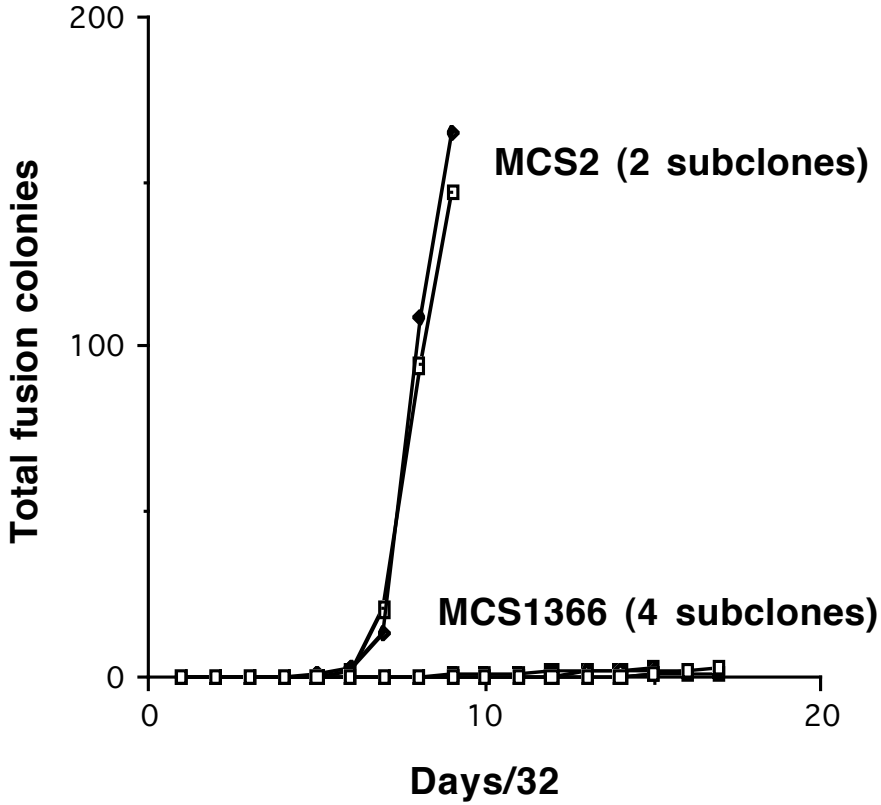
Counterfactuals:

- Mutagenic effects of chemicals and radiation
- Mutagenic effects of infection (virus, bacteria)
- Mutagenic effects of nutritional and physiological stress (starvation, temperature, osmotic pressure)
- Mutagenic effects of hybrid dysgenesis (inter-deme hybridization) and interspecific hybridization

==> genome change is sensitive to ecology & life history

Temporal & metabolic regulation of natural genetic engineering





Shapiro, J.A. 1984. Observations on the formation of clones containing *araB-lacZ* cistron fusions. Molec. Gen. Genet. **194,** 79-90/

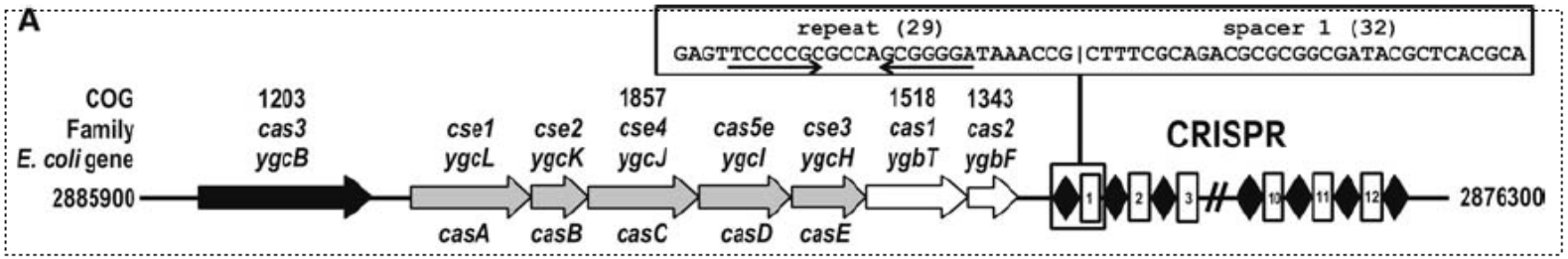
Shapiro, J.A. and D. Leach. 1990. Action of a transposable element in coding sequence fusions. *Genetics* **126**, 293-299.

Shapiro, J.A. 1997. Genome organization, natural genetic engineering, and adaptive mutation. *Trends in Genetics* **13**, 98-104

“Virus infection cannot induce DNA changes giving heritable resistance”

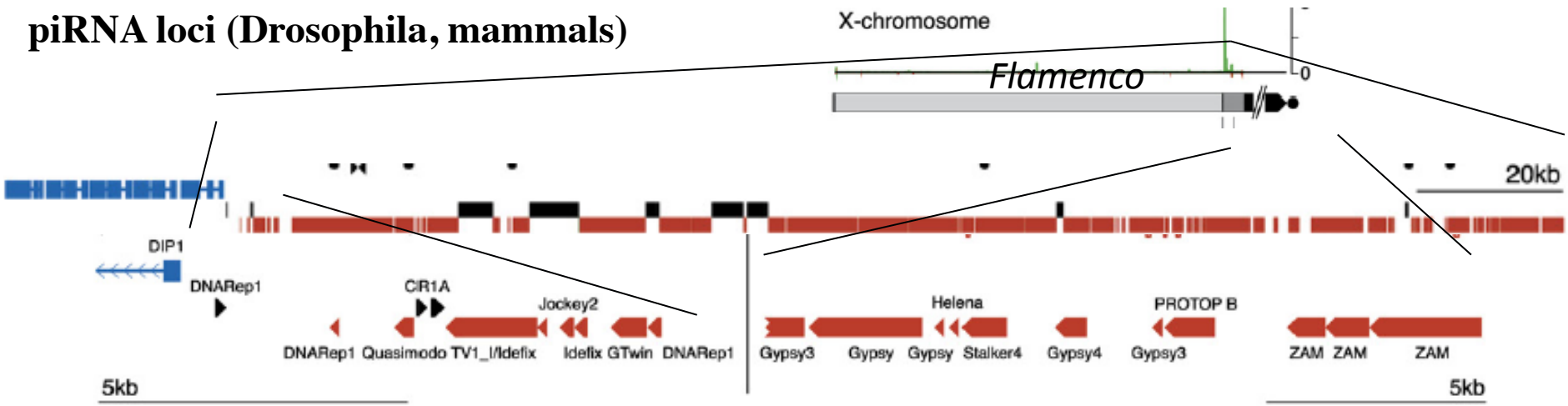
Counterfactuals:

CRISPRs (prokaryotes)



Brouns et al., Small CRISPR RNAs Guide Antiviral Defense in Prokaryotes. Science 321, 960 (2008)

piRNA loci (Drosophila, mammals)



Brennecke, et al. 2007. Discrete Small RNA Generating Loci as Master Regulators of Transposon Activity in *Drosophila*. *Cell, Vol 128, 1089-1103*

==> cells can retain a genomic memory of invading DNA and become immune.

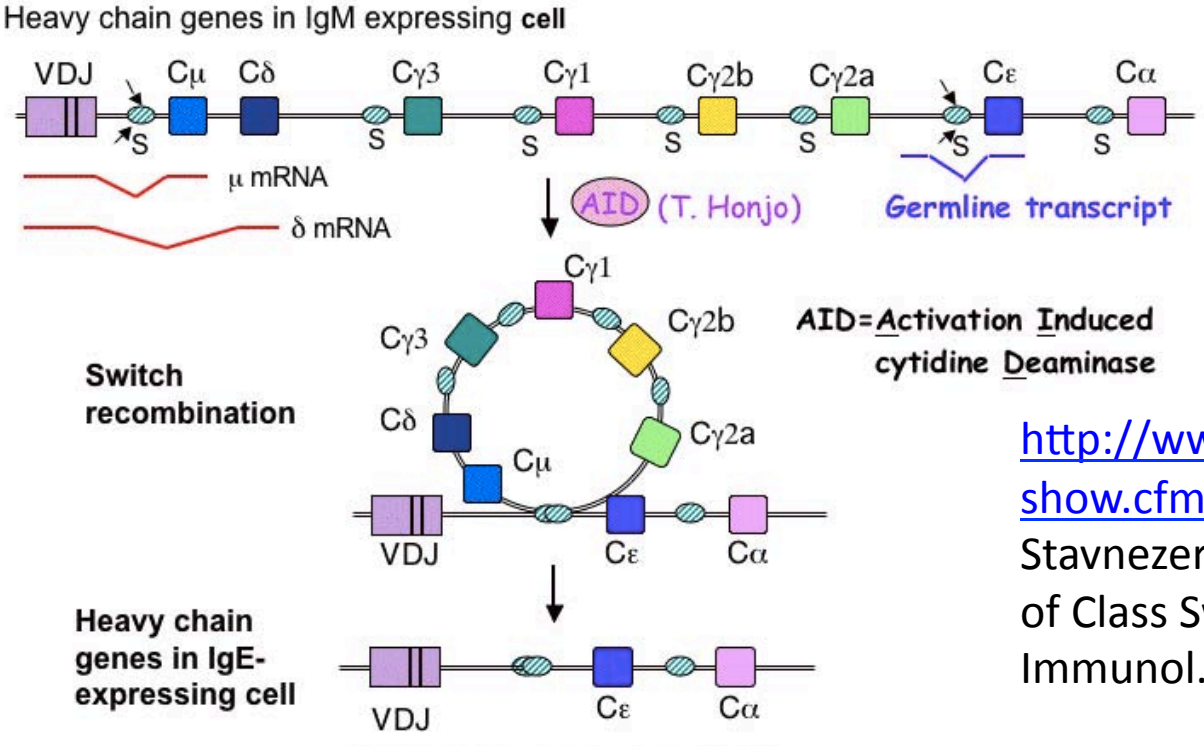
"Mutations cannot be targeted within the genome"

Counterfactuals:

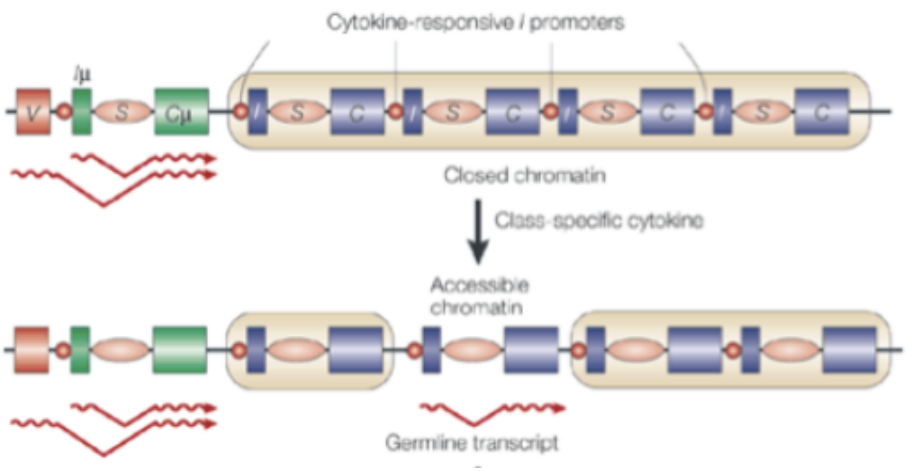
- Targeted DS breaks in mating type switching, insertion of inteins, group I introns, some retrotransposons
- Site-specific recombination for virus insertion
- Tn7 targeting to chromosome locus or replicating DNA
- Ty retroelement targeting to sites upstream of PolIII promoters (Ty1-4) or to silenced chromatin (Ty5)
- P element "homing"
- Immune system changes (VDJ joining at RSS; somatic hypermutation only of V region; isotype switching)

==> cells have molecular mechanisms to direct DNA changes to functionally defined locations in the genome.

Isotype Switching (Class Switch Recombination: **intercellular signaling to choose crossover site**)



http://www.umassmed.edu/faculty/show.cfm?start=0&faculty=300; see Stavnezer et al. Mechanism and Regulation of Class Switch Recombination. Annu. Rev. Immunol. 2008. 26:261–92



Linking class-switch recombination with somatic hypermutation. Kazuo Kinoshita & Tasuku Honjo*Nature Reviews Molecular Cell Biology 2, 493-503 (July 2001)*

“Spontaneous hereditary changes are localized and limited to those of small effect”

Counterfactuals:

- Protein evolution by domain swapping
- Homeotic transformations (Bateson, Goldschmidt)
- “Chromosome contamination” and chromosome rearrangements in hybrid dysgenesis
- Whole genome doubling (WGD) following interspecific hybridization
- Major phenotypic changes following interspecific hybridization

==> cells can restructure the whole genome in one generation with major changes in many characters.

Phenotypic changes after interspecific hybridization (and 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.

“Cells cannot integrate DNA change with biologically useful adaptive needs”

Counterfactuals:

- Induction of meiotic recombination by nucleases
- Mating-type switching in yeast
- Ciliate protozoa macronuclear development
- Microbial phase variation (homopolymer tracts, site-specific recombination, transposon insertion & excision)
- Microbial protein changes and antigenic variation (homologous cassette exchange, site-specific recombination, diversity-generating retroelements)
- Immune system rearrangements and targeted somatic hypermutation

==> cells have evolved multiple adaptive uses of DNA restructuring operators.

21st Century view of evolutionary change: a generalized scenario

- Ecological disruption ==> changes in biota (populations depleted), food sources, adaptive needs & organismal behavior.
- Macroevolution triggered by cell fusions & interspecific hybridizations (WGDs) leading to major episodes of horizontal transfer, genome rearrangements & novel symbiotic associations.
- Establishment of new cellular and genome system architectures; complex novelties arising from WGD and network exaptation.

  (A role for targeting and heuristics? Compare Watson, R. A. (2006). *Compositional Evolution: The impact of Sex, Symbiosis and Modularity on the Gradualist Framework of Evolution*, MIT Press; http://eprints.ecs.soton.ac.uk/12006/)
- Survival and proliferation of organisms with useful adaptive traits in depleted ecology; elimination of non-functional architectures; selection largely purifying.
- Microevolution by localized natural genetic engineering after ecological niches occupied (immune system model).

Darwin referring to “sports” and other sudden appearances of novel life forms:

"...variations which seem to us in our ignorance to arise spontaneously. It appears that I formerly underrated the frequency and value of these latter forms of variation, as leading to permanent modifications of structure independently of natural selection.” *Origin of Species*, 6th edition, Chapter XV, p. 395.