Cognitive Aspects of genome function

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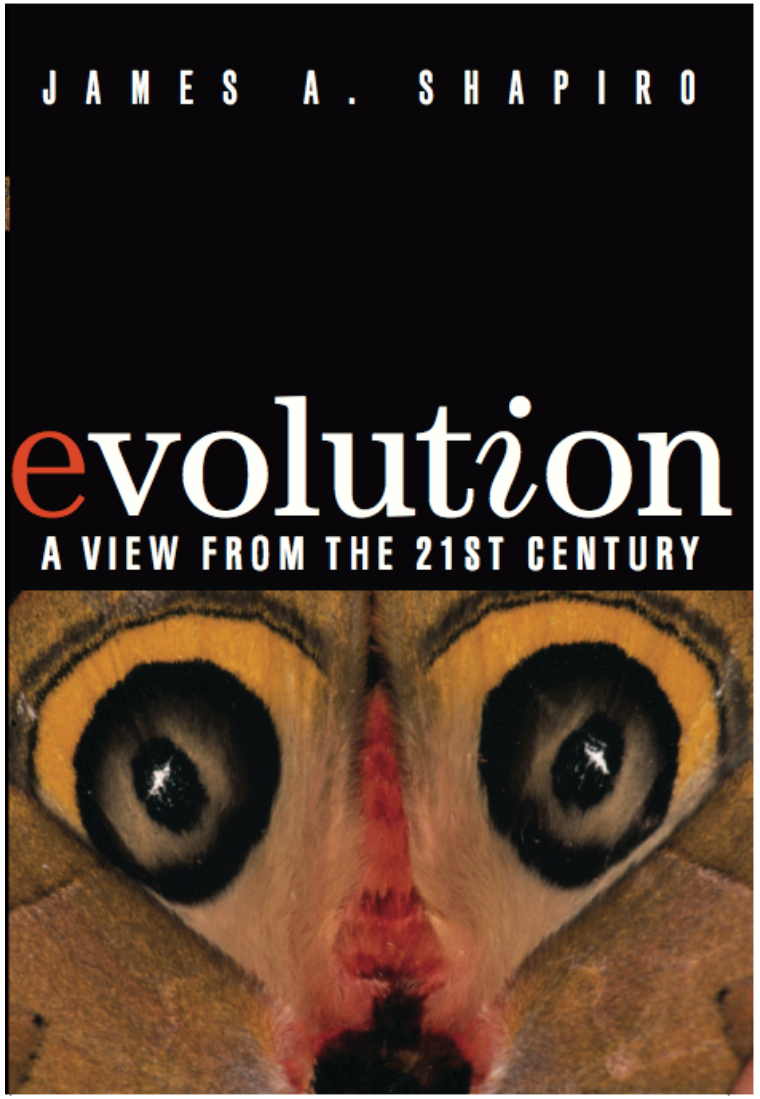


"In the future, attention undoubtedly will be centered on the genome, with greater appreciation of its significance as a highly sensitive organ of the cell that monitors genomic activities and corrects common errors, senses unusual and unexpected events, and responds to them, often by restructuring the genome."
McClintock, B., 1984 Significance of responses of the genome to challenge. Science **226**: 792-801. (Nobel Prize speech)

Philosophical Debates about the Organization and Evolution of Living Cells

- In response to Paley's "argument from design" for an intelligent Creator, Darwinists and neo-Darwinists insisted on the blind watchmaker rather than the operation of an engineering process (*i.e.* they explicitly excluded functional goals, design principles and self-evaluation).
- In the Mechanism vs. Vitalism debates of the 19th/ 20th Centuries (*e.g.* Driesch *vs.* Roux), purely hardwired explanations of life were adopted to avoid the need to accept some information-processing "vital force" to control growth and reproduction).

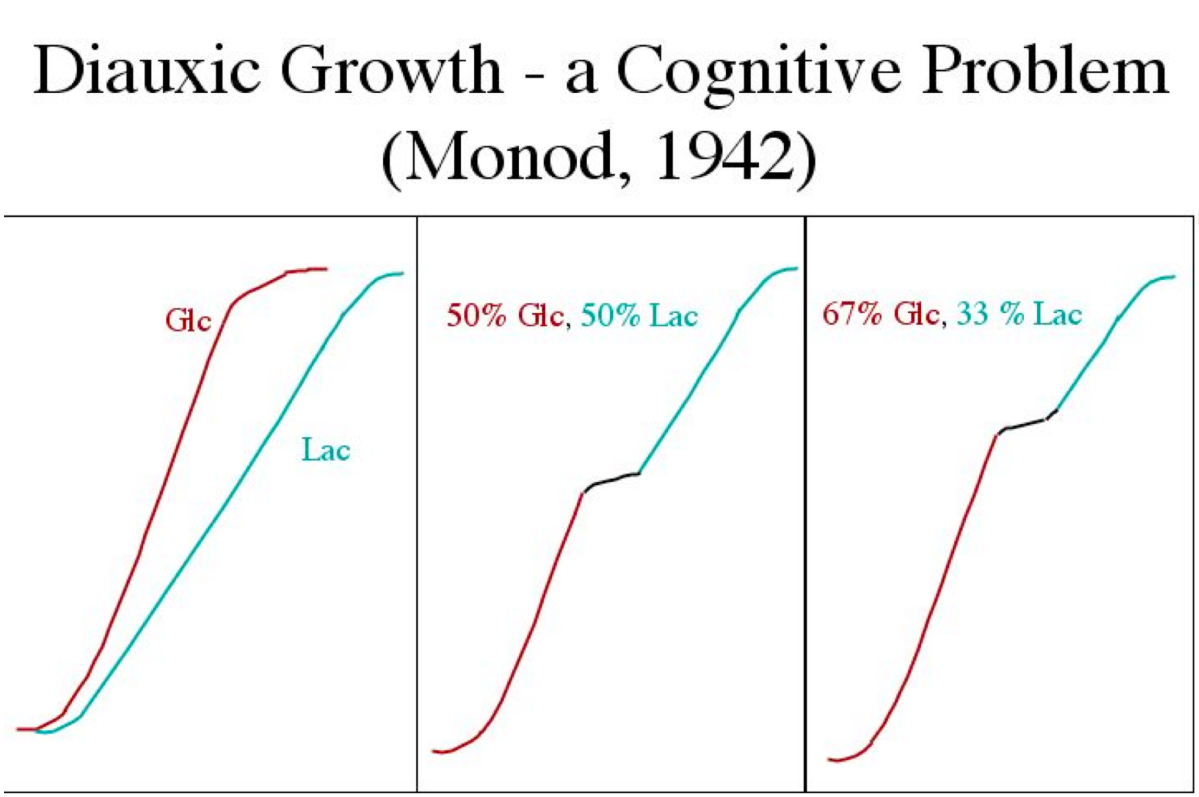
The basic argument

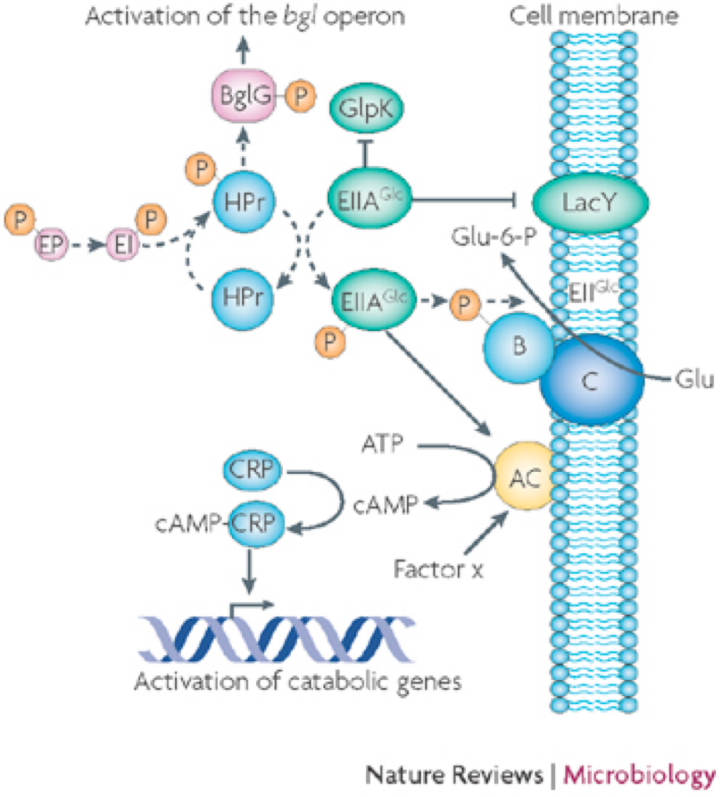
- Cells use cognitive processes (= action based on knowledge) in dealing with genomic information
- We know some of the molecules and mechanisms cells employ to gain & process knowledge relevant to genome action (sensing, signalling & computation by molecular networks)
- Cognitive functions affect both extracting information from and adding information to the genome (genome = Read-Write memory system)
- Cell cognition involved in all aspects of biological function, up to and including evolutionary change

Dennis Bray. 2009. *Wetware: A Computer in Every Living Cell*. Yale.

Antoine Danchin. 2009. Bacteria as computers making more computers. FEMS Microbiol Rev 33: 3-26.

Cognition in reading genomic data files: lactose utilization in E. coli

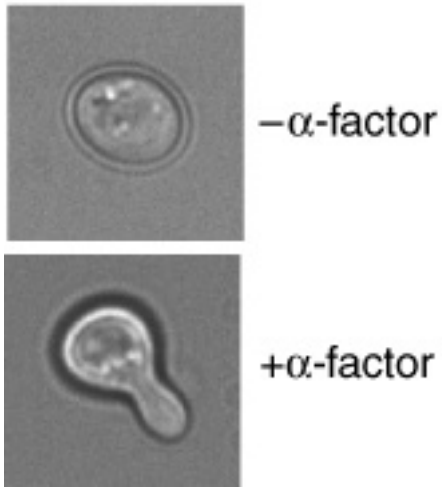




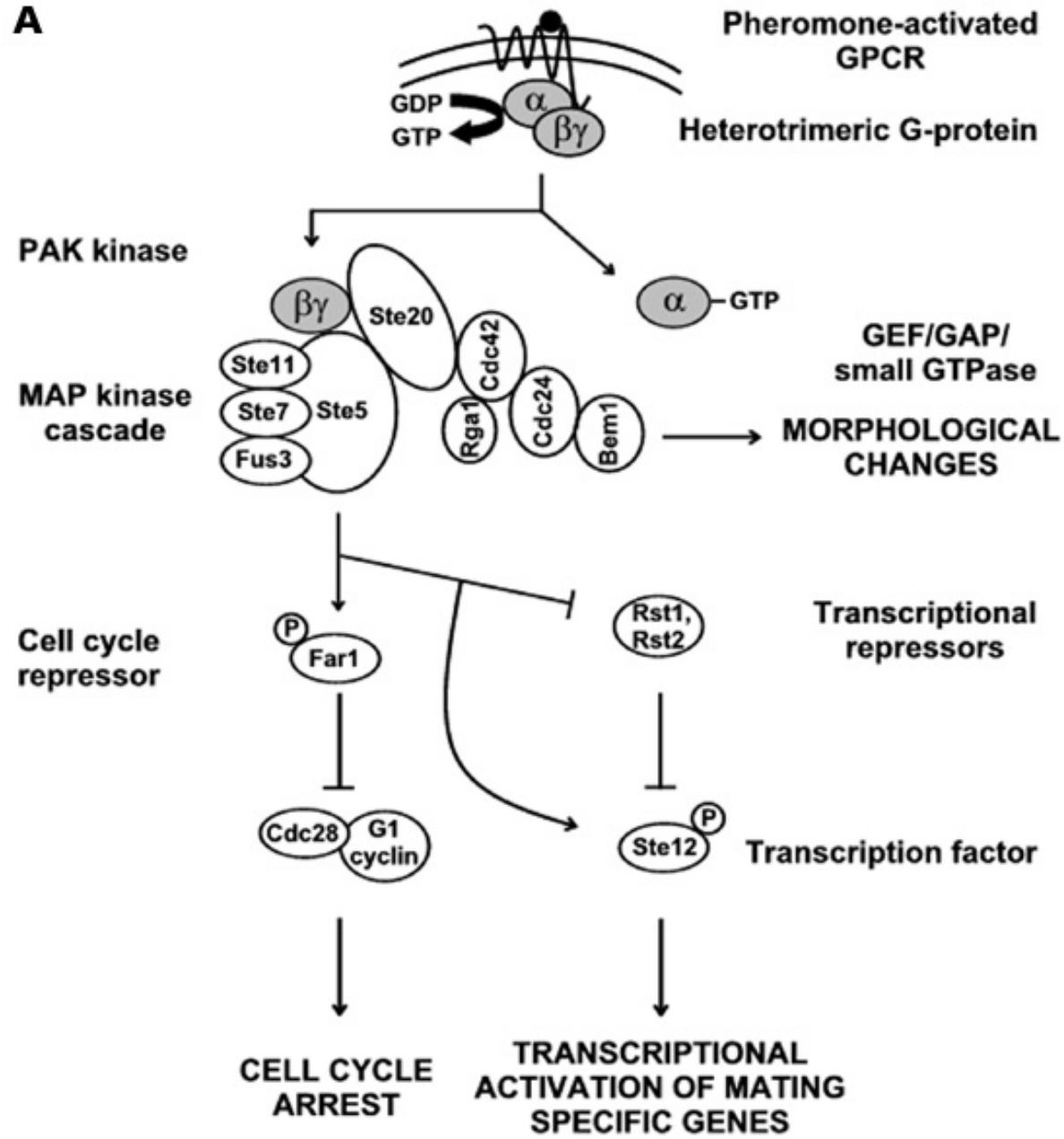
Synthesize lactose-metabolizing proteins when glucose is exhausted. How to sense glucose and lactose?

Görke B, Stülke J Carbon catabolite repression in bacteria: many ways to make the most out of nutrients. Nat Rev Microbiol. 2008 Aug;6(8): 613-24. Review

Cognition in reading the genome and growing the cell: yeast sexual arousal



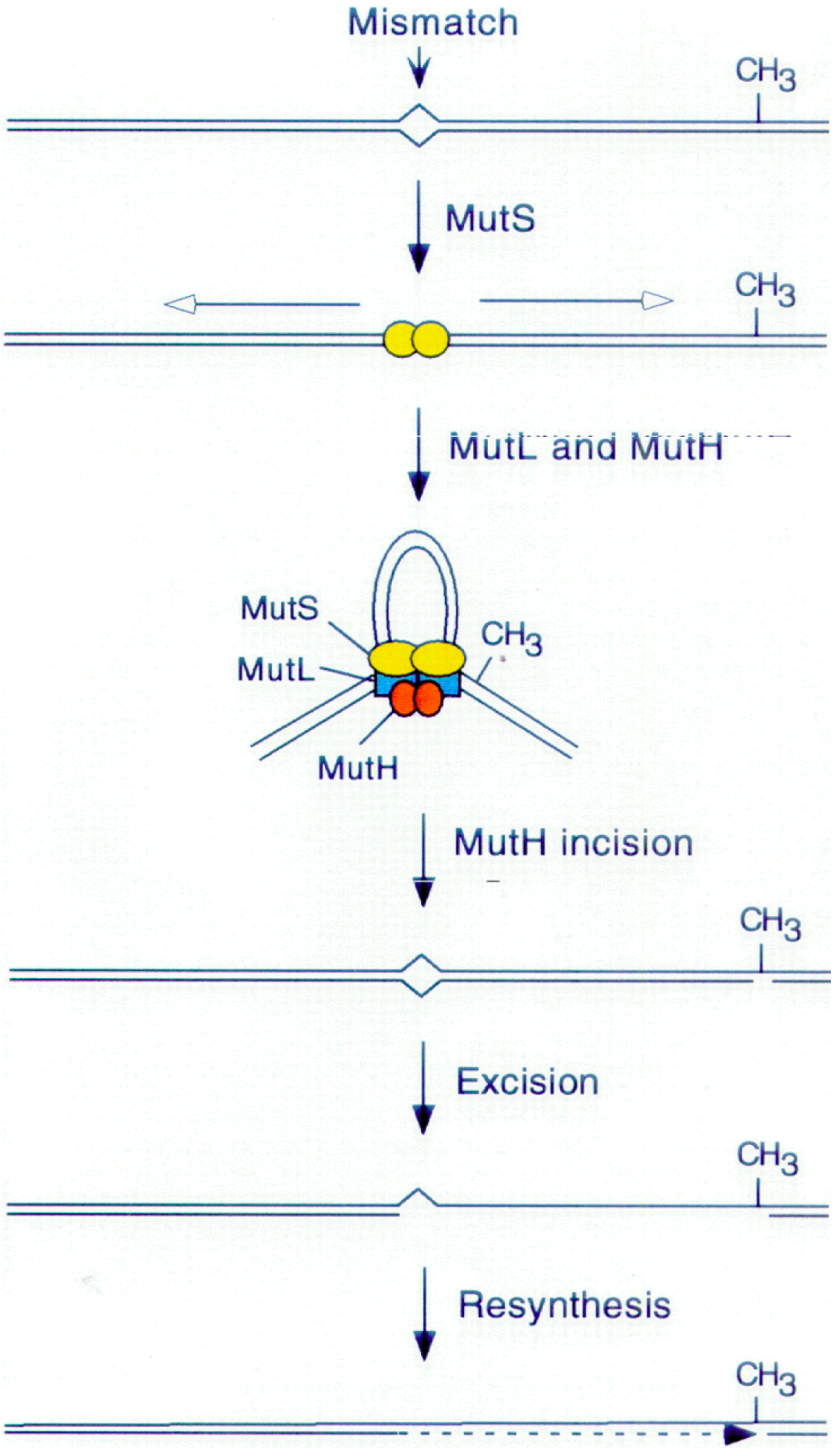
Pheromone Response
Frank van Drogen et al. MAP kinase dynamics in response to pheromones in budding yeast. Nature Cell Biology 3, 1051 - 1059 (2001).



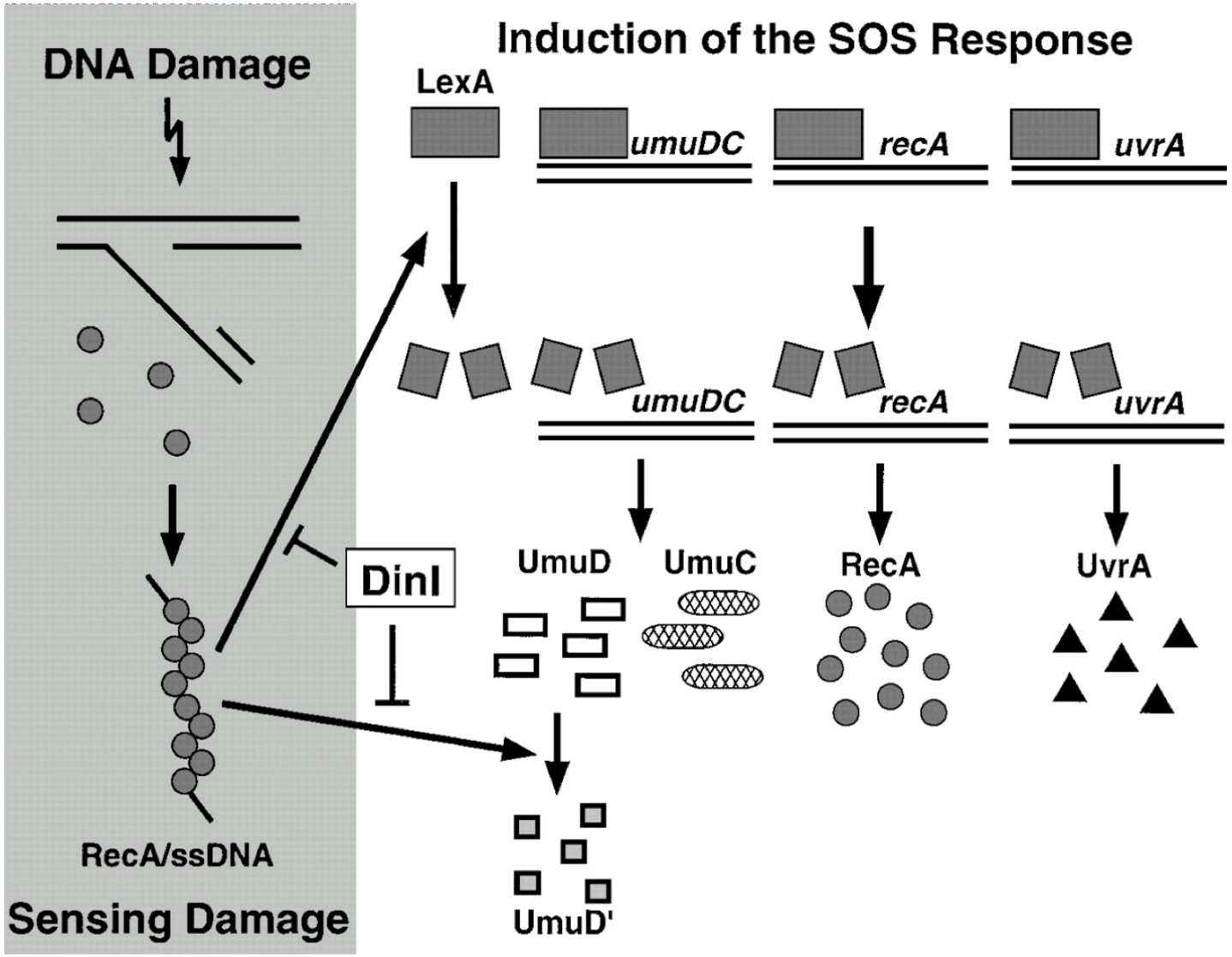
Mary J. Cismowski et al. Genetic screens in yeast to identify mammalian nonreceptor modulators of G-protein signaling. Nature Biotechnology 17, 878 - 883 (1999).

Cognition in proofreading DNA: mismatch excision repair

B. Harfe and S. Jinks-Robertson. DNA MISMATCH REPAIR AND GENETIC INSTABILITY. Annu. Rev. Genet. 2000. 34:359-399



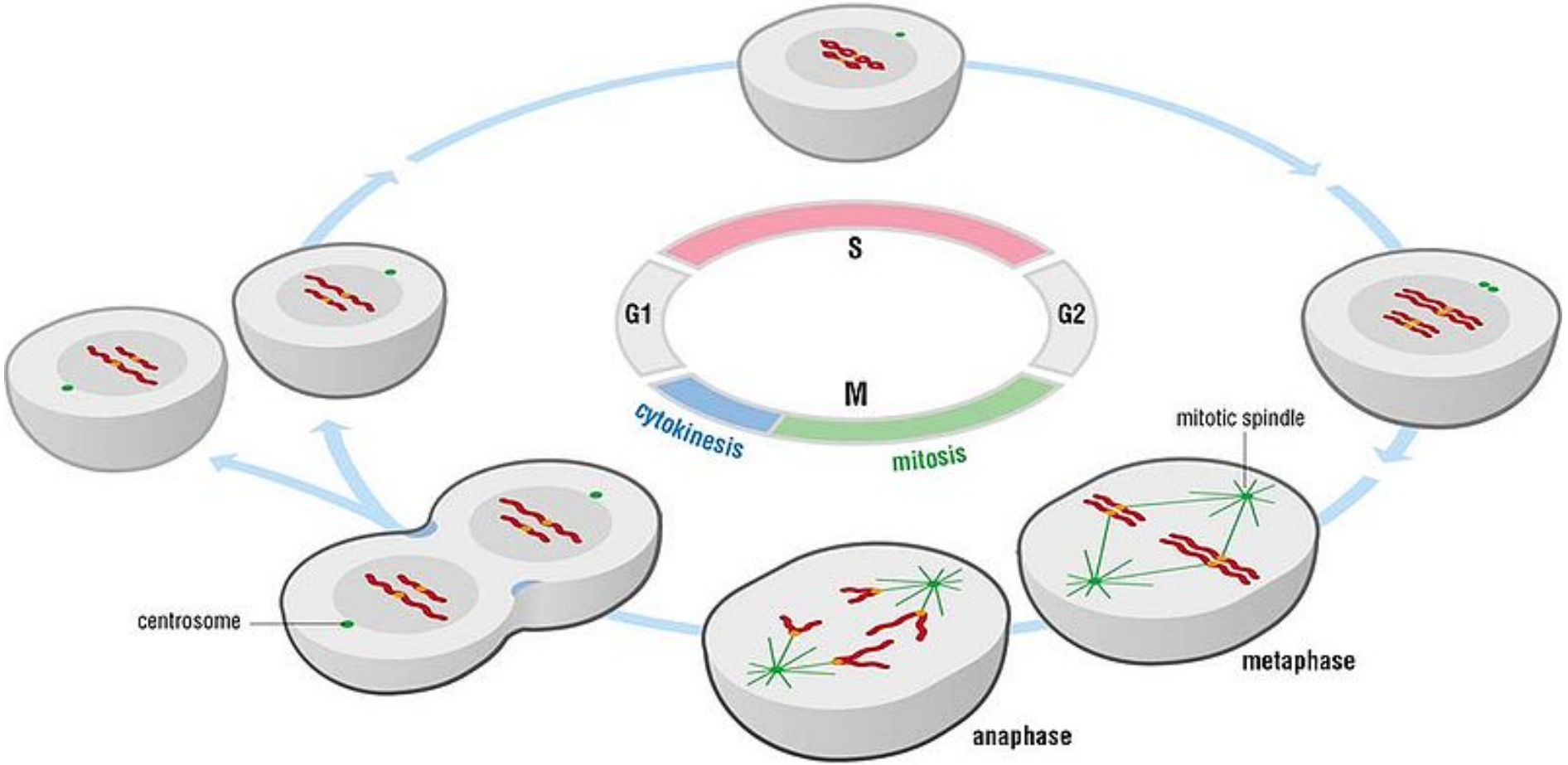
Cognition in proofreading and repairing DNA: RecA sensing and the SOS response



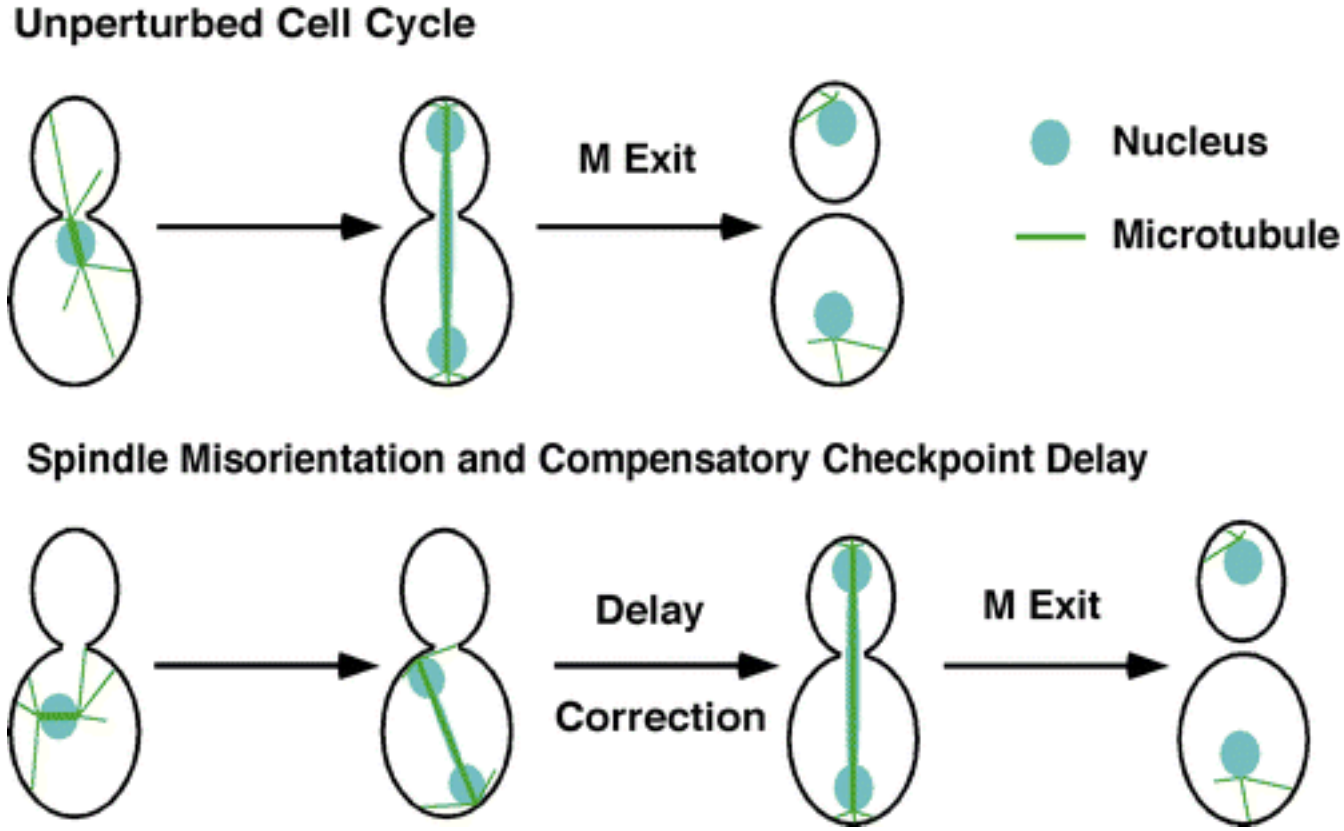
Sutton, et al. THE SOS RESPONSE: Recent Insights into umuDC- Dependent Mutagenesis and DNA Damage Tolerance. Annu. Rev. Genet. 2000. 34:479-497

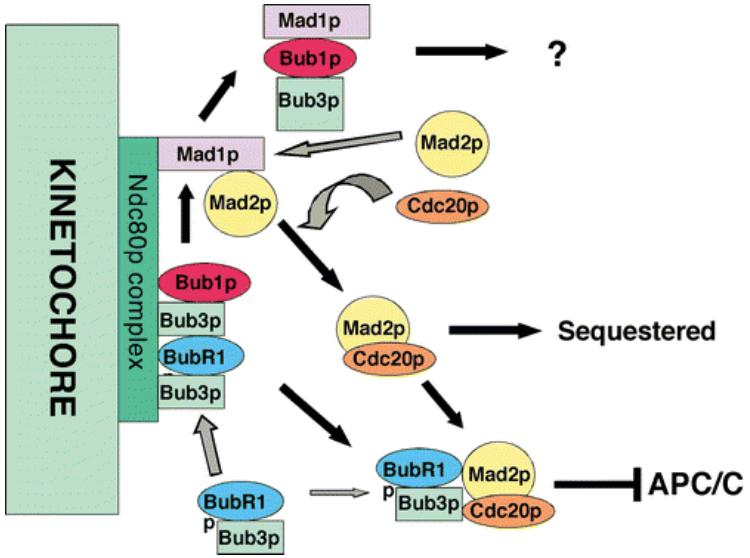
Cognitive functions in cell cycle control

From **The Cell Cycle: Principles of Control** by David O Morgan



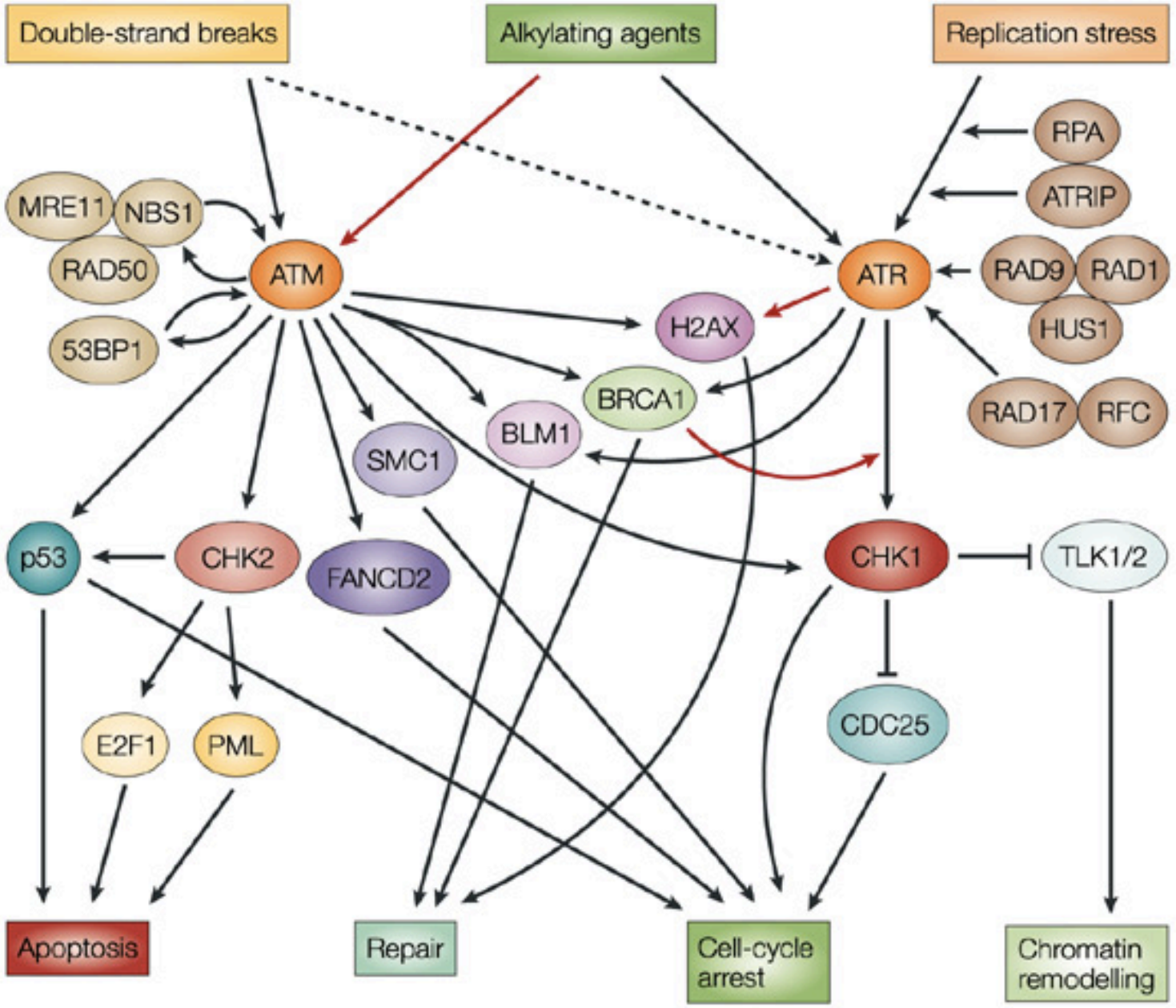
Cognition in cell cycle control: spindle orientation checkpoint in yeast





J. Lew and Daniel J. Burke.
THE SPINDLE ASSEMBLY AND SPINDLE POSITION CHECKPOINTS.
Annual Review of Genetics 37: 251-282 (2003)

Decision-making in the DNA damage response



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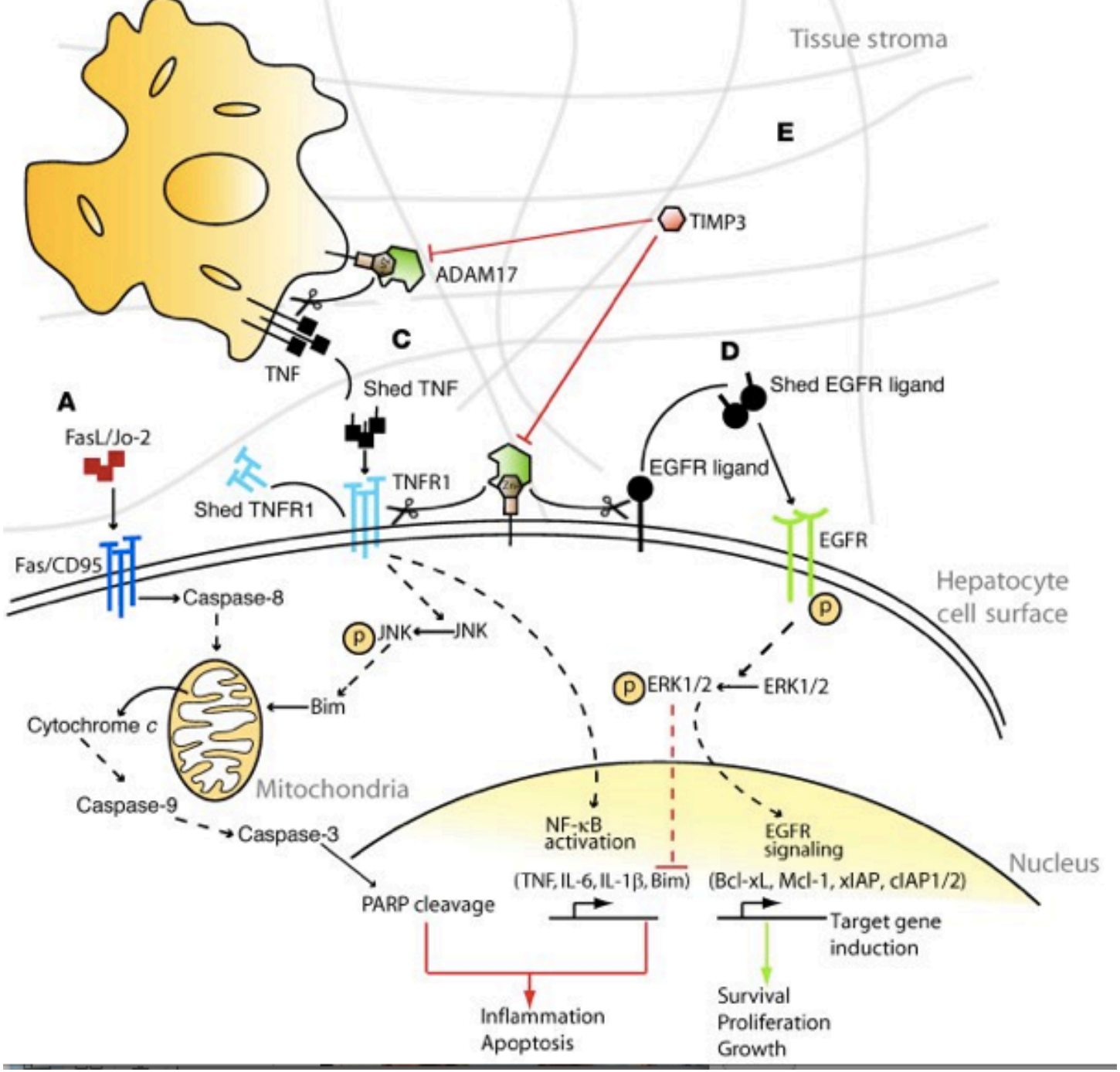
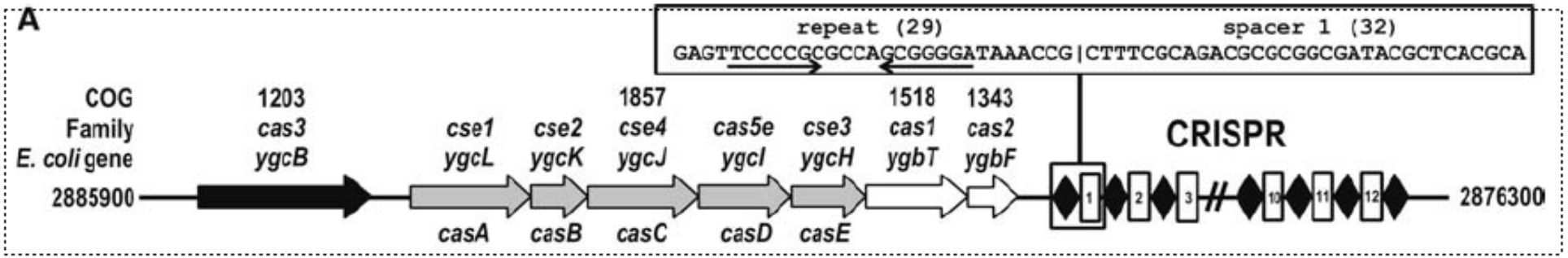
Cognition and decision-making in programmed cell death (apoptosis): Effect of cytokines on cell survival



Murthy et al. Ectodomain shedding of EGFR ligands and TNFR1 dictates hepatocyte apoptosis during fulminant hepatitis in mice. ***J Clin Invest. 2010; 120(8):2731–2744 doi:10.1172/JCI42686***

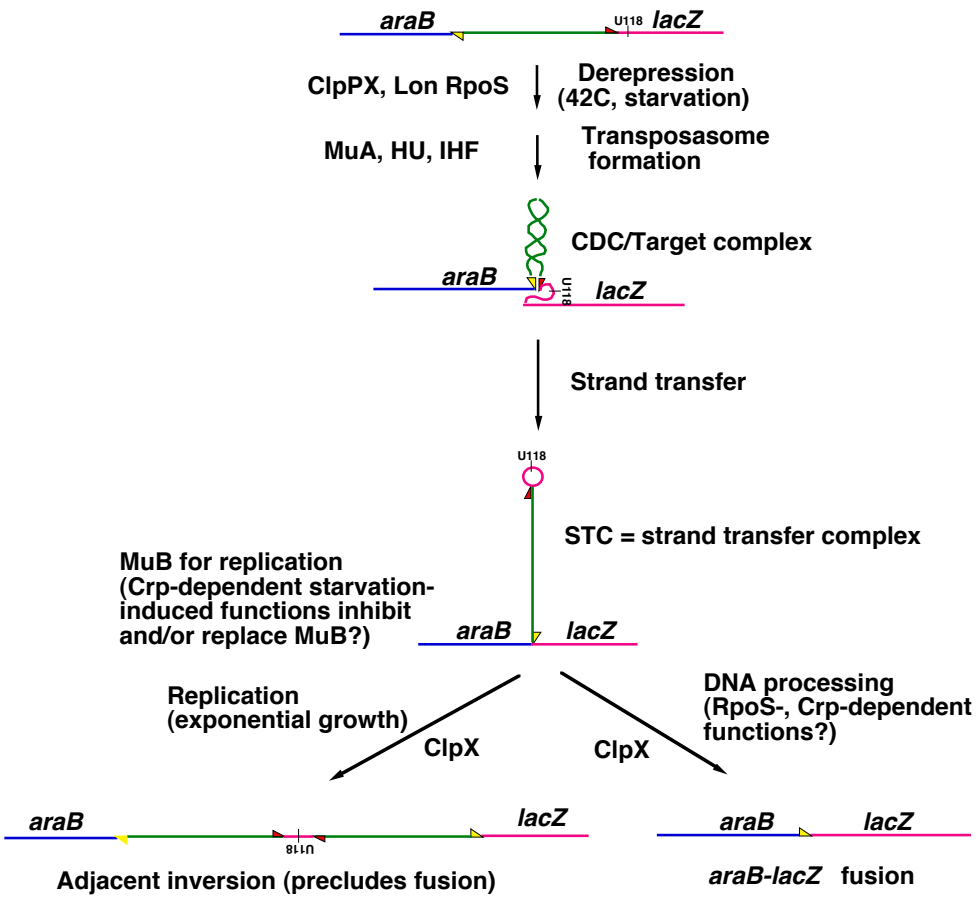
Cognition in genome defense: Developing immunity against invading DNA

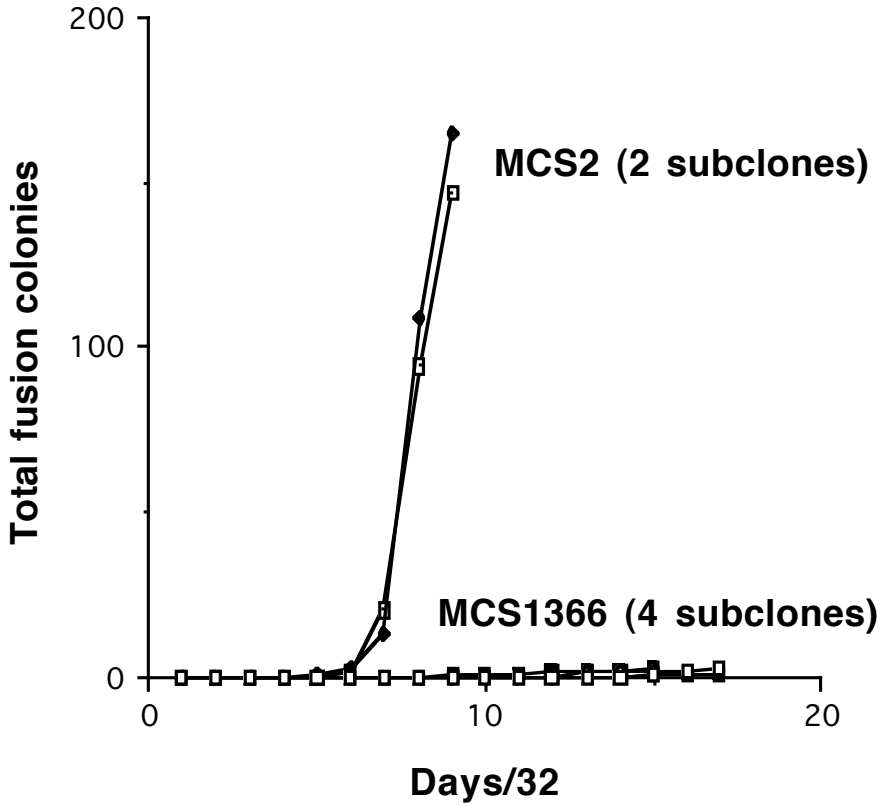
CRISPRs (Clustered Regularly Interspaced Short Palindromic Repeats)



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

Cognition in genome restructuring: Effect of starvation on araB-lacZ fusions





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

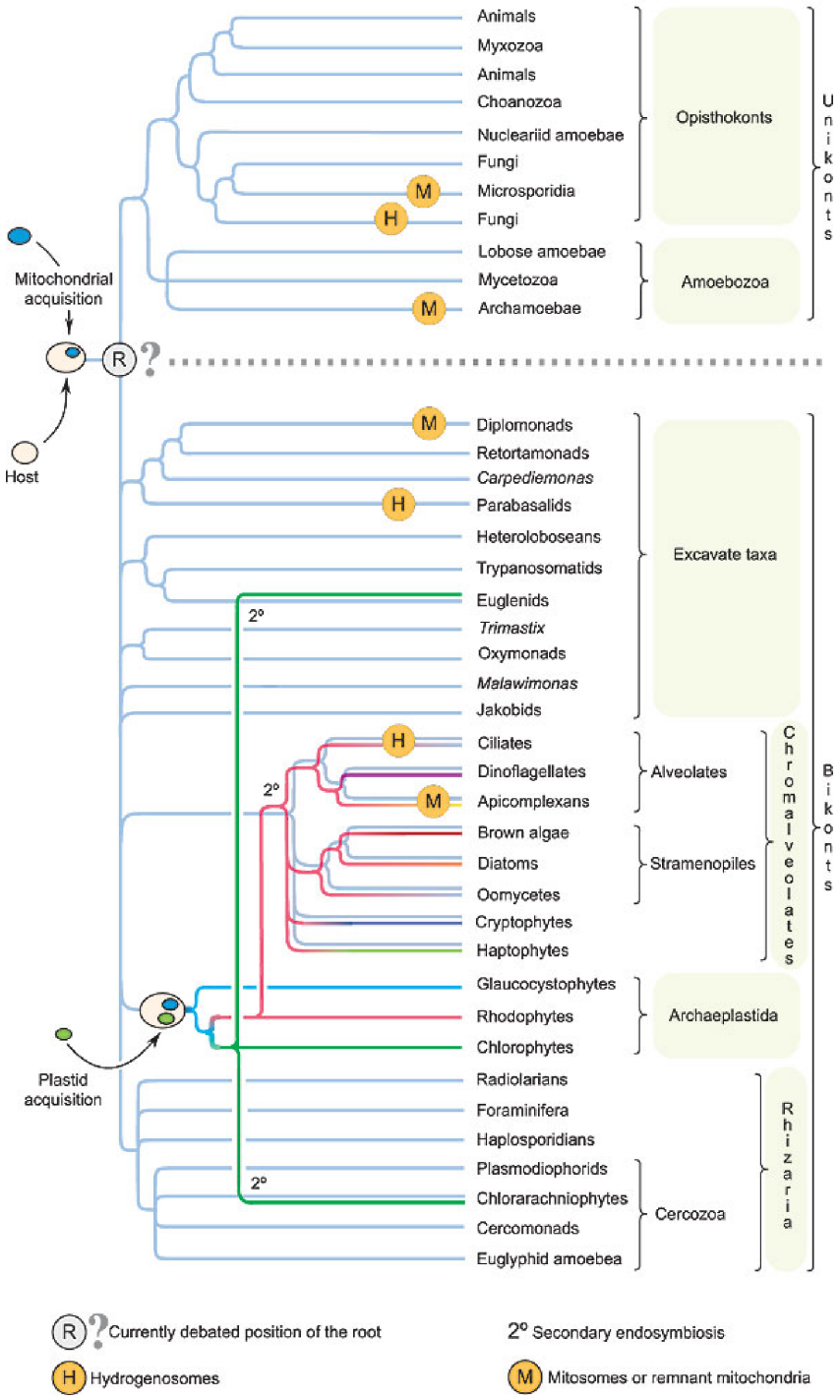
Cognition in genome restructuring:

Stimuli that alter epigenetic control of natural genetic engineering* and elevate genome variability

- Chromosome breaks (McClintock, 1944)
- Pheromones, hormones & cytokines
- **Starvation**
- DNA damage (mutagens)
- Telomere erosion
- Antibiotics, Phenolics, Osmolites, Oxidants
- Pressure, Temperature, Wounding
- Protoplasting & growth in tissue culture
- **Bacterial or fungal infection & endosymbiosis**
- **Changes in ploidy & DNA content (genome doubling)**
- **Hybridization (interspecific mating)**

* Mediated by CRISPR-like functions in *Drosophila* and other animals.

Cognition in evolution: symbiogenesis (merging cell cycles) at key points in evolution



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

How cognition may work in evolution:
ecological disruption affecting epigenetic regulation, population structures and genome stability

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