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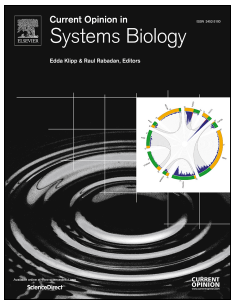

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Béla Novák, Frank Stefan Heldt, John J. Tyson

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Genome Stability during Cell Proliferation: A Systems Analysis of the Molecular Mechanisms Controlling Progression through the Eukaryotic Cell Cycle

Béla Novák[1], Frank Stefan Heldt[1] & John J. Tyson[2,3]

Addresses: [1]Department of Biochemistry, University of Oxford, UK; [2]Department of Biological Sciences, Virginia Tech, Blacksburg VA, USA; [3]Division of Systems Biology, Academy of Integrated Science, Virginia Tech, Blacksburg VA, USA.

Corresponding Authors: bela.novak@bioch.ox.ac.uk, tyson@vt.edu

Abstract

Well-nourished cells in a favorable environment (well supplied with growth factors, cytokines, and/or hormones and free from stresses, ionizing radiation, etc.) will grow, replicate their genome, and divide into two daughter cells, fully prepared to repeat the process. This cycle of DNA replication and division underlies all aspects of biological growth, reproduction, repair and development. As such, it is essential that the cell's genome be guarded against damage during the replication/division process, lest the error(s) be irrevocably passed down to all future generations of progeny. Hence, cell cycle progression is closely guarded against major sources of errors, in particular DNA damage and misalignment of replicated chromosomes on the mitotic spindle. In this review article we examine closely the molecular mechanisms that maintain genomic integrity during the cell division cycle, and we find an unexpected and intriguing arrangement of concatenated and nested bistable toggle switches. The topology of the network seems to play crucial roles in maintaining the stability of the genome during cell proliferation.