



TERRY L. ORR-WEAVER, Ph.D.

DEVELOPMENTAL REGULATION OF DNA REPLICATION
TO CONTROL CELL SIZE AND GENE COPY NUMBER

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Lectures will resume on August 30, 2018.

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Proper control of DNA replication and cell division are essential in development, yet alteration of DNA replication is used for particular developmental strategies. Throughout the plant and animal kingdoms there are tissues that need to have large cells, for example to provide barrier functions. These large increases in cell size are mediated by increasing DNA content through modification of the normal cell division cycle such that DNA replication but not cell division occur. This strategy is used in glial types in the *Drosophila* nervous system to ensure axonal ensheathment and that the blood-brain barrier is maintained during nervous system growth. Unexpectedly, we find that distribution of genomic DNA into multiple nuclei rather than a single nucleus within each cell impacts glial function. In addition to changes in the overall genomic DNA content, localized changes in gene copy number occur. We term the latter differential DNA replication and have exploited its ubiquitous presence in differentiated tissues in *Drosophila* to decipher the developmental control of origin firing and fork progression. We find that both constitutive genome architecture and tissue specificity impact the distribution of replication origins. Replication fork progression can be actively regulated in development, exhibiting both tissue and region-specific properties.



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Terry L. Orr-Weaver is an American Cancer Society Research Professor in the Department of Biology at MIT and a Member of the Whitehead Institute, which she initially joined in 1987. She obtained her Ph.D. in the laboratory of Dr. Jack Szostak at Harvard University in 1984 and did postdoctoral training in Dr. Allan Spradling's laboratory at the Carnegie Institution of Washington. Her research addresses regulation of cell division during development, and her laboratory has discovered crucial control proteins for chromosome segregation and DNA replication as well as providing key insights into how cell size is regulated. She served as President of the Genetics Society of America and of the National *Drosophila* Board of Directors. She was the chair of the Scientific Advisory Committee of Children's Hospital in Boston. She is an elected fellow of the American Academy of Microbiology, the American Association for the Advancement of Science, and a member of the National Academy of Sciences. She received the FASEB Excellence in Science award in 2013.