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The Cell Biology of the Germ Cell Life Cycle

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Each year Current Opinion in Cell Biology includes a section on Cell Differentiation. In many cases, a Cell Biologist thinks about their favorite model cell as having a single identity—its behavior may change with environment or manipulation, but its identity generally does not. Developmental Biologists, on the other hand, think about cell fate specification and how cell identity changes during development. The past few decades have seen an important merger of Cell Biology and Developmental Biology to study important questions of how a cell's identity influences its Cell Biology (e.g. cell shape and morphogenesis), and how basic Cell Biology controls a cell's identity (e.g. cytoplasmic determinants and asymmetric cell division). No place are these questions more relevant than in the Germ Cells, which are responsible for giving rise to the next generation of the species. In this issue, we explore how Germ Cell Differentiation controls, and is controlled by, Cell Biology throughout the life cycle of the germline.

Appropriately, we begin with Germ Cell formation. In many species, Germ Cells are formed from cells that inherit a localized cytoplasmic determinant, the germ plasm. One general characteristic of Germ Cell specification is that the expression of somatic genes must be repressed in order for the germ cell program to eventually be initiated. Nakamura and colleagues describe the cell biology of germ cell formation, along with how the germ plasm leads to the repression of somatic gene expression.

Another common feature of Germ Cell development is that the Germ Cells must often migrate from their site of origin to where the gonad will form. Thus, another key aspect of the germ cell program is to activate the cell migration machinery and the guidance mechanisms needed for them to find their way. In their paper, Tarbashevich and Raz focus on how germ cell migration is regulated in different species.

A critical aspect of Germ Cell Differentiation is that it is sex-specific; proper establishment of sexual identity in the germline is essential for controlling sexual development of the germ cells and their ability to produce such different cell types, the sperm or the egg. As with many aspects of Germ Cell development, sex determination in the germline requires close interactions between germ cells and somatic cells in the gonad, as described for different species in the paper by Murray *et al.*

One aspect of sex-specific development of the Germ Cells is their ability to produce male and, in some species, female Germline Stem Cells. The Germline Stem Cells enable an animal to produce large numbers of gametes throughout a large portion of its life, and

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represent excellent models for understanding adult stem cells in any organ. In their paper, Yamashita and colleagues review the Cell Biology of how Germline Stem Cells interact with their surrounding environment (niche) and how their division and maintenance are regulated.

The Cell Biology of chromatin regulation within the nucleus and throughout the cell cycle is also a critical aspect of Germ Cell Differentiation. First, Chen and colleagues describe how epigenetic regulation of the germline is regulated to control germ cell gene expression, and how this changes in the germline stem cells vs. during differentiation. Next, Judith Yanowitz reviews the specialized Cell Biology of the chromatin during the uniquely germline process of meiosis. Last, Bortvin and colleagues discuss how the germline chromatin is protected by the piRNA pathway from assault by transposable element mobilization. In particular, they discuss how the particular Cell Biological organization of piRNA components influences this pathway.

Finally, we complete the germline life cycle with the egg to embryo transition as the gametes, and the maternal and paternal pronuclei, fuse to form the totipotent zygote. Many of the key molecular and cellular changes that accompany this transition are regulated by proteolysis, which ensures that these events proceed in a tightly orchestrated manner. Verhlac and colleagues describe these events in the final paper. Thus, we are now back where we started; the complex process of Germ Cell Differentiation, and the key ways in which the Cell Biology machinery can regulate, and be regulated by the Germ Cell program, have brought us from embryo to highly differentiated gametes and back again. May the circle never be broken!

Biography

Mark Van Doren is on the faculty of Johns Hopkins University where his research focuses on the sexual development of the germ cells and gonads. In addition, he is director of an interdisciplinary graduate program in Cell, Molecular, Developmental Biology and Biophysics (<http://cmdb.jhu.edu/>).