



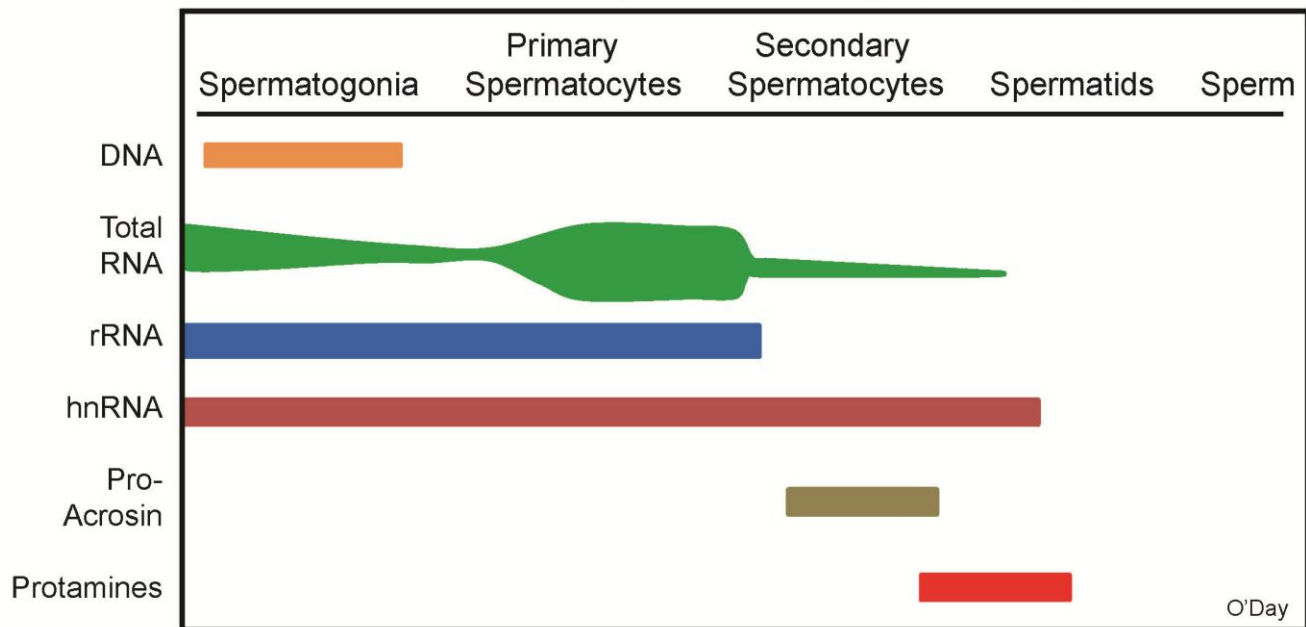
Sperm Nuclear Condensation and Male Pronucleus Formation: On-Line Self-Study

Goals of this exercise:

- To examine the events that shut down and reactivate the sperm nucleus
- To understand the reasons for these events
- To learn about the basic nucleoproteins involved in the events
- To learn the different roles the different nucleoproteins play
- To understand the first role of the egg cytoplasm in the start of embryogenesis

During spermatogenesis, the actively dividing spermatogonia are involved in the synthesis of large amounts of a diversity of macromolecules. As the process continues, there becomes a decreasing need for certain types of macromolecules as others become essential. As the spermatid develops and ultimately differentiates into a sperm, macromolecular synthesis essentially stops. Examine the following chart and list what macromolecular synthetic events are associated with which steps in spermatogenesis. Note how the changes are related to the specific events of spermatogenesis. Then we will focus on the changes in basic nuclear proteins.

Macromolecular synthesis during spermatogenesis

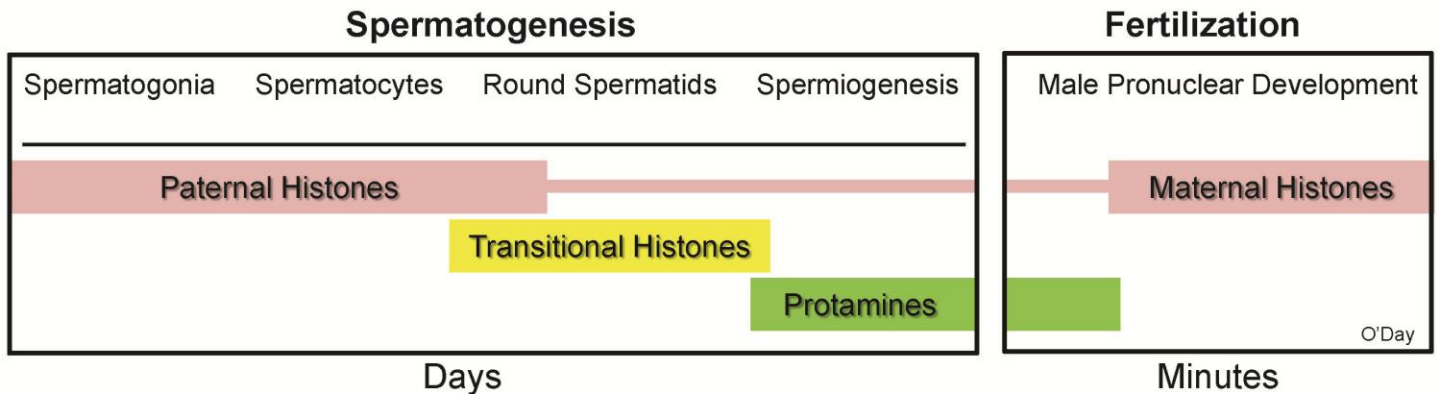


The Histone-Protamine Shift

It is important to understand the way DNA is packed and unpacked during spermatogenesis and fertilization because it has implications to human infertility as well as subsequent embryogenesis. As spermatogenesis progresses, the somatic histones become replaced with transitional histones which in turn get replaced by protamines as spermiogenesis proceeds. Check out the chart below noting some of specific changes that occur. This is a simplified version of the actual changes but reveals the essence of those changes. Based on what you learned in lecture, what is the significance of these changing patterns of histone presence?

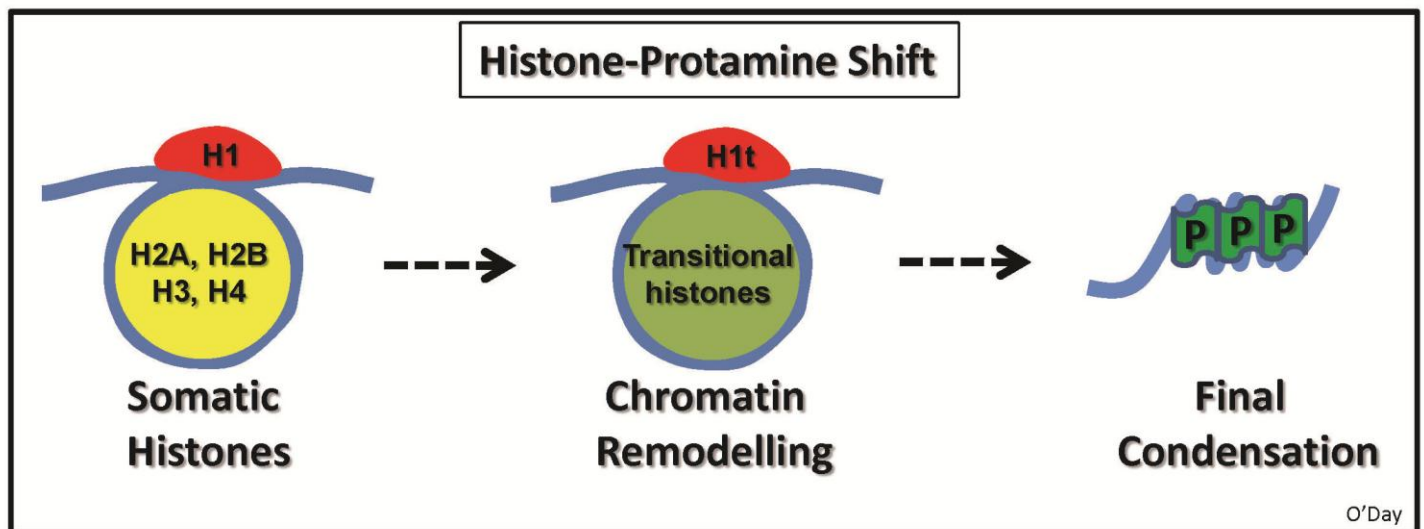
Events in Spermatogenesis and Male Pronucleus Formation

Basic nucleoprotein changes during spermatogenesis and fertilization



The Histone-Protamine Shift Affects Chromatin Packaging

Somatic histones organize chromatin in the classic nucleosome (beads on a string) structure. The transitional histones permit the shift from nucleosomal structure to an intermediate nucleosomal organization. This will in turn allow chromatin remodeling as the transitional histones are replaced by protamines. In humans, protamines P1 and P2 allow tighter chromatin packing which is the hallmark of sperm nuclei. This condensation and packing involves the formation of disulfide bridges between protamine proteins.



This overview doesn't address a number of events that are essential for these nucleoprotein transitions to occur. Histone acetylation and ubiquitination of specific histones are two of many essential events underlying the multi-step histone-protamine shift. In the end, the final human sperm chromatin still contains around 15% histone protein. Recent work has shown that this remaining histone maintains nucleosomal organization at the centromeres and telomeres. This appears to be critical for the subsequent decondensation and activation of the male genome that occurs at fertilization.

Male Pronucleus Formation Involves Re-Establishment of the Nucleosomal Structure

While the shutdown of nuclear synthetic activity is an essential stage in sperm formation, fertilization relieves the sperm nucleus from dormancy. This is important so that the male chromosomes can again function normally

Events in Spermatogenesis and Male Pronucleus Formation

in the upcoming events of cell division and gene activity that are required for continued development. As a result, fertilization leads to a protamine-histone shift ultimately re-instating the nucleosomal organization of the male chromatin. As the male pronucleus swells about three-fold, the sulfhydryl bonds between protamines are reduced. This allows the replacement of protamines with somatic histones. As yet the sequence of events has not been well established. However, one thing is clear. The histones that are used in the transition must come from the oocyte. Similarly the “chromatin remodeling factors” that allow the complete de-condensation and activation of the paternal chromatin are also from the egg cytoplasm. These events prepare the paternal genome for zygote nucleus formation as well as for the future gene regulation that underlies normal embryogenesis.

Reference

Martin, C. and Y. Zhang, 2007. Mechanisms of epigenetic inheritance. *Curr. Opin. Cell Biol.* 19: 266-272.

Ward, 2010. Function of sperm chromatin structural elements in fertilization and development. *Molecular Human Reproduction* 16: 30-36.

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