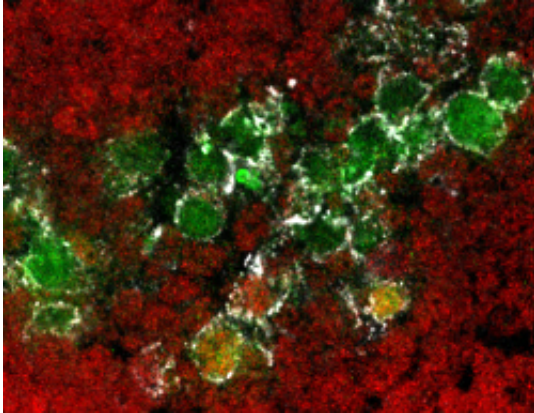


Timing germ cell development

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(Phys.org) —Scientists from the Friedrich Miescher Institute for Biomedical Research identify a novel mechanism in early germ cell development. They show how the chromatin modulator PRC1 coordinates the timing of sexual differentiation of germ cells during embryonic development. The study, which enhances our understanding of the mechanisms regulating stem-ness and cell fate determination, is published in the latest issue of *Nature*.

Like all Royal houses in Europe prepare their heirs to the throne, the body carefully develops its germ cells specifically and early on for their sole task of propagating the lineage. As the egg and the sperm fuse to form a zygote, a new being, they look back on an extensive "training" that separated them early on from other cells in the developing embryo.

During germ cell development, [gene expression](#) programs and chromatin states are prepared such that they support [embryonic development](#) after fertilization. What is more, the germ cells have to undergo an unusual type of cell division called meiosis to provide the correct set of chromosomes to the embryo. They have to reduce the two copies of each chromosome – one from the mother, one from the father – to one.

It has long been a mystery what enables germ cells to undergo meiosis. Antoine Peters, senior group leader at the Friedrich Miescher Institute for [Biomedical Research](#) and Adjunct Professor at the University of Basel, and his team have now been able to identify a major regulator of this switch in cell fate. As they report in the latest issue of *Nature*, they could show how the chromatin modifier and transcriptional repressor PRC1 controls the development of primordial germ cells and their entry into meiosis.

During embryonic development exposure to morphogens such as retinoic acid can change the fate of cells. For instance, it has been known that increasing levels of retinoic acid, secreted by surrounding [somatic cells](#), instruct primordial germ cells to differentiate and enter into meiosis. The mechanisms that confer responsiveness of cells to retinoic acid are, however, little understood. Chromatin-based mechanisms have been proposed to suppress changes in developmental fate by counteracting differentiation inducing cues. PRC1 is a multi-unit protein complex that controls chromatin configuration and suppresses expression of numerous genes that instruct cellular differentiation. The FMI scientists could now show in their elaborate study that PRC1 counterbalances retinoic acid signals from the environment in a gene dosage sensitive manner and thereby controls meiotic entry of female germ cells. It acts within the primordial germ cells and suppresses the genes necessary for differentiation. At the same time, it enables expression of transcription factors critical for self-renewal and stem-ness, such as Oct4 and Nanog. The study proposes that only as the levels of retinoic acid rise, the

suppressing function of PRC1 is specifically overcome at genes necessary for entry into meiosis. Genes specifying other differentiation pathways remain, however, repressed by PRC1.

"The better we understand the mechanisms controlling the development of [germ cells](#), the more we will learn about the essence of developmental potency of stem cells" comments Peters. "Our research allows us to dissect the roles of transcription factors, [chromatin](#) modulators and external signals in achieving, maintaining and exiting the stem cell state. Our novel findings underscore the importance of PRC1 in early developmental processes, at the transition between pluripotency and differentiation."

More information: Yokobayashi, S. et al. (2013) [PRC1 coordinates timing of sexual differentiation of female primordial germ cells](#). *Nature*, 495:236-240

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