## Seminar/Talk

# A checkpoint ensures repair of DNA lesions during zygotic reprogramming

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Sexual reproduction culminates in formation of a totipotent zygote with the potential to produce a whole organism. Sperm chromatin reorganization and epigenetic reprogramming involving changes in DNA and histone modifications generate a totipotent mouse embryo within one cell cycle. Active DNA demethylation of the paternal genome has been proposed to involve base excision and DNA repair-based mechanisms. The nature and consequence of DNA lesions generated during reprogramming is not known. Using mouse genetics and chemical biology, we discovered that Tet3-dependent zygotic reprogramming generates paternal DNA lesions that are monitored by a surveillance mechanism. In vivo structure-function rescue assays revealed that cohesin-dependent repair of paternal DNA lesions prevents activation of a Chk1-dependent checkpoint that delays mitotic entry. We propose the zygotic checkpoint senses DNA lesions generated during paternal DNA demethylation and ensures reprogrammed loci are repaired before mitosis to prevent chromosome fragmentation, embryo loss and infertility.

**Wednesday, March 15, 2017 11:00am - 12:00pm**
Seminar Room, Lab Building East

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