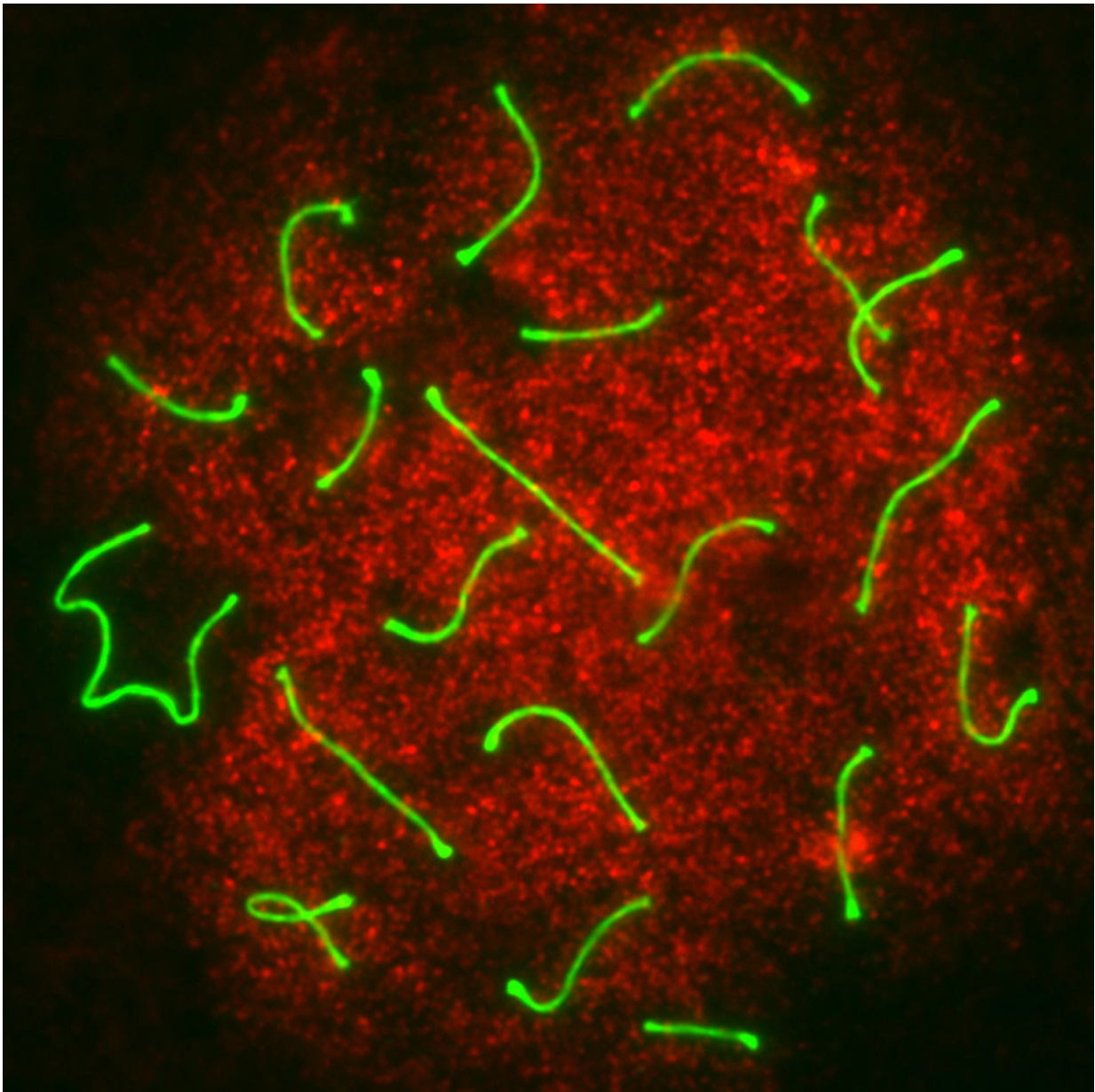


# Protein network linked to cancer is critical to male fertility

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This confocal microscope image from a study in the Oct. 18 online edition of *Cell Reports* shows spermatocytes in mice deficient for a Fanconi anemia pathway protein, *Fancd2*. The study from Cincinnati Children's Hospital Medical Center reports that mice lacking Fanconi anemia and DNA damage response proteins have disrupted sex chromosomes and are infertile, which the authors describe as a key finding in reproductive science. Credit: Cincinnati Children's

Researchers studying reproductive science identified a network of proteins often linked to cancer as also important to male fertility and the birth of healthy offspring, according to a study in the Oct. 18 online issue of *Cell Reports*.

The study by Satoshi Namewaka, PhD, and colleagues at Cincinnati Children's Hospital Medical Center focuses on the precise epigenetic regulation of the sex chromosomes, which is important to germline cells that make male sperm.

Epigenetics involves changes in organisms caused by modifications to gene expression, rather than alterations in the genetic code. Scientists increasingly study the epigenetics of reproduction to learn how environmental exposures or lifestyle may affect fertility or inherited traits in offspring.

The current study looks at the Fanconi anemia (FA) pathway, a network of 21 proteins that normally work to repair DNA damage in the body's cells. Mutations in the FA pathway can lead to severe anemia, genetic instability and different cancers. But the current study also uncovers roles in ensuring healthy human reproduction.

"Our data show the FA pathway regulates epigenetic programming in the germline and has an impact on reproduction," says Namewaka, lead

author in the Division of Reproductive Sciences at Cincinnati Children's. "Understanding the exact role of FA proteins in this regulation may also be important for understanding the substantial fertility defects associated with FA and the role of FA proteins in DNA repair."

The study is part of a much larger body of reproductive science exploring the causes of infertility, premature birth, birth defects and miscarriage - all still major health problems in the world.

Namekawa's team reports that during meiosis - a critical biological stage for the production of genetically healthy sperm - FA proteins accumulate on the male sex chromosomes. Certain FA proteins work with an enzyme called RNF8 to regulate histones, which form the spool that DNA wraps around inside a cell's nucleus.

The researchers tested the FA-DDR (DNA damage response) network's regulation of this process by studying meiosis in eight different mouse models. The mice were deficient for DDR proteins, including several Fanconi anemia proteins. This allowed the research team to unravel how FA-DDR proteins function in a pathway to regulate the male sex chromosomes, a key finding in reproductive science since disrupted sex chromosome regulation results in male infertility.

Data indicate that genetically modified mice lacking FA-DDR proteins are infertile and have substantial defects in the regulation of the male sex chromosomes during meiosis.

Scientists continue their research by digging deeper into how and when FA proteins and other DNA damage response proteins interact during meiosis, and how this affects sperm production and fertility in laboratory mouse models.

Provided by Cincinnati Children's Hospital Medical Center

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