SFU seeds discovery of mutant gene in chromosomes

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Simon Fraser University molecular biologists have discovered a gene whose job is to ensure that chromosomes are correctly distributed during the formation of eggs and sperm in mammals, including humans.

The discovery is a classic example of basic science leading to unanticipated results that may have important applications to treating and preventing gene-based diseases.

In this case, the researchers have isolated a genetic defect that causes chromosomal errors linked to infertility, Down's, Turner and Klinefelter's syndromes and many forms of cancer.

The thesis work of Lynnette Kuervers, a former doctoral student of SFU geneticist David Baillie, paved the way for Baillie and other North American scientists to uncover this new research.

They have pieced together how a genetic defect causes errors in the proper segregation of paired chromosomes into different cells, during meiosis, a process that generates eggs and sperm.

"Lynnette, who now lives in Ottawa, correctly concluded that a defective gene she discovered while studying other phenomena merited further investigation," says Baillie, a Canada Research chair in genomics. "She characterized the role of the gene in chromosome behaviour and her work was essential to further exploration of its importance."

While under Baillie's supervision in 2000, Kuervers discovered the defective gene X non-disjunction factor (xnd-1). At the time, she was studying genes involved in molting and reproduction of Caenorhabditis elegans (C. elegans), which are tiny worms.

The defective gene's name was inspired by Kuervers' discovery that it wreaked havoc on normal X chromosome behaviour during meiosis. The chromosome is key to reproduction and gender determination.

Over the last 10 years, Baillie and American scientists have built on Kuervers' work and now report that xnd-1 disrupts normal DNA swapping between chromosomes as they pair up in preparation for meiosis.

In the Oct. 14, 2010 issue of *Nature*, Baillie and his colleagues describe how xnd-1 in C. elegans causes DNA swapping to occur in gene-rich, central areas of chromosomes rather than at their gene-scarce ends. The defective gene also completely prevents the DNA swapping process in X chromosomes.

"My hope is that this work will help us better understand how genetic material is distributed through each generation of mammals, including humans," says Baillie. "We'll be able to do this by examining how mutations in xnd-1 interact with mutations in other genes known to act during meiosis to form eggs and sperm."

Caenorhabditis elegans (C. elegans) is a model organism. During the last 40 years, geneticists and molecular biologists have used the tiny worm to study the function of many genes, which are shared by many mammals, including humans.

Hundreds of labs worldwide, including five at SFU, work with this organism. All of Baillie's research over the last 36 years, including some

involving worms being sent to space to study radiation effects, has revolved around studying mutant C. elegans.

Baillie's lab works on about 8,000 genetic variants of C. elegans, most of which have been created at SFU.

xnd-1:
Crossovers of DNA information join duplicated meiotic chromosomes to facilitate their proper segregation. Crossover formation begins with the introduction of meiosis-specific double-strand breaks. The authors of this research have identified a new gene in C. elegans, xnd-1, that is required for crossover distribution on both the X and the autosomal (non-sex related) chromosomes. Preliminary findings suggest that xnd-1 does this by regulating certain proteins and enzymes.

Provided by Simon Fraser University