Study may lead to greater understanding of human genome regulation

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Many multi-cellular animals use sex chromosomes to determine sex. In fruit flies and in humans, this produces XX for females and XY for males. Cellular mechanisms then kick into gear to compensate the two-to-one imbalance of X-linked genes in females and males.

Victoria Meller, Ph.D., associate professor of biological sciences and resident of Huntington Woods, Mich., received $301,392 from the National Institute of General Medical Sciences of the National Institutes of Health to investigate the role of a type of RNA in the X chromosome dosage compensation of Drosophila, or fruit flies. The findings are likely to improve the understanding of gene regulation in humans, which employ similar cellular tools to regulate their complex genome.

Uncovering clues in genetic regulation in humans is instrumental in understanding a wide range of pathologies, including cancer, developmental abnormalities and some birth defects. The misregulation of large groups of genes is characteristic of these diseases.

There are significant differences in the way humans and fruit flies achieve X chromosome dosage compensation. "Humans double the expression of genes on the X chromosome, then deactivate one X chromosome in the female," Meller said. "Taking a much simpler approach, fruit flies double the X-expression from the male X chromosome and keep the female level the same."

Although these approaches differ, humans and flies both use regulatory

complexes that recognize the X chromosome. These complexes bind to and alter chromatin, the structure formed by DNA and associated proteins, to change the expression of the entire chromosome. "It's somewhat of a mystery, though, how these complexes identify the X chromosome," Meller said.

Recently, Meller's lab uncovered clues that a class of non-coding RNA called RNAi plays a role in X chromosome recognition. Her current study will explore the role of RNAi, along with short DNA sequences on the X chromosome, in X chromosome recognition.

Because of the similarities of human and fruit fly X chromosome recognition, findings from Meller's lab are likely to contribute to the understanding of gene regulation in humans. "Exploring how organisms achieve overall regulation of large groups of genes is basic research," said Meller. "Flies and mammals have the same tool kit for regulating their genome, and we are looking at how they use it."

"New information on how regulation works may lead to greater understanding of how those systems sometimes fail – and how future medical interventions can potentially treat these health problems," Meller said.

Provided by Wayne State University

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