Medical Xpress

Epigenetics helps explain early-onset puberty in females

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New research from Oregon Health & Science University has provided significant insight into the reasons why early-onset puberty occurs in females. The research, which was conducted at OHSU's Oregon National Primate Research Center, is published in the current early online edition of the journal *Nature Neuroscience*.

The paper explains how OHSU scientists are investigating the role of epigenetics in the control of puberty. Epigenetics refers to changes in gene activity linked to external factors that do not involve changes to the genetic code itself. The OHSU scientists believe improved understanding of these complex protein/gene interactions will lead to greater understanding of both early-onset (precocious) puberty and delayed puberty, and highlight new therapy avenues.

To conduct this research, scientists studied female rats, which like their human counterparts, go through puberty as part of their early aging process. These studies revealed that a group of proteins, called PcG proteins, regulate the activity of a gene called the Kiss1 gene, which is required for puberty to occur. When these PcG proteins diminish, Kiss1 is activated and puberty begins.

PcG proteins are produced by another set of genes that act as a biological switch during the embryonic stage of life. The role of these proteins is to turn off specific downstream genes at key developmental stages.

OHSU scientists found that both the activity of these "master" genes and their ability to turn off puberty are impacted by two forms of epigenetic control: a chemical modification of DNA known as DNA methylation, and changes in the composition of histones, a specialized set of proteins that modify gene activity by interacting with DNA.

Using this new information, researchers were then able to delay puberty in female rats. They accomplished this by increasing PcG protein levels in the hypothalamus of the brain using a targeted gene therapy approach so that Kiss1 activation failed to occur at the normal time in life. The hypothalamus is a region of the brain that controls reproductive development.

"While it was always understood that an organism's genes determine the timing of puberty, the role of epigenetics in this process has never been recorded until now," said Alejandro Lomniczi, Ph.D., a scientist in the Division of Neuroscience at the OHSU Oregon National Primate Research Center.

"Because epigenetic changes are driven by environmental, metabolic and cell-to-cell influences, these findings raise the possibility that a significant percentage of precocious and delayed puberty cases occurring in humans may be the result of environmental factors and other alterations in epigenetic control," said Sergio Ojeda, D.V.M, who is also a scientist in the Division of Neuroscience at the OHSU ONPRC.

"There is also much more to be learned about the way that epigenetic factors may link environmental factors such as nutrition, man-made chemicals, social interactions and other day-today influences to the timing and completion of normal puberty."

Provided by Oregon Health & Science University