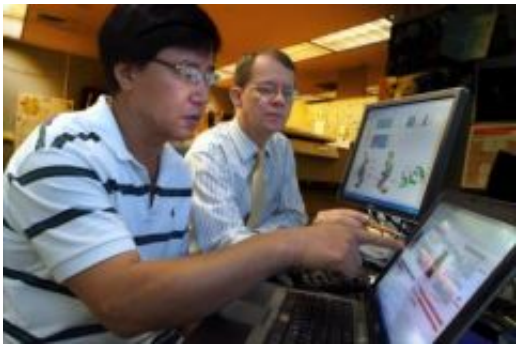
Scientists identify new gene responsible for puberty disorders

October 27 2008



A new gene responsible for some puberty disorders has been identified by Medical College of Georgia researchers. They found that the gene mutated in CHARGE syndrome -- a multi-system disorder characterized by diverse problems from heart defects to hearing loss to cleft lip and palate and mental retardation - also accounts for about 6 percent of two puberty disorders -- idiopathic hypogonadotropic hypogonadism, or IHH, and Kallmann syndrome. Credit: Medical College of Georgia

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They found that the gene mutated in CHARGE syndrome – a multi-system disorder characterized by diverse problems from heart defects to hearing loss to cleft lip and palate and mental retardation – also accounts for about 6 percent of two puberty disorders. These disorders – idiopathic hypogonadotropic hypogonadism, or IHH, and Kallmann

syndrome – short circuit puberty and can cause infertility. Kallmann syndrome is also marked by patients' inability to smell.

Dr. Lawrence Layman, chief of the MCG Section of Reproductive Endocrinology, Infertility and Genetics in the School of Medicine, and colleagues published an article in the October issue of *The American Journal of Human Genetics* linking the diseases.

CHARGE syndrome can also impair the sense of smell and inhibit production of sex steroids and hormones, so researchers suspected a common gene.

"Thinking that IHH and Kallmann syndrome could represent a milder version of CHARGE Syndrome, we set out to study the gene in a large sample of patients diagnosed with delayed puberty but not CHARGE," Dr. Layman says.

The identified gene is called chromodomain helicase DNA binding protein 7, or CHD7. In 101 people with IHH and Kallmann syndrome, researchers found seven mutations of CHD7 that weren't present in nearly 200 healthy individuals.

"This suggests that they were mutations causing the disorder, and we also showed that most of these mutations impaired the gene's function," Dr. Layman says.

Typically, puberty begins around age 10 in boys and age 8 or 9 in girls. It starts when the hypothalamus in the brain releases more gonadotropin releasing hormone, or GnRH, which stimulates the pituitary gland to make puberty-related hormones. This prompts ovaries to produce estrogen and eggs and testes to produce testosterone and sperm.

Pubertal disorders, Dr. Layman says, often begin long before that chain

of events begins.

He traces the defects to gestation, when neurons linked to reproduction and sense of smell fail to reach their destination together.

"While the discovery of additional genes involved in pubertal disorders is significant, we only know the cause for about one-third of all affected patients," says Hyung-Goo Kim, molecular geneticist in the Institute of Molecular Medicine and Genetics and the study's first author. "We know now that CHD7, only the second gene identified as a cause for IHH and Kallmann Syndrome, is a common culprit."

"There is still work to be done," says Dr. Layman, corresponding author. "But this work is important because it gives us cause for genetic counseling on patients with these mutations. And because these findings suggest that IHH and Kallmann Syndrome are mild variants of CHARGE, it also prompts us to look more carefully for heart problems, hearing loss and cleft lip/palate in patients with pubertal abnormalities."

Source: Medical College of Georgia