# ATA: mutation in X-linked gene tied to central hypothyroidism

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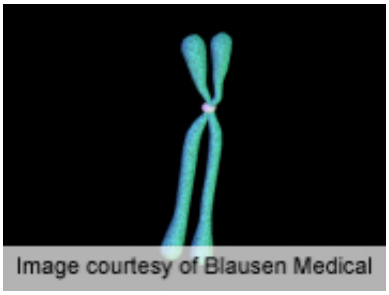


Mutations in the X-linked immunoglobulin superfamily member 1 gene, which encodes a pituitary-enriched plasma membrane glycoprotein, may play a role in central hypothyroidism, testicular enlargement, and variable prolactin deficiency, according to a study presented at the annual meeting of the American Thyroid Association, held from Sept. 19 to 23 in Montreal.

(HealthDay)—Mutations in the X-linked immunoglobulin superfamily member 1 (*IGSF1*) gene, which encodes a pituitary-enriched plasma membrane glycoprotein, may play a role in central hypothyroidism, testicular enlargement, and variable prolactin deficiency, according to a study presented at the annual meeting of the American Thyroid Association (ATA), held from Sept. 19 to 23 in Montreal.

Noting that specific mutations in the thyrotropin-releasing hormone receptor or thyroid-stimulating hormone (TSH)b subunit genes are the only known causes of isolated TSH deficiency, which can cause central hypothyroidism, Nadia Schoenmakers, Ph.D., from the University of

Cambridge in the United Kingdom, and colleagues used whole exome and candidate gene sequencing in 10 unrelated families with males exhibiting isolated TSH deficiency, testicular enlargement, and variably low serum prolactin levels.

In affected males, the researchers identified nine mutations in the *IGSF1* gene. Disease-associated mutations blocked *IGSF1* trafficking from the endoplasmic reticulum to the membrane, indicative of loss-of-function. Adult male *IGSF1* null mice exhibited similar features of the human disorder, including decreased pituitary TSH content and circulating thyroxine levels, in addition to increased body weight and fat mass.

"*IGSF1* involvement in central hypothyroidism is an important discovery because it creates inroads into our understanding of this rare syndrome, as well as new avenues by which it might be possible one day to control thyroid and testicular function," Douglas Forrest, Ph.D., program co-chair of the annual ATA meeting, said in a statement.

**More information:** Abstract No. Oral 1
More Information