MKRN3 Gene

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1. Introduction

The *MKRN3* gene provides instructions for making a protein called makorin ring finger protein 3 (MKRN3). This protein plays a role in directing the onset of puberty, which describes the changes in the body related to sexual development that normally occur in adolescence. Puberty begins when a gland in the brain called the hypothalamus is stimulated to release bursts of a hormone called gonadotropin releasing hormone (GnRH). This hormone triggers the release of other hormones that direct sexual development. Research suggests that the MKRN3 protein blocks (inhibits) the release of GnRH from the hypothalamus, thus holding off the onset of puberty.

The exact function of the MKRN3 protein is unknown. Based on its structure, the protein is thought to play a role in the cell machinery that breaks down (degrades) unwanted proteins, called the ubiquitin-proteasome system, by helping attach a molecule called ubiquitin to unwanted proteins. Ubiquitin acts as a signal to the ubiquitin-proteasome system to break the protein down. Researchers speculate that MKRN3 adds ubiquitin to proteins that would otherwise stimulate GnRH release. The breakdown of such proteins ensures that puberty does not begin until the right time.

For most genes, both copies of the gene (one copy inherited from each parent) are active in all cells. However, the activity of the *MKRN3* gene depends on which parent it was inherited from. Only the copy inherited from a person's father is active; the copy inherited from the mother is not active. This sort of parent-specific difference in gene activation is caused by a phenomenon called genomic imprinting.

2. Health Conditions Related to Genetic Changes

2.1. Central precocious puberty

More than 20 *MKRN3* gene mutations have been found to cause central precocious puberty. Individuals with this condition develop the signs of puberty earlier than normal, before age 8 in girls and before age 9 in boys. These signs include development of breasts and the start of a menstrual period in girls, enlargement of the testes and penis in boys, and development of pubic hair and a growth spurt in both girls and boys.

The *MKRN3* gene mutations involved in central precocious puberty are thought to lead to production of a nonfunctional MKRN3 protein from one copy of the gene. Because the other copy of the gene is inactive, affected individuals likely produce no functional MKRN3 protein. Although the mechanism is unclear, researchers speculate that without the MKRN3 protein to inhibit GnRH release, the hypothalamus releases bursts of the hormone, which stimulates the onset of puberty earlier than normal.

Because only the copy of the *MKRN3* gene from the father is active, the condition can only be inherited from a person's father.

3. Other Names for This Gene

- CPPB2
- D15S9
- MGC88288

- probable E3 ubiquitin-protein ligase makorin-3
- RING finger protein 63
- RNF63
- ZFP127
- zinc finger protein 127
- ZNF127

References

1. Abreu AP, Dauber A, Macedo DB, Noel SD, Brito VN, Gill JC, Cukier P, Thompson IR, Navarro VM, Gagliardi PC, Rodrigues T, Kochi C, Longui CA, Beckers D, deZegher F, Montenegro LR, Mendonca BB, Carroll RS, Hirschhorn JN, Latronico AC,Kaiser UB. Central precocious puberty caused by mutations in the imprinted geneMKRN3. N Engl J Med. 2013 Jun 27;368(26):2467-75. doi: 10.1056/NEJMoa1302160.
2. Hagen CP, Sørensen K, Mieritz MG, Johannsen TH, Almstrup K, Juul A.Circulating MKRN3 levels decline prior to pubertal onset and through puberty: alongitudinal study of healthy girls. J Clin Endocrinol Metab. 2015May;100(5):1920-6. doi: 10.1210/jc.2014-4462.
3. Neocleous V, Shammas C, Phelan MM, Nicolaou S, Phylactou LA, Skordis N. Insilico analysis of a novel MKRN3 missense mutation in familial central precociouspuberty. Clin Endocrinol (Oxf). 2016 Jan;84(1):80-4. doi: 10.1111/cen.12854.
4. Simon D, Ba I, Mekhail N, Ecosse E, Paulsen A, Zenaty D, Houang M, JesuranPerelroizen M, de Filippo GP, Salerno M, Simonin G, Reynaud R, Carel JC, Léger J,de Roux N. Mutations in the maternally imprinted gene MKRN3 are common infamilial central precocious puberty. Eur J Endocrinol. 2016 Jan;174(1):1-8. doi: 10.1530/EJE-15-0488.