MTOR Gene

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mechanistic target of rapamycin kinase

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1. Introduction

The *MTOR* gene provides instructions for making a protein called mTOR. This protein is found in various cell types throughout the body including brain cells. It interacts with other proteins to form two distinct protein groups, called mTOR complex 1 (mTORC1) and mTOR complex 2 (mTORC2). Both of these complexes transmit signals that direct the cells' function. Signaling through mTORC1 and mTORC2 regulate protein production, which influences cell growth, division, and survival. This mTOR signaling is especially important for growth and development of the brain, and it plays a role in a process called synaptic plasticity, which is the ability of the connections between nerve cells (synapses) to change and adapt over time in response to experience. Synaptic plasticity is critical for learning and memory.

2. Health Conditions Related to Genetic Changes

2.1. Smith-Kingsmore syndrome

Mutations in the *MTOR* gene cause a neurological disorder called Smith-Kingsmore syndrome. Individuals with this condition typically have a head that is larger than normal (macrocephaly), intellectual disability, and seizures. Affected individuals can also have unusual facial features, a behavioral condition called attention-deficit/hyperactivity disorder (ADHD), or autism spectrum disorder, which affects communication and social interaction.

MTOR gene mutations that cause Smith-Kingsmore syndrome are germline mutations, which means they are present in cells throughout the body. The most common mutation, found in nearly half of affected individuals, changes a single protein building block (amino acid) in the mTOR protein. Specifically, the amino acid glutamic acid is replaced by the amino acid lysine at protein position 1799 (written as Glu1799Lys or E1799K). This and other *MTOR* gene mutations are called "gain-of-function" because they increase the activity of the mTOR protein and, consequently, mTOR signaling. As a result, protein production normally regulated by mTORC1 or mTORC2 is uncontrolled, which impacts cell growth and division and other cellular processes. Too much mTOR signaling in brain cells disrupts brain growth and development and synaptic plasticity, leading to macrocephaly, intellectual disability, seizures, and other neurological problems in people with Smith-Kingsmore syndrome. Excessive mTOR signaling in other parts of the body likely underlies other, less common signs and symptoms of the condition.

2.2. Other disorders

Mutations in the *MTOR* gene can cause a spectrum of neurological disorders that result from abnormal development of the brain. This spectrum includes focal cortical dysplasia, which is characterized by malformation of the outer surface of the brain (the cerebral cortex), and hemimegalencephaly, which is enlargement of one side of the brain. These conditions are associated with recurrent seizures (epilepsy) that do not respond to treatment. The gene mutations involved in these disorders occur after conception and are not found in every cell in the body.

As in Smith-Kingsmore syndrome (described above), the genetic changes that cause focal cortical dysplasia and hemimegalencephaly are gain-of-function mutations. They abnormally increase mTOR signaling in brain cells, disrupting brain growth and development and leading to seizures.

3. Other Names for This Gene

- FK506 binding protein 12-rapamycin associated protein 2

- FK506-binding protein 12-rapamycin complex-associated protein 1
- FKBP-rapamycin associated protein
- FKBP12-rapamycin complex-associated protein 1
- FLJ44809
- FRAP
- FRAP1
- FRAP2
- mammalian target of rapamycin
- mechanistic target of rapamycin (serine/threonine kinase)
- RAFT1
- rapamycin and FKBP12 target 1
- rapamycin associated protein FRAP2
- rapamycin target protein 1
- RAPT1
- serine/threonine-protein kinase mTOR
- SKS

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