DOCK8 Gene

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Dedicator of Cytokinesis 8

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1. Normal Function

The *DOCK8* gene provides instructions for making a member of the DOCK family of proteins. The proteins in this family act as guanine nucleotide exchange factors (GEFs). GEFs turn on (activate) proteins called GTPases, which play an important role in chemical signaling within cells. Signaling stimulated by DOCK family proteins are typically involved in the arrangement of the structural framework inside cells (the cytoskeleton). By controlling the shape of the cytoskeleton, DOCK family proteins play a role in cell structure and movement (migration).

The DOCK8 protein is found most abundantly in cells of the immune system. This protein plays a critical role in the survival and function of several types of immune system cells, including T cells, NK cells, and B cells. T cells and NK cells recognize and attack foreign invaders, such as viruses, to prevent infection. B cells produce proteins called antibodies, which attach to foreign particles and germs and mark them for destruction.

Through its function as a GEF, the DOCK8 protein helps maintain the structure and integrity of T cells and NK cells. It also aids in the movement of these immune system cells to sites of infection, particularly the skin. The DOCK8 protein is also involved in chemical signaling pathways that stimulate B cells to mature and produce antibodies. The protein is also involved in the normal development and survival of other types of immune system cells.

2. Health Conditions Related to Genetic Changes

2.1 DOCK8 Immunodeficiency Syndrome

More than 130 mutations in the *DOCK8* gene have been found to cause DOCK8 immunodeficiency syndrome (also called autosomal recessive hyper-IgE syndrome or AR-HIES). DOCK8 immunodeficiency syndrome is an immune system disorder that causes recurrent severe infections of the skin and respiratory tract. Affected individuals may have other immune system problems, such as allergies, asthma, or an inflammatory skin disorder called eczema. Most of the mutations involved in DOCK8 immunodeficiency syndrome delete regions of DNA from the *DOCK8* gene. These deletions and other *DOCK8* gene mutations lead to production of an abnormally short protein or production of no protein. As a result, affected individuals have little or no functional DOCK8 protein.

A shortage of DOCK8 protein impairs normal immune cell development and function. It is thought that T cells lacking DOCK8 protein cannot maintain their shape as they move through dense spaces, such as those found within the skin. The abnormal cells die too easily, resulting in reduced numbers of these cells. A shortage of T cells impairs the immune response to foreign invaders, accounting for the severe skin infections common in DOCK8 immunodeficiency syndrome. A lack of DOCK8 protein also impairs B cell maturation and the production of certain antibodies. Impairment of this type of immune response leads to recurrent respiratory tract infections in people with this disorder.

For unknown reasons, a reduction of DOCK8 protein results in higher-than-normal production of an immune system protein known as immunoglobulin E (IgE), which plays a role in allergic reactions. As a result, people with DOCK8 immunodeficiency syndrome have an increased risk of food and environmental allergies.

3. Other Names for This Gene

- 1200017A24Rik

- dedicator of cytokinesis protein 8 isoform 1
- dedicator of cytokinesis protein 8 isoform 2
- dedicator of cytokinesis protein 8 isoform 3
- epididymis luminal protein 205
- FLJ00026
- FLJ00152
- FLJ00346
- HEL-205
- MRD2
- ZIR8

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