CARD14 Gene

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Contributor: Vicky Zhou

caspase recruitment domain family member 14

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1. Normal Function

The *CARD14* gene provides instructions for making a protein that turns on (activates) a group of interacting proteins known as nuclear factor-kappa-B (NF-κB). The NF-κB protein complex regulates the activity of multiple genes, including genes that control the body's immune responses and inflammatory reactions. Inflammation is a normal immune system response to injury and foreign invaders (such as bacteria). The NF-κB protein complex also protects cells from certain signals that would otherwise cause them to self-destruct (undergo apoptosis).

The CARD14 protein is found in many of the body's tissues, but it is particularly abundant in the skin. NF-κB signaling appears to play important roles in regulating inflammatory reactions in the skin and in promoting the survival of skin cells.

2. Health Conditions Related to Genetic Changes

2.1. Generalized Pustular Psoriasis

At least three *CARD14* gene mutations have been found in people with generalized pustular psoriasis (GPP), a rare and severe form of an inflammatory skin disorder called psoriasis. Individuals with GPP have repeated episodes in which large areas of skin become red and inflamed and develop small pus-filled blisters (pustules). The skin problems can be accompanied by fever and other signs of inflammation throughout the body (systemic inflammation). The episodes are thought to be triggered by infections, certain medications, pregnancy, or other stresses on the body. Most people with *CARD14*-associated GPP also have symptoms of the most common form of psoriasis called psoriasis vulgaris (PV), which is characterized by red, scaly patches of skin (plaques).

The *CARD14* gene mutations associated with GPP (including GPP with PV) lead to production of an altered CARD14 protein that more readily turns on NF-κB. Overactive NF-κB signaling increases the activity of genes involved in the body's inflammatory response. The resulting abnormal inflammation contributes to the skin problems characteristic of GPP and PV.

CARD14 gene mutations increase the risk of developing GPP. Not everyone with a mutation in this gene has the characteristic problems with inflammation. This complex condition is thought to arise from a combination of genetic and environmental factors.

2.2. Familial Pityriasis Rubra Pilaris

At least three mutations in the *CARD14* gene have been identified in people with familial pityriasis rubra pilaris, a rare hereditary skin condition characterized by a patchy, salmon-colored skin rash covered in fine scales. These mutations lead to overactivation of NF-κB signaling, which triggers an abnormal inflammatory response in the skin. Researchers are working to determine how these changes lead to the specific features of familial pityriasis rubra pilaris.

2.3. Psoriatic Arthritis

Psoriatic arthritis

2.4. Other Disorders

Changes in the *CARD14* gene may also contribute to other forms of psoriasis. At least two mutations have been identified in families with psoriasis. Several other rare variants of the *CARD14* gene have been associated with an increased risk of psoriasis in people without a family history of the disorder. Studies suggest that these genetic changes enhance activation of NF-κB, resulting in abnormal inflammation, which is a characteristic feature of psoriasis. However, *CARD14* gene mutations appear to be an uncommon risk factor for this condition. Additional factors in combination with the particular *CARD14* gene mutation may help determine which form of skin inflammation develops.

3. Other Names for This Gene

- bcl10-interacting maguk protein 2
- BIMP2
- CAR14_HUMAN
- CARD-containing MAGUK protein 2
- card-maguk protein 2
- carma 2
- CARMA2
- caspase recruitment domain family, member 14
- caspase recruitment domain-containing protein 14

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