

## CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME (CAPS)

### *A Rare Disease with High Unmet Medical Needs*

#### **What is CAPS?**

Cryopyrin-Associated Periodic Syndrome (CAPS) comprises a group of very rare, genetic and potentially life-threatening auto-inflammatory diseases with debilitating symptoms and limited treatment options. There are three recognized forms of CAPS disorders:

- Familial Cold Auto-inflammatory Syndrome (FCAS) - also known as Familial Cold Urticaria or Familial Cold Urticaria Syndrome
- Muckle-Wells Syndrome (MWS)
- Neonatal-Onset Multisystem Inflammatory Disease (NOMID) - also known as Chronic Infantile Neurological Cutaneous Articular Syndrome (CINCA).

These disorders are believed to represent related conditions along a spectrum of disease severity, with FCAS having the least severe physical manifestations of the disease and NOMID/CINCA sufferers experiencing the most severe physical manifestations.

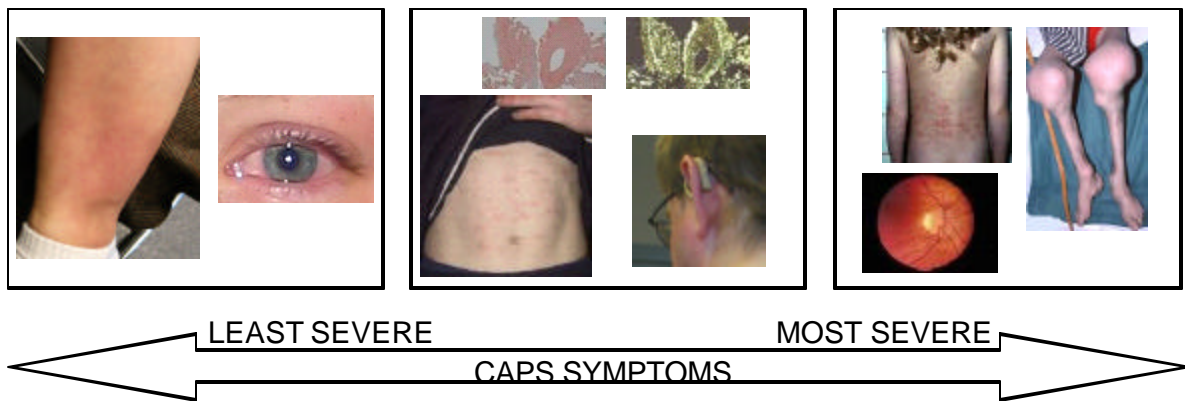


Figure 1: Severity of CAPS inflammation

#### **What symptoms are associated with CAPS?**

CAPS symptoms are almost always present from birth or infancy, and can occur daily throughout patients' lives. Symptoms include skin rash, fever, conjunctivitis, headaches and joint pain. Long-term consequences can be serious and potentially fatal, and include sensory-neural deafness, bone and joint deformities, central nervous system damage leading to visual loss, and amyloidosis, leading to renal failure and early death.

About 25% of patients develop amyloidosis that results in renal failure and can be life-threatening.

#### **What causes CAPS?**

FCAS, MWS and NOMID/CINCA are all caused by a mutation in the CIAS1 gene (also known as the NLRP3 gene).

The CIAS1 gene is responsible for production of a protein called cryopyrin that lends its name to the CAPS group of diseases. This protein plays important roles in controlling the body's defenses and regulating the production of molecules involved in helping the body fight off foreign invaders. The mutation of CIAS1 activates a complex cascade that ultimately results in the symptoms seen in CAPS.

In a healthy body, when triggered by a 'danger' signal, cryopyrin assembles with other molecules to coordinate an inflammatory response. This sensing and coordinating unit is called an inflammasome. This inflammatory response causes increased production of a molecule called interleukin-1 $\beta$  (IL-1 $\beta$ ), which is part of the body's immune system defenses and plays a key role in inflammation.

Researchers have found that mutations in the CIAS1 gene cause the cryopyrin protein to constantly overproduce IL-1 $\beta$  instead of producing it only in response to infection or injury. Overproduction of IL-1 $\beta$  leads the body to attack itself, causing inflammation and resulting in the symptoms seen in CAPS diseases.

### **How rare is CAPS?**

The mutation in the CIAS1 gene that causes CAPS is believed to occur in 1 out of 1 million people worldwide and there are believed to be around 300 people in the US with FCAS. However, these are only statistical estimates. Some believe that these disorders may be more prevalent, but due to lack of awareness and diagnosis – or misdiagnosis – the number of sufferers may be larger than estimated.

Traditionally, rare diseases like CAPS have been neglected, in terms of research, drug development and public awareness. Patients with rare diseases face many common problems, including delayed or incorrect diagnosis, lack of disease information or support resources, scarce scientific knowledge about their disease and lack of appropriate healthcare options.

Novartis is committed to collaborating with third-party medical and academic institutions to improve disease knowledge and resources for patients and families living with rare diseases and to develop innovative treatments to serve the unmet medical needs of those patients.

### **How is CAPS diagnosed?**

The CIAS1 genetic mutation is autosomal dominant, meaning that only one parent needs to be carrying the mutated CIAS1 gene in order for it to be passed on to the child. In FCAS and MWS, the gene mutation is usually passed down by one affected parent through many generations.

Mutation of the CIAS1 gene can also occur spontaneously at conception, as is often the case in NOMID/CINCA. However, some CAPS patients have no detectable genetic mutation. For this reason a clinical diagnosis based on symptoms is essential. The proper diagnosis of CAPS should include genetic testing for CIAS1 and other auto-inflammatory disorders, lab tests, a skin biopsy, a full evaluation of symptoms and a complete medical history from birth onwards.

Due to the rarity of CAPS disorders, patients can struggle for many years before being correctly diagnosed. Early and correct diagnosis is critical, as newer medications are being investigated that may help patients manage debilitating symptoms and prevent permanent damage caused by the long-term inflammation associated with CAPS.

**Further information**

A number of not-for-profit organizations operate with the aim of raising awareness of rare diseases such as CAPS. Further information on CAPS and rare diseases can be found by contacting the following organizations:

The NOMID Alliance  
P.O. Box 590354  
San Francisco, CA 94118  
United States of America  
Phone: +1 415-831-8782  
E-mail: [site\\_manager@nomidalliance.net](mailto:site_manager@nomidalliance.net)

National Organization for Rare Disorders (NORD)  
55 Kenosia Avenue  
PO Box 1968  
Danbury, CT 06813-1968  
United States of America  
Phone: +1 (203) 744 0100  
E-mail: [orphan@rarediseases.org](mailto:orphan@rarediseases.org)

OrphaNet  
Portal for rare diseases and orphan drugs  
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