# MUCKLE WELLS SYNDROME AS AN EXAMPLE OF HEREDITARY SYSTEMIC AUTOINFLAMMATORY DISEASE


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## 1.The Disease: Muckle Wells Syndrome (MWS)

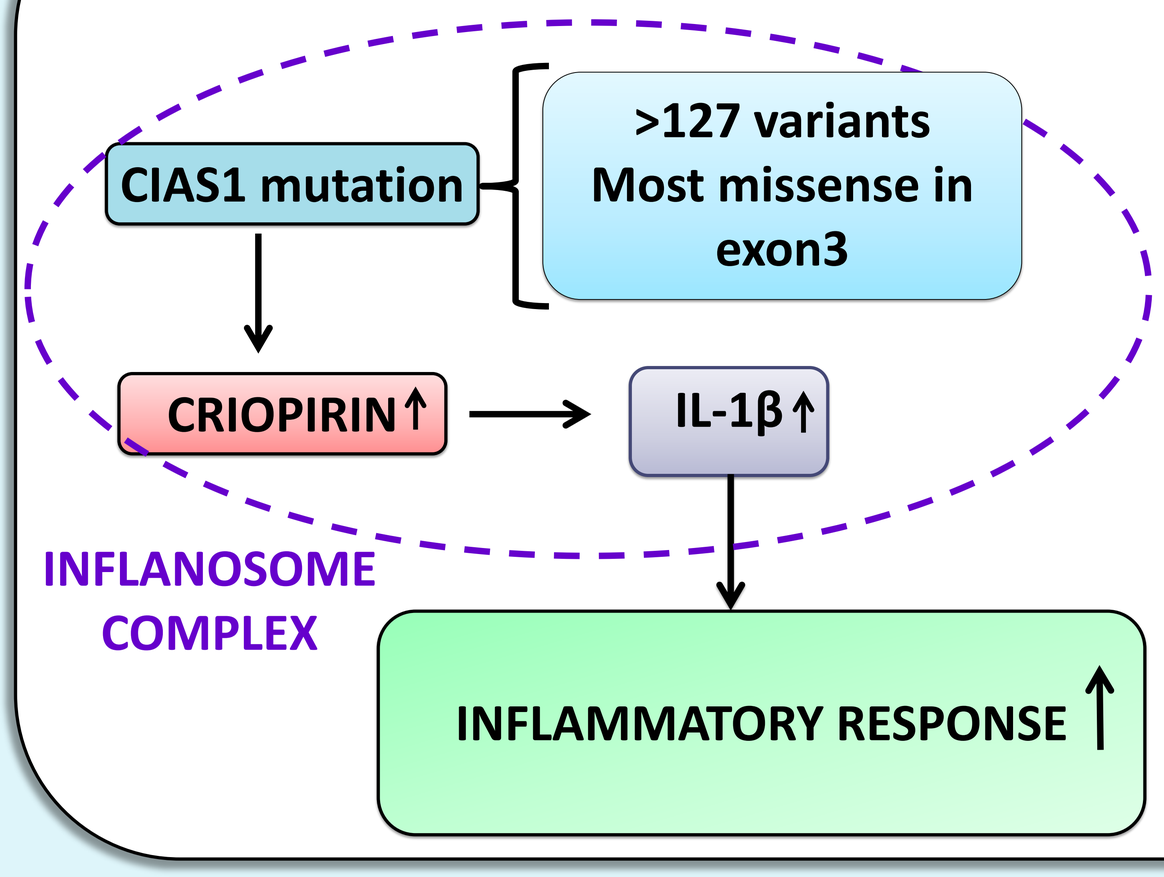
MWS is included in a group of inflammatory diseases called Criopirin Associated Periodic Syndrome (CAPS), at the same time, CAPS are included in a bigger group , Hereditary Systemic Autoinflammatory Diseases (HSAD). All of the syndromes included in CAPS, are associated with mutations in CIAS1 gene , which encodes the protein criopirin.

**MWS** is a rare disease (1:1.000.00) that has a high autoinflammatory component. Its inheritance is autosomical dominant. MWS patients show a chronic and systemic inflammation without reason for develop it (no infection, no neoplasic procedure…).

## 2. Targets

- Learn what is the origin of MWS
- What is the molecular mechanism of the disease
- What are the current treatments
- What are the worst symptom

## 3. Molecular Mechanism




**CIAS1 mutations cause a bigger gene expression**

**Criopirin levels increase in response at the bigger expression**

**IL-1 levels increase because criopirin turn on caspase-1, that cuts the IL-1 and makes it active**

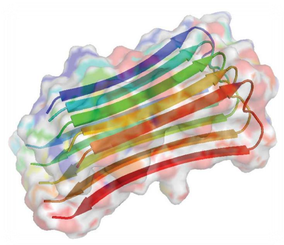
**IL-1 intermediate the inflammatory response by macrophages and monocytes and it is increased systemically**

References: (3)

## 4. Symptoms

Skin Rashes, Pain in the joints, Hearing loss, Fever, Headache, Conjunctivitis, Muscle pain, Proteinuria and **Potential AA Amiloidosis (25%)**

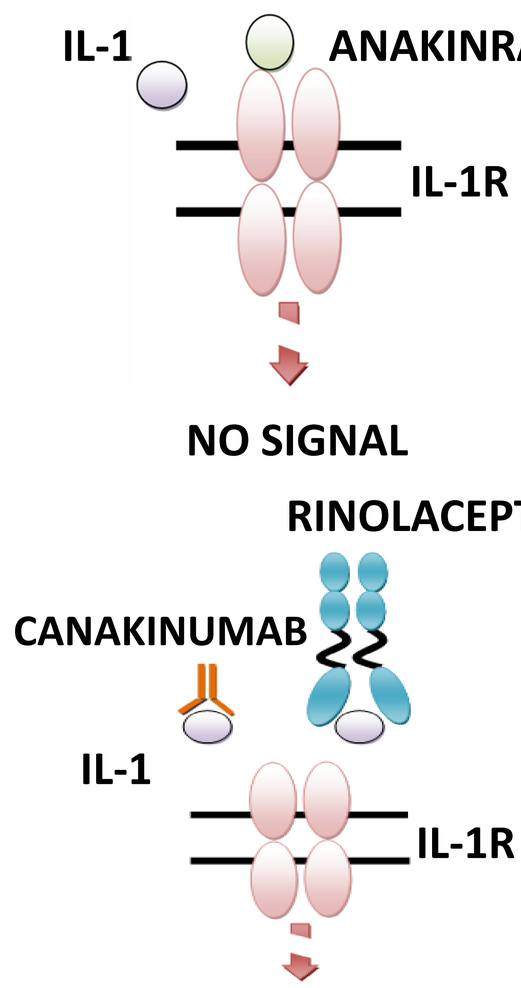
**Inflamation** → **IL-1, IL-6 , TNF↑** → **Increased SAA** → **Increased ability to form fibers and aggregates**



**Cross-β amyloid structure**. Image from Vanderbilt institute of Chemical Biology

References: (4)

## 5. Treatements




**ANAKINRA, IL-1R ANTAGONIST**

**RINOLACEPT, FUSION PROTEIN AGAINST IL-1β**

**CANAKINUMAB, HUMAN MONOCLONAL AB AGAINST IL-1 β**

References : (1), (2)

## 6. References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2. Hal M. Hoffman et. Al. Efficacy and Safety of Rinolacept (Interleukin-1 Trap) in Patients with Cryopyrin-Associated Periodic Syndromes. Atritis and Rheumatism 2008, 58; 2443-2452.
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4. Luis Bolaños,et al. Amiloidosis renal y tiroidea secundaria a síndrome periódico asociado a criopirinas (síndrome de Muckle-Wells) (mutación NLRP3). Nefrología, 2013, Vol33 ; nº 2.