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 (1:1,000,000) that has a high autoinflammatory component. Its inheritance is autosomal 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%)

Inflammation → 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. Treatments

ANAKINRA, IL-1R ANTAGONIST

RINOLACEPT, FUSION PROTEIN AGAINST IL-1β

CANAKINUMAB, HUMAN MONOCLONAL AB AGAINST IL-1β

References: (1), (2)

6. References