New targets for the treatment of autoinflammatory diseases

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The spectrum of autoinflammatory diseases (AID) is enlarging and overlapping with autoimmune and immunodeficiency disorders. The following treatment targets were mentioned:

Inflammasomopathies: Inflammasomes are important elements of the innate immune defense. The most common autoinflammatory syndromes, as well as a number of rare ones, are due to hereditary defects in the inflammasomes, hence are called inflammasomopathies (i.e. FMF, CAPS, HIDS/MKD). Activation of the inflammasomes results in the processing and subsequent secretion of the pro-inflammatory cytokines IL-1 beta and IL-18. Treatment target: Caspase 1, IL-1 beta and IL-18

NLRC4-MAS: NLRC4-Related Macrophage Activation Syndrome is an autoinflammatory syndrome caused by activating mutations in NLRC4. Macrophage Activation Syndrome (MAS) is a life-threatening systemic inflammatory complication of many rheumatic diseases and its causes are unknown. Treatment target: IL-18

Interferonopathies: Type I interferonopathies are a clinically heterogenic group of Mendelian inherited disorders(the inheritance of a single causative gene) linked to defective regulation of type I interferons (IFN), named type I interferonopathies. An increasing number of genetic diseases belonging to this family have later been discovered, including the Proteasome Associated Autoinflammatory Syndromes (PRAAS), IFN-stimulated gene 15 (ISG15) deficiency, Singleton-Merten syndrome and its atypical presentation (SMS), and stimulator of IFN genes (STING)-associated vasculopathy with onset in infancy (SAVI). Treatment target: Type I interferon

IL-36R: These cytokines have a central role in regulating inflammation, mediating many inflammatory diseases such as psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), ulcerative colitis and Crohn's disease. For patients with generalized pustular psoriasis (GPP), palmoplantar pustulosis (PPP) and DITRA, IL-36R Mab is being developed (ANB019). Treatment target: IL-36, IL-36R, IL-17, IL-23

DADA2: Deficiency of adenosine deaminase type 2 is an autosomal recessive (when you inherit two mutated genes, one from each parent) genetic disorder that involves inflammation of the body's tissues, especially the tissues that make up the blood vessels. Treatment target: TNF

TREATMENTS

There are two new anti-IL-1 agents for inflammasomopathies: RPH-104 (R-Pharm) and Lutikizumab (ABT-981), an anti-IL-1 alpha/IL-1 beta “dual variable domain” Mab.

As for targeting cytokines, the following treatments are used:
Anti-TNF: for patients with refractory arthritis, GI lesions
Tocilizumab: for patients with refractory arthritis, scleroderma-like lesions, in MKD and amyloidosis
Ustekinumab: for refractory patients with epithelial manifestations (i.e. pustular psoriasis)
Secukinumab: for refractory patients with epithelial manifestations (i.e. pustular psoriasis) or spondyloarthritis (concerns for IBD-like manifestations)

Treatments used for targeting proteins involved in immune activation are: Caspase 1 Belnacasan (VX 765, Vertex) and Caspase 1 inhibitor AC-201.