RESEARCH PROJECT:

Cryopyrin associated periodic syndromes (caps): investigations on patients blood cells and in a knock-in mouse model to exploit novel approaches for the modulation of the nlrp3 inflammasome

The aim of the research:

The cryopyrin associated periodic syndromes (CAPS) are a group of chronic or recurrent inflammatory diseases associated to mutations of a gene coding for Cryopyrin (NLRP3). This protein play a pivotal role in the regulation of production and secretion of IL-1β, one of the most potent pro-inflammatory cytokines via a important multi-protein complex called NLRP3 Inflammasome. The clinical manifestations associated with CAPS are: chronic systemic inflammation, urticarial rash, arthritis, chronic meningitis, sensorineural deafness and mental delay. Skeletal dysplasia may also be present, with variable limitation of daily activities. The beneficial effect of the recombinant IL-1 receptor antagonist (Anakinra) and anti.IL1 monoclonal antibody (Canakinumab) on the inflammatory manifestations of CAPS has been recently reported. However: i) not all CAPS-associated manifestations are controlled by anti-IL1 blockers (i.e. hearing loss, mental retardation and bone dysplasia, ii) some patients may gradually present a progressive resistance to Anakinra treatment; iii) the drug is expensive and not available in all Countries. In the former grant (GGP09127) we have analyzed a number of relevant pathogenic mechanisms associated to the disease. During the last year we have developed an animal mouse of CAPS, recapitulating the clinical and immunological features of huma disease. Aim of the present project is to identify new therapeutic approaches for the modulation of NLRP3 Inflammasome. These new approaches will applicable not only for CAPS, but for a number of other rare inherited inflammatory diseases (Autoinflammatory diseases) characterized by an over activation of NLRP3 Inflammasome.

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PRIVATE NON-PROFIT FUNDING BODY: FONDAZIONE TELETHON

Courtesy of Fondazione Telethon - C.F. 04879781005