Pavia, Italy  

Cryopyrin associated periodic syndromes (CAPS) are a group of autoinflammatory diseases linked to gain-of-function mutations in the NLRP3 inflammasome. These diseases are characterized by recurrent attacks of fever, inflammation, and tissue damage in multiple organ systems. Understanding the pathophysiology of CAPS is crucial for developing effective therapeutic strategies.

**Objectives:**
- To develop a novel NLRP3 knock-in (KI) mouse model of CAPS to evaluate amyloid deposition and to test alternative therapeutic approaches.

**Methods:**
- We generated Ki mice by engineering N475K mutation associated with CAPS phenotype into mouse Nlrp3 gene. Ki and Wild Type (WT) mice received PPIs or PBS intraperitoneally and were analyzed for survival, inflammation, cytokine secretion, and amyloidosis development.
- Cytokine secretion from bone marrow derived dendritic cells (BMDCs) and peritoneal macrophages (PMs) was evaluated by ELISA. Histological analysis of all organs was evaluated by hematoxylin and eosin staining. Amyloid deposition was quantified through Congo Red staining.

**Results:**
- Mutant NLRP3 Ki mice displayed features that recapitulate the immunological and clinical phenotype of CAPS. These mice had systemic inflammation, with high levels of serum pro-inflammatory cytokines compared to WT controls. Hystological analysis revealed the presence of acute and chronic inflammatory cell infiltrates and amyloid deposits in spleen, liver and kidneys. As in CAPS monocytes, BMDCs and PM from Ki mice showed a strong increase in IL-1β, IL-18, and IL-1α secretion and decreased levels in interleukin-1 receptor antagonist (IL-1Ra), the naturally occurring IL-1b inhibitor.

**Conclusion:**
- NLRP3 Ki mice display a strong clinical impact with improvement of inflammatory conditions and regression of amyloid deposits.

**Disclosure of Interests:**
- Yomei Shaw Grant/research support from: Unrestricted grant from MSD, Delphine Courvoisier/Grant/research support from: has received an unrestricted grant from MSD for this study, Consultant for: has received consulting fees from BMS, Pfizer, AB2 Bio and Janssens. 
- Paul J. Rothbard: None declared, Sabrina Chiesa: None declared, Marco Di Duca: None declared, Chiara Baldovini: None declared, Federica Penco: None declared, Anna Rubartelli: None declared, Laura Obici: None declared, Laura Obici: None declared. 

**References:**

**Disclosure of Interests:**
- Arinna Bertoni: None declared, Sonia Carta: None declared, Chiara Baldovini: None declared, Federica Penco: None declared, Enrica Balza: None declared, Silvia Borghini: None declared, Marco Di Duca: None declared, Emanuela Ogino: None declared, Paolo Nozza: None declared, Francesca Schena: None declared, Patricia Castellani: None declared, Lucia Pedroni: None declared, Laura Obici: None declared, Alberto Martini Consultant for: I do not have any conflict of interest to declare since starting from 1 March 2016 I became the Scientific Director of the G. Gaslini Hospital; therefore, my role does not allow me to render private consultancies resulting in personal income.
- I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below: AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.

The money received for these activities are directly transferred to the Gaslini Institute’s bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Isabella Ceccherini: None declared, Claudia Balza: None declared, Silvia Borghini: None declared, Marco Gattorno: None declared, Laura Obici: None declared.