P26 & FP – **Analysis of gut microbiota and immunological characterization in patients with Chronic Granulomatous Disease**

M. Pellicciotta[1,2], M. Chiriaco[3,4], S. Di Cesare[3,4], R. Rigoni[2,6], A. Finocchi[3] and B. Cassani [8,6]

[1] *Humanitas University, Rozzano, Italy*

[2] *Humanitas Clinical and Research Center, Rozzano, Italy*

[3] *University Department of Pediatrics, Childrens' Hospital Bambino Gesù, Rome, Italy*

[4] *Department of Systems Medicine, "University of Rome Tor Vergata", Italy*

[6] *IRGB, Milan Unit, CNR, Milan, Italy*

[8] *Fondazione Humanitas per la Ricerca, Rozzano, Italy*

Martina.pellicciotta@humanitasresearch.it

Background: Chronic granulomatous disease (CGD) is a primary immunodeficiency disorder of phagocytes, due to defect in the NADPH enzyme, resulting in impaired killing of bacteria and fungi. X-linked CGD is the most common genetic subgroup. In addition to phagocytes, the enzyme is expressed also in lymphocytes but its functional implication is still poorly characterized. Patients with CGD suffer from severe infections and deregulated inflammation. In particular, the mechanisms underlying the abnormal response of the intestinal immune system remain unclear.

Objective: To assess the link between microbiota and inflammation in condition of Nox-2 deficiency.

Methodology: PBMC of 13 CGD patients and 10 age-matched HD were analyzed by flow cytometry. The bacterial composition of fecal samples was determined, after DNA extraction, by 16S rRNA gene sequencing. Short Chain Fatty Acids (SCFAs) were quantified in fecal samples with a HPLC system. Fecal IgA were quantified by ELISA essay.

Results: Analysis at the enrollment showed diminished naïve CD4 and CD8 subsets and increased effector memory (CD45RA-CD27- and CD45RA-CCR7-) cells as well as a slight increase in the NKT subset. Despite normal B cell frequencies, the memory subsets (CD19+CD27+ unswitched and switched memory CD19+CD27+IgD-), were all below the normal range values. Analysis of intestinal microbiota composition revealed substantial differences between patients and age-matched healthy controls with a predominant skewing towards the inflammatory gamma-proteobacteria and enterobacteriacee species. Preliminary analysis of SCFAs showed a reduced faecal concentrations of butyric, acetic and propionic acid, both in adult and pediatric patients and decreased level of fecal IgA.

Conclusions / Implications for practice: Our studies will help to shed light on the pathogenic mechanisms underlying the IBD-like disease in CGD. We expect to identify a correlation between the type of mucosal and systemic immune responses, the composition of intestinal microbiota, and the clinical severity of intestinal pathology in patients. Studies are underway to investigate also the presence of rare genetic variants associated with IBD and, eventually, use them as biomarker and prognostic factor associated with the development of inflammatory intestinal manifestations, to redirect therapeutic approaches and improve the life quality of these patients.

References

-*Inflammatory bowel disease in chronic granulomatous disease: An emerging problem over a twenty years' experience*. Angelino G et al 2017