Microbiota Composition in HIV-positive and HIV-Exposed Uninfected Pediatric Subjects

E. Merlini[1*], M. Ficara[2], E. S. Cannizzo[1], F. Ferrari[2], C. Tincati[1], Laura Dotta[3], C. Tagliabue[4], A. Diana[5], V. Camelli[6], L. Iughetti[2,7], A. d'Arminio Monforte[1], M. Cellini[2], G. Marchetti[1] for the MIRROR Study Group

*(lead presenter) e-mail address of lead presenter: esther.merlini@gmail.com

[1]Clinic of Infectious Diseases, Dept Health Sciences, University of Milan, ASST Santi Paolo e Carlo, Milan, Italy; [2] Division of Paediatric Oncology-Haematology, Policlinico Hospital, Modena, Italy; [3]Clinica Pediatrica and "A. Nocivelli" Institute for Molecular Medicine, Department of Clinical and Experimental Sciences, University of Brescia, Spedali Civili Hospital, Brescia; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [5]Department of Translational Medical Science, Section of Pediatrics, University Federico II, Naples, Italy;[6] Dept of Sciences of Public Health and Pediatrics, University of Turin, Italy; [7]Pediatric Unit, Azienda Ospedaliero-Universitaria Policlinico, Modena, Italy

Keywords (maximum 8): microbiota, intestinal barrier, immune activation, pediatric individuals, HIV-exposed uninfected

A profound gut dysbiosis has been described in HIV+ adults, destabilizing the intestinal barrier and promoting disease progression. While in infants *in utero* HIV exposure and maternal microbiota seem to be the major players in shaping the microbiota composition and immune system, little is known on what happens in older pediatric subjects. We investigated fecal microbiota composition, intestinal barrier integrity and monocyte activation in HIV+ vs HIV-exposed uninfected (HEU) pediatric subjects.

We enrolled 80 children/adolescent (≤18 years), born from HIV+ mothers. Exclusion criteria: age <1year, hepatitis co-infection, prebiotic supplementation, antibiotic use in the past 2 weeks. Specimen: plasma, stool. Lab analyses: gut damage (I-FABP, E-Cadherin) and monocyte activation (sCD14) markers by ELISA; microbiota composition (alpha, beta diversity, relative abundance) by MiSeq Illumina tech. Statistical analyses as appropriate.

47 (59%) were HIV+ on cART, 33 (41%) HEU, with median age of 14 and 12 years respectively. The 2 groups significantly differ for feeding practice (p<.0001), delivery mode (p=.0005) and maternal cART during pregnancy (p<.0001). Interestingly, while I-FABP and E-Cadherin levels were similar (p=.960, p=.931), HIV+ showed higher sCD14 vs HEU (p<.0001). The gut microbiota analyses revealed a similar bacterial composition in terms of alpha diversity, beta diversity and relative abundance. Few differences were observed following the LEfSe analyses, with HIV+ showing bacteria belonging to the class of *Clostridia* alone, while HEU bacteria belonging to the class *Clostridia, Bacteroidetes*, *Alphaproteobacteria*. We restricted the analyses to individuals >5yrs (n=64), confirming no differences in microbiota composition. The LEfSe analyses highlighted higher prevalence of *Clostridia* in HIV+, *Bacteroidetes* and *Actinobacteria* in HEU.

In our cohort of HIV+ and HEU pediatric subjects, we describe similar gut microbiota and intestinal barrier integrity, yet higher sCD14 in HIV+. While the observation of comparable intestinal barrier integrity might support the positive role of cART in preserving gut integrity in pediatric subjects, the finding of higher monocyte activation seems to imply that residual inflammation, known driver of disease progression in the course of cART, lays its foundation already in the pediatric age.