P- 9 BIOMARKERS OF THE BACTERIAL, VIRAL AND HUMAN GUT TRANSCRIPTOME IN METABOLIC ASSOCIATED FATTY LIVER DISEASE (MAFLD) IN ARGENTINA

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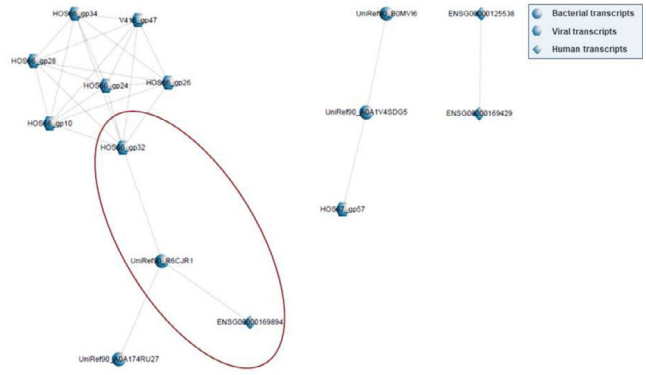
Introduction and Objectives: The functional dynamics of the gut microbiome and its interactions with the human transcriptome represent a niche for non-invasive biomarkers to risk-stratify MAFLD. This study aimed to identify gut transcriptomic signatures associated with MAFLD in Argentina.

Materials and Methods: Stool samples, diet, demographic and clinical data were obtained from 33 biopsy-proven MAFLD patients (12 simple steatosis -SS- and 21 steatohepatitis -SH-) and 19 healthy volunteers (HV). RNA-seq was performed in NovaSeq6000®. Data were analyzed with Maaslin2-v1.2.0, bioBakery-v1.8 and DESeq2-v4.1. Co-expression analysis was performed with Hmisc-v4.7-0.

Results: BMI was higher in MAFLD, particularly in SH patients ($q=4.49 \times 10^{-6}$). After adjusting for BMI, differentially expressed genes (DEGs) were found when comparing MAFLD *vs.* HV and SH *vs.* SS in bacterial (5 and 13, respectively), viral (112 and 26, respectively) and human (4 and 46, respectively), transcriptomes ($q<0.01$). Functional profiling of DEGs in MAFLD and SH patients revealed augmented bacterial sulfur and uric acid metabolisms, viral life cycle and viral regulation of the host immune system. Inflammatory regulation, lipid, iron and carbohydrate metabolisms, and response to oxidative stress were enhanced among human DEGs. After comparing transcript abundance, the most active bacterial families were *Bactereoidaceae*, *Rikenellaceae*, *Oscillospiraceae* and *Prevotellaceae* in all groups. *Bifidobacteriaceae* expression occurred mostly in HV, while *Prevotellaceae* prevailed in MAFLD patients. The *Firmicutes*/*Bacteroidetes* ratio was higher in MAFLD and SH. *Myoviridae*, *Podoviridae*, *Siphoviridae* and *Microviridae* were the most transcriptionally active viral families in all groups. *Myoviridae* and *Microviridae* showed up-regulated activity in MAFLD (FDR=0.006 for *Microviridae*) and SH groups (FDR=0.01 and 4.2×10^{-6}, respectively), whereas *Podoviridae* and *Siphoviridae* were less active in these groups. Significant correlations were observed between the expression of Faecalibacterium phage Mushu, *Prevotella copri* and the human mucin gene (Figure).

Conclusions: We identified specific signatures of the interaction between microbial and human gut transcriptomes that could be useful as non-invasive biomarkers of MAFLD diagnosis and progression.



Correlation network of the significant human, bacterial and viral transcriptome parameters of the MAFLD patients (p<0.01).
Edges represent positive correlations.
Significant correlations between expression of *Faecalibacterium phage Mushu* (HOS66_gp32), *Prevotella copri* (UniRef90_R6CJR1) and human mucin gene (ENSG00000169894) are highlighted.

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P-10 PATTERNS OF PROGRESSION AND TREATMENT DISCONTINUATION IN A REAL LIFE LATIN AMERICAN PROSPECTIVE COHORT STUDY OF INTERMEDIATE-ADVANCED HEPATOCELLULAR CARCINOMA: SECOND INTERIM ANALYSIS

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