

## **ALTERATIONS OF CIRCULATING MIRNAS AND MICROBIOME STRUCTURE IN SALIVA OF AUTISTIC CHILDREN ARE ASSOCIATED WITH COGNITIVE IMPAIRMENTS: POTENTIAL CROSS-TALKING AND DIAGNOSTIC APPLICATIONS**

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Recent evidence revealed that salivary molecules, as well as bacterial populations, can be perturbed by several pathological conditions, including neuro-psychiatric diseases. This relationship could be exploited to unveil new pathological mechanisms of elusive diseases, such as Autistic Spectrum Disorder (ASD) (1). We used a combined approach of miRNA expression profiling and microbiome analysis on saliva from 53 ASD and 27 NC children to investigate salivary ASD-related miRnome and microbiome alterations and their association with neuropsychological parameters.

After discovery and validation analysis, we demonstrated that 5 salivary miRNAs were statistically altered in ASD patients compared to NCs. Specifically, miR-29a-3p, -141-3p were upregulated, while let-7b-5p, miR-16-5p, -451a were downregulated in ASD saliva. The 16S rRNA microbiome sequencing analysis revealed statistically significant differences of abundance at the genus and species levels. In particular, *Rothia*, *Filifactor*, *Actinobacillus*, *Weeksellaceae*, *Ralstonia*, *Pasteurellaceae* and *Aggregatibacter* were increased in ASD patients, while *Tannerella*, *Moryella* and *TM7-3* were decreased. Variations of both miRNAs and microbes were statistically correlated to ASD related neuropsychological scores. Interestingly, we also found a negative correlation between miR-141-3p expression and *Tannerella* abundance. Univariate ROC curve analysis for miRNAs and bacteria showed moderate but significant AUCs; however, multivariate ROC curves, evaluating the combination of all miRNAs and bacteria, increased the predictive performance to discriminate ASD patients. In this study, we report that a potential cross-talking between salivary miRNAs and resident bacteria alterations could exist: these findings could pave the way to further dissect ASD molecular bases (2).

### References

- (1) Cirnigliaro et al., *Frontiers in Molecular Neuroscience*, 2017
- (2) Ragusa et al., *Molecular Autism*, 2019 (Submitted)