CO-REGULATORY NETWORK ANALYSIS: A COMBINED BIOINFORMATICS AND MOLECULAR STRATEGY FOR UNCOVERING GENETIC REGULATORY HUBS IN PAEDIATRIC MULTIPLE SCLEROSIS

Nicoletta Nuzziello[1]✉, Flavio Licciulli[1], Arianna Consiglio[1], Giorgio Grillo[1], Sabino Liuni[1], Maria Trojano[2], Maria Liguori[1]✉

[1]Institute of Biomedical Technologies, National Research Council, Bari Section, Bari
[2]Department of Basic Sciences, Neurosciences and Sense Organs, University of Bari

✉ nicoletta.nuzziello@ba.itb.cnr.it
maria.liguori@cnr.it

INTRODUCTION

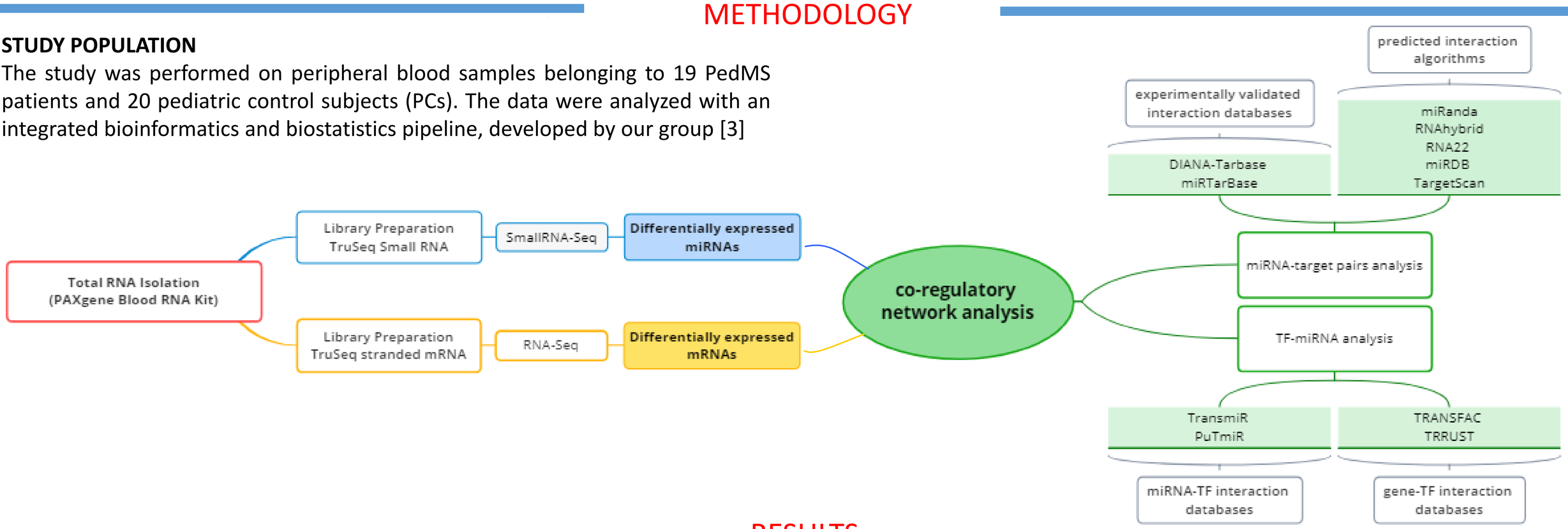
Multiple sclerosis (MS) is a chronic autoimmune complex disease of the Central Nervous System that primarily affects young adults, although approximately 3-10% of all patients complain the first symptoms during childhood and adolescence (so-called pediatric MS, PedMS) [1]. As the main regulators of gene expression, microRNAs (miRNAs) and transcription factors (TFs) seem to play key roles in MS by regulating their expression and the expression of their mutual targets through feedback loop (FBL) and feed-forward loop (FFL) modalities [2].

To better characterize the expression profiles of miRNome and its potential targetome in the peripheral blood of PedMS patients, we apply a High-Throughput Next-generation Sequencing (HT-NGS) approach, with the additional purpose to search for miRNA-TF co-regulatory networks possibly involved as hub genetic elements in the MS pathogenesis.

METHODOLOGY

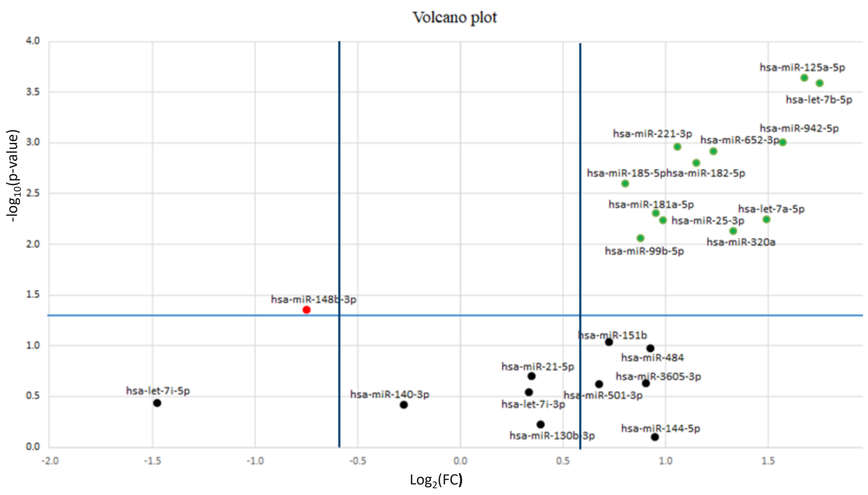
STUDY POPULATION

The study was performed on peripheral blood samples belonging to 19 PedMS patients and 20 pediatric control subjects (PCs). The data were analyzed with an integrated bioinformatics and biostatistics pipeline, developed by our group [3]

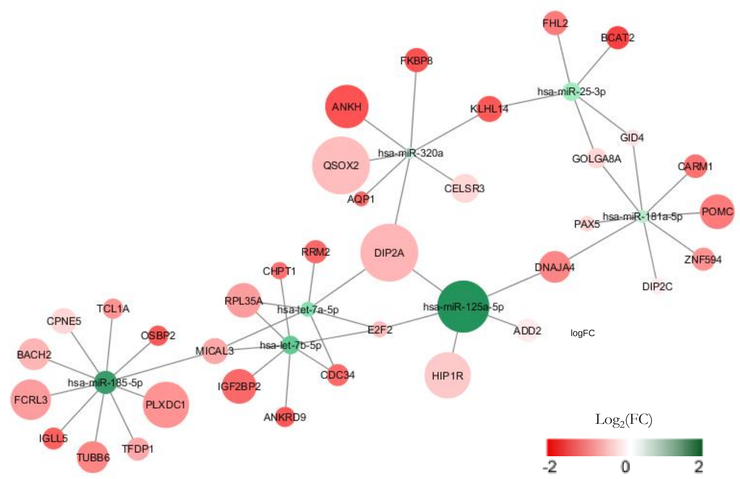


RESULTS

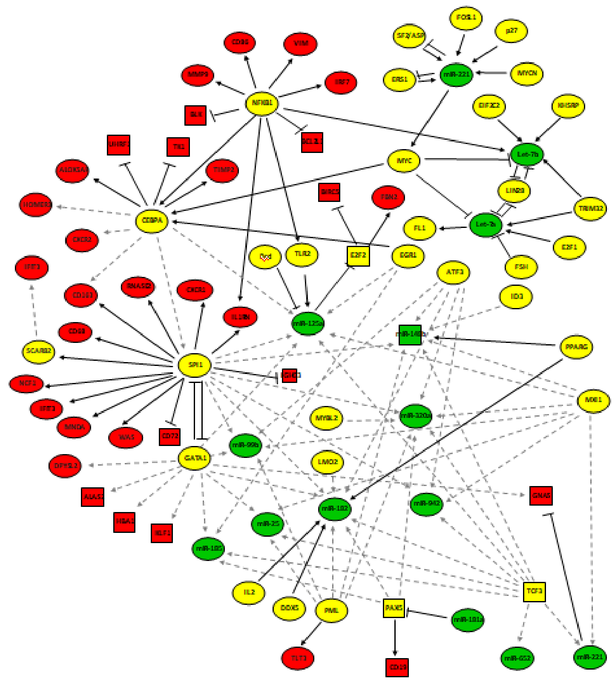
DIFFERENTIALLY EXPRESSED MIRNAS



MIRNA-TARGET NETWORK



TF-MIRNA CO-REGULATORY NETWORK



CONCLUSION

This integrated analysis enables to identify possible molecular signatures of PedMS, which is of great value considering the “environmentally naïve” status of the patients at the very beginning of their disease course. We were able to identify significant TF-miRNA co-regulatory networks, e.g. miR-125a-5p was activated by 7 TFs, was repressed by 1 TF and targeted E2F2; that, in turn, activated FBN2 and inhibited BIRC5.

[1] Banwell B. et al. Lancet Neurol. 2007, 6, 887-902
[2] Freiesleben S. et al. Scien. Rep. 2016, 6, 34512
[3] Liguori M. et al. Hum. Mol. Genet. 2018, 27, 66-79