***Supplementary Table 1*:** data referred to Spearman's correlation tests between the scores obtained at each NPS tests at follow-ups and the miRNAs expressions.

		hsa-miR-127-3p	hsa-miR-501-3p	hsa-miR-576-5p	hsa-miR-26b-5p	hsa-miR-1275	hsa-miR-182-5p	hsa-miR-451a	hsa-miR-486-5p	hsa-miR-320a-3p	hsa-miR-4742-3p	hsa-miR-192-5p	hsa-miR-548o-3p	hsa-miR-744-5p
Verbal memory														
SRT-LTS	Correlation Coefficient	0.035	0.117	0.433	0.333	0.45	0.583	0.5	0.267	-0.367	0.4	0.467	0.433	-0.45
	Sig. (2-tailed)	0.9	0.8	0.2	0.4	0.2	0.1	0.2	0.5	0.3	0.3	0.2	0.2	0.2
SRT-CLTR	Correlation Coefficient	-0.031	0.286	0.185	0.084	0.345	0.395	0.311	0.101	-0.235	0.151	0.252	0.252	-0.42
	Sig. (2-tailed)	0.9	0.5	0.6	0.8	0.4	0.3	0.4	0.8	0.5	0.7	0.5	0.5	0.3
SRT-D	Correlation Coefficient	-0.079	0.05	-0.16	-0.395	-0.034	-0.059	-0.16	0.101	-0.101	-0.336	-0.126	-0.185	-0.412
	Sig. (2-tailed)	0.8	0.9	0.7	0.3	0.9	0.9	0.7	0.8	0.8	0.4	0.7	0.6	0.3
Visual-spatial memory														
SPART	Correlation Coefficient	0.036	-0.145	0.145	-0.349	0.094	-0.068	-0.043	0.085	0.077	-0.051	0.009	0.17	-0.094
	Sig. (2-tailed)	0.9	0.7	0.7	0.4	0.8	0.9	0.9	0.8	0.8	0.8	0.9	0.7	0.8
SPART-D	Correlation Coefficient	-0.178	0.009	-0.179	-0.383	-0.026	-0.119	-0.187	0.077	-0.06	-0.366	-0.179	-0.221	-0.434
	Sig. (2-tailed)	0.7	0.9	0.6	0.3	0.9	0.8	0.6	0.8	0.9	0.3	0.6	0.6	0.2
Attention, IPS														
SDMT	Correlation Coefficient	-0.101	0.301	0.494	0.251	0.552	0.326	0.444	-0.251	0.218	0.46	0.351	0.653	0.017
	Sig. (2-tailed)	0.8	0.4	0.2	0.5	0.1	0.4	0.2	0.5	0.6	0.2	0.4	*0.06*	0.9
TMT-A	Correlation Coefficient	-0.127	0.059	-0.544	-0.653	0.067	-0.686	-0.519	-0.117	-0.695	-0.536	-0.678	-0.301	0.569
	Sig. (2-tailed)	0.7	0.9	0.1	*0.06*	0.9	0.04	0.2	0.8	0.04	0.1	0.05	0.4	0.1
TMT-B	Correlation Coefficient	0.165	0.133	0	-0.017	0.17	-0.1	0	-0.117	0.5	0.183	-0.067	0.233	0.617
	Sig. (2-tailed)	0.7	0.7	1	0.9	0.6	0.8	1	0.8	0.2	0.6	0.9	0.6	*0.07*
Expressive language														
SVFT	Correlation Coefficient	0.366	0.333	0.5	0.567	0.017	0.717	0.733	-0.1	-0.85	0.717	0.617	0.617	-0.017
	Sig. (2-tailed)	0.3	0.4	0.2	0.1	0.9	0.03	0.03	0.8	0.004	0.03	0.08	0.08	0.9
PVFT	Correlation Coefficient	0.249	0.561	0.318	0.351	0.293	0.594	0.636	-0.126	-0.536	0.519	0.427	0.577	0.059
	Sig. (2-tailed)	0.5	0.1	0.4	0.4	0.4	0.1	*0.07*	0.7	0.1	0.2	0.3	0.1	0.9

***Supplementary Table 2*:** Significant miRNAs/mRNAs pairs resulted from the analysis (adjusted p< 0.05); published associations with diseases (other than cancer) and/or functional activities (third column). Details of references in the following pages.

miRNAs	Targeted gene	Associations(*)
miR-576-5p, miR-26b-5p, miR-182-5p, miR-451a, miR-4742-3p, miR-548o-3p	TBL1XR1	autism [s1] mental retardation and immune response [s2] neurodevelopmental disorders [s3]
miR-127-3p, miR-1275, miR-320a-3p, miR-486-5p, miR-744-5p	SRCAP	rare Alzheimer's Disease [s4] FLOATing Horbor Syndrome [s5]
miR-127-3p, miR-1275, miR-486-5p, miR-744-5p	AC015813.2^	
miR-127-3p, miR-1275, miR-486-5p, miR-744-5p	AL591806.4^	
miR-127-3p, miR-1275, miR-501-3p, miR-744-5p	PDXP	GABA-synthesis in neuropsychiatry [s6]
miR-127-3p, miR-1275, miR-486-5p, miR-744-5p	STX16-NPEPL1	
miR-127-3p, miR-1275, miR-744-5p	AC022384.1^	
miR-192-5p, miR-26b-5p, miR-576-5p	ARL15	type-2 diabetes, AR, NF1 [s7] rheumatoid artheritis [s8] brain plasticity [s9]
miR-182-5p, miR-26b-5p, miR-576-5p	UBE2B	
miR-182-5p, miR-4742-3p	AC093512.2^	
miR-548o-3p, miR-4742-3p	AL162377.3^	
miR-182-5p, miR-548o-3p	GMFB	neurodegeneration, neuroinflammation [s10] memory impairment in mouse [s11] Parkinson's Disease [s12] brain ischemia [s13]
miR-4742-3p, miR-548o-3p	GNG11	HLA in complex disease [s14]
miR-182-5p, miR-4742-3p	MAP3K7CL	dermatomyosite animal model, beyond MHC [s15]
miR-192-5p, miR-26b-5p	C1D	schizophrenia [s16] RNA/DNA functions [s17] innate immunity [s18]
miR-182-5p, miR-26b-5p	SEC61G	Lupus, antigen presentation [s19]
miR-4742-3p, miR-548o-3p	SNRPE	
miR-4742-3p	DNAJC25-GNG10	
miR-4742-3p	GNG10	
miR-182-5p	PPBP	Alzheimer's Disease [s20] Microglia functioning [s21]
miR-127-3p	FMC1-LUC7L2	
miR-182-5p	NAMPTP1	
miR-4742-3p	PTP4A1	

^Novel transcript

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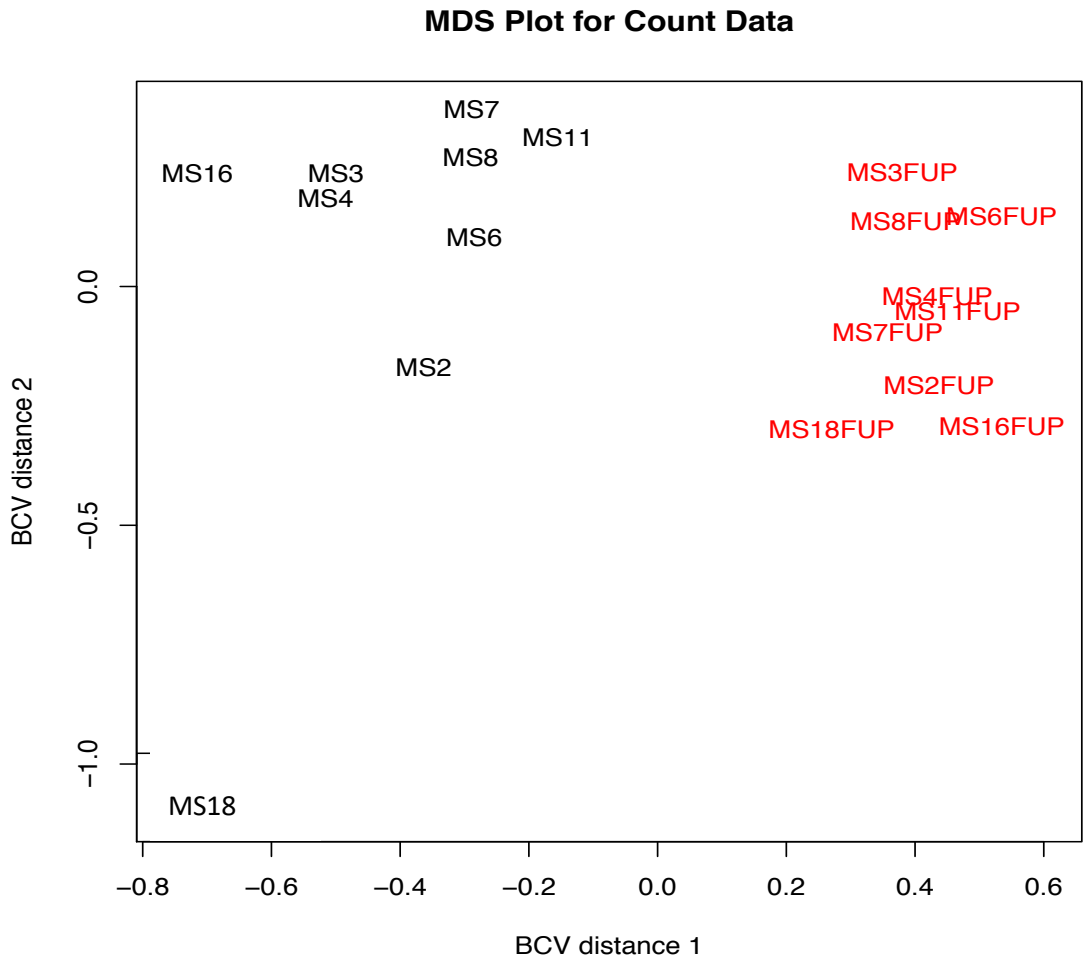
Supplementary Figure 1: Multidimensional scaling (MDS) plot of Dispersion Index between the miRNA expressions of all PedMS subjects at baseline (black) and at follow-up (red). Distances between individuals correspond to the leading biological coefficient of variation (BCV) that represents the biological (nontechnical) variation.



NOTE: As full disclosure, please note that, since the automatic legend of the plot (i.e. output of the MDS software) fall down in the MS18 spot, its box has been manually drawn by the leading Author in order to improve the quality of the image. The original image is available upon request.