miR-29a affects the progression of Alzheimer's Disease through one carbon-metabolism

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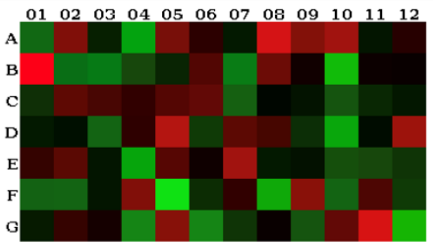
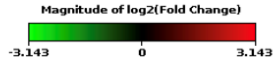
BACKGROUND: The Homocysteine (Hcy) pathway, also known as one-carbon metabolism, lead to the production of S-adenosylmethionine (SAM), the main donor of methyl groups. microRNAs (miRNAs) are emerging epigenetic factors linked to DNA methylation and associated to several diseases.

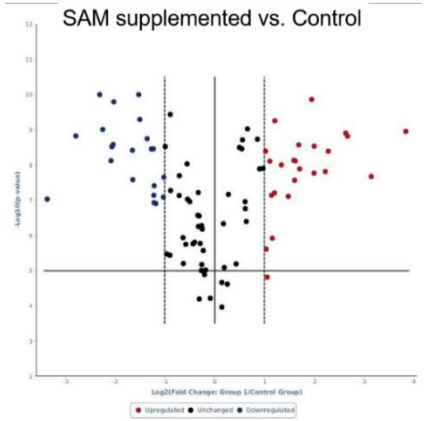
AIM: To test whether the modulation of the one-carbon metabolism, induced by B-vitamin deficiency and SAM-supplementation, could modulate the expression of miRNAs which are involved in the Alzheimer's disease.

METHODS: miR-29a has been assessed by a preliminary screening in SK-N-BE cells and then confirmed in more extended in vitro and in vivo analysis by Real-time PCR.

miRNAs PCR-array

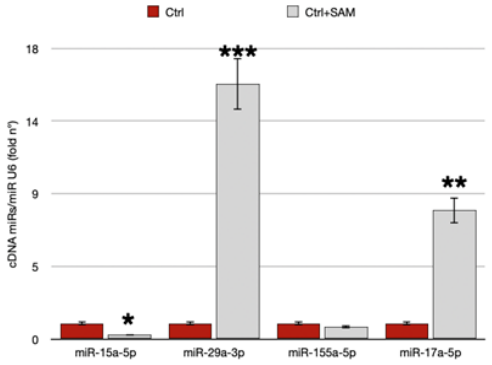




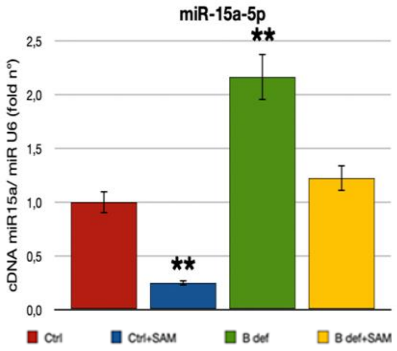


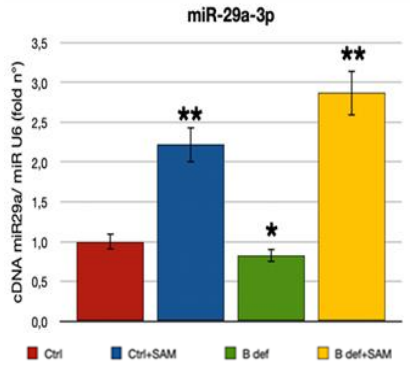
About 30% of miRNAs are modulated:
- 10 miRNAs up-regulated
- 12 miRNAa down-regulated

miRNAs expression in SK-N-BE cells



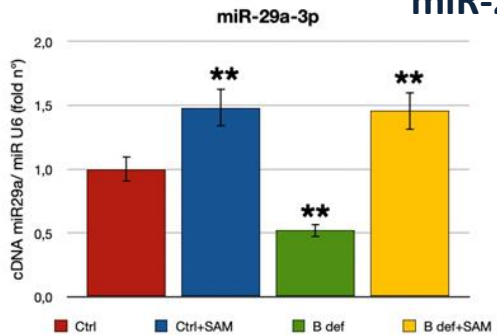
Real-time PCR analysis of modulated miRNAs in control and SAM-supplemented medium.



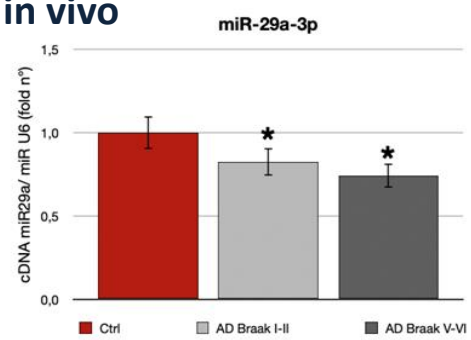


In SAM-supplemented and B-deficient conditions miR-15a and miR-29a show opposite expression profiles.

miR-29a expression in vivo



miR-29a is down-regulated in TgCRND8 mice brain in ipo-methylating conditions (B-deficiency)



miR-29a is down-regulated in brain samples from patients at different stages of the disease

CONCLUSIONS: miR-29a is modulated by one-carbon metabolism and regulates different AD-correlated genes. These findings suggests a possible role as novel therapeutic target in addressing nutritional-based interventions.