Altered miRNA in Amyotrophic Lateral Sclerosis: searching for the lowest common multiple

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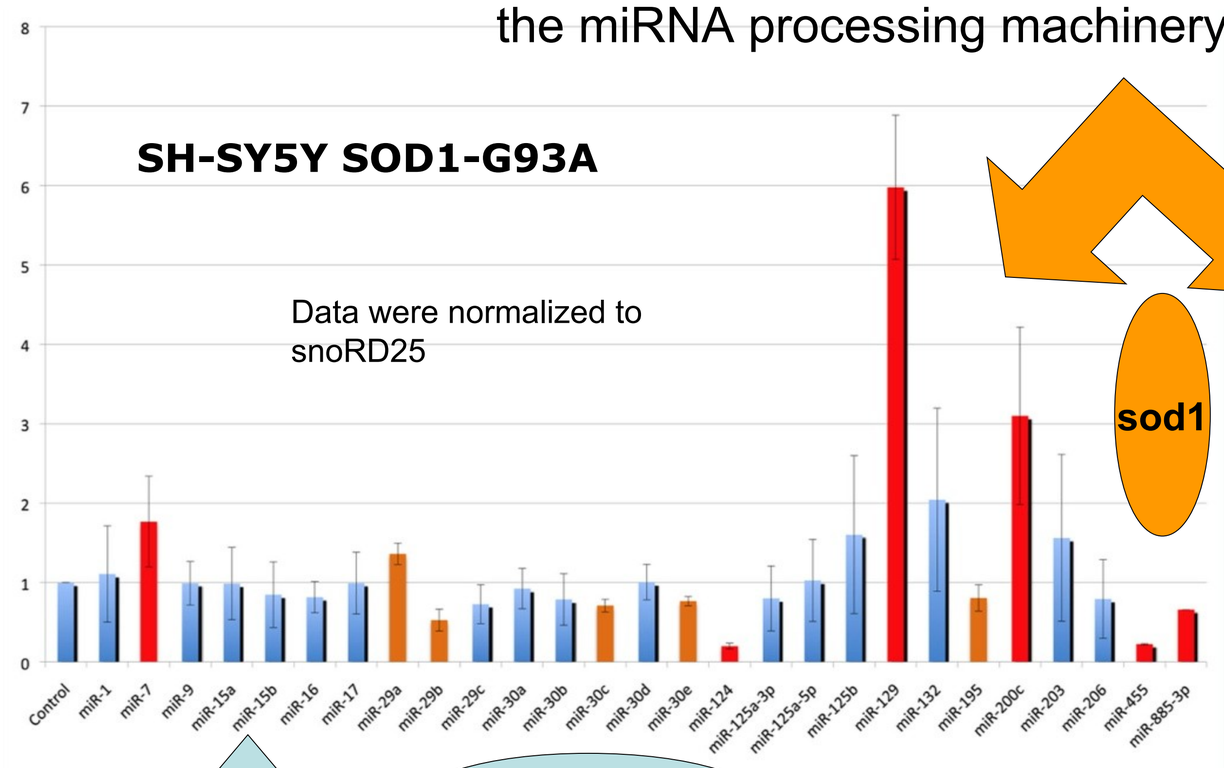
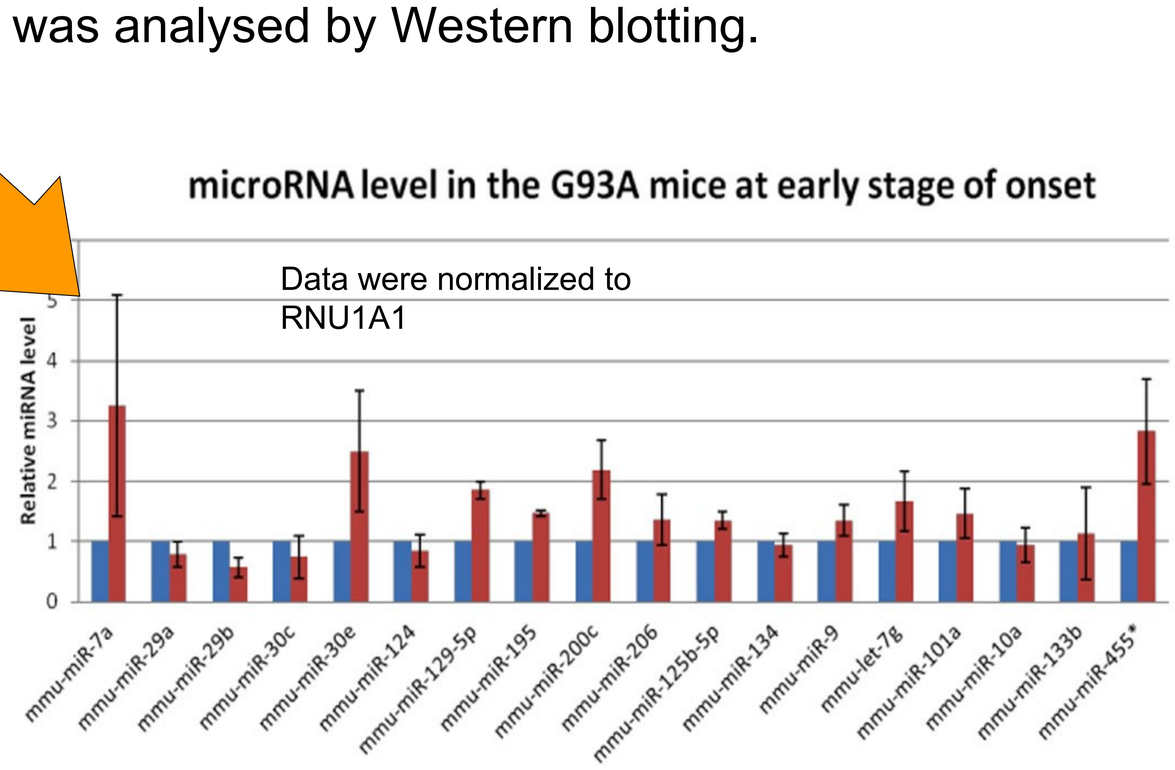
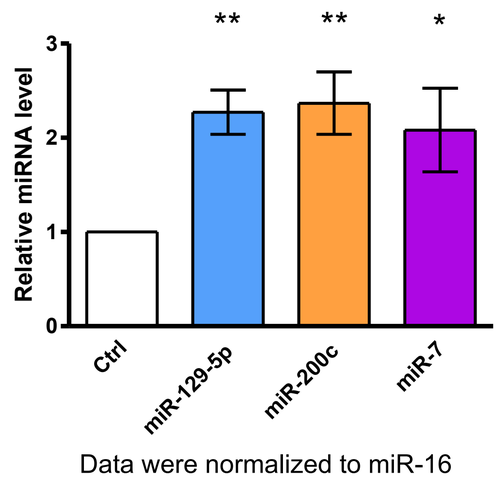
Micro RNAs (miRNAs) are small non-coding RNA that have the potential to regulate the expression of hundreds of different mRNA. Deregulation of miRNA expression has been reported in neurodegenerative disorders including amyotrophic lateral sclerosis (ALS). Aim of this work consisted in testing the hypothesis that altered expression of miRNAs may be a critical feature in ALS.

Methods: Using both deep Next Generation high through-put Sequencing (miRNA-seq) and bioinformatics analyses we identified a panel of differentially expressed miRNAs. The expression of these miRNAs was validated in cellular and animal models of SOD1-linked familial ALS, as well as in lymphomonocytes (PBMC) of sporadic ALS patients and of patients bearing SOD1 mutations. miRNA profiling was performed by RT-qPCR, while the expression of components of the miRNA processing machinery was analysed by Western blotting.







PBMC

	SALS (n=28)	**CTRL** (n=22)
Age	63.6 ± 12.6	62.9 ± 12.0
Gender (M/F)	15/13	11/11
Form (Spinal/Bulbar)	20/8	n/a
ALSFRS-R	23.3 ± 7.2	n/a
Disease duration (months)	32.5 ± 30.2	n/a

Results: Analysis in human neuroblastoma SH-SY5Y cells stably expressing the SOD1(G93A) mutation revealed the up-regulation of **mir-129** and **mir-200c**. The up-regulation of these two miRNAs was also observed in symptomatic SOD1(G93A) mice and in PBMC of ALS patients with respect to controls. We are currently validating potential target mRNAs. Finally, Western blot analysis in SH-SY5Y(SODG93A) cells revealed the differential expression of DCRG8, Dicer and EWS.

Conclusions: Our data uncover a potential role for mir-129-5p and mir-200c in ALS and suggest that misregulated expression of miRNAs may represent a common mechanism in different pathways leading to ALS pathology. We are currently increasing the analyzed samples for further substantiating these conclusions.