Myocyte Enhancer Factor-2 pathway is altered in Amyotrophic Lateral Sclerosis peripheral blood mononuclear cells

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Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neuromuscular disease characterized by motor neuron loss.

Myocyte enhancer factor 2 (MEF2) proteins are transcriptional factors playing a crucial role both in muscle and in neural development and maintenance. An important role in peripheral blood mononuclear cells (PBMC) has been also shown.

MEF2C was recently identified as potential genetic biomarker of longevity in transgenic SOD1^{G93A} ALS animal model (Calvo et al., 2012).

Material and Methods

In this study, we used peripheral blood mononuclear cells (PBMC) obtained from 30 sporadic ALS patients (sALS), 9 SOD1-mutated ALS patients (SOD1+ ALS) and 30 healthy controls.

PBMCs were isolated from whole blood by density gradient centrifugation; protein and gene expression was evaluated by western blot and qPCR while MEF2D and MEF2C localization was investigated by immunofluorescence.

Results

Our study showed increased MEF2D and MEF2C mRNA levels in sALS and in SOD1+ subjects (**Figure 1**) and, although protein levels were unchanged, an altered localization for MEF2D and MEF2C proteins in sALS cells was suggested (see **Figure 2**).

Moreover, MEF2 downstream targets (BDNF, KLF6 and RUFY3) were found significantly reduced in sporadic ALS patients and in subjects carrying SOD1 mutations (**Figure 3**), suggesting that MEF2D and MEF2C transcriptional function is disrupted in ALS PBMCs.

Conclusions

A systemic alteration of MEF2D and MEF2C pathways in both sporadic and familial ALS patients is present. Further studies on these pathways in affected tissues and animal models are needed to clarify the role of this dysregulation in disease onset and progression, possibly leading to the definition of novel promising therapeutic targets or novel biomarkers for early diagnosis.

References

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•Arosio, A., Sala, G., Rodriguez-Menendez, V., Gerardi, F., Lunetta, C., Ferrarese, C., Tremolizzo, L., 2015. Myocyte enhancer factor 2 pathway disruption in lymphomonocytes of patients with amyotrophic lateral sclerosis. *Submitted manuscript.*

Figure 1

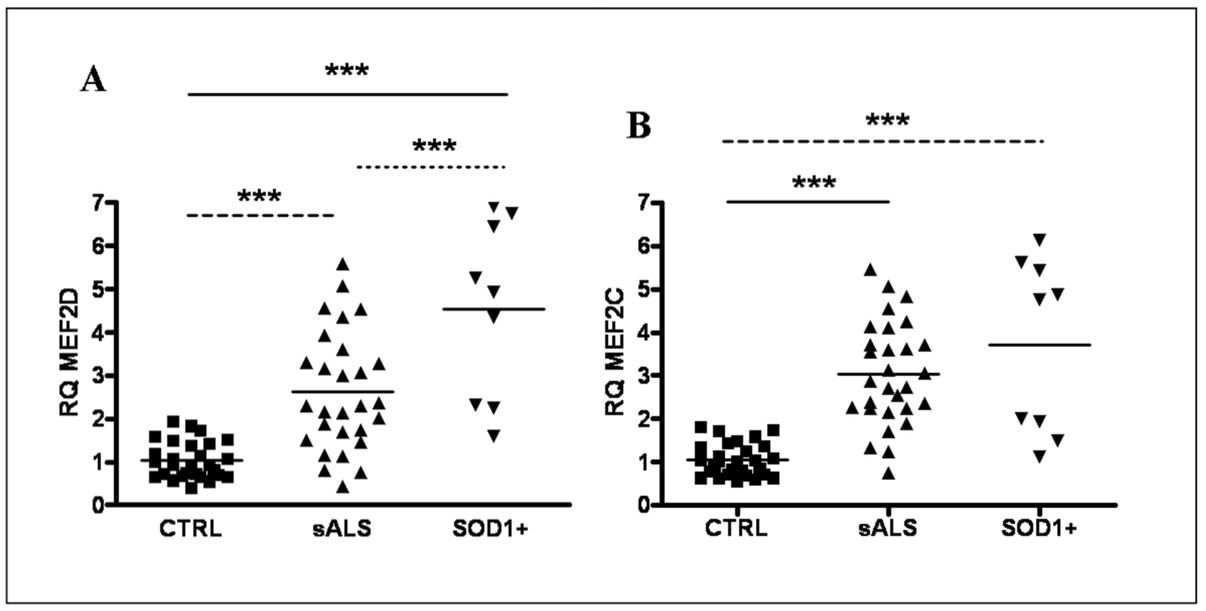


Figure 2

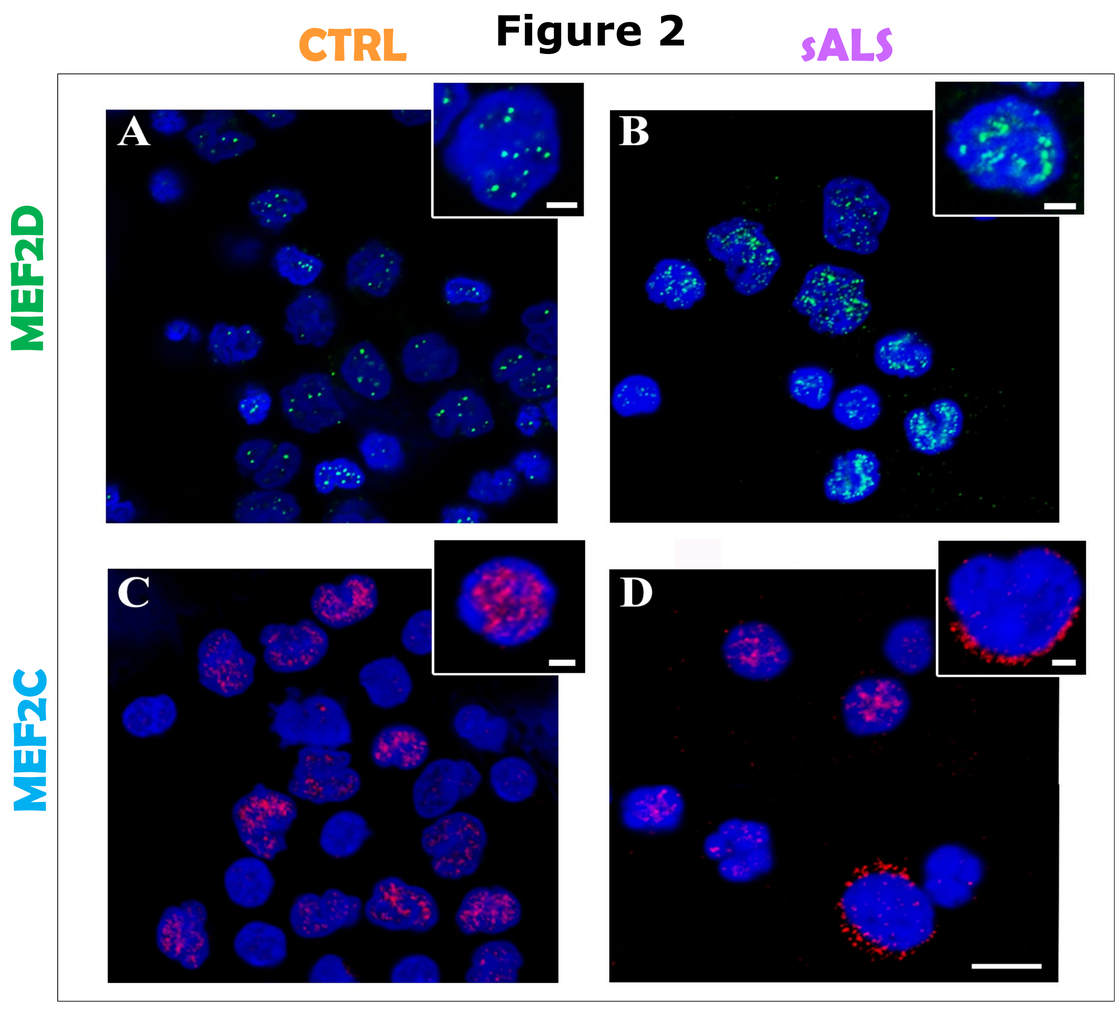
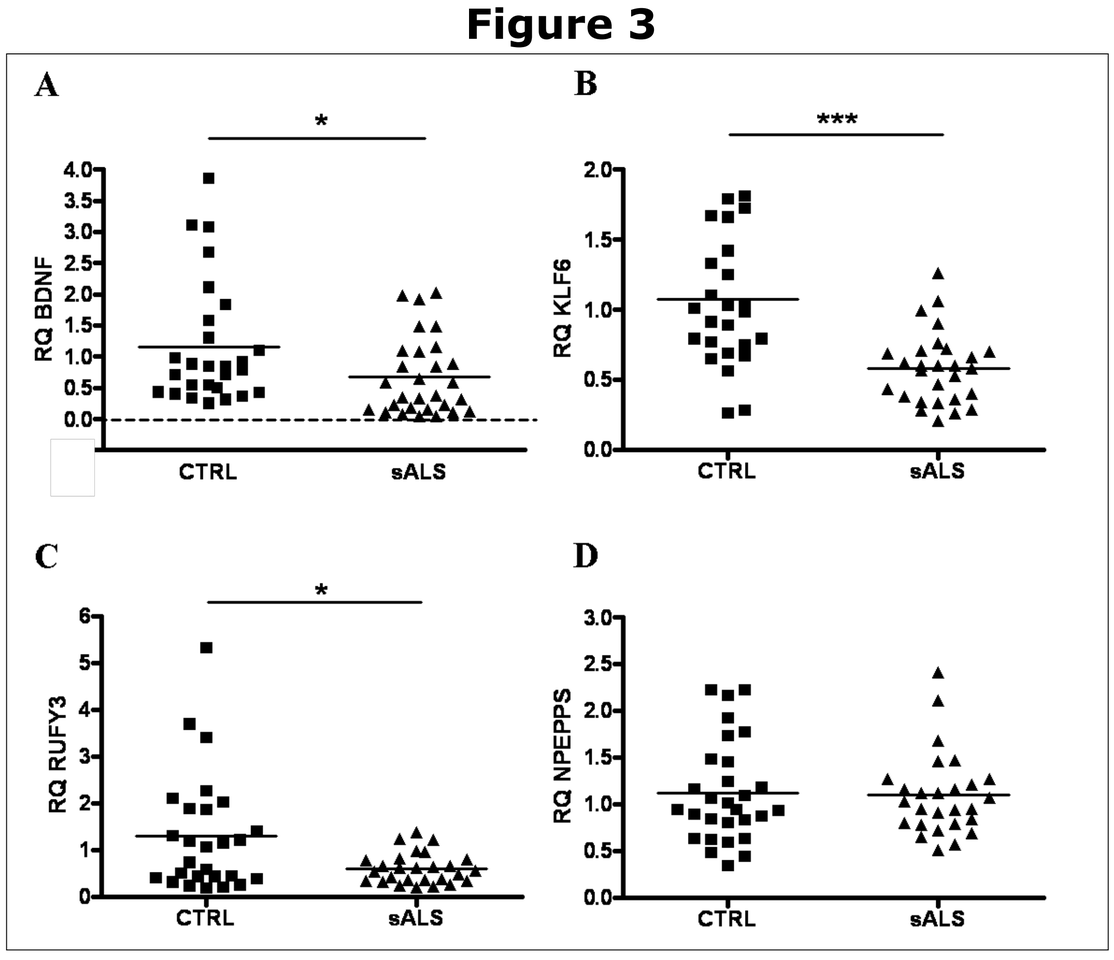


Figure 3



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