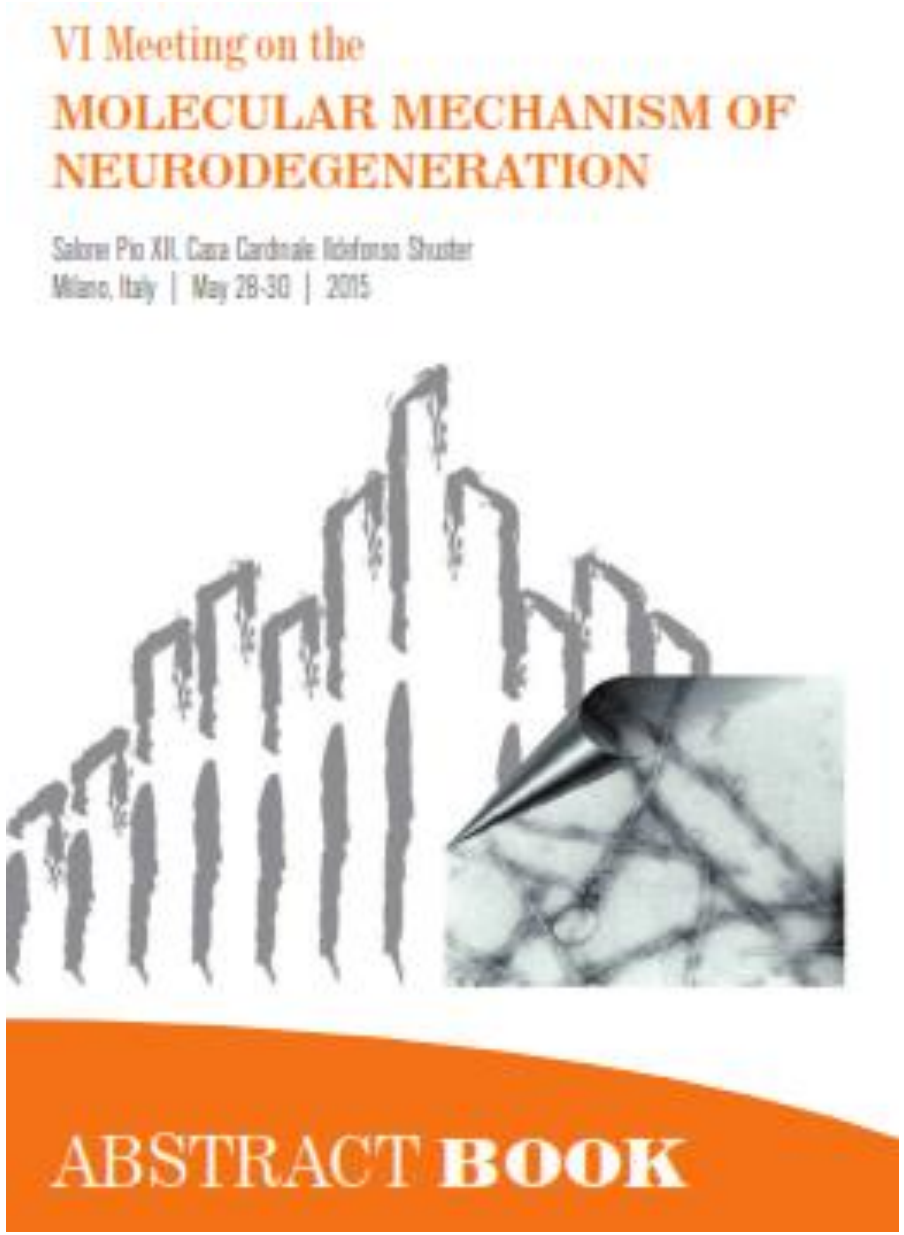

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TGFBETA1 EXPRESSION IN ALS MUSCLE AND SPINAL CORD

Galbiati M.[*1,2], *Meroni M.* [1], *Crippa V.* [1], *Rusmini P.* [1,2], *Cicardi M.* [1], *Cristofani R.* [1], *Messi E.* [1], *Pennuto M.* [2,3], *Poletti A.* [1,2]

[1] Dipartimento di Scienze Farmacologiche e Biomolecolari - Centre of Excellence on Neurodegenerative Diseases, Università degli Studi di Milano, Italia

[2] Centro InterUniversitario sulle Malattie Neurodegenerative, Università degli Studi di Firenze, Milano, Genova e Roma Tor Vergata (Italy)

[3] Dulbecco Telethon Institute Laboratory of Neurodegenerative Diseases, Centre for Integrative Biology (CIBIO), University of Trento, Italy

Some familial forms of Amyotrophic Lateral Sclerosis (ALS) are characterized by a dominant mutation in superoxide dismutase (SOD) 1 gene. Many evidence suggested that SOD1 toxicity is non-cell autonomous, involving multiple cell types: affected motor neurons, glial cells and muscle cells. In particular, muscle might be a primary source of toxicity. Indeed, it is reported that in mice the expression of mutated SOD1 in muscle cells is sufficient to induce motor neuron degeneration and muscle abnormalities already at the pre-symptomatic stage. TGFbeta1 is a growth factor known to be involved in neuron survival and in muscle development/maintenance. Furthermore, TGFbeta1 levels are increased in serum of ALS patients. On these bases, we decided to evaluate the expression of the TGFbeta1 gene in skeletal muscle and spinal cord of transgenic mice expressing mutated hSOD1 at different stages of the disease and taking in consideration mouse sex. The results indicate that in muscle TGFbeta1 expression is up-regulated by mutated hSOD1 at the symptomatic stage both in male and female, while at the pre-symptomatic stage TGFbeta1 mRNA levels are increased only in male. An high expression of TGFbeta1 might be responsible of muscle fibrosis. In spinal cord, the expression of TGFbeta1 decreases in the pre-symptomatic mice, indicating a drop in motorneuron protection. On the contrary, TGFbeta1 mRNA levels increase at the symptomatic stage, probably for the participation of other cell types. The analysis of the expression of Smad proteins, which are the main signalling molecules activated by TGFbeta, indicates a different regulation in muscle and spinal cord, and between male and female mice.

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