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TLQP peptides in Amyotrophic Lateral Sclerosis

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TLQP peptides (TLQPp) act on synaptic strengthening or against neuronal apoptosis but their involvement in Amyotrophic Lateral Sclerosis (ALS) is not well known. We used an ALS animal model (SOD1-G93A) and human tissues (plasma and fibroblasts from both patients and controls), to address the TLQPp expression and their modulation in ALS mechanisms. Mouse motor neuronal cells (NSC-34), were used to study the neuroprotective role of the TLQP-21 against oxidative stress induced by Sodium Arsenite. TLQPp were immunoquantified by ELISA, their cell expression studied by immunofluorescence while cell viability was addressed by MTT assay. In the NSC-34 naïve cells, TLQPp were found within the cytoplasm, axons and growth cones. Upon stress, they appeared immunolocalized exclusively within a cytoplasmatic area, close to the nucleus, (probably the Golgi). Moreover, under stress, TLQPp levels were reduced (42%, $p=3.1x10^{-6}$), while the exogenous increase of TLQP-21 improved cell viability (13%, p= 0.018). In naïve fibroblasts, TLQPp were also similarly localized in an area, likely the Golgi, of patients and controls while their reduction (31%, p=0.03) was observed in cells with TARDBP-A382T mutation. Stress granules only appeared after SA treatment, and did not contain TLQPp. In plasma, a reduced release of TLQPp was associated with the beginning of the clinical motor symptoms in patients (12%, p=0.026), and with a pre-symptomatic stage in mutant mice (26.3%, p=0.048). Finally, in mouse spinal cord we identified by vescicular acetylcholine transporter (VAChT) antibody, a specific localization of the TLQPp in the motor neurons with a reduction in the pre-symptomatic stage of mutant mice. In conclusion, TLQPp are reduced in the stressed NSC-34 cells, mutant mouse motor neurons as well as in fibroblasts with TARDBP-A382T mutation that also induces production of reactive oxygen specie. Hence, we suggest that their reduction may occur in response to oxidative stress. They could be also considered as early biomarkers, while TLQP-21 acts as neuroprotective factor.

Keywords
ALS, VGF, TLQP peptides, motor neurons