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Pulsed Electromagnetic Field (PEMF) and Amyotrophic Lateral Sclerosis (ALS): an innovative experimental cell model to evaluate the involvement of adenosine receptor A_{2A} in disease progression.

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Electromagnetic fields are emerging as a potential alternative to the pharmacological treatments in several inflammatory related pathologies. In this context, low-frequency, low-energy pulsed electromagnetic fields (PEMFs) have been largely demonstrated to be effective in contrasting the effects of inflammatory response, by acting on adenosine receptor A_{2A} [1]. This receptor is also involved in mediating the neuroinflammation in stroke [2] and in neurodegenerative disease [3].
Amyotrophic Lateral Sclerosis (ALS) is a fatal and aggressive adult neurodegenerative disease, characterized by neuromuscular junction disruption and motor neuron degeneration, typically leading to progressive paralysis and death within 2–5 years from symptoms appear. The onset of the disease is due to a complex interaction between genetic and molecular pathways which, up to now, has not been clarified. An important pathological hallmark in both familial and idiopathic ALS patients is the mis-localization of the primarily nuclear RNA and DNA binding protein TAR 43 (TDP-43), codified by *TARDP* gene, to the cytoplasm of motor neurons [4]. One of the mutations, with a dominant inheritance, found in TDP-43 is G376D, where the glycine in position 376 is replaced by an aspartic acid, responsible of TDP-43 translocation from the nucleus to the cytoplasm [5].
As for the other neurodegenerative diseases, A_{2A} receptor is deregulated in ALS pathology [6]. Literature data have demonstrated that A_{2A} receptor modulation, mediated by agonist interaction, rescues TDP-43 mis-localization and improve motor neurons survival [7].
Starting from the fibroblasts obtained from *TARDP (G376D)* ALS family at different stages of diseases [8], we investigated the possible therapeutic effect of PEMF, acting on A_{2A} receptor, and its role in ALS progression.
The experiments were performed on five cell models: CTR, healthy control; GAFU FIBRO, ALS early with mild symptoms; TARD GAFU, ALS late with severe symptoms; FUCHI ALS asynptomatic; MAFU, familiar control (member of the family without the mutation of *TARDP*). For cell exposure, carried out simultaneously for all cell lines and in experimental triplicate, three multiwells with eighteen wells in total were used within a double solenoid exposure system provided by IGEA, which implied the setting of a new dosimetric model to identify the proper uniformity volume and to evaluate the intensity and the homogeneity of the magnetic, electric and current density field distribution in each well.
Here we report the preliminary results of our study about the characterization of the response of ALS *TARDP (G376D)* cells to PEMF stimulation.

References

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