MEF2C and MEF2D alterations in sporadic and familial ALS patients: a possible correlation with disease progression?

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Objectives: Amyotrophic Lateral Sclerosis (ALS) is a lethal neurodegenerative disease affecting motor neurons very difficult to diagnose. For this reason, the identification of biomarkers useful to identify and to monitor the disease is an urgent goal. Since ALS is a neuromuscular disease, we assessed in accessible biofluids the potential involvement of two members of Myocyte Enhancer Factor 2 family (MEF2), a group of transcriptional factors regulating many important functions in central nervous system and muscle development and maintenance.

Materials: Peripheral Blood Mononuclear cells (PBMCs) obtained from 30 sporadic ALS patients (sALS), 9 subjects with SOD1 gene mutations (SOD1+) and 30 healthy controls (CTRL) were used for the analysis.

Method: PBMCs isolation; Real-time PCR (qPCR); Western blotting (WB); Immunofluorescence.

Results: We observed increased MEF2C and MEF2D mRNA levels in both sALS and SOD1+ patients with respect to controls. MEF2 altered intracellular localization and function were also reported in patient cells. Moreover, in 8 sALS patients MEF2C and MEF2D mRNA levels were re-evaluated at the follow-up showing a significant correlation with the disease progression index (DPI).

Discussion: MEF2C and MEF2D altered expressions were reported in circulating cells of patients suggesting the opportunity to test these parameters as possible biomarkers in ALS. Furthermore, preliminary results evidenced that MEF2 expression over time might be different between fast and slow progression patients.

Conclusions: A dedicated study will be planned to explore the eligibility of MEF2 as state marker of disease confirming previous results reporting that MEF2C mRNA levels negatively correlated with longevity in ALS animal model.

References

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In vitro activity and neurotoxicity of new promising metal-based anticancer complexes

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The approved platinum drugs continue to have a major role in cancer treatment. However, despite their efficacy, serious side effects often prevent their administration at full efficacious doses or may considerably affect patients' quality of life. Hence, there is an urgent need to find safer and better-tolerated chemotherapeutic drugs. In this work we investigated in vitro the activity and the neurotoxicity of new anticancer complexes based on copper ([Cu(PTA)4]PF6; [Cu(thp)4]PF6), gold ([Au(PTA)4]PF6) and platinum ([PtCl2(cis-1,4-DACH)]; [Pt(1,1'-CBDCA)(cis-1,4-DACH)]). Cytotoxicity was tested by MTT assay in a panel of human cancer cells. Neurotoxicity was evaluated by an in vitro model based on organotypic cultures of DRG from E15 rat embryos.

Since the ubiquitin-proteasome system is a cancer cell molecular target of copper and gold based-drugs, we evaluated, by fluorimetric assay, their ability to hinder the proteasome machinery in DRG neurons. At 48 hours, both copper compounds were not neurotoxic even at higher concentrations with respect to the IC50 calculated in cancer cells while [Au(PTA)4]PF6 was neurotoxic at lower concentration than IC50. [PtCl2(cis-1,4-DACH)] elicited a neurotoxicity slightly lower with respect to oxaliplatin. Conversely, [Pt(1,1'-CBDCA)(cis-1,4-DACH)] showed a reduced neurotoxicity compared with the reference drug. Both copper-based compounds, that are not neurotoxic, do not inhibit proteasome activity in DRG neurons. Contrarily, the neurotoxic complex [Au(PTA)4]PF6, induces a significant inhibition of proteasome activity. Our results, together with the low IC50 of the copper and platinum based complexes, suggest them as promising compounds providing support to further in vivo studies.

Cracking the Neural Code - A Gedanken Experiment: "The Alien Task"

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The concept of Spike is central in actual models of neural coding and the mean firing rate has been widely analyzed by information theory too as its most prominent aspect. Nevertheless, both computational models and clinical neurophysiology, are still lacking of an effective micro neurophysical theory for the underlying phenomena. A Gedanken-experiment might describe our actual knowledge of neural code as an "Alien-Task": "Alien scientists of a remote interstellar planet have been studying with their telescopes for a couple of centuries, the human knowledge transmission system in a primary school. Due to the perpendicular intergalactic perspective they ignore the existence of written signs and words on the vertical blackboard of the school. They have a well-established theory correlating the mean frequency of school chalkboard erasures, over years, months, days and hours with fluxes and progression of pupils from one class to the other, till the final school exit. As humans we know although that chalkboard erasure itself is meant simply as a tool to give space to new or updated information. A well-kept secret for aliens." The crucial point is that the spike itself is not the only carrier of information but, a sort of refresh system for the wired neuronal cell and and a fortifyer, of environmental field shaped wireless informations.The continuous flux of elisional events, occurring across neural membranes, gives the way to a sub microscopic field of informations, which is wired ,fortifyied and timed by the well-known events called spikes, themselves macro-elisional events.

References

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Effects of neoglycosylated collagen matrices on neuroblastoma and human stem cells: a new perspective for neuro-regeneration?

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Scope of the work: Regenerative medicine approaches based on scaffolds obtained form extracellular matrix (ECM) proteins are rapidly expanding. These scaffolds can be bioactivated with signalling cues in order to maintain cell viability and to control and guide cell behaviour. Among signalling molecules, carbohydrates play a key role. Given these premises, the scope of this work has been the evaluation of the effect of neoglycosylated collagen matrices on the behaviour of F11 neuroblastoma cell line, human umbilical cord blood- and bone marrow-derived mesenchymal stem cells in terms of viability and differentiation potential towards functionally active neuronal cells.

Materials and Methods: Collagen Type I from bovine Achilles tendon matrices were functionalised by reductive amination with maltose, lactose, cellobiose, 3'-sialyllactose, 3'-sialyllactose [1-3] leading to a covalent stable neoglycosylation pattern on the