

DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO

40° Cycle

Project proposal for a PhD scholarship

Title of the research: Identification of target molecules and development of therapeutic mRNA-based drugs for enhancing endogenous post-stroke human neurogenesis

Supervisor: Paola Piscopo, paola.piscopo@iss.it, Dipartimento di Neuroscienze – Istituto Superiore di Sanità

Tutor: Prof Ada Maria Tata, Dept. of Biology and Biotechnologies Charles Darwin, "Sapienza" University of Rome; adamaria.tata@uniroma1.it

Host Institution: Istituto Superiore di Sanità, Rome, Italy

Summary

Ischemic stroke (IS) may trigger proliferation, migration towards the ischemic lesion, and differentiation of neuroprogenitor cells into mature neurons. Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive technique inducing brain plasticity and enhances stroke recovery. Biomarkers such as miRNAs (miR) 17~92, Netrin-1 (Ntn-1) and Semaphorin 3A (Sema3A) play a role in neurogenesis/axonogenesis. The aim of the project is to study neurogenesis in IS patients who have received rTMS, investigating its effects on post-stroke neuroplasticity by dosing plasma miRs 17~92, Netrin-1 and Sema3A. The hypothesis is that rTMS stimulate certain biomarkers of neurogenesis/axonogenesis, such as Netrin-1 and Semaphorin (Sema3A) or exosomal miRNAs (miR)/miR, belonging to the miR17~92 family. Once the most promising miRs and proteins involved in post-stroke neurogenesis have been identified in humans (**Aim 1**), we will develop some cellular models of hypoxia with the aim of studying the functional relationship between these miRs and their target proteins (e.g. HMGB1) to confirm their role in neurogenesis. We will use both neuroblastoma cell lines and neural progenitor cells derived from induced pluripotent stem cells that will be exposed to oxygen and glucose deprivation conditions to mimic an in vitro ischemia model. (**Aim 2**) Moreover, we aim to increase neurogenesis and angiogenesis in in vitro models of cellular hypoxia by using a new nano-therapeutic approach (**Aim 3**).

References (other than publications of the proponent, if appropriate)

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Pertinent Publications of the proponent (last 5 years)

De Michele M, Piscopo P, Costanzo M, Lorenzano S, Crestini A, Rivabene R, Manzini V, Petraglia L, Iacobucci M, Berto I, Schiavo OG, Conte A, Belvisi D, Berardelli A, Toni D. Can Repetitive Transcranial Magnetic Stimulation (rTMS) Promote Neurogenesis and Axonogenesis in Subacute Human Ischemic Stroke? *Biomedicines.* 2024 Mar 17;12(3):670. doi: 10.3390/biomedicines12030670

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