

TOPIC PNRR5

Project title	Functional validation of RNA-based drugs in the CNS
Curriculum (standard or clinical)	Standard
Principal Investigator	Lodato Simona/Davide Pozzi
Lab name	Developmental Neurobiology
Main field of interest	Neuroscience
Abstract	<p>RNA therapy implies the use of RNA-based molecules to modulate biological pathways to cure specific conditions, and advancement in the RNA-targeting field allow a wide range of applications to treat rare and common diseases. RNA drugs can be classified into three categories: 1) antisense oligonucleotides or RNA interference for modifying gene expression; 2) RNA aptamers that can modulate the function of proteins; and 3) mRNA drugs encoding proteins. A major advantage of RNA drugs is the possibility to chemically modify them to improve their bioavailability and pharmacokinetics. In this project, we will employ multiple model systems (including pure cultures and co-cultures of neurons, astrocytes, and microglia obtained from the differentiation of patient-derived iPSC cells as well as 3D organoids and assembloids obtained from the differentiation of patient-derived iPSC cells, as well as microfluidic models of neurovascular barriers) to test new RNA drugs for the treatment of genetic diseases impacting on the central nervous system by exploiting novel strategies that allow an in-depth characterization of their pharmacodynamic profile and pharmacokinetics. Functional characterization of the lead compounds will be followed through both electrophysiological and molecular analysis in multiple model systems to allow a comprehensive and integrated evaluation of the drug properties.</p>
Brief description of the coherence of the Project in relation to the	This project is placed within the WP2–RNA drug pharmacodynamics of the SPOKE9 “From target to therapy: pharmacology, safety and regulatory competence center” of the National Center for Gene Therapy and Drug Development with RNA Technology (CN3, Mission 4 Component 2

PNRR objectives	Investment 1.4 of the NRP). The project will exploit the state-of-the-art multidisciplinary expertise and tools characterizing the Humanitas groups in the Neuro Center and collaborating with CNR groups to study and validate novel RNA drugs for the treatment of neurological diseases. The RNA drugs acting on the CNS are selected in collaboration with Spokes 1, 3, 6, 8 and Human Technopole.
PNRR project title	Multi scale functional validation of RNA-based drugs in the CNS (MULTIVAL) <i>“National Center for Gene Therapy and Drugs based on RNA Technology”.</i> <i>(CN3, Missione 4 Componente 2 Investimento 1.4 del PNRR).</i>
CUP	G43C22001360007
Required Skills to carry out the project	The ideal candidate must have basic skills in all or at least some of the following: cell culturing, microscopy, qPCR, western blot, tissue dissection, immunocytochemistry, extraction and purification of recombinant proteins from heterologous systems, enzymatic and binding assays.