ISTITUTO ITALIANO
DI TECNOLOGIA

PHD Neurosciences, curriculum “Neurosciences and Neurotechnologies, XXXVII cycle
Project title:

Advanced nanozymes to prevent ROS-induced neurodegeneration of the retina

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Neurodegeneration and neural cells death are at the origin of neurodegenerative diseases, which affect millions of people worldwide with significant social and economic impact. In most cases, no effective treatments are available, and, therefore, novel therapeutic strategies are in urgent demand. Neurodegenerative diseases are characterized by oxidative stress and inflammatory processes that combined represent a key hallmark during the disease's onset and progression. Catalytic nanoparticles, also called nanozymes, have recently shown an efficient capability to rescue oxidative stress by scavenging reactive oxygen species (ROS), behaving similarly to the most common intracellular enzymes for ROS regulation. The project aims to develop an engineered nanozyme-based platform to prevent and rescue ROS-induced neurodegeneration.

The antioxidant function of nanozymes will be studied in primary neurons or human neurons reprogrammed from induced pluripotent stem cells by evaluating: (i) the mechanisms of cellular uptake and the intracellular fate; (ii) the ability in decreasing endogenous ROS under various conditions of oxidative insults (hypoxia, strong oxidants, radiation); (iii) their effects on neuronal survival and on biomarkers of neurodegeneration; and (v) their ability to pass the blood-brain and blood-retinal barrier. The most effective nanozymes will be investigated *in vivo* for their ability to counteract neuronal degeneration induced by acute or chronic oxidative stress. Rat and mouse models of retinal photoreceptor degeneration acutely triggered by phototoxic damage or toxic agents (such as iodoacetic acid) or chronically developing as the result of mutations in photoreceptor or pigment epithelium genes will be used. Experimental animals will be injected either intravitreally or subretinally with nanozymes and their visual system performances followed over time using electrophysiological techniques. The idea of acting on mechanisms at the origin of the signaling cascade that ultimately leads to neural cell death will pave the way to novel therapeutic strategies based on injectable, biocompatible nanotools.

The successful candidate is a highly motivated scientist with a strong teamwork attitude and interest in disease-oriented research. She/he should have a Master degree in Life Sciences (Medicine, Biology, Pharmacy, Biotechnologies or similar), and a good background in neurobiology. Previous experience in animal studies is welcome. For information, please contact dr. Elisabetta Colombo (elisabetta.colombo@iit.it) and dr. Stefano Di Marco (stefano.dimarco@iit.it).