DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO

40° CYCLE

Research line for one DM630/2024 fellowship

Title: Molecular mechanisms of the gut-brain communication in neurodevelopmental disorders

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Summary

The mutation Arg451Cys (R451C) found in autistic children in the gene encoding for Neuroligin 3, a postsynaptic adhesion molecule involved in synaptic maturation, has been shown to cause a local misfolding in the protein, its retention in the endoplasmic reticulum (ER) and the activation of a stress condition of the ER known as the “unfolded protein response”. Moreover, the mutation alters the trafficking of the protein to the plasma membrane, where it carries out its functional role. The knockin mouse for the R451C mutation in NLGN3 is a recognized model of autism with behavioral alterations typical of the social sphere and functional alterations in neurotransmission. The mouse model also presents gastrointestinal deficits that have also been found in children with autism.
Recent data obtained in our laboratory, have highlighted that the chronic administration of a probiotic in the knockin mouse model of autism NLGN3 R451C, shows significant effects on the rescue of the social deficits and on the expression of synaptic proteins involved with neurotransmission.
The goal of the present project is to investigate the molecular basis of the effect of probiotics on the cellular phenotype of neural stem cells taken from the mouse R451C NLGN3 expressing the mutant protein endogenously. Specifically, we propose to investigate the cellular and molecular effects of probiotics directly on the "gut-brain" axis through the analysis of the metabolites released by intestinal cells after treatment with probiotics, and their effect on the neuronal cells.

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