Description form for PhD position

(1) University: University of Genoa
(2) Course and Curriculum: Neuroscienze. Curriculum Neuroscienze e Neurotecnologie
(3) Enrolling date: 01/03/2025

Short title (6 words max)	Drug screening in CTNNB1 syndrome
Expanded Title	Pharmacological treatment of the newly identified CTNNB1 syndrome
Background (optional, 150 words)	CTNNB1 syndrome is a novel syndrome caused by the complete or partial alteration of one allele of CTNNB1. Clinical features of the syndrome include developmental delay, intellectual disability (ID), speech impairment, autistic behaviors, microcephaly, and reduced motor capabilities, as well as characteristic craniofacial features and ocular anomalies. Our group, together with the Clinical Proteomics Department of the "G. Gaslini Hospital" belongs to a multidisciplinary network focused on exploring all possible treatment strategies for this disease.
Description (250 words)	We aim to explore novel potential treatments of CTNNB1 syndrome by investigating the effect of small molecules from a library that we designed in stabilizing the interaction between the two molecules β–catenin and N-cadherin, which we have previously shown to be decreased in the Batface (Bfc) mouse, a preclinical model of CTNNB1 syndrome. In collaboration with the Gaslini Hospital, we will use proteomic approaches, accompanied by the characterization of metabolites and lipids, which can generate insights and indications for drug discovery. We will also test a novel programmable epigenetic editing technology, designed in one of our labs, to modulate the expression of possible off-targets misregulated by the identified molecules. The project includes three main parts: 1) Molecules in the library will be screened in neurons cultured in vitro to test their efficacy in correcting the structural and functional changes caused by impaired β-catenin interactions with N-cadherin, taking into account the crucial role of the β-catenin signalling and modulating any possible off-target with a target-specific epigenetic writer. 2) The molecules and the epigenetic writers that show modulatory effects in cultured Bfc neurons will be tested in neurons differentiated from iPSCs that are isolated from patients with CTNNB1 syndrome. 3) Then, we will select the treatment that shows the highest efficacy and most minor toxicity from the in vitro screening, and we will perform molecular analysis of proteins, metabolites, and lipids combined with a thorough functional study that will help define potential drug targets as well as monitoring of its efficacy by features critically associated with disease and treatment.
References	Tucci, V., et al., Dominant beta-catenin mutations cause intellectual disability with recognizable syndromic features. J Clin Invest, 2014. 124(4): p. 1468-82.
Main Supervisor	Valter Tucci
Additional Supervisor(s)	Angelo Serani
Essential expertise (please provide always 4 criteria)	

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i)	degree in Biology-related fields
ii)	
iii)	
iv)	
Desirable expertise (please provide always 4 criteria)	
i)	Experience in iPS/ES cells or primary cultures
ii)	molecular biology techniques
iii)	RNA/DNA handling
iv)	bioinformatics