The Wnt/β-catenin pathway as therapeutic target for oncological and neurodegenerative diseases

The Wnt/β-catenin signaling is an evolutionarily conserved pathway that has a crucial role in embryonic and adult life. Dysregulation of Wnt/β-catenin pathway has been associated with various diseases, including cancer and neurodegenerative disorders, in particular Parkinson’s disease (PD) [1-3]. Several molecular components of the signaling have been proposed as innovative targets for cancer therapy, and very recently, some of them have been also evaluated as potential therapeutic targets for PD [1-3]. Our research group, led by Dr.ssa Annalucia Serafino has a longtime experience in the study of the molecular mechanisms involved in cancer, degenerative and neurodegenerative diseases, infectious diseases and deficits of the immune system, as well as in the use of preclinical models for testing the pharmacological activity of synthetic and nature-derived molecules. In the last years the lab focused the attention on the Wnt/β-catenin pathway as an innovative therapeutic target in oncological (mainly solid tumors) and neurodegenerative (mainly Parkinson's disease, PD) diseases, and on the validation of some components of this signaling as prognostic/diagnostic biomarkers that could also be predictive for the responsiveness to targeted anticancer therapies. In this context, we have identified and validated in vitro some natriuretic peptides (NPs) as molecules with antitumor, neuroprotective and neurorepair activities, that act by directly modulating the Wnt/β-catenin pathway [4, 6]. Results from these researches have been in part published [4, 6] and in part are under evaluation for a patent application. Moreover, our group, by using animal models of primary and metastatic colorectal cancer, has also demonstrated that the Wnt/β-catenin signaling not only dominates the early stages of sporadic colorectal cancer (CRC), but could also represent the connection between pre-cancer inflammation (inflammatory bowel diseases, IBD) and increased risk of developing CRC [5]. We also showed that some crucial components of the Wnt/β-catenin pathway, when evaluated by immunohistochemistry using a multiparametric approach that includes the analysis of both expression and localization, could be potent markers for diagnosis, prevention and therapy in IBD and CRC, also possessing a predictive value for responsiveness to targeted therapies [5]. This kind of multiparametric approach, that could in general represent a high-performance technological tool useful for designing personalized therapies, has been selected as technology of interest in the BioTTasa/CNR Project (http://biottasadb.cbm.fvg.it Scheda #52) and has been recently presented on the Promo-TT platform (https://promott.cnr.it/).

Our researches benefit from collaborations with the University of Rome Tor Vergata, and specifically with the Department of Biomedicine and Prevention (Prof.ssa F.C. Sanguolo), who provided IPSCs from human fibroblasts for the evaluation and characterization of NP efficacy on dopaminergic neuron differentiation, and with the Lab. of Experimental Ecology and Aquaculture (Prof. C. Boglione), where we set up a model of PD in zebrafish. Furthermore, our group has also established a close collaboration with some internal groups at IFT with expertise in neuroscience and neurodegenerative diseases (Dr. M. Cozzolino, Dr. L. Manni, Dr.ssa M. Soligo, Dr.ssa T. Bisogno) and in oncology and Regulatory Science (Dr. P. Pierimarchi)

References:

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