Novel serotoninergic ligands for breast cancer treatment

The biochemical signals of Serotonin, or 5-hydroxytryptamine, 5-HT, in mammary gland become dysregulated in cancer and contribute to proliferation, metastasis and angiogenesis. In particular, serotonin leads to fat accumulation in white adipose tissue. These adipose cells provide a significant contribution to the progression of breast cancer in the tumor microenvironment, being a prerequisite for invasion, metastasis and chemoresistance of cancer cell. The discovery of new molecules able to address the signal pathways of serotonin may pave the way toward modulation of the plasticity of peritumor and adipose cells, and also offer new prognostic tools and therapeutic opportunities for the treatment of breast cancer. The effect of 5-HT on both cancer and adipose cells is mainly mediated by the 5-HT_{2A} receptor. Our research team has long been involved in the synthesis of serotoninergic receptor ligands (5HTRs), focusing in particular on chemical entities acting as selective ligands of 5-HT_{1A}, 5-HT_{2A} and $5HT_{2C}$ receptors. The proposed project aims at the design and synthesis of new serotonin receptor ligands able to attack adipose cells and interfere with their ability to support the phenotype BC. The objective is the identification of molecules potentially usable in combination with endocrine therapy in order to improve the effectiveness on patients with ER+ BC. The impact of newly synthesized ligands on Mammary Adipose derived-Mesenchymal Stem Cells (MAd-MSCs) isolated from adipose tissue biopsies of healty women, will be investigated by the Research and Clinical Pathology Unit of the University of Naples Federico II. To reach this aim the appropriate dose of ligand will be considered in order to avoid any possible cytotoxic effects on MAd-MSCs.