Endocannabinoid System in Human Disorders

The evidence that Δ⁹-tetrahydrocannabinol (THC) binds to specific receptors in mammals led to ground-breaking insights into a whole endogenous signaling system now known as the endocannabinoid (eCB) system. This system encompasses two G protein-coupled receptors (GPCRs), cannabinoid receptor type-1 (CB₁) and cannabinoid receptor type-2 (CB₂), their most studied endogenous ligands, the “endocannabinoids” N-arachidonylethanolamine (anandamide) and 2-arachidonoylglycerol (2-AG), and enzymes responsible for eCB biosynthesis and hydrolytic inactivation. Starting from its identification, eCB system has been widely investigated as potential target to develop new therapeutic strategies that went far beyond what could be predicted from the pharmacological actions of THC. Indeed, alterations in eCB signalling, owing to changes in the expression and function of cannabinoid receptors and eCB metabolic enzymes, as well as modified eCB tissue concentrations, were found to be associated with diverse pathological conditions.

The research team led by Dr. Bisogno aims at better understanding molecular and cellular bases responsible of function and malfunction of eCB system, in both central and peripheral nervous system, in order to develop new diagnostic and therapeutic options. By means of multidisciplinary approaches we: a) unveiled the biosynthetic and metabolic pathways of the eCBs and of some eCB-like molecules, b) developed selective inhibitors of eCB inactivation and biosynthesis, c) studied of the regulation of eCB levels in tissues under physiological and pathological conditions and developed specific techniques for the lipidomic profiling of these molecules, d) identified the first endovanilloid and the relationships between eCBs and endovanilloids.

Our research contributed to highlight that in almost each of the major therapeutic areas of interest alterations in the eCB system are associated with the onset, progress and symptoms of diseases as well as to the preclinical use of cannabinoids and endocannabinoid-based drugs as potential therapies in human disorders.

The line of research takes advantage of the collaboration with international leaders in the field of endocannabinoids and bioactive lipid derivatives including the inventor of the names “endocannabinoids” and “endovanilloids” Dr. Di Marzo (Institute of Biomolecular Chemistry, CNR, Pozzuoli and Université Laval, Québec City, Canada).

References:

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