UNIVERSITÀ DEGLI STUDI DI PADOVA

PROJECT

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1) Project title
Investigating melatonin receptors as therapeutic targets in neuropsychiatric disorders
2)Abstract (max 500 words)
Melatonin (MLT), a neuromodulator predominantly acting through G-protein coupled receptors MT1 and MT2, regulates various brain functions, including circadian rhythms, mood, pain, and sleep. Clinical utilization of MLT and non-selective MT1/MT2 receptor agonists in neuropsychiatric and sleep disorders remains controversial regarding their efficacy. Ongoing investigations in our laboratory underscore the significance of selectively targeting either MT1 or MT2 receptors in elucidating disease pathophysiology and advancing psychopharmacological drug discovery. This is underpinned by dynamic changes in receptor density throughout the light/dark cycle and the differential distribution of MLT receptors in the different brain regions. Furthermore, MT1 and MT2 receptors seem to modulate distinct physiological responses as example in sleep, anxiety, pain, and depression. Nevertheless, the precise roles of MT1 and MT2 receptors in the brain, alongside their potential as targets for novel neuropsychiatric therapies, necessitate further detailed investigation. This project aims at investigating the neuropsychopharmacological profiles of novel and selective ligands for MT1 and/or MT2 receptors in murine models, employing well validated preclinical behavioural pharmacology paradigms encompassing depression, psychosis, anxiety, social behavior, and cognitive and motor functions. We also aim at delineating their neuronal mechanisms of action using in-vivo electrophysiology in anesthetized or freely moving mice and immunohistochemical techniques, along with neurochemical assays to measure their effects upon the serotonergic, dopaminergic, and glutamatergic neurotransmissions. Finally, these preclinical findings will be complemented by assessments in selected patient populations with unipolar or bipolar depression and schizophrenia. In particular, we will analyse the correlations between plasma and genetic biomarkers of the melatonin system and psychopathology. Collectively, this comprehensive approach aims to provide a robust neurobiological and pharmacological foundation for the development of selective MT1 and/or MT2 receptor ligands as innovative drugs in neuropsychopharmacology.