Adeno-associated vectors and neuropsychiatric disorders

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SUMMARY

Most of the medications used for neuropsychiatric disorders target G protein coupled receptors (GPCR). Over the last ten years our work evolves towards the understanding of mechanisms controlling GPCR responsiveness and desensitization. Among the most important players in GPCR function, RGS proteins (Regulators of G protein signaling) and their interactive partners, act in a highly selective manner to control various neuronal responses. A large amount of clinical and preclinical studies implicate members of the RGS family in the pathophysiology of disorders such as addiction, depression and schizophrenia. Moreover, complexes between RGS proteins, G alpha subunits and other scaffolding molecules appear to dynamically regulate the actions of several drugs used for the treatment of CNS diseases, including L-dopa, antidepressant agents and opiate analgesics. Our group combines genetic mouse models with biochemical and molecular biology approaches in order to understand the brain region/receptor selective actions of RGS family members, such as RGS9-2, RGS4, RGS2 and RGSz. Adeno-associated viral constructs (AAV) provided a very important tool for brain region selective overexpression or deletion of a protein, as they are nontoxic, they have a long half life and they selectively infect neurons. This presentation provides some examples of tissue specific interventions in RGS protein activity in animal models of addiction, neuropathic pain and depression.