

A Chemical Biology Approach to Control Endocannabinoid Biosynthesis

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Endocannabinoids play an essential role in human health and disease, regulating processes such as immunomodulation, energy balance and neurotransmission. Diacylglycerol lipase- α (DAGL- α) is responsible for the production of the endocannabinoid 2-arachidonoylglycerol (2-AG) in the central nervous system. It is a potential drug target for the treatment of obesity and neurodegenerative diseases. Currently, there are no selective inhibitors and activity-based probes available for its study. The identification of selective DAGL- α inhibitors is hampered by a lack of assays that make use of endogenous DAGL- α activity in proteomes. Determination of the selectivity of the inhibitors in native tissues is important, because DAGL- α belongs to the class of serine hydrolases, containing more than 200 members with various physiological functions. Here, I will present a chemical biology approach to identify and characterize highly selective chemical probes to study the function of this protein both in vitro and in vivo.