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AKAPs and Adenylyl Cyclase: the Next Dimension in cAMP Signaling

Carmen Dessauer, Ph. D.
(http://www.dessauer-lab.com)
Professor and Vice-Chair
Dept. of Integrative Biology and Pharmacology
McGovern Medical School
University of Texas Health Science Center, Houston, TX

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Science 2, room 109

The overall goal of my laboratory is to understand the regulation of adenylyl cyclase/cyclic AMP signaling in physiological and pathophysiological states. Over the years, we have elucidated mechanisms of adenylyl cyclase regulation by RGS proteins, heterotrimeric G protein alpha and beta-gamma subunits, and protein kinases. More recently we have explored the spatial and temporal regulation of cAMP signaling and identified scaffolding proteins, known as A Kinase Anchoring Proteins (AKAPs) that can bind to specific isoforms of adenylyl cyclase to temporally and spatially regulate cyclic AMP. These complexes clearly shape the dynamics of cyclic AMP production in terms of the magnitude of the signal, the temporal nature of PKA activation, and regulation of specific downstream targets, including TrpV1 and I_{Ks} (KCNQ1) channels. Projects in the lab include 1) kinetic and mechanistic studies of enzyme regulation, 2) roles for AKAPs and other scaffolding proteins in the spatial kinetics of adenylyl cyclase and cAMP signaling, 3) physiological roles for type 9 adenylyl cyclase in heart, and 4) pathophysiological roles for cAMP signaling in chronic pain after spinal cord injury.

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