Version 2.0

Abstract

Back to Hit List

Grant Number:	5K21DA000218-05
PI Name:	VON ZASTROW, MARK E.
PI Email:	zastrow@itsa.ucsf.edu
PI Title:	
Project Title:	MECHANISMS OF RECEPTOR INTERNALIZATION IN DRUG ADDICTION

Abstract: This is a request for a scientist Development Award to support training in molecular biological and biochemical approaches for studying receptor.based mechanisms of drug addiction The prolonged administration of certain addictive drugs causes sequestration and/or down regulation of G protein-coupled receptors. These phenomena involve drug-induced internalization of receptors from the plasma membrane and their delivery to specific populations of intracellular vesicles. The mechanisms that mediate and control this receptor internalization are not known. While several classes of cellular proteins have been identified that associate with receptors and mediate specific events in signal transduction, studies of mutant receptors and cell lines indicate that none of these associations is required for drug-induced receptor internalization. Therefore other, as yet unidentified, mechanisms must mediate and control drug-regulated internalization. By focusing on adrenergic receptors as a physiologically important and experimentally advantageous model system, the proposed studies will provide training in biochemical and molecular biological approaches to (1) define receptor domains that determine specific steps in the internalization mechanism, (2) identify cellular proteins that associate with receptors and mediate these steps, and (3) purify and clone these additional proteins. This work will elucidate, in molecular detail, fundamental biological mechanisms relevant to drug addiction.

Thesaurus Terms:
beta adrenergic receptor, drug receptor, protein structure /function, receptor binding chimeric protein, drug addiction, gene mutation, protein sequence, recombinant protein affinity chromatography, cell free system, molecular cloning

Institution: UNIVERSITY OF CALIFORNIA SAN FRANCISCO
500 PARNASSUS AVE
SAN FRANCISCO, CA 94143

Fiscal Year: 1998
Department: LANGLEY PORTER PSYCHIAT INST
Project Start: 30-SEP-1994
Project End: 31-AUG-1999
ICD: NATIONAL INSTITUTE ON DRUG ABUSE
IRG: SRCD

Version 2.0

Abstract

Back to Hit List

Grant Number:	5R29DA010711-02
PI Name:	VON ZASTROW, MARK E.
PI Email:	zastrow@itsa.ucsf.edu
PI Title:	
Project Title:	MEMBRANE TRAFFICKING OF OPIOID RECEPTORS

Abstract: DESCRIPTION: (Applicant's Abstract) Mechanisms that regulate opioid receptors play important roles in opiate drug action and are of fundamental importance to the biology of addiction. The proposed studies focus on the regulation of opioid receptors by rapid endocytosis. This process is of particular interest because (a) it distinguishes between structurally homologous types of cloned opioid receptor (delta, mu, and kappa); and (b) it is differentially regulated by opioid peptides and morphine. I propose to elucidate molecular mechanisms that mediate and regulate opioid receptor endocytosis, with the goal of understanding the remarkable type-selectivity and ligand-specificity of this process. The Specific Aims of the proposed studies are (1) to define endocytotic mechanisms that determine the type-selectivity and ligand-specificity of opioid receptor endocytosis, (2) to identify receptor domains that mediate type-selective differences in the endocytosis of cloned opioid receptors, and (3) to examine the effect of protein phosphorylation sites on type-selective and ligand-specific endocytosis of opioid receptors. These studies are directly relevant to the biology of opiate action and addiction. In addition, because the ability of different full agonist ligands to differentially regulate receptor endocytosis is a novel finding, these studies have general importance to the cell biology of G protein-coupled receptors.

Thesaurus Terms:
endocytosis, opioid receptor, protein structure /function, protein transport
ligand, phosphoprotein, receptor binding
molecular cloning, site directed mutagenesis, tissue /cell culture

Institution: UNIVERSITY OF CALIFORNIA SAN FRANCISCO
500 PARNASSUS AVE
SAN FRANCISCO, CA 94143
Fiscal Year: 1998
Department: LANGLEY PORTER PSYCHIAT INST
Project Start: 15-JAN-1997
Project End: 30-NOV-2001
ICD: NATIONAL INSTITUTE ON DRUG ABUSE
IRG: NIDA