Doctoral College
Metabolic & Cardiovascular Disease

GLUTAMATE RECEPTORS: OPTOGENETICS AND ORIGINS

GUEST LECTURE by

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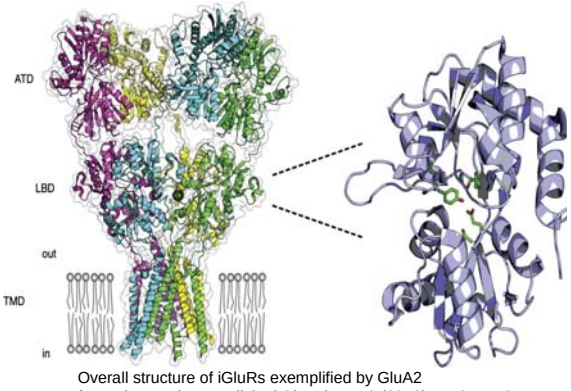
Wednesday, 15.02.2012
17:00h

SR 07.11, Preclinics, MUG (Harrachgasse 21)

Abstract

A major challenge in biology is to understand how cells sense and process signals from the environment. To understand cellular signaling we require technologies that generate well-controlled temporal and local stimulation. Our past work focused on ionotropic glutamate receptors (GluRs), which are the primary mediators of excitatory synaptic transmission in the mammalian central nervous system. In order to remote control neuronal signaling, we designed a novel GluR that is K^+-selective and light-gated [*Nature Neuroscience* (2010) 18: 1027-1032.]. This hyperpolarizing ion channel termed HyLighter is activated by millisecond light pulses and allows manipulating neuronal activity with unprecedented spatio-temporal resolution. In optogenetic experiments, HyLighter reversibly inhibits action potential firing in neuronal cultures and behavior in zebrafish. Inspired by the surprising compatibility of a K^+-selective pore with a GluR revealed in HyLighter, we discovered a new family of invertebrate glutamate receptors that combine a K^+ selectivity filter with glutamate sensing [*Nature Communications* (2011) 2: 232]. These receptors connect today's GluRs to their ancestral, prokaryotic ion channels and represent missing links in GluR evolution. The goal of our future work is to remote control signaling cascades with light to understand how cells orchestrate local and temporal signals into physiological responses.



Overall structure of iGluRs exemplified by GluA2
fom: Bioorganic & Medicinal Chemistry 18 (2010) 7759–7772

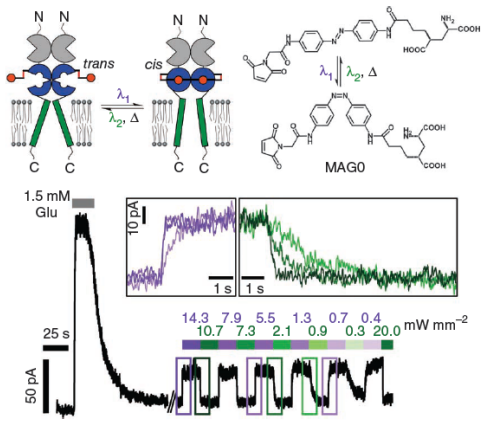


Photo-control of K^+ currents
from: Nature Neuroscience (2010) 18: 1027-1032