BBB Seminar (BMED380)

SCAN ME

Thursday, September 12. 14:30 at the BBB, Auditorium 4

Structure and regulation of AMPA glutamate receptor complexes

Ingo Greger
MRC Laboratory of Molecular Biology, UK

AMPA receptors (AMPARs) are cation channels that localize to neuronal synapses, where they are activated (gated) by the neurotransmitter L-glutamate. AMPARs mediate the majority of excitatory (depolarizing) neurotransmission in vertebrate brains and stand out for their diversity compared to other ionotropic glutamate receptors. These receptors are composed of four core subunits (GluA1-A4), which can assemble in various combinations and associate with a range of auxiliary subunits. Different receptor assemblies are characterized by specific gating and trafficking properties and can be selectively expressed in different brain circuits, and even within specific synapses in a given circuitry.

In this seminar, I will discuss the fundamental structure of AMPARs, including the differences between calcium-permeable (GluA2-lacking) and calcium-impermeable (GluA2-containing) forms, the organization of key auxiliary subunits, and how these architectural principles relate to their function and sub-synaptic organization.

Selected publications:

1. Ivica *et al.* Proton-triggered rearrangement of the AMPA receptor N-terminal domains impacts receptor kinetics and synaptic localization. ***Nat Struct Mol Biol.*** 2024 Aug 13.
2. Zhang *et al.* (2023) Structural mobility tunes signalling of the GluA1 AMPA glutamate receptor. ***Nature*** 621(7980): 877-882.
3. Zhang *et al.* (2021) Gating and modulation of a hetero-octameric AMPA glutamate receptor. ***Nature*** 594(7863): 454-458.
4. Herguedas *et al.* (2019) Architecture of the heteromeric GluA1/2 AMPA receptor in complex with the auxiliary subunit TARP γ8. ***Science*** 364(6438): pii: eaav9011.
5. Watson *et al.* (2017) Synaptic transmission and plasticity require AMPA receptor anchoring via its N-terminal domain. ***Elife*** 14;6: pii: e23024.
6. Greger *et al.* (2017) Structural and Functional Architecture of AMPA-Type Glutamate Receptors and Their Auxiliary Proteins. ***Neuron*** 94: (4):713-730.
7. Herguedas *et al.* (2016) Structure and organization of heteromeric AMPA-type glutamate receptors. ***Science*** 352: (6285):aad3873.
8. Cais *et al.* (2014) Mapping the interaction sites between AMPA receptors and TARPs reveals a role for the receptor N-terminal domain in channel gating. ***Cell Rep***. 9: 728-40.
9. Penn *et al.* (2012) Activity-mediated AMPA receptor remodeling, driven by alternative splicing in the ligand-binding domain. ***Neuron*** 76: 530-10.

Chairperson: Hongyu Zhang, Department of Biomedicine