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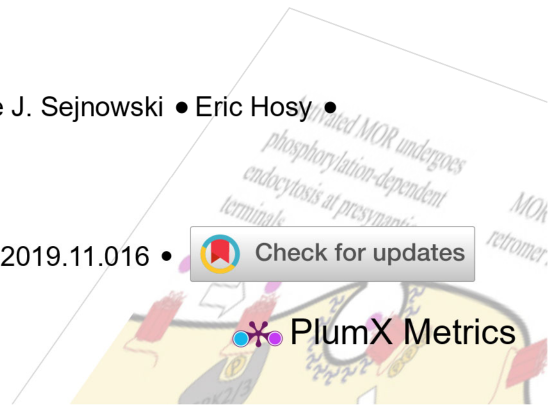
A Discrete Presynaptic Vesicle Cycle for Neuromodulator Receptors

Damien Jullié • Miriam Stoeber • Jean-Baptiste Sibarita • ... Terrence J. Sejnowski • Eric Hosy • Mark von Zastrow 8 • Show all authors • Show footnotes



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Highlights

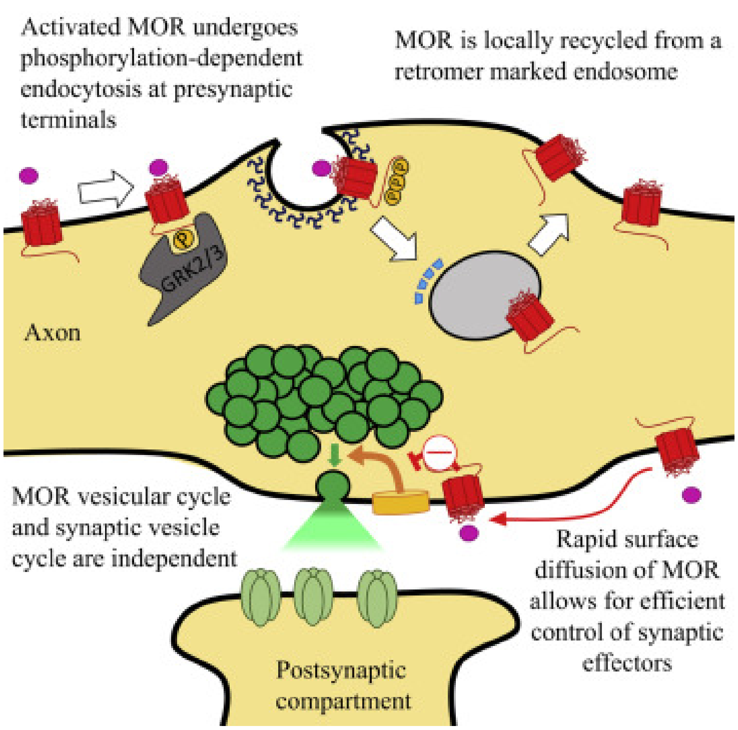
- Opioid receptors are diffusely distributed and laterally mobile on the axon surface
- Opioid receptors are phosphorylated and internalized at presynaptic terminals
- Opioid receptors locally recycle separately from the synaptic vesicle cycle
- Lateral mobility and allostery suggest a new strategy for presynaptic neuromodulation

Summary

or function of GPCRs is to inhibit presynaptic neurotransmitter release iiri
l-activated receptors to couple locally to effectors at terminals. The cur

specifically at presynaptic terminals. We delineate a parallel regulated endocytic cycle for GPCRs operating at the presynapse, separately from the synaptic vesicle cycle, which clears activated receptors from the surface of terminals and locally reinserts them to maintain the diffusible surface pool. We propose an alternate strategy for achieving local control of presynaptic effectors that, opposite to using receptor immobilization and enforced proximity, is based on lateral mobility of receptors and leverages the inherent allostery of GPCR-effector coupling.

Graphical Abstract



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