A novel trafficking pathway for NMDA receptors to synapses

J.M. Montgomery[1], O. Jeyfrous[2,3], T. Desilva[1], M. Schubert[1], C.G. Garner[2] and W.N Green,[3] [1]University of Auckland, New Zealand, [2]Stanford University, CA, USA, and [3]University of Chicago, IL, USA. (Introduced by John Bekkers)

Plasticity of the circuitry that wires the brain is a fundamental property of neurons that is thought to underlie learning and memory. We and others have shown that the development and elimination of synapses and changes in the strength of existing synapses in the hippocampus form the basis of this plasticity. The N-methyl-D-aspartate (NMDA)-type glutamate receptor expressed at synapses is required for learning and memory and is critical for normal brain function. At a cellular level, this receptor plays a pivotal role in triggering and controlling synapse plasticity. Our data show evidence for a unique trafficking pathway for the movement of NMDA receptors from the soma to synapses in rat hippocampal neurons. NMDA receptors, together with the synaptic scaffold protein SAP97, bud from somatic endoplasmic reticulum (ER) compartments and travel within dendrites in ER-derived vesicles. Live cell imaging of GFP-NR1 + DsRed-ER or GFP-NR1 + RFP-SAP97 shows these vesicles are highly mobile. NMDA receptors bypass somatic golgi as neither disruption of somatic golgi function with brefeldin A nor temperature shift to prevent protein exit from the golgi influence subcellular trafficking of NMDA receptors. These data provide evidence for a novel sorting mechanism for NMDA receptors resulting in a unique trafficking pathway to ensure specific, highly regulated synaptic NMDA receptor targeting.