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Advances in imaging, disease mechanisms, and therapies for ageing dementia research

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Title	Sorting nexin 27 (SNX27) is a substrate of the Ca2+/calmodulin-dependent protein kinase IIα (CaMKIIα)
Abstract (max 300w)	Ca2+/calmodulin-dependent protein kinase IIα (CaMKIIα) is an essential mediator of bidirectional plasticity, learning and memory. Upon activation, CaMKIIα undergoes a conformational change from an autoinhibited state to an "autonomously" active state that no longer requires the presence of Ca2+. Thus, it has long been regarded as a memory molecule. Here, we identify sorting nexin 27 (SNX27), a key regulator of endocytic recycling, as an interactor and substrate of CaMKIIα. The interaction between SNX27 and CaMKIIα involves a state-dependent switch from mainly the SNX27-PDZ domain during CaMKIIα autoinhibited state to the SNX27-FERM domain when the CaMKIIα is fully active. In addition, mass spectrometry analysis has identified serine residues within the SNX27-PDZ domain as CaMKIIα-dependent phosphorylation sites. Mutation of these serine residues modulates SNX27 binding to the GluN2A subunit of NMDA receptors (NMDARs), suggesting a role of CaMKIIα-dependent phosphorylation of SNX27 may regulate the endosomal recycling of NMDARs during synaptic plasticity.

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