

POSTER PRESENTATION

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The role of SorLA in neurotrophic activity and complex behavior

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SorLA binds amyloid precursor protein (APP) in the trans-Golgi network and protects it against proteolysis by both the alpha- and beta-secretases, preventing the generation of toxic amyloid-beta peptide. We have recently found that SorLA also affects neuronal function in a different manner by acting as sorting receptor for the neurotrophic factor GDNF and its receptors GFR α 1 and RET, directing them from the cell surface to endosomes. Through this mechanism, GDNF is targeted to lysosomes and degraded while GFR α 1 and RET recycles, creating an efficient GDNF clearance pathway. SorLA thereby influences a number of neuronal systems known to depend on GDNF activity including the dopaminergic system and the hippocampus. Accordingly, mice with altered SorLA expression exhibit altered reward and memory function, and a behavioral phenotype characterized by altered anxiety, hyperactivity, and response to psychostimulants.

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