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Board Number: B503**Competition in the postsynaptic density for PDZ domains of PSD-95.**T. Mastro¹, A. Preza¹, P. Kind², M.B. Kennedy¹;¹Biology and Biological Engineering, Caltech, Pasadena, CA, ²Centre for Integrative Physiology, The University of Edinburgh, Edinburgh, United Kingdom

Molecular mechanisms of synaptic plasticity are of great interest because derangement of synaptic plasticity contributes to neural diseases such as autism, schizophrenia, cognitive impairment, neuropathic pain, epilepsy, and stroke. This work addresses the molecular mechanisms underlying NMDA-type glutamate receptor-triggered plasticity at excitatory synapses. A critical step in this process is a change in the rate of trapping of AMPA-type receptors (AMPA) in the postsynaptic density (PSD), which increases the number of AMPARs and strengthens the electrical signal at the synapse. Our work aims to determine whether trapping of AMPARs in the PSD is mediated by rearrangement of the PSD scaffold caused by changes in the affinity of different PSD proteins for the PDZ domains of the major synaptic scaffold protein, PSD-95. Our earlier publication (1) supports this notion by showing that: 1. Phosphorylation of the abundant PSD protein synGAP by CaMKII reduces its affinity for the PDZ domains of PSD-95; and 2. The composition of the PSD is altered in synGAP deficient mice such that AMPAR-binding proteins with PDZ ligands, including TARPs and LRRTM2, are increased in concentration relative to PSD-95. We have now replicated these findings in synGAP-deficient rats. These findings suggest that the extent of binding of particular synaptic proteins to the PDZ domains of PSD-95 is regulated by activity-dependent phosphorylation of synGAP. We are testing this hypothesis in cultured rat neurons. We have isolated PSDs from neuronal cultures before and after induction of synGAP phosphorylation by pharmacological activation of NMDARs. The ratios of AMPAR-associated proteins to PSD-95 in the PSDs are determined by quantitative immunoblotting. We have found that the ratio of TARPs to PSD-95 is consistently increased in PSDs after chemical activation of synaptic NMDARs. We are using cultures from synGAP-deficient rats to determine if synGAP deficiency alters the composition of the PSD in rat cultures. We plan to transfect with a variety of synGAP mutant proteins in order to determine which domains or phosphorylation sites on synGAP are important for regulating PSD composition. 1.

Walkup, W. G. 3rd, Mastro, T. L., Schenker, L. T., Vielmetter, J., Hu, R., Iancu, A., Reghunathan, M., Bannon, B. D., and Kennedy, M. B. (2016) A model for regulation by synGAP- α 1 of binding of synaptic proteins to PDZ-domain 'slots' in the postsynaptic density. *Elife* 5, e16813.

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Board Number: B504**Nuclear Factor One (NFI)-Dependent Developmental Program Directs the Timing of Gene Expression in Maturing Neurons.**B. Ding^{1,2}, P. Dobner¹, D. Kilpatrick¹;¹Dept. of Microbiology and Physiological Systems and Program in Neuroscience, University of Massachusetts Medical School, Worcester, MA, ²Dept. of Molecular Biology, University of Texas Southwestern Medical Center, Dallas, TX

Developmental timing mechanisms play an essential role in nervous system development, and their disruption during synapse maturation is implicated in neurodevelopmental disorders. To examine how the timing of gene expression related to synapse formation is regulated during neuronal maturation, we used cerebellar tissues from gene knockout mouse and lentiviral transduction of mouse cerebellar