PROGRESS IN NEUROSCIENCE PINS

Seminar Series of the
Brain & Mind Research Institute
Weill Cornell Medical College (WCMC)
&
The Graduate Program in Neuroscience of
WCMC and Sloan Kettering Institute

Thursday, 10/2/14, 4 PM, coffee at 3:45 PM
Weill Auditorium

Are Neurotrophic Factors Relevant to Alzheimer's disease?

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Abstract:

Alterations in trophic factors have been associated with neurodegenerative disorders, such as Alzheimer's and Huntington's diseases, but the earliest events after a loss of neurotrophic factors have not been defined. Therefore, we performed transcriptional profiling in cultured rat hippocampal neurons to understand molecular and cellular mechanisms that follow the withdrawal of BDNF. We used a TrkB ligand scavenger (TrkB-F_c) to sequester endogenous neurotrophic factor activity in rat hippocampal cultures. Analysis of the transcriptional profile indicated an immediate change in gene expression at early time points (1.5 to 3 hrs). Withdrawal of BDNF leads to a significant decrease in genes associated with vesicular trafficking and synaptic plasticity, as well as selective increases in several protein phosphatases. Reduced neurotrophic factor support has been implicated as a mechanism to account for changes in synaptic plasticity during normal aging and neurodegenerative disorders. A comparison of these changes with recent studies of postmortem brain tissue from Alzheimer's disease revealed striking similarities in gene expression changes. These changes are relevant to a wide number of conditions in which levels of BDNF are compromised. Based on these findings, we hypothesize that loss of BDNF leads to changes in expression of synaptic proteins, which may reflect an early sign of vulnerability to neurodegeneration.

Recent relevant publications:

1 Scharfman, H.E. and Chao, M.V. (2013) The entorhinal cortex and neurotrophin signaling in Alzheimer's disease and other disorders. *Cognitive Neurosci* 4, 123-135.

Matrone, C., Barbagallo, A.P., La Rosa, L.R., Florenzano, F., Ciotti, M.T., Mercanti, D., Chao, M.V., Calissano, P.,D'Adamio, L. (2011) APP is phosphorylated by TrkA and regulates NGF/TrkA signaling. *J Neuroscience* 31, 11756-11761.

Arevalo, J.C., Wu, S.H., Takahashi, T., Zhang, H., Yu, T., Yano, H., Milner, T.A., Tessarollo, L., Ninan, I., Arancio, O. and Chao, M.V. (2010) The ARMS/Kidins220 scaffold protein modulates synaptic transmission. *Mol Cell Neurosci* 45, 92-100.

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