

# International Conference on Central Nervous System - Drug Effects & Novel Drug Development

September 5-7, 2012 DoubleTree by Hilton Philadelphia Center City, USA

## **A $\beta$ PP- CTF-AICD domains phosphorylation and interaction with adaptor proteins: Signal transduction and/or transcriptional role-relevance for Alzheimer pathology**

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In recent decades, the study of the amyloid precursor protein (APP) and of its proteolytic products carboxy terminal fragment (CTF), APP intracellular C-terminal domain (AICD) and amyloid beta has been mostly focussed on the role of APP as a producer of the toxic amyloid beta peptide. In my presentation I will reconsider the role of APP suggesting, in a provocative way, the protein as a central player in a putative signalling pathway. I highlight the presence in the cytosolic tail of APP of the YENPTY motif which is typical of tyrosine kinase receptors, the phosphorylation of the tyrosine, serine and threonine residues, the kinases involved and the interaction with intracellular adaptor proteins. In particular, I will discuss the interaction with Shc and Grb2 regulators, which through the activation of Ras proteins elicit downstream signalling events such as the MAPK pathway. I will also address the interaction of APP, CTFs and AICD with other adaptor proteins and in particular with Fe65 for nuclear transcriptional activity and the importance of phosphorylation for sorting the secretases involved in the amyloidogenic or non-amyloidogenic pathways. I will provide a novel perspective on Alzheimer's disease pathogenesis, focussing on the perturbation of the physiological activities of APP-CTFs and AICD as an alternative perspective from that which normally focuses on the accumulation of neurotoxic proteolytic fragments.

### **Biography**

Gennaro Schettini is Full Professor of Pharmacology at the School of Medicine and Pharmacy of University of Genova. Graduated magna cum laude at the University of Naples, Italy, spent 3 years at the University of Virginia, than at the New England Medical Center-Tufts University of Boston, at UCSD and lately at University of Melbourne. Has focused his research interests in the field of signal transduction involvement in neuronal survival and death and how it can relate to neurodegenerative diseases, namely Alzheimer Disease. His scientific production accounts for more than 225 scientific publications on international peer reviewed journals and the impact of his scientific production results in an H-index of 37.

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