

## The Astrocytes, not just Bystanders in Alzheimer's Disease (AD)

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There are two kinds of AD, the rare early onset AD (EOAD) and the slowly developing, late-onset AD (LOAD), which includes 95-99% of the cases. While the mutant driver genes of EOAD are known, the key LOAD drivers remain elusive. Hitherto, AD-related studies have mostly focused on neurons. But astrocytes connect to and collaborate with neurons in brain functions and are the stem cells for adult hippocampal neurogenesis. Therefore, we have developed a method of culturing phenotypically normal adult human astrocytes (NAHAs) directly following their isolation from the temporal cerebral cortex and are using such cultures to explore NAHAs roles in AD. Thus, we have shown that NAHAs react to the exposure to mixtures of proinflammatory cytokines and/or amyloid- $\beta$  peptides ( $A\beta$ ) by inducing GTP cyclohydrolase 1 (GCH1) and nitric oxide synthase-2 (NOS-2) thereby overproducing NO, and by synthesizing vascular endothelial growth-factor-A (VEGF-A) and  $A\beta$ 42 peptides. We are investigating the molecular mechanisms underlying such NAHAs responses to the indicated stimuli, including the involvement of plasmalemmal receptors and of their intracellular signalling pathways. In parallel, we are studying the effects of proinflammatory cytokines and/or  $A\beta$  peptides on cultured cerebral cortex normal adult human neurons (NAHNs) and the molecular interactions occurring in co-cultures of NAHAs with NAHNs. It is hoped that the results of our studies carried out on normal human adult nerve cells will expand our understanding of the molecular triggers and mechanisms underlying the development of AD and identify novel therapeutic targets to be translated into the clinical settings.

### Biography

Prof. Dr. Ubaldo Armato has completed his Medicine & Surgery courses at 24 years from Padua University (Italy). Next, he carried out his research work at Human Anatomy Institute, Padua Medical School, with stages at London School of Hygiene & Tropical Medicine (UK), and Canada's National Research Council (Ottawa, Ont.). Since 1986 he is Full Professor of Histology & Embryology and Director of the homonymous Section, Department of Life & Reproduction Sciences, Verona Medical School. He has published more than 90 papers in refereed journals and is an editorial board member of Journal of Alzheimer's Disease and Journal of Alzheimer's Disease & Parkinsonism.

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