

UNIVERSITÁ DEGLI STUDI DI BOLOGNA

## DIPARTIMENTO DI CHIMICA "GIACOMO CIAMICIAN"

VIA F. SELMI 2, 40126, BOLOGNA, (ITALY)

## AVVISO DI SEMINARIO

Giovedì 14 Febbraio, Aula I, ore 14.30

## **Dr. Mario Salmona**

Head, Department of Molecular Biochemistry and Pharmacology, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Via Giuseppe la Masa 19, 20156 Milan, Italy

## A bio-inspired therapeutic strategy for Alzheimer's disease

Alzheimer's disease (AD) is the most common form of dementia and a pressing challenge in countries with aging populations. Hence, the huge scientific and financial effort invested. The central feature in AD pathogenesis has been identified, i.e., the intracerebral accumulation of neurotoxic forms of amyloid-B peptide  $(A\beta)$  – which aggregate from small soluble oligomers. Nonetheless, the complexity of this disorder is such that more than 460 clinical trials searching for disease-modifying drugs, have dramatically failed and any effective treatments are still lacking. We believe that an advance in the compelling therapeutic issue can come from a radically different approach, subverting the ill-defined bottom-up track of previous attempts and transitioning to bioinspiration. Our aim is to develop a therapeutic strategy stemming from the illuminating clinical observation that naturally-occurring variants of A $\beta$  protect from this disease. In 2009, on the basis of a clinical case, we described a genetic variant of AB (ABA2V) with the prominent ability of hindering amyloidogenesis. More recently, another variant (ABA2T), involving the same codon, was found to be protective against AD. We think that the knowledge of the molecular mechanisms underlying the antiamyloidogenic properties of A2V and A2T begets a new scenario where efficient therapies against AD can be developed. To this end we carried out (i) the determination of the molecular machinery underlying the actual protective effects of A2V and A2T, and the development of lead compounds displaying A2V/A2T-like anti-amyloidogenic properties, by biophysical / biochemical / computational methods and cellular / nematode / mouse models; (ii) the preclinical assessment of their efficacy in cell and animal models.

Colleghi e studenti sono cordialmente invitati

Il Direttore del Dipartimento

Prof. F. Zerbetto

Prof. F. Paolucci