Epigenetic approaches for the treatment of Alzheimer’s disease

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Alzheimer’s disease (AD) drug development is mainly driven by the amyloid hypothesis. Unfortunately, the results of these drugs, that even may remove senile plaques, failed in reverting or stopping the dementia. Thus, it is emerging the idea that other pathways should be explored. Recent findings propose that epigenetic mechanisms, such as histone acetylation, are underlying memory deficits in AD. We become interested in Phenylbutyrate (PBA), as it is a drug that has potential properties that may be beneficial for AD. We demonstrated that PBA reverses memory deficits and the histopathological AD marks in the Tg2576 mouse model of the disease. HDAC inhibitors, like PBA, are being investigated for possible therapeutic effects in AD. It remains unclear which HDAC subtypes are involved in the pathophysiology of AD, and most of the HDACi tested are pan-HDACs. In terms of drug discovery, a greater selectivity may be required in terms of both specificity and safety. Specially, and since two isoforms, HDAC2 and HDAC6, seems to be the ones that may play a relevant role in the pathophysiology of AD, they should be the ones to be selectively inhibited. Based on this rational, in the last 2 years, we have been working in a novel strategy for the treatment of AD with a new generation of selective chemical compounds synthesized by the Small Molecule Drug Discovery platform at CIMA.

Biography

Mar Cuadrado-Tejedor got her PhD at University of Navarra, Spain in 2003. She is Associate Professor at the Department of Anatomy at School of Medicine at University of Navarra and forms part of Cellular and Molecular Neuropharmacology: Behaviour research team at the Center for Applied Medical Research (CIMA). Her research is mainly focused on finding new therapeutic targets for Alzheimer’s disease.

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