PREVENCIÓN DEL DOLOR POST-QUIRÚRGICO MEDIANTE EL USO DE UN OLIGODEOXYNUCLEÓTIDO INMUNOMODULADOR - EVIDENCIA PRE-CLÍNICA. PREVENTION OF POSTSURGICAL PAIN THROUGH USE OF AN IMMUNOMODULATING OLIGODEOXYNUCLEOTIDE – PRE-CLINICAL EVIDENCE.

Of the estimated 320 million people undergoing surgery each year, virtually all will develop acute postoperative pain, described as moderate, severe or extreme in 75% of the cases. Unsolved postoperative pain is detrimental for subsequent recovery and impacts the patient's quality of life. Moreover, it can lead to chronic postoperative pain in around 10% of patients with an estimated economic burden of US$43,000 per year/patient. In recent times, the role of the immune system in the mechanisms of pain is receiving serious attention, also for the development of new therapeutic agents. IMT504 is an oligodeoxynucleotide with immunomodulatory and tissue repair properties. Work in our laboratory for the past 15 years has exposed remarkable anti-allodynic and anti-inflammatory effects in various animal pain models. In the present talk, we will present novel data suggesting that, by targeting the immune system and MSCs, pre-emptive IMT504 modifies the response to surgical incision in an anti-allodynic and pro-resolution fashion. Moreover, we will reveal that this approach also results in opioid-sparing effects. Finally, we will address the steps taken thus far in relation to the validation of IMT504 as a therapeutic agent, with the aim of its future use in a variety of pain conditions.

Autores: Julia Rubione, Sandra Sbrascini, Bernardo Miguel, Candelaria Leiguarda, María Florencia Coronel, Carly McCarthy, Alejandro Montaner, Marcelo J. Villar, Pablo R. Brumovsky.

Afiliación: Instituto de Investigaciones en Medicina Traslacional, CONICET-Universidad Austral
Área de la Farmacología: Immunopharmacology
Dirección de Correo: pbrumovs@austral.edu.ar
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SIMPOSIO / SYMPOSIA 5

Coordinador Dr. Jorge Fuentealba (UdeC). Alzheimer Disease: an Update from basic to clinical research. Nibaldo Inestrosa (UMAG), Gonzalo Klassen (UdeC), Carlos Opazo (Florey Institute AU), Jorge Fuentealba (UdeC).

MENOPAUSIA Y DESARROLLO DE LA ENFERMEDAD DE ALZHEIMER. MENOPAUSE AND DEVELOPMENT OF ALZHEIMER´S DISEASE.

Late onset Alzheimer´s disease (AD) is a neurodegenerative disease with gender differences in its onset and progression. In fact, postmenopausal women are most frequently affected by sporadic AD in a ratio 3:1, differently from the incidence in the infrequent hereditary illness occurring in younger patients in a ratio 1:1. A particularly interesting aspect is the role of sex steroids on neuroprotection. Estrogen (E2) deficiency occurring in spontaneous or surgical menopause has been associated to cognitive decline; in this context, several studies have shown that early E2 replacement exerts neuroprotective effects. Here, we will address the role of estrogen deficiency and the role of Wnt signaling in the processes involved in the development of AD, including amyloid precursor protein (APP) processing to form senile plaques and Tau phosphorylation forming neurofibrillary tangles. Since AD is the most prevalent dementia and incurable disease, understanding its molecular pathogenesis could lead to the development of a specific therapeutic strategy.

Autores: Inestrosa NC.1,2 ; Villaseca P.1

Afiliación: 1Center of Excellence in Biomedicine of Magallanes (CEBIMA), University of Magallanes, Punta Arenas Chile, and 2Center for Aging and Regeneration (CARE), Pontifical Catholic University of Chile, Santiago, Chile.

Área de la Farmacología: Neuropharmacology
Dirección de Correo: ninestrosa@bio.puc.cl

LA ENFERMEDAD DE ALZHEIMER CONSTITUYE LA CAUSA MÁS FRECUENTE DE DEMENCIA. ALZHEIMER'S DISEASE IS THE MOST COMMON CAUSE OF DEMENTIA.

In the world, in 2019, around 55 million people had some type of dementia, a figure that is estimated to rise to 139 million in the year 2050. Currently in Chile, more than 200 thousand people live with dementia. It is a progressive disease that affects the cognitive functions of the individual, which significantly compromises their activities of daily living. Neuropsychiatric manifestations are also frequent. The most important neuropathological feature of Alzheimer's disease is the abnormal deposition of amyloid beta protein in the brain and the deposition of tau protein aggregates. It is known that such alterations can appear in the brain decades before clinical manifestations, a condition that has been called pre-clinical Alzheimer's disease. In recent times, the so-called biological markers of the disease have been developed, which have an important role in the understanding of pathophysiology, in the diagnosis and in clinical trials of drugs. It is a disease that has no treatment. There is a lot of ongoing research into therapies aimed at removing amyloid plaques from the brain. For this reason, it is known that prevention and intervention on modifiable risk factors play a fundamental role in reducing the incidence of the disease, thus being able to avoid or delay the onset of up to 40% of dementias.

Autores: Klassen G.

Afiliación: Faculty of Medicine, University of Concepcion

Área de la Farmacología: Neuropharmacology
Dirección de Correo: gklaasse@udec.cl

PROGRESOS EN LA CURA DEL ALZHEIMER. PROGRESS WITH THE CURE FOR ALZHEIMER'S DISEASE.

Alzheimer's disease (AD) is a debilitating aging-related disorder that has an enormous social and economic impact worldwide. Therefore, the quest to understand and treat AD is fundamental for neuropharmacology. Despite the identification of several genetic and risk factors associated with AD, the definite mechanism that may explain the onset and progress of this disease is unknow. Thus, an effective long-term treatment to prevent or treat its symptoms is still not available. The aim of this presentation is to describe and discuss the recent advances on factors that may contribute to the cognitive decline of this disease and the emerging therapeutic interventions that are currently under investigation. Considering that age is the most important risk factor for this disease, a special focus of this presentation will be the role of oxidate stress and redox-active metal dyshomeostasis on AD, with emphasis on the impact of the formation and clearance of proteins that are key to maintain proteostasis and synaptic function that are found altered in AD. Finally, a section of this presentation will be advocated to discuss the need of early and long-term interventions that will open a new opportunity for clinical trials that have failed to establish an effective therapy for AD.

Autores: Opazo C.

Afiliación: The Florey Institute of Neuroscience and Mental Health The University of Melbourne.

Área de la Farmacología: Neuropharmacology
Dirección de Correo: carlos.opazo@florey.edu.au

UN GRAN OLVIDADO: EL ROLE DEL RECEPTOR P2X2 EN LA ENFERMEDAD DE ALZHEIMER. A GREAT FORGOTTEN: THE ROLE OF P2X2 RECEPTORS IN ALZHEIMER'S DISEASE.

The soluble oligomers of beta amyloid peptide (SOAβ) are the principal neurotoxic agents that can explain the main symptoms of Alzheimer's disease (AD) at cellular levels. One of the main, the overload of intracellular Ca2+; however, in our group we have found there is evidence that SOAβ causes leakage of ATP to the extracellular space. It is well documented that extracellular ATP activates P2X receptors (P2XR), widely expressed in Central Nervous System (CNS) cells. Thus, P2XR act neuromodulating the synaptic activity, intracellular Ca2+ oscillations and facilitating neurotransmitter release. In our group we have demonstrated that the overexpression of P2X2R is upregulated induced by SOAβ, opening the possibility that this excess of P2X2R could potentiate the toxic mechanisms induced by SOAβ and contribute to physiopathology of AD. Importantly, we have observed the increase of P2X2Ris in cell lines, mice hippocampal neurons, and late Break stages of AD patients. These findings open a new pharmacological space to consider that the P2X2R as a key novel target to develop new therapeutic strategies to treat AD.

Autores: Fuentealba J, Godoy PA, Ramírez-Molina O, Panes JD., Flores-Núñez O., Gavilan J.
Afiliación: Laboratory of Screening of Neuroactive Compounds, Dept. Physiology, Fac. Biological Sciences, University of Concepcion.

Área de la Farmacología: Neuropharmacology
Dirección de Correo: jorgefuentealba@udec.cl
Agradecimientos: fondecyt 1200908 (JF), Beca ANID 21200612(JG); 21141247(JP); 21211001(ORM).