Neurodegeneration and Neuroprotection

Dra. CARME AULADELL

Position: Associate Professor

Research Interests

The research of our group is focused in the identification of new therapeutic targets to prevent neuronal degeneration through the study of cellular processes that occurs in neurodegenerative diseases.

The c-Jun N-terminal kinase (JNKs), also known as stress-activated protein kinase (SAPK), is activated in response to wide range of cellular stresses. Aberrant activation of JNK has been implicated in the pathogenesis of different neurodegenerative diseases as Alzheimer and Parkinson. Accordingly JNKs could be a potential target for preventing neurodegenerative disease. That is why we have focused our study on the function and the mechanisms of JNK pathway. There are three JNK isoforms (JNK1, JNK2 and JNK3) which mediate a plethora of physiological and pathological functions. However, only few data are available about the individual actions of specific JNK in brain functions. To analyze the particular implication of the JNK isoforms, in the apoptotic and inflammatory process, we use genetically modified mice, jnk1(-/-), jnk2(-/-) and jnk3(-/-) treated with kainic acid (KA), an analog of glutamate, that triggers temporal lobe epilepsy in humans. We have evidenced that the lack of jnk1 and jnk3 have a neuroprotective effect against KA, effect not observed in jnk2 null mice. Therefore, JNK1 or JNK3 are a promising target for blocking the brain damage induced by excitability. Thus, we are studying which pathways can be responsible for these differential effects. Further, understanding of the physiological function of JNK has come from target deletion of its activators, MKK4 and MKK7. In this way we are setting up conditional knockout mice for mkk4 and mkk7 genes using the Cre-LoxP recombination system, under specific promoters for glial and neuronal cells. In collaboration with the “Anatomía Patológica, Institut Hospital del Mar, Barcelona” we are studying the alterations of JNK pathway in post-mortem human brains patients affected with neurodegenerative diseases.

Current Research Lines

- Identification of new therapeutic targets to prevent neuronal degeneration
- Identification the role of JNK isoforms in the control of brain plasticity

Research team

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Technologies/methods:

- Detection of specific targets by Western Blot, hystochemistry and cytochemistry.
- Microarray analyses.
- Distribution pattern of mRNA by in situ hybridization.
- Nitric Oxide Assays and evaluation of free radicals assessment.

Recent Publications

Busquets O, Ettcheto M, Pallàs M, Beas-Zarate C, Verdaguer E, Auladell C, Folch J, Camins A.(2016). Long-term exposition to a high fat diet favors the appearance of β-amyloid depositions in the brain of C57BL/6J mice. A potential model of sporadic Alzheimer's disease. **Mech Ageing Dev.** 2016 Nov 15. pii: S0047-6374(16)30085-9. doi: 10.1016/j.mad.2016.11.002.

Auladell C, de Lemos L, Verdaguer E, Ettcheto M, Busquets O, Lazarowski A, Beas-Zarate C, Olloquequi J, Folch J, Camins A. (2016). Role of JNK isoforms in the kainic acid experimental model of epilepsy and neurodegeneration. **Front Biosci** (Landmark Ed). 2017 Jan 1;22:795-814.

Petrov D, Luque M, Pedrós I, Ettcheto M, Abad S, Pallàs M, Verdaguer E**,** Auladell C, Folch J, Camins A. (2016). Evaluation of the Role of JNK1 in the Hippocampus in an Experimental Model of Familial Alzheimer's Disease. **Mol Neurobiol**. 2016 Nov;53(9):6183-6193.

Verdaguer E., Brox S., Petrov D., Olloquequi J., Romero R., de Lemos M.L., Camins A., Auladell C. (2015). Vulnerability of calbindin, calretinin and parvalbumin in a transgenic/knock-in APPswe/PS1dE9 mouse model of Alzheimer disease together with disruption of hippocampal neurogenesis. **Exp Gerontol**. 2015 Sep;69:176-88.

Ettcheto M., Junyent F., de Lemos L., Pallas M., Folch J., Beas-Zarate C,, Verdaguer E., Gómez-Sintes R., Lucas J.J., Auladell C. Camins A. (2015). Mice Lacking Functional Fas Death Receptors Are Protected from Kainic Acid-Induced Apoptosis in the Hippocampus. **Mol Neurobiol.** 2015 Aug;52(1):120-9.

Redondo-Castro E., Romero R., Torres-Espín A., Utrera J., Duque D., Junyent F., Auladell C. (2014). Dithiocarb (N,N-diethyldithiocarbamate, DEDTC) decreases levels of biogenic monoamines in the adult mouse brain. **Neuropathol Appl Neurobiol**. 2014 Oct;40(6):747-58.

Junyent F., de Lemos L., Verdaguer E., Pallàs M., Folch J., Beas-Zárate C., Camins A., Auladell C. (2012).Lack of Jun-N-terminal kinase 3 (JNK3) does not protect against neurodegeneration induced by 3-nitropropionic acid. **Neuropathol Appl Neurobiol**. 2012 Jun;38(4):311-21.

Utrera J., Romero R., Verdaguer E., Junyent F., Auladell C. (2011). Recovery of axonal myelination sheath and axonal caliber in the mouse corpus callosum following damage induced by N,N-diethyldithiocarbamate. **Eur J Neurosci**. 2011 Dec;34(12):2007-14.

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