DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

AVVISO DI SEMINARIO

Il giorno **mercoledì 11 Dicembre 2018**
alle ore **11:00**,
presso l'Aula A
ex-farmacologia via Irnerio 48

la **Dott.ssa Lucia Hipolito, PhD**
Division of Pharmacy and Pharmaceutical Technology.
School of Pharmacy, University of Valencia, Spagna
(ospite Prof.ssa Romualdi)

terrà un seminario dal titolo:

SALSOLINOL, MESOLIMBIC DOPAMINE AND OPIOID SYSTEMS: A TALE OF PAIN AND ALCOHOL ADDICTION

I colleghi e gli studenti interessati sono cordialmente invitati

Commissione Ricerca e Attività Correlate - FaBiT

ABSTRACT

The action of ethanol in the central nervous system (CNS), concretely in the dopamine (DA) mesolimbic system, is a complex phenomenon and the participation of ethanol-derived compounds, such acetaldehyde and its derivatives is still a matter of debate. Since 1970, Salsolinol, a condensation product from DA and acetaldehyde, has been proposed to mediate the ethanol psychoactive effects. During the last ten years we have investigated the behavioural and neurochemical consequences derived from Salsolinol administration in the mesolimbic DA system, and its mechanism of action. Our data show that Salsolinol activates DA neurons located in the ventral tegmental area (VTA), leading to an increase of accumbal DA and consequently inducing DA related behaviours. Noteworthy, these Salsolinol derived effects are similar to those observed with ethanol but at lower doses, supporting that Salsolinol derived from ethanol metabolism may play a role in the rewarding effects of ethanol. Our data also confirmed that the blockade of the Mu opioid receptors (MORs) in the VTA impaired all salsolinol derived effects, uncovering its mechanism of action. Finally, we designed a therapeutic strategy based on impairing Salsolinol formation by sequestering acetaldehyde with DPenicillamine.

The treatment with D-Penicillamine not only prevented the alcohol relapse-like drinking in a preclinical model, but also increased the ability of naltrexone to prevent this behaviour. All together these data revealed the crucial role of MORs in alcohol addiction. Therefore, events that impact on opioid signalling may impact reward processes and consequently addiction to opioids but also to alcohol. Indeed, we have published that inflammatory pain desensitizes MORs in the mesolimbic pathway altering DA signalling and affecting the motivated behaviour of the rats. These changes impacted the heroin self-administration pattern, increasing it when very high doses are available. Based on these data, we designed a preclinical experiment combining an inflammatory pain rat model with an alcohol relapse model. Our data show that pain increases the vulnerability to relapse in females having no effect in male rats. All these data together with recent published data strongly supports the important role of the opioid system in alcohol addiction and also highlights the importance increasing our knowledge in this topic to better design new therapeutic approaches.

BIOGRAPHICAL SKETCH

Lucia Hipólito is lecturer of Pharmacy and Pharmaceutical technology in the University of Valencia. Since the start of her scientific career in 2005 she has been working on the field of neuropharmacology of addiction and specifically on alcohol addiction publishing more than 15 papers in well-known journals in the field. During her PhD period she joined the laboratory of Dr. JW Dalley and Dr. TW Robbins in the University Cambridge. This really fruitful research stay crystallized in extensive training, one highly cited publication and the present collaboration with Dr. David Belin (University of Cambridge). Right after finishing the PhD she obtained a Postdoctoral appointment in the Dr.JA Morón lab at the Dpt. of Anesthesiology of the Columbia University. During this time she started a project involving the study of pain and opioid addiction. Data obtained in this project had showed for the first time a dose dependent pain-increased heroin intake (Hipolito L 2015), being crucial in understanding the factors that contribute to the opioid epidemic that has been declared in the United States. Indeed, her research had a high impact in the field and Dr. Hipolito has received in 2016 the ESBRA Young Investigator Award, the Pain Award from the Valencian Society for the Studies and Treatment of Pain and the Valencian Young Investigator Award. Currently she is developing her investigation in the University of Valencia in the field of alcoholism and pain in collaboration with Dr. Moron and Dr. Bruchas (Washington University in St. Louis, MO, USA). She is also engaged with science outreach and is part of the organization committee of the Brain Awareness Week in Valencia and Woman in Science events.