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KChIP1 regulation of Kv 4.3 potassium channels and GABAergic transmission in primary hippocampal cells

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4-Aminopyridine (4-AP) is a potassium channel blocker used for the treatment of neuromuscular disorders. Otherwise, it has been described to produce a large number of adverse effects, among them cell death mediated mainly by blockage of K+ channels. Specifically, 4-AP has been reported to produce cell death in central nervous system on hippocampal cells. On the other hand, Kv channel interacting protein 1 (KChIP1) is a neuronal calcium sensor protein that is predominantly expressed at GABAergic synapses and it has been related with modulation of K+ channels, GABAergic transmission and cell death. According to this, KChIP1 could modulate K+ channels and GABAergic transmission, which mediate the toxic effects induced by 4-AP. We evaluated, in wild type and KChIP1 silenced primary hippocampal neurons, the effect of 4-AP (0.25 mM to 2 mM) with or without semicarbazide (0.3 M) co-treatment after 24 h and after 14 days 4-AP alone exposure on KChIP1 and Kv 4.3 potassium channels gene expression and GABAergic transmission. We observed that 4-AP modulates KChIP1 which regulates Kv 4.3 channels expression and GABAergic transmission. Our study suggests that KChIP1 is a key gene that may have a protective effect up to certain concentration after short-term 4-AP treatment, but this protection would be erased after long term exposure, due to KChIP1 down-regulation predisposing cell to 4-AP induced damages. These data might help to explain protective and toxic effects observed after overdose and long term exposure.

Biography

Javier del Pino has received his PharmD degree from the University Complutense University of Madrid in the year 2004. He has done two Master's in Sciences in the year 2009 and 2010. He did his Specialization in Neurotoxicology and Neurodevelopmental Toxicology and received his PhD in Toxicology in the year 2009. In 2010, he worked at Institute of Health Carlos III in the National Center of Environmental Health. From 2010 to 2012, he was an Associated Researcher at University of Massachusetts (UMASS), working at Sandra Petersen´s Lab in a National Institute of Health (NIH) project on developmental effects of TCDD endocrine disruptor on sexual differentiation. In 2016, he became an Associate Professor of Toxicology at the Complutense University of Madrid, Spain

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