Support for the Committee for Aid and Education in Neurochemistry (CAEN)

CATEGORY 1D: Career Interruption Re-entry Grant

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Report

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The last years, the kynurenine pathway metabolites have been involved in several neurodegenerative disorders and in aging process. However, the specific effect or mechanisms of these metabolites are still unknown; the main studies have been focus in their neuroactive properties. My investigation line is focus on the redox properties of kynurenines and their participation in neurodegenerative models. Our group and others have been proposed that endogenous tryptophan and their metabolites can interact and/or produce reactive oxygen species in tissues and cells. Specifically, the aim of this study was to investigate 3-HK and 3-HANA effects on mitochondrial and cellular function in rat cultured cortical astrocytes (rCCA) and in animals intrastriatally injected with these kynurenines as well as to determinate the ROS role on these effects. Our results show that both kynurenines decreased MTT reduction together with mitochondrial membrane potential. These observations were accompanied with increased cell death in rCCA and in circling behavior of injected animals. Interestingly, we found that ROS production was not increased in both *in vitro* and *in vivo* experiments, and accordingly lipid peroxidation (LP) was neither increased in striatal tissue of animals injected with both kynurenines. The lack of effect on these oxidative markers is in agreement with the •OH and $ONOO^-$ scavenging capacity of both kynurenines detected by chemical combinatorial assays. Altogether, these data indicate that both kynurenines exert toxic effects through mechanisms that include impairment of cellular energy metabolism which are not related to early ROS production.

Additionally, we continued studying the effect of the rest of kynurenine metabolites on mitochondrial function and the role of ROS in this paradigm both *in vivo* and *in vitro*.

It is important to mention that all the data obtained here are published in:

Reyes-Ocampo J, Ramírez-Ortega D, Vázquez Cervantes GI, Pineda B, Montes de Oca Balderas P, González-Esquivel D, Sánchez-Chapul L, Lugo-Huitrón R, Silva-Adaya D, Ríos C, Jiménez-Anguiano A, Pérez-de la Cruz V. 2015. **Mitochondrial dysfunction related to cell damage induced by 3-hydroxykynurenine and 3-hydroxyanthranilic acid: Non-dependent-effect of early reactive oxygen species production**. Neurotoxicology 50:81-91.

The fund was spent on a scholarship to Rafael Lugo Huitrón to get the master degree and obtaining the following chemicals:

JC-1 Mitochondrial membrane potential assay kit
Propidium iodide
Culture medium
Fetal bovine serum
3-hydroxykynurenine
3-hydroxyanthranilic acid
2-7-diclorofluorescein diacetate
Apomorphine
Salts and solvents