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Toxicogenomic profiles in neurons of male mice following early low exposure to the six indicator non-dioxin-like polychlorinated biphenyls

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We have previously shown neurobiological changes and developmental/behavioral performances in mice exposed during lactation to a representative environmental mixture of the six indicator non-dioxin-like polychlorinated biphenyls (∑6 NDL-PCBs) at low levels. In this study, we analyzed the global gene expression profile in cerebellar neurons isolated from male mice presenting the most significant induction of anxiety-like behavior in our previous study (10 ng/kg ∑6 NDL-PCBs). Our results revealed an up regulation in the expression of genes belonging to GO terms involved with the cell cycle, DNA replication, cell cycle checkpoint, response to DNA damage stimulus, regulation of RNA biosynthetic processes, and microtubule cytoskeleton organization. Down regulated genes belonged to terms involved with the transmission of nerve impulses, projection neurons, synapse hands, cell junctions, and regulation of RNA biosynthetic processes. Using qPCR, we quantified gene expression related to DNA damage and validated the transcriptomic study, as a significant over expression of *Atm, Atr, Bard1, Brca2, Fancd2, Figf, Mycn, p53* and *Rad51* was observed between groups. Finally, using immunoblots, we found significant changes in the protein expression of *Atm, Brca1, p53, Kcnma1, Npy4r* and *Scn1a* between exposed and control groups, indicating that the expression pattern of these proteins agreed with the expression pattern of their genes by qPCR, further validating our transcriptomic findings. In conclusion, our study showed that early life exposure of male mice to a low level of $\sum^6$ NDL-PCBs induced p53-dependent responses to cellular stress and a decrease in the expression of proteins involved in the generation, conduction, and transmission of electrical signals in neurons.

Biography

Arpiné Ardzivian Elnar has received a Diploma degree in chemistry from the Lebanese University of Beirut, Lebanon in 2008. She then shifted her academic focus towards pharmacokinetics in Mediterranean University of Marseille, France in 2009. She began her Ph.D. thesis in neurotoxicology at the University of Saarbrücken, Germany and University of Lorraine of Metz, France under Pr. Alexandra K. Kiemer and Pr. Rachid Soulimani. Her thesis focused on the evaluation of the short and long term neurotoxic effects following lactational exposure to the sum of the six non-dioxin-like polychlorinated biphenyls at low levels in offspring mice. Arpiné was awarded her Ph.D. in 2012 and continued her post-doc in University of Lorraine, Metz/Nancy, France in early 2013. Her current research focuses on the mechanisms of action and developmental neurotoxicity testing of chemicals at low environmental exposure.

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