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Transcriptomic, proteomic and metabolic studies of neuroblastoma cells to cytotoxicant, myricitrin

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Toxicity pathway studies by data, especially the upstream network of responses happening in toxicant-treated cells before their programmed cell death is reported to provide an unbiased approach to unravel changes deciding on the final fate of the cell. We studied the effect of the cytotoxicant, myricitrin, by a combined transcriptomic, proteomic and metabolomic approach on cellular adaptations upon exposure to cytotoxicant. Transcriptome changes preceding cell death upon myricitrin exposure by probe sets strongly pointed to changes in cluster related to genes with a role in chromosomal stability, eg., heterogeneous nuclear ribonucleoprotein (*HNRNPM*), that was downregulated. Those involved in adaptive carbon metabolism eg., argininosuccinate synthase (*ASS1*) were upregulated identified as intermediate response upon exposure to toxicant. Intracellular ATP and mitochondrial integrity were still close to control levels at 18 to 24 h of N2a cells subjected to cytotoxicant, with pronounced metabolome changes. Altered glucose levels and oxidative stress (methionine sulfoxide formation) as altered energy metabolism were detected. Consumption of phosphocreatine and a parallel accumulation of creatine indicated exhaustion of cellular energy buffer. The prominent role of GSH to counter increasing cell stress as early adaptation before breakdown of cellular homeostasis was observed. Direct data substantiating cell death by apoptosis with p38 map kinase mediated p53 activated upregulation of caspase 3 is reported and will be discussed.

Biography

Shailasree Sekhar received her PhD in Biochemistry as a fellow funded by CSIR, Govt. of India, in 2000. Currently, under the Institution of Excellence with the thrust area identified as the biodiversity of Western Ghats medicinal plants, with immunological affections and cancer prevention properties, due to location advantage of this hot spot to the University. With an active involvement in compilation of their scientific data as reviews resulted in bringing out a database on pharmacological properties of these medicinal plants of Western Ghats in an efficient way. Screening of medicinal plants with immunological affections used by tribes has resulted in identification of several of them with inflammation/cancer inhibiting property. Fingerprinting their metabolites and providing scientific valuation for traditional application has been her priority. She has published more than 30 papers in peer-reviewed journals, has 2 patents and is an adhoc reviewer of various journals. She has to her credit grants from National scientific agencies under Government of India.

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