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Mechanistic Studies on the Anti-Tumor Activities of Omega-3 Polyunsaturated Fatty Acids on the Human Neuroblastoma LA-N-1 Cells

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Abstract

Neuroblastoma is the most common extracranial solid cancer among infants and children. The prognosis of patients with advanced stages of neuroblastoma with N-myc amplification remains poor despite intense multimodality therapy, and there is a pressing need for alternative therapeutic strategies. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) are naturallyoccurring long-chain fatty acids containing a carbon-carbon double bond at the omega C-3 position. Although previous studies have demonstrated the anti-proliferative effect of n-3 PUFAs on different cancer cell lines in vitro, the anti-tumor effects and underlying molecular action mechanisms of n-3 PUFAs, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), on human neuroblastoma cells remained poorly understood. In this study, both DHA and EPA were shown to suppress the proliferation of two human neuroblastoma LA-N-1 and SH-SY5Y cell lines in a concentration- and timedependent manner.

Mechanistic studies using the LA-N-1 cells with N-myc amplification indicated that DHA and EPA could suppress N-myc expression and caused cell cycle arrest at the G0/G1 phase, which was accompanied by a decrease in CDK 2 and cyclin E protein expression. Remarkably, DHA and EPA could also trigger apoptosis in LA-N-1 cells by inducing DNA fragmentation and phosphatidylserine externalization. Increased in mitochondrial membrane depolarization and Cyt.C release, up-regulation of Bax, caspase-3 and caspase-9 proteins, and down-regulation of Bcl-XL protein suggested the possible involvement of the intrinsic apoptotic pathway. Interestingly, both DHA and EPA failed to induce neuronal differentiation in LA-N-1 cells, as judged by both morphological and functional criteria. Taken together, our results suggest that DHA and EPA might exhibit their anti-tumor effects on the human neuroblastoma LA-N-1 cells by triggering cell cycle arrest and by inducing apoptosis of the cancer cells. Therefore, n-3 PUFAs such as DHA and EPA are potential anti-cancer agents which can be used for the treatment of some forms of human neuroblastoma.

Biography:

Leung K N has received his BSc Degree (with First Class Honors) in Biochemistry from The Chinese University of Hong Kong (CUHK) and obtained PhD Degree in Microbiology and Immunology from The Australian National University. After two years of Post-doctoral work at the Pathology Department of the University of Cambridge, he returned to the CUHK as a Lecturer in the Department of Biochemistry in 1983. He was the former Dean of General Education in Chung Chi College, the Associate Dean of Science (Education) of CUHK and the Chairman of the Hong Kong Society for Immunology. He is now an Adjunct Professor in the School of Life Sciences, CUHK and the School of Science and Engineering, CUHK (Shenzhen). His main research interests include immunopharmacological studies of natural products and Chinese medicinal herbs; cancer immunotherapy; nutrition, immunity and cancer.