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1'-Acetoxychavicol acetate inhibits growth of human oral carcinoma xenograft in mice and potentiates cisplatin effect via proinflammatory microenvironment alterations

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Oral cancers although preventable, possess a low five-year survival rate which has remained unchanged over the past three decades. In an attempt to find a more safe, affordable and effective treatment option, we describe here the use of 1'S-1'-acetoxychavicol acetate (ACA), a component of the Malaysian ginger traditionally used for various medicinal purposes. Whether ACA can inhibit the growth of oral squamous cell carcinoma (SCC) cells alone or in combination with cisplatin (CDDP), was explored both in vitro and in vivo using Nu/Nu mice. Occurrence of apoptosis was assessed using PARP and DNA fragmentation assays, while the mode of action was elucidated through global expression profiling followed by Western blotting and IHC assays. We found that ACA alone inhibited the growth of oral SCC cells, induced apoptosis and suppressed its migration rate, while minimally affecting HMEC normal cell controls. ACA further enhanced the cytotoxic effects of CDDP in a synergistic manner as suggested by combination index studies, and inhibited the constitutive activation of NF-κB through suppression of IKKα/β activation. Human oral tumor xenografts studies in mice revealed that ACA alone was as effective as CDDP in reducing tumor volume, and further potentiated CDDP effects when used in combination, with reduced body weight loss. The effects of ACA also correlated with a down-regulation of NF-κB regulated genes (FasL and Bim), including proinflammatory (NF-κB and COX-2) and proliferative (cyclin D1) biomarkers in tumor tissue. Overall, our results suggest that ACA inhibits the growth of oral SCC and further potentiates the effect of standard CDDP treatment by modulation of the proinflammatory microenvironment. Current preclinical data forms the basis for further clinical trials to improve the current standards for oral cancer care.

Biography

Noor Hasima completed her PhD in immunogenetics from the University of Edinburgh in 1992, and post-doctoral studies on cancer immunotherapy in the University of California, Los Angeles, USA in 2005. She is currently an associate professor at the Institute of Biological Sciences, Faculty of Science, University Malaya, Malaysia. She was previously appointed as the deputy head of the Genetics and Molecular Biology division at University Malaya in 2007, and was the former president of the Malaysian Society for Molecular Biology Biotechnology. She is currently active in the field of cancer immunogenetics and immunotherapy, and has published over 10 research articles in reputable scientific journals.

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