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Involvement of TLR4/STAT3 signaling in the anti-melanoma effects of atractylenolide II

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Melanoma incidence and mortality rates are rapidly increasing. STAT3 (Signal Transducer and Activator of Transcription 3) and TLR4 (Toll-Like Receptor 4) have been shown to be activated in melanoma cells. Suppressing TLR4 or STAT3 signaling in tumor cells represents an antimelanoma strategy. Rhizoma Atractylodis Macrocephalae (Baizhu in Chinese), a Qi-tonifying Chinese medicinal herb, is commonly prescribed by traditional Chinese medicine doctors for treating melanoma. We have demonstrated that atractylenolide II (AT-II), isolated from Baizhu can significantly inhibit B16 tumor growth at non-toxic doses in mice which is associated with a potent suppression of STAT3 signaling. We have also found that AT-II inhibits melanoma metastasis in mice and cell migration in A375 and B16-F10 cells. Molecular docking indicated that AT-II could bind to TLR4/MD-2 receptor complex. MPLAs, specific TLR4 agonists, significantly diminish AT-II-afforded suppression on STAT3 phosphorylation/activation and melanoma cell migration. Based on these data, we concluded that inhibiting the TLR4/STAT3 pathway is involved in the anti-metastasis effects of AT-II. This study advances our understanding of the anti-melanoma mechanisms of AT-II and provides chemical and pharmacological justifications for the clinical application of Baizhu in melanoma treatment.

Biography

Xiu-Qiong Fu has completed her MPhil at Southern Medical University in Guangzhou, China. Presently, she is a PhD candidate of Hong Kong Baptist University. She has published more than ten papers in reputed journals. Her research work is in pharmacology of Chinese medicines.

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