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Inhibition of STAT3 signaling is associated with the anti-hepatocellular carcinoma effects of a triterpenoid-enriched extract from *Antrodia camphorate* mycelia

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Hepatocellular carcinoma (HCC), the major form of primary liver cancers, is the third leading cause of cancer-related death worldwide. Signal transducer and activator of transcription 3 (STAT3) signalling is persistently activated in HCC and has been proposed as a molecular target for the treatment and prevention of HCC. Antrodia camphorata (AC), especially its triterpenoids, has been reported to have anti-HCC effects. Zhankuic acid A, a triterpenoid isolated from AC, exerts anti-HCC effects by suppressing the activation/phosphorylation of JAK2 and STAT3 in HepG2 cells. In this study, we investigated the involvement of the STAT3 signaling pathway in the anti-HCC effects of a triterpenoid-enriched extract prepared from cultured AC mycelia (TEAC). HepG2, SMMC-7721 cell models and a SMMC-7721 xenografted mouse model were employed to evaluate the anti-HCC effects of TEAC. MTT assays showed that TEAC dose- and time-dependently inhibited the viability of HCC cells. TEAC also induced apoptosis in HepG2 and SMMC-7721 cells, which was confirmed by positive Annexin V/PI double staining, and the cleavage of poly (ADP-ribose) polymerase (PARP), caspases 3, 8, and 9. Moreover, TEAC retarded migration and invasion of cultured HepG2 cells. Mechanistic studies revealed that TEAC decreased the protein expression levels of phospho-STAT3 and phospho-JAK2 (a cytoplasmic kinase of STAT3), as well as total STAT3 in human HCC cells. STAT3 mRNA expression levels and STAT3-luciferase reporter activity were also reduced by TEAC. STAT3 targeted genes Bcl-xL and MMP2 were downregulated by TEAC. Overactivation of STAT3 diminished the cytotoxic effects of TEAC. In SMMC-7721-bearing mice, intragastric administration of TEAC (100 mg/kg) for 15 days significantly suppressed tumor growth. These results indicated that TEAC exerted *in vitro* and *in vivo* anti-HCC effects and the STAT3 signalling pathway was involved in the effects. This study provides a pharmacological basis for developing TEAC as an anti-HCC agent.

Biography

Peili Zhu is a PhD student in School of Chinese Medicine, Hong Kong Baptist University. She has specialization in Traditional Chinese Medicine. Her research interests are investigating the anti-cancer effects of traditional Chinese medicine and exploring the mechanism of action of these effects.

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