

Fucoidan inhibitory function in cancer *in vivo* and *in vitro*: Role in the development of human anti-cancer therapeutic intervention

Hsien-Yeh Hsu

National Yang-Ming University, Taiwan

Fucoidan, a polysaccharide extracted from brown seaweeds, reduces proliferation in a battery of tumor cells. In recent, we demonstrated that fucoidan reduces tumor size both in LLC1 lung cancer-xenograft male C57BL/6 mice and in 4T1 breast cancer-xenograft female Balb/c mice. As it is known, transforming growth factor β receptors (TGF β s) play important roles in the regulation of epithelial-mesenchymal transition (EMT) as well as of proliferation/progression and metastasis in cancer cells. Using these cancer cells, we found that fucoidan effectively up-regulates epithelial markers, down-regulates mesenchymal markers, and also decreases expression of transcriptional repressors Snail, Slug, and Twist. In addition, we found fucoidan inhibits TGF β -mediated migration and invasion of cancer cells. Moreover, we found fucoidan decreases TGFRI and TGFRII proteins *in vivo* and *in vitro*. To elucidate the mechanism by which fucoidan decreases TGFRI/II proteins in cancer cells, we found that fucoidan enhances ubiquitination proteasome pathway (UPP)-mediated degradation/ubiquitination of TGF β s. We further demonstrated fucoidan promotes Smurf2 and Smad7 to conjugate TGF β s, resulting in TGF β degradation. Together, we are the first to identify a novel mechanism for fucoidan anti-tumor activity, namely decreasing tumor growth by modulating TGF β proteins degradation, leading to reduction of TGF β -mediated signaling, and further inhibition of cancer cells *in vivo* and *in vitro*. Our current findings indicate that fucoidan is a potential therapeutic agent or dietary supplementation for cancers, acting via Smurf2-dependent ubiquitin degradation of TGF β s affecting the TGF β /Smad/Snail, Slug, Twist, and EMT axes.

Biography

Hsien-Yeh Hsu is a Molecular/Cellular biologist, and he obtained his Doctoral degree from Cornell University, USA. Later, he worked in various biotechnology companies in Boston, USA. In 1990, he returned to university, and later became Assistant Professor in Weill Cornell Medical College, NYC, USA. In 1997, he joined National Yang-Ming University, Taiwan. Currently, as Professor, he works at Department of Biotechnology and Laboratory Science in Medicine, and also as Research Fellow in Genomics Research Center, Academia Sinica. He is working on polysaccharides obtained from brown algae and medicinal mushroom *Ganoderma lucidum*, and focusing on anti-cancer functions in human clinical experiments. Moreover, he is engaged on examining anti-cancer therapeutic intervention and on developing anti-cancer drugs.

hsienyeh@gmail.com

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