The cytoprotective role of autophagy in CYT997 treated human head and neck squamous cell carcinoma

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Head and neck squamous cell carcinomas (HNSCC) exhibiting resistance to molecular-targeted therapeutics poses a challenge to their effective clinical management and alternate treatment strategies are actively sought to improve results. CYT997, a novel microtubule-disrupting agent, has shown anticancer activity in prostate cancer and other cancer types by inhibiting tubulin polymerization and disrupting cellular microtubules. Here, we report that CYT997 has considerable potential as a novel anticancer agent for HNSCC. CYT997 effectively abrogates mTOR signaling and induces significant cytotoxicity in HNSCC cells. Consequently, CYT997 treatment inhibits cell viability, migration and invasion and induces autophagy-associated apoptosis. CYT997 also suppresses tumor growth of HNSCC in a mouse xenograft model. Combined treatment with CYT997 and the autophagy inhibitor HCQ, but not 3-MA, overcomes autophagy blocked apoptosis and augments the anticancer activity of CYT997 *in vitro* and *in vivo*, suggesting that inhibition of mTOR-dependent autophagy sensitizes HNSCC cells to CYT997-induced apoptotic death. These findings underline the importance of autophagy in the anticancer activity of CYT997 and suggest that CYT997 may represent a potential therapeutic approach to treat HNSCC and pharmacologic autophagy blockade may enhance its efficacy. Therefore, our study has significant impact on the design and execution of effective therapy of patients with HNSCC.

Speaker Biography

Yong Teng was largely engaged in illustrating cancer metastatic signaling cascades and developing animal disease models for gene functional analysis and drug evaluation. Through his team work, he has identified several new molecular targets and signaling pathways which control cancer progression and metastasis and developed several novel anticancer strategies by modulating them. He is trying to bridge three major research themes, tumor microenvironment, autophagic survival and tumor metastasis, with an emphasis on a few central regulators. His ongoing projects seek to shift current research and clinical practice paradigm, which will directly impact the future development of effective therapy for cancer patients.

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