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Targeting hypoxia-induced accumulation of HIF-1α and inducing apoptosis in human colorectal cancer cells by Salternamide A, a marine natural product isolated from halophilic Streptomyces Sp.

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Hypoxia inducible factor-1α (HIF-1α) is an essential regulator of the cellular response to low oxygen concentrations, activating a broad range of genes that provide adaptive responses to oxygen deprivation. HIF-1α also plays a pivotal role in regulating the initiation of genes that are involved in decisive aspects of cancer biology, such as angiogenesis, cell survival, differentiation, invasion, tumor progression, and glucose metabolism. In general, HIF-1α is overexpressed in various cancers and therefore represents a considerable chemotherapeutic target. Salternamide A (SA), a novel small molecule that is isolated from a halophilic Streptomyces sp., is a potent cytotoxic agent against a variety of human cancer cell lines. However, the mechanisms by which SA inhibits tumor growth remain to be elucidated. In the present study, we demonstrate that SA efficiently inhibits the hypoxia-induced accumulation of HIF-1α in a time- and concentration-dependent manner in various human cancer cells. In addition, SA suppresses the upstream signaling of HIF-1α, such as PI3K/Akt/mTOR, p42/p44 MAPK, and STAT3 signaling under hypoxic conditions. Furthermore, we found that SA induces cell death by stimulating G2/M cell cycle arrest and apoptosis in human colorectal cancer cells. Taken together, SA was identified as a novel small molecule HIF-1α inhibitor from marine natural products and is potentially a leading candidate in the development of anticancer agents.

Biography

Jiyoung Hwang received a Bachelor's degree from College of Agriculture and Life Science, Seoul National University, South Korea in 2017. She is currently a Master's degree student at the College of Pharmacy, SNU, Seoul, South Korea. Her research is focused on identification of natural products-derived bioactive compounds in the fields of skin physiology and cancer biology.

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