

Enhanced anti-tumor effects of fluorouracil against gastric cancer by 5-aza-2'-deoxycytidine and trichostatin A

Shilian Hu

Anhui Provincial Hospital, China

Gastric cancer is one of the most common malignant tumors in the world, and only China contributes to almost half of all global new cases each year. Our previous studies have shown that the promoter hypermethylation of RUNX3 and E-cadherin plays an important role in the occurrence and development of gastric cancer. In this study, we analyzed the gene expression and inhibitive effects of gastric cancer cell lines MKN-45 and SGC-7901 treated with fluorouracil alone and in combination with 5-aza-2'-deoxycytidine (5-Aza-dC) or/and trichostatin A (TSA). Gastric cancer cell lines were treated with fluorouracil, with or without 5-aza-dC or/and TSA for different time and doses, and the inhibitive effects were measured by MTT kit to determine cell proliferation. The promoter methylation status and protein expression of RUNX3 and E-cadherin genes were analyzed by the methods of real-time quantified methylation-specific polymerase chain reaction (RTQ-MSP) and western blot, respectively. Treatment with 5-aza-dC or TSA alone was found not to inhibit the proliferation of gastric cancer cells as much as fluorouracil did, but the effect had a remarkable enhancement by fluorouracil combined with 5-aza-dC and TSA. The results showed that 5-aza-dC or TSA could reduce methylation and increase expression of RUNX3 and E-cadherin genes, and the combination of 5-aza-dC and TSA increased more, but fluorouracil did not affect their protein expression. Our findings imply that 5-aza-dC and TSA induce strong reactivation of RUNX3 and E-cadherin genes, and have potentials as therapeutic candidates alone or combination with other tumor-targeted drugs in gastric cancer therapy.

Biography

Shilian Hu has studied gastric cancer diagnostics, epigenetics and therapeutics more than 30 years, during which time she has authored more than 100 peer-reviewed papers. She has served as the editor-in-chief for the Journal of Chinese Clinical Healthcare and on the editorial boards for the Chinese Journal of Geriatrics. She is also the chairman of Anhui Provincial Health Administration Society and Anhui Provincial Geriatrics Society in China. Prof. Hu is a member of the Scientific Advisory Committees for the Chinese Geriatrics Society, and she has served on numerous review committees for clinical medicine journals and scientific foundations.

Calcium channels as targets in cancer therapy

Thierry Capiod

University of Paris, France

This lecture will address the role of calcium channels in cell proliferation and cell cycle progression and assess their potential use as therapeutical targets to cure cancer. Cell cycle progression requires precise timing of the intrinsic molecular steps and tight coordination with the environmental signals. Because of their great functional flexibility, calcium channels coordinate the upstream and downstream signals that converge on the cell cycle machinery. Calcium channels have been implicated in the control of different cell cycle checkpoints in normal as well as neoplastic cells. Direct conformational coupling with the cytoplasmic regulatory proteins will be discussed. Specific types of calcium channels have turned out to participate in the different stages of the tumor progression, in which cell heterogeneity is increased by the selection of malignant cells expressing the adequate calcium channel pattern that better support unrestrained growth. A comprehensive mechanistic picture of the functional relations between calcium channels and cell proliferation is therefore needed, opening up a new field of potential tumour progression blockers.

Biography

Thierry Capiod has studied calcium signaling for almost 30 years in France and UK. He more recently focused his research topics on the role of plasma membrane calcium channels in oncology with a particular attention on liver, prostate and breast cancers. He is a member of the Scientific Committee for the National Institute for Health and Medical Research (INSERM) in France and he is serving on the editorial board for the World Journal of Gastrointestinal Pharmacology and Therapeutics.