Abstract

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SAG-UPS regulates malignant transformation to confer survival advantage to early hepatocellular carcinoma

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Abstract

Chronic inflammation-mediated cell death/survival is an important risk factor to cancer development. However, the link between chronic inflammation and tumorigenesis is still unclear. Elucidating this link is needed for early diagnosis and development of therapeutics. Previously, we reported that SAG (sensitive to apoptosis gene) is a key regulator between immuneoveractivation and pro-tumorigenesis. Here, by retrospectively studying human primary hepatocellular carcinoma (HCC) tissues, we showed that SAG is up-regulated in the early stage of HCC, in conjunction with the increase in ubiquitination of specific suicide/apoptosis factors such as SARM and Noxa. We envisage that SAG-UPS (ubiquitin proteasome system) degrades apoptosis factors, thus conferring anti-apoptosis and uncontrolled cell survival strategy, which promotes liver cancer. We found that up-regulated SAG in HCC plays a key pro-tumorigenic role by perturbing the fine balance of the ratio of pro- and anti- apoptotic factors, as indicated by the production of pro- and anti-tumorigenic cytokines. This favors and exacerbates the vicious cycle of tumorigenic microenvironment for the progression of hepatoma. Our findings clearly established the power of SAG-UPS as a cell death/survival decision link between chronic inflammation and tumorigenesis. We propose SAGUPS to be an early diagnostic marker for HCC, and a potential target for therapeutics development.

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Biography

Shu-Chun Chang is an Assistant Professor of Translational Medicine, Taipei Medical University, Taiwan. She is trained in extracellular biology and glycobiology. Previously, she has worked in cancer research in Imperial College London. She is a Post-Doctorate in the field of Immunology/Inflammation at National University of Singapore. She has published more than 10 papers in reputed journals. Her research interests are in chronic inflammation-associated tumors (e.g., colon cancer and breast cancer) and this has a profound impact in identifying new molecular therapies for autoimmune diseases, immunodeficiency and cancers.

