Ann Surg Oncol (2011) 18:S239
DOI 10.1245/s10434-011-1789-x

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

LETTER TO THE EDITOR

Dual Role of Autophagy in Colon Cancer Cell Survival

TO THE EDITORS:

We read with interest the article by Li et al. that describes the association of autophagy with the 5-fluorouracil (5-FU)-induced apoptosis in colon cancer cells.[1] In the paper the authors found that the inhibition of autophagy enhances 5-FU-induced colon cancer cell apoptosis and improves the chemotherapeutic effect of 5-FU. Autophagy is a cellular process of autodigestion involving excess proteins and old organelles being recycled and is termed type II programmed cell death to distinguish it from apoptosis. Autophagy and apoptosis display large differences in cellular morphology and the molecular pathways that govern them. The relationship between them has not been well elicited. Although Li et al. showed that autophagy might play a role of self-defense in 5-FU-treated colon cancer cells, a recent study demonstrated that autophagic cell death might also be induced as an alternative cell death pathway in apoptosis-defective colon cancer cells.[1,2] These data suggest a paradoxical role of autophagy as a target for adjuvant therapy. On the one hand, it allows for cell survival against cytotoxicity of anticancer agents in apoptosis-competent cancer. On the other, it acts as a backup cell death mechanism in apoptosis-defective cancer.

Recently, our lab investigated the effects of autophagy in stressed and unstressed colon cancer cells. We found that in unstressed cells, inhibition of autophagy was associated with a significant growth advantage. Contrasting to this, in cells subjected to biological stress, inhibition of autophagy markedly reduced cell viability compared with control. This suggests autophagy has a dual role in colon cancer cells, pro-survival under biological stress and pro-death under normal conditions.

Several ways of manipulating autophagy have been proposed, allowing for both inhibition and enhancement of the process.[3,4] Before they become part of routine treatment two issues need addressing. First, accurate ways of determining a patient's unique cancer biology must be developed, allowing for a patient-tailored, either autophagy-inducing or autophagy-inhibiting, approach. Second, the agents already found effective in in vivo and in vitro studies require further testing to prove their suitability in a clinical setting.

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Published Online: 21 May 2011

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