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Modulatory effects of cetuximab and sodium butyrate on colon cancer biomarkers and mucous secreting cells during rat colon carcinogenesis

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It has been recently documented that mucin depletion in colonic epithelium is a hallmark for malignant transformation in human and rodents. To study the contribution of targeted therapy for mucous secreting cells during colon carcinogenesis, we used male rats divided into 5 groups. Group-1: Normal control, Group-2: 1,2-Dimethylhydrazine (DMH)-injected rats, Group-3: Rats injected with DMH then received 10 mg/kg/b.wt. Cetuximab, a monoclonal antibody that targets epidermal growth factor receptor (EGFR), Group-4: Rats injected with DMH then IP treated with Na-butyrate (200 mg/kg body weight), known to cause colonocytes and mucous cells differentiation and Group-5: Rats received DMH then treated with both cetuximab and Na-butyrate at the same doses. Rats from groups 3-5 had significant lower numbers of Aberrant Crypt Foci (ACF) and Mucin Depleted Foci (MDF), end point biomarkers for colon cancer, as compared with the DMH-administered group (G2). Combination therapy in G5 exerted most potent effect against ACF and MDF. All treatments retained the goblet cell numbers in colonic epithelium close to control levels with better effects obtained in G5. Moreover, all treatments have significantly inhibited the cellular proliferation levels of the colonic epithelia. Further, the drugs used have modulated the mRNA expression levels of MUC-2 and c-jun genes which are correlated with mucin secretion and early colon carcinogenesis respectively with most clear effects in G5. The data show that targeting epithelial and mucous cell growth and differentiation during carcinogenesis could recuperate the rats' colonic epithelium integrity and counter carcinogenesis and turnover towards malignancy. This could be of importance to colorectal cancer therapy.

Biography

Elsayed I Salim has his expertise in molecular carcinogenesis, toxicogenomic, anticancer drug discovery and cancer risk assessment. He has received his BSc and MSc degrees from Tanta University, Faculty of Science, Egypt and his Doctorate of Medical Sciences from Osaka City University Medical School, Japan in 2000.

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