ABSTRACT SUBMISSION FORM

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Title of your presentation

Mesenchymal Stem Cells Partially Cancel Azoxymethane-Induced Tumor Initiation

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Background: Although mesenchymal stem cells (MSCs) are a prime candidate for inflammatory bowel disease (IBD) therapy, the role of MSCs in tumorigenesis remains controversial. Therefore, the goal of our present study was to determine whether exogenous MSCs possess intrinsic anti-neoplastic or pro-neoplastic properties against azoxymethane (AOM)-induced colon carcinogenesis.
Methods: To gain the short- to long-term chemopreventive effects of MSCs and these mechanistic insights, we analyzed three rodent models *in vivo* and a MSCs co-culture model *in vitro*. First, evaluating the long-term effects of MSCs, we examined number of neoplasms per colon with or without intravenous injection of MSCs formed in the AOM/DSS model and the aberrant crypt foci (ACF) model. Next, investigating the short-term effects of MSCs, we evaluate the amount of the O^6 methylguanine (O^6MeG) adducts and the cell cycle machinery in the colonic epithelium after AOM exposure on the acute apoptotic response to genotoxic carcinogen (AARGC). Finally, we confirmed the effects of MSCs on proliferation, apoptosis and cell cycle machinery *in vitro* using IEC-6 cells under AOM treatment in a MSCs co-culture model.
Results: MSCs reduced the tumor formation although the tumor size was same in both groups, suggesting MSCs can partially cancel tumor initiation in the AOM-induced carcinogenesis model. MSCs inhibited the AARGC in the colonic epithelial cells, potentially due to their removal of the O^6MeG or prevention of DNA insults. Furthermore, MSCs broadly affected cell cycle-related proteins expression in the colonic epithelial cells, leading to G1 arrest or cell apoptosis.
Conclusions: We demonstrated that MSCs could reduce the formation of DNA adducts by alkylating carcinogens and/or potentially enhance apoptosis later in cells with critical DNA adducts, and these chemopreventive effects led to cancel the AOM-induced tumor initiation. This information has the potential to facilitate the clinical application of promising MSC therapy, even in cancer-prone IBD patients.