G protein-coupled estrogen receptor and nuclear estrogen receptors activity modulation in murine model of colitis-associated colorectal cancer

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The pathogenesis of many cancer types seems to be associated with an alterations of immunoregulation. Several lines of evidence suggest that estrogens play a role in the modulation of immune response and may be related to cancer etiology. However, impact of estrogen receptors i.e., G protein-coupled estrogen receptor (GPER) and nuclear estrogen receptors (ER\textsubscript{α} and ER\textsubscript{β}) on pathogenesis of colorectal cancer associated with inflammation is still elusive. The aim of our study was to determine contribution of estrogen signaling mediated by estrogen receptors in colitis-associated colorectal cancer. Azoxymethane (AOM) and dextran sulfate sodium (DSS)-induced murine model of colitis-associated colorectal cancer was used. Real-time PCR analysis revealed that GPER is down-regulated while both ER\textsubscript{α} and ER\textsubscript{β} are up-regulated in colitis-associated colorectal cancer. Interestingly, the administration of ICI 182,780 (fulvestrant), GPER agonist and nuclear estrogen receptor selective down-regulator did not lead to a reduction in the number of tumors and tumor area in the distal and proximal colon. No changes of colon macroscopic damage score such as colon length, thickness or width in ICI 182,780-treated mice with colitis-associated colorectal cancer was observed. These results indicate that dysregulation of estrogen receptors GPER, ER\textsubscript{α} and ER\textsubscript{β} expression may contribute to the development of colitis-associated colorectal cancer, being an effect rather than the cause of neoplastic transformation. To evaluate impact of estrogen signaling alteration in colitis-associated colorectal cancer further experiments are needed. This work was supported by grants (2015/17/N/NZ5/00336 and 2017/24/T/NZ5/00045 to DJ) from the National Science Center, Poland.