

Role of the Bone Marrow in TFF1 Knockout Mouse Gastric Adenomas

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The TFF-1 knockout [KO] mouse spontaneously develops antropyloric adenomas. To understand the potential role of bone marrow derived cells (BMDCs) in gastric carcinogenesis, we performed a sex-mismatched (male into female) bone marrow transplantation (BMT) experiment studying the following four groups: WT BM into WT mice, TFF-1 KO BM into WT, WT BM into TFF-1 KO, and TFF-1 KO BM into TFF-1 KO. We analysed the groups at 6 and 12 months after BMT to investigate long-term engraftment.

Histological analysis of tissues from the WT into WT mice showed normal morphology. KO into WT showed occasional hyperplasia and inflammation, but not the adenomas seen in KO into KO, which were tubulovillous, dysplastic, and often pedunculated. WT into KO mice showed no amelioration of KO tumours. Male bone-marrow derived myofibroblasts (Y chromosome ISH,  $\alpha$ -smooth muscle actin IHC) were found between glands and which were increased in the tumour stroma, especially nearer the lumen ( $P < 0.01$ ). ISH for Lgr5 revealed widespread expression within the gastric adenoma of one TFF-1 KO to KO mouse at 12 months. A trend was seen suggesting greater numbers of Y+ epithelial cells in the adenomas of this group. We have not formally excluded the possibility that these cells may be fusion events with CD45-positive BM cells.

We conclude that BM from TFF1 KO mice may on occasion be associated with inflammation and hyperplasia in WT recipients. The frequency of BM-derived myofibroblasts differs in adenomatous tissue. WT BM has no effect on the appearance of adenomas in KO mice.