Title: Hedgehog signaling mediates interferon-gamma induced mesenchymal stem cell proliferation and recruitment to the stomach

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Abstract:

Despite advances in treatment and declining incidence, gastric carcinoma remains one of the leading causes of cancer-related deaths in the world (Sherman, 2011; Zavros, 2011). Understanding the progression from chronic gastric inflammation to cancer is crucial in the development of novel therapies and strategies for treating gastric cancer (Sherman and Zavros, 2011). In the current study, we demonstrate that the Th1 pro-inflammatory cytokine interferon gamma (IFNy) induces mesenchymal stem cell proliferation and recruitment through the sonic hedgehog cell signaling pathway (Shh) during *H pylori* induced chronic inflammation. We have demonstrated here that *H pylori* infection is necessary in order to induce parietal cell atrophy and metaplasia. The data generated from the immunohistochemical analysis also indicates mice that have active sonic hedgehog signaling pathway (MSCvect) who were injected with IFNy had recruitment of mesenchymal stem cells. We also show that mice who did not have the active sonic hedgehog signaling component (MSCShhK0) injected with IFNy had no change in the amount of DNA synthesis or cell cycle progression. The results from the current study suggest that the Th1 cytokine IFNy induces the recruitment ofbone marrow-derived mesenchymal stem cells (BM-MSCs) to the site of chronic inflammation in response to the disruption of the gastric epithelium from *H pylori* infection.