

Thomas Tadros, Class of 2004
Department of Medicine, Division of Gastroenterology

CXCL12 expression in murine stomach regions, & lack of correlation between its expression and *H.felis*-induced gastritis and gastric carcinoma

Thomas Tadros, Shigeo Takaishi MD PhD, Jean Marie Houghton MD PhD, Calin Stoicov MD, Graham Barnard MD PhD

ABSTRACT: CXCL12 is a chemokine with diverse functions including: induction of chemotaxis and activation of leukocytes in response to pro-inflammatory mediators; murine B-cell lymphopoiesis, bone marrow myelopoiesis, & embryonic formation of the ventricular septum (Nagasawa et al., 1996); inhibition of HIV infection of T-cells (Oberlin et al., 1996); cell adhesion and migration (Peled et al., 2002; Gotoh et al., 1999). It has been shown that there is reduced expression of CXCL12 in many cancers, including hepato-cellular-, colon-, and esophageal cancers (Begum et al., 1996). However, in gastric cancer, both increased and decreased expression have been demonstrated (Shibuta et al., 1997). It is not known whether CXCL12 expression varies among the different regions of the stomach. *H.felis* infects the fundus and induces gastric carcinoma close to the gastroesophageal junction in mice. In humans, *H.pylori* infects the antrum and induces carcinoma in the non-cardia region of the stomach. Thus, regional variation in CXCL12 expression may exist in relation to these pathologies. The purpose of this experiment is: (1) to determine whether variation in expression of CXCL12 and its receptor CXCR4 exists in different regions of murine stomach; and (2) to determine whether expression of CXCL12 and CXCR4 changes during pathogenesis of *H.felis*-induced murine gastritis and gastric carcinoma. The hypothesis is that: (1) in normal mouse stomach, there will be no regional variation in expression of CXCL12 or CXCR4; and (2) in the inflammatory stage of *H.felis* infection, there will be increased expression of CXCL12 and CXCR4, while in the neoplastic and malignant stages there will be reduced expression. To test the hypothesis, mice were infected orally with *H.felis* to induce gastritis and gastric cancer. The stomachs of these mice and normal mice were procured. RNA was isolated from different regions of the stomach and reverse-transcribed to cDNA by oligo-dT priming. cDNA was amplified by real-time PCR using primers for CXCL12, CXCR4, and a control gene G3PDH. It was found that: (1) in mouse stomach, there is significantly greater expression of CXCL12 mRNA in the fundus (5.3 times greater) and lesser curvature (3.4 times greater) compared to the antrum; (2) there is a tendency towards increased expression of CXCL12 mRNA during the inflammatory phase with a subsequent reduced expression in the neoplastic phase; and (3) there is a tendency towards increased expression of the receptor CXCR4 mRNA in both inflammatory and neoplastic phases. Since changes in expression of CXCL12 and its receptor were not statistically-significant, increasing the number of gastritis and gastric cancer samples would help validate the results. Further, micro-dissection of stomach tissue using laser capture to separate cancer cells from stromal cells could more clearly demonstrate differences in CXCL12 and CXCR4 expression seen.

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