GROβ/CXCR2 autocrine loop in oesophageal squamous cell carcinoma.

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Growth-related oncogene (GRO), a CXC chemokine, plays a major role in inflammation, angiogenesis, tumorigenesis and wound healing. Recently, CXC chemokines have been extensively associated with metastasis and cellular transformation. Although aberrant expression of GRO has been reported in several human cancers, the expression of GRO and its receptor, CXCR2 in oesophageal squamous cell carcinoma (SCC) is unknown and the role of these genes in oesophageal carcinogenesis is poorly understood. Here we show that GROα, GROβ and CXCR2 are all up-regulated in oesophageal tumor tissue compared with corresponding normal tissue using cDNA microarray, Northern blot and immunohistochemical analysis. WHCO1, a oesophageal squamous cell carcinoma cell line, constitutively expresses GROα, GROβ and CXCR2. In the WHCO1 cell line, GROβ signalling is mediated in part by the Ras/Raf/MEK/ERK pathway, resulting in enhanced EGR-1 transcription. Treatment of WHCO1 with SB 225002 (specific inhibitor of CXCR2) and a specific antibody to GROβ blocks signalling via the Ras/Raf/MEK/ERK pathway and reduces EGR-1 transcription. MTT assay showed that proliferation of WHCO1 treated with SB 225002 is significantly (50%) inhibited compared with untreated cells. Elevated levels of EGR-1 may further induce the expression of downstream target genes related to tumor cell growth, proliferation, differentiation and metastasis. This autocrine signalling pathway may play a critical role in the development of oesophageal squamous cell carcinoma.