

Opioid growth factor (OGF) inhibits anchorage-independent growth in human cancer cells

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Abstract. Opioid growth factor (OGF) is a native endogenous opioid peptide ([Met⁵]-enkephalin) that interacts with the OGF receptor (OGFr), and serves as a tonically active negative growth factor in neoplasia. To inquire whether OGF modulates anchorage-independent growth, HT-29 human colon cancer cells were grown in soft agar and subjected to this peptide. In contrast to controls, HT-29 cells exposed to OGF had 57% fewer colonies, and these colonies were reduced in area by 75%. The changes induced by OGF were abolished by concomitant treatment with naloxone, indicating a receptor-mediated mechanism for peptide activity. Continuous blockade of opioid-receptor interactions with the potent and long-acting opioid antagonist, naltrexone (NTX), revealed an increase of 81 and 49% in the number and area, respectively, of colonies compared to control levels. These data suggest that OGF is tonically active in neoplastic cells growing in soft agar medium. HT-29 cells studied under anchorage-independent conditions were not influenced in growth by a variety of natural and synthetic opioids, including those selective for μ , δ , and κ opioid receptors. Similar effects on anchorage-independent growth by OGF and NTX observed for HT-29 cells were recorded in pancreatic adenocarcinoma cells (Mia PaCa-2, Panc-1) and squamous cell carcinoma of the head and neck (CAL-27). These results using anchorage-independent conditions are consistent with previous data showing that OGF can markedly influence tumor growth in xenografts, and suggest that clonogenic assays can be utilized as indicators of tumorigenicity when tumor transplantation experiments are restricted.