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Guanides as X4 HIV Inhibitors, Antibiotics and Inhibitors of Cancer Metastasis

Guanide and biguanide compounds synthesized by the Teintze lab have been found to bind to the CXCR4 chemokine receptor which is used by X4 strains of HIV to enter cells and is involved in cancer metastasis. Therefore, they may be able to inhibit both HIV infection and cancer metastasis. When the chemokine SDF-1 binds the CXCR4 receptor, it activates an intracellular signal transduction pathway triggering chemotaxis of cancer cells, which will metastasize toward a gradient of SDF-1. It's unknown whether the guanide compounds that bind CXCR4 activate the receptor which triggers the ERK MAPK1/3 pathway or are antagonists. For inhibiting either X4 HIV infection or cancer cell metastasis, the compounds should be antagonists. If they activated the receptor, they would cause inflammatory side effects or cell migration. To determine whether the compounds are antagonists, an ERK phosphorylation assay is being developed. CXCR4 over-expressing Cf2Th cells are grown in wells and treated with SDF-1 in the presence or absence of the guanide compounds. Duplicate western blots are run using the samples and probes with a monoclonal antibody to phosphorylated ERK and an antibody that recognizes all ERK, respectively. The chemiluminescence from the blots will be used to quantitatively determine whether the compounds are acting as antagonists or agonists.