Cell Screening Assay for Identifying Inhibitors of Eosinophil Proliferation

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Abstract:

The purpose of this study was to develop a cell-based screening assay for identification of small molecules for the treatment of asthma. Eosinophils are leukocytes that contribute to the pathology of asthma. Lidocaine inhibits interleukin-5 (IL-5)-mediated survival and activation of human eosinophils, and it is able to replace inhaled glucocorticoids for the treatment of asthma; however, lidocaine has many side effects, including anesthesia. Therefore, a collection of commercial and novel, synthesized lidocaine analogues were investigated for inhibitory activity of the IL-5-stimulated proliferation of TF-1 cells, a CD34+, cytokine-dependent, erythroleukemic cell line model for eosinophil growth. Among 74 investigated compounds, 10 were more potent inhibitors of cell proliferation than lidocaine (average IC50 = 223 µM), with IC50 values ranging within 1-119 µM. This cell-based assay is an effective method for screening chemical compounds and has revealed promising lead compounds for the treatment of asthma.

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