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Design, synthesis, and structure-activity-relationship of a novel series of CXCR4 antagonists

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Graphical Abstract

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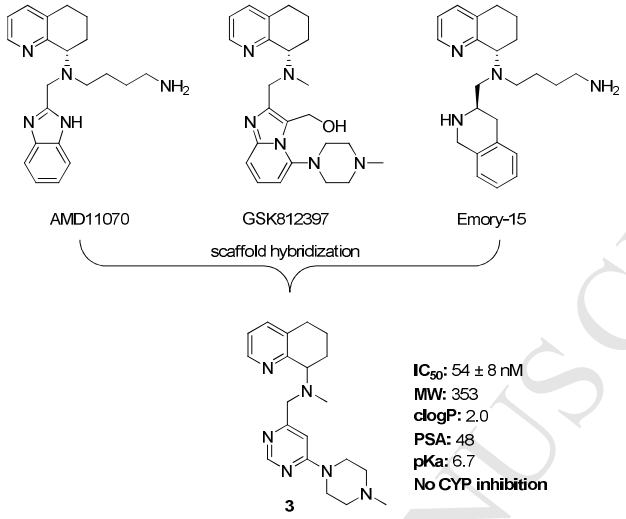

A novel series of CXCR4 antagonists was developed by a scaffold hybridization strategy. The most promising lead of this series, compound **3**, binds potently with CXCR4 receptor (IC_{50} = 54 nM) and inhibits CXCL12 induced cytosolic calcium increase (IC_{50} = 2.3 nM). Furthermore, compound **3** possesses good physicochemical properties (MW 353, clogP 2.0, PSA 48, pKa 6.7)，exhibits minimal CYP isozyme and hERG inhibition.