Supplemental Information About Pharmacological Agents:

Mepyramine: Selective inverse agonist for the H_1 receptor. Inhibits histamine induced inositol phosphate (InsP) production (log EC_{50} = -7.94) and intracellular calcium mobilization. Sequesters $G_{q/11}$ protein, reducing its availability for other receptors associated with the same signaling pathway (3).

Cetirizine dihydrochloride: This histamine H_1 receptor antagonist displays selectivity over other receptors at concentrations up to 10 μM (1).

Cimetidine: Widely used H_2 histamine antagonist, which has more recently been described as an inverse agonist (12).

Ciproxifan: A novel chemical series of histamine H_3-receptor antagonists. *In vitro*, it behaved as a competitive antagonist at the H_3 autoreceptor controlling ^3H histamine release from synaptosomes and displayed similar Ki values (0.5-1.9 nM) at the H_3 receptor controlling the electrically-induced contraction of guinea pig ileum or at the brain H_3 receptor labeled with ^{125}I-iodoproxyfan (10).

JNJ 7777120: H_4 receptor antagonist; displays high affinity (K_i = 4.5 nM) and is >1000-fold selective for H_4 over other histamine receptors (11).

H1152: Rho-kinase (ROCK) inhibitor that displays high selectivity over other protein kinases (cell-free in vitro kinase activity IC_{50} values are 0.012, 0.180, 0.360, 0.745, 3.03, 5.68 and 28.3 μM for ROCKII, CAMKII, PKG, Aurora A, PKA, PKC and MLCK respectively). Inhibits sulprostone-induced contractions in guinea pig aorta (IC_{50} = 190 nM) and displays proerectile effects in rats (2).

ML-7: Selective inhibitor of myosin light chain kinase (MLCK) (K_i = 0.3 μM). Exhibits more potent inhibition than the parent compound ML-9. Displays reversible, ATP-competitive inhibition of both Ca^{2+}-calmodulin-dependent and Ca^{2+}-calmodulin-independent smooth muscle MLCKs (9).

GFX109203X: Very potent and selective inhibitor of protein kinase C, selective for the α and β1 isoforms (cell-free in vitro kinase IC_{50} values are 0.0084, 0.0180, 0.210, 0.132, and 5.8 μM for α, β1, δ, ε and ζ isoforms respectively). Selective over MLCK, PKG and PKA (IC_{50} values are 0.6, 4.6, and 33 μM respectively). Potent antagonist at the 5-HT_3receptor (K_i = 29.5 nM) (8).

PI828: PI 3-Kinase inhibitor (cell-free in vitro kinase IC_{50} values are 0.098, 0.183, 0.227 and 1.967 μM for p110β, p110α, p110δ and p110γ respectively) that displays higher potency than LY 294002 (4).

Immepip dihydrobromide: Potent histamine H_3 receptor agonist. Also binds to H_4 receptors (K_i values are 0.4 and 9 nM at human recombinant H_3 and

H_4 receptors respectively). Equipotent to or slightly more active than (R)-α-methylhistamine at H_3 receptors (5).

SB203580: Selective inhibitor of p38 mitogen-activated protein kinase (Cell-free in vitro kinase assay IC_{50} values are 50 and 500 nM for SAPK2a/p38 and SAPK2b/p38β2 respectively). Displays 100-500-fold selectivity over LCK, GSK-3β and PKBα (6).

Y16: A cell-permeable pyrazolidinedione compound that is shown to target RhoGEF DH-PH domain junction with high affinity (K_d = 65 nM) and effetively prevent RhoGEFs LARG, p115, and PDZ from interacting with RhoA, while displaying little potency against DBL-RhoA, LBC-RhoA, intersectin-Cdc42, or TrioN-Cdc42 interaction. Shown to completely prevent serum-induced activation of cellular RhoA, but not Cdc42 or Rac1, in NIH-3T3 cultures (10 μM) and RhoA downstream signaling events. Greatly synergizes with Rho GEF-binding domain blocker Rhosin in blocking RhoA-LARG interaction and in preventing cellular RhoA activation (both drugs at 5 μM) (7).

Additional Information:

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