

SUPPLEMENTAL DATA

Manuscript title: Detailed analysis of biased histamine H₄ receptor signalling by JNJ7777120 analogues

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Supplemental Table 1. Overview of potency and intrinsic activity values in a β -arrestin2 recruitment and CRE-luciferase assay. Intrinsic activity is calculated as percentage of maximal histamine (HA) response. Data shown are pooled data from at least three experiments performed in duplicate. Error bars indicate SEM values.

Supplemental Figure 1. Effect of different basic side chains influence compound intrinsic activity in β -arrestin2 recruitment. U2OS-H₄R cells were stimulated with indicated amount of indolecarboxamides. A) R5-Cl, R7-CH₃ B) R7-F C) R7-CH₃. Intrinsic activity is plotted as percentage of maximal histamine (HA) response. Data shown are pooled data from at least three experiments performed in duplicate. Error bars indicate SEM values.

Compound		β-arrestin2 recruitment		Compound		β-arrestin2 recruitment	
#	Structure	pEC ₅₀	Intrinsic act. (%HA)	#	Structure	pEC ₅₀	Intrinsic act. (%HA)
75*		6.0(0.09)	95 (4.1)	26		5.4(0.08)	44 (6.1)
35		6.4(0.12)	75 (4.8)	41		7.8(0.10)	44 (4.1)
48		8.0(0.11)	63 (4.5)	22		6.1(0.06)	42 (4.0)
50		7.8(0.10)	63 (4.0)	59		5.8(0.10)	41 (3.9)
28		7.0(0.03)	62 (4.3)	21		5.6(0.02)	39 (3.5)
1		8.0(0.12)	62 (4.2)	46		6.8(0.13)	38 (2.2)
47		8.3(0.13)	59 (1.1)	72		6.2(0.09)	37 (2.5)
51		8.2(0.20)	58 (4.2)	20		6.2(0.00)	37 (1.3)
29		7.4(0.07)	57 (2.8)	67		7.5(0.19)	36 (3.3)
49		7.9(0.12)	57 (2.4)	69		6.2(0.07)	36 (2.2)
76		6.9(0.12)	57 (1.5)	64		6.4(0.06)	36 (1.3)
2		7.5(0.12)	56 (3.6)	19		5.3(0.08)	36 (0.9)
70		7.3(0.06)	55 (4.0)	71		7.2(0.12)	35 (0.8)
18		7.0(0.12)	53 (0.8)	63		7.1(0.09)	33 (4.7)
12		6.5(0.12)	52 (2.8)	54		6.2(0.12)	33 (1.6)
17		6.9(0.07)	52 (1.3)	57		5.6(0.07)	32 (3.5)
56		6.5(0.09)	51 (3.8)	31		6.8(0.09)	30 (1.4)
74		7.4(0.06)	50 (0.4)	45		5.9(0.09)	29 (2.5)
36		7.2(0.13)	49 (3.9)	61		5.4(0.07)	28 (3.2)
43		7.0(0.10)	48 (4.8)	66		5.6(0.08)	24 (2.3)
55		7.1(0.03)	48 (4.8)	73		6.6(0.11)	19 (1.9)
10		7.2(0.07)	47 (4.2)	53		6.6(0.07)	18 (2.4)
77		6.7(0.09)	46 (1.9)	44		6.0(0.07)	14 (3.4)
68		6.7(0.13)	45 (2.3)	65		6.0(0.12)	13 (2.5)

*NB. **75** is the only compound that displays agonism in CRE luciferase assay:
 Eff=105±5%, pEC₅₀=6.4±0.1

Supplemental Figure 1

