The efficacy of β2-adrenoceptor agonists in human bronchial smooth muscle cells and human bronchial epithelial cells compared with that seen in transfected CHO-K1 cell lines.

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Agonist ligands have two properties – affinity (ability to bind to a given receptor) and efficacy (ability to induce a response; Strange 2008). Full agonists are able to stimulate maximum responses whilst less efficacious ligands only induce partial agonist responses. Thus agonist ligands can be ranked in order of efficacy by the proportion of the maximal response they are able to stimulate (Kenakin 1999, Strange 2008). A recent study has examined the efficacy of a range of β-adrenoceptor ligands at the human β-adrenoceptors expressed in CHO-K1 cells (Baker 2010). A criticism of this study is that the human receptors are overexpressed by transfection into rodent cells, rather than being studied in their native environment. This study therefore examined the responses to several β-adrenoceptor agonists in human airway smooth muscle cells (HASM), human bronchial epithelial cells (BE; both expressing native β2-adrenoceptors) and compared the rank order of efficacy of these ligands to that seen in stably transfected CHOK1-cell lines, one with a high level of β2-adrenoceptor expression (CHO-β2-high) and one with a low-level of human-β2-adrenoceptor expression (CHO-β2-low).

3H-cAMP accumulation assays were performed as described in Baker 2010 and an incubation time of 5 hours was used to maximise the accuracy of the small response measurements.

Fenoterol stimulated a response in all 4 cell lines that was inhibited by ICI 118551 to yield log K_D values of -9.64±0.04 (n=11), -9.68±0.17 (n=4), -9.84±0.05 (n=15) and -9.69±0.06 (n=7) in the HASM, BE, CHO-β2-high and CHO-β2-low cell lines respectively. The affinity for CGP 20712A (log K_D) was -6.04±0.07 (n=4), -6.06±0.13 (n=13), -6.14±0.13 (n=6) and -6.14±0.05 (n=4) respectively thus confirming the presence of the human β2-adrenoceptor (and not the human β1-adrenoceptor) in each cell line. Adrenaline stimulated responses that were 98.1±3.7% (n=8), 89.2±2.8% (n=6), 100.6±2.5% (n=6) and 89.9±6.0% (n=6) of the maximum response to isoprenaline at each cell line respectively (HASM, BE, CHO-β2-high and CHO-β2-low). Noradrenaline was found to be less efficacious in all cell lines with responses of 55.9±1.9% (n=7), 72.6±11.3% (n=6), 91.6±2.6% (n=6) and 81.4±5.4% (n=5). BRL37344 was the least efficacious ligand in all lines with response of 9.1±0.5% (n=4), 21.8±3.8% (n=3), 47.5±3.8% (n=6) and 40.1±5.4% (n=6) respectively.

The overall rank order of efficacy of the ligands was isoprenaline > adrenaline > formoterol > fenoterol > cimaterol > noradrenaline > terbutaline > salbutamol > salmeterol > clenbuterol > ractopamine > BRL35135A > BRL 37344.

In conclusion, the rank order of ligand efficacies for the human β2-adrenoceptor as determined in the transfected CHO-K1 cell lines is the same as that seen in for native β2-adrenoceptors expressed in human bronchial epithelial and airway smooth muscle cells.

Baker 2010 The selectivity of β-adrenoceptor agonists at the human β1, β2 and β3-adrenoceptors. Brit J Pharmacol 160: 1048-1061
