Cystic fibrosis (CF) is a common lethal inherited disease of Caucasians, characterised as an exocrineopathy [1]. The CF gene protein, the cystic fibrosis transmembrane conductance regulator (CFTR) acts as a cyclic AMP-dependent CF channel [2] and also plays a key role in regulating secretion of mucus and serous proteins [3-6]. Thus, an antibody raised against a synthetic peptide from the first nucleotide binding domain (NBD) of CFTR inhibited β-adrenergic stimulated mucin secretion, when introduced into living rat submandibular cells by hypotonic swelling [5]. The CFTR antibody containing cells showed the same phenotype as submandibular cells from CF individuals [3], thus providing a good model for investigating correction of the CFTR defect. Cells transfected with CFTR also showed increased cyclic AMP dependent endocytosis and exocytosis [7] and mucin secretion [8]. Pharmacological correction of the CFTR-mediated mucin secretion defect has been demonstrated [3,9]. Thus, defective β-adrenergic stimulation of mucin secretion in CF cells and in CFTR antibody containing cells was corrected by the non-selective agonist 3-isobutyl-1-methylxanthine (IBMX). IBMX was also shown to activate CF transport in cells expressing ΔF508 CFTR [10]. IBMX acts as an adenine receptor antagonist and inhibits cyclic nucleotide phosphodiesterases and protein phosphatases. The present study has used the CFTR antibody inhibited submandibular cell model to directly investigate the role of adenine receptor antagonists in the correction of defective CFTR-mediated mucin secretion and whether excessive increase in cyclic AMP is required. Production of CFTR antibodies raised against a peptide (524-537), in the first NBD of CFTR was carried out as described [5]. Incorporation of antibodies into intact rat submandibular acini and measurement of mucin secretion was as described [5]. Acini were pulse-chase labelled with [3H]-glucosamine and suspended in TES-buffered saline, pH 7.4 containing 1mg/ml BSA [5]. To 200μl of acini suspension, 800μl of either 10mM TES, pH 7.4 (swollen) or TES-buffered saline (unswollen), each containing 5mM ATP and antibody (approx. 0.2mg IgG/mI) was added for 1.5 min at room temperature, followed by washing and resuspension in buffer containing 20mg/ml BSA. Following a 15 min recovery, acini were washed and incubated under experimental conditions at 37°C. [3H]-labelled mucin release was measured as described [5]. Cyclic AMP content was measured by radioimmunoassay [5]. The actions of the selective A1 and A2 receptor antagonists, 8-cyclopentyl theophylline (CPT) and 3,7-dimethyl-1-propargylxanthine (DMPX) on correction of CFTR-antibody-inhibited β-adrenergic stimulation of mucin secretion has been investigated. CPT and DMPX stimulated mucin secretion from normal rat submandibular acini in a dose-dependent manner; at a concentration of 1 mM, CPT increased mucin secretion by 228.2 ± 25.6 % basal (n=4) and DMPX by 434.0 ± 85.3 % basal (n=4). Doses of CPT close to the Ki for A1 adenose receptor antagonism did not stimulate mucin secretion (10nM CPT, 104.3 % basal, n=2). The data indicate that the effect of CPT in increasing mucin secretion is unlikely to be related to A1 receptor antagonism; although an A2 agonist effect cannot be ruled out. Correction of CFTR antibody inhibited β-adrenergic mucin secretion response was seen using CPT but not DMPX; Table 1 shows the isoproterenol-inhibited mucin secretion response in CFTR antibody containing cells and restoration by CPT. Isoproterenol response in cells containing non-immune serum was 228 ± 17.5 % basal (n=4, p<0.05 for difference from cells containing CFTR antibody). It can be seen (Table 1) that DMPX was ineffective at restoring secretion whereas CPT was almost as effective as cAMP (1 mM).