Research Article

Receptor(s) activation and cAMP elevation by the PGE1 analogue, Misoprostol in cultured human fibroblast cell line (W138).

Sankar P. Mitra

Sepracor Inc, 84 Waterford Drive, Marlborough, MA 01752, USA

Address: Sankar P. Mitra Ph.D, 102, Vassar Street, Worcester, MA 01602

E-mail: smitra3554@gmail.com
*Corresponding author

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ABSTRACT

Misoprostol is a racemate of synthetic PGE1 analog and an agonist to the EP receptors. The drug elevates cAMP level dose-dependently (EC_{50} ~ 7.0 µM) in human lung fibroblast cell line, W138. Both free acid and its methyl ester are seen to be equally potent in that act. The specific PGE1 receptor (EP2) antagonist AH6809 inhibits the effect of cAMP elevation (EC_{50} ~ 10µM) almost ~ 90 %. Pre-treating the cells with Pertussis toxin (PTx) enhances the cAMP level considerably whereas Cholera toxin (CTx) instead of elevating it lowers the level by ~ 25 % in presence of Miso. The events characteriscally indicate that Miso works by activating both Gs and G_i associated with its receptor(s). The anti-mitotic drug Colchicine lowers the basal production of cAMP but also suppresses the elevating effect by Miso. On the other hand the action of Forskolin (FSK) in its presence shows only an additive effect. All these facts strongly suggest that either the agonist interaction may proceed via a single receptor which is promiscuously associated with both stimulatory (G_s) and inhibitory (G_i) G -proteins or else the W138 cell line expresses both EP2 and EP3 (subtype EP3α) which are respectively connected to them while acting simultaneously.