**What are G Protein Coupled Receptors?**

G Protein Coupled Receptor (GPCR) are receptors which mediate the responses to many signal molecules such as hormones, neurotransmitters and mediators. They are only found in eukaryotes with more than 1000 known types of GPCR (Alberts, 2002 & Alberts, 2013). They are also the largest family of cell surface receptors in which more than half of all known drugs works via G-protein coupled receptors. Some well-known drug which uses G-protein coupled receptors are Ventolin (salbutamol) and Telfast (fexofenadine hydrochloride) (Alberts, 2013). GPCR indirectly activate or inactivate plasma-membrane bound enzymes via trimeric GTP-binding proteins (G-proteins) in which serves as relay molecules as they couple receptor to enzyme (Alberts, 2002 & Alberts, 2013).

GPCR are single polypeptide chain which threads back and forth across membrane (extracellular side and the cytosol side). The receptor changes shape when bonded with a ligand in which then activates G-proteins. G-proteins are made up of three protein subunits $\alpha$, $\beta$, & $\gamma$. There are many different types of G-protein in which is specific to a set of receptors. They include Gs (stimulatory) which activates adenylyl cyclase, Gi (inhibition) which inhibits adenylyl cyclase and Gq which activates phospholipase C-$\beta$.

**How Does G Protein Coupled Receptors Work?**

1. The G-protein has guanosine diphosphate (GDP) attached. The G-protein is current inactive; hence GDP is in excess. (Alberts, 2002)
2. Signal molecules such as hormones or neurotransmitters binds in the GPCR on the extracellular side in which the GPCR undergoes a conformational change (Alberts, 2002).
3. The G-protein is activated and binds with GPCR (Alberts, 2002).
4. The activated receptor induces a conformational change to the $\alpha$ subunit of G-protein in which causes the exchanges GDP to guanosine triphosphate (GTP) via dissociation (Alberts, 2002).
5. GTP binding to the $\alpha$ subunit causes a further conformational change which causes the $\alpha$ subunit to dissociate and move away from the $\beta$ & $\gamma$ subunit or the $\alpha$, $\beta$ & $\gamma$ subunit can stay together (Alberts, 2002).
6. G-protein can now control the activity of target protein such as enzymes that produces second messenger. These second messenger can cause the activation and inhibition of many processes in the human body (Alberts, 2002).
7. The $\alpha$ subunit hydrolyses the GTP to GDP in which causes the $\alpha$ subunit to dissociate from the target molecule. This step can be accelerated by the binding of another protein called regulator of G-protein signaling (RGS) (Alberts, 2002).
8. The $\alpha$, $\beta$ & $\gamma$ subunit is reformed and is in the inactivated stage (Alberts, 2002).

This process can continuously occur as long as signal molecules are bound to the receptor however, if this process continues, the receptor can become inactive even if the signal molecules is still attached.
**What is Asthma?**

GPCR and G-protein mechanism can be seen in allergenic asthma. About 25 million Americans are affected by asthma in which 60% of those people are affected by allergenic asthma (Asthma and Allergy Foundation America 2015). These allergens include dust mites, mold, pets, pollen or mold (Asthma and Allergy Foundation America 2015).

Asthma causes the walls of airways to become sore and swollen (Asthma Australia, n.d.). This causes the airway to become narrower thus less air gets to the lungs. Narrowing of the airways can cause wheezing, coughing, chest tightness or troubled breathing (Asthma Australia, n.d.).

**Asthma Relationship to GPCR**

Histamine couples with the G-protein $G_{q}$ in which activates the enzyme phospholipase C-$eta$ (Alberts 2002 & Penn, Bond & Walker 2014). The activated phospholipase C-$eta$ cleaves phosphatidylinositol 4,5-bisphosphate (PIP$_2$) into diacyl glycerol and inositol 1,4,5-triphosphate (IP$_3$) (Alberts 2002, Penn, Bond & Walker 2014 & Deshpande & Penn 2006). This process release calcium ion from the endoplasmic reticulum in which causes the contraction of the smooth muscle in the airways (Alberts 2002, Penn, Bond & Walker 2014 & Deshpande & Penn 2006).

Ventolin or salbutamol can help relax the smooth muscle in the airways. Salbutamol is a $\beta_2$-agonist which can bind to $\beta_2$-adrenoceptor to activate adenylyl cyclase (Alberts 2002, Billington et al 2013 & Deshpande & Penn 2006). Activation of adenylyl cyclase causes the synthesis of 3'-5'-cyclic adenosine monophosphate (cAMP) which lowers the concentration of calcium ion release. This process causes the smooth muscle in the airway to relax (Alberts 2002, Billington et al 2013 & Deshpande & Penn 2006) which makes it easy to breathe.
Reference:


