We’ve all heard of growth factors but what do we really know about how they work?
Delving further into this relation between receptors and growth factors we also begin to uncover some nasty truths about them and why sometimes it’s best if they aren’t in use.

WHAT ARE RECEPTORS?
Serving as the processing and distribution centre much like that of a postal service are cell-surface receptors which lay embedded within the cell membrane. These receptors process either drugs, signalling proteins or ligands present which then go on to initiate an appropriate response. However, with an address stamped on to these molecules, they will only be posted to the specific receptor.

These receptors are generally transmembrane proteins with a structure which we can separate into 3 regions, extracellular, plasma and intracellular. Upon the binding of a specific molecule from the extracellular region to the plasma region of the receptor, a conformational or activity change takes place. At the intracellular region, the message is distributed to its designated location which in most cases is the nucleus.

THE FAMILY OF RECEPTORS
With a focus on the family of Kinase-Linked Receptors, their most frequent forms are concerned with cell division and differentiation. Responsible for the formation of new tissue, this form is receptive to various growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF) and vascular endothelial growth factor (VEGF) \[^{[1]}\]. In its other forms, it may either regard glucose and glycogen metabolism with the reception of insulin or the initiation of an inflammatory response with the reception of cytokines \[^{[2]}\].

FACT
There are over 50 Receptor Tyrosine Kinases belonging to at least 18 families!
Have we only scratched the surface of this family tree?

TYPES OF KINASE-LINKED RECEPTORS
Being split further on from this ‘family’ of receptors, there are various types of Kinase-Linked Receptors where the main 3 include:

1. Receptor Tyrosine Kinase (RTK)
2. Receptor Serine/Threonine Kinase
3. Receptor Guanylyl Cyclases

(Khanacademy.org)
HOW DO RECEPTOR TYROSINE KINASES WORK?

So what actually goes on within the processing centre of this postal service? It is suggested that upon the arrival and binding of a signalling molecule to the receptor a process known as 'dimerization' occurs where the two kinase domains are brought together leading to the activation of the receptor. Upon the completion of this stage, phosphorylation of tyrosine residue occurs at the adjacent receptor. With some RTKs, the phosphorylation of particular tyrosines amplify kinase activity. In the grand scheme of things however, this process serves as a call for downstream molecules to form signalling complexes.

Based upon the recognition of these phosphorylated tyrosines by Src Homology 2 (SH2) domains further signalling events can be dictated.

THE ROLE OF RTKs AND ITS DOWNFALL

As previously introduced, RTKs take up the role of forming a response with the introduction of extracellular growth factors. This ultimately leads to processes concerning cell growth, differentiation and proliferation. It is here however where we find the nasty aspects of the business.

It is here where we find that the dysregulation of RTK signalling plays a role in the development of neoplasia.

WHAT IS TO BE DONE?

How are we taking control?

Sometimes, messages are best undelivered and when we’re talking about the body, it’s for the better of our overall health.

Regarding this, we can consider Receptor Tyrosine Inhibitors as a 'No Junk Mail' sign. Doing exactly this and serving as the first of it’s kind, Imatinib is an example of such which is used as a chemotherapy drug. In preventing the phosphorylation that would usually occur to promote cancerous cell division, the kinase receptor is instead blocked from the very beginning.

Working as a competitive inhibitor, it binds to the standard structure without any need of a structural rearrangement. This involves the positioning and activation of an A-loop. When active, the A-loop is in an ‘open’ conformation where it swings away from the centre of the kinase.
References


