10/08/18

Cell communication II: propagation of the signal:

What is an example of an internal signal receptor?

-estrogen receptor

What is the immediate effect of a steroid hormone binding to its receptor?

-Changes in gene expression

Receptor Tyrosine Kinases (RTKs)

-Receptor tyrosine kinases are membrane receptors that attach phosphates to tyrosine

-A receptor tyrosine kinase can trigger multiple signal transduction pathways at once.

-abnormal functioning of RTKs is associated with many types of cancers

Target for new therapies

Herceptin

Transphosphorylation

Which amino acid sidechain can be phosphorylated?

-tyrosine

-Serine

-threonine

Protein phosphorylation: a molecular switch

What is the source of phosphate group that is transferred to the RTK?

-ATP

Outside of cell

Adapter proteins

Ras: rat sarcoma virus known to carry the gene around

-a form of a g-protein

GDP inactive

GTP active and binds to another protein (Raf)

Gene expression is always the end of signaling receptive pathways

Stimulates: cell proliferation, angiogenesis, cell migration

Inhibits: cell death (apoptosis)

Phosphorylation

Transduction: cascades of molecular interactions relay signals from receptors to target molecules in the cell

-How can the transduction cascade be regulated and how can other

More than 30% of all human cancers are driven by mutations of RAS genes

Ras is also known as “oncogene”

How likely is it that mutations impacting signal transduction pathways are inherited from one generation to another?

Signal transduction pathways are important for many fundamental functions.

Embryonic development is critically dependent on the proper function signal transduction pathways

Disturbances in signal transduction lead to catastrophic consequences during embryogenesis

Only very few mutations with subtle effects are tolerated and thus be inherited from one generation to another.

Second messengers:   
small molecules and ions as second messengers

Cyclic AMP

Cyclic amp (cAMP) is one of the most widely used second messengers

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Second messenger vs protein-mediated transduction

Protein mediated transduction

-enzymes are specific for one substrate

-enzymes are often localized in the cell, with limited diffusion

-sustained response to signals

Second messenger system

Second messengers can activate multiple downstream effectors

-small molecules and ions diffuse rapidly throughout the cell

Fine tuning the response:

Amplification

Specificity

Efficiency

Integration

Termination

Scaffolding proteins are large relay proteins to which other relay proteins are attached

Multiple signals can generate a combinatorial code that causes cells to react in very different ways.