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The results of the training recognize the role of phosphorylation in the transmission of intracellular signals. Assessment of the role of the second messengers in the transmission of signal induction signal path depends on the modification of the cellular component by the enzyme. There are many enzymatic changes that can occur and they are recognized to turn the next component downstream. Below are some of the most common intracellular alarm events. Phosphorylation Figure 1. The protein phosphorylation to the residues of the amino acids serine, threonine and tyrosine is added to the phosphate group (PO<sub>4</sub>-3). One of the most common chemical modifications that occurs in signaling pathways is the addition of a phosphate group (PO<sub>4</sub>-3) to a molecule such as protein in a process called phosphorylation. Phosphate can be added to nucleotide, such as GMP for GDP formation or TPP. Phosphates are also often added to serine, threonine and tyrosine protein residues, where they replace the hydroxyl group of amino acids (Figure 1). Transmission of phosphate is catalyzed by an enzyme called kinase. Different kinases are named after the substrate they are phosphorylate. Phosphorylation of the remnants of serine and threonine often activates enzymes. Phosphorylation of tyrosine residues can either affect the activity of the enzyme, or create a binder that interacts with the descending components in the signal cascade. Phosphorylation can activate or inactivate enzymes, and the reversal of phosphorylation, dephosphorylation of phosphatase, will change the effect. The second messenger of the Second Messenger are small molecules that spread the signal after it has been initiated by binding the signaling molecule to the receptor. These molecules help to spread the signal through the cytoplasm, altering the behavior of some cellular proteins. Calcium ion is a widely used second messenger. The free concentration of calcium ions (Ca<sup>2+</sup>) in the cell is very low, because the ion pumps in the plasma membrane constantly use adenosine-5-triphosphate (ATP) to remove it. For signaling purposes, Ca<sup>2+</sup> is stored in cytoplasmic bubbles such as endoplasmic reticulum, or access from outside the cell. When signaling calcium ion channels closed by ligand, allow higher levels of Ca<sup>2+</sup>, which are present outside the cell (or intracellular storage compartments), to enter the cytoplasm, which increases the concentration of cytoplasmic Ca<sup>2+</sup>. The reaction to the increase in Ca<sup>2+</sup> varies, depending on the type of cell involved. For example, in  $\beta$  cells of the pancreas, Ca<sup>2+</sup> signaling leads to the release of insulin, and in muscle cells, an increase in Ca<sup>2+</sup> leads to muscle contractions. Another second messenger used in many different cell types is the cyclical AMP (cAMP). Cyclic AMP is synthesized by the enzyme adenylyl cyclase from ATP (Figure 2). The main role cAMP in cells to bind and activate an enzyme called cAMP-dependent kinase (A-kinase). A-kinase regulates many vital metabolic pathways: it phosphorylates the serine and threonine remnants of its target proteins, activating them in the process. A-kinase is found in many different cell types, and the target proteins in each cell are different. The differences will have variations of responses to cAMP in different cells. Figure 2. This diagram shows the mechanism for the formation of a cyclical AMP (cAMP). cAMP serves as a second messenger to activate or inactivate proteins inside the cell. The signal stops when an enzyme called phosphodiesterase converts cAMP into AMP. Present in small concentrations in the plasma membrane, inositol phospholipid lipids, which can also be converted into second messengers. Because these molecules are membrane components, they are located near membrane receptors and can easily interact with them. Phosphatidylinositol (PI) is the main phospholipid that plays a role in cellular signaling. Enzymes known as kinases are PI phosphorylate for the formation of PI-phosphate (PIP) and PI-bisphosphate (PIP<sub>2</sub>). Enzyme phospholipase C breaks down PIP<sub>2</sub> to form diacylglycerol (DAG) and triphosphate inositol (IP<sub>3</sub>) (Figure 3). These PIP<sub>2</sub> cleavage products serve as second messengers. Diacylglycerol (DAG) remains in the plasma membrane and activates protein kinase C (PKC), which then phosphorylates serine and threonine residues in the targeted proteins. IP<sub>3</sub> dissipates in the cytoplasm and binds to the ligand-closed calcium channels in the endoplasmic reticulum for the release of Ca<sup>2+</sup>, which continues to signal the cascade. Figure 3. The enzyme phospholipase C breaks down PIP<sub>2</sub> on IP<sub>3</sub> and DAG, both of which serve as second messengers. Ligand binding to the receptor allows for the transmission of the signal through the cell. The chain of events that transmits the signal through the cell is called a signal path or cascade. Signaling pathways are often very complex due to interactions between different proteins. The main component of cellular signal cascades is the phosphorylation of molecules by enzymes known as kinases. Phosphorylation adds a phosphate group to the serine, threonine and tyrosine in the protein, altering their forms, activating or inactivating the protein. Small molecules, such as nucleotides, can also be phosphorylated. The second messengers are small, non-protein molecules that are used to transmit a signal inside a cell. Examples of second messengers are calcium ions (Ca<sup>2+</sup>), cyclical AMP (cAMP), diacylglycerol (DAG) and inositol triphosphate (IP<sub>3</sub>). 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