

Cell and Molecular Biology
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Week 05
Cellular Communications
Lecture - 19
Cellular Communication (Part 2)

Hello everyone, this is Dr. Vishal Trivedi from the Department of Biosciences and Bioengineering, IIT Guwahati. And what we were discussing was the cell signaling in this particular module. So far, what we have discussed is the importance of cell signaling in regulating the different types of cellular events. So in this context, we have discussed the role of cell signaling in cell growth and division. Cell differentiation, metabolism, and homeostasis.

We have discussed how cell signaling regulates the different types of reactions within the immune system and how cell signaling also regulates the different types of events related to cell death, such as apoptosis. How the cell signaling starting from the receptor is activating the different types of caspases and so on. And then we also discuss how the cell is communicating with another cell with the help of cell signaling. And apart from that, we also discuss how cell signaling is being triggered by different types of environmental factors such as humidity, temperature, pH, osmolality, and so on.

So it is very clear that cell signaling is very, very important for the survival and successful completion of the life cycle of an organism. Now, in this context, in the previous lecture, we discussed that cell signaling is of three different types. We have autocrine signaling, paracrine signaling, and then we also have endocrine signaling. In the auto-crime signaling, we are, you know, talking to our next colleagues or we are actually talking to someone who is very close to each other. And we are also going to talk to each other, right? So, in auto-crime signaling, it's like you are talking to yourself and things like that.

Then, in the para-crime signaling, you are talking to your neighbor, who is in the next balcony. And this means you are actually sending the signal to the nearby cell, and that's how you are communicating to give the instructions so that the neighboring cells should give you the desirable outcomes. One of the classical examples is how the signal from one neuron gets into the different neurons, and then lastly, we are talking about endocrine signaling. In endocrine signaling, you are secreting the molecules. Then it is traveling through the bloodstream, and then it is going to very distant locations far away.

Now, talking about endocrine signaling, we also have, you know, the different types of

hormones that are responsible for endocrine signaling. So, in this context, we have said that we are actually going to discuss animal hormones. We are also going to discuss the plant hormones. And then we are also going to discuss their importance in regulating the important physiological functions within the particular organisms. In this context, if you recall, in the previous lecture, we discussed that animal hormones could be of three different types: animal hormones that are peptide or protein in nature, animal hormones that are steroidal in nature, and then we also have animal hormones that belong to other categories.

Most of the peptide-based animal hormones are water-soluble hormones. Then the steroids are the fat-soluble hormones, and so on. Animal hormones regulate the different types of functions within animals. So they are regulating growth and metabolism. They are actually regulating the metabolic reactions.

So in this context, we discuss glucagon and insulin. And then you also regulate the different types of reproductive activity. So in that context, we discuss the role of follicular stimulating hormones, oxytocin, and all those kinds of hormones. And then we also discuss how it is regulating mood, homeostasis, sleep cycles, and so on. So in the previous lecture, we discussed the peptide-based hormones.

And in today's lecture, we are actually going to discuss the steroid hormone. So, as the name suggests, steroid hormones are actually fat-soluble hormones. Right. And you know the advantage of fat-soluble hormones.

Right. Fat-soluble hormones are actually, if you recall, in the previous module we discussed the transport of the material, right? And what we said is that anything which is hydrophobic in nature is actually going to cross the plasma membrane very easily because the plasma membrane is made up of lipids, and that's how it is actually going to get inside the cell, or it is going to reach the cytosol, or it can actually reach the nucleus as well, right? So basically, all the steroid hormones are fat-soluble hormones, and they can easily cross the plasma membrane, which is how they can either reach the cytosol or the nucleus. And once they reach the nucleus, they are actually going to activate or behave like a transcription factor, or they are actually going to activate the production of different types of transcription factors. And that's how it is actually going to start the cell signaling now within the steroid hormones. This is what is written here: the steroid hormones are lipid-soluble hormones, and they are mostly derived from cholesterol. Unlike peptide hormones, they are hydrophobic and can freely cross the plasma membrane of target cells.

Once inside the cell, they typically bind to the intracellular receptors located either in the

cytoplasm or the nucleus. The hormone receptor complex then acts as a transcription factor, and it regulates the gene expression directly. Pteridine hormones vary in their structure and function but generally consist of four fused carbon rings forming the pteridine backbone. Now talking about the more properties of steroid hormones. So they are synthesized mainly in the adrenal gland, gonads, and the placenta, and include key hormones such as cortisol, adrosterone, testosterone, estradiol, and progesterone.

The majority of the steroid hormones actually play a very crucial role in the reproductive cycles of the animals. Due to their lipid nature, they are not stored in vesicles; they are synthesized on demand and then transported into the blood bound to a specific carrier protein. So all steroid hormones are synthesized from the central molecule, which is called cholesterol, and is either taken up from the LDL in the blood or synthesized de novo in the steroidogenic cells. Steroid hormones are synthesized in cells rich in smooth endoplasmic reticulum or the SER and the mitochondria, primarily in the adrenal cortex, gonads, and placenta. Cholesterol is transported into the mitochondria by the steroidogenic acute regulatory protein, or StAR.

And in the mitochondria, cholesterol is converted into pregnenolone by the cholesterol side chain cleavage enzyme, which is called P450 ssc or CYP11A1. Now, these are the complicated pathways that people are using for steroid synthesis, right? So, pregnenolone serves as the precursor for all the other steroid hormones and is further modified by the various cytochrome P450 enzymes and the hydroxysteroid dehydrogenases in the smooth endoplasmic reticulum and the mitochondria to produce the different types of hormones. So you are actually having cholesterol, which is going to be processed by CYP11A. And that's how you're actually going to produce pregnenolone. And the pregnenolone is actually going to be fractionated into the different types of enzymes.

So pregnenolone will be a basic molecule. Which is going to be processed by the CYP17A1, and that's how you are actually going to produce the 17-alpha-hydroxypregnenolone, right? And then this 17-hydroxypregnenolone is going to be processed again by the CYP17A1, and that's how you are actually going to produce the DHEA. And the DHEA is then going to be processed by another enzyme called SALT; that's how you are actually going to produce the DHEA, okay? This is a steroid hormone. Similarly, the pregnenolone is going to be converted into the three beta HSD, right? And that three beta HSD is going to be converted into the progesterone, right? And then the progesterone is going to be fractionated into the two pathways. In one pathway, the SIP 17 alpha 1 again is going to process the progesterone to produce the 17 alpha hydroxy progesterone, right? And this 17 alpha hydroxypregnenolone can also be produced from the 17 hydroxypregnenolone, you know, by an intermediate called 3 beta HSD, right? And then this 17 alpha hydroxyprogesterone is going to be processed by CYP21, which is another

cytochrome

P450

enzyme.

And then it is going to form deoxycortisol. And then deoxycortisol is going to be processed by an enzyme called CYP11B1. And then it is going to form cortisol. And the cortisol is going to be converted into 11 beta HSD2 or 11 beta HSD1. And that is eventually going to convert it into cortisone.

And the cortisone is going to be called glucocorticoid. Similarly, the progesterone that is being formed from the pregnenolone is going to be processed by the CYP21 to form the deoxycorticosterone. And then deoxycorticosterone is going to be processed by CYP11B1 to form corticosterone, and then corticosterone is going to be processed by CYP11B2 to form aldosterone, and aldosterone is going to be a mineralocorticoid. Similarly, some of these enzymes are actually going to be, you know, for example, the 17 beta hydroxypregnenolone is going to be converted into DHEA, right? And then DHEA is going to be converted into 3 beta HSD. And then it is going to be converted into androstenedione.

And then it is going to be converted into 17 beta HSD3. And that is going to get converted into testosterone. And the testosterone is also going to be processed by the 5 alpha reductase to form dihydrotestosterone, right? So, these are the sex hormones, right? And the DHEA and the L-pro-steroidine, when they are going to be processed by the CYP19A1, another cytochrome enzyme. And then it is going to form the androstenedione.

Right. And then the androstenedione is going to be converted into 17 beta HSD1. And that is going to form the androstenedione, and the androstenedione is going to be converted into testosterone. So all these enzymes are the sex hormones. Right. So you see that there are three categories of steroid hormones that are going to be produced by this complicated process.

Interactions of the cholesterol with this cytochrome P450 enzyme system. So, it is going to form the mineralocorticoid, the glucocorticoid, and the sex hormones. So one of the very important features is that steroid hormones are not being stored. Steroid hormones, since they readily cross the plasma membrane, do not need to be stored in vesicles, and they are synthesized as soon as there is a demand. So there will be a demand, then it is actually going to be secreted, and then it is going to be secreted outside, and that's how it will reach the target cells, right? And this process is going to be very, very fast.

Now let's talk about the classification of the steroid hormones. Steroid hormones can be classified based on their primary site of synthesis, which includes the adrenal cortex, gonads, and placenta. Within each site, the different classes of steroid hormones, such as glucocorticoids, mineralocorticoids, and sex steroids, are produced, each with distinct

physiological roles. Now, let's see how these steroid hormones are produced from the different sites and what their physiological role is. So, first are the steroid hormones that are going to be produced by the adrenal cortex.

So, you have the cortisol, right, which actually belongs to the glucocorticoids, and cortisol regulates metabolism, stress responses, and suppresses inflammation. And in the deficiency of cortisol, it is causing Addison's disease, fatigue, and low blood sugar. Then we have aldosterone. So aldosterone is a mineralocorticoid, and it maintains the balance of sodium and water.

It regulates blood pressure. In the absence of aldosterone or if there is a deficiency of aldosterone, it will cause low blood pressure, hyperkalemia, and dehydration. Then we have DHEA, which is actually a weak androgen, and it is a precursor for the sex steroids that contribute to the secondary sexual characteristics, such as moustaches and all that. It is often asymptomatic and may affect libido or mood. Then we have the steroid hormones, which are produced by the gonads. So you have testosterone, estradiol, and progesterone.

Testosterone belongs to androgens and promotes male secondary sexual characteristics and spermatogenesis. In the deficiency of testosterone, it is going to delay puberty. It is going to cause infertility, and there will be reduced muscle mass. Whereas estradiol belongs to the class of estrogen and regulates the female reproductive cycles. It maintains the uterine lining and is also causing the bone length.

Remember that the majority of estrogen is a very important hormone for female health. The right to female reproductive health and, many times, even estrogen is responsible for the development of osteoporosis or bone health-related issues. So, if there is a deficiency of estrogens, then it is going to cause irregular menstrual cycles, osteoporosis, and also infertility. Then we have progesterone, which is the hormone that prepares the uterus for implantation and supports pregnancy. In the absence of progesterone, it is going to cause infertility and menstrual cycle irregularities.

Then we have the steroid hormones from the placenta, correct? So the placenta is going to produce progesterone and estrogens. Progesterone belongs to a class of hormones and it maintains the endometrium, inhibits uterine contractions during pregnancy. So it is actually a good hormone that is going to maintain the pregnancy. So it has been a hormone that is required for the maintenance of pregnancy. So if there is a deficiency of progesterone, then it is actually going to cause abortions or preterm labor.

Then we have estrogen. So estrogen belongs to the estrogen class. It promotes uterine

blood flow and fetal development. In the absence of estrogen, it will actually cause impaired fetal growth and placental functions. Then we have another class of steroid hormones which are called cortisol. So this is just one classical example of the steroid hormones, just to explain to you how the steroid hormones are produced, how they cross the plasma membranes, how they actually initiate cell signaling, and how they are regulated, along with the different types of events.

So cortisol is one of the glucocorticoids and plays a crucial role in the body's response to stress, metabolic regulation, and immune regulation. How are you going to do the synthesis of cortisol? So cortisol is synthesized in the zona fasciculata of the adrenal cortex from cholesterol. We have already seen how cortisol or the cortisol-derived hormones are produced in the previous slides. The synthesis begins when the acetylcholinotropic hormone binds to its receptor on the adrenal cell, stimulating the uptake of cholesterol and its transport into the mitochondria via a protein called an SPR protein. So when there is a need to synthesize cortisol, the adrenocorticotropic hormone is actually going to be produced, and then it is actually going to bind to its receptor on the adrenal cells, and that is actually going to initiate the uptake of cholesterol from the blood, right? So it is actually going to initiate the uptake of cholesterol from the blood, right? And then it is going to be transported to the mitochondria with this particular protein.

Inside the mitochondria, cholesterol is converted into pregnenolone by CYP11A1, and after a series of enzymatic steps, cortisol is produced. And all these steps we discussed in a previous slide, right? How steroid hormones are being produced. As a steroid hormone, it is not stored but is synthesized and secreted on demand into the bloodstream. So as soon as the steroid hormones are synthesized, they are transported into the blood, and then they reach their final site of action. Now, what happens at the site of action is that it actually catalyzes the cell signaling.

Right? So, being lipophilic, cortisol easily diffuses across the plasma membrane of the target cell. Once it is in the blood, right? Then it is actually reaching its target site. So, this is the target site. And since this is, you know, hydrophobic in nature, it is crossing the membrane and also reaching inside the target cells. Inside the cytoplasm, it binds to the glucocorticoid receptors, which are normally held inactive by the heat shock proteins.

Upon binding, the receptor undergoes a conformational change, dissociating from the HSPs, and the glucocorticoid complex is translocated to the nucleus, right? In the nucleus, it binds to the glucocorticoid response element or the GREs on the DNA and functions as a transcription factor, either up-regulating or down-regulating the expression of target genes. This genomic signaling pathway influences gluconeogenesis, protein

breakdown, and immune responses. So cortisol synthesis is under the control of the hypothalamic-pituitary-adrenal axis. So remember that the ACTH is actually the initiator of starting the synthesis of cortisol.

So that is being completely secreted by the pituitary. And that's how the complete cortisol synthesis is actually going to be regulated by the brain. So in response to stress or low cortisol levels, the hypothalamus secretes the corticotropin-releasing hormone (CRH), which stimulates the anterior pituitary to release ACTH, which in turn promotes cortisol production. Now, one interesting thing is that you see that many of these hormones, like ACTH and corticotropin-releasing hormone, and so on. They are actually peptide hormones, right? I'm sure you might recall from the previous lecture that these are the peptide hormones secreted from the brain, right? So peptide hormones are actually regulating the synthesis of the steroid hormones. And many of these steroid hormones actually regulate the synthesis of the peptide hormone.

So basically, you have the peptide hormone, you have the steroid, and in many places, the peptide hormones are regulating or initiating the synthesis of the steroid hormones, and the steroid hormones are actually regulating the synthesis of the peptide hormone, and that's why there is a complete cascade of the peptide hormones and steroid hormones, and they both are actually working in coordination with each other. So there are many places where the peptide hormones are actually under the tight control of the steroid hormones. And there are places where the activity of steroid hormones or their synthesis is under the tight control of peptide hormones. Now cortisol exerts negative feedback on the hypothalamus, and we treat it to further suppress the release of CRH and ACTH. So from the regulatory signal, this is what it is written here.

So from the regulatory signals, it is actually stimulating the hypothalamus, and then the hypothalamus is secreting the CRH. Then CRH stimulates the anterior pituitary, and the anterior pituitary secretes ACTH. And then ACTH stimulates the adrenal cortex to synthesize cortisol, and then cortisol actually acts on different parts of the brain, right? And that's how it activates some of the genes for its final functions. Now, what will be the outcomes of cortisol signaling? So it maintains the blood glucose levels during stress and fasting.

It stimulates gluconeogenesis in the liver. It inhibits glucose uptake in muscles and adipose tissues. Promotes protein catabolism in muscles to provide amino acids for gluconeogenesis, enhances lipolysis in adipose tissues, suppresses immune and inflammatory responses, and supports blood pressure regulation by enhancing vasoconstriction. Now let's move on to the next class, which is called the monoamines. So we discussed the peptide hormones, we discussed the steroid hormones, and now

there's a third class, which is called the monoamines. Now, what are monoamines? So monoamine hormones are small biologically active molecules derived from aromatic amino acids like tyrosine and tryptophan.

So these are the hormones that are being synthesized from the aromatic amino acids such as tyrosine and tryptophan. They are synthesized by modifying these amino acids through decarboxylation and hydroxylation reactions. Monoamines are typically water-soluble and exert their effects by binding to the cell surface receptors, primarily the GPCRs or the ionotropic receptors. GPCR stands for G protein-coupled receptors. However, some, like thyroid hormones, are lipophilic and act via the intracellular nuclear receptors.

Monoamines include the important hormones that play a vital role in regulating moods, sleep, metabolism, cardiovascular functions, and stress responses. So you see, the monoamines are actually falling into two categories. One, they are water-soluble, and the second is that they are fat-soluble, right? Water-soluble examples include some of the thyroid hormones, such as T3 and T4, which are water-soluble, while fat-soluble hormones, like T3 and T4, have nuclear receptors. In contrast, many proteins and monoamines, which are water-soluble, bind to cell surface receptors. Now, how is the synthesis of the monoamines? So, you remember that the precursors of the monoamines are two hormones, which are tyrosine and tryptophan, right? So, monoamine hormones are synthesized from the aromatic amino acids, primarily tyrosine and tryptophan.

Tyrosine serves as a precursor for catecholamines, such as dopamine, norepinephrine, epinephrine, and thyroid hormones. While tryptophan gives rise to serotonin and melatonin. Remember, all these hormones are very, very important for mood swings. They are important for the different types of stress responses, and so on. So in the catecholamine pathway, tyrosine is converted into L-DOPA, right? By the tyrosine hydroxylase, then the dopamine is produced by the dopa carboxylase.

Remember that dopamine is a pleasure hormone; it actually causes a very good mood. So, dopamine is further converted into norepinephrine by the dopamine beta hydroxylase, and in the adrenal medulla, the PNMT converts norepinephrine into epinephrine. Tryptophan is first hydroxylated to form 5-hydroxytryptophan, which is then decarboxylated to produce serotonin. So in the previous slide, you have seen that tyrosine is being modified to form norepinephrine, epinephrine, and dopamine. In this case, the tryptophan is hydroxylated to form 5-hydroxytryptophan, and then it is decarboxylated to produce serotonin.

In the pineal gland, serotonin is converted into melatonin through the sequential action of N-acetyltransferase and hydroxylamine indole O-ethyltransferase, and the thyroid

hormones T3 and T4 are synthesized differentially, involving the adonation of the tyrosine residue into the hieroglobin within the thyroid gland. So, monoamines are a very, very important class of hormones; they are required for different types of functions, regulating metabolism, moods, preparing the cell for various types of stress responses, and so on. So, because of that, the monoamines are also classified based on the precursor amino acids; thus, you are actually going to have the monoamines derived from tyrosine or the monoamines derived from tryptophan. So monoamine hormones can be classified based on their precursor amino acids and cytosynthesis, reflecting their structural differences and specialized functions in the body.

So you have the tryptophan-derived monoamine hormones. So you have melatonin and serotonin. Melatonin is produced by the pineal gland. It regulates the circadian rhythm and the sleep-wake cycle; this means that melatonin is actually regulating sleep. You might have seen that many times you are not getting good sleep, and that good sleep comes from the production of melatonin. And that's why it is important that you take the different diets into account in your diet so that you will get the different types of amino acids.

If you take the same kind of diet every day, then you may actually get rid of important amino acids such as tryptophan or tyrosine, and you may experience a shortage of melatonin production. So melatonin is going to regulate the circadian rhythm, which means it is actually going to control when you wake up and when you sleep. And if there is a shortage of melatonin, it is actually going to directly affect sleep disturbances. It is going to disturb the circadian rhythm. And it's going to cause different types of sleep-related disorders, so once sleep is disturbed, it is actually going to lead to more and more complications in terms of that; it is going to disturb digestion, cause headaches, and all those kinds of things.

The second hormone is serotonin. Right, so serotonin is a hormone that is synthesized by the central nervous system. Enterochromaffin cells in the GI tract and the platelets. And serotonin is required for the regulation of mood, sleep, appetite, gastrointestinal motility, and vascular tone. So serotonin is actually important for moods. And it is if there will be a shortage of serotonin that is linked to depression, anxiety, irritable bowel syndrome, and migraines.

Then we have the tyrosine-derived monoamines. So we have dopamine, norepinephrine, and epinephrine. So dopamine is secreted from the hypothalamus, and it inhibits prolactin secretion, modulates motor activities, and affects mood rewards. So if there is a shortage of dopamine, it will actually be responsible for Parkinson's disease or hyperprolactinemia. Then we have norepinephrine. So norepinephrine is going to be

secreted from the adrenal medulla and the central nervous system or from the neurons.

And the norepinephrine is causing vasoconstriction, increasing blood pressure and part of the flight or fight response. Vasoconstriction means the narrowing of the blood vessels, right? So when there is a narrowing of the blood vessel, it is actually going to increase the blood pressure. If there is a shortage of norepinephrine, then it is actually going to cause the low BP.

It is going to cause depression. It is going to impair the stress response. Similarly, we have epinephrine. So, epinephrine is also being secreted from the adrenal medulla. It increases the heart rate. It increases the blood glucose levels and also causes bronchodilation. So epinephrine is going to reduce the stress responses if there is a shortage of epinephrine, which means it's also going to be a part of the fight or flight responses.

And it is also going to cause hypoglycemia in the case of stress, right? So remember, in the case of stress, you're supposed to have a very high glucose level so that you can actually have a lot of energy to use for the fight or flight responses. If there is a shortage of epinephrine, then it is actually going to do the reverse. So, to explain the different properties of the monoamines, you know, monoamine hormones, I have taken an example of epinephrine. So, whatever we are going to discuss regarding epinephrine, the general mechanisms of all the monoamine hormones are going to remain the same, except for their target hormone cells, their target receptors, and all those kinds of information, which could be different. So epinephrine, epinephrine, it is a catecholamine derived from tyrosine and plays a major role in the fight or flight responses by preparing the body for acute stress.

Remember, when we discussed the hormones, or when we discuss cell signaling, we discuss this response. So this response is when you are actually going to see the lion, right? So, if you see or encounter the lion, you have the option to either fight it or run. So, either you fight, or you run. In either of these cases, it is actually going to be responsible and it requires one of the monoamines, which is called epinephrine. How does the synthesis of epinephrine work, right? So, epinephrine is synthesized in the adrenal medulla, right? So, within the adrenal medulla, tyrosine is going to be transported into the adrenal chromaffin cells, and then it is actually going to be hydroxylated to form dopa, and then dopa is going to be converted to dopamine, right? And then dopamine is actually going to enter here, and that is how it is actually going to form norepinephrine, which, through a series of reactions, is going to be converted into epinephrine.

So, the process begins with the tyrosine, and it is converted into L-dopa, then dopamine,

and then norepinephrine. In chromaffin cells, norepinephrine is methylated by PNMT, or phenylethanolamine N-methyltransferase, to form epinephrine. This synthesis is stimulated by the stress signal through the sympathetic nervous system. And once you synthesize epinephrine, it is actually going to cause the signaling because remember that all these hormones are, you know, behaving like steroid hormones or peptide hormones.

So, epinephrine is a water-soluble hormone. It cannot cross the plasma membrane and thus binds to the endogenous receptors, which are GPCRs located on the surface of the target cell. So, basically, epinephrine will bind to the beta-adrenergic receptor, which is actually a GPCR, or G protein-coupled receptor, which means it is going to be coupled to the G protein. And then these G proteins are actually going to activate adenylate cyclase. So, the specific signaling pathway is activated by the receptor subtype and the tissue involved. So in the liver and the skeletal muscles, epinephrine primarily binds to the beta-adrenergic receptors, which activate the GS protein.

And the GS protein is actually going to activate adenylate cyclase. And then adenylate cyclase is actually going to convert ATP into cyclic AMP, right? So, it triggers a signaling cascade by activating adenylate cyclase, which increases the level of cyclic AMP, and as soon as the cyclic AMP level goes up, it will actually activate protein kinase A, right? And once protein kinase A is formed, it is actually going to activate phosphorylase A. And phosphorylase A is an enzyme that actually breaks down glycogen to form glucose 1-phosphate, and then glucose 1-phosphate is converted into glucose 6-phosphate by the enzyme called isomerase. And glucose 6-phosphate is then going to give up its phosphate, right, and will form glucose, and then this glucose is actually going to go out of the body. So this is actually the blood, right? So from the blood, the epinephrine comes, it binds to the beta adrenergic receptor that activates the GS. GS activates the adenylate cyclase, which then converts ATP into cyclic AMP, and then cyclic AMP activates protein kinase A to form the active protein kinase A, which then forms the active phosphorylase A.

And that is going to start catalyzing the breakdown of glycogen into glucose 1-phosphate, and then there will be a conversion of glucose 1-phosphate into glucose 6-phosphate with the help of isomerase. And then from this, there will be a dephosphorylation to form glucose, and then this glucose is going to be transported, and that is how it is actually going to increase the blood glucose. So, this rise in cyclic AMP activates protein kinase A by converting it from its inactive form to active PKA, and then it actually forms the PKA phosphorylase enzyme, like phosphorylase B. And that converting into the active phosphorylase A and then analyzing the breakdown of glycogen to glucose 1-phosphate, and then glucose 1-phosphate is going to be converted into glucose 6-phosphate, and then ultimately glucose is going to be produced, and that

glucose is going to be transported. Now, in vascular smooth muscles, epinephrine may bind to the alpha-1 adrenergic receptor, triggering the Gq protein pathway, right? So, in this case, the adapter protein is going to be different.

And that is how it is actually going to activate the activation of phospholipase C, which produces IP3 and DAG, right. and resulting in the calcium release from the endoplasmic reticulum and the activation of protein kinase C. These efforts help regulate the vascular tone, cardiac output, and other physiological responses necessary for fight or flight situations. So in this case, in the muscle cell, the epinephrine is going to bind to the alpha-1 adrenergic receptors, which are linked to the Gq, and the Gq is activated.

So remember that in that one, the GS is involved. In this one, the GQ is involved. So, it is actually going to activate phospholipase C, and that phospholipase C is going to process PIP2 to form IP3 and DAG. And both of these molecules are going to activate the release of calcium from the ER. So it is actually going to be stored calcium that is going to be released from the endoplasmic reticulum, and then this calcium is actually going to initiate the reactions or it is actually going to initiate the muscle contractions. And that's how the person will actually start contracting the muscles, and it is actually going to be used for the fight or flight situations. So how is the regulation of epinephrine signaling? So, epinephrine release is tightly regulated by the sympathetic nervous system.

Stress, physical exertion, or hypoglycemia stimulates the hypothalamus, leading to the sympathetic nervous activation of the adrenal medulla and the rapid secretion of epinephrine. Epinephrine is inactivated by an enzyme called catechol-O-methyltransferase or monoamine oxidase and has a short half-life. So, catecholamine, as soon as the epinephrine function is over, these enzymes are actually going to degrade epinephrine, and that is how all the reactions related to epinephrine are going to be downregulated. Its effects are also regulated by the receptor density and the downregulation after prolonged exposure. So what is the outcome of the epinephrine signaling? It is actually going to increase the blood glucose level, right? It is going to increase the heart rate and the cardiac output.

It is going to cause bronchodilation, which means the relaxation of the bronchial smooth muscles. Then it's going to cause vasodilation in the skeletal muscles or vasoconstriction in the skin or the GI, and it's also going to cause rapid mobilization during stress. Apart from these three hormones, such as the peptide-based hormones, the steroid hormones, or the monoamine hormones, we also have other types of hormones, or animal hormones, which also participate in cell signaling. So other types of hormones, in addition to the peptide, steroid, and monoamine hormones, are also produced by the body, such as eicosanoids and vitamin-derived hormones. So you have the eicosanoids, which are

actually prostaglandins or leukotrienes, right? And these are the hormones that are being produced by arachidonic acid. Arachidonic acid is a molecule that is present within the cell membrane and actually has a function in inflammation, immunity, and platelet function.

Similarly, we have vitamin-derived hormones like vitamin D hormones, such as calcitriol, which are also produced by the skin, liver, and kidneys. And this has been required for the calcium and phosphate regulation. So, so far what we have discussed is the cell signaling and what the requirements of cell signaling are. And in the previous lecture, we discussed the peptide-based hormones. And in this current lecture, we have also discussed the steroid-based hormones, monoamines, and the other types of hormones.

Animal hormones are very much required, and we have also studied the different functions of these animal hormones and how their deficiency could be responsible for various types of pathological conditions. So, with this brief discussion about animal hormones, I would like to conclude my lecture here. In our subsequent lecture, we are going to discuss plant hormones. Thank you.