Cell and Molecular Biology
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Week 05
Cellular Communications
Lecture - 18
Cellular Communication (Part 1)

Hello, everyone. This is Dr. Vishal Tevedi from the Department of Biosciences and Bioengineering, IIT Guwahati. And what were we discussing? We were discussing the different aspects of cell and molecular biology in this particular course. So far, what we have discussed is the origin of life and evolution in the first module. Following that, we have discussed the cellular structures, cell growth, apoptosis, and the different parameters to monitor growth, and in this previous module, we have also discussed cellular transport.

And how the cells are taking up the nutrients from the environment, how they are actually going to take up the molecules, what the different mechanisms are by which the molecules are being transported inside the cell, and how the cell's intercellular trafficking system is distributing these materials to the different organelles. Now, these molecules are interacting with the cell, and as a result, these cells are responding to these treatments, which are mostly supportive of growth, meaning they support the growth of the cell. Sometimes these molecules are not good for the cell, so the cell is responding in such a way that it is either going to undergo apoptosis, autophagy, or necrosis; in either case, the cell is continuously responding to the environment. Whether it is the molecules or the environmental factors, such as light, water, pH, humidity, and so on.

And these responses come from a very well-developed network of proteins that are present inside the cell. This protein network is, you know, taking up the responses from the cell surface and then delineating these responses to the nucleus in response to these treatments. The nucleus is modulating different types of activities; for example, if there is a cell that is responding to the glucose present in the environment. Then the cellular system is going to start responding in a positive manner, and it is actually going to start synthesizing the molecules that are required for the metabolism of these particular molecules. Right.

And all these events are tightly regulated. All these events are interrelated. And all these events are part of cell signaling, which means that the cell is actually going to respond to the external environment. So in this particular module, we are discussing cell signaling, the different components of cell signaling, how these components are connected to each other, how these components regulate the entire event, and the downstream effects when these components come together. So, as you can see, cell signaling is a very important parameter, right? So it is required for different types of functions, including cell growth and division.

It is required for metabolism, hemostasis, immune response, cell death, and so forth. So,

what are the different functions of cell signaling? So it regulates cell growth and division, which means it actually ensures proper tissue development and repair. So the first aspect is that it is actually going to regulate cell growth and division. Then it is also going to control cell differentiation, which means if a cell is differentiating, it is, you know, making the different types of organelles or different types of cells; that also has to be tightly regulated. So the first event is that it controls cell growth and division.

Remember, we discussed a lot about this when we were discussing cyclins and cyclin-dependent protein kinases and how they regulate the switch from the G1 to S phase, S to G2 phase, and G2 to M phase, and so on. Apart from that, it is also going to regulate cell differentiation, which means it will regulate the stem cells or the primary cells to differentiate and form specialized cells. Then it is also going to regulate metabolism and homeostasis. One of the classical examples is, you know, what we discussed when we discussed glucose, right? So when there is an uptake of glucose, the glucose will be utilized in downstream carbohydrate metabolism, right? So that is required for maintaining the internal balance by responding to the nutrient and energy levels.

Right. And then the number four is actually going to mediate immune responses. So this is number one. This is number two. And this is number three. The fourth aspect is that it is actually going to control immune responses.

So it helps to detect the pathogens. It is going to help initiate the inflammation and coordinate the defense. Then we also require cell signaling to regulate cell death, right? So, we have discussed apoptosis. There are so many caspases: initiator caspases and executor caspases are required. So that is also required for eliminating damage or unnecessary tissue in a controlled manner, which means we are talking about apoptosis.

And then we are also going to facilitate communication between the cells. Right. So there are neurotransmitters. There are different types of cells that communicate with each other with the help of cell signaling. So it enables coordination in development, repair, and immune function.

All these examples we are going to see when we go through this topic in this module. And then we are also going to integrate the environmental cues. So basically, cell signaling detects different types of environmental factors. So it is going to be different regarding the abiotic stress. It is going to detect the toxins.

It is going to detect the light, osmolality, pH, humidity, and all those kinds of things, and that is going to help in maintaining the internal environment and addressing human stresses. Then it is also going to support tissue and organ function, so it is going to synchronize activity across the different tissues for proper organization. For example, if you have studied digestion, right? So digestion starts in the stomach, then the food goes into the small intestine, then it goes from there to the large intestine, and then it is excreted. All these compartments that are present within the digestive system coordinate with each other, right? Once digestion in the stomach is over, the pyloric sphincter will open, and only then will the food from the stomach enter the small intestine. The same is

true when it goes from the small intestine into the large intestine so that water and other micronutrients can be absorbed from the undigested food, and that's how it actually forms feces.

Cell signaling is an essential and integrated component of the cell, enabling it to perform many different functions, all of which are required for maintaining the homeostasis of that particular cell, allowing it to grow and differentiate into different types of cells. Now, talking about why there is a need to do cell signaling. So cell signaling is required for survival and efficient functioning. Organisms may quickly respond to sudden changes. And this is very, very important.

If you don't have cell signaling, you will not be able to respond to incoming threats. Incoming threats could probably come from many types and many places. It could be from internal sources or external sources. A classical example is how the body reacts to acute stress, such as facing a threat or experiencing fear. For example, when it is very dark, when there is lightning, or when there is a cloud bursting, and all those kinds of things.

So it actually creates fear, doesn't it? And it creates a fear so that your body is ready for incoming problems and threats. And this situation activates different types of highly coordinated signaling events. But one of the logical examples is the fight-or-flight response to stress. Suppose you see a lion, or if you encounter a lion or a dog, for example, on your street. Now, when you encounter a dog, you have two options.

Either you will go and fight with this particular dog, and he will run away, or you will actually decide that, OK, I will not fight; I will run away. OK, so these kinds of decisions come as soon as you see the specific threats. If the threat is manageable, like when it is a lion, you will decide to run. If it is a dog, you could probably think about whether I can manage this particular thing or not. If you can manage, then you will fight.

If you cannot manage, then you will run away. So these kinds of options come, or these kinds of things come from a response that is called the fight or flight response, and these are all linked to cell signaling. So cell signaling, one of the integral parts of cell signaling, is the perception of stress. Right. You first have to detect the incoming threats.

You have to detect the incoming stress, right? And that occurs or happens in the brain. Right. So the brain, especially the hypothalamus, detects threats and activates the sympathetic nervous system. So it actually signals to the adrenal glands, or it actually involves systemic hormonal signaling. So it gives a signal to the adrenal glands, and no impulse stimulates the adrenal medulla, which secretes epinephrine, right? And that epinephrine is actually going to ask you to decide whether you want to fight or flee because, accordingly, the body is going to prepare the muscles, the body is going to prepare the blood pressure, and those kinds of events, and that's how it is actually going to control those events.

So then adrenaline travels to multiple organs and binds to the endogenous receptor on

the target cell, and that's how it actually prepares the body for different types of threats. And then you are going to have the third event, which is the cellular responses. So, if you see the cell signaling, it is a multi-step process. In the first step, you are going to respond to the stress. In the second event, you are going to ask the cellular system to respond.

So this triggers various intercellular signaling cascades that lead to an increased heart rate and blood pressure to pump more oxygen. Dilation of the airway improves oxygen intake. Conversion of glycogen to glucose provides a sufficient amount of glucose available for utilization when you want to run away and engage in similar activities. to provide the immediate energy, right? Because the immediate energy comes from glucose and not from fat or other biomolecules. Then it's going to reduce digestive activity so that you can conserve energy.

And it is also going to dilate the pupils so that you can look under very low-light conditions, allowing more and more light to enter your eyes. So these are the cellular responses that will occur when you encounter a lion or a dog and are under the fight-or-flight response. Which is going to be, you know, governed by cell signaling. Then there will be a contraction of the skeletal muscles, which is going to improve strength and responsiveness, correct? And what will the outcome be? The outcome is that the organism becomes physically and mentally prepared for fight or flight, right? And these two events are very important, aren't they? Because the last judgment is whether I could fight a particular stress or whether I should flee from this particular place, is what you are going to do, right? So the fight-or-flight response is actually a response in which the whole body is involved, right? You are actually going to illuminate the ice so that you can see under the dim light. The brain is actually going to give you the signal to the adrenal glands, and the adrenal glands are going to start secreting epinephrine, which will actually increase blood pressure.

It is actually going to increase the supply of blood to the heart and other organs, and then your heartbeat will go up so that more and more blood can be supplied to the different organs of the body. It is actually going to start catalyzing the conversion of glycogen into glucose so that there is a greater amount of glucose present in the bloodstream. And then I am also going to prepare the muscles so that they have more oxygen and more glucose, and they will be ready to act, right? So they will be ready to, you know, fight, right? And then there would be a retardation or inhibition of the digestive system so that more and more energy would be utilized for this particular response. Now, as far as cell signaling is concerned, the signaling in the organism could be of three different types: it could be autocrine signaling, paracrine signaling, or endocrine signaling. And all these signaling events can be compared with the different types of interactions; for example, when you interact with your friends who are sitting next to you on your bench, right? Or you can actually talk to the same friend when he is at home, or you can talk to him when he is in another city or another country.

So the auto crime signaling means that you are going to talk to yourself. Okay, so if you compare it with that, then you are talking to yourself. Many times, it happens that you talk to yourself when you are making a plan, arranging the material, or, suppose you are

going on a trip, right? Then you talk to yourself and say, "Okay, I need these materials, these are the clothes I require, and these are the dress materials I require." So first, you make the list, and then you talk to yourself and start taking note of what materials you have taken, what materials you have left, and so on. And then we have the paracrine signaling where you actually talk to your friend who is your neighbor or who is on the next bench.

Which means very close, right? And then the endocrine signaling means you talk to your friend, but he is in another city. Okay, so first we will discuss autocrine signaling. So autocrine signaling means that when you talk to yourself, a cell is present; this is a nucleus, and the cell itself is going to secrete a material or start secreting a ligand. And that ligand will go and bind to a particular receptor on the cell surface, and then it will start sending the signal to the cell. This happens because you want a very good microenvironment around you.

So every cell is secreting molecules outside so that it can actually maintain a local environment. And those molecules are actually going and binding to the receptor and then returning back to the cell, right? So this actually creates the microenvironment of a particular cell, which provides supportive growth for this cell, and that is how this cell feels good. So, what is autocrine signaling? Autocrine signaling is a form of cell communication in which a cell secretes signaling molecules, such as cytokines or growth factors, that bind to a receptor on the same cell that produced them. In some cases, neighboring cells of the same type can also respond to these signals. This type of signaling allows the cell to regulate its own activity and reinforce specific responses.

It is especially important for cell growth and differentiation, immune cell activation, inflammatory responses, and embryonic development. Cell growth and differentiation have been discussed a lot when we talked about, you know, the transition of the cells from the G1 to S phase and from the S to G2 phase and all that. Even for differentiation, many types of cells secrete molecules, which then come back and bind to a specific receptor. And that is how they are generating the specific type of cell signaling, and that cell signaling is also changing the transcriptomic analysis, or transcriptome, of a particular cell, and eventually the proteome of the cell, basically changing the outcome, right? For example, our cell wants to change into an epithelial cell, doesn't it? The stem cell wants to change into an epithelial cell. It is actually going to secrete some of the signaling molecules so that they will bind to their own receptors, and then the downstream signaling of those receptors will start changing the different types of transcription factors present within the cell.

As a result, it's actually going to start activating the transcription of these specific genes, and the gene products of those genes are going to start changing the outcomes. Similarly, you have the immune cell activations that we will discuss in detail in a future module. But you have seen the T cell, how the T cell is activated, and how the B cell is activated. So it is secreting the antibodies, and these antibodies are binding to the B cell on its own. And that's how it is actually increasing the proliferation of B cells.

And that's how a particular clone, when selected for conversion into plasma cells so that it actually starts secreting antibodies, is done only this way. So you know that when there is clonal selection, the antibodies are secreted, and then the receptors engage with a particular antigen or those kinds of things. And that's how it is actually going to remain in the, you know, proliferation stage, and that's how clonal selection works. In fact, for other cell types or other immune cell types as well, autocrine signaling activates and prompts them to secrete different types of cytokines.

Then we also have the inflammatory responses. In the same way, the inflammatory cells, like mast cells and some dendritic cells, also secrete a lot of inflammatory molecules when they undergo autocrine signaling, and we have a similar process in embryonic development and so on. So there are, you know, cell signaling events controlling this in a very, very regulated manner. So autocrine signaling ensures rapid localized feedback and is critical in tightly controlled processes like T-cell proliferation and cell fate determination during development. So, you also have pain perception and apoptosis during infections.

Now let's take an example. So, we have an example of T-cell activation. So, these are the antigen-presenting cells. This is the NAV T cell. And when the antigen-presenting cell is presenting the antigen to the MSCs, it is recognized by the T cell receptor present on the T cells.

And that's how it is actually secreting IL-2. And then these IL-2 are binding to the T cell, and that's how they are converting this naive T cell into activated T cells. So autocrine signaling plays a crucial role in the activation and clonal expansion of T cells, particularly CD4-positive T helper cells, during an immune response. So, antigen recognition is important. So, a NAV CD4 positive T cell recognized a specific antigen presented on the MHC class II via its T cell receptor, and then these active interactions, along with the co-stimulatory molecule, activated the T cells. And then there are so many, you know, that the cytokines are going to be secreted by the naive T cells.

So there will be IL-2 secretion and there will be receptor expansions. So the activated T cell begins to produce IL-2 and simultaneously upregulates the IL-2 receptor on its surface. And then IL-2 binds to the IL-2 receptor on the same T cell, forming an autocrine loop. Which means these IL-2 will bind to the IL-2-containing T cells. They will go and bind, and then they will ask for the secretion of more and more IL-2, and that's how there will be an expansion of this activation.

And then this signaling drives the proliferation of the activated T cells, creating more identical T cells capable of responding to the antigen. So, there is another example of the regulation of apoptosis. So IL-2 signaling also influences whether the activated T cell will survive or undergo programmed cell death, thereby helping to maintain immune balance. This autocrine loop ensures that only antigen-specific T cells expand, making the immune response both efficient and highly specific. So this is just a single example of how autocrine signaling helps with immune responses, T cell activation, and differentiation.

Now let's move on to the next mode and the next mode is called as the paracrine signaling. So, as I said, paracrine signaling means talking to your friend who is sitting on the next bench or at his home. Right? So paracrine signaling means this is you. This is you, and this is your friend. OK, so you are talking to your friend, who is not very close but is not very far either.

So you can be. So what you are doing is secreting the molecules. It means you are sending the signal. And your friend who actually has the receptor for this particular signal is receiving those signals. And that's how this cell is actually going to respond to your signal.

OK. That means you are actually going to talk to your friend, and he is sitting next to you. So this is only if it is adjacent to the target cells. Right. So in paracrine signaling, the signaling molecules can be secreted into the extracellular fluid. These molecules act as local mediators and target the cells neighboring the signaling through local diffusion.

The signaling can aid in the exchange of information between cells using a soluble signal that can diffuse from one cell to another, which means that this signaling is happening over short distances. The signaling can have a high local concentration of signaling molecules. The signal can include growth factors, cytokines, hormones, prostaglandins, and so on. So, these are the signaling molecules, right? So it is secreting the molecules, and then they are being received by the target cells that are present within the vicinity. So it is secreting the molecule that is received by a target cell that is within the vicinity.

And that's how it is actually amplifying this signal. So one of the classical examples is neurotransmitters carrying signals between nerve cells using paracrine signaling. A pound released at the postsynaptic end, the neurotransmitters diffuse across the synaptic gap to adjacent postsynaptic neurons or effector cells. Another example can be the action of cytokines on the neoplastic cell using the immune responses and inflammation. Testosterone released by the Leydig cells binds to the androgen receptor in neighboring Sertoli cells to regulate spermatogenesis. And then you also have an example of cell differentiation, proliferation, and migration during embryonic development, which is regulated by paracrine signaling from factors such as growth factors.

So paracrine signaling means talking to your friend who is sitting adjacent to you. So you're giving a signal, maybe in your classroom, right? So, for example, if you're trying to give some signal to your friend who's sitting in the same room, that is also part of paracrine signaling. Then we are coming back to the third one, which is called endocrine signaling. So endocrine signaling means talking to your friend who is sitting in another city or very far away, okay? So, what are you doing? The signaling cell is secreting the ligands or signaling molecules. Then it goes through the bloodstream and reaches the target cell, which is very, very far away.

For example, you are secreting the molecules into the brain. For example, you are secreting the molecule from the brain, and then it reaches the liver. That is endocrine

signaling. Endocrine signaling involves the release of signaling molecules called hormones by specialized endocrine cells. These hormones travel throughout the bloodstream to act on distant target cells, correct? So these are the cells, these are the targets, and these are the secretory cells, right? They have secreted a molecule that will enter the bloodstream and then reach a target cell that has a receptor, and that's why it will bind. The endocrine cells are typically located in the endocrine glands, such as the thyroid, pituitary, and adrenal glands, and they secrete molecules that then reach the target cells.

We have many examples. So endocrine signaling can happen in different types of organisms, right? So it is mostly done by the hormones, right? So, hormones could be present in all eukaryotic cells. Right. So mostly, the hormones are present in multicellular organisms. So hormones are present in the animals, right? Or hormones could be present in plants, and they are regulating different types of activities, right? So they are regulating metabolism, they are regulating cellular functions, and so on, right? So in endocrine signaling, first we will discuss animal hormones, and second, we will discuss plant hormones.

So, the first is animal hormones. The term "hormone" was first used by the physiologist Ernest Henry Starling in 1905. Hormones were described as substances produced by glands with internal secretion, which serve to carry signals in the blood to the target organs. But there were many exceptions. Thus, there have been some ways to define it. One such definition is that a hormone is an organic compound secreted by a plant or an animal that helps regulate physiological processes and maintain internal balance or homeostasis.

Now let's first talk about animal hormones. So animal hormones are, you know, widely distributed throughout the body, right? And they are performing different types of functions. Animal hormones are, you know, regulating growth and development. Animal hormones regulate metabolism and energy. Animal hormones regulate the reproductive system. Animal hormones regulate the flight and fright responses to different types of stress, such as injury stress and environmental factors; they also maintain mood and behavior.

And then, also maintaining homeostasis, they are maintaining sleep or the sleep cycle as well. Hormones are the chemical messengers that transmit signals into the bloodstream and tissues; they act slowly and influence a wide variety of functions. Imbalanced hormones can lead to various disorders. One hormone can regulate more than one biological function. Multiple hormones can also be involved in the regulation of biological functions, and hormone production can be regulated by negative feedback controls, right? Chemically, hormones can be classified into two main groups based on their solubility.

So, you can have lipid-soluble hormones or water-soluble hormones. So, what is the general mechanism of hormone signaling? The endocrine glands release hormones into the extracellular space, from where they enter the capillaries and travel throughout the

bloodstream to reach the distant target cells, enabling the systemic effect. So, this is the endocrine gland, right? And it is actually secreting the hormone. Then it goes into the bloodstream. Then, hormone-producing cells are specialized and release the hormone via exocytosis or other membrane transport mechanisms. These transport mechanisms we discussed in detail in the previous module, right? How are the molecules being transported? And then they reach the target cells or their target organs, actually.

So this is the endocrine gland, which secretes the molecules into the bloodstream; then they travel throughout the bloodstream until they reach the target cells, and the target cells actually have the receptors. These receptors bind these hormones, and that's how they function. regulating or relaying the signal within the cell. Sometimes, these receptors are not present outdoors. These receptors might be present inside the nucleus; accordingly, the animal hormones could be of different types, right? As we said, animal hormones could be lipid-soluble or water-soluble hormones.

Target cells for a hormone can be of various cell types distributed across different tissues. Hormones act by binding to specific receptors either on the cell surface or within the cell, depending on their chemical nature. This receptor binding initiates the downstream signaling events that may ultimately lead to changes in gene expression. The response of target cells may be detected by the original hormone-producing cells, resulting in reduced hormonal control. This response is a negative feedback mechanism, which means that if this is the hormone-producing cell, hormone-producing organ, or glands, when it secretes the hormone and the hormone reaches a receptor-containing cell, then when it binds to this cell, this cell also starts responding, and this cell is actually going to secrete the molecules or give you the signal to these glands.

that we have enough hormones and there is no need to secrete any more. And that's how the production of this hormone is also going to be reduced. And this kind of mechanism is called a feedback mechanism. Feedback mechanism means I have enough amount of supply stop supply by enemy. Okay. So that's how this is called a feedback mechanism, which means that you're going to give feedback to your supplier that you have enough quantity of this particular material.

There's no need to secrete it or supply it anymore. And that's how it is actually going to reduce the supply. Now, based on their chemical nature, the hormones could be of three different types.

It could be a peptide hormone. It could be a steroid hormone. It could be monoamines. So, let's talk about peptide hormones. The peptide hormones are composed of amino acids linked by peptide bonds, with lengths ranging from three to 200 residues. Sometimes, they may also be glycosylated, affecting their stability and activity. They are water-soluble and cannot cross the plasma membrane.

It means they will actually bind to the receptors that are present on the cell surface. Therefore, they primarily bind to the cell surface receptors to initiate cell signaling. Although rare, some peptide hormones can also act in intracrine signaling, where they

function through intracellular or nuclear receptors within the same cell that synthesizes them. These hormones vary significantly in terms of size, structure, and biological functions, regulating processes such as metabolism, growth, fluid balance, and immune response. Peptide hormone production occurs in specialized secretory cells rich in endoplasmic reticulum and the Golgi apparatus, which are responsible for protein synthesis, modification, and packaging. Remember when we were discussing intracellular trafficking and cellular structures? You have seen that the endoplasmic reticulum, Golgi apparatus, and lysosomes are the three organelles that are very active in regulating cell secretions.

So the cells that are actually going to produce the hormones will have a very high quantity of these organelles. Hormones are stored in secretory vesicles, which release upon the appropriate stimulus, allowing for a rapid response to physical cues. The main step in the synthesis of the peptide hormone works, doesn't it? The main steps in the synthesis of peptide hormones include first the transcription and second the post-transcriptional modification. So in the first step, the DNA will form the messenger RNA, which is called transcription, right? And in all these events, we are going to discuss how transcription works and how replication works in the subsequent modules. And then the messenger RNA is going to be crude messenger RNA, right? And then it is actually going to be, you know, doing the post-transcriptional modifications that we are also going to discuss in a subsequent module.

Then the messenger RNA is going to undergo capping, splicing, and polyadenylation to form mature messenger RNA. And then once it forms the mature messenger RNA, the mature messenger RNA will produce the peptide hormone, and then the peptide hormone will be put into the secretory pathway, and that's how it will be secreted out of the cell. So then it is going to be, you know, once the mature messenger RNA is formed, the ribosome in the rough area translates the messenger RNA into precursor polypeptides. Then co-translational and post-transcriptional modification signal peptides are cleaved to form the prohormones, and they may be folded, glycosylated, and cleaved into the active form before being packed into the vesicle for storage and release upon stimulation. These peptide hormones can be of different types depending on the organ they are actually going to produce.

So, peptide hormones can be classified based on their site of synthesis, as this determines their specific functions, target organs, and physiological roles. Now, let's look at the different types of peptide hormones. And as I said, you know, peptide hormones are classified based on their origin, right? Peptide hormones can be secreted from the hypothalamus. So remember that a peptide hormone will be secreted from different organs.

It is going to be secreted by the digestive system. It is going to be secreted by the brain. It is going to be secreted by the other endocrine glands. So, the first is the hypothalamus, right? So for the hypothalamus, a large number of peptide hormones is going to be secreted. One is the antidiuretic hormone, or ADH, right? And ADH, what is its function? It is actually going to promote water reabsorption in the kidneys and regulate blood

osmolarity. And if there is a deficiency of this particular hormone, the person will develop diabetes insipidus, which causes excessive urination and dehydration.

Then we have the CRH, or corticotropin-releasing hormone. It actually stimulates the ACTH release from the anterior pituitary, and if there is not enough TRH, then there will be a lower production of the acetylcholine receptor or ACTH, and that is actually going to be responsible for adrenal insufficiency or fatigue. Then we also have the growth hormone-releasing hormone. So that is also going to stimulate the secretion of growth hormone from the anterior pituitary gland. And the growth, if there will be a lower production of the growth hormone, then there will be a growth retardation, especially into the children. So that is actually going to cause the dwarfism, right? And then you also have the gonadotropin-releasing hormone.

So that is also going to stimulate the production of luteinizing hormone and follicle-stimulating hormone from the NTGP3. And that is also going to be caused by. So there will be a reduction in GnRH. Then it is actually going to cause hypogonadism and infertility. Because if you don't produce LH or FSH, there will be less production of eggs, which is also going to cause infertility.

Then we also have oxytocin, which stimulates uterine contractions and milk ejections in lactating females, and a deficiency of oxytocin can actually cause poor labor and impaired milk production. Then we have somatostatin. Somatostatin inhibits the growth hormone and TSH secretions, and excessive levels can lead to growth or metabolism-related issues. So don't worry; it's not like the hormone deficiency only causes the disease.

An excess of hormones can also cause a disease. Then we have thyrotropin-releasing hormone, or TRH, which stimulates thyroid-stimulating hormone and may promote prolactin secretion from the anterior pituitary. And if there is a deficiency of TRH, it will actually reduce the production of TSH, which will then cause hypothyroidism. Then you also have the peptide hormones from the anterior pituitary gland. So this is another part of the brain from which you are going to receive the peptide hormones. So you have the ACTH, which stimulates the cortisol secretion from the anterior cortex, and if there is a deficiency of ACTH, it will actually affect the cartilage or cause low blood pressure.

If you have FSH or the follicle-stimulating hormone that stimulates follicle development in the ovary and spermatogenesis in the testes. If there is a deficiency of FSH, then it will cause infertility, irregular menstrual cycles, or reduced sperm counts. Then we have LH, or luteinizing hormone. So LH is going to trigger ovulation and corpus luteum formation in females, and testosterone production in males. And if there is a reduction in LH production, it is going to cause infertility, menstrual disorders, and low testosterone.

Then we have growth hormones. Growth hormone stimulates growth, cell reproduction, and regeneration, and there will be a reduction in these processes. Then it is going to cause stunted growth in children, fatigue, and low muscle mass in adults. Then we have prolactin. The prolactin stimulates milk production in lactating women and prevents

inadequate lactation. Then we have TSH, or thyroid-stimulating hormone, which stimulates the production of thyroid hormones and can cause hypothyroidism, weight gain, or fatigue.

Then we have the peptide hormones, which are produced by the parathyroid glands. So parathyroid glands release parathyroid hormone and calcitonin. Calcitonin lowers the blood calcium level by inhibiting osteoclast activity, promoting calcium excretion by the kidneys, and reducing calcium levels, which can cause mild effects in humans; deficiency is usually not clinically significant. Then we have parathyroid hormone, or PTH, which increases blood calcium by stimulating the osteoclasts, enhancing calcium reabsorption in the kidneys, and activating vitamin D. If there is a reduction in PTH, it will cause hypocalcemia, muscle cramps, and tetany or seizures. Then we also have the peptide hormones from the heart, right? And it is going to be atrial natriuretic peptide, or ANP.

And ANP promotes sodium and water secretion by the kidneys and lowers blood volume and pressure. And if there is a reduction of ANP, it is actually going to cause hypertension and fluid retention. Then we also have the brain natriuretic peptide, or BNP, which is similar to ANP but is secreted mainly from the ventricles under pressure or volume overload. This reduces the ability to compensate for cardiac stress and is used as a heart failure marker. Then we have the peptide hormones from the digestive system. So you have cholecystokinin, or CCK, which stimulates the release of bile from the gallbladder, pancreatic enzyme secretions, and slows gastric emptying.

And if there is a deficiency, then it is actually going to affect fat digestion and reduce satisfaction, which means it is going to lower your satisfaction level when you eat the food. Then you also have gastrin. Gastrin actually stimulates gastric acid secretion from the parietal cells, and if there is a deficiency of gastrin, it will lead to low stomach acid, which means it will reduce the production of HCl and also affect digestion.

Then we have this. So it is actually going to stimulate appetite and promote GH release. And if there is a reduction, then there will be less hunger and possible growth issues. Then we have the glucagon-like peptides, which enhance insulin secretion, inhibit glucagon release, and slow gastric emptying. If there is a reduction of this or a deficiency, then there will be impaired glucose regulation and possible postprandial hypoglycemia. Then we have the glucose-dependent insulinotropic peptide that stimulates insulin secretion in response to oral glucose.

And if there is a deficiency, there will eventually be decreased insulin responses to the meals. Then we also have oxygen modeling, or OXM. Right. And that reduces the appetite, inhibits gastric motility, and decreases acid secretions. And if there is a deficiency, it is going to cause a potential imbalance in weight regulation.

Then we have a secretion that stimulates bicarbonate secretion from the pancreas and inhibits gastric acid secretion. If there is a deficiency, then it is going to impair the pH buffering of the chyme and affect digestion in the small intestine. Then we also have peptide hormones from the liver. The liver is secreting one peptide hormone, which is

insulin-like growth factor one, that mediates many of the growth hormone's effects, promoting systemic body growth, especially of bones and muscles. If there is a reduction in this, then there will be growth failures in children's muscle mass and bone density.

Then we have the peptide hormones from the kidneys. So, it's going to be arthropoietin and renin. Arthropoietin stimulates red cell production in the bone marrow, and if there is a reduction in erythropoietin, it will actually cause anemia, especially in chronic kidney disease. We have renin, so renin is initiating the renin-angiotensin-aldosterone system, regulating blood pressure and fluid balance, and if there is a reduction in renin production, it will cause hypotension, electrolyte imbalance, and impaired RAAS responses; we also have peptide hormones from fat tissue or adipose tissue. So those are called adiponectin, leptin, and resistin. And the adiponectin enhances insulin sensitivity, the inflammatory response, and promotes lipid oxidation. If there is a reduction in adiponectin, it will actually cause insulin resistance, an increased risk of metabolic syndrome, and obesity.

Then we have leptin. Leptin regulates appetite and energy expenditure by acting on the hypothalamus, resulting in a reduction of appetite. Then it is going to cause an uncontrolled appetite, obesity, and metabolic dysregulation. Then we have resistance. Resistance impairs insulin sensitivity and has a potential role in inflammation if dysregulated.

Then we also have the peptide hormones from the pancreas. So, peptide hormones are like insulin, glucagon, amylin, pancreatic polypeptide, somatostatin, and vasoactive intestinal peptide. So insulin lowers the blood glucose level, glucagon raises the blood glucose level, and amylin slows gastric emptying, suppresses glucagon, and promotes satiety. Then we have pancreatic polypeptide, which regulates exocrine pancreatic secretion and influences hepatic glycogen levels and GI motility.

Then we have somatostatin. Somatostatin inhibits the secretion of insulin, glucagon, GH, and many gastrointestinal hormones. And then we have a vasoactive intestinal peptide that relaxes the GI smooth muscles, stimulating the secretion of water and electrolytes into the intestine. And as far as the deficiency is concerned, the insulin deficiency is actually going to cause diabetes mellitus. With the deficiency of glucagon, it will actually cause hypoglycemia, and it happens especially during fasting. Then amylin is causing postprandial glucose spikes or impaired satiety.

Then we have pancreatic polypeptide, which causes the altered release of digestive enzymes and the gastrointestinal modality. Then we have somatostatin, which causes excess glucose release and early isolated deficiency. Then you have a vasoactive intestinal peptide that causes malabsorption, and if in excess, it causes unclear deficiency effects. So these are the peptide hormones that have been secreted by the different organs present within the animal body. All these peptide hormones mostly act through specific pathways, so their receptors are different, their machinery is different, but their mechanisms for how they actually function are more or less the same.

So, to explain these mechanisms, I have taken an example of glucagon to illustrate how the cell signaling of glucagon works. Right, so glucagon signaling is different from insulin signaling. Glucagon signaling is different from amylin, but the events are the same when we explain that glucagon does not mean that the other hormones are also going to follow a similar kind of machinery. The machinery is going to be different, but the events will be the same. Now, talking about glucagon, it is a very simple and well-characterized peptide hormone that plays a central role in maintaining blood glucose levels during fasting.

How is glucagon synthesized? So glucagon is synthesized by the alpha cells of the pancreatic islets of Langerhans. It is initially produced as a larger precursor, preproglucagon, encoded by the GCG gene. Inside the rough endoplasmic reticulum, the signal peptide is cleaved to form proglucagon, which is further processed in the secretory vesicle to yield the 29-amino-acid-long glucagon. These vesicles store glucagon until secretion is triggered by a drop in blood glucose levels. So, glucagon and insulin are working in the opposite direction, right? So, if you have glucose, and if the glucose level goes up, then it is actually going to induce the secretion of insulin.

If the glucose level goes down, it will actually induce the production of glucagon. So glucagon's job is to maintain blood glucose levels. Insulin's job is to decrease the glucose levels. Insulin's job is to reduce glucose levels. So insulin is actually going to take the glucose from the blood and store it in the liver. Glucagon is going to do the reverse.

It is going to take glycogen from the liver, convert it into glucose, and put the glucose into the bloodstream. What is the signaling mechanism of glucagon? So, glucagon exerts its effects by binding to the glucagon receptor. GPCR, right, is predominantly expressed in the liver and to a lesser extent in the kidney, pancreas, and other tissues. Upon activation, the receptor activates the GS and Gq proteins.

So, this is the GCG receptor. So when glucagon comes and binds to this, it actually activates the GS and GQ proteins. GS stimulates the adenylate cyclase, increasing the cyclic AMP level and activating the protein kinase A, which then phosphorylates transcription factors like CRB to promote gene expression. So when the GS is activated, it will actually convert the ATB into cyclic AMP with the help of the direct cyclase. And then the AMP is actually going to activate the protein kinase A, and protein kinase C is going to activate the CREB.

And CREB is actually going to work as the transcription factor. So GQ activation leads to the activation of phospholipase C. So, on the other hand, the GQ is going to activate the phospholipase C, right? And the phospholipase C is going to convert DPHP2 into IP3, right? which play a role in calcium release from the ER, further enhancing the CREB-dependent transcription via the CREB-regulated transcription factors. Besides the CREB and CRT-C2 pathways, glucagon is also known to activate several other inter-circular signaling cascades. So basically, this receptor, GCG, actually has the GS and GQ proteins when they get activated. The GS is going to activate the adenylate cyclase, which is going to convert ATP into cyclic AMP.

Cyclic AMP will bind to protein kinase A, and protein kinase A will activate the CRB. Similarly, GQ is going to activate the phospholipase C, and the phospholipase C is going to start converting the PIP2 into IP3, and IP3 is going to activate the endoplasmic reticulum, which is the ER, to release the calcium. And once the intercellular calcium of the cell goes up, it will actually delineate the calcium-dependent signaling within the cell, and that is how it will actually activate the CRTCS C2 signaling, and these two pathways are actually going to increase the blood calcium level. These coordinated signaling events demonstrate how peptide hormones like glucagon use multiple intracellular pathways to regulate gene expression and maintain physiological balance, highlighting the complexity and precision of the cell signaling mechanisms. Now, how is the glucagon signaling going to be regulated? So glucagon secretion is stimulated by hypoglycemia, which means low blood glucose, amino acid intake, and catecholamines during stress. It is inhibited by the insulin, which signals high blood glucose, and by the somatostatin, which acts as a general inhibitor of pancreatic hormone release.

So basically, glucagon signaling is regulated first at the level of ligands, such as low blood glucose. So if there is low blood glucose, it is going to stimulate. If there is high blood glucose, it is going to downregulate the production of glucagon. In addition, when there is secretion of insulin, it will inhibit the production of glucagon. Similarly, somatostatin is also going to inhibit insulin production.

Intracellularly, the signal is terminated by phosphodiesterase, which degrades cyclic AMP. Remember, in the first step, adenylate cyclase is processing the ATP and producing the cyclic AMP, which is activating the protein kinase A. So if in the cell, the phosphodiesterase is degrading the cyclic AMP, then there will be no activation of protein kinase A, and that's how it is actually going to cease or inhibit the cell signaling. And through receptor desensitization, if glucagon levels remain elevated for too long, this tight regulation ensures that blood glucose remains within a narrow physiological range. Now, what is the outcome of glucagon signaling? So it is actually going to increase the blood glucose levels.

It is going to stimulate glycogenolysis in the liver. It is going to enhance glycogenolysis. It is going to inhibit blood glucose synthesis. And it's going to promote lipolysis in the adipose tissue, which means it is going to increase the availability of fat for energy and also maintain blood glucose during fasting or between meals. So this is all about what we have discussed regarding animal hormones. So far, we have discussed the different types of cell signaling, including autocrine signaling, paracrine signaling, and endocrine signaling. So far, what we have discussed includes the peptide hormones, and within the peptide hormones, we have talked about the peptide hormones secreted from the liver, heart, pancreas, brain, and so on.

With this, I would like to conclude my lecture here. In our subsequent lecture, we are going to discuss some more animal hormones. And then we are also going to discuss the plant hormone. Thank you.