Introduction to Developmental Biology

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Lecture No – 27

Evolutionary Developmental Biology (Part 2 of 3)

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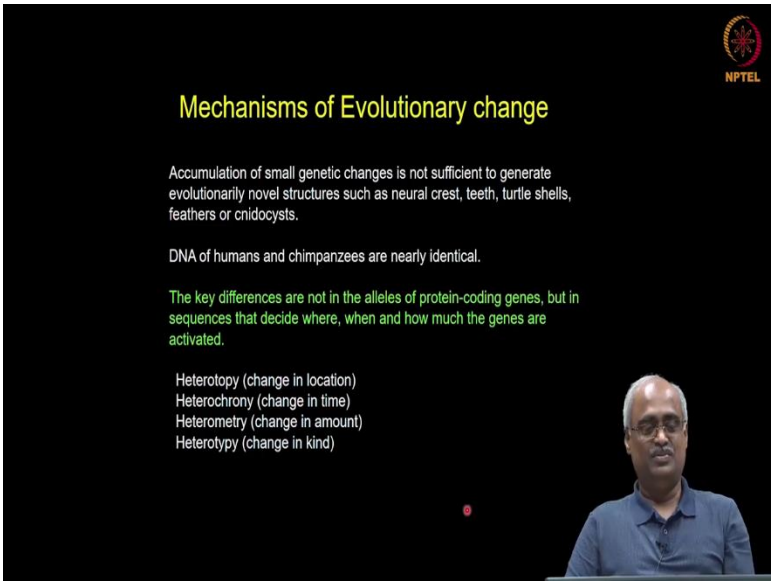

Students welcome back to developmental biology class. So today, we will continue on the developmental mechanisms that are the basis for evolutionary adaptation. So yesterday, I introduced four types of changes. I briefly mentioned that the genome sequence differences are not so much compared to the morphology changes and other aspects of different groups of organisms.

Those differences come from not the sequence difference per se but from changes in the sequence that determines where a gene is expressed and when it is expressed and how long it is expressed; by varying those things, most of the anatomical and morphological differences are brought about. Besides, changes, of course, in protein sequence also matters. And these changes can be grouped into four groups. They are heterotopy; change in location and heterochrony change in time, and heterometry change in the amount and heterotypy is the protein sequence change; that changes the protein's function.

So we will see examples of each of these and make these concepts clearer, so we will proceed from there. So first, let us take up heterotopy, change in location. A change in the location of a gene expression can lead to anatomical and morphological changes within a lineage. Therefore variations are possible with a given theme of body plan.

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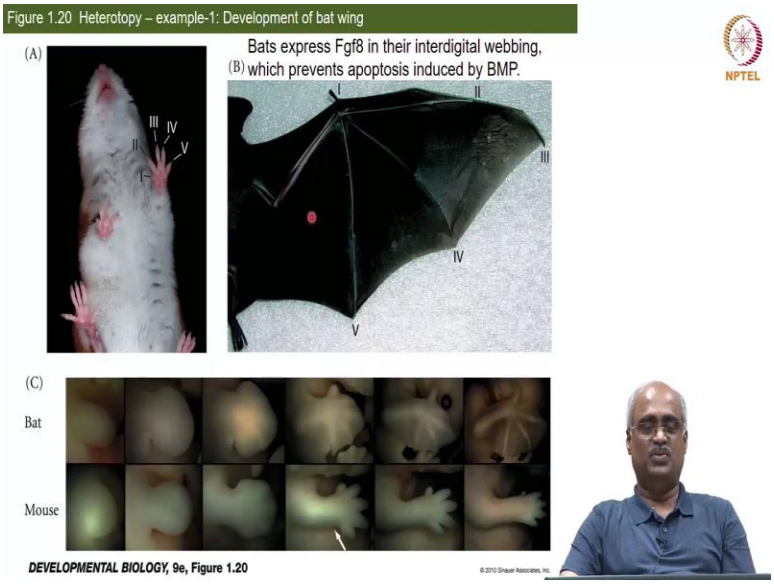

So this is an example that is familiar to you, so we discussed this when we talked about the link between Von Baer's principles and Darwin's theory of descent with modification. There, we discussed how one could look at the diversity among organisms and think about the variations that have been developed over a long period or look at the embryonic similarities and very diverse adult features.

But if you go back to the same organisms' embryos, there are a lot of similarities. One could look at those embryonic similarities and think about how you know the descent, which is an evolutionary progression of one species giving rise to another species and so on, has happened by modifying the same thing. That is why the early stages of embryos have similarities. So a very similar thing can be varied to generate the adaptations.

So you could look at both diversity and unity, so that is the context in which we saw this example earlier. So we will revisit this as an example of the change in location of gene expression. If you look at the left top image, this is a mouse, and you have the digits or the forelimb's fingers, so there are five of them, but there they are independent (Fig 1A). There is no web-like connection between two fingers. So they are separate, but if you look at this right image top and this is again forelimb (Fig 4B). So you see two noticeable differences; one is the length of the fingers. It is also numbered, number one is extremely short compared

to the other ones, and they are all, except number one, a lot longer than the ones you see in the mouse. Both are mammals with forelimb modification. They are very different, so the variation is obvious, but it is by modifying a slight change in what you already have.

To get rid of the web-like thing that starts if you look at the lower panel, if you compare the top and the bottom, both have similar limb buds, which expands to make these finger-like structures. The web exists in the third image between both of them. But as time progresses, the web disappears in mouse, but not in the bat. That is primarily because of a change in the location of expression of the gene FGF-8. This FGF-8 is expressed in the interdigital tissue only in the bat but not in the mouse. Due to that, BMP, one of the TGT ß members, is suppressed in the bat's web area. This ectopic expression of FGF-8 is a heterotopy. It is not expressed in another mammal in the same area due to BMP, and as a result, BMP, which usually promotes apoptosis, meaning programmed cell death in the interdigital web, is not active. As a result, no apoptosis; therefore, the web persists.

On the other hand, in mice, no FGF-8 is absent in the web area, and due to that, BMP is active, and BMP promotes apoptosis. So the web cells die, and the web disappears. So this is an adaptation; converting your hand into a batwing so that it could fly. This shows a big change or big adaptation but coming from this modular use of one gene being expressed in one place, which only has the effect only in that place. Here, FGF8 is expressed in a location where it usually is not expressed in closely related other mammals.

So that is why it is an example of heterotopy. This is how the bat got its wing, just one gene expression in a different place.

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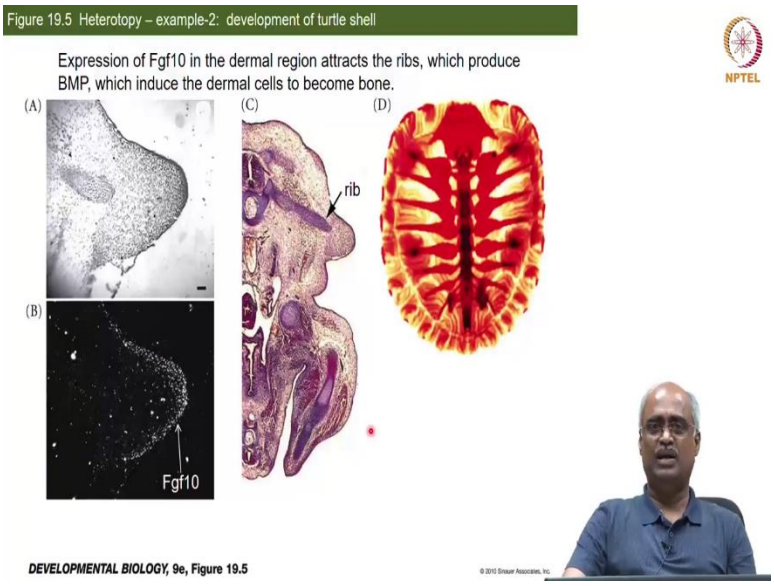

The next example is even more dramatic; again, you will see how very simple molecular changes can account for profound anatomical change and, therefore, a new evolutionary adaptation. Here we are looking at how the turtle got its shell. So the turtle is closely related to vertebrates. While other vertebrates have a ribcage protecting the internal organs like lungs and heart in a human, the turtle does not have it. Instead, it seemed to have that ribcage converted to be a bony structure on the back which is its shell. So let us see how such a major change happened. If you look at the example in the slide, when the early structure starts to form in the dorsal or epidermal area, this area expresses FGF-10. So this is an ectopic expression, hetrotopy.

So here in the slide, you have the bright field image and in-situ hybridization image for FGF-10. So FGF signal is seen at the edges here, which draws the rib primordium to grow towards this region. So instead of going down, it goes up because of the FGF-10 signal. And when the rib grows into that area, what the rib does is it secrets BMP, bone morphogenetic factor. The dermal or the skin cells can respond to BMP, and when they respond to BMP, they develop into bone. So you got rib into this area, and that rib converted the skin into bone here, which is how turtle shell forms.

So Figure C is a cross-section of a later stage embryo. So this is the rib that has nicely grown here and then a much later stage as you see in Figure D, the red color is a dye that stains bone, and you can see wherever the rib has grown in those areas, the new bone starts to form. So this is how the turtle got its shell, due to the heterotopic expression of FGF-10 and that alone seems to be enough, given the basic body plan of a vertebrate. The body plan means being the rib cage being normally formed and could be modified by simply

changing one signaling molecule's expression. These two are really good examples of heterotopy; change in gene expression leads to a major variation in the anatomy and morphology, leading to different evolutionary adaptations.

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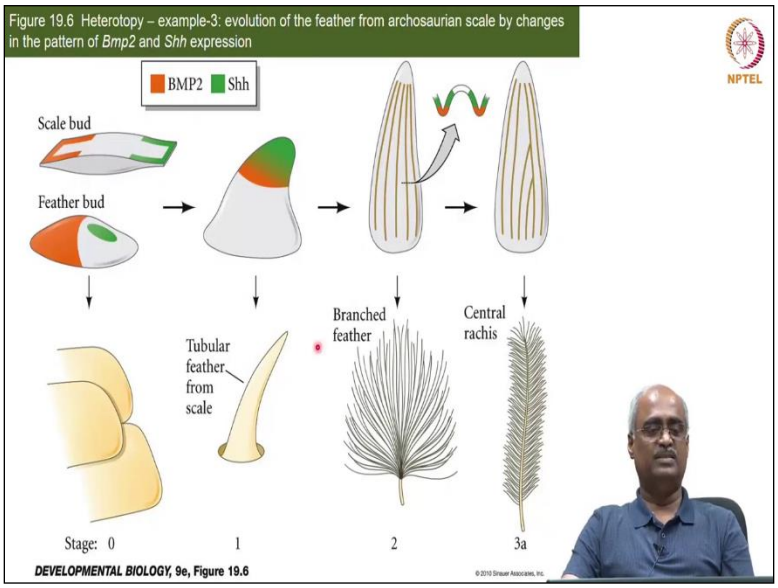

So we will look at two more examples of heterotopy. We saw how the bat got its wings, and we saw how the turtle got its shell. Now we will also see how birds got their feathers. These are evolutionary novel structures, only birds have wings with the feathers, and you do not see that kind of a wing elsewhere among the vertebrates.

For a long time, evolutionary biologists knew that the modification of reptilian scales was feathers. If you can remember, I told a few classes ago that birds and mammals are descendants of two different reptilian ancestors. So in reptiles like lizard or crocodile, they have nice scales, and the modifications of those scales happened in birds to make the feathers. So that is determined by the expression domain of a BMP ortholog, BMP-2, and Sonic hedgehog. So we learned about the hedgehog pathway quite some time ago in the very early classes. These two are expressed in these domains as cartooned here on the top left; that is how it is in the reptiles' scales. But in birds, their spatial expression domains are changed. It leads to a mount-like structure and finally creates two adjacent instead of two separate domains of expression, so you get two adjacent domains of expression. And that leads to this tube-like feather formation in the very ancient reptile that leads to bird transition. And once these tube-like structures form, again by setting up different similar domains of these two gene expressions, you create an axis, from which you then derive branched feathers or a central rachis. So this is another example of heterotopy.

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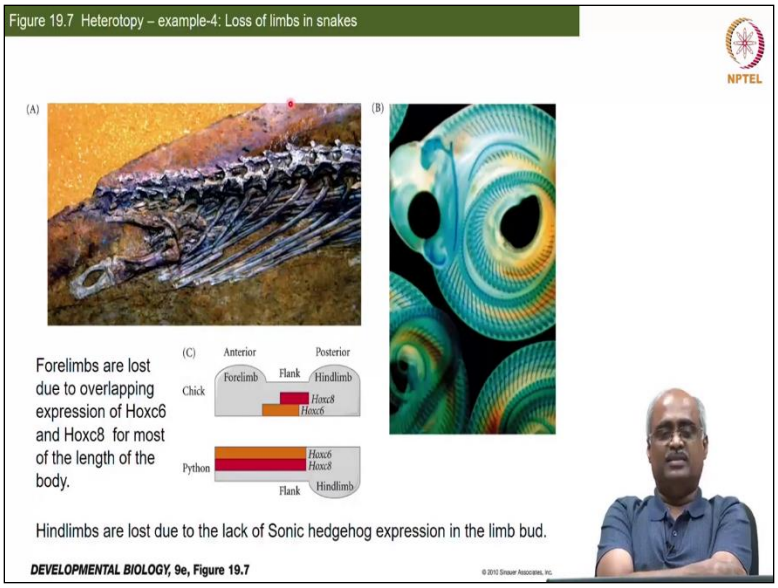

And the last example that we are going to look at is how the snake lost its forelimb. First of all, you need to understand that the snakes evolved from the tetrapod ancestor having forelimbs, two at the front and two at the back, so two forelimbs and two hind limbs.

So it originated from a tetrapod, and during evolution, it lost its limbs. So how did it lose its forelimbs is quite simple. So we already know Hox genes and Hox code, which states that the combination of Hox genes determines the segment identity along the anterior to the posterior axis. If you look at it figure A in the slide, this is a fossil skeleton of an ancestral snake, you can see it is a hind limb a very short structure, but you can make out the limb structure. But the primary thing is this, so it seemed to have rib all over the body. So the Hox genes responsible for making the ribcage are expressed throughout the body in snakes.

So this cartoon explains the expression domain in the chick. This Hoxc is the third gene, 8th paralog, and the other paralog Hoxc6 overlap the middle part of the body. And if you have Hox6, where its domain of expression ends, you have the forelimbs, and similarly, where you have the Hoxc8 ends, you get the hind limb. So this is the expression pattern that determines the initiation of forelimbs.

So essentially, you should not have Hoxc6 to initiate the forelimb, but if you look at an ancestral snake-like python, what happens is both of them are expressed all through that is because Hox6 does not get expressed without Hox8, and in this case, they both express all through and when they both express you make the ribs and as a result, you make rib like vertebrae from the anterior to posterior, and that is how the snake skeleton is formed.

So due to the heterotopic expression of Hox 6c, the forelimbs are lost. The hindlimbs are lost primarily due to the absence of sonic hedgehog expression in the limb bud. And sonic hedgehog is required for the limb bud to grow. So hind limbs are also lost in modern-day snakes. So this is how snakes lost their limbs; again, a heterotopic expression of genes.

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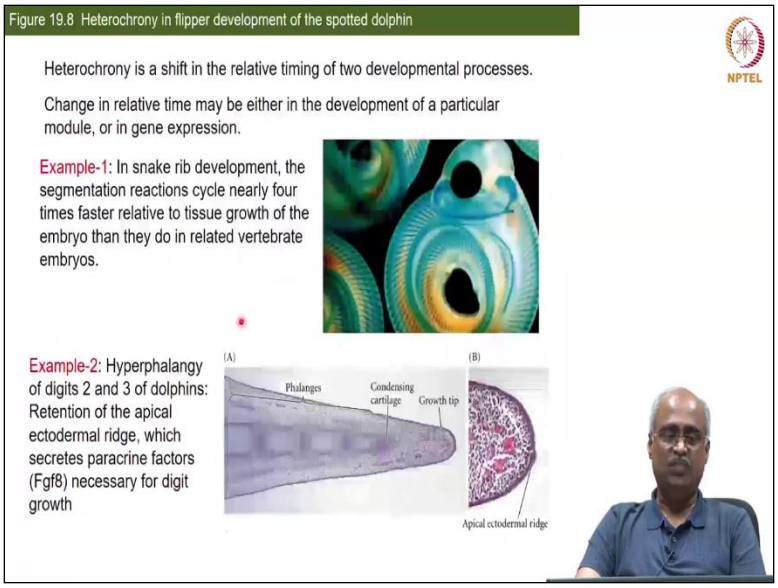

Next, we are going to see an example of temporal expression change, meaning time difference. When a gene is expressed and for how long it is expressed. Both are important even if something is to be expressed for a short period at a certain developmental stage; instead, if it is expressed for a longer period, it will impact. So that is heterochrony, so chrony the word derives from how it connects to time and change. So the actual start of expression can also be a different time point; the duration of expression can also vary. Both kinds of chronological changes are possible, and both can lead to anatomical and morphological changes within a single lineage. We will see a couple of examples; here, we saw earlier, but we did not focus on this particular feature.

When we looked at the snake, we focused only on how it lost its limbs. But we did not seriously think about why it is long and why it has too many vertebrae. During the rib development, the segmentation reaction cycles nearly four times faster than the rest of the embryonic tissue growth when you compare with what happens between the cycle times compared to the rest of the embryonic development in other vertebrates. Whatever be the rate of segmentation cycle compared to the rest of the embryo in other vertebrates in snakes, that rate is four times faster.

As a result, it ends up creating many segments and forms a lot of vertebrae. So that is one example, and another example where we are seeing is called a hyperphalangy. So this is common among cetacean mammals like whales and dolphins. So it will be interesting for you to do homework, read upon, and find out the evolutionary ancestors of these mammals that have gone back to the marine environment. So I will not explain the evolutionary ancestry of these cetaceans; cetaceans is a common name for whale-like organisms.

So in them, the phalanges, phalanges means like our finger digits (1,2,3,4,5)other bone structures. So these bones at which you can tone your finger. So these phalanges can be longer or shorter. So when it is longer, it is called hyperphalangy, which has happened in the forelimbs of cetaceans; for example, in dolphins.

We are looking at digit 2 and 3 in dolphin. So these phalanges have become long, and therefore it could make a long flipper. When a forelimb like ours is converted into a fin-like structure, they are called flippers instead of fins in the fish. Fish fin did not evolve by converting a forelimb like ours into a fin-like structure and therefore, these are called flippers. And in the dolphin flipper, if you look at, the digits 2 and 3 are very long because these phalanges expanded more compared to what happens in closely related mammals. And that is because, in this apical ectodermal ridge, the skin-forming cells maintained a signal secretion ability that promotes these phalanges to grow and because they extend along. So they are expressed for a more extended period. Here it is not an ectopic expression; they usually are needed for the phalanges to grow; it is just that they stayed too long, and as a result, the phalanges become longer. So it is chronological, that is, temporal variation longer time it existed. And that is why you have long digits in these dolphins.

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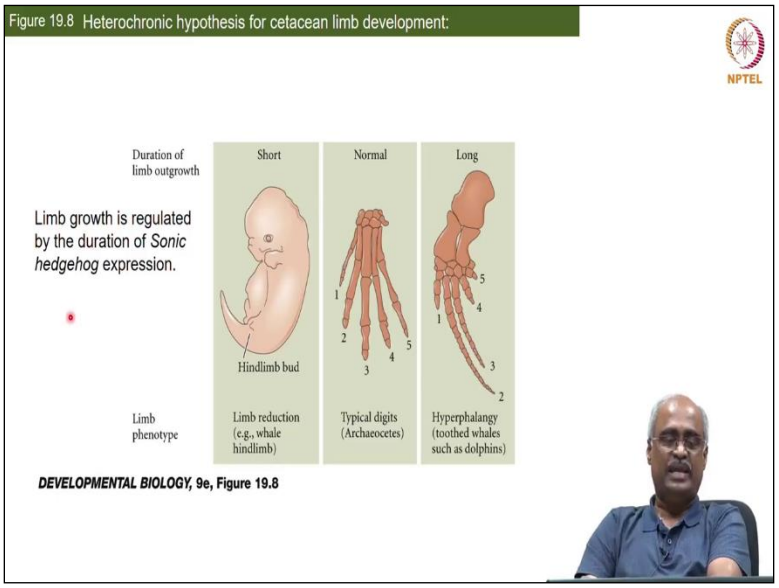

Then let's see a similar example in the same group that is the limb bud. So how long the limb bud continues to grow also facilitates the longer phalanges ending up in longer digits. So, this limb bud growing we saw when we were discussing the hind limb of snakes. So the Sonic hedgehog expression in the apical ectodermal ridge of the limb bud, in this case, is the reason for it.

So if the Sonic hedgehog expression duration is shorter, it forms very short hind limbs and shorter digits. So this is what is found in the whale's hind limbs. But if you look at ancestral whale-like archaeocetes, there you have a normal level of Sonic hedgehog expression and, as a result, normal limb growth. Here, the Sonic hedgehog expression remains for a longer period; thus, everything ends up longer. So this is also the limb development promoting gene that is sonic hedgehog and signals that promote the phalange growth both staying longer ended up having longer limb with longer digits. So this is how the whales got their flippers, a good example of heterochrony.

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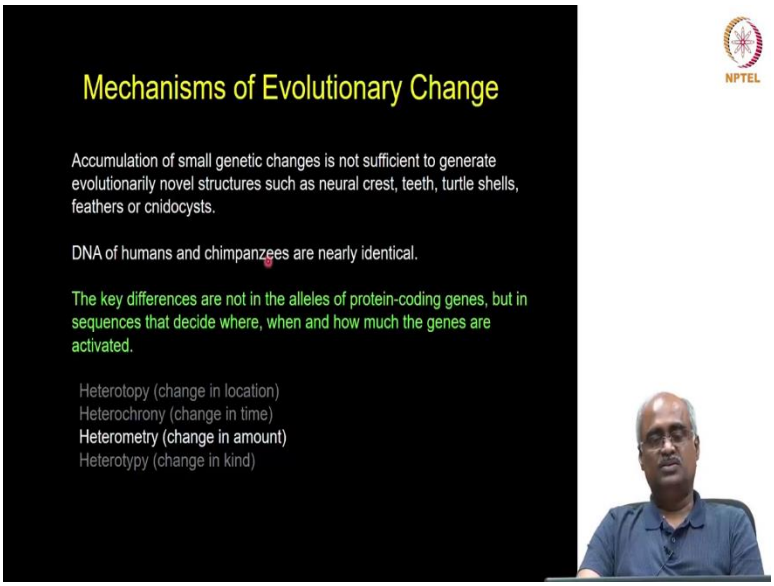

So let us look at a different mechanism which is heterometry. So the amount of gene expression, like the protein product being less or more, can also vary the tissue changes. Here in each one of these, you see the developmental modules helping in varying certain structures without varying rest of the embryo. These variations of certain structures are essential adaptations.

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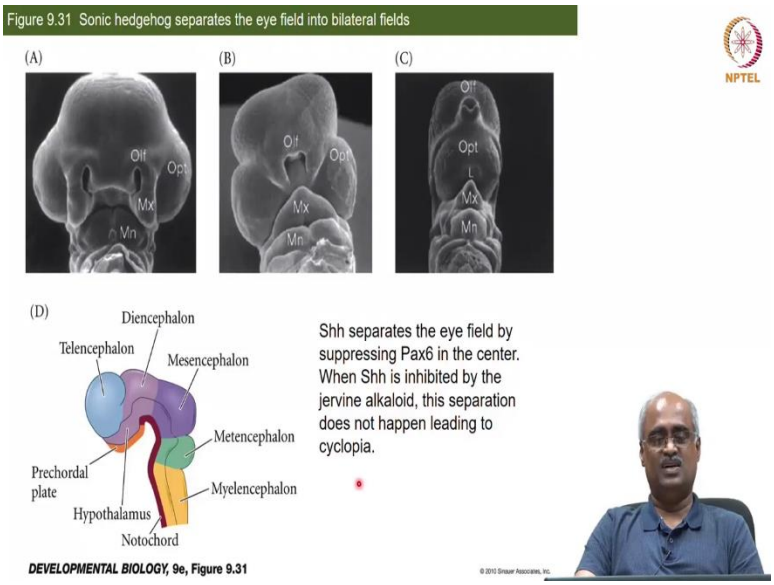

Here, we see an example of an interesting fish species that lives in underwater caves with absolutely no light there and has no use for eyes. But it is not that it does not want to have eyes but to develop other senses to live in that kind of an environment whatever modification needed ending up eliminating eyes. So, let us see this example of heterometry.

So this is a normal mouse embryo here. The Figure in the slide shows the head region of the mouse embryo. You are looking at its head from the front. So you see the two-nose circle where the two nose cavity is going to form. The adjacent regions are the optic vesicles where the eyes will develop. So you see two of the optical vesicle, and that is because of the precaudal plate. During embryonic development, the orange structure cartooned here, the precaudal plate produces a Sonic hedgehog that inhibits Pax-6 expression. As you are very familiar with already, Pax-6 is required for the optic vesicle development lens formation. So, it is essentially Pax-6 equals eye development, no Pax-6, no eye. And this normal level of Sonic hedgehog ends up inhibiting Pax-6 in the central region; thus, this I field splits into two. So Pax-6 is inhibited in the center but allowed expression on the two sides, so you end up getting two eyes.

If you remember, the hedgehog is cholesterol modified, and if we inhibit cholesterol biosynthesis like using this jervine alkaloid, then the hedgehog signaling will be reduced. If you partially reduce hedgehog signaling, then the field does not split well so both the optic vesicle remains close, and the nasal cavity does not bifurcate and forms a weird structure. And if you abolish hedgehog, then the split does not happen, and you get one single eye developing, a condition called cyclopia. So this is because Pax-6 expression has not been reduced in the center. So this is what happens when you reduce the quantity of expression. So this is a mutant condition we are talking about; this is not an evolutionary adaptation. So this is our background

preparation to understand how the cavefish lost its eye, which I just mentioned at the beginning to see that in the next one. So here is the result where you have no Sonic hedgehog.

Now let us think of a situation where you have too much sonic hedgehog. Instead of suppressing Pax-6 only at the centre, now you have it suppressed all over meaning no eye optic vesicle forming and therefore absolutely no eye, which is what happened in the cavefish.

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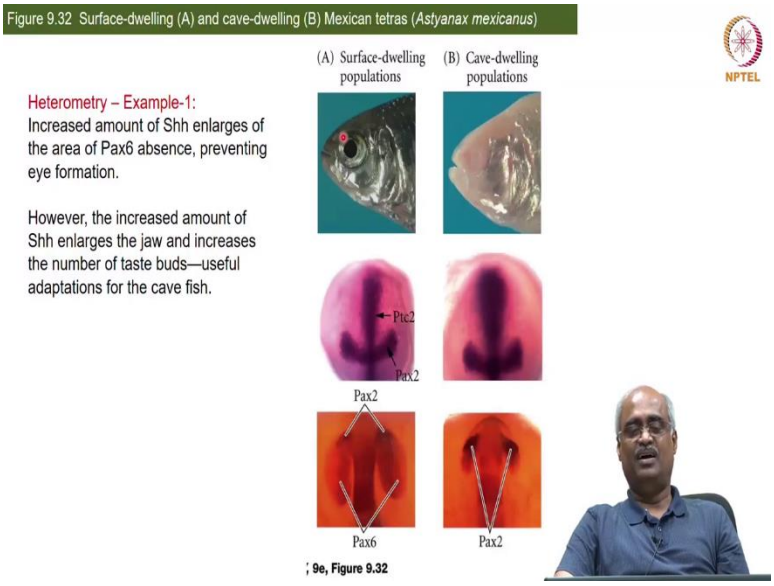

So this is a surface-dwelling fish in the same area belonging to the same group; they are very closely related species. And this one lived in the caves for more than 10000 years, and it had no use for light, but that was not the reason it lost the eye. The change in gene expression helped it adapt to that cave environment, making a bigger jaw and a better sense of taste. And these two were useful adaptations in the dark environment and helped by more expression of Sonic hedgehog. So the quantity that we are talking about, heterometry, so more expression; thus, its downstream targets like Patched-2 and the Pax-2 are affected compared to the surface-dwelling of fishes. So in these embryos, the dark colors show the expression of these two genes. In cave-dwelling fish, the embryo patched-2 expression domain is bigger, leading to a bigger jaw and more taste buds. Its gustatory sense is much more than the other fish.

Due to the sonic hedgehog's expression, the Pax-6 expression is absent in the cave-dwelling fish. As a result, the optic vesicle is not formed, and the Pax-2 which is expressed very little in the normal fish embryo is expressed more in the other one, leading to more taste buds. Quantitatively, more expression of Sonic hedgehog helped in adapting to the cave environment by making bigger jaws led to the loss of the light-sensing organ eye, which did not matter because it had no use for the eyes in that environment.

So this is how a quantitative variation has also helped in the evolution to modify the same basic developmental module. Here, the eye field still exists; it is just that it has been modified into that required variation by changing one gene expression.

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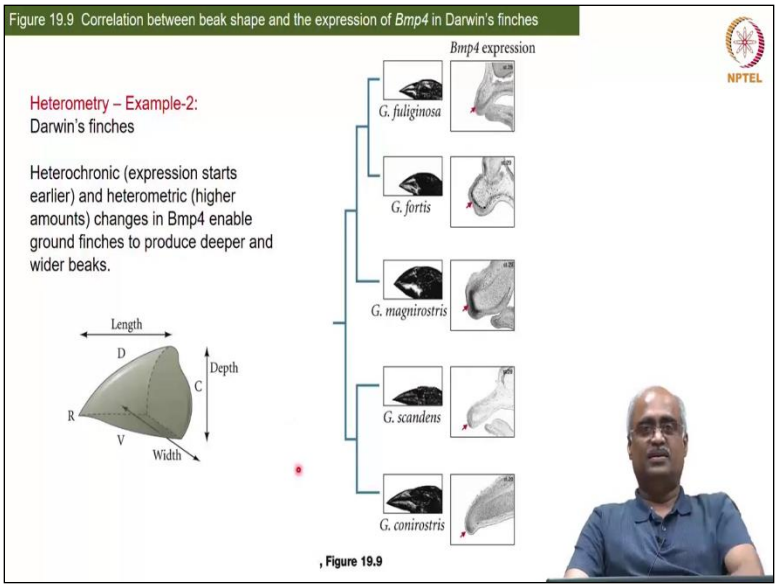

So this is the famous example of Darwin's finches. These are birds that live in Galapagos islands where Darwin visited during his South America voyage in the early 1800s. There he saw these variations in closely related birds, which are called finches. These are barbless related birds from the South American mainland that got adapted to different islands based on what food source was available there.

And that is primarily by modifying the three-dimensional aspects of the beak-like the height, width, and depth of the beak by changing the level of protein expression. Both heterochronic and heterometric variations led to variations of this beak, and that is what we are going to see here.

So the first example we are going to see is heterochronic and heterometric variation. This gene will be expressed for longer or shorter time, and more or less quantity, both variations we are going to see, and the gene again is familiar. It is a small tool kit it is not like a whole lot of tools that are being used, and it is BMP again. So if you look at the first three beaks, these are the ground finches. So these things poke open the seeds that are lying on the ground and then eat the seeds' contents. So they need to break hard shells, so they need a deeper and wider but shorter beak that helps in breaking open the seed cases, and that is made possible by having more BMP expression in this embryonic frontal nasal mesenchyme area. On that area in the embryo, you have more BMP expression (third beak from top), and then you get a deeper and wider

beak, but then it is shorter and gives it an application of more force in breaking the seeds. Then you see this one slightly smaller (second beak from top), and it has slightly less expression and further smaller it does even less expression (first beak from top), but the last two beaks have far lower expressions. So these are the cactus finches. These have tapered long beaks that help them search inside the cactus flowers for insects and other food. So these benefited by having longer and narrower beaks. The ground finches benefited by having a shorter but wider and deeper dimension that is more pronounced.

And this variation is made possible by having varying quantities of BMP-4, and that is the heterometry. But in these species, the expression starts very early as well. So expression started earlier than these and expressed more than these, and the finches beak story doesn't end there. So there is one more molecule we are going to look.

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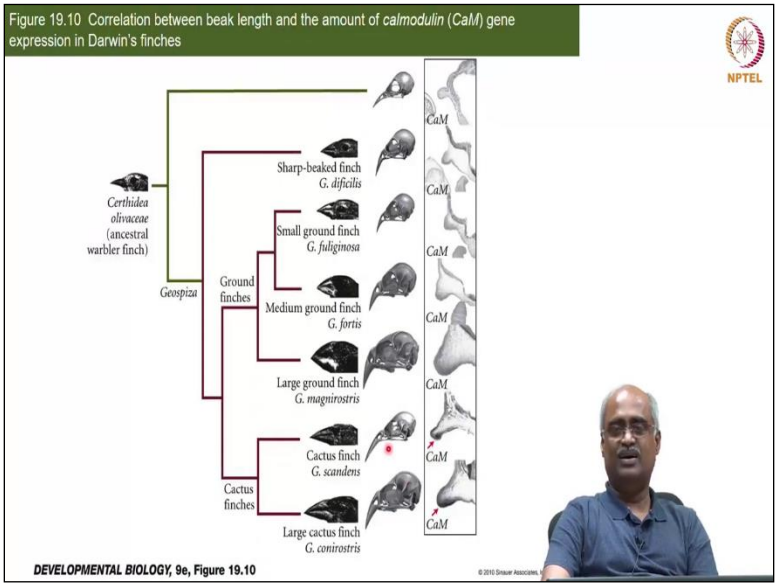

By playing the concentrations of these two, you can create varieties of beaks. It gives you a three-dimensional coordinate for the relative concentrations of these two molecules, and therefore you can generate a variety of beak sizes and shapes. So the molecule responsible for it is calmodulin. So calmodulin is a protein that binds to calcium and then interacts with other proteins and modifies their activity. That is why it is called calmodulin.

So the calmodulin expression also matters. When it comes to the beak length, calmodulin and the BMP-4 act as antagonists, meaning we just saw that more BMP shorter beak although it is wider and deeper. With calmodulin, the opposite is true; the more calmodulin, the longer the beak. More the calmodulin and less BMP-4, you get a longer beak, as you see here in the cactus finches.

Here in the slide, as you can see, the primordial embryonic structure in the bottom most express more calmodulin than the ones you go up. So these two are the cactus finches. They have tapered longer beaks, and these are the ground ones. This has a lot of BMP-4, which started expressing early as well. And here you have less calmodulin compared to these, and as you go further, you have a very low amount of calmodulin that makes shorter beaks.

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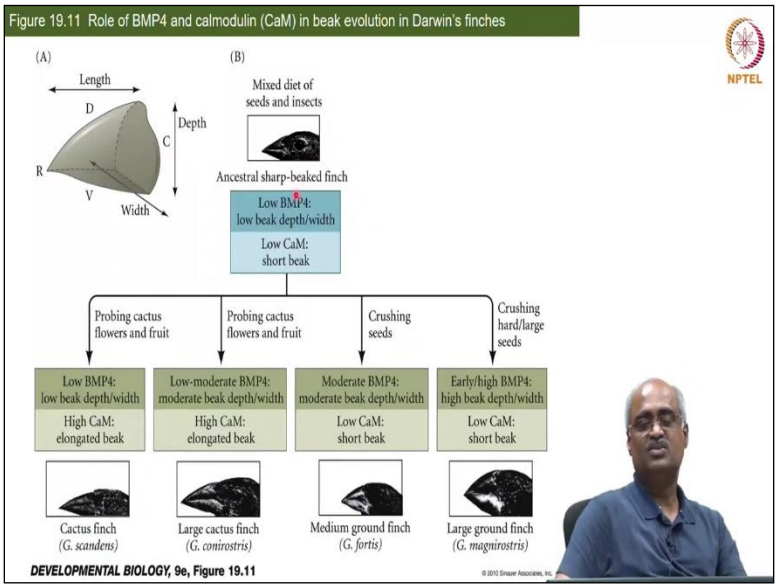

And this is explained further here. So this (Figure B) is like the ancestral bird from the South American mainland where it was probably breaking some seeds and probing some flowers. And that had a low level of both, and it had this shape. So this is like the starting point, ancestral. And by varying the quantity of both these protein expressions and then the duration. So by changing these two, you create all these variations.

So in one case, the cactus finches have low BMP and high calmodulin, and as a result, you have longer beaks that are narrower; therefore, it can readily get deeper into the flower and search through the flower structures. Then you have some that are not so specialized to probe the flowers so deep. And they have slightly more BMP-4 than these and the same level of calmodulin as this or a slightly lower amount of calmodulin.

But as you progress towards these crushing seeds, you almost have more BMP-4 and but less calmodulin, and as a result, you have medium ground finches. This is not that deeper or wider than these, but it is deeper

and wider and shorter than these. And when you have high BMP-4 and low calmodulin, you get a shorter beak wider and deeper, so this can break and crush hard and large seeds (large ground finch).

Here, what we are seeing is a significant anatomical variation generated by simply varying the timing and quantity of just a couple of molecules. So, this is how you connect morphology the molecular biology via developmental mechanisms to evolutionary adaptation. So without understanding the developmental mechanisms of how beak forms and the underlying molecular biology, that is, the expression of these molecules and what these molecules do, you will not explain how these adaptations have happened actually during evolution.

So this is the connection between developmental mechanisms and evolutionary adaptation. So here you are, throwing up in a population an enormous variations. Natural selection can select among those variations, and these variations have been generated in three-dimensional by merely varying the expression pattern of two different proteins.

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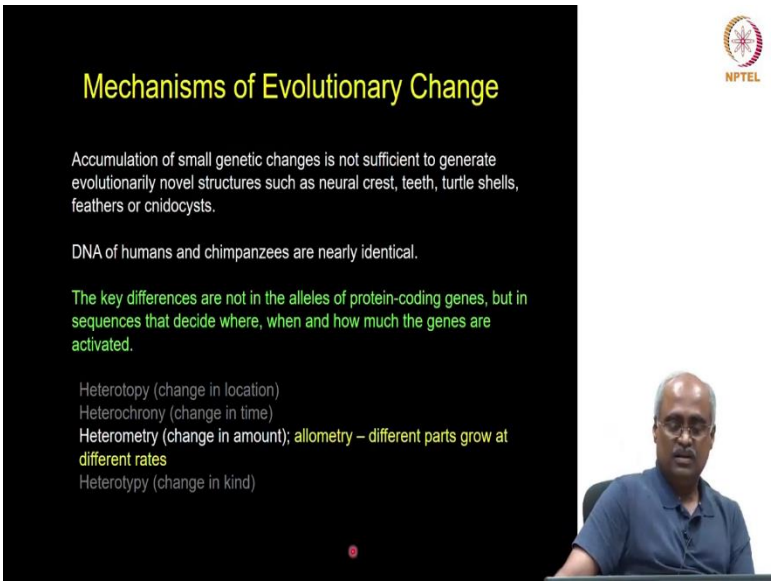

So there is a small variation in the theme of heterometry, and that small variation is allometry. So till now, we saw quantitative variation. The next one we will see is the quantitation variation of a structure for the rest of the embryo. So the different parts grow at different rates; thus, one part becomes way too big compared to the rest of it. So it is not proportional compared to an ancestral organism in the same lineage.

So that is allometry. We will see this through a couple of examples. One example for which I do not have images here is that we have five toes, but the horse has only one toe. The horse is also a tetrapod. Since it

uses both pairs of limbs as legs, we do not call them fingers; we only call toes. So it is single-toed as if these are all gone and only one finger is there or one toe in the foot is present. That is an allometric growth, one being so dominant compared to the rest. But even in your toe, the middle ones are longer than the other. They are not of the same size, and that is because of the allometric growth of the interdigital regions. And that is what led to the eventually in horses one finger being its functional foot.

The other example we are going to see is the whales. So whales are mammals, have lungs like us, breathe air, and do not have the gill apparatus to take oxygen from water. So how do they breathe? It lives in the sea. So it should be able to breathe very comfortably while swimming, it should need to turn its head up and down as we swim, and interesting allometry does that, illustrated in the next slide.

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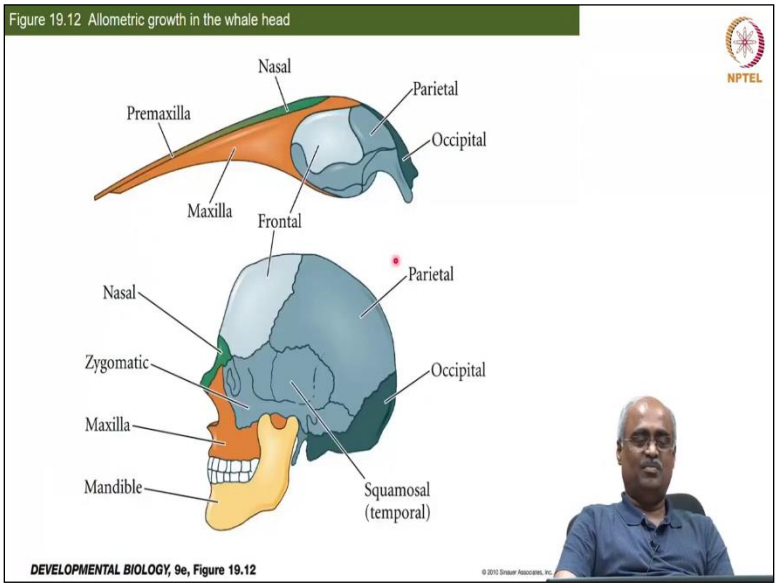

So here is the comparison, this lower jaw, the mandible, is not shown here for the whale; otherwise, this whole structure is shown here. And where I was hoping you could draw your attention is to look at this upper jaw or the maxilla. So this has grown too long compared to the rest of the craniofacial structure. So that is the allometry. It is not proportional compared to the rest of it; as you see in another vertebrate, this has grown too long.

So probably, the primordial cells that produce this were more sensitive to certain signals. Therefore, they responded more, or that signal was produced more in this organism than here and thus grew longer. So the same structure significantly varied, but what is the big deal of making this grow big? Just think about what will happen. If you make this maxilla grow, this nasal part goes to the top. So the nasal cavity opens on the

top; therefore, it could be comfortable swimming without turning its head left and right all the time, and it can breathe.

So its nose is on the top of its head instead of on the side. So this is an example of allometry; the maxillary bone grew a lot more than the rest of the body. So the difference in the proportion here is called allometry. We will see the last variation is not changing the timing or space, or quantity; instead, changing the molecule itself. So that is what is heterotypy. So we will see some examples of heterotypy in the next few slides.

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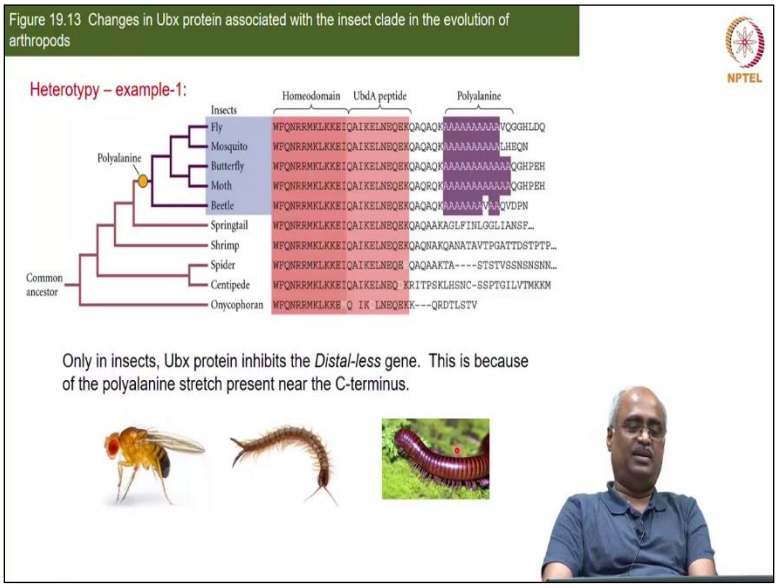

So here is one good example. If you look at insects, you may be thinking that insects have too many legs compared to us. Let us take our hands, we have four limbs, and they have six, so they are more, but instead of asking they have more, you should look at its close relatives like centipede and millipede. They have many legs; every segment is producing a pair of legs while only the thoracic segments produce legs.

So in insects, why not the abdomen segments or the head segments develop legs? That is because of the variation in this ultrabithorax. So in the insect's ultrabithorax, the protein sequence has more polyalanine stretches, as marked here in the slide. So this is like drosophila ultrabithorax to refresh your memory; it is a posterior Hox gene a homeotic gene. And its homeodomain is very well conserved.

But if you look at the C-terminal region, it ended up adding a lot more polyalanine due to a mutation somewhere in this ancestor. A splice junction difference or change in this stop codon extended into the further sequence, adding up more polyalanine. So what is the big deal of having polyalanine?. The polyalanine stretch in the C-terminus of ultrabithorax ends up inhibiting this distal-less, the gene that we talked about yesterday.

So distal-less, we have multiple copies, each one expressing in different locations. We saw this in the last class. But insects have only one, and when that is inhibited, that leads to the inhibition of leg development in other segments. So in the posterior segments, which are controlled by the ultrabithorax, their distal-less is not expressed, and as a result, they do not form the legs, and whereas in other species these do not have poly-alanine stretch, they have a normal Distal-less expression which stimulates the leg formation in all the segments. And that is how the insects lost the legs in the posterior segments. So this is an example of the protein sequence varying heterotypy variation in the type.

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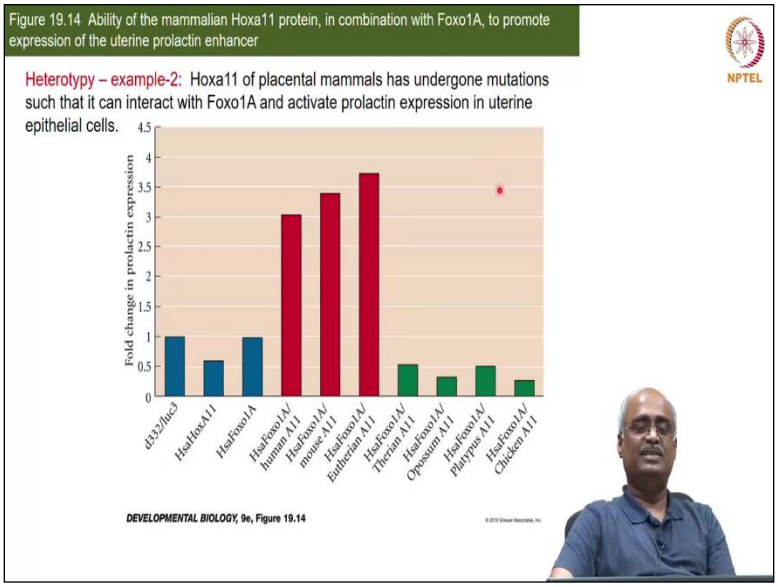

So this is another good example of the extensive placental connection in mammals between the mother and the fetus via placenta having decidua and chorion. We learned a lot from the embryos' point of view but let us look at the mother's point of view. So you have to modify the oviduct into a large uterus, and the uterus epithelium should be able to form the blood vessels to get nutrients towards the embryo. And it should be able to accommodate the embryo itself, and it also promotes trophoblast proliferation, which helps the embryo gets implanted in the uterine wall.

All these are all significant modification of the uterus epithelium and made possible in these mammalian vertebrates by producing a prolactin hormone. How do you end up producing more prolactin only in mammals, and that is simply by changing a subtle change in the protein sequence of a Hox gene.

So this Hox gene we discussed in the last class also, Hoxa11. The Hoxa11 of placental mammals have significant changes from the Hoxa11 of other vertebrates such that this Hoxa11 of placental mammals have acquired the ability to interact with this transcription factor Foxo1A. This Foxo1A, when bound by Hoxa11,

activates prolactin expression and the prolactin hormone is enough to do all those modifications. I described just now the uterus epithelium, and this is an experimental illustration of that. So here it is a reporter control a non-specific protein that does not induce prolactin expression.

Here you have just the human Hoxa11 but no Foxo1A, which does not again promote prolactin, and here you have Foxo1A alone with no human Hoxa11, and that also does not promote prolactin expression. But when you have both now, you have a lot of prolactin produced. And the Foxo1A from a human with a different placental mammal mouse also does it, and any Eutherian mammal does it. But then if you go back to the non-placental mammals, if you take Therian and Opossum Platypus or bird, they do not do it.
It is the placental mammal Hoxa11 that is capable of interacting with Foxo1A and promoting prolactin expression. A sequence variation on the same basic protein that is the heterotypy led to a change in anatomy and, as a result, an evolutionary adaptation. So if you consider the anatomical changes, it is dramatic, making a placenta and having an embryo grow in your body. Just look at the birds; they just throw it away, insects do the same thing, reptiles do the same thing.

But mammals keep the embryo in them, and that requires an enormous change, and all of that does not require a wholesale reworking of the fundamental body plan; you just need to vary a little bit, and that could be accomplished by varying subtle changes in the function of a protein. It is now changing the protein function, not the expression time or spatial changes. So this is how placental mammals have developed that adaptation.

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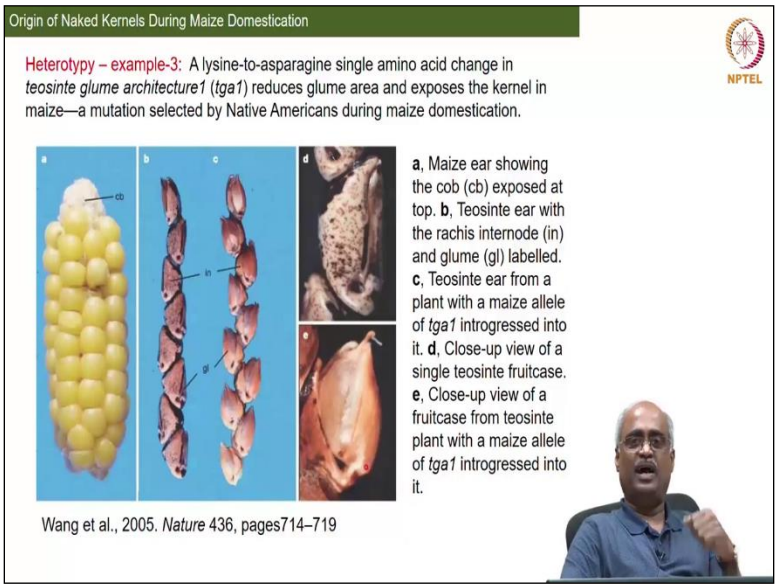

So this is another example of heterotypy. So I have one more example that is from the plants. This is a remarkable thing. Here again, I will not have the time to explain the whole detail of this amazing crop's evolutionary history. So in India, we may not be dependent on this crop maize a lot for our food source. If we are unable to grow maize, we are not going to have a famine. But in other parts of the world, for example if you take North America and the North American maize exported to you Europe in both these places, they are heavily dependent on maize.

It is an important crop; it is just that it is fed, secondarily you do not directly eat the maize, maize is fed to cows, and then the beef industry provides the meat to the human population. So a large part of the human population is dependent on this particular crop. So it is worth your time to find out how this maize evolved? Is it natural selection, or was there any human intervention? So go ahead and figure out on your own how this happened.

But here, we are going to use this as an example for heterotypy. In corn, if you look at its base at each one of these kernels. This whole structure is cob the top portion does not have the kernels, which is attached to the kernel, and at that place, there is a covering which is not visible here, in the next one I will show you.

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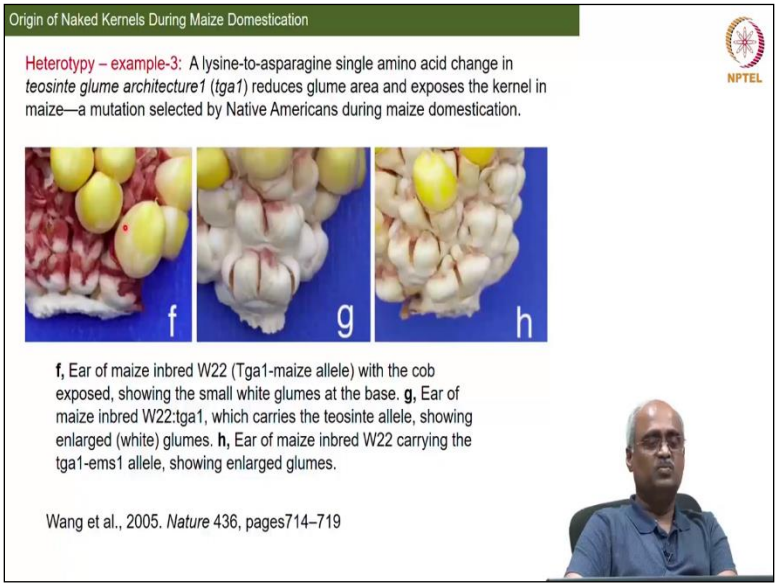

So this portion, this white structure so here the kernel is removed, and you only see this cover. This cover is called glume.

(refer to the previous slide) If this glume is really big and seriously protecting this kernel, it is not easy to harvest it. And this is how the ancestral monocot from which this organism came about looked like a seed

has a very hard, fully protective seed cover, and this is its glume. And this plant is called teosinte, so in this plant, if you express the normal maize version of this gene called teosinte glume architecture1 or TGA1 you get softer kernels The difference between gene sequence in maize and teosinte, its ancestor is just one amino acid. One amino acid change on lysine to asparagine change leads to glume being very short and as a result, it exposes the kernel. So here, instead of asparagine, when you have lysine, it is big and closes. So this in fig b you see the wild type teosinte. And then here, what you have is the maize allele gotten through genetic crosses. As a result, instead of this hard and fully covering glume (fig d), this makes a soft and short one, and the seed is more exposed(fig e). So just one amino acid mutation and a dramatic change are better shown in this mutant version.

(Refer to the above slide) So this is called wild type (fig f) because this is what is commonly grown, and here this is how the glume is (this white structure) and when you have that one amino acid mutation in the maize crop, the glume is very big and it covers the seed very thoroughly (fig g). This can also be obtained by introducing the teosinte's allele into maize (fig f). So a change in one amino acid and therefore a change in the type of the same basic protein you have the glume being bigger or smaller, which is an adaptation.

So with this, I will stop for this lecture; in the next lecture, what we are going to do is now that we are familiar with the developmental mechanisms of certain body parts, how they are formed, and how you can vary them. Now we will look at the constraints of this body plan and how those constraints end up limiting the variations in the adaptations that are possible.

Every possible structure that would help an environment may not be possible given these developmental mechanisms. So we need to remember natural selection does not produce any structure; natural selection selects among the variations that exist based on which variation fits in a given environment. So that means those variations must already exist and from what we have learned.

So far, it becomes abundantly clear that there will be limits to the types of variations that are possible. And as a result, among what structures are can and cannot evolve be predicted. And those developmental constraints that provide a trajectory to evolution are going to be the topic of our next lecture.