 The end of last lecture I got an interesting question about apoptosis which I covered very briefly towards the end of that lecture. And the question was this: Do healthy cells tell sick cells to die?

Or in turn, do sick cells tell healthy cells to die?

So, is there some kind of communication between cells as to who is healthy and who is not healthy? For those of you who are just coming in, there is a handout outside, and up front, it's the same thing. And that's actually a very interesting question because they really does seem, in the body, to be some sense of monitoring whether cells are healthy or not.

Now, a lot of the time, cells that are not healthy intrinsically activate their own death program, or they have the ability, they gain the ability to respond to some kind of extrinsic signals. And in fact, signals could be sent both ways, we believe, where sick cells will tell healthy cells to die under conditions that are obviously not favorable to the organism, but more important, that healthy cells can tell sick cells not to survive. So, the balance of apoptosis and cell survival is a very delicate one and regulated by many, many things. So, it's a good question. All right, we move on. We move on to a new module. So, you have, in fact, covered the foundations of modern biology. You've covered them in a very superficial way. And I want to emphasize that. You should, by now, know how to take a piece of DNA, conceptually turn it into RNA, and conceptually turn that into a protein. You should know what to do if the DNA sequence is changed. You should have the expectation that the RNA and protein that are made from it will be changed, too, and you should have various other nuggets of information that are covered by foundations. These foundations are not going to go away. We're going to use them throughout the rest of these uncovered black boxes. And I'm going to assume that you remember a bunch of stuff as I go through the material in the next several lectures. But we are going to move in to the formation module. And today, we are going to talk about things in a kind of overview way. And I'm going to tell you five major things that are important. And I'm going to write them on the board, and some of the things they need to know about them. And we will use the slides as well. So, what is formation? What is this module all about? Well, it's about something called "development," where development is the process by which one cell, the fertilized egg or the zygote goes on to make a multi-cellular and complex organism.

This is not about squishy little embryos. OK, this is about life as it began, as it continues in your own bodies.

And it has immense applications for multiple biomedical and bioengineering processes that I'll talk about as we go through. The first thing you need to know is what's written up here is that the development occurs over time and space.

And that's one of the things that makes it an incredibly complex set of processes to think about. The overtime can

be a long time. And what's important to understand is that developmental processes occur throughout life. Initially, in the formation of the organism from a single cell, the fertilized egg, the zygote, and later on, early in the formation of the embryo, and later, in the renewal of the adult.

And this is where the stem cells come in. And we'll have a lecture on stem cells later on. But development is something that occurs throughout life. And in fact, I teach an upper-class course on development to graduate students. And the first thing I tell them when I start to teach them is really there is no such subject as developmental biology because it covers, it includes, it encompasses biochemistry, genetics, molecular biology, protein structure, and many different disciplines. And it occurs throughout life. So, it really covers everything. But we have put these things together in the formation module, and I think you will find them interesting. OK, so here's a schematic of how things work courtesy of Picasso. And really, this whole process is quite remarkable. It starts with two dying cells.

The egg and the sperm, haploid cells that have a half-life that have a life of about 12 hours up to which they are dead. But when they fuse, there's magic that happens, and you get a viable cell, the zygote, that has the capacity to go on and divide many, many times to form an embryo and ultimately an adult organism. And as we've mentioned many times, it is estimated that there are about ten to the 14th cells in the human. In the adults, and even in young adults, there is much replacement of cells throughout life. And this whole process obviously takes place over time. But that's important because the time component means that things change over time. And in order to understand this entire slide, you have to factor in this fourth dimension.

So, what are some of the things that we're going to cover in this module, and why are we bothering to talk to you about the subject?

Well, one of the things that's of interest is the effect of chemicals on the formation of a normal body. So, there are these things called teratogens, which are chemicals that affect formation of early steps in development of the embryo. This is a famous one, the effects of a famous one called thalidomide that was given as an anti-nausea medication during pregnancy some decades ago.

It has no effect on rodents on which it was tested, but it was not tested on primates before you give it to people, and it has the devastating effect of preventing limb formation, and a number of people were born in the late 1940s, early 1950s, who lacked limbs because of the effect of thalidomide. And I have to tell you, this is very interesting for those of you who are interested in chemistry. Thalidomide has a pretty simple chemical structure. It has been studied for many, many decades. It's a very interesting drug because it turns out it prevents cachexia, which is the wasting that occurs with many disorders including HIV-AIDS infection. So, thalidomide is a very, very useful drug. It has a simple chemical structure. It's been studied for decades, and we do not know its mechanism

of action. OK, here's another one that you might be familiar with, the drug, not the syndrome, I hope.

So, fetal alcohol syndrome, so, a normal brain, this is a brain taken from a fetus. That is the late stage gestation human whose mother drink excessive amounts of alcohol during pregnancy. So, during the early stages of pregnancy the first few months, alcohol is devastating to formation of the brain and also to the bones of the face. And even a reasonable number of drinks, apparently, just a few can significantly lower the IQ points of a baby. And so, it's a good reason not to drink if you're pregnant. This was a very devastating case.

You can see the brain is very smooth. It doesn't have those nice valleys and hills, the sulci and the gyri, that the normal brain has, and this fetus would not have been able to survive. Here's one. This is the dream of all biologists, developmental or otherwise. It's a dream of bioengineers. It's probably the dream of everybody. Someone cuts off their arm in an accident: can we grow a new one? Well, newts can. So, in this example, newts can. So, in this example, the newt limb, this poor animal was amputated just above the elbow. But over a period of a few months, another limb grew back, smaller than the original but perfectly functional.

We can't do that. How do newts do it, and how could we use that information to help people grow new limbs, or new hearts, or new eyes? Fish, for example, the fisheye work on zebrafish can grow a new heart. You can cut the heart into two. Take away half of it. It'll regenerate a new heart.

There are animals were you can remove half of the retina or all of the retina, and it will regenerate a new retina. We do some regeneration. You can take away two thirds of the liver, and new liver will grow back. And that's one of the principles behind liver transplants. But we can't do things like regenerate eyes, and hearts, and limbs. It's been the focus of study for a long time to try to figure out how newts do it, and to ask whether we can capitalize on that knowledge. And I have to tell you, it's been a very tough area of biology, still wide open. And that's where the great god of stem cells comes in. Because it's been so difficult to get limb regeneration, for example, and heart regeneration, there is a sense that perhaps we could get groups of cells to repair damaged organs.

And stem cells are the things that hold this promise. And we'll have a whole lecture on this later. And part and parcel of stem cells is the very newsworthy issue of human cloning, making identical replicas of things. And we'll talk about this also in a separate lecture. OK, all right, so let's move on to the next set of things that you need to know. And that's the notion that there are multiple processes that are involved in setting up development formation of any multi-cellular organism.

So, multiple processes are involved. And these are cell division, right, a single cell, so, ten to the 14th cells. You figure out how many rounds of cell division at us. Actually, that's a tough question.

You could go and do that, OK, and over spring break if you're lying on the beach or hanging out on a mountain, if

you can find any snow you can go and figure out how many cell divisions it takes to get ten to the 14th cells. But it's not so easy because cells don't just divide from one to ten to the 14th. As they are dividing, there's a balance of cell division, and as we talked about last lecture, of cell death. OK, so cell division versus cell death, and so I can't tell you how many divisions that takes because there are a lot of cells that die along the way to those ten to the 14th cells. Here's another one: cell type.

What's cell type? Different kinds of cells in the body, we mentioned this right at the beginning of the course. Skin cells, cells that produce the hair, nerve cells, red blood cells, and so on. There are probably 500 different cell types, and these each have specific functions. And the definition of a cell type really is a group of cells with a particular function. Something else that's interesting about turning that single cell into a multi-cellular organism is the notion of position. So, if you look at yourself in the mirror with all your imperfections, you likely have your arms coming out of your shoulders, and your head coming up above your shoulders also. Something has made the decision to put those parts of your body in their correct place. And that system is a set of positional information. It's kind of like a map. And as you're going from a single cell to a multi-cellular organism, there is a set of molecular information that really puts the coordinates on a map just as it you had a blank map of the world and you put on the Cartesian coordinates. So you would do that to the developing embryo. So, there's something called positional information, and the final thing is three-dimensional structure.

And we'll have a whole lecture on 3-D structure. But suffice to say for now, cells do not work as single entities. The blood subsystem, the hematopoietic system, is the only real example in the body of cells working as single systems.

And even there, they don't really. In all cases, cells group together to form tissues, and is tissues grouped together to form organs. And the precise three-dimensional structure by which they form is really important. So, here are some examples. I'm going to show you a movie of some stages of human development. This is taken from material collected a long time ago. And what I want you to see is that over a period of a few weeks how the sides of the embryo changes due to cell division. OK, so -- So these are all taken at the same magnification. And you can see that as time progresses, the size of the embryo changes, and this was all due to cell division. You can see that shape changes as well, and this is due to various processes including modeling through cell death. One of the interesting things about this, and this will be on your website. You can look at it.

One of the interesting things about this is that early human embryos have a tail. So, you had a tail, a really pretty good tail until you were about 56 days old. And then, it disappeared. And in these early embryos, if you go back and look at this again, you will see the embryo has a tail. So, this is a manifestation over the tremendous change in size of a human embryo caused by changes in the number of cells. This cell death, duck feet, chicken feet, chicken feet are not web. Duck feet are webbed. They start off looking almost identical. And the difference is that

between the digits, between the fingers or the toes, the cells die in the case of the chicken, and they do not die in the case of the duck. And if you go back and look at this, you will see that there are little dots between the digits of the chick, and not the digits of the duck, and those are the cells dying. So, there is a controlled process of cell death that's very important. Tissues, cell type, this is really one of the most extraordinary examples in the body of different cell types, and different cell types working together to a common function. This is a diagram of the retina that I took from your book, and it exemplifies two things: one, a bunch of different cell types. These are all nerve cells that are in the retina, and they are nerve cells that in various ways, either sense light or transmit the signal of the light once the light has been sensed to other nerve cells.

You can see, firstly, there are these different cell types, and you can see secondly, represented by colors, you can see that they're organized in layers. There is a very precise and very important layering of cell types in the retina. If you disrupt that layering, the retina doesn't work. And in many cases of retinal degeneration, the retina doesn't work because the cells have, the layering has been disorganized, and the cells can't make the proper contacts with one another. Position: we talk about axes in the animal, and in the adult as well. We talk about an anterior, posterior axis, which is the set of organs from the head to the tail.

We talk about a dorsal, ventral axis from the back of the animal to the belly. And we talk about a left-right axis from the left to the right. So, if you look at yourself in a mirror again, you'll look pretty symmetric. If you were to peel back your body wall and look at your organs inside, you will see that you are not symmetric at all. You have an asymmetry along your left-right axis. OK, so you will need to know these terms: anterior, posterior, dorsal, ventral, and left-right is easy. And finally, here's three dimensional structure. Here is the heart.

The heart is a muscle. It's actually got several different cell types. But it is mostly muscle where the muscle is arrayed in various, precise, organization. And it's this precise organization of the cells that allows the heart to pump. How do you get this organization? We'll talk about that later on in the course. Can you regenerate this organization either artificially, or in some kind of tissue culture system?

Very tough to do, and as you may know, there is no good artificial heart out there right now. This is a great thing for some of you to think about for your future careers. It's wide open. Are there circumstances where we could regenerate a human heart in a test tube or in a large test tube on a Petri plate, for example?

It would have to be a very large test tube, right, a box, a test box? I don't think so. I think that is really going to be very, very tough to do, and I think we have to think more carefully about how we are going to repair damaged hearts. Again, we'll talk more about this.

So, what I'm going to do now is to show you a movie of the development of an early fish embryo. The kind of fish is called a zebra fish. I work on these in my laboratory. I have about 10, 00 of them there, and I'm going to use

them. Yes, I have 10,000 fish. If you want to come and visit my laboratory and see my fish, you can. It's a fantastic model system.

And I'm going to use this movie and this embryo to show you something about the sequence of events that take place during development. I want you to look for cell division, and I want you to look for structural changes as you watch the movie. Let's look at the movie again without the music. And let me show you what you're looking at. So, to zebra fish, like the chicken, and actually almost like the human develops as a disk of cells, or from a little disk of cells. I'll show this to you again when it starts again, that sits on top of a yolk cell. Chickens have got a yolk cell. That's the yolk of egg. Humans don't. But otherwise things are very similar. Let me try to start that. OK, good. So, we're going to look at this again. Here is the yolk cell.

This big round ball here is the so-called yolk cell, and that's going to be the food of the embryo. These two bumps on top are two cells. This is a two cell stage embryo.

And as you watch the movie for the last time, and I'll post it on your website so you can watch it as much as you want, you'll see these two cells divide into four cells, and eight cells, and 16 cells, and so on, until they've made a little dome of cells sitting on top of the yolk cell. And then, at that point, suddenly at some point, and this is very interesting. That group of cells realizes that there's enough of them, and they start to move. And they spread out to cover the whole yolk cell.

And as they do this, a bunch of them also move to the right hand side of the board. And if you watch, you could see stuff happening. And at the end of the movie, you could see something that might have been somewhat recognizable to you as a developing little animal in that it had an eye, and I'll point this out, and it had a tail. So, let's watch it again and I'll stop it at various points, and I will point out stuff.

Where did my mouse go? There it is. OK, so here's the cell division. Cells are dividing. They are dividing, they're dividing, they're dividing, and making this little dome on top of the embryo on top of the yolk. So, this little group of cells is going to give rise to the whole fish. And although humans don't have a yolk cell like this, human embryos look very similar.

And now, this group of cells is going to spread out. You will see a kind of haze spreading out over this yolk cell.

That's the cells moving. There they go. They're moving, moving, moving, moving, moving down. And at the same time, a bunch of them are moving to the side of the embryo. And as you watch, take a look. Here is the high. This oval is the eye and the brain is going to develop up here. And watch these little shiver and shaky things on the side as well. Those are the developing muscles.

OK, and so, there it goes, a lot of shape forming.

And we are going to move on from there. OK, so go and take a look at this at your leisure. We are going to talk about some of those processes again. So, let's move on to the next point that we need to deal with, and that is a point that I've called here cell fate requires differential gene expression. But I'm going to state it more simply on the boards, which are now not responsive.

OK, here's an easy way to state this. Genes control development.

OK, well, that doesn't sound so surprising. Genes control everything as far as you've been told, but let's talk about that in a bit more detail. And there are three things you should know about this. Firstly, the function of a cell depends on the specific proteins present.

So, cell function depends on specific proteins.

Second thing: all cells contain the same genes or the same set of genes -- And the third thing is that only some of those genes are used in each cell type.

And I'm going to use the term expressed, which we've encountered before. Only some genes are expressed in each cell type. And I'm also going to introduce to you a term called fate where the term is similarly used to the English term fate, but not quite, where fate and development refers to the final form and function of a cell.

All right, so let's see what we have. Here's something we've seen before, this kind of tiresome diagram that's useful and that should be really familiar to you, the passage of information from DNA through an RNA intermediate to a protein product. And the formation of the final product from the gene is termed gene expression. Cell types are different because they make different proteins. We've talked about these three cell types previously.

Erythrocytes are so because they're making globin, which carries oxygen around the body. Neurons are making proteins, which send out the filaments, and chemicals that allow nerves to communicate with each other and so on. Number 15 on your hand out, the first slide on your handout, you need to know this really, really clearly. This is important.

And part of the deal here is something I'm going to write on the board, firstly, that in any process of figuring out what a cell is going to become, there are multiple steps to a final fate. It doesn't just happen at once.

And secondly, I want to make the distinction between regulatory genes and differentiation genes -- -- where regulatory genes, we can rephrase this, control cell fate, and differentiation genes affect cell fate.

They carry out cell fate. And here is a litany that I've written out for you that is important that you know. In the life

of a cell, as it's deciding what to become, it goes through multiple stages. It starts off not knowing what it's going to become, and we call those uncommitted cells. Kind of like you when you came to MIT, you were uncommitted and perhaps still are as to what you're going to do next. But over time, through the passage of time, you get various inputs and you decide what you are going to become either as a cell or as an MIT student. And at that point, you are called committed or determined. That's the jargon. You need to know it. It's very important. Committed or determined cells have made the decision what to be. But they haven't gone on and become the final thing that they're going to be. So, maybe you are premed, and by now you have committed to being premed. So, you are different than when you came in here, but you certainly are not a qualified physician at this point. In order to do that, you're going to have to go through another bunch of steps and find your final form. You're going to have to differentiate into a physician or into a cell type. So, this uncommitted-committed differentiated litany triad is something we're going to talk about over and over. It's going to come up throughout the course probably in most of the lectures that both I and Professor Jacks will give you. During this passage, and you've got the slide, this is the slide you actually have, is two sets of genes are activated, regulatory genes and differentiation genes. As the uncommitted cells decide what they're going to be, regulatory genes are activated.

As the committed cells go on to read out the final thing, their final function, the activation of differentiation genes takes place. So, how does it work? How does a cell decide what to become, and how do different cells decide to become different things? Well, this is the way I think about this. This isn't the way your book thinks about it, but this is the way I think about it. I think that there is a combinatorial regulatory code that controls cell type.

And so, let's have an example of the three cell types I've talked about before, your erythrocyte neuron and sperm. And let's look at the regulatory genes that each expresses. You can look on the screen. You have this in front of you as a handout. So, I've arbitrarily said that an erythrocyte is expressing regulatory genes, R, F, and K, the neurons expressing A, I, and K, and the sperm is expressing A, F, and K.

OK, now let's look at those. Those three groups of three letters are different from one another. And so, for each of these cell types, there is a unique set of letters or a unique regulatory code. What's this code made up of? Well, it's made up of cell type specific factors, or cell type specific regulatory genes, regulatory gene products. RNI are expressed in just the erythrocyte, or just the neuron. They are cell type specific regulators. General factors, K is expressed in all of the cells, and restricted factors, F and A, are expressed in just two of the three cells. And you can do that for any cell type. You can come up with some kind of combinatorial code of gene expression of regulatory genes that control cell fate. Now, these regulatory genes will go on to activate the expression of a whole bunch of differentiation genes. And usually a small set of regulatory genes will activate a large set of differentiation genes that carry out the final function.

So, here I've given you an example for erythrocytes. It's, again, on your handouts. The regulatory code for

erythrocytes, RFK, a small regulatory code, actually it's probably about 20 genes, will go on and activate at least a hundred genes which will be the gene products that actually carry out the function of red blood cells. OK, so regulatory genes activate differentiation genes. What's all this regulatory stuff?

What are these regulatory genes? So, here you have to think back to previous lectures. Remember this diagram? You have it.

You've had it several times. This is the hierarchy of things that happened from the gene in the nucleus to the final, modified, localized protein products. You can control, the cell can control gene expression at any point along this hierarchy.

It can control transcription, initiation, or termination, RNA splicing, stability or exports, translation, the initiation or elongation. It can control export of proteins to different parts of the cell through protein trafficking, modification and control of protein stability. And there are more. OK, this is some of the list of steps at which gene expression can be regulated. And those hypothetical regulatory factors I told you about in the last couple of slides can be anything that affect any of these steps from the gene to the final product. OK, all right, so here's another one that you need to know.

Complexity increases with developmental age.

And what I'm going to tell you about is how as development proceeds, as you get different cell types forming, you have to make groups of cells with specific regulatory codes.

And these cells -- And these regulatory codes will lead to a specific fate. So, here's a nice example just by looking at development of an organ, for example, and this is important if you're going to try to engineer an organ through tissue engineering. You have to understand there are normally many, many steps involved. These are the beginning steps in formation of the eye.

And it doesn't matter what each of these steps are, but if you look at the progression of cells, each of these lines are groups of cells. You can see that they organized in different ways.

They fold. Bits break off, and you'll end up with a structure that's a lot more complex just in a pictorial way than it was in the beginning. And that is true in terms of every aspect of this organ.

It is more complex at the end than at the beginning. And somewhere through here, you have to increase the complexity of this developing tissue. So, how do you do it?

This is the way I like to think about this, and this is number 20 of your handout. Here's an egg or a zygote, if you

like, a one cell embryo. It's one cell. There's only one kind of cell there.

Or, I like to think in terms of territories. There's only one territory there. Now, I've also put a red dot in the cell. And this red dot can be anything.

But it really is in terms of our conversation a group of regulatory gene products, or one regulatory gene product.

Watch what happens when in my hypothetical example the cell divides. The red dot goes to one cell, and not the other cell. And so, now I've got two different kinds of cells. The regulators are in one cell and not in the other cell. And then, I've gone through this and done it again. When the cells go to four cells, suddenly I've magically put a blue dot in one of the cells, and there's a red dot in another cell, and there's some cells with no dots. And those give me three different kinds of cells, or if you like, three different kinds of territories. And for territories, you can read regulatory code, set of regulatory gene products. So, what have we done?

What we have done in this example is to take a zygote or an egg, if you like, that is symmetric at least along one axis, and to divide it so that it's now got two daughters cells that are different from one another. So, there is a breaking of symmetry somewhere in this process. Now, in actual fact, if you look at the egg, it's really only symmetric in one axis. And so, it's not uniformly symmetric. But one of the things we think about in development is that every time you make a new cell type, you have to break symmetry. You get two different kinds of cell from one kind of cell. All right -- So, I'll come back to that diagram in a moment, but I want to, the fifth point I want to give you is that regulatory factors act within cells and between cells.

Really important, that's why it's up on the screen and it's on the board. I'm going to tell you about three things. I'm going to tell you about regulatory factors that are given the term, determinants that work in a cell autonomous way. That means with inside the cell that carries them. I want to tell you about regulators called inducers that act between cells or in cell-cell signaling.

And I'm going to tell you about a subset of inducers called morphogens, which work in a concentration dependent way.

So, this is a kind of magic, and it isn't a kind of magic. The molecules I'll tell you about our molecules that you've heard about previously, OK?

The phrasing, the jargon is a little different and you need to learn it because this is jargon that's used throughout biology. Let's first of all talk about these things called determinants. And the notion here is that cells become different because of what they inherit. And I've drawn for you here, and this is number 21 on your handout, I've drawn for you here a cell, this blue thing with squares in it. The squares are determinants, and determinants are some kind of regulatory factor. They may be one regulatory factor, maybe more than one regulatory factor. They

may be transcription factors. They may be splicing factors. They may be micro-RNA's. They may be all the things we've talked about in previous lectures, but I've drawn them as squares.

And here's a cell with those little squares. And I've drawn it so that all the squares are on one side and not the other. And of course, you're sitting there asking, how did the squares get on one side but not the other? And that is a really good question. And I'm not going to tell you how to get on one side but not the other. But there is a whole system in the cell of pulleys using things like microtubules where specific squares, specific molecules, can actually be pulled to one side of the cell or the other. And then, you're going to ask me, well, how do they know which side of the cell to move to?

And that's another great question that I'm not going to answer. But suffice to say there is a whole molecular machinery that can move regulatory molecules to different places in the cell. But let's go back to our cell that's got squares on one side and not on the other. When it divides, it gives rise to a cell that's got lots of squares, lots of determinants, and another cell that doesn't have any.

The cell with the determinants goes on to make cell type one because it has a specific set of regulatory factors. The cell without them goes on to make another cell type. It's not that it doesn't have any regulators; it just doesn't have the ones in the squares. So, cells are different because of what they inherit. Here is a fantastic example. These are early worm embryos, early embryos of [scientific name]. We mentioned this last time that Professor Horvitz in the biology department got the Nobel Prize for it several years ago. And this is an example of determinants moving to different cells during development. So, the top row are cells that have been stained for their nuclei. And you can see one cell, two cell, and 32 cell stage embryo. These bottom pictures are florescent pictures of things called pea granules. These are determinants. And you can see even at the one cell stage, there are all located on one side of the cell. At the two cell stage, they all go to one of the two cells. And at the 32 cell stage, they are all in the cell over here. And those cells or that cell is going to give rise to the egg and sperm of [scientific name] , and those pea granules are determinants for the germ cells.

Here's the other big thing. Cell-cell signaling: cells may secrete an inducer. This is a ligand. Remember signal transduction that you talked about in cell biology II?

Those same ligands that are secreted by cells bind to receptors on target cells. Receptor ligand interaction leads to activation of signal transduction pathways, again, from cell biology II. And that over time can change the genes that a cell is expressing and changed the fate of the cell. So, we call these things inducers because of the specific assays involved. But really, they're ligands, often proteins, sometimes lipids, that bind receptors, activate signal transduction, and change cell fate.

This is number 23 on your handout. So, induction: a process by which cells become different because their neighbors tell them to do so, and a variation of induction, oh, here's an example of induction, sea urchin embryo, the induction is everywhere.

But I've picked this one example. Sea urchin embryo goes on through time to make this little thing called a pluteus larva. If you remove the bottom half of the embryo, it goes on. The rest goes on to make a kind of a round thing with lots of cilia sticking out. And you can take four little cells that were right on the bottom of the normal embryo called micro-mirrors and stick them back on this top half of the embryo that didn't make a normal one.

And it will restore a pretty normal embryo. And it's not that the red cells have made all the parts of the embryo that we're missing, or the parts of the larva that were missing. It's that those red cells have sent out a signal, and that signal has told other cells what to become. And in the case of the sea urchin, part of that signal is something called the delta protein. This is a micrograph of the a sea urchin embryo at a very early stage, and this brown-purple group of cells here are those cells that contain the delta protein. These are the micro-mirrors, and these are involved in inducing the rest of the embryo to become what it does. Now, inducers, ligands, can be tricky.

They can act in different ways at different concentrations. And this is one of the big questions of biology. How do they do this?

So, for example, if you have a lot of an inducer, it may tell cells to become cell type one. If you have a little bit of an inducer, it may tell cells to become cell type two. And we'll talk about in a subsequent lecture the molecular basis for this. So, an inducer that can induce different fates at different concentrations is terms a morphogen --