Activity 1: Fact or Fiction?

Based on video and online text content

15 minutes (10 minutes before and 5 minutes after the video)

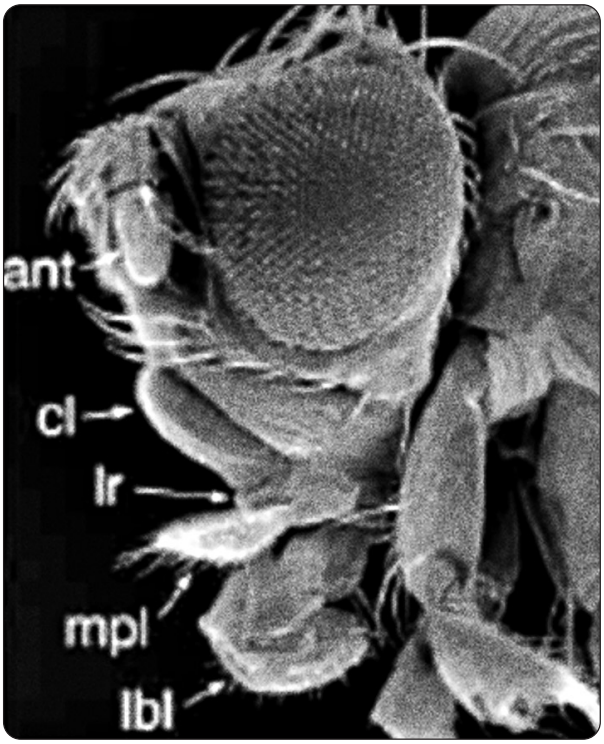
Setup

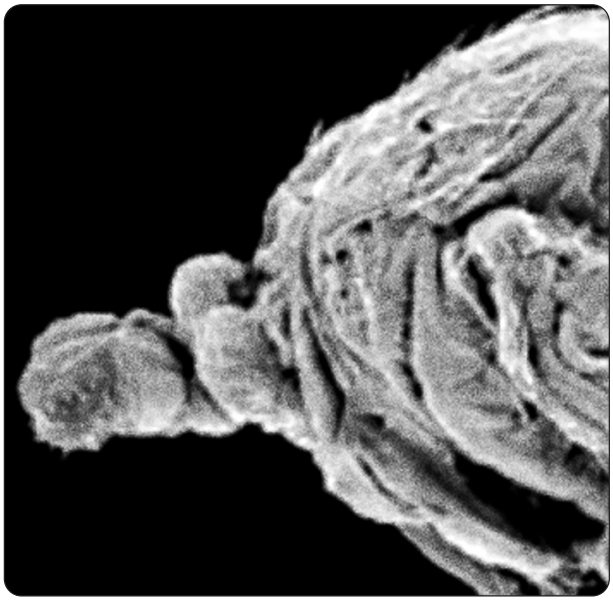
Recent results in developmental genetics have been eye-popping—literally. The electron micrographs on the overhead transparency show a normal fruit fly on the left; and, on the right, a fruit fly that has developed without eyes and several other head structures. In this unit, we'll see more of the revelations that have come from the study of developing organisms. Before viewing the video, look at 10 statements about developmental genetics. All sound surprising, and half are actually true. Just based on your instincts, which do you think are the true statements? After watching the video, review your choices. Information on some statements can be found in the online text chapter.

Materials

- One transparency of the *Drosophila* Head Micrographs
- One copy of the Statements per person (master copy provided)
- One copy of the Genetics of Development online text chapter per two people (available online at http://www.learner.org/channel/courses/biology)
- Tips and Suggested Answers

Drosophila Head Micrographs





Statements

All of these statements about developmental biology sound unbelievable, but five are actually true. Can you choose the five statements that are *entirely* true? Even if you don't know anything about this subject, just take a educated guess. Answers, found in Tips and Suggested Answers, will be discussed after watching the video.

1. The phenotype of the fly in the electron micrograph on the left is caused by altering the expression of a single gene, called *eyeless*.
2. One of the most commonly used organisms for developmental research is the zebra, because of the universality of its developmental processes and its surprisingly brief gestation period.
3. In animals, most genes are not grouped together by function. However, the Hox genes that regulate development are grouped together by function, and arranged in order of the body segment they control and the time they are expressed.
4. A compound made by the corn lilly plant blocks a receptor required for signaling during animal development. Sheep that are exposed to the compound in utero have a cyclops phenotype.
5. Women who are trying to become pregnant are advised not to take an anti-acne drug called Accutane because it triggers a response similar to fertilization, resulting in a haploid embryo that cannot complete development.
6. The most promising medical feature of embryonic stem cells is that they can be transplanted into any adult without being rejected.
7. A gene called Hedgehog is a crucial signal-transduction component of animal development. The gene got its name because mutations cause fruit fly embryos to have a spiny appearance.
8. There are some developmental genes, encoding MADs box transcription factors, that are so highly conserved that they are found in both plants and animals.
9. The *C. elegans* species of nematode worms is an excellent model organism for development: each worm develops in a slightly different way and ends up with a different number of cells, just like a human.
10. After the age of about 25, a human no longer has any stem cells.

Source of micrographs: Jiao, R. et al. 2001. *Development* 128:3307

Fact or Fiction? Answers

1. True.
2. False, but zebra*fish* are a commonly used organism for developmental research.
3. True.
4. True.
5. False. Accutane is contraindicated for pregnant women, but it is because it triggers incorrect expression of Hox genes during development.
6. False. Embryonic stem cells come from an embryo that resulted from fusion of a sperm and an egg. As a result, it has a unique genetic makeup and novel combination of cell surface antigens that could be rejected by the immune system of a transplant recipient.
7. True.
8. True.
9. False. The nematode worm *C. elegans* is used as a model organism because the developmental fate of every cell has been determined, and every non-mutant individual has a precise number of cells: 1031 in the males and 959 in the hermaphrodites.
10. False. Adults have stem cells that are continually dividing to generate replacements for skin, sperm, blood, and other cells.

Activity 2: Mommie Dearest

Based on video and online text content

45 minutes

Setup

A breakthrough in the genetics of development was recognized with the 1995 Nobel Prize in Physiology and Medicine, given to Edward B. Lewis, Christiane Nüsslein-Volhard, and Eric F. Weischaus for their work on maternal effect genes. Although inherited as nuclear genes, their phenotypic effects depend on the genotype of the mother, not the individual. In this exercise, work in pairs to read about these genes and their role in development from the Genetics of Development online text chapter. Then, set up some fruit fly crosses that involve mutations in maternal effect genes. Follow several generations in the crosses to see how maternal effect genes are inherited and how they exert their phenotypic effects.

Materials

- One copy of the Readings, Worksheet, and Discussion Questions per person (master copy provided)
- Tips and Suggested Answers

Readings, Worksheet, and Discussion Questions

Part 1: Readings

Before starting on the problems, familiarize yourself with maternal effect genes by reading this excerpt from the Genetics of Development online text chapter (available online at http://www.learner.org/channel/courses/biology).

Establishing the Gradient and Coordinate Genes

Development is a process where the products of some genes turn other genes on or off. But how does the process start? Even before fertilization, development is occurring. We normally think of an egg as a storehouse of energy supply and nutrients that the embryo will use as it develops. While this is true, the egg also supplies information to establish a molecular coordinate system. This coordinate system provides a way to tell "which end is up"; in other words, the location of the embryo's head is determined even before the egg is fertilized.

Coordinate genes are named because they establish the primary coordinate system for what will become the embryo. One important example of a coordinate gene is bicoid, which is involved in establishing the anterior-posterior polarity in *Drosophila*. How does bicoid do this? To understand this process, we need to first discuss how bicoid gets to the anterior part of the egg. Nurse cells surround the anterior region of the egg in *Drosophila* and other flies. Cytoplasmic bridges allow various substances—in this case mRNA from bicoid—to be transported from the nurse cells into the egg. The bicoid mRNA is then trapped by proteins produced by other genes. The result is a concentration gradient of bicoid mRNA: the anterior end has the highest concentration and the posterior end lacks it. Translation of bicoid is inhibited until after fertilization, leading to a bicoid protein concentration gradient.

In addition to bicoid, other coordinate genes help establish an anterior-posterior polarity. Still other coordinate genes allow the establishment of a dorsal-ventral gradient. These coordinate genes, like bicoid, are sometimes called maternal effect genes. **Maternal effect** occurs when the phenotype of the individual is dependent on its mother's genotype, not its own. In cases of maternal effect, the transmission pattern of the alleles is the same as in standard Mendelian genetics but the action of the gene occurs a generation later. For example, consider a maternal effect gene where the mutant allele (m) is recessive to the wild-type allele. In the cross of homozygous, wild-type females to homozygous, mutant males, all the F1 offspring are heterozygotes and appear normal. In the reciprocal cross, all of the F1 offspring are heterozygotes but have the mutant phenotype. Although the F1 offspring are genotypically identical in the reciprocal crosses, they are phenotypically different. This is because phenotype is due to the action of the mothers' genotype. Maternal effect is not the same thing as maternal inheritance, such as in mitochondria, where the genetic material is transmitted only across maternal lines.

Responses to the Concentration Gradient

Coordinate genes such as bicoid lay down the grand plan, so to speak, upon which the genes downstream will act. The pattern of the developing embryo arises as these downstream genes are activated or repressed.

Like many of the other coordinate genes, bicoid encodes a transcription factor; thus, there is a concentration gradient of a transcription factor. The next genes in this developmental cascade, the "gap genes," possess binding sites for this transcription factor. Gap genes are so named because mutations in these genes can produce larvae with "gaps" (missing several segments). These genes differ in how many bicoid binding sites they have and, thus, vary in their sensitivity to this transcription factor. Some gap genes will become active at low concentrations of bicoid, while the activation of others will require higher concentrations. Due to the concentration gradient, different regions of the developing embryo will activate different gap genes.

Unlike the coordinate genes, the gap genes are not maternal effect genes. The activities of the embryo's gap genes (and not those of the mother's genes) determine the phenotype. Gap genes also encode for transcription factors, and these affect the transcription of genes that further refine the patterning of the *Drosophila* embryo.

Part 2: Worksheet

Now that you are familiar with maternal effect genes, work through these problems. Some answers can be found in Tips and Suggested Answers.

1. An example of a maternal effect coordinate gene that is expressed in the anterior section of the fly embryo is *bicoid*. Null alleles of *bicoid* have recessive effects, and *bicoid* is an autosomal locus.
    a. Draw the cross between a female fly that is a heterozygote of a null and a wild-type allele, with a male that is also a heterozygote. (Write the genotypes of the parents and all possible offspring.) The null allele is designated *bcd* and the wild-type is designed bcd+.

    b. What are the expected genotypes of the offspring (and in what ratios) from such a cross?

    c. What are the expected phenotypes of the embryos from this cross?

    d. What would you expect for the phenotype of an embryo that is the result of a homozygous *bicoid* null mother mated to a homozygous wild-type male? Draw out this cross as well.

2. The protein from the *bicoid* gene is a transcription factor that turns on expression of *hunchback*, a gap gene. Like *bicoid*, *hunchback* is also on the third chromosome.
    a. Draw the cross of a female that is homozygous for the null allele of *bicoid* and wild-type for *hunchback*, with a male that is homozygous for the wild type allele of *bicoid* and homozygous for the null allele of *hunchback*. The wild-type allele of *hunchback* is designated hb+ and the mutant is *hb*.

    b. Given a *Drosophila* embryo with a mother that was homozygous for a *bicoid* null allele, what would you expect for the expression pattern of the hunchback protein?

    c. What would be the expression pattern of bicoid protein in a *Drosophila* embryo that was homozygous for the wild-type allele of *bicoid*, but was homozygous for a null allele of *hunchback*?

Part 3: Discussion Questions

1. How is maternal effect inheritance different from mitochondrial inheritance? In particular:
   a. Which genes are nuclear? Which are cytoplasmic?

   b. In which type of inheritance do the mother and offspring always share phenotypes?

   c. In which type of inheritance are alleles inherited equally from the mother and the father?

2. Challenge question (may be more difficult): Two species of fruit flies each have very similar patterns of abdominal bristles; however, hybrids between these species often have deformed bristles. Recent studies have found that the gene (*shaven baby*) involved in making those bristles has fourfold lower expression in the hybrids than in the pure species.

   Based on what you have learned developmental genetics, propose an explanation for these results. Hint: Think about what might be different in the two species.

Mommie Dearest, Suggested Answers

Part 2: Worksheet

1. a. 25% *bcd+/bcd+*, 50% *bcd/bcd+*, 25% *bcd/bcd*
   b. The gene is maternal effect, and null alleles are recessive. Given that the mother is heterozygote, all embryos should be phenotypically normal.
   c. Even though the offspring is a heterozygote, its phenotype is determined by the maternal genotype, and the mother is a homozygous null. Individuals without any *bicoid* expression would lack anterior segments—the head and thorax—and would likely have two tails.
   d. Even though the offspring is a heterozygote, its phenotype is determined by the maternal genotype, and the mother is a homozygous null. Individuals without any *bicoid* expression would lack anterior segments—the head and thorax—and would likely have two tails.

2. b. The embryo would not express hunchback protein, because it lacked the bicoid protein.
   c. The expression of bicoid would be normal—expressed in the anterior of the fly and not the posterior—because hunchback expression doesn't affect *bicoid* expression.

Part 3: Discussion Questions

2. The species have diverged in both the promoter of *shaven baby* and the transcription factor(s) that bind to that promoter. In each of the pure species, binding between the transcription factors and the promoter is normal. The hybrids, however, have the wrong combinations of transcription factors and promoter.

Activity 3: Small Cells, Big Controversies

Based on video and online text content

60 minutes

Setup

Stem cell research has yielded key insights into the fundamentals of development. It has also promised great medical advances, especially in tissue transplants. Because this area of research includes work on stem cells that come from embryos, this field is also the center of much controversy. *Rediscovering Biology* interviewed a leading stem cell researcher, Dr. Markus Grompe of Oregon Health and Sciences University. Read excerpts of his interview and, in teams of three or four, discuss the scientific facts and the public opinions about stem cells.

Materials

- One copy of the Discussion Questions per person (master copy provided)
- One copy of the Interview Transcript Excerpts per person (master copy provided)

Discussion Questions

1. Read Excerpt 1, and then discuss these questions:
    a. What are the developmental differences between totipotent and pluripotent stem cells? How are they different in potential medical functions?

    b. How would you explain the differences between embryonic, prenatal, and adult stem cells?

    c. Dr. Grompe, in his interview for *Rediscovering Biology*, says that embryonic stem cells are "not really little human beings" because they are not totipotent—they cannot generate a placenta. Is he splitting hairs when he distinguishes between embryonic and prenatal, totipotent, and pluripotent? Or are these useful distinctions for scientific and public policy discussions?

    d. As we just read, embryonic stems are obtained directly from embryos. One way to obtain human embryos is to combine a donated sperm and a donated egg in a test tube, and let the zygote begin to divide in vitro. State all possible opinions in favor and against generating embryos this way for the purpose of obtaining embryonic stem cells. If you feel comfortable doing so, state your own personal opinion.

    Stem cells have also been taken from embryos that were generated as part of an infertile couple's therapy. State all possible opinions in favor and against taking stem cells from the unused embryos of an in vitro fertilization procedure. If you feel comfortable doing so, state your own personal opinion.

2. Read Excerpt 2, and then discuss these questions:
    a. What are the political and ethical connections between the issues of embryonic stem cells and human cloning? Do you think people have difficulty seeing the difference between these procedures? If so, what can be done to make the issues more clear?

    b. In August 2001, President George W. Bush announced that federally funded labs could work with only those embryonic stem cell lines that were established before the announcement. Of course, privately funded labs and labs in countries with other regulations are not subject to these rules: they can generate new embryonic stem cell lines from embryos that were not used after an in vitro fertilization, or from embryos generated solely for the purpose of extracting stem cells. What factors were involved in this decision by President Bush's administration?

    c. How can the government effectively regulate the use of stem cells in research? Who should decide which cells should be made available for research? Is this an issue for state, federal, or global authorities to decide and regulate?

d. Does the policy accurately reflect public opinion about embryonic stem cells and their uses?

e. What effect, if any, has this policy had on public health in the U.S.? Will basic research be affected?

f. In September 2000, several celebrities with diseases and disabilities that might benefit from stem cell research—such as Mary Tyler Moore, Christopher Reeve, and Michael J. Fox—asked Congress to allow federal funds to be used for embryonic stem cell research. Do you think this kind of publicity affects public opinion or federal policy?

g. What diseases and medical conditions could potentially be treated or cured through stem cell therapy?

3. Read Excerpt 3, and then discuss these questions:
   a. Which do you think is more promising for research on development: adult or embryonic stem cells?

   b. Which do you think is more promising for medical treatments like transplants: adult or embryonic stem cells?

   c. Is it necessary to use embryonic stem cells? Or can adult stem cells serve the same research purposes?

   d. Would you be able to discuss these topics in your high school biology classes? Or are the issues too sensitive? If you would be able to discuss it, would you allow the expression of personal opinions? If so, how would you moderate the discussion?

Interview Transcript Excerpts

Excerpts from a 2003 interview with Dr. Markus Grompe of Oregon Health and Sciences University, for the *Rediscovering Biology* Genetics of Development unit. The entire interview transcript is available online at http://www.learner.org/channel/courses/biology.

Excerpt 1:

Q: Can you please define a stem cell?

A stem cell is a cell in the body that is responsible for renewing other tissues. It is not a differentiated functioning cell, but it is a cell that's sort of the reservoir for other cells that are needed in the body. Stem cells exist both before birth—prenatal stem cells—and they continue to exist in the adult organism.

An "embryonic" stem cell is actually a cell that doesn't naturally exist in humans or in animals. It's actually a kind of a laboratory stem cell that has been used extensively since the late 1980s for experimental biology. This very specific kind of cell [is] derived from early embryos and is used in the lab. Those are now available for human and mouse and a variety of other species. I tend to refer to the cells that naturally exist in the early developing organism as "prenatal" stem cells, because the term "embryonic" stem cell is already basically very narrowly defined as that particular kind of cell.

It all starts with the fertilized embryo when the sperm and the egg come together and that's the only cell really that one would describe as a totipotent stem cell, in the sense that that first one- or two- or four-celled embryo has the ability to give rise to the entire fetus as well as the placenta. So the difference between a totipotent and a multi- or pluripotent cell is that only the totipotent cells can give rise to both the placenta and the embryo both.

The embryonic stem cells that have been talked about so much are actually cells that can give rise to virtually all the tissues of the fetus and the adult organism, but they do not make placenta. So those embryonic stem cells that are talked about quite a bit in the newspapers and so forth, are not totipotent, they're not really little human beings. They have the capability to making all the tissues of the fetus, but not the placenta.

Q: And the placenta is necessary for the fetus?

For complete development, yes. The very earliest cells are the ones with the most developmental potential. The embryonic stem cells that people are beginning to use for tissue repair studies and so forth are derived from the very early embryo at the so-called blastocyst stage, which is where the embryo has first developed a cavity within it and there's a group of cells in there called the inner cell mass. What people do for mouse and human and primate embryonic stem cells, is pick out those inner cell mass cells and then grow them in the laboratory. What's been learned from the mouse in particular is that you can actually culture these cells in a dish for many many generations and then inject them back into blastocysts and they have the capacity to develop back into a full adult mouse, which is the basis of a lot of the genetic manipulation of mice that we use in the laboratory.

I think that the distinction between totipotent and pluripotent is important in regards to the ethics of this discussion, because some people are under the impression that embryonic stem cells are little people being grown in the tissue culture dish in the lab. These are not embryos; they're embryo-derived. So in the process of generating embryonic stem cells an embryo is destroyed, but it's not the same thing as cloning or actually having the equivalent to a human conceptus in the lab.

Q: What's the process to obtaining embryonic stem cells?

The procedure by which embryonic stem cells are made differs a little bit from species to species, but basically fertilized embryos are taken in the tissue culture dish and they are allowed to develop to the blastocyst stage, which consists of 32 to 64 cells. You can see that under the microscope, it takes several days for that to happen. At the blastocyst stage there will be a group of cells on the inside of the embryo called the inner cell mass. They are dissected out under the microscope and then they are dispersed and grown on a group of cells that we call feeder cells. They essentially then start to grow like bacteria, doubling and doubling and doubling again with virtually unlimited capacity for that process.

The nice thing about embryonic stem cells is, though, they haven't forgotten how to go back and be differentiated and stop growing. So that if they are put back into an environment such as a developing embryo where they get the right signals, they stop growing uncontrolled and they start behaving like a proper inner cell mass again.

Excerpt 2:

Q: Because there has been controversy about this and there are ethical questions, are there some labs that have been using the totipotent cells? Is there advantage to doing research with that and has it happened?

Well, there are labs that work with actual human embryos. Those are particularly—in terms of the research applications—the people interested in cloning. Those cells actually grow very very poorly and so you really don't have the ability to propagate them extensively and use them for tissue repair studies. What people have been using them for is to basically try to put into these embryos the nuclei from adult cells and that's called cloning.

That's what we've been hearing about here the last few weeks or months, is basically killing a human embryo and transferring the nucleus of an adult cell into it. I think the ethics with embryonic stem cells come from the fact that to get them you have to destroy an embryo. But once they're there and exist and can be grown, there are no further ethical problems at that point.

I think this is where the policy of the Bush government has come from, is the fact that [it is OK to use] the already existing lines.

Q: So the ethical question for using the pluripotent cells arises because the embryo at that early early stage is essentially destroyed?

Yes. So, basically, to get embryonic stem cells, the embryo is allowed to progress to the blastocyst stage, which is 32 or 64 cells, and is harvested essentially at that point, or a portion of the embryo is cut out. Basically that's the end of that embryo except for the cells in the inner cell mass that can then essentially grow indefinitely; they're in a sense immortal.

Excerpt 3:

Q: Now can you talk about adult stem cells?

Adult stem cells are, for the most part, tissue-specific adult stem cells; meaning that for a certain tissue, you need in some instances a stem cell that continuously divides and spawns new cells to stay alive. There are tissues that turn over all the time and you basically need stem cells—so that would be blood, skin, intestine, or sperm production. Those are all examples of tissues where there's continuous cell division going on and all of those tissues have stem cells that are responsible for tissue renewal.

People have known and written about [these] for a considerable length of time. It's now become apparent that most, if not all, tissues actually have stem cells. Although most tissues are not continually dividing all the time, there are cells that are responsible for tissue repair in the case of injury. So for example, let's say your liver gets hurt by a virus or something like that. Even though liver cells on average only divide once a year in a normal person, you can wipe out your liver with a virus or an injury quite drastically and then you might need stem cells. These are adult stem cells that we call facultative, meaning they are only activated when they're needed as opposed to those in the tissues like blood that are always activated and continuously dividing.

Finally there's a new concept in terms of adult stem cells, which is the idea that adult organisms, including people, continue to harbor some of these very early stem cells like the embryonic stem cells, basically pluripotent stem cells. That's really a concept that's only emerged in the last five, six years and has generated a lot of excitement in terms of the therapeutic potential of those cells.

Q: What are the advantages of using embryonic stem cells or prenatal stem cells for research?

The reasons embryonic stem cells are advantageous for research are many-fold. The main advantage that I see in terms of practical use is the fact that these cells can grow virtually indefinitely in the tissue culture dish. It's possible to share cells between laboratories, it's possible to have comparison of results between different laboratories. But just the sheer fact that they are what we would call immortal allows very very easy experimental manipulation of the cells.

Embryonic stem cells have the other advantage that they are multipotent and can turn into many different types of tissue in culture, and therefore it's possible to learn from studying embryonic stem cells how differentiation occurs. Basically, how you go from multipotent to developmentally restricted and finally differentiated. People are using them for that purpose.

Q: Are there advantages of using adult stem cells for the same type of research?

The adult stem cells have the advantage of the fact that you can have many more cell donors; it's easy to get the cells. For example, it should at least in theory be possible to get adult stem cells from any person who wishes to donate cells. In terms of research, they have really not many advantages over embryonic stem cells, with the possible exception that what we learn about differentiation from embryonic stem cells could potentially only pertain to embryonic differentiation.

There's a paradigm in developmental biology that says that the way a liver stem cell becomes a hepatocyte—for example, in the embryo—is the same process in principle that happens later in life when a liver stem cell becomes a hepatocyte. But that is only a hypothesis at this point. We really don't know in most cases whether adult stem cell differentiation mimics embryonic stem cell differentiation. It's possible that what you would learn from embryonic stem cell differentiation would not apply to adult stem cells.

Q: Can you summarize in a "compare and contrast" fashion the use of embryonic versus adult stem cells?

Embryonic stem cells and adult stem cells can be both used for research. There are several advantages and disadvantages to both. Again, the most important advantage of embryonic stem cells is that they can be easily grown to large numbers; it takes a very short period of time to grow a lot of them, which makes it easy to study. Also the fact that they can develop into multiple tissues makes it possible to study those processes.

The disadvantage of adult stem cells in comparison is that they grow much more slowly and at lower density, so it takes a long time to make lots of adult stem cells. However, the advantage of using the multipotent adult progenitor cells is that they would potentially teach you about developmental processes in the adult, which could be very different from embryonic stem cells. So, in that sense, even though they grow in a more difficult system, they have the advantage of probably reflecting the status of adult stem cells more readily.

In terms of clinical application, there are also quite important differences between embryonic stem cells and adult progenitor cells. The most important one is that embryonic stem cells are derived from donor fetuses that are immunologically mismatched to the person you'd want to be treating. You would have the same issues as you currently have with organ transplantation or with blood transfusions, where you might have to actually use immunosuppression to be able to use those cells. With the adult stem cells it should be possible to derive those cells from the patient herself, so you at least in theory may be able to get away completely from using immune suppression. So the immunological mismatch is a problem.

The other issue with embryonic stem cells is that when they're injected or when they're transplanted without additional modification, in animals at least they form tumors very easily. There is a significant safety issue with embryonic stem cells. Whereas the adult stem cells as they've been studied to date, do not form tumors in any kind of setting. So there are differences for clinical use in that regard.

Q: Would another disadvantages of using adult stem cells for clinical use be that the genetic makeup of that cell is going to be the same as the person you're putting it back into and the same mutations may be there?

Adult stem cells are thought by some to have the disadvantage of being a problem with genetic disease. For example, if you derive adult stem cells from a person with a lung genetic disease, the cells that you derive from that person are also of course going to have that same genetic disorder. Even though they're immunologically matched, you couldn't do a cure with them because they have the same genetic defect. However, that problem is easily surmounted, because like embryonic stem cells, adult stem cells grow extensively in tissue culture. It is possible to correct the genetic defect first *in vitro* and then use those genetically modified cells. The only difference between the stem cells and the patient are that the stem cells have been cured of the genetic defect.

Q: Can you talk about the pros and cons of a patient receiving his or her own cells?

There are disadvantages and advantages to using the patient's own cells for the treatment of Type I diabetes in terms of stem cell therapy. It's important to note that Type I diabetes comes about by immunological rejection of the patient's own beta cells. So, the thinking is that if you were to generate beta cells from that patient's own tissue, you would basically restart the entire process. In other words, the immune system would come after those beta cells again unless you use immune suppression. If you use embryonic stem cells from a donor that's not tissue matched to the person with diabetes, it could have both a positive or a negative effect. The negative effect would be that the immune system might also attack those cells because they are foreign. The positive effect might be that that immunological rejection may be more easily managed than the original immune rejection of the beta cells.

Until those kind of experiments or studies are done, it's really impossible to know whether that would be an advantage or disadvantage to use tissue matched or non-matched cells. But the immune rejection is going to be an issue with Type I diabetes whether you use the patient's own cells or not.