

## **Arlotta Clip 6 Transcript**

PAOLA ARLOTTA: So this is incredible because the retina has many, many, many different types of cells in there. It has a specific structure. It requires these morphogenetic movements that the tissue made in vitro. Yes.

STUDENT: What are the hypothesis for why this happens? Is it like proteins?

PAOLA ARLOTTA: Well it's many, many mechanisms. But all of these mechanical movements of development are so key during the embryo, are all controlled, of course, by the identity of the cells involved, but by the fact that the physical properties of cells in specific locations, like at the edges of this invaginated epithelium will be different. And their shape will change. And their connectivity in addition will be different, their stiffness will be different.

STUDENT: Like similar to axonal guidance, like guidepost cells and stuff, do you think there's something like--

PAOLA ARLOTTA: Signals.

STUDENT: Yeah, the theory of something like that in the cell?

PAOLA ARLOTTA: There will be patterning signals that will tell the cells who to be and how to behave at a certain given time. But eventually, there will also be coordinated interaction among the cells, which in a certain position will have to bend.

STUDENT: Because what I didn't get is, naturally if you just put that in a dish it would seem to that it would just want-- the expanding out makes sense, but the invagination--

PAOLA ARLOTTA: Exactly. How do they know when to stop the expand and begin to invaginate. That's not completely known, but there are some molecules that have been identified for the fact that at the edges you're going to have these cells that pushed them in.

And it might be in certain organism size, like when you reach a certain size there is a certain pressure. And here, certainly, if the bubble was too big it wouldn't invaginate. And if it was too small, it wouldn't invaginate. So it might be something with size. Yes.

STUDENT: Sorry, just to clarify. What was the starting cell for this?

PAOLA ARLOTTA: An embryonic stem cell.

STUDENT: It's just a vanilla generic?

PAOLA ARLOTTA: Vanilla genetic embryonic stem cell that is pushed though to become an embryo body, which is a spherical structure. And that then forms neuro ectoderm. So it's not that it will form endoderm and mesoderm. But largely neuro ectoderm. But from the same kind of structure-- and I'll show you the slide-- Georgia can make human brain organoids.

STUDENT: What's the difference?

PAOLA ARLOTTA: What's the difference. What's the difference, Georgia? Let's go there so we can talk about the difference. Because there is not much of a difference, yet the tissue is different in the end. I'm going to get to that slide and then come back.

So basically, it has been discovered-- sorry, go ahead.

STUDENT: I was wondering if it's just neuroectoderm, are we just assuming that that's like the retina and the neural portion?

PAOLA ARLOTTA: Right, so that neuroectoderm can make all sorts of things of neuroectodermal origin. And then the media in which you culture that structure, and the substrate in which you coat that structure will affect what you preferentially make. But for example, when we make brain we also make retina in the same organoid. In a way some of the principles that self-organize, self pattern, and self build the nervous system are shared among these different regions. At some point though, there has to be specialization because the type of cells you make and the type of movement you make are different. And

STUDENT: So you're not saying the entire eye, as in lens, iris.

PAOLA ARLOTTA: So in this context, the cup can be made without the need for any external other tissue. But if you want to make the cornea, or if you want to make the crystalline, or if you want to make other parts of the eye, that typically requires the presence of other cells around it that will induce it. So there is, of course-- I'm not trying to eliminate the external patterning. There's still external patterning, but a lot can be self-assembled.