Arlotta Clip 3 Transcript

PAOLA ARLOTTA: There is also the fact that this brain literally develops within the embryo differently than that. So there are new progenitor cells that are present in the human cerebral cortex not present in the mouse that allow that expansion. So even understanding this human brain development by studying that, you can see how it pales compared to the actual tissue that you should be studying. That's why it's so important to look at human, human, human. OK, yes?

STUDENT: Could you also argue that even if mice brains were more analogous to human brains, there's not really a way for us to measure the same. They can't communicate.

PAOLA ARLOTTA: Can't ask them anything, right?

STUDENT: Sorry.

PAOLA ARLOTTA: Go ahead.

STUDENT: Couldn't you also say that for like organoids though? Like, how would you measure?

PAOLA ARLOTTA: Or could we use those to do what mice can't? Hold that thought. We're going to go there. Yes?

STUDENT: I was going to answer that.

PAOLA ARLOTTA: Answer that. I like it.

STUDENT: Transplant it.

PAOLA ARLOTTA: We transplant an organ. No, we won't transplant a brain organoid. Well, one could transplant it in an animal model to try to make it become a more mature, more whatever. Yes?

STUDENT: Something that also is slightly confusing to me is the fact that with a neurodegenerative disease you can point at something and say this is ALS, this is Alzheimer's. But I don't quite understand-- and I guess this might be a limit of my own knowledge, how can we definitively say, this human schizophrenia versus depression?

PAOLA ARLOTTA: Good question.

STUDENT: Like, how would you use that in our labs.

PAOLA ARLOTTA: What do you think? How do you think it's done today?

STUDENT: I know they use the DSM guidelines, but how can you create something like that for a mouse? And even then, there are mistakes that are made with humans.

PAOLA ARLOTTA: You know, you touch such an important point here. A major limitation of all of this field that has been dormant basically forever is the fact that we classify still patients based on clinical symptoms, and patients that may have a completely different etiology of the disease get put in the same bucket because they may have some similar symptomatology, basically. But they could have a completely different disease that affects a completely different part of the brain, or only partly overlapping. And there is no good way, or no scientifically driven way to classify and stratify the population of patients to have any predictive value for where one drug would work and when one drug will not work.

And so maybe-- I was going to tell you later, but let me give you an example of work that is partially contested. So you need to know this, but I'll ask you why you think that people contest this, that may help us understand these patients better, classify them more correctly, and then develop a treatment that is more personalized and likely to work.