WEBVTT

NOTE duration:"00:19:30"

NOTE recognizability:0.923

NOTE language:en-us

NOTE Confidence: 0.946962533333333

00:00:00.000 --> 00:00:03.428 Let me introduce Doctor Andrelevchenko,

NOTE Confidence: 0.946962533333333

00:00:03.428 --> 00:00:05.398 who is the next speaker.

NOTE Confidence: 0.946962533333333

00:00:05.400 --> 00:00:07.625 He graduated from the Moscow

NOTE Confidence: 0.946962533333333

00:00:07.625 --> 00:00:09.850 Institute of Physics and Technology

NOTE Confidence: 0.946962533333333

00:00:09.928 --> 00:00:11.600 and obtained his doctor,

NOTE Confidence: 0.946962533333333

00:00:11.600 --> 00:00:14.255 obtained his doctoral degree from

NOTE Confidence: 0.946962533333333

00:00:14.255 --> 00:00:16.506 Columbia University and after

NOTE Confidence: 0.946962533333333

00:00:16.506 --> 00:00:18.878 postdoctoral experience at Caltech,

NOTE Confidence: 0.946962533333333

00:00:18.880 --> 00:00:21.088 he started his independent position at

NOTE Confidence: 0.946962533333333

00:00:21.088 --> 00:00:23.768 Johns Hopkins in 2001 and was recruited

NOTE Confidence: 0.946962533333333

00:00:23.768 --> 00:00:26.660 as the founding director of the Ill

NOTE Confidence: 0.946962533333333

00:00:26.660 --> 00:00:29.043 Systems Biology Institute in 2015.

NOTE Confidence: 0.946962533333333

00:00:29.043 --> 00:00:32.181 And he's also the John Malone

NOTE Confidence: 0.946962533333333

00:00:32.181 --> 00:00:34.496 professor of biomedical Engineering

NOTE Confidence: 0.946962533333333

00:00:34.496 --> 00:00:37.120 and professor of physics.

NOTE Confidence: 0.946962533333333

00:00:37.120 --> 00:00:37.600 Please.

NOTE Confidence: 0.94528523

00:00:44.160 --> 00:00:45.756 Hello and thanks for inviting me.

NOTE Confidence: 0.94528523

00:00:45.760 --> 00:00:50.212 And as as Angelica just said for

NOTE Confidence: 0.94528523

00:00:50.212 --> 00:00:52.864 engineers and physicists to be in the

NOTE Confidence: 0.94528523

00:00:52.864 --> 00:00:54.786 in the room with all of you is, is,

NOTE Confidence: 0.94528523

00:00:54.786 --> 00:00:57.874 is always the great pleasure and and very,

NOTE Confidence: 0.94528523

00:00:57.880 --> 00:01:00.600 very interesting to us.

NOTE Confidence: 0.94528523

00:01:00.600 --> 00:01:02.316 It's of course I'm an engineer,

NOTE Confidence: 0.94528523

00:01:02.320 --> 00:01:04.400 but I'm actually we do do quite a

NOTE Confidence: 0.94528523

00:01:04.400 --> 00:01:06.565 bit of biology and what you learn

NOTE Confidence: 0.94528523

00:01:06.565 --> 00:01:08.684 of course is being an engineer.

NOTE Confidence: 0.94528523

00:01:08.684 --> 00:01:11.400 If you develop tools and we know,

NOTE Confidence: 0.94528523

00:01:11.400 --> 00:01:14.540 all know with with tools you

NOTE Confidence: 0.94528523

00:01:14.540 --> 00:01:16.515 get to discover new tools,

NOTE Confidence: 0.94528523

00:01:16.520 --> 00:01:19.165 new discoveries and that's something

NOTE Confidence: 0.94528523

00:01:19.165 --> 00:01:21.810 that we've really enjoyed thoroughly

NOTE Confidence: 0.94528523

00:01:21.889 --> 00:01:23.622 on different different scales.

NOTE Confidence: 0.94528523

00:01:23.622 --> 00:01:26.208 And what I'd like to illustrate

NOTE Confidence: 0.94528523

00:01:26.208 --> 00:01:28.848 today is the use of these tools.

NOTE Confidence: 0.94528523

00:01:28.850 --> 00:01:30.838 And some insights that we can gain

NOTE Confidence: 0.94528523

00:01:30.838 --> 00:01:32.892 from them and the fact that you

NOTE Confidence: 0.94528523

00:01:32.892 --> 00:01:34.596 actually can do it on multiple

NOTE Confidence: 0.94528523

00:01:34.661 --> 00:01:39.322 different scales in terms of sales,

NOTE Confidence: 0.94528523

00:01:39.322 --> 00:01:44.850 small organoids or even larger structures,

NOTE Confidence: 0.94528523

00:01:44.850 --> 00:01:48.850 okay. So let's see if this. Yeah.

NOTE Confidence: 0.94528523

00:01:48.850 --> 00:01:50.929 So I always run out of time,

NOTE Confidence: 0.94528523

00:01:50.930 --> 00:01:52.214 hopefully not today.

NOTE Confidence: 0.94528523

00:01:52.214 --> 00:01:55.210 So I'd like to immediately thank all

NOTE Confidence: 0.94528523

00:01:55.287 --> 00:01:57.658 the people who helped us do this,

NOTE Confidence: 0.94528523

00:01:57.658 --> 00:01:59.646 as our collaborators as well as the

NOTE Confidence: 0.94528523

00:01:59.646 --> 00:02:01.790 members of the lab were truly in the

NOTE Confidence: 0.94528523

00:02:01.790 --> 00:02:03.329 trenches doing all of this work.

NOTE Confidence: 0.94528523

00:02:03.330 --> 00:02:07.848 Particularly for a lot of the

NOTE Confidence: 0.94528523

00:02:07.850 --> 00:02:09.608 work towards the ends of flora,

NOTE Confidence: 0.94528523

00:02:09.610 --> 00:02:11.086 because this has been a very,

NOTE Confidence: 0.94528523

00:02:11.090 --> 00:02:12.308 very exciting collaboration

NOTE Confidence: 0.94528523

00:02:12.308 --> 00:02:14.744 with the factory in the lab.

NOTE Confidence: 0.94528523

00:02:14.750 --> 00:02:17.980 And a lot of things are not shown are also

NOTE Confidence: 0.94528523

00:02:18.063 --> 00:02:20.989 very interesting to us and are always,

NOTE Confidence: 0.94528523

00:02:20.990 --> 00:02:22.750 almost always products of collaboration.

NOTE Confidence: 0.94528523

00:02:22.750 --> 00:02:24.310 And as on the hill,

NOTE Confidence: 0.94528523

00:02:24.310 --> 00:02:25.350 like I mentioned for example,

NOTE Confidence: 0.94528523

00:02:25.350 --> 00:02:27.037 we have been doing a lot of

NOTE Confidence: 0.94528523

00:02:27.037 --> 00:02:28.189 interesting things with her lab,

NOTE Confidence: 0.94528523

00:02:28.190 --> 00:02:30.470 which has been amazing.

NOTE Confidence: 0.94528523

00:02:30.470 --> 00:02:35.336 So what I'd like to really focus on

NOTE Confidence: 0.94528523

00:02:35.336 --> 00:02:37.439 is this combination of difference

NOTE Confidence: 0.94528523

00:02:37.439 --> 00:02:40.295 approaches and how they come together

NOTE Confidence: 0.94528523

00:02:40.295 --> 00:02:42.558 more specifically in the context of.

NOTE Confidence: 0.94528523

00:02:42.560 --> 00:02:45.488 The fact that as we've already

NOTE Confidence: 0.94528523

00:02:45.488 --> 00:02:48.090 heard the tissues and you know,

NOTE Confidence: 0.94528523

00:02:48.090 --> 00:02:50.365 even if you go smaller on the

NOTE Confidence: 0.94528523

00:02:50.365 --> 00:02:52.000 level of digital cells,

NOTE Confidence: 0.94528523

00:02:52.000 --> 00:02:53.992 what you see is that the

NOTE Confidence: 0.94528523

00:02:53.992 --> 00:02:55.320 environment is not uniform.

NOTE Confidence: 0.94528523

00:02:55.320 --> 00:02:57.430 The environment can present cells

NOTE Confidence: 0.94528523

00:02:57.430 --> 00:02:59.118 and tissues with gradients,

NOTE Confidence: 0.94528523

00:02:59.120 --> 00:03:02.600 for example of cues of morphogens.

NOTE Confidence: 0.94528523

00:03:02.600 --> 00:03:06.253 And this can occur both for stages

NOTE Confidence: 0.94528523

00:03:06.253 --> 00:03:08.518 in development or in cancer,

NOTE Confidence: 0.94528523

00:03:08.520 --> 00:03:10.420 for example, progression where

NOTE Confidence: 0.94528523

00:03:10.420 --> 00:03:12.320 cells may migrate gradients.

NOTE Confidence: 0.94528523

00:03:12.320 --> 00:03:16.037 Could be in collective cell migration or

NOTE Confidence: 0.94528523

00:03:16.037 --> 00:03:18.919 reorganization of tissues in development.

NOTE Confidence: 0.94528523

00:03:18.920 --> 00:03:23.048 It could be in homeostasis and wound repair.

NOTE Confidence: 0.94528523

00:03:23.048 --> 00:03:25.370 So many, many instances.

NOTE Confidence: 0.94528523

00:03:25.370 --> 00:03:28.400 And of course if you take

NOTE Confidence: 0.94528523

00:03:28.400 --> 00:03:29.040 developmental biology,

NOTE Confidence: 0.94528523

00:03:29.040 --> 00:03:31.640 I guess more or less,

NOTE Confidence: 0.94528523

00:03:31.640 --> 00:03:33.128 you know, almost anywhere,

NOTE Confidence: 0.94528523

00:03:33.128 --> 00:03:35.360 at least where I took it,

NOTE Confidence: 0.94528523

00:03:35.360 --> 00:03:37.117 you find that there is this model,

NOTE Confidence: 0.94528523

00:03:37.120 --> 00:03:40.438 beautiful model due to Lewis Wolpert.

NOTE Confidence: 0.94528523

00:03:40.440 --> 00:03:41.884 Of the French flag,

NOTE Confidence: 0.94528523

00:03:41.884 --> 00:03:43.328 essentially suggesting that in

NOTE Confidence: 0.94528523

00:03:43.328 --> 00:03:44.920 the gradient of morphogens,

NOTE Confidence: 0.94528523

00:03:44.920 --> 00:03:47.830 you can have multiple different

NOTE Confidence: 0.94528523

00:03:47.830 --> 00:03:50.960 fates emerging due to the overall

NOTE Confidence: 0.94528523

00:03:50.960 --> 00:03:52.160 level of morphogens,

NOTE Confidence: 0.94528523

00:03:52.160 --> 00:03:53.770 sort of sort of like the cells

NOTE Confidence: 0.94528523

00:03:53.770 --> 00:03:54.800 responding to the doses,

NOTE Confidence: 0.94528523

00:03:54.800 --> 00:03:56.680 different doses of the input.

NOTE Confidence: 0.94528523

00:03:56.680 --> 00:03:59.746 And it does frequently happen in

NOTE Confidence: 0.94528523

00:03:59.746 --> 00:04:01.800 tissues and hopefully towards the

NOTE Confidence: 0.94528523

00:04:01.800 --> 00:04:03.880 end I'm going to show you an example

NOTE Confidence: 0.94528523

00:04:03.880 --> 00:04:09.046 that Flora has really introduced us to.

NOTE Confidence: 0.94528523

00:04:09.050 --> 00:04:09.363 Now,

NOTE Confidence: 0.94528523

00:04:09.363 --> 00:04:11.800 so how do you do experiments to

NOTE Confidence: 0.94528523

00:04:11.800 --> 00:04:13.975 try to understand the influence

NOTE Confidence: 0.94528523

00:04:13.975 --> 00:04:14.845 of graded

NOTE Confidence: 0.950316941

00:04:14.850 --> 00:04:18.378 inputs, whether you look at cell migration

NOTE Confidence: 0.950316941

00:04:18.378 --> 00:04:21.340 or this developmental processes where

NOTE Confidence: 0.950316941

00:04:21.340 --> 00:04:24.965 you have multiple different responses.

NOTE Confidence: 0.950316941

00:04:24.970 --> 00:04:26.722 So there are there's a tradition

NOTE Confidence: 0.950316941

00:04:26.722 --> 00:04:28.566 in by engineering that you may or

NOTE Confidence: 0.950316941

00:04:28.566 --> 00:04:30.686 may not be aware of for kind of a

NOTE Confidence: 0.950316941

00:04:30.686 --> 00:04:32.482 progression of different steps in

NOTE Confidence: 0.950316941

00:04:32.482 --> 00:04:34.226 development of different tools.

NOTE Confidence: 0.950316941

00:04:34.230 --> 00:04:37.222 And these are just some of the examples

NOTE Confidence: 0.950316941

00:04:37.222 --> 00:04:38.680 essentially historically how the

NOTE Confidence: 0.950316941

00:04:38.680 --> 00:04:40.638 gradient studies have been done and

NOTE Confidence: 0.950316941

00:04:40.638 --> 00:04:43.262 almost always what you see and the ones

NOTE Confidence: 0.950316941

00:04:43.262 --> 00:04:46.669 at the bottom are the ones that we developed.

NOTE Confidence: 0.950316941

00:04:46.670 --> 00:04:48.567 The ones at the top are the

NOTE Confidence: 0.950316941

00:04:48.567 --> 00:04:50.229 ones that were used before.

NOTE Confidence: 0.950316941

00:04:50.230 --> 00:04:51.882 You see that it's a kind of

NOTE Confidence: 0.950316941

00:04:51.882 --> 00:04:52.590 two different ideas.

NOTE Confidence: 0.950316941

00:04:52.590 --> 00:04:54.282 One is the flow.

NOTE Confidence: 0.950316941

00:04:54.282 --> 00:04:57.110 In the flow you have mixing of

NOTE Confidence: 0.950316941

00:04:57.110 --> 00:04:58.885 liquids and within liquids you

NOTE Confidence: 0.950316941

00:04:58.885 --> 00:05:00.660 can have different doses of.

NOTE Confidence: 0.950316941

00:05:00.660 --> 00:05:03.174 Compound that you're interested in and

NOTE Confidence: 0.950316941

00:05:03.174 --> 00:05:05.740 that gradually may generate the gradient.

NOTE Confidence: 0.950316941

00:05:05.740 --> 00:05:07.420 The issue is that of course

NOTE Confidence: 0.950316941

00:05:07.420 --> 00:05:09.179 cells don't like flow of liquid.

NOTE Confidence: 0.950316941

00:05:09.180 --> 00:05:10.780 For the most part,

NOTE Confidence: 0.950316941

00:05:10.780 --> 00:05:12.380 they die almost immediately.

NOTE Confidence: 0.950316941

00:05:12.380 --> 00:05:13.156 They're very,

NOTE Confidence: 0.950316941

00:05:13.156 --> 00:05:15.096 very sensitive to what happens

NOTE Confidence: 0.950316941

00:05:15.096 --> 00:05:16.260 with the environment.

NOTE Confidence: 0.950316941

00:05:16.260 --> 00:05:18.899 If you shake, you know your flask.

NOTE Confidence: 0.950316941

00:05:18.900 --> 00:05:21.096 Sometimes you'll see a cell death,

NOTE Confidence: 0.950316941

00:05:21.100 --> 00:05:23.188 and that's what you face when you try

NOTE Confidence: 0.950316941

00:05:23.188 --> 00:05:25.143 to introduce cells into anything that

NOTE Confidence: 0.950316941

00:05:25.143 --> 00:05:26.858 flows when you hear microfluidics,

NOTE Confidence: 0.950316941

00:05:26.860 --> 00:05:29.170 microfluidics.

NOTE Confidence: 0.950316941

00:05:29.170 --> 00:05:32.344 Fluidics parts should really generate

NOTE Confidence: 0.950316941

00:05:32.344 --> 00:05:35.014 immediately some trepidation for you

NOTE Confidence: 0.950316941

00:05:35.014 --> 00:05:37.688 because anything again that flows

NOTE Confidence: 0.950316941

00:05:37.688 --> 00:05:39.993 almost always there are instances

NOTE Confidence: 0.950316941

00:05:39.993 --> 00:05:42.569 where flow is important for sure,

NOTE Confidence: 0.950316941

00:05:42.570 --> 00:05:44.088 for example in the material cells,

NOTE Confidence: 0.950316941

00:05:44.090 --> 00:05:45.920 but generally cells are really sensitive

NOTE Confidence: 0.950316941

00:05:45.920 --> 00:05:48.327 to that and they really don't like it.

NOTE Confidence: 0.950316941

00:05:48.330 --> 00:05:51.172 So that is something that we recognized

NOTE Confidence: 0.950316941

00:05:51.172 --> 00:05:52.762 almost immediately started when

NOTE Confidence: 0.950316941

00:05:52.762 --> 00:05:54.604 we started working with cells and

NOTE Confidence: 0.950316941

00:05:54.604 --> 00:05:57.202 then we had to develop a different.

NOTE Confidence: 0.950316941

00:05:57.202 --> 00:05:59.682 Series of devices where it's

NOTE Confidence: 0.950316941

00:05:59.682 --> 00:06:01.546 really all diffusion, right?

NOTE Confidence: 0.950316941

00:06:01.546 --> 00:06:03.050 It's not nothing flows.

NOTE Confidence: 0.950316941

00:06:03.050 --> 00:06:05.444 The cells are actually in this beautiful,

NOTE Confidence: 0.950316941

00:06:05.450 --> 00:06:06.629 very steady environment,

NOTE Confidence: 0.950316941

00:06:06.629 --> 00:06:10.890 but there are gradients and so with that.

NOTE Confidence: 0.950316941

00:06:10.890 --> 00:06:12.888 So you have this example on

NOTE Confidence: 0.950316941

00:06:12.888 --> 00:06:14.930 the left here where you have.

NOTE Confidence: 0.851849155

00:06:16.970 --> 00:06:19.458 I'm not, I'm not going to mess it. Okay.

NOTE Confidence: 0.851849155

00:06:19.458 --> 00:06:22.402 So you have this idea of a source,

NOTE Confidence: 0.851849155

00:06:22.410 --> 00:06:24.810 for example of growth factory GF.

NOTE Confidence: 0.851849155

00:06:24.810 --> 00:06:26.495 And the cells in between

NOTE Confidence: 0.851849155

00:06:26.495 --> 00:06:27.843 looking like fish here,

NOTE Confidence: 0.851849155

00:06:27.850 --> 00:06:31.002 but this is a cell and there are this

NOTE Confidence: 0.851849155

00:06:31.002 --> 00:06:33.242 nice channels connecting source of

NOTE Confidence: 0.851849155

00:06:33.242 --> 00:06:36.380 the GF and medium without the GF and

NOTE Confidence: 0.851849155

00:06:36.380 --> 00:06:38.387 the certain gradient developing and

NOTE Confidence: 0.851849155

00:06:38.387 --> 00:06:40.169 the the cells actually do respond.

NOTE Confidence: 0.851849155

00:06:40.170 --> 00:06:43.146 And so you start seeing how they run

NOTE Confidence: 0.851849155

00:06:43.146 --> 00:06:45.290 very happily, they run into each other,

NOTE Confidence: 0.851849155

00:06:45.290 --> 00:06:46.038 they collide.

NOTE Confidence: 0.851849155

00:06:46.038 --> 00:06:48.656 You can study what happens when that

NOTE Confidence: 0.851849155

00:06:48.656 --> 00:06:51.350 when that occurs and you see this

NOTE Confidence: 0.851849155

00:06:51.350 --> 00:06:55.690 beautiful chains of cells going up and down.

NOTE Confidence: 0.851849155

00:06:55.690 --> 00:06:58.342 And let me try again,

NOTE Confidence: 0.851849155

00:06:58.342 --> 00:07:01.770 maybe it will work, maybe not.

NOTE Confidence: 0.851849155

00:07:01.770 --> 00:07:04.116 So we wanted to really extend

NOTE Confidence: 0.851849155

00:07:04.116 --> 00:07:06.586 that a little bit to you know,

NOTE Confidence: 0.851849155

00:07:06.586 --> 00:07:08.882 we've heard that cells actually live in

NOTE Confidence: 0.851849155

00:07:08.882 --> 00:07:11.088 softer media and they're surrounded by

NOTE Confidence: 0.851849155

00:07:11.088 --> 00:07:13.730 the cells that communicate the form tissues,

NOTE Confidence: 0.851849155

00:07:13.730 --> 00:07:14.944 tissue ensembles.

NOTE Confidence: 0.851849155

00:07:14.944 --> 00:07:18.586 And so can we really extend

NOTE Confidence: 0.851849155

00:07:18.586 --> 00:07:20.629 this analysis now to?

NOTE Confidence: 0.851849155

00:07:20.630 --> 00:07:22.990 What really is at the center of today's

NOTE Confidence: 0.851849155

00:07:22.990 --> 00:07:24.669 workshop and that is organized.

NOTE Confidence: 0.851849155

00:07:24.670 --> 00:07:27.141 And so this paper was the first

NOTE Confidence: 0.851849155

00:07:27.141 --> 00:07:29.994 attempt to do that where it wasn't.

NOTE Confidence: 0.851849155

00:07:29.994 --> 00:07:33.228 It was an organoid of breast tissue

NOTE Confidence: 0.851849155

00:07:33.230 --> 00:07:37.009 that you'll see next and rather than.

NOTE Confidence: 0.851849155

00:07:37.009 --> 00:07:39.760 Brain tissue that we'll see a bit

NOTE Confidence: 0.851849155

00:07:39.846 --> 00:07:42.040 later and this was surf the question,

NOTE Confidence: 0.851849155

00:07:42.040 --> 00:07:42.472 okay.

NOTE Confidence: 0.851849155

00:07:42.472 --> 00:07:43.768 So what happens,

NOTE Confidence: 0.851849155

00:07:43.768 --> 00:07:47.528 we know that in the breast there's branching,

NOTE Confidence: 0.851849155

00:07:47.528 --> 00:07:51.032 there's in the periods of lactation

NOTE Confidence: 0.851849155

00:07:51.032 --> 00:07:53.265 especially or around that time

NOTE Confidence: 0.851849155

00:07:53.265 --> 00:07:55.395 there may be a very significant

NOTE Confidence: 0.851849155

00:07:55.395 --> 00:07:56.998 reorganization of the breast tissue.

NOTE Confidence: 0.851849155

00:07:57.000 --> 00:07:59.674 And in that process in the adults

NOTE Confidence: 0.851849155

00:07:59.674 --> 00:08:02.421 what happens is there is a growth

NOTE Confidence: 0.851849155

00:08:02.421 --> 00:08:04.378 and branching of various surf.

NOTE Confidence: 0.851849155

00:08:04.378 --> 00:08:07.650 Parts of the of the tissue and that

NOTE Confidence: 0.851849155

00:08:07.741 --> 00:08:10.493 is is triggered by e.g F the same

NOTE Confidence: 0.851849155

00:08:10.500 --> 00:08:12.943 same compound that I showed you in

NOTE Confidence: 0.851849155

00:08:12.943 --> 00:08:15.496 the in the last movie can trigger

NOTE Confidence: 0.851849155

00:08:15.496 --> 00:08:18.100 migration of cells in a directive way.

NOTE Confidence: 0.851849155

00:08:18.100 --> 00:08:20.540 So what happens with tissues?

NOTE Confidence: 0.851849155

00:08:20.540 --> 00:08:22.340 And So what you can see is that

NOTE Confidence: 0.851849155

00:08:22.340 --> 00:08:24.229 you again you can sort of extend

NOTE Confidence: 0.851849155

00:08:24.229 --> 00:08:25.940 this technology to the same idea,

NOTE Confidence: 0.851849155

00:08:25.940 --> 00:08:28.796 have a gradient now if e.g F over

NOTE Confidence: 0.851849155

00:08:28.796 --> 00:08:30.993 much larger distance and organized

NOTE Confidence: 0.851849155

00:08:30.993 --> 00:08:33.795 are embedded now in the space.

NOTE Confidence: 0.851849155

00:08:33.800 --> 00:08:35.798 And you start seeing that they

NOTE Confidence: 0.851849155

00:08:35.798 --> 00:08:36.797 actually start branching.

NOTE Confidence: 0.851849155

00:08:36.800 --> 00:08:38.485 This organoid that initially was

NOTE Confidence: 0.851849155

00:08:38.485 --> 00:08:40.600 the kind of a spherical thing,

NOTE Confidence: 0.851849155

00:08:40.600 --> 00:08:42.945 begins to branch in a very directed

NOTE Confidence: 0.851849155

00:08:42.945 --> 00:08:46.118 way towards the source of e.g F

NOTE Confidence: 0.851849155

00:08:46.120 --> 00:08:48.046 what's interesting is that you can

NOTE Confidence: 0.851849155

00:08:48.046 --> 00:08:50.171 either induce it or naturally have

NOTE Confidence: 0.851849155

00:08:50.171 --> 00:08:52.428 some single cells around and they

NOTE Confidence: 0.851849155

00:08:52.428 --> 00:08:54.198 actually don't sense these gradients.

NOTE Confidence: 0.851849155

00:08:54.200 --> 00:08:56.064 So in spite of the movie that I

NOTE Confidence: 0.851849155

00:08:56.064 --> 00:08:57.677 just showed you in the previous,

NOTE Confidence: 0.851849155

00:08:57.680 --> 00:08:59.200 the the ligand concentration

NOTE Confidence: 0.851849155

00:08:59.200 --> 00:09:02.070 gradients in this case are so shallow.

NOTE Confidence: 0.851849155

00:09:02.070 --> 00:09:03.786 That individual cells just don't respond,

NOTE Confidence: 0.851849155

00:09:03.790 --> 00:09:05.110 they don't sense the gradients,

NOTE Confidence: 0.851849155

00:09:05.110 --> 00:09:07.546 only the tissues can sense the gradients,

NOTE Confidence: 0.851849155

00:09:07.550 --> 00:09:08.990 which implies that there is some

NOTE Confidence: 0.851849155

00:09:08.990 --> 00:09:10.670 sort of cell cell communication.

NOTE Confidence: 0.851849155

00:09:10.670 --> 00:09:15.020 And so our analysis suggested that's

NOTE Confidence: 0.851849155

00:09:15.020 --> 00:09:18.030 really the cell cell communication

NOTE Confidence: 0.851849155

00:09:18.030 --> 00:09:20.310 mechanisms in this process,

NOTE Confidence: 0.851849155

00:09:20.310 --> 00:09:23.400 this one branch forming here that

NOTE Confidence: 0.851849155

00:09:23.400 --> 00:09:25.299 will branch more is,

NOTE Confidence: 0.851849155

00:09:25.299 --> 00:09:27.742 is really all of that is mediated

NOTE Confidence: 0.851849155

00:09:27.742 --> 00:09:29.250 by calcium signaling.

NOTE Confidence: 0.851849155

00:09:29.250 --> 00:09:31.930 And calcium communication between the

NOTE Confidence: 0.942682696551724

00:09:31.930 --> 00:09:33.358 channels connecting the cells.

NOTE Confidence: 0.942682696551724

00:09:33.358 --> 00:09:35.916 So one thing that I want to

NOTE Confidence: 0.942682696551724

00:09:35.916 --> 00:09:37.666 emphasize already in the two

NOTE Confidence: 0.942682696551724

00:09:37.666 --> 00:09:39.758 examples that I showed you where

NOTE Confidence: 0.942682696551724

00:09:39.758 --> 00:09:41.928 you in both cases you saw movies,

NOTE Confidence: 0.942682696551724

00:09:41.930 --> 00:09:43.982 is that you really benefit not

NOTE Confidence: 0.942682696551724

00:09:43.982 --> 00:09:46.393 only from the ability to generate

NOTE Confidence: 0.942682696551724

00:09:46.393 --> 00:09:48.698 gradients or grows such organoids.

NOTE Confidence: 0.942682696551724

00:09:48.700 --> 00:09:50.620 But also from the fact that

NOTE Confidence: 0.942682696551724

00:09:50.620 --> 00:09:52.659 you can really peer into life,

NOTE Confidence: 0.942682696551724

00:09:52.660 --> 00:09:54.772 either life cells or life in

NOTE Confidence: 0.942682696551724

00:09:54.772 --> 00:09:56.180 this case life organoias,

NOTE Confidence: 0.942682696551724

00:09:56.180 --> 00:09:58.294 and see the dynamics of the processes

NOTE Confidence: 0.942682696551724

00:09:58.294 --> 00:10:00.258 that are of interest to you.

NOTE Confidence: 0.942682696551724

00:10:00.260 --> 00:10:04.420 So these devices really allow you to analyze,

NOTE Confidence: 0.942682696551724

00:10:04.420 --> 00:10:05.082 you know,

NOTE Confidence: 0.942682696551724

00:10:05.082 --> 00:10:06.737 communication between the cells and

NOTE Confidence: 0.942682696551724

00:10:06.737 --> 00:10:09.700 what happens with the cells and

NOTE Confidence: 0.942682696551724

00:10:09.700 --> 00:10:12.112 shoot movies like that and analyze

NOTE Confidence: 0.942682696551724

00:10:12.112 --> 00:10:15.219 in this case the calcium signaling.

NOTE Confidence: 0.942682696551724

00:10:15.220 --> 00:10:17.005 So we wanted to really continue doing

NOTE Confidence: 0.942682696551724

00:10:17.005 --> 00:10:19.525 this and of course the challenge the the

NOTE Confidence: 0.942682696551724

00:10:19.525 --> 00:10:21.220 more interesting structures the more

NOTE Confidence: 0.942682696551724

00:10:21.276 --> 00:10:23.256 complex structures occur in the brain.

NOTE Confidence: 0.942682696551724

00:10:23.260 --> 00:10:25.996 And in the brain there may be different

NOTE Confidence: 0.942682696551724

00:10:25.996 --> 00:10:28.639 types of analysis and this was termed

NOTE Confidence: 0.942682696551724

00:10:28.639 --> 00:10:31.459 for the first time brain on the chip.

NOTE Confidence: 0.942682696551724

00:10:31.460 --> 00:10:34.772 Now in the Community of Engineers,

NOTE Confidence: 0.942682696551724

00:10:34.772 --> 00:10:36.220 anything on a chip, you'll,

NOTE Confidence: 0.942682696551724

00:10:36.220 --> 00:10:37.420 you'll hear longer on the chip,

NOTE Confidence: 0.942682696551724

00:10:37.420 --> 00:10:39.652 brain on chip it's just a big name

NOTE Confidence: 0.942682696551724

00:10:39.652 --> 00:10:41.479 it's it's not more than that.

NOTE Confidence: 0.942682696551724

00:10:41.480 --> 00:10:42.947 But here it's,

NOTE Confidence: 0.942682696551724

00:10:42.947 --> 00:10:43.436 it's,

NOTE Confidence: 0.942682696551724

00:10:43.436 --> 00:10:45.881 it's it's something that allows

NOTE Confidence: 0.942682696551724

00:10:45.881 --> 00:10:48.820 you to start modeling the presence

NOTE Confidence: 0.942682696551724

00:10:48.820 --> 00:10:52.680 of multiple cell types in the self

NOTE Confidence: 0.942682696551724

00:10:52.680 --> 00:10:54.852 organizing networks and again do it

NOTE Confidence: 0.942682696551724

00:10:54.852 --> 00:10:57.480 in such a way that can visualize this

NOTE Confidence: 0.942682696551724

00:10:57.480 --> 00:11:01.036 in great detail and see what happens.

NOTE Confidence: 0.942682696551724

00:11:01.040 --> 00:11:03.008 So here again you can start

NOTE Confidence: 0.942682696551724

00:11:03.008 --> 00:11:04.320 with the progenitor cells.

NOTE Confidence: 0.942682696551724

00:11:04.320 --> 00:11:06.518 They will not necessarily form and organize,

NOTE Confidence: 0.942682696551724

00:11:06.520 --> 00:11:09.068 they can form clusters of cells that

NOTE Confidence: 0.942682696551724

00:11:09.068 --> 00:11:11.399 are connected by bundles of axons.

NOTE Confidence: 0.942682696551724

00:11:11.400 --> 00:11:14.271 At some point you can couple that to a

NOTE Confidence: 0.942682696551724

00:11:14.271 --> 00:11:17.392 layer of endothelial cells and mimic the

NOTE Confidence: 0.942682696551724

00:11:17.392 --> 00:11:20.360 blood brain barrier that actually forms here.

NOTE Confidence: 0.942682696551724

00:11:20.360 --> 00:11:22.117 And you can introduce some drugs here,

NOTE Confidence: 0.942682696551724

00:11:22.120 --> 00:11:22.776 for example,

NOTE Confidence: 0.942682696551724

00:11:22.776 --> 00:11:23.760 on this side,

NOTE Confidence: 0.942682696551724

00:11:23.760 --> 00:11:27.239 and study how they can potentially be

NOTE Confidence: 0.942682696551724

00:11:27.240 --> 00:11:29.480 penetrating this blood brain barrier.

NOTE Confidence: 0.942682696551724

00:11:29.480 --> 00:11:30.780 There's a basement membrane

NOTE Confidence: 0.942682696551724

00:11:30.780 --> 00:11:32.080 that will form here.

NOTE Confidence: 0.942682696551724

00:11:32.080 --> 00:11:33.388 And so even though of course

NOTE Confidence: 0.942682696551724

00:11:33.388 --> 00:11:34.640 it's not the real tissue,

NOTE Confidence: 0.942682696551724

00:11:34.640 --> 00:11:36.400 it starts having some interesting

NOTE Confidence: 0.942682696551724

00:11:36.400 --> 00:11:38.160 features that you can use.

NOTE Confidence: 0.942682696551724

00:11:38.160 --> 00:11:40.280 To start exploring what happens,

NOTE Confidence: 0.942682696551724

00:11:40.280 --> 00:11:43.115 there is a communication as was just

NOTE Confidence: 0.942682696551724

00:11:43.115 --> 00:11:45.372 mentioned by antalicate between the

NOTE Confidence: 0.942682696551724

00:11:45.372 --> 00:11:47.832 neuronal cells as they different

NOTE Confidence: 0.942682696551724

00:11:47.832 --> 00:11:49.800 shades and endothelial cells.

NOTE Confidence: 0.942682696551724

00:11:49.800 --> 00:11:50.648 And it can introduce,

NOTE Confidence: 0.942682696551724

00:11:50.648 --> 00:11:51.920 which we did in this case.

NOTE Confidence: 0.942682696551724

00:11:51.920 --> 00:11:54.626 Also project cells into a more

NOTE Confidence: 0.942682696551724

00:11:54.626 --> 00:11:57.203 developed network and see how the

NOTE Confidence: 0.942682696551724

00:11:57.203 --> 00:11:59.861 presence of both neuronal cells and

NOTE Confidence: 0.942682696551724

00:11:59.861 --> 00:12:02.920 in the field cells make may control

NOTE Confidence: 0.942682696551724

00:12:02.920 --> 00:12:05.120 the behavior of this progenitor

NOTE Confidence: 0.942682696551724

00:12:05.120 --> 00:12:06.880 cells neural progeneral cells.

NOTE Confidence: 0.942682696551724

00:12:06.880 --> 00:12:09.344 And you can again introduce the gradients

NOTE Confidence: 0.942682696551724

00:12:09.344 --> 00:12:11.598 now of variety of different cues.

NOTE Confidence: 0.942682696551724

00:12:11.600 --> 00:12:16.456 So I could be B&P we've heard about some

NOTE Confidence: 0.942682696551724

00:12:16.456 --> 00:12:18.582 examples have already been enunciated

NOTE Confidence: 0.942682696551724

00:12:18.582 --> 00:12:20.874 and so you can have introduction

NOTE Confidence: 0.942682696551724

00:12:20.874 --> 00:12:22.828 of multiple gradients can attended

NOTE Confidence: 0.942682696551724

00:12:22.828 --> 00:12:24.678 that can potentially either Dr.

NOTE Confidence: 0.942682696551724

00:12:24.680 --> 00:12:27.158 migration of the cells and how they

NOTE Confidence: 0.942682696551724

00:12:27.158 --> 00:12:29.202 position them themselves now in the

NOTE Confidence: 0.942682696551724

00:12:29.202 --> 00:12:31.656 more realistic model of this brain

NOTE Confidence: 0.942682696551724

00:12:31.656 --> 00:12:34.918 tissue or what happens to them in different.

NOTE Confidence: 0.942682696551724

00:12:34.920 --> 00:12:37.160 Concentration within this gradient,

NOTE Confidence: 0.942682696551724

00:12:37.160 --> 00:12:37.720 right.

NOTE Confidence: 0.942682696551724

00:12:37.720 --> 00:12:40.432 And so you can study that and of

NOTE Confidence: 0.942682696551724

00:12:40.432 --> 00:12:41.712 course again you can visualize

NOTE Confidence: 0.942682696551724

00:12:41.712 --> 00:12:42.480 what happens within

NOTE Confidence: 0.949478315833333

00:12:42.534 --> 00:12:43.818 the clusters. So again,

NOTE Confidence: 0.949478315833333

00:12:43.818 --> 00:12:45.912 this is calcium imaging before you

NOTE Confidence: 0.949478315833333

00:12:45.912 --> 00:12:48.012 saw that in the memory tissue,

NOTE Confidence: 0.949478315833333

00:12:48.012 --> 00:12:49.876 organoid in this case,

NOTE Confidence: 0.949478315833333

00:12:49.880 --> 00:12:52.358 it's neural tissue, not yet organoid,

NOTE Confidence: 0.949478315833333

00:12:52.360 --> 00:12:54.280 it's cluster of cells,

NOTE Confidence: 0.949478315833333

00:12:54.280 --> 00:12:57.640 but you can already see how they

NOTE Confidence: 0.949478315833333

00:12:57.640 --> 00:12:58.712 show this neuronal phenotypes,

NOTE Confidence: 0.949478315833333

00:12:58.712 --> 00:13:00.052 how they communicate with each

NOTE Confidence: 0.949478315833333

00:13:00.052 --> 00:13:01.340 other and they can visualize

NOTE Confidence: 0.949478315833333

00:13:01.340 --> 00:13:02.320 calcium signaling in them.

NOTE Confidence: 0.907636881111111

00:13:05.420 --> 00:13:08.402 So of course I already mentioned

NOTE Confidence: 0.907636881111111

00:13:08.402 --> 00:13:10.932 flora multiple times, and I think

NOTE Confidence: 0.907636881111111

00:13:10.932 --> 00:13:13.340 she's going to talk about that more.

NOTE Confidence: 0.907636881111111

00:13:13.340 --> 00:13:16.580 So I'm not going to go into biology of

NOTE Confidence: 0.907636881111111

00:13:16.580 --> 00:13:19.154 of what happens with embryos and what

NOTE Confidence: 0.907636881111111

00:13:19.154 --> 00:13:21.481 happens with the development of the brain

NOTE Confidence: 0.907636881111111

00:13:21.481 --> 00:13:23.740 very much other than to say that again,

NOTE Confidence: 0.907636881111111

00:13:23.740 --> 00:13:26.140 there are gradients, of course,

NOTE Confidence: 0.907636881111111

00:13:26.140 --> 00:13:28.124 in the developing embryo.

NOTE Confidence: 0.907636881111111

00:13:28.124 --> 00:13:30.108 Of multiple morphogens and

NOTE Confidence: 0.907636881111111

00:13:30.108 --> 00:13:32.458 multiple signals that really

NOTE Confidence: 0.907636881111111

00:13:32.458 --> 00:13:34.710 define axis for developing embryo.

NOTE Confidence: 0.907636881111111

00:13:34.710 --> 00:13:37.535 And it again is of interest to see

NOTE Confidence: 0.907636881111111

00:13:37.535 --> 00:13:39.405 what happens either with cells,

NOTE Confidence: 0.907636881111111

00:13:39.410 --> 00:13:40.930 single cells or cell ensembles

NOTE Confidence: 0.907636881111111

00:13:40.930 --> 00:13:42.450 that they just showed you,

NOTE Confidence: 0.907636881111111

00:13:42.450 --> 00:13:45.579 or even with organoids that may be

NOTE Confidence: 0.907636881111111

00:13:45.579 --> 00:13:47.766 exposed the gradients of various

NOTE Confidence: 0.907636881111111

00:13:47.766 --> 00:13:50.433 cues and it could be the actual.

NOTE Confidence: 0.907636881111111

00:13:50.440 --> 00:13:51.696 Signaling molecules for something

NOTE Confidence: 0.907636881111111

00:13:51.696 --> 00:13:52.638 that mimics them.

NOTE Confidence: 0.907636881111111

00:13:52.640 --> 00:13:53.260 For example,

NOTE Confidence: 0.907636881111111

00:13:53.260 --> 00:13:55.430 this G SK3 inhibitor is widely used

NOTE Confidence: 0.907636881111111

00:13:55.430 --> 00:13:57.355 and used by flora quite a bit.

NOTE Confidence: 0.907636881111111

00:13:57.360 --> 00:14:00.416 And so we tried to develop this radiance

NOTE Confidence: 0.907636881111111

00:14:00.416 --> 00:14:02.800 and analyze the outcomes of that.

NOTE Confidence: 0.907636881111111

00:14:02.800 --> 00:14:05.160 And again as I said,

NOTE Confidence: 0.907636881111111

00:14:05.160 --> 00:14:05.916 Flora will likely,

NOTE Confidence: 0.907636881111111

00:14:05.916 --> 00:14:07.176 I don't know exactly what

NOTE Confidence: 0.907636881111111

00:14:07.176 --> 00:14:08.359 she's going to talk about,

NOTE Confidence: 0.907636881111111

00:14:08.360 --> 00:14:10.256 but she will talk a little

NOTE Confidence: 0.907636881111111

00:14:10.256 --> 00:14:11.520 bit more about this.

NOTE Confidence: 0.907636881111111

00:14:11.520 --> 00:14:13.434 And so this devices again are

NOTE Confidence: 0.907636881111111

00:14:13.434 --> 00:14:15.160 very similar in some sense,

NOTE Confidence: 0.907636881111111

00:14:15.160 --> 00:14:17.098 but but have now been optimized

NOTE Confidence: 0.907636881111111

00:14:17.098 --> 00:14:18.710 and developed and that does

NOTE Confidence: 0.907636881111111

00:14:18.710 --> 00:14:20.246 take quite a bit of time.

NOTE Confidence: 0.907636881111111

00:14:20.250 --> 00:14:22.255 Forebrain organize that are much

NOTE Confidence: 0.907636881111111

00:14:22.255 --> 00:14:24.260 more complex than the ensembles

NOTE Confidence: 0.907636881111111

00:14:24.332 --> 00:14:26.087 that they showed you before.

NOTE Confidence: 0.907636881111111

00:14:26.090 --> 00:14:27.566 And this is what you do,

NOTE Confidence: 0.907636881111111

00:14:27.570 --> 00:14:29.290 is you try to optimize all of this.

NOTE Confidence: 0.907636881111111

00:14:29.290 --> 00:14:33.280 You do both analysis and experiments and

NOTE Confidence: 0.907636881111111

00:14:33.280 --> 00:14:35.488 modeling of what happens in such devices.

NOTE Confidence: 0.907636881111111

00:14:35.490 --> 00:14:35.970 Ultimately,

NOTE Confidence: 0.907636881111111

00:14:35.970 --> 00:14:39.330 of course what you look at is

NOTE Confidence: 0.907636881111111

00:14:39.330 --> 00:14:41.770 the outcome of the genetic level

NOTE Confidence: 0.907636881111111

00:14:41.770 --> 00:14:43.082 of expression of different

NOTE Confidence: 0.907636881111111

00:14:43.082 --> 00:14:44.722 markers of different tissues you

NOTE Confidence: 0.907636881111111

00:14:44.722 --> 00:14:46.409 can play with concentrations,

NOTE Confidence: 0.907636881111111

00:14:46.410 --> 00:14:49.130 different concentrations you can.

NOTE Confidence: 0.907636881111111

00:14:49.130 --> 00:14:52.770 Do different types of analysis in

NOTE Confidence: 0.907636881111111

00:14:52.770 --> 00:14:55.050 terms of for example different

NOTE Confidence: 0.907636881111111

00:14:55.050 --> 00:14:56.810 hydrogel composition of collagen.

NOTE Confidence: 0.907636881111111

00:14:56.810 --> 00:14:59.690 We just again heard from Angelica

NOTE Confidence: 0.907636881111111

00:14:59.690 --> 00:15:01.640 that the extra cell metrics is

NOTE Confidence: 0.907636881111111

00:15:01.640 --> 00:15:03.678 very important and so how does

NOTE Confidence: 0.907636881111111

00:15:03.678 --> 00:15:05.760 it affected how the gradients of

NOTE Confidence: 0.907636881111111

00:15:05.838 --> 00:15:07.258 different morphogens affected.

NOTE Confidence: 0.907636881111111

00:15:07.258 --> 00:15:09.562 And of course even visually you

NOTE Confidence: 0.907636881111111

00:15:09.562 --> 00:15:11.460 can see that depending on where

NOTE Confidence: 0.907636881111111

00:15:11.460 --> 00:15:12.810 you are in the gradient,

NOTE Confidence: 0.907636881111111

00:15:12.810 --> 00:15:16.618 in this case still 1 dimensional gradient.

NOTE Confidence: 0.907636881111111

00:15:16.620 --> 00:15:18.750 It really defines the outcome in

NOTE Confidence: 0.907636881111111

00:15:18.750 --> 00:15:20.756 terms of the differentiation and

NOTE Confidence: 0.907636881111111

00:15:20.756 --> 00:15:23.096 expression of the differentiation markers.

NOTE Confidence: 0.907636881111111

00:15:23.100 --> 00:15:25.137 Now we want to really take it

NOTE Confidence: 0.907636881111111

00:15:25.140 --> 00:15:27.600 beyond this and since there are

NOTE Confidence: 0.907636881111111

00:15:27.600 --> 00:15:29.428 multiple axis for differentiation,

NOTE Confidence: 0.907636881111111

00:15:29.428 --> 00:15:34.059 if you have dorsal ventral AT axis and so on,

NOTE Confidence: 0.907636881111111

00:15:34.060 --> 00:15:35.950 it would be wonderful to develop

NOTE Confidence: 0.907636881111111

00:15:35.950 --> 00:15:37.640 now fields of this morphogens

NOTE Confidence: 0.907636881111111

00:15:37.640 --> 00:15:39.824 that may be 2 dimensional or

NOTE Confidence: 0.907636881111111

00:15:39.824 --> 00:15:41.774 high dimensional so that embryos

NOTE Confidence: 0.907636881111111

00:15:41.774 --> 00:15:44.138 positioned in different parts of this.

NOTE Confidence: 0.907636881111111

00:15:44.140 --> 00:15:47.460 Field can have different combinations

NOTE Confidence: 0.907636881111111

00:15:47.460 --> 00:15:51.322 of morphogens affecting their

NOTE Confidence: 0.907636881111111

00:15:51.322 --> 00:15:54.646 differentiation and So what you really

NOTE Confidence: 0.907636881111111

00:15:54.646 --> 00:15:57.340 get if you succeed in experiment

NOTE Confidence: 0.907636881111111

00:15:57.340 --> 00:15:59.976 like this is a really snapshot of

NOTE Confidence: 0.907636881111111

00:15:59.976 --> 00:16:02.070 not just one combination of different

NOTE Confidence: 0.907636881111111

00:16:02.134 --> 00:16:03.818 inputs or different factors,

NOTE Confidence: 0.907636881111111

00:16:03.820 --> 00:16:06.385 but multiple combinations present in

NOTE Confidence: 0.907636881111111

00:16:06.385 --> 00:16:09.948 a sort of A2 dimensional those distribution.

NOTE Confidence: 0.907636881111111

00:16:09.948 --> 00:16:13.364 And of course by modulating what you.

NOTE Confidence: 0.907636881111111

00:16:13.370 --> 00:16:15.232 Do with these devices you can get

NOTE Confidence: 0.907636881111111

00:16:15.232 --> 00:16:17.178 all sorts of different gradients

NOTE Confidence: 0.907636881111111

00:16:17.178 --> 00:16:18.810 and gradient distributions,

NOTE Confidence: 0.907636881111111

00:16:18.810 --> 00:16:20.988 and again you can do various

NOTE Confidence: 0.907636881111111

00:16:20.988 --> 00:16:22.440 types of experimental tests

NOTE Confidence: 0.943608176666667

00:16:22.512 --> 00:16:24.327 and simulations of all this.

NOTE Confidence: 0.943608176666667

00:16:24.330 --> 00:16:26.406 But ultimately, again as we make

NOTE Confidence: 0.943608176666667

00:16:26.410 --> 00:16:28.318 hopefully we'll hear from Flora and

NOTE Confidence: 0.943608176666667

00:16:28.318 --> 00:16:30.730 this is done very much with her lab,

NOTE Confidence: 0.943608176666667

00:16:30.730 --> 00:16:34.531 you can really now begin to examine

NOTE Confidence: 0.943608176666667

00:16:34.531 --> 00:16:36.770 within this two-dimensional fields

NOTE Confidence: 0.943608176666667

00:16:36.770 --> 00:16:39.250 what happens with the expression

NOTE Confidence: 0.943608176666667

00:16:39.250 --> 00:16:43.260 now of markers that will tell you.

NOTE Confidence: 0.943608176666667

00:16:43.260 --> 00:16:47.012 About the AP&DV or Dorsodential

NOTE Confidence: 0.943608176666667

00:16:47.012 --> 00:16:49.522 here access imposed by Sony

NOTE Confidence: 0.943608176666667

00:16:49.522 --> 00:16:51.492 Hedgehog and this compound that

NOTE Confidence: 0.943608176666667

00:16:51.492 --> 00:16:53.623 they mentioned before which is the

NOTE Confidence: 0.943608176666667

00:16:53.623 --> 00:16:56.468 G SK3 inhibitor and really look at

NOTE Confidence: 0.943608176666667

00:16:56.468 --> 00:16:59.552 the rated changes in distribution

NOTE Confidence: 0.943608176666667

00:16:59.552 --> 00:17:02.417 of multiple expression markers and

NOTE Confidence: 0.943608176666667

00:17:02.417 --> 00:17:05.531 ultimately how it corresponds to the

NOTE Confidence: 0.943608176666667

00:17:05.531 --> 00:17:07.857 differentiation in the actual embryo now.

NOTE Confidence: 0.940253532962963

00:17:10.470 --> 00:17:12.084 I meant to insert conclusion slide

NOTE Confidence: 0.940253532962963

00:17:12.084 --> 00:17:14.070 but it didn't come out and so well

NOTE Confidence: 0.940253532962963

00:17:14.070 --> 00:17:15.689 I'll tell you a little bit just

NOTE Confidence: 0.940253532962963

00:17:15.689 --> 00:17:17.387 to summarize a couple of thoughts,

NOTE Confidence: 0.940253532962963

00:17:17.390 --> 00:17:20.225 I'll leave you with that and also

NOTE Confidence: 0.940253532962963

00:17:20.230 --> 00:17:23.429 with what we want to do next.

NOTE Confidence: 0.940253532962963

00:17:23.430 --> 00:17:26.031 So again I think one of the things I

NOTE Confidence: 0.940253532962963

00:17:26.031 --> 00:17:27.990 would like to, I wanted to illustrate

NOTE Confidence: 0.940253532962963

00:17:27.990 --> 00:17:29.550 it's no not the only challenge,

NOTE Confidence: 0.940253532962963

00:17:29.550 --> 00:17:31.790 but one of the challenges again is how

NOTE Confidence: 0.940253532962963

00:17:31.790 --> 00:17:34.130 do you screen multiple conditions,

NOTE Confidence: 0.940253532962963

00:17:34.130 --> 00:17:38.109 how do you explore the influence of graded?

NOTE Confidence: 0.940253532962963

00:17:38.110 --> 00:17:40.470 Inputs, it could be attractants,

NOTE Confidence: 0.940253532962963

00:17:40.470 --> 00:17:43.428 growth factors, it could be morphogens,

NOTE Confidence: 0.940253532962963

00:17:43.430 --> 00:17:44.590 could be other things.

NOTE Confidence: 0.940253532962963

00:17:44.590 --> 00:17:47.370 So how do you study that and do you

NOTE Confidence: 0.940253532962963

00:17:47.370 --> 00:17:49.308 really have technologies to do that?

NOTE Confidence: 0.940253532962963

00:17:49.310 --> 00:17:51.109 And the answer is that the technology,

NOTE Confidence: 0.940253532962963

00:17:51.110 --> 00:17:52.270 at least for that part,

NOTE Confidence: 0.940253532962963

00:17:52.270 --> 00:17:54.700 is becoming more and more mature

NOTE Confidence: 0.940253532962963

00:17:54.700 --> 00:17:56.870 and applicable to multiple scales.

NOTE Confidence: 0.940253532962963

00:17:56.870 --> 00:17:58.270 You know, you can play with cells,

NOTE Confidence: 0.940253532962963

00:17:58.270 --> 00:18:01.430 you can play with cell small cell

NOTE Confidence: 0.940253532962963

00:18:01.430 --> 00:18:04.230 ensembles or even larger organized

NOTE Confidence: 0.940253532962963

00:18:04.230 --> 00:18:05.916 and you really can explore that.

NOTE Confidence: 0.940253532962963

00:18:05.920 --> 00:18:07.640 One huge limitation of course,

NOTE Confidence: 0.940253532962963

00:18:07.640 --> 00:18:09.684 is the actual size of the organoids

NOTE Confidence: 0.940253532962963

00:18:09.684 --> 00:18:13.280 that we are playing with, which is,

NOTE Confidence: 0.940253532962963

00:18:13.280 --> 00:18:14.440 as already has been mentioned,

NOTE Confidence: 0.940253532962963

00:18:14.440 --> 00:18:15.502 is really limited.

NOTE Confidence: 0.940253532962963

00:18:15.502 --> 00:18:17.435 For example by the vascularization.

NOTE Confidence: 0.940253532962963

00:18:17.435 --> 00:18:20.010 We don't really have vascularization

NOTE Confidence: 0.940253532962963

00:18:20.010 --> 00:18:21.040 of organoids,

NOTE Confidence: 0.940253532962963

00:18:21.040 --> 00:18:23.060 and therefore whatever nutrients

NOTE Confidence: 0.940253532962963

00:18:23.060 --> 00:18:25.080 or oxygen they get,

NOTE Confidence: 0.940253532962963

00:18:25.080 --> 00:18:26.930 they get by diffusion from

NOTE Confidence: 0.940253532962963

00:18:26.930 --> 00:18:28.040 the surrounding medium,

NOTE Confidence: 0.940253532962963

00:18:28.040 --> 00:18:29.792 and that means that you cannot

NOTE Confidence: 0.940253532962963

00:18:29.792 --> 00:18:31.838 grow them beyond a certain size

NOTE Confidence: 0.940253532962963

00:18:31.838 --> 00:18:33.466 before they become necrotic.

NOTE Confidence: 0.940253532962963

00:18:33.470 --> 00:18:36.350 In the at the center and that means

NOTE Confidence: 0.940253532962963

00:18:36.350 --> 00:18:38.060 that that's actually one of the

NOTE Confidence: 0.940253532962963

00:18:38.060 --> 00:18:39.693 bigger challenges that flora and I

NOTE Confidence: 0.940253532962963

00:18:39.693 --> 00:18:41.067 have been discussing quite a bit.

NOTE Confidence: 0.940253532962963

00:18:41.070 --> 00:18:43.310 And then and Helica mentioned as well,

NOTE Confidence: 0.940253532962963

00:18:43.310 --> 00:18:45.464 how do you really vascularize organoids

NOTE Confidence: 0.940253532962963

00:18:45.464 --> 00:18:48.629 and how do you introduce that component,

NOTE Confidence: 0.940253532962963

00:18:48.630 --> 00:18:50.709 especially because vascular

NOTE Confidence: 0.940253532962963

00:18:50.709 --> 00:18:53.183 component can affect formation

NOTE Confidence: 0.940253532962963

00:18:53.183 --> 00:18:55.148 of this structures as well.

NOTE Confidence: 0.940253532962963

00:18:55.150 --> 00:18:57.858 So there's crosstalk between

NOTE Confidence: 0.940253532962963

00:18:57.858 --> 00:19:00.566 vasculature and neural tissue.

NOTE Confidence: 0.940253532962963

00:19:00.570 --> 00:19:02.593 So this it's a huge challenge for

NOTE Confidence: 0.940253532962963

00:19:02.593 --> 00:19:04.045 the whole community and we're

NOTE Confidence: 0.940253532962963

00:19:04.045 --> 00:19:05.370 trying to tackle it now.

NOTE Confidence: 0.940253532962963

00:19:05.370 --> 00:19:07.490 And beyond that of course,

NOTE Confidence: 0.940253532962963

00:19:07.490 --> 00:19:09.586 how can we really build it up in

NOTE Confidence: 0.940253532962963

00:19:09.586 --> 00:19:12.089 terms of the complexity of both the

NOTE Confidence: 0.940253532962963

00:19:12.089 --> 00:19:14.004 tissues themselves and the fields

NOTE Confidence: 0.940253532962963

00:19:14.072 --> 00:19:16.406 of different inputs that this such

NOTE Confidence: 0.940253532962963

00:19:16.406 --> 00:19:18.870 tissues can experience and do it in

NOTE Confidence: 0.940253532962963

00:19:18.870 --> 00:19:20.370 the relatively high throughput fashion.

NOTE Confidence: 0.940253532962963

00:19:20.370 --> 00:19:22.058 So this is what we are super excited

NOTE Confidence: 0.940253532962963

00:19:22.058 --> 00:19:23.769 right now about and this technology

NOTE Confidence: 0.940253532962963

00:19:23.769 --> 00:19:25.009 really has been progressing.

NOTE Confidence: 0.940253532962963

00:19:25.010 --> 00:19:27.180 So hopefully it will be widely used.

NOTE Confidence: 0.940253532962963

00:19:27.180 --> 00:19:29.098 As as it becomes available to you.

NOTE Confidence: 0.940253532962963

00:19:29.100 --> 00:19:30.000 Thank you very much.