WEBVTT

NOTE duration:”00:21:26”

NOTE recognizability:0.931

NOTE language:en-us

NOTE Confidence: 0.943128857142857

00:00:00.000 --> 00:00:02.198 We're moving now to the next speaker,

NOTE Confidence: 0.943128857142857

00:00:02.200 --> 00:00:03.258 Angelica Gonzalez.

NOTE Confidence: 0.943128857142857

00:00:03.258 --> 00:00:06.432 She's a associate professor of biomedical

NOTE Confidence: 0.943128857142857

00:00:06.432 --> 00:00:09.358 engineering at the Yale School of

NOTE Confidence: 0.943128857142857

00:00:09.358 --> 00:00:11.154 Engineering and Applied Science.

NOTE Confidence: 0.943128857142857

00:00:11.160 --> 00:00:14.044 Her appointment is an association with the

NOTE Confidence: 0.943128857142857

00:00:14.044 --> 00:00:16.720 vascular Biology and Therapeutics program.

NOTE Confidence: 0.943128857142857

00:00:16.720 --> 00:00:19.010 We should provide the convenient

NOTE Confidence: 0.943128857142857

00:00:19.010 --> 00:00:20.842 platform for her research.

NOTE Confidence: 0.943128857142857

00:00:20.850 --> 00:00:22.720 Research is focused on the

NOTE Confidence: 0.943128857142857

00:00:22.720 --> 00:00:24.216 development of biomaterials for

NOTE Confidence: 0.943128857142857

00:00:24.216 --> 00:00:26.168 use as investigational tools,

NOTE Confidence: 0.943128857142857

00:00:26.170 --> 00:00:28.378 particularly for the investigation

NOTE Confidence: 0.943128857142857

00:00:28.378 --> 00:00:30.034 of immunological responses

NOTE Confidence: 0.943128857142857

00:00:30.034 --> 00:00:31.690 to inflammatory signals.

NOTE Confidence: 0.943128857142857

00:00:31.690 --> 00:00:32.530 Thank you very much.

NOTE Confidence: 0.94226628

00:00:53.830 --> 00:00:55.510 Thank you to the organizers

NOTE Confidence: 0.94226628

00:00:55.510 --> 00:00:57.190 for having me here today.

NOTE Confidence: 0.94226628

00:00:57.190 --> 00:01:00.070 I am, As for indicated,

NOTE Confidence: 0.94226628

00:01:00.070 --> 00:01:03.190 a biomedical engineer, so don't really

NOTE Confidence: 0.94226628

00:01:03.190 --> 00:01:04.905 see myself in these spaces very often.

NOTE Confidence: 0.94226628

00:01:04.910 --> 00:01:07.150 So I'm flattered to have been invited and

NOTE Confidence: 0.94226628

00:01:07.150 --> 00:01:10.896 I hope this is informative to your group.

NOTE Confidence: 0.94226628

00:01:10.900 --> 00:01:13.462 The work that my lab does really

NOTE Confidence: 0.94226628

00:01:13.462 --> 00:01:16.035 focuses on the idea that organs,

NOTE Confidence: 0.94226628

00:01:16.035 --> 00:01:20.205 organoids really require the the aid

NOTE Confidence: 0.94226628

00:01:20.205 --> 00:01:22.922 of microvasculature specifically to

NOTE Confidence: 0.94226628

00:01:22.922 --> 00:01:25.627 feed the cells the multicellular.

NOTE Confidence: 0.94226628

00:01:25.630 --> 00:01:27.370 Constructs within the structures

NOTE Confidence: 0.94226628

00:01:27.370 --> 00:01:29.545 in order to deliver nutrients,

NOTE Confidence: 0.94226628

00:01:29.550 --> 00:01:32.214 oxygen, but also when you add

NOTE Confidence: 0.94226628

00:01:32.214 --> 00:01:33.990 vascular structures into anything,

NOTE Confidence: 0.94226628

00:01:33.990 --> 00:01:37.510 you increase the multicellular interactions.

NOTE Confidence: 0.94226628

00:01:37.510 --> 00:01:39.890 We consider the vasculature itself

NOTE Confidence: 0.94226628

00:01:39.890 --> 00:01:42.270 a multicellular structure and it

NOTE Confidence: 0.94226628

00:01:42.350 --> 00:01:44.770 increases the complexity of these.

NOTE Confidence: 0.94226628

00:01:44.770 --> 00:01:45.978 These organisms,

NOTE Confidence: 0.94226628

00:01:45.978 --> 00:01:50.206 but it's as tissue engineering has developed,

NOTE Confidence: 0.94226628

00:01:50.210 --> 00:01:51.454 as organoids are continuing

NOTE Confidence: 0.94226628

00:01:51.454 --> 00:01:53.009 to develop in their systems,

NOTE Confidence: 0.94226628

00:01:53.010 --> 00:01:54.495 it's clear that an understanding

NOTE Confidence: 0.94226628

00:01:54.495 --> 00:01:55.683 of the microvascular structure,

NOTE Confidence: 0.94226628

00:01:55.690 --> 00:01:57.490 in particular its diversity,

NOTE Confidence: 0.94226628

00:01:57.490 --> 00:01:59.290 the way it grows,

NOTE Confidence: 0.94226628

00:01:59.290 --> 00:02:01.510 and the way it maintains homeostatic

NOTE Confidence: 0.94226628

00:02:01.510 --> 00:02:03.850 and converts into a pathological

NOTE Confidence: 0.94226628

00:02:03.850 --> 00:02:06.820 structure is important to understand.

NOTE Confidence: 0.94226628

00:02:06.820 --> 00:02:08.820 And so that's what my lab has come to do.

NOTE Confidence: 0.94226628

00:02:08.820 --> 00:02:10.398 Over over years,

NOTE Confidence: 0.94226628

00:02:10.398 --> 00:02:13.522 we have us come to appreciate

NOTE Confidence: 0.94226628

00:02:13.522 --> 00:02:15.578 that the multicellular constructs,

NOTE Confidence: 0.94226628

00:02:15.580 --> 00:02:18.020 endothelial cells and the parasites

NOTE Confidence: 0.94226628

00:02:18.020 --> 00:02:20.970 are required for formation of

NOTE Confidence: 0.94226628

00:02:20.970 --> 00:02:22.740 a healthy vasculature.

NOTE Confidence: 0.94226628

00:02:22.740 --> 00:02:25.521 So what you see up on the upper right

NOTE Confidence: 0.94226628

00:02:25.521 --> 00:02:28.328 hand corner is a placental organ where

NOTE Confidence: 0.94226628

00:02:28.328 --> 00:02:31.218 you can see microvascular structure both.

NOTE Confidence: 0.94226628

00:02:31.218 --> 00:02:32.654 Let's see.

NOTE Confidence: 0.94226628

00:02:32.654 --> 00:02:35.280 Longitudinally and transected and

NOTE Confidence: 0.94226628

00:02:35.280 --> 00:02:38.100 cut in the transverse of supported

NOTE Confidence: 0.94226628

00:02:38.100 --> 00:02:39.981 within these structures that

NOTE Confidence: 0.94226628

00:02:39.981 --> 00:02:42.345 we outgrow in order to isolate

NOTE Confidence: 0.94226628

00:02:42.345 --> 00:02:44.440 a human vascular structures.

NOTE Confidence: 0.94226628

00:02:44.440 --> 00:02:46.652 You can also see that the structure

NOTE Confidence: 0.94226628

00:02:46.652 --> 00:02:47.600 of the microvasculature,

NOTE Confidence: 0.94226628

00:02:47.600 --> 00:02:49.696 and this is in human lung tissue that

NOTE Confidence: 0.94226628

00:02:49.696 --> 00:02:51.678 we sliced can be is quite apparent.

NOTE Confidence: 0.94226628

00:02:51.680 --> 00:02:53.145 The individual cells line the

NOTE Confidence: 0.94226628

00:02:53.145 --> 00:02:54.317 lumen of the vessel.

NOTE Confidence: 0.94226628

00:02:54.320 --> 00:02:55.922 The parasites are in the outside

NOTE Confidence: 0.94226628

00:02:55.922 --> 00:02:57.520 of that supporting that structure.

NOTE Confidence: 0.94226628

00:02:57.520 --> 00:02:59.554 In this auto fluorescent image and

NOTE Confidence: 0.94226628

00:02:59.554 --> 00:03:01.342 in the second harmonic generated

NOTE Confidence: 0.94226628

00:03:01.342 --> 00:03:03.520 generation image you can see the

NOTE Confidence: 0.94226628

00:03:03.520 --> 00:03:05.570 complexity and the support required

NOTE Confidence: 0.94226628

00:03:05.570 --> 00:03:07.358 of the extracellular matrix,

NOTE Confidence: 0.94226628

00:03:07.360 --> 00:03:10.528 another component of this complex structure.

NOTE Confidence: 0.94226628

00:03:10.530 --> 00:03:12.945 And within the actual wall of the

NOTE Confidence: 0.94226628

00:03:12.945 --> 00:03:14.778 microvasculature is what we consider

NOTE Confidence: 0.94226628

00:03:14.778 --> 00:03:16.968 a basic called the basement membrane.

NOTE Confidence: 0.94226628

00:03:16.970 --> 00:03:18.650 It supports the growth of the

NOTE Confidence: 0.94226628

00:03:18.650 --> 00:03:20.184 endothelial cells and the pericides

NOTE Confidence: 0.94226628

00:03:20.184 --> 00:03:21.969 within these structures as well.

NOTE Confidence: 0.94226628

00:03:21.970 --> 00:03:24.406 And so all of these cells again

NOTE Confidence: 0.94226628

00:03:24.410 --> 00:03:26.982 work together in order to deliver

NOTE Confidence: 0.94226628

00:03:26.982 --> 00:03:28.630 nutrients support the structure

NOTE Confidence: 0.94226628

00:03:28.630 --> 00:03:31.082 of full organs are are natural

NOTE Confidence: 0.94226628

00:03:31.082 --> 00:03:32.687 organs as well as the

NOTE Confidence: 0.949198844444445

00:03:34.930 --> 00:03:36.634 as well as organoids that are

NOTE Confidence: 0.949198844444445

00:03:36.634 --> 00:03:37.486 now becoming vascularized.

NOTE Confidence: 0.944027375

00:03:39.510 --> 00:03:41.400 So as an engineer, what we've come

NOTE Confidence: 0.944027375

00:03:41.400 --> 00:03:44.261 to do is really think about how most

NOTE Confidence: 0.944027375

00:03:44.261 --> 00:03:46.241 systems rely on biochemical signals

NOTE Confidence: 0.944027375

00:03:46.312 --> 00:03:48.344 and cell cell interactions that

NOTE Confidence: 0.944027375

00:03:48.344 --> 00:03:50.708 that are required in these organs.

NOTE Confidence: 0.944027375

00:03:50.710 --> 00:03:52.995 But there's an increasing appreciation

NOTE Confidence: 0.944027375

00:03:52.995 --> 00:03:55.746 that the extracellular matrix itself is

NOTE Confidence: 0.944027375

00:03:55.746 --> 00:03:57.756 essential for promoting self organization

NOTE Confidence: 0.944027375

00:03:57.756 --> 00:04:00.099 and other cues within the tissue.

NOTE Confidence: 0.944027375

00:04:00.100 --> 00:04:02.480 In fact, the extracellular matrix

NOTE Confidence: 0.944027375

00:04:02.480 --> 00:04:04.860 is a reciprocal communicating device

NOTE Confidence: 0.944027375

00:04:04.934 --> 00:04:07.628 between cells where they inform the

NOTE Confidence: 0.944027375

00:04:07.628 --> 00:04:09.700 extracellular matrix and cells are

NOTE Confidence: 0.944027375

00:04:09.700 --> 00:04:12.955 driven to in their functions by the

NOTE Confidence: 0.944027375

00:04:12.955 --> 00:04:14.350 extracellular matrix themselves.

NOTE Confidence: 0.944027375

00:04:14.350 --> 00:04:17.070 Is you, you can see here in collagen

NOTE Confidence: 0.944027375

00:04:17.070 --> 00:04:19.222 gels that we've created dependent

NOTE Confidence: 0.944027375

00:04:19.222 --> 00:04:20.950 on the structure here,

NOTE Confidence: 0.944027375

00:04:20.950 --> 00:04:23.950 the fibrillarity of the collagen gel,

NOTE Confidence: 0.944027375

00:04:23.950 --> 00:04:26.477 whether it's a small thin fiber full

NOTE Confidence: 0.944027375

00:04:26.477 --> 00:04:28.907 of small pores or a larger fiber,

NOTE Confidence: 0.944027375

00:04:28.910 --> 00:04:31.590 it really directs the morphology,

NOTE Confidence: 0.944027375

00:04:31.590 --> 00:04:34.320 but also the phenotypes of the

NOTE Confidence: 0.944027375

00:04:34.320 --> 00:04:36.350 expression of contractile fibers,

NOTE Confidence: 0.944027375

00:04:36.350 --> 00:04:38.692 proteins like alphasin, muscle, actin.

NOTE Confidence: 0.944027375

00:04:38.692 --> 00:04:41.009 Not only do we think about the

NOTE Confidence: 0.944027375

00:04:41.009 --> 00:04:42.481 architecture of the extracellular

NOTE Confidence: 0.944027375

00:04:42.481 --> 00:04:43.917 matrix as an informing,

NOTE Confidence: 0.944027375

00:04:43.920 --> 00:04:46.678 as a tool in informing the structure

NOTE Confidence: 0.944027375

00:04:46.678 --> 00:04:48.360 and organization of cells,

NOTE Confidence: 0.944027375

00:04:48.360 --> 00:04:50.496 but we also know that the composition of

NOTE Confidence: 0.944027375

00:04:50.496 --> 00:04:51.999 the extracellular matrix is important,

NOTE Confidence: 0.944027375

00:04:52.000 --> 00:04:54.400 and that means the presentation of

NOTE Confidence: 0.944027375

00:04:54.400 --> 00:04:56.544 specific proteins like collagens,

NOTE Confidence: 0.944027375

00:04:56.544 --> 00:04:59.152 laminins and pyronectin and the

NOTE Confidence: 0.944027375

00:04:59.152 --> 00:05:01.224 biomechanics of those structures.

NOTE Confidence: 0.944027375

00:05:01.230 --> 00:05:02.494 And as an engineer,

NOTE Confidence: 0.944027375

00:05:02.494 --> 00:05:04.752 again that's really where we focus on

NOTE Confidence: 0.944027375

00:05:04.752 --> 00:05:06.880 most of our attention is thinking about

NOTE Confidence: 0.944027375

00:05:06.880 --> 00:05:08.726 how these elements independently and

NOTE Confidence: 0.944027375

00:05:08.726 --> 00:05:11.470 in concert work to direct cell behavior.

NOTE Confidence: 0.942266279999999

00:05:14.110 --> 00:05:15.902 So we first started in my lab a

NOTE Confidence: 0.942266279999999

00:05:15.902 --> 00:05:17.719 number of years ago in developing

NOTE Confidence: 0.942266279999999

00:05:17.719 --> 00:05:19.359 novel polymers that would allow

NOTE Confidence: 0.942266279999999

00:05:19.359 --> 00:05:21.542 that would allow us to invest cells

NOTE Confidence: 0.942266279999999

00:05:21.542 --> 00:05:23.142 both 2 dimensionally and three

NOTE Confidence: 0.942266279999999

00:05:23.142 --> 00:05:24.710 dimensionally into their structures,

NOTE Confidence: 0.942266279999999

00:05:24.710 --> 00:05:26.468 but really with the idea of.

NOTE Confidence: 0.942266279999999

00:05:26.470 --> 00:05:29.010 Turning polymers that looks like

NOTE Confidence: 0.942266279999999

00:05:29.010 --> 00:05:31.182 non porous flat structures into

NOTE Confidence: 0.942266279999999

00:05:31.182 --> 00:05:33.102 something that looked much more

NOTE Confidence: 0.942266279999999

00:05:33.102 --> 00:05:35.110 like a basement membrane.

NOTE Confidence: 0.942266279999999

00:05:35.110 --> 00:05:37.446 So here what I'm showing you is the

NOTE Confidence: 0.942266279999999

00:05:37.446 --> 00:05:38.910 polyethylene glycol in different

NOTE Confidence: 0.942266279999999

00:05:38.910 --> 00:05:41.110 molecular weights so changing the

NOTE Confidence: 0.942266279999999

00:05:41.110 --> 00:05:42.846 the length of the chain but can

NOTE Confidence: 0.942266279999999

00:05:42.846 --> 00:05:44.459 be modified to look more fibrillar

NOTE Confidence: 0.942266279999999

00:05:44.459 --> 00:05:46.349 or pour rated much more like a

NOTE Confidence: 0.942266279999999

00:05:46.404 --> 00:05:48.454 human extracellular matrix than our

NOTE Confidence: 0.942266279999999

00:05:48.454 --> 00:05:50.094 standard polycarbonate transfers that

NOTE Confidence: 0.942266279999999

00:05:50.094 --> 00:05:54.175 we use through creation of either

NOTE Confidence: 0.942266279999999

00:05:54.175 --> 00:05:57.107 sacrificial crystal structures or.

NOTE Confidence: 0.942266279999999

00:05:57.110 --> 00:05:57.942 Salt structures.

NOTE Confidence: 0.942266279999999

00:05:57.942 --> 00:06:00.854 What this does is not only gives

NOTE Confidence: 0.942266279999999

00:06:00.854 --> 00:06:02.446 us an altered architecture,

NOTE Confidence: 0.942266279999999

00:06:02.446 --> 00:06:04.406 but also changes the mechanics

NOTE Confidence: 0.942266279999999

00:06:04.406 --> 00:06:06.621 of the environment to be more

NOTE Confidence: 0.942266279999999

00:06:06.621 --> 00:06:08.667 replicative of that that a cell

NOTE Confidence: 0.942266279999999

00:06:08.738 --> 00:06:10.508 would want to see in tissue.

NOTE Confidence: 0.942266279999999

00:06:10.510 --> 00:06:12.715 So the polycarbonate transwell is on the

NOTE Confidence: 0.942266279999999

00:06:12.715 --> 00:06:15.268 order of two gigapascals and stiffness,

NOTE Confidence: 0.942266279999999

00:06:15.270 --> 00:06:16.506 something like bone.

NOTE Confidence: 0.942266279999999

00:06:16.506 --> 00:06:18.154 Whereas the polyethylene glycol

NOTE Confidence: 0.942266279999999

00:06:18.154 --> 00:06:20.074 structure can be modified vastly

NOTE Confidence: 0.942266279999999

00:06:20.074 --> 00:06:22.446 to be very soft and viscoelastic

NOTE Confidence: 0.942266279999999

00:06:22.446 --> 00:06:26.422 and modified to be stiff as well.

NOTE Confidence: 0.942266279999999

00:06:26.430 --> 00:06:27.350 And so as I mentioned,

NOTE Confidence: 0.942266279999999

00:06:27.350 --> 00:06:29.354 composition is also a key component

NOTE Confidence: 0.942266279999999

00:06:29.354 --> 00:06:31.649 of how we understand the structure of

NOTE Confidence: 0.942266279999999

00:06:31.649 --> 00:06:34.790 the tissue that supports the cells.

NOTE Confidence: 0.942266279999999

00:06:34.790 --> 00:06:36.134 And that can mean that we can

NOTE Confidence: 0.942266279999999

00:06:36.134 --> 00:06:36.710 take whole tissue.

NOTE Confidence: 0.942266279999999

00:06:36.710 --> 00:06:38.710 So we've taken skin,

NOTE Confidence: 0.942266279999999

00:06:38.710 --> 00:06:40.710 lung and other organs,

NOTE Confidence: 0.942266279999999

00:06:40.710 --> 00:06:42.545 decellularize them and then reconstitute

NOTE Confidence: 0.942266279999999

00:06:42.545 --> 00:06:44.858 the proteins that make up these

NOTE Confidence: 0.942266279999999

00:06:44.858 --> 00:06:46.546 tissues within these structures.

NOTE Confidence: 0.942266279999999

00:06:46.550 --> 00:06:48.310 You can do that with cell derived proteins.

NOTE Confidence: 0.942266279999999

00:06:48.310 --> 00:06:50.291 And so here I'm showing you that

NOTE Confidence: 0.942266279999999

00:06:50.291 --> 00:06:51.720 endothelial cells and pericytes.

NOTE Confidence: 0.942266279999999

00:06:51.720 --> 00:06:53.600 Can be cultured, decellularized,

NOTE Confidence: 0.942266279999999

00:06:53.600 --> 00:06:55.480 their extracellular matrix evaluated,

NOTE Confidence: 0.942266279999999

00:06:55.480 --> 00:06:57.512 and then encompassed into

NOTE Confidence: 0.942266279999999

00:06:57.512 --> 00:06:59.036 these polymeric structures.

NOTE Confidence: 0.942266279999999

00:06:59.040 --> 00:07:01.077 Or we can take peptide sequences that

NOTE Confidence: 0.942266279999999

00:07:01.077 --> 00:07:02.800 are very specific for immigrants,

NOTE Confidence: 0.942266279999999

00:07:02.800 --> 00:07:05.110 for example adhesive moieties that

NOTE Confidence: 0.942266279999999

00:07:05.110 --> 00:07:07.420 could drive cellular function for

NOTE Confidence: 0.942266279999999

00:07:07.498 --> 00:07:09.538 investigation or for function.

NOTE Confidence: 0.942266279999999

00:07:09.540 --> 00:07:10.780 And as I mentioned,

NOTE Confidence: 0.942266279999999

00:07:10.780 --> 00:07:12.640 not just fibrillarity can be modified

NOTE Confidence: 0.942266279999999

00:07:12.699 --> 00:07:14.655 in our architecture of the scaffold,

NOTE Confidence: 0.942266279999999

00:07:14.660 --> 00:07:16.970 but we also think about pore

NOTE Confidence: 0.942266279999999

00:07:16.970 --> 00:07:18.544 diameter or distribution across

NOTE Confidence: 0.942266279999999

00:07:18.544 --> 00:07:20.956 these structures so that we can

NOTE Confidence: 0.942266279999999

00:07:20.956 --> 00:07:23.327 modify them to look much more like

NOTE Confidence: 0.942266279999999

00:07:23.327 --> 00:07:25.340 a specific type of human tissue.

NOTE Confidence: 0.942266279999999

00:07:25.340 --> 00:07:27.482 And what I've described to you is

NOTE Confidence: 0.942266279999999

00:07:27.482 --> 00:07:29.425 much of the bulk characteristics

NOTE Confidence: 0.942266279999999

00:07:29.425 --> 00:07:32.140 of such tissues and we've also

NOTE Confidence: 0.942266279999999

00:07:32.140 --> 00:07:34.340 moved forward to thinking about

NOTE Confidence: 0.942266279999999

00:07:34.340 --> 00:07:37.050 new methods or additional methods.

NOTE Confidence: 0.942266279999999

00:07:37.050 --> 00:07:39.690 To look at the micro environment,

NOTE Confidence: 0.942266279999999

00:07:39.690 --> 00:07:41.796 so as we know when we think about the

NOTE Confidence: 0.942266279999999

00:07:41.796 --> 00:07:43.087 extracellular matrix or bulk tissue,

NOTE Confidence: 0.942266279999999

00:07:43.090 --> 00:07:44.330 we're thinking about a mix

NOTE Confidence: 0.942266279999999

00:07:44.330 --> 00:07:45.730 of proteins and a mix of

NOTE Confidence: 0.944827872727273

00:07:48.010 --> 00:07:49.714 elements. But if you think about

NOTE Confidence: 0.944827872727273

00:07:49.714 --> 00:07:51.170 what the cell actually sees,

NOTE Confidence: 0.944827872727273

00:07:51.170 --> 00:07:53.454 it's a single protein,

NOTE Confidence: 0.944827872727273

00:07:53.454 --> 00:07:56.253 it's a single fiber for example.

NOTE Confidence: 0.944827872727273

00:07:56.253 --> 00:07:58.419 And so by using Electro spinning

NOTE Confidence: 0.944827872727273

00:07:58.419 --> 00:07:59.768 techniques here shown here,

NOTE Confidence: 0.944827872727273

00:07:59.770 --> 00:08:03.166 we can create scaffolds that allow for

NOTE Confidence: 0.944827872727273

00:08:03.166 --> 00:08:05.856 single cell interactions with fibers.

NOTE Confidence: 0.944827872727273

00:08:05.860 --> 00:08:07.988 We can make these fibers in a way

NOTE Confidence: 0.944827872727273

00:08:07.988 --> 00:08:09.678 that their mechanics are more

NOTE Confidence: 0.944827872727273

00:08:09.678 --> 00:08:11.972 replicative of those of human collagen,

NOTE Confidence: 0.944827872727273

00:08:11.972 --> 00:08:12.916 for example,

NOTE Confidence: 0.944827872727273

00:08:12.916 --> 00:08:16.220 and also modify single fiber so that

NOTE Confidence: 0.944827872727273

00:08:16.300 --> 00:08:18.925 they present either these adhesive

NOTE Confidence: 0.944827872727273

00:08:18.925 --> 00:08:22.020 moieties or parts of human proteins.

NOTE Confidence: 0.944566485714286

00:08:24.560 --> 00:08:26.177 So what I'm going to describe to

NOTE Confidence: 0.944566485714286

00:08:26.177 --> 00:08:27.900 you are some experiments that we've

NOTE Confidence: 0.944566485714286

00:08:27.900 --> 00:08:29.844 done in both 2 dimensional systems

NOTE Confidence: 0.944566485714286

00:08:29.844 --> 00:08:31.792 using these scaffolds as a planer

NOTE Confidence: 0.944566485714286

00:08:31.792 --> 00:08:33.432 structures in which endothelial cells

NOTE Confidence: 0.944566485714286

00:08:33.432 --> 00:08:35.571 and pericides can be cultured and will

NOTE Confidence: 0.944566485714286

00:08:35.571 --> 00:08:37.677 add neural stem cells to these as well.

NOTE Confidence: 0.944566485714286

00:08:37.680 --> 00:08:39.752 Or what I'm showing you here is work

NOTE Confidence: 0.944566485714286

00:08:39.752 --> 00:08:41.834 by a collaborator, Andre Lechenko,

NOTE Confidence: 0.944566485714286

00:08:41.834 --> 00:08:44.193 who you'll be hearing from next that

NOTE Confidence: 0.944566485714286

00:08:44.193 --> 00:08:46.849 was published in 2019 that describes

NOTE Confidence: 0.944566485714286

00:08:46.849 --> 00:08:48.653 endothelial cell pericide interactions

NOTE Confidence: 0.944566485714286

00:08:48.653 --> 00:08:51.088 and how we used his models to further

NOTE Confidence: 0.944566485714286

00:08:51.088 --> 00:08:53.026 investigate the role of vascular

NOTE Confidence: 0.944566485714286

00:08:53.026 --> 00:08:54.556 cells in contributing to disease.

NOTE Confidence: 0.944566485714286

00:08:54.560 --> 00:08:58.212 State. So as I mentioned,

NOTE Confidence: 0.944566485714286

00:08:58.212 --> 00:09:00.330 when we're thinking about how to

NOTE Confidence: 0.944566485714286

00:09:00.407 --> 00:09:03.317 replicate human microvasculature in vitro,

NOTE Confidence: 0.944566485714286

00:09:03.320 --> 00:09:05.144 we're thinking quite a bit about

NOTE Confidence: 0.944566485714286

00:09:05.144 --> 00:09:06.710 not just collecting the cells

NOTE Confidence: 0.944566485714286

00:09:06.710 --> 00:09:08.474 and putting them into the space,

NOTE Confidence: 0.944566485714286

00:09:08.480 --> 00:09:10.240 but also what they're looking

NOTE Confidence: 0.944566485714286

00:09:10.240 --> 00:09:11.648 like in these spaces.

NOTE Confidence: 0.944566485714286

00:09:11.650 --> 00:09:13.325 So just by simple modification

NOTE Confidence: 0.944566485714286

00:09:13.325 --> 00:09:14.330 of the architecture,

NOTE Confidence: 0.944566485714286

00:09:14.330 --> 00:09:16.290 what you can see here is that parasites

NOTE Confidence: 0.944566485714286

00:09:16.290 --> 00:09:18.167 can look like more stilt formation,

NOTE Confidence: 0.944566485714286

00:09:18.170 --> 00:09:19.850 they can have multiple extensions,

NOTE Confidence: 0.944566485714286

00:09:19.850 --> 00:09:22.688 they can look elongated or very

NOTE Confidence: 0.944566485714286

00:09:22.688 --> 00:09:25.533 rounded and depending on these the

NOTE Confidence: 0.944566485714286

00:09:25.533 --> 00:09:27.305 presentation of these fibriller

NOTE Confidence: 0.944566485714286

00:09:27.305 --> 00:09:30.026 structures you can also get these

NOTE Confidence: 0.944566485714286

00:09:30.026 --> 00:09:33.580 changes in expression and protein.

NOTE Confidence: 0.944566485714286

00:09:33.580 --> 00:09:35.146 Even the collagen that so many

NOTE Confidence: 0.944566485714286

00:09:35.146 --> 00:09:37.806 of us use in lab can be modified

NOTE Confidence: 0.944566485714286

00:09:37.806 --> 00:09:39.746 very simply through changes in

NOTE Confidence: 0.944566485714286

00:09:39.746 --> 00:09:41.538 concentration or curing temperature.

NOTE Confidence: 0.944566485714286

00:09:41.540 --> 00:09:43.605 So what I'm showing you here is

NOTE Confidence: 0.944566485714286

00:09:43.605 --> 00:09:46.300 that whether room temperature or

NOTE Confidence: 0.944566485714286

00:09:46.300 --> 00:09:51.160 additional changes in or at different
NOTE Confidence: 0.944566485714286
00:09:51.160 --> 00:09:52.780 temperatures and concentrations,
NOTE Confidence: 0.944566485714286
00:09:52.780 --> 00:09:56.402 you can alter the fibrillerity and the
NOTE Confidence: 0.944566485714286
00:09:56.402 --> 00:09:58.988 density of these collagen fibers that
NOTE Confidence: 0.944566485714286
00:09:58.988 --> 00:10:01.456 would subsequently change the way the
NOTE Confidence: 0.944566485714286
00:10:01.456 --> 00:10:03.760 cells are responding to these systems.
NOTE Confidence: 0.944566485714286
00:10:03.760 --> 00:10:05.580 So what I hope to have given you so far
NOTE Confidence: 0.944566485714286
00:10:05.630 --> 00:10:07.358 is the idea that matrix architecture,
NOTE Confidence: 0.944566485714286
00:10:07.360 --> 00:10:09.570 composition and mechanics can influence
NOTE Confidence: 0.944566485714286
00:10:09.570 --> 00:10:12.559 cells behavior at the single cell level.
NOTE Confidence: 0.944566485714286
00:10:12.560 --> 00:10:14.268 So what I'm going to describe to
NOTE Confidence: 0.944566485714286
00:10:14.268 --> 00:10:16.503 you now is how we look use these
NOTE Confidence: 0.944566485714286
00:10:16.503 --> 00:10:17.948 engineered models to start to
NOTE Confidence: 0.944566485714286
00:10:18.010 --> 00:10:20.025 understand better the complexity of
NOTE Confidence: 0.944566485714286
00:10:20.025 --> 00:10:22.040 cellular interactions and what that
NOTE Confidence: 0.944566485714286
00:10:22.040 --> 00:10:26.000 means for development of disease

NOTE Confidence: 0.944566485714286

00:10:26.000 --> 00:10:27.260 and development of therapeutics.

NOTE Confidence: 0.944566485714286

00:10:27.260 --> 00:10:29.757 The first story I'm going to tell you

NOTE Confidence: 0.944566485714286

00:10:29.757 --> 00:10:31.682 is a little bit about the microvascular

NOTE Confidence: 0.944566485714286

00:10:31.690 --> 00:10:37.650 and the role of parasites in fibrosis.

NOTE Confidence: 0.944566485714286

00:10:37.650 --> 00:10:38.994 As I mentioned,

NOTE Confidence: 0.944566485714286

00:10:38.994 --> 00:10:41.234 human parasites that we've taken

NOTE Confidence: 0.944566485714286

00:10:41.234 --> 00:10:44.042 from the placenta were we've

NOTE Confidence: 0.944566485714286

00:10:44.042 --> 00:10:46.982 created structures where we could

NOTE Confidence: 0.944566485714286

00:10:46.982 --> 00:10:49.447 incorporate into these polymers a

NOTE Confidence: 0.944566485714286

00:10:49.450 --> 00:10:53.517 healthy human lung tissue or an IPF

NOTE Confidence: 0.944566485714286

00:10:53.517 --> 00:10:55.800 idiopathic pulmonary fibrotic lung.

NOTE Confidence: 0.944566485714286

00:10:55.800 --> 00:10:57.500 We've put these into scaffolds

NOTE Confidence: 0.944566485714286

00:10:57.500 --> 00:10:59.200 that were either very soft,

NOTE Confidence: 0.944566485714286

00:10:59.200 --> 00:11:01.153 so on the order of 1 kilopascal

NOTE Confidence: 0.944566485714286

00:11:01.153 --> 00:11:02.480 like a healthy tissue,

NOTE Confidence: 0.944566485714286

00:11:02.480 --> 00:11:04.175 or very stiff 20 kilopascals

NOTE Confidence: 0.944566485714286

00:11:04.175 --> 00:11:06.400 like that of a fibrotic tissue.

NOTE Confidence: 0.944566485714286

00:11:06.400 --> 00:11:09.207 What this did was it enabled us

NOTE Confidence: 0.944566485714286

00:11:09.207 --> 00:11:11.470 to determine whether or not the

NOTE Confidence: 0.944566485714286

00:11:11.470 --> 00:11:15.000 effect of the protein changes were

NOTE Confidence: 0.944566485714286

00:11:15.000 --> 00:11:17.995 sufficient to drive the morphological

NOTE Confidence: 0.944566485714286

00:11:17.995 --> 00:11:20.605 changes and the tip changes that

NOTE Confidence: 0.944566485714286

00:11:20.605 --> 00:11:22.799 Perry sites often exhibit when

NOTE Confidence: 0.944566485714286

00:11:22.800 --> 00:11:24.960 they are in a fibrotic environment.

NOTE Confidence: 0.944566485714286

00:11:24.960 --> 00:11:26.850 What we found was it is really

NOTE Confidence: 0.944566485714286

00:11:26.850 --> 00:11:28.640 the stiffness of the environment,

NOTE Confidence: 0.944566485714286

00:11:28.640 --> 00:11:30.120 not the presence of collagen,

NOTE Confidence: 0.944566485714286

00:11:30.120 --> 00:11:31.600 not the presence of laminin,

NOTE Confidence: 0.944566485714286

00:11:31.600 --> 00:11:34.480 that drives these phenotypic changes.

NOTE Confidence: 0.944566485714286

00:11:34.480 --> 00:11:35.398 So as you can see here,

NOTE Confidence: 0.944566485714286

00:11:35.400 --> 00:11:38.120 the parasites extend uniformly when

NOTE Confidence: 0.944566485714286

00:11:38.120 --> 00:11:40.840 they're on a stiffer environment,

NOTE Confidence: 0.944566485714286

00:11:40.840 --> 00:11:43.996 increasing their alpha smooth methyl actin,

NOTE Confidence: 0.8482625

00:11:44.000 --> 00:11:47.480 which is also a marker of Myo fibroblastness,

NOTE Confidence: 0.8482625

00:11:47.480 --> 00:11:49.331 their trends differentiation

NOTE Confidence: 0.8482625

00:11:49.331 --> 00:11:51.799 into a fibrotic state.

NOTE Confidence: 0.8482625

00:11:51.800 --> 00:11:53.250 So having confirmed that these

NOTE Confidence: 0.8482625

00:11:53.250 --> 00:11:54.700 cells were actually able to

NOTE Confidence: 0.8482625

00:11:54.756 --> 00:11:56.360 respond to the microenvironment,

NOTE Confidence: 0.8482625

00:11:56.360 --> 00:11:57.600 so mechanical sensing and

NOTE Confidence: 0.8482625

00:11:57.600 --> 00:11:58.840 we created the system,

NOTE Confidence: 0.8482625

00:11:58.840 --> 00:12:01.160 we got to talk with our collaborators in

NOTE Confidence: 0.9219367

00:12:03.440 --> 00:12:05.468 pulmonary medicine about the

NOTE Confidence: 0.9219367

00:12:05.468 --> 00:12:07.496 occurrence of myofiberblast trans

NOTE Confidence: 0.9219367

00:12:07.496 --> 00:12:09.390 differentiation in human tissue.

NOTE Confidence: 0.9219367

00:12:09.390 --> 00:12:12.120 And so Erica Herzog here in pulmonary

NOTE Confidence: 0.9219367

00:12:12.120 --> 00:12:14.358 medicine helped us to obtain human lung

NOTE Confidence: 0.9219367

00:12:14.358 --> 00:12:17.324 tissue and in our control you can see

NOTE Confidence: 0.9219367

00:12:17.324 --> 00:12:19.409 that in these tissues microvasculature

NOTE Confidence: 0.9219367

00:12:19.409 --> 00:12:22.710 that's N G2 positive of a parasite

NOTE Confidence: 0.9219367

00:12:22.710 --> 00:12:24.374 marker parasites are abundant in

NOTE Confidence: 0.9219367

00:12:24.374 --> 00:12:26.716 the lung and they are well aligned

NOTE Confidence: 0.9219367

00:12:26.716 --> 00:12:30.161 along the the micro vessel actually.

NOTE Confidence: 0.9219367

00:12:30.161 --> 00:12:33.216 Disassemble and while the parasites,

NOTE Confidence: 0.9219367

00:12:33.220 --> 00:12:34.684 the N G2 positive cells are

NOTE Confidence: 0.9219367

00:12:34.684 --> 00:12:35.660 still alive in there,

NOTE Confidence: 0.9219367

00:12:35.660 --> 00:12:38.180 they're now positive for alpha SMA,

NOTE Confidence: 0.9219367

00:12:38.180 --> 00:12:39.524 indicating their contribution

NOTE Confidence: 0.9219367

00:12:39.524 --> 00:12:41.340 to the fibrotic foci,

NOTE Confidence: 0.9219367

00:12:41.340 --> 00:12:43.640 so contributing to collagen deposition

NOTE Confidence: 0.9219367

00:12:43.640 --> 00:12:46.778 and changes in the extracellular matrix.

NOTE Confidence: 0.9219367

00:12:46.780 --> 00:12:48.838 This is the first time anyone has

NOTE Confidence: 0.9219367

00:12:48.838 --> 00:12:50.130 shown that parasites microvascular

NOTE Confidence: 0.9219367

00:12:50.130 --> 00:12:52.254 cells could leave the vessel wall

NOTE Confidence: 0.9219367

00:12:52.254 --> 00:12:53.944 and contribute to the formation

NOTE Confidence: 0.9219367

00:12:53.944 --> 00:12:56.180 of a disease lesion in human IPF.

NOTE Confidence: 0.9219367

00:12:56.180 --> 00:12:59.464 And in fact about 15% of the

NOTE Confidence: 0.9219367

00:12:59.464 --> 00:13:01.653 cells in these lesions were at

NOTE Confidence: 0.9219367

00:13:01.653 --> 00:13:04.018 G2 positive and LSMA positive.

NOTE Confidence: 0.951658786666667

00:13:07.170 --> 00:13:09.672 So as I mentioned when thinking

NOTE Confidence: 0.951658786666667

00:13:09.672 --> 00:13:11.961 about these parasites and their

NOTE Confidence: 0.951658786666667

00:13:11.961 --> 00:13:14.129 contribution to disease states,

NOTE Confidence: 0.951658786666667

00:13:14.130 --> 00:13:16.608 the initiating factor would have to be

NOTE Confidence: 0.951658786666667

00:13:16.608 --> 00:13:18.834 departed with their departure from the

NOTE Confidence: 0.951658786666667

00:13:18.834 --> 00:13:22.810 vessel wall in about 2007 through 2011,

NOTE Confidence: 0.951658786666667

00:13:22.810 --> 00:13:25.340 Boris Hines and Jeremy Duffield

NOTE Confidence: 0.951658786666667

00:13:25.340 --> 00:13:28.672 had demonstrated that in in kidney

NOTE Confidence: 0.951658786666667

00:13:28.672 --> 00:13:32.320 disease they in kidney disease wrap.

NOTE Confidence: 0.951658786666667

00:13:32.320 --> 00:13:33.880 Mouse and rabbit models,

NOTE Confidence: 0.951658786666667

00:13:33.880 --> 00:13:35.580 they were able to observe

NOTE Confidence: 0.951658786666667

00:13:35.580 --> 00:13:37.280 parasites leaving the vessel wall,

NOTE Confidence: 0.951658786666667

00:13:37.280 --> 00:13:39.320 but no one had observed that

NOTE Confidence: 0.951658786666667

00:13:39.320 --> 00:13:40.790 of the the human.

NOTE Confidence: 0.951658786666667

00:13:40.790 --> 00:13:43.950 And so with the tools made by our

NOTE Confidence: 0.951658786666667

00:13:44.042 --> 00:13:45.986 collaborator Andre Luvchenko,

NOTE Confidence: 0.951658786666667

00:13:45.986 --> 00:13:49.792 we were able to evaluate the extent to

NOTE Confidence: 0.951658786666667

00:13:49.792 --> 00:13:52.382 which parasites would actually depart

NOTE Confidence: 0.951658786666667

00:13:52.382 --> 00:13:55.652 the vessel wall after a TGF beta,

NOTE Confidence: 0.951658786666667

00:13:55.652 --> 00:13:58.411 transforming growth factor beta stimulus

NOTE Confidence: 0.951658786666667

00:13:58.411 --> 00:14:01.357 to move into the interstitial tissue.

NOTE Confidence: 0.951658786666667

00:14:01.360 --> 00:14:03.586 What this suggested was that the

NOTE Confidence: 0.951658786666667

00:14:03.586 --> 00:14:05.535 same signals that induce fibrosis

NOTE Confidence: 0.951658786666667

00:14:05.535 --> 00:14:07.881 in the human lung could actually

NOTE Confidence: 0.951658786666667

00:14:07.881 --> 00:14:10.320 induce the initial departure of the

NOTE Confidence: 0.951658786666667

00:14:10.320 --> 00:14:12.315 parasite from the vascular wall.

NOTE Confidence: 0.925274907142857

00:14:14.400 --> 00:14:16.176 Not only do these parasites leave

NOTE Confidence: 0.925274907142857

00:14:16.176 --> 00:14:18.229 the vascular wall and migrate into

NOTE Confidence: 0.925274907142857

00:14:18.229 --> 00:14:20.320 the interstitial, but if we put

NOTE Confidence: 0.925274907142857

00:14:20.320 --> 00:14:22.610 them onto a human healthy lung and.

NOTE Confidence: 0.925274907142857

00:14:22.610 --> 00:14:24.450 We activated them with the TGF beta signal.

NOTE Confidence: 0.925274907142857

00:14:24.450 --> 00:14:26.574 We saw a significant deposition of

NOTE Confidence: 0.925274907142857

00:14:26.574 --> 00:14:28.750 collagen 1 suggesting that these cells

NOTE Confidence: 0.925274907142857

00:14:28.750 --> 00:14:30.490 are in fact depositing extracellular

NOTE Confidence: 0.925274907142857

00:14:30.490 --> 00:14:32.530 matrix in a very robust way.

NOTE Confidence: 0.925274907142857

00:14:32.530 --> 00:14:35.330 Not only do they deposit new collagen one,

NOTE Confidence: 0.925274907142857

00:14:35.330 --> 00:14:37.316 but they also increase their expression

NOTE Confidence: 0.925274907142857

00:14:37.316 --> 00:14:39.362 without the SMA confirming that they

NOTE Confidence: 0.925274907142857

00:14:39.362 --> 00:14:40.706 actually are trans differentiating

NOTE Confidence: 0.925274907142857

00:14:40.706 --> 00:14:42.730 into a mild fibroblast like cell.

NOTE Confidence: 0.94830432

00:14:44.990 --> 00:14:46.430 What's interesting for us also,

NOTE Confidence: 0.94830432

00:14:46.430 --> 00:14:47.810 as again at thinking about

NOTE Confidence: 0.94830432

00:14:47.810 --> 00:14:49.190 the mechanics of the system,

NOTE Confidence: 0.94830432

00:14:49.190 --> 00:14:51.087 is that where a healthy lung again

NOTE Confidence: 0.94830432

00:14:51.087 --> 00:14:53.507 is on the order of two kilopascals,

NOTE Confidence: 0.94830432

00:14:53.510 --> 00:14:55.886 a lung of IPF idiopathic pulmonary

NOTE Confidence: 0.94830432

00:14:55.886 --> 00:15:00.110 fibrosis is on the order of 25K pascals,

NOTE Confidence: 0.94830432

00:15:00.110 --> 00:15:03.686 the transformed TGF beta activated lung.

NOTE Confidence: 0.94830432

00:15:03.686 --> 00:15:06.110 In which the parasites receded is

NOTE Confidence: 0.94830432

00:15:06.181 --> 00:15:08.617 now on the order of 18 kilopascals.

NOTE Confidence: 0.94830432

00:15:08.620 --> 00:15:10.384 So these cells were really capable of

NOTE Confidence: 0.94830432

00:15:10.384 --> 00:15:12.160 not just migrating or get away from

NOTE Confidence: 0.94830432

00:15:12.160 --> 00:15:13.618 the vessel wall and these constructs,

NOTE Confidence: 0.94830432

00:15:13.620 --> 00:15:16.040 but now transforming that collagen

NOTE Confidence: 0.94830432

00:15:16.040 --> 00:15:18.844 based extracellular matrix into a

NOTE Confidence: 0.94830432

00:15:18.844 --> 00:15:22.300 stiffer and remodeled environment.

NOTE Confidence: 0.94830432

00:15:22.300 --> 00:15:24.868 We take this information from these

NOTE Confidence: 0.94830432

00:15:24.868 --> 00:15:27.445 engineered tools and we now go

NOTE Confidence: 0.94830432

00:15:27.445 --> 00:15:29.797 into humans to understand more and

NOTE Confidence: 0.94830432

00:15:29.797 --> 00:15:32.128 confirm that these findings are

NOTE Confidence: 0.94830432

00:15:32.128 --> 00:15:34.072 actually are important for humans.

NOTE Confidence: 0.94830432

00:15:34.072 --> 00:15:36.250 So this work with Erica Herzog,

NOTE Confidence: 0.94830432

00:15:36.250 --> 00:15:38.378 we then worked with BI to try

NOTE Confidence: 0.94830432

00:15:38.378 --> 00:15:39.800 out the tentative therapeutics

NOTE Confidence: 0.94830432

00:15:39.800 --> 00:15:41.330 that were initially

NOTE Confidence: 0.947633426666667

00:15:43.890 --> 00:15:45.682 evaluated for IPF patients,

NOTE Confidence: 0.947633426666667

00:15:45.682 --> 00:15:48.897 but now have moved into really thinking

NOTE Confidence: 0.947633426666667

00:15:48.897 --> 00:15:51.680 about whether or not these cells

NOTE Confidence: 0.947633426666667

00:15:51.680 --> 00:15:55.414 exist in all forms of their process,

NOTE Confidence: 0.947633426666667

00:15:55.414 --> 00:15:57.706 their transformation process.

NOTE Confidence: 0.947633426666667

00:15:57.706 --> 00:16:01.950 In humans, so with our collaborators,

NOTE Confidence: 0.947633426666667

00:16:01.950 --> 00:16:05.247 we have used single cell RNA SEQ

NOTE Confidence: 0.947633426666667

00:16:05.247 --> 00:16:08.430 analysis to identify what is now

NOTE Confidence: 0.947633426666667

00:16:08.430 --> 00:16:11.230 currently an unclassified cell of

NOTE Confidence: 0.947633426666667

00:16:11.230 --> 00:16:15.550 parasite ancestry within the lungs of

NOTE Confidence: 0.947633426666667

00:16:15.550 --> 00:16:17.790 interstitial lung disease patients,

NOTE Confidence: 0.947633426666667

00:16:17.790 --> 00:16:21.198 IPF patients and other patients that

NOTE Confidence: 0.947633426666667

00:16:21.198 --> 00:16:23.786 that present with lung disease.

NOTE Confidence: 0.947633426666667

00:16:23.786 --> 00:16:25.976 This novel cell population is

NOTE Confidence: 0.947633426666667

00:16:25.976 --> 00:16:27.928 correlated to an increasingly

NOTE Confidence: 0.947633426666667

00:16:27.928 --> 00:16:30.728 present in these fibrotic states,

NOTE Confidence: 0.947633426666667

00:16:30.730 --> 00:16:32.898 and the unknown population,

NOTE Confidence: 0.947633426666667

00:16:32.898 --> 00:16:35.608 again with a parasite ancestry,

NOTE Confidence: 0.947633426666667

00:16:35.610 --> 00:16:37.230 seems to localize itself

NOTE Confidence: 0.947633426666667

00:16:37.230 --> 00:16:38.445 in perinkable regions,

NOTE Confidence: 0.947633426666667

00:16:38.450 --> 00:16:40.586 suggesting that it is migrating away

NOTE Confidence: 0.947633426666667

00:16:40.586 --> 00:16:42.509 from the vessel and contributing

NOTE Confidence: 0.947633426666667

00:16:42.509 --> 00:16:44.237 to the fibrotic foci.

NOTE Confidence: 0.947633426666667

00:16:44.240 --> 00:16:45.864 What is increasingly interesting

NOTE Confidence: 0.947633426666667

00:16:45.864 --> 00:16:48.300 though is that what our findings

NOTE Confidence: 0.947633426666667

00:16:48.368 --> 00:16:50.618 are suggesting is that these cells

NOTE Confidence: 0.947633426666667

00:16:50.618 --> 00:16:53.070 in the intermediate state are also

NOTE Confidence: 0.947633426666667

00:16:53.070 --> 00:16:55.920 much more reflective of stem cells.

NOTE Confidence: 0.947633426666667

00:16:55.920 --> 00:16:59.840 They are Mick Kayla, 4C D 146 positive.

NOTE Confidence: 0.947633426666667

00:16:59.840 --> 00:17:03.280 It's very similar to also 4 positive as

NOTE Confidence: 0.950317

00:17:05.560 --> 00:17:08.611 identified by our collaborators at UVA.

NOTE Confidence: 0.950317

00:17:08.611 --> 00:17:10.735 So our. Engineered systems

NOTE Confidence: 0.950317

00:17:10.735 --> 00:17:13.390 are now helping us inform,

NOTE Confidence: 0.950317

00:17:13.390 --> 00:17:16.230 helping to inform us as to how to

NOTE Confidence: 0.950317

00:17:16.230 --> 00:17:21.110 evaluate the data from human patients.

NOTE Confidence: 0.950317

00:17:21.110 --> 00:17:22.986 So briefly, I'll tell you a little

NOTE Confidence: 0.950317

00:17:22.986 --> 00:17:25.010 bit about how we're thinking now about

NOTE Confidence: 0.950317

00:17:25.010 --> 00:17:27.291 using the same kind of engineered

NOTE Confidence: 0.950317

00:17:27.291 --> 00:17:29.754 extracellular matrix scaffolds

NOTE Confidence: 0.950317

00:17:29.754 --> 00:17:33.038 to treat neurological injury.

NOTE Confidence: 0.950317

00:17:33.040 --> 00:17:34.156 So as many of you know,

NOTE Confidence: 0.950317

00:17:34.160 --> 00:17:36.160 there is a vast complexity

NOTE Confidence: 0.950317

00:17:36.160 --> 00:17:37.760 of the neurovascular niche.

NOTE Confidence: 0.950317

00:17:37.760 --> 00:17:41.064 It's not completely well understood how the

NOTE Confidence: 0.950317

00:17:41.064 --> 00:17:43.560 vasculature contributes to the maturation,

NOTE Confidence: 0.950317

00:17:43.560 --> 00:17:46.180 the quiescence and even the

NOTE Confidence: 0.950317

00:17:46.180 --> 00:17:48.800 migration of neural stem cells.

NOTE Confidence: 0.950317

00:17:48.800 --> 00:17:49.394 In particular,

NOTE Confidence: 0.950317

00:17:49.394 --> 00:17:51.473 we know that there is an abundance

NOTE Confidence: 0.950317

00:17:51.473 --> 00:17:53.434 of neural stem cells in the

NOTE Confidence: 0.950317

00:17:53.434 --> 00:17:55.034 SVZ or the subventricular zone,

NOTE Confidence: 0.950317

00:17:55.040 --> 00:17:57.608 and it's been suggested that as

NOTE Confidence: 0.950317

00:17:57.608 --> 00:17:59.565 the neural stem cells migrate from

NOTE Confidence: 0.950317

00:17:59.565 --> 00:18:01.528 the SVZ to the olfactory mold

NOTE Confidence: 0.950317

00:18:01.528 --> 00:18:03.036 through the rostal migratory.

NOTE Confidence: 0.950317

00:18:03.040 --> 00:18:04.696 Or a stream.

NOTE Confidence: 0.950317

00:18:04.696 --> 00:18:07.240 The the contact with the

NOTE Confidence: 0.950317

00:18:07.240 --> 00:18:09.702 vasculature really drives its again,

NOTE Confidence: 0.950317

00:18:09.702 --> 00:18:10.244 quiescence,

NOTE Confidence: 0.950317

00:18:10.244 --> 00:18:12.954 migration and survival and maturation.

NOTE Confidence: 0.950317

00:18:12.960 --> 00:18:16.786 So by taking cues from the work

NOTE Confidence: 0.950317

00:18:16.786 --> 00:18:18.826 that had been done historically

NOTE Confidence: 0.950317

00:18:18.826 --> 00:18:21.556 in around the neural vascular

NOTE Confidence: 0.950317

00:18:21.560 --> 00:18:22.800 niche and neural stem cell

NOTE Confidence: 0.864214078571429

00:18:26.080 --> 00:18:29.650 research, we. Ought to try to

NOTE Confidence: 0.864214078571429

00:18:29.650 --> 00:18:32.194 develop very specific regions,

NOTE Confidence: 0.864214078571429

00:18:32.194 --> 00:18:36.082 regional mimics of the the brain.

NOTE Confidence: 0.864214078571429

00:18:36.090 --> 00:18:37.035 What's becomes very

NOTE Confidence: 0.864214078571429

00:18:37.035 --> 00:18:38.610 important is as I mentioned,

NOTE Confidence: 0.864214078571429

00:18:38.610 --> 00:18:42.180 we typically use in and in tissue

NOTE Confidence: 0.864214078571429

00:18:42.180 --> 00:18:44.305 culture things on the order substrates

NOTE Confidence: 0.864214078571429

00:18:44.305 --> 00:18:46.770 on the order of two gigapascals,

NOTE Confidence: 0.864214078571429

00:18:46.770 --> 00:18:49.370 but when we're working with lung or skin,

NOTE Confidence: 0.864214078571429

00:18:49.370 --> 00:18:53.064 we're on the order of about 20 kilopascals.

NOTE Confidence: 0.864214078571429

00:18:53.064 --> 00:18:55.986 And brain is much more viscoelastic,

NOTE Confidence: 0.864214078571429

00:18:55.990 --> 00:18:56.870 much softer.

NOTE Confidence: 0.864214078571429

00:18:56.870 --> 00:18:59.950 So this meant creating new systems that

NOTE Confidence: 0.864214078571429

00:18:59.950 --> 00:19:02.734 allowed us to template or mimic in this

NOTE Confidence: 0.864214078571429

00:19:02.734 --> 00:19:05.469 case the SPZ much more realistically

NOTE Confidence: 0.864214078571429

00:19:05.470 --> 00:19:08.781 with on the with our mechanics on

NOTE Confidence: 0.864214078571429

00:19:08.781 --> 00:19:12.155 the order of less than 1000 Pascals.

NOTE Confidence: 0.864214078571429

00:19:12.155 --> 00:19:15.395 We also stain tissues of the tissues in

NOTE Confidence: 0.864214078571429

00:19:15.395 --> 00:19:18.003 order to determine which compositional

NOTE Confidence: 0.864214078571429

00:19:18.003 --> 00:19:21.195 proteins are part of these structures.

NOTE Confidence: 0.864214078571429

00:19:21.200 --> 00:19:22.440 And together with that information,

NOTE Confidence: 0.864214078571429

00:19:22.440 --> 00:19:26.726 we can incorporate those proteins and into

NOTE Confidence: 0.864214078571429

00:19:26.726 --> 00:19:29.642 our templated mimics to represent more

NOTE Confidence: 0.864214078571429

00:19:29.642 --> 00:19:32.057 closely specific regions of the roster,

NOTE Confidence: 0.864214078571429

00:19:32.057 --> 00:19:34.799 migratory stream SBZ and olfactory bowl.

NOTE Confidence: 0.864214078571429

00:19:34.800 --> 00:19:37.016 So what you'll see here is that if

NOTE Confidence: 0.864214078571429

00:19:37.016 --> 00:19:38.851 we culture endothelial cells and

NOTE Confidence: 0.864214078571429

00:19:38.851 --> 00:19:41.275 parasites with our neural stem cells,

NOTE Confidence: 0.864214078571429

00:19:41.280 --> 00:19:43.776 we can start to observe neural

NOTE Confidence: 0.864214078571429

00:19:43.776 --> 00:19:45.024 stem cell clustering.

NOTE Confidence: 0.864214078571429

00:19:45.030 --> 00:19:47.022 This is a phenomenon that it's

NOTE Confidence: 0.864214078571429

00:19:47.022 --> 00:19:48.590 important and required for the

NOTE Confidence: 0.864214078571429

00:19:48.590 --> 00:19:50.830 functional migration of the NSC

NOTE Confidence: 0.864214078571429

00:19:50.830 --> 00:19:53.070 through the rosto migratory stream.

NOTE Confidence: 0.864214078571429

00:19:53.070 --> 00:19:55.058 And in fact the creation of these

NOTE Confidence: 0.864214078571429

00:19:55.058 --> 00:19:56.847 tools allows us to observe first

NOTE Confidence: 0.864214078571429

00:19:56.847 --> 00:19:59.030 hand the migration of these cells,

NOTE Confidence: 0.864214078571429

00:19:59.030 --> 00:20:00.630 observe also their clustering

NOTE Confidence: 0.864214078571429

00:20:00.630 --> 00:20:02.110 and chain migration,

NOTE Confidence: 0.864214078571429

00:20:02.110 --> 00:20:04.180 but helps us to understand that

NOTE Confidence: 0.864214078571429

00:20:04.180 --> 00:20:06.113 in fact it's the endothelial

NOTE Confidence: 0.864214078571429

00:20:06.113 --> 00:20:09.920 cells that are driving these NSC.

NOTE Confidence: 0.864214078571429

00:20:09.920 --> 00:20:12.060 Clustering functions and we were

NOTE Confidence: 0.864214078571429

00:20:12.060 --> 00:20:14.200 able to isolate more specifically

NOTE Confidence: 0.864214078571429

00:20:14.269 --> 00:20:16.810 that the secretion of M MP2 from

NOTE Confidence: 0.864214078571429

00:20:16.810 --> 00:20:18.346 endothelial cells could allow

NOTE Confidence: 0.864214078571429

00:20:18.346 --> 00:20:20.236 for an head hearing cleavage.

NOTE Confidence: 0.864214078571429

00:20:20.240 --> 00:20:22.415 That then facilitated this clustering

NOTE Confidence: 0.864214078571429

00:20:22.415 --> 00:20:24.684 and chain migration because we

NOTE Confidence: 0.864214078571429

00:20:24.684 --> 00:20:27.576 now have a clear understanding of.

NOTE Confidence: 0.864214078571429

00:20:27.580 --> 00:20:29.608 What the endothelial cells of these

NOTE Confidence: 0.864214078571429

00:20:29.608 --> 00:20:31.370 constructs and what is healthy

NOTE Confidence: 0.864214078571429

00:20:31.370 --> 00:20:32.420 for these cells?

NOTE Confidence: 0.864214078571429

00:20:32.420 --> 00:20:35.240 We were able to coencapsulate the

NOTE Confidence: 0.864214078571429

00:20:35.240 --> 00:20:37.595 endothelial cells and neural stem

NOTE Confidence: 0.864214078571429

00:20:37.595 --> 00:20:40.348 cells into a biomimetic of this SPZ

NOTE Confidence: 0.864214078571429

00:20:40.348 --> 00:20:43.116 that keeps them quiescent and deliver

NOTE Confidence: 0.864214078571429

00:20:43.116 --> 00:20:47.092 those into a brain structure and brain

NOTE Confidence: 0.864214078571429

00:20:47.092 --> 00:20:51.280 injury model with our collaborators at.

NOTE Confidence: 0.864214078571429

00:20:51.280 --> 00:20:52.640 University of Pittsburgh what we

NOTE Confidence: 0.864214078571429

00:20:52.640 --> 00:20:54.908 were able to show is that we could

NOTE Confidence: 0.864214078571429

00:20:54.908 --> 00:20:56.606 actually allow these cells to escape

NOTE Confidence: 0.864214078571429

00:20:56.606 --> 00:20:58.676 from these constructs and embed and

NOTE Confidence: 0.864214078571429

00:20:58.676 --> 00:21:00.584 graph themselves within the brain.

NOTE Confidence: 0.864214078571429

00:21:00.584 --> 00:21:03.720 The the stroked region.

NOTE Confidence: 0.864214078571429

00:21:03.720 --> 00:21:05.784 So what I hope to have shared with

NOTE Confidence: 0.864214078571429

00:21:05.784 --> 00:21:07.644 you is that biomatic scaffolds

NOTE Confidence: 0.864214078571429

00:21:07.644 --> 00:21:09.352 can enhance our understanding

NOTE Confidence: 0.864214078571429

00:21:09.352 --> 00:21:11.531 of matrix cell interactions and

NOTE Confidence: 0.864214078571429

00:21:11.531 --> 00:21:13.596 how they drive cell behavior,

NOTE Confidence: 0.864214078571429

00:21:13.600 --> 00:21:16.840 but we can also use cues from these such

NOTE Confidence: 0.864214078571429

00:21:16.840 --> 00:21:20.980 models to inform therapeutic development.

NOTE Confidence: 0.864214078571429

00:21:20.980 --> 00:21:21.500 Thank you,

NOTE Confidence: 0.864214078571429

00:21:21.500 --> 00:21:23.060 and I think all my collaborators

NOTE Confidence: 0.864214078571429

00:21:23.060 --> 00:21:26.000 brought their aid in this work.