WEBVTT

NOTE duration: ”00:25:41.930”

NOTE Confidence: 0.83322746

00:00:00.080 --> 00:00:01.280 Thanks up and also wrapping

NOTE Confidence: 0.83322746

00:00:01.280 --> 00:00:02.800 up the workshop. It's the

NOTE Confidence: 0.83322746

00:00:02.800 --> 00:00:03.780 second keynote,

NOTE Confidence: 0.91378003

00:00:04.160 --> 00:00:05.299 doctor Wendell Lim,

NOTE Confidence: 0.9815973

00:00:05.759 --> 00:00:07.859 who's, visiting us from UCSF.

NOTE Confidence: 0.95622367

00:00:08.559 --> 00:00:10.160 He actually, did his postdoc

NOTE Confidence: 0.95622367

00:00:10.160 --> 00:00:10.719 at Yale,

NOTE Confidence: 0.8713746

00:00:11.200 --> 00:00:12.400 and then he got his,

NOTE Confidence: 0.96978915

00:00:13.115 --> 00:00:14.735 undergrad from Harvard and PhD,

NOTE Confidence: 0.99650145

00:00:15.035 --> 00:00:15.695 in biochemistry

NOTE Confidence: 0.94904983

00:00:16.315 --> 00:00:18.015 and biophysics in MIT.

NOTE Confidence: 0.91425574

00:00:18.715 --> 00:00:19.835 And Doctor Lim has made,

NOTE Confidence: 0.91425574

00:00:20.075 --> 00:00:22.235 pioneering contributions to multiple fields,

NOTE Confidence: 0.91425574

00:00:22.235 --> 00:00:23.375 including cell signaling,

NOTE Confidence: 0.91913855

00:00:23.755 --> 00:00:25.515 systems, synthetic biology, and more

NOTE Confidence: 0.91913855

00:00:25.515 --> 00:00:27.134 recently in immune cell engineering.

NOTE Confidence: 0.9725325

00:00:27.470 --> 00:00:28.430 And so he's currently the

NOTE Confidence: 0.9725325

00:00:28.430 --> 00:00:29.810 Bayer's distinguished professor,

NOTE Confidence: 0.9260572

00:00:31.470 --> 00:00:32.930 of cellular molecular pharmacology

NOTE Confidence: 0.9700021

00:00:33.309 --> 00:00:34.430 and the director of the

NOTE Confidence: 0.9700021

00:00:34.430 --> 00:00:36.530 Cell Design Institute at UCSF.

NOTE Confidence: 0.9700021

00:00:36.829 --> 00:00:37.710 So I'm gonna hand it

NOTE Confidence: 0.9700021

00:00:37.710 --> 00:00:38.989 over to Wendell. Thanks for

NOTE Confidence: 0.9700021

00:00:38.989 --> 00:00:39.489 coming.

NOTE Confidence: 0.92631763

00:00:40.055 --> 00:00:41.495 This works for me. Okay.

NOTE Confidence: 0.92631763

00:00:41.495 --> 00:00:42.215 Hi, everyone.

NOTE Confidence: 0.9864946

00:00:42.614 --> 00:00:43.574 So it's great to be

NOTE Confidence: 0.9864946

00:00:43.574 --> 00:00:45.015 here. And what I'm gonna

NOTE Confidence: 0.9864946

00:00:45.015 --> 00:00:46.055 do is tell you about

NOTE Confidence: 0.9864946

00:00:46.055 --> 00:00:46.635 our work,

NOTE Confidence: 0.9911898

00:00:47.894 --> 00:00:49.114 trying to engineer,

NOTE Confidence: 0.9993972

00:00:50.214 --> 00:00:51.434 new cellular behaviors.

NOTE Confidence: 0.96434927

00:00:51.894 --> 00:00:52.934 So what's shown here on

NOTE Confidence: 0.96434927

00:00:52.934 --> 00:00:54.030 this slide is a a

NOTE Confidence: 0.96434927

00:00:54.110 --> 00:00:55.550 really beautiful movie by Alex

NOTE Confidence: 0.96434927

00:00:55.550 --> 00:00:56.510 Ritter. It's a light sheet,

NOTE Confidence: 0.96434927

00:00:56.829 --> 00:00:58.910 microscopy movie of a, a

NOTE Confidence: 0.96434927

00:00:58.910 --> 00:01:00.190 t cell. And we have,

NOTE Confidence: 0.96434927

00:01:00.190 --> 00:01:01.550 as you know, these cells

NOTE Confidence: 0.96434927

00:01:01.550 --> 00:01:02.589 running around your body. They're

NOTE Confidence: 0.96434927

00:01:02.589 --> 00:01:03.710 patrolling your body, and they're

NOTE Confidence: 0.96434927

00:01:03.710 --> 00:01:05.390 able to defend you, from

NOTE Confidence: 0.96434927

00:01:05.390 --> 00:01:07.330 various infections and and diseases.

NOTE Confidence: 0.9634411

00:01:08.265 --> 00:01:09.784 And, you know, we are

NOTE Confidence: 0.9634411

00:01:09.784 --> 00:01:10.905 very interested in,

NOTE Confidence: 0.98832273

00:01:11.465 --> 00:01:12.905 harnessing those capabilities and asking,

NOTE Confidence: 0.98832273

00:01:12.905 --> 00:01:14.604 can we ask these cells

NOTE Confidence: 0.98832273

00:01:14.825 --> 00:01:15.865 to do new things that

NOTE Confidence: 0.98832273

00:01:15.865 --> 00:01:17.244 they don't normally do?

NOTE Confidence: 0.98366696

00:01:17.784 --> 00:01:19.225 And we're that's also a

NOTE Confidence: 0.98366696

00:01:19.225 --> 00:01:20.505 very fundamental question that we're

NOTE Confidence: 0.98366696

00:01:20.505 --> 00:01:21.564 interested in because,

NOTE Confidence: 0.99842435

00:01:22.185 --> 00:01:23.520 in general, you know,

NOTE Confidence: 0.95093155

00:01:24.000 --> 00:01:25.039 cells are the sort of

NOTE Confidence: 0.95093155

00:01:25.039 --> 00:01:26.719 smallest living unit of of

NOTE Confidence: 0.95093155

00:01:26.719 --> 00:01:28.560 life that really do complex

NOTE Confidence: 0.95093155

00:01:28.560 --> 00:01:29.859 level functions. And,

NOTE Confidence: 0.99588937

00:01:30.399 --> 00:01:31.679 they're able to sense lots

NOTE Confidence: 0.99588937

00:01:31.679 --> 00:01:33.219 of things, integrate that information,

NOTE Confidence: 0.97770345

00:01:33.679 --> 00:01:35.119 make lots of complex decisions,

NOTE Confidence: 0.97770345

00:01:35.119 --> 00:01:36.259 and they have this capability

NOTE Confidence: 0.97770345

00:01:36.319 --> 00:01:38.399 that molecular systems really by

NOTE Confidence: 0.97770345

00:01:38.399 --> 00:01:39.975 themselves don't do. They they

NOTE Confidence: 0.97770345

00:01:39.975 --> 00:01:41.175 are a set of molecules

NOTE Confidence: 0.97770345

00:01:41.175 --> 00:01:42.795 that work in concert together.

NOTE Confidence: 0.9738241

00:01:43.815 --> 00:01:44.315 So,

NOTE Confidence: 0.9843514

00:01:44.855 --> 00:01:46.455 when we are in this

NOTE Confidence: 0.9843514

00:01:46.455 --> 00:01:48.615 case, you know, traditionally, biology

NOTE Confidence: 0.9843514

00:01:48.615 --> 00:01:49.495 has been a field of

NOTE Confidence: 0.9843514

00:01:49.495 --> 00:01:51.015 of studying these, you know,

NOTE Confidence: 0.9843514

00:01:51.015 --> 00:01:53.015 complex evolved organisms and trying

NOTE Confidence: 0.9843514

00:01:53.015 --> 00:01:54.100 to take them apart. And

NOTE Confidence: 0.9843514

00:01:54.100 --> 00:01:55.300 we've gone through the era

NOTE Confidence: 0.9843514

00:01:55.300 --> 00:01:56.500 of really kind of now

NOTE Confidence: 0.9843514

00:01:56.500 --> 00:01:57.800 understanding the genomes,

NOTE Confidence: 0.9879645

00:01:58.180 --> 00:01:59.220 and the parts of all

NOTE Confidence: 0.9879645

00:01:59.220 --> 00:02:00.200 these things. But,

NOTE Confidence: 0.91354007

00:02:00.580 --> 00:02:01.620 for the test that we're

NOTE Confidence: 0.91354007

00:02:01.620 --> 00:02:02.680 talking about, really,

NOTE Confidence: 0.9911394

00:02:03.140 --> 00:02:04.180 what we need to do

NOTE Confidence: 0.9911394

00:02:04.180 --> 00:02:04.680 is,

NOTE Confidence: 0.92590714

00:02:05.460 --> 00:02:06.740 if we eventually want to

NOTE Confidence: 0.92590714

00:02:06.740 --> 00:02:07.460 be able to have, like,

NOTE Confidence: 0.92590714

00:02:07.460 --> 00:02:09.380 a chat PTP equivalent that

NOTE Confidence: 0.92590714

00:02:09.380 --> 00:02:10.715 says, we wanted to sell

NOTE Confidence: 0.92590714

00:02:10.715 --> 00:02:11.775 that can do x,

NOTE Confidence: 0.96629536

00:02:12.555 --> 00:02:13.674 and then hope that it

NOTE Confidence: 0.96629536

00:02:13.674 --> 00:02:15.055 would spit out some genetic

NOTE Confidence: 0.96629536

00:02:15.114 --> 00:02:16.875 information that we've upload into

NOTE Confidence: 0.96629536

00:02:16.875 --> 00:02:18.155 that cell. We really need

NOTE Confidence: 0.96629536

00:02:18.155 --> 00:02:20.155 to understand this the hierarchies

NOTE Confidence: 0.96629536

00:02:20.155 --> 00:02:21.674 of of biological language and

NOTE Confidence: 0.96629536

00:02:21.674 --> 00:02:23.215 encoding in a much

NOTE Confidence: 0.72219205

00:02:23.514 --> 00:02:24.330 deeper way.

NOTE Confidence: 0.97795755

00:02:24.810 --> 00:02:25.450 That is, you know, we

NOTE Confidence: 0.97795755

00:02:25.450 --> 00:02:27.370 know everything is encoded ultimately

NOTE Confidence: 0.97795755

00:02:27.370 --> 00:02:28.650 as sets of molecules and

NOTE Confidence: 0.97795755

00:02:28.650 --> 00:02:30.270 genes, but that these,

NOTE Confidence: 0.9871121

00:02:31.370 --> 00:02:32.590 molecules come together,

NOTE Confidence: 0.9504877

00:02:32.889 --> 00:02:34.490 in various cellular circuits and

NOTE Confidence: 0.9504877

00:02:34.490 --> 00:02:36.010 subroutines and then the cells,

NOTE Confidence: 0.9504877

00:02:36.010 --> 00:02:37.130 of course, have to talk

NOTE Confidence: 0.9504877

00:02:37.130 --> 00:02:37.950 to one another,

NOTE Confidence: 0.9940826

00:02:38.544 --> 00:02:40.065 and that much of the

NOTE Confidence: 0.9940826

00:02:40.065 --> 00:02:41.264 the the complex behavior that

NOTE Confidence: 0.9940826

00:02:41.264 --> 00:02:43.125 we see in real biology

NOTE Confidence: 0.9940826

00:02:43.185 --> 00:02:45.105 comes from many different layers

NOTE Confidence: 0.9940826

00:02:45.105 --> 00:02:46.145 like this. And so that's

NOTE Confidence: 0.9940826

00:02:46.145 --> 00:02:47.105 a lot like a very

NOTE Confidence: 0.9940826

00:02:47.105 --> 00:02:48.005 complex grammar.

NOTE Confidence: 0.97236794

00:02:48.465 --> 00:02:49.985 So I'm also gonna reference

NOTE Confidence: 0.97236794

00:02:49.985 --> 00:02:50.485 Hamlet,

NOTE Confidence: 0.9889491

00:02:50.865 --> 00:02:51.825 but we have, you know,

NOTE Confidence: 0.9889491

00:02:51.825 --> 00:02:53.490 these basic words that,

NOTE Confidence: 0.9770327

00:02:53.970 --> 00:02:55.330 we want to understand how

NOTE Confidence: 0.9770327

00:02:55.330 --> 00:02:56.450 we put them together to

NOTE Confidence: 0.9770327

00:02:56.450 --> 00:02:58.290 build sentences, to build essays,

NOTE Confidence: 0.9770327

00:02:58.290 --> 00:02:59.490 to make arguments, to write

NOTE Confidence: 0.9770327

00:02:59.490 --> 00:03:00.770 books. And we want to

NOTE Confidence: 0.9770327

00:03:00.770 --> 00:03:02.470 not just take apart classics,

NOTE Confidence: 0.9770327

00:03:02.530 --> 00:03:03.490 but we wanna be able

NOTE Confidence: 0.9770327

00:03:03.490 --> 00:03:04.770 to write our own, new

NOTE Confidence: 0.9770327

00:03:04.770 --> 00:03:06.794 books. So that's we're now

NOTE Confidence: 0.9770327

00:03:06.875 --> 00:03:07.915 thinking about this as more

NOTE Confidence: 0.9770327

00:03:07.915 --> 00:03:09.215 like generative biology

NOTE Confidence: 0.9849099

00:03:09.514 --> 00:03:10.555 that we wanna try to

NOTE Confidence: 0.9849099

00:03:10.555 --> 00:03:11.855 understand this hierarchical,

NOTE Confidence: 0.99362135

00:03:12.794 --> 00:03:13.694 sort of structure

NOTE Confidence: 0.91247743

00:03:13.995 --> 00:03:15.535 or grammar of biology.

NOTE Confidence: 0.9809657

00:03:16.155 --> 00:03:17.755 And then can that really

NOTE Confidence: 0.9809657

00:03:17.755 --> 00:03:18.495 help us,

NOTE Confidence: 0.9782394

00:03:18.970 --> 00:03:20.489 to design cells that do,

NOTE Confidence: 0.9782394

00:03:20.810 --> 00:03:22.750 really complex and important things?

NOTE Confidence: 0.96525586

00:03:25.130 --> 00:03:27.470 So the, let's see. Okay.

NOTE Confidence: 0.9236733

00:03:29.290 --> 00:03:31.209 Okay. So, we're working on

NOTE Confidence: 0.9236733

00:03:31.209 --> 00:03:32.410 a couple different problems, but,

NOTE Confidence: 0.9236733

00:03:32.410 --> 00:03:33.209 you know, in in all

NOTE Confidence: 0.9236733

00:03:33.209 --> 00:03:34.330 cases, you need to kind

NOTE Confidence: 0.9236733

00:03:34.330 --> 00:03:36.305 of rephrase a traditional problem

NOTE Confidence: 0.9236733

00:03:36.305 --> 00:03:37.425 like in immunology. You might

NOTE Confidence: 0.9236733

00:03:37.425 --> 00:03:38.385 ask how to how to

NOTE Confidence: 0.9236733

00:03:38.385 --> 00:03:40.405 immune cells recognize and kill,

NOTE Confidence: 0.9919174

00:03:40.865 --> 00:03:42.545 disease causing foreign cells that,

NOTE Confidence: 0.9919174

00:03:42.865 --> 00:03:44.485 without causing broad damage.

NOTE Confidence: 0.9794212

00:03:44.865 --> 00:03:46.645 We're also working on development.

NOTE Confidence: 0.9794212

00:03:46.705 --> 00:03:47.665 I'm not gonna talk about

NOTE Confidence: 0.9794212

00:03:47.665 --> 00:03:48.865 that today, but in the

NOTE Confidence: 0.9794212

00:03:48.865 --> 00:03:50.700 case of of, immunology,

NOTE Confidence: 0.96382153

00:03:51.640 --> 00:03:53.660 to rephrase this, as a

NOTE Confidence: 0.96382153

00:03:53.800 --> 00:03:55.100 generative design question,

NOTE Confidence: 0.9615047

00:03:55.800 --> 00:03:57.320 we want to ask if

NOTE Confidence: 0.9615047

00:03:57.320 --> 00:03:58.680 we understand the design logic

NOTE Confidence: 0.9615047

00:03:58.680 --> 00:04:00.520 of biological systems, how can

NOTE Confidence: 0.9615047

00:04:00.520 --> 00:04:02.200 we, for example, engineer immune

NOTE Confidence: 0.9615047

00:04:02.200 --> 00:04:03.980 cells to precisely recognize,

NOTE Confidence: 0.95311743

00:04:04.515 --> 00:04:06.114 and kill solid tumors that

NOTE Confidence: 0.95311743

00:04:06.114 --> 00:04:07.474 normally that evade the natural

NOTE Confidence: 0.95311743

00:04:07.474 --> 00:04:08.375 immune system,

NOTE Confidence: 0.95036346

00:04:09.155 --> 00:04:10.935 or other sorts of, complex

NOTE Confidence: 0.95036346

00:04:11.155 --> 00:04:11.655 disease,

NOTE Confidence: 0.8929877

00:04:12.355 --> 00:04:14.295 tissue based diseases like autoimmunity,

NOTE Confidence: 0.97844285

00:04:14.595 --> 00:04:15.655 fibrosis, etcetera.

NOTE Confidence: 0.9627032

00:04:17.160 --> 00:04:18.460 So as I said before,

NOTE Confidence: 0.95045686

00:04:19.000 --> 00:04:19.880 you know, right now, the

NOTE Confidence: 0.95045686

00:04:19.880 --> 00:04:21.080 way that we interface with

NOTE Confidence: 0.95045686

00:04:21.080 --> 00:04:23.480 disease is largely, not always,

NOTE Confidence: 0.95045686

00:04:23.480 --> 00:04:25.480 but, through molecules, small molecules

NOTE Confidence: 0.95045686

00:04:25.480 --> 00:04:26.220 or biologics.

NOTE Confidence: 0.9528787

00:04:27.000 --> 00:04:28.760 And these are very, very,

NOTE Confidence: 0.9528787

00:04:28.760 --> 00:04:29.260 obviously,

NOTE Confidence: 0.71264005

00:04:30.164 --> 00:04:30.565 amazing,

NOTE Confidence: 0.93673813

00:04:30.964 --> 00:04:32.645 entities, but they tend to,

NOTE Confidence: 0.93673813

00:04:32.645 --> 00:04:34.425 again, have these systemic activities,

NOTE Confidence: 0.98587656

00:04:35.125 --> 00:04:36.724 and that and whereas, you

NOTE Confidence: 0.98587656

00:04:36.724 --> 00:04:37.925 know, what we're hoping is

NOTE Confidence: 0.98587656

00:04:37.925 --> 00:04:39.525 that cells have this ability

NOTE Confidence: 0.98587656

00:04:39.525 --> 00:04:41.845 to migrate, to sense different

NOTE Confidence: 0.98587656

00:04:41.845 --> 00:04:43.384 things at these different scales,

NOTE Confidence: 0.9826679

00:04:43.949 --> 00:04:45.069 and and decide when and

NOTE Confidence: 0.9826679

00:04:45.069 --> 00:04:46.210 where they will function,

NOTE Confidence: 0.9592727

00:04:46.830 --> 00:04:48.589 and, that they can, as

NOTE Confidence: 0.9592727

00:04:48.589 --> 00:04:49.630 I said, migrate, they can

NOTE Confidence: 0.9592727

00:04:49.630 --> 00:04:50.669 adhere, they can decide to

NOTE Confidence: 0.9592727

00:04:50.669 --> 00:04:51.970 stay somewhere, they can proliferate,

NOTE Confidence: 0.9592727

00:04:52.110 --> 00:04:53.069 they can talk to other

NOTE Confidence: 0.9592727

00:04:53.069 --> 00:04:54.430 cells. So we think it

NOTE Confidence: 0.9592727

00:04:54.430 --> 00:04:56.110 is, possibly a much more

NOTE Confidence: 0.9592727

00:04:56.110 --> 00:04:58.289 powerful way to interface, especially

NOTE Confidence: 0.9982567

00:04:58.735 --> 00:05:00.035 with complex diseases.

NOTE Confidence: 0.96980923

00:05:01.375 --> 00:05:02.415 And so when we wanna

NOTE Confidence: 0.96980923

00:05:02.415 --> 00:05:03.695 try to program cells, I

NOTE Confidence: 0.96980923

00:05:03.695 --> 00:05:04.815 mean, many people, of course,

NOTE Confidence: 0.96980923

00:05:04.815 --> 00:05:05.875 are familiar with,

NOTE Confidence: 0.95791125

00:05:06.255 --> 00:05:07.455 the great success of CAR

NOTE Confidence: 0.95791125

00:05:07.455 --> 00:05:09.475 T cells, chimeric antigen receptors,

NOTE Confidence: 0.95791125

00:05:09.695 --> 00:05:10.735 T cells that are able

NOTE Confidence: 0.95791125

00:05:10.735 --> 00:05:12.255 to redirect a T cell

NOTE Confidence: 0.95791125

00:05:12.255 --> 00:05:13.154 killing response

NOTE Confidence: 0.88440305

00:05:14.710 --> 00:05:14.950 to a a a a

NOTE Confidence: 0.88440305

00:05:14.950 --> 00:05:17.450 specific tumor antigen bearing cell.

NOTE Confidence: 0.97485185

00:05:18.310 --> 00:05:18.810 And,

NOTE Confidence: 0.96131414

00:05:19.190 --> 00:05:20.470 but, you know, although that's,

NOTE Confidence: 0.96131414

00:05:20.470 --> 00:05:22.070 you know, recognizing one thing,

NOTE Confidence: 0.96131414

00:05:22.070 --> 00:05:23.029 in many ways, we know

NOTE Confidence: 0.96131414

00:05:23.029 --> 00:05:24.070 that the CAR T is

NOTE Confidence: 0.96131414

00:05:24.070 --> 00:05:25.510 really about interacting with a

NOTE Confidence: 0.96131414

00:05:25.510 --> 00:05:27.005 network that's in the tissue

NOTE Confidence: 0.96131414

00:05:27.005 --> 00:05:28.044 in the body. They have

NOTE Confidence: 0.96131414

00:05:28.044 --> 00:05:29.165 to interact with the tumor,

NOTE Confidence: 0.96131414

00:05:29.165 --> 00:05:31.005 the stroma, other immune cells,

NOTE Confidence: 0.96131414

00:05:31.005 --> 00:05:32.764 and really, so, you know,

NOTE Confidence: 0.96131414

00:05:32.764 --> 00:05:33.964 I think in many cases

NOTE Confidence: 0.96131414

00:05:33.964 --> 00:05:35.264 in normal biology,

NOTE Confidence: 0.95923406

00:05:35.805 --> 00:05:37.404 physiology, as well as things

NOTE Confidence: 0.95923406

00:05:37.404 --> 00:05:38.205 that we'd like to do

NOTE Confidence: 0.95923406

00:05:38.205 --> 00:05:39.750 in terms of remodeling or

NOTE Confidence: 0.95923406

00:05:39.750 --> 00:05:41.270 treating disease. This is about

NOTE Confidence: 0.95923406

00:05:41.270 --> 00:05:42.490 kind of trying to rewire

NOTE Confidence: 0.9718083

00:05:42.870 --> 00:05:45.130 these cellular conversations and circuits.

NOTE Confidence: 0.95215493

00:05:46.950 --> 00:05:48.150 And so what is it

NOTE Confidence: 0.95215493

00:05:48.150 --> 00:05:49.110 that we want to do?

NOTE Confidence: 0.95215493

00:05:49.110 --> 00:05:49.990 If if we wanted to,

NOTE Confidence: 0.95215493

00:05:49.990 --> 00:05:51.190 like, draw in new new

NOTE Confidence: 0.95215493

00:05:51.190 --> 00:05:52.010 circuit connections,

NOTE Confidence: 0.9947527

00:05:52.470 --> 00:05:53.430 how do we connect these

NOTE Confidence: 0.9947527

00:05:53.430 --> 00:05:54.925 cells? And so,

NOTE Confidence: 0.9563795

00:05:55.385 --> 00:05:56.345 there are obviously a lot

NOTE Confidence: 0.9563795

00:05:56.345 --> 00:05:57.545 of different ways, but, I

NOTE Confidence: 0.9563795

00:05:57.545 --> 00:05:58.765 guess, one of the simplifications

NOTE Confidence: 0.9563795

00:05:58.904 --> 00:05:59.705 we're trying to make is

NOTE Confidence: 0.9563795

00:05:59.705 --> 00:06:00.825 to say that really there

NOTE Confidence: 0.9563795

00:06:00.825 --> 00:06:01.785 there are just a few

NOTE Confidence: 0.9563795

00:06:01.785 --> 00:06:03.065 types of state changes that

NOTE Confidence: 0.9563795

00:06:03.065 --> 00:06:04.345 you see when one cell

NOTE Confidence: 0.9563795

00:06:04.345 --> 00:06:05.625 talks to another cell.

NOTE Confidence: 0.9446365

00:06:05.945 --> 00:06:07.464 So if this particular cell

NOTE Confidence: 0.9446365

00:06:07.464 --> 00:06:08.585 here in node saw x,

NOTE Confidence: 0.9446365

00:06:08.585 --> 00:06:10.105 y, or z from another

NOTE Confidence: 0.9446365

00:06:10.105 --> 00:06:11.570 cell, it could turn on

NOTE Confidence: 0.9446365

00:06:11.570 --> 00:06:13.330 new new signals. It could

NOTE Confidence: 0.9446365

00:06:13.330 --> 00:06:14.610 turn on receptors that allow

NOTE Confidence: 0.9446365

00:06:14.610 --> 00:06:15.890 it to sense things. It

NOTE Confidence: 0.9446365

00:06:15.890 --> 00:06:17.170 could move or change its

NOTE Confidence: 0.9446365

00:06:17.170 --> 00:06:18.529 shape. It could adhere to

NOTE Confidence: 0.9446365

00:06:18.529 --> 00:06:19.490 things and stay in one

NOTE Confidence: 0.9446365

00:06:19.490 --> 00:06:21.010 place or could divide and

NOTE Confidence: 0.9446365

00:06:21.010 --> 00:06:21.510 grow,

NOTE Confidence: 0.9992808

00:06:21.890 --> 00:06:22.545 or die.

NOTE Confidence: 0.98228633

00:06:23.265 --> 00:06:24.945 And so we're interested in

NOTE Confidence: 0.98228633

00:06:24.945 --> 00:06:26.485 trying to build sort of,

NOTE Confidence: 0.97448325

00:06:27.025 --> 00:06:28.865 in a sense, domesticated modules

NOTE Confidence: 0.97448325

00:06:28.865 --> 00:06:30.065 that we can utilize to

NOTE Confidence: 0.97448325

00:06:30.065 --> 00:06:31.605 execute these sorts of functions,

NOTE Confidence: 0.97448325

00:06:31.825 --> 00:06:33.345 genetically encoded elements that we

NOTE Confidence: 0.97448325

00:06:33.345 --> 00:06:35.045 can put in. We're inspired

NOTE Confidence: 0.97448325

00:06:35.105 --> 00:06:36.305 by the the the cars,

NOTE Confidence: 0.97448325

00:06:36.305 --> 00:06:37.185 as I said, which is

NOTE Confidence: 0.97448325

00:06:37.185 --> 00:06:37.665 taking,

NOTE Confidence: 0.9898867

00:06:37.985 --> 00:06:39.720 an an antibody that recognizes

NOTE Confidence: 0.9898867

00:06:39.720 --> 00:06:41.080 an antigen of the user's

NOTE Confidence: 0.9898867

00:06:41.080 --> 00:06:41.580 choice,

NOTE Confidence: 0.970393

00:06:42.200 --> 00:06:43.820 and fuses it to elements

NOTE Confidence: 0.970393

00:06:43.880 --> 00:06:45.180 from the t cell receptor,

NOTE Confidence: 0.970393

00:06:45.320 --> 00:06:47.000 which now allows when that

NOTE Confidence: 0.970393

00:06:47.000 --> 00:06:49.240 t cell recognizes that target

NOTE Confidence: 0.970393

00:06:49.240 --> 00:06:51.080 antigen, it now launches this

NOTE Confidence: 0.970393

00:06:51.080 --> 00:06:52.540 complex t cell response,

NOTE Confidence: 0.97787637

00:06:53.080 --> 00:06:53.740 to proliferate,

NOTE Confidence: 0.96299475

00:06:54.125 --> 00:06:55.565 kill, and secrete. And that's

NOTE Confidence: 0.96299475

00:06:55.565 --> 00:06:56.925 the basis of our, CAR

NOTE Confidence: 0.96299475

00:06:56.925 --> 00:06:57.585 T therapies.

NOTE Confidence: 0.95440006

00:06:58.205 --> 00:06:59.325 We've been building a number

NOTE Confidence: 0.95440006

00:06:59.325 --> 00:07:00.365 of other things. One of

NOTE Confidence: 0.95440006

00:07:00.365 --> 00:07:01.565 them is the the synthetic

NOTE Confidence: 0.95440006

00:07:01.565 --> 00:07:02.945 NASH or syn NASH receptor.

NOTE Confidence: 0.92251927

00:07:03.245 --> 00:07:05.404 This is a, another chimeric

NOTE Confidence: 0.92251927

00:07:05.404 --> 00:07:07.005 type receptor that is actually,

NOTE Confidence: 0.92251927

00:07:07.005 --> 00:07:08.465 we think, much more flexible,

NOTE Confidence: 0.92251927

00:07:08.685 --> 00:07:09.825 allows us to connect,

NOTE Confidence: 0.9972906

00:07:10.419 --> 00:07:11.940 almost any input to any

NOTE Confidence: 0.9972906

00:07:11.940 --> 00:07:13.379 output. The idea here is

NOTE Confidence: 0.9972906

00:07:13.379 --> 00:07:13.879 that,

NOTE Confidence: 0.88772476

00:07:14.259 --> 00:07:15.639 based on the notch receptor,

NOTE Confidence: 0.7187147

00:07:16.419 --> 00:07:16.919 the,

NOTE Confidence: 0.9719894

00:07:17.300 --> 00:07:18.840 you can put a, extracellular

NOTE Confidence: 0.9719894

00:07:19.139 --> 00:07:20.419 antibody on the outside for

NOTE Confidence: 0.9719894

00:07:20.419 --> 00:07:21.860 an antigen of choice. And

NOTE Confidence: 0.9719894

00:07:21.860 --> 00:07:22.659 then the middle part of

NOTE Confidence: 0.9719894

00:07:22.659 --> 00:07:24.375 it, actually, when this binding

NOTE Confidence: 0.9719894

00:07:24.375 --> 00:07:26.295 is engaged, it cleaves the

NOTE Confidence: 0.9719894

00:07:26.295 --> 00:07:27.435 receptor and releases

NOTE Confidence: 0.9840058

00:07:27.735 --> 00:07:29.895 an intracellular transcription factor that

NOTE Confidence: 0.9840058

00:07:29.895 --> 00:07:31.115 can go into the nucleus

NOTE Confidence: 0.9840058

00:07:31.175 --> 00:07:32.375 and turn on a target

NOTE Confidence: 0.9840058

00:07:32.375 --> 00:07:34.295 gene that's driven by by

NOTE Confidence: 0.9840058

00:07:34.295 --> 00:07:36.295 the recognized the cognate promoter.

NOTE Confidence: 0.9840058

00:07:36.295 --> 00:07:37.255 And so what's great is

NOTE Confidence: 0.9840058

00:07:37.255 --> 00:07:38.520 you can change what the

NOTE Confidence: 0.9840058

00:07:38.520 --> 00:07:39.880 cell senses, and you can

NOTE Confidence: 0.9840058

00:07:39.880 --> 00:07:41.560 plug in any genetically encoded

NOTE Confidence: 0.9840058

00:07:41.560 --> 00:07:42.780 element here in the payload

NOTE Confidence: 0.9840058

00:07:42.920 --> 00:07:44.280 or multiple ones and create

NOTE Confidence: 0.9840058

00:07:44.280 --> 00:07:45.800 your own programs of x

NOTE Confidence: 0.9840058

00:07:45.800 --> 00:07:46.780 turns to y.

NOTE Confidence: 0.9534038

00:07:47.160 --> 00:07:48.440 So that's very flexible. We

NOTE Confidence: 0.9534038

00:07:48.440 --> 00:07:49.160 can do things like we

NOTE Confidence: 0.9534038

00:07:49.160 --> 00:07:50.300 can turn on a car

NOTE Confidence: 0.9534038

00:07:50.360 --> 00:07:51.960 in series after a Synash

NOTE Confidence: 0.9534038

00:07:51.960 --> 00:07:53.235 and actually have two different

NOTE Confidence: 0.9534038

00:07:53.235 --> 00:07:54.835 antigens that are required in

NOTE Confidence: 0.9534038

00:07:54.835 --> 00:07:55.335 sequence

NOTE Confidence: 0.99579716

00:07:55.715 --> 00:07:56.995 to, give you much more

NOTE Confidence: 0.99579716

00:07:56.995 --> 00:07:57.495 control.

NOTE Confidence: 0.9495373

00:07:57.955 --> 00:07:59.735 Another thing is, the synthetic

NOTE Confidence: 0.9495373

00:07:59.795 --> 00:08:01.475 adhesion molecules. We found that

NOTE Confidence: 0.9495373

00:08:01.475 --> 00:08:02.775 you can take a antibody,

NOTE Confidence: 0.9495373

00:08:02.995 --> 00:08:04.195 a tunable antibody, and then

NOTE Confidence: 0.9495373

00:08:04.195 --> 00:08:05.655 link it to different intracellular

NOTE Confidence: 0.9495373

00:08:05.715 --> 00:08:07.395 domains that are associated with

NOTE Confidence: 0.9495373

00:08:07.395 --> 00:08:09.270 cell adhesion. These engage with

NOTE Confidence: 0.9495373

00:08:09.270 --> 00:08:11.110 the cytoskeleton and create force

NOTE Confidence: 0.9495373

00:08:11.110 --> 00:08:12.490 and can create really strong

NOTE Confidence: 0.9495373

00:08:12.550 --> 00:08:14.010 and different kinds of attachments.

NOTE Confidence: 0.9495373

00:08:14.230 --> 00:08:15.590 And that's another important thing

NOTE Confidence: 0.9495373

00:08:15.590 --> 00:08:16.570 is that cells,

NOTE Confidence: 0.9395696

00:08:16.950 --> 00:08:18.970 they physically organize into tissues

NOTE Confidence: 0.9395696

00:08:19.190 --> 00:08:21.290 or, they bind to partners,

NOTE Confidence: 0.9395696

00:08:21.350 --> 00:08:22.870 recognize partners. And so really

NOTE Confidence: 0.9395696

00:08:22.870 --> 00:08:23.370 this,

NOTE Confidence: 0.9703081

00:08:23.845 --> 00:08:24.965 being able to both tune

NOTE Confidence: 0.9703081

00:08:24.965 --> 00:08:26.645 their physical organization kinda how

NOTE Confidence: 0.9703081

00:08:26.645 --> 00:08:27.925 they're physically wired with how

NOTE Confidence: 0.9703081

00:08:27.925 --> 00:08:29.525 they're biochemically wired is, I

NOTE Confidence: 0.9703081

00:08:29.525 --> 00:08:30.965 think, a really powerful thing.

NOTE Confidence: 0.9703081

00:08:30.965 --> 00:08:32.085 And then another example is

NOTE Confidence: 0.9703081

00:08:32.085 --> 00:08:33.365 we have recently gotten some,

NOTE Confidence: 0.9703081

00:08:33.605 --> 00:08:35.065 nice results on some synthetic,

NOTE Confidence: 0.9506039

00:08:35.445 --> 00:08:36.804 chemokines. This is very important

NOTE Confidence: 0.9506039

00:08:36.804 --> 00:08:38.085 for the immune system because,

NOTE Confidence: 0.9506039

00:08:38.085 --> 00:08:39.179 of course, as well as

NOTE Confidence: 0.9506039

00:08:39.179 --> 00:08:40.380 in development because,

NOTE Confidence: 0.9784446

00:08:40.780 --> 00:08:41.500 a lot of what a

NOTE Confidence: 0.9784446

00:08:41.500 --> 00:08:43.179 cell does is is determined

NOTE Confidence: 0.9784446

00:08:43.179 --> 00:08:44.540 by, where it's told to

NOTE Confidence: 0.9784446

00:08:44.540 --> 00:08:46.160 go. So these chemokine receptors,

NOTE Confidence: 0.9421835

00:08:46.540 --> 00:08:47.900 specify that cells to, for

NOTE Confidence: 0.9421835

00:08:47.900 --> 00:08:48.940 example, go to the lymph

NOTE Confidence: 0.9421835

00:08:48.940 --> 00:08:49.900 nodes and talk to other

NOTE Confidence: 0.9421835

00:08:49.900 --> 00:08:51.020 cells that have the same

NOTE Confidence: 0.9421835

00:08:51.020 --> 00:08:51.980 receptors. So it's a way

NOTE Confidence: 0.9421835

00:08:51.980 --> 00:08:54.014 for to mediate at this

NOTE Confidence: 0.9421835

00:08:54.014 --> 00:08:55.615 sort of high level, large

NOTE Confidence: 0.9421835

00:08:55.615 --> 00:08:56.115 scale,

NOTE Confidence: 0.99654925

00:08:56.574 --> 00:08:58.834 coordination and communication between cells.

NOTE Confidence: 0.9800955

00:09:00.415 --> 00:09:01.934 Okay. So oh, okay. This

NOTE Confidence: 0.9800955

00:09:01.934 --> 00:09:03.615 is screwed up. Sorry. So

NOTE Confidence: 0.9800955

00:09:03.615 --> 00:09:04.815 I'm gonna tell you about

NOTE Confidence: 0.9800955

00:09:04.815 --> 00:09:06.434 two things very briefly today,

NOTE Confidence: 0.9790421

00:09:07.019 --> 00:09:08.079 just as examples,

NOTE Confidence: 0.96142554

00:09:08.459 --> 00:09:09.820 of things that we're we're

NOTE Confidence: 0.96142554

00:09:09.820 --> 00:09:10.699 trying to do and have

NOTE Confidence: 0.96142554

00:09:10.699 --> 00:09:12.160 had had some success in.

NOTE Confidence: 0.98400766

00:09:12.620 --> 00:09:14.220 One is actually the idea

NOTE Confidence: 0.98400766

00:09:14.220 --> 00:09:15.179 of trying to,

NOTE Confidence: 0.97872484

00:09:15.899 --> 00:09:17.759 engineer cells to recognize,

NOTE Confidence: 0.9266768

00:09:18.795 --> 00:09:19.755 a a tissue, in this

NOTE Confidence: 0.9266768

00:09:19.755 --> 00:09:21.434 case, the brain. The idea

NOTE Confidence: 0.9266768

00:09:21.434 --> 00:09:22.654 is that can we actually

NOTE Confidence: 0.9908807

00:09:22.955 --> 00:09:24.955 combine kind of molecular scale

NOTE Confidence: 0.9908807

00:09:24.955 --> 00:09:25.455 recognition

NOTE Confidence: 0.99411094

00:09:25.915 --> 00:09:26.395 with,

NOTE Confidence: 0.9812673

00:09:26.795 --> 00:09:28.554 anatomical recognition. So I'll tell

NOTE Confidence: 0.9812673

00:09:28.554 --> 00:09:30.154 you about developing this kind

NOTE Confidence: 0.9812673

00:09:30.154 --> 00:09:31.135 of tissue GPS

NOTE Confidence: 0.96225893

00:09:31.670 --> 00:09:33.290 sensor, that can deliver,

NOTE Confidence: 0.9799854

00:09:33.670 --> 00:09:35.190 cellular actions to the brain

NOTE Confidence: 0.9799854

00:09:35.190 --> 00:09:35.910 and then how we can

NOTE Confidence: 0.9799854

00:09:35.910 --> 00:09:37.670 use that in different directions

NOTE Confidence: 0.9799854

00:09:37.670 --> 00:09:39.449 to either attack brain cancers

NOTE Confidence: 0.97345835

00:09:39.750 --> 00:09:41.209 or to, for example, attack,

NOTE Confidence: 0.97345835

00:09:41.509 --> 00:09:42.170 or treat,

NOTE Confidence: 0.93488824

00:09:42.630 --> 00:09:43.130 neuroinflammation.

NOTE Confidence: 0.97218084

00:09:44.149 --> 00:09:44.790 And then,

NOTE Confidence: 0.9054483

00:09:45.269 --> 00:09:46.389 related to that, I'll also

NOTE Confidence: 0.9054483

00:09:46.389 --> 00:09:47.425 talk about our our efforts

NOTE Confidence: 0.9054483

00:09:47.425 --> 00:09:49.465 to actually create cells that

NOTE Confidence: 0.9054483

00:09:49.465 --> 00:09:49.965 generate,

NOTE Confidence: 0.96700233

00:09:50.585 --> 00:09:51.085 customized

NOTE Confidence: 0.87541515

00:09:51.545 --> 00:09:52.045 multifactor,

NOTE Confidence: 0.99360144

00:09:52.825 --> 00:09:53.325 immunosuppressive

NOTE Confidence: 0.9471022

00:09:53.705 --> 00:09:54.205 programs,

NOTE Confidence: 0.9464882

00:09:54.665 --> 00:09:56.125 that, for example, can protect,

NOTE Confidence: 0.7591288

00:09:56.665 --> 00:09:57.885 against neuro inflammation

NOTE Confidence: 0.97542226

00:09:58.345 --> 00:09:59.565 or can protect transplanted

NOTE Confidence: 0.94500923

00:10:01.650 --> 00:10:02.690 organs, for example, in this

NOTE Confidence: 0.94500923

00:10:02.690 --> 00:10:04.929 case, beta islets from, immune

NOTE Confidence: 0.94500923

00:10:04.929 --> 00:10:05.429 rejection.

NOTE Confidence: 0.97560734

00:10:06.130 --> 00:10:07.250 So let me talk first

NOTE Confidence: 0.97560734

00:10:07.250 --> 00:10:09.010 about the brain, this kind

NOTE Confidence: 0.97560734

00:10:09.010 --> 00:10:10.390 of idea of a GPS

NOTE Confidence: 0.97560734

00:10:10.690 --> 00:10:11.730 in the cells that they

NOTE Confidence: 0.97560734

00:10:11.730 --> 00:10:13.184 can know where they have

NOTE Confidence: 0.97560734

00:10:13.184 --> 00:10:14.065 to go and and turn

NOTE Confidence: 0.97560734

00:10:14.065 --> 00:10:15.204 on specific responses.

NOTE Confidence: 0.95709026

00:10:16.065 --> 00:10:17.505 And this is we we

NOTE Confidence: 0.95709026

00:10:17.505 --> 00:10:18.704 were really interested in trying

NOTE Confidence: 0.95709026

00:10:18.704 --> 00:10:19.764 to do this in conceptually

NOTE Confidence: 0.96547866

00:10:20.225 --> 00:10:21.505 because, as I said, one

NOTE Confidence: 0.96547866

00:10:21.505 --> 00:10:22.804 of the things about molecular

NOTE Confidence: 0.96547866

00:10:23.105 --> 00:10:23.605 therapeutics

NOTE Confidence: 0.9643704

00:10:24.144 --> 00:10:25.184 is that even if you

NOTE Confidence: 0.9643704

00:10:25.184 --> 00:10:26.304 target a CAR T with

NOTE Confidence: 0.9643704

00:10:26.304 --> 00:10:27.649 just, you know, one antigen,

NOTE Confidence: 0.9643704

00:10:27.870 --> 00:10:28.850 is that those,

NOTE Confidence: 0.9835731

00:10:29.470 --> 00:10:31.070 that we have the same

NOTE Confidence: 0.9835731

00:10:31.070 --> 00:10:32.829 molecules, they operate in many

NOTE Confidence: 0.9835731

00:10:32.829 --> 00:10:34.029 different places in the body.

NOTE Confidence: 0.9835731

00:10:34.029 --> 00:10:35.389 So inherently, that's why you

NOTE Confidence: 0.9835731

00:10:35.389 --> 00:10:36.190 get a lot of cross

NOTE Confidence: 0.9835731

00:10:36.190 --> 00:10:37.250 reactions and toxicities.

NOTE Confidence: 0.986117

00:10:38.269 --> 00:10:39.149 What we would love to

NOTE Confidence: 0.986117

00:10:39.149 --> 00:10:39.950 be able to do is

NOTE Confidence: 0.986117

00:10:39.950 --> 00:10:40.995 to be able to restrict

NOTE Confidence: 0.986117

00:10:41.075 --> 00:10:42.515 a drug to act only

NOTE Confidence: 0.986117

00:10:42.515 --> 00:10:43.795 in a target tissue, say,

NOTE Confidence: 0.986117

00:10:43.795 --> 00:10:45.154 like the brain, so that

NOTE Confidence: 0.986117

00:10:45.154 --> 00:10:46.455 you get much more specificity.

NOTE Confidence: 0.986117

00:10:46.515 --> 00:10:47.635 And this is really kind

NOTE Confidence: 0.986117

00:10:47.635 --> 00:10:48.835 of like saying, well, if

NOTE Confidence: 0.986117

00:10:48.835 --> 00:10:49.795 you only had a street

NOTE Confidence: 0.986117

00:10:49.795 --> 00:10:51.154 address to mail a letter,

NOTE Confidence: 0.986117

00:10:51.154 --> 00:10:52.035 it could go to many

NOTE Confidence: 0.986117

00:10:52.035 --> 00:10:52.855 different cities.

NOTE Confidence: 0.98745596

00:10:53.315 --> 00:10:54.275 But if you combine a

NOTE Confidence: 0.98745596

00:10:54.275 --> 00:10:55.795 street address with this higher

NOTE Confidence: 0.98745596

00:10:55.795 --> 00:10:57.010 scale thing like a ZIP

NOTE Confidence: 0.98745596

00:10:57.010 --> 00:10:58.050 code, you get the it

NOTE Confidence: 0.98745596

00:10:58.050 --> 00:10:59.270 gets to the right place.

NOTE Confidence: 0.97114116

00:11:00.050 --> 00:11:01.650 And so, this kind of

NOTE Confidence: 0.97114116

00:11:01.650 --> 00:11:02.929 thing is very difficult for

NOTE Confidence: 0.97114116

00:11:02.929 --> 00:11:04.210 a molecule to do, but

NOTE Confidence: 0.97114116

00:11:04.210 --> 00:11:05.089 a living cell, this is

NOTE Confidence: 0.97114116

00:11:05.089 --> 00:11:06.130 really what they do for

NOTE Confidence: 0.97114116

00:11:06.130 --> 00:11:06.710 a living.

NOTE Confidence: 0.9872528

00:11:07.170 --> 00:11:08.690 They can integrate information at

NOTE Confidence: 0.9872528

00:11:08.690 --> 00:11:10.184 multiple scales. Okay?

NOTE Confidence: 0.9554611

00:11:10.985 --> 00:11:12.585 So, Milos Simic is a

NOTE Confidence: 0.9554611

00:11:12.585 --> 00:11:13.705 a fellow, in in our

NOTE Confidence: 0.9554611

00:11:13.705 --> 00:11:15.225 institute that really took this

NOTE Confidence: 0.9554611

00:11:15.225 --> 00:11:16.345 on, and he asked, how

NOTE Confidence: 0.9554611

00:11:16.345 --> 00:11:17.545 can we try to do

NOTE Confidence: 0.9554611

00:11:17.545 --> 00:11:18.825 this? And the idea was

NOTE Confidence: 0.9554611

00:11:18.825 --> 00:11:19.065 to,

NOTE Confidence: 0.99666655

00:11:19.865 --> 00:11:20.605 use bioinformatics

NOTE Confidence: 0.95578355

00:11:20.985 --> 00:11:21.965 to screen for,

NOTE Confidence: 0.9769558

00:11:22.345 --> 00:11:24.205 BRAIN or CNS specific extracellular

NOTE Confidence: 0.9769558

00:11:24.505 --> 00:11:25.865 antigens, some kind of marker

NOTE Confidence: 0.9769558

00:11:25.865 --> 00:11:27.139 that we could recognize

NOTE Confidence: 0.91495967

00:11:27.519 --> 00:11:28.959 and then design a synapse

NOTE Confidence: 0.91495967

00:11:28.959 --> 00:11:30.399 receptor that could detect that

NOTE Confidence: 0.91495967

00:11:30.399 --> 00:11:31.440 and then use that to

NOTE Confidence: 0.91495967

00:11:31.440 --> 00:11:31.940 induce,

NOTE Confidence: 0.9682636

00:11:32.639 --> 00:11:33.620 in t cells,

NOTE Confidence: 0.9225893

00:11:34.079 --> 00:11:35.679 expression of a therapeutic payload,

NOTE Confidence: 0.9225893

00:11:35.679 --> 00:11:36.959 either a car that could

NOTE Confidence: 0.9225893

00:11:36.959 --> 00:11:38.559 attack a brain tumor or

NOTE Confidence: 0.9225893

00:11:38.559 --> 00:11:39.459 say a suppressive

NOTE Confidence: 0.978953

00:11:40.035 --> 00:11:41.735 cytokine that could suppress neuroinflammation.

NOTE Confidence: 0.9414435

00:11:43.394 --> 00:11:44.834 So, we worked with Olga

NOTE Confidence: 0.9414435

00:11:44.834 --> 00:11:45.334 Tronskaya,

NOTE Confidence: 0.7163631

00:11:45.635 --> 00:11:46.214 a bioinformaticsist

NOTE Confidence: 0.99018604

00:11:46.755 --> 00:11:47.894 colleague at Princeton,

NOTE Confidence: 0.95946133

00:11:48.595 --> 00:11:49.075 and,

NOTE Confidence: 0.9510624

00:11:49.554 --> 00:11:50.915 looked for what were good

NOTE Confidence: 0.9510624

00:11:50.915 --> 00:11:51.415 candidates.

NOTE Confidence: 0.930629

00:11:52.195 --> 00:11:53.394 And, and then we also

NOTE Confidence: 0.930629

00:11:53.394 --> 00:11:55.075 worked with, Deb Sidu,

NOTE Confidence: 0.93583965

00:11:55.500 --> 00:11:56.940 a colleague who who's who,

NOTE Confidence: 0.9203436

00:11:57.420 --> 00:11:58.960 pans for, antibodies.

NOTE Confidence: 0.9321597

00:11:59.500 --> 00:12:00.940 And, what we found is

NOTE Confidence: 0.9321597

00:12:00.940 --> 00:12:01.580 that there are a couple

NOTE Confidence: 0.9321597

00:12:01.580 --> 00:12:02.540 different things that you could

NOTE Confidence: 0.9321597

00:12:02.540 --> 00:12:03.900 recognize in the brain, unique

NOTE Confidence: 0.9321597

00:12:03.900 --> 00:12:05.420 molecule markers. There were markers

NOTE Confidence: 0.9321597

00:12:05.420 --> 00:12:06.620 that were unique on neurons

NOTE Confidence: 0.9321597

00:12:06.620 --> 00:12:08.780 like this, neuro neural specific,

NOTE Confidence: 0.9696423

00:12:09.245 --> 00:12:11.404 cadherin. There are various, molecules

NOTE Confidence: 0.9696423

00:12:11.404 --> 00:12:12.524 that are specific to the

NOTE Confidence: 0.9696423

00:12:12.524 --> 00:12:13.024 myelin.

NOTE Confidence: 0.9469736

00:12:13.804 --> 00:12:15.165 But then, but one thing

NOTE Confidence: 0.9469736

00:12:15.165 --> 00:12:16.125 that I didn't realize at

NOTE Confidence: 0.9469736

00:12:16.125 --> 00:12:17.005 times that the brain has

NOTE Confidence: 0.9469736

00:12:17.005 --> 00:12:19.024 a very unique extracellular matrix.

NOTE Confidence: 0.9469736

00:12:19.084 --> 00:12:20.204 It forms, for example, the

NOTE Confidence: 0.9469736

00:12:20.204 --> 00:12:21.824 perineal nets around synapses,

NOTE Confidence: 0.94479364

00:12:22.365 --> 00:12:23.404 very important for that. And

NOTE Confidence: 0.94479364

00:12:23.404 --> 00:12:23.964 there are a bunch of

NOTE Confidence: 0.94479364

00:12:23.964 --> 00:12:25.880 molecules that are quite unique.

NOTE Confidence: 0.94479364

00:12:25.880 --> 00:12:27.100 One of them is Brevacan

NOTE Confidence: 0.94479364

00:12:27.160 --> 00:12:27.980 or BCAN,

NOTE Confidence: 0.9114316

00:12:28.600 --> 00:12:29.639 and we were able to

NOTE Confidence: 0.9114316

00:12:29.639 --> 00:12:30.759 find that this was we

NOTE Confidence: 0.9114316

00:12:30.759 --> 00:12:31.899 raised the Synash

NOTE Confidence: 0.9679149

00:12:32.759 --> 00:12:34.759 receptor against this and found

NOTE Confidence: 0.9679149

00:12:34.759 --> 00:12:35.639 that, in the end, this

NOTE Confidence: 0.9679149

00:12:35.639 --> 00:12:36.440 was one of the best

NOTE Confidence: 0.9679149

00:12:36.440 --> 00:12:37.559 ones that we we had.

NOTE Confidence: 0.9679149

00:12:37.559 --> 00:12:38.360 So I'll tell you about

NOTE Confidence: 0.9679149

00:12:38.360 --> 00:12:38.860 that.

NOTE Confidence: 0.9685858

00:12:40.254 --> 00:12:41.535 Okay. So how do we

NOTE Confidence: 0.9685858

00:12:41.535 --> 00:12:43.154 design a brain primed glioblastoma,

NOTE Confidence: 0.86700994

00:12:44.654 --> 00:12:46.675 cell therapy? There's a lethal,

NOTE Confidence: 0.9914529

00:12:47.134 --> 00:12:48.035 brain cancer.

NOTE Confidence: 0.98220795

00:12:48.975 --> 00:12:49.475 So

NOTE Confidence: 0.97752357

00:12:50.095 --> 00:12:50.894 it's been known for a

NOTE Confidence: 0.97752357

00:12:50.894 --> 00:12:52.254 long time that, a lot

NOTE Confidence: 0.97752357

00:12:52.254 --> 00:12:52.495 of,

NOTE Confidence: 0.92214215

00:12:53.090 --> 00:12:54.929 glioblastomas and other brain tumors,

NOTE Confidence: 0.92214215

00:12:54.929 --> 00:12:56.130 and in fact, many tumors

NOTE Confidence: 0.92214215

00:12:56.130 --> 00:12:57.190 have these common,

NOTE Confidence: 0.8833955

00:12:57.809 --> 00:12:58.790 tumor antigens,

NOTE Confidence: 0.95482254

00:12:59.170 --> 00:13:00.770 mostly embryonic sort of proteins

NOTE Confidence: 0.95482254

00:13:00.770 --> 00:13:02.309 that are expressed, improperly.

NOTE Confidence: 0.9350631

00:13:03.570 --> 00:13:04.530 And f a two and

NOTE Confidence: 0.9350631

00:13:04.530 --> 00:13:05.490 I l thirteen r a

NOTE Confidence: 0.9350631

00:13:05.490 --> 00:13:06.929 two are examples of antibody

NOTE Confidence: 0.9350631

00:13:07.010 --> 00:13:07.670 of antigens

NOTE Confidence: 0.9565138

00:13:08.015 --> 00:13:09.695 that are commonly expressed on

NOTE Confidence: 0.9565138

00:13:09.695 --> 00:13:10.195 many

NOTE Confidence: 0.76437795

00:13:10.895 --> 00:13:11.395 gliomas,

NOTE Confidence: 0.94900817

00:13:12.095 --> 00:13:13.455 but, but the but the

NOTE Confidence: 0.94900817

00:13:13.455 --> 00:13:14.335 problem is that these are

NOTE Confidence: 0.94900817

00:13:14.335 --> 00:13:15.695 also expressed in a lot

NOTE Confidence: 0.94900817

00:13:15.695 --> 00:13:16.895 of normal tissues in in

NOTE Confidence: 0.94900817

00:13:16.895 --> 00:13:18.355 lower levels maybe elsewhere,

NOTE Confidence: 0.9849844

00:13:18.895 --> 00:13:19.775 not in the brain, but

NOTE Confidence: 0.9849844

00:13:19.775 --> 00:13:21.630 elsewhere. So the idea here

NOTE Confidence: 0.93704194

00:13:22.030 --> 00:13:23.309 was could we improve on

NOTE Confidence: 0.93704194

00:13:23.309 --> 00:13:24.590 these by combining them and

NOTE Confidence: 0.93704194

00:13:24.590 --> 00:13:26.750 integrating multiple antigens? The idea

NOTE Confidence: 0.93704194

00:13:26.750 --> 00:13:28.030 being that let's take a

NOTE Confidence: 0.93704194

00:13:28.030 --> 00:13:29.870 SynNotch that recognizes a BCAN,

NOTE Confidence: 0.93704194

00:13:29.870 --> 00:13:30.830 and that's gonna be the

NOTE Confidence: 0.93704194

00:13:30.830 --> 00:13:32.830 priming interaction that will now

NOTE Confidence: 0.93704194

00:13:32.830 --> 00:13:34.345 turn on the expression of

NOTE Confidence: 0.93704194

00:13:34.345 --> 00:13:35.385 a car. Now this case,

NOTE Confidence: 0.93704194

00:13:35.385 --> 00:13:36.605 the car is two headed,

NOTE Confidence: 0.9459811

00:13:38.105 --> 00:13:39.385 for both of these things.

NOTE Confidence: 0.9459811

00:13:39.385 --> 00:13:40.265 So we one of the

NOTE Confidence: 0.9459811

00:13:40.265 --> 00:13:41.145 things that a lot of

NOTE Confidence: 0.9459811

00:13:41.145 --> 00:13:42.184 these tumors do is they

NOTE Confidence: 0.9459811

00:13:42.184 --> 00:13:43.785 escape if you need to

NOTE Confidence: 0.9459811

00:13:43.785 --> 00:13:45.085 kill one of those things.

NOTE Confidence: 0.9459811

00:13:45.145 --> 00:13:46.505 So we're gonna use the

NOTE Confidence: 0.9459811

00:13:46.505 --> 00:13:48.410 the brain to trigger everything.

NOTE Confidence: 0.9459811

00:13:48.630 --> 00:13:49.510 And the great thing is

NOTE Confidence: 0.9459811

00:13:49.510 --> 00:13:50.950 that, like, you the the

NOTE Confidence: 0.9459811

00:13:50.950 --> 00:13:52.150 the the tumor can't get

NOTE Confidence: 0.9459811

00:13:52.150 --> 00:13:53.850 a grant advantage by mutating

NOTE Confidence: 0.86046803

00:13:54.230 --> 00:13:55.589 BKAN in the brain. There's

NOTE Confidence: 0.86046803

00:13:55.589 --> 00:13:56.809 no selectable advantage.

NOTE Confidence: 0.9632586

00:13:57.190 --> 00:13:58.309 But then we're gonna cast

NOTE Confidence: 0.9632586

00:13:58.309 --> 00:14:00.165 this more complete net of

NOTE Confidence: 0.9632586

00:14:00.165 --> 00:14:02.325 killing two common antigens. But

NOTE Confidence: 0.9632586

00:14:02.325 --> 00:14:03.945 that what, and and importantly

NOTE Confidence: 0.9632586

00:14:04.005 --> 00:14:05.285 to know is that that,

NOTE Confidence: 0.9632586

00:14:05.445 --> 00:14:06.565 when a synosh when a

NOTE Confidence: 0.9632586

00:14:06.565 --> 00:14:07.684 t cell gets activated by

NOTE Confidence: 0.9632586

00:14:07.684 --> 00:14:08.885 synosh, there's kind of this

NOTE Confidence: 0.9632586

00:14:08.885 --> 00:14:10.084 blast radius of about a

NOTE Confidence: 0.9632586

00:14:10.084 --> 00:14:11.605 hundred microns where it can

NOTE Confidence: 0.9632586

00:14:11.605 --> 00:14:13.045 operate and start killing once

NOTE Confidence: 0.9632586

00:14:13.045 --> 00:14:13.679 the CAR

NOTE Confidence: 0.99842894

00:14:14.080 --> 00:14:14.660 is expressed.

NOTE Confidence: 0.94213337

00:14:15.120 --> 00:14:16.240 And as I said, these

NOTE Confidence: 0.94213337

00:14:16.240 --> 00:14:17.679 two antigens, the killing ones

NOTE Confidence: 0.94213337

00:14:17.679 --> 00:14:18.960 actually are are not expressed

NOTE Confidence: 0.94213337

00:14:18.960 --> 00:14:20.320 in the normal brain. So

NOTE Confidence: 0.94213337

00:14:20.320 --> 00:14:21.940 lobosoma is the only place

NOTE Confidence: 0.94213337

00:14:22.160 --> 00:14:23.839 where brain plus these two

NOTE Confidence: 0.94213337

00:14:23.839 --> 00:14:24.339 antigens,

NOTE Confidence: 0.99931306

00:14:24.880 --> 00:14:25.380 works.

NOTE Confidence: 0.96871567

00:14:26.000 --> 00:14:28.100 So, what's shown here is,

NOTE Confidence: 0.9250586

00:14:28.795 --> 00:14:29.295 hopefully

NOTE Confidence: 0.94418424

00:14:29.675 --> 00:14:30.955 okay. Yeah. Is a movie

NOTE Confidence: 0.94418424

00:14:30.955 --> 00:14:31.915 of a a t cell

NOTE Confidence: 0.94418424

00:14:31.915 --> 00:14:33.755 with this SynNotch and with

NOTE Confidence: 0.94418424

00:14:33.755 --> 00:14:35.035 a green reporter that turns

NOTE Confidence: 0.94418424

00:14:35.035 --> 00:14:35.915 on when the SynNotch is

NOTE Confidence: 0.94418424

00:14:35.915 --> 00:14:37.435 activated and it's interacting with,

NOTE Confidence: 0.94418424

00:14:37.755 --> 00:14:39.135 the surroundings of an astrocyte,

NOTE Confidence: 0.9291494

00:14:39.595 --> 00:14:41.515 which expresses BCAN in this

NOTE Confidence: 0.9291494

00:14:41.515 --> 00:14:43.050 ECM and it turns on,

NOTE Confidence: 0.9291494

00:14:43.290 --> 00:14:44.570 goes from green blue to

NOTE Confidence: 0.9291494

00:14:44.570 --> 00:14:45.470 green. I'm sorry.

NOTE Confidence: 0.9817178

00:14:45.930 --> 00:14:47.209 And so we can take,

NOTE Confidence: 0.9817178

00:14:47.450 --> 00:14:47.950 these,

NOTE Confidence: 0.9678814

00:14:48.410 --> 00:14:49.850 this kind of cell and,

NOTE Confidence: 0.9678814

00:14:49.850 --> 00:14:50.970 for example, turn on a

NOTE Confidence: 0.9678814

00:14:50.970 --> 00:14:51.470 car,

NOTE Confidence: 0.9710894

00:14:52.490 --> 00:14:53.790 and we can look at

NOTE Confidence: 0.9710894

00:14:53.810 --> 00:14:55.370 the retrieve the cells from

NOTE Confidence: 0.9710894

00:14:55.370 --> 00:14:56.170 the brain as well as

NOTE Confidence: 0.9710894

00:14:56.170 --> 00:14:57.130 the spleen spleen in the

NOTE Confidence: 0.9710894

00:14:57.130 --> 00:14:58.089 blood, and we only see

NOTE Confidence: 0.9710894

00:14:58.089 --> 00:14:59.355 strong activation,

NOTE Confidence: 0.95470923

00:14:59.975 --> 00:15:01.115 by a GFP marker,

NOTE Confidence: 0.9608271

00:15:01.735 --> 00:15:02.935 in the brain. So it's

NOTE Confidence: 0.9608271

00:15:02.935 --> 00:15:03.435 selectively,

NOTE Confidence: 0.9645299

00:15:03.975 --> 00:15:05.335 primed in the brain. And

NOTE Confidence: 0.9645299

00:15:05.335 --> 00:15:06.295 then when we when we,

NOTE Confidence: 0.9645299

00:15:06.535 --> 00:15:07.575 put a brain tumor in

NOTE Confidence: 0.9645299

00:15:07.575 --> 00:15:08.075 here

NOTE Confidence: 0.9613507

00:15:08.615 --> 00:15:10.135 and then we, give them

NOTE Confidence: 0.9613507

00:15:10.135 --> 00:15:11.335 the the these cells, you

NOTE Confidence: 0.9613507

00:15:11.335 --> 00:15:12.615 can see they, are able

NOTE Confidence: 0.9613507

00:15:12.615 --> 00:15:13.815 to clear that tumor,

NOTE Confidence: 0.9956199

00:15:14.300 --> 00:15:15.740 completely and give you really

NOTE Confidence: 0.9956199

00:15:15.740 --> 00:15:16.560 great survival.

NOTE Confidence: 0.9527067

00:15:17.100 --> 00:15:17.819 This is one of the

NOTE Confidence: 0.9527067

00:15:17.819 --> 00:15:19.579 best, results that we've seen

NOTE Confidence: 0.9527067

00:15:19.579 --> 00:15:20.620 in this kind of animal

NOTE Confidence: 0.9527067

00:15:20.620 --> 00:15:22.300 model. I should say also

NOTE Confidence: 0.9527067

00:15:22.300 --> 00:15:22.860 we see,

NOTE Confidence: 0.9192421

00:15:24.100 --> 00:15:25.259 a hundred days later, we

NOTE Confidence: 0.9192421

00:15:25.259 --> 00:15:26.379 still see after the tumor

NOTE Confidence: 0.9192421

00:15:26.379 --> 00:15:28.079 is cleared, we still see,

NOTE Confidence: 0.9541528

00:15:28.715 --> 00:15:30.315 a resident memory like cells,

NOTE Confidence: 0.9541528

00:15:30.555 --> 00:15:31.995 of these these CAR Ts

NOTE Confidence: 0.9541528

00:15:31.995 --> 00:15:33.195 in the brain, and they

NOTE Confidence: 0.9541528

00:15:33.195 --> 00:15:34.895 are the mice are resistant

NOTE Confidence: 0.9541528

00:15:35.115 --> 00:15:35.775 to rechallenge

NOTE Confidence: 0.9870098

00:15:36.235 --> 00:15:37.855 with even in the contralateral

NOTE Confidence: 0.9870098

00:15:37.995 --> 00:15:38.495 hemisphere.

NOTE Confidence: 0.9930939

00:15:39.195 --> 00:15:41.035 So so, it seems to

NOTE Confidence: 0.9930939

00:15:41.035 --> 00:15:42.370 be working really well.

NOTE Confidence: 0.99460137

00:15:42.990 --> 00:15:44.450 And then, in addition,

NOTE Confidence: 0.99435157

00:15:45.070 --> 00:15:46.589 we have done experiments where

NOTE Confidence: 0.99435157

00:15:46.589 --> 00:15:47.149 we put,

NOTE Confidence: 0.9775426

00:15:47.630 --> 00:15:48.750 the same tumors in the

NOTE Confidence: 0.9775426

00:15:48.750 --> 00:15:50.130 brain or in the flank,

NOTE Confidence: 0.94226545

00:15:50.510 --> 00:15:51.470 and what you can see

NOTE Confidence: 0.94226545

00:15:51.470 --> 00:15:52.830 is that on and then

NOTE Confidence: 0.94226545

00:15:52.830 --> 00:15:54.625 inject the cells and these

NOTE Confidence: 0.94226545

00:15:54.625 --> 00:15:55.505 tumors are in the same

NOTE Confidence: 0.94226545

00:15:55.505 --> 00:15:56.785 animal, but only the ones

NOTE Confidence: 0.94226545

00:15:56.785 --> 00:15:58.065 in the brain are cleared.

NOTE Confidence: 0.94226545

00:15:58.065 --> 00:15:59.024 The ones in the flank

NOTE Confidence: 0.94226545

00:15:59.024 --> 00:16:00.305 are not. And I should

NOTE Confidence: 0.94226545

00:16:00.305 --> 00:16:01.985 say that these are are

NOTE Confidence: 0.94226545

00:16:01.985 --> 00:16:02.565 are BKAN,

NOTE Confidence: 0.9785337

00:16:02.944 --> 00:16:04.545 sensors are responsive to both

NOTE Confidence: 0.9785337

00:16:04.545 --> 00:16:06.305 human and mouse. So it's

NOTE Confidence: 0.9785337

00:16:06.305 --> 00:16:07.505 really priming based on the

NOTE Confidence: 0.9785337

00:16:07.505 --> 00:16:08.565 endogenous mouse,

NOTE Confidence: 0.9945684

00:16:09.024 --> 00:16:09.524 BKAN.

NOTE Confidence: 0.86865526

00:16:11.530 --> 00:16:13.370 So, yeah, we see, brain

NOTE Confidence: 0.86865526

00:16:13.370 --> 00:16:15.050 restricted activity. Now,

NOTE Confidence: 0.9332352

00:16:15.450 --> 00:16:17.210 Milosz, wanted to also say

NOTE Confidence: 0.9332352

00:16:17.210 --> 00:16:18.090 if we have this kind

NOTE Confidence: 0.9332352

00:16:18.090 --> 00:16:18.670 of general,

NOTE Confidence: 0.92265284

00:16:19.370 --> 00:16:20.650 module that can say this

NOTE Confidence: 0.92265284

00:16:20.650 --> 00:16:21.870 is where you're gonna act,

NOTE Confidence: 0.9388627

00:16:22.585 --> 00:16:24.345 anatomically, could we use it

NOTE Confidence: 0.9388627

00:16:24.345 --> 00:16:25.465 to produce different kinds of

NOTE Confidence: 0.9388627

00:16:25.465 --> 00:16:26.585 payloads that would maybe push

NOTE Confidence: 0.9388627

00:16:26.585 --> 00:16:28.025 things in the opposite direction

NOTE Confidence: 0.9388627

00:16:28.025 --> 00:16:29.245 like in, neuroinflammation?

NOTE Confidence: 0.9839142

00:16:29.945 --> 00:16:30.665 And one,

NOTE Confidence: 0.9759692

00:16:31.625 --> 00:16:33.385 cytokine that's been shown to

NOTE Confidence: 0.9759692

00:16:33.385 --> 00:16:34.505 to have some effects if

NOTE Confidence: 0.9759692

00:16:34.505 --> 00:16:35.785 you, for example, express it

NOTE Confidence: 0.9759692

00:16:35.785 --> 00:16:36.525 by AAV

NOTE Confidence: 0.83077496

00:16:36.870 --> 00:16:37.910 in the brain is aisle

NOTE Confidence: 0.83077496

00:16:37.910 --> 00:16:38.410 ten.

NOTE Confidence: 0.96457416

00:16:38.950 --> 00:16:40.070 And but it can't be

NOTE Confidence: 0.96457416

00:16:40.070 --> 00:16:41.589 systemically injected because it's not

NOTE Confidence: 0.96457416

00:16:41.589 --> 00:16:42.630 stable enough to half life

NOTE Confidence: 0.96457416

00:16:42.630 --> 00:16:43.510 is really long. It doesn't

NOTE Confidence: 0.96457416

00:16:43.510 --> 00:16:44.470 get into the brain very

NOTE Confidence: 0.96457416

00:16:44.470 --> 00:16:46.010 well. So he worked with,

NOTE Confidence: 0.9312333

00:16:47.430 --> 00:16:48.650 several of our neurology

NOTE Confidence: 0.9073851

00:16:48.965 --> 00:16:50.325 colleagues and used the EAE

NOTE Confidence: 0.9073851

00:16:50.325 --> 00:16:52.405 model for multiple sclerosis. This

NOTE Confidence: 0.9073851

00:16:52.405 --> 00:16:53.705 is something where you induce

NOTE Confidence: 0.9073851

00:16:53.925 --> 00:16:55.365 an autoimmune response against a

NOTE Confidence: 0.9073851

00:16:55.365 --> 00:16:57.365 myelin protein, and then asked

NOTE Confidence: 0.9073851

00:16:57.365 --> 00:16:58.565 if we dose them with

NOTE Confidence: 0.9073851

00:16:58.565 --> 00:16:59.065 these,

NOTE Confidence: 0.966374

00:16:59.445 --> 00:17:01.605 suppressor cells, these designer suppressor

NOTE Confidence: 0.966374

00:17:01.605 --> 00:17:02.885 cells, could we reduce the

NOTE Confidence: 0.966374

00:17:02.885 --> 00:17:04.085 kind of paralysis that you

NOTE Confidence: 0.966374

00:17:04.085 --> 00:17:04.770 see in these,

NOTE Confidence: 0.88522196

00:17:05.170 --> 00:17:06.630 neurological like exams?

NOTE Confidence: 0.9507552

00:17:07.250 --> 00:17:08.710 And so what's shown here

NOTE Confidence: 0.9507552

00:17:08.770 --> 00:17:09.650 is that we, in fact,

NOTE Confidence: 0.9507552

00:17:09.650 --> 00:17:11.250 see a significant suppression of

NOTE Confidence: 0.9507552

00:17:11.250 --> 00:17:13.250 this is essentially paralysis in

NOTE Confidence: 0.9507552

00:17:13.250 --> 00:17:14.230 a longer life,

NOTE Confidence: 0.8714047

00:17:14.850 --> 00:17:16.869 survival. So hopefully oh,

NOTE Confidence: 0.9925636

00:17:18.050 --> 00:17:18.550 okay.

NOTE Confidence: 0.99947345

00:17:20.684 --> 00:17:22.125 Well, I can't figure out

NOTE Confidence: 0.99947345

00:17:22.125 --> 00:17:23.025 how to do that.

NOTE Confidence: 0.9557464

00:17:23.725 --> 00:17:24.845 Okay. I'll just actually stick

NOTE Confidence: 0.9557464

00:17:24.845 --> 00:17:25.804 with that. Anyway, you'll you

NOTE Confidence: 0.9557464

00:17:25.804 --> 00:17:26.765 would see that you'll see

NOTE Confidence: 0.9557464

00:17:26.765 --> 00:17:28.205 that the mice, by twelve

NOTE Confidence: 0.9557464

00:17:28.205 --> 00:17:29.405 days that were not treated

NOTE Confidence: 0.9557464

00:17:29.405 --> 00:17:30.765 were really pretty much paralyzed,

NOTE Confidence: 0.9557464

00:17:30.765 --> 00:17:31.725 but the ones that were

NOTE Confidence: 0.9557464

00:17:31.725 --> 00:17:32.125 treated,

NOTE Confidence: 0.94194365

00:17:32.525 --> 00:17:33.345 were were not.

NOTE Confidence: 0.8964515

00:17:35.010 --> 00:17:35.510 So,

NOTE Confidence: 0.9335283

00:17:35.810 --> 00:17:37.730 and then in another, related,

NOTE Confidence: 0.88997227

00:17:38.050 --> 00:17:39.410 intersecting paper, Nish Reddy, a

NOTE Confidence: 0.88997227

00:17:39.410 --> 00:17:41.650 former post student graduate student

NOTE Confidence: 0.88997227

00:17:41.650 --> 00:17:42.390 in the lab,

NOTE Confidence: 0.9256108

00:17:42.770 --> 00:17:44.450 Ashley asked, could we instead

NOTE Confidence: 0.9256108

00:17:44.450 --> 00:17:45.490 of just looking at aisle

NOTE Confidence: 0.9256108

00:17:45.490 --> 00:17:45.650 ten

NOTE Confidence: 0.75881493

00:17:52.445 --> 00:17:53.345 Okay. K.

NOTE Confidence: 0.8654947

00:17:53.725 --> 00:17:54.225 Cool.

NOTE Confidence: 0.9358575

00:17:55.565 --> 00:17:56.685 Could we now kind of

NOTE Confidence: 0.9358575

00:17:56.685 --> 00:17:58.285 make custom programs that have

NOTE Confidence: 0.9358575

00:17:58.285 --> 00:17:59.905 different suppressive cytokines,

NOTE Confidence: 0.93283796

00:18:00.445 --> 00:18:01.585 antibodies, etcetera?

NOTE Confidence: 0.83085954

00:18:02.445 --> 00:18:02.685 And,

NOTE Confidence: 0.96557045

00:18:03.630 --> 00:18:05.150 he then screened these for

NOTE Confidence: 0.96557045

00:18:05.150 --> 00:18:06.510 for how effective they were

NOTE Confidence: 0.96557045

00:18:06.510 --> 00:18:07.330 at suppressing,

NOTE Confidence: 0.78419095

00:18:07.790 --> 00:18:09.490 a t cell killing response.

NOTE Confidence: 0.97414243

00:18:10.030 --> 00:18:11.630 And, this is just summarizing

NOTE Confidence: 0.97414243

00:18:11.630 --> 00:18:13.390 this plot here. Basically, he,

NOTE Confidence: 0.97414243

00:18:13.630 --> 00:18:15.150 in the middle there, he

NOTE Confidence: 0.97414243

00:18:15.150 --> 00:18:16.270 saw that that the best

NOTE Confidence: 0.97414243

00:18:16.270 --> 00:18:17.970 payloads were these specific combinations.

NOTE Confidence: 0.95143795

00:18:18.270 --> 00:18:19.365 They turn out to be

NOTE Confidence: 0.95143795

00:18:19.365 --> 00:18:20.645 things that look that in

NOTE Confidence: 0.95143795

00:18:20.645 --> 00:18:22.085 which a normal Treg would

NOTE Confidence: 0.95143795

00:18:22.085 --> 00:18:23.365 fit. They are a combination

NOTE Confidence: 0.95143795

00:18:23.365 --> 00:18:24.665 of a suppressive cytokine

NOTE Confidence: 0.8028869

00:18:25.045 --> 00:18:26.405 or a suppressor agent, even

NOTE Confidence: 0.8028869

00:18:26.405 --> 00:18:27.465 anti PD one,

NOTE Confidence: 0.94255775

00:18:28.965 --> 00:18:30.244 PDL one. I'm sorry. And

NOTE Confidence: 0.94255775

00:18:30.244 --> 00:18:30.565 then,

NOTE Confidence: 0.8397321

00:18:32.010 --> 00:18:33.450 with a a sync for

NOTE Confidence: 0.8397321

00:18:33.450 --> 00:18:34.970 inflammatory cytokines like a like,

NOTE Confidence: 0.8397321

00:18:34.970 --> 00:18:36.010 CD twenty five, which is

NOTE Confidence: 0.8397321

00:18:36.010 --> 00:18:37.690 a sync for for IL

NOTE Confidence: 0.8397321

00:18:37.690 --> 00:18:39.150 two, the the required,

NOTE Confidence: 0.9961418

00:18:40.170 --> 00:18:41.390 inflammatory cytokine,

NOTE Confidence: 0.98918444

00:18:42.010 --> 00:18:43.690 which also leads to enhanced

NOTE Confidence: 0.98918444

00:18:43.690 --> 00:18:45.210 proliferation of these cells, the

NOTE Confidence: 0.98918444

00:18:45.210 --> 00:18:46.815 suppressor cells. And then he

NOTE Confidence: 0.98918444

00:18:46.815 --> 00:18:47.934 was able to show with,

NOTE Confidence: 0.98918444

00:18:48.174 --> 00:18:48.835 in collaboration

NOTE Confidence: 0.8455259

00:18:49.135 --> 00:18:50.674 with Matthias Heebrock's lab,

NOTE Confidence: 0.9812951

00:18:51.054 --> 00:18:52.275 that we could transplant,

NOTE Confidence: 0.9699548

00:18:52.655 --> 00:18:53.955 beta beta cell,

NOTE Confidence: 0.93767935

00:18:54.655 --> 00:18:55.955 islet, organoids,

NOTE Confidence: 0.94462323

00:18:56.655 --> 00:18:58.494 into mice and that these

NOTE Confidence: 0.94462323

00:18:58.494 --> 00:18:59.775 would be normally killed by,

NOTE Confidence: 0.94462323

00:19:00.015 --> 00:19:01.320 T cells, but that we

NOTE Confidence: 0.94462323

00:19:01.320 --> 00:19:02.359 could protect them for a

NOTE Confidence: 0.94462323

00:19:02.359 --> 00:19:04.119 number of days, with these

NOTE Confidence: 0.94462323

00:19:04.119 --> 00:19:05.480 these enhanced programs. And we're

NOTE Confidence: 0.94462323

00:19:05.480 --> 00:19:06.380 hoping to to,

NOTE Confidence: 0.9364782

00:19:07.320 --> 00:19:09.480 improve these and, improve these

NOTE Confidence: 0.9364782

00:19:09.480 --> 00:19:10.679 and and and apply them

NOTE Confidence: 0.9364782

00:19:10.679 --> 00:19:11.740 towards, neuroinflammation

NOTE Confidence: 0.9939878

00:19:12.279 --> 00:19:12.779 also.

NOTE Confidence: 0.9576397

00:19:13.159 --> 00:19:13.480 So,

NOTE Confidence: 0.9442176

00:19:14.279 --> 00:19:14.520 the,

NOTE Confidence: 0.9875144

00:19:16.184 --> 00:19:17.144 hopefully, I've shown you that

NOTE Confidence: 0.9875144

00:19:17.144 --> 00:19:18.024 we can engineer,

NOTE Confidence: 0.93665886

00:19:18.424 --> 00:19:20.024 immune cells that use multi

NOTE Confidence: 0.93665886

00:19:20.024 --> 00:19:20.924 receptor circuits,

NOTE Confidence: 0.95665264

00:19:21.945 --> 00:19:22.445 to,

NOTE Confidence: 0.96864957

00:19:22.984 --> 00:19:24.125 to integrate information,

NOTE Confidence: 0.9521869

00:19:24.825 --> 00:19:26.105 at different scales and that

NOTE Confidence: 0.9521869

00:19:26.105 --> 00:19:27.244 can make very precise

NOTE Confidence: 0.87141734

00:19:27.625 --> 00:19:29.244 disease specific decisions.

NOTE Confidence: 0.99245214

00:19:29.970 --> 00:19:31.429 In the example of glioblastoma,

NOTE Confidence: 0.97499067

00:19:31.809 --> 00:19:33.109 we've been able to engineer,

NOTE Confidence: 0.9116669

00:19:34.530 --> 00:19:36.450 precision brain cancer therapies in

NOTE Confidence: 0.9116669

00:19:36.450 --> 00:19:37.809 which we program a cell

NOTE Confidence: 0.9116669

00:19:37.809 --> 00:19:39.490 that one recognizes that it's

NOTE Confidence: 0.9116669

00:19:39.490 --> 00:19:40.450 in the brain and two

NOTE Confidence: 0.9116669

00:19:40.450 --> 00:19:41.109 that induces

NOTE Confidence: 0.9168678

00:19:41.410 --> 00:19:42.470 a killing response,

NOTE Confidence: 0.9013001

00:19:42.994 --> 00:19:43.494 locally.

NOTE Confidence: 0.9536838

00:19:43.955 --> 00:19:45.255 And it's a powerful combination

NOTE Confidence: 0.9536838

00:19:45.315 --> 00:19:47.095 of kind of anatomical molecular

NOTE Confidence: 0.9536838

00:19:47.235 --> 00:19:48.595 specificity. And I think that

NOTE Confidence: 0.9536838

00:19:48.595 --> 00:19:50.295 kind of multi scale functionality

NOTE Confidence: 0.9536838

00:19:50.435 --> 00:19:51.395 is really part of the

NOTE Confidence: 0.9536838

00:19:51.395 --> 00:19:52.455 key of what living,

NOTE Confidence: 0.92836833

00:19:52.835 --> 00:19:53.795 systems can do and then

NOTE Confidence: 0.92836833

00:19:53.875 --> 00:19:54.869 and the challenge of how

NOTE Confidence: 0.92836833

00:19:54.950 --> 00:19:56.630 how we understand biological function,

NOTE Confidence: 0.92836833

00:19:56.630 --> 00:19:57.290 of course.

NOTE Confidence: 0.9883865

00:19:57.670 --> 00:19:58.950 And then these tissue sensing

NOTE Confidence: 0.9883865

00:19:58.950 --> 00:20:00.150 cells can be used in

NOTE Confidence: 0.9883865

00:20:00.150 --> 00:20:01.990 a disease agnostic manner to

NOTE Confidence: 0.9883865

00:20:01.990 --> 00:20:02.470 deliver,

NOTE Confidence: 0.9512835

00:20:03.350 --> 00:20:04.730 immune suppressive payloads,

NOTE Confidence: 0.9473984

00:20:05.350 --> 00:20:06.090 for neuroinflammation,

NOTE Confidence: 0.98955274

00:20:06.950 --> 00:20:08.090 as well as potentially

NOTE Confidence: 0.9815511

00:20:08.575 --> 00:20:09.935 regenerative payloads for things like

NOTE Confidence: 0.9815511

00:20:09.935 --> 00:20:10.435 neurodegeneration,

NOTE Confidence: 0.9745042

00:20:10.975 --> 00:20:12.435 and we can create customized

NOTE Confidence: 0.9745042

00:20:12.734 --> 00:20:13.795 multifactor programs.

NOTE Confidence: 0.9889612

00:20:14.494 --> 00:20:15.535 So I wanna just end

NOTE Confidence: 0.9889612

00:20:15.535 --> 00:20:16.734 by giving you some update

NOTE Confidence: 0.9889612

00:20:16.734 --> 00:20:17.535 on some of the the

NOTE Confidence: 0.9889612

00:20:17.535 --> 00:20:19.295 clinical things. We're we're, very

NOTE Confidence: 0.9889612

00:20:19.295 --> 00:20:20.494 excited to try to really

NOTE Confidence: 0.9889612

00:20:20.494 --> 00:20:22.095 push these through to the

NOTE Confidence: 0.9889612

00:20:22.095 --> 00:20:23.715 clinic, as soon as possible.

NOTE Confidence: 0.97543573

00:20:24.630 --> 00:20:25.109 And,

NOTE Confidence: 0.90647304

00:20:25.510 --> 00:20:27.910 we have, one one, phase

NOTE Confidence: 0.90647304

00:20:27.910 --> 00:20:28.869 one trial that we've already

NOTE Confidence: 0.90647304

00:20:28.869 --> 00:20:30.250 opened, which is called eSync.

NOTE Confidence: 0.90647304

00:20:30.310 --> 00:20:31.430 This is actually a synapse

NOTE Confidence: 0.90647304

00:20:31.430 --> 00:20:32.950 of our circuit that is

NOTE Confidence: 0.90647304

00:20:32.950 --> 00:20:34.790 actually primed by a,

NOTE Confidence: 0.92199284

00:20:35.430 --> 00:20:36.330 tumor specific

NOTE Confidence: 0.95864004

00:20:36.790 --> 00:20:39.015 GBM specific neoantigen. So it's

NOTE Confidence: 0.95864004

00:20:39.015 --> 00:20:40.695 absolutely unique. The problem is

NOTE Confidence: 0.95864004

00:20:40.695 --> 00:20:41.195 it's

NOTE Confidence: 0.93330956

00:20:41.655 --> 00:20:43.015 it's very heterogeneous. So if

NOTE Confidence: 0.93330956

00:20:43.015 --> 00:20:44.615 you only attack that, you

NOTE Confidence: 0.93330956

00:20:44.615 --> 00:20:45.355 get escape,

NOTE Confidence: 0.9388826

00:20:46.135 --> 00:20:47.494 because of the heterogeneity. But

NOTE Confidence: 0.9388826

00:20:47.494 --> 00:20:48.455 in this case, we're only

NOTE Confidence: 0.9388826

00:20:48.455 --> 00:20:49.575 using it for to flag

NOTE Confidence: 0.9388826

00:20:49.575 --> 00:20:51.030 the location and then killing

NOTE Confidence: 0.9388826

00:20:51.030 --> 00:20:52.869 more broadly. So that, is,

NOTE Confidence: 0.9388826

00:20:53.110 --> 00:20:54.790 already, down three patients have

NOTE Confidence: 0.9388826

00:20:54.790 --> 00:20:56.070 been dosed. And then this

NOTE Confidence: 0.9388826

00:20:56.070 --> 00:20:57.110 other one, the b sync

NOTE Confidence: 0.9388826

00:20:57.110 --> 00:20:58.550 is the brain priming using

NOTE Confidence: 0.9388826

00:20:58.550 --> 00:21:00.230 BECAN. That one we're gonna

NOTE Confidence: 0.9388826

00:21:00.230 --> 00:21:01.590 file, hopefully, by the end

NOTE Confidence: 0.9388826

00:21:01.590 --> 00:21:03.030 of this year, and start

NOTE Confidence: 0.9388826

00:21:03.030 --> 00:21:04.615 the trial next year. But

NOTE Confidence: 0.9388826

00:21:04.615 --> 00:21:05.734 this is we're really excited

NOTE Confidence: 0.9388826

00:21:05.734 --> 00:21:06.554 by it because,

NOTE Confidence: 0.9620677

00:21:07.095 --> 00:21:08.215 in this case, this is

NOTE Confidence: 0.9620677

00:21:08.215 --> 00:21:08.934 one of the first cases

NOTE Confidence: 0.9620677

00:21:08.934 --> 00:21:10.075 where you're actually using

NOTE Confidence: 0.9039852

00:21:10.455 --> 00:21:12.534 a non tumor antigen to

NOTE Confidence: 0.9039852

00:21:12.615 --> 00:21:13.914 as part of the recognition.

NOTE Confidence: 0.9772434

00:21:14.534 --> 00:21:15.654 And so that means what's

NOTE Confidence: 0.9772434

00:21:15.654 --> 00:21:16.549 exciting is, like, in the

NOTE Confidence: 0.9772434

00:21:16.549 --> 00:21:17.429 first one, we have to

NOTE Confidence: 0.9772434

00:21:17.429 --> 00:21:18.549 screen the patients to find

NOTE Confidence: 0.9772434

00:21:18.549 --> 00:21:19.530 which subpopulation

NOTE Confidence: 0.97092867

00:21:19.910 --> 00:21:21.210 has that neoantigen.

NOTE Confidence: 0.98221135

00:21:21.510 --> 00:21:22.790 But in this case, everyone

NOTE Confidence: 0.98221135

00:21:22.790 --> 00:21:24.710 has BCAN, so everyone can

NOTE Confidence: 0.98221135

00:21:24.710 --> 00:21:26.309 can is there can can

NOTE Confidence: 0.98221135

00:21:26.309 --> 00:21:27.590 be part of this. In

NOTE Confidence: 0.98221135

00:21:27.590 --> 00:21:28.090 addition,

NOTE Confidence: 0.9722789

00:21:28.414 --> 00:21:30.414 these these, killing antigens are

NOTE Confidence: 0.9722789

00:21:30.414 --> 00:21:31.955 found in many different tumors.

NOTE Confidence: 0.98276144

00:21:32.335 --> 00:21:33.774 So this this these look

NOTE Confidence: 0.98276144

00:21:33.774 --> 00:21:35.135 like they're they could work

NOTE Confidence: 0.98276144

00:21:35.135 --> 00:21:36.414 for a lot of pediatric

NOTE Confidence: 0.98276144

00:21:36.414 --> 00:21:36.914 gliomas,

NOTE Confidence: 0.8821659

00:21:37.294 --> 00:21:38.835 many brain cancers, including,

NOTE Confidence: 0.9633839

00:21:39.455 --> 00:21:40.830 brain mets from things like

NOTE Confidence: 0.9633839

00:21:40.830 --> 00:21:42.910 breast and lung, etcetera. So

NOTE Confidence: 0.9633839

00:21:42.910 --> 00:21:44.109 it's really interesting that that,

NOTE Confidence: 0.9633839

00:21:44.109 --> 00:21:45.789 you know, we're we've focused

NOTE Confidence: 0.9633839

00:21:45.789 --> 00:21:46.590 a lot of kind of

NOTE Confidence: 0.9633839

00:21:46.590 --> 00:21:48.190 targeting things to very specific

NOTE Confidence: 0.9633839

00:21:48.190 --> 00:21:50.830 molecular, sort of, individuals and

NOTE Confidence: 0.9633839

00:21:50.830 --> 00:21:52.429 these personalized things. But there

NOTE Confidence: 0.9633839

00:21:52.429 --> 00:21:53.869 is the capability in in

NOTE Confidence: 0.9633839

00:21:53.869 --> 00:21:54.990 this case to kind of

NOTE Confidence: 0.9633839

00:21:54.990 --> 00:21:56.325 cast the net at different

NOTE Confidence: 0.9633839

00:21:56.325 --> 00:21:57.445 levels and then get something

NOTE Confidence: 0.9633839

00:21:57.445 --> 00:21:58.965 that really could be very

NOTE Confidence: 0.9633839

00:21:58.965 --> 00:22:00.484 precise but still used for

NOTE Confidence: 0.9633839

00:22:00.484 --> 00:22:01.865 a large number of patients.

NOTE Confidence: 0.97107774

00:22:03.684 --> 00:22:04.725 And so let me end

NOTE Confidence: 0.97107774

00:22:04.804 --> 00:22:05.764 it's going back to this.

NOTE Confidence: 0.97107774

00:22:05.764 --> 00:22:06.505 We are,

NOTE Confidence: 0.9971341

00:22:07.044 --> 00:22:08.424 we we are very interested

NOTE Confidence: 0.9971341

00:22:08.484 --> 00:22:09.544 in trying to

NOTE Confidence: 0.96594274

00:22:10.480 --> 00:22:12.899 apply AI and and predictive,

NOTE Confidence: 0.9835403

00:22:13.279 --> 00:22:13.779 methods,

NOTE Confidence: 0.96201015

00:22:14.320 --> 00:22:15.679 that allow us to design

NOTE Confidence: 0.96201015

00:22:15.679 --> 00:22:16.799 things. We have been working

NOTE Confidence: 0.96201015

00:22:16.799 --> 00:22:17.679 a lot on we worked

NOTE Confidence: 0.96201015

00:22:17.679 --> 00:22:19.359 with IBM on a number

NOTE Confidence: 0.96201015

00:22:19.359 --> 00:22:21.539 of, sort of modular motifs

NOTE Confidence: 0.96201015

00:22:21.600 --> 00:22:23.440 within CARs and other receptors

NOTE Confidence: 0.96201015

00:22:23.440 --> 00:22:24.480 to try to understand what

NOTE Confidence: 0.96201015

00:22:24.480 --> 00:22:25.759 their phenotypes would be, but

NOTE Confidence: 0.96201015

00:22:25.759 --> 00:22:26.265 we'd really

NOTE Confidence: 0.9760984

00:22:28.185 --> 00:22:28.785 like to be able to,

NOTE Confidence: 0.9760984

00:22:28.905 --> 00:22:29.505 do this and operate at

NOTE Confidence: 0.9760984

00:22:29.505 --> 00:22:30.984 these different scales and have

NOTE Confidence: 0.9760984

00:22:30.984 --> 00:22:32.185 predictions at that level. And

NOTE Confidence: 0.9760984

00:22:32.185 --> 00:22:32.925 part of our,

NOTE Confidence: 0.97769046

00:22:33.305 --> 00:22:34.425 sort of our strategy is

NOTE Confidence: 0.97769046

00:22:34.425 --> 00:22:35.865 to to simplify the the

NOTE Confidence: 0.97769046

00:22:35.865 --> 00:22:37.145 the alphabet of kind of

NOTE Confidence: 0.97769046

00:22:37.145 --> 00:22:38.600 components or words that we

NOTE Confidence: 0.97769046

00:22:38.600 --> 00:22:39.180 use and

NOTE Confidence: 0.9286272

00:22:39.640 --> 00:22:41.240 and that that we understand

NOTE Confidence: 0.9286272

00:22:41.240 --> 00:22:42.440 well and use these in

NOTE Confidence: 0.9286272

00:22:42.440 --> 00:22:43.260 big combinations,

NOTE Confidence: 0.9936677

00:22:43.560 --> 00:22:44.520 generate a lot of data

NOTE Confidence: 0.9936677

00:22:44.520 --> 00:22:46.040 from that, and then,

NOTE Confidence: 0.96192336

00:22:46.520 --> 00:22:47.820 try to, you know, predict

NOTE Confidence: 0.96192336

00:22:48.119 --> 00:22:49.320 what we can build, in

NOTE Confidence: 0.96192336

00:22:49.320 --> 00:22:51.525 that way. So, let me,

NOTE Confidence: 0.96192336

00:22:51.765 --> 00:22:53.365 also just thank, the people

NOTE Confidence: 0.96192336

00:22:53.365 --> 00:22:54.325 from my group and in

NOTE Confidence: 0.96192336

00:22:54.325 --> 00:22:54.825 particular,

NOTE Confidence: 0.9292603

00:22:55.365 --> 00:22:56.725 Milos who led the work

NOTE Confidence: 0.9292603

00:22:56.725 --> 00:22:58.165 on the brain targeting with

NOTE Confidence: 0.9292603

00:22:58.165 --> 00:22:59.685 our colleagues, Sudayo and Scott

NOTE Confidence: 0.9292603

00:22:59.685 --> 00:23:01.205 Zamvil, and then Nish Reddy

NOTE Confidence: 0.9292603

00:23:01.205 --> 00:23:02.405 who, led the work on

NOTE Confidence: 0.9292603

00:23:02.405 --> 00:23:04.665 the synthetic suppressor cells. Alright.

NOTE Confidence: 0.9292603

00:23:04.885 --> 00:23:05.625 Thank you.

NOTE Confidence: 0.88857365

00:23:11.660 --> 00:23:13.280 Thanks, Vandal. That was

NOTE Confidence: 0.93792224

00:23:13.820 --> 00:23:14.320 nominal.

NOTE Confidence: 0.954204

00:23:17.500 --> 00:23:19.180 Yeah. Wonderful talk, Vandal, as

NOTE Confidence: 0.954204

00:23:19.180 --> 00:23:19.680 always.

NOTE Confidence: 0.9008473

00:23:20.234 --> 00:23:21.595 What do you think, the

NOTE Confidence: 0.9008473

00:23:21.595 --> 00:23:22.955 knowledge gaps do we need

NOTE Confidence: 0.9008473

00:23:22.955 --> 00:23:24.075 for the AI to tell

NOTE Confidence: 0.9008473

00:23:24.075 --> 00:23:26.095 us which, the synthetic circuit

NOTE Confidence: 0.9008473

00:23:26.155 --> 00:23:28.155 field, that logic that allows

NOTE Confidence: 0.9008473

00:23:28.155 --> 00:23:29.115 you to do this, let

NOTE Confidence: 0.9008473

00:23:29.115 --> 00:23:30.234 us all do this? Yeah.

NOTE Confidence: 0.9008473

00:23:30.554 --> 00:23:31.054 Well,

NOTE Confidence: 0.98274326

00:23:31.355 --> 00:23:32.155 I mean, that's a great

NOTE Confidence: 0.98274326

00:23:32.155 --> 00:23:33.275 question. I'm open to lots

NOTE Confidence: 0.98274326

00:23:33.275 --> 00:23:34.619 of different ideas. I mean,

NOTE Confidence: 0.98274326

00:23:34.619 --> 00:23:35.740 look. I'm I mean, I'm

NOTE Confidence: 0.98274326

00:23:35.740 --> 00:23:37.740 a simple biochemist, so I

NOTE Confidence: 0.98274326

00:23:37.740 --> 00:23:38.940 think about these pieces and

NOTE Confidence: 0.98274326

00:23:38.940 --> 00:23:39.820 kind of how they're put

NOTE Confidence: 0.98274326

00:23:39.820 --> 00:23:40.320 together.

NOTE Confidence: 0.98364335

00:23:41.100 --> 00:23:42.300 You know, how to represent

NOTE Confidence: 0.98364335

00:23:42.300 --> 00:23:43.820 that information at these different

NOTE Confidence: 0.98364335

00:23:43.820 --> 00:23:44.940 scales, I think, is is,

NOTE Confidence: 0.98364335

00:23:44.940 --> 00:23:46.140 you know, something that I'd

NOTE Confidence: 0.98364335

00:23:46.140 --> 00:23:48.080 like to to explore more.

NOTE Confidence: 0.7971215

00:23:51.755 --> 00:23:53.595 Randall. Hi, Risa. Great great

NOTE Confidence: 0.7971215

00:23:53.595 --> 00:23:54.095 thoughts.

NOTE Confidence: 0.9648166

00:23:55.674 --> 00:23:57.135 Are you trying to find

NOTE Confidence: 0.9648166

00:23:57.195 --> 00:23:59.615 similar approach to identify this,

NOTE Confidence: 0.9781377

00:23:59.994 --> 00:24:00.494 glioblastoma

NOTE Confidence: 0.98985606

00:24:01.434 --> 00:24:03.515 specific antigens to find something

NOTE Confidence: 0.98985606

00:24:03.515 --> 00:24:05.054 that you can use on

NOTE Confidence: 0.9995851

00:24:05.640 --> 00:24:06.859 endothelial cells

NOTE Confidence: 0.901395

00:24:08.440 --> 00:24:09.960 for organ and tissue specific

NOTE Confidence: 0.901395

00:24:09.960 --> 00:24:11.160 targeting that would not be

NOTE Confidence: 0.901395

00:24:11.160 --> 00:24:13.000 dependent just on inflammation and

NOTE Confidence: 0.901395

00:24:13.000 --> 00:24:14.040 when t cells will go

NOTE Confidence: 0.901395

00:24:14.040 --> 00:24:15.980 there anyway. Yeah. When you

NOTE Confidence: 0.9949072

00:24:16.600 --> 00:24:18.380 use this approach to induce

NOTE Confidence: 0.9949072

00:24:18.440 --> 00:24:18.940 extravasation

NOTE Confidence: 0.9490658

00:24:19.560 --> 00:24:21.365 by detecting. Yeah. Because there

NOTE Confidence: 0.9490658

00:24:21.365 --> 00:24:22.465 there are now,

NOTE Confidence: 0.8552823

00:24:23.005 --> 00:24:23.505 datasets

NOTE Confidence: 0.9995142

00:24:24.365 --> 00:24:25.345 available about

NOTE Confidence: 0.9729303

00:24:25.805 --> 00:24:27.805 organ specific endothelial. Yes. Yeah.

NOTE Confidence: 0.9729303

00:24:27.805 --> 00:24:29.005 So we're very excited about

NOTE Confidence: 0.9729303

00:24:29.005 --> 00:24:29.805 that. I mean, I think

NOTE Confidence: 0.9729303

00:24:29.805 --> 00:24:30.305 that,

NOTE Confidence: 0.99705416

00:24:31.085 --> 00:24:32.285 we came up with this

NOTE Confidence: 0.99705416

00:24:32.285 --> 00:24:32.725 ECM.

NOTE Confidence: 0.9211567

00:24:33.165 --> 00:24:34.445 We're looking into whether there's

NOTE Confidence: 0.9211567

00:24:34.445 --> 00:24:36.680 other tissue specific ECM. The

NOTE Confidence: 0.94971675

00:24:37.260 --> 00:24:38.180 and, yes, there's a lot

NOTE Confidence: 0.94971675

00:24:38.180 --> 00:24:39.560 of endothelial specificity,

NOTE Confidence: 0.9776556

00:24:39.860 --> 00:24:40.900 which is weird to me,

NOTE Confidence: 0.9776556

00:24:40.900 --> 00:24:41.060 but,

NOTE Confidence: 0.97788197

00:24:41.860 --> 00:24:42.660 it seems to be that

NOTE Confidence: 0.97788197

00:24:42.660 --> 00:24:43.700 way. And and we're actually

NOTE Confidence: 0.97788197

00:24:43.700 --> 00:24:45.380 excited because we some we

NOTE Confidence: 0.97788197

00:24:45.380 --> 00:24:46.420 think we have some ways

NOTE Confidence: 0.97788197

00:24:46.420 --> 00:24:47.790 to increase, transmigration,

NOTE Confidence: 0.95723766

00:24:50.595 --> 00:24:52.134 engineered interactions. So I think

NOTE Confidence: 0.95723766

00:24:52.195 --> 00:24:53.494 that could be interesting.

NOTE Confidence: 0.9937576

00:24:54.195 --> 00:24:55.414 And then there's also

NOTE Confidence: 0.97668755

00:24:55.715 --> 00:24:57.475 a lot of, information about,

NOTE Confidence: 0.97668755

00:24:57.715 --> 00:24:59.494 sort of combinations of proteases

NOTE Confidence: 0.97668755

00:24:59.634 --> 00:25:01.190 that are organ specific.

NOTE Confidence: 0.99626994

00:25:02.130 --> 00:25:02.630 So,

NOTE Confidence: 0.96717066

00:25:03.409 --> 00:25:04.850 you know, we're we're interested

NOTE Confidence: 0.96717066

00:25:04.850 --> 00:25:05.730 in looking at those and

NOTE Confidence: 0.96717066

00:25:05.730 --> 00:25:07.109 whether we can sense those.

NOTE Confidence: 0.96717066

00:25:07.169 --> 00:25:08.850 Yeah. And and quick related

NOTE Confidence: 0.96717066

00:25:08.850 --> 00:25:09.510 to that,

NOTE Confidence: 0.90924704

00:25:09.890 --> 00:25:11.669 speaking of VCM, the tenascin

NOTE Confidence: 0.90924704

00:25:11.730 --> 00:25:12.929 c is one of this

NOTE Confidence: 0.90924704

00:25:12.929 --> 00:25:14.695 ECM components. It's It's in

NOTE Confidence: 0.90924704

00:25:14.695 --> 00:25:16.375 brionic, but, in adults, it's

NOTE Confidence: 0.90924704

00:25:16.375 --> 00:25:17.494 mostly in tumors that will

NOTE Confidence: 0.90924704

00:25:17.494 --> 00:25:18.635 be in the main target.

NOTE Confidence: 0.90924704

00:25:18.695 --> 00:25:19.535 Yeah. Well, I mean, yes.

NOTE Confidence: 0.90924704

00:25:19.535 --> 00:25:20.295 A lot of these I

NOTE Confidence: 0.90924704

00:25:20.295 --> 00:25:21.975 mean, in in fibrotic tumors,

NOTE Confidence: 0.90924704

00:25:21.975 --> 00:25:23.494 that's another thing we that

NOTE Confidence: 0.90924704

00:25:23.494 --> 00:25:24.855 overlaps with this. There's a

NOTE Confidence: 0.90924704

00:25:24.855 --> 00:25:25.335 lot of,

NOTE Confidence: 0.98272544

00:25:26.615 --> 00:25:28.295 recognition of those, as a

NOTE Confidence: 0.98272544

00:25:28.295 --> 00:25:28.795 component,

NOTE Confidence: 0.90954494

00:25:29.160 --> 00:25:31.420 for, say, pancreatic, ovarian, etcetera,

NOTE Confidence: 0.991297

00:25:31.880 --> 00:25:33.180 and fibrosis too.

NOTE Confidence: 0.94111717

00:25:33.480 --> 00:25:34.400 So that's the thing. This

NOTE Confidence: 0.94111717

00:25:34.400 --> 00:25:35.880 is sort of general flavors

NOTE Confidence: 0.94111717

00:25:35.880 --> 00:25:37.800 of things that are normal.

NOTE Confidence: 0.94111717

00:25:37.800 --> 00:25:39.320 Right? And and and but

NOTE Confidence: 0.94111717

00:25:39.320 --> 00:25:40.840 in the wrong combinations, they're

NOTE Confidence: 0.94111717

00:25:40.840 --> 00:25:41.340 disease.