WEBVTT

NOTE duration: ”00:22:59.071”

NOTE Confidence: 0.928172

00:00:00.080 --> 00:00:01.599 So, kicking us off in

NOTE Confidence: 0.928172

00:00:01.599 --> 00:00:02.480 session two, it's,

NOTE Confidence: 0.80424714

00:00:03.199 --> 00:00:04.340 Steve, Kleinstein,

NOTE Confidence: 0.9237188

00:00:04.880 --> 00:00:06.399 to who's the Anthony Brady

NOTE Confidence: 0.9237188

00:00:06.399 --> 00:00:07.839 professor of pathology here at

NOTE Confidence: 0.9237188

00:00:07.839 --> 00:00:09.139 the Yale School of Medicine.

NOTE Confidence: 0.8586859

00:00:09.599 --> 00:00:10.719 He also co directs the

NOTE Confidence: 0.8586859

00:00:10.719 --> 00:00:11.440 grad program in computational biology

NOTE Confidence: 0.8586859

00:00:11.440 --> 00:00:11.940 and

NOTE Confidence: 0.6344995

00:00:13.055 --> 00:00:14.115 biomedical informatics,

NOTE Confidence: 0.9815299

00:00:14.575 --> 00:00:16.995 with secondary appointments in immunobiology

NOTE Confidence: 0.9714197

00:00:17.535 --> 00:00:19.055 and the new department of

NOTE Confidence: 0.9714197

00:00:19.055 --> 00:00:21.075 biomedical informatics and data science.

NOTE Confidence: 0.97061193

00:00:21.935 --> 00:00:23.375 And so Steve, came to

NOTE Confidence: 0.97061193

00:00:23.375 --> 00:00:25.454 immunology from computer science, and

NOTE Confidence: 0.97061193

00:00:25.454 --> 00:00:27.135 he's been a leader working

NOTE Confidence: 0.97061193

00:00:27.135 --> 00:00:27.635 on

NOTE Confidence: 0.99615985

00:00:28.510 --> 00:00:29.790 various aspects of the immune

NOTE Confidence: 0.99615985

00:00:29.790 --> 00:00:31.150 system for the last, two

NOTE Confidence: 0.99615985

00:00:31.150 --> 00:00:32.930 decades. So welcome, Steve.

NOTE Confidence: 0.9367962

00:00:35.790 --> 00:00:36.610 Thank you.

NOTE Confidence: 0.95748276

00:00:39.070 --> 00:00:40.670 It's, re really nice to

NOTE Confidence: 0.95748276

00:00:40.670 --> 00:00:41.790 see all all the energy

NOTE Confidence: 0.95748276

00:00:41.790 --> 00:00:42.590 and all the all the,

NOTE Confidence: 0.95748276

00:00:43.284 --> 00:00:44.405 collaborations that are starting up,

NOTE Confidence: 0.95748276

00:00:44.645 --> 00:00:45.525 here at Yale in this

NOTE Confidence: 0.95748276

00:00:45.525 --> 00:00:47.945 area of, computational systems, immunology,

NOTE Confidence: 0.84505767

00:00:48.565 --> 00:00:49.465 AI and engineering.

NOTE Confidence: 0.9923274

00:00:50.165 --> 00:00:51.364 So I am going to,

NOTE Confidence: 0.968425

00:00:52.485 --> 00:00:53.205 hit on a lot of

NOTE Confidence: 0.968425

00:00:53.205 --> 00:00:54.165 the themes that so a

NOTE Confidence: 0.968425

00:00:54.165 --> 00:00:55.045 a bunch of the previous

NOTE Confidence: 0.968425

00:00:55.045 --> 00:00:57.270 speakers already, already touched upon.

NOTE Confidence: 0.968425

00:00:57.570 --> 00:00:59.170 And broadly speaking, we are,

NOTE Confidence: 0.968425

00:00:59.410 --> 00:01:00.690 we are interested in how

NOTE Confidence: 0.968425

00:01:00.690 --> 00:01:02.470 to read an individual's immunological

NOTE Confidence: 0.968425

00:01:02.770 --> 00:01:04.369 state. So there's lots of

NOTE Confidence: 0.968425

00:01:04.369 --> 00:01:06.130 new and emerging experimental methods

NOTE Confidence: 0.968425

00:01:06.130 --> 00:01:07.409 that allow one to profile

NOTE Confidence: 0.968425

00:01:07.409 --> 00:01:08.565 somebody's immune state,

NOTE Confidence: 0.96503955

00:01:09.125 --> 00:01:10.245 at at very high throughput

NOTE Confidence: 0.96503955

00:01:10.245 --> 00:01:12.265 ranging from things like transcriptomics,

NOTE Confidence: 0.99121386

00:01:13.045 --> 00:01:14.905 single cell transcriptomics, metabolomics,

NOTE Confidence: 0.81689066

00:01:15.925 --> 00:01:16.425 proteomics,

NOTE Confidence: 0.904302

00:01:17.045 --> 00:01:18.245 and also profiling of the

NOTE Confidence: 0.904302

00:01:18.245 --> 00:01:20.405 adaptive immune receptor repertoire, b

NOTE Confidence: 0.904302

00:01:20.405 --> 00:01:22.040 and t cell receptor repertoires.

NOTE Confidence: 0.93759376

00:01:22.899 --> 00:01:24.899 My lab both, develops novel

NOTE Confidence: 0.93759376

00:01:24.899 --> 00:01:27.079 computational methods to, analyze,

NOTE Confidence: 0.98214275

00:01:27.540 --> 00:01:28.899 and, deal with a lot

NOTE Confidence: 0.98214275

00:01:28.899 --> 00:01:30.180 of these new, and emerging

NOTE Confidence: 0.98214275

00:01:30.180 --> 00:01:30.920 data types,

NOTE Confidence: 0.98993033

00:01:31.220 --> 00:01:32.180 as well as working with

NOTE Confidence: 0.98993033

00:01:32.180 --> 00:01:33.780 clinical and experimental groups to

NOTE Confidence: 0.98993033

00:01:33.780 --> 00:01:34.680 apply those,

NOTE Confidence: 0.9143382

00:01:35.115 --> 00:01:36.495 those techno those techniques,

NOTE Confidence: 0.9790639

00:01:37.115 --> 00:01:38.235 to real to real data

NOTE Confidence: 0.9790639

00:01:38.235 --> 00:01:39.295 to understand immunological

NOTE Confidence: 0.97597575

00:01:39.595 --> 00:01:40.955 state. And the kinds of

NOTE Confidence: 0.97597575

00:01:40.955 --> 00:01:42.395 questions we're broadly interested in

NOTE Confidence: 0.97597575

00:01:42.395 --> 00:01:43.035 are some of the kind

NOTE Confidence: 0.97597575

00:01:43.115 --> 00:01:43.995 some of the questions that

NOTE Confidence: 0.97597575

00:01:43.995 --> 00:01:45.675 John already already touched on.

NOTE Confidence: 0.97831887

00:01:45.995 --> 00:01:46.795 So how do we you

NOTE Confidence: 0.97831887

00:01:46.795 --> 00:01:47.675 know, can we take these

NOTE Confidence: 0.97831887

00:01:47.675 --> 00:01:48.895 immunological measurements,

NOTE Confidence: 0.99295104

00:01:49.350 --> 00:01:50.790 and say something about the

NOTE Confidence: 0.99295104

00:01:50.790 --> 00:01:51.690 exposure history,

NOTE Confidence: 0.96699923

00:01:52.070 --> 00:01:53.030 of the individual? Right? The

NOTE Confidence: 0.96699923

00:01:53.030 --> 00:01:54.550 immune system encodes to some

NOTE Confidence: 0.96699923

00:01:54.550 --> 00:01:55.990 degree our history of prior

NOTE Confidence: 0.96699923

00:01:55.990 --> 00:01:57.030 exposure. So can we say

NOTE Confidence: 0.96699923

00:01:57.030 --> 00:01:58.310 something about whether an individual

NOTE Confidence: 0.96699923

00:01:58.310 --> 00:01:59.270 has been exposed to, say,

NOTE Confidence: 0.96699923

00:01:59.270 --> 00:02:00.710 SARS COV two? Does the

NOTE Confidence: 0.96699923

00:02:00.710 --> 00:02:02.470 individual carry protective memory from

NOTE Confidence: 0.96699923

00:02:02.470 --> 00:02:03.770 this, from this infection?

NOTE Confidence: 0.9857473

00:02:04.505 --> 00:02:06.265 Talking about current immunological state,

NOTE Confidence: 0.9857473

00:02:06.265 --> 00:02:07.945 can we profile somebody's immune

NOTE Confidence: 0.9857473

00:02:07.945 --> 00:02:09.625 system, and make an inference

NOTE Confidence: 0.9857473

00:02:09.625 --> 00:02:11.065 about whether they have are

NOTE Confidence: 0.9857473

00:02:11.065 --> 00:02:12.125 are currently undergoing

NOTE Confidence: 0.9796247

00:02:12.505 --> 00:02:13.785 an acute infection? With what

NOTE Confidence: 0.9796247

00:02:13.785 --> 00:02:15.225 virus are they currently infected

NOTE Confidence: 0.9796247

00:02:15.225 --> 00:02:16.505 with? Can we say something

NOTE Confidence: 0.9796247

00:02:16.505 --> 00:02:17.544 about the future? Will the

NOTE Confidence: 0.9796247

00:02:17.544 --> 00:02:19.330 outcome of that, that infection

NOTE Confidence: 0.9796247

00:02:19.330 --> 00:02:20.129 be sort of a mild

NOTE Confidence: 0.9796247

00:02:20.129 --> 00:02:21.889 infection that resolves quickly, or

NOTE Confidence: 0.9796247

00:02:21.889 --> 00:02:22.849 will it be more more

NOTE Confidence: 0.9796247

00:02:22.849 --> 00:02:23.349 severe?

NOTE Confidence: 0.9814855

00:02:23.889 --> 00:02:24.849 And we can we also

NOTE Confidence: 0.9814855

00:02:24.849 --> 00:02:25.889 wanna be able to ask

NOTE Confidence: 0.9814855

00:02:25.889 --> 00:02:27.730 questions about, the the the

NOTE Confidence: 0.9814855

00:02:27.730 --> 00:02:28.610 outcome of different,

NOTE Confidence: 0.9510668

00:02:29.169 --> 00:02:30.950 interventions or things like vaccinations.

NOTE Confidence: 0.9510668

00:02:31.125 --> 00:02:32.345 We give someone a vaccine,

NOTE Confidence: 0.99558276

00:02:32.885 --> 00:02:34.285 how does their immunological state

NOTE Confidence: 0.99558276

00:02:34.405 --> 00:02:35.445 can we predict what the

NOTE Confidence: 0.99558276

00:02:35.445 --> 00:02:36.645 outcome of that vaccine will

NOTE Confidence: 0.99558276

00:02:36.645 --> 00:02:37.685 be? Will they generate good

NOTE Confidence: 0.99558276

00:02:37.685 --> 00:02:38.905 protective, immunological

NOTE Confidence: 0.9621765

00:02:39.205 --> 00:02:40.725 memory? So I'm gonna talk

NOTE Confidence: 0.9621765

00:02:40.725 --> 00:02:42.725 at, somewhat high level about

NOTE Confidence: 0.9621765

00:02:42.725 --> 00:02:43.685 a few of the different

NOTE Confidence: 0.9621765

00:02:43.685 --> 00:02:44.805 projects going on in my

NOTE Confidence: 0.9621765

00:02:44.805 --> 00:02:45.845 lab to touch on on

NOTE Confidence: 0.9621765

00:02:45.845 --> 00:02:46.825 these different aspects.

NOTE Confidence: 0.98816824

00:02:47.220 --> 00:02:48.419 So first, let's talk about

NOTE Confidence: 0.98816824

00:02:48.419 --> 00:02:50.980 identifying immunological exposures from somebody's

NOTE Confidence: 0.98816824

00:02:50.980 --> 00:02:52.840 host, host response profile.

NOTE Confidence: 0.97894764

00:02:53.299 --> 00:02:54.500 So the idea here is

NOTE Confidence: 0.97894764

00:02:54.500 --> 00:02:55.780 that we're going from a,

NOTE Confidence: 0.9664602

00:02:56.180 --> 00:02:57.379 a population of people. We

NOTE Confidence: 0.9664602

00:02:57.379 --> 00:02:58.340 take some kind of blood

NOTE Confidence: 0.9664602

00:02:58.340 --> 00:02:59.894 or tissue sample, and we

NOTE Confidence: 0.9664602

00:02:59.894 --> 00:03:01.334 profile that sample. So here,

NOTE Confidence: 0.9664602

00:03:01.334 --> 00:03:02.694 for example, we're looking at

NOTE Confidence: 0.9664602

00:03:02.694 --> 00:03:04.635 transcriptional profiles that we take,

NOTE Confidence: 0.97539276

00:03:05.334 --> 00:03:06.534 so we measure different gene

NOTE Confidence: 0.97539276

00:03:06.534 --> 00:03:07.814 expression levels, genes on the

NOTE Confidence: 0.97539276

00:03:07.814 --> 00:03:09.415 x axis, samples from those

NOTE Confidence: 0.97539276

00:03:09.415 --> 00:03:10.534 individuals on the y axis.

NOTE Confidence: 0.97539276

00:03:10.534 --> 00:03:11.415 So we get these different

NOTE Confidence: 0.97539276

00:03:11.415 --> 00:03:13.014 gene expression profiles, and we

NOTE Confidence: 0.97539276

00:03:13.014 --> 00:03:14.375 wanna make some inferences. So,

NOTE Confidence: 0.97539276

00:03:14.375 --> 00:03:15.389 for example, can we look

NOTE Confidence: 0.97539276

00:03:15.389 --> 00:03:17.090 at those gene expression profiles

NOTE Confidence: 0.97539276

00:03:17.310 --> 00:03:18.430 and discern a pattern that

NOTE Confidence: 0.97539276

00:03:18.430 --> 00:03:19.310 might tell us, hey. This

NOTE Confidence: 0.97539276

00:03:19.310 --> 00:03:20.210 group of individuals

NOTE Confidence: 0.9805037

00:03:20.590 --> 00:03:22.110 is currently undergoing an acute

NOTE Confidence: 0.9805037

00:03:22.110 --> 00:03:23.470 response to West Nile virus

NOTE Confidence: 0.9805037

00:03:23.470 --> 00:03:23.970 infection.

NOTE Confidence: 0.9520247

00:03:24.270 --> 00:03:25.150 So there are a lot

NOTE Confidence: 0.9520247

00:03:25.150 --> 00:03:26.350 of publications, a lot of

NOTE Confidence: 0.9520247

00:03:26.350 --> 00:03:27.630 studies that try to develop

NOTE Confidence: 0.9520247

00:03:27.630 --> 00:03:29.004 these types of signatures. Right?

NOTE Confidence: 0.9520247

00:03:29.004 --> 00:03:30.444 You recruiting a cohort of

NOTE Confidence: 0.9520247

00:03:30.444 --> 00:03:31.504 people with an infection,

NOTE Confidence: 0.9887006

00:03:32.044 --> 00:03:33.424 some kind of control populations,

NOTE Confidence: 0.9887006

00:03:33.565 --> 00:03:35.165 profile them, do some machine

NOTE Confidence: 0.9887006

00:03:35.165 --> 00:03:37.025 learning, some differential expression analysis,

NOTE Confidence: 0.9887006

00:03:37.084 --> 00:03:37.965 come up with some set

NOTE Confidence: 0.9887006

00:03:37.965 --> 00:03:39.245 of genes or metabolites or

NOTE Confidence: 0.9887006

00:03:39.245 --> 00:03:41.084 proteins that are characteristic of

NOTE Confidence: 0.9887006

00:03:41.084 --> 00:03:42.625 that, of that infection.

NOTE Confidence: 0.9928611

00:03:43.370 --> 00:03:44.010 So we set out a

NOTE Confidence: 0.9928611

00:03:44.010 --> 00:03:45.370 few years ago to evaluate

NOTE Confidence: 0.9928611

00:03:45.370 --> 00:03:46.489 some of these signatures that

NOTE Confidence: 0.9928611

00:03:46.489 --> 00:03:47.790 have been proposed in literature.

NOTE Confidence: 0.8452795

00:03:48.250 --> 00:03:50.110 CBB graduate student, Jan Chawla,

NOTE Confidence: 0.95317876

00:03:50.730 --> 00:03:51.770 wanted to ask a couple

NOTE Confidence: 0.95317876

00:03:51.770 --> 00:03:52.430 of questions.

NOTE Confidence: 0.97486967

00:03:52.890 --> 00:03:54.170 Particularly, he wanted to look

NOTE Confidence: 0.97486967

00:03:54.170 --> 00:03:55.610 at the the signatures that

NOTE Confidence: 0.97486967

00:03:55.610 --> 00:03:56.915 were in the literature and

NOTE Confidence: 0.97486967

00:03:56.915 --> 00:03:58.595 assessed how, robust they were.

NOTE Confidence: 0.97486967

00:03:58.595 --> 00:03:59.635 So to what extent you

NOTE Confidence: 0.97486967

00:03:59.635 --> 00:04:00.755 could take a signature from

NOTE Confidence: 0.97486967

00:04:00.755 --> 00:04:02.755 one study and, apply that

NOTE Confidence: 0.97486967

00:04:02.755 --> 00:04:03.975 signature to an independent,

NOTE Confidence: 0.96720856

00:04:04.355 --> 00:04:05.315 cohort and have it be

NOTE Confidence: 0.96720856

00:04:05.315 --> 00:04:07.255 predictive and also cross reactivity.

NOTE Confidence: 0.96720856

00:04:07.395 --> 00:04:08.435 So to what extent could

NOTE Confidence: 0.96720856

00:04:08.435 --> 00:04:09.395 you take a signature of,

NOTE Confidence: 0.96720856

00:04:09.395 --> 00:04:10.835 say, for some particular virus

NOTE Confidence: 0.96720856

00:04:10.835 --> 00:04:11.335 infection,

NOTE Confidence: 0.7701931

00:04:11.909 --> 00:04:12.969 like a like an influenza

NOTE Confidence: 0.7701931

00:04:13.109 --> 00:04:13.609 infection?

NOTE Confidence: 0.9630362

00:04:13.909 --> 00:04:15.030 And to what extent was

NOTE Confidence: 0.9630362

00:04:15.030 --> 00:04:16.789 that signature specific to that

NOTE Confidence: 0.9630362

00:04:16.789 --> 00:04:18.150 infection or would it what

NOTE Confidence: 0.9630362

00:04:18.150 --> 00:04:19.509 we call cross react? Would

NOTE Confidence: 0.9630362

00:04:19.509 --> 00:04:21.029 that signature also come up,

NOTE Confidence: 0.9630362

00:04:21.270 --> 00:04:22.070 in a lot of other

NOTE Confidence: 0.9630362

00:04:22.070 --> 00:04:23.589 viral infections or bacteria or

NOTE Confidence: 0.9630362

00:04:23.589 --> 00:04:24.710 or other types of infections

NOTE Confidence: 0.9630362

00:04:24.710 --> 00:04:25.529 like a bacterial?

NOTE Confidence: 0.89115036

00:04:25.935 --> 00:04:26.895 So we put together a

NOTE Confidence: 0.89115036

00:04:26.895 --> 00:04:28.654 cohort of about, at the

NOTE Confidence: 0.89115036

00:04:28.654 --> 00:04:29.455 time of the publication, it

NOTE Confidence: 0.89115036

00:04:29.455 --> 00:04:30.335 was a hundred and fifty

NOTE Confidence: 0.89115036

00:04:30.335 --> 00:04:31.695 datasets and a a a

NOTE Confidence: 0.89115036

00:04:31.695 --> 00:04:32.995 bit over seventeen thousand,

NOTE Confidence: 0.82882965

00:04:33.775 --> 00:04:34.995 transcriptional profiles

NOTE Confidence: 0.98488075

00:04:35.295 --> 00:04:36.975 encompassing a whole variety of

NOTE Confidence: 0.98488075

00:04:36.975 --> 00:04:39.555 viral, viral infections, bacterial infections,

NOTE Confidence: 0.98488075

00:04:39.695 --> 00:04:40.915 as well as some noninfections,

NOTE Confidence: 0.9699836

00:04:41.680 --> 00:04:42.960 conditions that we thought might,

NOTE Confidence: 0.9699836

00:04:43.360 --> 00:04:44.560 might be similar, might look

NOTE Confidence: 0.9699836

00:04:44.560 --> 00:04:46.160 similar transcriptionally to a,

NOTE Confidence: 0.934742

00:04:46.639 --> 00:04:47.860 to an infection response.

NOTE Confidence: 0.9951723

00:04:48.240 --> 00:04:50.020 And he evaluated those signatures,

NOTE Confidence: 0.9708948

00:04:50.400 --> 00:04:51.839 for their robustness and cross

NOTE Confidence: 0.9708948

00:04:51.839 --> 00:04:52.339 reactivity

NOTE Confidence: 0.9281042

00:04:52.800 --> 00:04:53.760 and brought you know, high

NOTE Confidence: 0.9281042

00:04:53.760 --> 00:04:54.800 level what we found from,

NOTE Confidence: 0.9281042

00:04:55.154 --> 00:04:56.275 from the study is one,

NOTE Confidence: 0.9281042

00:04:56.275 --> 00:04:57.315 a lot of the signatures

NOTE Confidence: 0.9281042

00:04:57.315 --> 00:04:57.975 that were,

NOTE Confidence: 0.96767205

00:04:58.915 --> 00:05:00.435 proposed in literature, in fact,

NOTE Confidence: 0.96767205

00:05:00.435 --> 00:05:02.355 were quite robust. Generally speaking,

NOTE Confidence: 0.96767205

00:05:02.355 --> 00:05:03.555 if you developed a signature

NOTE Confidence: 0.96767205

00:05:03.555 --> 00:05:04.435 that was supposed to be

NOTE Confidence: 0.96767205

00:05:04.435 --> 00:05:06.055 predictive of some virus response,

NOTE Confidence: 0.9867526

00:05:06.595 --> 00:05:08.275 it was reproducible in in,

NOTE Confidence: 0.9867526

00:05:08.595 --> 00:05:09.875 other studies of the of

NOTE Confidence: 0.9867526

00:05:09.875 --> 00:05:11.430 that virus response. But there

NOTE Confidence: 0.9867526

00:05:11.430 --> 00:05:12.390 was also a large amount

NOTE Confidence: 0.9867526

00:05:12.390 --> 00:05:14.070 of cross reactivity, and maybe

NOTE Confidence: 0.9867526

00:05:14.070 --> 00:05:14.890 this is something,

NOTE Confidence: 0.9967971

00:05:15.350 --> 00:05:16.490 that's not too surprising.

NOTE Confidence: 0.9584457

00:05:16.950 --> 00:05:17.990 A lot of these a

NOTE Confidence: 0.9584457

00:05:17.990 --> 00:05:18.950 lot of these studies, you

NOTE Confidence: 0.9584457

00:05:18.950 --> 00:05:20.470 will get, you know, for

NOTE Confidence: 0.9584457

00:05:20.470 --> 00:05:21.990 example, like an interferon signature

NOTE Confidence: 0.9584457

00:05:21.990 --> 00:05:22.790 that will come up in

NOTE Confidence: 0.9584457

00:05:22.790 --> 00:05:23.670 almost every virus,

NOTE Confidence: 0.9673307

00:05:24.154 --> 00:05:25.775 virus response that you study.

NOTE Confidence: 0.9673307

00:05:25.835 --> 00:05:26.795 And you might expect if

NOTE Confidence: 0.9673307

00:05:26.795 --> 00:05:27.995 you don't account for that,

NOTE Confidence: 0.9673307

00:05:27.995 --> 00:05:29.195 that signature is also gonna

NOTE Confidence: 0.9673307

00:05:29.195 --> 00:05:30.395 be predictive of multiple other

NOTE Confidence: 0.9673307

00:05:30.395 --> 00:05:30.895 viruses.

NOTE Confidence: 0.97610205

00:05:31.275 --> 00:05:32.715 We also found those signatures

NOTE Confidence: 0.97610205

00:05:32.715 --> 00:05:33.595 cross react with a lot

NOTE Confidence: 0.97610205

00:05:33.595 --> 00:05:35.115 of noninfectious conditions. So here

NOTE Confidence: 0.97610205

00:05:35.115 --> 00:05:36.089 you see, for example, we

NOTE Confidence: 0.97610205

00:05:36.250 --> 00:05:37.130 we evaluated a bunch of

NOTE Confidence: 0.97610205

00:05:37.130 --> 00:05:39.210 different, signatures for virus infections

NOTE Confidence: 0.97610205

00:05:39.210 --> 00:05:40.730 along the x axis and

NOTE Confidence: 0.97610205

00:05:40.730 --> 00:05:42.330 evaluated their ability to predict,

NOTE Confidence: 0.97610205

00:05:42.570 --> 00:05:44.410 aging. So just comparing young

NOTE Confidence: 0.97610205

00:05:44.410 --> 00:05:46.410 versus older older individuals. And

NOTE Confidence: 0.97610205

00:05:46.410 --> 00:05:47.130 you can see a lot

NOTE Confidence: 0.97610205

00:05:47.130 --> 00:05:47.949 of these signatures,

NOTE Confidence: 0.9924102

00:05:48.490 --> 00:05:49.529 as measured by the area

NOTE Confidence: 0.9924102

00:05:49.529 --> 00:05:50.650 under the curve for predicting

NOTE Confidence: 0.9924102

00:05:50.650 --> 00:05:52.275 old versus young are highly

NOTE Confidence: 0.9924102

00:05:52.275 --> 00:05:54.035 predictive of age, and only

NOTE Confidence: 0.9924102

00:05:54.035 --> 00:05:55.235 a subset of signatures is

NOTE Confidence: 0.9924102

00:05:55.235 --> 00:05:56.195 not. So for so we

NOTE Confidence: 0.9924102

00:05:56.195 --> 00:05:56.995 are getting a lot of

NOTE Confidence: 0.9924102

00:05:56.995 --> 00:05:58.035 cross reactivity, and you have

NOTE Confidence: 0.9924102

00:05:58.035 --> 00:05:58.995 to account for this if

NOTE Confidence: 0.9924102

00:05:58.995 --> 00:06:00.215 you wanna use these signatures,

NOTE Confidence: 0.9265752

00:06:00.915 --> 00:06:02.455 for, predictive responses.

NOTE Confidence: 0.9857472

00:06:02.835 --> 00:06:03.955 And in general, we are

NOTE Confidence: 0.9857472

00:06:03.955 --> 00:06:05.395 interest often interested in what

NOTE Confidence: 0.9857472

00:06:05.395 --> 00:06:06.750 makes a response unique. Right?

NOTE Confidence: 0.9857472

00:06:06.830 --> 00:06:08.029 In general, we don't necessarily

NOTE Confidence: 0.9857472

00:06:08.029 --> 00:06:08.830 wanna pick out, oh, we're

NOTE Confidence: 0.9857472

00:06:08.830 --> 00:06:10.290 getting an interferon response,

NOTE Confidence: 0.95711106

00:06:10.830 --> 00:06:12.029 in in in coming up

NOTE Confidence: 0.95711106

00:06:12.029 --> 00:06:12.990 in response to a viral

NOTE Confidence: 0.95711106

00:06:12.990 --> 00:06:14.029 infection. We wanna know what's

NOTE Confidence: 0.95711106

00:06:14.029 --> 00:06:15.550 specific about a SARS COV

NOTE Confidence: 0.95711106

00:06:15.550 --> 00:06:16.990 two infection that makes it

NOTE Confidence: 0.95711106

00:06:16.990 --> 00:06:18.529 different from a typical antiviral

NOTE Confidence: 0.95711106

00:06:18.589 --> 00:06:19.870 response, or what's different about

NOTE Confidence: 0.95711106

00:06:19.870 --> 00:06:20.370 this,

NOTE Confidence: 0.9604513

00:06:21.035 --> 00:06:23.115 vaccine response, this influenza vaccine

NOTE Confidence: 0.9604513

00:06:23.115 --> 00:06:23.615 response,

NOTE Confidence: 0.9473862

00:06:24.075 --> 00:06:25.435 when it doesn't generate protective

NOTE Confidence: 0.9473862

00:06:25.435 --> 00:06:26.555 memory that makes it different

NOTE Confidence: 0.9473862

00:06:26.555 --> 00:06:28.095 from other types of, responses?

NOTE Confidence: 0.9473862

00:06:28.315 --> 00:06:29.355 So we've also worked on

NOTE Confidence: 0.9473862

00:06:29.355 --> 00:06:31.035 methods in collaboration with, Elena

NOTE Confidence: 0.9473862

00:06:31.035 --> 00:06:33.135 Daslavsky's group at Mount Sinai

NOTE Confidence: 0.9473862

00:06:33.435 --> 00:06:34.875 to as methods to generate

NOTE Confidence: 0.9473862

00:06:34.875 --> 00:06:36.235 robust signatures that are not

NOTE Confidence: 0.9473862

00:06:36.235 --> 00:06:37.890 cross reactive. And this takes

NOTE Confidence: 0.9473862

00:06:37.890 --> 00:06:39.730 advantage of the massive public

NOTE Confidence: 0.9473862

00:06:39.730 --> 00:06:40.790 data that's available,

NOTE Confidence: 0.9582438

00:06:41.490 --> 00:06:43.190 profiling different types of responses.

NOTE Confidence: 0.9582438

00:06:43.330 --> 00:06:44.210 So if we have our

NOTE Confidence: 0.9582438

00:06:44.210 --> 00:06:46.050 response, our our our dataset

NOTE Confidence: 0.9582438

00:06:46.050 --> 00:06:47.250 of interest, so for example,

NOTE Confidence: 0.9582438

00:06:47.250 --> 00:06:49.074 disease versus a control, we

NOTE Confidence: 0.9582438

00:06:49.074 --> 00:06:50.754 can also integrate all sorts

NOTE Confidence: 0.9582438

00:06:50.754 --> 00:06:52.194 of control samples from other

NOTE Confidence: 0.9582438

00:06:52.194 --> 00:06:53.315 diseases that are in the

NOTE Confidence: 0.9582438

00:06:53.315 --> 00:06:54.514 public domain to come up

NOTE Confidence: 0.9582438

00:06:54.514 --> 00:06:55.875 with our signature that's specific.

NOTE Confidence: 0.9582438

00:06:55.875 --> 00:06:57.154 So for example, if we're

NOTE Confidence: 0.9582438

00:06:57.154 --> 00:06:58.294 profiling the influenza,

NOTE Confidence: 0.9574334

00:06:58.675 --> 00:07:00.435 an influenza infection response, we

NOTE Confidence: 0.9574334

00:07:00.435 --> 00:07:01.555 might pull from the literature

NOTE Confidence: 0.9574334

00:07:01.555 --> 00:07:02.455 lots of other

NOTE Confidence: 0.8406037

00:07:11.900 --> 00:07:13.520 specificities, so gene expression,

NOTE Confidence: 0.9589427

00:07:13.900 --> 00:07:15.580 protein expression signatures are are

NOTE Confidence: 0.9589427

00:07:15.580 --> 00:07:16.960 nice, but the immune system,

NOTE Confidence: 0.9709168

00:07:17.264 --> 00:07:18.705 we can take advantage already

NOTE Confidence: 0.9709168

00:07:18.705 --> 00:07:19.905 has a a sort of

NOTE Confidence: 0.9709168

00:07:19.905 --> 00:07:21.505 component built in that's highly

NOTE Confidence: 0.9709168

00:07:21.505 --> 00:07:22.005 specific,

NOTE Confidence: 0.96746033

00:07:22.465 --> 00:07:23.745 for the for the response

NOTE Confidence: 0.96746033

00:07:23.745 --> 00:07:24.785 being generated, and that is

NOTE Confidence: 0.96746033

00:07:24.785 --> 00:07:26.384 the the the adaptive immune

NOTE Confidence: 0.96746033

00:07:26.384 --> 00:07:27.505 response, the b cells and

NOTE Confidence: 0.96746033

00:07:27.505 --> 00:07:29.104 the t cells, that compose

NOTE Confidence: 0.96746033

00:07:29.104 --> 00:07:30.065 the adaptive arms of the

NOTE Confidence: 0.96746033

00:07:30.065 --> 00:07:31.770 immune response. I'm gonna focus

NOTE Confidence: 0.96746033

00:07:31.770 --> 00:07:32.810 on b cells. My lab

NOTE Confidence: 0.96746033

00:07:32.810 --> 00:07:34.169 focuses works a lot on

NOTE Confidence: 0.96746033

00:07:34.169 --> 00:07:35.790 b cell receptor, responses.

NOTE Confidence: 0.98876226

00:07:36.169 --> 00:07:37.690 So b cells have antibody

NOTE Confidence: 0.98876226

00:07:37.690 --> 00:07:39.050 receptors on their surface that

NOTE Confidence: 0.98876226

00:07:39.050 --> 00:07:40.030 give them specificity,

NOTE Confidence: 0.98499656

00:07:40.730 --> 00:07:42.270 to recognize different pathogens.

NOTE Confidence: 0.9700573

00:07:42.905 --> 00:07:44.345 The naive repertoire coming out

NOTE Confidence: 0.9700573

00:07:44.345 --> 00:07:45.225 of the bone marrow, so

NOTE Confidence: 0.9700573

00:07:45.225 --> 00:07:46.825 our our immune system constantly

NOTE Confidence: 0.9700573

00:07:46.825 --> 00:07:48.425 produces naive b cells with,

NOTE Confidence: 0.9700573

00:07:48.745 --> 00:07:50.185 pretty much a unique receptor

NOTE Confidence: 0.9700573

00:07:50.185 --> 00:07:51.545 on every cell that's generated

NOTE Confidence: 0.9700573

00:07:51.545 --> 00:07:52.905 from the bone marrow, and

NOTE Confidence: 0.9700573

00:07:52.905 --> 00:07:54.105 that gives those cells their,

NOTE Confidence: 0.9700573

00:07:54.345 --> 00:07:55.785 a unique ability to recognize

NOTE Confidence: 0.9700573

00:07:55.785 --> 00:07:57.740 different pathogens. So some cells

NOTE Confidence: 0.9700573

00:07:57.740 --> 00:07:58.620 coming out of the bone

NOTE Confidence: 0.9700573

00:07:58.620 --> 00:07:59.900 marrow might, have a have

NOTE Confidence: 0.9700573

00:07:59.900 --> 00:07:59.980 a,

NOTE Confidence: 0.9522133

00:08:00.940 --> 00:08:03.100 innate specificity for the influenza

NOTE Confidence: 0.9522133

00:08:03.100 --> 00:08:04.460 virus. Others might have an

NOTE Confidence: 0.9522133

00:08:04.460 --> 00:08:05.980 innate specificity for,

NOTE Confidence: 0.94238955

00:08:06.460 --> 00:08:08.300 for SARS CoV two. Once

NOTE Confidence: 0.94238955

00:08:08.300 --> 00:08:09.660 you get once you encounter

NOTE Confidence: 0.94238955

00:08:09.660 --> 00:08:11.100 a a pathogen, you're confronted

NOTE Confidence: 0.94238955

00:08:11.100 --> 00:08:12.535 with pathogenic challenge, whether it

NOTE Confidence: 0.94238955

00:08:12.535 --> 00:08:14.055 be a natural infection, or

NOTE Confidence: 0.94238955

00:08:14.055 --> 00:08:14.715 a vaccine.

NOTE Confidence: 0.9684023

00:08:15.095 --> 00:08:16.215 Some of those naive b

NOTE Confidence: 0.9684023

00:08:16.215 --> 00:08:18.215 cells are stimulated, activated into

NOTE Confidence: 0.9684023

00:08:18.215 --> 00:08:19.815 the response, and they undergo

NOTE Confidence: 0.9684023

00:08:19.815 --> 00:08:22.135 a process of, rapid tonal

NOTE Confidence: 0.9684023

00:08:22.135 --> 00:08:23.915 expansion and somatic hypermutation.

NOTE Confidence: 0.9954184

00:08:24.599 --> 00:08:26.120 So these cells introduce point

NOTE Confidence: 0.9954184

00:08:26.120 --> 00:08:27.639 mutations into the DNA that

NOTE Confidence: 0.9954184

00:08:27.639 --> 00:08:29.000 codes for their receptor. This

NOTE Confidence: 0.9954184

00:08:29.000 --> 00:08:30.199 is a really scary process

NOTE Confidence: 0.9954184

00:08:30.199 --> 00:08:31.159 when I first learned about

NOTE Confidence: 0.9954184

00:08:31.159 --> 00:08:31.659 it,

NOTE Confidence: 0.9927306

00:08:31.960 --> 00:08:33.079 but it's actually quite,

NOTE Confidence: 0.99185956

00:08:33.800 --> 00:08:35.000 quite good because it allows

NOTE Confidence: 0.99185956

00:08:35.000 --> 00:08:36.440 our bodies to learn about

NOTE Confidence: 0.99185956

00:08:36.440 --> 00:08:37.740 the pathogenic environment.

NOTE Confidence: 0.99260944

00:08:38.135 --> 00:08:39.255 And through a process of

NOTE Confidence: 0.99260944

00:08:39.255 --> 00:08:40.774 mutation and selection, we can

NOTE Confidence: 0.99260944

00:08:40.774 --> 00:08:42.295 generate higher and higher affinity

NOTE Confidence: 0.99260944

00:08:42.295 --> 00:08:43.975 receptors for the pathogen that

NOTE Confidence: 0.99260944

00:08:43.975 --> 00:08:45.015 we're confronted with. So we

NOTE Confidence: 0.99260944

00:08:45.015 --> 00:08:46.315 can learn about the pathogenic

NOTE Confidence: 0.99260944

00:08:46.375 --> 00:08:47.975 environment through our, throughout our

NOTE Confidence: 0.99260944

00:08:47.975 --> 00:08:48.475 lifetime.

NOTE Confidence: 0.94354874

00:08:49.495 --> 00:08:50.934 And this occurs in specialized

NOTE Confidence: 0.94354874

00:08:50.934 --> 00:08:53.050 structures called, germinal centers in

NOTE Confidence: 0.94354874

00:08:53.050 --> 00:08:54.589 our secondary lymphoid organs.

NOTE Confidence: 0.94930756

00:08:54.970 --> 00:08:56.269 And here you see actually

NOTE Confidence: 0.94930756

00:08:56.490 --> 00:08:57.690 a a germinal center. The

NOTE Confidence: 0.94930756

00:08:57.690 --> 00:08:58.889 b cells are ingrained from

NOTE Confidence: 0.94930756

00:08:58.889 --> 00:09:01.050 a live anesthetized mouse, undergoing

NOTE Confidence: 0.94930756

00:09:01.050 --> 00:09:02.010 an immune response. This is

NOTE Confidence: 0.94930756

00:09:02.010 --> 00:09:02.809 work we did with Anne

NOTE Confidence: 0.94930756

00:09:02.809 --> 00:09:03.309 Haberman,

NOTE Confidence: 0.9812935

00:09:03.690 --> 00:09:05.290 with two photon microscopy over,

NOTE Confidence: 0.9812935

00:09:05.404 --> 00:09:07.165 over a decade ago. So

NOTE Confidence: 0.9812935

00:09:07.165 --> 00:09:08.845 this process results in affinity

NOTE Confidence: 0.9812935

00:09:08.845 --> 00:09:10.385 maturation of the b cell

NOTE Confidence: 0.9842298

00:09:10.845 --> 00:09:11.965 repertoire, and you can imagine

NOTE Confidence: 0.9842298

00:09:11.965 --> 00:09:12.845 that we can learn a

NOTE Confidence: 0.9842298

00:09:12.845 --> 00:09:13.965 lot about the history of

NOTE Confidence: 0.9842298

00:09:13.965 --> 00:09:14.465 immunological

NOTE Confidence: 0.99460036

00:09:14.845 --> 00:09:16.925 exposures by studying these, the,

NOTE Confidence: 0.99460036

00:09:17.245 --> 00:09:18.125 the set of b cell

NOTE Confidence: 0.99460036

00:09:18.125 --> 00:09:19.665 receptors carried by an individual.

NOTE Confidence: 0.9663443

00:09:20.230 --> 00:09:21.429 Since two thousand nine, we've

NOTE Confidence: 0.9663443

00:09:21.429 --> 00:09:22.790 had the ability to sequence

NOTE Confidence: 0.9663443

00:09:22.790 --> 00:09:24.230 the b cell receptors at

NOTE Confidence: 0.9663443

00:09:24.230 --> 00:09:24.970 a high throughput,

NOTE Confidence: 0.9339235

00:09:25.750 --> 00:09:26.490 both with,

NOTE Confidence: 0.97805756

00:09:27.270 --> 00:09:29.050 both with bulk sequencing technologies

NOTE Confidence: 0.97805756

00:09:29.110 --> 00:09:29.910 where we can take a

NOTE Confidence: 0.97805756

00:09:29.910 --> 00:09:30.809 tissue sample,

NOTE Confidence: 0.9524348

00:09:31.110 --> 00:09:32.309 sequence the b cell receptor

NOTE Confidence: 0.9524348

00:09:32.309 --> 00:09:33.830 using PCR amplification and high

NOTE Confidence: 0.9524348

00:09:33.830 --> 00:09:35.345 throughput sequencing. That gives us

NOTE Confidence: 0.9524348

00:09:35.345 --> 00:09:37.425 anywhere from hundreds of thousands

NOTE Confidence: 0.9524348

00:09:37.425 --> 00:09:38.785 to millions of b cell

NOTE Confidence: 0.9524348

00:09:38.785 --> 00:09:40.004 receptors in a sample,

NOTE Confidence: 0.9318578

00:09:40.384 --> 00:09:41.824 and more recently through single

NOTE Confidence: 0.9318578

00:09:41.824 --> 00:09:43.345 cell technologies where we can

NOTE Confidence: 0.9318578

00:09:43.345 --> 00:09:44.865 get individual from a single

NOTE Confidence: 0.9318578

00:09:44.865 --> 00:09:46.165 cell, the b cell receptor

NOTE Confidence: 0.9318578

00:09:46.384 --> 00:09:47.764 along with the pair transcriptome

NOTE Confidence: 0.9318578

00:09:47.985 --> 00:09:49.105 for tens of thousands of

NOTE Confidence: 0.9318578

00:09:49.105 --> 00:09:50.490 cells, at a time.

NOTE Confidence: 0.9713913

00:09:50.970 --> 00:09:52.010 And, of course, the challenge

NOTE Confidence: 0.9713913

00:09:52.010 --> 00:09:53.370 is now once we're once

NOTE Confidence: 0.9713913

00:09:53.370 --> 00:09:54.730 we have these receptors, how

NOTE Confidence: 0.9713913

00:09:54.730 --> 00:09:55.309 do we

NOTE Confidence: 0.97745174

00:09:55.929 --> 00:09:57.130 how do we interpret them?

NOTE Confidence: 0.97745174

00:09:57.130 --> 00:09:58.250 So the typical data we

NOTE Confidence: 0.97745174

00:09:58.250 --> 00:09:59.610 get kinda looks like this.

NOTE Confidence: 0.97745174

00:09:59.610 --> 00:10:00.570 Right? We get the b

NOTE Confidence: 0.97745174

00:10:00.570 --> 00:10:02.089 cell receptor sequence. Each row

NOTE Confidence: 0.97745174

00:10:02.089 --> 00:10:03.050 is a b cell receptor

NOTE Confidence: 0.97745174

00:10:03.050 --> 00:10:03.550 sequence,

NOTE Confidence: 0.98399884

00:10:04.694 --> 00:10:05.735 associated with the cell. And

NOTE Confidence: 0.98399884

00:10:05.735 --> 00:10:06.934 now we wanna we wanna

NOTE Confidence: 0.98399884

00:10:06.934 --> 00:10:07.815 know things like, well, which

NOTE Confidence: 0.98399884

00:10:07.815 --> 00:10:08.615 one of these b cells

NOTE Confidence: 0.98399884

00:10:08.774 --> 00:10:09.495 which one of these b

NOTE Confidence: 0.98399884

00:10:09.495 --> 00:10:10.235 cell receptors,

NOTE Confidence: 0.97200173

00:10:10.934 --> 00:10:12.535 is is specific or binds

NOTE Confidence: 0.97200173

00:10:12.535 --> 00:10:13.834 to the influenza hemagglutinin,

NOTE Confidence: 0.91776127

00:10:14.295 --> 00:10:15.334 molecule, or which one of

NOTE Confidence: 0.91776127

00:10:15.334 --> 00:10:16.375 these are specific for the

NOTE Confidence: 0.91776127

00:10:16.375 --> 00:10:17.880 SARS CoV two spike protein.

NOTE Confidence: 0.89538056

00:10:18.440 --> 00:10:19.559 And I wanna thank Deepa

NOTE Confidence: 0.89538056

00:10:19.559 --> 00:10:20.760 for for introducing these,

NOTE Confidence: 0.9637826

00:10:21.960 --> 00:10:23.880 representation learning approaches because that's

NOTE Confidence: 0.9637826

00:10:23.880 --> 00:10:24.600 one of the things we

NOTE Confidence: 0.9637826

00:10:24.600 --> 00:10:25.900 do with b cell receptors

NOTE Confidence: 0.9637826

00:10:26.200 --> 00:10:27.559 is we take advantage of

NOTE Confidence: 0.9637826

00:10:27.559 --> 00:10:29.640 these, language based language based

NOTE Confidence: 0.9637826

00:10:29.640 --> 00:10:30.140 models

NOTE Confidence: 0.870731

00:10:30.464 --> 00:10:31.425 to, develop,

NOTE Confidence: 0.9789047

00:10:32.144 --> 00:10:33.505 embedding approaches where we can

NOTE Confidence: 0.9789047

00:10:33.505 --> 00:10:34.625 learn we can take those

NOTE Confidence: 0.9789047

00:10:34.625 --> 00:10:35.605 b cell receptors,

NOTE Confidence: 0.9813576

00:10:35.985 --> 00:10:36.944 map them into a lower

NOTE Confidence: 0.9813576

00:10:36.944 --> 00:10:38.625 dimensional space where we can

NOTE Confidence: 0.9813576

00:10:38.625 --> 00:10:38.944 then,

NOTE Confidence: 0.9725971

00:10:39.505 --> 00:10:41.425 develop classification models and do

NOTE Confidence: 0.9725971

00:10:41.425 --> 00:10:43.184 analysis and learn, learn all

NOTE Confidence: 0.9725971

00:10:43.184 --> 00:10:44.464 sorts of interesting things about

NOTE Confidence: 0.9725971

00:10:44.464 --> 00:10:45.444 the b cell receptor.

NOTE Confidence: 0.9613555

00:10:46.070 --> 00:10:46.790 So one of the things

NOTE Confidence: 0.9613555

00:10:46.790 --> 00:10:47.830 we wanted to learn about

NOTE Confidence: 0.9613555

00:10:47.830 --> 00:10:48.710 and one of the, sort

NOTE Confidence: 0.9613555

00:10:48.710 --> 00:10:50.070 of important key challenges for

NOTE Confidence: 0.9613555

00:10:50.070 --> 00:10:51.929 the community is learning specificity.

NOTE Confidence: 0.9613555

00:10:51.990 --> 00:10:52.710 So we would like to

NOTE Confidence: 0.9613555

00:10:52.710 --> 00:10:53.510 be able to take a

NOTE Confidence: 0.9613555

00:10:53.510 --> 00:10:55.429 b cell receptor sequence and

NOTE Confidence: 0.9613555

00:10:55.429 --> 00:10:56.710 predict that this b cell

NOTE Confidence: 0.9613555

00:10:56.710 --> 00:10:57.830 receptor is going to bind,

NOTE Confidence: 0.9613555

00:10:57.830 --> 00:10:59.030 for example, to SARS CoV

NOTE Confidence: 0.9613555

00:10:59.030 --> 00:11:00.945 two spike protein. A graduate

NOTE Confidence: 0.9613555

00:11:00.945 --> 00:11:02.704 student, Mimi Wang, from the

NOTE Confidence: 0.9613555

00:11:02.704 --> 00:11:03.684 CBB program,

NOTE Confidence: 0.90137386

00:11:04.304 --> 00:11:05.345 did a did a study

NOTE Confidence: 0.90137386

00:11:05.345 --> 00:11:06.565 a couple of years ago,

NOTE Confidence: 0.9290298

00:11:07.024 --> 00:11:08.545 looking actually, just just was

NOTE Confidence: 0.9290298

00:11:08.545 --> 00:11:10.065 published this, this past year

NOTE Confidence: 0.9290298

00:11:10.225 --> 00:11:11.684 early early this year, actually.

NOTE Confidence: 0.9791625

00:11:12.065 --> 00:11:14.020 Looking at multiple embedding methods.

NOTE Confidence: 0.9791625

00:11:14.100 --> 00:11:15.220 Some of these are general

NOTE Confidence: 0.9791625

00:11:15.220 --> 00:11:16.500 protein embedding methods that were

NOTE Confidence: 0.9791625

00:11:16.500 --> 00:11:18.100 generated not for antibody receptors,

NOTE Confidence: 0.9791625

00:11:18.100 --> 00:11:19.460 but to embed general protein

NOTE Confidence: 0.9791625

00:11:19.460 --> 00:11:19.960 sequences,

NOTE Confidence: 0.88795334

00:11:20.580 --> 00:11:21.779 and others, such as this

NOTE Confidence: 0.88795334

00:11:21.779 --> 00:11:23.700 AnteBERTy were developed specifically to

NOTE Confidence: 0.88795334

00:11:23.700 --> 00:11:24.600 embed antibody

NOTE Confidence: 0.97803724

00:11:24.900 --> 00:11:25.400 receptors.

NOTE Confidence: 0.96134526

00:11:25.755 --> 00:11:27.455 And she evaluated the ability

NOTE Confidence: 0.96134526

00:11:27.595 --> 00:11:28.955 of these, of these different

NOTE Confidence: 0.96134526

00:11:28.955 --> 00:11:30.554 embedding methods to predict SARS

NOTE Confidence: 0.96134526

00:11:30.554 --> 00:11:32.095 CoV two spike binding.

NOTE Confidence: 0.95464355

00:11:32.635 --> 00:11:33.995 There's a background control where

NOTE Confidence: 0.95464355

00:11:33.995 --> 00:11:35.295 we scrambled up the sequences

NOTE Confidence: 0.95464355

00:11:35.355 --> 00:11:36.795 shown in gray here, that

NOTE Confidence: 0.95464355

00:11:36.795 --> 00:11:37.770 has the expected

NOTE Confidence: 0.93207496

00:11:39.050 --> 00:11:40.010 f ones. And you can

NOTE Confidence: 0.93207496

00:11:40.010 --> 00:11:41.610 see on the real data

NOTE Confidence: 0.93207496

00:11:41.610 --> 00:11:42.809 shown in the colored, in

NOTE Confidence: 0.93207496

00:11:42.809 --> 00:11:43.770 the colored bar too, we

NOTE Confidence: 0.93207496

00:11:43.770 --> 00:11:44.809 actually get a pretty good

NOTE Confidence: 0.93207496

00:11:44.809 --> 00:11:45.309 ability,

NOTE Confidence: 0.95437914

00:11:45.770 --> 00:11:46.730 a very good ability to

NOTE Confidence: 0.95437914

00:11:46.730 --> 00:11:48.010 predict SARS CoV two spike

NOTE Confidence: 0.95437914

00:11:48.010 --> 00:11:48.510 binding,

NOTE Confidence: 0.9540283

00:11:48.970 --> 00:11:50.410 from these, from the, from

NOTE Confidence: 0.9540283

00:11:50.410 --> 00:11:51.950 these embedded b cell receptors.

NOTE Confidence: 0.9770769

00:11:52.485 --> 00:11:53.285 And in fact, some of

NOTE Confidence: 0.9770769

00:11:53.285 --> 00:11:54.485 the, you know, the the

NOTE Confidence: 0.9770769

00:11:54.485 --> 00:11:55.925 generic method, the general methods

NOTE Confidence: 0.9770769

00:11:55.925 --> 00:11:56.965 actually work pretty well. We

NOTE Confidence: 0.9770769

00:11:56.965 --> 00:11:57.684 do get a little bit

NOTE Confidence: 0.9770769

00:11:57.684 --> 00:11:59.445 of a performance boost, from

NOTE Confidence: 0.9770769

00:11:59.445 --> 00:12:00.645 the models that were developed

NOTE Confidence: 0.9770769

00:12:00.645 --> 00:12:02.345 specifically on antibody receptors.

NOTE Confidence: 0.9850563

00:12:02.804 --> 00:12:03.765 We have a newer study

NOTE Confidence: 0.9850563

00:12:03.765 --> 00:12:05.045 that's on bioRxiv now where

NOTE Confidence: 0.9850563

00:12:05.045 --> 00:12:05.925 we've shown that if you

NOTE Confidence: 0.9850563

00:12:05.925 --> 00:12:07.519 take these, general methods and

NOTE Confidence: 0.9850563

00:12:07.519 --> 00:12:08.399 you actually do a little

NOTE Confidence: 0.9850563

00:12:08.399 --> 00:12:09.440 bit of fine tuning on

NOTE Confidence: 0.9850563

00:12:09.440 --> 00:12:10.899 them specific to the problem,

NOTE Confidence: 0.9850563

00:12:10.959 --> 00:12:12.320 we can actually boost, that

NOTE Confidence: 0.9850563

00:12:12.320 --> 00:12:13.620 power to predict specificity,

NOTE Confidence: 0.9997378

00:12:14.399 --> 00:12:15.139 even further.

NOTE Confidence: 0.99743897

00:12:15.600 --> 00:12:16.559 So that's the power to

NOTE Confidence: 0.99743897

00:12:16.559 --> 00:12:18.160 predict specificity on a single

NOTE Confidence: 0.99743897

00:12:18.160 --> 00:12:20.019 sequence. What about whole repertoires?

NOTE Confidence: 0.99743897

00:12:20.145 --> 00:12:20.945 So when we take a

NOTE Confidence: 0.99743897

00:12:20.945 --> 00:12:22.065 blood sample or a tissue

NOTE Confidence: 0.99743897

00:12:22.065 --> 00:12:23.184 sample from a person, we

NOTE Confidence: 0.99743897

00:12:23.184 --> 00:12:24.405 don't get a single sequence.

NOTE Confidence: 0.99743897

00:12:24.705 --> 00:12:25.825 We actually get tens of

NOTE Confidence: 0.99743897

00:12:25.825 --> 00:12:27.665 thousands to to potentially millions

NOTE Confidence: 0.99743897

00:12:27.665 --> 00:12:28.325 of sequences.

NOTE Confidence: 0.9551669

00:12:28.785 --> 00:12:29.745 It looks something like this.

NOTE Confidence: 0.9551669

00:12:29.745 --> 00:12:30.625 This is actually a blood

NOTE Confidence: 0.9551669

00:12:30.625 --> 00:12:32.465 repertoire from somebody undergoing, an

NOTE Confidence: 0.9551669

00:12:32.465 --> 00:12:34.065 actual vaccine response seven days

NOTE Confidence: 0.9551669

00:12:34.065 --> 00:12:34.705 post the response,

NOTE Confidence: 0.9136701

00:12:35.529 --> 00:12:36.250 where each of the points

NOTE Confidence: 0.9136701

00:12:36.250 --> 00:12:37.290 in these trees a leaf

NOTE Confidence: 0.9136701

00:12:37.290 --> 00:12:38.089 and each of those,

NOTE Confidence: 0.9368375

00:12:38.650 --> 00:12:39.630 and each of those,

NOTE Confidence: 0.9550499

00:12:40.330 --> 00:12:42.170 sort of circle diagrams represent

NOTE Confidence: 0.9550499

00:12:42.170 --> 00:12:43.850 a clonal expansion starting from

NOTE Confidence: 0.9550499

00:12:43.850 --> 00:12:44.890 a starting from a naive

NOTE Confidence: 0.9550499

00:12:44.890 --> 00:12:46.250 b cell. So you can

NOTE Confidence: 0.9550499

00:12:46.250 --> 00:12:47.050 see there is a bunch

NOTE Confidence: 0.9550499

00:12:47.050 --> 00:12:48.410 of clonal expansions in the

NOTE Confidence: 0.9550499

00:12:48.410 --> 00:12:48.910 blood.

NOTE Confidence: 0.98690903

00:12:49.245 --> 00:12:50.605 So that's pretty indicative of

NOTE Confidence: 0.98690903

00:12:50.605 --> 00:12:52.465 of, an actual ongoing infection.

NOTE Confidence: 0.98690903

00:12:52.605 --> 00:12:54.205 Generally speaking, in a in

NOTE Confidence: 0.98690903

00:12:54.205 --> 00:12:55.804 a healthy human, at rest,

NOTE Confidence: 0.98690903

00:12:55.804 --> 00:12:57.005 you don't have large clonal

NOTE Confidence: 0.98690903

00:12:57.005 --> 00:12:57.505 expansions,

NOTE Confidence: 0.9683595

00:12:58.125 --> 00:12:59.325 in your blood. But now

NOTE Confidence: 0.9683595

00:12:59.325 --> 00:13:00.765 can we tell what infection

NOTE Confidence: 0.9683595

00:13:00.765 --> 00:13:02.205 or what vaccination this person

NOTE Confidence: 0.9683595

00:13:02.205 --> 00:13:03.899 is actually responding to? So

NOTE Confidence: 0.9683595

00:13:03.899 --> 00:13:04.940 one simple thing we can

NOTE Confidence: 0.9683595

00:13:04.940 --> 00:13:05.820 do is take all of

NOTE Confidence: 0.9683595

00:13:05.820 --> 00:13:07.500 the b cell receptor sequences

NOTE Confidence: 0.9683595

00:13:07.500 --> 00:13:09.100 in these clones, calculate the

NOTE Confidence: 0.9683595

00:13:09.100 --> 00:13:10.380 probability of it being a

NOTE Confidence: 0.9683595

00:13:10.380 --> 00:13:12.300 SARS CoV-two specific clone, and

NOTE Confidence: 0.9683595

00:13:12.300 --> 00:13:13.600 just average over the repertoire.

NOTE Confidence: 0.9683595

00:13:13.740 --> 00:13:14.540 And you can see that

NOTE Confidence: 0.9683595

00:13:14.540 --> 00:13:15.579 actually gives us a pretty

NOTE Confidence: 0.9683595

00:13:15.579 --> 00:13:17.360 good power to predict, individuals

NOTE Confidence: 0.9683595

00:13:17.420 --> 00:13:18.459 who are twenty eight days

NOTE Confidence: 0.9683595

00:13:18.459 --> 00:13:19.934 post SARS COV two vaccine,

NOTE Confidence: 0.9683595

00:13:20.235 --> 00:13:21.434 shown here on the right,

NOTE Confidence: 0.9683595

00:13:21.434 --> 00:13:23.035 versus a control population at

NOTE Confidence: 0.9683595

00:13:23.035 --> 00:13:24.654 rest pre vac pre vaccination.

NOTE Confidence: 0.98095167

00:13:25.915 --> 00:13:26.634 We do a lot of

NOTE Confidence: 0.98095167

00:13:26.634 --> 00:13:27.595 work like this with b

NOTE Confidence: 0.98095167

00:13:27.595 --> 00:13:29.194 cell receptors. As I mentioned,

NOTE Confidence: 0.98095167

00:13:29.194 --> 00:13:30.154 we we do all sorts

NOTE Confidence: 0.98095167

00:13:30.154 --> 00:13:32.074 of methods for preprocessing, population

NOTE Confidence: 0.98095167

00:13:32.074 --> 00:13:33.855 structure inference, and repertoire analysis.

NOTE Confidence: 0.89299303

00:13:34.309 --> 00:13:35.990 And BILab makes available a

NOTE Confidence: 0.89299303

00:13:35.990 --> 00:13:37.589 a computational framework called called

NOTE Confidence: 0.89299303

00:13:37.589 --> 00:13:38.089 incantation,

NOTE Confidence: 0.9990952

00:13:39.029 --> 00:13:39.990 to deal with all sorts

NOTE Confidence: 0.9990952

00:13:39.990 --> 00:13:41.110 of analysis of these kinds

NOTE Confidence: 0.9990952

00:13:41.110 --> 00:13:41.690 of data,

NOTE Confidence: 0.99599177

00:13:42.389 --> 00:13:43.589 which is pretty widely used

NOTE Confidence: 0.99599177

00:13:43.589 --> 00:13:44.709 by the by the community.

NOTE Confidence: 0.99599177

00:13:44.949 --> 00:13:45.670 And I'll just take a

NOTE Confidence: 0.99599177

00:13:45.670 --> 00:13:46.630 moment to plug. We are

NOTE Confidence: 0.99599177

00:13:46.630 --> 00:13:47.910 having our twenty twenty five

NOTE Confidence: 0.99599177

00:13:47.910 --> 00:13:49.589 users group meeting on January

NOTE Confidence: 0.99599177

00:13:49.589 --> 00:13:51.095 thirtieth. If you are interested

NOTE Confidence: 0.99599177

00:13:51.095 --> 00:13:52.054 in joining us for that,

NOTE Confidence: 0.99599177

00:13:52.295 --> 00:13:53.495 please do please do sign

NOTE Confidence: 0.99599177

00:13:53.495 --> 00:13:54.695 up. It's free. If you've

NOTE Confidence: 0.99599177

00:13:54.695 --> 00:13:55.815 ever used our tools and

NOTE Confidence: 0.99599177

00:13:55.815 --> 00:13:56.934 are interested in submitting an

NOTE Confidence: 0.99599177

00:13:56.934 --> 00:13:58.535 abstract, the abstract deadline is

NOTE Confidence: 0.99599177

00:13:58.535 --> 00:13:59.495 just about a week from

NOTE Confidence: 0.99599177

00:13:59.495 --> 00:13:59.995 now.

NOTE Confidence: 0.96589106

00:14:01.095 --> 00:14:02.135 So now let me move

NOTE Confidence: 0.96589106

00:14:02.135 --> 00:14:03.575 to an, beyond just sort

NOTE Confidence: 0.96589106

00:14:03.575 --> 00:14:04.774 of looking at the current

NOTE Confidence: 0.96589106

00:14:04.774 --> 00:14:05.835 state of an individual,

NOTE Confidence: 0.92851996

00:14:06.510 --> 00:14:07.710 into the problem of can

NOTE Confidence: 0.92851996

00:14:07.710 --> 00:14:09.170 we predict how an individual

NOTE Confidence: 0.92851996

00:14:09.230 --> 00:14:10.430 respond to a to a

NOTE Confidence: 0.92851996

00:14:10.430 --> 00:14:12.990 certain immunological exposure? John already

NOTE Confidence: 0.92851996

00:14:12.990 --> 00:14:14.430 introduced this idea of of

NOTE Confidence: 0.92851996

00:14:14.430 --> 00:14:16.050 variable you know, human variability

NOTE Confidence: 0.92851996

00:14:16.110 --> 00:14:17.970 to the same immunological exposure.

NOTE Confidence: 0.96409386

00:14:18.285 --> 00:14:19.404 So for example, in a

NOTE Confidence: 0.96409386

00:14:19.404 --> 00:14:20.845 vaccine response, if we take

NOTE Confidence: 0.96409386

00:14:20.845 --> 00:14:22.144 a bunch of young adults,

NOTE Confidence: 0.97683764

00:14:22.524 --> 00:14:23.805 shown along the x axis

NOTE Confidence: 0.97683764

00:14:23.805 --> 00:14:24.845 here, we give them the

NOTE Confidence: 0.97683764

00:14:24.845 --> 00:14:26.204 seasonal flu vaccine and we

NOTE Confidence: 0.97683764

00:14:26.204 --> 00:14:27.725 measure their antibody response on

NOTE Confidence: 0.97683764

00:14:27.725 --> 00:14:29.084 the y axis. You can

NOTE Confidence: 0.97683764

00:14:29.084 --> 00:14:30.225 see there's a whole,

NOTE Confidence: 0.95552874

00:14:30.925 --> 00:14:32.945 wide variety of different, responses.

NOTE Confidence: 0.95552874

00:14:33.245 --> 00:14:35.420 Some people barely generate any,

NOTE Confidence: 0.95552874

00:14:35.640 --> 00:14:37.000 or actually generate no boost

NOTE Confidence: 0.95552874

00:14:37.000 --> 00:14:38.760 in their antibody titers, while

NOTE Confidence: 0.95552874

00:14:38.760 --> 00:14:40.520 other individuals generate, you know,

NOTE Confidence: 0.95552874

00:14:40.520 --> 00:14:41.800 orders of magnitude increase in

NOTE Confidence: 0.95552874

00:14:41.800 --> 00:14:43.400 their, in their titers. So

NOTE Confidence: 0.95552874

00:14:43.400 --> 00:14:44.360 we wanna know, can we

NOTE Confidence: 0.95552874

00:14:44.360 --> 00:14:45.720 predict the response to this

NOTE Confidence: 0.95552874

00:14:45.720 --> 00:14:47.500 vax to to influenza vaccination?

NOTE Confidence: 0.96231085

00:14:47.880 --> 00:14:49.500 And more broadly, can we

NOTE Confidence: 0.96231085

00:14:49.595 --> 00:14:50.635 predict the response to other

NOTE Confidence: 0.96231085

00:14:50.635 --> 00:14:52.155 vaccinations? Is there a universal

NOTE Confidence: 0.96231085

00:14:52.155 --> 00:14:53.355 signature? Is this are the

NOTE Confidence: 0.96231085

00:14:53.355 --> 00:14:55.675 same biological mechanisms, the same

NOTE Confidence: 0.96231085

00:14:55.675 --> 00:14:57.035 signatures that are associated with

NOTE Confidence: 0.96231085

00:14:57.035 --> 00:14:58.955 good flu vaccine responses? Do

NOTE Confidence: 0.96231085

00:14:58.955 --> 00:15:00.075 those also hold for things

NOTE Confidence: 0.96231085

00:15:00.075 --> 00:15:01.615 like yellow fever, for smallpox,

NOTE Confidence: 0.9114661

00:15:01.915 --> 00:15:03.030 for SARS CoV two?

NOTE Confidence: 0.9556235

00:15:03.830 --> 00:15:04.630 And to do that, we

NOTE Confidence: 0.9556235

00:15:04.630 --> 00:15:05.590 leveraged the power of a

NOTE Confidence: 0.9556235

00:15:05.590 --> 00:15:06.790 consortium that we're involved in.

NOTE Confidence: 0.9556235

00:15:07.110 --> 00:15:08.950 John already mentioned, HIPSI, the

NOTE Confidence: 0.9556235

00:15:08.950 --> 00:15:11.290 human human immunologic human immunology

NOTE Confidence: 0.9556235

00:15:11.350 --> 00:15:12.170 project consortium.

NOTE Confidence: 0.9711867

00:15:13.030 --> 00:15:14.470 This is some a consortium

NOTE Confidence: 0.9711867

00:15:14.470 --> 00:15:15.590 that's been funded since two

NOTE Confidence: 0.9711867

00:15:15.590 --> 00:15:16.550 thousand and ten. We've had

NOTE Confidence: 0.9711867

00:15:16.550 --> 00:15:17.510 one of the centers here

NOTE Confidence: 0.9711867

00:15:17.510 --> 00:15:18.170 at Yale.

NOTE Confidence: 0.921491

00:15:18.475 --> 00:15:19.755 It's currently co directed by

NOTE Confidence: 0.921491

00:15:19.755 --> 00:15:21.115 Ruth Montgomery and and David

NOTE Confidence: 0.921491

00:15:21.115 --> 00:15:22.395 Hafler, and we've been part

NOTE Confidence: 0.921491

00:15:22.395 --> 00:15:23.775 of it since the beginning

NOTE Confidence: 0.921491

00:15:23.835 --> 00:15:24.815 in twenty ten.

NOTE Confidence: 0.9555089

00:15:25.595 --> 00:15:26.555 HiPSI does a lot of

NOTE Confidence: 0.9555089

00:15:26.555 --> 00:15:29.015 high throughput profiling of of,

NOTE Confidence: 0.9342196

00:15:29.435 --> 00:15:31.530 humans in diverse immunological states.

NOTE Confidence: 0.9342196

00:15:31.850 --> 00:15:32.890 All of the data is

NOTE Confidence: 0.9342196

00:15:32.890 --> 00:15:34.730 deposited into a repository called

NOTE Confidence: 0.9342196

00:15:34.730 --> 00:15:35.230 import.

NOTE Confidence: 0.99669915

00:15:35.690 --> 00:15:37.130 There's over a hundred different

NOTE Confidence: 0.99669915

00:15:37.130 --> 00:15:37.630 studies,

NOTE Confidence: 0.97209907

00:15:37.930 --> 00:15:39.850 over, almost eight thousand different

NOTE Confidence: 0.97209907

00:15:39.850 --> 00:15:41.210 individuals and lots and lots

NOTE Confidence: 0.97209907

00:15:41.210 --> 00:15:42.030 of measurements.

NOTE Confidence: 0.9813059

00:15:42.890 --> 00:15:44.030 As part of this consortium,

NOTE Confidence: 0.9813059

00:15:44.090 --> 00:15:45.370 we put together a data

NOTE Confidence: 0.9813059

00:15:45.370 --> 00:15:47.005 resource of all the studies

NOTE Confidence: 0.9813059

00:15:47.005 --> 00:15:48.925 that were done, profiling human

NOTE Confidence: 0.9813059

00:15:48.925 --> 00:15:49.825 vaccine responses.

NOTE Confidence: 0.83653325

00:15:50.365 --> 00:15:51.425 In the end, we profiles

NOTE Confidence: 0.9573628

00:15:51.805 --> 00:15:53.325 of thirteen different vaccines where

NOTE Confidence: 0.9573628

00:15:53.325 --> 00:15:55.265 we could relate transcriptional profiles,

NOTE Confidence: 0.94773865

00:15:55.725 --> 00:15:57.825 to antibody tighter, tighter responses.

NOTE Confidence: 0.9620452

00:15:58.300 --> 00:15:59.580 From the analysis of those

NOTE Confidence: 0.9620452

00:15:59.580 --> 00:16:00.620 data, we did two different

NOTE Confidence: 0.9620452

00:16:00.620 --> 00:16:01.740 things. One is we looked

NOTE Confidence: 0.9620452

00:16:01.740 --> 00:16:03.760 for baseline immune states.

NOTE Confidence: 0.9910113

00:16:04.380 --> 00:16:05.820 So could you take somebody's

NOTE Confidence: 0.9910113

00:16:05.820 --> 00:16:07.760 immunological state prior to vaccination

NOTE Confidence: 0.9902043

00:16:08.140 --> 00:16:09.180 and predict how they were

NOTE Confidence: 0.9902043

00:16:09.180 --> 00:16:10.220 gonna respond to the to

NOTE Confidence: 0.9902043

00:16:10.220 --> 00:16:11.280 the to the vaccine?

NOTE Confidence: 0.95717245

00:16:11.985 --> 00:16:13.145 So we could, in fact,

NOTE Confidence: 0.95717245

00:16:13.505 --> 00:16:15.265 generate identify those kinds of

NOTE Confidence: 0.95717245

00:16:15.265 --> 00:16:17.025 profiles as well as temporal

NOTE Confidence: 0.95717245

00:16:17.025 --> 00:16:18.305 profiles. So could you look

NOTE Confidence: 0.95717245

00:16:18.305 --> 00:16:19.425 a day or a week

NOTE Confidence: 0.95717245

00:16:19.425 --> 00:16:20.165 post vaccination

NOTE Confidence: 0.98481846

00:16:20.785 --> 00:16:21.985 and predict the longer term

NOTE Confidence: 0.98481846

00:16:21.985 --> 00:16:23.505 antibody response to vaccine? It

NOTE Confidence: 0.98481846

00:16:23.505 --> 00:16:24.305 turns out you can do

NOTE Confidence: 0.98481846

00:16:24.305 --> 00:16:25.665 that, you can do that

NOTE Confidence: 0.98481846

00:16:25.665 --> 00:16:26.325 as well.

NOTE Confidence: 0.97024137

00:16:26.769 --> 00:16:27.730 And just to show you

NOTE Confidence: 0.97024137

00:16:27.730 --> 00:16:28.230 one,

NOTE Confidence: 0.9986814

00:16:28.930 --> 00:16:29.670 one aspect

NOTE Confidence: 0.95941585

00:16:30.130 --> 00:16:31.250 of that and the just

NOTE Confidence: 0.95941585

00:16:31.250 --> 00:16:32.529 to emphasize the importance of

NOTE Confidence: 0.95941585

00:16:32.529 --> 00:16:33.649 kinetics and and and sort

NOTE Confidence: 0.95941585

00:16:33.649 --> 00:16:34.870 of timing of the response.

NOTE Confidence: 0.95941585

00:16:35.089 --> 00:16:36.550 So here you see a

NOTE Confidence: 0.95941585

00:16:36.610 --> 00:16:37.649 a bunch of those different

NOTE Confidence: 0.95941585

00:16:37.649 --> 00:16:39.089 vaccines that we profiled. Each

NOTE Confidence: 0.95941585

00:16:39.089 --> 00:16:39.935 one is shown by a

NOTE Confidence: 0.95941585

00:16:39.935 --> 00:16:42.035 different line, days post vaccination

NOTE Confidence: 0.95941585

00:16:42.095 --> 00:16:43.375 on the x axis, and

NOTE Confidence: 0.95941585

00:16:43.375 --> 00:16:44.574 the y axis shows the

NOTE Confidence: 0.95941585

00:16:44.574 --> 00:16:45.855 ability of a plasma cell

NOTE Confidence: 0.95941585

00:16:45.855 --> 00:16:47.795 signature to predict the antibody

NOTE Confidence: 0.95941585

00:16:47.855 --> 00:16:49.055 titers of the response at

NOTE Confidence: 0.95941585

00:16:49.055 --> 00:16:50.415 each at different days post

NOTE Confidence: 0.95941585

00:16:50.415 --> 00:16:50.915 vaccination.

NOTE Confidence: 0.9955654

00:16:51.774 --> 00:16:52.495 And you can see for

NOTE Confidence: 0.9955654

00:16:52.495 --> 00:16:53.615 the flu vaccine, if you

NOTE Confidence: 0.9955654

00:16:53.615 --> 00:16:55.475 look seven days post vaccination,

NOTE Confidence: 0.9157328

00:16:55.910 --> 00:16:56.790 we know that there's a

NOTE Confidence: 0.9157328

00:16:56.790 --> 00:16:57.990 burst of plasma blasts that

NOTE Confidence: 0.9157328

00:16:57.990 --> 00:16:59.110 are generally observed in the

NOTE Confidence: 0.9157328

00:16:59.110 --> 00:17:00.950 blood, post vaccination in the

NOTE Confidence: 0.9157328

00:17:00.950 --> 00:17:02.470 flu response. And in fact,

NOTE Confidence: 0.9157328

00:17:02.470 --> 00:17:03.830 those that plasma blast is

NOTE Confidence: 0.9157328

00:17:03.830 --> 00:17:05.430 just highly predictive of the

NOTE Confidence: 0.9157328

00:17:05.430 --> 00:17:07.590 ultimate antibody response, to flu

NOTE Confidence: 0.9157328

00:17:07.590 --> 00:17:08.090 vaccine.

NOTE Confidence: 0.9805224

00:17:08.470 --> 00:17:09.530 A lot of other vaccines

NOTE Confidence: 0.9805224

00:17:09.590 --> 00:17:10.570 share those characteristics,

NOTE Confidence: 0.96480274

00:17:10.984 --> 00:17:12.105 but notably not the yellow

NOTE Confidence: 0.96480274

00:17:12.105 --> 00:17:13.785 fever vaccine. So in yellow

NOTE Confidence: 0.96480274

00:17:13.785 --> 00:17:14.585 fever, if you look at

NOTE Confidence: 0.96480274

00:17:14.585 --> 00:17:15.465 seven days and you look

NOTE Confidence: 0.96480274

00:17:15.465 --> 00:17:16.585 for that signature, you don't

NOTE Confidence: 0.96480274

00:17:16.585 --> 00:17:17.545 see it. But if you

NOTE Confidence: 0.96480274

00:17:17.545 --> 00:17:18.585 look a little bit later,

NOTE Confidence: 0.96480274

00:17:18.585 --> 00:17:19.145 say say,

NOTE Confidence: 0.9505914

00:17:20.345 --> 00:17:21.305 ten days or or a

NOTE Confidence: 0.9505914

00:17:21.305 --> 00:17:22.665 couple weeks after the vaccine

NOTE Confidence: 0.9505914

00:17:22.665 --> 00:17:24.179 response, then in fact, you

NOTE Confidence: 0.9505914

00:17:24.179 --> 00:17:25.539 actually do see that signature

NOTE Confidence: 0.9505914

00:17:25.539 --> 00:17:26.840 and coming out as predictive.

NOTE Confidence: 0.9505914

00:17:26.900 --> 00:17:28.020 So in fact, it's the

NOTE Confidence: 0.9505914

00:17:28.020 --> 00:17:29.299 same biology in both those

NOTE Confidence: 0.9505914

00:17:29.299 --> 00:17:31.240 cases that drives a successful

NOTE Confidence: 0.9505914

00:17:31.299 --> 00:17:32.900 response, but it's very important

NOTE Confidence: 0.9505914

00:17:32.900 --> 00:17:33.780 sort of when during the

NOTE Confidence: 0.9505914

00:17:33.780 --> 00:17:34.840 course of the response,

NOTE Confidence: 0.9760343

00:17:35.140 --> 00:17:36.520 that we, that we look.

NOTE Confidence: 0.9942086

00:17:37.265 --> 00:17:38.544 If you're interested in those

NOTE Confidence: 0.9942086

00:17:38.544 --> 00:17:39.845 kinds of of predictions,

NOTE Confidence: 0.97144467

00:17:40.304 --> 00:17:41.345 I'll make one other plug

NOTE Confidence: 0.97144467

00:17:41.345 --> 00:17:42.144 is that we are part

NOTE Confidence: 0.97144467

00:17:42.144 --> 00:17:42.885 of a center,

NOTE Confidence: 0.8956549

00:17:44.144 --> 00:17:46.065 center for modeling immunity, along

NOTE Confidence: 0.8956549

00:17:46.065 --> 00:17:47.105 with Bjorn Peters at the

NOTE Confidence: 0.8956549

00:17:47.105 --> 00:17:48.085 La Jolla Institute,

NOTE Confidence: 0.94669086

00:17:48.544 --> 00:17:49.664 and we run an annual

NOTE Confidence: 0.94669086

00:17:49.664 --> 00:17:51.970 challenge contest for predicting the,

NOTE Confidence: 0.94669086

00:17:52.290 --> 00:17:53.970 vaccine response. So the CMI

NOTE Confidence: 0.94669086

00:17:53.970 --> 00:17:54.790 PB challenge.

NOTE Confidence: 0.9868318

00:17:55.250 --> 00:17:56.530 And so the idea is

NOTE Confidence: 0.9868318

00:17:56.530 --> 00:17:58.710 that, we provide you data,

NOTE Confidence: 0.57552403

00:17:59.090 --> 00:17:59.590 multiomics,

NOTE Confidence: 0.9674246

00:18:00.130 --> 00:18:00.630 profiles,

NOTE Confidence: 0.92002916

00:18:01.490 --> 00:18:02.770 at baseline, so prior to

NOTE Confidence: 0.92002916

00:18:02.770 --> 00:18:03.670 getting a vaccine,

NOTE Confidence: 0.9819771

00:18:04.024 --> 00:18:05.065 and it's your job to

NOTE Confidence: 0.9819771

00:18:05.065 --> 00:18:05.945 try to come up with

NOTE Confidence: 0.9819771

00:18:05.945 --> 00:18:07.065 a model to predict the

NOTE Confidence: 0.9819771

00:18:07.065 --> 00:18:08.345 vaccine response. We provide a

NOTE Confidence: 0.9819771

00:18:08.345 --> 00:18:09.384 couple of cohorts of data

NOTE Confidence: 0.9819771

00:18:09.384 --> 00:18:10.345 where we have the,

NOTE Confidence: 0.98358804

00:18:10.744 --> 00:18:12.284 profiles and also the endpoints,

NOTE Confidence: 0.98358804

00:18:12.424 --> 00:18:13.544 and there's some data that's

NOTE Confidence: 0.98358804

00:18:13.544 --> 00:18:15.225 held out, and there are

NOTE Confidence: 0.98358804

00:18:15.225 --> 00:18:16.380 there are prizes for the

NOTE Confidence: 0.98358804

00:18:16.460 --> 00:18:17.740 teams that, that do the

NOTE Confidence: 0.98358804

00:18:17.740 --> 00:18:18.940 best. So if you're interested

NOTE Confidence: 0.98358804

00:18:18.940 --> 00:18:19.920 in that kind of work,

NOTE Confidence: 0.98358804

00:18:19.980 --> 00:18:21.260 please do, check it out.

NOTE Confidence: 0.98358804

00:18:21.260 --> 00:18:22.859 The submission deadline is, for

NOTE Confidence: 0.98358804

00:18:22.940 --> 00:18:24.300 on November twenty second. You've

NOTE Confidence: 0.98358804

00:18:24.300 --> 00:18:25.260 got just about a month

NOTE Confidence: 0.98358804

00:18:25.260 --> 00:18:26.859 to develop, to develop your

NOTE Confidence: 0.98358804

00:18:26.859 --> 00:18:27.359 models.

NOTE Confidence: 0.9502848

00:18:28.885 --> 00:18:30.085 Okay. And so now I

NOTE Confidence: 0.9502848

00:18:30.085 --> 00:18:31.445 wanna touch, for a minute

NOTE Confidence: 0.9502848

00:18:31.445 --> 00:18:32.184 on multiomics.

NOTE Confidence: 0.929217

00:18:33.285 --> 00:18:34.725 So previously, I was just

NOTE Confidence: 0.929217

00:18:34.725 --> 00:18:36.244 talking, for for HiPSI. We

NOTE Confidence: 0.929217

00:18:36.244 --> 00:18:37.304 looked a lot of transcriptional

NOTE Confidence: 0.929217

00:18:37.445 --> 00:18:38.885 signatures, and those are, those

NOTE Confidence: 0.929217

00:18:38.885 --> 00:18:40.244 are very powerful. But it

NOTE Confidence: 0.929217

00:18:40.244 --> 00:18:41.445 was mentioned a couple times

NOTE Confidence: 0.929217

00:18:41.445 --> 00:18:42.740 already. Increasingly,

NOTE Confidence: 0.95819783

00:18:43.280 --> 00:18:44.400 a lot of our experimental

NOTE Confidence: 0.95819783

00:18:44.400 --> 00:18:46.400 data encompasses multiple different types

NOTE Confidence: 0.95819783

00:18:46.400 --> 00:18:48.600 of measurements, transcriptional profiles, met

NOTE Confidence: 0.9269029

00:18:49.280 --> 00:18:51.619 metabolomic profiles, proteomic profiles,

NOTE Confidence: 0.96571785

00:18:52.080 --> 00:18:53.359 all together. And one one

NOTE Confidence: 0.96571785

00:18:53.359 --> 00:18:54.720 of the challenges, how do

NOTE Confidence: 0.96571785

00:18:54.720 --> 00:18:56.855 we integrate those data together

NOTE Confidence: 0.96571785

00:18:56.855 --> 00:18:57.815 in order to come up

NOTE Confidence: 0.96571785

00:18:57.815 --> 00:18:58.715 with, predictive

NOTE Confidence: 0.9962489

00:18:59.255 --> 00:19:00.775 responses and understand the the

NOTE Confidence: 0.9962489

00:19:00.775 --> 00:19:01.275 immunological

NOTE Confidence: 0.99804693

00:19:01.575 --> 00:19:03.095 mechanisms that are driving those

NOTE Confidence: 0.99804693

00:19:03.095 --> 00:19:03.595 differential,

NOTE Confidence: 0.9032026

00:19:04.055 --> 00:19:05.035 differential outcomes.

NOTE Confidence: 0.8899949

00:19:05.575 --> 00:19:06.695 And here I wanna highlight

NOTE Confidence: 0.8899949

00:19:06.695 --> 00:19:07.895 a a method that, we've

NOTE Confidence: 0.8899949

00:19:07.895 --> 00:19:09.815 been developed in collaboration, with

NOTE Confidence: 0.8899949

00:19:09.815 --> 00:19:11.580 Liang who spoke spoke earlier,

NOTE Confidence: 0.9351304

00:19:11.980 --> 00:19:13.500 and a graduate student, Jeremy

NOTE Confidence: 0.9351304

00:19:13.500 --> 00:19:15.679 Geege, another CBB graduate student.

NOTE Confidence: 0.9539418

00:19:16.059 --> 00:19:17.019 And the idea here is

NOTE Confidence: 0.9539418

00:19:17.019 --> 00:19:17.899 a lot of times where

NOTE Confidence: 0.9539418

00:19:17.899 --> 00:19:19.019 we have these multi omics

NOTE Confidence: 0.9539418

00:19:19.019 --> 00:19:20.380 data, the common way to

NOTE Confidence: 0.9539418

00:19:20.380 --> 00:19:21.740 analyze those data is to

NOTE Confidence: 0.9539418

00:19:21.740 --> 00:19:22.940 take the data and do

NOTE Confidence: 0.9539418

00:19:22.940 --> 00:19:24.539 some dimensionality reduction. Right? So

NOTE Confidence: 0.9539418

00:19:24.539 --> 00:19:25.690 you have those, you know,

NOTE Confidence: 0.9190917

00:19:26.674 --> 00:19:28.035 potentially hundreds of thousands of

NOTE Confidence: 0.9190917

00:19:28.035 --> 00:19:29.554 measurements of genes and proteins

NOTE Confidence: 0.9190917

00:19:29.554 --> 00:19:30.535 and and and metabolites

NOTE Confidence: 0.98585683

00:19:31.234 --> 00:19:32.835 to reduce the dimensionality of

NOTE Confidence: 0.98585683

00:19:32.835 --> 00:19:34.595 those into some smaller, some

NOTE Confidence: 0.98585683

00:19:34.595 --> 00:19:36.035 smaller space and then do

NOTE Confidence: 0.98585683

00:19:36.035 --> 00:19:37.475 machine learning. And one of

NOTE Confidence: 0.98585683

00:19:37.475 --> 00:19:38.515 the things we found is

NOTE Confidence: 0.98585683

00:19:38.515 --> 00:19:39.715 that doing doing it that

NOTE Confidence: 0.98585683

00:19:39.715 --> 00:19:40.980 way actually could be suboptimal

NOTE Confidence: 0.98585683

00:19:41.140 --> 00:19:42.260 because you would actually you

NOTE Confidence: 0.98585683

00:19:42.260 --> 00:19:43.480 could actually miss variation

NOTE Confidence: 0.99387354

00:19:43.859 --> 00:19:44.980 that was important for the

NOTE Confidence: 0.99387354

00:19:44.980 --> 00:19:45.480 response,

NOTE Confidence: 0.9625366

00:19:45.859 --> 00:19:47.059 of interest. And so we

NOTE Confidence: 0.9625366

00:19:47.059 --> 00:19:48.580 developed a method called, SPEAR,

NOTE Confidence: 0.9625366

00:19:48.580 --> 00:19:49.880 which is a sparse supervised

NOTE Confidence: 0.9625366

00:19:49.940 --> 00:19:51.240 Bayesian factor model,

NOTE Confidence: 0.94105583

00:19:51.540 --> 00:19:53.059 where in generating the lower

NOTE Confidence: 0.94105583

00:19:53.059 --> 00:19:54.119 dimensional representation,

NOTE Confidence: 0.9755208

00:19:54.585 --> 00:19:56.024 we took into account both

NOTE Confidence: 0.9755208

00:19:56.024 --> 00:19:57.225 the variation in the multi

NOTE Confidence: 0.9755208

00:19:57.225 --> 00:19:58.664 omic data as well as

NOTE Confidence: 0.9755208

00:19:58.664 --> 00:20:00.424 the response of interest. And

NOTE Confidence: 0.9755208

00:20:00.424 --> 00:20:01.865 the the method learns to

NOTE Confidence: 0.9755208

00:20:01.865 --> 00:20:03.625 adaptively balance how much to

NOTE Confidence: 0.9755208

00:20:03.625 --> 00:20:04.984 try and explain the variability

NOTE Confidence: 0.9755208

00:20:04.984 --> 00:20:06.105 in the data and how

NOTE Confidence: 0.9755208

00:20:06.105 --> 00:20:07.145 much to try and explain

NOTE Confidence: 0.9755208

00:20:07.145 --> 00:20:08.505 the response of interest in

NOTE Confidence: 0.9755208

00:20:08.505 --> 00:20:09.544 coming up with those lower

NOTE Confidence: 0.9755208

00:20:09.544 --> 00:20:10.044 dimensional,

NOTE Confidence: 0.9953346

00:20:10.640 --> 00:20:11.700 lower dimensional factors.

NOTE Confidence: 0.9852269

00:20:12.640 --> 00:20:13.760 And finally, what I'll end

NOTE Confidence: 0.9852269

00:20:13.760 --> 00:20:15.120 with is the the importance

NOTE Confidence: 0.9852269

00:20:15.120 --> 00:20:15.780 of genetics.

NOTE Confidence: 0.99013776

00:20:16.160 --> 00:20:17.600 So so all of these,

NOTE Confidence: 0.99013776

00:20:17.920 --> 00:20:19.040 responses and all of these

NOTE Confidence: 0.99013776

00:20:19.040 --> 00:20:20.720 signatures are often modulated by

NOTE Confidence: 0.99013776

00:20:20.720 --> 00:20:21.860 the genetic background,

NOTE Confidence: 0.94711775

00:20:22.320 --> 00:20:24.055 of of the individual. And

NOTE Confidence: 0.94711775

00:20:24.055 --> 00:20:25.575 in particularly, it's an emerging

NOTE Confidence: 0.94711775

00:20:25.575 --> 00:20:27.575 area to understand to what

NOTE Confidence: 0.94711775

00:20:27.575 --> 00:20:29.175 extent the genetics of the

NOTE Confidence: 0.94711775

00:20:29.175 --> 00:20:30.234 b cell receptor,

NOTE Confidence: 0.6010582

00:20:31.095 --> 00:20:31.595 repertoire

NOTE Confidence: 0.9686893

00:20:31.975 --> 00:20:33.175 and the components of the

NOTE Confidence: 0.9686893

00:20:33.175 --> 00:20:33.994 b cell receptor

NOTE Confidence: 0.96807736

00:20:34.295 --> 00:20:35.734 influence the ability of people

NOTE Confidence: 0.96807736

00:20:35.734 --> 00:20:36.955 to respond to infection,

NOTE Confidence: 0.9734162

00:20:37.470 --> 00:20:38.130 and vaccination.

NOTE Confidence: 0.94506854

00:20:38.750 --> 00:20:39.790 And I'll show one example

NOTE Confidence: 0.94506854

00:20:39.790 --> 00:20:40.290 here,

NOTE Confidence: 0.98886573

00:20:40.669 --> 00:20:42.850 from, showing the influence of

NOTE Confidence: 0.8942216

00:20:43.309 --> 00:20:44.669 a b cell receptor variable

NOTE Confidence: 0.8942216

00:20:44.669 --> 00:20:46.190 gene, a gene called, IGH

NOTE Confidence: 0.8942216

00:20:46.190 --> 00:20:47.809 v one one sixty nine,

NOTE Confidence: 0.9570908

00:20:48.109 --> 00:20:49.650 on the flu vaccine response.

NOTE Confidence: 0.9570908

00:20:49.869 --> 00:20:51.090 So here you see,

NOTE Confidence: 0.981859

00:20:51.935 --> 00:20:53.455 there's a position, in this,

NOTE Confidence: 0.981859

00:20:53.775 --> 00:20:54.895 in this gene, which can

NOTE Confidence: 0.981859

00:20:54.895 --> 00:20:55.855 either be an f or

NOTE Confidence: 0.981859

00:20:55.855 --> 00:20:57.295 an l. And depending on

NOTE Confidence: 0.981859

00:20:57.295 --> 00:20:58.755 the genotype of the individual,

NOTE Confidence: 0.97516173

00:20:59.535 --> 00:21:01.455 that individual will generate different

NOTE Confidence: 0.97516173

00:21:01.455 --> 00:21:04.175 titers of broadly neutralizing antibody

NOTE Confidence: 0.97516173

00:21:04.175 --> 00:21:05.695 in response to, in response

NOTE Confidence: 0.97516173

00:21:05.695 --> 00:21:06.494 to the flu vaccine. You

NOTE Confidence: 0.97516173

00:21:06.494 --> 00:21:07.234 see the micro

NOTE Confidence: 0.986223

00:21:07.590 --> 00:21:08.950 titers, on the y on

NOTE Confidence: 0.986223

00:21:08.950 --> 00:21:10.010 the y axis here.

NOTE Confidence: 0.99879754

00:21:10.549 --> 00:21:11.750 And so it's really an

NOTE Confidence: 0.99879754

00:21:11.750 --> 00:21:13.109 emerging area to try and

NOTE Confidence: 0.99879754

00:21:13.109 --> 00:21:14.789 understand how the genetics of

NOTE Confidence: 0.99879754

00:21:14.789 --> 00:21:16.010 the antibody repertoire

NOTE Confidence: 0.91938573

00:21:16.390 --> 00:21:17.850 influence the response to vaccination,

NOTE Confidence: 0.9492954

00:21:18.309 --> 00:21:19.049 and infection.

NOTE Confidence: 0.9939823

00:21:19.429 --> 00:21:20.309 And there's not been a

NOTE Confidence: 0.9939823

00:21:20.309 --> 00:21:21.130 lot of associations,

NOTE Confidence: 0.9662263

00:21:21.645 --> 00:21:22.685 that have been discovered so

NOTE Confidence: 0.9662263

00:21:22.685 --> 00:21:24.205 far. In part, I think

NOTE Confidence: 0.9662263

00:21:24.205 --> 00:21:25.244 this is because in all

NOTE Confidence: 0.9662263

00:21:25.244 --> 00:21:26.625 of the genome wide association

NOTE Confidence: 0.9662263

00:21:26.685 --> 00:21:28.285 studies that are done, the

NOTE Confidence: 0.9662263

00:21:28.285 --> 00:21:30.285 immunoglobulin locus is generally not

NOTE Confidence: 0.9662263

00:21:30.285 --> 00:21:31.565 included in any of those

NOTE Confidence: 0.9662263

00:21:31.565 --> 00:21:33.005 studies. So it's not there's

NOTE Confidence: 0.9662263

00:21:33.005 --> 00:21:33.984 very low representation

NOTE Confidence: 0.9696861

00:21:34.285 --> 00:21:35.725 on the, SNP arrays that

NOTE Confidence: 0.9696861

00:21:35.725 --> 00:21:36.540 are that are used.

NOTE Confidence: 0.95947915

00:21:37.020 --> 00:21:38.220 And in general, one can't

NOTE Confidence: 0.95947915

00:21:38.220 --> 00:21:39.100 get this from the short

NOTE Confidence: 0.95947915

00:21:39.100 --> 00:21:40.400 read sequencing

NOTE Confidence: 0.93872637

00:21:41.900 --> 00:21:43.340 data because the region is

NOTE Confidence: 0.93872637

00:21:43.340 --> 00:21:44.960 highly, highly repetitive.

NOTE Confidence: 0.9214178

00:21:45.740 --> 00:21:46.940 And so with the postdoc

NOTE Confidence: 0.9214178

00:21:46.940 --> 00:21:47.680 in the lab,

NOTE Confidence: 0.91618073

00:21:48.380 --> 00:21:49.500 Dylan, who's one of the,

NOTE Confidence: 0.91618073

00:21:49.980 --> 00:21:52.145 Gale BI data science fellows.

NOTE Confidence: 0.91618073

00:21:52.365 --> 00:21:53.885 He's actually developed a,

NOTE Confidence: 0.99652535

00:21:54.205 --> 00:21:55.325 an approach now where we

NOTE Confidence: 0.99652535

00:21:55.325 --> 00:21:56.685 can go in from short

NOTE Confidence: 0.99652535

00:21:56.685 --> 00:21:58.765 read DNA sequencing data and

NOTE Confidence: 0.99652535

00:21:58.765 --> 00:21:59.984 genotype the immunoglobulin

NOTE Confidence: 0.9785071

00:22:00.285 --> 00:22:01.565 locus. And the way he's

NOTE Confidence: 0.9785071

00:22:01.565 --> 00:22:02.525 able to do this is

NOTE Confidence: 0.9785071

00:22:02.525 --> 00:22:03.265 by leveraging,

NOTE Confidence: 0.94358444

00:22:03.565 --> 00:22:05.005 a pangeneome graph. So this

NOTE Confidence: 0.94358444

00:22:05.005 --> 00:22:06.685 is a graphical representation of

NOTE Confidence: 0.94358444

00:22:06.685 --> 00:22:07.960 a genome where instead of

NOTE Confidence: 0.94358444

00:22:07.960 --> 00:22:09.559 having a single linear reference

NOTE Confidence: 0.94358444

00:22:09.559 --> 00:22:11.080 as is commonly used today,

NOTE Confidence: 0.94358444

00:22:11.080 --> 00:22:12.600 we can actually represent and

NOTE Confidence: 0.94358444

00:22:12.600 --> 00:22:13.580 encode the diversity,

NOTE Confidence: 0.9933056

00:22:14.200 --> 00:22:15.480 of the population into a

NOTE Confidence: 0.9933056

00:22:15.480 --> 00:22:17.240 single graphical representation of the

NOTE Confidence: 0.9933056

00:22:17.240 --> 00:22:17.740 genome.

NOTE Confidence: 0.99063873

00:22:18.279 --> 00:22:19.799 And by and by leveraging

NOTE Confidence: 0.99063873

00:22:19.799 --> 00:22:21.035 that structure, we can take

NOTE Confidence: 0.99063873

00:22:21.035 --> 00:22:22.955 those short read, DNA sequencing

NOTE Confidence: 0.99063873

00:22:22.955 --> 00:22:23.455 data,

NOTE Confidence: 0.97223055

00:22:23.994 --> 00:22:24.795 map it to this pan

NOTE Confidence: 0.97223055

00:22:24.795 --> 00:22:26.575 genome graph, and discover variability

NOTE Confidence: 0.97223055

00:22:26.795 --> 00:22:28.335 in the, in the immunoglobulin

NOTE Confidence: 0.97223055

00:22:28.475 --> 00:22:29.835 locus. And what we're gearing

NOTE Confidence: 0.97223055

00:22:29.835 --> 00:22:30.715 up to do now is

NOTE Confidence: 0.97223055

00:22:30.715 --> 00:22:31.915 to actually use this method

NOTE Confidence: 0.97223055

00:22:31.915 --> 00:22:33.195 on biobank data because we

NOTE Confidence: 0.97223055

00:22:33.195 --> 00:22:34.895 now have public data sources

NOTE Confidence: 0.96067166

00:22:35.650 --> 00:22:37.330 of massive numbers of individuals

NOTE Confidence: 0.96067166

00:22:37.330 --> 00:22:39.170 with, short read DNA sequencing

NOTE Confidence: 0.96067166

00:22:39.170 --> 00:22:40.450 data, and a lot of

NOTE Confidence: 0.96067166

00:22:40.450 --> 00:22:42.130 interesting clinical and other, and

NOTE Confidence: 0.96067166

00:22:42.130 --> 00:22:42.869 other phenotypes.

NOTE Confidence: 0.9880353

00:22:43.410 --> 00:22:44.770 And so we're we're planning

NOTE Confidence: 0.9880353

00:22:44.770 --> 00:22:45.730 to use this approach to

NOTE Confidence: 0.9880353

00:22:45.730 --> 00:22:47.170 mine those biobanks and find

NOTE Confidence: 0.9880353

00:22:47.170 --> 00:22:47.670 interesting,

NOTE Confidence: 0.9389264

00:22:48.130 --> 00:22:50.150 connections between the immunoglobulin locus,

NOTE Confidence: 0.99664736

00:22:50.686 --> 00:22:51.907 and and those outcomes.

NOTE Confidence: 0.96928656

00:22:52.607 --> 00:22:53.487 And so I think I

NOTE Confidence: 0.96928656

00:22:53.487 --> 00:22:55.427 will, stop there because I'm,

NOTE Confidence: 0.9055362

00:22:55.727 --> 00:22:56.847 out of time. And,

NOTE Confidence: 0.96010286

00:22:57.407 --> 00:22:58.446 thank you and take any

NOTE Confidence: 0.96010286

00:22:58.446 --> 00:22:58.946 questions.