WEBVTT

NOTE duration:"00:30:39.0400000"

NOTE recognizability:0.932

NOTE language:en-us

NOTE Confidence: 0.93200886

00:00:00.000 --> 00:00:02.332 So first, David Martinez.

NOTE Confidence: 0.93200886

00:00:02.332 --> 00:00:04.664 He joined the immunobiology

NOTE Confidence: 0.93200886

00:00:04.664 --> 00:00:07.359 department just three months ago,

NOTE Confidence: 0.93200886

00:00:07.360 --> 00:00:10.080 so welcome to Yale.

NOTE Confidence: 0.93200886

00:00:10.080 --> 00:00:12.117 So David grew up in El Salvador

NOTE Confidence: 0.93200886

00:00:12.117 --> 00:00:14.478 and he came to the United States,

NOTE Confidence: 0.93200886

00:00:14.480 --> 00:00:16.762 where he had the opportunity to work

NOTE Confidence: 0.93200886

00:00:16.762 --> 00:00:18.440 with very prominent scientists.

NOTE Confidence: 0.93200886

00:00:18.440 --> 00:00:22.136 So Sally Permars, who is a prominent

NOTE Confidence: 0.93200886

00:00:22.136 --> 00:00:23.720 immunologist and vaccinologist.

NOTE Confidence: 0.93200886

00:00:23.720 --> 00:00:27.073 She was his advisor during his doctoral

NOTE Confidence: 0.93200886

00:00:27.073 --> 00:00:30.496 studies at Duke University and then he

NOTE Confidence: 0.93200886

00:00:30.496 --> 00:00:32.890 joined Ralph Barrick's lab at UNC Chapel

NOTE Confidence: 0.93200886

00:00:32.963 --> 00:00:35.268 Hill from his postdoctoral studies.

NOTE Confidence: 0.93200886

00:00:35.270 --> 00:00:37.650 And David's core expertise

NOTE Confidence: 0.93200886

00:00:37.650 --> 00:00:40.030 is vaccinology and virology,

NOTE Confidence: 0.93200886

00:00:40.030 --> 00:00:42.518 focusing focusing on inflated

NOTE Confidence: 0.93200886

00:00:42.518 --> 00:00:44.384 viruses and coronaviruses.

NOTE Confidence: 0.93200886

00:00:44.390 --> 00:00:46.130 And I wanted to highlight that

NOTE Confidence: 0.93200886

00:00:46.130 --> 00:00:48.330 not only has he made very

NOTE Confidence: 0.93200886

00:00:48.330 --> 00:00:50.266 interesting observations for dengue,

NOTE Confidence: 0.93200886

00:00:50.270 --> 00:00:53.532 but he also has been very involved

NOTE Confidence: 0.93200886

00:00:53.532 --> 00:00:55.258 throughout the pandemic and

NOTE Confidence: 0.93200886

00:00:55.258 --> 00:00:56.799 he helps to understand.

NOTE Confidence: 0.93200886

00:00:56.799 --> 00:00:59.397 So to inform on the development

NOTE Confidence: 0.93200886

00:00:59.397 --> 00:01:00.939 of the vaccines,

NOTE Confidence: 0.93200886

00:01:00.940 --> 00:01:03.460 the Moderna and the J&J,

NOTE Confidence: 0.93200886

00:01:03.460 --> 00:01:04.740 as well as the antibody,

NOTE Confidence: 0.93200886

00:01:04.740 --> 00:01:06.428 the antivirals from Eli,

NOTE Confidence: 0.93200886

00:01:06.428 --> 00:01:07.694 Lilly and AstraZeneca,

NOTE Confidence: 0.93200886

00:01:07.700 --> 00:01:09.048 which is really impressive.

NOTE Confidence: 0.93200886

00:01:09.048 --> 00:01:10.733 He's also a Hannah Gray,

NOTE Confidence: 0.93200886

00:01:10.740 --> 00:01:12.860 faculty fellow of the HTMI.

NOTE Confidence: 0.93200886

00:01:12.860 --> 00:01:14.694 And so please join me in welcoming

NOTE Confidence: 0.93200886

00:01:14.694 --> 00:01:17.096 David for his first talk at Yale as

NOTE Confidence: 0.93200886

00:01:17.096 --> 00:01:18.651 a tenure track assistant professor.

NOTE Confidence: 0.937298

00:01:36.530 --> 00:01:38.210 All right, Well, thank you very much,

NOTE Confidence: 0.937298

00:01:38.210 --> 00:01:40.850 Nicole, for that very kind introduction.

NOTE Confidence: 0.937298

00:01:40.850 --> 00:01:43.343 Thank you all for joining the launch of the

NOTE Confidence: 0.937298

00:01:43.343 --> 00:01:45.649 Yale Center for Infection and Immunity.

NOTE Confidence: 0.937298

00:01:45.650 --> 00:01:48.008 I'm incredibly excited to be here

NOTE Confidence: 0.937298

00:01:48.010 --> 00:01:51.448 enjoying such an outstanding but also

NOTE Confidence: 0.937298

00:01:51.448 --> 00:01:53.818 incredibly friendly and supportive group.

NOTE Confidence: 0.937298

00:01:53.818 --> 00:01:56.086 Also, thank you to the Dean for

NOTE Confidence: 0.937298

00:01:56.086 --> 00:01:58.418 the support of the Center for

NOTE Confidence: 0.937298

00:01:58.418 --> 00:02:02.724 Infection and Immunity and as well,

NOTE Confidence: 0.937298

00:02:02.724 --> 00:02:04.746 Nicole, for planning this and and

NOTE Confidence: 0.937298

00:02:04.746 --> 00:02:06.808 and just getting this set up.

NOTE Confidence: 0.937298

00:02:06.810 --> 00:02:09.609 So I'd like to tell you a little bit

NOTE Confidence: 0.937298

00:02:09.609 --> 00:02:11.782 about some of the approaches that we've

NOTE Confidence: 0.937298

00:02:11.782 --> 00:02:14.076 been thinking about over the last really

NOTE Confidence: 0.937298

00:02:14.076 --> 00:02:16.844 3 1/2 years in terms of tackling these

NOTE Confidence: 0.937298

00:02:16.850 --> 00:02:19.770 preemergent and pandemic coronaviruses.

NOTE Confidence: 0.92680395

00:02:22.290 --> 00:02:24.496 So this is I think, information

NOTE Confidence: 0.92680395

00:02:24.496 --> 00:02:26.726 that's hopefully familiar by now.

NOTE Confidence: 0.92680395

00:02:26.730 --> 00:02:28.970 But you know, we really have around,

NOTE Confidence: 0.92680395

00:02:28.970 --> 00:02:30.170 depending on who,

NOTE Confidence: 0.92680395

00:02:30.170 --> 00:02:33.088 how we define viral families, 24 to 26

NOTE Confidence: 0.92680395

00:02:33.088 --> 00:02:34.924 viral families that can infect humans.

NOTE Confidence: 0.92680395

00:02:34.930 --> 00:02:38.186 This is one of those viral families that

NOTE Confidence: 0.92680395

00:02:38.186 --> 00:02:41.009 includes members of the family Corona Verde.

NOTE Confidence: 0.92680395

00:02:41.010 --> 00:02:43.628 And from these family we really have

NOTE Confidence: 0.92680395

00:02:43.628 --> 00:02:46.470 a four genera that exists in in here.

NOTE Confidence: 0.92680395

00:02:46.470 --> 00:02:47.830 And from these four genera,

NOTE Confidence: 0.92680395

00:02:47.830 --> 00:02:49.990 two of them are more common

NOTE Confidence: 0.92680395

00:02:49.990 --> 00:02:51.070 commonly infecting humans.

NOTE Confidence: 0.92680395

00:02:51.070 --> 00:02:53.470 So these include the alpha coronaviruses

NOTE Confidence: 0.92680395

00:02:53.470 --> 00:02:56.526 that are shown here in in this cluster,

NOTE Confidence: 0.92680395

00:02:56.526 --> 00:02:59.105 as well as the beta coronaviruses that

NOTE Confidence: 0.92680395

00:02:59.105 --> 00:03:02.140 are shown here by these pink clusters

NOTE Confidence: 0.92680395

00:03:02.140 --> 00:03:05.301 from the beta coronavirus genus.

NOTE Confidence: 0.92680395

00:03:05.301 --> 00:03:07.107 We really have two major groups

NOTE Confidence: 0.92680395

00:03:07.107 --> 00:03:09.039 that are known to infect humans.

NOTE Confidence: 0.92680395

00:03:09.040 --> 00:03:10.960 These include the group to be

NOTE Confidence: 0.92680395

00:03:10.960 --> 00:03:12.720 sarbecoviruses or SARS related viruses,

NOTE Confidence: 0.92680395

00:03:12.720 --> 00:03:14.664 which of course include members of

NOTE Confidence: 0.92680395

00:03:14.664 --> 00:03:16.345 that we're familiar with including

NOTE Confidence: 0.92680395

00:03:16.345 --> 00:03:18.277 SARS COVID One which emerged in

NOTE Confidence: 0.92680395

00:03:18.280 --> 00:03:20.512 2003 and SARS COVID 2A virus

NOTE Confidence: 0.92680395

00:03:20.512 --> 00:03:23.140 that now needs no introduction.

NOTE Confidence: 0.92680395

00:03:23.140 --> 00:03:25.308 We also have the group to see Merbeka

NOTE Confidence: 0.92680395

00:03:25.308 --> 00:03:27.100 viruses or MERS related viruses.

NOTE Confidence: 0.92680395

00:03:27.100 --> 00:03:28.960 So really it wasn't until the

NOTE Confidence: 0.92680395

00:03:28.960 --> 00:03:30.909 early 2000s that people began to

NOTE Confidence: 0.92680395

00:03:30.909 --> 00:03:32.534 pay attention to these groups.

NOTE Confidence: 0.92680395

00:03:32.540 --> 00:03:34.904 Whenever SARS coronavirus emerged

NOTE Confidence: 0.92680395

00:03:34.904 --> 00:03:37.859 and infected over 8000 people

NOTE Confidence: 0.92680395

00:03:37.860 --> 00:03:39.940 and caused around 800 deaths,

NOTE Confidence: 0.92680395

00:03:39.940 --> 00:03:43.160 so about 10% mortality rate.

NOTE Confidence: 0.92680395

00:03:43.160 --> 00:03:44.310 Some of these other viruses

NOTE Confidence: 0.92680395

00:03:44.310 --> 00:03:45.000 are more pathogenic,

NOTE Confidence: 0.92680395

00:03:45.000 --> 00:03:46.320 including MERS coronavirus.

NOTE Confidence: 0.92680395

00:03:46.320 --> 00:03:48.520 It's estimated to cause around

NOTE Confidence: 0.92680395

00:03:48.520 --> 00:03:50.302 a 30% mortality rate.

NOTE Confidence: 0.92680395

00:03:50.302 --> 00:03:53.008 And the reasons underlying the higher

NOTE Confidence: 0.92680395

00:03:53.008 --> 00:03:55.640 mortality rate of the virus are unknown,

NOTE Confidence: 0.92680395

00:03:55.640 --> 00:03:57.004 although it's speculated that

NOTE Confidence: 0.92680395

00:03:57.004 --> 00:03:59.534 some of the genes and the virus

NOTE Confidence: 0.92680395

00:03:59.534 --> 00:04:01.614 itself and the accessory orbs

NOTE Confidence: 0.92680395

00:04:01.614 --> 00:04:03.278 are potentially responsible for

NOTE Confidence: 0.92680395

00:04:03.341 --> 00:04:05.078 this increased pathogenesis.

NOTE Confidence: 0.92680395

00:04:05.080 --> 00:04:07.495 So in thinking about how to tackle

NOTE Confidence: 0.92680395

00:04:07.495 --> 00:04:09.040 these genetically divergent viruses,

NOTE Confidence: 0.92680395

00:04:09.040 --> 00:04:11.680 we began to look at one of these

NOTE Confidence: 0.94126415

00:04:13.870 --> 00:04:15.710 subgenera of the Sarbeca viruses.

NOTE Confidence: 0.94126415

00:04:15.710 --> 00:04:16.990 So these include the zoonotic,

NOTE Confidence: 0.94126415

00:04:16.990 --> 00:04:18.550 SARS like viruses.

NOTE Confidence: 0.94126415

00:04:18.550 --> 00:04:20.630 And this similarity plotter,

NOTE Confidence: 0.94126415

00:04:20.630 --> 00:04:22.082 still called Simplot,

NOTE Confidence: 0.94126415

00:04:22.082 --> 00:04:24.018 really depicts the genetic

NOTE Confidence: 0.94126415

00:04:24.018 --> 00:04:26.562 diversity within this subgenus of

NOTE Confidence: 0.94126415

00:04:26.562 --> 00:04:28.746 viruses throughout its genome.

NOTE Confidence: 0.94126415

00:04:28.750 --> 00:04:30.906 So these are fairly large RNA viruses,

NOTE Confidence: 0.94126415

00:04:30.910 --> 00:04:32.885 around 30 KB depending on

NOTE Confidence: 0.94126415

00:04:32.885 --> 00:04:34.860 which virus we're looking at.

NOTE Confidence: 0.94126415

00:04:34.860 --> 00:04:37.751 And these viruses on the right here

NOTE Confidence: 0.94126415

00:04:37.751 --> 00:04:40.144 are zoonotic viruses of bad origin,

NOTE Confidence: 0.94126415

00:04:40.144 --> 00:04:42.490 as well as human epidemic viruses

NOTE Confidence: 0.94126415

00:04:42.563 --> 00:04:44.379 or other zoonotic viruses.

NOTE Confidence: 0.94126415

00:04:44.380 --> 00:04:46.140 And what I want to draw your attention

NOTE Confidence: 0.94126415

00:04:46.140 --> 00:04:47.530 to in this particular similarity

NOTE Confidence: 0.94126415

00:04:47.530 --> 00:04:49.630 plot is that these viruses have a

NOTE Confidence: 0.94126415

00:04:49.680 --> 00:04:51.540 great degree of genetic diversity in

NOTE Confidence: 0.94126415

00:04:51.540 --> 00:04:53.268 various portions of their genomes,

NOTE Confidence: 0.94126415

00:04:53.268 --> 00:04:56.684 in particular the subunit one that is

NOTE Confidence: 0.94126415

00:04:56.684 --> 00:04:59.298 depicted here by the spike that I've laid,

NOTE Confidence: 0.94126415

00:04:59.300 --> 00:05:01.900 this ribbon model that have

NOTE Confidence: 0.94126415

00:05:01.900 --> 00:05:03.856 laid sort of parallel to this.

NOTE Confidence: 0.94126415

00:05:03.860 --> 00:05:05.972 So when we began to think about how

NOTE Confidence: 0.94126415

00:05:05.972 --> 00:05:08.686 do we begin to tackle these viruses

NOTE Confidence: 0.94126415

00:05:08.686 --> 00:05:10.378 that are genetically diverse,

NOTE Confidence: 0.94126415

00:05:10.380 --> 00:05:12.036 how are we going to deal with the

NOTE Confidence: 0.94126415

00:05:12.036 --> 00:05:13.180 genetic diversity of these viruses?

NOTE Confidence: 0.94126415

00:05:13.180 --> 00:05:15.336 So this depicted the bigger the dip,

NOTE Confidence: 0.94126415

00:05:15.340 --> 00:05:17.240 then the more genetic diversity

NOTE Confidence: 0.94126415

00:05:17.240 --> 00:05:19.140 we have among these viruses.

NOTE Confidence: 0.94126415

00:05:19.140 --> 00:05:20.538 So to begin to do this,

NOTE Confidence: 0.94126415

00:05:20.540 --> 00:05:22.514 we turn to patients that have

NOTE Confidence: 0.94126415

00:05:22.514 --> 00:05:24.279 been infected with the original

NOTE Confidence: 0.94126415

00:05:24.279 --> 00:05:25.905 SARS COVID from 2003.

NOTE Confidence: 0.94126415

00:05:25.905 --> 00:05:29.300 So this was a highly collaborative study

NOTE Confidence: 0.94126415

00:05:29.300 --> 00:05:34.208 spanning the NIAID Vaccine Research Center,

NOTE Confidence: 0.94126415

00:05:34.210 --> 00:05:34.650 UNC,

NOTE Confidence: 0.94126415

00:05:34.650 --> 00:05:37.290 Duke University and and other collaborators.

NOTE Confidence: 0.94126415

00:05:37.290 --> 00:05:40.714 So what we did is we got a hold of

NOTE Confidence: 0.94126415

00:05:40.714 --> 00:05:43.010 a convalescent PBMC samples and we

NOTE Confidence: 0.94126415

00:05:43.010 --> 00:05:44.942 began to study monoclonal antibodies

NOTE Confidence: 0.94126415

00:05:44.942 --> 00:05:47.126 from these from this particular patient.

NOTE Confidence: 0.94126415

00:05:47.130 --> 00:05:48.607 So this was a patient that I,

NOTE Confidence: 0.94126415

00:05:48.610 --> 00:05:50.374 like I said had been infected with

NOTE Confidence: 0.94126415

00:05:50.374 --> 00:05:53.810 SARS COVID in 2003 and by standard

NOTE Confidence: 0.94126415

00:05:53.810 --> 00:05:56.074 approaches that have been developed

NOTE Confidence: 0.94126415

00:05:56.074 --> 00:05:58.030 by others and also utilized by

NOTE Confidence: 0.94126415

00:05:58.030 --> 00:05:59.470 us and many others.

NOTE Confidence: 0.94126415

00:05:59.470 --> 00:06:02.104 Then we began to isolate antigen

NOTE Confidence: 0.94126415

00:06:02.104 --> 00:06:04.971 specific memory B cells by essentially

NOTE Confidence: 0.94126415

00:06:04.971 --> 00:06:07.546 taking an antigen bait protein,

NOTE Confidence: 0.94126415

00:06:07.550 --> 00:06:08.955 labeling it and then sorting

NOTE Confidence: 0.94126415

00:06:08.955 --> 00:06:10.874 those memory B cells and cloning

NOTE Confidence: 0.94126415

00:06:10.874 --> 00:06:12.230 out monoclonal antibodies.

NOTE Confidence: 0.94126415

00:06:12.230 --> 00:06:14.575 And we began to triage the antibodies

NOTE Confidence: 0.94126415

00:06:14.575 --> 00:06:17.121 and study them in a way that we could

NOTE Confidence: 0.94126415

00:06:17.121 --> 00:06:19.456 begin to map to where they bound on

NOTE Confidence: 0.94126415

00:06:19.456 --> 00:06:22.110 the spike protein on the SARS Kobe 2 virus,

NOTE Confidence: 0.94126415

00:06:22.110 --> 00:06:24.786 but also other SARS related viruses.

NOTE Confidence: 0.94126415

00:06:24.790 --> 00:06:26.654 And I'm going to tell you a little

NOTE Confidence: 0.94126415

00:06:26.654 --> 00:06:28.670 bit about those monoclonal antibodies.

NOTE Confidence: 0.94126415

00:06:28.670 --> 00:06:30.710 But first I want to just for the,

NOTE Confidence: 0.94126415

00:06:30.710 --> 00:06:31.790 so that my talk is clear,

NOTE Confidence: 0.94126415

00:06:31.790 --> 00:06:34.107 just want to introduce this other concept.

NOTE Confidence: 0.94126415

00:06:34.110 --> 00:06:35.832 So I think this is something that

NOTE Confidence: 0.94126415

00:06:35.832 --> 00:06:37.535 we're all familiar with by now just

NOTE Confidence: 0.94126415

00:06:37.535 --> 00:06:39.204 you know given what we've heard in

NOTE Confidence: 0.94126415

00:06:39.204 --> 00:06:40.961 the media over the last few years

NOTE Confidence: 0.94126415

00:06:40.961 --> 00:06:42.478 about antibodies to the coronavirus.

NOTE Confidence: 0.94126415

00:06:42.478 --> 00:06:44.494 But I think it's an important

NOTE Confidence: 0.94126415

00:06:44.494 --> 00:06:46.546 concept just for clarity of my talk.

NOTE Confidence: 0.94126415

00:06:46.550 --> 00:06:49.030 So antibodies have multiple functions.

NOTE Confidence: 0.94126415

00:06:49.030 --> 00:06:52.046 They can have antiviral functions

NOTE Confidence: 0.94126415

00:06:52.046 --> 00:06:54.556 like nonneutralizing functions like a

NOTE Confidence: 0.94126415

00:06:54.556 --> 00:06:56.512 BCC or various phagocytic functions.

NOTE Confidence: 0.94126415

00:06:56.512 --> 00:06:59.089 But one of the functions that they

NOTE Confidence: 0.94126415

00:06:59.089 --> 00:07:01.099 do not on the nonneutralizing side,

NOTE Confidence: 0.94126415

00:07:01.100 --> 00:07:03.500 but the other function is neutralization.

NOTE Confidence: 0.94126415

00:07:03.500 --> 00:07:05.488 So this is the literal ability of

NOTE Confidence: 0.94126415

00:07:05.488 --> 00:07:07.395 the Mal antibody molecule to stop

NOTE Confidence: 0.94126415

00:07:07.395 --> 00:07:09.375 the virus from delivering its its

NOTE Confidence: 0.94126415

00:07:09.375 --> 00:07:11.019 genetic cargo inside the cell.

NOTE Confidence: 0.94126415

00:07:11.020 --> 00:07:12.760 So for a lot of the data that I'm going

NOTE Confidence: 0.9325602

00:07:12.805 --> 00:07:14.848 to show you, when I say neutralization,

NOTE Confidence: 0.9325602

00:07:14.848 --> 00:07:16.733 I'm literally talking about this.

NOTE Confidence: 0.9325602

00:07:16.740 --> 00:07:19.452 So antibodies can neutralize by essentially

NOTE Confidence: 0.9325602

00:07:19.452 --> 00:07:21.215 stopping the conformational change of

NOTE Confidence: 0.9325602

00:07:21.215 --> 00:07:23.256 the spike protein which is, you know,

NOTE Confidence: 0.9325602

00:07:23.256 --> 00:07:24.796 essentially a spring loaded molecule.

NOTE Confidence: 0.9325602

00:07:24.800 --> 00:07:25.980 And in doing so,

NOTE Confidence: 0.9325602

00:07:25.980 --> 00:07:28.524 it can prevent the delivery of the viral

NOTE Confidence: 0.9325602

00:07:28.524 --> 00:07:31.190 cargo that the genetic cargo into the cell.

NOTE Confidence: 0.9325602

00:07:31.190 --> 00:07:33.488 So we screened over 1700 monoclonal

NOTE Confidence: 0.9325602

00:07:33.488 --> 00:07:35.020 antibodies that were isolated

NOTE Confidence: 0.9325602

00:07:35.081 --> 00:07:36.789 from this particular patient.

NOTE Confidence: 0.9325602

00:07:36.790 --> 00:07:38.494 And I don't have time to talk about

NOTE Confidence: 0.9325602

00:07:38.494 --> 00:07:40.309 all the 1700 monoclonal antibodies,

NOTE Confidence: 0.9325602

00:07:40.310 --> 00:07:41.766 but I want to draw your attention to

NOTE Confidence: 0.9325602

00:07:41.766 --> 00:07:43.126 four of these monoclonal antibodies

NOTE Confidence: 0.9325602

00:07:43.126 --> 00:07:44.706 that really caught our attention.

NOTE Confidence: 0.9325602

00:07:44.710 --> 00:07:47.164 So these were antibodies that could

NOTE Confidence: 0.9325602

00:07:47.164 --> 00:07:49.350 neutralize various SARS related viruses,

NOTE Confidence: 0.9325602

00:07:49.350 --> 00:07:52.070 including viruses of zoonotic origin

NOTE Confidence: 0.9325602

00:07:52.070 --> 00:07:54.212 from bat species as well as the

NOTE Confidence: 0.9325602

00:07:54.212 --> 00:07:57.137 SARS Co V2 pandemic virus and the

NOTE Confidence: 0.9325602

00:07:57.137 --> 00:07:59.647 original SARS coronavirus from 2003.

NOTE Confidence: 0.9325602

00:07:59.647 --> 00:08:03.109 So from these four monoclonal antibodies,

NOTE Confidence: 0.9325602

00:08:03.110 --> 00:08:04.916 what this data told us is that

NOTE Confidence: 0.9325602

00:08:04.916 --> 00:08:06.340 despite the genetic diversity within

NOTE Confidence: 0.9325602

00:08:06.340 --> 00:08:08.426 the subunit 1 portion of the spike,

NOTE Confidence: 0.9325602

00:08:08.430 --> 00:08:10.726 then clearly there were sites that were

NOTE Confidence: 0.9325602

00:08:10.726 --> 00:08:12.332 so-called Achilles heels within these

NOTE Confidence: 0.9325602

00:08:12.332 --> 00:08:14.306 viruses that could be targeted by the

NOTE Confidence: 0.9325602

00:08:14.306 --> 00:08:16.389 host immune response and in particular,

NOTE Confidence: 0.9325602

00:08:16.390 --> 00:08:18.230 the human immune response,

NOTE Confidence: 0.9325602

00:08:18.230 --> 00:08:21.226 which was not really known at the time.

NOTE Confidence: 0.9325602

00:08:21.230 --> 00:08:22.760 So we began to study these

NOTE Confidence: 0.9325602

00:08:22.760 --> 00:08:23.270 monoclonal antibodies,

NOTE Confidence: 0.9325602

00:08:23.270 --> 00:08:25.230 not just in vitro but also in vivo.

NOTE Confidence: 0.9325602

00:08:25.230 --> 00:08:27.220 So for for much of the data that I'm going

NOTE Confidence: 0.9325602

00:08:27.269 --> 00:08:29.188 to show you in this portion of my talk,

NOTE Confidence: 0.9325602

00:08:29.190 --> 00:08:31.475 then it really involves characterizing

NOTE Confidence: 0.9325602

00:08:31.475 --> 00:08:33.760 the antiviral functions of these

NOTE Confidence: 0.9325602

00:08:33.824 --> 00:08:36.269 monoclonal antibodies in mouse models.

NOTE Confidence: 0.9325602

00:08:36.270 --> 00:08:38.555 And just to give you a brief overview

NOTE Confidence: 0.9325602

00:08:38.555 --> 00:08:40.515 of how the experiments are being set up

NOTE Confidence: 0.9325602

00:08:40.515 --> 00:08:42.210 and they're essentially two different

NOTE Confidence: 0.9325602

00:08:42.210 --> 00:08:44.304 ways that we evaluated these antibodies,

NOTE Confidence: 0.9325602

00:08:44.310 --> 00:08:46.638 either in a prophylactic or preventative

NOTE Confidence: 0.9325602

00:08:46.638 --> 00:08:48.820 setting or in a therapeutic setting.

NOTE Confidence: 0.9325602

00:08:48.820 --> 00:08:51.670 So in these various animal models

NOTE Confidence: 0.9325602

00:08:51.670 --> 00:08:53.095 of coronavirus pathogenesis,

NOTE Confidence: 0.9325602

00:08:53.100 --> 00:08:55.578 then peak virus replication is around

NOTE Confidence: 0.9325602

00:08:55.578 --> 00:08:58.140 2 days post infection or 48 hours.

NOTE Confidence: 0.9325602

00:08:58.140 --> 00:09:00.408 So we want to evaluate the antibodies

NOTE Confidence: 0.9325602

00:09:00.408 --> 00:09:03.302 in a manner that we can test whether or

NOTE Confidence: 0.9325602

00:09:03.302 --> 00:09:05.546 not viral replication and the relevant

NOTE Confidence: 0.9325602

00:09:05.546 --> 00:09:08.007 tissues of these mice like the lung or

NOTE Confidence: 0.9325602

00:09:08.007 --> 00:09:10.267 the upper Airways can in fact be dampen.

NOTE Confidence: 0.9325602

00:09:10.270 --> 00:09:12.510 So we either treated the mice at 12

NOTE Confidence: 0.9325602

00:09:12.510 --> 00:09:15.079 or or 12 hours before infection or 12

NOTE Confidence: 0.9325602

00:09:15.079 --> 00:09:17.502 hours post infection or even at times

NOTE Confidence: 0.9325602

00:09:17.502 --> 00:09:19.227 later post infection to determine

NOTE Confidence: 0.9325602

00:09:19.227 --> 00:09:21.998 whether or not the antibodies had any

NOTE Confidence: 0.9325602

00:09:21.998 --> 00:09:24.508 efficacy against these various viruses.

NOTE Confidence: 0.9325602

00:09:24.510 --> 00:09:26.870 So looking at this data,

NOTE Confidence: 0.9325602

00:09:26.870 --> 00:09:29.696 we first began to evaluate the

NOTE Confidence: 0.9325602

00:09:29.696 --> 00:09:31.854 antiviral function of four of these,

NOTE Confidence: 0.9325602

00:09:31.854 --> 00:09:32.350 you know,

NOTE Confidence: 0.9325602

00:09:32.350 --> 00:09:33.880 broadly neutralizing crossreactive

NOTE Confidence: 0.9325602

00:09:33.880 --> 00:09:36.430 antibodies against the original SARS.

NOTE Confidence: 0.9325602

00:09:36.430 --> 00:09:39.409 So this is SARS Co V1 and a highly

NOTE Confidence: 0.9325602

00:09:39.409 --> 00:09:40.699 pathogenic mouse model.

NOTE Confidence: 0.9325602

00:09:40.700 --> 00:09:42.240 So from this data,

NOTE Confidence: 0.9325602

00:09:42.240 --> 00:09:44.140 whenever we compared the ability

NOTE Confidence: 0.9325602

00:09:44.140 --> 00:09:46.300 of these antibodies to block virus

NOTE Confidence: 0.9325602

00:09:46.300 --> 00:09:48.501 replication in the lungs of these

NOTE Confidence: 0.9325602

00:09:48.501 --> 00:09:50.271 animals compared to a negative

NOTE Confidence: 0.9325602

00:09:50.271 --> 00:09:52.220 controlled flu monoclonal antibody,

NOTE Confidence: 0.9325602

00:09:52.220 --> 00:09:55.690 then only one of these antibodies was really

NOTE Confidence: 0.9325602

00:09:55.690 --> 00:09:57.820 able to fully suppress virus replication.

NOTE Confidence: 0.9325602

00:09:57.820 --> 00:09:59.182 So for the remainder of this

NOTE Confidence: 0.9325602

00:09:59.182 --> 00:10:00.812 particular part of my talk that I'm

NOTE Confidence: 0.9325602

00:10:00.812 --> 00:10:02.373 going to focus on telling you about

NOTE Confidence: 0.9325602

00:10:02.420 --> 00:10:04.060 that particular monoclonal antibody,

NOTE Confidence: 0.9325602

00:10:04.060 --> 00:10:05.236 which is called DH1047.

NOTE Confidence: 0.9325602

00:10:05.236 --> 00:10:07.000 So we wanted to know whether

NOTE Confidence: 0.935195495454545

00:10:07.057 --> 00:10:08.887 or not this antibody could not

NOTE Confidence: 0.935195495454545

00:10:08.887 --> 00:10:10.790 only prevent disease in these mice,

NOTE Confidence: 0.935195495454545

00:10:10.790 --> 00:10:12.848 but could it also dampen virus

NOTE Confidence: 0.935195495454545

00:10:12.848 --> 00:10:14.750 replication in a therapeutic setting?

NOTE Confidence: 0.935195495454545

00:10:14.750 --> 00:10:16.388 So once the mice are infected,

NOTE Confidence: 0.935195495454545

00:10:16.390 --> 00:10:17.940 if we treat them with

NOTE Confidence: 0.935195495454545

00:10:17.940 --> 00:10:18.870 this particular antibody,

NOTE Confidence: 0.935195495454545

00:10:18.870 --> 00:10:21.908 can we mitigate signs of viral pathogenesis?

NOTE Confidence: 0.935195495454545

00:10:21.910 --> 00:10:24.606 And that is in fact what we saw

NOTE Confidence: 0.935195495454545

00:10:24.606 --> 00:10:26.628 whenever mice were treated with

NOTE Confidence: 0.935195495454545

00:10:26.630 --> 00:10:28.630 DH1047 in a therapeutic setting,

NOTE Confidence: 0.935195495454545

00:10:28.630 --> 00:10:31.108 then we could reduce lung virus

NOTE Confidence: 0.935195495454545

00:10:31.108 --> 00:10:33.405 replication as well as other

NOTE Confidence: 0.935195495454545

00:10:33.405 --> 00:10:35.669 measures of viral pathogenesis.

NOTE Confidence: 0.935195495454545

00:10:35.670 --> 00:10:38.652 We then wanted to expand our breath

NOTE Confidence: 0.935195495454545

00:10:38.652 --> 00:10:40.562 of studying this monoclonal antibody

NOTE Confidence: 0.935195495454545

00:10:40.562 --> 00:10:43.234 and also evaluate the ability of this

NOTE Confidence: 0.935195495454545

00:10:43.234 --> 00:10:44.670 particular antibody isolated from

NOTE Confidence: 0.935195495454545

00:10:44.670 --> 00:10:47.520 a human and blocking these various

NOTE Confidence: 0.935195495454545

00:10:47.520 --> 00:10:50.470 coronaviruses and mouse animal models.

NOTE Confidence: 0.935195495454545

00:10:50.470 --> 00:10:53.326 So we looked at A2 zoonotic

NOTE Confidence: 0.935195495454545

00:10:53.326 --> 00:10:55.773 preemergent viruses that I'll note

NOTE Confidence: 0.935195495454545

00:10:55.773 --> 00:10:58.396 that whenever you take these two

NOTE Confidence: 0.935195495454545

00:10:58.396 --> 00:11:00.026 coronaviruses that are shown here,

NOTE Confidence: 0.935195495454545

00:11:00.030 --> 00:11:01.554 they're isolated from a bat and

NOTE Confidence: 0.935195495454545

00:11:01.554 --> 00:11:03.453 you put them in human primary

NOTE Confidence: 0.935195495454545

00:11:03.453 --> 00:11:04.686 airway epithelial cells,

NOTE Confidence: 0.935195495454545

00:11:04.690 --> 00:11:07.030 they grow efficiently well and they

NOTE Confidence: 0.935195495454545

00:11:07.030 --> 00:11:09.458 can evade many of the commonly used

NOTE Confidence: 0.935195495454545

00:11:09.458 --> 00:11:10.878 countermeasures at least against SARS

NOTE Confidence: 0.935195495454545

00:11:10.878 --> 00:11:12.570 COVID and and also against SARS,

NOTE Confidence: 0.935195495454545

00:11:12.570 --> 00:11:13.514 COVID too.

NOTE Confidence: 0.935195495454545

00:11:13.514 --> 00:11:14.930 So but this,

NOTE Confidence: 0.935195495454545

00:11:14.930 --> 00:11:16.665 this monoclonal antibody that we

NOTE Confidence: 0.935195495454545

00:11:16.665 --> 00:11:19.015 isolated from a human then could not

NOTE Confidence: 0.935195495454545

00:11:19.015 --> 00:11:20.750 only prevent the virus infection

NOTE Confidence: 0.935195495454545

00:11:20.750 --> 00:11:21.845 and pretreated mice,

NOTE Confidence: 0.935195495454545

00:11:21.850 --> 00:11:23.758 but could also treat the virus

NOTE Confidence: 0.935195495454545

00:11:23.758 --> 00:11:25.030 infection in these mice.

NOTE Confidence: 0.935195495454545

00:11:25.030 --> 00:11:26.962 Suggesting that within these

NOTE Confidence: 0.935195495454545

00:11:26.962 --> 00:11:28.894 highly genetically diverse subunit

NOTE Confidence: 0.935195495454545

00:11:28.894 --> 00:11:31.484 1 portion of the spike then this

NOTE Confidence: 0.935195495454545

00:11:31.484 --> 00:11:33.547 was again pointing to an Achilles

NOTE Confidence: 0.935195495454545

00:11:33.547 --> 00:11:35.594 heel within these various viruses.

NOTE Confidence: 0.935195495454545

00:11:35.594 --> 00:11:38.310 And then also in looking at again

NOTE Confidence: 0.935195495454545

00:11:38.380 --> 00:11:40.372 looking at more breadth of this

NOTE Confidence: 0.935195495454545

00:11:40.372 --> 00:11:42.658 virus as we also evaluated another

NOTE Confidence: 0.935195495454545

00:11:42.658 --> 00:11:45.304 SARS related virus called WIV 16.

NOTE Confidence: 0.935195495454545

00:11:45.310 --> 00:11:47.756 And then we could similarly treat

NOTE Confidence: 0.935195495454545

00:11:47.756 --> 00:11:50.388 these mice in a preventative or or

NOTE Confidence: 0.935195495454545

00:11:50.388 --> 00:11:52.145 therapeutic setting and also against

NOTE Confidence: 0.935195495454545

00:11:52.145 --> 00:11:54.336 a SARS two related virus that was

NOTE Confidence: 0.935195495454545

00:11:54.405 --> 00:11:57.420 isolated from an animal called a pangolin.

NOTE Confidence: 0.935195495454545

00:11:57.420 --> 00:11:58.632 So clearly the,

NOTE Confidence: 0.935195495454545

00:11:58.632 --> 00:12:00.652 the footprint bound by this

NOTE Confidence: 0.935195495454545

00:12:00.652 --> 00:12:02.678 monoclonal antibody then it's highly

NOTE Confidence: 0.935195495454545

00:12:02.678 --> 00:12:04.214 must be highly conserved.

NOTE Confidence: 0.935195495454545

00:12:04.220 --> 00:12:06.444 So we were interested in also

NOTE Confidence: 0.935195495454545

00:12:06.444 --> 00:12:08.268 testing the ability of this antibody

NOTE Confidence: 0.935195495454545

00:12:08.268 --> 00:12:09.820 against the SARS 2 variants,

NOTE Confidence: 0.935195495454545

00:12:09.820 --> 00:12:11.210 at least the variants that

NOTE Confidence: 0.935195495454545

00:12:11.210 --> 00:12:12.600 were prevalent at the time.

NOTE Confidence: 0.935195495454545

00:12:12.600 --> 00:12:15.198 So you know,

NOTE Confidence: 0.935195495454545

00:12:15.198 --> 00:12:16.794 this was totally unexpected

NOTE Confidence: 0.935195495454545

00:12:16.794 --> 00:12:19.279 because what we found was that

NOTE Confidence: 0.935195495454545

00:12:19.279 --> 00:12:21.309 this monoclonal antibody could not

NOTE Confidence: 0.935195495454545

00:12:21.309 --> 00:12:23.340 only have this wide diverse breath

NOTE Confidence: 0.935195495454545

00:12:23.340 --> 00:12:24.636 against these zoonotic viruses,

NOTE Confidence: 0.935195495454545

00:12:24.640 --> 00:12:27.280 but it could also block all

NOTE Confidence: 0.935195495454545

00:12:27.280 --> 00:12:28.600 the various variants.

NOTE Confidence: 0.935195495454545

00:12:28.600 --> 00:12:30.520 At the time that we published a study,

NOTE Confidence: 0.935195495454545

00:12:30.520 --> 00:12:32.291 the delta was sort of the prevalent

NOTE Confidence: 0.935195495454545

00:12:32.291 --> 00:12:34.080 variant but it could potently

NOTE Confidence: 0.935195495454545

00:12:34.080 --> 00:12:36.960 neutralize these various variants

NOTE Confidence: 0.935195495454545

00:12:36.960 --> 00:12:39.370 at I see 50 levels in the sub

NOTE Confidence: 0.935195495454545

00:12:39.370 --> 00:12:40.600 100 microgram levels.

NOTE Confidence: 0.935195495454545

00:12:40.600 --> 00:12:43.060 And then finally in collaboration with

NOTE Confidence: 0.935195495454545

00:12:43.127 --> 00:12:45.402 Primavera Chara at Duke University

NOTE Confidence: 0.935195495454545

00:12:45.402 --> 00:12:47.222 who's a structural biologist.

NOTE Confidence: 0.935195495454545

00:12:47.230 --> 00:12:51.590 Then we solve the structure for

NOTE Confidence: 0.935195495454545

00:12:51.590 --> 00:12:53.984 DH1047 bound to the source Kobe 1RB.

NOTE Confidence: 0.935195495454545

00:12:53.990 --> 00:12:54.984 DI don't have time to tell you,

NOTE Confidence: 0.935195495454545

00:12:54.990 --> 00:12:56.790 tell you all about the details,

NOTE Confidence: 0.935195495454545

00:12:56.790 --> 00:12:59.030 but what I want to just briefly

NOTE Confidence: 0.935195495454545

00:12:59.030 --> 00:13:01.105 tell you is that the DH1047,

NOTE Confidence: 0.935195495454545

00:13:01.105 --> 00:13:03.280 this broadly neutralizing and broadly

NOTE Confidence: 0.935195495454545

00:13:03.280 --> 00:13:05.020 protective antibody against our

NOTE Confidence: 0.935195495454545

00:13:05.077 --> 00:13:06.907 Becca viruses then actually binds to

NOTE Confidence: 0.935195495454545

00:13:06.907 --> 00:13:09.539 the inner side of this or Becca virus RBD.

NOTE Confidence: 0.935195495454545

00:13:09.540 --> 00:13:11.332 So in a more detailed paper that

NOTE Confidence: 0.935195495454545

00:13:11.332 --> 00:13:12.779 was published by Eric Holman,

NOTE Confidence: 0.935195495454545

00:13:12.780 --> 00:13:14.990 Sapphire and colleagues then an

NOTE Confidence: 0.935195495454545

00:13:14.990 --> 00:13:17.200 antibody that they described called

NOTE Confidence: 0.9340599

00:13:17.273 --> 00:13:19.753 RB D6 or COVID 250 then actually has

NOTE Confidence: 0.9340599

00:13:19.753 --> 00:13:22.430 almost the identical footprint of this

NOTE Confidence: 0.9340599

00:13:22.430 --> 00:13:24.620 particular antibody that I told you.

NOTE Confidence: 0.9340599

00:13:24.620 --> 00:13:27.500 So not only did we demonstrate that a

NOTE Confidence: 0.9340599

00:13:27.500 --> 00:13:29.418 DH1047 has his broad activity in mice,

NOTE Confidence: 0.9340599

00:13:29.420 --> 00:13:31.418 but on a more practical level,

NOTE Confidence: 0.9340599

00:13:31.420 --> 00:13:33.541 we think that the epitope or the

NOTE Confidence: 0.9340599

00:13:33.541 --> 00:13:35.383 footprint bound by this antibody

NOTE Confidence: 0.9340599

00:13:35.383 --> 00:13:37.553 is actually a rational target

NOTE Confidence: 0.9340599

00:13:37.553 --> 00:13:38.855 for panzerbecovirus vaccines.

NOTE Confidence: 0.9340599

00:13:38.860 --> 00:13:41.098 And we're actually interested in utilizing

NOTE Confidence: 0.9340599

00:13:41.098 --> 00:13:43.012 this knowledge for deploying and

NOTE Confidence: 0.9340599

00:13:43.012 --> 00:13:45.240 developing optimal vaccination strategies

NOTE Confidence: 0.9340599

00:13:45.240 --> 00:13:49.580 against this group of SARS related viruses.

NOTE Confidence: 0.9340599

00:13:49.580 --> 00:13:51.362 In fact, that some of our

NOTE Confidence: 0.9340599

00:13:51.362 --> 00:13:52.940 work also spans this area.

NOTE Confidence: 0.9340599

00:13:52.940 --> 00:13:55.996 So I think it's also clear that no

NOTE Confidence: 0.9340599

00:13:55.996 --> 00:13:57.725 universal vaccines exist against

NOTE Confidence: 0.9340599

00:13:57.725 --> 00:14:00.377 this group of SARS related viruses,

NOTE Confidence: 0.9340599

00:14:00.380 --> 00:14:02.036 although we have a number of

NOTE Confidence: 0.9340599

00:14:02.036 --> 00:14:03.505 individuals that are working on

NOTE Confidence: 0.9340599

00:14:03.505 --> 00:14:05.445 approaches that have so far proved

NOTE Confidence: 0.9340599

00:14:05.445 --> 00:14:07.600 to be successful in animal models.

NOTE Confidence: 0.9340599

00:14:07.600 --> 00:14:09.634 So we designed a vaccine approach

NOTE Confidence: 0.9340599

00:14:09.634 --> 00:14:11.634 that we were interested in really

NOTE Confidence: 0.9340599

00:14:11.634 --> 00:14:13.380 based on a heterologous boost to

NOTE Confidence: 0.9340599

00:14:13.380 --> 00:14:15.877 try to harness the immune system to

NOTE Confidence: 0.9340599

00:14:15.877 --> 00:14:17.988 target these cross reactive B cells

NOTE Confidence: 0.9340599

00:14:17.988 --> 00:14:19.558 to these conserve sites including

NOTE Confidence: 0.9340599

00:14:19.558 --> 00:14:21.696 the site that is targeted by DH1047

NOTE Confidence: 0.9340599

00:14:21.696 --> 00:14:23.712 or even more conserve sites within

NOTE Confidence: 0.9340599

00:14:23.712 --> 00:14:25.600 the machinery of the S2 domain.

NOTE Confidence: 0.9340599

00:14:25.600 --> 00:14:28.001 So the subunit 2 or the stock

NOTE Confidence: 0.9340599

00:14:28.001 --> 00:14:30.228 that is shown here in green.

NOTE Confidence: 0.9340599

00:14:30.230 --> 00:14:32.904 So some of these conserve sites include

NOTE Confidence: 0.9340599

00:14:32.910 --> 00:14:35.024 the fusion peptide as well as the

NOTE Confidence: 0.9340599

00:14:35.024 --> 00:14:37.531 stem Helix loop that have now been

NOTE Confidence: 0.9340599

00:14:37.531 --> 00:14:39.829 described by David Weissler and colleagues.

NOTE Confidence: 0.9340599

00:14:39.830 --> 00:14:42.044 And these sites can actually are

NOTE Confidence: 0.9340599

00:14:42.044 --> 00:14:44.070 highly conserved among these viruses.

NOTE Confidence: 0.9340599

00:14:44.070 --> 00:14:45.588 And not just within these viruses,

NOTE Confidence: 0.9340599

00:14:45.590 --> 00:14:47.430 but the fusion peptide is sort of a,

NOTE Confidence: 0.9340599

00:14:47.430 --> 00:14:49.428 you know, this,

NOTE Confidence: 0.9340599

00:14:49.430 --> 00:14:50.998 you know,

NOTE Confidence: 0.9340599

00:14:50.998 --> 00:14:55.009 general type of protein motif on

NOTE Confidence: 0.9340599

00:14:55.009 --> 00:14:58.327 type 1 membranes of these various

NOTE Confidence: 0.9340599

00:14:58.327 --> 00:15:01.420 infectious viruses that infect humans.

NOTE Confidence: 0.9340599

00:15:01.420 --> 00:15:02.724 So I don't have time to tell you

NOTE Confidence: 0.9340599

00:15:02.724 --> 00:15:04.059 all about the details of this data.

NOTE Confidence: 0.9340599

00:15:04.060 --> 00:15:06.260 But utilizing the design of

NOTE Confidence: 0.9340599

00:15:06.260 --> 00:15:07.580 these chimeric spikes,

NOTE Confidence: 0.9340599

00:15:07.580 --> 00:15:09.974 then we aim to boost mice in a manner

NOTE Confidence: 0.9340599

00:15:09.974 --> 00:15:12.405 that could direct their immune systems

NOTE Confidence: 0.9340599

00:15:12.405 --> 00:15:14.500 to these highly conserved areas.

NOTE Confidence: 0.9340599

00:15:14.500 --> 00:15:16.600 And we aim to try to increase

NOTE Confidence: 0.9340599

00:15:16.600 --> 00:15:17.934 immune coverage against these

NOTE Confidence: 0.9340599

00:15:17.934 --> 00:15:19.056 genetically divergent Sarbeca

NOTE Confidence: 0.9340599

00:15:19.056 --> 00:15:21.687 viruses that are shown here on the

NOTE Confidence: 0.9340599

00:15:21.687 --> 00:15:23.337 left by this phylogenetic tree.

NOTE Confidence: 0.9340599

00:15:23.340 --> 00:15:24.572 So just to tell you a little

NOTE Confidence: 0.9340599

00:15:24.572 --> 00:15:26.098 bit of the details of this data.

NOTE Confidence: 0.9340599

00:15:26.100 --> 00:15:28.350 Then the chimeric spike boosted mice

NOTE Confidence: 0.9340599

00:15:28.350 --> 00:15:31.555 that I I am telling you about are

NOTE Confidence: 0.9340599

00:15:31.555 --> 00:15:34.699 actually shown in Group one or group 2.

NOTE Confidence: 0.9340599

00:15:34.700 --> 00:15:37.238 So they were either given to the mice in

NOTE Confidence: 0.9340599

00:15:37.238 --> 00:15:40.220 a Multiplex manner or boosted separately.

NOTE Confidence: 0.9340599

00:15:40.220 --> 00:15:43.156 And the what I want to draw your

NOTE Confidence: 0.9340599

00:15:43.156 --> 00:15:45.811 attention to is that Group 4 is

NOTE Confidence: 0.9340599

00:15:45.811 --> 00:15:47.664 actually AM RNA vaccinated mouse

NOTE Confidence: 0.9340599

00:15:47.664 --> 00:15:49.890 group that received a similar vaccine

NOTE Confidence: 0.9340599

00:15:49.952 --> 00:15:52.016 to the Pfizer and Moderna vaccine.

NOTE Confidence: 0.9340599

00:15:52.020 --> 00:15:53.964 So whenever we vaccinate these mice

NOTE Confidence: 0.9340599

00:15:53.964 --> 00:15:56.211 and begin to compare the neutralizing

NOTE Confidence: 0.9340599

00:15:56.211 --> 00:15:57.991 activities of these various

NOTE Confidence: 0.9340599

00:15:57.991 --> 00:15:59.771 vaccines including our vaccines,

NOTE Confidence: 0.9340599

00:15:59.780 --> 00:16:01.454 then what we observed with our

NOTE Confidence: 0.9340599

00:16:01.454 --> 00:16:03.763 vaccines is that we were able to

NOTE Confidence: 0.9340599

00:16:03.763 --> 00:16:05.279 elicit broadly neutralizing antibodies

NOTE Confidence: 0.9340599

00:16:05.279 --> 00:16:07.416 not just against the original SARS

NOTE Confidence: 0.9340599

00:16:07.416 --> 00:16:09.740 and SARS Co V2 but also against

NOTE Confidence: 0.9340599

00:16:09.812 --> 00:16:12.048 these more genetically divergent

NOTE Confidence: 0.9340599

00:16:12.048 --> 00:16:14.284 preemergent SARS related viruses.

NOTE Confidence: 0.9340599

00:16:14.290 --> 00:16:16.198 More importantly and I think a

NOTE Confidence: 0.9340599

00:16:16.198 --> 00:16:18.222 far more stringent test is that

NOTE Confidence: 0.9340599

00:16:18.222 --> 00:16:19.248 whenever we introduce

NOTE Confidence: 0.927624013333333

00:16:19.250 --> 00:16:21.326 viruses that were not included in

NOTE Confidence: 0.927624013333333

00:16:21.326 --> 00:16:23.390 the vaccine cocktail to these mice

NOTE Confidence: 0.927624013333333

00:16:23.390 --> 00:16:25.244 including a heterologous WI V1 or

NOTE Confidence: 0.927624013333333

00:16:25.244 --> 00:16:27.570 even a very hard to neutralize at

NOTE Confidence: 0.927624013333333

00:16:27.570 --> 00:16:29.727 the time the so-called beta variant,

NOTE Confidence: 0.927624013333333

00:16:29.727 --> 00:16:32.312 then our vaccines can fully

NOTE Confidence: 0.927624013333333

00:16:32.312 --> 00:16:34.965 protect mice against both lower and

NOTE Confidence: 0.927624013333333

00:16:34.965 --> 00:16:36.425 upper airway virus replication.

NOTE Confidence: 0.927624013333333

00:16:36.430 --> 00:16:38.670 So we think that this could be a

NOTE Confidence: 0.927624013333333

00:16:38.670 --> 00:16:41.190 potentially a strategy among many strategies.

NOTE Confidence: 0.927624013333333

00:16:41.190 --> 00:16:43.206 So this is by no means you know that

NOTE Confidence: 0.927624013333333

00:16:43.206 --> 00:16:46.158 one of the by no means the only approach

NOTE Confidence: 0.927624013333333

00:16:46.158 --> 00:16:48.330 that different individuals are pursuing.

NOTE Confidence: 0.927624013333333

00:16:48.330 --> 00:16:51.632 But we think that this could be a

NOTE Confidence: 0.927624013333333

00:16:51.632 --> 00:16:53.900 strategy to to have a tool in our

NOTE Confidence: 0.927624013333333

00:16:53.900 --> 00:16:55.452 armamentarium for dealing with these

NOTE Confidence: 0.927624013333333

00:16:55.452 --> 00:16:56.856 genetically divergent viruses that

NOTE Confidence: 0.927624013333333

00:16:56.856 --> 00:16:59.439 could emerge at a later point in time.

NOTE Confidence: 0.927624013333333

00:16:59.440 --> 00:17:01.386 And we think that this could perhaps

NOTE Confidence: 0.927624013333333

00:17:01.386 --> 00:17:03.120 be a strategy for preventing,

NOTE Confidence: 0.927624013333333

00:17:03.120 --> 00:17:03.944 God forbid,

NOTE Confidence: 0.927624013333333

00:17:03.944 --> 00:17:07.240 a future starts Kobe 3 virus emergence event.

NOTE Confidence: 0.927624013333333

00:17:07.240 --> 00:17:09.165 So this is clearly one of the

NOTE Confidence: 0.927624013333333

00:17:09.165 --> 00:17:10.988 approaches that we think is successful.

NOTE Confidence: 0.927624013333333

00:17:10.988 --> 00:17:12.573 But there are other approaches

NOTE Confidence: 0.927624013333333

00:17:12.573 --> 00:17:13.598 that not only us,

NOTE Confidence: 0.927624013333333

00:17:13.600 --> 00:17:15.959 but others are pursuing in the field.

NOTE Confidence: 0.927624013333333

00:17:15.960 --> 00:17:17.451 And one of the approaches that I

NOTE Confidence: 0.927624013333333

00:17:17.451 --> 00:17:20.022 want to sort of end with in terms of

NOTE Confidence: 0.927624013333333

00:17:20.022 --> 00:17:21.912 the coronavirus aspect of my talk is

NOTE Confidence: 0.927624013333333

00:17:21.912 --> 00:17:23.998 to tell you a little bit about how

NOTE Confidence: 0.927624013333333

00:17:23.998 --> 00:17:25.788 we're thinking about dealing with

NOTE Confidence: 0.927624013333333

00:17:25.788 --> 00:17:28.819 more of the breadth of these various

NOTE Confidence: 0.927624013333333

00:17:28.819 --> 00:17:30.355 highly pathogenic coronaviruses.

NOTE Confidence: 0.927624013333333

00:17:30.360 --> 00:17:33.356 So in a collaboration with Duke University,

NOTE Confidence: 0.927624013333333

00:17:33.360 --> 00:17:36.708 then what we began to do is to engineer

NOTE Confidence: 0.927624013333333

00:17:36.708 --> 00:17:38.858 nanoparticles by including various RBD's.

NOTE Confidence: 0.927624013333333

00:17:38.858 --> 00:17:41.242 So the RBD remember is a site that

NOTE Confidence: 0.927624013333333

00:17:41.242 --> 00:17:42.945 contains these Achilles heels on

NOTE Confidence: 0.927624013333333

00:17:42.945 --> 00:17:45.355 these various viruses and one of the

NOTE Confidence: 0.927624013333333

00:17:45.355 --> 00:17:47.494 areas that we're interested in is to

NOTE Confidence: 0.927624013333333

00:17:47.494 --> 00:17:49.048 be able to expand the immune breath,

NOTE Confidence: 0.927624013333333

00:17:49.050 --> 00:17:50.630 the protective immune breath

NOTE Confidence: 0.927624013333333

00:17:50.630 --> 00:17:52.210 against these various viruses.

NOTE Confidence: 0.927624013333333

00:17:52.210 --> 00:17:54.721 So in a proof of concept study that I'm

NOTE Confidence: 0.927624013333333

00:17:54.721 --> 00:17:57.169 going to just tell you about real quick,

NOTE Confidence: 0.927624013333333

00:17:57.170 --> 00:18:00.455 then what we decided to do was to expand

NOTE Confidence: 0.927624013333333

00:18:00.455 --> 00:18:02.698 the breath of our our vaccine that

NOTE Confidence: 0.927624013333333

00:18:02.698 --> 00:18:04.960 I'm going to tell you about not just

NOTE Confidence: 0.927624013333333

00:18:04.960 --> 00:18:06.844 against group to be Cerbecca viruses,

NOTE Confidence: 0.927624013333333

00:18:06.850 --> 00:18:08.101 but also group,

NOTE Confidence: 0.927624013333333

00:18:08.101 --> 00:18:10.186 group to see Marbecca viruses.

NOTE Confidence: 0.927624013333333

00:18:10.190 --> 00:18:13.790 So we engineered A ferritin nanoparticle

NOTE Confidence: 0.927624013333333

00:18:13.790 --> 00:18:16.135 vaccine and tagged three of these

NOTE Confidence: 0.927624013333333

00:18:16.135 --> 00:18:17.531 various receptor binding domains

NOTE Confidence: 0.927624013333333

00:18:17.531 --> 00:18:19.269 from not only group to obese,

NOTE Confidence: 0.927624013333333

00:18:19.270 --> 00:18:21.670 but also group to C sarbacoviruses.

NOTE Confidence: 0.927624013333333

00:18:21.670 --> 00:18:24.022 And we began to study the immunogenicity

NOTE Confidence: 0.927624013333333

00:18:24.022 --> 00:18:26.370 and the ability of the epitopes on

NOTE Confidence: 0.927624013333333

00:18:26.370 --> 00:18:27.960 the receptor binding domains to

NOTE Confidence: 0.927624013333333

00:18:27.960 --> 00:18:30.231 be presented in a manner that the

NOTE Confidence: 0.927624013333333

00:18:30.231 --> 00:18:31.836 immune system immune system could

NOTE Confidence: 0.927624013333333

00:18:31.836 --> 00:18:33.823 see them and generate optimal immune

NOTE Confidence: 0.927624013333333

00:18:33.823 --> 00:18:36.070 responses in at least in mouse models.

NOTE Confidence: 0.927624013333333

00:18:36.070 --> 00:18:37.710 So I don't have time to tell you

NOTE Confidence: 0.927624013333333

00:18:37.710 --> 00:18:39.389 all about the details of that data,

NOTE Confidence: 0.927624013333333

00:18:39.390 --> 00:18:41.766 but I'll show you some of the data

NOTE Confidence: 0.927624013333333

00:18:41.766 --> 00:18:43.954 that we think is important and and

NOTE Confidence: 0.927624013333333

00:18:43.954 --> 00:18:46.519 being able to guide universal vaccine

NOTE Confidence: 0.927624013333333

00:18:46.519 --> 00:18:47.139 approaches.

NOTE Confidence: 0.927624013333333

00:18:47.140 --> 00:18:48.939 So the first question that we asked

NOTE Confidence: 0.927624013333333

00:18:48.939 --> 00:18:50.918 is whether or not this multimeric

NOTE Confidence: 0.927624013333333

00:18:50.918 --> 00:18:52.833 nanoparticle RBD vaccine could elicit

NOTE Confidence: 0.927624013333333

00:18:52.833 --> 00:18:54.427 this protective immunity against

NOTE Confidence: 0.927624013333333

00:18:54.427 --> 00:18:55.959 these genetically divergent not

NOTE Confidence: 0.927624013333333

00:18:55.959 --> 00:18:57.491 just SARS related virus,

NOTE Confidence: 0.927624013333333

00:18:57.500 --> 00:19:00.380 but also MERS related viruses that

NOTE Confidence: 0.927624013333333

00:19:00.380 --> 00:19:02.858 we know are poised for emergence

NOTE Confidence: 0.927624013333333

00:19:02.858 --> 00:19:04.889 since MERS coronavirus continues to

NOTE Confidence: 0.927624013333333

00:19:04.889 --> 00:19:07.059 emerge each year in the Middle East.

NOTE Confidence: 0.927624013333333

00:19:07.060 --> 00:19:10.196 But we wanted to test these viruses,

NOTE Confidence: 0.91796273

00:19:10.200 --> 00:19:12.260 test these this vaccine against

NOTE Confidence: 0.91796273

00:19:12.260 --> 00:19:14.785 these viruses not just in stringent

NOTE Confidence: 0.91796273

00:19:14.785 --> 00:19:18.040 in vitro assays but also in highly

NOTE Confidence: 0.91796273

00:19:18.040 --> 00:19:20.617 pathogenic animal models of of disease.

NOTE Confidence: 0.91796273

00:19:20.620 --> 00:19:22.908 So when we evaluated the ability of these

NOTE Confidence: 0.91796273

00:19:22.908 --> 00:19:25.517 of the vaccine to elicit protective

NOTE Confidence: 0.91796273

00:19:25.517 --> 00:19:27.493 immunity in particular neutralizing

NOTE Confidence: 0.91796273

00:19:27.493 --> 00:19:29.619 antibodies against authentic viruses.

NOTE Confidence: 0.91796273

00:19:29.620 --> 00:19:32.092 So this this is not pseudovirus

NOTE Confidence: 0.91796273

00:19:32.092 --> 00:19:33.740 but actually authentic virus.

NOTE Confidence: 0.91796273

00:19:33.740 --> 00:19:37.240 Then this Multimeric RBD vaccine not only

NOTE Confidence: 0.91796273

00:19:37.240 --> 00:19:40.222 elicited high levels of neutralizing

NOTE Confidence: 0.91796273

00:19:40.222 --> 00:19:43.018 antibodies against zoonotic viruses,

NOTE Confidence: 0.91796273

00:19:43.020 --> 00:19:46.185 also the original sarscovy from 2003,

NOTE Confidence: 0.91796273

00:19:46.185 --> 00:19:48.855 but we could also elicit whenever

NOTE Confidence: 0.91796273

00:19:48.855 --> 00:19:52.628 we begin to add more relevant RBD's

NOTE Confidence: 0.91796273

00:19:52.628 --> 00:19:55.100 neutralizing antibodies against

NOTE Confidence: 0.91796273

00:19:55.100 --> 00:19:57.602 this other group to see MERS, MERS,

NOTE Confidence: 0.91796273

00:19:57.602 --> 00:19:59.414 coronavirus as well as a whole

NOTE Confidence: 0.91796273

00:19:59.414 --> 00:20:01.660 host of other MERS related viruses.

NOTE Confidence: 0.91796273

00:20:01.660 --> 00:20:04.020 Which I don't have time to tell you

NOTE Confidence: 0.91796273

00:20:04.020 --> 00:20:06.360 about that data and a more stringent

NOTE Confidence: 0.91796273

00:20:06.360 --> 00:20:08.490 test whenever we evaluate the vaccine

NOTE Confidence: 0.91796273

00:20:08.559 --> 00:20:10.549 and not just protecting against

NOTE Confidence: 0.91796273

00:20:10.549 --> 00:20:12.539 mortality and a highly pathogenic

NOTE Confidence: 0.91796273

00:20:12.607 --> 00:20:14.038 SARS Co V1 mouse model,

NOTE Confidence: 0.91796273

00:20:14.038 --> 00:20:17.310 but what we what we see is that.

NOTE Confidence: 0.91796273

00:20:17.310 --> 00:20:19.185 The multimeric vaccine can not

NOTE Confidence: 0.91796273

00:20:19.185 --> 00:20:21.060 only protect against lung virus

NOTE Confidence: 0.91796273

00:20:21.129 --> 00:20:23.189 replication relative to a control,

NOTE Confidence: 0.91796273

00:20:23.190 --> 00:20:25.614 but it can also protect against

NOTE Confidence: 0.91796273

00:20:25.614 --> 00:20:27.230 upper airway virus replication.

NOTE Confidence: 0.91796273

00:20:27.230 --> 00:20:29.288 And then similarly whenever we evaluate

NOTE Confidence: 0.91796273

00:20:29.288 --> 00:20:31.556 the ability of this trivalent or

NOTE Confidence: 0.91796273

00:20:31.556 --> 00:20:33.646 multimeric vaccine to protect against

NOTE Confidence: 0.91796273

00:20:33.646 --> 00:20:36.064 MERS coronavirus then we see fairly

NOTE Confidence: 0.91796273

00:20:36.064 --> 00:20:37.894 stringent protection against both lower

NOTE Confidence: 0.91796273

00:20:37.894 --> 00:20:41.189 and upper airway virus replication.

NOTE Confidence: 0.91796273

00:20:41.190 --> 00:20:43.614 So I'm in conclusion then this is another

NOTE Confidence: 0.91796273

00:20:43.614 --> 00:20:45.389 approach that we're excited about.

NOTE Confidence: 0.91796273

00:20:45.390 --> 00:20:47.735 So the so-called multimeric vaccine

NOTE Confidence: 0.91796273

00:20:47.735 --> 00:20:50.080 expressing various Group 2B and

NOTE Confidence: 0.91796273

00:20:50.150 --> 00:20:51.928 Group 2C receptor binding domains

NOTE Confidence: 0.91796273

00:20:51.928 --> 00:20:54.364 to elicit these types of broadly

NOTE Confidence: 0.91796273

00:20:54.364 --> 00:20:55.470 neutralizing antibodies.

NOTE Confidence: 0.91796273

00:20:55.470 --> 00:20:57.558 And we think that this could be one

NOTE Confidence: 0.91796273

00:20:57.558 --> 00:20:59.915 of the many strategies that not only

NOTE Confidence: 0.91796273

00:20:59.915 --> 00:21:02.018 us but in other individuals that

NOTE Confidence: 0.91796273

00:21:02.018 --> 00:21:03.330 are pursuing similar strategies.

NOTE Confidence: 0.91796273

00:21:03.330 --> 00:21:04.000 In particular,

NOTE Confidence: 0.91796273

00:21:04.000 --> 00:21:06.010 I'm David Viessler from the University

NOTE Confidence: 0.91796273

00:21:06.010 --> 00:21:07.664 of Washington and Howard Hughes

NOTE Confidence: 0.91796273

00:21:07.664 --> 00:21:09.524 Medical Institute as well as Pamela

NOTE Confidence: 0.91796273

00:21:09.524 --> 00:21:11.602 Bjorkman who also have other really

NOTE Confidence: 0.91796273

00:21:11.602 --> 00:21:12.288 promising approaches.

NOTE Confidence: 0.91796273

00:21:12.290 --> 00:21:14.425 So I would be remiss not to

NOTE Confidence: 0.91796273

00:21:14.425 --> 00:21:16.010 mention their work in this area,

NOTE Confidence: 0.91796273

00:21:16.010 --> 00:21:19.640 which I think is also critically

NOTE Confidence: 0.91796273

00:21:19.640 --> 00:21:21.358 important and some future directions,

NOTE Confidence: 0.91796273

00:21:21.358 --> 00:21:23.568 at least for this particular part of my talk.

NOTE Confidence: 0.91796273

00:21:23.570 --> 00:21:24.551 Then you know,

NOTE Confidence: 0.91796273

00:21:24.551 --> 00:21:26.186 we're of course interested in

NOTE Confidence: 0.91796273

00:21:26.186 --> 00:21:27.567 evaluating whether or not we can

NOTE Confidence: 0.91796273

00:21:27.570 --> 00:21:30.027 begin to boost some of these conserved

NOTE Confidence: 0.91796273

00:21:30.027 --> 00:21:31.929 epitopes within the S2 machinery.

NOTE Confidence: 0.91796273

00:21:31.930 --> 00:21:33.484 So in particular the fusion peptide

NOTE Confidence: 0.91796273

00:21:33.484 --> 00:21:35.410 as well as the same Helix loop,

NOTE Confidence: 0.91796273

00:21:35.410 --> 00:21:36.718 irrelevant animal models,

NOTE Confidence: 0.91796273

00:21:36.718 --> 00:21:39.770 as well as these more multimeric vaccines.

NOTE Confidence: 0.91796273

00:21:39.770 --> 00:21:41.894 And not just their ability to

NOTE Confidence: 0.91796273

00:21:41.894 --> 00:21:43.396 prevent mortality and highly

NOTE Confidence: 0.91796273

00:21:43.396 --> 00:21:44.924 pathogenic disease in mice,

NOTE Confidence: 0.91796273

00:21:44.930 --> 00:21:47.222 but also the ability to prevent

NOTE Confidence: 0.91796273

00:21:47.222 --> 00:21:49.285 the transmission of these highly

NOTE Confidence: 0.91796273

00:21:49.285 --> 00:21:51.580 transmissible SARS Cov 2 variants.

NOTE Confidence: 0.91796273

00:21:51.580 --> 00:21:53.380 Another area that I'm actually

NOTE Confidence: 0.91796273

00:21:53.380 --> 00:21:55.285 just super interested in and will

NOTE Confidence: 0.91796273

00:21:55.285 --> 00:21:57.907 be an area that the lab will be

NOTE Confidence: 0.91796273

00:21:57.907 --> 00:21:59.590 expanding into is understanding

NOTE Confidence: 0.91796273

00:21:59.590 --> 00:22:02.115 sort of more fundamental mechanisms

NOTE Confidence: 0.91796273

00:22:02.115 --> 00:22:04.677 of the induction and generation

NOTE Confidence: 0.91796273

00:22:04.677 --> 00:22:06.766 and maintenance of plasma cells.

NOTE Confidence: 0.91796273

00:22:06.766 --> 00:22:08.356 And in particular long lived

NOTE Confidence: 0.91796273

00:22:08.356 --> 00:22:10.290 plasma cells and relevant tissues.

NOTE Confidence: 0.91796273

00:22:10.290 --> 00:22:11.490 Not just in the bone marrow,

NOTE Confidence: 0.91796273

00:22:11.490 --> 00:22:14.394 but also in relevant areas including

NOTE Confidence: 0.91796273

00:22:14.394 --> 00:22:16.730 the lemon appropriate or even

NOTE Confidence: 0.91796273

00:22:16.730 --> 00:22:18.728 in the upper and lower airway.

NOTE Confidence: 0.91796273

00:22:18.730 --> 00:22:21.555 Utilizing this really nice and

NOTE Confidence: 0.91796273

00:22:21.555 --> 00:22:24.328 elegant system for time stamping

NOTE Confidence: 0.91796273

00:22:24.328 --> 00:22:27.604 and being able to track the

NOTE Confidence: 0.9366321

00:22:27.610 --> 00:22:29.186 generation and longevity of

NOTE Confidence: 0.9366321

00:22:29.186 --> 00:22:31.156 these cells in various tissues.

NOTE Confidence: 0.9366321

00:22:31.160 --> 00:22:32.770 So in the last couple minutes then

NOTE Confidence: 0.9366321

00:22:32.770 --> 00:22:34.635 I just want to just briefly tell

NOTE Confidence: 0.9366321

00:22:34.635 --> 00:22:36.315 you about another group of viruses.

NOTE Confidence: 0.9366321

00:22:36.320 --> 00:22:37.760 So I I mentioned very early

NOTE Confidence: 0.9366321

00:22:37.760 --> 00:22:39.304 in my talk about, you know,

NOTE Confidence: 0.9366321

00:22:39.304 --> 00:22:41.640 the 26 viral families that can infect humans.

NOTE Confidence: 0.9366321

00:22:41.640 --> 00:22:43.089 So Corona Verde is one of those

NOTE Confidence: 0.9366321

00:22:43.089 --> 00:22:44.638 families that I just told you about.

NOTE Confidence: 0.9366321

00:22:44.640 --> 00:22:46.640 But another of those families

NOTE Confidence: 0.9366321

00:22:46.640 --> 00:22:48.240 includes the Flavy Verde,

NOTE Confidence: 0.9366321

00:22:48.240 --> 00:22:53.800 which as we also know has been a a major,

NOTE Confidence: 0.9366321

00:22:53.800 --> 00:22:57.855 you know, source of human infections.

NOTE Confidence: 0.9366321

00:22:57.855 --> 00:22:59.070 And in particular,

NOTE Confidence: 0.9366321

00:22:59.070 --> 00:23:01.095 including members from from from

NOTE Confidence: 0.9366321

00:23:01.095 --> 00:23:03.822 this group have made many important

NOTE Confidence: 0.9366321

00:23:03.822 --> 00:23:05.942 contributions whenever Zika virus which

NOTE Confidence: 0.9366321

00:23:05.942 --> 00:23:08.713 is a flaming virus emerged in 2015.

NOTE Confidence: 0.9366321

00:23:08.713 --> 00:23:11.114 But a virus that I'm actually really

NOTE Confidence: 0.9366321

00:23:11.114 --> 00:23:12.849 interested in is dengue virus.

NOTE Confidence: 0.9366321

00:23:12.850 --> 00:23:15.251 And the reason why I'm interested in

NOTE Confidence: 0.9366321

00:23:15.251 --> 00:23:17.542 this virus because it actually breaks

NOTE Confidence: 0.9366321

00:23:17.542 --> 00:23:19.936 the many of the canonical immunological

NOTE Confidence: 0.9366321

00:23:19.936 --> 00:23:22.683 rules that we typically think of in

NOTE Confidence: 0.9366321

00:23:22.683 --> 00:23:24.698 terms of understanding antibody responses.

NOTE Confidence: 0.9366321

00:23:24.698 --> 00:23:27.138 So this virus is transmitted

NOTE Confidence: 0.9366321

00:23:27.138 --> 00:23:29.090 by a many vectors.

NOTE Confidence: 0.9366321

00:23:29.090 --> 00:23:31.757 One of these vectors includes 80S aegypti

NOTE Confidence: 0.9366321

00:23:31.757 --> 00:23:34.221 and it's highly prevalent in tropical

NOTE Confidence: 0.9366321

00:23:34.221 --> 00:23:37.126 areas including my very own El Salvador.

NOTE Confidence: 0.9366321

00:23:37.130 --> 00:23:39.050 And it infects upwards of

NOTE Confidence: 0.9366321

00:23:39.050 --> 00:23:40.970 400 million people each year.

NOTE Confidence: 0.9366321

00:23:40.970 --> 00:23:43.268 And the group that's most afflicted

NOTE Confidence: 0.9366321

00:23:43.268 --> 00:23:45.801 by the most severe forms of

NOTE Confidence: 0.9366321

00:23:45.801 --> 00:23:47.645 the disease includes children.

NOTE Confidence: 0.9366321

00:23:47.650 --> 00:23:50.154 And one of the areas that I'm interested

NOTE Confidence: 0.9366321

00:23:50.154 --> 00:23:52.001 in studying Danga virus is really

NOTE Confidence: 0.9366321

00:23:52.001 --> 00:23:54.220 more on the immune side of things.

NOTE Confidence: 0.9366321

00:23:54.220 --> 00:23:57.900 So and now a published paper as well

NOTE Confidence: 0.9366321

00:23:57.900 --> 00:24:01.450 as other epidemiologic papers in

NOTE Confidence: 0.9366321

00:24:01.450 --> 00:24:03.340 the New England Journal of Medicine.

NOTE Confidence: 0.9366321

00:24:03.340 --> 00:24:06.470 Then it's become increasingly clear

NOTE Confidence: 0.9366321

00:24:06.470 --> 00:24:08.840 that in zero negative children that

NOTE Confidence: 0.9366321

00:24:08.840 --> 00:24:11.100 received the only FDA approved vaccine,

NOTE Confidence: 0.9366321

00:24:11.100 --> 00:24:12.411 the socalled Invaxia,

NOTE Confidence: 0.9366321

00:24:12.411 --> 00:24:14.596 then these children have higher

NOTE Confidence: 0.9366321

00:24:14.596 --> 00:24:17.388 incidence of hospitalization in very

NOTE Confidence: 0.9366321

00:24:17.388 --> 00:24:19.932 young children compared to children who

NOTE Confidence: 0.9366321

00:24:19.932 --> 00:24:22.580 have had a prior dengue virus infection.

NOTE Confidence: 0.9366321

00:24:22.580 --> 00:24:23.492 So if you have,

NOTE Confidence: 0.9366321

00:24:23.492 --> 00:24:24.860 if you're a zero negative child,

NOTE Confidence: 0.9366321

00:24:24.860 --> 00:24:27.416 you live in an endemic area,

NOTE Confidence: 0.9366321

00:24:27.420 --> 00:24:28.938 you cannot actually get the vaccine.

NOTE Confidence: 0.9366321

00:24:28.940 --> 00:24:30.311 It's actually contraindicated

NOTE Confidence: 0.9366321

00:24:30.311 --> 00:24:32.139 in this particular group.

NOTE Confidence: 0.9366321

00:24:32.140 --> 00:24:36.476 So Aravinda De Silva is one of my

NOTE Confidence: 0.9366321

00:24:36.480 --> 00:24:38.990 postdoc mentors and he's actually

NOTE Confidence: 0.9366321

00:24:38.990 --> 00:24:41.704 supporting my program by letting me

NOTE Confidence: 0.9366321

00:24:41.704 --> 00:24:44.168 access PBMC samples from a cohort from

NOTE Confidence: 0.9366321

00:24:44.168 --> 00:24:46.576 the Philippines that which contains 0

NOTE Confidence: 0.9366321

00:24:46.576 --> 00:24:48.460 negative and 0 positive children who

NOTE Confidence: 0.9366321

00:24:48.517 --> 00:24:50.357 were vaccinated with being vaccia.

NOTE Confidence: 0.9366321

00:24:50.360 --> 00:24:52.645 So I'm actually really interested

NOTE Confidence: 0.9366321

00:24:52.645 --> 00:24:54.473 in understanding the fundamental

NOTE Confidence: 0.9366321

00:24:54.473 --> 00:24:56.104 properties of those monoclonal

NOTE Confidence: 0.9366321

00:24:56.104 --> 00:24:58.320 antibodies from these by basic groups

NOTE Confidence: 0.9366321

00:24:58.320 --> 00:25:00.840 of of children in terms of their

NOTE Confidence: 0.9366321

00:25:00.840 --> 00:25:03.003 baseline status and understanding what

NOTE Confidence: 0.9366321

00:25:03.003 --> 00:25:05.222 is particular about these antibody

NOTE Confidence: 0.9366321

00:25:05.222 --> 00:25:07.327 properties and these children that

NOTE Confidence: 0.9366321

00:25:07.327 --> 00:25:09.820 could potentially lead to enhanced disease.

NOTE Confidence: 0.9366321

00:25:09.820 --> 00:25:11.800 So just again,

NOTE Confidence: 0.9366321

00:25:11.800 --> 00:25:13.288 not really give you everything,

NOTE Confidence: 0.9366321

00:25:13.288 --> 00:25:14.981 but just to give you a little bit

NOTE Confidence: 0.9366321

00:25:14.981 --> 00:25:16.402 of the flavor of the things that

NOTE Confidence: 0.9366321

00:25:16.402 --> 00:25:17.848 we're interested in for the future.

NOTE Confidence: 0.9366321

00:25:17.850 --> 00:25:18.870 So with that,

NOTE Confidence: 0.9366321

00:25:18.870 --> 00:25:20.832 I'd like to acknowledge members who

NOTE Confidence: 0.9366321

00:25:20.832 --> 00:25:22.404 contributed to the to these studies,

NOTE Confidence: 0.9366321

00:25:22.410 --> 00:25:25.850 including members from UNC particular,

NOTE Confidence: 0.9366321

00:25:25.850 --> 00:25:28.225 my postdoctoral advisor Ralph Barrick

NOTE Confidence: 0.9366321

00:25:28.225 --> 00:25:31.522 and Aravinda De Silva from Duke University,

NOTE Confidence: 0.9366321

00:25:31.522 --> 00:25:32.450 Bart Haynes,

NOTE Confidence: 0.9366321

00:25:32.450 --> 00:25:33.330 Kevin Saunders.

NOTE Confidence: 0.9366321

00:25:33.330 --> 00:25:35.970 And then our collaborator on all

NOTE Confidence: 0.9366321

00:25:35.970 --> 00:25:37.410 the mRNA work,

NOTE Confidence: 0.9366321

00:25:37.410 --> 00:25:40.352 Drew Wiseman and also a nascent

NOTE Confidence: 0.9366321

00:25:40.352 --> 00:25:42.236 collaborator who's also assistant

NOTE Confidence: 0.9366321

00:25:42.236 --> 00:25:44.120 professor at University of

NOTE Confidence: 0.93936396

00:25:44.192 --> 00:25:46.010 Pennsylvania Norbert Party,

NOTE Confidence: 0.93936396

00:25:46.010 --> 00:25:47.846 who did his post for Drew.

NOTE Confidence: 0.93936396

00:25:47.850 --> 00:25:49.530 We're also going to be collaborating

NOTE Confidence: 0.93936396

00:25:49.530 --> 00:25:51.422 with him on on mRNA approaches

NOTE Confidence: 0.93936396

00:25:51.422 --> 00:25:52.966 to emerging flaving viruses.

NOTE Confidence: 0.93936396

00:25:52.970 --> 00:25:55.208 So more to come on that.

NOTE Confidence: 0.93936396

00:25:55.210 --> 00:25:57.090 Also my funding acknowledgements from

NOTE Confidence: 0.93936396

00:25:57.090 --> 00:25:58.970 the Howard Hughes Medical Institute.

NOTE Confidence: 0.93936396

00:25:58.970 --> 00:26:00.170 Thank you very much for your attention. So

NOTE Confidence: 0.93663293

00:26:11.280 --> 00:26:13.200 you're good with time. So we can take

NOTE Confidence: 0.93663293

00:26:13.200 --> 00:26:14.559 some questions from the audience.

NOTE Confidence: 0.917228

00:26:23.040 --> 00:26:24.160 So I have the microphone.

NOTE Confidence: 0.917228

00:26:30.930 --> 00:26:32.890 Excellent talk. Thank you, David.

NOTE Confidence: 0.917228

00:26:32.890 --> 00:26:34.890 My question is about the

NOTE Confidence: 0.917228

00:26:34.890 --> 00:26:36.562 conserved epitope to you.

NOTE Confidence: 0.917228

00:26:36.562 --> 00:26:38.652 You found that the monocle

NOTE Confidence: 0.917228

00:26:38.652 --> 00:26:40.766 Ronnie body binds to has that.

NOTE Confidence: 0.917228

00:26:40.770 --> 00:26:44.250 How is it resistant to evasion

NOTE Confidence: 0.917228

00:26:44.250 --> 00:26:45.894 and is that there's some kind

NOTE Confidence: 0.917228

00:26:45.894 --> 00:26:47.324 of a critical function that

NOTE Confidence: 0.917228

00:26:47.324 --> 00:26:48.689 the virus has to preserve?

NOTE Confidence: 0.917228

00:26:48.690 --> 00:26:49.955 And is it also preserved

NOTE Confidence: 0.917228

00:26:49.955 --> 00:26:50.967 in the Omicron linear?

NOTE Confidence: 0.93565387

00:26:51.250 --> 00:26:54.484 Yeah. So if if you incubate the

NOTE Confidence: 0.93565387

00:26:54.484 --> 00:26:56.523 antibody with Omicron and this

NOTE Confidence: 0.93565387

00:26:56.523 --> 00:26:58.007 various lineages for longer,

NOTE Confidence: 0.93565387

00:26:58.010 --> 00:27:00.170 you can have some neutralization.

NOTE Confidence: 0.93565387

00:27:00.170 --> 00:27:03.544 So even though many of the Omicron

NOTE Confidence: 0.93565387

00:27:03.544 --> 00:27:05.610 lineages haven't necessarily mutated

NOTE Confidence: 0.93565387

00:27:05.610 --> 00:27:07.370 the footprint of the antibody,

NOTE Confidence: 0.93565387

00:27:07.370 --> 00:27:09.190 then additional mutations within the

NOTE Confidence: 0.93565387

00:27:09.190 --> 00:27:11.921 RBD that are distal to the actual

NOTE Confidence: 0.93565387

00:27:11.921 --> 00:27:14.021 footprint epitope can actually alter

NOTE Confidence: 0.93565387

00:27:14.021 --> 00:27:16.090 the accessibility of the epitope.

NOTE Confidence: 0.93565387

00:27:16.090 --> 00:27:20.130 So you know much like many of the

NOTE Confidence: 0.93565387

00:27:20.130 --> 00:27:22.570 monoclonal antibody therapies then

NOTE Confidence: 0.93565387

00:27:22.570 --> 00:27:24.570 Omicron and its various lineages

NOTE Confidence: 0.93565387

00:27:24.570 --> 00:27:26.977 including you know the latest XBB

NOTE Confidence: 0.93565387

00:27:26.977 --> 00:27:29.419 1.5 and its various lineages then

NOTE Confidence: 0.93565387

00:27:29.419 --> 00:27:31.081 have demonstrated the ability

NOTE Confidence: 0.93565387

00:27:31.081 --> 00:27:34.180 to evade this DH1047 antibody.

NOTE Confidence: 0.93565387

00:27:34.180 --> 00:27:35.044 So that's unfortunately,

NOTE Confidence: 0.93565387

00:27:35.044 --> 00:27:37.300 you know, just a a,

NOTE Confidence: 0.93565387

00:27:37.300 --> 00:27:41.575 a problem that the field has and and

NOTE Confidence: 0.93565387

00:27:41.575 --> 00:27:44.415 something that the virus has figured out by,

NOTE Confidence: 0.93565387

00:27:44.420 --> 00:27:45.042 you know,

NOTE Confidence: 0.93565387

00:27:45.042 --> 00:27:46.908 mutating sort of these distal and

NOTE Confidence: 0.93565387

00:27:46.908 --> 00:27:48.738 outside parts within the footprint,

NOTE Confidence: 0.93565387

00:27:48.740 --> 00:27:51.740 not even necessarily the footprint

NOTE Confidence: 0.93565387

00:27:51.740 --> 00:27:54.477 but but you know we're still excited

NOTE Confidence: 0.93565387

00:27:54.477 --> 00:27:56.518 about the ability of this to,

NOTE Confidence: 0.93565387

00:27:56.520 --> 00:27:57.278 you know,

NOTE Confidence: 0.93565387

00:27:57.278 --> 00:27:59.552 retain its function against these number

NOTE Confidence: 0.93565387

00:27:59.552 --> 00:28:01.638 of different zoonotic viruses that

NOTE Confidence: 0.93565387

00:28:01.640 --> 00:28:04.517 we know are poised for human emergence.

NOTE Confidence: 0.93565387

00:28:04.520 --> 00:28:06.080 David. Hey David, great talk.

NOTE Confidence: 0.93565387

00:28:06.080 --> 00:28:07.012 Thank you.

NOTE Confidence: 0.93565387

00:28:07.012 --> 00:28:07.478 I'm

NOTE Confidence: 0.942856

00:28:07.480 --> 00:28:09.532 curious what your your choice of

NOTE Confidence: 0.942856

00:28:09.532 --> 00:28:11.600 nanoparticles and is it important for the

NOTE Confidence: 0.942856

00:28:12.280 --> 00:28:13.204 these multivalent vaccines

NOTE Confidence: 0.942856

00:28:13.204 --> 00:28:14.436 for them to actually

NOTE Confidence: 0.942856

00:28:14.440 --> 00:28:17.317 be attached to a a particle or

NOTE Confidence: 0.942856

00:28:17.320 --> 00:28:19.320 that's is that advantageous compared

NOTE Confidence: 0.926569908571429

00:28:19.320 --> 00:28:22.386 to just having mix of proteins injected.

NOTE Confidence: 0.926569908571429

00:28:22.390 --> 00:28:24.062 Yeah, you know we think it we we

NOTE Confidence: 0.926569908571429

00:28:24.062 --> 00:28:25.979 think it might be and you know this

NOTE Confidence: 0.926569908571429

00:28:25.979 --> 00:28:27.701 this is certainly on on you know

NOTE Confidence: 0.926569908571429

00:28:27.701 --> 00:28:29.346 the more practical side is this is

NOTE Confidence: 0.926569908571429

00:28:29.350 --> 00:28:31.191 reflected by the by the potency and

NOTE Confidence: 0.926569908571429

00:28:31.191 --> 00:28:33.267 the amount of immune response we see.

NOTE Confidence: 0.926569908571429

00:28:33.270 --> 00:28:36.474 In particular you know the levels

NOTE Confidence: 0.926569908571429

00:28:36.474 --> 00:28:39.208 of serum neutralizing antibodies are

NOTE Confidence: 0.926569908571429

00:28:39.208 --> 00:28:41.648 greatly exceeded whenever we couple

NOTE Confidence: 0.926569908571429

00:28:41.648 --> 00:28:43.856 you know whatever protein of choice

NOTE Confidence: 0.926569908571429

00:28:43.856 --> 00:28:46.136 in this case that receptor binding

NOTE Confidence: 0.926569908571429

00:28:46.136 --> 00:28:49.120 domain in a multi in a multimaric form.

NOTE Confidence: 0.926569908571429

00:28:49.120 --> 00:28:51.280 You know for probably for reasons

NOTE Confidence: 0.926569908571429

00:28:51.280 --> 00:28:53.518 of you know activating you know

NOTE Confidence: 0.926569908571429

00:28:53.518 --> 00:28:56.676 besyl receptors in a in a better way

NOTE Confidence: 0.926569908571429

00:28:56.676 --> 00:28:59.280 potentially or in a more potent way.

NOTE Confidence: 0.926569908571429

00:28:59.280 --> 00:29:02.880 But that seems to be a feature that confers,

NOTE Confidence: 0.926569908571429

00:29:02.880 --> 00:29:05.949 you know, these B cells to to make far

NOTE Confidence: 0.926569908571429

00:29:05.949 --> 00:29:09.238 more potent levels of antibody responses.

NOTE Confidence: 0.926569908571429

00:29:09.240 --> 00:29:10.404 And this is not something that

NOTE Confidence: 0.926569908571429

00:29:10.404 --> 00:29:11.800 we just see with coronaviruses,

NOTE Confidence: 0.926569908571429

00:29:11.800 --> 00:29:14.817 but also with other viruses that are

NOTE Confidence: 0.926569908571429

00:29:14.817 --> 00:29:17.279 genetically divergent like HIV for example.

NOTE Confidence: 0.926569908571429

00:29:17.280 --> 00:29:18.700 So let me just quick follow up.

NOTE Confidence: 0.926569908571429

00:29:18.700 --> 00:29:19.720 That's really interesting.

NOTE Confidence: 0.9320592

00:29:20.280 --> 00:29:22.480 Is it important that individual

NOTE Confidence: 0.9320592

00:29:22.480 --> 00:29:24.680 particles be multivalent or if

NOTE Confidence: 0.9320592

00:29:24.752 --> 00:29:27.800 you took a mixture of particles,

NOTE Confidence: 0.9320592

00:29:27.800 --> 00:29:31.358 1 coated with this receptor binding domain,

NOTE Confidence: 0.9320592

00:29:31.360 --> 00:29:33.610 another particle coded with that one,

NOTE Confidence: 0.9320592

00:29:33.610 --> 00:29:35.164 mix them together and then inject it,

NOTE Confidence: 0.9320592

00:29:35.170 --> 00:29:36.730 would that work equally well? Yeah.

NOTE Confidence: 0.9320592

00:29:36.730 --> 00:29:38.410 So that's that's a great question.

NOTE Confidence: 0.9320592

00:29:38.410 --> 00:29:42.069 So you know based on data that from

NOTE Confidence: 0.9320592

00:29:42.069 --> 00:29:44.930 from our group actually you know with

NOTE Confidence: 0.9320592

00:29:44.930 --> 00:29:47.080 the with the chimeric mRNA vaccines

NOTE Confidence: 0.9320592

00:29:47.080 --> 00:29:49.570 when you give them all together

NOTE Confidence: 0.9320592

00:29:49.570 --> 00:29:51.579 even though you may have breath you

NOTE Confidence: 0.9320592

00:29:51.579 --> 00:29:53.288 actually lose some of the potency.

NOTE Confidence: 0.9320592

00:29:53.290 --> 00:29:55.218 You know and you know we could go

NOTE Confidence: 0.9320592

00:29:55.218 --> 00:29:57.260 on about you know like theoretical

NOTE Confidence: 0.9320592

00:29:57.260 --> 00:29:59.130 reasons underlying this actual you

NOTE Confidence: 0.9320592

00:29:59.130 --> 00:30:00.984 know phenotype you know but it

NOTE Confidence: 0.9320592

00:30:00.984 --> 00:30:02.687 could just be that you just have

NOTE Confidence: 0.9320592

00:30:02.687 --> 00:30:04.132 you know multiple different clones

NOTE Confidence: 0.9320592

00:30:04.132 --> 00:30:06.310 of B cells that are being selected

NOTE Confidence: 0.9320592

00:30:06.310 --> 00:30:07.915 against the various antigens as

NOTE Confidence: 0.9320592

00:30:07.915 --> 00:30:10.585 opposed to you know more potent and

NOTE Confidence: 0.9320592

00:30:10.585 --> 00:30:12.610 higher affinity clones against the

NOTE Confidence: 0.9320592

00:30:12.678 --> 00:30:15.034 the the single particle with say

NOTE Confidence: 0.9320592

00:30:15.034 --> 00:30:17.638 like a single protein for example.

NOTE Confidence: 0.9320592

00:30:17.640 --> 00:30:19.628 But we we definitely lose some of

NOTE Confidence: 0.9320592

00:30:19.628 --> 00:30:21.400 the potency when we include more

NOTE Confidence: 0.9320592

00:30:21.400 --> 00:30:24.720 antigens and and give them all at once.

NOTE Confidence: 0.9320592

00:30:24.720 --> 00:30:26.968 So but but but definitely I that's an

NOTE Confidence: 0.9320592

00:30:26.968 --> 00:30:28.149 interesting question and something

NOTE Confidence: 0.9320592

00:30:28.149 --> 00:30:29.835 that we've thought about a lot

NOTE Confidence: 0.9320592

00:30:29.835 --> 00:30:31.280 in optimizing these strategies.

NOTE Confidence: 0.9320592

00:30:31.280 --> 00:30:31.600 Thank you.

NOTE Confidence: 0.9324823

00:30:32.120 --> 00:30:34.395 That's a great talk and great discussion.

NOTE Confidence: 0.9324823

00:30:34.400 --> 00:30:36.479 I am fascinated by these same topics.

NOTE Confidence: 0.9324823

00:30:36.480 --> 00:30:37.710 So we'll be sure to continue

NOTE Confidence: 0.9324823

00:30:37.710 --> 00:30:39.040 over the lunch break asking you.