

WEBVTT

NOTE duration:"01:32:46.8050000"

NOTE language:en-us

NOTE Confidence: 0.8432005

00:00:00.000 --> 00:00:02.947 We're going to start with a few

NOTE Confidence: 0.8432005

00:00:02.947 --> 00:00:04.653 introductory remarks from the

NOTE Confidence: 0.8432005

00:00:04.653 --> 00:00:06.805 head of our Cancer Center, Dr.

NOTE Confidence: 0.8432005

00:00:06.805 --> 00:00:09.245 Fuchs, and then we'll go into a few

NOTE Confidence: 0.8432005

00:00:09.245 --> 00:00:11.514 short presentations by really outstanding

NOTE Confidence: 0.8432005

00:00:11.514 --> 00:00:14.358 panelists from our center and also

NOTE Confidence: 0.8432005

00:00:14.431 --> 00:00:16.596 Doctor IRA Melman from Jeanetta.

NOTE Confidence: 0.8432005

00:00:16.600 --> 00:00:18.973 And after that will be opening up

NOTE Confidence: 0.8432005

00:00:18.973 --> 00:00:21.470 the program to questions and answers

NOTE Confidence: 0.8432005

00:00:21.470 --> 00:00:23.805 and hopefully a freeform discussion

NOTE Confidence: 0.8432005

00:00:23.805 --> 00:00:26.297 to cover some of these topics.

NOTE Confidence: 0.8432005

00:00:26.300 --> 00:00:27.473 We really know.

NOTE Confidence: 0.8432005

00:00:27.473 --> 00:00:30.820 We know that that in order to treat.

NOTE Confidence: 0.8432005

00:00:30.820 --> 00:00:33.166 To effectively develop cures for cancer,

NOTE Confidence: 0.8432005

00:00:33.170 --> 00:00:35.900 there has to be a collaboration between

NOTE Confidence: 0.8432005

00:00:35.900 --> 00:00:38.670 industry, academics, government.

NOTE Confidence: 0.8432005

00:00:38.670 --> 00:00:40.710 It's really very, very important,

NOTE Confidence: 0.8432005

00:00:40.710 --> 00:00:43.128 and we designed this session specifically

NOTE Confidence: 0.8432005

00:00:43.128 --> 00:00:45.609 to build connections between your medicine,

NOTE Confidence: 0.8432005

00:00:45.610 --> 00:00:47.650 Yale science and industry leaders.

NOTE Confidence: 0.8432005

00:00:47.650 --> 00:00:49.785 We've collected your questions in

NOTE Confidence: 0.8432005

00:00:49.785 --> 00:00:52.827 advance and we invite you to submit

NOTE Confidence: 0.8432005

00:00:52.827 --> 00:00:55.305 your questions at during the time

NOTE Confidence: 0.8432005

00:00:55.305 --> 00:00:57.439 of discussion in the chat room.

NOTE Confidence: 0.8432005

00:00:57.440 --> 00:00:59.888 We also encourage you to share

NOTE Confidence: 0.8432005

00:00:59.888 --> 00:01:01.520 your questions with everyone.

NOTE Confidence: 0.85950565

00:01:03.750 --> 00:01:05.958 Heading into engaging in the discussion,

NOTE Confidence: 0.85950565

00:01:05.960 --> 00:01:08.616 we know that we have a wealth of

NOTE Confidence: 0.85950565

00:01:08.616 --> 00:01:10.758 expertise in the audience today.

NOTE Confidence: 0.85950565

00:01:10.760 --> 00:01:13.336 Not only do we have outstanding panelists,  
NOTE Confidence: 0.85950565

00:01:13.340 --> 00:01:16.184 we have an amazing list of  
NOTE Confidence: 0.85950565

00:01:16.184 --> 00:01:17.606 participants from industry.  
NOTE Confidence: 0.85950565

00:01:17.610 --> 00:01:19.270 Will review the chat room  
NOTE Confidence: 0.85950565

00:01:19.270 --> 00:01:21.333 throughout and will pull a number  
NOTE Confidence: 0.85950565

00:01:21.333 --> 00:01:23.355 of the questions for for ants.  
NOTE Confidence: 0.85950565

00:01:23.360 --> 00:01:25.364 For discussion in the question and  
NOTE Confidence: 0.85950565

00:01:25.364 --> 00:01:27.440 answer portion of the session will  
NOTE Confidence: 0.85950565

00:01:27.440 --> 00:01:29.480 also have a staff member monitoring  
NOTE Confidence: 0.85950565

00:01:29.480 --> 00:01:31.859 the chat room and if we're unable  
NOTE Confidence: 0.85950565

00:01:31.859 --> 00:01:33.499 to answer your question today,  
NOTE Confidence: 0.85950565

00:01:33.500 --> 00:01:35.860 will try and follow up as soon  
NOTE Confidence: 0.85950565

00:01:35.860 --> 00:01:36.855 as as possible.  
NOTE Confidence: 0.85950565

00:01:36.855 --> 00:01:38.745 And please also know that the  
NOTE Confidence: 0.85950565

00:01:38.745 --> 00:01:40.260 webinar is being recorded.  
NOTE Confidence: 0.85950565

00:01:40.260 --> 00:01:42.956 Let me now just welcome doctor Charlie Fuchs.

NOTE Confidence: 0.85950565

00:01:42.960 --> 00:01:45.326 He's the head of our Cancer Center.

NOTE Confidence: 0.85950565

00:01:45.330 --> 00:01:47.520 He's a Richard Sackler and Jonathan

NOTE Confidence: 0.85950565

00:01:47.520 --> 00:01:48.980 Sackler Professor of Medicine.

NOTE Confidence: 0.85950565

00:01:48.980 --> 00:01:51.005 And professor of chronic disease

NOTE Confidence: 0.85950565

00:01:51.005 --> 00:01:51.410 Epidemiology.

NOTE Confidence: 0.85950565

00:01:51.410 --> 00:01:52.460 As I said,

NOTE Confidence: 0.85950565

00:01:52.460 --> 00:01:54.910 he's a director of the Yale Cancer

NOTE Confidence: 0.85950565

00:01:54.993 --> 00:01:57.248 Center and also the physician

NOTE Confidence: 0.85950565

00:01:57.248 --> 00:01:59.503 in chief of Smilow Hospital.

NOTE Confidence: 0.85950565

00:01:59.510 --> 00:02:01.706 Charlie has brought an amazing vision

NOTE Confidence: 0.85950565

00:02:01.706 --> 00:02:04.155 of building science at this Institute

NOTE Confidence: 0.85950565

00:02:04.155 --> 00:02:05.987 is be immeasurably successful.

NOTE Confidence: 0.85950565

00:02:05.990 --> 00:02:06.800 Charlie please.

NOTE Confidence: 0.8715226

00:02:07.620 --> 00:02:10.404 Error, thank you and thank you

NOTE Confidence: 0.8715226

00:02:10.404 --> 00:02:13.645 for your leadership and I want to

NOTE Confidence: 0.8715226

00:02:13.645 --> 00:02:16.225 welcome or many attendees today to.  
NOTE Confidence: 0.8715226

00:02:16.230 --> 00:02:19.846 What is the 1st of a new series,  
NOTE Confidence: 0.8715226

00:02:19.850 --> 00:02:22.268 namely Yale engage cancer which is  
NOTE Confidence: 0.8715226

00:02:22.268 --> 00:02:24.859 really intended to be to stimulate  
NOTE Confidence: 0.8715226

00:02:24.859 --> 00:02:27.577 discussion and collaboration in what is  
NOTE Confidence: 0.8715226

00:02:27.577 --> 00:02:30.720 our mutual interest in combatting cancer?  
NOTE Confidence: 0.8715226

00:02:30.720 --> 00:02:33.438 And this first one, I think,  
NOTE Confidence: 0.8715226

00:02:33.440 --> 00:02:35.468 really highlights the great  
NOTE Confidence: 0.8715226

00:02:35.468 --> 00:02:38.003 depth at our center has.  
NOTE Confidence: 0.8715226

00:02:38.010 --> 00:02:40.368 Enemy know biology and Immuno Oncology.  
NOTE Confidence: 0.8715226

00:02:40.370 --> 00:02:41.950 Mario certainly are our  
NOTE Confidence: 0.8715226

00:02:41.950 --> 00:02:43.530 leader for the session.  
NOTE Confidence: 0.8715226

00:02:43.530 --> 00:02:45.840 Has has really had an incredibly  
NOTE Confidence: 0.8715226

00:02:45.840 --> 00:02:47.842 accomplished career in science and  
NOTE Confidence: 0.8715226

00:02:47.842 --> 00:02:49.827 drug development in Iowan recently.  
NOTE Confidence: 0.8715226

00:02:49.830 --> 00:02:51.800 The president of the Society

NOTE Confidence: 0.8715226

00:02:51.800 --> 00:02:53.376 of immunotherapy and cancer.

NOTE Confidence: 0.8715226

00:02:53.380 --> 00:02:55.350 But obviously, as you'll hear,

NOTE Confidence: 0.8715226

00:02:55.350 --> 00:02:57.365 we have assembled Marios assembled

NOTE Confidence: 0.8715226

00:02:57.365 --> 00:02:59.815 an extraordinary talent to team to

NOTE Confidence: 0.8715226

00:02:59.815 --> 00:03:01.650 really engage in this discussion.

NOTE Confidence: 0.8715226

00:03:01.650 --> 00:03:04.359 You know, we I joined the Kansas

NOTE Confidence: 0.8715226

00:03:04.359 --> 00:03:06.379 center about four years ago,

NOTE Confidence: 0.8715226

00:03:06.380 --> 00:03:09.989 and you know what attracted me here was the.

NOTE Confidence: 0.8715226

00:03:09.990 --> 00:03:12.768 Great depth of talent and accomplishment.

NOTE Confidence: 0.8715226

00:03:12.770 --> 00:03:15.548 The science here is really unparalleled

NOTE Confidence: 0.8715226

00:03:15.548 --> 00:03:18.324 in terms of genetics, cell biology,

NOTE Confidence: 0.8715226

00:03:18.324 --> 00:03:19.710 pharmacology among others,

NOTE Confidence: 0.8715226

00:03:19.710 --> 00:03:21.006 and most notably,

NOTE Confidence: 0.8715226

00:03:21.006 --> 00:03:23.166 today Immunobiology and beyond that

NOTE Confidence: 0.8715226

00:03:23.166 --> 00:03:25.730 I think the clinical operation.

NOTE Confidence: 0.8715226

00:03:25.730 --> 00:03:26.281 Frankly,  
NOTE Confidence: 0.8715226

00:03:26.281 --> 00:03:29.587 the 10th anniversary of swallow cancer  
NOTE Confidence: 0.8715226

00:03:29.587 --> 00:03:32.243 hospital has enabled an incredible  
NOTE Confidence: 0.8715226

00:03:32.243 --> 00:03:35.931 growth of a clinical operation it now sees.  
NOTE Confidence: 0.8715226

00:03:35.940 --> 00:03:38.586 48% of all cancer patients in the  
NOTE Confidence: 0.8715226

00:03:38.586 --> 00:03:40.969 state of Connecticut and is enabled  
NOTE Confidence: 0.8715226

00:03:40.969 --> 00:03:42.934 a fourfold increase in trials,  
NOTE Confidence: 0.8715226

00:03:42.940 --> 00:03:44.110 clinical trial enrollment,  
NOTE Confidence: 0.8715226

00:03:44.110 --> 00:03:46.060 and Moreover, actually this year.  
NOTE Confidence: 0.8715226

00:03:46.060 --> 00:03:49.243 Yale had studies that have that have enabled  
NOTE Confidence: 0.8715226

00:03:49.243 --> 00:03:52.275 4 new drug approvals in the cancer space.  
NOTE Confidence: 0.8715226

00:03:52.280 --> 00:03:53.058 You know,  
NOTE Confidence: 0.8715226

00:03:53.058 --> 00:03:53.447 obviously,  
NOTE Confidence: 0.8715226

00:03:53.447 --> 00:03:56.170 we're in the midst of a pandemic,  
NOTE Confidence: 0.8715226

00:03:56.170 --> 00:03:58.110 and we're focused on kovid.  
NOTE Confidence: 0.8715226

00:03:58.110 --> 00:04:00.050 But we all recognize that

NOTE Confidence: 0.8715226

00:04:00.050 --> 00:04:01.602 in the 21st century,

NOTE Confidence: 0.8715226

00:04:01.610 --> 00:04:04.137 cancer is really the great landscape for

NOTE Confidence: 0.8715226

00:04:04.137 --> 00:04:07.450 for what we want to accomplish in medicine.

NOTE Confidence: 0.8715226

00:04:07.450 --> 00:04:09.790 And I think I owe.

NOTE Confidence: 0.8715226

00:04:09.790 --> 00:04:12.142 Is an important leg that's going

NOTE Confidence: 0.8715226

00:04:12.142 --> 00:04:15.538 to get us to where we need to be.

NOTE Confidence: 0.8715226

00:04:15.540 --> 00:04:17.898 We really value the partnerships that

NOTE Confidence: 0.8715226

00:04:17.898 --> 00:04:20.641 we develop at Yale with our colleagues

NOTE Confidence: 0.8715226

00:04:20.641 --> 00:04:23.196 and industry and so many of you.

NOTE Confidence: 0.8715226

00:04:23.200 --> 00:04:25.110 Perhaps all of you with

NOTE Confidence: 0.8715226

00:04:25.110 --> 00:04:26.256 backgrounds and industry,

NOTE Confidence: 0.8715226

00:04:26.260 --> 00:04:28.927 an biotech and related areas are obviously

NOTE Confidence: 0.8715226

00:04:28.927 --> 00:04:31.619 sharing a mutual interest in this fight.

NOTE Confidence: 0.8715226

00:04:31.620 --> 00:04:32.386 You know,

NOTE Confidence: 0.8715226

00:04:32.386 --> 00:04:35.067 we welcome your participation in this forum.

NOTE Confidence: 0.8715226



00:04:35.070 --> 00:04:35.836 But Moreover,  
NOTE Confidence: 0.8715226

00:04:35.836 --> 00:04:38.517 either during or even after the webinar,  
NOTE Confidence: 0.8715226

00:04:38.520 --> 00:04:39.664 we would like to.  
NOTE Confidence: 0.8715226

00:04:39.664 --> 00:04:41.380 Engage with you in terms of  
NOTE Confidence: 0.8715226

00:04:41.449 --> 00:04:43.549 conversations and collaborations.  
NOTE Confidence: 0.8715226

00:04:43.550 --> 00:04:45.046 'cause first and foremost,  
NOTE Confidence: 0.8715226

00:04:45.046 --> 00:04:47.720 we know it takes a village to  
NOTE Confidence: 0.8715226

00:04:47.720 --> 00:04:49.838 combat cancer and we hope with  
NOTE Confidence: 0.8715226

00:04:49.838 --> 00:04:51.889 this does beyond other things.  
NOTE Confidence: 0.8715226

00:04:51.890 --> 00:04:53.780 Is actually enable new collaboration.  
NOTE Confidence: 0.8715226

00:04:53.780 --> 00:04:56.060 So please reach out to me.  
NOTE Confidence: 0.8715226

00:04:56.060 --> 00:04:58.106 Mario or the other panelists because  
NOTE Confidence: 0.8715226

00:04:58.106 --> 00:05:01.091 we want this to be the beginning of  
NOTE Confidence: 0.8715226

00:05:01.091 --> 00:05:02.639 conversations and new engagements  
NOTE Confidence: 0.8715226

00:05:02.639 --> 00:05:05.063 as we work together to leverage  
NOTE Confidence: 0.8715226

00:05:05.063 --> 00:05:07.427 the great work in Immuno Oncology.

NOTE Confidence: 0.8715226

00:05:07.430 --> 00:05:10.550 So Mario, thank you for allowing me to.

NOTE Confidence: 0.8715226

00:05:10.550 --> 00:05:11.908 To share a few thoughts and I

NOTE Confidence: 0.8715226

00:05:11.908 --> 00:05:13.179 look forward to this symposium.

NOTE Confidence: 0.88338006

00:05:14.930 --> 00:05:17.120 Thank you Charlie.

NOTE Confidence: 0.88338006

00:05:17.120 --> 00:05:19.432 I just again want to repeat that our

NOTE Confidence: 0.88338006

00:05:19.432 --> 00:05:21.461 format today will be a combination

NOTE Confidence: 0.88338006

00:05:21.461 --> 00:05:23.201 of brief introductory comments by

NOTE Confidence: 0.88338006

00:05:23.201 --> 00:05:25.803 our panelists and then a moderated

NOTE Confidence: 0.88338006

00:05:25.803 --> 00:05:27.559 discussion including your questions.

NOTE Confidence: 0.88338006

00:05:27.560 --> 00:05:29.360 We've invited our faculty to

NOTE Confidence: 0.88338006

00:05:29.360 --> 00:05:30.800 briefly address several questions,

NOTE Confidence: 0.88338006

00:05:30.800 --> 00:05:32.960 including what their core expertise says,

NOTE Confidence: 0.88338006

00:05:32.960 --> 00:05:35.120 what questions are driving their research,

NOTE Confidence: 0.88338006

00:05:35.120 --> 00:05:37.640 how can we work with the corporate

NOTE Confidence: 0.88338006

00:05:37.640 --> 00:05:40.160 sector in order to address this disease,

NOTE Confidence: 0.88338006

00:05:40.160 --> 00:05:42.320 and finally, what types of resources,  
NOTE Confidence: 0.88338006

00:05:42.320 --> 00:05:42.680 capabilities,  
NOTE Confidence: 0.88338006

00:05:42.680 --> 00:05:44.810 and partnerships align with those brought  
NOTE Confidence: 0.88338006

00:05:44.810 --> 00:05:47.860 to bear by the corporate sector to advance.  
NOTE Confidence: 0.88338006

00:05:47.860 --> 00:05:49.804 This work remind all the speakers  
NOTE Confidence: 0.88338006

00:05:49.804 --> 00:05:52.059 that you have 5 minutes to speak  
NOTE Confidence: 0.88338006

00:05:52.059 --> 00:05:55.420 and then I will cut you off.  
NOTE Confidence: 0.88338006

00:05:55.420 --> 00:05:57.883 Very nicely because we want to get  
NOTE Confidence: 0.88338006

00:05:57.883 --> 00:05:59.643 on to the discussion afterwards.  
NOTE Confidence: 0.88338006

00:05:59.643 --> 00:06:01.047 After the Yale speakers,  
NOTE Confidence: 0.88338006

00:06:01.050 --> 00:06:02.458 I'll then introduce Doctor  
NOTE Confidence: 0.88338006

00:06:02.458 --> 00:06:03.866 IRA Melman from genetic.  
NOTE Confidence: 0.88338006

00:06:03.870 --> 00:06:04.926 So with that,  
NOTE Confidence: 0.88338006

00:06:04.926 --> 00:06:07.390 let me just go ahead and proceed.  
NOTE Confidence: 0.88338006

00:06:07.390 --> 00:06:09.145 Our first speaker will be  
NOTE Confidence: 0.88338006

00:06:09.145 --> 00:06:10.198 doctor Marcus Bosenberg.

NOTE Confidence: 0.88338006

00:06:10.200 --> 00:06:11.960 He's The Professor of dermatology,

NOTE Confidence: 0.88338006

00:06:11.960 --> 00:06:13.016 pathology and Immunobiology

NOTE Confidence: 0.88338006

00:06:13.016 --> 00:06:15.146 at the El School of Medicine.

NOTE Confidence: 0.88338006

00:06:15.146 --> 00:06:16.936 He's currently the interim director

NOTE Confidence: 0.88338006

00:06:16.936 --> 00:06:19.107 of the Yale Center framing oncology

NOTE Confidence: 0.88338006

00:06:19.107 --> 00:06:21.183 and he's also the director for

NOTE Confidence: 0.88338006

00:06:21.183 --> 00:06:22.949 the Center for position cans

NOTE Confidence: 0.88338006

00:06:22.949 --> 00:06:24.989 for modeling and the director of

NOTE Confidence: 0.88338006

00:06:24.990 --> 00:06:27.310 the elsewhere in skin cancer.

NOTE Confidence: 0.88338006

00:06:27.310 --> 00:06:29.830 And also the Co leader of the genetics,

NOTE Confidence: 0.88338006

00:06:29.830 --> 00:06:30.829 genomics and epigenetics.

NOTE Confidence: 0.88338006

00:06:30.829 --> 00:06:33.160 So I've now taken up almost all

NOTE Confidence: 0.88338006

00:06:33.221 --> 00:06:35.111 of the five minutes with Retitles

NOTE Confidence: 0.88338006

00:06:35.111 --> 00:06:37.079 Marcus and I'll turn it over to.

NOTE Confidence: 0.82695603

00:06:39.600 --> 00:06:41.184 Thanks Mario would have the

NOTE Confidence: 0.82695603

00:06:41.184 --> 00:06:43.080 next slide that be great thanks.

NOTE Confidence: 0.82695603

00:06:43.080 --> 00:06:45.264 I had the great pleasure of working

NOTE Confidence: 0.82695603

00:06:45.264 --> 00:06:47.204 with Mario on a regular basis

NOTE Confidence: 0.82695603

00:06:47.204 --> 00:06:49.077 as part of the Melanoma team.

NOTE Confidence: 0.82695603

00:06:49.077 --> 00:06:50.345 As a practicing dramatic

NOTE Confidence: 0.82695603

00:06:50.345 --> 00:06:52.235 pathologist and I think you know,

NOTE Confidence: 0.82695603

00:06:52.240 --> 00:06:53.675 the Yale Center for immuno

NOTE Confidence: 0.82695603

00:06:53.675 --> 00:06:55.110 oncology in this session is

NOTE Confidence: 0.82695603

00:06:55.169 --> 00:06:56.979 really focused on Immuno Oncology.

NOTE Confidence: 0.82695603

00:06:56.980 --> 00:07:00.023 Is kind of at the center of a hub of a

NOTE Confidence: 0.82695603

00:07:00.023 --> 00:07:02.669 number of very important pieces at Yale.

NOTE Confidence: 0.82695603

00:07:02.670 --> 00:07:04.255 So doctor Fuchs really nicely

NOTE Confidence: 0.82695603

00:07:04.255 --> 00:07:05.840 summarized some of the really

NOTE Confidence: 0.82695603

00:07:05.893 --> 00:07:07.717 impact that the Cancer Center has.

NOTE Confidence: 0.82695603

00:07:07.720 --> 00:07:09.911 I think many of you are aware

NOTE Confidence: 0.82695603

00:07:09.911 --> 00:07:11.620 of the sort of world.

NOTE Confidence: 0.82695603

00:07:11.620 --> 00:07:13.650 Leading world renowned capability of

NOTE Confidence: 0.82695603

00:07:13.650 --> 00:07:15.680 the Immunobiology Department at Yale,

NOTE Confidence: 0.82695603

00:07:15.680 --> 00:07:17.785 traditionally with real strengths in

NOTE Confidence: 0.82695603

00:07:17.785 --> 00:07:19.890 basic immunology but now branching

NOTE Confidence: 0.82695603

00:07:19.956 --> 00:07:21.360 out toward human translation.

NOTE Confidence: 0.82695603

00:07:21.360 --> 00:07:22.090 Menology Ann.

NOTE Confidence: 0.82695603

00:07:22.090 --> 00:07:25.460 Really one of my jobs is to try to

NOTE Confidence: 0.82695603

00:07:25.460 --> 00:07:28.380 bring folks into the realm of IO from

NOTE Confidence: 0.82695603

00:07:28.380 --> 00:07:31.510 that Department which has really been,

NOTE Confidence: 0.82695603

00:07:31.510 --> 00:07:32.324 I think,

NOTE Confidence: 0.82695603

00:07:32.324 --> 00:07:34.359 a great success so far.

NOTE Confidence: 0.82695603

00:07:34.360 --> 00:07:37.856 A couple of the talks here from doctor

NOTE Confidence: 0.82695603

00:07:37.856 --> 00:07:41.222 ring and Doctor Wisocky sort of are

NOTE Confidence: 0.82695603

00:07:41.222 --> 00:07:43.976 related to some of those efforts.

NOTE Confidence: 0.82695603

00:07:43.980 --> 00:07:46.492 Also kind of giving you a feel for

NOTE Confidence: 0.82695603

00:07:46.492 --> 00:07:49.155 the landscape and this is really just  
NOTE Confidence: 0.82695603

00:07:49.155 --> 00:07:51.120 an introductory session with myself.  
NOTE Confidence: 0.82695603

00:07:51.120 --> 00:07:53.208 There's also the advanced cell therapy  
NOTE Confidence: 0.82695603

00:07:53.208 --> 00:07:55.318 lab that Diane Kraus directs and  
NOTE Confidence: 0.82695603

00:07:55.318 --> 00:07:57.593 had established an it's a full GNP  
NOTE Confidence: 0.82695603

00:07:57.593 --> 00:08:00.050 facility that can harvest to multithreading.  
NOTE Confidence: 0.82695603

00:08:00.050 --> 00:08:01.740 Lymphocytes expand and then allow  
NOTE Confidence: 0.82695603

00:08:01.740 --> 00:08:03.871 that product to be reinfused into  
NOTE Confidence: 0.82695603

00:08:03.871 --> 00:08:05.399 patients runs clinical trials.  
NOTE Confidence: 0.82695603

00:08:05.400 --> 00:08:07.619 This is a real opportunity for Yale  
NOTE Confidence: 0.82695603

00:08:07.619 --> 00:08:09.705 to move forward on the scientific  
NOTE Confidence: 0.82695603

00:08:09.705 --> 00:08:11.835 front with regard to cell therapies  
NOTE Confidence: 0.82695603

00:08:11.835 --> 00:08:14.057 and we're really positioned well.  
NOTE Confidence: 0.82695603

00:08:14.060 --> 00:08:15.227 To do that,  
NOTE Confidence: 0.82695603

00:08:15.227 --> 00:08:17.172 doctor Herbst will be talking  
NOTE Confidence: 0.82695603

00:08:17.172 --> 00:08:19.972 right after me about some of the

NOTE Confidence: 0.82695603

00:08:19.972 --> 00:08:21.917 translation TLE efforts at Yale,

NOTE Confidence: 0.82695603

00:08:21.920 --> 00:08:24.278 and I'll let him do so.

NOTE Confidence: 0.82695603

00:08:24.280 --> 00:08:26.863 As doctor snow mentioned in my role

NOTE Confidence: 0.82695603

00:08:26.863 --> 00:08:29.695 in as directing the Yale Sport and

NOTE Confidence: 0.82695603

00:08:29.695 --> 00:08:31.750 skin cancer with Harriet Cougar,

NOTE Confidence: 0.82695603

00:08:31.750 --> 00:08:33.318 there's really excellent access

NOTE Confidence: 0.82695603

00:08:33.318 --> 00:08:34.494 to patient samples,

NOTE Confidence: 0.82695603

00:08:34.500 --> 00:08:36.064 patient materials through now.

NOTE Confidence: 0.82695603

00:08:36.064 --> 00:08:38.029 Doctor Hertz will explain 3

NOTE Confidence: 0.82695603

00:08:38.030 --> 00:08:40.000 now spore grants at Yale,

NOTE Confidence: 0.82695603

00:08:40.000 --> 00:08:41.960 and we're coordinating these efforts,

NOTE Confidence: 0.82695603

00:08:41.960 --> 00:08:44.165 especially with regard to Iota

NOTE Confidence: 0.82695603

00:08:44.165 --> 00:08:45.929 getting access to specimens.

NOTE Confidence: 0.82695603

00:08:45.930 --> 00:08:48.751 Which I think will be important for

NOTE Confidence: 0.82695603

00:08:48.751 --> 00:08:49.960 industrial academic collaborations

NOTE Confidence: 0.82695603



00:08:50.024 --> 00:08:51.119 in my role now too.  
NOTE Confidence: 0.82695603

00:08:51.120 --> 00:08:53.000 I also tend to be at a lot of the  
NOTE Confidence: 0.82695603

00:08:53.062 --> 00:08:55.118 discussions related to industrial  
NOTE Confidence: 0.82695603

00:08:55.118 --> 00:08:56.660 academic collaborations between  
NOTE Confidence: 0.82695603

00:08:56.660 --> 00:08:58.728 other entities, aniele with respect.  
NOTE Confidence: 0.82695603

00:08:58.728 --> 00:09:00.488 And, you know, oncology Ann,  
NOTE Confidence: 0.82695603

00:09:00.488 --> 00:09:02.283 I really enjoy that interaction  
NOTE Confidence: 0.82695603

00:09:02.283 --> 00:09:04.308 an obviously try to move those  
NOTE Confidence: 0.82695603

00:09:04.308 --> 00:09:06.078 things forward in the way that's  
NOTE Confidence: 0.82695603

00:09:06.078 --> 00:09:07.929 most productive for both parties  
NOTE Confidence: 0.82695603

00:09:07.929 --> 00:09:09.794 in each of those interactions.  
NOTE Confidence: 0.82695603

00:09:09.800 --> 00:09:13.260 So if we can go on to the next slide,  
NOTE Confidence: 0.82695603

00:09:13.260 --> 00:09:16.196 I'll talk about the remaining thing on the.  
NOTE Confidence: 0.82695603

00:09:16.200 --> 00:09:17.094 We'll hear so,  
NOTE Confidence: 0.82695603

00:09:17.094 --> 00:09:18.584 and that's the Center for  
NOTE Confidence: 0.82695603

00:09:18.584 --> 00:09:20.119 precision cut cancer modeling,

NOTE Confidence: 0.82695603  
00:09:20.120 --> 00:09:22.124 which I also direct with vision  
NOTE Confidence: 0.82695603  
00:09:22.124 --> 00:09:24.050 with Sammy and what this is,  
NOTE Confidence: 0.82695603  
00:09:24.050 --> 00:09:26.008 is a state of the art  
NOTE Confidence: 0.82695603  
00:09:26.008 --> 00:09:26.986 preclinical testing facility.  
NOTE Confidence: 0.82695603  
00:09:26.990 --> 00:09:29.558 It's really focused on Immuno Oncology.  
NOTE Confidence: 0.82695603  
00:09:29.560 --> 00:09:31.499 And we will do testing of agents  
NOTE Confidence: 0.82695603  
00:09:31.499 --> 00:09:33.460 with respect to syngenetic models and  
NOTE Confidence: 0.82695603  
00:09:33.460 --> 00:09:35.602 other things that have been developed  
NOTE Confidence: 0.82695603  
00:09:35.602 --> 00:09:37.700 at Yale that are unique to Yale.  
NOTE Confidence: 0.82695603  
00:09:37.700 --> 00:09:39.020 We have sponsored research  
NOTE Confidence: 0.82695603  
00:09:39.020 --> 00:09:40.340 agreements with some members  
NOTE Confidence: 0.82695603  
00:09:40.340 --> 00:09:42.497 who are on this call related to  
NOTE Confidence: 0.82695603  
00:09:42.497 --> 00:09:43.937 things like class one deficient  
NOTE Confidence: 0.8345073  
00:09:43.995 --> 00:09:45.540 models that were uniquely developed  
NOTE Confidence: 0.8345073  
00:09:45.540 --> 00:09:47.716 at Yale that don't have to be  
NOTE Confidence: 0.8345073

00:09:47.716 --> 00:09:49.907 licensed out as a result of that,  
NOTE Confidence: 0.8345073

00:09:49.910 --> 00:09:52.126 and we have a lot of experience which  
NOTE Confidence: 0.8345073

00:09:52.126 --> 00:09:54.288 some of which will hear about in  
NOTE Confidence: 0.8345073

00:09:54.288 --> 00:09:56.579 later talks just after me looking at  
NOTE Confidence: 0.8345073

00:09:56.579 --> 00:09:58.973 responses to IO agents in these models,  
NOTE Confidence: 0.8345073

00:09:58.980 --> 00:09:59.943 what were particularly.  
NOTE Confidence: 0.8345073

00:09:59.943 --> 00:10:02.615 Cited about right now is the idea of  
NOTE Confidence: 0.8345073

00:10:02.615 --> 00:10:04.811 doing patient derived explant studies to  
NOTE Confidence: 0.8345073

00:10:04.811 --> 00:10:06.870 evaluate human immuno oncology agents.  
NOTE Confidence: 0.8345073

00:10:06.870 --> 00:10:09.355 So the idea here is you take  
NOTE Confidence: 0.8345073

00:10:09.355 --> 00:10:10.420 fragments of tumors,  
NOTE Confidence: 0.8345073

00:10:10.420 --> 00:10:12.758 embed them in a proprietary 3D matrix  
NOTE Confidence: 0.8345073

00:10:12.758 --> 00:10:15.308 and then use agents that might be  
NOTE Confidence: 0.8345073

00:10:15.308 --> 00:10:17.516 biologics that are using humans to  
NOTE Confidence: 0.8345073

00:10:17.587 --> 00:10:19.675 test responses in those samples and  
NOTE Confidence: 0.8345073

00:10:19.675 --> 00:10:22.410 on the right you can see this is

NOTE Confidence: 0.8345073

00:10:22.410 --> 00:10:24.970 an example of a mouse based tumor,

NOTE Confidence: 0.8345073

00:10:24.970 --> 00:10:27.578 but one in which when we gave a

NOTE Confidence: 0.8345073

00:10:27.578 --> 00:10:29.513 checkpoint inhibitor we see a

NOTE Confidence: 0.8345073

00:10:29.513 --> 00:10:31.129 compute complete curatives response.

NOTE Confidence: 0.8345073

00:10:31.130 --> 00:10:32.846 And so we're looking at readouts

NOTE Confidence: 0.8345073

00:10:32.846 --> 00:10:33.704 for these systems.

NOTE Confidence: 0.8345073

00:10:33.710 --> 00:10:35.824 But the idea is to have personalized

NOTE Confidence: 0.8345073

00:10:35.824 --> 00:10:37.375 immunotherapy where you can actually

NOTE Confidence: 0.8345073

00:10:37.375 --> 00:10:39.157 look at different combinations in a

NOTE Confidence: 0.8345073

00:10:39.157 --> 00:10:41.057 patient in real time and decide what

NOTE Confidence: 0.8345073

00:10:41.057 --> 00:10:42.607 might work best for that patient.

NOTE Confidence: 0.8345073

00:10:42.607 --> 00:10:44.329 And we're not fully there yet,

NOTE Confidence: 0.8345073

00:10:44.330 --> 00:10:46.220 but we think we're pretty close and

NOTE Confidence: 0.8345073

00:10:46.220 --> 00:10:48.335 hope to have this available for others

NOTE Confidence: 0.8345073

00:10:48.335 --> 00:10:50.649 within the next six months to a year.

NOTE Confidence: 0.8345073

00:10:50.650 --> 00:10:52.456 So I'll stop there and allow  
NOTE Confidence: 0.8345073

00:10:52.456 --> 00:10:54.089 the next speakers to go on.  
NOTE Confidence: 0.76468164

00:10:57.900 --> 00:10:59.758 Argus tanky, with the next  
NOTE Confidence: 0.76468164

00:10:59.758 --> 00:11:01.618 speaker is doctor Roy Herbst.  
NOTE Confidence: 0.76468164

00:11:01.620 --> 00:11:03.846 He's the head of medical oncology,  
NOTE Confidence: 0.76468164

00:11:03.850 --> 00:11:05.890 Yale Cancer Center and smile cancer  
NOTE Confidence: 0.76468164

00:11:05.890 --> 00:11:07.677 hospital and The Associated Cancer  
NOTE Confidence: 0.76468164

00:11:07.677 --> 00:11:09.145 Center director for Translational  
NOTE Confidence: 0.76468164

00:11:09.145 --> 00:11:11.462 research and a professor of Medicine  
NOTE Confidence: 0.76468164

00:11:11.462 --> 00:11:13.520 and professor of pharmacology, Roy.  
NOTE Confidence: 0.84727836

00:11:15.060 --> 00:11:16.955 Thanks Mary, and thanks to  
NOTE Confidence: 0.84727836

00:11:16.955 --> 00:11:18.850 everyone for being here today.  
NOTE Confidence: 0.84727836

00:11:18.850 --> 00:11:21.321 So in my role as the associate  
NOTE Confidence: 0.84727836

00:11:21.321 --> 00:11:23.020 director of Translational Research,  
NOTE Confidence: 0.84727836

00:11:23.020 --> 00:11:25.642 I just want to describe, you know,  
NOTE Confidence: 0.84727836

00:11:25.642 --> 00:11:27.838 a little bit about your disease

NOTE Confidence: 0.84727836

00:11:27.838 --> 00:11:30.060 programs or so-called darts and what

NOTE Confidence: 0.84727836

00:11:30.060 --> 00:11:32.870 you can see is UCR disease programs,

NOTE Confidence: 0.84727836

00:11:32.870 --> 00:11:34.010 immunology, population Sciences,

NOTE Confidence: 0.84727836

00:11:34.010 --> 00:11:34.770 Developmental Therapeutics,

NOTE Confidence: 0.84727836

00:11:34.770 --> 00:11:35.904 microbiology, cell signaling,

NOTE Confidence: 0.84727836

00:11:35.904 --> 00:11:36.660 radiation genetics,

NOTE Confidence: 0.84727836

00:11:36.660 --> 00:11:38.560 and all of these disease

NOTE Confidence: 0.84727836

00:11:38.560 --> 00:11:39.700 programs are amazing,

NOTE Confidence: 0.84727836

00:11:39.700 --> 00:11:42.548 but we want to interact them with the

NOTE Confidence: 0.84727836

00:11:42.548 --> 00:11:45.090 clinic with the clinical teams have.

NOTE Confidence: 0.84727836

00:11:45.090 --> 00:11:47.208 Access to patient specimens move move

NOTE Confidence: 0.84727836

00:11:47.208 --> 00:11:50.068 new drugs from the the lab to the clinic,

NOTE Confidence: 0.84727836

00:11:50.070 --> 00:11:52.240 and I think we're doing that quite

NOTE Confidence: 0.84727836

00:11:52.240 --> 00:11:54.388 well and we form these darts.

NOTE Confidence: 0.84727836

00:11:54.390 --> 00:11:55.730 Diseased aligned research teams

NOTE Confidence: 0.84727836

00:11:55.730 --> 00:11:57.740 and that's where we build our  
NOTE Confidence: 0.84727836

00:11:57.798 --> 00:11:59.253 industry alliances in our spores  
NOTE Confidence: 0.84727836

00:11:59.253 --> 00:12:01.504 and we have a number of industry  
NOTE Confidence: 0.84727836

00:12:01.504 --> 00:12:03.349 alliances right now with Genentech,  
NOTE Confidence: 0.84727836

00:12:03.350 --> 00:12:03.826 Astra Zeneca,  
NOTE Confidence: 0.84727836

00:12:03.826 --> 00:12:05.730 Eli Lilly to name a few and these  
NOTE Confidence: 0.84727836

00:12:05.783 --> 00:12:07.555 darts promote translational research  
NOTE Confidence: 0.84727836

00:12:07.555 --> 00:12:09.327 through the scientific discovery.  
NOTE Confidence: 0.84727836

00:12:09.330 --> 00:12:11.010 We test new discoveries in  
NOTE Confidence: 0.84727836

00:12:11.010 --> 00:12:13.089 our clinics as I mentioned and  
NOTE Confidence: 0.84727836

00:12:13.089 --> 00:12:15.099 really take ideas back and forth.  
NOTE Confidence: 0.84727836

00:12:15.100 --> 00:12:16.794 We've worked very hard this last year  
NOTE Confidence: 0.84727836

00:12:16.794 --> 00:12:18.631 too and to improve integration to  
NOTE Confidence: 0.84727836

00:12:18.631 --> 00:12:20.396 increase the number of investigator  
NOTE Confidence: 0.84727836

00:12:20.396 --> 00:12:21.957 trials that we have at Yale.  
NOTE Confidence: 0.84727836

00:12:21.960 --> 00:12:23.676 Now in this day and age,

NOTE Confidence: 0.84727836

00:12:23.680 --> 00:12:24.960 investigator initiated trials can

NOTE Confidence: 0.84727836

00:12:24.960 --> 00:12:27.706 be where we hold the Ind or it can

NOTE Confidence: 0.84727836

00:12:27.706 --> 00:12:29.230 be a small trial with industry

NOTE Confidence: 0.84727836

00:12:29.230 --> 00:12:30.540 where they hold the Ind.

NOTE Confidence: 0.84727836

00:12:30.540 --> 00:12:32.563 But at least we are closely involved

NOTE Confidence: 0.84727836

00:12:32.563 --> 00:12:34.265 in the correlative studies or it's

NOTE Confidence: 0.84727836

00:12:34.265 --> 00:12:36.429 built on Yale Science and we want to

NOTE Confidence: 0.84727836

00:12:36.429 --> 00:12:38.550 build clinical basic teams to move forward.

NOTE Confidence: 0.84727836

00:12:38.550 --> 00:12:42.519 So in the next slide I'll just show you.

NOTE Confidence: 0.84727836

00:12:42.520 --> 00:12:44.650 We've been very successful in this,

NOTE Confidence: 0.84727836

00:12:44.650 --> 00:12:45.772 and you know,

NOTE Confidence: 0.84727836

00:12:45.772 --> 00:12:47.642 there was already an existing

NOTE Confidence: 0.84727836

00:12:47.642 --> 00:12:49.618 Melanoma spore here 10 years ago.

NOTE Confidence: 0.84727836

00:12:49.620 --> 00:12:52.653 But now with the support of the darts and

NOTE Confidence: 0.84727836

00:12:52.653 --> 00:12:56.008 with some monies that we were able to supply,

NOTE Confidence: 0.84727836



00:12:56.010 --> 00:12:58.850 Marcus and Harry have renewed the skins for,

NOTE Confidence: 0.84727836

00:12:58.850 --> 00:13:00.980 so it's a third renewal now.

NOTE Confidence: 0.84727836

00:13:00.980 --> 00:13:01.910 A third span.

NOTE Confidence: 0.84727836

00:13:01.910 --> 00:13:03.770 For that we formed a new

NOTE Confidence: 0.84727836

00:13:03.770 --> 00:13:05.599 lung cancer spore myself,

NOTE Confidence: 0.84727836

00:13:05.600 --> 00:13:07.016 with leaping as leaders.

NOTE Confidence: 0.84727836

00:13:07.016 --> 00:13:09.500 We did this now six years ago.

NOTE Confidence: 0.84727836

00:13:09.500 --> 00:13:11.915 We just renewed it building a large

NOTE Confidence: 0.84727836

00:13:11.915 --> 00:13:14.787 part on the immunology from his lab.

NOTE Confidence: 0.84727836

00:13:14.790 --> 00:13:16.686 One of the trials that really,

NOTE Confidence: 0.84727836

00:13:16.690 --> 00:13:18.755 I think propelled this forward was a

NOTE Confidence: 0.84727836

00:13:18.755 --> 00:13:21.022 signal 15 for which it was developed

NOTE Confidence: 0.84727836

00:13:21.022 --> 00:13:23.002 in the lab paper nature medicine,

NOTE Confidence: 0.84727836

00:13:23.010 --> 00:13:24.270 and then of course,

NOTE Confidence: 0.84727836

00:13:24.270 --> 00:13:25.215 clinical trials ongoing.

NOTE Confidence: 0.84727836

00:13:25.220 --> 00:13:26.800 Really proud that Barbara Burtneess,

NOTE Confidence: 0.84727836

00:13:26.800 --> 00:13:28.060 who actually was recruited

NOTE Confidence: 0.84727836

00:13:28.060 --> 00:13:29.635 in the last 10 years,

NOTE Confidence: 0.84727836

00:13:29.640 --> 00:13:31.747 built a head and neck program and

NOTE Confidence: 0.84727836

00:13:31.747 --> 00:13:33.429 with support working with surgery,

NOTE Confidence: 0.84727836

00:13:33.430 --> 00:13:35.010 working with some of the

NOTE Confidence: 0.84727836

00:13:35.010 --> 00:13:35.958 great scientific leaders,

NOTE Confidence: 0.84727836

00:13:35.960 --> 00:13:38.192 now hasn't had an export and we actually

NOTE Confidence: 0.84727836

00:13:38.192 --> 00:13:41.019 have a group that's working in brain cancer.

NOTE Confidence: 0.84727836

00:13:41.020 --> 00:13:41.650 They've submitted.

NOTE Confidence: 0.84727836

00:13:41.650 --> 00:13:42.910 They're working on it.

NOTE Confidence: 0.84727836

00:13:42.910 --> 00:13:43.652 Pat Larusso,

NOTE Confidence: 0.84727836

00:13:43.652 --> 00:13:45.878 who I think you all know.

NOTE Confidence: 0.84727836

00:13:45.880 --> 00:13:48.202 Or many of you will know has been working

NOTE Confidence: 0.84727836

00:13:48.202 --> 00:13:50.879 on something in phase One South DNA repair,

NOTE Confidence: 0.84727836

00:13:50.880 --> 00:13:52.446 so we have many many translations

NOTE Confidence: 0.84727836

00:13:52.446 --> 00:13:54.514 from lab to clinic programs and these  
NOTE Confidence: 0.84727836

00:13:54.514 --> 00:13:56.124 are great opportunities for specimens  
NOTE Confidence: 0.84727836

00:13:56.124 --> 00:13:58.230 to work with industry for new drugs.  
NOTE Confidence: 0.84727836

00:13:58.230 --> 00:14:00.518 We these things will only survive if we  
NOTE Confidence: 0.84727836

00:14:00.518 --> 00:14:02.637 have alliances with the outside next slide.  
NOTE Confidence: 0.82979816

00:14:02.640 --> 00:14:04.944 So I just want to give one example  
NOTE Confidence: 0.82979816

00:14:04.944 --> 00:14:06.969 today and I know iris on the  
NOTE Confidence: 0.82979816

00:14:06.969 --> 00:14:08.810 phone and he's going to speak.  
NOTE Confidence: 0.82979816

00:14:08.810 --> 00:14:10.889 So I've known IRA for quite some  
NOTE Confidence: 0.82979816

00:14:10.889 --> 00:14:12.628 time longer than either of us.  
NOTE Confidence: 0.82979816

00:14:12.630 --> 00:14:13.870 Would like to know.  
NOTE Confidence: 0.82979816

00:14:13.870 --> 00:14:15.420 Actually took a course at  
NOTE Confidence: 0.82979816

00:14:15.420 --> 00:14:16.926 Rockefeller University as a student  
NOTE Confidence: 0.82979816

00:14:16.926 --> 00:14:18.624 when he was a guest lecture.  
NOTE Confidence: 0.82979816

00:14:18.630 --> 00:14:21.267 But of course, IRA has a history with Yale,  
NOTE Confidence: 0.82979816

00:14:21.270 --> 00:14:22.938 so I was approached nine years

NOTE Confidence: 0.82979816

00:14:22.938 --> 00:14:25.078 ago with a drug called MPL 3280.

NOTE Confidence: 0.82979816

00:14:25.080 --> 00:14:27.468 It was a PDL one inhibitor.

NOTE Confidence: 0.82979816

00:14:27.470 --> 00:14:28.825 We already knew that these

NOTE Confidence: 0.82979816

00:14:28.825 --> 00:14:29.909 drugs sort of work.

NOTE Confidence: 0.82979816

00:14:29.910 --> 00:14:31.566 The PD one inhibitors cause Mario

NOTE Confidence: 0.82979816

00:14:31.566 --> 00:14:33.159 his office right across the Hall,

NOTE Confidence: 0.82979816

00:14:33.160 --> 00:14:35.128 but we studied this drug and you can

NOTE Confidence: 0.82979816

00:14:35.128 --> 00:14:37.227 see on the left you know activity.

NOTE Confidence: 0.82979816

00:14:37.230 --> 00:14:38.540 You know your complete response

NOTE Confidence: 0.82979816

00:14:38.540 --> 00:14:40.434 in a patient but will yell was

NOTE Confidence: 0.82979816

00:14:40.434 --> 00:14:42.036 able to offer along with many

NOTE Confidence: 0.82979816

00:14:42.036 --> 00:14:43.459 colleagues from around the world.

NOTE Confidence: 0.82979816

00:14:43.460 --> 00:14:44.924 It was a multi national study

NOTE Confidence: 0.82979816

00:14:44.924 --> 00:14:46.689 but we were able to get biopsies

NOTE Confidence: 0.82979816

00:14:46.689 --> 00:14:48.397 and this was the work of Katie

NOTE Confidence: 0.82979816

00:14:48.455 --> 00:14:50.020 Poletti and Scott Gettinger and  
NOTE Confidence: 0.82979816

00:14:50.020 --> 00:14:51.860 others so we could actually define  
NOTE Confidence: 0.82979816

00:14:51.860 --> 00:14:52.940 the adaptive immune response.  
NOTE Confidence: 0.82979816

00:14:52.940 --> 00:14:54.724 So I think if we hit one more  
NOTE Confidence: 0.82979816

00:14:54.724 --> 00:14:56.541 time so we actually could see  
NOTE Confidence: 0.82979816

00:14:56.541 --> 00:14:58.497 what happened in a patient that.  
NOTE Confidence: 0.82979816

00:14:58.500 --> 00:15:00.656 Responded but we also could see what  
NOTE Confidence: 0.82979816

00:15:00.656 --> 00:15:02.299 happens in patients that didn't.  
NOTE Confidence: 0.82979816

00:15:02.300 --> 00:15:03.251 And you know,  
NOTE Confidence: 0.82979816

00:15:03.251 --> 00:15:04.836 this was an important observation.  
NOTE Confidence: 0.82979816

00:15:04.840 --> 00:15:06.136 Working closely with Iran,  
NOTE Confidence: 0.82979816

00:15:06.136 --> 00:15:08.080 the team danshen this was actually  
NOTE Confidence: 0.82979816

00:15:08.134 --> 00:15:09.820 published in nature and it really  
NOTE Confidence: 0.82979816

00:15:09.820 --> 00:15:11.337 defined some of the parameters  
NOTE Confidence: 0.82979816

00:15:11.337 --> 00:15:13.341 of immune resistance and now of  
NOTE Confidence: 0.82979816

00:15:13.341 --> 00:15:15.506 course the challenge is to use this

NOTE Confidence: 0.82979816

00:15:15.506 --> 00:15:16.951 knowledge in the future prospectively

NOTE Confidence: 0.82979816

00:15:16.951 --> 00:15:18.470 with combinations of agents,

NOTE Confidence: 0.82979816

00:15:18.470 --> 00:15:20.670 and that's something we're doing

NOTE Confidence: 0.82979816

00:15:20.670 --> 00:15:23.450 right now on the next slide.

NOTE Confidence: 0.82979816

00:15:23.450 --> 00:15:25.196 And we had the opportunity to

NOTE Confidence: 0.82979816

00:15:25.196 --> 00:15:26.069 take it further.

NOTE Confidence: 0.82979816

00:15:26.070 --> 00:15:27.210 So then, you know,

NOTE Confidence: 0.82979816

00:15:27.210 --> 00:15:28.920 as a lung cancer investigator and

NOTE Confidence: 0.82979816

00:15:28.976 --> 00:15:30.728 having a very robust long group,

NOTE Confidence: 0.82979816

00:15:30.730 --> 00:15:32.809 you know doing phase three all the

NOTE Confidence: 0.82979816

00:15:32.809 --> 00:15:34.799 way from phase one with a spore.

NOTE Confidence: 0.82979816

00:15:34.800 --> 00:15:35.631 As I mentioned,

NOTE Confidence: 0.82979816

00:15:35.631 --> 00:15:38.000 we were the lead site for this trial.

NOTE Confidence: 0.82979816

00:15:38.000 --> 00:15:39.722 The empower 110 trial which actually

NOTE Confidence: 0.82979816

00:15:39.722 --> 00:15:41.918 look at this drug and PDL 3280

NOTE Confidence: 0.82979816

00:15:41.918 --> 00:15:43.568 became a Tesla Zimride compared  
NOTE Confidence: 0.82979816

00:15:43.568 --> 00:15:45.013 with chemotherapy and this trial  
NOTE Confidence: 0.82979816

00:15:45.013 --> 00:15:46.721 if we hit again this trial just  
NOTE Confidence: 0.82979816

00:15:46.730 --> 00:15:48.290 recently reported in the New  
NOTE Confidence: 0.82979816

00:15:48.290 --> 00:15:49.850 England Journal of Medicine two  
NOTE Confidence: 0.82979816

00:15:49.904 --> 00:15:51.941 weeks ago was a positive result and  
NOTE Confidence: 0.82979816

00:15:51.941 --> 00:15:53.824 actually resulted in the drug being  
NOTE Confidence: 0.82979816

00:15:53.824 --> 00:15:55.414 approved in the frontline setting.  
NOTE Confidence: 0.82979816

00:15:55.420 --> 00:15:56.730 The reason I showed this,  
NOTE Confidence: 0.82979816

00:15:56.730 --> 00:15:58.647 if we go to the next hit is we  
NOTE Confidence: 0.82979816

00:15:58.647 --> 00:16:00.674 will look at some of the different  
NOTE Confidence: 0.82979816

00:16:00.674 --> 00:16:02.210 PDL one markers in this.  
NOTE Confidence: 0.82979816

00:16:02.210 --> 00:16:04.559 So we were able to move one metal up.  
NOTE Confidence: 0.82979816

00:16:04.560 --> 00:16:06.066 It wasn't the first drug approved  
NOTE Confidence: 0.82979816

00:16:06.066 --> 00:16:07.965 in this space the 2nd but were able  
NOTE Confidence: 0.82979816

00:16:07.965 --> 00:16:09.908 to look at SP142 and 22C3 which are

NOTE Confidence: 0.82979816

00:16:09.908 --> 00:16:11.458 different biomarkers but even more

NOTE Confidence: 0.82979816

00:16:11.458 --> 00:16:13.690 critical not known to many on this call.

NOTE Confidence: 0.82979816

00:16:13.690 --> 00:16:15.184 Kurt shoppers now working with these

NOTE Confidence: 0.82979816

00:16:15.184 --> 00:16:16.492 specimens with some amino quantitative

NOTE Confidence: 0.82979816

00:16:16.492 --> 00:16:18.389 studies that he's developed here at Yale.

NOTE Confidence: 0.82979816

00:16:18.390 --> 00:16:19.824 So now we have randomized data

NOTE Confidence: 0.82979816

00:16:19.824 --> 00:16:21.683 that we can look at even more

NOTE Confidence: 0.82979816

00:16:21.683 --> 00:16:22.819 exploratory biomarkers and then

NOTE Confidence: 0.82979816

00:16:22.819 --> 00:16:24.476 on the very final slide we're

NOTE Confidence: 0.82979816

00:16:24.476 --> 00:16:26.536 anxious to work with all of you we.

NOTE Confidence: 0.82979816

00:16:26.536 --> 00:16:28.748 No, here this is very interesting story.

NOTE Confidence: 0.80423737

00:16:28.750 --> 00:16:30.610 I forgot to put this in.

NOTE Confidence: 0.80423737

00:16:30.610 --> 00:16:32.787 This is looking at tumor mutational burden.

NOTE Confidence: 0.80423737

00:16:32.790 --> 00:16:34.692 This is blood based tumor mutational

NOTE Confidence: 0.80423737

00:16:34.692 --> 00:16:36.326 burden as done by Foundation

NOTE Confidence: 0.80423737



00:16:36.326 --> 00:16:38.156 Medicine and you can see when  
NOTE Confidence: 0.80423737

00:16:38.156 --> 00:16:40.250 you have TM be greater than 16.  
NOTE Confidence: 0.80423737

00:16:40.250 --> 00:16:42.427 You can see that in this trial.  
NOTE Confidence: 0.80423737

00:16:42.430 --> 00:16:43.674 That's a predictive marker  
NOTE Confidence: 0.80423737

00:16:43.674 --> 00:16:44.918 with significance for activity.  
NOTE Confidence: 0.80423737

00:16:44.920 --> 00:16:46.164 For intensive over chemotherapy.  
NOTE Confidence: 0.80423737

00:16:46.164 --> 00:16:47.719 So new markers being developed.  
NOTE Confidence: 0.80423737

00:16:47.720 --> 00:16:50.558 So then on the next slide.  
NOTE Confidence: 0.80423737

00:16:50.560 --> 00:16:52.485 This is what I, my final slide.  
NOTE Confidence: 0.80423737

00:16:52.490 --> 00:16:54.366 We have a whole office of Translational  
NOTE Confidence: 0.80423737

00:16:54.366 --> 00:16:56.127 research and this actually expands now  
NOTE Confidence: 0.80423737

00:16:56.127 --> 00:16:57.632 throughout the Cancer Center 'cause  
NOTE Confidence: 0.80423737

00:16:57.632 --> 00:16:59.759 we work with other teams but with Ed  
NOTE Confidence: 0.80423737

00:16:59.759 --> 00:17:01.290 Captain who's been just a wonderful  
NOTE Confidence: 0.80423737

00:17:01.290 --> 00:17:03.490 colleague and friend for now 6 1/2 years.  
NOTE Confidence: 0.80423737

00:17:03.490 --> 00:17:05.182 We've really built this office where

NOTE Confidence: 0.80423737

00:17:05.182 --> 00:17:07.152 we have the ability to bring these

NOTE Confidence: 0.80423737

00:17:07.152 --> 00:17:08.986 proposals in and then to execute you.

NOTE Confidence: 0.80423737

00:17:08.990 --> 00:17:10.908 It's very easy to make the deal,

NOTE Confidence: 0.80423737

00:17:10.910 --> 00:17:12.786 but to actually execute on the deal

NOTE Confidence: 0.80423737

00:17:12.786 --> 00:17:14.488 is important so I'll stop there.

NOTE Confidence: 0.80423737

00:17:14.490 --> 00:17:15.860 Happy to answer questions later.

NOTE Confidence: 0.80423737

00:17:15.860 --> 00:17:17.510 Anxious to work with as many

NOTE Confidence: 0.80423737

00:17:17.510 --> 00:17:18.610 collaborators as makes sense.

NOTE Confidence: 0.80423737

00:17:18.610 --> 00:17:19.160 Thank you.

NOTE Confidence: 0.77084476

00:17:20.370 --> 00:17:22.146 Right, thank you. I'd like to

NOTE Confidence: 0.77084476

00:17:22.146 --> 00:17:23.920 introduce the next speaker ehrenring.

NOTE Confidence: 0.77084476

00:17:23.920 --> 00:17:26.174 He's an assistant professor of email biology,

NOTE Confidence: 0.77084476

00:17:26.180 --> 00:17:28.764 one of the most creative minds I've met.

NOTE Confidence: 0.77084476

00:17:28.770 --> 00:17:31.031 Among all the wealth of talent that

NOTE Confidence: 0.77084476

00:17:31.031 --> 00:17:33.292 we have here, Aaron, you have some

NOTE Confidence: 0.77084476

00:17:33.292 --> 00:17:34.907 very interesting things to describe.  
NOTE Confidence: 0.77084476

00:17:34.910 --> 00:17:35.870 Please please proceed.  
NOTE Confidence: 0.8315963

00:17:36.830 --> 00:17:38.590 Yeah, thanks so much Mario.  
NOTE Confidence: 0.8315963

00:17:38.590 --> 00:17:40.876 So the focus of my research is to use  
NOTE Confidence: 0.8315963

00:17:40.876 --> 00:17:42.327 structure based protein engineering  
NOTE Confidence: 0.8315963

00:17:42.327 --> 00:17:43.843 to develop pharmacological tools  
NOTE Confidence: 0.8315963

00:17:43.843 --> 00:17:46.741 that we can use to dissecting probe  
NOTE Confidence: 0.8315963

00:17:46.741 --> 00:17:48.445 complicated immuno regulatory pathways.  
NOTE Confidence: 0.8315963

00:17:48.450 --> 00:17:49.437 That's a mouthful.  
NOTE Confidence: 0.8315963

00:17:49.437 --> 00:17:51.411 I should say what we're really  
NOTE Confidence: 0.8315963

00:17:51.411 --> 00:17:53.303 primarily focused on are these  
NOTE Confidence: 0.8315963

00:17:53.303 --> 00:17:54.428 proteins called cytokines,  
NOTE Confidence: 0.8315963

00:17:54.430 --> 00:17:56.125 which are small hormone like  
NOTE Confidence: 0.8315963

00:17:56.125 --> 00:17:57.820 molecules of the immune system  
NOTE Confidence: 0.8315963

00:17:57.885 --> 00:17:59.580 have exerted very powerful effects  
NOTE Confidence: 0.8315963

00:17:59.580 --> 00:18:01.709 on nearly all aspects of immune

NOTE Confidence: 0.8315963

00:18:01.709 --> 00:18:03.929 Physiology and biology is really cool,

NOTE Confidence: 0.8315963

00:18:03.930 --> 00:18:05.490 but what's really important

NOTE Confidence: 0.8315963

00:18:05.490 --> 00:18:07.440 in the context of cancer?

NOTE Confidence: 0.8315963

00:18:07.440 --> 00:18:09.712 Is the study kind for the very first

NOTE Confidence: 0.8315963

00:18:09.712 --> 00:18:11.913 agents that prove the principle that the

NOTE Confidence: 0.8315963

00:18:11.913 --> 00:18:14.548 immune system could be a target of cancer?

NOTE Confidence: 0.8315963

00:18:14.550 --> 00:18:16.601 And that's evident from this this very

NOTE Confidence: 0.8315963

00:18:16.601 --> 00:18:18.817 seminal report on the activity of high

NOTE Confidence: 0.8315963

00:18:18.817 --> 00:18:20.417 dose interleukin two and Melanoma,

NOTE Confidence: 0.8315963

00:18:20.420 --> 00:18:22.787 and you can see that a small fraction of

NOTE Confidence: 0.8315963

00:18:22.787 --> 00:18:25.047 patients actually had very durable responses.

NOTE Confidence: 0.8315963

00:18:25.050 --> 00:18:27.606 In fact, you could call them cures and you

NOTE Confidence: 0.8315963

00:18:27.606 --> 00:18:30.310 see that first tail in the survival curve,

NOTE Confidence: 0.8315963

00:18:30.310 --> 00:18:32.494 and I'll just note that you know

NOTE Confidence: 0.8315963

00:18:32.494 --> 00:18:34.628 a major leader in this work was,

NOTE Confidence: 0.8315963

00:18:34.630 --> 00:18:36.070 of course, our colleague,  
NOTE Confidence: 0.8315963

00:18:36.070 --> 00:18:37.870 my good friend Mario snow.  
NOTE Confidence: 0.8315963

00:18:37.870 --> 00:18:39.782 You know who's been leading the way so  
NOTE Confidence: 0.8315963

00:18:39.782 --> 00:18:42.012 we can advance the next slide, please.  
NOTE Confidence: 0.8315963

00:18:42.012 --> 00:18:44.844 So in the past four years,  
NOTE Confidence: 0.8315963

00:18:44.850 --> 00:18:47.076 my lab has gotten really interested  
NOTE Confidence: 0.8315963

00:18:47.076 --> 00:18:48.560 in one particular cytokine,  
NOTE Confidence: 0.8315963

00:18:48.560 --> 00:18:49.838 called Interleukin 18.  
NOTE Confidence: 0.8315963

00:18:49.838 --> 00:18:52.394 What makes this study kind compelling  
NOTE Confidence: 0.8315963

00:18:52.394 --> 00:18:54.919 is it has really strong activities in  
NOTE Confidence: 0.8315963

00:18:54.919 --> 00:18:57.826 vitro in a dish on two key cell types.  
NOTE Confidence: 0.8315963

00:18:57.830 --> 00:18:59.574 Tumor infiltrating T cells,  
NOTE Confidence: 0.8315963

00:18:59.574 --> 00:19:01.318 which recognize specific tumor  
NOTE Confidence: 0.8315963

00:19:01.318 --> 00:19:03.453 antigens in are proven to be  
NOTE Confidence: 0.8315963

00:19:03.453 --> 00:19:05.247 the some of the most important,  
NOTE Confidence: 0.8315963

00:19:05.250 --> 00:19:07.105 if not most important targets

NOTE Confidence: 0.8315963

00:19:07.105 --> 00:19:08.218 in cancer immunotherapy.

NOTE Confidence: 0.8315963

00:19:08.220 --> 00:19:09.261 I liked it.

NOTE Confidence: 0.8315963

00:19:09.261 --> 00:19:10.996 Also stimulates another class of

NOTE Confidence: 0.8315963

00:19:10.996 --> 00:19:13.040 cells called natural killer cells,

NOTE Confidence: 0.8315963

00:19:13.040 --> 00:19:14.084 which are emerging.

NOTE Confidence: 0.8315963

00:19:14.084 --> 00:19:15.476 As key immune effectors,

NOTE Confidence: 0.8315963

00:19:15.480 --> 00:19:17.045 particularly in the setting of

NOTE Confidence: 0.8315963

00:19:17.045 --> 00:19:17.984 immune checkpoint resistance,

NOTE Confidence: 0.8315963

00:19:17.990 --> 00:19:20.430 as Roy was just alluding to in the

NOTE Confidence: 0.8315963

00:19:20.430 --> 00:19:22.677 setting of image C Class one loss,

NOTE Confidence: 0.8315963

00:19:22.680 --> 00:19:24.558 if you can advance one click

NOTE Confidence: 0.8315963

00:19:24.558 --> 00:19:25.810 that was really shocking,

NOTE Confidence: 0.8315963

00:19:25.810 --> 00:19:26.102 though,

NOTE Confidence: 0.8315963

00:19:26.102 --> 00:19:28.146 as we dug into the biology violate

NOTE Confidence: 0.8315963

00:19:28.146 --> 00:19:30.643 teams that have been tried in clinical

NOTE Confidence: 0.8315963

00:19:30.643 --> 00:19:32.123 trials before GlaxoSmithKline had  
NOTE Confidence: 0.8315963

00:19:32.123 --> 00:19:34.139 taken it through a phase two trial  
NOTE Confidence: 0.8315963

00:19:34.139 --> 00:19:35.476 of over 60 Melanoma patients.  
NOTE Confidence: 0.8315963

00:19:35.476 --> 00:19:37.408 What they found was that it was  
NOTE Confidence: 0.8315963

00:19:37.408 --> 00:19:39.270 very well tolerated for cytokine,  
NOTE Confidence: 0.8315963

00:19:39.270 --> 00:19:40.835 but it completely bombed due  
NOTE Confidence: 0.8315963

00:19:40.835 --> 00:19:42.087 to lack of Efficacy.  
NOTE Confidence: 0.8315963

00:19:42.090 --> 00:19:43.920 Only one out of 60 three  
NOTE Confidence: 0.8315963

00:19:43.920 --> 00:19:45.800 patients had a partial response.  
NOTE Confidence: 0.8315963

00:19:45.800 --> 00:19:46.458 Next slide,  
NOTE Confidence: 0.8315963

00:19:46.458 --> 00:19:46.787 please.  
NOTE Confidence: 0.8315963

00:19:46.787 --> 00:19:49.090 So what we discovered in my lab  
NOTE Confidence: 0.8315963

00:19:49.160 --> 00:19:51.645 is that the activity of Alateen is  
NOTE Confidence: 0.8315963

00:19:51.645 --> 00:19:53.619 highly restricted by a molecule  
NOTE Confidence: 0.8315963

00:19:53.619 --> 00:19:55.719 produced by tumors within tumors  
NOTE Confidence: 0.8315963

00:19:55.719 --> 00:19:57.694 called Interleukin 18 binding protein.

NOTE Confidence: 0.8315963

00:19:57.694 --> 00:20:00.193 This is an ultra high affinity inhibitor.

NOTE Confidence: 0.8315963

00:20:00.200 --> 00:20:01.247 Violating that binds.

NOTE Confidence: 0.8315963

00:20:01.247 --> 00:20:03.341 I'll 18 inhibits its ability to

NOTE Confidence: 0.8315963

00:20:03.341 --> 00:20:04.927 interact with its receptor on,

NOTE Confidence: 0.8315963

00:20:04.930 --> 00:20:05.918 till and NK cells.

NOTE Confidence: 0.8315963

00:20:05.918 --> 00:20:08.545 And So what we did is we use directed

NOTE Confidence: 0.8315963

00:20:08.545 --> 00:20:10.699 evolution to create a version of

NOTE Confidence: 0.8315963

00:20:10.699 --> 00:20:12.350 violating that was completely

NOTE Confidence: 0.8315963

00:20:12.350 --> 00:20:14.400 impervious to the decoy receptor,

NOTE Confidence: 0.8315963

00:20:14.400 --> 00:20:16.871 but was still able to engage with

NOTE Confidence: 0.8315963

00:20:16.871 --> 00:20:18.625 highlighting receptor on until and

NOTE Confidence: 0.8315963

00:20:18.625 --> 00:20:21.153 what we found in mouse models with cancer.

NOTE Confidence: 0.8315963

00:20:21.160 --> 00:20:23.050 This is a very close collaboration

NOTE Confidence: 0.8315963

00:20:23.050 --> 00:20:25.098 with Marcus Bosenberg in the Center

NOTE Confidence: 0.8315963

00:20:25.098 --> 00:20:26.558 for precision cancer modeling.

NOTE Confidence: 0.79149914



00:20:26.560 --> 00:20:28.708 Is that just like in patients  
NOTE Confidence: 0.79149914

00:20:28.708 --> 00:20:30.390 natural wild type Interleukin 18?  
NOTE Confidence: 0.79149914

00:20:30.390 --> 00:20:31.965 That's the blue survival curve  
NOTE Confidence: 0.79149914

00:20:31.965 --> 00:20:33.225 here was entirely ineffective.  
NOTE Confidence: 0.79149914

00:20:33.230 --> 00:20:35.072 It had no ability to slow  
NOTE Confidence: 0.79149914

00:20:35.072 --> 00:20:36.710 tumor growth or cure mice.  
NOTE Confidence: 0.79149914

00:20:36.710 --> 00:20:38.290 Where's the decoy resistant variant?  
NOTE Confidence: 0.79149914

00:20:38.290 --> 00:20:40.216 Had single agent activity that could  
NOTE Confidence: 0.79149914

00:20:40.216 --> 00:20:42.092 clear two well established tumors from  
NOTE Confidence: 0.79149914

00:20:42.092 --> 00:20:43.982 the door to these mice with activity  
NOTE Confidence: 0.79149914

00:20:43.982 --> 00:20:46.380 that was commensurate in fact a bit  
NOTE Confidence: 0.79149914

00:20:46.380 --> 00:20:47.764 better than checkpoint immunotherapy.  
NOTE Confidence: 0.79149914

00:20:47.770 --> 00:20:48.715 And of course,  
NOTE Confidence: 0.79149914

00:20:48.715 --> 00:20:50.605 it synergized which equity mean therapy.  
NOTE Confidence: 0.79149914

00:20:50.610 --> 00:20:52.506 We describe these findings in that  
NOTE Confidence: 0.79149914

00:20:52.506 --> 00:20:53.770 recent publication in nature.

NOTE Confidence: 0.79149914

00:20:53.770 --> 00:20:54.718 Earlier this summer.

NOTE Confidence: 0.79149914

00:20:54.718 --> 00:20:57.090 Next slide, please.

NOTE Confidence: 0.79149914

00:20:57.090 --> 00:20:58.562 Now, obviously we're tremendously

NOTE Confidence: 0.79149914

00:20:58.562 --> 00:21:00.034 excited about the potential

NOTE Confidence: 0.79149914

00:21:00.034 --> 00:21:01.639 impact of the decor Resistant

NOTE Confidence: 0.79149914

00:21:01.639 --> 00:21:03.529 Valley Team D R18 in the clinic,

NOTE Confidence: 0.79149914

00:21:03.530 --> 00:21:05.095 and we particularly want to

NOTE Confidence: 0.79149914

00:21:05.095 --> 00:21:07.070 test it out here at Yale.

NOTE Confidence: 0.79149914

00:21:07.070 --> 00:21:09.310 We have such a leading phase one unit

NOTE Confidence: 0.79149914

00:21:09.310 --> 00:21:11.690 and an experience with set of kind

NOTE Confidence: 0.79149914

00:21:11.690 --> 00:21:13.830 of new therapies instead of that.

NOTE Confidence: 0.79149914

00:21:13.830 --> 00:21:15.762 And I recently started a company

NOTE Confidence: 0.79149914

00:21:15.762 --> 00:21:16.728 called Simcha Therapeutics.

NOTE Confidence: 0.79149914

00:21:16.730 --> 00:21:18.644 We've raised over \$25,000,000 to advance

NOTE Confidence: 0.79149914

00:21:18.644 --> 00:21:20.296 this molecule that was developed

NOTE Confidence: 0.79149914

00:21:20.296 --> 00:21:22.210 here at Yale into clinical trials,  
NOTE Confidence: 0.79149914

00:21:22.210 --> 00:21:24.660 and I'm excited to say that there  
NOTE Confidence: 0.79149914

00:21:24.660 --> 00:21:26.864 will be dosing the first patient  
NOTE Confidence: 0.79149914

00:21:26.864 --> 00:21:29.370 in the first half of next year.  
NOTE Confidence: 0.79149914

00:21:29.370 --> 00:21:31.590 Next slide, please.  
NOTE Confidence: 0.79149914

00:21:31.590 --> 00:21:34.110 So finally I want to tell you about  
NOTE Confidence: 0.79149914

00:21:34.110 --> 00:21:36.027 some emerging research in my lab.  
NOTE Confidence: 0.79149914

00:21:36.030 --> 00:21:37.298 We're missing a slide,  
NOTE Confidence: 0.79149914

00:21:37.298 --> 00:21:39.200 so I'll just briefly mention it.  
NOTE Confidence: 0.79149914

00:21:39.200 --> 00:21:40.148 Here we go,  
NOTE Confidence: 0.79149914

00:21:40.148 --> 00:21:42.044 which is that one more forward,  
NOTE Confidence: 0.79149914

00:21:42.050 --> 00:21:43.928 which is that we're not just  
NOTE Confidence: 0.79149914

00:21:43.928 --> 00:21:45.180 interested in making pharmacologic  
NOTE Confidence: 0.79149914

00:21:45.231 --> 00:21:47.115 tools drugs against the immune system,  
NOTE Confidence: 0.79149914

00:21:47.120 --> 00:21:49.190 but we're also really interested in  
NOTE Confidence: 0.79149914

00:21:49.190 --> 00:21:50.570 developing technologies in profiling

NOTE Confidence: 0.79149914

00:21:50.626 --> 00:21:52.041 the drugs that are naturally

NOTE Confidence: 0.79149914

00:21:52.041 --> 00:21:53.456 produced by the immune system.

NOTE Confidence: 0.79149914

00:21:53.460 --> 00:21:54.576 That is to say,

NOTE Confidence: 0.79149914

00:21:54.576 --> 00:21:55.971 antibodies in one thing that's

NOTE Confidence: 0.79149914

00:21:55.971 --> 00:21:57.700 becoming increasingly clear is that

NOTE Confidence: 0.79149914

00:21:57.700 --> 00:21:59.800 immunotherapy doesn't just affect T cells,

NOTE Confidence: 0.79149914

00:21:59.800 --> 00:22:02.752 but it also seems to be able to affect.

NOTE Confidence: 0.79149914

00:22:02.760 --> 00:22:04.686 Other branch of the immune system.

NOTE Confidence: 0.79149914

00:22:04.690 --> 00:22:05.332 B cells,

NOTE Confidence: 0.79149914

00:22:05.332 --> 00:22:06.616 and the moral immunity,

NOTE Confidence: 0.79149914

00:22:06.620 --> 00:22:08.230 and we hypothesize that that

NOTE Confidence: 0.79149914

00:22:08.230 --> 00:22:09.196 many cancer patients,

NOTE Confidence: 0.79149914

00:22:09.200 --> 00:22:10.810 particularly those true with immunotherapy,

NOTE Confidence: 0.79149914

00:22:10.810 --> 00:22:12.555 may be making protective anti

NOTE Confidence: 0.79149914

00:22:12.555 --> 00:22:13.951 cancer antibodies or antibodies

NOTE Confidence: 0.79149914

00:22:13.951 --> 00:22:15.458 that activate the immune system

NOTE Confidence: 0.79149914

00:22:15.458 --> 00:22:17.504 and we want to learn from these

NOTE Confidence: 0.79149914

00:22:17.504 --> 00:22:18.860 clinical trials of nature.

NOTE Confidence: 0.79149914

00:22:18.860 --> 00:22:20.425 Seeing what drugs patients made

NOTE Confidence: 0.79149914

00:22:20.425 --> 00:22:22.364 and potentially get ideas for new

NOTE Confidence: 0.79149914

00:22:22.364 --> 00:22:23.954 drug targets and potentially even

NOTE Confidence: 0.79149914

00:22:23.954 --> 00:22:25.606 new therapies from these patients

NOTE Confidence: 0.79149914

00:22:25.606 --> 00:22:27.544 and so that end we've developed

NOTE Confidence: 0.79149914

00:22:27.544 --> 00:22:29.152 this technology called Reprap index

NOTE Confidence: 0.79149914

00:22:29.152 --> 00:22:30.416 approach to management profiling

NOTE Confidence: 0.79149914

00:22:30.416 --> 00:22:32.430 that we've used to discover new

NOTE Confidence: 0.79149914

00:22:32.430 --> 00:22:33.468 auto antibody targets.

NOTE Confidence: 0.79149914

00:22:33.470 --> 00:22:35.146 We've profiled extensively in

NOTE Confidence: 0.79149914

00:22:35.146 --> 00:22:36.822 autoimmune diseases like this

NOTE Confidence: 0.79149914

00:22:36.822 --> 00:22:39.080 one here shown called ape said,

NOTE Confidence: 0.79149914

00:22:39.080 --> 00:22:41.432 but we're also now applying it

NOTE Confidence: 0.79149914

00:22:41.432 --> 00:22:43.398 together with samples from the

NOTE Confidence: 0.79149914

00:22:43.398 --> 00:22:45.336 various spores that we have here

NOTE Confidence: 0.79149914

00:22:45.336 --> 00:22:48.269 at Yale of patients treated with

NOTE Confidence: 0.79149914

00:22:48.269 --> 00:22:50.785 immunotherapy in monitored longitudinally.

NOTE Confidence: 0.79149914

00:22:50.790 --> 00:22:51.190 So yeah,

NOTE Confidence: 0.79149914

00:22:51.190 --> 00:22:52.190 thank you for your attention.

NOTE Confidence: 0.8024929

00:22:54.930 --> 00:22:57.625 And thank you, that's it's amazing science.

NOTE Confidence: 0.8024929

00:22:57.630 --> 00:23:00.325 It's my pleasure to introduce Grace Chan.

NOTE Confidence: 0.8024929

00:23:00.330 --> 00:23:02.260 She's a relatively recent recruited.

NOTE Confidence: 0.8024929

00:23:02.260 --> 00:23:04.395 Yeah, who's using really fascinating

NOTE Confidence: 0.8024929

00:23:04.395 --> 00:23:08.236 work on circular RNAs and could lead to a

NOTE Confidence: 0.8024929

00:23:08.236 --> 00:23:10.678 potential new target for immune modulation.

NOTE Confidence: 0.8024929

00:23:10.680 --> 00:23:11.868 Grace please go ahead.

NOTE Confidence: 0.8592195

00:23:14.970 --> 00:23:17.330 Hi everybody, I'm excited to great.

NOTE Confidence: 0.859219500000001

00:23:17.330 --> 00:23:19.836 Excited to tell you about my research

NOTE Confidence: 0.859219500000001

00:23:19.836 --> 00:23:22.533 program so we know that cells need  
NOTE Confidence: 0.8592195000000001

00:23:22.533 --> 00:23:24.849 to be able to recognize pathogenic  
NOTE Confidence: 0.8592195000000001

00:23:24.929 --> 00:23:27.039 RNA's to prevent infection but  
NOTE Confidence: 0.8592195000000001

00:23:27.039 --> 00:23:29.544 also recognize their own self our  
NOTE Confidence: 0.8592195000000001

00:23:29.544 --> 00:23:31.120 days to prevent autoimmunity.  
NOTE Confidence: 0.8592195000000001

00:23:31.120 --> 00:23:33.090 And so my research program  
NOTE Confidence: 0.8592195000000001

00:23:33.090 --> 00:23:34.666 has two main questions.  
NOTE Confidence: 0.8592195000000001

00:23:34.670 --> 00:23:37.330 One we're trying to understand where the  
NOTE Confidence: 0.8592195000000001

00:23:37.330 --> 00:23:39.341 molecular mechanisms for maintaining this  
NOTE Confidence: 0.8592195000000001

00:23:39.341 --> 00:23:41.753 vital balance and recognition of self,  
NOTE Confidence: 0.8592195000000001

00:23:41.760 --> 00:23:44.848 nonself and then also how can we capitalize  
NOTE Confidence: 0.8592195000000001

00:23:44.848 --> 00:23:47.740 on this distinction to develop new?  
NOTE Confidence: 0.8592195000000001

00:23:47.740 --> 00:23:51.796 Cancer therapies. And so we had.  
NOTE Confidence: 0.8592195000000001

00:23:51.800 --> 00:23:54.446 Discovered that you carry out excels,  
NOTE Confidence: 0.8592195000000001

00:23:54.450 --> 00:23:57.054 have a way to distinguish between  
NOTE Confidence: 0.8592195000000001

00:23:57.054 --> 00:23:59.310 foreign circular RNAs and self

NOTE Confidence: 0.859219500000001

00:23:59.310 --> 00:24:01.515 circular maze or circular RNAs.

NOTE Confidence: 0.859219500000001

00:24:01.520 --> 00:24:03.914 Are this newly discovered class of

NOTE Confidence: 0.859219500000001

00:24:03.914 --> 00:24:06.093 endogenous RNAs that are abundant

NOTE Confidence: 0.859219500000001

00:24:06.093 --> 00:24:08.149 and ubiquitous in eukaryotes?

NOTE Confidence: 0.859219500000001

00:24:08.150 --> 00:24:10.814 And so, with this distinction between

NOTE Confidence: 0.859219500000001

00:24:10.814 --> 00:24:13.020 foreign and self circular RNAs,

NOTE Confidence: 0.859219500000001

00:24:13.020 --> 00:24:15.385 we hypothesize that we could

NOTE Confidence: 0.859219500000001

00:24:15.385 --> 00:24:17.277 engineer foreign circular RNA's

NOTE Confidence: 0.859219500000001

00:24:17.277 --> 00:24:20.090 to be a potent vaccine agg event.

NOTE Confidence: 0.859219500000001

00:24:20.090 --> 00:24:24.036 And if you go to the next slide, please.

NOTE Confidence: 0.859219500000001

00:24:24.036 --> 00:24:27.364 We found that if we deliver born circular

NOTE Confidence: 0.859219500000001

00:24:27.364 --> 00:24:30.209 RNAs into mice and then challenged

NOTE Confidence: 0.859219500000001

00:24:30.209 --> 00:24:32.559 with cancer b16 Melanoma cells,

NOTE Confidence: 0.859219500000001

00:24:32.560 --> 00:24:36.208 we were able to protect the mice against

NOTE Confidence: 0.859219500000001

00:24:36.208 --> 00:24:38.778 those subsequent sort of initiation of

NOTE Confidence: 0.859219500000001



00:24:38.778 --> 00:24:42.259 the tumor as well as growth of the tumor,  
NOTE Confidence: 0.8592195000000001

00:24:42.260 --> 00:24:44.882 and we're excited to work with  
NOTE Confidence: 0.8592195000000001

00:24:44.882 --> 00:24:47.178 the Center for precision cancer  
NOTE Confidence: 0.8592195000000001

00:24:47.178 --> 00:24:49.518 modeling to continue to investigate  
NOTE Confidence: 0.8592195000000001

00:24:49.518 --> 00:24:53.162 one of the scope and effects of the  
NOTE Confidence: 0.8592195000000001

00:24:53.162 --> 00:24:55.688 circular RNAs as a cancer vaccine.  
NOTE Confidence: 0.8592195000000001

00:24:55.690 --> 00:24:56.574 Next please.  
NOTE Confidence: 0.8592195000000001

00:24:56.574 --> 00:24:59.668 Another area of my program is to  
NOTE Confidence: 0.8592195000000001

00:24:59.668 --> 00:25:02.282 understand what are the features of  
NOTE Confidence: 0.8592195000000001

00:25:02.282 --> 00:25:05.850 the circular RNA that allows a cell to  
NOTE Confidence: 0.8592195000000001

00:25:05.850 --> 00:25:08.170 distinguish between self and foreign,  
NOTE Confidence: 0.8592195000000001

00:25:08.170 --> 00:25:10.230 and we identify the specific  
NOTE Confidence: 0.8592195000000001

00:25:10.230 --> 00:25:12.290 RNA modification called N 6,  
NOTE Confidence: 0.8592195000000001

00:25:12.290 --> 00:25:14.350 methyl adenosine or M6 say.  
NOTE Confidence: 0.8592195000000001

00:25:14.350 --> 00:25:17.094 So we saw that self circular RNAs  
NOTE Confidence: 0.8592195000000001

00:25:17.094 --> 00:25:19.201 associated with these enzymes that

NOTE Confidence: 0.859219500000001

00:25:19.201 --> 00:25:21.769 recognize M6A or interact with M6A,

NOTE Confidence: 0.859219500000001

00:25:21.770 --> 00:25:23.414 whereas these foreign circular

NOTE Confidence: 0.859219500000001

00:25:23.414 --> 00:25:24.647 armies did not,

NOTE Confidence: 0.859219500000001

00:25:24.650 --> 00:25:28.026 and so we thought we could target the.

NOTE Confidence: 0.859219500000001

00:25:28.030 --> 00:25:31.735 An enzyme that installs this

NOTE Confidence: 0.859219500000001

00:25:31.735 --> 00:25:33.958 modifications next please.

NOTE Confidence: 0.859219500000001

00:25:33.960 --> 00:25:36.032 Next slide,

NOTE Confidence: 0.859219500000001

00:25:36.032 --> 00:25:37.068 please.

NOTE Confidence: 0.859219500000001

00:25:37.070 --> 00:25:39.950 And we saw that and breast cancer

NOTE Confidence: 0.859219500000001

00:25:39.950 --> 00:25:42.245 epithelial cells type 3 interferons

NOTE Confidence: 0.859219500000001

00:25:42.245 --> 00:25:44.797 were specifically upregulated when

NOTE Confidence: 0.859219500000001

00:25:44.797 --> 00:25:47.349 M6A modification is decreased,

NOTE Confidence: 0.859219500000001

00:25:47.350 --> 00:25:50.365 whereas type one interference are

NOTE Confidence: 0.859219500000001

00:25:50.365 --> 00:25:54.230 not changed and so next please.

NOTE Confidence: 0.859219500000001

00:25:54.230 --> 00:25:57.422 My program has been interested in both

NOTE Confidence: 0.859219500000001

00:25:57.422 --> 00:25:59.338 uncovering the molecular mechanism  
NOTE Confidence: 0.8592195000000001

00:25:59.338 --> 00:26:01.693 for how RNA modification controls  
NOTE Confidence: 0.8592195000000001

00:26:01.693 --> 00:26:04.802 an immune response as well as to  
NOTE Confidence: 0.8592195000000001

00:26:04.802 --> 00:26:07.106 understand if there are targets along  
NOTE Confidence: 0.8592195000000001

00:26:07.106 --> 00:26:10.140 that pathway that we can identify two  
NOTE Confidence: 0.8592195000000001

00:26:10.140 --> 00:26:12.350 to specifically target cancer cells.  
NOTE Confidence: 0.8592195000000001

00:26:12.350 --> 00:26:13.240 Thank you.  
NOTE Confidence: 0.90042603

00:26:20.770 --> 00:26:22.738 Great, thank you.  
NOTE Confidence: 0.90042603

00:26:22.740 --> 00:26:25.604 I I I I don't think the next  
NOTE Confidence: 0.90042603

00:26:25.604 --> 00:26:27.859 speaker needs any introduction.  
NOTE Confidence: 0.90042603

00:26:27.860 --> 00:26:30.849 Doctor Who Saki has become world famous  
NOTE Confidence: 0.90042603

00:26:30.849 --> 00:26:33.842 was before but now really very well  
NOTE Confidence: 0.90042603

00:26:33.842 --> 00:26:36.824 known for all her work in COVID-19.  
NOTE Confidence: 0.90042603

00:26:36.830 --> 00:26:39.396 She's an outstanding immunologist and also  
NOTE Confidence: 0.90042603

00:26:39.396 --> 00:26:42.811 has a research interest in cancer also Kiko,  
NOTE Confidence: 0.90042603

00:26:42.811 --> 00:26:44.518 please, please go ahead.

NOTE Confidence: 0.82971156

00:26:45.520 --> 00:26:46.798 Thank you Mario.

NOTE Confidence: 0.82971156

00:26:46.798 --> 00:26:48.928 I'm delighted to be here.

NOTE Confidence: 0.82971156

00:26:48.930 --> 00:26:51.282 So today I'm just going to start

NOTE Confidence: 0.82971156

00:26:51.282 --> 00:26:52.994 with this principle guiding

NOTE Confidence: 0.82971156

00:26:52.994 --> 00:26:54.887 effective cancer immunotherapy.

NOTE Confidence: 0.82971156

00:26:54.890 --> 00:26:57.837 And I'm borrowing a page from Doctor

NOTE Confidence: 0.82971156

00:26:57.837 --> 00:26:59.987 IRA Mehlman's cancer immunity cycle

NOTE Confidence: 0.82971156

00:26:59.987 --> 00:27:02.829 book as any anyone on this call

NOTE Confidence: 0.82971156

00:27:02.829 --> 00:27:05.487 probably has seen this but essentially

NOTE Confidence: 0.82971156

00:27:05.487 --> 00:27:08.139 just wanted to highlight that there

NOTE Confidence: 0.82971156

00:27:08.139 --> 00:27:10.484 are steps in immune surveillance

NOTE Confidence: 0.82971156

00:27:10.484 --> 00:27:13.570 and clearance of cancer that is not

NOTE Confidence: 0.82971156

00:27:13.570 --> 00:27:15.838 working very well and that's Why.

NOTE Confidence: 0.82971156

00:27:15.840 --> 00:27:18.312 People develop cancer and some of

NOTE Confidence: 0.82971156

00:27:18.312 --> 00:27:20.556 them are treatable with checkpoint

NOTE Confidence: 0.82971156

00:27:20.556 --> 00:27:23.146 inhibitors while others are not.  
NOTE Confidence: 0.82971156

00:27:23.150 --> 00:27:25.904 So my laboratory has started to  
NOTE Confidence: 0.82971156

00:27:25.904 --> 00:27:27.740 really examine these fundamental  
NOTE Confidence: 0.82971156

00:27:27.821 --> 00:27:31.034 issues relating to all those stages of  
NOTE Confidence: 0.82971156

00:27:31.034 --> 00:27:33.209 recognition and clearance of cancer.  
NOTE Confidence: 0.82971156

00:27:33.210 --> 00:27:36.234 So the immune surveillance begins by  
NOTE Confidence: 0.82971156

00:27:36.234 --> 00:27:38.890 dendritic cells within the cancer.  
NOTE Confidence: 0.82971156

00:27:38.890 --> 00:27:41.404 Carrying the The Antigen to the  
NOTE Confidence: 0.82971156

00:27:41.404 --> 00:27:44.072 draining lymph node and that stimulates  
NOTE Confidence: 0.82971156

00:27:44.072 --> 00:27:47.271 T cells that are specific to cancer  
NOTE Confidence: 0.82971156

00:27:47.271 --> 00:27:49.903 antigens and those T cells can  
NOTE Confidence: 0.82971156

00:27:49.903 --> 00:27:51.998 divide and become effector cells.  
NOTE Confidence: 0.82971156

00:27:52.000 --> 00:27:54.534 They will migrate back to the site  
NOTE Confidence: 0.82971156

00:27:54.534 --> 00:27:56.950 of cancer to infiltrate into that  
NOTE Confidence: 0.82971156

00:27:56.950 --> 00:28:00.459 issue and that allows for T cells to  
NOTE Confidence: 0.82971156

00:28:00.459 --> 00:28:03.039 recognize cancer cells through specific

NOTE Confidence: 0.82971156

00:28:03.039 --> 00:28:05.984 antigen and clearance of the cancer.

NOTE Confidence: 0.82971156

00:28:05.984 --> 00:28:08.605 Using cytotoxic mechanisms and of course,

NOTE Confidence: 0.82971156

00:28:08.605 --> 00:28:09.956 checkpoint inhibitors can.

NOTE Confidence: 0.82971156

00:28:09.956 --> 00:28:13.162 Really engage in in this whole cycle

NOTE Confidence: 0.82971156

00:28:13.162 --> 00:28:16.001 by allowing the effector function of

NOTE Confidence: 0.82971156

00:28:16.001 --> 00:28:19.550 T cells to occur more more robustly.

NOTE Confidence: 0.82971156

00:28:19.550 --> 00:28:20.783 Next slide, please.

NOTE Confidence: 0.82971156

00:28:20.783 --> 00:28:24.273 So we began to sort of try to

NOTE Confidence: 0.82971156

00:28:24.273 --> 00:28:26.863 understand why this immunity cycle

NOTE Confidence: 0.82971156

00:28:26.863 --> 00:28:29.570 doesn't work in most cases,

NOTE Confidence: 0.82971156

00:28:29.570 --> 00:28:32.902 and one of the issues that we

NOTE Confidence: 0.82971156

00:28:32.902 --> 00:28:33.854 tackled recently,

NOTE Confidence: 0.82971156

00:28:33.860 --> 00:28:36.240 which was this paper that

NOTE Confidence: 0.82971156

00:28:36.240 --> 00:28:38.144 published earlier this year,

NOTE Confidence: 0.82971156

00:28:38.150 --> 00:28:39.982 we discovered that the.

NOTE Confidence: 0.82971156

00:28:39.982 --> 00:28:42.730 Lymphatics that are draining the brain,  
NOTE Confidence: 0.82971156

00:28:42.730 --> 00:28:45.560 which is the meningeal lymphatics.  
NOTE Confidence: 0.82971156

00:28:45.560 --> 00:28:48.881 Do not do not drain that issue as well  
NOTE Confidence: 0.82971156

00:28:48.881 --> 00:28:52.490 as other lymphatics found in the skin.  
NOTE Confidence: 0.82971156

00:28:52.490 --> 00:28:55.154 For example and by increasing the  
NOTE Confidence: 0.82971156

00:28:55.154 --> 00:28:56.930 drainage through the meningeal  
NOTE Confidence: 0.82971156

00:28:57.008 --> 00:28:58.843 lymphatics by introducing into the  
NOTE Confidence: 0.82971156

00:28:58.843 --> 00:29:02.169 CSF or veg of see we can actually  
NOTE Confidence: 0.82971156

00:29:02.169 --> 00:29:04.061 increase the immune surveillance  
NOTE Confidence: 0.82971156

00:29:04.061 --> 00:29:06.442 and better priming for glioblastoma  
NOTE Confidence: 0.82971156

00:29:06.442 --> 00:29:09.809 and also other brain meds and so  
NOTE Confidence: 0.82971156

00:29:09.809 --> 00:29:13.508 this is so it's driven us to in new  
NOTE Confidence: 0.82971156

00:29:13.508 --> 00:29:16.168 technology we call in faxes where.  
NOTE Confidence: 0.82971156

00:29:16.170 --> 00:29:18.252 Doctor Alan Ring and I are  
NOTE Confidence: 0.82971156

00:29:18.252 --> 00:29:20.510 collaborating to make a better sort  
NOTE Confidence: 0.82971156

00:29:20.510 --> 00:29:22.886 of more specific agent that can

NOTE Confidence: 0.82971156

00:29:22.886 --> 00:29:24.809 stimulate the meningeal lymphatics

NOTE Confidence: 0.82971156

00:29:24.809 --> 00:29:26.921 to increase immune surveillance

NOTE Confidence: 0.82971156

00:29:26.921 --> 00:29:29.033 in clearance of cancer.

NOTE Confidence: 0.82971156

00:29:29.040 --> 00:29:29.900 Next please.

NOTE Confidence: 0.83901122222222

00:29:32.030 --> 00:29:33.056 Next please.

NOTE Confidence: 0.83901122222222

00:29:33.056 --> 00:29:36.647 The other key issue is the antigen,

NOTE Confidence: 0.83901122222222

00:29:36.650 --> 00:29:39.200 so in addition to the mutation

NOTE Confidence: 0.83901122222222

00:29:39.200 --> 00:29:41.520 load that accumulates in cancer,

NOTE Confidence: 0.83901122222222

00:29:41.520 --> 00:29:44.262 there's also this other type of

NOTE Confidence: 0.83901122222222

00:29:44.262 --> 00:29:46.400 antigen that we're focusing on,

NOTE Confidence: 0.83901122222222

00:29:46.400 --> 00:29:48.610 which is the endogenous retrovirus

NOTE Confidence: 0.83901122222222

00:29:48.610 --> 00:29:50.378 which Anderson at Nosiness.

NOTE Confidence: 0.83901122222222

00:29:50.380 --> 00:29:53.488 Retroviruses are occupy 8% of our genome,

NOTE Confidence: 0.83901122222222

00:29:53.490 --> 00:29:56.584 and many of them have coding capacity,

NOTE Confidence: 0.83901122222222

00:29:56.590 --> 00:29:58.880 and many are mostly silenced

NOTE Confidence: 0.83901122222222



00:29:58.880 --> 00:30:00.254 after developmental stage.  
NOTE Confidence: 0.8390112222222222

00:30:00.260 --> 00:30:01.595 Early developmental stage,  
NOTE Confidence: 0.8390112222222222

00:30:01.595 --> 00:30:03.820 but can be reactivated during  
NOTE Confidence: 0.8390112222222222

00:30:03.820 --> 00:30:05.873 oncogenesis and so we're targeting  
NOTE Confidence: 0.8390112222222222

00:30:05.873 --> 00:30:07.698 and what first identifying what  
NOTE Confidence: 0.8390112222222222

00:30:07.698 --> 00:30:09.394 kinds of endogenous retroviruses  
NOTE Confidence: 0.8390112222222222

00:30:09.394 --> 00:30:12.100 or reactivated in some cancers and  
NOTE Confidence: 0.8390112222222222

00:30:12.100 --> 00:30:14.710 targeting this using a new tool  
NOTE Confidence: 0.8390112222222222

00:30:14.710 --> 00:30:17.260 that we created called Earth map.  
NOTE Confidence: 0.8390112222222222

00:30:17.260 --> 00:30:21.145 And this is also an ongoing collaboration  
NOTE Confidence: 0.8390112222222222

00:30:21.145 --> 00:30:24.022 with Marcus Bosenberg's group as well  
NOTE Confidence: 0.8390112222222222

00:30:24.022 --> 00:30:27.806 as Grace Chen to look at these or of  
NOTE Confidence: 0.8390112222222222

00:30:27.806 --> 00:30:31.004 dysregulation in cancer tissues next please.  
NOTE Confidence: 0.8390112222222222

00:30:31.010 --> 00:30:33.000 So once these thank you,  
NOTE Confidence: 0.8390112222222222

00:30:33.000 --> 00:30:34.584 once these energies are  
NOTE Confidence: 0.8390112222222222

00:30:34.584 --> 00:30:36.168 recognized by T cells,

NOTE Confidence: 0.83901122222222

00:30:36.170 --> 00:30:37.990 diesel still have to migrate

NOTE Confidence: 0.83901122222222

00:30:37.990 --> 00:30:40.328 back into the tumor tissue to

NOTE Confidence: 0.83901122222222

00:30:40.328 --> 00:30:42.128 perform its cytolytic function.

NOTE Confidence: 0.83901122222222

00:30:42.130 --> 00:30:44.722 And what we're trying to do is to

NOTE Confidence: 0.83901122222222

00:30:44.722 --> 00:30:46.773 encourage this process by stimulating

NOTE Confidence: 0.83901122222222

00:30:46.773 --> 00:30:48.998 the local micro environment using

NOTE Confidence: 0.83901122222222

00:30:48.998 --> 00:30:51.650 short RNA that stimulates free guy,

NOTE Confidence: 0.83901122222222

00:30:51.650 --> 00:30:54.429 which we call stem Blue Barney SLR.

NOTE Confidence: 0.83901122222222

00:30:54.430 --> 00:30:56.415 This is a collaboration with

NOTE Confidence: 0.83901122222222

00:30:56.415 --> 00:30:58.003 an appliance group here,

NOTE Confidence: 0.83901122222222

00:30:58.010 --> 00:31:00.644 and we've just formed a new

NOTE Confidence: 0.83901122222222

00:31:00.644 --> 00:31:02.400 company called rig immune.

NOTE Confidence: 0.83901122222222

00:31:02.400 --> 00:31:04.410 Which is really inoculation of

NOTE Confidence: 0.83901122222222

00:31:04.410 --> 00:31:07.351 this LR into the tumor to stimulate

NOTE Confidence: 0.83901122222222

00:31:07.351 --> 00:31:09.466 not only T cell migration,

NOTE Confidence: 0.83901122222222

00:31:09.470 --> 00:31:11.780 but also priming of tumor specific

NOTE Confidence: 0.8390112222222222

00:31:11.780 --> 00:31:14.294 T cell and possibly Rick Kumanan

NOTE Confidence: 0.8390112222222222

00:31:14.294 --> 00:31:16.534 clearance of this these tumors,

NOTE Confidence: 0.8390112222222222

00:31:16.540 --> 00:31:17.396 and finally,

NOTE Confidence: 0.8390112222222222

00:31:17.396 --> 00:31:19.536 in order for the checkpoint

NOTE Confidence: 0.8390112222222222

00:31:19.536 --> 00:31:21.120 inhibitors to work in,

NOTE Confidence: 0.8390112222222222

00:31:21.120 --> 00:31:23.265 you know privileged organs like

NOTE Confidence: 0.8390112222222222

00:31:23.265 --> 00:31:25.847 the brain we are allowing those

NOTE Confidence: 0.8390112222222222

00:31:25.847 --> 00:31:28.374 antibodies such as anti PD L1 to

NOTE Confidence: 0.8390112222222222

00:31:28.374 --> 00:31:31.430 come into that issue using a BBB

NOTE Confidence: 0.8390112222222222

00:31:31.430 --> 00:31:33.234 access technology we developed.

NOTE Confidence: 0.8390112222222222

00:31:33.240 --> 00:31:34.884 We call synaxis an.

NOTE Confidence: 0.8390112222222222

00:31:34.884 --> 00:31:37.350 It allows the baby to transient

NOTE Confidence: 0.8390112222222222

00:31:37.433 --> 00:31:40.422 Lee open to enable any kind of

NOTE Confidence: 0.8390112222222222

00:31:40.422 --> 00:31:42.656 macromolecules to come into the

NOTE Confidence: 0.8390112222222222

00:31:42.656 --> 00:31:44.831 brain for transition time period

NOTE Confidence: 0.83901122222222

00:31:44.831 --> 00:31:46.570 for a better access.

NOTE Confidence: 0.83901122222222

00:31:46.570 --> 00:31:48.720 An better clearance of glioblastoma

NOTE Confidence: 0.83901122222222

00:31:48.720 --> 00:31:51.300 so I'll end there. Thank you.

NOTE Confidence: 0.81744766

00:31:54.480 --> 00:31:55.880 OK, cool, thank you.

NOTE Confidence: 0.81744766

00:31:55.880 --> 00:31:57.993 It's really outstanding science so it's

NOTE Confidence: 0.81744766

00:31:57.993 --> 00:32:00.099 my pleasure to introduce our moment.

NOTE Confidence: 0.81744766

00:32:00.100 --> 00:32:02.550 He's as you know, the vice president.

NOTE Confidence: 0.81744766

00:32:02.550 --> 00:32:03.978 Cancer immunology for Genentech.

NOTE Confidence: 0.81744766

00:32:03.978 --> 00:32:05.049 Professor of biochemistry

NOTE Confidence: 0.81744766

00:32:05.049 --> 00:32:06.410 and biophysics at UCSF,

NOTE Confidence: 0.81744766

00:32:06.410 --> 00:32:08.867 but formerly before all of those was

NOTE Confidence: 0.81744766

00:32:08.867 --> 00:32:11.678 actually ahead of cell biology here at Yale.

NOTE Confidence: 0.81744766

00:32:11.680 --> 00:32:14.264 Higher first of all, let me thank you

NOTE Confidence: 0.81744766

00:32:14.264 --> 00:32:16.587 for agreeing to provide some comments.

NOTE Confidence: 0.81744766

00:32:16.590 --> 00:32:20.100 We just like to ask you to to give you.

NOTE Confidence: 0.81744766

00:32:20.100 --> 00:32:21.780 Give us briefly your thoughts  
NOTE Confidence: 0.81744766

00:32:21.780 --> 00:32:23.124 about challenges and opportunities  
NOTE Confidence: 0.81744766

00:32:23.124 --> 00:32:24.320 in Immuno Oncology.  
NOTE Confidence: 0.81744766

00:32:24.320 --> 00:32:26.756 Highlight those that you think might be  
NOTE Confidence: 0.81744766

00:32:26.756 --> 00:32:29.069 might benefit from collaborations with.  
NOTE Confidence: 0.81744766

00:32:29.070 --> 00:32:30.470 With academics for example.  
NOTE Confidence: 0.83307904

00:32:31.970 --> 00:32:34.160 Thanks Mario Dan Hyder. All my  
NOTE Confidence: 0.83307904

00:32:34.160 --> 00:32:36.859 friends who there is been alluded to.  
NOTE Confidence: 0.83307904

00:32:36.860 --> 00:32:39.485 I do have multiple connections to deal.  
NOTE Confidence: 0.83307904

00:32:39.490 --> 00:32:41.734 In fact, we've spent probably well  
NOTE Confidence: 0.83307904

00:32:41.734 --> 00:32:44.749 more than half of my adult life there,  
NOTE Confidence: 0.83307904

00:32:44.750 --> 00:32:47.006 so I left back in 2007.  
NOTE Confidence: 0.83307904

00:32:47.010 --> 00:32:49.266 Really for the purpose of trying  
NOTE Confidence: 0.83307904

00:32:49.266 --> 00:32:50.770 to accelerate this field,  
NOTE Confidence: 0.83307904

00:32:50.770 --> 00:32:53.002 feeling that what was really needed  
NOTE Confidence: 0.83307904

00:32:53.002 --> 00:32:55.330 in the first instance was the

NOTE Confidence: 0.83307904

00:32:55.330 --> 00:32:56.870 production of experimental agents

NOTE Confidence: 0.83307904

00:32:56.870 --> 00:32:59.754 that we could get into patients and

NOTE Confidence: 0.83307904

00:32:59.754 --> 00:33:01.874 sample what is actually happening.

NOTE Confidence: 0.83307904

00:33:01.880 --> 00:33:03.510 As a consequence of therapy,

NOTE Confidence: 0.83307904

00:33:03.510 --> 00:33:06.320 in order to understand it.

NOTE Confidence: 0.83307904

00:33:06.320 --> 00:33:08.448 As I think I often find myself

NOTE Confidence: 0.83307904

00:33:08.448 --> 00:33:10.421 saying the only model for human

NOTE Confidence: 0.83307904

00:33:10.421 --> 00:33:12.731 cancer is human cancer in the end,

NOTE Confidence: 0.83307904

00:33:12.740 --> 00:33:14.991 and it's not to say that you

NOTE Confidence: 0.83307904

00:33:14.991 --> 00:33:15.954 can't learn many,

NOTE Confidence: 0.83307904

00:33:15.954 --> 00:33:17.559 many critical things from mice,

NOTE Confidence: 0.83307904

00:33:17.560 --> 00:33:19.821 but if you actually want to reduce

NOTE Confidence: 0.83307904

00:33:19.821 --> 00:33:21.789 to practice what it is you're

NOTE Confidence: 0.83307904

00:33:21.789 --> 00:33:23.649 trying to do in the laboratory,

NOTE Confidence: 0.83307904

00:33:23.650 --> 00:33:25.897 you need access not only to patients,

NOTE Confidence: 0.83307904

00:33:25.900 --> 00:33:27.505 but to experimental drugs that  
NOTE Confidence: 0.83307904

00:33:27.505 --> 00:33:28.789 you can actually perform.  
NOTE Confidence: 0.83307904

00:33:28.790 --> 00:33:31.037 These types of critical studies in patients.  
NOTE Confidence: 0.83307904

00:33:31.040 --> 00:33:33.752 And it turns out that that's a very  
NOTE Confidence: 0.83307904

00:33:33.752 --> 00:33:35.698 difficult thing to do in academia.  
NOTE Confidence: 0.83307904

00:33:35.700 --> 00:33:37.968 And moving to a biotech company.  
NOTE Confidence: 0.83307904

00:33:37.970 --> 00:33:39.870 Large one is genetic really  
NOTE Confidence: 0.83307904

00:33:39.870 --> 00:33:41.010 provided that opportunity.  
NOTE Confidence: 0.83307904

00:33:41.010 --> 00:33:43.308 So that's something that the companies  
NOTE Confidence: 0.83307904

00:33:43.308 --> 00:33:46.427 do well and I think one reason I  
NOTE Confidence: 0.83307904

00:33:46.427 --> 00:33:48.683 chose or took the opportunity to  
NOTE Confidence: 0.83307904

00:33:48.762 --> 00:33:51.289 move to Genetec as opposed to other  
NOTE Confidence: 0.83307904

00:33:51.289 --> 00:33:54.270 places was because it is a very  
NOTE Confidence: 0.83307904

00:33:54.270 --> 00:33:55.782 highly researched based place.  
NOTE Confidence: 0.83307904

00:33:55.790 --> 00:33:56.921 In other words,  
NOTE Confidence: 0.83307904

00:33:56.921 --> 00:34:00.339 we are as serious I think as you are,

NOTE Confidence: 0.83307904

00:34:00.340 --> 00:34:03.212 or I was well also faculty member in

NOTE Confidence: 0.83307904

00:34:03.212 --> 00:34:05.808 pushing the field of basic research.

NOTE Confidence: 0.83307904

00:34:05.810 --> 00:34:10.864 Particularly in this area, as as anyone.

NOTE Confidence: 0.83307904

00:34:10.870 --> 00:34:14.430 Part of that was to try and breakdown.

NOTE Confidence: 0.82013416

00:34:16.510 --> 00:34:18.234 With biomarker studies understanding

NOTE Confidence: 0.82013416

00:34:18.234 --> 00:34:21.211 what the various steps in cancer had

NOTE Confidence: 0.82013416

00:34:21.211 --> 00:34:23.486 to be overcome in order to generate

NOTE Confidence: 0.82013416

00:34:23.486 --> 00:34:25.200 a productive immune response,

NOTE Confidence: 0.82013416

00:34:25.200 --> 00:34:29.280 and Akiko is kindly already referred to this.

NOTE Confidence: 0.82013416

00:34:29.280 --> 00:34:31.982 But again, the main reason was really

NOTE Confidence: 0.82013416

00:34:31.982 --> 00:34:34.675 the production of agents that that we

NOTE Confidence: 0.82013416

00:34:34.675 --> 00:34:37.360 could use to study these various steps

NOTE Confidence: 0.82013416

00:34:37.360 --> 00:34:39.886 and so called cancer immunity cycle.

NOTE Confidence: 0.82013416

00:34:39.890 --> 00:34:41.860 Now, OK, we've done that.

NOTE Confidence: 0.82013416

00:34:41.860 --> 00:34:44.956 We have a variety of agents in the clinic

NOTE Confidence: 0.82013416



00:34:44.956 --> 00:34:47.749 and they're starting to study them.

NOTE Confidence: 0.82013416

00:34:47.750 --> 00:34:49.735 These range from the checkpoint

NOTE Confidence: 0.82013416

00:34:49.735 --> 00:34:52.070 inhibitors such as the PD one,

NOTE Confidence: 0.82013416

00:34:52.070 --> 00:34:54.305 blockers that Roy Herbst is

NOTE Confidence: 0.82013416

00:34:54.305 --> 00:34:56.540 already brought to your attention

NOTE Confidence: 0.82013416

00:34:56.617 --> 00:34:58.669 and everybody already knows.

NOTE Confidence: 0.82013416

00:34:58.670 --> 00:35:00.462 Second generation checkpoint inhibitors.

NOTE Confidence: 0.82013416

00:35:00.462 --> 00:35:03.150 The one that we have advanced

NOTE Confidence: 0.82013416

00:35:03.223 --> 00:35:04.887 in something called Tigit.

NOTE Confidence: 0.82013416

00:35:04.890 --> 00:35:06.750 We seem to be performing quite

NOTE Confidence: 0.82013416

00:35:06.750 --> 00:35:08.725 well in the clinic thus far

NOTE Confidence: 0.82013416

00:35:08.725 --> 00:35:10.395 in a variety of indications,

NOTE Confidence: 0.82013416

00:35:10.400 --> 00:35:12.020 but I think more importantly,

NOTE Confidence: 0.82013416

00:35:12.020 --> 00:35:14.029 the next major goal is going to

NOTE Confidence: 0.82013416

00:35:14.029 --> 00:35:15.909 be to address those patients.

NOTE Confidence: 0.82013416

00:35:15.910 --> 00:35:17.030 As Akiko was saying,

NOTE Confidence: 0.82013416

00:35:17.030 --> 00:35:19.529 that do not exhibit much in the way

NOTE Confidence: 0.82013416

00:35:19.529 --> 00:35:21.409 of response to checkpoint inhibitors.

NOTE Confidence: 0.82013416

00:35:21.410 --> 00:35:23.030 In order to do this,

NOTE Confidence: 0.82013416

00:35:23.030 --> 00:35:25.294 you need to have a holistic view of

NOTE Confidence: 0.82013416

00:35:25.294 --> 00:35:27.339 various steps and potential rate limiting

NOTE Confidence: 0.82013416

00:35:27.339 --> 00:35:29.842 steps that impede the progress of an

NOTE Confidence: 0.82013416

00:35:29.842 --> 00:35:31.774 immune response in a cancer patient.

NOTE Confidence: 0.82013416

00:35:31.780 --> 00:35:34.426 The one that I think we find.

NOTE Confidence: 0.82013416

00:35:34.430 --> 00:35:36.270 Most daunting at the moment.

NOTE Confidence: 0.82013416

00:35:36.270 --> 00:35:38.616 Certainly the most common is found

NOTE Confidence: 0.82013416

00:35:38.616 --> 00:35:41.040 here between steps 5 and step 6,

NOTE Confidence: 0.82013416

00:35:41.040 --> 00:35:42.870 which is the egress or.

NOTE Confidence: 0.834624588

00:35:45.240 --> 00:35:47.720 Tumor reactive T cells.

NOTE Confidence: 0.834624588

00:35:47.720 --> 00:35:50.178 Or other cells from the blood

NOTE Confidence: 0.834624588

00:35:50.178 --> 00:35:52.272 got into the tumor because most

NOTE Confidence: 0.834624588

00:35:52.272 --> 00:35:54.658 tumors are not just sitting there  
NOTE Confidence: 0.834624588

00:35:54.658 --> 00:35:56.673 waiting to receive these cells,  
NOTE Confidence: 0.834624588

00:35:56.680 --> 00:35:59.655 but rather are invested by a highly  
NOTE Confidence: 0.834624588

00:35:59.655 --> 00:36:01.289 immunosuppressive and physical blockade  
NOTE Confidence: 0.834624588

00:36:01.289 --> 00:36:03.880 in the form of the Peri Tumoral Strama,  
NOTE Confidence: 0.834624588

00:36:03.880 --> 00:36:05.014 which basically Christy  
NOTE Confidence: 0.834624588

00:36:05.014 --> 00:36:06.526 cells and inactivates them.  
NOTE Confidence: 0.834624588

00:36:06.530 --> 00:36:09.490 So I think one of the major scientific  
NOTE Confidence: 0.834624588

00:36:09.490 --> 00:36:12.208 challenges we have is to how to  
NOTE Confidence: 0.834624588

00:36:12.208 --> 00:36:13.728 overcome that stromal barrier,  
NOTE Confidence: 0.834624588

00:36:13.730 --> 00:36:15.486 and by doing so,  
NOTE Confidence: 0.834624588

00:36:15.486 --> 00:36:18.120 we feel we can probably unlock.  
NOTE Confidence: 0.834624588

00:36:18.120 --> 00:36:20.826 The benefits of even just first  
NOTE Confidence: 0.834624588

00:36:20.826 --> 00:36:22.630 generation checkpoint inhibitors to  
NOTE Confidence: 0.834624588

00:36:22.706 --> 00:36:24.769 as many as 50% more cancer patients  
NOTE Confidence: 0.834624588

00:36:24.769 --> 00:36:26.634 than are currently being addressed

NOTE Confidence: 0.834624588

00:36:26.634 --> 00:36:28.681 with just checkpoint inhibitors alone

NOTE Confidence: 0.834624588

00:36:28.681 --> 00:36:30.746 or in combination with chemotherapy

NOTE Confidence: 0.834624588

00:36:30.746 --> 00:36:33.128 or other types of targeted therapy.

NOTE Confidence: 0.834624588

00:36:33.130 --> 00:36:36.478 Now this is where the partnership

NOTE Confidence: 0.834624588

00:36:36.478 --> 00:36:38.152 comes in because.

NOTE Confidence: 0.834624588

00:36:38.160 --> 00:36:40.108 To add a company,

NOTE Confidence: 0.834624588

00:36:40.108 --> 00:36:43.030 we don't have a medical school

NOTE Confidence: 0.834624588

00:36:43.135 --> 00:36:45.470 or a hospital and less.

NOTE Confidence: 0.834624588

00:36:45.470 --> 00:36:48.755 Happened to be in a John Le Carre novel

NOTE Confidence: 0.834624588

00:36:48.755 --> 00:36:51.890 which didn't workout too well for them.

NOTE Confidence: 0.834624588

00:36:51.890 --> 00:36:54.846 But traditional relationship

NOTE Confidence: 0.834624588

00:36:54.846 --> 00:36:56.458 between companies and academic

NOTE Confidence: 0.834624588

00:36:56.458 --> 00:36:58.579 institutions is to fill that gap.

NOTE Confidence: 0.834624588

00:36:58.580 --> 00:36:59.672 In other words,

NOTE Confidence: 0.834624588

00:36:59.672 --> 00:37:01.856 when trials are run of new

NOTE Confidence: 0.834624588

00:37:01.856 --> 00:37:02.730 investigational agents,  
NOTE Confidence: 0.834624588

00:37:02.730 --> 00:37:04.242 they run at hospitals.  
NOTE Confidence: 0.834624588

00:37:04.242 --> 00:37:05.754 To a first approximation,  
NOTE Confidence: 0.834624588

00:37:05.760 --> 00:37:08.028 those hospitals are in academic centers,  
NOTE Confidence: 0.834624588

00:37:08.030 --> 00:37:10.760 but that's again a really one way  
NOTE Confidence: 0.834624588

00:37:10.760 --> 00:37:12.804 relationship that allows you to  
NOTE Confidence: 0.834624588

00:37:12.804 --> 00:37:14.819 generate some important clinical data  
NOTE Confidence: 0.834624588

00:37:14.819 --> 00:37:17.847 on the Efficacy and safety of a new agent,  
NOTE Confidence: 0.834624588

00:37:17.850 --> 00:37:19.862 but doesn't really allow  
NOTE Confidence: 0.834624588

00:37:19.862 --> 00:37:22.377 anybody to learn very much.  
NOTE Confidence: 0.834624588

00:37:22.380 --> 00:37:24.893 That can only be done by having  
NOTE Confidence: 0.834624588

00:37:24.893 --> 00:37:27.400 a joint enterprise that is still  
NOTE Confidence: 0.834624588

00:37:27.400 --> 00:37:29.660 as committed to pushing forward  
NOTE Confidence: 0.834624588

00:37:29.660 --> 00:37:31.909 and understanding the science that  
NOTE Confidence: 0.834624588

00:37:31.909 --> 00:37:34.019 underlies all of these events.  
NOTE Confidence: 0.834624588

00:37:34.020 --> 00:37:36.260 And do that in partnership.

NOTE Confidence: 0.834624588

00:37:36.260 --> 00:37:38.768 Where where on the company size

NOTE Confidence: 0.834624588

00:37:38.768 --> 00:37:41.755 early on the genetic side we can

NOTE Confidence: 0.834624588

00:37:41.755 --> 00:37:44.215 bring to bear many assays and

NOTE Confidence: 0.834624588

00:37:44.215 --> 00:37:46.706 resources and insights that we've

NOTE Confidence: 0.834624588

00:37:46.706 --> 00:37:49.201 gotten from our experience by

NOTE Confidence: 0.834624588

00:37:49.201 --> 00:37:51.488 treating thousands and thousands of

NOTE Confidence: 0.834624588

00:37:51.488 --> 00:37:53.723 cancer patients with these agents,

NOTE Confidence: 0.834624588

00:37:53.730 --> 00:37:56.526 together with the rare an insightful

NOTE Confidence: 0.834624588

00:37:56.526 --> 00:37:59.289 cyantific insight that one can find

NOTE Confidence: 0.834624588

00:37:59.289 --> 00:38:01.349 at a top academic institution,

NOTE Confidence: 0.834624588

00:38:01.350 --> 00:38:04.140 and they all certainly for us.

NOTE Confidence: 0.834624588

00:38:04.140 --> 00:38:07.028 Is it's always at the top of the

NOTE Confidence: 0.834624588

00:38:07.028 --> 00:38:09.688 list and not only because of

NOTE Confidence: 0.834624588

00:38:09.688 --> 00:38:11.536 my own filial loyalty,

NOTE Confidence: 0.834624588

00:38:11.540 --> 00:38:14.326 but simply be cause the focus on

NOTE Confidence: 0.834624588

00:38:14.326 --> 00:38:16.550 immunology and how that interfaces  
NOTE Confidence: 0.834624588

00:38:16.550 --> 00:38:19.406 with human biology at Yale has  
NOTE Confidence: 0.834624588

00:38:19.406 --> 00:38:21.808 really emerged over the last 10  
NOTE Confidence: 0.834624588

00:38:21.808 --> 00:38:26.060 years or so is really being quite.  
NOTE Confidence: 0.834624588

00:38:26.060 --> 00:38:28.216 Quite inspiring and I also find  
NOTE Confidence: 0.834624588

00:38:28.216 --> 00:38:30.844 it much more easy to deal with the  
NOTE Confidence: 0.834624588

00:38:30.844 --> 00:38:32.968 culture and the commitment of the  
NOTE Confidence: 0.834624588

00:38:32.968 --> 00:38:34.923 faculty and the administration to  
NOTE Confidence: 0.834624588

00:38:34.923 --> 00:38:37.188 actually advancing these types of studies.  
NOTE Confidence: 0.834624588

00:38:37.190 --> 00:38:39.726 Then I find in many of our other  
NOTE Confidence: 0.834624588

00:38:39.726 --> 00:38:41.217 partner institutions where often  
NOTE Confidence: 0.834624588

00:38:41.217 --> 00:38:43.207 unfortunately one finds a variety  
NOTE Confidence: 0.834624588

00:38:43.207 --> 00:38:44.003 of roadblocks.  
NOTE Confidence: 0.834624588

00:38:44.010 --> 00:38:45.810 So I think you know,  
NOTE Confidence: 0.834624588

00:38:45.810 --> 00:38:49.128 Yale provides a really good substrate to  
NOTE Confidence: 0.834624588

00:38:49.128 --> 00:38:52.407 actually get these kinds of studies done.

NOTE Confidence: 0.834624588

00:38:52.410 --> 00:38:54.601 What's needed is to get together on

NOTE Confidence: 0.834624588

00:38:54.601 --> 00:38:57.180 the types of samples that are needed,

NOTE Confidence: 0.834624588

00:38:57.180 --> 00:38:59.226 what types of analytics are required,

NOTE Confidence: 0.834624588

00:38:59.230 --> 00:39:02.038 and then in the matter of any good

NOTE Confidence: 0.834624588

00:39:02.038 --> 00:39:04.114 collaboration each party brings to the

NOTE Confidence: 0.834624588

00:39:04.114 --> 00:39:06.729 table what that party is best at doing.

NOTE Confidence: 0.834624588

00:39:06.730 --> 00:39:08.440 And in our Case No.

NOTE Confidence: 0.834624588

00:39:08.440 --> 00:39:11.850 We believe we have a lot of science to offer,

NOTE Confidence: 0.8434615

00:39:11.850 --> 00:39:13.550 not just support and funding,

NOTE Confidence: 0.8434615

00:39:13.550 --> 00:39:15.620 and in your case certainly got

NOTE Confidence: 0.8434615

00:39:15.620 --> 00:39:17.639 more than just patients to offer.

NOTE Confidence: 0.8434615

00:39:17.640 --> 00:39:20.709 There is a enormous amount of as I said,

NOTE Confidence: 0.8434615

00:39:20.710 --> 00:39:22.520 scientific expertise and insight that.

NOTE Confidence: 0.8434615

00:39:22.520 --> 00:39:25.058 Will turn out to be critical.

NOTE Confidence: 0.8434615

00:39:25.060 --> 00:39:28.071 I think to solving these various problems.

NOTE Confidence: 0.8434615



00:39:28.071 --> 00:39:31.130 So with that I think I probably  
NOTE Confidence: 0.8434615

00:39:31.210 --> 00:39:33.075 end my remarks and continue  
NOTE Confidence: 0.8434615

00:39:33.075 --> 00:39:35.660 on to the next next element.  
NOTE Confidence: 0.87899816

00:39:36.570 --> 00:39:38.430 Alright, thank you very much and  
NOTE Confidence: 0.87899816

00:39:38.430 --> 00:39:40.419 thank you for the kind words.  
NOTE Confidence: 0.87899816

00:39:40.420 --> 00:39:42.443 Let me please invite all the panelists  
NOTE Confidence: 0.87899816

00:39:42.443 --> 00:39:44.626 to turn on their microphones in their  
NOTE Confidence: 0.87899816

00:39:44.626 --> 00:39:47.260 in their videos and I want to remind  
NOTE Confidence: 0.87899816

00:39:47.260 --> 00:39:49.696 all the attendees to please submit your  
NOTE Confidence: 0.87899816

00:39:49.696 --> 00:39:53.090 questions through the chat feature.  
NOTE Confidence: 0.87899816

00:39:53.090 --> 00:39:54.680 I might I might just start.  
NOTE Confidence: 0.87899816

00:39:54.680 --> 00:39:56.270 I see a couple of questions,  
NOTE Confidence: 0.87899816

00:39:56.270 --> 00:39:58.470 but I might just start with just a  
NOTE Confidence: 0.87899816

00:39:58.470 --> 00:39:59.820 challenging question to the panelists  
NOTE Confidence: 0.87899816

00:39:59.820 --> 00:40:01.792 and any. Body can take this.  
NOTE Confidence: 0.87899816

00:40:01.792 --> 00:40:03.632 What do you think we've,

NOTE Confidence: 0.87899816

00:40:03.640 --> 00:40:05.487 you know, as you know,

NOTE Confidence: 0.87899816

00:40:05.487 --> 00:40:07.946 the problem in the clinic is that

NOTE Confidence: 0.87899816

00:40:07.946 --> 00:40:10.468 a subset respond to anti PD one

NOTE Confidence: 0.87899816

00:40:10.468 --> 00:40:12.498 and PDL one few combinations.

NOTE Confidence: 0.87899816

00:40:12.500 --> 00:40:14.230 The majority of patients don't

NOTE Confidence: 0.87899816

00:40:14.230 --> 00:40:15.268 respond obviously although

NOTE Confidence: 0.87899816

00:40:15.268 --> 00:40:16.929 we've made enormous progress.

NOTE Confidence: 0.87899816

00:40:16.930 --> 00:40:19.828 What do you think we've learned from

NOTE Confidence: 0.87899816

00:40:19.828 --> 00:40:22.095 mechanisms of response to anti PD

NOTE Confidence: 0.87899816

00:40:22.095 --> 00:40:24.307 one or video one that would drive?

NOTE Confidence: 0.8349594

00:40:26.500 --> 00:40:28.680 Future targets future development.

NOTE Confidence: 0.834106

00:40:32.640 --> 00:40:35.646 Maybe I'll start with that one if that's OK,

NOTE Confidence: 0.834106

00:40:35.650 --> 00:40:37.974 Miro and I'll let others jump in.

NOTE Confidence: 0.834106

00:40:37.980 --> 00:40:41.814 So I think you know it's been a bit

NOTE Confidence: 0.834106

00:40:41.814 --> 00:40:44.520 frustrating on those fronts in that.

NOTE Confidence: 0.834106

00:40:44.520 --> 00:40:45.753 Mechanisms of resistance  
NOTE Confidence: 0.834106

00:40:45.753 --> 00:40:46.986 have been determined,  
NOTE Confidence: 0.834106

00:40:46.990 --> 00:40:50.572 one of which is loss of MH C Class  
NOTE Confidence: 0.834106

00:40:50.572 --> 00:40:54.602 one or reduction of MH C Class one  
NOTE Confidence: 0.834106

00:40:54.602 --> 00:40:57.689 through a variety of mechanisms.  
NOTE Confidence: 0.834106

00:40:57.690 --> 00:40:59.440 You know there are some.  
NOTE Confidence: 0.834106

00:40:59.440 --> 00:41:01.743 You know reasons why that you'd think  
NOTE Confidence: 0.834106

00:41:01.743 --> 00:41:04.319 that might not result in an resistance,  
NOTE Confidence: 0.834106

00:41:04.320 --> 00:41:05.860 because natural killer cells might  
NOTE Confidence: 0.834106

00:41:05.860 --> 00:41:07.883 be able to kill those tumors  
NOTE Confidence: 0.834106

00:41:07.883 --> 00:41:09.559 without that inhibitory signal.  
NOTE Confidence: 0.834106

00:41:09.560 --> 00:41:11.926 I'd like to highlight for those of  
NOTE Confidence: 0.834106

00:41:11.926 --> 00:41:13.740 you haven't followed Aaron rings,  
NOTE Confidence: 0.834106

00:41:13.740 --> 00:41:16.071 I'll 18 story that this is one of the  
NOTE Confidence: 0.834106

00:41:16.071 --> 00:41:18.086 few therapies that's actually effective  
NOTE Confidence: 0.834106

00:41:18.086 --> 00:41:21.070 on both class one proficient in class,

NOTE Confidence: 0.834106  
00:41:21.070 --> 00:41:22.150 one deficient tumors,  
NOTE Confidence: 0.834106  
00:41:22.150 --> 00:41:23.950 but that's still a pretty  
NOTE Confidence: 0.834106  
00:41:23.950 --> 00:41:25.260 small minority of cases.  
NOTE Confidence: 0.834106  
00:41:25.260 --> 00:41:27.714 I think there are also issues with.  
NOTE Confidence: 0.834106  
00:41:27.714 --> 00:41:28.776 Low mutation burden.  
NOTE Confidence: 0.834106  
00:41:28.776 --> 00:41:29.838 Lack of antigenicity.  
NOTE Confidence: 0.834106  
00:41:29.840 --> 00:41:32.376 I think I referred to T cell trafficking  
NOTE Confidence: 0.834106  
00:41:32.376 --> 00:41:35.058 as well and the reasons why T cells  
NOTE Confidence: 0.834106  
00:41:35.058 --> 00:41:37.082 traffic and actually I would say  
NOTE Confidence: 0.834106  
00:41:37.082 --> 00:41:39.301 that as a pathologist we don't know  
NOTE Confidence: 0.834106  
00:41:39.301 --> 00:41:41.895 if T cells were there and then left.  
NOTE Confidence: 0.834106  
00:41:41.900 --> 00:41:43.525 We typically get one snapshot  
NOTE Confidence: 0.834106  
00:41:43.525 --> 00:41:44.825 and we you know,  
NOTE Confidence: 0.834106  
00:41:44.830 --> 00:41:47.764 we know that they're not there when we look,  
NOTE Confidence: 0.834106  
00:41:47.770 --> 00:41:49.874 but I think there's a number of things  
NOTE Confidence: 0.834106

00:41:49.874 --> 00:41:51.990 that we just simply don't understand  
NOTE Confidence: 0.834106

00:41:51.990 --> 00:41:54.288 about how anti cancer immunity happens  
NOTE Confidence: 0.834106

00:41:54.290 --> 00:41:56.865 even to the level of our the till  
NOTE Confidence: 0.834106

00:41:56.865 --> 00:41:59.498 are the cells that are in the tumor.  
NOTE Confidence: 0.834106

00:41:59.500 --> 00:42:00.475 Actually what's responding  
NOTE Confidence: 0.834106

00:42:00.475 --> 00:42:01.775 to PD one blockade?  
NOTE Confidence: 0.834106

00:42:01.780 --> 00:42:02.800 Or is it?  
NOTE Confidence: 0.834106

00:42:02.800 --> 00:42:04.160 Something outside of that,  
NOTE Confidence: 0.834106

00:42:04.160 --> 00:42:06.068 and those are pretty basic questions.  
NOTE Confidence: 0.834106

00:42:06.070 --> 00:42:08.219 I think that's where yell could help  
NOTE Confidence: 0.834106

00:42:08.219 --> 00:42:10.200 others workout how these things work.  
NOTE Confidence: 0.834106

00:42:10.200 --> 00:42:12.601 So I think the mechanisms of resistance  
NOTE Confidence: 0.834106

00:42:12.601 --> 00:42:14.968 are still need quite a bit of work.  
NOTE Confidence: 0.8047646

00:42:16.650 --> 00:42:19.930 If you do any of you think that there's a,  
NOTE Confidence: 0.8047646

00:42:19.930 --> 00:42:22.198 how would we approach those low mutation  
NOTE Confidence: 0.8047646

00:42:22.198 --> 00:42:24.522 tumors that the tumors that have load

NOTE Confidence: 0.8047646

00:42:24.522 --> 00:42:26.490 the mutation burdens may be endogenous?

NOTE Confidence: 0.8047646

00:42:26.490 --> 00:42:28.130 Retrovirus would be a target,

NOTE Confidence: 0.8047646

00:42:28.130 --> 00:42:29.770 but are there other targets?

NOTE Confidence: 0.8047646

00:42:29.770 --> 00:42:31.846 Or will we eventually need to

NOTE Confidence: 0.8047646

00:42:31.846 --> 00:42:33.894 isolate out rare specific T cells

NOTE Confidence: 0.8047646

00:42:33.894 --> 00:42:35.994 and clone out the T cell receptors?

NOTE Confidence: 0.8047646

00:42:36.000 --> 00:42:37.966 What do you think are the

NOTE Confidence: 0.8047646

00:42:37.966 --> 00:42:39.278 approaches to address those?

NOTE Confidence: 0.8047646

00:42:39.280 --> 00:42:41.024 Those types of tumors?

NOTE Confidence: 0.8047646

00:42:41.024 --> 00:42:43.276 Akiko, maybe I can ask you to address that,

NOTE Confidence: 0.8047646

00:42:43.280 --> 00:42:44.420 since you are the world

NOTE Confidence: 0.8047646

00:42:44.420 --> 00:42:45.560 expert on an 8 immunology.

NOTE Confidence: 0.8360967

00:42:46.390 --> 00:42:47.706 Oh, thank you, yeah,

NOTE Confidence: 0.8360967

00:42:47.706 --> 00:42:50.090 so that's the issue that you know.

NOTE Confidence: 0.8360967

00:42:50.090 --> 00:42:52.610 First there has to be some sort of

NOTE Confidence: 0.8360967

00:42:52.610 --> 00:42:54.552 antigen that T cells can recognize  
NOTE Confidence: 0.8360967

00:42:54.552 --> 00:42:57.581 unless we go into the NK type of therapy  
NOTE Confidence: 0.8360967

00:42:57.581 --> 00:43:00.164 that Aaron might want to comment later.  
NOTE Confidence: 0.8360967

00:43:00.170 --> 00:43:01.850 But but you know what?  
NOTE Confidence: 0.8360967

00:43:01.850 --> 00:43:04.642 We are kind of not looking at is  
NOTE Confidence: 0.8360967

00:43:04.642 --> 00:43:07.220 really the endogenous retrovirus.  
NOTE Confidence: 0.8360967

00:43:07.220 --> 00:43:08.720 Sodium in the cancer,  
NOTE Confidence: 0.8360967

00:43:08.720 --> 00:43:10.595 and whether those are many,  
NOTE Confidence: 0.8360967

00:43:10.600 --> 00:43:12.132 are coding capable sequences  
NOTE Confidence: 0.8360967

00:43:12.132 --> 00:43:14.047 that are dysregulated and up  
NOTE Confidence: 0.8360967

00:43:14.047 --> 00:43:15.867 regulated and expressed in cancer,  
NOTE Confidence: 0.8360967

00:43:15.870 --> 00:43:17.916 and so right now what we're  
NOTE Confidence: 0.8360967

00:43:17.916 --> 00:43:20.576 trying to do is to elude the  
NOTE Confidence: 0.8360967

00:43:20.576 --> 00:43:23.006 peptides from the MHC of cancers.  
NOTE Confidence: 0.8360967

00:43:23.010 --> 00:43:24.138 Different cancer cells.  
NOTE Confidence: 0.8360967

00:43:24.138 --> 00:43:24.890 Jeff issues.

NOTE Confidence: 0.8360967

00:43:24.890 --> 00:43:27.170 You and I are actually collaborating

NOTE Confidence: 0.8360967

00:43:27.170 --> 00:43:29.905 on this project so we can actually

NOTE Confidence: 0.8360967

00:43:29.905 --> 00:43:32.185 identify if there are peptides that

NOTE Confidence: 0.8360967

00:43:32.185 --> 00:43:34.401 are derived from herbs that can

NOTE Confidence: 0.8360967

00:43:34.401 --> 00:43:36.526 become target of T cell recognition.

NOTE Confidence: 0.8360967

00:43:36.526 --> 00:43:39.018 And can we? Take advantage of that.

NOTE Confidence: 0.66061544

00:43:40.210 --> 00:43:42.130 And methods to upregulate those antigens?

NOTE Confidence: 0.66061544

00:43:42.130 --> 00:43:44.370 I guess you're also working on it

NOTE Confidence: 0.66061544

00:43:44.370 --> 00:43:45.970 at this time. Yes, Marcus.

NOTE Confidence: 0.825603

00:43:49.390 --> 00:43:51.700 I'm going to take a question from

NOTE Confidence: 0.825603

00:43:51.700 --> 00:43:52.690 the audience intermittently,

NOTE Confidence: 0.825603

00:43:52.690 --> 00:43:54.340 as we're addressing these questions.

NOTE Confidence: 0.825603

00:43:54.340 --> 00:43:56.320 One was are there treatments coming

NOTE Confidence: 0.825603

00:43:56.320 --> 00:43:57.970 along for for glioblastomas? Now?

NOTE Confidence: 0.825603

00:43:57.970 --> 00:44:00.206 I'm not a glioblastoma expert, but akiko.

NOTE Confidence: 0.825603



00:44:00.206 --> 00:44:02.257 I'll just turn that over to you  
NOTE Confidence: 0.825603

00:44:02.257 --> 00:44:03.808 because I think your research  
NOTE Confidence: 0.825603

00:44:03.808 --> 00:44:05.602 address is perhaps one of the  
NOTE Confidence: 0.825603

00:44:05.663 --> 00:44:07.539 bigger problems in glioblastoma.  
NOTE Confidence: 0.7951604

00:44:08.460 --> 00:44:09.852 Right, so glioblastoma,  
NOTE Confidence: 0.7951604

00:44:09.852 --> 00:44:12.636 unlike other non non brain tumors,  
NOTE Confidence: 0.7951604

00:44:12.640 --> 00:44:15.418 have an extra layer of challenge,  
NOTE Confidence: 0.7951604

00:44:15.420 --> 00:44:18.912 which is the there's very little  
NOTE Confidence: 0.7951604

00:44:18.912 --> 00:44:20.658 immunosurveillance that's occurring  
NOTE Confidence: 0.7951604

00:44:20.658 --> 00:44:23.879 in the brain due to a limited  
NOTE Confidence: 0.7951604

00:44:23.879 --> 00:44:26.570 drainage by the meningeal lymphatics.  
NOTE Confidence: 0.7951604

00:44:26.570 --> 00:44:28.796 And the fact that you know,  
NOTE Confidence: 0.7951604

00:44:28.800 --> 00:44:31.626 you know priming T cells and T cells are  
NOTE Confidence: 0.7951604

00:44:31.626 --> 00:44:34.379 not migrating into the tissue either.  
NOTE Confidence: 0.7951604

00:44:34.380 --> 00:44:37.026 So one of the ways in which we're trying  
NOTE Confidence: 0.7951604

00:44:37.026 --> 00:44:40.064 to overcome this is to increase immune

NOTE Confidence: 0.7951604

00:44:40.064 --> 00:44:42.190 surveillance by injecting veg FCI.

NOTE Confidence: 0.7951604

00:44:42.190 --> 00:44:44.437 Referred to that in my slide and

NOTE Confidence: 0.7951604

00:44:44.437 --> 00:44:46.755 we're calling it lymph axis and

NOTE Confidence: 0.7951604

00:44:46.755 --> 00:44:48.890 essentially to increase the drainage.

NOTE Confidence: 0.7951604

00:44:48.890 --> 00:44:51.333 An stimulation of T cells against you

NOTE Confidence: 0.7951604

00:44:51.333 --> 00:44:54.099 manage and in the draining lymph node.

NOTE Confidence: 0.7951604

00:44:54.100 --> 00:44:56.410 And once that happens, these diesels

NOTE Confidence: 0.7951604

00:44:56.410 --> 00:44:58.680 can migrate back into the brain.

NOTE Confidence: 0.7951604

00:44:58.680 --> 00:45:00.204 And tackle the CIMA.

NOTE Confidence: 0.7951604

00:45:00.204 --> 00:45:00.966 Ran it.

NOTE Confidence: 0.7951604

00:45:00.970 --> 00:45:02.875 It obviously works well with

NOTE Confidence: 0.7951604

00:45:02.875 --> 00:45:04.399 checkpoint inhibitors as well,

NOTE Confidence: 0.7951604

00:45:04.400 --> 00:45:06.632 so and we're also collaborating with

NOTE Confidence: 0.7951604

00:45:06.632 --> 00:45:09.442 Aaron's lab to make a better reagent

NOTE Confidence: 0.7951604

00:45:09.442 --> 00:45:11.532 that can more specifically stimulate

NOTE Confidence: 0.7951604

00:45:11.532 --> 00:45:14.807 visit for three to be able to do this

NOTE Confidence: 0.7951604

00:45:14.807 --> 00:45:16.602 efficiently without any side effects.

NOTE Confidence: 0.7951604

00:45:16.602 --> 00:45:18.918 So that's one possible way that

NOTE Confidence: 0.7951604

00:45:18.918 --> 00:45:21.157 we're trying to tackle this issue.

NOTE Confidence: 0.848862

00:45:21.860 --> 00:45:23.036 That's excellent Roy maybe.

NOTE Confidence: 0.848862

00:45:23.036 --> 00:45:24.835 Yeah, I was wondering if you

NOTE Confidence: 0.848862

00:45:24.835 --> 00:45:26.340 could address the brain tumors

NOTE Confidence: 0.848862

00:45:26.398 --> 00:45:28.225 for also that maybe that could be

NOTE Confidence: 0.848862

00:45:28.225 --> 00:45:30.090 a project in this war actually,

NOTE Confidence: 0.848862

00:45:30.090 --> 00:45:31.818 but but other other approaches not

NOTE Confidence: 0.848862

00:45:31.818 --> 00:45:33.568 only within immunology but also to

NOTE Confidence: 0.848862

00:45:33.568 --> 00:45:35.212 mention that there other Yale engage

NOTE Confidence: 0.848862

00:45:35.212 --> 00:45:36.443 sessions with other approaches

NOTE Confidence: 0.848862

00:45:36.443 --> 00:45:38.028 to glioblastoma is also right.

NOTE Confidence: 0.848862

00:45:38.030 --> 00:45:39.210 Well, there is this

NOTE Confidence: 0.848862

00:45:39.210 --> 00:45:40.992 more group and they are studying

NOTE Confidence: 0.848862

00:45:40.992 --> 00:45:42.730 that and I think he goes.

NOTE Confidence: 0.848862

00:45:42.730 --> 00:45:44.500 Approach would be a good one,

NOTE Confidence: 0.848862

00:45:44.500 --> 00:45:46.460 but I did want to mention Mario was

NOTE Confidence: 0.848862

00:45:46.460 --> 00:45:47.999 the need to personalize immunotherapy

NOTE Confidence: 0.848862

00:45:47.999 --> 00:45:50.302 and I think we're right on the

NOTE Confidence: 0.848862

00:45:50.361 --> 00:45:52.721 precipice of doing that in a place like

NOTE Confidence: 0.848862

00:45:52.721 --> 00:45:55.486 yellow should be able to do that so.

NOTE Confidence: 0.848862

00:45:55.490 --> 00:45:57.080 We already heard that you know,

NOTE Confidence: 0.848862

00:45:57.080 --> 00:45:59.042 if you don't have MHT one or you don't

NOTE Confidence: 0.848862

00:45:59.042 --> 00:46:00.788 have the adaptive immune response,

NOTE Confidence: 0.848862

00:46:00.790 --> 00:46:02.910 and that's being shown for 456 years now.

NOTE Confidence: 0.848862

00:46:02.910 --> 00:46:05.830 But what do you do if you have a cold tumor?

NOTE Confidence: 0.848862

00:46:05.830 --> 00:46:08.480 If you have a tumor that doesn't have HD one,

NOTE Confidence: 0.848862

00:46:08.480 --> 00:46:10.328 no capability had a paper on that.

NOTE Confidence: 0.848862

00:46:10.330 --> 00:46:11.920 It's about 5% of lung cancers,

NOTE Confidence: 0.848862

00:46:11.920 --> 00:46:13.754 so I'd like to propose that you  
NOTE Confidence: 0.848862

00:46:13.754 --> 00:46:16.172 know what we need to do is we need  
NOTE Confidence: 0.848862

00:46:16.172 --> 00:46:17.750 to dissect tumors out, you know.  
NOTE Confidence: 0.848862

00:46:17.750 --> 00:46:19.340 And just like we would profile  
NOTE Confidence: 0.848862

00:46:19.340 --> 00:46:20.404 a tumor in genetically,  
NOTE Confidence: 0.848862

00:46:20.404 --> 00:46:22.006 we need to profile the immune  
NOTE Confidence: 0.848862

00:46:22.006 --> 00:46:23.318 microenvironment and these cold tumors.  
NOTE Confidence: 0.848862

00:46:23.320 --> 00:46:25.560 These tumors that might not be driven.  
NOTE Confidence: 0.848862

00:46:25.560 --> 00:46:27.331 PDL one or perhaps ticket is involved  
NOTE Confidence: 0.848862

00:46:27.331 --> 00:46:29.803 as we heard tomorrow we need to start  
NOTE Confidence: 0.848862

00:46:29.803 --> 00:46:31.458 thinking about the right combinations,  
NOTE Confidence: 0.848862

00:46:31.460 --> 00:46:33.212 but you know the biggest problem  
NOTE Confidence: 0.848862

00:46:33.212 --> 00:46:35.021 is we're just flying blind and  
NOTE Confidence: 0.848862

00:46:35.021 --> 00:46:36.774 the clinical world will do. That.  
NOTE Confidence: 0.848862

00:46:36.774 --> 00:46:39.126 Will go on for years if not stopped.  
NOTE Confidence: 0.848862

00:46:39.130 --> 00:46:40.605 You know just combining different

NOTE Confidence: 0.848862

00:46:40.605 --> 00:46:41.785 drugs and using them,

NOTE Confidence: 0.848862

00:46:41.790 --> 00:46:43.827 but I think you know right now

NOTE Confidence: 0.848862

00:46:43.827 --> 00:46:45.933 it's a perfect time and you and

NOTE Confidence: 0.848862

00:46:45.933 --> 00:46:47.395 I have talked about this.

NOTE Confidence: 0.848862

00:46:47.395 --> 00:46:49.165 It's very complicated in refractory setting.

NOTE Confidence: 0.848862

00:46:49.165 --> 00:46:50.345 Someone gets chemo immunotherapy

NOTE Confidence: 0.848862

00:46:50.345 --> 00:46:51.230 and then refractory.

NOTE Confidence: 0.848862

00:46:51.230 --> 00:46:52.886 There could be thousands of different

NOTE Confidence: 0.848862

00:46:52.886 --> 00:46:54.344 mechanisms put in the frontline

NOTE Confidence: 0.848862

00:46:54.344 --> 00:46:55.544 setting primary resistance and

NOTE Confidence: 0.848862

00:46:55.544 --> 00:46:57.420 we know that with Atez Alisme,

NOTE Confidence: 0.848862

00:46:57.420 --> 00:46:57.996 Abbott Pembrolizumab.

NOTE Confidence: 0.848862

00:46:57.996 --> 00:46:59.672 Half the patients about will respond

NOTE Confidence: 0.848862

00:46:59.672 --> 00:47:01.528 when you have the high PD L1 Group,

NOTE Confidence: 0.848862

00:47:01.528 --> 00:47:02.456 the other half don't.

NOTE Confidence: 0.848862

00:47:02.460 --> 00:47:03.909 I would suggest that the group to  
NOTE Confidence: 0.848862

00:47:03.909 --> 00:47:05.369 look for some of the mechanisms  
NOTE Confidence: 0.848862

00:47:05.369 --> 00:47:06.425 we've heard about today.  
NOTE Confidence: 0.848862

00:47:06.430 --> 00:47:08.760 I can't wait to get my hands on Aaron's drug,  
NOTE Confidence: 0.848862

00:47:08.760 --> 00:47:09.224 you know,  
NOTE Confidence: 0.848862

00:47:09.224 --> 00:47:12.250 and look at that and things like that.  
NOTE Confidence: 0.85154384

00:47:12.250 --> 00:47:14.986 You know, maybe I can ask her to comment,  
NOTE Confidence: 0.85154384

00:47:14.990 --> 00:47:16.510 because obviously that's a major.  
NOTE Confidence: 0.85154384

00:47:16.510 --> 00:47:18.662 You know you. You need to know what  
NOTE Confidence: 0.85154384

00:47:18.662 --> 00:47:20.586 the mechanisms of resistance are in  
NOTE Confidence: 0.85154384

00:47:20.586 --> 00:47:22.584 Biomarkers for development of your drugs.  
NOTE Confidence: 0.85154384

00:47:22.590 --> 00:47:24.704 So how do you approach that internally?  
NOTE Confidence: 0.85154384

00:47:24.710 --> 00:47:25.926 And also in collaboration  
NOTE Confidence: 0.85154384

00:47:25.926 --> 00:47:26.838 with academic institutions?  
NOTE Confidence: 0.8751713

00:47:28.040 --> 00:47:30.685 I think you know the the problem  
NOTE Confidence: 0.8751713

00:47:30.685 --> 00:47:32.560 of resistance has even a

NOTE Confidence: 0.8751713

00:47:32.639 --> 00:47:34.167 darker aspect to it,

NOTE Confidence: 0.8751713

00:47:34.170 --> 00:47:36.080 which is we don't really,

NOTE Confidence: 0.8751713

00:47:36.080 --> 00:47:38.655 truly understand the mechanism of

NOTE Confidence: 0.8751713

00:47:38.655 --> 00:47:41.760 why things work when they work.

NOTE Confidence: 0.8751713

00:47:41.760 --> 00:47:43.720 Someone's were diluted to this,

NOTE Confidence: 0.8751713

00:47:43.720 --> 00:47:45.670 but our understanding of how

NOTE Confidence: 0.8751713

00:47:45.670 --> 00:47:47.230 these checkpoint inhibitors work.

NOTE Confidence: 0.8751713

00:47:47.230 --> 00:47:48.794 Even Witcher vision Lee

NOTE Confidence: 0.8751713

00:47:48.794 --> 00:47:50.749 was framed by off bias,

NOTE Confidence: 0.8751713

00:47:50.750 --> 00:47:53.806 all based in the series of assumptions as

NOTE Confidence: 0.8751713

00:47:53.806 --> 00:47:56.616 reversing this process of T cell exhaustion,

NOTE Confidence: 0.8751713

00:47:56.620 --> 00:47:58.575 thereby acting in the tumor

NOTE Confidence: 0.8751713

00:47:58.575 --> 00:48:00.139 to reactivate T cells,

NOTE Confidence: 0.8751713

00:48:00.140 --> 00:48:02.870 either certainly is not the whole story.

NOTE Confidence: 0.8751713

00:48:02.870 --> 00:48:04.825 In fact, maybe only marginally

NOTE Confidence: 0.8751713



00:48:04.825 --> 00:48:06.389 true in some patients.  
NOTE Confidence: 0.8751713

00:48:06.390 --> 00:48:09.518 So if in fact the PD one PD,  
NOTE Confidence: 0.8751713

00:48:09.520 --> 00:48:11.780 L1 or Tigit Axis along  
NOTE Confidence: 0.8751713

00:48:11.780 --> 00:48:13.588 with simulate 4C28 Axis.  
NOTE Confidence: 0.8751713

00:48:13.590 --> 00:48:15.564 Full works in lymphoid tissues to  
NOTE Confidence: 0.8751713

00:48:15.564 --> 00:48:17.720 expand the T cell compartment.  
NOTE Confidence: 0.8751713

00:48:17.720 --> 00:48:20.247 Then that means we have the entire  
NOTE Confidence: 0.8751713

00:48:20.247 --> 00:48:22.969 mechanism of how PD one blockade works.  
NOTE Confidence: 0.8751713

00:48:22.970 --> 00:48:25.220 Not quite right if not incorrect.  
NOTE Confidence: 0.8751713

00:48:25.220 --> 00:48:26.536 If that's the case,  
NOTE Confidence: 0.8751713

00:48:26.536 --> 00:48:28.510 it's very difficult to know how  
NOTE Confidence: 0.8751713

00:48:28.582 --> 00:48:31.473 to improve upon that or how to  
NOTE Confidence: 0.8751713

00:48:31.473 --> 00:48:32.712 understand resistance mechanisms.  
NOTE Confidence: 0.8751713

00:48:32.720 --> 00:48:35.352 If you don't really know the mechanism  
NOTE Confidence: 0.8751713

00:48:35.352 --> 00:48:37.279 of immune mechanism that Modulated  
NOTE Confidence: 0.8751713

00:48:37.279 --> 00:48:39.469 as a consequence of your drug.

NOTE Confidence: 0.8751713

00:48:39.470 --> 00:48:43.478 So I think it's important to.

NOTE Confidence: 0.8751713

00:48:43.480 --> 00:48:44.276 You know,

NOTE Confidence: 0.8751713

00:48:44.276 --> 00:48:47.062 even just as a basic science project,

NOTE Confidence: 0.8751713

00:48:47.070 --> 00:48:48.900 be sure that we really understand

NOTE Confidence: 0.8751713

00:48:48.900 --> 00:48:51.067 that all of the predictions associated

NOTE Confidence: 0.8751713

00:48:51.067 --> 00:48:53.719 with a presumed mechanism of action

NOTE Confidence: 0.8751713

00:48:53.719 --> 00:48:56.024 are actually correct before we

NOTE Confidence: 0.8751713

00:48:56.024 --> 00:48:57.836 can really understand resistance,

NOTE Confidence: 0.8751713

00:48:57.840 --> 00:48:58.760 you know.

NOTE Confidence: 0.8751713

00:48:58.760 --> 00:48:59.680 That said,

NOTE Confidence: 0.8751713

00:48:59.680 --> 00:49:01.520 there's certain aspects of

NOTE Confidence: 0.8751713

00:49:01.520 --> 00:49:04.121 resistance that are that are

NOTE Confidence: 0.8751713

00:49:04.121 --> 00:49:05.726 finding increasingly important.

NOTE Confidence: 0.8751713

00:49:05.730 --> 00:49:08.138 We've invested very heavily

NOTE Confidence: 0.8751713

00:49:08.138 --> 00:49:09.944 in tumor antigens,

NOTE Confidence: 0.8751713

00:49:09.950 --> 00:49:15.984 particularly mutant knew antigens as well as.  
NOTE Confidence: 0.8751713

00:49:15.990 --> 00:49:18.666 Endogenous elements that Akiko is setting.  
NOTE Confidence: 0.8751713

00:49:18.670 --> 00:49:20.900 Chloe Arbiser line elements and  
NOTE Confidence: 0.8751713

00:49:20.900 --> 00:49:23.130 transposable elements as potential antigens,  
NOTE Confidence: 0.8751713

00:49:23.130 --> 00:49:24.910 'cause they certainly a  
NOTE Confidence: 0.8751713

00:49:24.910 --> 00:49:26.690 great antigens in mice,  
NOTE Confidence: 0.8751713

00:49:26.690 --> 00:49:29.506 but we find that you know the context  
NOTE Confidence: 0.8751713

00:49:29.506 --> 00:49:32.934 of our vaccine programs you see as  
NOTE Confidence: 0.8751713

00:49:32.934 --> 00:49:36.060 significant debilitating amount of MSE loss.  
NOTE Confidence: 0.8751713

00:49:36.060 --> 00:49:38.682 Sometimes it's a hard loss which  
NOTE Confidence: 0.8751713

00:49:38.682 --> 00:49:40.430 means loss of heterozygosity  
NOTE Confidence: 0.8751713

00:49:40.507 --> 00:49:42.299 for particular MA serial.  
NOTE Confidence: 0.8751713

00:49:42.300 --> 00:49:45.868 Other times it means soft loss which is  
NOTE Confidence: 0.8751713

00:49:45.868 --> 00:49:48.099 just simply transcriptional repression.  
NOTE Confidence: 0.8751713

00:49:48.100 --> 00:49:49.972 And you need to workout computational  
NOTE Confidence: 0.8751713

00:49:49.972 --> 00:49:51.596 workflows so that you could

NOTE Confidence: 0.8751713

00:49:51.596 --> 00:49:53.206 actually examine patients on a

NOTE Confidence: 0.8751713

00:49:53.206 --> 00:49:55.050 patient by patient basis to find

NOTE Confidence: 0.8751713

00:49:55.050 --> 00:49:56.786 out not only what the range of

NOTE Confidence: 0.8751713

00:49:56.786 --> 00:49:58.312 antigens are that they're making,

NOTE Confidence: 0.8751713

00:49:58.312 --> 00:50:00.860 so that you can design an appropri.

NOTE Confidence: 0.8751713

00:50:00.860 --> 00:50:02.129 Vaccine in fact,

NOTE Confidence: 0.8751713

00:50:02.129 --> 00:50:04.667 that was that that's your goal.

NOTE Confidence: 0.8751713

00:50:04.670 --> 00:50:06.358 Or design an appropriate

NOTE Confidence: 0.8751713

00:50:06.358 --> 00:50:08.046 type of cell therapy,

NOTE Confidence: 0.8751713

00:50:08.050 --> 00:50:10.588 but also to know how that

NOTE Confidence: 0.8751713

00:50:10.588 --> 00:50:11.857 patient is reacting,

NOTE Confidence: 0.8751713

00:50:11.860 --> 00:50:13.960 whether the patient responds or

NOTE Confidence: 0.8751713

00:50:13.960 --> 00:50:16.555 doesn't respond at the genetic level

NOTE Confidence: 0.8751713

00:50:16.555 --> 00:50:19.537 in the tumor in terms of whether

NOTE Confidence: 0.8751713

00:50:19.537 --> 00:50:21.251 transcriptional patterns are different

NOTE Confidence: 0.8751713

00:50:21.251 --> 00:50:23.699 that now create a resistance environment,  
NOTE Confidence: 0.8751713

00:50:23.700 --> 00:50:27.408 perhaps by losing irrelevant MSE molecule.  
NOTE Confidence: 0.8751713

00:50:27.410 --> 00:50:29.510 Or again bye bye genetic loss,  
NOTE Confidence: 0.8751713

00:50:29.510 --> 00:50:31.960 which is something that the tumors do.  
NOTE Confidence: 0.8751713

00:50:31.960 --> 00:50:34.606 Unfortunately very very well and has been  
NOTE Confidence: 0.8751713

00:50:34.606 --> 00:50:37.628 a real problem even be targeted therapies.  
NOTE Confidence: 0.8751713

00:50:37.630 --> 00:50:38.602 So you know,  
NOTE Confidence: 0.8751713

00:50:38.602 --> 00:50:38.926 again,  
NOTE Confidence: 0.8751713

00:50:38.926 --> 00:50:41.968 I think this type of work can really only  
NOTE Confidence: 0.8751713

00:50:41.968 --> 00:50:44.850 be done on a patient by patient basis,  
NOTE Confidence: 0.8751713

00:50:44.850 --> 00:50:47.279 and it's not something if we use  
NOTE Confidence: 0.8751713

00:50:47.279 --> 00:50:49.330 clinical sites just to run trials.  
NOTE Confidence: 0.8751713

00:50:49.330 --> 00:50:51.730 And if you use us just to give  
NOTE Confidence: 0.8751713

00:50:51.730 --> 00:50:54.139 you drugs to run clinical trials,  
NOTE Confidence: 0.8751713

00:50:54.140 --> 00:50:55.860 that's not going to work.  
NOTE Confidence: 0.8751713

00:50:55.860 --> 00:50:57.930 That's not new advanced the field.

NOTE Confidence: 0.8751713

00:50:57.930 --> 00:51:02.218 I think there really does need to be.

NOTE Confidence: 0.9031921

00:51:02.220 --> 00:51:04.380 An interface which is developing

NOTE Confidence: 0.9031921

00:51:04.380 --> 00:51:06.540 but really needs to be.

NOTE Confidence: 0.9031921

00:51:06.540 --> 00:51:08.104 Advanced around the science,

NOTE Confidence: 0.9031921

00:51:08.104 --> 00:51:10.059 even forgetting about the clinical

NOTE Confidence: 0.9031921

00:51:10.059 --> 00:51:11.647 development issues for the moment,

NOTE Confidence: 0.9031921

00:51:11.650 --> 00:51:13.058 but just, you know,

NOTE Confidence: 0.9031921

00:51:13.058 --> 00:51:14.466 really concentrated on the

NOTE Confidence: 0.9031921

00:51:14.466 --> 00:51:16.353 science that that is controlling

NOTE Confidence: 0.9031921

00:51:16.353 --> 00:51:18.218 response and lack of response,

NOTE Confidence: 0.9031921

00:51:18.220 --> 00:51:19.680 either as primary resistance

NOTE Confidence: 0.9031921

00:51:19.680 --> 00:51:20.775 or acquired resistance.

NOTE Confidence: 0.8219428

00:51:22.690 --> 00:51:24.430 Thank you, I mean, you know.

NOTE Confidence: 0.8219428

00:51:24.430 --> 00:51:25.845 Obviously I followed your work

NOTE Confidence: 0.8219428

00:51:25.845 --> 00:51:27.900 about the way PD one worked and

NOTE Confidence: 0.8219428

00:51:27.900 --> 00:51:29.646 the effects on CD 28 signaling,  
NOTE Confidence: 0.8219428

00:51:29.650 --> 00:51:31.546 and there's been a lot of data about  
NOTE Confidence: 0.8219428

00:51:31.546 --> 00:51:33.527 the need for new for it's the early  
NOTE Confidence: 0.8219428

00:51:33.527 --> 00:51:35.312 stem cells that are generating the  
NOTE Confidence: 0.8219428

00:51:35.312 --> 00:51:37.586 anti tumor response and not the  
NOTE Confidence: 0.8219428

00:51:37.586 --> 00:51:38.607 terminally differentiated cells.  
NOTE Confidence: 0.8219428

00:51:38.607 --> 00:51:40.663 There's a lot of data out there that  
NOTE Confidence: 0.8219428

00:51:40.663 --> 00:51:42.703 makes the whole mechanism of how anti  
NOTE Confidence: 0.8219428

00:51:42.703 --> 00:51:44.440 PD one works relatively confusing,  
NOTE Confidence: 0.8219428

00:51:44.440 --> 00:51:46.225 but I just want to address maybe  
NOTE Confidence: 0.8219428

00:51:46.225 --> 00:51:48.338 a couple of issues 'cause we have  
NOTE Confidence: 0.8219428

00:51:48.338 --> 00:51:49.948 some expertise on the panel,  
NOTE Confidence: 0.8219428

00:51:49.950 --> 00:51:51.134 one based on errands,  
NOTE Confidence: 0.8219428

00:51:51.134 --> 00:51:54.268 work on our 18 and again going back to Akiko.  
NOTE Confidence: 0.8219428

00:51:54.270 --> 00:51:56.538 And maybe grace on on innate immunity.  
NOTE Confidence: 0.8219428

00:51:56.540 --> 00:51:57.494 How do you?

NOTE Confidence: 0.8219428

00:51:57.494 --> 00:51:59.720 How do you view the in patients

NOTE Confidence: 0.8219428

00:51:59.796 --> 00:52:02.127 who lose class one and and maybe

NOTE Confidence: 0.8219428

00:52:02.127 --> 00:52:04.308 don't have a lot of T cells?

NOTE Confidence: 0.8219428

00:52:04.310 --> 00:52:06.722 How do you think that we can Co opt

NOTE Confidence: 0.8219428

00:52:06.722 --> 00:52:09.170 innate immunity to treat those patients?

NOTE Confidence: 0.8219428

00:52:09.170 --> 00:52:11.270 Let me just start with them because

NOTE Confidence: 0.8219428

00:52:11.270 --> 00:52:13.193 I think he has some interesting

NOTE Confidence: 0.8219428

00:52:13.193 --> 00:52:15.837 data with I'll 18 and it may be

NOTE Confidence: 0.8219428

00:52:15.837 --> 00:52:18.210 good at Grayson Akiko and see what

NOTE Confidence: 0.8219428

00:52:18.210 --> 00:52:19.868 their thoughts are about this.

NOTE Confidence: 0.7817753

00:52:21.540 --> 00:52:23.265 And this is obviously a

NOTE Confidence: 0.7817753

00:52:23.265 --> 00:52:24.990 topic that here at Yale,

NOTE Confidence: 0.7817753

00:52:24.990 --> 00:52:27.750 we have a really keen an intense interest.

NOTE Confidence: 0.7817753

00:52:27.750 --> 00:52:29.948 You know from some of the initial

NOTE Confidence: 0.7817753

00:52:29.948 --> 00:52:31.488 observations that that loss of

NOTE Confidence: 0.7817753



00:52:31.488 --> 00:52:33.371 beta 2 micro Glenn was for current  
NOTE Confidence: 0.7817753

00:52:33.371 --> 00:52:35.625 theme of patients who acquired  
NOTE Confidence: 0.7817753

00:52:35.625 --> 00:52:37.068 secondary resistance immunotherapy.  
NOTE Confidence: 0.7817753

00:52:37.070 --> 00:52:39.526 So Marcus and I have been working on  
NOTE Confidence: 0.7817753

00:52:39.526 --> 00:52:41.409 this problem looking for preclinical  
NOTE Confidence: 0.7817753

00:52:41.409 --> 00:52:43.815 agents that could that could treat  
NOTE Confidence: 0.7817753

00:52:43.815 --> 00:52:45.849 mouse tumors where we have deleted  
NOTE Confidence: 0.7817753

00:52:45.849 --> 00:52:48.142 MHT class one or take tumors that  
NOTE Confidence: 0.7817753

00:52:48.142 --> 00:52:50.308 naturally have loss of other components  
NOTE Confidence: 0.7817753

00:52:50.308 --> 00:52:52.609 of antigen presentation like tapasin.  
NOTE Confidence: 0.7817753

00:52:52.610 --> 00:52:55.266 As well and then we see you know,  
NOTE Confidence: 0.7817753

00:52:55.270 --> 00:52:58.267 as you may expect, that you know me loud.  
NOTE Confidence: 0.7817753

00:52:58.270 --> 00:53:00.466 Immunological dogma is that NK cells  
NOTE Confidence: 0.7817753

00:53:00.466 --> 00:53:02.581 should recognize these cells that have  
NOTE Confidence: 0.7817753

00:53:02.581 --> 00:53:04.925 lost image C Class one this marker itself.  
NOTE Confidence: 0.7817753

00:53:04.930 --> 00:53:07.594 But we know that the truthfully NK cells,

NOTE Confidence: 0.7817753

00:53:07.600 --> 00:53:09.260 particularly the tumor micro environment,

NOTE Confidence: 0.7817753

00:53:09.260 --> 00:53:10.930 become rapidly energetic or exhausted,

NOTE Confidence: 0.7817753

00:53:10.930 --> 00:53:13.254 depending on what terminology want to use.

NOTE Confidence: 0.7817753

00:53:13.260 --> 00:53:15.916 This is work by David Relay and others.

NOTE Confidence: 0.7817753

00:53:15.920 --> 00:53:18.989 And so it is clear preclinically that we can

NOTE Confidence: 0.7817753

00:53:18.989 --> 00:53:21.247 reinvigorate some of those NK cell response.

NOTE Confidence: 0.7817753

00:53:21.250 --> 00:53:22.910 But we started kind therapies.

NOTE Confidence: 0.7817753

00:53:22.910 --> 00:53:25.180 Others have started to use.

NOTE Confidence: 0.7817753

00:53:25.180 --> 00:53:26.760 Agents against NK cell receptors,

NOTE Confidence: 0.7817753

00:53:26.760 --> 00:53:28.650 like agonists of the NK G2D.

NOTE Confidence: 0.7817753

00:53:28.650 --> 00:53:31.476 That's like sort of as best you could say,

NOTE Confidence: 0.7817753

00:53:31.480 --> 00:53:34.216 TC are equivalent and NK cells or inhibiting

NOTE Confidence: 0.7817753

00:53:34.216 --> 00:53:36.208 key receptors like the anti NK G2A.

NOTE Confidence: 0.7817753

00:53:36.210 --> 00:53:38.100 That's the Mona Lisa map drug.

NOTE Confidence: 0.7817753

00:53:38.100 --> 00:53:39.990 It actually has some activity when

NOTE Confidence: 0.7817753

00:53:39.990 --> 00:53:41.250 combined with monoclonal antibodies.

NOTE Confidence: 0.7817753

00:53:41.250 --> 00:53:43.448 I think one thing that is underexplored,

NOTE Confidence: 0.7817753

00:53:43.450 --> 00:53:45.882 but it's going to be a major challenge

NOTE Confidence: 0.7817753

00:53:45.882 --> 00:53:47.550 in harnessing NK cell activity,

NOTE Confidence: 0.7817753

00:53:47.550 --> 00:53:48.922 particularly against these tumors.

NOTE Confidence: 0.7817753

00:53:48.922 --> 00:53:51.678 Last class one is a lot of these

NOTE Confidence: 0.7817753

00:53:51.678 --> 00:53:53.592 preclinical models and work guilty of

NOTE Confidence: 0.7817753

00:53:53.592 --> 00:53:56.010 it here at Yale are not amino edited.

NOTE Confidence: 0.7817753

00:53:56.010 --> 00:53:58.282 So in the same way that tumors become

NOTE Confidence: 0.7817753

00:53:58.282 --> 00:54:00.503 amino edited against T cells they can

NOTE Confidence: 0.7817753

00:54:00.503 --> 00:54:02.500 become Immuno edited against NK cells.

NOTE Confidence: 0.7817753

00:54:02.500 --> 00:54:04.210 In loss of self antigens is

NOTE Confidence: 0.7817753

00:54:04.210 --> 00:54:05.900 not enough to drive killing.

NOTE Confidence: 0.7817753

00:54:05.900 --> 00:54:06.208 Sorry.

NOTE Confidence: 0.7817753

00:54:06.208 --> 00:54:08.364 Lots of markers himself like image C

NOTE Confidence: 0.7817753

00:54:08.364 --> 00:54:10.838 Class one is not enough to drive killing.

NOTE Confidence: 0.7817753

00:54:10.840 --> 00:54:12.700 You need you need other signals.

NOTE Confidence: 0.7817753

00:54:12.700 --> 00:54:13.021 NK,

NOTE Confidence: 0.7817753

00:54:13.021 --> 00:54:14.626 activator signals antagonist signals in

NOTE Confidence: 0.7817753

00:54:14.626 --> 00:54:16.708 tumor cells appear to edit those out.

NOTE Confidence: 0.7817753

00:54:16.710 --> 00:54:18.942 For a great example of that has been

NOTE Confidence: 0.7817753

00:54:18.942 --> 00:54:21.182 seen in lymphoma where we know that

NOTE Confidence: 0.7817753

00:54:21.182 --> 00:54:23.819 that you know class one loss is common.

NOTE Confidence: 0.7817753

00:54:23.820 --> 00:54:26.016 But what usually Co occurs almost.

NOTE Confidence: 0.7817753

00:54:26.020 --> 00:54:27.838 Always is loss of CD 2,

NOTE Confidence: 0.7817753

00:54:27.840 --> 00:54:29.360 which is an important molecule

NOTE Confidence: 0.7817753

00:54:29.360 --> 00:54:30.880 that drives NK cell killing,

NOTE Confidence: 0.7817753

00:54:30.880 --> 00:54:33.445 and so I think really we need to think

NOTE Confidence: 0.7817753

00:54:33.445 --> 00:54:35.792 about how can we do more than just

NOTE Confidence: 0.7817753

00:54:35.792 --> 00:54:37.880 this inhibit or activate NK cells.

NOTE Confidence: 0.7817753

00:54:37.880 --> 00:54:40.001 But how do we really direct the

NOTE Confidence: 0.7817753

00:54:40.001 --> 00:54:40.607 tumor engagement?  
NOTE Confidence: 0.7817753

00:54:40.610 --> 00:54:42.344 I think there's some really exciting  
NOTE Confidence: 0.7817753

00:54:42.344 --> 00:54:44.259 programs like the dragon fight programs,  
NOTE Confidence: 0.7817753

00:54:44.260 --> 00:54:44.942 monoclonal antibodies.  
NOTE Confidence: 0.7817753

00:54:44.942 --> 00:54:47.670 Of course we're good at that and something  
NOTE Confidence: 0.7817753

00:54:47.731 --> 00:54:49.723 that we really keenly have our eye on,  
NOTE Confidence: 0.7817753

00:54:49.730 --> 00:54:51.266 something that Marcus and I are  
NOTE Confidence: 0.7817753

00:54:51.266 --> 00:54:53.125 working on at the Center for  
NOTE Confidence: 0.7817753

00:54:53.125 --> 00:54:54.286 precision cancer modeling.  
NOTE Confidence: 0.8589774

00:54:55.840 --> 00:54:59.116 And Grace, What do you think about your rig?  
NOTE Confidence: 0.8589774

00:54:59.120 --> 00:55:01.654 I agonist or that would they be  
NOTE Confidence: 0.8589774

00:55:01.660 --> 00:55:03.480 able to address this issue?  
NOTE Confidence: 0.8589774

00:55:03.480 --> 00:55:06.224 Yeah, I think these are really important  
NOTE Confidence: 0.8589774

00:55:06.224 --> 00:55:08.076 questions and highlights the point  
NOTE Confidence: 0.8589774

00:55:08.076 --> 00:55:10.225 that I read brought up about coupling  
NOTE Confidence: 0.8589774

00:55:10.225 --> 00:55:12.499 the basic science with the translation

NOTE Confidence: 0.8589774

00:55:12.499 --> 00:55:14.737 all aspects right because we think

NOTE Confidence: 0.8589774

00:55:14.737 --> 00:55:16.759 that there are potentially new types

NOTE Confidence: 0.8589774

00:55:16.759 --> 00:55:18.619 of science that's happening within

NOTE Confidence: 0.8589774

00:55:18.619 --> 00:55:20.584 different types of immune cells,

NOTE Confidence: 0.8589774

00:55:20.590 --> 00:55:22.776 either in response to new antigens

NOTE Confidence: 0.8589774

00:55:22.776 --> 00:55:24.268 or under normal conditions,

NOTE Confidence: 0.8589774

00:55:24.268 --> 00:55:26.900 and that would be important to understand.

NOTE Confidence: 0.8589774

00:55:26.900 --> 00:55:30.824 Or how we can then address in disease states.

NOTE Confidence: 0.8589774

00:55:30.830 --> 00:55:33.015 So, for example, there's pulmonary

NOTE Confidence: 0.8589774

00:55:33.015 --> 00:55:34.763 evidence that RNA modifications,

NOTE Confidence: 0.8589774

00:55:34.770 --> 00:55:37.392 and specifically the N 6 methyl

NOTE Confidence: 0.8589774

00:55:37.392 --> 00:55:39.140 adenosine that I mentioned.

NOTE Confidence: 0.8589774

00:55:39.140 --> 00:55:42.224 The levels are different in, you know,

NOTE Confidence: 0.8589774

00:55:42.224 --> 00:55:44.032 cancer situations versus healthy

NOTE Confidence: 0.8589774

00:55:44.032 --> 00:55:46.723 situations and that they change in

NOTE Confidence: 0.8589774

00:55:46.723 --> 00:55:48.748 different types of immune cells.

NOTE Confidence: 0.8589774

00:55:48.750 --> 00:55:51.210 So given that Arnie modifications is

NOTE Confidence: 0.8589774

00:55:51.210 --> 00:55:53.560 like an epic transcriptomic regulator,

NOTE Confidence: 0.8589774

00:55:53.560 --> 00:55:56.476 it controls all sorts of different

NOTE Confidence: 0.8589774

00:55:56.476 --> 00:55:58.950 aspects and within a cell.

NOTE Confidence: 0.8589774

00:55:58.950 --> 00:56:01.488 M6A has been shown to control

NOTE Confidence: 0.8589774

00:56:01.488 --> 00:56:03.760 the transcript stability as well

NOTE Confidence: 0.8589774

00:56:03.760 --> 00:56:05.776 as its cellular localization,

NOTE Confidence: 0.8589774

00:56:05.780 --> 00:56:09.420 as well as its ability to be translated.

NOTE Confidence: 0.8589774

00:56:09.420 --> 00:56:12.252 So we have data showing that

NOTE Confidence: 0.8589774

00:56:12.252 --> 00:56:14.880 depending on the level of M6A,

NOTE Confidence: 0.8589774

00:56:14.880 --> 00:56:17.150 the Genomic Architecture is different,

NOTE Confidence: 0.8589774

00:56:17.150 --> 00:56:19.460 and the Genomic confirmation then

NOTE Confidence: 0.8589774

00:56:19.460 --> 00:56:21.770 affects the types of transcripts

NOTE Confidence: 0.8589774

00:56:21.840 --> 00:56:23.520 that are being produced,

NOTE Confidence: 0.8589774

00:56:23.520 --> 00:56:25.875 and subsequently the proteins that

NOTE Confidence: 0.8589774

00:56:25.875 --> 00:56:28.230 could be expressed from those

NOTE Confidence: 0.8589774

00:56:28.303 --> 00:56:31.099 transcripts and stuff we can identify.

NOTE Confidence: 0.8589774

00:56:31.100 --> 00:56:33.595 Key aspects that are differentially

NOTE Confidence: 0.8589774

00:56:33.595 --> 00:56:36.090 changing between cancer states or

NOTE Confidence: 0.8589774

00:56:36.163 --> 00:56:38.635 healthy States and or the different

NOTE Confidence: 0.8589774

00:56:38.635 --> 00:56:41.658 types of immune cells in a cancer state.

NOTE Confidence: 0.8589774

00:56:41.660 --> 00:56:42.050 Potentially,

NOTE Confidence: 0.8589774

00:56:42.050 --> 00:56:45.170 we have new targets to then go after

NOTE Confidence: 0.8589774

00:56:45.170 --> 00:56:47.817 in sort of difficult situations.

NOTE Confidence: 0.7929867

00:56:49.080 --> 00:56:51.256 Let me let akiko in an Marcus comment

NOTE Confidence: 0.7929867

00:56:51.256 --> 00:56:54.019 'cause I you know this is an area that's

NOTE Confidence: 0.7929867

00:56:54.019 --> 00:56:55.890 become a substantial interest to us,

NOTE Confidence: 0.7929867

00:56:55.890 --> 00:56:57.126 including the myeloid component.

NOTE Confidence: 0.7929867

00:56:57.126 --> 00:56:59.283 So maybe you can comment a little

NOTE Confidence: 0.7929867

00:56:59.283 --> 00:57:00.918 bit on that. Akiko and Marcus.

NOTE Confidence: 0.808472900000001



00:57:03.100 --> 00:57:06.259 Thank you so since the NK issue is so  
NOTE Confidence: 0.8084729000000001

00:57:06.259 --> 00:57:09.148 nicely covered by air and I'm just going  
NOTE Confidence: 0.8084729000000001

00:57:09.148 --> 00:57:12.913 to sort of mention another thing that it's  
NOTE Confidence: 0.8084729000000001

00:57:12.913 --> 00:57:15.965 fundamental to immuno oncology Ann yet  
NOTE Confidence: 0.8084729000000001

00:57:15.965 --> 00:57:18.040 really hasn't garnered enough attention,  
NOTE Confidence: 0.8084729000000001

00:57:18.040 --> 00:57:21.505 which is the sort of immunosuppressive state.  
NOTE Confidence: 0.8084729000000001

00:57:21.510 --> 00:57:25.092 Of tumor burden and this I learned kind of,  
NOTE Confidence: 0.8084729000000001

00:57:25.100 --> 00:57:26.492 you know, through experiment.  
NOTE Confidence: 0.8084729000000001

00:57:26.492 --> 00:57:29.743 So the rest of my lab does antiviral  
NOTE Confidence: 0.8084729000000001

00:57:29.743 --> 00:57:32.150 immunity, and so we've been looking  
NOTE Confidence: 0.8084729000000001

00:57:32.150 --> 00:57:34.444 at what happens to antiviral immunity  
NOTE Confidence: 0.8084729000000001

00:57:34.444 --> 00:57:36.950 in mice that are bearing tumors an  
NOTE Confidence: 0.8084729000000001

00:57:36.950 --> 00:57:39.469 they are really immuno suppressed.  
NOTE Confidence: 0.8084729000000001

00:57:39.470 --> 00:57:41.460 They cannot generate diesel immunity.  
NOTE Confidence: 0.8084729000000001

00:57:41.460 --> 00:57:43.854 In case else you know their  
NOTE Confidence: 0.8084729000000001

00:57:43.854 --> 00:57:45.450 dendritic cells are wacky.

NOTE Confidence: 0.808472900000001  
00:57:45.450 --> 00:57:48.798 So I think before we can even start thinking  
NOTE Confidence: 0.808472900000001  
00:57:48.798 --> 00:57:51.560 about how to improve immune oncology.  
NOTE Confidence: 0.808472900000001  
00:57:51.560 --> 00:57:53.492 We have to deal with this impact  
NOTE Confidence: 0.808472900000001  
00:57:53.492 --> 00:57:55.265 of tumor burden and what it's  
NOTE Confidence: 0.808472900000001  
00:57:55.265 --> 00:57:56.740 doing to the immune system.  
NOTE Confidence: 0.808472900000001  
00:57:56.740 --> 00:57:59.044 I don't think we understand that very well.  
NOTE Confidence: 0.808472900000001  
00:57:59.050 --> 00:58:00.772 Or maybe I'm just being ignorant  
NOTE Confidence: 0.808472900000001  
00:58:00.772 --> 00:58:01.633 of those facts,  
NOTE Confidence: 0.808472900000001  
00:58:01.640 --> 00:58:03.212 but I feel like that's something  
NOTE Confidence: 0.808472900000001  
00:58:03.212 --> 00:58:05.499 that we need to deal with no matter  
NOTE Confidence: 0.808472900000001  
00:58:05.499 --> 00:58:06.974 what the immunotherapy is going  
NOTE Confidence: 0.808472900000001  
00:58:06.974 --> 00:58:09.097 to be in order to really elicit  
NOTE Confidence: 0.808472900000001  
00:58:09.097 --> 00:58:10.570 a robust immunity against tumors.  
NOTE Confidence: 0.79807854  
00:58:12.690 --> 00:58:14.210 Marcus, if you could comment,  
NOTE Confidence: 0.79807854  
00:58:14.210 --> 00:58:15.119 yeah, that's excellent.  
NOTE Confidence: 0.79807854

00:58:15.120 --> 00:58:17.248 Sure, yeah. I think it's really interesting.  
NOTE Confidence: 0.79807854

00:58:17.250 --> 00:58:19.350 IRA also had kind of touched on  
NOTE Confidence: 0.79807854

00:58:19.350 --> 00:58:21.522 this to talking about how I mean  
NOTE Confidence: 0.79807854

00:58:21.522 --> 00:58:23.322 1 version of MHT class losses,  
NOTE Confidence: 0.79807854

00:58:23.330 --> 00:58:24.850 sort of by allelic beta,  
NOTE Confidence: 0.79807854

00:58:24.850 --> 00:58:27.090 two microglobulin loss and everything is gone  
NOTE Confidence: 0.79807854

00:58:27.090 --> 00:58:29.710 and you expect NK cells perhaps to hit those,  
NOTE Confidence: 0.79807854

00:58:29.710 --> 00:58:31.838 but it's probably more subtle than that.  
NOTE Confidence: 0.79807854

00:58:31.840 --> 00:58:33.360 Frequently have specific MHT class,  
NOTE Confidence: 0.79807854

00:58:33.360 --> 00:58:34.880 one alleles or even specific  
NOTE Confidence: 0.79807854

00:58:34.880 --> 00:58:36.400 antigens that are really important.  
NOTE Confidence: 0.79807854

00:58:36.400 --> 00:58:38.792 Antigens that are lost and it's really hard  
NOTE Confidence: 0.79807854

00:58:38.792 --> 00:58:41.269 to know how that happens along the way,  
NOTE Confidence: 0.79807854

00:58:41.270 --> 00:58:43.398 but I think one of the things  
NOTE Confidence: 0.79807854

00:58:43.398 --> 00:58:44.610 that's been surprising too.  
NOTE Confidence: 0.79807854

00:58:44.610 --> 00:58:46.830 I think many immuno oncology field.

NOTE Confidence: 0.79807854

00:58:46.830 --> 00:58:49.350 Is the demonstration by a lot of different

NOTE Confidence: 0.79807854

00:58:49.350 --> 00:58:50.794 approaches that interferon gamma

NOTE Confidence: 0.79807854

00:58:50.794 --> 00:58:52.669 reception or interferon reception and

NOTE Confidence: 0.79807854

00:58:52.669 --> 00:58:54.945 tumor cells is really critical for being

NOTE Confidence: 0.79807854

00:58:54.945 --> 00:58:57.190 able to be killed by the immune system?

NOTE Confidence: 0.79807854

00:58:57.190 --> 00:58:59.630 And it seems that one of the principle

NOTE Confidence: 0.79807854

00:58:59.695 --> 00:59:01.495 things that that does is upregulate

NOTE Confidence: 0.79807854

00:59:01.495 --> 00:59:03.824 MHC class one in the tumor cells

NOTE Confidence: 0.79807854

00:59:03.824 --> 00:59:05.252 so the transcriptional regulation

NOTE Confidence: 0.79807854

00:59:05.252 --> 00:59:07.790 of MFC class one in tumor cells is

NOTE Confidence: 0.79807854

00:59:07.790 --> 00:59:09.617 really really important and some of

NOTE Confidence: 0.79807854

00:59:09.617 --> 00:59:11.465 the approaches that people have been

NOTE Confidence: 0.79807854

00:59:11.465 --> 00:59:13.537 referring to with innate immunity and

NOTE Confidence: 0.79807854

00:59:13.537 --> 00:59:15.347 even things like cytosolic nucleic

NOTE Confidence: 0.79807854

00:59:15.347 --> 00:59:17.232 acid sensing like Regai agonism.

NOTE Confidence: 0.79807854

00:59:17.232 --> 00:59:20.440 And things like that were in our hands.  
NOTE Confidence: 0.79807854

00:59:20.440 --> 00:59:22.900 Irv reactivation is great at Reactivating.  
NOTE Confidence: 0.79807854

00:59:22.900 --> 00:59:24.544 You know interferon secretion  
NOTE Confidence: 0.79807854

00:59:24.544 --> 00:59:25.777 and sometimes type.  
NOTE Confidence: 0.79807854

00:59:25.780 --> 00:59:28.080 One interferon can substitute for  
NOTE Confidence: 0.79807854

00:59:28.080 --> 00:59:30.845 Interferon Gamma at least an upregulation  
NOTE Confidence: 0.79807854

00:59:30.845 --> 00:59:33.933 of MFC Class 1 SI think things that  
NOTE Confidence: 0.79807854

00:59:33.933 --> 00:59:36.993 are locally going to be inducing the T  
NOTE Confidence: 0.79807854

00:59:36.993 --> 00:59:39.978 cell tumor cell interaction in that fashion.  
NOTE Confidence: 0.79807854

00:59:39.978 --> 00:59:41.846 An override whatever local  
NOTE Confidence: 0.79807854

00:59:41.846 --> 00:59:43.489 immunosuppressive effects that are  
NOTE Confidence: 0.79807854

00:59:43.489 --> 00:59:45.094 there will really be critical.  
NOTE Confidence: 0.79807854

00:59:45.100 --> 00:59:47.698 I think one of the difficulties  
NOTE Confidence: 0.79807854

00:59:47.698 --> 00:59:48.997 that we've had.  
NOTE Confidence: 0.79807854

00:59:49.000 --> 00:59:49.738 In studying.  
NOTE Confidence: 0.79807854

00:59:49.738 --> 00:59:51.583 The tumor microenvironment is that

NOTE Confidence: 0.79807854

00:59:51.583 --> 00:59:53.350 it's been very difficult.

NOTE Confidence: 0.79807854

00:59:53.350 --> 00:59:55.163 For instance, I mean T regs have

NOTE Confidence: 0.79807854

00:59:55.163 --> 00:59:57.010 a very well established role,

NOTE Confidence: 0.79807854

00:59:57.010 --> 00:59:58.535 but other aspects, like whatever

NOTE Confidence: 0.79807854

00:59:58.535 --> 01:00:00.460 versions one will call different MD.

NOTE Confidence: 0.79807854

01:00:00.460 --> 01:00:00.778 Yes,

NOTE Confidence: 0.79807854

01:00:00.778 --> 01:00:02.050 sees things like that,

NOTE Confidence: 0.79807854

01:00:02.050 --> 01:00:03.710 so myeloid derived factors that

NOTE Confidence: 0.79807854

01:00:03.710 --> 01:00:05.370 can be suppressive than tumor

NOTE Confidence: 0.79807854

01:00:05.430 --> 01:00:06.790 environment or hard to entirely

NOTE Confidence: 0.79807854

01:00:06.790 --> 01:00:08.700 get rid of in most contexts.

NOTE Confidence: 0.79807854

01:00:08.700 --> 01:00:10.285 And you can't really study

NOTE Confidence: 0.79807854

01:00:10.285 --> 01:00:11.553 them adequately in human.

NOTE Confidence: 0.79807854

01:00:11.560 --> 01:00:13.968 So I think their roles an exactly what

NOTE Confidence: 0.79807854

01:00:13.968 --> 01:00:16.310 they're doing has been harder to determine,

NOTE Confidence: 0.79807854

01:00:16.310 --> 01:00:17.650 but.

NOTE Confidence: 0.79807854

01:00:17.650 --> 01:00:20.882 I'd refer back to some comments about the

NOTE Confidence: 0.79807854

01:00:20.882 --> 01:00:22.770 personalized immunotherapy and how you know,

NOTE Confidence: 0.79807854

01:00:22.770 --> 01:00:25.230 with these explant assays you can

NOTE Confidence: 0.79807854

01:00:25.230 --> 01:00:27.903 actually do these things and we can

NOTE Confidence: 0.79807854

01:00:27.903 --> 01:00:30.129 keep tumors alive for over a month

NOTE Confidence: 0.79807854

01:00:30.208 --> 01:00:32.686 with all the sto kiamat re preserved

NOTE Confidence: 0.79807854

01:00:32.686 --> 01:00:34.482 and one could reconstitute tumors

NOTE Confidence: 0.79807854

01:00:34.482 --> 01:00:36.678 to take out my load components.

NOTE Confidence: 0.79807854

01:00:36.680 --> 01:00:38.990 So I think I'm very enthusiastic about

NOTE Confidence: 0.79807854

01:00:38.990 --> 01:00:41.070 this approach to actually evaluate

NOTE Confidence: 0.79807854

01:00:41.070 --> 01:00:42.902 how different cell types contribute

NOTE Confidence: 0.79807854

01:00:42.902 --> 01:00:44.366 to localized immune suppression,

NOTE Confidence: 0.79807854

01:00:44.370 --> 01:00:45.830 which hopefully will lead

NOTE Confidence: 0.79807854

01:00:45.830 --> 01:00:46.925 to mechanistic advances,

NOTE Confidence: 0.79807854

01:00:46.930 --> 01:00:47.660 an understanding.

NOTE Confidence: 0.84946245  
01:00:48.700 --> 01:00:51.348 Let me just ask you one more question  
NOTE Confidence: 0.84946245  
01:00:51.348 --> 01:00:54.238 before I want to turn out back to Iran.  
NOTE Confidence: 0.84946245  
01:00:54.240 --> 01:00:56.109 Ask him a couple of questions but  
NOTE Confidence: 0.84946245  
01:00:56.109 --> 01:00:58.402 the do you think that there's a role  
NOTE Confidence: 0.84946245  
01:00:58.402 --> 01:01:00.394 for purely non T cell dependent  
NOTE Confidence: 0.84946245  
01:01:00.394 --> 01:01:02.386 mechanisms in cancer treatment?  
NOTE Confidence: 0.84946245  
01:01:02.390 --> 01:01:04.469 Do you think that we could without  
NOTE Confidence: 0.84946245  
01:01:04.469 --> 01:01:06.299 getting any T cell response,  
NOTE Confidence: 0.84946245  
01:01:06.300 --> 01:01:07.930 activate NK cells, myeloid cells,  
NOTE Confidence: 0.84946245  
01:01:07.930 --> 01:01:09.585 macrophages in a sufficient way  
NOTE Confidence: 0.84946245  
01:01:09.585 --> 01:01:11.240 or modulate their function that  
NOTE Confidence: 0.84946245  
01:01:11.295 --> 01:01:12.870 you could see significant anti  
NOTE Confidence: 0.84946245  
01:01:12.870 --> 01:01:14.445 tumor activity in the clinic?  
NOTE Confidence: 0.8413477  
01:01:16.230 --> 01:01:18.846 I think you know there's a couple examples,  
NOTE Confidence: 0.8413477  
01:01:18.850 --> 01:01:20.806 so at the NK approaches, ankhar,  
NOTE Confidence: 0.8413477



01:01:20.806 --> 01:01:23.415 NK and things like that, I think that  
NOTE Confidence: 0.8413477

01:01:23.415 --> 01:01:26.369 it is likely to be possible to do that.  
NOTE Confidence: 0.81358355

01:01:28.430 --> 01:01:29.960 Other things that, for instance,  
NOTE Confidence: 0.81358355

01:01:29.960 --> 01:01:32.408 one of our researchers here at Yale Allies,  
NOTE Confidence: 0.81358355

01:01:32.410 --> 01:01:34.545 who is looking at using Carty with  
NOTE Confidence: 0.81358355

01:01:34.545 --> 01:01:36.078 myeloid cells, like with basophils,  
NOTE Confidence: 0.81358355

01:01:36.078 --> 01:01:36.996 another Excel types,  
NOTE Confidence: 0.81358355

01:01:37.000 --> 01:01:38.758 and that this approach might be  
NOTE Confidence: 0.81358355

01:01:38.758 --> 01:01:40.360 something that would be really,  
NOTE Confidence: 0.81358355

01:01:40.360 --> 01:01:41.584 really could work well,  
NOTE Confidence: 0.81358355

01:01:41.584 --> 01:01:42.808 and that's oppressive pathways.  
NOTE Confidence: 0.81358355

01:01:42.810 --> 01:01:44.340 Might not actually work as well  
NOTE Confidence: 0.81358355

01:01:44.340 --> 01:01:46.504 against a non T cell because that's  
NOTE Confidence: 0.81358355

01:01:46.504 --> 01:01:47.956 typically how the suppression  
NOTE Confidence: 0.81358355

01:01:47.956 --> 01:01:49.540 would be expected to work.  
NOTE Confidence: 0.81358355

01:01:49.540 --> 01:01:51.250 I think there's still some work

NOTE Confidence: 0.81358355

01:01:51.250 --> 01:01:53.219 to be done in those areas,

NOTE Confidence: 0.81358355

01:01:53.220 --> 01:01:55.665 but you know I I'm open to the

NOTE Confidence: 0.81358355

01:01:55.665 --> 01:01:56.912 possibility that other things

NOTE Confidence: 0.81358355

01:01:56.912 --> 01:01:59.110 can work and I think it's worth.

NOTE Confidence: 0.81358355

01:01:59.110 --> 01:02:01.132 Pursuing it based on the preliminary

NOTE Confidence: 0.81358355

01:02:01.132 --> 01:02:03.388 data that you're seeing in those areas.

NOTE Confidence: 0.81358355

01:02:03.390 --> 01:02:05.358 So I am enthusiastic about that.

NOTE Confidence: 0.84732705

01:02:06.610 --> 01:02:08.423 Interesting, so I just want to ask

NOTE Confidence: 0.84732705

01:02:08.423 --> 01:02:10.584 you a question you you know you lead

NOTE Confidence: 0.84732705

01:02:10.584 --> 01:02:12.802 development in a company and I wonder you

NOTE Confidence: 0.84732705

01:02:12.802 --> 01:02:14.762 know that when you look at combinations,

NOTE Confidence: 0.84732705

01:02:14.770 --> 01:02:17.158 all the combinations that we've done.

NOTE Confidence: 0.84732705

01:02:17.160 --> 01:02:19.240 One is not overwhelmed by the by the

NOTE Confidence: 0.84732705

01:02:19.240 --> 01:02:21.559 level of activity that's been observed.

NOTE Confidence: 0.84732705

01:02:21.560 --> 01:02:23.125 Maybe it's because we don't

NOTE Confidence: 0.84732705

01:02:23.125 --> 01:02:24.377 have the right biomarkers.  
NOTE Confidence: 0.84732705

01:02:24.380 --> 01:02:26.200 Have you taken home any any lessons  
NOTE Confidence: 0.84732705

01:02:26.200 --> 01:02:28.276 from the the three that seemed to  
NOTE Confidence: 0.84732705

01:02:28.276 --> 01:02:29.821 have worked CTA for chemotherapy  
NOTE Confidence: 0.84732705

01:02:29.821 --> 01:02:31.599 and vege perceptor Inhibitors,  
NOTE Confidence: 0.84732705

01:02:31.600 --> 01:02:33.616 which seem to be the ones that  
NOTE Confidence: 0.84732705

01:02:33.616 --> 01:02:36.000 are sort of at the forefront now,  
NOTE Confidence: 0.84732705

01:02:36.000 --> 01:02:37.256 notwithstanding the early Dec  
NOTE Confidence: 0.84732705

01:02:37.256 --> 01:02:39.140 with digit but but but those?  
NOTE Confidence: 0.84732705

01:02:39.140 --> 01:02:41.024 Those seem to have sort of  
NOTE Confidence: 0.84732705

01:02:41.024 --> 01:02:42.280 moved to the front,  
NOTE Confidence: 0.84732705

01:02:42.280 --> 01:02:44.512 which are not the ones that other than  
NOTE Confidence: 0.84732705

01:02:44.512 --> 01:02:47.013 CTA four chemotherapy and the veg F  
NOTE Confidence: 0.84732705

01:02:47.013 --> 01:02:48.888 Receptor Inhibitors would have been.  
NOTE Confidence: 0.84732705

01:02:48.890 --> 01:02:51.095 The top ones on my list 10 years ago.  
NOTE Confidence: 0.8577246

01:02:52.640 --> 01:02:54.616 No, you're actually right.

NOTE Confidence: 0.8577246

01:02:54.616 --> 01:02:58.380 Mario. I mean when we decided

NOTE Confidence: 0.8577246

01:02:58.380 --> 01:03:01.650 to go into using chemotherapy.

NOTE Confidence: 0.8577246

01:03:01.650 --> 01:03:03.806 Theoretical pieces for that was not well,

NOTE Confidence: 0.8577246

01:03:03.810 --> 01:03:07.850 Gee, maybe some of them if they're not.

NOTE Confidence: 0.8577246

01:03:07.850 --> 01:03:08.516 Therefore, blade,

NOTE Confidence: 0.8577246

01:03:08.516 --> 01:03:10.514 if you can choose those properties,

NOTE Confidence: 0.8577246

01:03:10.520 --> 01:03:12.655 maybe they'll cause some type of information

NOTE Confidence: 0.8577246

01:03:12.655 --> 01:03:14.727 or immunogenic cell death that will

NOTE Confidence: 0.8577246

01:03:14.727 --> 01:03:16.199 somehow synergized with immunotherapy.

NOTE Confidence: 0.8577246

01:03:16.200 --> 01:03:19.540 I think that's turned out not to be the case.

NOTE Confidence: 0.8577246

01:03:19.540 --> 01:03:22.230 That my guess is now.

NOTE Confidence: 0.8577246

01:03:22.230 --> 01:03:25.042 No looking having book

NOTE Confidence: 0.8577246

01:03:25.042 --> 01:03:27.854 for epitope spreading and.

NOTE Confidence: 0.8577246

01:03:27.860 --> 01:03:30.485 Expansion of TC Arts Fidelity and stuff.

NOTE Confidence: 0.8577246

01:03:30.490 --> 01:03:32.370 In lot of these patients.

NOTE Confidence: 0.8577246

01:03:32.370 --> 01:03:34.326 I just think that's an additive  
NOTE Confidence: 0.8577246

01:03:34.326 --> 01:03:37.029 effect that you get a certain amount  
NOTE Confidence: 0.8577246

01:03:37.029 --> 01:03:38.797 of tumor debulking associated  
NOTE Confidence: 0.8577246

01:03:38.797 --> 01:03:40.881 with chemotherapy that then allows  
NOTE Confidence: 0.8577246

01:03:40.881 --> 01:03:42.957 the immunotherapy to do what it's  
NOTE Confidence: 0.8577246

01:03:42.957 --> 01:03:44.991 going to do almost separately.  
NOTE Confidence: 0.8577246

01:03:44.991 --> 01:03:48.793 So I think that the idea that at  
NOTE Confidence: 0.8577246

01:03:48.793 --> 01:03:51.109 least most conventional chemo.  
NOTE Confidence: 0.8577246

01:03:51.110 --> 01:03:53.262 Immunotherapy combinations are synergistic.  
NOTE Confidence: 0.8577246

01:03:53.262 --> 01:03:55.952 That's that's still waiting for  
NOTE Confidence: 0.8577246

01:03:55.952 --> 01:03:58.040 good evidence that case of.  
NOTE Confidence: 0.8362142

01:04:00.160 --> 01:04:01.840 Antagonist is an interesting  
NOTE Confidence: 0.8362142

01:04:01.840 --> 01:04:04.360 one where I think that is.  
NOTE Confidence: 0.8362142

01:04:04.360 --> 01:04:07.335 That's one of the examples where I  
NOTE Confidence: 0.8362142

01:04:07.335 --> 01:04:10.657 think we really need to look into that.  
NOTE Confidence: 0.8362142

01:04:10.660 --> 01:04:14.020 From a mechanistic POV in HTC for example,

NOTE Confidence: 0.8362142

01:04:14.020 --> 01:04:16.648 the that particular combination is really

NOTE Confidence: 0.8362142

01:04:16.648 --> 01:04:18.640 quite effective from surprisingly so,

NOTE Confidence: 0.8362142

01:04:18.640 --> 01:04:19.480 especially considering

NOTE Confidence: 0.8362142

01:04:19.480 --> 01:04:21.580 that in renal it's not.

NOTE Confidence: 0.8362142

01:04:21.580 --> 01:04:23.420 So what's with that?

NOTE Confidence: 0.8362142

01:04:23.420 --> 01:04:26.684 Because both of the system app on

NOTE Confidence: 0.8362142

01:04:26.684 --> 01:04:29.526 it by itself is supposed to have.

NOTE Confidence: 0.8362142

01:04:29.530 --> 01:04:32.484 Activity and in both of those indications,

NOTE Confidence: 0.8362142

01:04:32.490 --> 01:04:35.838 so I take that to suggest that it's not

NOTE Confidence: 0.8362142

01:04:35.838 --> 01:04:38.410 necessarily an additive phenomenon there,

NOTE Confidence: 0.8362142

01:04:38.410 --> 01:04:40.470 but there's something that specific

NOTE Confidence: 0.8362142

01:04:40.470 --> 01:04:43.464 that's going on in ACC that is

NOTE Confidence: 0.8362142

01:04:43.464 --> 01:04:45.599 being addressed by the definition,

NOTE Confidence: 0.8362142

01:04:45.600 --> 01:04:47.898 which could actually have to do

NOTE Confidence: 0.8362142

01:04:47.898 --> 01:04:49.988 with myeloid cell suppression or

NOTE Confidence: 0.8362142

01:04:49.988 --> 01:04:51.948 overcoming mile itself suppressions,  
NOTE Confidence: 0.8362142

01:04:51.950 --> 01:04:54.694 and certainly by Jeff is one way that  
NOTE Confidence: 0.8362142

01:04:54.694 --> 01:04:58.426 one can use to turn off dendritic cell  
NOTE Confidence: 0.8362142

01:04:58.426 --> 01:05:00.406 activity and antigen presentation,  
NOTE Confidence: 0.8362142

01:05:00.410 --> 01:05:01.182 so perhaps.  
NOTE Confidence: 0.8362142

01:05:01.182 --> 01:05:03.112 That's slowing down what aspect  
NOTE Confidence: 0.8362142

01:05:03.112 --> 01:05:04.270 of the problem.  
NOTE Confidence: 0.8362142

01:05:04.270 --> 01:05:07.222 So there again, is just a plea for saying,  
NOTE Confidence: 0.8362142

01:05:07.230 --> 01:05:07.894 You know,  
NOTE Confidence: 0.8362142

01:05:07.894 --> 01:05:10.218 we need to look into that from  
NOTE Confidence: 0.8362142

01:05:10.218 --> 01:05:11.510 mechanistic point of view,  
NOTE Confidence: 0.8362142

01:05:11.510 --> 01:05:13.478 better than we have thus far.  
NOTE Confidence: 0.84984183

01:05:15.560 --> 01:05:20.910 In terms of no future combinations. My.  
NOTE Confidence: 0.84892386

01:05:24.240 --> 01:05:25.899 What I keep trying to push is  
NOTE Confidence: 0.84892386

01:05:25.899 --> 01:05:27.959 to take a mechanistic approach,  
NOTE Confidence: 0.84892386

01:05:27.960 --> 01:05:29.796 look at the tumors and figure

NOTE Confidence: 0.84892386  
01:05:29.796 --> 01:05:31.680 out what what's wrong with them.  
NOTE Confidence: 0.84892386  
01:05:31.680 --> 01:05:33.850 What is the rate limiting step here?  
NOTE Confidence: 0.84892386  
01:05:33.850 --> 01:05:35.446 What is the rate limiting step  
NOTE Confidence: 0.84892386  
01:05:35.446 --> 01:05:37.658 there and then try and pick apart  
NOTE Confidence: 0.84892386  
01:05:37.658 --> 01:05:39.114 mechanisms associated with them,  
NOTE Confidence: 0.84892386  
01:05:39.120 --> 01:05:41.541 and I think it markets are just saying and  
NOTE Confidence: 0.84892386  
01:05:41.541 --> 01:05:44.078 I think it increasing number of cases.  
NOTE Confidence: 0.84892386  
01:05:44.080 --> 01:05:46.366 It does look like the myeloid  
NOTE Confidence: 0.84892386  
01:05:46.366 --> 01:05:47.890 compartment is playing a.  
NOTE Confidence: 0.84892386  
01:05:47.890 --> 01:05:50.008 Important, but as yet poorly understood,  
NOTE Confidence: 0.84892386  
01:05:50.010 --> 01:05:52.140 role in a lot of this,  
NOTE Confidence: 0.84892386  
01:05:52.140 --> 01:05:54.702 and I think it's it's more than  
NOTE Confidence: 0.84892386  
01:05:54.702 --> 01:05:58.333 high time to go back and look more  
NOTE Confidence: 0.84892386  
01:05:58.333 --> 01:06:00.783 seriously at the myeloid compartment.  
NOTE Confidence: 0.84892386  
01:06:00.790 --> 01:06:03.136 The whole field of so-called mileage  
NOTE Confidence: 0.84892386



01:06:03.136 --> 01:06:05.418 derived suppressor cells that I think is,  
NOTE Confidence: 0.84892386

01:06:05.420 --> 01:06:07.388 is still very very sketchy in  
NOTE Confidence: 0.84892386

01:06:07.388 --> 01:06:09.549 terms of the precision with which  
NOTE Confidence: 0.84892386

01:06:09.549 --> 01:06:11.105 those cells are described.  
NOTE Confidence: 0.84892386

01:06:11.110 --> 01:06:12.976 What they do and who they  
NOTE Confidence: 0.84892386

01:06:12.976 --> 01:06:15.389 are and how to modulate them.  
NOTE Confidence: 0.84892386

01:06:15.390 --> 01:06:17.875 So I think we have to kind  
NOTE Confidence: 0.84892386

01:06:17.875 --> 01:06:20.005 of back off in some way,  
NOTE Confidence: 0.84892386

01:06:20.010 --> 01:06:22.080 at least as scientists and understand  
NOTE Confidence: 0.84892386

01:06:22.080 --> 01:06:23.914 the basic immunology and cell  
NOTE Confidence: 0.84892386

01:06:23.914 --> 01:06:25.474 biology before really designing  
NOTE Confidence: 0.84892386

01:06:25.474 --> 01:06:27.424 and knowing precisely what agents  
NOTE Confidence: 0.84892386

01:06:27.485 --> 01:06:29.267 to bring forward in the interim.  
NOTE Confidence: 0.84892386

01:06:29.270 --> 01:06:30.638 Obviously we don't as.  
NOTE Confidence: 0.84892386

01:06:30.638 --> 01:06:32.348 Conditions don't want to wait  
NOTE Confidence: 0.84892386

01:06:32.348 --> 01:06:33.889 around for the basic scientists

NOTE Confidence: 0.84892386

01:06:33.889 --> 01:06:35.830 to figure it all out for us,

NOTE Confidence: 0.84892386

01:06:35.830 --> 01:06:38.548 assuming that they'll even do that.

NOTE Confidence: 0.84892386

01:06:38.550 --> 01:06:41.398 But agents are coming out all the time

NOTE Confidence: 0.84892386

01:06:41.398 --> 01:06:45.120 and I think crafting combinations of them,

NOTE Confidence: 0.84892386

01:06:45.120 --> 01:06:47.310 which I find in companies,

NOTE Confidence: 0.84892386

01:06:47.310 --> 01:06:49.938 is often akin to just throwing

NOTE Confidence: 0.84892386

01:06:49.938 --> 01:06:51.690 spaghetti against the wall.

NOTE Confidence: 0.84892386

01:06:51.690 --> 01:06:54.798 Still has to be.

NOTE Confidence: 0.84892386

01:06:54.800 --> 01:06:57.334 In a fashion that has some some

NOTE Confidence: 0.84892386

01:06:57.334 --> 01:06:58.840 logic associated with that,

NOTE Confidence: 0.84892386

01:06:58.840 --> 01:07:01.129 and I think that's that's a struggle

NOTE Confidence: 0.84892386

01:07:01.129 --> 01:07:03.439 in both of our communities to

NOTE Confidence: 0.84892386

01:07:03.439 --> 01:07:05.947 just keep people from doing stuff

NOTE Confidence: 0.84892386

01:07:05.947 --> 01:07:08.482 because it can be done and instead

NOTE Confidence: 0.84892386

01:07:08.482 --> 01:07:10.610 spending your time and effort and

NOTE Confidence: 0.84892386

01:07:10.610 --> 01:07:12.890 the commitment of patients to doing  
NOTE Confidence: 0.84892386

01:07:12.890 --> 01:07:14.978 those things that have the best  
NOTE Confidence: 0.84892386

01:07:14.978 --> 01:07:16.868 chance of working based on the  
NOTE Confidence: 0.84892386

01:07:16.941 --> 01:07:19.389 science as we currently understand it.  
NOTE Confidence: 0.8220813

01:07:21.130 --> 01:07:21.672 Thanks, Alright,  
NOTE Confidence: 0.8220813

01:07:21.672 --> 01:07:23.027 I'm glad you mentioned mileage,  
NOTE Confidence: 0.8220813

01:07:23.030 --> 01:07:23.846 so you're interested.  
NOTE Confidence: 0.8220813

01:07:23.846 --> 01:07:24.934 Also were very interested.  
NOTE Confidence: 0.8220813

01:07:24.940 --> 01:07:26.300 I think Marcus is prioritizing.  
NOTE Confidence: 0.8220813

01:07:26.300 --> 01:07:28.092 That is one of the areas of  
NOTE Confidence: 0.8220813

01:07:28.092 --> 01:07:29.769 research for the El Senor de  
NOTE Confidence: 0.8220813

01:07:29.769 --> 01:07:31.184 mean onkologie and we have.  
NOTE Confidence: 0.8220813

01:07:31.190 --> 01:07:32.822 You know, we can't bring everybody  
NOTE Confidence: 0.8220813

01:07:32.822 --> 01:07:33.910 onto the phone conversation.  
NOTE Confidence: 0.8220813

01:07:33.910 --> 01:07:35.542 We have a lot of expertise  
NOTE Confidence: 0.8220813

01:07:35.542 --> 01:07:36.358 here in immunobiology,

NOTE Confidence: 0.8220813

01:07:36.360 --> 01:07:38.110 in that area that that again we

NOTE Confidence: 0.8220813

01:07:38.110 --> 01:07:39.503 just can't fit everybody into

NOTE Confidence: 0.8220813

01:07:39.503 --> 01:07:41.255 one hour and a half session.

NOTE Confidence: 0.8220813

01:07:41.260 --> 01:07:43.404 So I just want to maybe just turn

NOTE Confidence: 0.8220813

01:07:43.404 --> 01:07:45.695 to Roy for a second before you go

NOTE Confidence: 0.8220813

01:07:45.695 --> 01:07:48.099 back to more of the basic science.

NOTE Confidence: 0.8220813

01:07:48.100 --> 01:07:49.140 Well, there's a question

NOTE Confidence: 0.8220813

01:07:49.140 --> 01:07:50.180 about rare tumor initiatives,

NOTE Confidence: 0.8220813

01:07:50.180 --> 01:07:52.260 so I wanted to ask you 2 questions.

NOTE Confidence: 0.8220813

01:07:52.260 --> 01:07:53.820 What do we do here about

NOTE Confidence: 0.8220813

01:07:53.820 --> 01:07:54.860 rare tumors and what?

NOTE Confidence: 0.8220813

01:07:54.860 --> 01:07:56.680 What are the efforts that we have?

NOTE Confidence: 0.8220813

01:07:56.680 --> 01:07:57.980 And the other question that

NOTE Confidence: 0.8220813

01:07:57.980 --> 01:07:59.800 I have for you is, you know.

NOTE Confidence: 0.8220813

01:07:59.800 --> 01:08:01.880 Now, now that you've heard all this way,

NOTE Confidence: 0.8220813

01:08:01.880 --> 01:08:02.125 where?  
NOTE Confidence: 0.8220813

01:08:02.125 --> 01:08:03.595 Where do you think the field  
NOTE Confidence: 0.8220813

01:08:03.595 --> 01:08:05.000 is headed in lung cancer?  
NOTE Confidence: 0.8220813

01:08:05.000 --> 01:08:06.560 For Immunobiology and even on Koleji.  
NOTE Confidence: 0.76484925

01:08:07.840 --> 01:08:09.784 Well, the second question is a  
NOTE Confidence: 0.76484925

01:08:09.784 --> 01:08:12.147 lot easier for me to answer than  
NOTE Confidence: 0.76484925

01:08:12.147 --> 01:08:14.133 the first rare tumors we send  
NOTE Confidence: 0.76484925

01:08:14.133 --> 01:08:16.426 them to Pat Larusso in phase one.  
NOTE Confidence: 0.76484925

01:08:16.430 --> 01:08:18.260 So we know where we're growing.  
NOTE Confidence: 0.76484925

01:08:18.260 --> 01:08:20.726 You know, the yell when I row is the  
NOTE Confidence: 0.76484925

01:08:20.726 --> 01:08:23.136 director of the deputy director of science.  
NOTE Confidence: 0.76484925

01:08:23.140 --> 01:08:24.970 You know we're seeing a couple  
NOTE Confidence: 0.76484925

01:08:24.970 --> 01:08:26.190 of 1000 patients now.  
NOTE Confidence: 0.76484925

01:08:26.190 --> 01:08:28.122 We have about eight 9000 a year  
NOTE Confidence: 0.76484925

01:08:28.122 --> 01:08:30.323 and we have a large number of  
NOTE Confidence: 0.76484925

01:08:30.323 --> 01:08:32.285 care centers 15 around the state,

NOTE Confidence: 0.76484925

01:08:32.290 --> 01:08:34.120 so we are seeing you know,

NOTE Confidence: 0.76484925

01:08:34.120 --> 01:08:35.650 like sarcoma is an issue.

NOTE Confidence: 0.76484925

01:08:35.650 --> 01:08:37.650 You know we see enough of those now

NOTE Confidence: 0.76484925

01:08:37.650 --> 01:08:39.816 that we probably need to form more

NOTE Confidence: 0.76484925

01:08:39.816 --> 01:08:41.830 full fledged order that area and

NOTE Confidence: 0.76484925

01:08:41.830 --> 01:08:43.575 certainly even more rare tumors.

NOTE Confidence: 0.76484925

01:08:43.580 --> 01:08:45.320 You know, skin tumors you know

NOTE Confidence: 0.76484925

01:08:45.320 --> 01:08:47.432 you see some of those, right?

NOTE Confidence: 0.76484925

01:08:47.432 --> 01:08:49.440 Merkel cell tumor approved.

NOTE Confidence: 0.76484925

01:08:49.440 --> 01:08:51.624 You know agents so as this happens,

NOTE Confidence: 0.76484925

01:08:51.630 --> 01:08:54.118 we're getting to do more and more of

NOTE Confidence: 0.76484925

01:08:54.118 --> 01:08:56.339 that where we're at the point now.

NOTE Confidence: 0.76484925

01:08:56.340 --> 01:08:57.984 We're probably going to have to

NOTE Confidence: 0.76484925

01:08:57.984 --> 01:09:00.212 set up a unknown tumor clinic or

NOTE Confidence: 0.76484925

01:09:00.212 --> 01:09:01.997 something for the everything else,

NOTE Confidence: 0.76484925

01:09:02.000 --> 01:09:04.504 'cause we're seeing more and more of that.  
NOTE Confidence: 0.76484925

01:09:04.510 --> 01:09:07.014 And we are moving towards a tumor agnostic,  
NOTE Confidence: 0.76484925

01:09:07.020 --> 01:09:07.648 you know,  
NOTE Confidence: 0.76484925

01:09:07.648 --> 01:09:10.160 sort of treatment with some of these agents.  
NOTE Confidence: 0.76484925

01:09:10.160 --> 01:09:10.848 You know,  
NOTE Confidence: 0.76484925

01:09:10.848 --> 01:09:12.912 the Pember Lizum app was just  
NOTE Confidence: 0.76484925

01:09:12.912 --> 01:09:14.239 approved based on AT MB,  
NOTE Confidence: 0.76484925

01:09:14.240 --> 01:09:16.466 so I think with more advanced Genomic  
NOTE Confidence: 0.76484925

01:09:16.466 --> 01:09:18.030 profiling and immune profiling.  
NOTE Confidence: 0.76484925

01:09:18.030 --> 01:09:19.794 I think that might be one way to deal  
NOTE Confidence: 0.76484925

01:09:19.794 --> 01:09:21.658 or deal with the more we are tumors.  
NOTE Confidence: 0.76484925

01:09:21.660 --> 01:09:23.810 As far as lung cancer.  
NOTE Confidence: 0.76484925

01:09:23.810 --> 01:09:24.136 No,  
NOTE Confidence: 0.76484925

01:09:24.136 --> 01:09:27.070 I've been doing this now for almost 25 years,  
NOTE Confidence: 0.76484925

01:09:27.070 --> 01:09:29.345 certainly in the area of targeted therapy.  
NOTE Confidence: 0.76484925

01:09:29.350 --> 01:09:30.670 I think we've done.

NOTE Confidence: 0.76484925

01:09:30.670 --> 01:09:32.940 We're doing what we need to do.

NOTE Confidence: 0.76484925

01:09:32.940 --> 01:09:34.830 I remember when we first with

NOTE Confidence: 0.76484925

01:09:34.830 --> 01:09:36.486 John Mendelsohn started to look

NOTE Confidence: 0.76484925

01:09:36.486 --> 01:09:37.497 at EGFR inhibitors.

NOTE Confidence: 0.76484925

01:09:37.500 --> 01:09:40.107 We treated everyone we saw a 10% response.

NOTE Confidence: 0.76484925

01:09:40.107 --> 01:09:42.069 We were thrilled drugs became approved.

NOTE Confidence: 0.76484925

01:09:42.070 --> 01:09:44.026 It was seven years before the

NOTE Confidence: 0.76484925

01:09:44.026 --> 01:09:45.330 EGFR mutation was developed,

NOTE Confidence: 0.76484925

01:09:45.330 --> 01:09:47.610 and then once that happened, of course.

NOTE Confidence: 0.76484925

01:09:47.610 --> 01:09:49.235 Still not a home run.

NOTE Confidence: 0.76484925

01:09:49.240 --> 01:09:50.272 'cause of resistance.

NOTE Confidence: 0.76484925

01:09:50.272 --> 01:09:52.336 But then we started to treat

NOTE Confidence: 0.76484925

01:09:52.336 --> 01:09:54.197 patients in the frontline setting.

NOTE Confidence: 0.76484925

01:09:54.200 --> 01:09:55.574 And now just recently there are

NOTE Confidence: 0.76484925

01:09:55.574 --> 01:09:57.155 data now in the agement setting

NOTE Confidence: 0.76484925



01:09:57.155 --> 01:09:58.997 with some of these agents where  
NOTE Confidence: 0.76484925

01:09:58.997 --> 01:10:00.538 perhaps they'll be more potent or.  
NOTE Confidence: 0.76484925

01:10:00.540 --> 01:10:01.980 Early on, before resistance develops,  
NOTE Confidence: 0.76484925

01:10:01.980 --> 01:10:03.996 I think we're at a point in  
NOTE Confidence: 0.76484925

01:10:03.996 --> 01:10:04.860 lung cancer immunotherapy.  
NOTE Confidence: 0.76484925

01:10:04.860 --> 01:10:06.876 We have to take a deep breath,  
NOTE Confidence: 0.76484925

01:10:06.880 --> 01:10:08.596 and it's hard because Iris said,  
NOTE Confidence: 0.76484925

01:10:08.600 --> 01:10:10.392 it's very hard for a company or  
NOTE Confidence: 0.76484925

01:10:10.392 --> 01:10:12.504 group not to just add on and  
NOTE Confidence: 0.76484925

01:10:12.504 --> 01:10:13.784 start to build combinations.  
NOTE Confidence: 0.76484925

01:10:13.790 --> 01:10:15.225 Who would have thought chemotherapy  
NOTE Confidence: 0.76484925

01:10:15.225 --> 01:10:16.373 combinations would have worked?  
NOTE Confidence: 0.76484925

01:10:16.380 --> 01:10:17.169 In fact, no.  
NOTE Confidence: 0.76484925

01:10:17.169 --> 01:10:19.404 I led the trial of a Tesla might  
NOTE Confidence: 0.76484925

01:10:19.404 --> 01:10:20.700 as a single agent.  
NOTE Confidence: 0.76484925

01:10:20.700 --> 01:10:22.140 I was offered the combo.

NOTE Confidence: 0.76484925

01:10:22.140 --> 01:10:23.176 I didn't want it.

NOTE Confidence: 0.76484925

01:10:23.176 --> 01:10:25.599 I talked to a few people here leaping.

NOTE Confidence: 0.76484925

01:10:25.600 --> 01:10:26.748 I didn't think chemotherapy

NOTE Confidence: 0.76484925

01:10:26.748 --> 01:10:27.896 would be the reason.

NOTE Confidence: 0.76484925

01:10:27.900 --> 01:10:29.628 And I totally agree with IRA,

NOTE Confidence: 0.76484925

01:10:29.630 --> 01:10:31.508 I think it's an additive approach.

NOTE Confidence: 0.76484925

01:10:31.510 --> 01:10:32.154 They're not.

NOTE Confidence: 0.76484925

01:10:32.154 --> 01:10:34.020 They're not antagonistic, but but still.

NOTE Confidence: 0.76484925

01:10:34.020 --> 01:10:36.979 The thing that bothers me is in lung cancer.

NOTE Confidence: 0.76484925

01:10:36.980 --> 01:10:38.590 We those are the agents,

NOTE Confidence: 0.76484925

01:10:38.590 --> 01:10:40.200 you know, see TLA four.

NOTE Confidence: 0.76484925

01:10:40.200 --> 01:10:41.810 A little bit vague, Jeff,

NOTE Confidence: 0.76484925

01:10:41.810 --> 01:10:44.386 you know their number of Axl Mer TK.

NOTE Confidence: 0.7647381

01:10:44.390 --> 01:10:46.316 We have some with Carla Rothlin.

NOTE Confidence: 0.7647381

01:10:46.320 --> 01:10:48.246 We have some some expertise there.

NOTE Confidence: 0.7647381

01:10:48.250 --> 01:10:50.122 I think some of these approaches  
NOTE Confidence: 0.7647381

01:10:50.122 --> 01:10:51.800 that we heard from Aaron,  
NOTE Confidence: 0.7647381

01:10:51.800 --> 01:10:53.726 you know, 50% of lung cancers,  
NOTE Confidence: 0.7647381

01:10:53.730 --> 01:10:56.322 maybe 60% when the ping and David rim  
NOTE Confidence: 0.7647381

01:10:56.322 --> 01:10:58.876 and Kurt look at them have no tail.  
NOTE Confidence: 0.7647381

01:10:58.880 --> 01:11:01.584 So so, so there's clearly a need to.  
NOTE Confidence: 0.7647381

01:11:01.590 --> 01:11:03.375 Personalized this therapy and I  
NOTE Confidence: 0.7647381

01:11:03.375 --> 01:11:05.839 think the next step really has to be,  
NOTE Confidence: 0.7647381

01:11:05.840 --> 01:11:07.975 and I know I was actually going  
NOTE Confidence: 0.7647381

01:11:07.975 --> 01:11:10.096 to ask you a question, Mario,  
NOTE Confidence: 0.7647381

01:11:10.096 --> 01:11:12.378 why don't we do more of this?  
NOTE Confidence: 0.7647381

01:11:12.380 --> 01:11:14.669 Why five years now after chemo immunotherapy?  
NOTE Confidence: 0.7647381

01:11:14.670 --> 01:11:17.604 I mean, do we not know what's going on?  
NOTE Confidence: 0.7647381

01:11:17.610 --> 01:11:18.782 What's the sweet spot?  
NOTE Confidence: 0.7647381

01:11:18.782 --> 01:11:20.247 Went to work when patients  
NOTE Confidence: 0.7647381

01:11:20.247 --> 01:11:21.858 become have primary resistance,

NOTE Confidence: 0.7647381

01:11:21.860 --> 01:11:23.588 we need to obtain more samples

NOTE Confidence: 0.7647381

01:11:23.588 --> 01:11:25.541 and it's very hard because those

NOTE Confidence: 0.7647381

01:11:25.541 --> 01:11:27.749 studies are very in labor intensive.

NOTE Confidence: 0.7647381

01:11:27.750 --> 01:11:29.706 Specially now in this covid area.

NOTE Confidence: 0.7647381

01:11:29.710 --> 01:11:31.996 Or we just want to survive.

NOTE Confidence: 0.7647381

01:11:32.000 --> 01:11:33.939 But we need samples, we need biopsies.

NOTE Confidence: 0.7647381

01:11:33.940 --> 01:11:36.424 We need to take him to our labs pressing.

NOTE Confidence: 0.7647381

01:11:36.430 --> 01:11:37.820 Pressing has to be quick,

NOTE Confidence: 0.7647381

01:11:37.820 --> 01:11:39.620 but you know I reset the best model

NOTE Confidence: 0.7647381

01:11:39.620 --> 01:11:41.984 sort of human and all the animal models

NOTE Confidence: 0.7647381

01:11:41.984 --> 01:11:43.910 we've mentioned are fraught with issues.

NOTE Confidence: 0.7647381

01:11:43.910 --> 01:11:45.566 So I would say right now.

NOTE Confidence: 0.7647381

01:11:45.570 --> 01:11:46.678 Lung cancer. It's amazing.

NOTE Confidence: 0.7647381

01:11:46.678 --> 01:11:48.063 You know you know therapy.

NOTE Confidence: 0.7647381

01:11:48.070 --> 01:11:50.290 I just got the.

NOTE Confidence: 0.7647381

01:11:50.290 --> 01:11:51.980 Five year results now with  
NOTE Confidence: 0.7647381

01:11:51.980 --> 01:11:54.020 with drugs 30% survival in an  
NOTE Confidence: 0.7647381

01:11:54.020 --> 01:11:55.380 untreated metastatic lung cancer,  
NOTE Confidence: 0.7647381

01:11:55.380 --> 01:11:58.770 no PDL 1 high but you know PDL 1 low.  
NOTE Confidence: 0.7647381

01:11:58.770 --> 01:12:01.066 It's a lot different and many patients  
NOTE Confidence: 0.7647381

01:12:01.066 --> 01:12:02.963 don't benefit klemen they want what  
NOTE Confidence: 0.7647381

01:12:02.963 --> 01:12:04.951 they see in the commercials and many  
NOTE Confidence: 0.7647381

01:12:05.007 --> 01:12:06.899 patients have acquired resistance.  
NOTE Confidence: 0.7647381

01:12:06.900 --> 01:12:09.490 This field is perfect for the alliance  
NOTE Confidence: 0.7647381

01:12:09.490 --> 01:12:11.259 between industry and academia to  
NOTE Confidence: 0.7647381

01:12:11.259 --> 01:12:13.324 you know of course you've got to  
NOTE Confidence: 0.7647381

01:12:13.324 --> 01:12:15.379 do the big phase three trials.  
NOTE Confidence: 0.7647381

01:12:15.380 --> 01:12:19.110 I would do that too if I was in the company,  
NOTE Confidence: 0.7647381

01:12:19.110 --> 01:12:20.800 but we've got it in.  
NOTE Confidence: 0.7647381

01:12:20.800 --> 01:12:21.848 Have a few studies.  
NOTE Confidence: 0.7647381

01:12:21.848 --> 01:12:23.749 That are really focusing on the mechanism

NOTE Confidence: 0.7647381

01:12:23.749 --> 01:12:25.688 and either taking the new drugs and

NOTE Confidence: 0.7647381

01:12:25.688 --> 01:12:27.478 like you know with Aaron's drug,

NOTE Confidence: 0.7647381

01:12:27.480 --> 01:12:29.432 you know the first trials will have to

NOTE Confidence: 0.7647381

01:12:29.432 --> 01:12:31.665 be just to show some activity in safety,

NOTE Confidence: 0.7647381

01:12:31.670 --> 01:12:33.504 but then they have to move forward

NOTE Confidence: 0.7647381

01:12:33.504 --> 01:12:35.247 with liepins drug, the cyclic 15.

NOTE Confidence: 0.7647381

01:12:35.247 --> 01:12:37.790 There have been responses in the phase one.

NOTE Confidence: 0.7647381

01:12:37.790 --> 01:12:39.392 But are there enough well that

NOTE Confidence: 0.7647381

01:12:39.392 --> 01:12:40.193 time will tell,

NOTE Confidence: 0.7647381

01:12:40.200 --> 01:12:42.344 but now it's time to develop an assay.

NOTE Confidence: 0.7647381

01:12:42.350 --> 01:12:44.384 So what we've been able to do here at

NOTE Confidence: 0.7647381

01:12:44.384 --> 01:12:46.634 Yale in partnership is we early on got

NOTE Confidence: 0.7647381

01:12:46.634 --> 01:12:48.509 David Rimm working closely with next.

NOTE Confidence: 0.7647381

01:12:48.510 --> 01:12:50.082 You're one of the companies that

NOTE Confidence: 0.7647381

01:12:50.082 --> 01:12:51.677 John will tell you was developed

NOTE Confidence: 0.7647381

01:12:51.677 --> 01:12:53.399 here and it's taken a few years  
NOTE Confidence: 0.7647381

01:12:53.399 --> 01:12:54.937 to develop a good bioassay.  
NOTE Confidence: 0.7647381

01:12:54.940 --> 01:12:56.708 But now we can start to treat patients  
NOTE Confidence: 0.7647381

01:12:56.708 --> 01:12:58.144 based on the biomarker because  
NOTE Confidence: 0.7647381

01:12:58.144 --> 01:13:00.028 science is going to prevail otherwise.  
NOTE Confidence: 0.7647381

01:13:00.030 --> 01:13:00.298 No,  
NOTE Confidence: 0.7647381

01:13:00.298 --> 01:13:02.710 it it's going to be random and there's just,  
NOTE Confidence: 0.7647381

01:13:02.710 --> 01:13:03.264 you know,  
NOTE Confidence: 0.7647381

01:13:03.264 --> 01:13:05.792 you and I talk about this all the time  
NOTE Confidence: 0.7647381

01:13:05.792 --> 01:13:08.719 in the Hall and we now and I see each other.  
NOTE Confidence: 0.7647381

01:13:08.720 --> 01:13:09.190 Occasionally now,  
NOTE Confidence: 0.7647381

01:13:09.190 --> 01:13:10.835 'cause we're all locked in their offices,  
NOTE Confidence: 0.7647381

01:13:10.840 --> 01:13:12.020 but every once in awhile  
NOTE Confidence: 0.7647381

01:13:12.020 --> 01:13:13.200 we bump into each other.  
NOTE Confidence: 0.7647381

01:13:13.200 --> 01:13:14.859 That's going to be the key thing.  
NOTE Confidence: 0.7647381

01:13:14.860 --> 01:13:16.306 How do we figure out resistance

NOTE Confidence: 0.7647381  
01:13:16.306 --> 01:13:17.270 and be proactive about  
NOTE Confidence: 0.84427387  
01:13:17.316 --> 01:13:17.450 it?  
NOTE Confidence: 0.8292841  
01:13:19.150 --> 01:13:20.094 Yeah, by the way,  
NOTE Confidence: 0.8292841  
01:13:20.094 --> 01:13:21.876 I was wondering once we told you  
NOTE Confidence: 0.8292841  
01:13:21.876 --> 01:13:23.416 not to bother with chemotherapy,  
NOTE Confidence: 0.8292841  
01:13:23.420 --> 01:13:25.289 and I think that just reflects how  
NOTE Confidence: 0.8292841  
01:13:25.289 --> 01:13:27.154 humbling it is to where you are.  
NOTE Confidence: 0.8292841  
01:13:27.154 --> 01:13:28.491 The biggest influence bending and  
NOTE Confidence: 0.8292841  
01:13:28.491 --> 01:13:29.828 mad at you for awhile.  
NOTE Confidence: 0.8292841  
01:13:29.830 --> 01:13:31.426 Yeah yeah, yeah, the so we.  
NOTE Confidence: 0.8292841  
01:13:31.430 --> 01:13:33.404 You know it's the biology is very  
NOTE Confidence: 0.8292841  
01:13:33.404 --> 01:13:35.175 complex and one of the reasons  
NOTE Confidence: 0.8292841  
01:13:35.175 --> 01:13:36.903 why I started that question is  
NOTE Confidence: 0.8292841  
01:13:36.903 --> 01:13:39.002 that when I look at CTA four I can  
NOTE Confidence: 0.8292841  
01:13:39.002 --> 01:13:40.452 think of 10 different reasons why  
NOTE Confidence: 0.8292841



01:13:40.452 --> 01:13:42.380 it might make anti PD one better.

NOTE Confidence: 0.8292841

01:13:42.380 --> 01:13:43.742 But in any individual patient I

NOTE Confidence: 0.8292841

01:13:43.742 --> 01:13:45.329 can't tell which of those mechanisms

NOTE Confidence: 0.8292841

01:13:45.329 --> 01:13:46.914 might be active for chemotherapy.

NOTE Confidence: 0.8292841

01:13:46.920 --> 01:13:49.090 I mean you could do be doing

NOTE Confidence: 0.8292841

01:13:49.090 --> 01:13:50.020 10 different things.

NOTE Confidence: 0.8292841

01:13:50.020 --> 01:13:51.976 I think the exploration of email

NOTE Confidence: 0.8292841

01:13:51.976 --> 01:13:53.606 object is really important and

NOTE Confidence: 0.8292841

01:13:53.606 --> 01:13:55.461 that's why I like this focus on

NOTE Confidence: 0.8292841

01:13:55.461 --> 01:13:57.050 really going back to the tumor,

NOTE Confidence: 0.8292841

01:13:57.050 --> 01:13:58.362 immunobiology and actually to

NOTE Confidence: 0.8292841

01:13:58.362 --> 01:14:00.002 thank Charlie for his commitment

NOTE Confidence: 0.8292841

01:14:00.002 --> 01:14:01.874 to recruiting people who who are

NOTE Confidence: 0.8292841

01:14:01.874 --> 01:14:03.657 focusing on that area because I

NOTE Confidence: 0.8292841

01:14:03.657 --> 01:14:05.351 think as we build our strength and

NOTE Confidence: 0.8292841

01:14:05.351 --> 01:14:07.215 continue to build our strength in that

NOTE Confidence: 0.8292841

01:14:07.215 --> 01:14:09.070 area and were very strong already,

NOTE Confidence: 0.8292841

01:14:09.070 --> 01:14:10.630 we may actually get the answer

NOTE Confidence: 0.8292841

01:14:10.630 --> 01:14:12.290 to some of these questions.

NOTE Confidence: 0.8292841

01:14:12.290 --> 01:14:14.124 So let me just ask one question

NOTE Confidence: 0.8292841

01:14:14.124 --> 01:14:15.834 here that I can answer because

NOTE Confidence: 0.8292841

01:14:15.834 --> 01:14:17.836 I don't know is you know the

NOTE Confidence: 0.8292841

01:14:17.906 --> 01:14:19.808 there was a question related to

NOTE Confidence: 0.8292841

01:14:19.808 --> 01:14:21.486 nano particles in an Atom.

NOTE Confidence: 0.8292841

01:14:21.486 --> 01:14:25.490 Articles fit in into the world of of baby no.

NOTE Confidence: 0.8292841

01:14:25.490 --> 01:14:26.862 Biology and Immuno Oncology

NOTE Confidence: 0.8292841

01:14:26.862 --> 01:14:29.510 or any of you in the capable

NOTE Confidence: 0.8292841

01:14:29.510 --> 01:14:31.570 of addressing that question.

NOTE Confidence: 0.8292841

01:14:31.570 --> 01:14:32.380 I'm not.

NOTE Confidence: 0.846941

01:14:34.980 --> 01:14:37.716 I can take a stab at it.

NOTE Confidence: 0.846941

01:14:37.720 --> 01:14:39.680 I don't know it entirely,

NOTE Confidence: 0.846941

01:14:39.680 --> 01:14:42.704 but I do know I think John is also  
NOTE Confidence: 0.846941

01:14:42.704 --> 01:14:45.835 put some comments in the the chat  
NOTE Confidence: 0.846941

01:14:45.835 --> 01:14:48.699 for attendees to look at as well.  
NOTE Confidence: 0.846941

01:14:48.700 --> 01:14:51.584 So Mark Salzman's been a central player  
NOTE Confidence: 0.846941

01:14:51.584 --> 01:14:53.798 in the Nanoparticle area at Yale,  
NOTE Confidence: 0.846941

01:14:53.800 --> 01:14:56.928 and more broadly for a very long time,  
NOTE Confidence: 0.846941

01:14:56.930 --> 01:14:59.282 and I believe with Mike Gerardi  
NOTE Confidence: 0.846941

01:14:59.282 --> 01:15:00.850 is also recently started.  
NOTE Confidence: 0.846941

01:15:00.850 --> 01:15:03.196 A company called stratify that also  
NOTE Confidence: 0.846941

01:15:03.196 --> 01:15:05.230 is likely interested in using.  
NOTE Confidence: 0.846941

01:15:05.230 --> 01:15:06.434 Anna particle based approaches  
NOTE Confidence: 0.846941

01:15:06.434 --> 01:15:07.337 to enhance immunotherapy's.  
NOTE Confidence: 0.846941

01:15:07.340 --> 01:15:08.845 So there certainly are efforts  
NOTE Confidence: 0.846941

01:15:08.845 --> 01:15:10.964 along those lines and it's not just  
NOTE Confidence: 0.846941

01:15:10.964 --> 01:15:12.364 mark that are additional people  
NOTE Confidence: 0.846941

01:15:12.364 --> 01:15:14.258 at Yahoo are doing these things.

NOTE Confidence: 0.846941

01:15:14.260 --> 01:15:16.297 All the platforms tend to be quite

NOTE Confidence: 0.846941

01:15:16.297 --> 01:15:18.155 different and I think if one

NOTE Confidence: 0.846941

01:15:18.155 --> 01:15:20.003 actually follows up and looks at

NOTE Confidence: 0.846941

01:15:20.003 --> 01:15:21.832 Akiko's paper related to the rig

NOTE Confidence: 0.846941

01:15:21.832 --> 01:15:23.892 immune with Anna pile and we help

NOTE Confidence: 0.846941

01:15:23.892 --> 01:15:25.397 with some of those studies.

NOTE Confidence: 0.846941

01:15:25.400 --> 01:15:27.290 But looking at EPS copal affects

NOTE Confidence: 0.846941

01:15:27.290 --> 01:15:29.271 for nanoparticles I think part of

NOTE Confidence: 0.846941

01:15:29.271 --> 01:15:30.926 the difficulty has been getting

NOTE Confidence: 0.846941

01:15:30.926 --> 01:15:32.674 trafficking to tumors are not like

NOTE Confidence: 0.846941

01:15:32.674 --> 01:15:34.430 T cells which seem to be really

NOTE Confidence: 0.846941

01:15:34.430 --> 01:15:35.810 good at finding tumors.

NOTE Confidence: 0.846941

01:15:35.810 --> 01:15:37.610 Nanoparticles have a harder time

NOTE Confidence: 0.846941

01:15:37.610 --> 01:15:39.897 and tend to end up in macrophages,

NOTE Confidence: 0.846941

01:15:39.900 --> 01:15:42.035 so a lot of those efforts tended

NOTE Confidence: 0.846941

01:15:42.035 --> 01:15:44.052 to be intratumoral and then trying  
NOTE Confidence: 0.846941

01:15:44.052 --> 01:15:45.787 to see these so-called abscopal  
NOTE Confidence: 0.846941

01:15:45.787 --> 01:15:47.687 effects or distant effects for  
NOTE Confidence: 0.846941

01:15:47.687 --> 01:15:49.979 intratumoral agents is one of the  
NOTE Confidence: 0.846941

01:15:49.979 --> 01:15:51.414 challenges that frequently happens,  
NOTE Confidence: 0.846941

01:15:51.414 --> 01:15:53.502 and again at the center position,  
NOTE Confidence: 0.846941

01:15:53.510 --> 01:15:55.040 counseling were particularly well set  
NOTE Confidence: 0.846941

01:15:55.040 --> 01:15:57.430 up to help those folks evaluate whether  
NOTE Confidence: 0.846941

01:15:57.430 --> 01:15:59.435 they're seeing these abscopal affects,  
NOTE Confidence: 0.846941

01:15:59.440 --> 01:16:00.840 but that's kind of,  
NOTE Confidence: 0.846941

01:16:00.840 --> 01:16:01.540 I think,  
NOTE Confidence: 0.846941

01:16:01.540 --> 01:16:03.976 a broader scope across yell as to  
NOTE Confidence: 0.846941

01:16:03.976 --> 01:16:04.672 what's happening.  
NOTE Confidence: 0.8830849

01:16:06.360 --> 01:16:09.306 I think Mario is in the.  
NOTE Confidence: 0.8830849

01:16:09.310 --> 01:16:11.430 In the back scene area,  
NOTE Confidence: 0.8830849

01:16:11.430 --> 01:16:14.475 not a particles have been in use

NOTE Confidence: 0.8830849

01:16:14.475 --> 01:16:16.939 and are increasingly being in use.

NOTE Confidence: 0.8830849

01:16:16.940 --> 01:16:19.060 It certainly the RNA vaccine

NOTE Confidence: 0.8830849

01:16:19.060 --> 01:16:21.180 we're developing with buying tech.

NOTE Confidence: 0.8830849

01:16:21.180 --> 01:16:23.295 Is it basically an added

NOTE Confidence: 0.8830849

01:16:23.295 --> 01:16:24.564 particle based approach,

NOTE Confidence: 0.8830849

01:16:24.570 --> 01:16:28.200 as is the cold vaccine that

NOTE Confidence: 0.8830849

01:16:28.200 --> 01:16:31.070 they're developing as well as.

NOTE Confidence: 0.8830849

01:16:31.070 --> 01:16:35.610 Moderna there are a number of.

NOTE Confidence: 0.8830849

01:16:35.610 --> 01:16:37.010 Ways of using them?

NOTE Confidence: 0.8830849

01:16:37.010 --> 01:16:39.110 I think the first incarnation was

NOTE Confidence: 0.8830849

01:16:39.178 --> 01:16:41.158 to try and use that particles.

NOTE Confidence: 0.8830849

01:16:41.160 --> 01:16:43.308 That's kind of surrogate or artificial

NOTE Confidence: 0.8830849

01:16:43.308 --> 01:16:45.438 antigen presenting cells so far that

NOTE Confidence: 0.8830849

01:16:45.438 --> 01:16:47.358 hasn't really worked out that well

NOTE Confidence: 0.8830849

01:16:47.358 --> 01:16:48.762 because Antigen presenting cells

NOTE Confidence: 0.8830849

01:16:48.762 --> 01:16:50.880 are more than simply inert surface.  
NOTE Confidence: 0.8830849

01:16:50.880 --> 01:16:52.412 Is that present antigens.  
NOTE Confidence: 0.8830849

01:16:52.412 --> 01:16:55.053 They actually act and perform a complex  
NOTE Confidence: 0.8830849

01:16:55.053 --> 01:16:57.474 POD to do with the T cells and B  
NOTE Confidence: 0.8830849

01:16:57.544 --> 01:16:59.896 cells that they are presenting too,  
NOTE Confidence: 0.8830849

01:16:59.900 --> 01:17:02.280 but using them as delivery vehicles for  
NOTE Confidence: 0.8830849

01:17:02.280 --> 01:17:04.759 RNA has actually worked out pretty well,  
NOTE Confidence: 0.8830849

01:17:04.760 --> 01:17:06.590 but it also turns out.  
NOTE Confidence: 0.8830849

01:17:06.590 --> 01:17:07.036 Surprisingly,  
NOTE Confidence: 0.8830849

01:17:07.036 --> 01:17:08.820 when they work well,  
NOTE Confidence: 0.8830849

01:17:08.820 --> 01:17:11.496 they can also be quite toxic,  
NOTE Confidence: 0.8830849

01:17:11.500 --> 01:17:14.684 and I think a lot of the adverse  
NOTE Confidence: 0.8830849

01:17:14.684 --> 01:17:16.969 events associated with either the  
NOTE Confidence: 0.8830849

01:17:16.969 --> 01:17:19.314 cancer vaccines over the covid  
NOTE Confidence: 0.8830849

01:17:19.314 --> 01:17:22.156 vaccines can be attributed as much  
NOTE Confidence: 0.8830849

01:17:22.156 --> 01:17:24.880 to the data particle themselves and

NOTE Confidence: 0.8830849

01:17:24.880 --> 01:17:27.450 its ability to trigger inflammasome

NOTE Confidence: 0.8830849

01:17:27.450 --> 01:17:30.716 responses as the RNA another adjutants

NOTE Confidence: 0.8830849

01:17:30.716 --> 01:17:33.160 that data particles contain.

NOTE Confidence: 0.8830849

01:17:33.160 --> 01:17:35.278 I've worked with Mark and with

NOTE Confidence: 0.8830849

01:17:35.278 --> 01:17:37.536 Tarek Fahmi and I actually get

NOTE Confidence: 0.8830849

01:17:37.536 --> 01:17:39.834 a princely sum every month for

NOTE Confidence: 0.8830849

01:17:39.834 --> 01:17:42.322 being on the patent that controls

NOTE Confidence: 0.8830849

01:17:42.322 --> 01:17:45.388 these princely sum I think gets me

NOTE Confidence: 0.8830849

01:17:45.388 --> 01:17:48.916 coffee at the corner coffee store.

NOTE Confidence: 0.8830849

01:17:48.920 --> 01:17:50.384 But nevertheless, you know,

NOTE Confidence: 0.8830849

01:17:50.384 --> 01:17:52.580 I think they're very interesting platforms,

NOTE Confidence: 0.8830849

01:17:52.580 --> 01:17:54.734 but they haven't really been put

NOTE Confidence: 0.8830849

01:17:54.734 --> 01:17:57.830 into into play it in a way that's

NOTE Confidence: 0.8830849

01:17:57.830 --> 01:17:59.410 that really establishes what

NOTE Confidence: 0.8830849

01:17:59.410 --> 01:18:01.360 the future is going to be.

NOTE Confidence: 0.8830849



01:18:01.360 --> 01:18:04.288 That's not to say they shouldn't be studied.

NOTE Confidence: 0.8830849

01:18:04.290 --> 01:18:06.882 One thing it hasn't come up that in

NOTE Confidence: 0.8830849

01:18:06.882 --> 01:18:09.458 this context I'd like to make bring

NOTE Confidence: 0.8830849

01:18:09.458 --> 01:18:11.313 up for the group's consideration

NOTE Confidence: 0.8830849

01:18:11.390 --> 01:18:13.078 is actually self therapy.

NOTE Confidence: 0.8830849

01:18:13.080 --> 01:18:15.270 When we think of cell therapy,

NOTE Confidence: 0.8830849

01:18:15.270 --> 01:18:19.082 we think of car T cells, which I think are.

NOTE Confidence: 0.8830849

01:18:19.082 --> 01:18:21.097 It can be extraordinarily effective

NOTE Confidence: 0.8830849

01:18:21.097 --> 01:18:23.812 in heme onc setting, certain of them,

NOTE Confidence: 0.8830849

01:18:23.812 --> 01:18:27.419 but thus far less so in solid tumor settings,

NOTE Confidence: 0.8830849

01:18:27.420 --> 01:18:29.345 and it's probably wide variety

NOTE Confidence: 0.8830849

01:18:29.345 --> 01:18:30.885 of reasons for that.

NOTE Confidence: 0.8830849

01:18:30.890 --> 01:18:33.155 We have only ourselves recently

NOTE Confidence: 0.8830849

01:18:33.155 --> 01:18:35.420 started getting into this area.

NOTE Confidence: 0.8830849

01:18:35.420 --> 01:18:38.370 I'm not sure what Yale's

NOTE Confidence: 0.8830849

01:18:38.370 --> 01:18:40.140 involvement has been,

NOTE Confidence: 0.8830849

01:18:40.140 --> 01:18:44.536 but I do think despite my reluctance

NOTE Confidence: 0.8830849

01:18:44.536 --> 01:18:48.399 to embrace cartis in our own shop,

NOTE Confidence: 0.8830849

01:18:48.400 --> 01:18:52.140 I do think that.

NOTE Confidence: 0.8830849

01:18:52.140 --> 01:18:54.365 Cells engineered cells are the

NOTE Confidence: 0.8830849

01:18:54.365 --> 01:18:57.037 nanoparticles of the future in terms

NOTE Confidence: 0.8830849

01:18:57.037 --> 01:18:59.592 of being able to engineer and design

NOTE Confidence: 0.8830849

01:18:59.592 --> 01:19:02.299 them in ways that will allow them

NOTE Confidence: 0.8830849

01:19:02.299 --> 01:19:04.602 not only to be therapeutic agents,

NOTE Confidence: 0.8830849

01:19:04.602 --> 01:19:06.210 but also per say,

NOTE Confidence: 0.8830849

01:19:06.210 --> 01:19:09.140 but also delivers of therapeutic

NOTE Confidence: 0.8830849

01:19:09.140 --> 01:19:12.070 agents such that you can.

NOTE Confidence: 0.8830849

01:19:12.070 --> 01:19:13.594 Get them to use.

NOTE Confidence: 0.8830849

01:19:13.594 --> 01:19:16.412 Make use of their of the cells

NOTE Confidence: 0.8830849

01:19:16.412 --> 01:19:19.034 ability to find out where it

NOTE Confidence: 0.8830849

01:19:19.034 --> 01:19:21.738 is you would like it to go.

NOTE Confidence: 0.8830849

01:19:21.740 --> 01:19:24.212 Get to that spot and then turn it  
NOTE Confidence: 0.8830849

01:19:24.212 --> 01:19:26.980 on to generate other activities,  
NOTE Confidence: 0.8830849

01:19:26.980 --> 01:19:28.995 possibly even the release and  
NOTE Confidence: 0.8830849

01:19:28.995 --> 01:19:30.204 secretion of Biotherapeutics,  
NOTE Confidence: 0.8830849

01:19:30.210 --> 01:19:32.195 which would change entirely business  
NOTE Confidence: 0.8830849

01:19:32.195 --> 01:19:35.440 of how we make drugs and the patients.  
NOTE Confidence: 0.8830849

01:19:35.440 --> 01:19:41.110 So I think this is this is an area that.  
NOTE Confidence: 0.86137027

01:19:41.110 --> 01:19:43.100 I find personally very exciting.  
NOTE Confidence: 0.86137027

01:19:43.100 --> 01:19:46.600 We are investing heavily in.  
NOTE Confidence: 0.86137027

01:19:46.600 --> 01:19:49.966 Looking at how to do I  
NOTE Confidence: 0.86137027

01:19:49.966 --> 01:19:51.649 PSC technology perhaps?  
NOTE Confidence: 0.86137027

01:19:51.650 --> 01:19:54.650 Diane sender at the Yelton can help push  
NOTE Confidence: 0.86137027

01:19:54.650 --> 01:19:56.863 this forward collaboratively because this  
NOTE Confidence: 0.86137027

01:19:56.863 --> 01:20:00.437 is just again at the very beginning, but.  
NOTE Confidence: 0.86137027

01:20:00.437 --> 01:20:02.519 But this is a place right?  
NOTE Confidence: 0.86137027

01:20:02.520 --> 01:20:04.760 I do see a very remarkable future.

NOTE Confidence: 0.8344973

01:20:06.600 --> 01:20:08.160 Thank you for making it.

NOTE Confidence: 0.8344973

01:20:08.160 --> 01:20:10.954 As a matter of fact, we we do have

NOTE Confidence: 0.8344973

01:20:10.954 --> 01:20:12.509 a large clinical Carty program.

NOTE Confidence: 0.8344973

01:20:12.510 --> 01:20:14.534 We've we've done a great deal of work

NOTE Confidence: 0.8344973

01:20:14.534 --> 01:20:16.858 with til cells actually actually sending.

NOTE Confidence: 0.8344973

01:20:16.860 --> 01:20:18.729 This sells out and infusing them here

NOTE Confidence: 0.8344973

01:20:18.729 --> 01:20:21.357 so we have a very well oiled machine

NOTE Confidence: 0.8344973

01:20:21.357 --> 01:20:22.769 for administering self therapy.

NOTE Confidence: 0.8344973

01:20:22.770 --> 01:20:24.474 We've also done some cell generation

NOTE Confidence: 0.8344973

01:20:24.474 --> 01:20:26.947 of our own and there's a huge amount

NOTE Confidence: 0.8344973

01:20:26.947 --> 01:20:28.855 of work in Immunobiology looking at

NOTE Confidence: 0.8344973

01:20:28.916 --> 01:20:30.824 targets within T cells that could

NOTE Confidence: 0.8344973

01:20:30.824 --> 01:20:32.640 be used as intellectual property

NOTE Confidence: 0.8344973

01:20:32.640 --> 01:20:34.800 for T cell Engineering.

NOTE Confidence: 0.8344973

01:20:34.800 --> 01:20:38.022 So there is a nascent program here in in.

NOTE Confidence: 0.8344973

01:20:38.030 --> 01:20:42.146 In some areas, in some well developed.

NOTE Confidence: 0.8344973

01:20:42.150 --> 01:20:43.944 Well developed in other areas and

NOTE Confidence: 0.8344973

01:20:43.944 --> 01:20:45.619 we are very interested in that.

NOTE Confidence: 0.85761327

01:20:46.190 --> 01:20:48.098 And I mean we only have

NOTE Confidence: 0.857613270000001

01:20:48.100 --> 01:20:49.960 about, I think 10 more minutes

NOTE Confidence: 0.857613270000001

01:20:49.960 --> 01:20:52.345 and I just want to spend a few

NOTE Confidence: 0.857613270000001

01:20:52.345 --> 01:20:54.773 minutes on an area that I think is

NOTE Confidence: 0.857613270000001

01:20:54.773 --> 01:20:56.993 a particular strength here at Dale,

NOTE Confidence: 0.857613270000001

01:20:57.000 --> 01:20:58.330 which is the animal modeling

NOTE Confidence: 0.857613270000001

01:20:58.330 --> 01:21:00.145 and how important it is towards

NOTE Confidence: 0.857613270000001

01:21:00.145 --> 01:21:01.447 Immunooncology and Marcus.

NOTE Confidence: 0.857613270000001

01:21:01.450 --> 01:21:03.042 And perhaps you might make

NOTE Confidence: 0.857613270000001

01:21:03.042 --> 01:21:03.996 some comments again,

NOTE Confidence: 0.857613270000001

01:21:03.996 --> 01:21:05.268 because you just mentioned

NOTE Confidence: 0.857613270000001

01:21:05.268 --> 01:21:06.540 some of the resource,

NOTE Confidence: 0.857613270000001

01:21:06.540 --> 01:21:08.829 but there's a huge number of resources

NOTE Confidence: 0.857613270000001

01:21:08.829 --> 01:21:10.990 related to animal modeling and how it

NOTE Confidence: 0.85761327

01:21:10.990 --> 01:21:12.580 fits in with with testing.

NOTE Confidence: 0.85761327

01:21:12.580 --> 01:21:15.226 Well, this has been a tough crowd

NOTE Confidence: 0.85761327

01:21:15.226 --> 01:21:16.970 for traditional animal model I.

NOTE Confidence: 0.85761327

01:21:16.970 --> 01:21:19.714 No IRA's point of view and respected

NOTE Confidence: 0.85761327

01:21:19.714 --> 01:21:21.842 an remember seeing him at the

NOTE Confidence: 0.85761327

01:21:21.842 --> 01:21:23.886 back of a city workshop that I

NOTE Confidence: 0.85761327

01:21:23.963 --> 01:21:26.459 organized on animal modeling in IO.

NOTE Confidence: 0.85761327

01:21:26.460 --> 01:21:28.931 I view that as a compliment even

NOTE Confidence: 0.85761327

01:21:28.931 --> 01:21:31.568 if it wasn't intended to be one.

NOTE Confidence: 0.85761327

01:21:31.570 --> 01:21:34.034 But what I would say is our lab

NOTE Confidence: 0.85761327

01:21:34.034 --> 01:21:36.194 has developed a number of immuno

NOTE Confidence: 0.85761327

01:21:36.194 --> 01:21:38.039 genic syngeneic lines that are

NOTE Confidence: 0.85761327

01:21:38.039 --> 01:21:40.330 used widely including by Pharma.

NOTE Confidence: 0.85761327

01:21:40.330 --> 01:21:42.160 These Yale University mouse, Melanoma,

NOTE Confidence: 0.85761327

01:21:42.160 --> 01:21:44.330 Yum and Yum are lines that enable  
NOTE Confidence: 0.85761327

01:21:44.330 --> 01:21:46.979 people to see responses to checkpoints.  
NOTE Confidence: 0.85761327

01:21:46.980 --> 01:21:49.124 And sort of tune your system so you  
NOTE Confidence: 0.85761327

01:21:49.124 --> 01:21:51.322 can see either additive or synergistic  
NOTE Confidence: 0.85761327

01:21:51.322 --> 01:21:53.716 effects by adding a second agent.  
NOTE Confidence: 0.85761327

01:21:53.720 --> 01:21:55.350 Obviously that's harder to tell  
NOTE Confidence: 0.85761327

01:21:55.350 --> 01:21:57.430 whether that will happen in humans,  
NOTE Confidence: 0.85761327

01:21:57.430 --> 01:21:59.446 in which humans that will happen.  
NOTE Confidence: 0.85761327

01:21:59.450 --> 01:22:01.480 But to get some kind of enthusiasm  
NOTE Confidence: 0.85761327

01:22:01.480 --> 01:22:03.564 or not for your agent certainly  
NOTE Confidence: 0.85761327

01:22:03.564 --> 01:22:05.844 has been used on those purposes.  
NOTE Confidence: 0.85761327

01:22:05.850 --> 01:22:07.691 One of the things I'd like to  
NOTE Confidence: 0.85761327

01:22:07.691 --> 01:22:10.162 focus on is there's a recent nature  
NOTE Confidence: 0.85761327

01:22:10.162 --> 01:22:12.586 biotechnology paper by Nick Joshis lab,  
NOTE Confidence: 0.85761327

01:22:12.590 --> 01:22:14.613 so Joshi and it uses a very  
NOTE Confidence: 0.85761327

01:22:14.613 --> 01:22:16.639 controlled way of antigen delivery.

NOTE Confidence: 0.85761327  
01:22:16.640 --> 01:22:18.470 Digital model antigens from LCMV.  
NOTE Confidence: 0.85761327  
01:22:18.470 --> 01:22:20.438 Both class one and Class 2,  
NOTE Confidence: 0.85761327  
01:22:20.440 --> 01:22:22.525 but it allows for modeling of  
NOTE Confidence: 0.85761327  
01:22:22.525 --> 01:22:24.350 immune related adverse events in  
NOTE Confidence: 0.85761327  
01:22:24.350 --> 01:22:26.324 ways that we haven't really been  
NOTE Confidence: 0.85761327  
01:22:26.324 --> 01:22:28.670 able to do to this point in time,  
NOTE Confidence: 0.85761327  
01:22:28.670 --> 01:22:30.966 so you can specifically turn antigens on,  
NOTE Confidence: 0.85761327  
01:22:30.970 --> 01:22:33.133 either in the context of a cancer  
NOTE Confidence: 0.85761327  
01:22:33.133 --> 01:22:34.920 elsewhere or even without that,  
NOTE Confidence: 0.85761327  
01:22:34.920 --> 01:22:36.560 and look at immune checkpoint  
NOTE Confidence: 0.85761327  
01:22:36.560 --> 01:22:37.216 inhibitor induced.  
NOTE Confidence: 0.81051123  
01:22:39.420 --> 01:22:41.737 IR A's that I think that has  
NOTE Confidence: 0.81051123  
01:22:41.737 --> 01:22:44.348 been a big lack in this area.  
NOTE Confidence: 0.81051123  
01:22:44.350 --> 01:22:46.110 There was recently an NCI  
NOTE Confidence: 0.81051123  
01:22:46.110 --> 01:22:47.518 meeting related to that.  
NOTE Confidence: 0.81051123



01:22:47.520 --> 01:22:50.124 Also sort of suggesting the same Katie  
NOTE Confidence: 0.81051123

01:22:50.124 --> 01:22:52.753 Palitti who was had been at yell out  
NOTE Confidence: 0.81051123

01:22:52.753 --> 01:22:55.431 for about 10 years as well as very  
NOTE Confidence: 0.81051123

01:22:55.431 --> 01:22:57.366 active and lung cancer modeling.  
NOTE Confidence: 0.81051123

01:22:57.370 --> 01:23:00.538 So I do agree that we have great strengths.  
NOTE Confidence: 0.81051123

01:23:00.540 --> 01:23:02.652 Yeah I would again for this  
NOTE Confidence: 0.81051123

01:23:02.652 --> 01:23:04.060 particular group as well.  
NOTE Confidence: 0.81051123

01:23:04.060 --> 01:23:06.216 As for I think these other groups  
NOTE Confidence: 0.81051123

01:23:06.216 --> 01:23:08.108 that are developing these patients  
NOTE Confidence: 0.81051123

01:23:08.108 --> 01:23:09.928 arrive explant models including.  
NOTE Confidence: 0.81051123

01:23:09.930 --> 01:23:11.735 The National Cancer Institute in  
NOTE Confidence: 0.81051123

01:23:11.735 --> 01:23:13.899 Amsterdam and Daniella Talmon and Tom  
NOTE Confidence: 0.81051123

01:23:13.899 --> 01:23:15.675 Schumacher the big challenge in this  
NOTE Confidence: 0.81051123

01:23:15.675 --> 01:23:17.879 area has been A to keep things alive,  
NOTE Confidence: 0.81051123

01:23:17.880 --> 01:23:20.416 and I've mentioned that we can do that.  
NOTE Confidence: 0.81051123

01:23:20.420 --> 01:23:22.611 But also what the readouts are that

NOTE Confidence: 0.81051123

01:23:22.611 --> 01:23:24.559 correspond to responses in human patients.

NOTE Confidence: 0.81051123

01:23:24.560 --> 01:23:26.646 I think there's all sorts of biology

NOTE Confidence: 0.81051123

01:23:26.646 --> 01:23:28.690 you can do in those systems,

NOTE Confidence: 0.81051123

01:23:28.690 --> 01:23:30.598 but there's obviously a lot of

NOTE Confidence: 0.81051123

01:23:30.598 --> 01:23:31.870 interest in personalized therapy.

NOTE Confidence: 0.81051123

01:23:31.870 --> 01:23:33.778 To see how those responses are,

NOTE Confidence: 0.81051123

01:23:33.780 --> 01:23:35.370 and they haven't published yet,

NOTE Confidence: 0.81051123

01:23:35.370 --> 01:23:38.223 it will be interesting to see when people do.

NOTE Confidence: 0.81051123

01:23:38.230 --> 01:23:40.894 Right now, it seems to be elicited cytokines.

NOTE Confidence: 0.81051123

01:23:40.900 --> 01:23:42.420 Of certain profiles that seem

NOTE Confidence: 0.81051123

01:23:42.420 --> 01:23:43.948 to be the best answer,

NOTE Confidence: 0.81051123

01:23:43.948 --> 01:23:45.784 but I think there's more work

NOTE Confidence: 0.81051123

01:23:45.784 --> 01:23:47.588 to be done on those areas,

NOTE Confidence: 0.81051123

01:23:47.590 --> 01:23:48.622 but I would agree,

NOTE Confidence: 0.81051123

01:23:48.622 --> 01:23:50.170 and the other thing that Yale

NOTE Confidence: 0.81051123

01:23:50.232 --> 01:23:52.314 has an advantage is for these  
NOTE Confidence: 0.81051123

01:23:52.314 --> 01:23:53.355 different syngenetic models.  
NOTE Confidence: 0.81051123

01:23:53.360 --> 01:23:54.880 We've developed many crisper derived  
NOTE Confidence: 0.81051123

01:23:54.880 --> 01:23:56.710 genetic mutants like beta two microglia  
NOTE Confidence: 0.81051123

01:23:56.710 --> 01:23:58.790 knockout so forth that make it easy  
NOTE Confidence: 0.81051123

01:23:58.790 --> 01:24:00.941 for Pharma to come in and just  
NOTE Confidence: 0.81051123

01:24:00.941 --> 01:24:03.397 establish an SRA to look at class one.  
NOTE Confidence: 0.81051123

01:24:03.400 --> 01:24:05.388 Deficient models of a variety of types  
NOTE Confidence: 0.81051123

01:24:05.388 --> 01:24:07.650 that can be responsive to mu agent,  
NOTE Confidence: 0.81051123

01:24:07.650 --> 01:24:09.940 so it's kind of a broader swath of  
NOTE Confidence: 0.81051123

01:24:09.940 --> 01:24:11.949 and that's all centered really through  
NOTE Confidence: 0.81051123

01:24:11.949 --> 01:24:14.029 the center precision cancer modeling.  
NOTE Confidence: 0.81051123

01:24:14.030 --> 01:24:15.526 Nearly all of that except for next stuff.  
NOTE Confidence: 0.8158064

01:24:16.150 --> 01:24:18.322 Could you just mention briefly the  
NOTE Confidence: 0.8158064

01:24:18.322 --> 01:24:20.369 humanized mouse models and with what  
NOTE Confidence: 0.8158064

01:24:20.370 --> 01:24:23.114 they will might be, so that was a

NOTE Confidence: 0.8158064

01:24:23.114 --> 01:24:25.297 fairly large mistake on my part.

NOTE Confidence: 0.8158064

01:24:25.300 --> 01:24:27.406 So Richard Flavelle is probably developed.

NOTE Confidence: 0.8158064

01:24:27.410 --> 01:24:29.930 You know, the I would argue amongst the

NOTE Confidence: 0.8158064

01:24:29.930 --> 01:24:31.990 most advanced humanized mouse models.

NOTE Confidence: 0.8158064

01:24:31.990 --> 01:24:34.742 These so called Mr G mice which have

NOTE Confidence: 0.8158064

01:24:34.742 --> 01:24:38.029 not kins of human cytokines for various

NOTE Confidence: 0.8158064

01:24:38.029 --> 01:24:40.940 cytokines that are really important for.

NOTE Confidence: 0.8158064

01:24:40.940 --> 01:24:42.650 Full development and re engraftment

NOTE Confidence: 0.8158064

01:24:42.650 --> 01:24:44.018 of different components of

NOTE Confidence: 0.8158064

01:24:44.018 --> 01:24:45.449 the hematopoietic system,

NOTE Confidence: 0.8158064

01:24:45.450 --> 01:24:48.834 and I think the real strength with the Mr.

NOTE Confidence: 0.8158064

01:24:48.840 --> 01:24:51.624 G model is that it in graphs various

NOTE Confidence: 0.8158064

01:24:51.624 --> 01:24:53.716 components of the myeloid derivatives

NOTE Confidence: 0.8158064

01:24:53.716 --> 01:24:56.350 much better than most other models

NOTE Confidence: 0.8158064

01:24:56.350 --> 01:24:58.605 have up to this point in time.

NOTE Confidence: 0.8158064

01:24:58.610 --> 01:25:00.866 So there's two papers of note  
NOTE Confidence: 0.8158064

01:25:00.866 --> 01:25:01.994 related to that,  
NOTE Confidence: 0.8158064

01:25:02.000 --> 01:25:04.709 so one is related to modeling multiple  
NOTE Confidence: 0.8158064

01:25:04.709 --> 01:25:06.510 human multiple myeloma and mice,  
NOTE Confidence: 0.8158064

01:25:06.510 --> 01:25:08.880 which was done with MoD adopt  
NOTE Confidence: 0.8158064

01:25:08.880 --> 01:25:10.950 carp a couple years back.  
NOTE Confidence: 0.8158064

01:25:10.950 --> 01:25:13.180 And they would Stephanie Hellena  
NOTE Confidence: 0.8158064

01:25:13.180 --> 01:25:14.964 they've modeled MD's AML,  
NOTE Confidence: 0.8158064

01:25:14.970 --> 01:25:16.506 engraftment into these models.  
NOTE Confidence: 0.8158064

01:25:16.506 --> 01:25:19.256 The difficulty with a lot of these  
NOTE Confidence: 0.8158064

01:25:19.256 --> 01:25:21.518 models has been that to actually  
NOTE Confidence: 0.8158064

01:25:21.518 --> 01:25:23.569 test whether agents work on them,  
NOTE Confidence: 0.8158064

01:25:23.570 --> 01:25:24.440 they've been very,  
NOTE Confidence: 0.8158064

01:25:24.440 --> 01:25:27.149 very good to show that you can re in  
NOTE Confidence: 0.8158064

01:25:27.149 --> 01:25:28.997 Grafton get these different things to  
NOTE Confidence: 0.8158064

01:25:28.997 --> 01:25:31.358 work and you can look at additional

NOTE Confidence: 0.8158064

01:25:31.358 --> 01:25:33.734 genetic changes that happen in those models,

NOTE Confidence: 0.8158064

01:25:33.734 --> 01:25:35.444 but the remaining challenges to

NOTE Confidence: 0.8158064

01:25:35.444 --> 01:25:37.479 use these to then say how is,

NOTE Confidence: 0.8158064

01:25:37.480 --> 01:25:39.762 say an immune checkpoint or a new

NOTE Confidence: 0.8158064

01:25:39.762 --> 01:25:41.905 therapy going to help in that context.

NOTE Confidence: 0.8158064

01:25:41.905 --> 01:25:43.849 But the other issue until more

NOTE Confidence: 0.8158064

01:25:43.849 --> 01:25:45.847 recently was that Regenerx on had

NOTE Confidence: 0.8158064

01:25:45.847 --> 01:25:47.129 participated in the generation

NOTE Confidence: 0.8158064

01:25:47.129 --> 01:25:48.614 of those models which made.

NOTE Confidence: 0.8158064

01:25:48.620 --> 01:25:50.876 A little bit complex to work with other

NOTE Confidence: 0.8158064

01:25:50.876 --> 01:25:52.830 companies and outside of Richard's lab,

NOTE Confidence: 0.8158064

01:25:52.830 --> 01:25:54.636 but I think that's at least

NOTE Confidence: 0.8158064

01:25:54.636 --> 01:25:55.539 possibly being solved,

NOTE Confidence: 0.8158064

01:25:55.540 --> 01:25:57.346 and I wouldn't view that as

NOTE Confidence: 0.8158064

01:25:57.346 --> 01:25:58.249 an impediment now.

NOTE Confidence: 0.8670489

01:26:00.550 --> 01:26:03.166 OK, I'm going to ask one more question.

NOTE Confidence: 0.8670489

01:26:03.170 --> 01:26:05.852 I don't see a whole lot of the questions

NOTE Confidence: 0.8670489

01:26:05.852 --> 01:26:08.344 from the chat before I turn it back

NOTE Confidence: 0.8670489

01:26:08.344 --> 01:26:10.718 over to Charlie for closing comments.

NOTE Confidence: 0.8670489

01:26:10.720 --> 01:26:11.650 One challenging question,

NOTE Confidence: 0.8670489

01:26:11.650 --> 01:26:13.820 you know every day I read a

NOTE Confidence: 0.8670489

01:26:13.886 --> 01:26:15.944 new paper about another T cell

NOTE Confidence: 0.8670489

01:26:15.944 --> 01:26:17.610 checkpoint inhibitor and you know,

NOTE Confidence: 0.8670489

01:26:17.610 --> 01:26:19.566 I I probably can't count on,

NOTE Confidence: 0.8670489

01:26:19.570 --> 01:26:22.194 you know 100 hands and fingers and toes.

NOTE Confidence: 0.8670489

01:26:22.200 --> 01:26:24.090 How many things actually block T cell

NOTE Confidence: 0.8670489

01:26:24.090 --> 01:26:26.130 function in the tumor microenvironment?

NOTE Confidence: 0.8670489

01:26:26.130 --> 01:26:26.738 Or peripherally,

NOTE Confidence: 0.8670489

01:26:26.738 --> 01:26:28.866 how does one know which those are

NOTE Confidence: 0.8670489

01:26:28.866 --> 01:26:30.980 the critical non redundant targets?

NOTE Confidence: 0.8670489

01:26:30.980 --> 01:26:31.980 For therapy.

NOTE Confidence: 0.83682704

01:26:38.990 --> 01:26:40.220 How do you

NOTE Confidence: 0.85308512

01:26:40.220 --> 01:26:42.586 know well? I mean, I just have

NOTE Confidence: 0.85308512

01:26:42.586 --> 01:26:44.898 how OK I'll give you a hug.

NOTE Confidence: 0.85308512

01:26:44.900 --> 01:26:45.725 You approach it.

NOTE Confidence: 0.85308512

01:26:45.725 --> 01:26:47.100 How do you approach it?

NOTE Confidence: 0.85308512

01:26:47.100 --> 01:26:48.750 Because I you know. I mean,

NOTE Confidence: 0.85308512

01:26:48.750 --> 01:26:51.500 I can list 15 in the back of my head.

NOTE Confidence: 0.85308512

01:26:51.500 --> 01:26:53.700 I don't know how to decide is it.

NOTE Confidence: 0.85308512

01:26:53.700 --> 01:26:55.625 Is it true that they're all important?

NOTE Confidence: 0.85308512

01:26:55.630 --> 01:26:57.000 It's just an individual patients?

NOTE Confidence: 0.85308512

01:26:57.000 --> 01:26:58.778 Or are they are some of them

NOTE Confidence: 0.85308512

01:26:58.778 --> 01:27:00.579 redundant or in the same pathway?

NOTE Confidence: 0.85308512

01:27:00.580 --> 01:27:02.092 Or is biology not important that

NOTE Confidence: 0.85308512

01:27:02.092 --> 01:27:03.901 some of this biology is just not

NOTE Confidence: 0.85308512

01:27:03.901 --> 01:27:05.389 important in cancer but may be

NOTE Confidence: 0.85308512



01:27:05.389 --> 01:27:06.959 important in other settings like  
NOTE Confidence: 0.85308512

01:27:06.959 --> 01:27:08.549 infectious disease or something else?  
NOTE Confidence: 0.3591845

01:27:10.300 --> 01:27:13.991 I'm. I mean, how do you know is  
NOTE Confidence: 0.3591845

01:27:13.991 --> 01:27:16.834 I think it's all tide up with the  
NOTE Confidence: 0.3591845

01:27:16.834 --> 01:27:19.400 beginning theme of this whole meeting,  
NOTE Confidence: 0.3591845

01:27:19.400 --> 01:27:22.418 which is you have to understand  
NOTE Confidence: 0.3591845

01:27:22.418 --> 01:27:25.439 mechanism and understand the science so.  
NOTE Confidence: 0.3591845

01:27:25.440 --> 01:27:27.010 Back and how long ago.  
NOTE Confidence: 0.3591845

01:27:27.010 --> 01:27:28.894 10 years ago when these things  
NOTE Confidence: 0.3591845

01:27:28.894 --> 01:27:30.460 were first being laid out.  
NOTE Confidence: 0.3591845

01:27:30.460 --> 01:27:31.816 I remember you know,  
NOTE Confidence: 0.3591845

01:27:31.816 --> 01:27:33.511 constructing a diagram with the  
NOTE Confidence: 0.3591845

01:27:33.511 --> 01:27:34.821 negative and positive regulators  
NOTE Confidence: 0.3591845

01:27:34.821 --> 01:27:36.956 that were known at the time and  
NOTE Confidence: 0.3591845

01:27:37.018 --> 01:27:38.626 which one should we look out,  
NOTE Confidence: 0.3591845

01:27:38.630 --> 01:27:42.158 which was which one should we look at?

NOTE Confidence: 0.3591845

01:27:42.160 --> 01:27:45.184 And I think a lot of investigators and

NOTE Confidence: 0.3591845

01:27:45.184 --> 01:27:48.132 companies went off just to look at them

NOTE Confidence: 0.3591845

01:27:48.132 --> 01:27:50.137 all without really understanding what

NOTE Confidence: 0.3591845

01:27:50.137 --> 01:27:52.119 the relative contributions of them were.

NOTE Confidence: 0.3591845

01:27:52.120 --> 01:27:55.432 We decided to look at one which was tigt.

NOTE Confidence: 0.3591845

01:27:55.440 --> 01:27:56.436 And you know,

NOTE Confidence: 0.3591845

01:27:56.436 --> 01:27:58.760 that emerged as a consequence of perhaps

NOTE Confidence: 0.3591845

01:27:58.826 --> 01:28:00.976 we're deluding ourselves into this,

NOTE Confidence: 0.3591845

01:28:00.980 --> 01:28:03.620 but that emerged as a consequence

NOTE Confidence: 0.3591845

01:28:03.620 --> 01:28:05.380 of increased understanding as

NOTE Confidence: 0.3591845

01:28:05.453 --> 01:28:07.613 to how it is that PD one works.

NOTE Confidence: 0.3591845

01:28:07.620 --> 01:28:09.654 So if the current hypothesis is

NOTE Confidence: 0.3591845

01:28:09.654 --> 01:28:11.787 that PD one blockade causes an

NOTE Confidence: 0.3591845

01:28:11.787 --> 01:28:14.251 increase in the number of this self

NOTE Confidence: 0.3591845

01:28:14.251 --> 01:28:16.180 renewing stem light compartment.

NOTE Confidence: 0.3591845

01:28:16.180 --> 01:28:19.420 That generates effector T cells.  
NOTE Confidence: 0.3591845

01:28:19.420 --> 01:28:23.910 Then what else is there?  
NOTE Confidence: 0.3591845

01:28:23.910 --> 01:28:26.690 If you're trying to add to that and forget  
NOTE Confidence: 0.3591845

01:28:26.690 --> 01:28:29.008 about the reversal of exhaustion business,  
NOTE Confidence: 0.3591845

01:28:29.010 --> 01:28:30.002 if you do that,  
NOTE Confidence: 0.3591845

01:28:30.002 --> 01:28:31.978 it turns out that the only other  
NOTE Confidence: 0.3591845

01:28:31.978 --> 01:28:33.678 negative regulator that's expressed  
NOTE Confidence: 0.3591845

01:28:33.678 --> 01:28:35.803 on the SCM compartment engine,  
NOTE Confidence: 0.3591845

01:28:35.810 --> 01:28:38.420 and so if that and it also turns out  
NOTE Confidence: 0.3591845

01:28:38.420 --> 01:28:40.910 that we haven't published this yet,  
NOTE Confidence: 0.3591845

01:28:40.910 --> 01:28:43.325 that PD one is actually  
NOTE Confidence: 0.3591845

01:28:43.325 --> 01:28:45.257 what regulates CD 226.  
NOTE Confidence: 0.3591845

01:28:45.260 --> 01:28:48.305 Enzymatically and tigit with a regular C226.  
NOTE Confidence: 0.3591845

01:28:48.310 --> 01:28:50.920 Only by competing for like end.  
NOTE Confidence: 0.3591845

01:28:50.920 --> 01:28:53.530 OK so that means that there's  
NOTE Confidence: 0.3591845

01:28:53.530 --> 01:28:55.270 a close Functional Association.

NOTE Confidence: 0.3591845

01:28:55.270 --> 01:28:58.310 And so if you want to enhance

NOTE Confidence: 0.3591845

01:28:58.310 --> 01:29:00.710 the function then you have to

NOTE Confidence: 0.3591845

01:29:00.710 --> 01:29:03.529 go after both of those things.

NOTE Confidence: 0.3591845

01:29:03.530 --> 01:29:06.143 Assuming you correct with respect to

NOTE Confidence: 0.3591845

01:29:06.143 --> 01:29:08.926 understanding what is the target cell

NOTE Confidence: 0.3591845

01:29:08.926 --> 01:29:12.350 type that that that you're dealing with.

NOTE Confidence: 0.3591845

01:29:12.350 --> 01:29:14.126 No interesting if you look

NOTE Confidence: 0.3591845

01:29:14.126 --> 01:29:15.774 at the exhausted cells.

NOTE Confidence: 0.3591845

01:29:15.780 --> 01:29:17.976 There's lots of digit on them,

NOTE Confidence: 0.3591845

01:29:17.980 --> 01:29:19.820 but there's no CD 226,

NOTE Confidence: 0.3591845

01:29:19.820 --> 01:29:22.021 so unless you know there's another

NOTE Confidence: 0.3591845

01:29:22.021 --> 01:29:24.590 element of the mechanism that we missing,

NOTE Confidence: 0.3591845

01:29:24.590 --> 01:29:27.810 which is entirely possible.

NOTE Confidence: 0.3591845

01:29:27.810 --> 01:29:31.758 Blockade in exhaust itself can't be

NOTE Confidence: 0.3591845

01:29:31.758 --> 01:29:35.240 expected to reactivate its client.

NOTE Confidence: 0.3591845

01:29:35.240 --> 01:29:36.692 A positive rate costimulatory  
NOTE Confidence: 0.3591845

01:29:36.692 --> 01:29:38.144 molecule that's a costimulatory  
NOTE Confidence: 0.3591845

01:29:38.150 --> 01:29:40.670 molecule isn't even there.  
NOTE Confidence: 0.3591845

01:29:40.670 --> 01:29:42.784 So you know those types of considerations.  
NOTE Confidence: 0.3591845

01:29:42.790 --> 01:29:44.464 I think you know one really  
NOTE Confidence: 0.3591845

01:29:44.464 --> 01:29:46.120 needs to think them through,  
NOTE Confidence: 0.3591845

01:29:46.120 --> 01:29:48.248 not just believe what's in the literature,  
NOTE Confidence: 0.3591845

01:29:48.250 --> 01:29:50.056 but set up your own systems,  
NOTE Confidence: 0.3591845

01:29:50.060 --> 01:29:51.878 often in mice to figure out.  
NOTE Confidence: 0.3591845

01:29:51.880 --> 01:29:52.789 And in fact,  
NOTE Confidence: 0.3591845

01:29:52.789 --> 01:29:55.340 if if your hypothesis holds any water.  
NOTE Confidence: 0.3591845

01:29:55.340 --> 01:29:57.264 'cause these are big decisions you make  
NOTE Confidence: 0.3591845

01:29:57.264 --> 01:29:58.920 you enter into a development program.  
NOTE Confidence: 0.3591845

01:29:58.920 --> 01:30:00.698 Whether you doing it in an academ.  
NOTE Confidence: 0.3591845

01:30:00.700 --> 01:30:03.260 Lab or industrial lab.  
NOTE Confidence: 0.3591845

01:30:03.260 --> 01:30:05.484 You know it takes 2 years at least

NOTE Confidence: 0.3591845

01:30:05.484 --> 01:30:07.497 to select the best antibody and then

NOTE Confidence: 0.3591845

01:30:07.497 --> 01:30:09.839 to grow it up and then you know,

NOTE Confidence: 0.3591845

01:30:09.840 --> 01:30:11.550 put it in patients you're out.

NOTE Confidence: 0.3591845

01:30:11.550 --> 01:30:12.086 You know,

NOTE Confidence: 0.3591845

01:30:12.086 --> 01:30:13.694 with a huge investment of money

NOTE Confidence: 0.3591845

01:30:13.694 --> 01:30:15.791 and time at least five years before

NOTE Confidence: 0.3591845

01:30:15.791 --> 01:30:16.694 you know anything.

NOTE Confidence: 0.85898066

01:30:17.930 --> 01:30:19.225 Yeah, we're actually gonna validating

NOTE Confidence: 0.85898066

01:30:19.225 --> 01:30:20.965 some of those targets with some of

NOTE Confidence: 0.85898066

01:30:20.965 --> 01:30:22.177 the resources that we have here.

NOTE Confidence: 0.85898066

01:30:22.180 --> 01:30:22.885 Thank you. Alright,

NOTE Confidence: 0.85898066

01:30:22.885 --> 01:30:24.295 it's always been a vexing question.

NOTE Confidence: 0.85898066

01:30:24.300 --> 01:30:26.188 I could talk to you all all day.

NOTE Confidence: 0.85898066

01:30:26.190 --> 01:30:27.835 Actually, it's my favorite thing to do,

NOTE Confidence: 0.85898066

01:30:27.840 --> 01:30:29.233 but I think at this point I

NOTE Confidence: 0.85898066

01:30:29.233 --> 01:30:30.969 want to turn it over back over  
NOTE Confidence: 0.85898066

01:30:30.969 --> 01:30:32.324 to Charlie for closing remarks,  
NOTE Confidence: 0.85898066

01:30:32.330 --> 01:30:34.185 and I want to thank all the  
NOTE Confidence: 0.85898066

01:30:34.185 --> 01:30:35.870 participants for all their comments.  
NOTE Confidence: 0.85898066

01:30:35.870 --> 01:30:37.028 Charlie, please go  
NOTE Confidence: 0.84907657

01:30:37.030 --> 01:30:39.702 ahead. Thank you and I just want to  
NOTE Confidence: 0.84907657

01:30:39.702 --> 01:30:42.757 thank all of our panelists for superb  
NOTE Confidence: 0.84907657

01:30:42.757 --> 01:30:45.478 discussion and obviously think IRA for  
NOTE Confidence: 0.84907657

01:30:45.478 --> 01:30:48.182 taking the time out to join us today.  
NOTE Confidence: 0.84907657

01:30:48.190 --> 01:30:50.120 You know, as you've heard,  
NOTE Confidence: 0.84907657

01:30:50.120 --> 01:30:51.656 we've had great advances,  
NOTE Confidence: 0.84907657

01:30:51.656 --> 01:30:53.576 probably unprecedented advances in io,  
NOTE Confidence: 0.84907657

01:30:53.580 --> 01:30:56.010 but clearly the next generation is  
NOTE Confidence: 0.84907657

01:30:56.010 --> 01:30:58.401 going to require innovation at a  
NOTE Confidence: 0.84907657

01:30:58.401 --> 01:31:00.507 level that builds on terrific science.  
NOTE Confidence: 0.84907657

01:31:00.510 --> 01:31:02.820 Outstanding science moves into the clinic,

NOTE Confidence: 0.84907657

01:31:02.820 --> 01:31:05.884 and I'm I'm so proud of the fact

NOTE Confidence: 0.84907657

01:31:05.884 --> 01:31:08.158 that everyone of our panelists.

NOTE Confidence: 0.84907657

01:31:08.160 --> 01:31:10.602 Is innovating in that space and

NOTE Confidence: 0.84907657

01:31:10.602 --> 01:31:13.042 many others who we said they

NOTE Confidence: 0.84907657

01:31:13.042 --> 01:31:15.078 couldn't include in the forum.

NOTE Confidence: 0.84907657

01:31:15.078 --> 01:31:18.340 In fact 1.0. I'll mention a city Chen,

NOTE Confidence: 0.84907657

01:31:18.340 --> 01:31:20.776 one of our leading investigators who

NOTE Confidence: 0.84907657

01:31:20.780 --> 01:31:22.406 company being launched tomorrow,

NOTE Confidence: 0.84907657

01:31:22.406 --> 01:31:23.624 evolve immune therapeutics.

NOTE Confidence: 0.84907657

01:31:23.624 --> 01:31:26.480 Looking at the T cell targeting space.

NOTE Confidence: 0.84907657

01:31:26.480 --> 01:31:29.231 Just one of the many things that

NOTE Confidence: 0.84907657

01:31:29.231 --> 01:31:31.360 are our investigators are leading.

NOTE Confidence: 0.84907657

01:31:31.360 --> 01:31:32.084 You know,

NOTE Confidence: 0.84907657

01:31:32.084 --> 01:31:34.618 I want to thank all the attendees

NOTE Confidence: 0.84907657

01:31:34.618 --> 01:31:37.216 for joining us today and again

NOTE Confidence: 0.84907657



01:31:37.216 --> 01:31:39.932 want to emphasize this should be  
NOTE Confidence: 0.84907657

01:31:39.932 --> 01:31:42.307 the beginning of the conversation.  
NOTE Confidence: 0.84907657

01:31:42.310 --> 01:31:44.210 Please reach out to us.  
NOTE Confidence: 0.84907657

01:31:44.210 --> 01:31:46.826 We will be following up with you because  
NOTE Confidence: 0.84907657

01:31:46.826 --> 01:31:49.528 we want to build more collaborations,  
NOTE Confidence: 0.84907657

01:31:49.530 --> 01:31:50.470 more conversations.  
NOTE Confidence: 0.84907657

01:31:50.470 --> 01:31:53.760 And finally want to thank Kathy Lynch  
NOTE Confidence: 0.84907657

01:31:53.760 --> 01:31:56.621 and her team for organizing this and  
NOTE Confidence: 0.84907657

01:31:56.621 --> 01:31:59.467 remind all of you that we actually  
NOTE Confidence: 0.84907657

01:31:59.467 --> 01:32:02.323 have two more forms of cancer engage  
NOTE Confidence: 0.84907657

01:32:02.330 --> 01:32:04.736 on November 5th or novel cancer  
NOTE Confidence: 0.84907657

01:32:04.736 --> 01:32:06.340 therapeutics and delivery system.  
NOTE Confidence: 0.84907657

01:32:06.340 --> 01:32:08.340 And then on December 9th,  
NOTE Confidence: 0.84907657

01:32:08.340 --> 01:32:09.916 defining mechanisms and biomarkers  
NOTE Confidence: 0.84907657

01:32:09.916 --> 01:32:11.886 of sensitivity and resistance to  
NOTE Confidence: 0.84907657

01:32:11.886 --> 01:32:13.559 answer Anti cancer treatments.

NOTE Confidence: 0.84907657

01:32:13.560 --> 01:32:16.220 So really key topics beyond IO that

NOTE Confidence: 0.84907657

01:32:16.220 --> 01:32:17.970 our investigators are leading.

NOTE Confidence: 0.84907657

01:32:17.970 --> 01:32:20.370 So again thank all of you.

NOTE Confidence: 0.84907657

01:32:20.370 --> 01:32:22.776 Mario, thank you for your leadership.

NOTE Confidence: 0.84907657

01:32:22.780 --> 01:32:24.380 Any final. Large meal.

NOTE Confidence: 0.8735408

01:32:25.290 --> 01:32:27.236 No, I want to thank you Charlie.

NOTE Confidence: 0.8735408

01:32:27.240 --> 01:32:28.640 Thanks to all the panelists,

NOTE Confidence: 0.8735408

01:32:28.640 --> 01:32:30.312 all the people who participated today.

NOTE Confidence: 0.8735408

01:32:30.312 --> 01:32:31.146 Please contact us.

NOTE Confidence: 0.8735408

01:32:31.146 --> 01:32:32.536 We are very interested in

NOTE Confidence: 0.8735408

01:32:32.536 --> 01:32:33.092 developing collaborations.

NOTE Confidence: 0.8735408

01:32:33.100 --> 01:32:35.324 We have an enormous wealth of talent here.

NOTE Confidence: 0.8735408

01:32:35.330 --> 01:32:36.450 Hope will be working

NOTE Confidence: 0.8735408

01:32:36.450 --> 01:32:37.850 with you in the future.

NOTE Confidence: 0.8735408

01:32:37.850 --> 01:32:38.678 Thank you again.