WEBVTT

NOTE duration:"00:30:49.5570000"

NOTE language:en-us

NOTE Confidence: 0.885055780410767

00:00:00.000 --> 00:00:03.108 Both in cancer and and obviously

NOTE Confidence: 0.885055780410767

00:00:03.108 --> 00:00:05.980 immunology and response to viruses.

NOTE Confidence: 0.885055780410767

00:00:05.980 --> 00:00:08.724 And we'll start with our first speaker,

NOTE Confidence: 0.885055780410767

00:00:08.730 --> 00:00:09.909 doctor lash boost.

NOTE Confidence: 0.885055780410767

00:00:09.909 --> 00:00:11.908 I allows is, you know,

NOTE Confidence: 0.885055780410767

00:00:11.908 --> 00:00:14.362 is a professor of Medicine at

NOTE Confidence: 0.885055780410767

00:00:14.362 --> 00:00:16.977 the school of Madison at the US.

NOTE Confidence: 0.885055780410767

00:00:16.980 --> 00:00:18.162 Will Medison Co.

NOTE Confidence: 0.885055780410767

00:00:18.162 --> 00:00:19.738 Leader of the genetics,

NOTE Confidence: 0.885055780410767

00:00:19.740 --> 00:00:21.970 genomics and epigenetics research program

NOTE Confidence: 0.885055780410767

00:00:21.970 --> 00:00:24.200 and director of Translational research

NOTE Confidence: 0.885055780410767

00:00:24.262 --> 00:00:26.439 for breast cancer in our Cancer Center.

NOTE Confidence: 0.885055780410767

00:00:26.440 --> 00:00:28.885 Having received his medical degree

NOTE Confidence: 0.885055780410767

00:00:28.885 --> 00:00:31.330 in Budapest and his subsequent

NOTE Confidence: 0.885055780410767

00:00:31.408 --> 00:00:33.853 doctorate at the University of

NOTE Confidence: 0.885055780410767

00:00:33.853 --> 00:00:36.298 Oxford blouse is really committed.

NOTE Confidence: 0.885055780410767

00:00:36.300 --> 00:00:38.994 His career to really understanding the

NOTE Confidence: 0.885055780410767

00:00:38.994 --> 00:00:41.877 biology of breast cancer and leveraging

NOTE Confidence: 0.885055780410767

00:00:41.877 --> 00:00:43.901 that understanding to fundamentally

NOTE Confidence: 0.885055780410767

00:00:43.901 --> 00:00:47.638 improving our way to deliver more efficient,

NOTE Confidence: 0.885055780410767

00:00:47.640 --> 00:00:48.624 more effective,

NOTE Confidence: 0.885055780410767

00:00:48.624 --> 00:00:51.084 and more successful clinical care.

NOTE Confidence: 0.885055780410767

00:00:51.090 --> 00:00:52.076 You know,

NOTE Confidence: 0.885055780410767

00:00:52.076 --> 00:00:54.048 through his laboratory work,

NOTE Confidence: 0.885055780410767

00:00:54.050 --> 00:00:55.890 his work in translation,

NOTE Confidence: 0.885055780410767

00:00:55.890 --> 00:00:57.270 Medison And frankly,

NOTE Confidence: 0.885055780410767

00:00:57.270 --> 00:00:58.710 his leadership of clinical

NOTE Confidence: 0.885055780410767

00:00:58.710 --> 00:01:00.150 trials in clinic research,

NOTE Confidence: 0.885055780410767

00:01:00.150 --> 00:01:02.280 which have not only investigated new

NOTE Confidence: 0.885055780410767

00:01:02.280 --> 00:01:04.470 drugs but also leverage new technologies

NOTE Confidence: 0.885055780410767

00:01:04.470 --> 00:01:06.600 to better define and predict how

NOTE Confidence: 0.885055780410767

00:01:06.600 --> 00:01:08.790 women will best respond to therapy.

NOTE Confidence: 0.885055780410767

00:01:08.790 --> 00:01:11.058 He really has been the triple thread

NOTE Confidence: 0.885055780410767

00:01:11.058 --> 00:01:13.110 and actually have academic Medison,

NOTE Confidence: 0.885055780410767

00:01:13.110 --> 00:01:15.371 and we're pleased to have him today

NOTE Confidence: 0.885055780410767

00:01:15.371 --> 00:01:17.967 to share his work in translation and

NOTE Confidence: 0.885055780410767

00:01:17.967 --> 00:01:20.307 research in breast cancer so loud.

NOTE Confidence: 0.885055780410767

00:01:20.310 --> 00:01:22.470 Thank you for Evergreen speak today.

NOTE Confidence: 0.927787184715271

00:01:23.380 --> 00:01:25.282 Thank you Charlie, for them the

NOTE Confidence: 0.927787184715271

00:01:25.282 --> 00:01:27.554 opportunity to to give a brief update

NOTE Confidence: 0.927787184715271

00:01:27.554 --> 00:01:29.738 on some of the translation of projects

NOTE Confidence: 0.927787184715271

00:01:29.797 --> 00:01:31.897 that we actually have been involved in

NOTE Confidence: 0.927787184715271

00:01:31.897 --> 00:01:35.850 the past few years here at Yale. Um?

NOTE Confidence: 0.893426477909088

00:01:42.370 --> 00:01:45.233 So this is my a disclosure slide

NOTE Confidence: 0.893426477909088

00:01:45.233 --> 00:01:48.606 and I would like to cover 3 areas.

NOTE Confidence: 0.893426477909088

00:01:48.610 --> 00:01:51.172 When is exploiting the emu micro environment

NOTE Confidence: 0.893426477909088

00:01:51.172 --> 00:01:54.429 of a breast cancer for therapeutic purposes,

NOTE Confidence: 0.893426477909088

00:01:54.430 --> 00:01:56.342 some potential metabolic vulnerabilities

NOTE Confidence: 0.893426477909088

00:01:56.342 --> 00:01:59.886 in breast cancer I think exists and I'd

NOTE Confidence: 0.893426477909088

00:01:59.886 --> 00:02:02.326 like to challenge you to think and you

NOTE Confidence: 0.893426477909088

00:02:02.396 --> 00:02:04.651 knew very about cancer predisposition

NOTE Confidence: 0.893426477909088

00:02:04.651 --> 00:02:07.249 or cancer risk category cancer risk.

NOTE Confidence: 0.893426477909088

00:02:07.249 --> 00:02:10.795 So the road from an idea to a clinical trial

NOTE Confidence: 0.893426477909088

00:02:10.795 --> 00:02:13.707 or clinical trial result is really very

NOTE Confidence: 0.893426477909088

00:02:13.707 --> 00:02:17.235 long and often times very sort of tortuous.

NOTE Confidence: 0.893426477909088

00:02:17.240 --> 00:02:18.596 So as an example,

NOTE Confidence: 0.893426477909088

00:02:18.596 --> 00:02:21.067 about 10 years ago we published this

NOTE Confidence: 0.893426477909088

00:02:21.067 --> 00:02:23.587 paper very show at the presence of

NOTE Confidence: 0.893426477909088

00:02:23.587 --> 00:02:25.630 immune cells in primary tumors,

NOTE Confidence: 0.893426477909088

00:02:25.630 --> 00:02:27.820 either ER positive or triple negative,

NOTE Confidence: 0.893426477909088

00:02:27.820 --> 00:02:30.221 or her two positive breast cancer service

NOTE Confidence: 0.893426477909088

00:02:30.221 --> 00:02:31.840 usually associated with prognosis.

NOTE Confidence: 0.893426477909088

00:02:31.840 --> 00:02:33.660 Let's outcome in patients receiving

NOTE Confidence: 0.893426477909088

00:02:33.660 --> 00:02:34.388 order surgery.

NOTE Confidence: 0.893426477909088

00:02:34.390 --> 00:02:36.706 Now the treatment and surgery so

NOTE Confidence: 0.893426477909088

00:02:36.706 --> 00:02:38.849 that people was published in 2010.

NOTE Confidence: 0.893426477909088

00:02:38.850 --> 00:02:41.370 I'd like to remind you that in 2010

NOTE Confidence: 0.893426477909088

00:02:41.370 --> 00:02:43.704 there is no effective, you know,

NOTE Confidence: 0.893426477909088

00:02:43.704 --> 00:02:45.439 therapy in any disease type.

NOTE Confidence: 0.893426477909088

00:02:45.440 --> 00:02:47.869 So we cause this the closing sentence.

NOTE Confidence: 0.893426477909088

00:02:47.870 --> 00:02:49.178 This paper was, well,

NOTE Confidence: 0.893426477909088

00:02:49.178 --> 00:02:50.813 it remains unknown whether the

NOTE Confidence: 0.893426477909088

00:02:50.813 --> 00:02:52.286 Indians selectivity is simply

NOTE Confidence: 0.893426477909088

00:02:52.286 --> 00:02:54.464 associated with with a better outcome,

NOTE Confidence: 0.893426477909088

00:02:54.470 --> 00:02:56.396 or it's really the cause of

NOTE Confidence: 0.893426477909088

00:02:56.396 --> 00:02:58.280 the battle outcome in disease.

NOTE Confidence: 0.893426477909088

00:02:58.280 --> 00:03:00.730 So around the same time in another

NOTE Confidence: 0.893426477909088

00:03:00.730 --> 00:03:03.138 project with a postdoc in my lab,

NOTE Confidence: 0.893426477909088

00:03:03.140 --> 00:03:05.732 we also looked at what sort of biological

NOTE Confidence: 0.893426477909088

00:03:05.732 --> 00:03:07.650 processes or or gene expressions,

NOTE Confidence: 0.893426477909088

00:03:07.650 --> 00:03:09.054 signatures or patterns are

NOTE Confidence: 0.893426477909088

00:03:09.054 --> 00:03:10.458 associated with the response.

NOTE Confidence: 0.893426477909088

00:03:10.460 --> 00:03:11.396 Show me legend.

NOTE Confidence: 0.893426477909088

00:03:11.396 --> 00:03:11.708 Chemotherapy.

NOTE Confidence: 0.893426477909088

00:03:11.708 --> 00:03:13.580 Sony rejoin chemotherapy is really a

NOTE Confidence: 0.893426477909088

00:03:13.627 --> 00:03:15.523 perfect setting where you can correlate

NOTE Confidence: 0.893426477909088

00:03:15.523 --> 00:03:17.139 a particular biomarker with sensitive

NOTE Confidence: 0.893426477909088

00:03:17.139 --> 00:03:18.921 to the treatment because you can

NOTE Confidence: 0.893426477909088

00:03:18.921 --> 00:03:20.756 directly measure the effect of the

NOTE Confidence: 0.893426477909088

00:03:20.756 --> 00:03:22.940 treatment at the time of the surgery.

NOTE Confidence: 0.893426477909088

00:03:22.940 --> 00:03:24.188 Patients have no residual

NOTE Confidence: 0.893426477909088

00:03:24.188 --> 00:03:25.436 cancer after the chemo.

NOTE Confidence: 0.893426477909088

00:03:25.440 --> 00:03:27.000 They tend to do really,

NOTE Confidence: 0.893426477909088

00:03:27.000 --> 00:03:28.866 really well and we call this

NOTE Confidence: 0.893426477909088

00:03:28.866 --> 00:03:29.799 pathological complete response.

NOTE Confidence: 0.893426477909088

00:03:29.800 --> 00:03:30.622 So be selling.

NOTE Confidence: 0.893426477909088

00:03:30.622 --> 00:03:33.240 This is again a number of immune signatures.

NOTE Confidence: 0.893426477909088

00:03:33.240 --> 00:03:34.920 Are Indian related markers fell

NOTE Confidence: 0.893426477909088

00:03:34.920 --> 00:03:36.945 out so obviously the big question

NOTE Confidence: 0.893426477909088

00:03:36.945 --> 00:03:38.877 is so is this a mere Association

NOTE Confidence: 0.893426477909088

00:03:38.877 --> 00:03:40.757 or A cause and effect and?

NOTE Confidence: 0.893426477909088

00:03:40.760 --> 00:03:42.256 Right around that time,

NOTE Confidence: 0.893426477909088

00:03:42.256 --> 00:03:44.500 in the second half of 2010,

NOTE Confidence: 0.893426477909088

00:03:44.500 --> 00:03:47.004 the 1st paper came out in the New

NOTE Confidence: 0.893426477909088

00:03:47.004 --> 00:03:49.034 England Journal of Medicine and eating

NOTE Confidence: 0.893426477909088

00:03:49.034 --> 00:03:51.646 woman at that have shown that actually

NOTE Confidence: 0.893426477909088

00:03:51.646 --> 00:03:53.846 manipulating an immune checkpoint,

NOTE Confidence: 0.893426477909088

00:03:53.850 --> 00:03:56.244 so we'd illumi map could improve the

NOTE Confidence: 0.893426477909088

00:03:56.244 --> 00:03:58.710 survival of patients in metastatic Melanoma,

NOTE Confidence: 0.893426477909088

00:03:58.710 --> 00:04:01.454 so that really created an opportunity to test

NOTE Confidence: 0.893426477909088

00:04:01.454 --> 00:04:03.947 this Kozera fact versus Amir Association.

NOTE Confidence: 0.893426477909088

00:04:03.950 --> 00:04:04.251 2012,

NOTE Confidence: 0.893426477909088

00:04:04.251 --> 00:04:05.756 which is actually the year

NOTE Confidence: 0.893426477909088

00:04:05.756 --> 00:04:07.270 when I joined the air.

NOTE Confidence: 0.893426477909088

00:04:07.270 --> 00:04:09.582 We proposed the new edgmont trial to be

NOTE Confidence: 0.893426477909088

00:04:09.582 --> 00:04:12.405 an S and ask them would repeal me map.

NOTE Confidence: 0.893426477909088

00:04:12.410 --> 00:04:13.830 It could improve the pathological

NOTE Confidence: 0.893426477909088

00:04:13.830 --> 00:04:14.966 complete response rate when

NOTE Confidence: 0.893426477909088

00:04:14.966 --> 00:04:16.030 combined with chemotherapy.

NOTE Confidence: 0.893426477909088

00:04:16.030 --> 00:04:17.238 So PMS said, well,

NOTE Confidence: 0.893426477909088

00:04:17.238 --> 00:04:18.748 now that's a good idea,

NOTE Confidence: 0.893426477909088

00:04:18.750 --> 00:04:20.946 but it's really too toxic and

NOTE Confidence: 0.893426477909088

00:04:20.946 --> 00:04:22.410 it's way too early.

NOTE Confidence: 0.893426477909088

00:04:22.410 --> 00:04:24.682 So it went to look and proposed them

NOTE Confidence: 0.893426477909088

00:04:24.682 --> 00:04:27.269 the same thing and you ain't even prior,

NOTE Confidence: 0.893426477909088

00:04:27.270 --> 00:04:28.790 but also for good measure,

NOTE Confidence: 0.893426477909088

00:04:28.790 --> 00:04:30.578 he asked them whether they would

NOTE Confidence: 0.893426477909088

00:04:30.578 --> 00:04:32.140 be interested in Edgmont Prial,

NOTE Confidence: 0.893426477909088

00:04:32.140 --> 00:04:34.114 since since a lot of immune cells

NOTE Confidence: 0.893426477909088

00:04:34.114 --> 00:04:35.346 in the microenvironment predicted

NOTE Confidence: 0.893426477909088

00:04:35.346 --> 00:04:36.996 better outcome of the surgery.

NOTE Confidence: 0.868568539619446

00:04:37.000 --> 00:04:38.925 So for the new regiment they actually

NOTE Confidence: 0.868568539619446

00:04:38.925 --> 00:04:41.127 sent me this lovely letter that I

NOTE Confidence: 0.868568539619446

00:04:41.127 --> 00:04:43.084 thought it's interesting to read, right?

NOTE Confidence: 0.868568539619446

00:04:43.084 --> 00:04:44.908 So read the actual date first,

NOTE Confidence: 0.868568539619446

00:04:44.910 --> 00:04:46.728 so it's 18th of September 2012.

NOTE Confidence: 0.868568539619446

00:04:46.730 --> 00:04:47.642 The ordinary nice,

NOTE Confidence: 0.868568539619446

00:04:47.642 --> 00:04:48.858 polite rejection that well,

NOTE Confidence: 0.868568539619446

00:04:48.860 --> 00:04:50.295 we are unable to provide

NOTE Confidence: 0.868568539619446

00:04:50.295 --> 00:04:52.129 either funding or drug for this

NOTE Confidence: 0.868568539619446

00:04:52.129 --> 00:04:53.819 project because of the unclear.

NOTE Confidence: 0.868568539619446

00:04:53.820 --> 00:04:56.172 FDA regularly path forward.

NOTE Confidence: 0.868568539619446

00:04:56.172 --> 00:04:58.524 Either there is well,

NOTE Confidence: 0.868568539619446

00:04:58.530 --> 00:05:01.288 sort of tried the road for edge

NOTE Confidence: 0.868568539619446

00:05:01.288 --> 00:05:03.189 event registrations and they agreed

NOTE Confidence: 0.868568539619446

00:05:03.189 --> 00:05:05.765 to do an agent trial which led to

NOTE Confidence: 0.868568539619446

00:05:05.843 --> 00:05:08.279 this spoke as 1418 konnakol trial,

NOTE Confidence: 0.868568539619446

00:05:08.280 --> 00:05:10.542 so not as 40 actually means

NOTE Confidence: 0.868568539619446

00:05:10.542 --> 00:05:12.779 that it was started in 2014,

NOTE Confidence: 0.868568539619446

00:05:12.780 --> 00:05:15.255 so it took about two years to the NCI

NOTE Confidence: 0.868568539619446

00:05:15.255 --> 00:05:18.403 to really put together this large of

NOTE Confidence: 0.868568539619446

00:05:18.403 --> 00:05:20.271 the randomized registration trial.

NOTE Confidence: 0.868568539619446

00:05:20.280 --> 00:05:22.155 After Merck supported it in

NOTE Confidence: 0.868568539619446

00:05:22.155 --> 00:05:23.280 2012 in principle.

NOTE Confidence: 0.868568539619446

00:05:23.280 --> 00:05:25.905 So I'm kind of tenacious and not

NOTE Confidence: 0.868568539619446

00:05:25.905 --> 00:05:27.852 very aggressive, but I I tenacious.

NOTE Confidence: 0.868568539619446

00:05:27.852 --> 00:05:30.385 So I supposed to say my dear again

NOTE Confidence: 0.868568539619446

00:05:30.385 --> 00:05:32.709 to Med immune in the same year,

NOTE Confidence: 0.868568539619446

00:05:32.710 --> 00:05:34.498 maybe even at that time was

NOTE Confidence: 0.868568539619446

00:05:34.498 --> 00:05:35.392 a startup company.

NOTE Confidence: 0.868568539619446

00:05:35.400 --> 00:05:37.472 They had do volume app and now they're

NOTE Confidence: 0.868568539619446

00:05:37.472 --> 00:05:39.712 part of easiest is Erica and being

NOTE Confidence: 0.868568539619446

00:05:39.712 --> 00:05:41.372 smaller than they actually said?

NOTE Confidence: 0.868568539619446

00:05:41.380 --> 00:05:42.250 Yeah, why not?

NOTE Confidence: 0.868568539619446

00:05:42.250 --> 00:05:43.990 So we propose them to studies

NOTE Confidence: 0.868568539619446

00:05:43.990 --> 00:05:45.560 and they agreed to both.

NOTE Confidence: 0.868568539619446

00:05:45.560 --> 00:05:47.060 What was the single agent,

NOTE Confidence: 0.868568539619446

00:05:47.060 --> 00:05:49.450 I mean a single arm phase, one phase,

NOTE Confidence: 0.868568539619446

00:05:49.450 --> 00:05:51.906 two trial at Yale, and the randomized trial.

NOTE Confidence: 0.868568539619446

00:05:51.906 --> 00:05:54.230 So the I spy consortium combined it all,

NOTE Confidence: 0.868568539619446

00:05:54.230 --> 00:05:56.030 Apple event added to pocket back.

NOTE Confidence: 0.868568539619446

00:05:56.030 --> 00:05:58.470 So our study at year was just simply.

NOTE Confidence: 0.868568539619446

00:05:58.470 --> 00:05:58.981 So.

NOTE Confidence: 0.868568539619446

00:05:58.981 --> 00:05:59.492 Hum.

NOTE Confidence: 0.868568539619446

00:05:59.492 --> 00:06:02.558 So I could be presented last

NOTE Confidence: 0.868568539619446

00:06:02.558 --> 00:06:05.968 year the results of the year

NOTE Confidence: 0.868568539619446

00:06:05.968 --> 00:06:08.808 phase one phase two trial.

NOTE Confidence: 0.868568539619446

00:06:08.810 --> 00:06:10.425 There's a historical interest because

NOTE Confidence: 0.868568539619446

00:06:10.425 --> 00:06:12.753 this was the first knew edgmont even

NOTE Confidence: 0.868568539619446

00:06:12.753 --> 00:06:14.733 oncology trial anywhere in the world.

NOTE Confidence: 0.868568539619446

00:06:14.740 --> 00:06:17.364 So the first patient was enrolled in 2015.

NOTE Confidence: 0.868568539619446

00:06:17.370 --> 00:06:19.994 It was a phase one phase two trial,

NOTE Confidence: 0.868568539619446

00:06:20.000 --> 00:06:21.680 and because this has never been

NOTE Confidence: 0.868568539619446

00:06:21.680 --> 00:06:23.269 done in the collective setting

NOTE Confidence: 0.868568539619446

00:06:23.269 --> 00:06:24.929 combined with chemotherapy food,

NOTE Confidence: 0.868568539619446

00:06:24.930 --> 00:06:25.307 though,

NOTE Confidence: 0.868568539619446

00:06:25.307 --> 00:06:27.192 is chemotherapy before surgery FT

NOTE Confidence: 0.868568539619446

00:06:27.192 --> 00:06:29.358 require that the first three patients

NOTE Confidence: 0.868568539619446

00:06:29.358 --> 00:06:31.423 is watch for 9 months each week

NOTE Confidence: 0.868568539619446

00:06:31.423 --> 00:06:33.549 for the next lot could be entered.

NOTE Confidence: 0.868568539619446

00:06:33.550 --> 00:06:35.998 So it looks like it was a long

NOTE Confidence: 0.868568539619446

00:06:35.998 --> 00:06:37.420 time to complete.

NOTE Confidence: 0.868568539619446

00:06:37.420 --> 00:06:39.375 The results showed that the

NOTE Confidence: 0.868568539619446

00:06:39.375 --> 00:06:40.548 pathological complete eradication

NOTE Confidence: 0.868568539619446

00:06:40.548 --> 00:06:42.699 rate in the rest was about 44%.

NOTE Confidence: 0.868568539619446

00:06:42.700 --> 00:06:44.108 The same chemotherapy regimen

NOTE Confidence: 0.868568539619446

00:06:44.108 --> 00:06:45.516 in a similar trial,

NOTE Confidence: 0.868568539619446

00:06:45.520 --> 00:06:47.977 and by by the sea by smog.

NOTE Confidence: 0.868568539619446

00:06:47.980 --> 00:06:49.360 Southwestern college group resulted

NOTE Confidence: 0.868568539619446

00:06:49.360 --> 00:06:51.430 in a PCR or pathological covered

NOTE Confidence: 0.868568539619446

00:06:51.487 --> 00:06:52.907 response with different 29%.

NOTE Confidence: 0.868568539619446

00:06:52.910 --> 00:06:55.016 So we also noted that there,

NOTE Confidence: 0.868568539619446

00:06:55.020 --> 00:06:56.484 as you would expect,

NOTE Confidence: 0.868568539619446

00:06:56.484 --> 00:06:58.680 you cancel each other higher PD

NOTE Confidence: 0.868568539619446

00:06:58.750 --> 00:07:00.772 leg and one expression or more

NOTE Confidence: 0.868568539619446

00:07:00.772 --> 00:07:03.183 sites at a higher PCR eight more

NOTE Confidence: 0.868568539619446

00:07:03.183 --> 00:07:05.358 closer to 60% rather than.

NOTE Confidence: 0.868568539619446

00:07:05.358 --> 00:07:07.140 44 So remember,

NOTE Confidence: 0.868568539619446

00:07:07.140 --> 00:07:10.196 parallel with this and the other study was

NOTE Confidence: 0.868568539619446

00:07:10.196 --> 00:07:12.610 running through the I spy that I was so.

NOTE Confidence: 0.868568539619446

00:07:12.610 --> 00:07:15.730 Lad and he showed the results of the

NOTE Confidence: 0.868568539619446

00:07:15.730 --> 00:07:18.608 Plenary session of the EC are this year on.

NOTE Confidence: 0.868568539619446

00:07:18.610 --> 00:07:20.934 The study shows 9 the randomized setting

NOTE Confidence: 0.868568539619446

00:07:20.934 --> 00:07:23.198 that indeed leave this door vulnerable.

NOTE Confidence: 0.868568539619446

00:07:23.200 --> 00:07:25.015 A product combination improved the

NOTE Confidence: 0.868568539619446

00:07:25.015 --> 00:07:26.467 pathological can't response rate

NOTE Confidence: 0.868568539619446

00:07:26.467 --> 00:07:28.499 in both the triple negative group,

NOTE Confidence: 0.868568539619446

00:07:28.500 --> 00:07:30.385 which was the results were

NOTE Confidence: 0.868568539619446

00:07:30.385 --> 00:07:32.270 very eerily similar in terms

NOTE Confidence: 0.864236354827881

00:07:32.342 --> 00:07:34.852 of the PCI rate, 47 versus 44% in

NOTE Confidence: 0.864236354827881

00:07:34.852 --> 00:07:36.970 our little negative study at Yale,

NOTE Confidence: 0.864236354827881

00:07:36.970 --> 00:07:38.735 and we also notice that

NOTE Confidence: 0.864236354827881

00:07:38.735 --> 00:07:40.500 actually this drug also work.

NOTE Confidence: 0.864236354827881

00:07:40.500 --> 00:07:41.948 That is combination worked.

NOTE Confidence: 0.864236354827881

00:07:41.948 --> 00:07:44.714 It was added to chemotherapy. You have to.

NOTE Confidence: 0.864236354827881

00:07:44.714 --> 00:07:46.940 I mean it hormone receptor HR stands

NOTE Confidence: 0.864236354827881

00:07:47.010 --> 00:07:49.090 for hormone receptor resolution,

NOTE Confidence: 0.864236354827881

00:07:49.090 --> 00:07:50.395 receptor positive disease.

NOTE Confidence: 0.864236354827881

00:07:50.395 --> 00:07:53.005 However, the result might this reason

NOTE Confidence: 0.864236354827881

00:07:53.005 --> 00:07:55.499 why this was picked for a plenary

NOTE Confidence: 0.864236354827881

00:07:55.499 --> 00:07:57.860 session is actually in the next slide,

NOTE Confidence: 0.864236354827881

00:07:57.860 --> 00:08:00.556 so we stumbled upon a remarkably sort of

NOTE Confidence: 0.864236354827881

00:08:00.556 --> 00:08:03.716 simple and clear way to isolate out among

NOTE Confidence: 0.864236354827881

00:08:03.716 --> 00:08:05.860 the estrogen receptor positive tumors,

NOTE Confidence: 0.864236354827881

00:08:05.860 --> 00:08:07.765 the ones which really benefited

NOTE Confidence: 0.864236354827881

00:08:07.765 --> 00:08:09.670 versus those who did not.

NOTE Confidence: 0.864236354827881

00:08:09.670 --> 00:08:12.110 There was no editing benefit.

NOTE Confidence: 0.864236354827881

00:08:12.110 --> 00:08:14.666 So if you split these estrogen

NOTE Confidence: 0.864236354827881

00:08:14.666 --> 00:08:16.370 receptor hormone receptor positive

NOTE Confidence: 0.864236354827881

00:08:16.439 --> 00:08:18.797 group into two more likely subtypes,

NOTE Confidence: 0.864236354827881

00:08:18.800 --> 00:08:21.968 let me call your MP1 and MP2MP one

NOTE Confidence: 0.864236354827881

00:08:21.968 --> 00:08:24.657 this crap sort of Mamma print.

NOTE Confidence: 0.864236354827881

00:08:24.660 --> 00:08:27.196 The lower end of the moment I grew

NOTE Confidence: 0.864236354827881

00:08:27.196 --> 00:08:30.516 up in the MP two is the Momma Prince

NOTE Confidence: 0.864236354827881

00:08:30.516 --> 00:08:32.830 Super High score on my printer.

NOTE Confidence: 0.864236354827881

00:08:32.830 --> 00:08:34.825 Similar sort of predictor that we used

NOTE Confidence: 0.864236354827881

00:08:34.825 --> 00:08:36.948 to to identify patients who benefit

NOTE Confidence: 0.864236354827881

00:08:36.948 --> 00:08:38.963 from Edgmont chemotherapy in hormone

NOTE Confidence: 0.864236354827881

00:08:38.963 --> 00:08:40.640 receptor positive diseases score.

NOTE Confidence: 0.864236354827881

00:08:40.640 --> 00:08:42.908 So what we're showing here that this

NOTE Confidence: 0.864236354827881

00:08:42.908 --> 00:08:45.123 core itself has a meaning and just

NOTE Confidence: 0.864236354827881

00:08:45.123 --> 00:08:47.461 being called high risk or or benefiting

NOTE Confidence: 0.864236354827881

00:08:47.461 --> 00:08:49.509 from chemotherapy is valuable,

NOTE Confidence: 0.864236354827881

00:08:49.510 --> 00:08:52.086 but you actually can also split this look

NOTE Confidence: 0.864236354827881

00:08:52.086 --> 00:08:54.886 into that really super sensitive to adding.

NOTE Confidence: 0.864236354827881

00:08:54.890 --> 00:08:56.518 Uh, in Indian checkpoint

NOTE Confidence: 0.864236354827881

00:08:56.518 --> 00:08:58.146 inhibitor to the chemotherapy.

NOTE Confidence: 0.864236354827881

00:08:58.150 --> 00:08:59.782 So in that group,

NOTE Confidence: 0.864236354827881

00:08:59.782 --> 00:09:02.840 the pathological CR equals 64% versus 22%.

NOTE Confidence: 0.864236354827881

00:09:02.840 --> 00:09:04.860 In the chemotherapy alone.

NOTE Confidence: 0.864236354827881

00:09:04.860 --> 00:09:07.020 So what is this MP group?

NOTE Confidence: 0.864236354827881

00:09:07.020 --> 00:09:08.730 So this NP group actually is

NOTE Confidence: 0.864236354827881

00:09:08.730 --> 00:09:11.131 the group which has a very high

NOTE Confidence: 0.864236354827881

00:09:11.131 --> 00:09:12.723 proliferation and the relatively

NOTE Confidence: 0.864236354827881

00:09:12.723 --> 00:09:14.580 low estrogen receptors signaling,

NOTE Confidence: 0.864236354827881

00:09:14.580 --> 00:09:16.740 or estrogen receptor sort of activity.

NOTE Confidence: 0.864236354827881

00:09:16.740 --> 00:09:18.900 Read out that you can capture

NOTE Confidence: 0.864236354827881

00:09:18.900 --> 00:09:20.340 Biostar generating wearing jeans,

NOTE Confidence: 0.864236354827881

00:09:20.340 --> 00:09:22.332 and that's an important sort of

NOTE Confidence: 0.864236354827881

00:09:22.332 --> 00:09:24.462 piece of information to design the

NOTE Confidence: 0.864236354827881

00:09:24.462 --> 00:09:25.934 follow-up registration trial for

NOTE Confidence: 0.864236354827881

00:09:25.934 --> 00:09:28.260 base that we have working with.

NOTE Confidence: 0.864236354827881

00:09:28.260 --> 00:09:29.776 Because this guy proliferation

NOTE Confidence: 0.864236354827881

00:09:29.776 --> 00:09:31.671 most regions signaling group is

NOTE Confidence: 0.864236354827881

00:09:31.671 --> 00:09:34.045 the group that is the least likely

NOTE Confidence: 0.864236354827881

00:09:34.045 --> 00:09:35.850 to benefit from endocrine therapy.

NOTE Confidence: 0.864236354827881

00:09:35.850 --> 00:09:37.662 Gotta hand it most likely to

NOTE Confidence: 0.864236354827881

00:09:37.662 --> 00:09:38.266 benefit chemotherapy,

NOTE Confidence: 0.864236354827881

00:09:38.270 --> 00:09:40.424 and we think that this benefit

NOTE Confidence: 0.864236354827881

00:09:40.424 --> 00:09:42.258 could be further augmented by

NOTE Confidence: 0.864236354827881

00:09:42.258 --> 00:09:43.888 by adding indoor follow map.

NOTE Confidence: 0.864236354827881

00:09:43.890 --> 00:09:46.210 So we want to get back to this

NOTE Confidence: 0.864236354827881

00:09:46.210 --> 00:09:48.678 letter in September 2012 from work.

NOTE Confidence: 0.864236354827881

00:09:48.680 --> 00:09:51.067 So a year later, in September 30th,

NOTE Confidence: 0.864236354827881

00:09:51.070 --> 00:09:51.360 2013,

NOTE Confidence: 0.864236354827881

00:09:51.360 --> 00:09:53.390 the FDA approved the first sort of

NOTE Confidence: 0.864236354827881

00:09:53.390 --> 00:09:55.584 drug to be based on pathological

NOTE Confidence: 0.864236354827881

00:09:55.584 --> 00:09:57.906 company response rate in breast cancer,

NOTE Confidence: 0.864236354827881

00:09:57.910 --> 00:09:59.314 and that was purchased.

NOTE Confidence: 0.864236354827881

00:09:59.314 --> 00:10:01.069 So purchasing have improved the

NOTE Confidence: 0.864236354827881

00:10:01.069 --> 00:10:02.448 pathological computer response rate

NOTE Confidence: 0.864236354827881

00:10:02.448 --> 00:10:04.398 in her two positive disease and

NOTE Confidence: 0.864236354827881

00:10:04.398 --> 00:10:06.117 lettered registration of this drug.

NOTE Confidence: 0.864236354827881

00:10:06.120 --> 00:10:07.830 So not respecting the idea,

NOTE Confidence: 0.864236354827881

00:10:07.830 --> 00:10:09.702 and they actually lounge the large

NOTE Confidence: 0.864236354827881

00:10:09.702 --> 00:10:11.929 randomized trial with a pathological CRS,

NOTE Confidence: 0.864236354827881

00:10:11.930 --> 00:10:13.988 their endpoint, and to their credit,

NOTE Confidence: 0.864236354827881

00:10:13.990 --> 00:10:16.166 they invited me back.

NOTE Confidence: 0.864236354827881

00:10:16.166 --> 00:10:17.798 To the app.

NOTE Confidence: 0.864236354827881

00:10:17.800 --> 00:10:20.596 Leadership of the trial and the

NOTE Confidence: 0.864236354827881

00:10:20.596 --> 00:10:22.924 results were actually published this

NOTE Confidence: 0.864236354827881

00:10:22.924 --> 00:10:25.619 year in the new invention of Madison

NOTE Confidence: 0.864236354827881

00:10:25.619 --> 00:10:28.239 because it did confirm that indeed,

NOTE Confidence: 0.864236354827881

00:10:28.240 --> 00:10:30.732 adding parallelism after chemotherapy

NOTE Confidence: 0.864236354827881

00:10:30.732 --> 00:10:33.224 improves the pathological computer

NOTE Confidence: 0.864236354827881

00:10:33.224 --> 00:10:35.422 education rate improved the

NOTE Confidence: 0.864236354827881

00:10:35.422 --> 00:10:37.607 recurrence free survival even after

NOTE Confidence: 0.864236354827881

00:10:37.607 --> 00:10:40.209 18 months of median follow up.

NOTE Confidence: 0.864236354827881

00:10:40.210 --> 00:10:41.545 So this is the research

NOTE Confidence: 0.864236354827881

00:10:41.545 --> 00:10:42.880 study that sort of was

NOTE Confidence: 0.894069969654083

00:10:42.939 --> 00:10:45.029 largely based on these observations.

NOTE Confidence: 0.894069969654083

00:10:45.030 --> 00:10:47.590 Remember 10 years ago, so it took six.

NOTE Confidence: 0.894069969654083

00:10:47.590 --> 00:10:50.190 It looks 40 years to actually start this

NOTE Confidence: 0.894069969654083

00:10:50.190 --> 00:10:52.409 study another six years to complete it,

NOTE Confidence: 0.894069969654083

00:10:52.410 --> 00:10:54.978 and it would have been completed by now,

NOTE Confidence: 0.894069969654083

00:10:54.980 --> 00:10:56.384 not for the coded.

NOTE Confidence: 0.894069969654083

00:10:56.384 --> 00:10:59.665 So it has accrued 923 patients out of 1000

NOTE Confidence: 0.894069969654083

00:10:59.665 --> 00:11:02.227 and the results probably will be become

NOTE Confidence: 0.894069969654083

00:11:02.298 --> 00:11:05.234 available in the next two to three years.

NOTE Confidence: 0.894069969654083

00:11:05.240 --> 00:11:08.078 So so some cancers that high,

NOTE Confidence: 0.894069969654083

00:11:08.080 --> 00:11:09.724 you know, you know.

NOTE Confidence: 0.894069969654083

00:11:09.724 --> 00:11:11.368 Union presence know why

NOTE Confidence: 0.894069969654083

00:11:11.368 --> 00:11:13.459 so often suffer numbers.

NOTE Confidence: 0.894069969654083

00:11:13.460 --> 00:11:15.434 Medical student at Yale took on

NOTE Confidence: 0.894069969654083

00:11:15.434 --> 00:11:17.223 this project to actually look

NOTE Confidence: 0.894069969654083

00:11:17.223 --> 00:11:18.867 into the molecular background,

NOTE Confidence: 0.894069969654083

00:11:18.870 --> 00:11:20.675 or why sometimes have a

NOTE Confidence: 0.894069969654083

00:11:20.675 --> 00:11:22.480 lot of lymphocytes at this.

NOTE Confidence: 0.894069969654083

00:11:22.480 --> 00:11:24.646 Last one is now medical country

NOTE Confidence: 0.894069969654083

00:11:24.646 --> 00:11:26.090 fellow at Sloan Kettering.

NOTE Confidence: 0.894069969654083

00:11:26.090 --> 00:11:28.169 So we did these families pcga let

NOTE Confidence: 0.894069969654083

00:11:28.169 --> 00:11:30.334 me show that many other people

NOTE Confidence: 0.894069969654083

00:11:30.334 --> 00:11:32.339 did before that triple negative

NOTE Confidence: 0.894069969654083

00:11:32.339 --> 00:11:34.759 cancer's had a higher notation count,

NOTE Confidence: 0.894069969654083

00:11:34.760 --> 00:11:36.565 highly antigen mode and more

NOTE Confidence: 0.894069969654083

00:11:36.565 --> 00:11:37.648 cytotoxic T cells.

NOTE Confidence: 0.894069969654083

00:11:37.650 --> 00:11:38.012 However,

NOTE Confidence: 0.894069969654083

00:11:38.012 --> 00:11:41.640 when you look at the actual group On its own,

NOTE Confidence: 0.894069969654083

00:11:41.640 --> 00:11:43.746 like triple negative disease or ER

NOTE Confidence: 0.894069969654083

00:11:43.746 --> 00:11:45.854 positive cancer, her two positive cancer.

NOTE Confidence: 0.894069969654083

00:11:45.854 --> 00:11:47.258 These associations suddenly flip.

NOTE Confidence: 0.894069969654083

00:11:47.260 --> 00:11:49.010 This is a correlation matrix.

NOTE Confidence: 0.894069969654083

00:11:49.010 --> 00:11:51.818 I don't expect you to see the numbers,

NOTE Confidence: 0.894069969654083

00:11:51.820 --> 00:11:54.034 but the colors indicate you the

NOTE Confidence: 0.894069969654083

00:11:54.034 --> 00:11:55.510 the positive correlation when

NOTE Confidence: 0.894069969654083

00:11:55.576 --> 00:11:57.086 it's Brown and it's blue,

NOTE Confidence: 0.894069969654083

00:11:57.090 --> 00:11:58.845 it's negative and anti correlation

NOTE Confidence: 0.894069969654083

00:11:58.845 --> 00:12:00.600 and the deeper the color,

NOTE Confidence: 0.894069969654083

00:12:00.600 --> 00:12:02.350 the higher the correlation value.

NOTE Confidence: 0.894069969654083

00:12:02.350 --> 00:12:04.870 So you can see that the Indian signatures

NOTE Confidence: 0.894069969654083

00:12:04.870 --> 00:12:07.269 are highly correlated with one another.

NOTE Confidence: 0.894069969654083

00:12:07.270 --> 00:12:09.020 But on the other hand,

NOTE Confidence: 0.894069969654083

00:12:09.020 --> 00:12:10.825 is Genomic metrics of generic

NOTE Confidence: 0.894069969654083

00:12:10.825 --> 00:12:11.908 complexities such as.

NOTE Confidence: 0.894069969654083

00:12:11.910 --> 00:12:14.244 Mutation load or New Antigen Lord

NOTE Confidence: 0.894069969654083

00:12:14.244 --> 00:12:15.800 or deletions or amplifications,

NOTE Confidence: 0.894069969654083

00:12:15.800 --> 00:12:17.320 loads or como complexity.

NOTE Confidence: 0.894069969654083

00:12:17.320 --> 00:12:19.220 We actually are inversely associated

NOTE Confidence: 0.894069969654083

00:12:19.220 --> 00:12:21.230 with immune Indian presence in

NOTE Confidence: 0.894069969654083

00:12:21.230 --> 00:12:23.185 triple negative disease and disease,

NOTE Confidence: 0.894069969654083

00:12:23.190 --> 00:12:25.140 so that was pretty counterintuitive.

NOTE Confidence: 0.894069969654083

00:12:25.140 --> 00:12:26.692 Counter intuitive in 2017.

NOTE Confidence: 0.894069969654083

00:12:26.692 --> 00:12:27.080 OK,

NOTE Confidence: 0.894069969654083

00:12:27.080 --> 00:12:30.572 so you're moving in says you have a simpler.

NOTE Confidence: 0.894069969654083

00:12:30.580 --> 00:12:32.914 We can suggest the fewer than

NOTE Confidence: 0.894069969654083

00:12:32.914 --> 00:12:34.470 your hand surgeons are.

NOTE Confidence: 0.894069969654083

00:12:34.470 --> 00:12:37.200 So when I see things like this,

NOTE Confidence: 0.894069969654083

00:12:37.200 --> 00:12:39.150 I try to confirm it.

NOTE Confidence: 0.894069969654083

00:12:39.150 --> 00:12:41.376 So we reached out collaborator and

NOTE Confidence: 0.894069969654083

00:12:41.376 --> 00:12:43.983 friend Thomas card and ask him to

NOTE Confidence: 0.894069969654083

00:12:43.983 --> 00:12:46.089 actually replicate this or with a

NOTE Confidence: 0.894069969654083

00:12:46.089 --> 00:12:47.705 different methodology and Thomas

NOTE Confidence: 0.894069969654083

00:12:47.705 --> 00:12:50.087 actually find exact same thing that

NOTE Confidence: 0.894069969654083

00:12:50.087 --> 00:12:52.010 in primary triple negative disease,

NOTE Confidence: 0.894069969654083

00:12:52.010 --> 00:12:54.650 the fewer the immune cells they hire.

NOTE Confidence: 0.894069969654083

00:12:54.650 --> 00:12:56.158 The Genomic heterogeneity and

NOTE Confidence: 0.894069969654083

00:12:56.158 --> 00:12:58.036 the worst prognosis. So worse.

NOTE Confidence: 0.894069969654083

00:12:58.036 --> 00:13:00.274 Prognosis means that you have a

NOTE Confidence: 0.894069969654083

00:13:00.274 --> 00:13:01.830 higher probability for methods.

NOTE Confidence: 0.894069969654083

00:13:01.830 --> 00:13:04.557 This is so and let us do this hypothesis

NOTE Confidence: 0.894069969654083

00:13:04.557 --> 00:13:06.625 that maybe the metastatic lesions

NOTE Confidence: 0.894069969654083

00:13:06.625 --> 00:13:09.780 are actually immune refugees or or escapes.

NOTE Confidence: 0.894069969654083

00:13:09.780 --> 00:13:12.510 So there are more immune in Earth

NOTE Confidence: 0.894069969654083

00:13:12.510 --> 00:13:14.523 that Michael Environment is more

NOTE Confidence: 0.894069969654083

00:13:14.523 --> 00:13:16.443 immune inert and these three

NOTE Confidence: 0.894069969654083

00:13:16.443 --> 00:13:18.914 brilliant woman took on this project

NOTE Confidence: 0.894069969654083

00:13:18.914 --> 00:13:20.999 or parasitically was a visiting

NOTE Confidence: 0.894069969654083

00:13:20.999 --> 00:13:23.384 scientist from Hungary or so with.

NOTE Confidence: 0.894069969654083

00:13:23.384 --> 00:13:26.590 Smoking baby that his lab in Charlotte.

NOTE Confidence: 0.894069969654083

00:13:26.590 --> 00:13:27.724 With me and.

NOTE Confidence: 0.894069969654083

00:13:27.724 --> 00:13:30.370 More Gerstein so we rounded up samples

NOTE Confidence: 0.894069969654083

00:13:30.449 --> 00:13:33.249 which will pair primaries and meds and

NOTE Confidence: 0.894069969654083

00:13:33.249 --> 00:13:35.940 also a separate Court of primaries.

NOTE Confidence: 0.894069969654083

00:13:35.940 --> 00:13:38.299 And that's not from the same patient,

NOTE Confidence: 0.894069969654083

00:13:38.300 --> 00:13:40.911 and subjected them to a whole series

NOTE Confidence: 0.894069969654083

00:13:40.911 --> 00:13:43.018 of molecular studies to test it in.

NOTE Confidence: 0.894069969654083

00:13:43.020 --> 00:13:44.700 You micro environment is the

NOTE Confidence: 0.894069969654083

00:13:44.700 --> 00:13:45.708 same or different,

NOTE Confidence: 0.894069969654083

00:13:45.710 --> 00:13:47.095 so this is just really

NOTE Confidence: 0.894069969654083

00:13:47.095 --> 00:13:48.480 examples of three sort of

NOTE Confidence: 0.843152046203613

00:13:48.540 --> 00:13:49.731 simple and straightforward

NOTE Confidence: 0.843152046203613

00:13:49.731 --> 00:13:52.113 findings with teal comes the tumor.

NOTE Confidence: 0.843152046203613

00:13:52.120 --> 00:13:54.064 Infiltrating info sites are lower in

NOTE Confidence: 0.843152046203613

00:13:54.064 --> 00:13:55.765 maximum primary tumors in matched

NOTE Confidence: 0.843152046203613

00:13:55.765 --> 00:13:57.505 and unmatched chords be dealing.

NOTE Confidence: 0.843152046203613

00:13:57.510 --> 00:13:59.670 Expression is the same, it slower.

NOTE Confidence: 0.843152046203613

00:13:59.670 --> 00:14:01.542 In in the matter equations and

NOTE Confidence: 0.843152046203613

00:14:01.542 --> 00:14:03.719 also a whole lot of different

NOTE Confidence: 0.843152046203613

00:14:03.719 --> 00:14:05.854 Indian signatures are all lower,

NOTE Confidence: 0.843152046203613

00:14:05.860 --> 00:14:08.170 consistently showing that there are less

NOTE Confidence: 0.843152046203613

00:14:08.170 --> 00:14:10.588 Indians and less activity in the breast.

NOTE Confidence: 0.843152046203613

00:14:10.590 --> 00:14:12.322 Cancer metastatic micro environment.

NOTE Confidence: 0.843152046203613

00:14:12.322 --> 00:14:14.920 Why don't was really interesting though?

NOTE Confidence: 0.843152046203613

00:14:14.920 --> 00:14:17.206 Is that while most of the

NOTE Confidence: 0.843152046203613

00:14:17.206 --> 00:14:18.730 emu markers went down,

NOTE Confidence: 0.843152046203613

00:14:18.730 --> 00:14:20.764 some of the Indian targets actually

NOTE Confidence: 0.843152046203613

00:14:20.764 --> 00:14:23.049 remain high or or even increased

NOTE Confidence: 0.843152046203613

00:14:23.049 --> 00:14:25.199 in the meta static environments.

NOTE Confidence: 0.843152046203613

00:14:25.200 --> 00:14:27.498 And these IO targets are potential

NOTE Confidence: 0.843152046203613

00:14:27.498 --> 00:14:29.780 good set of candidates for offer.

NOTE Confidence: 0.843152046203613

00:14:29.780 --> 00:14:32.440 Testing them in the meta static setting,

NOTE Confidence: 0.843152046203613

00:14:32.440 --> 00:14:34.350 either alone or in combination.

NOTE Confidence: 0.843152046203613

00:14:34.350 --> 00:14:36.630 Also in combination with established agents.

NOTE Confidence: 0.843152046203613

00:14:36.630 --> 00:14:39.290 So we selected the group of this

NOTE Confidence: 0.843152046203613

00:14:39.290 --> 00:14:41.906 preserved IO targets for a clinical trial

NOTE Confidence: 0.843152046203613

00:14:41.906 --> 00:14:44.660 that we hope to conduct this support.

NOTE Confidence: 0.843152046203613

00:14:44.660 --> 00:14:46.430 Clinical trials it's called rustic

NOTE Confidence: 0.843152046203613

00:14:46.430 --> 00:14:49.250 and this is sort of a scheme of it.

NOTE Confidence: 0.843152046203613

00:14:49.250 --> 00:14:49.960 And again,

NOTE Confidence: 0.843152046203613

00:14:49.960 --> 00:14:52.445 this takes this immune targets that we

NOTE Confidence: 0.843152046203613

00:14:52.445 --> 00:14:54.430 preserved in the meta static setting

NOTE Confidence: 0.843152046203613

00:14:54.430 --> 00:14:56.429 and testing in the clinic whether

NOTE Confidence: 0.843152046203613

00:14:56.429 --> 00:14:58.649 they really have a functional role.

NOTE Confidence: 0.843152046203613

00:14:58.650 --> 00:15:00.438 In suppressing the new Micro Hood,

NOTE Confidence: 0.843152046203613

00:15:00.440 --> 00:15:02.302 so because of lack of time I

NOTE Confidence: 0.843152046203613

00:15:02.302 --> 00:15:04.163 can't really talk about all the

NOTE Confidence: 0.843152046203613

00:15:04.163 --> 00:15:05.828 other Indian projects every day,

NOTE Confidence: 0.843152046203613

00:15:05.830 --> 00:15:07.622 but I just thought I list them here

NOTE Confidence: 0.843152046203613

00:15:07.622 --> 00:15:09.793 so we did compare changes in the

NOTE Confidence: 0.843152046203613

00:15:09.793 --> 00:15:11.458 micro environment before and after

NOTE Confidence: 0.843152046203613

00:15:11.521 --> 00:15:13.597 therapy and the shouts only published.

NOTE Confidence: 0.843152046203613

00:15:13.600 --> 00:15:15.952 This give us some ideas what to add

NOTE Confidence: 0.843152046203613

00:15:15.952 --> 00:15:17.909 to Pembrolizumab Order Volume app to

NOTE Confidence: 0.843152046203613

00:15:17.909 --> 00:15:19.877 make the treatment even more effective

NOTE Confidence: 0.843152046203613

00:15:19.934 --> 00:15:21.629 than you actually and setting.

NOTE Confidence: 0.843152046203613

00:15:21.630 --> 00:15:23.862 Homes we also compared to same

NOTE Confidence: 0.843152046203613

00:15:23.862 --> 00:15:25.350 day the immune reach,

NOTE Confidence: 0.843152046203613

00:15:25.350 --> 00:15:27.540 triple negative and the energy or

NOTE Confidence: 0.843152046203613

00:15:27.540 --> 00:15:30.282 positive Kansas to see that there is

NOTE Confidence: 0.843152046203613

00:15:30.282 --> 00:15:32.302 differences in their micro environments

NOTE Confidence: 0.843152046203613

00:15:32.302 --> 00:15:34.842 and that was done by Paso mirror

NOTE Confidence: 0.843152046203613

00:15:34.842 --> 00:15:37.254 medical students who is now a resident

NOTE Confidence: 0.843152046203613

00:15:37.254 --> 00:15:39.858 at the Harvard system the same way.

NOTE Confidence: 0.843152046203613

00:15:39.860 --> 00:15:41.530 So we did similar comparisons

NOTE Confidence: 0.843152046203613

00:15:41.530 --> 00:15:43.950 by by race and King blindness.

NOTE Confidence: 0.843152046203613

00:15:43.950 --> 00:15:46.934 Scientists in my lab is working or not.

NOTE Confidence: 0.843152046203613

00:15:46.940 --> 00:15:49.684 Of data from a number of different new

NOTE Confidence: 0.843152046203613

00:15:49.684 --> 00:15:51.919 agent trials that seems to do well.

NOTE Confidence: 0.843152046203613

00:15:51.920 --> 00:15:53.575 Map kind of what precisely

NOTE Confidence: 0.843152046203613

00:15:53.575 --> 00:15:54.237 defined predictors,

NOTE Confidence: 0.843152046203613

00:15:54.240 --> 00:15:56.124 and he rosenblit is Medical College

NOTE Confidence: 0.843152046203613

00:15:56.124 --> 00:15:58.674 of fellow with a very nice people and

NOTE Confidence: 0.843152046203613

00:15:58.674 --> 00:16:00.966 actually looking at in a large pool

NOTE Confidence: 0.843152046203613

00:16:00.966 --> 00:16:02.876 of data from Foundation Medicine.

NOTE Confidence: 0.843152046203613

00:16:02.880 --> 00:16:04.782 Be like an expression across different

NOTE Confidence: 0.843152046203613

00:16:04.782 --> 00:16:06.859 meta static sites in breast cancer.

NOTE Confidence: 0.843152046203613

00:16:06.860 --> 00:16:09.038 And there are some really substantial

NOTE Confidence: 0.843152046203613

00:16:09.038 --> 00:16:10.904 differences in people like an

NOTE Confidence: 0.843152046203613

00:16:10.904 --> 00:16:12.689 expression depending on what site

NOTE Confidence: 0.843152046203613

00:16:12.689 --> 00:16:14.117 you are actually sampling.

NOTE Confidence: 0.843152046203613

00:16:14.120 --> 00:16:16.728 I'm going to move on to something else

NOTE Confidence: 0.843152046203613

00:16:16.728 --> 00:16:19.206 that really got me excited in the past.

NOTE Confidence: 0.843152046203613

00:16:19.210 --> 00:16:21.436 So if you a few months so.

NOTE Confidence: 0.843152046203613

00:16:21.440 --> 00:16:23.045 Many metabolic processes are catalyzed

NOTE Confidence: 0.843152046203613

00:16:23.045 --> 00:16:25.016 by multiple different isozymes or or

NOTE Confidence: 0.843152046203613

00:16:25.016 --> 00:16:26.300 proteins that really capitalizes.

NOTE Confidence: 0.843152046203613

00:16:26.300 --> 00:16:27.272 Same enzymatic reaction.

NOTE Confidence: 0.843152046203613

00:16:27.272 --> 00:16:29.540 Normal cells usually have many of these,

NOTE Confidence: 0.843152046203613

00:16:29.540 --> 00:16:31.274 and oftentimes in cancer you actually

NOTE Confidence: 0.843152046203613

00:16:31.274 --> 00:16:34.078 see that one of the isoforms become dominant,

NOTE Confidence: 0.843152046203613

00:16:34.080 --> 00:16:36.664 so that's the schema on this figure, right?

NOTE Confidence: 0.843152046203613

00:16:36.664 --> 00:16:38.608 So normal tissue is both sides.

NOTE Confidence: 0.843152046203613

00:16:38.610 --> 00:16:41.194 When I sent to our expressed in cancer,

NOTE Confidence: 0.843152046203613

00:16:41.200 --> 00:16:43.524 I just have one becomes a dominant

NOTE Confidence: 0.843152046203613

00:16:43.524 --> 00:16:44.520 and the other

NOTE Confidence: 0.857035517692566

00:16:44.590 --> 00:16:47.219 one is lost. So we asked how often do we

NOTE Confidence: 0.857035517692566

00:16:47.219 --> 00:16:50.565 see this in cancer and do this sort of isis

NOTE Confidence: 0.857035517692566

00:16:50.565 --> 00:16:52.960 and expression changes could could harbor.

NOTE Confidence: 0.857035517692566

00:16:52.960 --> 00:16:56.688 Or or include enzymes that we could target

NOTE Confidence: 0.857035517692566

00:16:56.688 --> 00:16:59.228 metabolically somaca March secret visiting

NOTE Confidence: 0.857035517692566

00:16:59.228 --> 00:17:02.288 scientist faculty from from a Polish

NOTE Confidence: 0.857035517692566

00:17:02.288 --> 00:17:05.099 University to this project on and device.

NOTE Confidence: 0.857035517692566

00:17:05.100 --> 00:17:07.435 This sort of strategy to

NOTE Confidence: 0.857035517692566

00:17:07.435 --> 00:17:09.303 look at humanizing forms.

NOTE Confidence: 0.857035517692566

00:17:09.310 --> 00:17:11.418 Isozymes managed matched primary

NOTE Confidence: 0.857035517692566

00:17:11.418 --> 00:17:14.053 tumors in the metastatic lesions

NOTE Confidence: 0.857035517692566

00:17:14.053 --> 00:17:16.437 sorry match the normal tissue.

NOTE Confidence: 0.857035517692566

00:17:16.440 --> 00:17:18.680 The DC area across 14 different cancer

NOTE Confidence: 0.857035517692566

00:17:18.680 --> 00:17:21.075 types where this was available than the

NOTE Confidence: 0.857035517692566

00:17:21.075 --> 00:17:23.133 validated the results in cell lines.

NOTE Confidence: 0.857035517692566

00:17:23.140 --> 00:17:25.036 Make sure that this is really

NOTE Confidence: 0.857035517692566

00:17:25.036 --> 00:17:27.068 observed in the purest system and

NOTE Confidence: 0.857035517692566

00:17:27.068 --> 00:17:29.168 not just an artifact of difference.

NOTE Confidence: 0.857035517692566

00:17:29.170 --> 00:17:31.205 He still different issue compositions

NOTE Confidence: 0.857035517692566

00:17:31.205 --> 00:17:33.240 and then says the functionality

NOTE Confidence: 0.857035517692566

00:17:33.308 --> 00:17:35.786 in this depth map data which is

NOTE Confidence: 0.857035517692566

00:17:35.786 --> 00:17:37.374 basically complete knockdown of all

NOTE Confidence: 0.857035517692566

00:17:37.374 --> 00:17:39.214 human jeans in about 7 or 8 cell

NOTE Confidence: 0.857035517692566

00:17:39.220 --> 00:17:41.230 lines and then the conference hits.

NOTE Confidence: 0.857035517692566

00:17:41.230 --> 00:17:43.240 We validated in the manual screen.

NOTE Confidence: 0.857035517692566

00:17:43.240 --> 00:17:45.256 This is an example for you

NOTE Confidence: 0.857035517692566

00:17:45.256 --> 00:17:46.600 how this exactly looks.

NOTE Confidence: 0.857035517692566

00:17:46.600 --> 00:17:51.836 404 Kansas so this is Csea enzyme.

NOTE Confidence: 0.857035517692566

00:17:51.840 --> 00:17:53.127 2 forms ACA&B.

NOTE Confidence: 0.857035517692566

00:17:53.127 --> 00:17:56.919 Plots show you that how they still the ACA,

NOTE Confidence: 0.857035517692566

00:17:56.920 --> 00:18:00.060 which is the red and be which is the blue,

NOTE Confidence: 0.857035517692566

00:18:00.060 --> 00:18:02.564 had the expression a normal and an action.

NOTE Confidence: 0.857035517692566

00:18:02.570 --> 00:18:04.747 Cancer tissues and you can see that

NOTE Confidence: 0.857035517692566

00:18:04.747 --> 00:18:06.959 the Blues all go down and cancel.

NOTE Confidence: 0.857035517692566

00:18:06.960 --> 00:18:08.530 That means that the expression

NOTE Confidence: 0.857035517692566

00:18:08.530 --> 00:18:09.786 of this is lost,

NOTE Confidence: 0.857035517692566

00:18:09.790 --> 00:18:11.355 whereas the red remains stable

NOTE Confidence: 0.857035517692566

00:18:11.355 --> 00:18:13.240 and the red is the sea.

NOTE Confidence: 0.857035517692566

00:18:13.240 --> 00:18:15.124 So this thing this is a

NOTE Confidence: 0.857035517692566

00:18:15.124 --> 00:18:16.066 potentially interesting target.

NOTE Confidence: 0.857035517692566

00:18:16.070 --> 00:18:18.177 So when you look at this across

NOTE Confidence: 0.857035517692566

00:18:18.177 --> 00:18:19.463 different cancer types and

NOTE Confidence: 0.857035517692566

00:18:19.463 --> 00:18:21.088 indeed app map validation data,

NOTE Confidence: 0.857035517692566

00:18:21.090 --> 00:18:23.082 then actually what really fell out on the

NOTE Confidence: 0.857035517692566

00:18:23.082 --> 00:18:25.240 top is this questionnaire carboxylase.

NOTE Confidence: 0.857035517692566

00:18:25.240 --> 00:18:28.174 Which show this loss of isoenzyme

NOTE Confidence: 0.857035517692566

00:18:28.174 --> 00:18:30.130 diversity intro different cancer

NOTE Confidence: 0.857035517692566

00:18:30.211 --> 00:18:32.701 types and was socially but nine

NOTE Confidence: 0.857035517692566

00:18:32.701 --> 00:18:35.107 different cell lines and each cancer

NOTE Confidence: 0.857035517692566

00:18:35.107 --> 00:18:37.771 types in in the depth map so that

NOTE Confidence: 0.857035517692566

00:18:37.780 --> 00:18:40.293 map has like several dozens of cell

NOTE Confidence: 0.857035517692566

00:18:40.293 --> 00:18:43.209 lines for a particular cancer type,

NOTE Confidence: 0.857035517692566

00:18:43.210 --> 00:18:44.323 like breast cancer.

NOTE Confidence: 0.857035517692566

00:18:44.323 --> 00:18:46.549 Nine of these showed the same

NOTE Confidence: 0.857035517692566

00:18:46.549 --> 00:18:48.230 loss of heterozygosity,

NOTE Confidence: 0.857035517692566

00:18:48.230 --> 00:18:50.340 loss of diversity as we

NOTE Confidence: 0.857035517692566

00:18:50.340 --> 00:18:52.450 saw in the human data.

NOTE Confidence: 0.857035517692566

00:18:52.450 --> 00:18:53.689 Different cancer types.

NOTE Confidence: 0.857035517692566

00:18:53.689 --> 00:18:56.580 And in this case is also validated,

NOTE Confidence: 0.857035517692566

00:18:56.580 --> 00:18:58.771 so most of the cell lines there

NOTE Confidence: 0.857035517692566

00:18:58.771 --> 00:19:00.898 where the CSC was knocked out.

NOTE Confidence: 0.857035517692566

00:19:00.900 --> 00:19:02.886 If it had the dominant expression,

NOTE Confidence: 0.857035517692566

00:19:02.890 --> 00:19:04.318 it really impact viability.

NOTE Confidence: 0.857035517692566

00:19:04.318 --> 00:19:07.125 But the real kicker is that when we

NOTE Confidence: 0.857035517692566

00:19:07.125 --> 00:19:09.197 look up what is known about this,

NOTE Confidence: 0.857035517692566

00:19:09.200 --> 00:19:11.819 it turns out that Pfizer has a drug that

NOTE Confidence: 0.857035517692566

00:19:11.819 --> 00:19:14.314 they put through phase one and phase

NOTE Confidence: 0.857035517692566

00:19:14.314 --> 00:19:16.839 two trials for diabetes and fatty liver,

NOTE Confidence: 0.857035517692566

00:19:16.840 --> 00:19:18.500 and actually showed all the

NOTE Confidence: 0.857035517692566

00:19:18.500 --> 00:19:20.160 metabolic effects that we expected.

NOTE Confidence: 0.857035517692566

00:19:20.160 --> 00:19:21.320 But they discontinued development

NOTE Confidence: 0.857035517692566

00:19:21.320 --> 00:19:23.060 last year or two years ago

NOTE Confidence: 0.857035517692566

00:19:23.114 --> 00:19:24.470 because of thrombocytopenia,

NOTE Confidence: 0.857035517692566

00:19:24.470 --> 00:19:25.652 which is wonderful.

NOTE Confidence: 0.857035517692566

00:19:25.652 --> 00:19:27.228 Because don't beside opinion

NOTE Confidence: 0.857035517692566

00:19:27.228 --> 00:19:28.756 through megakaryocytes really rely

NOTE Confidence: 0.857035517692566

00:19:28.756 --> 00:19:30.226 on the normal lipid synthesis,

NOTE Confidence: 0.857035517692566

00:19:30.230 --> 00:19:32.561 because from both sides bought off and

NOTE Confidence: 0.857035517692566

00:19:32.561 --> 00:19:35.555 every time I turn both sides come off

NOTE Confidence: 0.857035517692566

00:19:35.555 --> 00:19:37.880 from the surface supermodel career site,

NOTE Confidence: 0.857035517692566

00:19:37.880 --> 00:19:38.948 it takes lipids.

NOTE Confidence: 0.857035517692566

00:19:38.948 --> 00:19:41.084 Membranes made it so we answered

NOTE Confidence: 0.857035517692566

00:19:41.084 --> 00:19:43.343 the proof that is really works

NOTE Confidence: 0.857035517692566

00:19:43.343 --> 00:19:44.807 the way it's supposed.

NOTE Confidence: 0.857035517692566

00:19:44.810 --> 00:19:46.562 So the Anthony to collaboration with

NOTE Confidence: 0.857035517692566

00:19:46.562 --> 00:19:48.482 Pfizer to to do some additional

NOTE Confidence: 0.857035517692566

00:19:48.482 --> 00:19:49.874 preclinical studies and bring

NOTE Confidence: 0.857035517692566

00:19:49.874 --> 00:19:51.266 it in the clinic

NOTE Confidence: 0.862062811851501

00:19:51.323 --> 00:19:52.387 if it validates so,

NOTE Confidence: 0.862062811851501

00:19:52.390 --> 00:19:54.448 we simply throw validation is pre

NOTE Confidence: 0.862062811851501

00:19:54.448 --> 00:19:56.181 clinical validation is falling on

NOTE Confidence: 0.862062811851501

00:19:56.181 --> 00:19:58.011 the shoulders of Julia fold even

NOTE Confidence: 0.862062811851501

00:19:58.011 --> 00:19:59.844 offer Medical College of Fellows and

NOTE Confidence: 0.862062811851501

00:19:59.844 --> 00:20:01.560 finish with scientists in my lab.

NOTE Confidence: 0.862062811851501

00:20:01.560 --> 00:20:03.808 So before the coveted broke we had a

NOTE Confidence: 0.862062811851501

00:20:03.808 --> 00:20:05.900 chance to look at 10 different cell

NOTE Confidence: 0.862062811851501

00:20:05.900 --> 00:20:08.511 lines and you see that in the human

NOTE Confidence: 0.862062811851501

00:20:08.511 --> 00:20:09.951 sort of achievable concentrations

NOTE Confidence: 0.862062811851501

00:20:09.951 --> 00:20:12.620 that you can get in the human serum.

NOTE Confidence: 0.862062811851501

00:20:12.620 --> 00:20:15.168 It says a pretty broad inhibitory effect.

NOTE Confidence: 0.862062811851501

00:20:15.170 --> 00:20:17.795 And the army is not for coffee.

NOTE Confidence: 0.862062811851501

00:20:17.800 --> 00:20:19.680 I could probably show you,

NOTE Confidence: 0.862062811851501

00:20:19.680 --> 00:20:22.015 said the combinatorial screen results

NOTE Confidence: 0.862062811851501

00:20:22.015 --> 00:20:24.350 from the high throughputs combinatorial

NOTE Confidence: 0.862062811851501

00:20:24.410 --> 00:20:26.699 screen that we initially is doing in

NOTE Confidence: 0.862062811851501

00:20:26.699 --> 00:20:29.030 our core facility at the West campus

NOTE Confidence: 0.862062811851501

00:20:29.030 --> 00:20:30.635 and also collaborating in jacks

NOTE Confidence: 0.862062811851501

00:20:30.635 --> 00:20:33.216 to test this drug in PDX models.

NOTE Confidence: 0.862062811851501

00:20:33.220 --> 00:20:36.595 And we hope to bring this to the clinic.

NOTE Confidence: 0.862062811851501

00:20:36.600 --> 00:20:38.036 Maybe the year 2.

NOTE Confidence: 0.862062811851501

00:20:38.036 --> 00:20:40.557 So finally the last five minutes I

NOTE Confidence: 0.862062811851501

00:20:40.557 --> 00:20:42.853 wanna spend on an idea that we kind

NOTE Confidence: 0.862062811851501

00:20:42.853 --> 00:20:45.376 of stumbled upon off awhile back.

NOTE Confidence: 0.862062811851501

00:20:45.380 --> 00:20:46.950 This is not our paper,

NOTE Confidence: 0.862062811851501

00:20:46.950 --> 00:20:49.054 it's the people from nature of it shows

NOTE Confidence: 0.862062811851501

00:20:49.054 --> 00:20:51.031 you the distribution of different sort

NOTE Confidence: 0.862062811851501

00:20:51.031 --> 00:20:53.570 of mutations in large cities of Kansas.

NOTE Confidence: 0.862062811851501

00:20:53.570 --> 00:20:55.568 So the striking thing about this

NOTE Confidence: 0.862062811851501

00:20:55.568 --> 00:20:57.986 is that there are these set of

NOTE Confidence: 0.862062811851501

00:20:57.986 --> 00:21:00.020 jeans that affected more than 65

NOTE Confidence: 0.862062811851501

00:21:00.020 --> 00:21:02.300 cases out of close to 3000 Kansas.

NOTE Confidence: 0.862062811851501

00:21:02.300 --> 00:21:04.580 And even in this sort of very modern

NOTE Confidence: 0.862062811851501

00:21:04.580 --> 00:21:06.669 and high sort of accuracy study,

NOTE Confidence: 0.862062811851501

00:21:06.670 --> 00:21:08.225 about 9% of Kansas said

NOTE Confidence: 0.862062811851501

00:21:08.225 --> 00:21:09.158 no driver alterations.

NOTE Confidence: 0.862062811851501

00:21:09.160 --> 00:21:11.344 English challenge you to think about anyway.

NOTE Confidence: 0.862062811851501

00:21:11.350 --> 00:21:14.090 What you think you mean by a driver, Jean.

NOTE Confidence: 0.862062811851501

00:21:14.090 --> 00:21:15.590 So is it a statistical construct

NOTE Confidence: 0.862062811851501

00:21:15.590 --> 00:21:17.245 from any sort of statisticians

NOTE Confidence: 0.862062811851501

00:21:17.245 --> 00:21:18.517 in computational biologist?

NOTE Confidence: 0.862062811851501

00:21:18.520 --> 00:21:20.398 It is actually a statistical construct,

NOTE Confidence: 0.862062811851501

00:21:20.400 --> 00:21:22.672 but of course many of you think about

NOTE Confidence: 0.862062811851501

00:21:22.672 --> 00:21:25.079 this is gene that caused the cancer.

NOTE Confidence: 0.862062811851501

00:21:25.080 --> 00:21:27.740 The way I think about this is

NOTE Confidence: 0.862062811851501

00:21:27.740 --> 00:21:30.310 actually it's just a narrative tool.

NOTE Confidence: 0.862062811851501

00:21:30.310 --> 00:21:32.090 To kill a good story.

NOTE Confidence: 0.862062811851501

00:21:32.090 --> 00:21:34.474 So this is actually from the same paper

NOTE Confidence: 0.862062811851501

00:21:34.474 --> 00:21:37.058 from but from the supplementary figures,

NOTE Confidence: 0.862062811851501

00:21:37.060 --> 00:21:38.950 but it shows you the enormous amount

NOTE Confidence: 0.862062811851501

00:21:38.950 --> 00:21:40.687 of model of Genomic abnormalities

NOTE Confidence: 0.862062811851501

00:21:40.687 --> 00:21:42.419 that any particular cancer

NOTE Confidence: 0.862062811851501

00:21:42.419 --> 00:21:44.151 has so retro transpositions,

NOTE Confidence: 0.862062811851501

00:21:44.160 --> 00:21:46.638 a few dozen number of structural variants,

NOTE Confidence: 0.862062811851501

00:21:46.640 --> 00:21:48.770 several dozen to several, several 1000.

NOTE Confidence: 0.862062811851501

00:21:48.770 --> 00:21:51.458 So these are big chunks of the DNA

NOTE Confidence: 0.862062811851501

00:21:51.458 --> 00:21:53.154 chromosomes missing very larger than

NOTE Confidence: 0.862062811851501

00:21:53.154 --> 00:21:55.869 the thousands of in Dallas and 10s of

NOTE Confidence: 0.862062811851501

00:21:55.869 --> 00:21:57.999 thousands of single included variance.

NOTE Confidence: 0.862062811851501

00:21:58.000 --> 00:21:58.355 Incidentally,

NOTE Confidence: 0.862062811851501

00:21:58.355 --> 00:22:01.195 you also see this actually in the CIS,

NOTE Confidence: 0.862062811851501

00:22:01.200 --> 00:22:02.970 which is a premalignant lesion,

NOTE Confidence: 0.862062811851501

00:22:02.970 --> 00:22:04.780 so these services, all the.

NOTE Confidence: 0.862062811851501

00:22:04.780 --> 00:22:05.138 Well,

NOTE Confidence: 0.862062811851501

00:22:05.138 --> 00:22:06.570 marks off of cancer,

NOTE Confidence: 0.862062811851501

00:22:06.570 --> 00:22:08.360 except it's not really cancer,

NOTE Confidence: 0.862062811851501

00:22:08.360 --> 00:22:11.616 but it has the same B 53 mutations

NOTE Confidence: 0.862062811851501

00:22:11.616 --> 00:22:12.830 clarifications or not.

NOTE Confidence: 0.862062811851501

00:22:12.830 --> 00:22:14.874 Just the game keeps you big pools,

NOTE Confidence: 0.862062811851501

00:22:14.880 --> 00:22:15.873 better weather really.

NOTE Confidence: 0.862062811851501

00:22:15.873 --> 00:22:17.859 The function of this these jeans

NOTE Confidence: 0.862062811851501

00:22:17.859 --> 00:22:19.876 and then the individual jeans is.

NOTE Confidence: 0.862062811851501

00:22:19.880 --> 00:22:21.735 So this is a people that many

NOTE Confidence: 0.862062811851501

00:22:21.735 --> 00:22:23.738 years ago we did nearby Sunday.

NOTE Confidence: 0.862062811851501

00:22:23.740 --> 00:22:26.116 She was that he was a medical student.

NOTE Confidence: 0.862062811851501

00:22:26.120 --> 00:22:26.672 That year.

NOTE Confidence: 0.862062811851501

00:22:26.672 --> 00:22:28.604 Now is a faculty at Sloan Kettering

NOTE Confidence: 0.862062811851501

00:22:28.604 --> 00:22:30.634 and what I want to illustrate here

NOTE Confidence: 0.862062811851501

00:22:30.634 --> 00:22:32.462 is that every single cancer which

NOTE Confidence: 0.862062811851501

00:22:32.462 --> 00:22:34.709 is a column as really a different

NOTE Confidence: 0.862062811851501

00:22:34.709 --> 00:22:35.624 combination of abnormalities.

NOTE Confidence: 0.862062811851501

00:22:35.624 --> 00:22:38.000 So if you think about it that way,

NOTE Confidence: 0.862062811851501

00:22:38.000 --> 00:22:39.480 maybe it's really the reason.

NOTE Confidence: 0.886608481407166

00:22:39.480 --> 00:22:41.256 Why cancel the have different layers?

NOTE Confidence: 0.886608481407166

00:22:41.260 --> 00:22:42.745 Because because of this combinatorial

NOTE Confidence: 0.886608481407166

00:22:42.745 --> 00:22:43.933 difference that they have.

NOTE Confidence: 0.886608481407166

00:22:43.940 --> 00:22:45.848 So if each of these contributes

NOTE Confidence: 0.886608481407166

00:22:45.848 --> 00:22:48.069 something then their net effect is

NOTE Confidence: 0.886608481407166

00:22:48.069 --> 00:22:49.849 really really heterogeneous behavior.

NOTE Confidence: 0.886608481407166

00:22:49.850 --> 00:22:52.106 But maybe it's even more interesting.

NOTE Confidence: 0.886608481407166

00:22:52.110 --> 00:22:54.648 Is this work with DVR? She was.

NOTE Confidence: 0.886608481407166

00:22:54.648 --> 00:22:56.916 The students at that time at Yale

NOTE Confidence: 0.886608481407166

00:22:56.916 --> 00:22:59.510 and now it's a medical student pad.

NOTE Confidence: 0.886608481407166

00:22:59.510 --> 00:23:01.382 You sequence all the human kindness

NOTE Confidence: 0.886608481407166

00:23:01.382 --> 00:23:03.570 ease in 90 two breast cancer,

NOTE Confidence: 0.886608481407166

00:23:03.570 --> 00:23:05.950 only to see whether there are any.

NOTE Confidence: 0.886608481407166

00:23:05.950 --> 00:23:08.008 Lowering additional kindness is that it?

NOTE Confidence: 0.886608481407166

00:23:08.010 --> 00:23:09.798 I guess we didn't find any,

NOTE Confidence: 0.886608481407166

00:23:09.800 --> 00:23:11.100 but we really observe though

NOTE Confidence: 0.886608481407166

00:23:11.100 --> 00:23:13.150 is that there is a very large

NOTE Confidence: 0.886608481407166

00:23:13.150 --> 00:23:14.885 number of high functional impact.

NOTE Confidence: 0.886608481407166

00:23:14.890 --> 00:23:17.698 Variance in kindness is bigger germline.

NOTE Confidence: 0.886608481407166

00:23:17.700 --> 00:23:19.870 I'm still think about for a second,

NOTE Confidence: 0.886608481407166

00:23:19.870 --> 00:23:22.003 so you actually carry a bunch of germ line

NOTE Confidence: 0.886608481407166

00:23:22.003 --> 00:23:24.516 so the mutations that inactivator overactive.

NOTE Confidence: 0.886608481407166

00:23:24.520 --> 00:23:27.000 It kinda seems like PSC kinase or whatnot.

NOTE Confidence: 0.886608481407166

00:23:27.000 --> 00:23:29.510 So what does it mean?

NOTE Confidence: 0.886608481407166

00:23:29.510 --> 00:23:32.198 So please give us this idea

NOTE Confidence: 0.886608481407166

00:23:32.198 --> 00:23:33.990 that maybe it's really.

NOTE Confidence: 0.886608481407166

00:23:33.990 --> 00:23:35.700 He just focused too narrowly

NOTE Confidence: 0.886608481407166

00:23:35.700 --> 00:23:36.726 on driver mutations,

NOTE Confidence: 0.886608481407166

00:23:36.730 --> 00:23:39.817 which are only four of five in a cancel.

NOTE Confidence: 0.886608481407166

00:23:39.820 --> 00:23:41.794 What actually would be probably also

NOTE Confidence: 0.886608481407166

00:23:41.794 --> 00:23:44.049 helpful is to look at the context

NOTE Confidence: 0.886608481407166

00:23:44.049 --> 00:23:45.807 in which this is happening and

NOTE Confidence: 0.886608481407166

00:23:45.807 --> 00:23:47.738 the constant Israeli hundreds of

NOTE Confidence: 0.886608481407166

00:23:47.738 --> 00:23:50.102 additional variants that come in from

NOTE Confidence: 0.886608481407166

00:23:50.110 --> 00:23:53.246 the somatic or the germ line angle.

NOTE Confidence: 0.886608481407166

00:23:53.250 --> 00:23:55.416 So he proposed this idea that

NOTE Confidence: 0.886608481407166

00:23:55.416 --> 00:23:56.860 really functional German variance,

NOTE Confidence: 0.886608481407166

00:23:56.860 --> 00:23:59.026 conkle, jeans and it's the totality

NOTE Confidence: 0.886608481407166

00:23:59.026 --> 00:24:00.470 of the functional impact.

NOTE Confidence: 0.886608481407166

00:24:00.470 --> 00:24:01.914 High functional impact German

NOTE Confidence: 0.886608481407166

00:24:01.914 --> 00:24:03.719 variants in cancer Lady Jeans.

NOTE Confidence: 0.886608481407166

00:24:03.720 --> 00:24:05.886 They could actually determine cancer risk.

NOTE Confidence: 0.886608481407166

00:24:05.890 --> 00:24:07.732 So we know that there are

NOTE Confidence: 0.886608481407166

00:24:07.732 --> 00:24:09.860 a few very high penetrance.

NOTE Confidence: 0.886608481407166

00:24:09.860 --> 00:24:11.660 Cancer is chains like Bronco,

NOTE Confidence: 0.886608481407166

00:24:11.660 --> 00:24:13.802 but it's really is the minority

NOTE Confidence: 0.886608481407166

00:24:13.802 --> 00:24:15.989 women who carry this even very,

NOTE Confidence: 0.886608481407166

00:24:15.990 --> 00:24:17.434 very strong family history.

NOTE Confidence: 0.886608481407166

00:24:17.434 --> 00:24:19.600 So what's accounts for dismissing heredity?

NOTE Confidence: 0.886608481407166

00:24:19.600 --> 00:24:21.814 You think it's the totality of

NOTE Confidence: 0.886608481407166

00:24:21.814 --> 00:24:23.620 the defects that actually are.

NOTE Confidence: 0.886608481407166

00:24:23.620 --> 00:24:26.470 Embedded in a whole lot of

NOTE Confidence: 0.886608481407166

00:24:26.470 --> 00:24:28.370 individually non sort of.

NOTE Confidence: 0.886608481407166

00:24:28.370 --> 00:24:29.687 Cannot translate that.

NOTE Confidence: 0.886608481407166

00:24:29.687 --> 00:24:32.760 And then the next iteration of this,

NOTE Confidence: 0.886608481407166

00:24:32.760 --> 00:24:34.530 that's really the combined effect

NOTE Confidence: 0.886608481407166

00:24:34.530 --> 00:24:36.756 of the germline and somatic events

NOTE Confidence: 0.886608481407166

00:24:36.756 --> 00:24:39.090 that really lead to the malignant

NOTE Confidence: 0.886608481407166

00:24:39.090 --> 00:24:41.138 transformation rather than a few

NOTE Confidence: 0.886608481407166

00:24:41.138 --> 00:24:42.359 individually dramatic effect.

NOTE Confidence: 0.886608481407166

00:24:42.360 --> 00:24:44.514 And it's a project that talking

NOTE Confidence: 0.886608481407166

00:24:44.514 --> 00:24:46.845 is pursuing in my lap towers

NOTE Confidence: 0.886608481407166

00:24:46.845 --> 00:24:48.885 visiting post doc from from.

NOTE Confidence: 0.886608481407166

00:24:48.890 --> 00:24:51.738 And that is so if it's really true,

NOTE Confidence: 0.886608481407166

00:24:51.740 --> 00:24:54.169 then we would expect that woman who

NOTE Confidence: 0.886608481407166

00:24:54.169 --> 00:24:56.245 developed cancer the younger age will

NOTE Confidence: 0.886608481407166

00:24:56.245 --> 00:24:58.499 have a lot more sort of deleterious

NOTE Confidence: 0.886608481407166

00:24:58.570 --> 00:25:00.880 germline events in cancer jeans then

NOTE Confidence: 0.886608481407166

00:25:00.880 --> 00:25:03.156 people who develop cancer the later

NOTE Confidence: 0.886608481407166

00:25:03.156 --> 00:25:04.996 age because it's ultimately the

NOTE Confidence: 0.886608481407166

00:25:04.996 --> 00:25:07.175 combined effect of the acquired and

NOTE Confidence: 0.886608481407166

00:25:07.175 --> 00:25:09.534 the inborn errors that lead to Kansas.

NOTE Confidence: 0.886608481407166

00:25:09.540 --> 00:25:11.878 So if you are born with a

NOTE Confidence: 0.886608481407166

00:25:11.878 --> 00:25:14.170 lot of errors to start with,

NOTE Confidence: 0.886608481407166

00:25:14.170 --> 00:25:16.738 it gonna take a fewer or shorter time

NOTE Confidence: 0.886608481407166

00:25:16.738 --> 00:25:19.580 to get to reach this critical level.

NOTE Confidence: 0.886608481407166

00:25:19.580 --> 00:25:20.582 And long, behold,

NOTE Confidence: 0.886608481407166

00:25:20.582 --> 00:25:22.920 that's exactly what he observed in a

NOTE Confidence: 0.886608481407166

00:25:22.988 --> 00:25:25.212 bunch of large series like that ECA or

NOTE Confidence: 0.886608481407166

00:25:25.212 --> 00:25:27.913 the UK biobank and now just published

NOTE Confidence: 0.886608481407166

00:25:27.913 --> 00:25:29.988 this paper in Nature Communications.

NOTE Confidence: 0.886608481407166

00:25:29.990 --> 00:25:32.942 I want to just point out to you because

NOTE Confidence: 0.886608481407166

00:25:32.942 --> 00:25:35.885 time is short on this very last figure,

NOTE Confidence: 0.886608481407166

00:25:35.890 --> 00:25:37.620 which is the the comparison,

NOTE Confidence: 0.886608481407166

00:25:37.620 --> 00:25:39.000 the relationship between the

NOTE Confidence: 0.886608481407166

00:25:39.000 --> 00:25:41.070 mutation than in the cancer versus

NOTE Confidence: 0.870644629001617

00:25:41.132 --> 00:25:42.644 the variant, the German

NOTE Confidence: 0.870644629001617

00:25:42.644 --> 00:25:44.779 variant burden by age groups.

NOTE Confidence: 0.870644629001617

00:25:44.780 --> 00:25:49.082 So he he means younger than 30 and the

NOTE Confidence: 0.870644629001617

00:25:49.082 --> 00:25:53.147 other advocating speak louder than 80.

NOTE Confidence: 0.870644629001617

00:25:53.150 --> 00:25:55.316 The installation ship is actually remarkable,

NOTE Confidence: 0.870644629001617

00:25:55.320 --> 00:25:57.742 so yo patience young who are who

NOTE Confidence: 0.870644629001617

00:25:57.742 --> 00:26:00.271 have cancer at a younger age and

NOTE Confidence: 0.870644629001617

00:26:00.271 --> 00:26:02.839 it's it across all the cancers that

NOTE Confidence: 0.870644629001617

00:26:02.839 --> 00:26:05.415 letter TCG ahead or the UK biobank.

NOTE Confidence: 0.870644629001617

00:26:05.420 --> 00:26:07.947 We also get consider the 30s, forties,

NOTE Confidence: 0.870644629001617

00:26:07.947 --> 00:26:10.089 50s have a much higher germline

NOTE Confidence: 0.870644629001617

00:26:10.089 --> 00:26:12.278 variant burden in cancer Lee jeans,

NOTE Confidence: 0.870644629001617

00:26:12.280 --> 00:26:15.890 and this is like 5 or 6 only jeans then.

NOTE Confidence: 0.870644629001617

00:26:15.890 --> 00:26:18.172 Then people who get cancer the older

NOTE Confidence: 0.870644629001617

00:26:18.172 --> 00:26:20.689 age and on the other hand most

NOTE Confidence: 0.870644629001617

00:26:20.689 --> 00:26:22.891 folks have a much higher mutation

NOTE Confidence: 0.870644629001617

00:26:22.968 --> 00:26:24.978 somatic mutation so they can.

NOTE Confidence: 0.870644629001617

00:26:24.980 --> 00:26:27.269 So so then that led to us

NOTE Confidence: 0.870644629001617

00:26:27.269 --> 00:26:28.939 another idea that So what?

NOTE Confidence: 0.870644629001617

00:26:28.940 --> 00:26:31.580 Actually the cancer jeans are in this thing?

NOTE Confidence: 0.870644629001617

00:26:31.580 --> 00:26:33.506 That it's probably a lot broader

NOTE Confidence: 0.870644629001617

00:26:33.506 --> 00:26:35.185 sort of repertoire then then

NOTE Confidence: 0.870644629001617

00:26:35.185 --> 00:26:36.855 no one Canonical cancel jeans.

NOTE Confidence: 0.870644629001617

00:26:36.860 --> 00:26:39.786 So you could think that this study?

NOTE Confidence: 0.870644629001617

00:26:39.790 --> 00:26:40.537 The Dom Hussein,

NOTE Confidence: 0.870644629001617

00:26:40.537 --> 00:26:42.280 who is a PhD student in the

NOTE Confidence: 0.870644629001617

00:26:42.341 --> 00:26:43.925 computational biology program and

NOTE Confidence: 0.870644629001617

00:26:43.925 --> 00:26:46.301 supervised by Mian Mar Gerstein too.

NOTE Confidence: 0.870644629001617

00:26:46.310 --> 00:26:48.585 So how many jeans are actually connected,

NOTE Confidence: 0.870644629001617

00:26:48.590 --> 00:26:50.654 one step or two step or three step

NOTE Confidence: 0.870644629001617

00:26:50.654 --> 00:26:52.783 away in a pretty important interaction

NOTE Confidence: 0.870644629001617

00:26:52.783 --> 00:26:55.105 network from from a cancer gene.

NOTE Confidence: 0.870644629001617

00:26:55.110 --> 00:26:57.718 So if they are immediately next to it,

NOTE Confidence: 0.870644629001617

00:26:57.720 --> 00:26:59.020 then they probably influence

NOTE Confidence: 0.870644629001617

00:26:59.020 --> 00:27:00.645 the affective for cancer gene.

NOTE Confidence: 0.870644629001617

00:27:00.650 --> 00:27:02.280 If they're two step removed,

NOTE Confidence: 0.870644629001617

00:27:02.280 --> 00:27:04.236 they still probably influence over less,

NOTE Confidence: 0.870644629001617

00:27:04.240 --> 00:27:07.175 so there actually a whole lot of jeans, but.

NOTE Confidence: 0.870644629001617

00:27:07.175 --> 00:27:09.125 Half of all human jeans are

NOTE Confidence: 0.870644629001617

00:27:09.125 --> 00:27:09.775 actually connected.

NOTE Confidence: 0.870644629001617

00:27:09.780 --> 00:27:11.718 One or two steps away from

NOTE Confidence: 0.870644629001617

00:27:11.718 --> 00:27:13.010 from cancer hub gene.

NOTE Confidence: 0.870644629001617

00:27:13.010 --> 00:27:15.594 Most of these are not implicated in cancer,

NOTE Confidence: 0.870644629001617

00:27:15.600 --> 00:27:18.328 and if you look at their sort of

NOTE Confidence: 0.870644629001617

00:27:18.328 --> 00:27:19.947 functional importance in this gap

NOTE Confidence: 0.870644629001617

00:27:19.947 --> 00:27:21.977 database and it turns out that the

NOTE Confidence: 0.870644629001617

00:27:22.048 --> 00:27:24.640 further away you get from the cancer hub,

NOTE Confidence: 0.870644629001617

00:27:24.640 --> 00:27:26.782 the less important they seem to be

NOTE Confidence: 0.870644629001617

00:27:26.782 --> 00:27:29.090 in survival in the depth map data

NOTE Confidence: 0.870644629001617

00:27:29.090 --> 00:27:31.076 which supports the idea that there

NOTE Confidence: 0.870644629001617

00:27:31.142 --> 00:27:33.050 are lot more jeans involved in

NOTE Confidence: 0.870644629001617

00:27:33.050 --> 00:27:35.308 cancer than what you think you see

NOTE Confidence: 0.870644629001617

00:27:35.308 --> 00:27:37.590 the same when you look at weather.

NOTE Confidence: 0.870644629001617

00:27:37.590 --> 00:27:39.970 There is an evolutionary pressure to to

NOTE Confidence: 0.870644629001617

00:27:39.970 --> 00:27:41.779 preserve truncating mutations in these jeans,

NOTE Confidence: 0.870644629001617

00:27:41.780 --> 00:27:43.390 and again the further away.

NOTE Confidence: 0.870644629001617

00:27:43.390 --> 00:27:45.371 So the jeans which are one Step

NOTE Confidence: 0.870644629001617

00:27:45.371 --> 00:27:47.496 2 step three step away from a

NOTE Confidence: 0.870644629001617

00:27:47.496 --> 00:27:49.746 concert Hall gene and less and less

NOTE Confidence: 0.870644629001617

00:27:49.746 --> 00:27:51.581 evolutionary pressure on them into

NOTE Confidence: 0.870644629001617

00:27:51.581 --> 00:27:53.810 four through 4 to exclude truncations.

NOTE Confidence: 0.870644629001617

00:27:53.810 --> 00:27:56.090 And it was so carry actually

NOTE Confidence: 0.870644629001617

00:27:56.090 --> 00:27:58.490 somatic mutations. So that's.

NOTE Confidence: 0.859965562820435

00:28:01.910 --> 00:28:03.890 Personalized sort of Jim Langley scored.

NOTE Confidence: 0.859965562820435

00:28:03.890 --> 00:28:06.067 That's sums up all these effects that

NOTE Confidence: 0.859965562820435

00:28:06.067 --> 00:28:08.179 people are born with cancer chains,

NOTE Confidence: 0.859965562820435

00:28:08.180 --> 00:28:09.825 and that's a project that

NOTE Confidence: 0.859965562820435

00:28:09.825 --> 00:28:11.810 that we actually got to ask.

NOTE Confidence: 0.859965562820435

00:28:11.810 --> 00:28:13.130 Or young investigator award

NOTE Confidence: 0.859965562820435

00:28:13.130 --> 00:28:14.780 to pursue together with cow.

NOTE Confidence: 0.859965562820435

00:28:14.780 --> 00:28:16.430 And we say this too

NOTE Confidence: 0.859965562820435

00:28:16.430 --> 00:28:17.750 gruesome pictures out here.

NOTE Confidence: 0.859965562820435

00:28:17.750 --> 00:28:19.400 Just remind you guys that

NOTE Confidence: 0.859965562820435

00:28:19.400 --> 00:28:21.050 this is how airplanes crash.

NOTE Confidence: 0.859965562820435

00:28:21.050 --> 00:28:22.880 They actually don't crash because

NOTE Confidence: 0.859965562820435

00:28:22.880 --> 00:28:24.710 there is a statistically significant

NOTE Confidence: 0.859965562820435

00:28:24.769 --> 00:28:26.491 losses of the wings or the engines

NOTE Confidence: 0.859965562820435

00:28:26.491 --> 00:28:28.381 or not every single plane crashes

NOTE Confidence: 0.859965562820435

00:28:28.381 --> 00:28:30.211 caused by a different combination

NOTE Confidence: 0.859965562820435

00:28:30.211 --> 00:28:31.560 of individually nonlethal events.

NOTE Confidence: 0.859965562820435

00:28:31.560 --> 00:28:34.000 So they fall into groups like human error,

NOTE Confidence: 0.859965562820435

00:28:34.000 --> 00:28:35.180 which is almost always there,

NOTE Confidence: 0.859965562820435

00:28:35.180 --> 00:28:36.818 but it's not the same human error.

NOTE Confidence: 0.859965562820435

00:28:36.820 --> 00:28:38.465 It's a different kind of human error.

NOTE Confidence: 0.859965562820435

00:28:38.470 --> 00:28:39.880 There's always some kind of a

NOTE Confidence: 0.859965562820435

00:28:39.880 --> 00:28:40.820 mechanical or instrumental failure,

NOTE Confidence: 0.859965562820435

00:28:40.820 --> 00:28:43.460 but it's never the same instrument.

NOTE Confidence: 0.859965562820435

00:28:43.460 --> 00:28:45.160 So that's my final slide,

NOTE Confidence: 0.859965562820435

00:28:45.160 --> 00:28:47.200 really studying the new micro environment.

NOTE Confidence: 0.859965562820435

00:28:47.200 --> 00:28:49.118 Let us to some some useful ideas

NOTE Confidence: 0.859965562820435

00:28:49.118 --> 00:28:50.791 about clinical trials are very

NOTE Confidence: 0.859965562820435

00:28:50.791 --> 00:28:52.391 excited about exploring metabolic

NOTE Confidence: 0.859965562820435

00:28:52.391 --> 00:28:53.991 adaptations for therapeutic targets,

NOTE Confidence: 0.859965562820435

00:28:54.000 --> 00:28:56.320 and we submitted the DOD grant with this

NOTE Confidence: 0.859965562820435

00:28:56.320 --> 00:28:58.759 with a group of other investigators,

NOTE Confidence: 0.859965562820435

00:28:58.760 --> 00:29:01.016 and I think I really think that the

NOTE Confidence: 0.859965562820435

00:29:01.016 --> 00:29:02.840 universe is functionally cancel.

NOTE Confidence: 0.859965562820435

00:29:02.840 --> 00:29:04.694 Event chains is much larger than

NOTE Confidence: 0.859965562820435

00:29:04.694 --> 00:29:06.919 we think it is interested in.

NOTE Confidence: 0.859965562820435

00:29:06.920 --> 00:29:09.496 More stuff at the bottom of the

NOTE Confidence: 0.859965562820435

00:29:09.496 --> 00:29:11.926 slide shows takes you through the

NOTE Confidence: 0.859965562820435

00:29:11.926 --> 00:29:14.428 list of publications by our group.

NOTE Confidence: 0.859965562820435

00:29:14.430 --> 00:29:18.438 So thank you, and this is my lab.

NOTE Confidence: 0.859965562820435

00:29:18.440 --> 00:29:19.070 Each other.

NOTE Confidence: 0.893206596374512

00:29:21.130 --> 00:29:22.228 Wow, thank you.

NOTE Confidence: 0.893206596374512

00:29:22.228 --> 00:29:24.424 That was a an impressive array

NOTE Confidence: 0.893206596374512

00:29:24.424 --> 00:29:26.590 of work on so many fronts.

NOTE Confidence: 0.893206596374512

00:29:26.590 --> 00:29:28.768 And congratulations on all of it.

NOTE Confidence: 0.893206596374512

00:29:28.770 --> 00:29:32.046 I know where we're a little late on time,

NOTE Confidence: 0.893206596374512

00:29:32.050 --> 00:29:34.954 so let me just offer up one question.

NOTE Confidence: 0.893206596374512

00:29:34.960 --> 00:29:37.150 You know? I think you oppose.

NOTE Confidence: 0.893206596374512

00:29:37.150 --> 00:29:39.118 Obviously a very good case that

NOTE Confidence: 0.893206596374512

00:29:39.118 --> 00:29:40.905 it's a combination of germline

NOTE Confidence: 0.893206596374512

00:29:40.905 --> 00:29:42.965 asmatic events and I'm curious,

NOTE Confidence: 0.893206596374512

00:29:42.970 --> 00:29:45.518 do you think breast is is different?

NOTE Confidence: 0.893206596374512

00:29:45.520 --> 00:29:47.740 Breast cancer is different than other

NOTE Confidence: 0.893206596374512

00:29:47.740 --> 00:29:49.670 solid to malignancy's because obviously

NOTE Confidence: 0.893206596374512

00:29:49.670 --> 00:29:51.645 germline and semantic events are.

NOTE Confidence: 0.893206596374512

00:29:51.650 --> 00:29:52.278 Install cancers,

NOTE Confidence: 0.893206596374512

00:29:52.278 --> 00:29:53.848 but you think breast is

NOTE Confidence: 0.893206596374512

00:29:53.848 --> 00:29:55.240 somehow different that respect.

NOTE Confidence: 0.859023571014404

00:29:55.240 --> 00:29:57.840 Yes, it's different. It's a matter of fact,

NOTE Confidence: 0.859023571014404

00:29:57.840 --> 00:30:00.031 so you can group really Kansas even

NOTE Confidence: 0.859023571014404

00:30:00.031 --> 00:30:02.641 in this paper that that I refer to

NOTE Confidence: 0.859023571014404

00:30:02.641 --> 00:30:04.690 be looked at different cancer types,

NOTE Confidence: 0.859023571014404

00:30:04.690 --> 00:30:06.818 and this Association starts to fall apart

NOTE Confidence: 0.859023571014404

00:30:06.818 --> 00:30:09.497 in Kansas that actually have a very high

NOTE Confidence: 0.859023571014404

00:30:09.497 --> 00:30:11.499 environments or customer on exposure, right?

NOTE Confidence: 0.859023571014404

00:30:11.499 --> 00:30:13.233 Because that in this sort of

NOTE Confidence: 0.859023571014404

00:30:13.233 --> 00:30:15.119 message of this new relationship.

NOTE Confidence: 0.859023571014404

00:30:15.120 --> 00:30:17.076 So this relationship is less strong

NOTE Confidence: 0.859023571014404

00:30:17.076 --> 00:30:18.710 in lung cancer, bladder cancer,

NOTE Confidence: 0.859023571014404

00:30:18.710 --> 00:30:20.010 and some other cancers.

NOTE Confidence: 0.859023571014404

00:30:20.010 --> 00:30:22.622 So the real picture of course, is nuance.

NOTE Confidence: 0.859023571014404

00:30:22.622 --> 00:30:23.926 It's much more nuanced.

NOTE Confidence: 0.859023571014404

00:30:23.930 --> 00:30:25.294 And the same way.

NOTE Confidence: 0.859023571014404

00:30:25.294 --> 00:30:28.124 So the jeans we chat important so the

NOTE Confidence: 0.859023571014404

00:30:28.124 --> 00:30:30.609 cancer gene is probably also vary from

NOTE Confidence: 0.859023571014404

00:30:30.609 --> 00:30:33.029 some tissue types of tissue type.

NOTE Confidence: 0.859023571014404

00:30:33.030 --> 00:30:34.395 So these are the refinements

NOTE Confidence: 0.859023571014404

00:30:34.395 --> 00:30:35.960 that we are actually working on.

NOTE Confidence: 0.859023571014404

00:30:35.960 --> 00:30:38.112 Is just that I wanted to give you

NOTE Confidence: 0.859023571014404

00:30:38.112 --> 00:30:39.948 a repertoire of things that we do,

NOTE Confidence: 0.859023571014404

00:30:39.950 --> 00:30:41.570 but that's exactly what we actually

NOTE Confidence: 0.859023571014404

00:30:41.570 --> 00:30:43.139 addressing in this project right now.

NOTE Confidence: 0.900047183036804

00:30:44.120 --> 00:30:46.184 Thank you and I know just for time

NOTE Confidence: 0.900047183036804

00:30:46.184 --> 00:30:47.746 will will move on, but obviously

NOTE Confidence: 0.900047183036804

00:30:47.746 --> 00:30:49.552 folks can certainly email allow us to.