WEBVTT

00:00:05.570 --> 00:00:09.665 OK, well it's 1232. Let's get started.

00:00:09.670 --> 00:00:12.268 Welcome everyone to pathology grand rounds.

00:00:12.270 --> 00:00:16.239 It is my distinct pleasure to introduce

00:00:16.239 --> 00:00:20.450 my good friend Bob Anders to the group.

00:00:20.450 --> 00:00:24.296 Today. Very excited about his lecture.

00:00:24.300 --> 00:00:27.762 Doctor Anders earned his medical and

00:00:27.762 --> 00:00:31.111 molecular biology graduate degrees at the

00:00:31.111 --> 00:00:33.973 Mayo Clinic Medical and Graduate School.

00:00:33.980 --> 00:00:36.941 He then completed his anatomic and clinical

00:00:36.941 --> 00:00:39.713 pathology residency and a fellowship in

00:00:39.713 --> 00:00:41.625 gastrointestinal and liver pathology.

00:00:41.630 --> 00:00:45.030 And postdoctoral training in immunology

00:00:45.030 --> 00:00:47.340 at the University of Chicago.

00:00:47.340 --> 00:00:49.836 With our good friend John Hart.

NOTE Confidence: 0.937411687142857

00:00:49.840 --> 00:00:52.234 He joined the faculty at Johns Hopkins

NOTE Confidence: 0.937411687142857

00:00:52.234 --> 00:00:55.000 School of Medicine in 2005 as an

NOTE Confidence: 0.937411687142857

00:00:55.000 --> 00:00:58.120 assistant professor in the Division of

NOTE Confidence: 0.937411687142857

00:00:58.120 --> 00:01:00.355 Gastrointestinal and Liver Pathology and

NOTE Confidence: 0.937411687142857

00:01:00.355 --> 00:01:03.840 is soon to be full professor in that lab.

NOTE Confidence: 0.937411687142857

00:01:03.840 --> 00:01:06.934 He also serves as the Co director of

NOTE Confidence: 0.937411687142857

00:01:06.934 --> 00:01:08.690 the tumor microenvironment laboratory

NOTE Confidence: 0.937411687142857

00:01:08.690 --> 00:01:11.070 in the Bloomberg Kimmel Institute

NOTE Confidence: 0.937411687142857

00:01:11.070 --> 00:01:12.974 for Immune Cancer Therapy.

NOTE Confidence: 0.937411687142857

00:01:12.980 --> 00:01:15.476 But in addition to his duties as a

NOTE Confidence: 0.937411687142857

00:01:15.476 --> 00:01:17.920 practicing GI liver surgical pathologist,

NOTE Confidence: 0.937411687142857

00:01:17.920 --> 00:01:20.755 a Bob is one of those rare breeds of

NOTE Confidence: 0.937411687142857

00:01:20.755 --> 00:01:23.047 diagnostic pathologists who runs an

NOTE Confidence: 0.937411687142857

00:01:23.047 --> 00:01:24.951 independently funded research lab

NOTE Confidence: 0.937411687142857

00:01:24.951 --> 00:01:27.318 that focuses on tumor immunology.

00:01:27.320 --> 00:01:29.600 His interest in immunology developed while

00:01:29.600 --> 00:01:32.036 he was studying liver immunology and

00:01:32.036 --> 00:01:34.580 regeneration at the University of Chicago.

00:01:34.580 --> 00:01:37.276 And in his early years at Johns Hopkins,

00:01:37.280 --> 00:01:39.084 his current interests are

00:01:39.084 --> 00:01:40.437 in tumor immunology,

00:01:40.440 --> 00:01:42.216 and specifically interrogating the

00:01:42.216 --> 00:01:44.436 immune microenvironment in tumor tissue.

00:01:44.440 --> 00:01:47.340 Obviously a very hot topic.

00:01:47.340 --> 00:01:50.161 He first began examining human tissue for

00:01:50.161 --> 00:01:52.807 the expression of our good friend PD1,

00:01:52.810 --> 00:01:55.480 and PDL one in 2006.

00:01:55.480 --> 00:01:57.382 At the encouragement of his K

00:01:57.382 --> 00:01:59.020 8 mentor doctor Liping Chen,

00:01:59.020 --> 00:02:00.528 who's currently at Yale.

00:02:00.528 --> 00:02:02.790 And he continues this research on

NOTE Confidence: 0.937411687142857

00:02:02.861 --> 00:02:05.135 human in inhuman and marine cancer.

NOTE Confidence: 0.937411687142857

00:02:05.140 --> 00:02:08.128 I mean analogy using single and

NOTE Confidence: 0.937411687142857

00:02:08.128 --> 00:02:10.120 multi color immunostaining couple

NOTE Confidence: 0.937411687142857

00:02:10.205 --> 00:02:12.197 to digital image analysis.

NOTE Confidence: 0.937411687142857

00:02:12.200 --> 00:02:14.492 In addition to all these accompanying

NOTE Confidence: 0.937411687142857

00:02:14.492 --> 00:02:16.020 this area of interest,

NOTE Confidence: 0.937411687142857

00:02:16.020 --> 00:02:18.360 his CV boast hundreds of publications

NOTE Confidence: 0.937411687142857

00:02:18.360 --> 00:02:20.750 and he is invited to something

NOTE Confidence: 0.937411687142857

00:02:20.750 --> 00:02:22.625 like 50 lectures a year,

NOTE Confidence: 0.937411687142857

00:02:22.630 --> 00:02:26.774 a giving courses and and interacting is very,

NOTE Confidence: 0.937411687142857

00:02:26.780 --> 00:02:30.200 very active and sought after collaborator.

NOTE Confidence: 0.937411687142857

00:02:30.200 --> 00:02:33.086 So really, the model of physician,

NOTE Confidence: 0.937411687142857

00:02:33.090 --> 00:02:35.310 scientist in pathology and I'm

NOTE Confidence: 0.937411687142857

00:02:35.310 --> 00:02:38.209 delighted to welcome you to his

NOTE Confidence: 0.937411687142857

00:02:38.209 --> 00:02:40.585 lecture entitled Immune based

NOTE Confidence: 0.937411687142857

00:02:40.585 --> 00:02:42.367 cancer treatment biomarkers.

NOTE Confidence: 0.937411687142857

00:02:42.370 --> 00:02:44.738 The pathologist's critical role.

NOTE Confidence: 0.937411687142857

00:02:44.740 --> 00:02:45.000 Bob,

NOTE Confidence: 0.937411687142857

00:02:45.000 --> 00:02:45.520 thank you.

NOTE Confidence: 0.640507146666667

00:02:46.170 --> 00:02:48.018 Yeah, thanks Marie,

NOTE Confidence: 0.640507146666667

00:02:48.018 --> 00:02:49.866 that's very generous.

NOTE Confidence: 0.640507146666667

00:02:49.870 --> 00:02:51.151 Introduction that would

NOTE Confidence: 0.640507146666667

00:02:51.151 --> 00:02:52.859 make my parents proud.

NOTE Confidence: 0.640507146666667

00:02:52.860 --> 00:02:56.598 Thanks. So this is a great.

NOTE Confidence: 0.640507146666667

00:02:56.600 --> 00:02:58.890 Time to be a pathologist,

NOTE Confidence: 0.640507146666667

00:02:58.890 --> 00:03:02.978 and that's sort of my my message here.

NOTE Confidence: 0.640507146666667

00:03:02.980 --> 00:03:06.172 So I receive funding and and

NOTE Confidence: 0.640507146666667

00:03:06.172 --> 00:03:08.910 consult for these in these.

NOTE Confidence: 0.89365533625

00:03:13.170 --> 00:03:17.538 Institutions, but it won't affect what I say.

NOTE Confidence: 0.89365533625

00:03:17.540 --> 00:03:20.372 So the plan here is to talk about

NOTE Confidence: 0.89365533625

00:03:20.372 --> 00:03:22.618 biomarkers in cancer or talk

NOTE Confidence: 0.89365533625

00:03:22.618 --> 00:03:24.558 about immune based biomarkers,

NOTE Confidence: 0.89365533625

00:03:24.560 --> 00:03:26.156 and then you know kind of the.

NOTE Confidence: 0.89365533625

00:03:26.160 --> 00:03:29.142 So the story of how DNA

NOTE Confidence: 0.89365533625

00:03:29.142 --> 00:03:30.633 based immune biomarkers.

NOTE Confidence: 0.926997395714286

00:03:33.170 --> 00:03:35.318 Developed and then something

NOTE Confidence: 0.926997395714286

00:03:35.318 --> 00:03:37.734 that shouldn't be, you know,

NOTE Confidence: 0.926997395714286

00:03:37.734 --> 00:03:41.281 foreign to to most of you with the efforts

NOTE Confidence: 0.926997395714286

00:03:41.281 --> 00:03:44.280 of Doctor Shelper and and and Doctor Rim.

NOTE Confidence: 0.926997395714286

00:03:44.280 --> 00:03:46.452 And that's you know how do

NOTE Confidence: 0.926997395714286

00:03:46.452 --> 00:03:47.900 we find new biomarkers?

NOTE Confidence: 0.926997395714286

00:03:47.900 --> 00:03:49.484 So biomarkers it.

NOTE Confidence: 0.926997395714286

00:03:49.484 --> 00:03:52.124 Turns out from the beginning.

NOTE Confidence: 0.926997395714286

00:03:52.130 --> 00:03:54.330 There's confusion.

NOTE Confidence: 0.926997395714286

00:03:54.330 --> 00:03:57.146 So prognostic biomarkers that's

NOTE Confidence: 0.926997395714286

00:03:57.146 --> 00:04:00.666 about how patients will do,

NOTE Confidence: 0.926997395714286

00:04:00.670 --> 00:04:02.024 essentially untreated,

NOTE Confidence: 0.926997395714286

00:04:02.024 --> 00:04:06.086 or with definitive treatment like surgery.

NOTE Confidence: 0.926997395714286

00:04:06.090 --> 00:04:08.691 But most of what we talk about these days

NOTE Confidence: 0.926997395714286

00:04:08.691 --> 00:04:11.550 is is really about predictive biomarkers,

NOTE Confidence: 0.926997395714286

00:04:11.550 --> 00:04:14.568 and that's and that's personalized medicine.

NOTE Confidence: 0.926997395714286

00:04:14.570 --> 00:04:16.500 It's what it's what we've

NOTE Confidence: 0.926997395714286

00:04:16.500 --> 00:04:18.430 wanted for the longest time.

NOTE Confidence: 0.926997395714286

00:04:18.430 --> 00:04:20.719 It's how to select the the patients

NOTE Confidence: 0.926997395714286

00:04:20.719 --> 00:04:23.060 that will benefit from a given therapy.

NOTE Confidence: 0.932919251

00:04:25.400 --> 00:04:27.556 And this is great.

NOTE Confidence: 0.932919251

00:04:27.556 --> 00:04:30.251 This is great for pathologists

NOTE Confidence: 0.932919251

00:04:30.251 --> 00:04:33.145 because you know human human tissue

NOTE Confidence: 0.932919251

00:04:33.145 --> 00:04:35.320 is a prognostic biomarker, right?

NOTE Confidence: 0.859660446363636

00:04:37.550 --> 00:04:42.102 This was so clear even it was even

NOTE Confidence: 0.859660446363636

00:04:42.102 --> 00:04:46.564 clearer to a surgeon back in 1932,

NOTE Confidence: 0.859660446363636

00:04:46.564 --> 00:04:48.950 right with the Dukes classification.

NOTE Confidence: 0.859660446363636

00:04:48.950 --> 00:04:52.850 You know, if a if a colon cancer

NOTE Confidence: 0.859660446363636

00:04:52.850 --> 00:04:55.680 penetrated deeper into a colon.

NOTE Confidence: 0.859660446363636

00:04:55.680 --> 00:04:59.298 The patients didn't do as well.

NOTE Confidence: 0.859660446363636

00:04:59.300 --> 00:05:02.268 Fast forward Banta 2006,

NOTE Confidence: 0.859660446363636

00:05:02.268 --> 00:05:05.978 where Jerome Galand showed that.

NOTE Confidence: 0.859660446363636

00:05:05.980 --> 00:05:08.775 The tight density and location

NOTE Confidence: 0.859660446363636

00:05:08.775 --> 00:05:11.570 of immune cells were oops.

NOTE Confidence: 0.859660446363636

00:05:11.570 --> 00:05:13.466 He didn't mean predictive.

NOTE Confidence: 0.859660446363636

00:05:13.466 --> 00:05:16.518 He meant prognostic of of clinical outcome,

NOTE Confidence: 0.859660446363636

00:05:16.518 --> 00:05:19.869 and I will tell you that I presented

NOTE Confidence: 0.859660446363636

00:05:19.869 --> 00:05:22.496 this paper at our Journal Club.

NOTE Confidence: 0.859660446363636

00:05:22.496 --> 00:05:26.440 And and there were people who walked out

NOTE Confidence: 0.859660446363636

00:05:26.538 --> 00:05:29.919 of that room saying this is nonsense.

NOTE Confidence: 0.859660446363636

00:05:29.920 --> 00:05:33.628 And why were they so perplexed?

NOTE Confidence: 0.859660446363636

00:05:33.630 --> 00:05:34.207 Essentially,

NOTE Confidence: 0.859660446363636

00:05:34.207 --> 00:05:38.246 you had patients with stage one or

NOTE Confidence: 0.859660446363636

00:05:38.246 --> 00:05:41.357 two that's shown in the in the in

NOTE Confidence: 0.859660446363636

00:05:41.357 --> 00:05:44.378 the red and green regions of this

NOTE Confidence: 0.859660446363636

00:05:44.380 --> 00:05:48.139 Kaplan Meier curve who didn't do well?

NOTE Confidence: 0.866695171666667

00:05:51.450 --> 00:05:52.425 After the diagnosis,

NOTE Confidence: 0.866695171666667

00:05:52.425 --> 00:05:55.429 you know that that sort of didn't make sense.

NOTE Confidence: 0.866695171666667

00:05:55.430 --> 00:05:58.118 Well, it turns out that our immune

NOTE Confidence: 0.866695171666667

00:05:58.118 --> 00:06:00.158 system really is quite important,

NOTE Confidence: 0.866695171666667

00:06:00.158 --> 00:06:03.266 which will be the message for the

NOTE Confidence: 0.866695171666667

00:06:03.266 --> 00:06:05.968 rest of the of the lecture here.

NOTE Confidence: 0.866695171666667

00:06:05.970 --> 00:06:09.025 So you can go back as far as 2012

NOTE Confidence: 0.866695171666667

00:06:09.025 --> 00:06:11.455 and you know 120 articles and

NOTE Confidence: 0.866695171666667

00:06:11.455 --> 00:06:14.939 in in 20 different cancer types,

NOTE Confidence: 0.866695171666667

00:06:14.940 --> 00:06:17.607 showing that you know the type of

NOTE Confidence: 0.866695171666667

00:06:17.607 --> 00:06:19.705 immune cells that are infiltrating

NOTE Confidence: 0.866695171666667

00:06:19.705 --> 00:06:22.339 at patients tumor or the till.

NOTE Confidence: 0.866695171666667

00:06:22.340 --> 00:06:25.238 If you will, is really important

NOTE Confidence: 0.866695171666667

00:06:25.240 --> 00:06:26.956 and you know it's not surprising,

NOTE Confidence: 0.866695171666667

00:06:26.960 --> 00:06:29.608 it's great to have CD 8 cells that

NOTE Confidence: 0.866695171666667

00:06:29.608 --> 00:06:31.519 are secreting interferon gamma.

NOTE Confidence: 0.866695171666667

00:06:31.520 --> 00:06:35.060 We would call them TH one.

NOTE Confidence: 0.866695171666667

00:06:35.060 --> 00:06:38.441 In your in your cancer compared to

NOTE Confidence: 0.866695171666667

00:06:38.441 --> 00:06:41.695 you know things that are suppressive

NOTE Confidence: 0.866695171666667

00:06:41.695 --> 00:06:45.109 of of the immune based response.

NOTE Confidence: 0.866695171666667

00:06:45.110 --> 00:06:46.798 OK, so that's prognostic.

NOTE Confidence: 0.866695171666667

00:06:46.798 --> 00:06:48.908 What about human tissue as

NOTE Confidence: 0.866695171666667

00:06:48.908 --> 00:06:51.060 a predictive biomarker?

NOTE Confidence: 0.866695171666667

00:06:51.060 --> 00:06:51.880 You know,

NOTE Confidence: 0.866695171666667

00:06:51.880 --> 00:06:53.930 this is really talking about

NOTE Confidence: 0.866695171666667

00:06:53.930 --> 00:06:55.659 whether patients will respond

NOTE Confidence: 0.866695171666667

00:06:55.659 --> 00:06:57.769 or benefit from from therapy.

NOTE Confidence: 0.866695171666667

00:06:57.770 --> 00:06:58.736 And you know,

NOTE Confidence: 0.866695171666667

00:06:58.736 --> 00:07:00.024 we've been promising patients

NOTE Confidence: 0.866695171666667

00:07:00.024 --> 00:07:01.649 this for a long time.

NOTE Confidence: 0.866695171666667

00:07:01.650 --> 00:07:02.793 And you know,

NOTE Confidence: 0.866695171666667

00:07:02.793 --> 00:07:04.698 I breakdown the predictive biomarkers

NOTE Confidence: 0.866695171666667

00:07:04.698 --> 00:07:06.950 into in the three generations.

NOTE Confidence: 0.866695171666667

00:07:06.950 --> 00:07:07.341 First,

NOTE Confidence: 0.866695171666667

00:07:07.341 --> 00:07:09.296 it was important for oncologists

NOTE Confidence: 0.866695171666667

00:07:09.296 --> 00:07:11.575 to know whether something was a

NOTE Confidence: 0.866695171666667

00:07:11.575 --> 00:07:13.205 lymphoma or a colorectal cancer.

NOTE Confidence: 0.866695171666667

00:07:13.210 --> 00:07:15.320 I mean, this really changed.

NOTE Confidence: 0.866695171666667

00:07:15.320 --> 00:07:17.600 How they treated a patient.

NOTE Confidence: 0.866695171666667

00:07:17.600 --> 00:07:19.600 The second generation really

NOTE Confidence: 0.866695171666667

00:07:19.600 --> 00:07:21.875 came on and this is,

NOTE Confidence: 0.866695171666667

00:07:21.875 --> 00:07:24.425 you know work that Doctor Rim

NOTE Confidence: 0.866695171666667

00:07:24.425 --> 00:07:27.332 is is doing in really trying to

NOTE Confidence: 0.866695171666667

00:07:27.332 --> 00:07:31.740 get down to how much a cancer

NOTE Confidence: 0.866695171666667

00:07:31.740 --> 00:07:34.920 expresses a particular biomarker,

NOTE Confidence: 0.866695171666667

00:07:34.920 --> 00:07:36.372 not just any biomarker,

NOTE Confidence: 0.866695171666667

00:07:36.372 --> 00:07:38.187 but actually a biomarker that

NOTE Confidence: 0.866695171666667

00:07:38.187 --> 00:07:40.363 we can target and her two new

NOTE Confidence: 0.866695171666667

00:07:40.363 --> 00:07:42.120 would be a perfect example.

NOTE Confidence: 0.866695171666667

00:07:42.120 --> 00:07:44.717 And now we're into the third generation.

NOTE Confidence: 0.866695171666667

00:07:44.720 --> 00:07:47.240 You know, by my definitions of.

NOTE Confidence: 0.866695171666667

00:07:47.240 --> 00:07:50.280 You know how many immune cells are present?

NOTE Confidence: 0.866695171666667

00:07:50.280 --> 00:07:53.418 What are what's the immune contexture?

NOTE Confidence: 0.866695171666667

00:07:53.420 --> 00:07:55.940 What immune inhibitors are present?

NOTE Confidence: 0.866695171666667

00:07:55.940 --> 00:07:58.800 Which ones aren't present so,

NOTE Confidence: 0.866695171666667

00:07:58.800 --> 00:08:02.418 as pathologists are our goal actually,

NOTE Confidence: 0.866695171666667

00:08:02.420 --> 00:08:03.912 or are, you know,

NOTE Confidence: 0.866695171666667

00:08:03.912 --> 00:08:05.777 has gotten much more complicated?

NOTE Confidence: 0.866695171666667

00:08:05.780 --> 00:08:06.564 You know,

NOTE Confidence: 0.866695171666667

00:08:06.564 --> 00:08:09.308 telling some telling us something was a,

NOTE Confidence: 0.866695171666667

00:08:09.310 --> 00:08:11.330 you know an adenocarcinoma versus

NOTE Confidence: 0.866695171666667

00:08:11.330 --> 00:08:14.220 lymphoma is a lot different than saying,

NOTE Confidence: 0.866695171666667

00:08:14.220 --> 00:08:17.244 Oh well, there's a lot of

NOTE Confidence: 0.866695171666667

00:08:17.244 --> 00:08:18.756 tumor infiltrating lymphocytes.

NOTE Confidence: 0.866695171666667

00:08:18.760 --> 00:08:19.750 So immune therapy.

NOTE Confidence: 0.866695171666667

00:08:19.750 --> 00:08:21.049 What is it? Well,

NOTE Confidence: 0.866695171666667

00:08:21.049 --> 00:08:24.120 it turns out this guy knew a lot about it.

NOTE Confidence: 0.866695171666667

00:08:24.120 --> 00:08:26.648 This is Doctor Coley,

NOTE Confidence: 0.866695171666667

00:08:26.650 --> 00:08:28.274 and if you don't know much about him,

NOTE Confidence: 0.866695171666667

00:08:28.280 --> 00:08:31.395 I highly encourage you to Google him.

NOTE Confidence: 0.866695171666667

00:08:31.400 --> 00:08:33.260 You know he.

NOTE Confidence: 0.866695171666667

00:08:33.260 --> 00:08:35.740 He essentially was rubbing.

NOTE Confidence: 0.866695171666667

00:08:35.740 --> 00:08:38.908 Bacteria into the skin of patients

NOTE Confidence: 0.866695171666667

00:08:38.908 --> 00:08:41.744 with advanced cancers and showing

NOTE Confidence: 0.866695171666667

00:08:41.744 --> 00:08:44.899 that their cancers were regressing.

NOTE Confidence: 0.866695171666667

00:08:44.900 --> 00:08:46.800 Now he was a surgeon,

NOTE Confidence: 0.866695171666667

00:08:46.800 --> 00:08:49.600 so he was much maligned for his approach,

NOTE Confidence: 0.866695171666667

00:08:49.600 --> 00:08:51.560 'cause essentially he was

NOTE Confidence: 0.866695171666667

00:08:51.560 --> 00:08:52.540 giving chemotherapy,

NOTE Confidence: 0.866695171666667

00:08:52.540 --> 00:08:56.332 which went when you know conventional

NOTE Confidence: 0.866695171666667

00:08:56.332 --> 00:08:59.688 thought was that this should be

NOTE Confidence: 0.866695171666667

00:08:59.688 --> 00:09:02.330 more of a surgical approach and

NOTE Confidence: 0.866695171666667

00:09:02.330 --> 00:09:05.780 you know it was so hard for him.

NOTE Confidence: 0.866695171666667

00:09:05.780 --> 00:09:08.080 To get his message out,

NOTE Confidence: 0.866695171666667

00:09:08.080 --> 00:09:09.788 he had to travel all the way

NOTE Confidence: 0.866695171666667

00:09:09.788 --> 00:09:10.870 down from New York,

NOTE Confidence: 0.866695171666667

00:09:10.870 --> 00:09:13.159 which is where he was from down

NOTE Confidence: 0.866695171666667

00:09:13.159 --> 00:09:15.099 to Johns Hopkins in Baltimore,

NOTE Confidence: 0.866695171666667

00:09:15.100 --> 00:09:17.543 and this is a picture of him

14

NOTE Confidence: 0.866695171666667

00:09:17.543 --> 00:09:19.040 lecturing in Heard Hall.

NOTE Confidence: 0.866695171666667

00:09:19.040 --> 00:09:22.112 And this is exactly where pathology

NOTE Confidence: 0.866695171666667

00:09:22.112 --> 00:09:26.137 grand rounds is still conducted to the day,

NOTE Confidence: 0.866695171666667

00:09:26.140 --> 00:09:30.484 and I can identify this as as as.

NOTE Confidence: 0.863899206666667

00:09:30.490 --> 00:09:33.478 Heard Hall because we have these,

NOTE Confidence: 0.863899206666667

00:09:33.480 --> 00:09:36.434 you know, flags displayed in at the

NOTE Confidence: 0.863899206666667

00:09:36.434 --> 00:09:39.430 margins of of the lecture system.

NOTE Confidence: 0.863899206666667

00:09:39.430 --> 00:09:41.002 So what's immune therapy?

NOTE Confidence: 0.863899206666667

00:09:41.002 --> 00:09:42.632 You know, it's it's.

NOTE Confidence: 0.863899206666667

00:09:42.632 --> 00:09:45.695 It's basically the idea that a patient's

NOTE Confidence: 0.863899206666667

00:09:45.695 --> 00:09:48.905 immune system can eliminate a cancer.

NOTE Confidence: 0.863899206666667

00:09:48.910 --> 00:09:50.950 This is very patient empowering.

NOTE Confidence: 0.863899206666667

00:09:50.950 --> 00:09:53.841 I had the misfortune of spending a

NOTE Confidence: 0.863899206666667

00:09:53.841 --> 00:09:57.197 lot of time in a in a cancer immuno

NOTE Confidence: 0.863899206666667

00:09:57.197 --> 00:10:01.306 or in a cancer therapy setting and

NOTE Confidence: 0.863899206666667

00:10:01.306 --> 00:10:06.234 it was amazing to to to witness how

NOTE Confidence: 0.863899206666667

00:10:06.234 --> 00:10:10.302 patients responded to the fact that.

NOTE Confidence: 0.863899206666667

00:10:10.310 --> 00:10:12.610 They were mounting in.

NOTE Confidence: 0.863899206666667

00:10:12.610 --> 00:10:15.485 Immune response to their cancer.

NOTE Confidence: 0.863899206666667

00:10:15.490 --> 00:10:19.928 They just needed a little help removing.

NOTE Confidence: 0.863899206666667

00:10:19.930 --> 00:10:22.070 The break.

NOTE Confidence: 0.863899206666667

00:10:22.070 --> 00:10:25.556 So cancer immune therapy is is best,

NOTE Confidence: 0.863899206666667

00:10:25.560 --> 00:10:27.906 you know understood with you know

NOTE Confidence: 0.863899206666667

00:10:27.906 --> 00:10:31.650 anyone who drives a car, right?

NOTE Confidence: 0.863899206666667

00:10:31.650 --> 00:10:35.528 So we thought the problem with cancer

NOTE Confidence: 0.863899206666667

00:10:35.528 --> 00:10:38.898 therapy or tumor immuno tumor immunology

NOTE Confidence: 0.863899206666667

00:10:38.898 --> 00:10:42.850 was just that we we needed to press

NOTE Confidence: 0.863899206666667

00:10:42.953 --> 00:10:47.139 the accelerator harder but anyone who knows.

NOTE Confidence: 0.863899206666667

00:10:47.140 --> 00:10:49.184 Anything about you know driving a car

NOTE Confidence: 0.863899206666667

00:10:49.184 --> 00:10:51.489 if you have your foot on the brake,

NOTE Confidence: 0.863899206666667

00:10:51.490 --> 00:10:53.680 it doesn't matter really how hard

NOTE Confidence: 0.863899206666667

00:10:53.680 --> 00:10:55.140 you press the accelerator.

NOTE Confidence: 0.863899206666667

00:10:55.140 --> 00:11:00.168 It's all about releasing the brake.

NOTE Confidence: 0.863899206666667

00:11:00.170 --> 00:11:03.455 And that was recognized formally

NOTE Confidence: 0.863899206666667

00:11:03.455 --> 00:11:06.083 with the Nobel laureates.

NOTE Confidence: 0.863899206666667

00:11:06.090 --> 00:11:07.506 Here, Doctor,

NOTE Confidence: 0.863899206666667

00:11:07.506 --> 00:11:09.630 Allison and Honjo.

NOTE Confidence: 0.863899206666667

00:11:09.630 --> 00:11:10.240 Day.

NOTE Confidence: 0.863899206666667

00:11:10.240 --> 00:11:12.070 And you know,

NOTE Confidence: 0.863899206666667

00:11:12.070 --> 00:11:14.510 essentially both of these

NOTE Confidence: 0.863899206666667

00:11:14.510 --> 00:11:17.196 individuals were were studying

NOTE Confidence: 0.863899206666667

00:11:17.196 --> 00:11:22.412 immune based therapy in terms of uh,

NOTE Confidence: 0.863899206666667

00:11:22.412 --> 00:11:23.998 immune inhibitors,

NOTE Confidence: 0.863899206666667

00:11:24.000 --> 00:11:25.923 not immune stimulators,

NOTE Confidence: 0.863899206666667

00:11:25.923 --> 00:11:28.487 but immune inhibitor inhibitors.

NOTE Confidence: 0.863899206666667

00:11:28.490 --> 00:11:30.758 So what I've done here is,

NOTE Confidence: 0.863899206666667

00:11:30.760 --> 00:11:33.918 I've lined up the immune synapse between

00:11:33.918 --> 00:11:38.062 antigen presenting cells and and and T cells.

00:11:38.070 --> 00:11:40.576 And I think all of us recognize

00:11:40.576 --> 00:11:43.080 that we need a signal,

00:11:43.080 --> 00:11:46.290 one that's MHC engaging the T

00:11:46.409 --> 00:11:50.338 cell receptor and then signal 2

00:11:50.338 --> 00:11:52.654 here is what's responsible for,

00:11:52.654 --> 00:11:55.742 you know, driving the immune system.

00:11:55.742 --> 00:11:58.532 But then it's these breaks.

00:11:58.540 --> 00:11:59.953 It's the brace.

00:11:59.953 --> 00:12:02.308 It's the inhibitors of the

00:12:02.308 --> 00:12:04.996 immune system that went on to win

00:12:04.996 --> 00:12:06.580 the Nobel prizes here,

00:12:06.580 --> 00:12:08.215 and I would point out

00:12:08.215 --> 00:12:09.523 very important fact here.

00:12:11.780 --> 00:12:13.670 And I have the utmost respect

NOTE Confidence: 0.895689038888889

00:12:13.670 --> 00:12:15.306 for Doctor Handjo, who personally

NOTE Confidence: 0.895689038888889

00:12:15.306 --> 00:12:17.707 invited me to to give a talk.

NOTE Confidence: 0.870413867777778

00:12:20.070 --> 00:12:22.681 It it was, it was actually Doctor

NOTE Confidence: 0.870413867777778

00:12:22.681 --> 00:12:25.558 Liping Chen, one of your tumor,

NOTE Confidence: 0.870413867777778

00:12:25.558 --> 00:12:27.299 immunologists, who really figured

NOTE Confidence: 0.870413867777778

00:12:27.299 --> 00:12:30.480 out what PDL one did it in in.

NOTE Confidence: 0.870413867777778

00:12:30.480 --> 00:12:32.440 In fact it was misnamed, it was.

NOTE Confidence: 0.870413867777778

00:12:32.440 --> 00:12:33.945 It was thought to be a program,

NOTE Confidence: 0.870413867777778

00:12:33.950 --> 00:12:36.626 death ligands and it was Doctor

NOTE Confidence: 0.870413867777778

00:12:36.626 --> 00:12:39.841 Chen who figured out that that PDL

NOTE Confidence: 0.870413867777778

00:12:39.841 --> 00:12:43.267 one was actually a very critical

NOTE Confidence: 0.870413867777778

00:12:43.267 --> 00:12:46.137 immune inhibitor and ultimately the

NOTE Confidence: 0.870413867777778

00:12:46.137 --> 00:12:50.649 key to unlocking tumor immunology.

NOTE Confidence: 0.870413867777778

00:12:50.650 --> 00:12:57.640 So how do we reconcile CTL A4 versus PDL one?

NOTE Confidence: 0.870413867777778

00:12:57.640 --> 00:12:59.620 You know, for me,

NOTE Confidence: 0.870413867777778

19

00:12:59.620 --> 00:13:01.516 CTL A4 works in the periphery,

NOTE Confidence: 0.870413867777778

00:13:01.520 --> 00:13:04.628 it's an early part of the immune

NOTE Confidence: 0.870413867777778

00:13:04.628 --> 00:13:07.543 response where PDL one is a little

NOTE Confidence: 0.870413867777778

00:13:07.543 --> 00:13:10.400 bit later and occurs in the tumor.

NOTE Confidence: 0.870413867777778

00:13:10.400 --> 00:13:14.588 That's the key then to the

NOTE Confidence: 0.870413867777778

00:13:14.588 --> 00:13:15.984 pathologist because.

NOTE Confidence: 0.870413867777778

00:13:15.990 --> 00:13:18.432 Our ability to look in the

NOTE Confidence: 0.870413867777778

00:13:18.432 --> 00:13:20.500 tumor is very helpful. Why?

NOTE Confidence: 0.870413867777778

00:13:20.500 --> 00:13:23.580 Why are we even talking about this?

NOTE Confidence: 0.870413867777778

00:13:23.580 --> 00:13:27.180 I mean the the rate of.

NOTE Confidence: 0.870413867777778

00:13:27.180 --> 00:13:31.115 Of FDA approval for cancer

NOTE Confidence: 0.870413867777778

00:13:31.115 --> 00:13:33.476 therapies is unprecedented.

NOTE Confidence: 0.870413867777778

00:13:33.480 --> 00:13:36.805 In the last 10 to 15 years,

NOTE Confidence: 0.870413867777778

00:13:36.810 --> 00:13:40.368 the rate of cancer therapies approval

NOTE Confidence: 0.870413867777778

00:13:40.368 --> 00:13:44.461 with the FDA keeping in mind this

NOTE Confidence: 0.870413867777778

00:13:44.461 --> 00:13:47.146 is a very conservative group.

NOTE Confidence: 0.870413867777778

00:13:47.150 --> 00:13:49.730 Has just accelerated, you know,

NOTE Confidence: 0.870413867777778

00:13:49.730 --> 00:13:52.810 you know I kind of stopped updating my

NOTE Confidence: 0.870413867777778

00:13:52.810 --> 00:13:55.868 slide here about 2019 and it's 26 more.

NOTE Confidence: 0.870413867777778

00:13:55.870 --> 00:13:59.086 It's probably 50 more by now.

NOTE Confidence: 0.870413867777778

00:13:59.090 --> 00:14:02.290 You know this is really.

NOTE Confidence: 0.870413867777778

00:14:02.290 --> 00:14:07.104 Frighteningly fast approval in

NOTE Confidence: 0.870413867777778

00:14:07.104 --> 00:14:10.608 in terms of of tumor immunity.

NOTE Confidence: 0.870413867777778

00:14:10.610 --> 00:14:11.066 OK,

NOTE Confidence: 0.870413867777778

00:14:11.066 --> 00:14:14.258 so let's let's take a step back

NOTE Confidence: 0.870413867777778

00:14:14.258 --> 00:14:17.175 and you know the first person

NOTE Confidence: 0.870413867777778

00:14:17.175 --> 00:14:20.830 to look at A at a cancer.

NOTE Confidence: 0.870413867777778

00:14:20.830 --> 00:14:24.150 That had undergone PD1 blockade,

NOTE Confidence: 0.870413867777778

00:14:24.150 --> 00:14:28.270 and biopsy is me.

NOTE Confidence: 0.870413867777778

00:14:28.270 --> 00:14:30.278 You know, so how did we get here?

NOTE Confidence: 0.870413867777778

00:14:30.280 --> 00:14:33.076 So let's talk about PDL one

NOTE Confidence: 0.870413867777778

00:14:33.076 --> 00:14:36.330 as a as a biomarker.

NOTE Confidence: 0.870413867777778

00:14:36.330 --> 00:14:39.319 So we have this paper here which

NOTE Confidence: 0.870413867777778

00:14:39.319 --> 00:14:43.322 you know back in 2012. Explored the.

NOTE Confidence: 0.870413867777778

00:14:43.322 --> 00:14:48.206 This was really a safety paper.

NOTE Confidence: 0.870413867777778

00:14:48.210 --> 00:14:52.656 This was a phase one trial.

NOTE Confidence: 0.870413867777778

00:14:52.660 --> 00:14:56.156 About can patients even

NOTE Confidence: 0.870413867777778

00:14:56.156 --> 00:14:58.778 tolerate PD1 blockade?

NOTE Confidence: 0.870413867777778

00:14:58.780 --> 00:15:01.230 And.

NOTE Confidence: 0.870413867777778

00:15:01.230 --> 00:15:04.359 You can see that very important you

NOTE Confidence: 0.870413867777778

00:15:04.359 --> 00:15:07.121 know individuals to to Johns Hopkins as

NOTE Confidence: 0.870413867777778

00:15:07.121 --> 00:15:10.510 well as as to Yale or are listed here,

NOTE Confidence: 0.870413867777778

00:15:10.510 --> 00:15:14.976 because this is really a landmark paper.

NOTE Confidence: 0.870413867777778

00:15:14.980 --> 00:15:16.720 And I was fortunate enough to

NOTE Confidence: 0.870413867777778

00:15:16.720 --> 00:15:18.844 be in the right place at the

NOTE Confidence: 0.870413867777778

00:15:18.844 --> 00:15:20.688 right time and and what what?

NOTE Confidence: 0.870413867777778

00:15:20.688 --> 00:15:23.007 My laboratory at the time was really

NOTE Confidence: 0.870413867777778

00:15:23.007 --> 00:15:25.251 good at measuring was the expression

NOTE Confidence: 0.870413867777778

00:15:25.251 --> 00:15:30.192 of PD L1 protein in the tumor and

NOTE Confidence: 0.870413867777778

00:15:30.192 --> 00:15:33.076 the results of what we found are

NOTE Confidence: 0.870413867777778

00:15:33.076 --> 00:15:35.309 summarized in this graph here.

NOTE Confidence: 0.870413867777778

00:15:35.310 --> 00:15:38.397 And you can see that if patients

NOTE Confidence: 0.870413867777778

00:15:38.397 --> 00:15:41.102 were deemed to be PD L1 positive,

NOTE Confidence: 0.870413867777778

00:15:41.102 --> 00:15:43.650 we can argue about what that means.

NOTE Confidence: 0.870413867777778

00:15:43.650 --> 00:15:47.756 They had about a 5050 chance of response,

NOTE Confidence: 0.870413867777778

00:15:47.756 --> 00:15:50.966 but. And very important here.

NOTE Confidence: 0.870413867777778

00:15:50.970 --> 00:15:53.180 If patients were deemed to

NOTE Confidence: 0.870413867777778

00:15:53.180 --> 00:15:54.948 be PDL one negative.

NOTE Confidence: 0.926375558333334

00:15:57.660 --> 00:16:00.960 They had no chance of responding.

NOTE Confidence: 0.926375558333334

00:16:00.960 --> 00:16:04.915 And that's very helpful as an oncologist.

NOTE Confidence: 0.926375558333334

00:16:04.920 --> 00:16:08.120 If something has a 100%.

NOTE Confidence: 0.926375558333334

00:16:08.120 --> 00:16:10.904 Predictive power that means

NOTE Confidence: 0.926375558333334

00:16:10.904 --> 00:16:13.518 that it's as an oncologist.

NOTE Confidence: 0.926375558333334

00:16:13.518 --> 00:16:15.548 You move that patient on

NOTE Confidence: 0.926375558333334

00:16:15.548 --> 00:16:17.180 to something different,

NOTE Confidence: 0.926375558333334

00:16:17.180 --> 00:16:21.835 and this publication here is really the

NOTE Confidence: 0.926375558333334

00:16:21.835 --> 00:16:24.772 key to springing everything forward

NOTE Confidence: 0.926375558333334

00:16:24.772 --> 00:16:29.260 to PDL one as a predictive biomarker.

NOTE Confidence: 0.926375558333334

00:16:29.260 --> 00:16:31.620 Now it turns out that.

NOTE Confidence: 0.926375558333334

00:16:31.620 --> 00:16:34.130 That 100% predictive negative predictive

NOTE Confidence: 0.926375558333334

00:16:34.130 --> 00:16:37.840 value was was a little bit overblown,

NOTE Confidence: 0.926375558333334

00:16:37.840 --> 00:16:41.640 and it we can talk about the details of that,

NOTE Confidence: 0.926375558333334

00:16:41.640 --> 00:16:45.702 but it wasn't completely wrong either.

NOTE Confidence: 0.926375558333334

00:16:45.702 --> 00:16:47.274 So what I'm showing you here

NOTE Confidence: 0.926375558333334

00:16:47.274 --> 00:16:48.919 is one of our brilliant,

NOTE Confidence: 0.926375558333334

00:16:48.920 --> 00:16:51.600 now few faculty member members,

NOTE Confidence: 0.926375558333334

00:16:51.600 --> 00:16:52.616 Jill Sunshine,

NOTE Confidence: 0.926375558333334

00:16:52.616 --> 00:16:56.680 and what they did is they looked at

NOTE Confidence: 0.926375558333334

00:16:56.680 --> 00:16:58.700 all the different Dwan treatments

NOTE Confidence: 0.926375558333334

00:16:58.700 --> 00:17:01.080 there are listed on the top.

NOTE Confidence: 0.926375558333334

00:17:01.080 --> 00:17:03.000 All the different cancer types.

NOTE Confidence: 0.926375558333334

00:17:03.000 --> 00:17:05.796 Listed on the bottom and the

NOTE Confidence: 0.926375558333334

00:17:05.796 --> 00:17:08.477 response rate listed on the Y

NOTE Confidence: 0.926375558333334

00:17:08.477 --> 00:17:11.349 axis here and what you can see is.

NOTE Confidence: 0.926375558333334

00:17:11.350 --> 00:17:14.136 That patients who are PDL 1 positive

NOTE Confidence: 0.926375558333334

00:17:14.136 --> 00:17:17.002 again we can debate about what that

NOTE Confidence: 0.926375558333334

00:17:17.002 --> 00:17:20.236 means had about a 50% response rate

NOTE Confidence: 0.926375558333334

00:17:20.236 --> 00:17:24.597 and if they were PDL one negative.

NOTE Confidence: 0.926375558333334

00:17:24.600 --> 00:17:28.091 They had about a Tanner of 15 response rate.

NOTE Confidence: 0.926375558333334

00:17:28.091 --> 00:17:30.688 OK, so this is a little different

NOTE Confidence: 0.926375558333334

00:17:30.688 --> 00:17:33.280 than 100% negative predictive rate,

NOTE Confidence: 0.926375558333334

00:17:33.280 --> 00:17:35.500 but it it helps.

NOTE Confidence: 0.926375558333334

00:17:35.500 --> 00:17:38.580 So the most common question that I'm asked.

NOTE Confidence: 0.926375558333334

00:17:38.580 --> 00:17:43.410 Is is PDL 1A good biomarker?

NOTE Confidence: 0.926375558333334

00:17:43.410 --> 00:17:43.891 Well.

NOTE Confidence: 0.926375558333334

00:17:43.891 --> 00:17:47.258 It's not, it's it's not an end,

NOTE Confidence: 0.926375558333334

00:17:47.260 --> 00:17:49.480 it's it's not a perfect biomarker.

NOTE Confidence: 0.926375558333334

00:17:49.480 --> 00:17:50.402 It's imperfect.

NOTE Confidence: 0.926375558333334

00:17:50.402 --> 00:17:53.168 And what it does is it

NOTE Confidence: 0.926375558333334

00:17:53.168 --> 00:17:55.180 enriches for responders.

NOTE Confidence: 0.926375558333334

00:17:55.180 --> 00:17:57.250 So if you're an individual

NOTE Confidence: 0.926375558333334

00:17:57.250 --> 00:17:59.550 patient and you're deemed to be

NOTE Confidence: 0.926375558333334

00:17:59.550 --> 00:18:01.360 PD L1 positive or negative,

NOTE Confidence: 0.926375558333334

00:18:01.360 --> 00:18:03.580 you know Doctor Robert or myself.

NOTE Confidence: 0.926375558333334

00:18:03.580 --> 00:18:05.686 Look at your specimen in our

NOTE Confidence: 0.926375558333334

00:18:05.686 --> 00:18:08.103 expert weighs and and and call

NOTE Confidence: 0.926375558333334

00:18:08.103 --> 00:18:09.975 something positive or negative.

NOTE Confidence: 0.926375558333334

00:18:09.980 --> 00:18:13.664 You you probably have about a 50% fifty 50%.

NOTE Confidence: 0.926375558333334

00:18:13.664 --> 00:18:15.710 Or or or?

NOTE Confidence: 0.926375558333334

00:18:15.710 --> 00:18:16.480 I'm sorry,

NOTE Confidence: 0.926375558333334

00:18:16.480 --> 00:18:18.405 a 5050 chance of responding.

NOTE Confidence: 0.866535091666667

00:18:20.750 --> 00:18:25.846 But if you take 100 patients and you

NOTE Confidence: 0.866535091666667

00:18:25.846 --> 00:18:28.702 pick only the patients that are PDL,

NOTE Confidence: 0.866535091666667

00:18:28.710 --> 00:18:31.930 1 positive again by an expert reviewer,

NOTE Confidence: 0.866535091666667

00:18:31.930 --> 00:18:35.808 you pick out a lot of winners.

NOTE Confidence: 0.866535091666667

00:18:35.810 --> 00:18:40.076 So is PDL 1A great biomarker?

NOTE Confidence: 0.866535091666667

00:18:40.080 --> 00:18:44.808 It depends if you're a physician trying to,

NOTE Confidence: 0.866535091666667

00:18:44.810 --> 00:18:46.658 you know, treat an individual patient.

NOTE Confidence: 0.866535091666667

00:18:46.660 --> 00:18:49.506 No, it's not. It's a 5050, you know.

NOTE Confidence: 0.866535091666667

00:18:49.506 --> 00:18:50.538 Sort of coin toss.

NOTE Confidence: 0.866535091666667

00:18:50.540 --> 00:18:52.801 But if you're a far if you're

NOTE Confidence: 0.866535091666667

00:18:52.801 --> 00:18:54.330 a large pharmaceutical company.

NOTE Confidence: 0.866535091666667

00:18:54.330 --> 00:18:56.801 And you wish to find the patients

NOTE Confidence: 0.866535091666667

00:18:56.801 --> 00:18:59.290 that are most likely to benefit.

NOTE Confidence: 0.866535091666667

00:18:59.290 --> 00:19:01.850 Then it's a fabulous biomarker,

NOTE Confidence: 0.866535091666667

00:19:01.850 --> 00:19:04.520 because you're a you're a

NOTE Confidence: 0.866535091666667

00:19:04.520 --> 00:19:06.980 affectively picking 50% winners.

NOTE Confidence: 0.946057189285714

00:19:09.530 --> 00:19:12.505 OK, so maybe the maybe the issue

NOTE Confidence: 0.946057189285714

00:19:12.505 --> 00:19:15.667 is we just need to do better.

NOTE Confidence: 0.946057189285714

00:19:15.670 --> 00:19:19.726 We need to do PDL 1 determination,

NOTE Confidence: 0.946057189285714

00:19:19.726 --> 00:19:22.954 immunohistochemistry, test performance.

NOTE Confidence: 0.946057189285714

00:19:22.954 --> 00:19:24.598 Better you know,

NOTE Confidence: 0.946057189285714

00:19:24.598 --> 00:19:27.200 maybe when it was first done in my lab.

NOTE Confidence: 0.946057189285714

00:19:27.200 --> 00:19:30.686 You know back almost you know

NOTE Confidence: 0.946057189285714

00:19:30.686 --> 00:19:33.010 10 plus years ago.

NOTE Confidence: 0.946057189285714

00:19:33.010 --> 00:19:34.870 You know, I hadn't considered everything,

NOTE Confidence: 0.946057189285714

00:19:34.870 --> 00:19:38.134 so the thing about PDL one expression is

NOTE Confidence: 0.946057189285714

00:19:38.134 --> 00:19:40.753 we're asking pathologists to do things

NOTE Confidence: 0.946057189285714

00:19:40.753 --> 00:19:44.190 that we've never asked them to do before.

NOTE Confidence: 0.946057189285714

00:19:44.190 --> 00:19:46.934 First off PDL one can be expressed

NOTE Confidence: 0.946057189285714

00:19:46.934 --> 00:19:48.850 on different types of cells.

NOTE Confidence: 0.946057189285714

00:19:48.850 --> 00:19:50.488 It could be in a histiocyte,

NOTE Confidence: 0.946057189285714

00:19:50.490 --> 00:19:53.290 a malignant cell or even a lymphocyte.

NOTE Confidence: 0.946057189285714

00:19:53.290 --> 00:19:55.288 It can even change its location.

NOTE Confidence: 0.946057189285714

00:19:55.290 --> 00:19:57.348 Sometimes it can be in the cytoplasm,

NOTE Confidence: 0.946057189285714

00:19:57.350 --> 00:19:59.350 other times it can be in the membrane.

NOTE Confidence: 0.946057189285714

00:19:59.350 --> 00:20:01.978 And then we're even further asking

NOTE Confidence: 0.946057189285714

00:20:01.978 --> 00:20:04.570 the pathologist to consider all these

NOTE Confidence: 0.946057189285714

00:20:04.570 --> 00:20:08.820 different cell types and say how many?

NOTE Confidence: 0.946057189285714

00:20:08.820 --> 00:20:13.196 How many cells are positive and this is

NOTE Confidence: 0.946057189285714

00:20:13.196 --> 00:20:16.588 really outside of what pathologists can do.

NOTE Confidence: 0.946057189285714

00:20:16.588 --> 00:20:20.863 And then on top of that we have

NOTE Confidence: 0.946057189285714

00:20:20.863 --> 00:20:24.151 different scoring systems so again

NOTE Confidence: 0.946057189285714

00:20:24.151 --> 00:20:27.658 I'm going to go over this quickly.

NOTE Confidence: 0.946057189285714

00:20:27.660 --> 00:20:29.755 Sometimes it's the number of

NOTE Confidence: 0.946057189285714

00:20:29.755 --> 00:20:31.850 tumor cells that are positive.

NOTE Confidence: 0.946057189285714

00:20:31.850 --> 00:20:34.364 Sometimes it's the number of tumor

NOTE Confidence: 0.946057189285714

00:20:34.364 --> 00:20:36.525 cells and inflammatory cells that

NOTE Confidence: 0.946057189285714

00:20:36.525 --> 00:20:38.575 are positive over a denominator.

NOTE Confidence: 0.946057189285714

00:20:38.580 --> 00:20:40.600 That's just the cancer cells.

NOTE Confidence: 0.946057189285714

00:20:40.600 --> 00:20:43.256 I mean, this is starting to get crazy.

NOTE Confidence: 0.946057189285714

00:20:43.260 --> 00:20:44.604 I mean,

NOTE Confidence: 0.946057189285714

00:20:44.604 --> 00:20:48.636 it's not practical for us to

NOTE Confidence: 0.946057189285714

00:20:48.636 --> 00:20:51.660 expect pathologists to be able to,

NOTE Confidence: 0.946057189285714

00:20:51.660 --> 00:20:53.520 you know.

NOTE Confidence: 0.946057189285714

00:20:53.520 --> 00:20:55.945 Find down this granularity and

NOTE Confidence: 0.946057189285714

00:20:55.945 --> 00:20:57.885 this was beautifully displayed

NOTE Confidence: 0.946057189285714

00:20:57.885 --> 00:21:00.417 in a study by Doctor Rim who,

NOTE Confidence: 0.946057189285714

00:21:00.420 --> 00:21:03.708 which I was fortunate enough to be part

NOTE Confidence: 0.946057189285714

00:21:03.708 --> 00:21:06.166 of and and basically what we showed

NOTE Confidence: 0.946057189285714

00:21:06.166 --> 00:21:08.588 or what doctor Rimm showed is that.

NOTE Confidence: 0.932407768333333

00:21:11.140 --> 00:21:14.098 If you ask us, the proportion,

NOTE Confidence: 0.932407768333333

00:21:14.100 --> 00:21:16.605 that's the percentage of tumor

NOTE Confidence: 0.932407768333333

00:21:16.605 --> 00:21:18.609 cells that are positive.

NOTE Confidence: 0.932407768333333

00:21:18.610 --> 00:21:21.305 Houses pathologists we can agree on this,

NOTE Confidence: 0.932407768333333

00:21:21.310 --> 00:21:24.831 but if you start making the equation

NOTE Confidence: 0.932407768333333

00:21:24.831 --> 00:21:28.369 more complicated and say well you should

NOTE Confidence: 0.932407768333333

00:21:28.369 --> 00:21:31.900 include immune cells but not plasma cells.

NOTE Confidence: 0.932407768333333

00:21:31.900 --> 00:21:36.032 The Inter rater of their agreement falls

NOTE Confidence: 0.932407768333333

00:21:36.032 --> 00:21:41.238 apart precipitously, so a .86% or a

NOTE Confidence: 0.932407768333333

00:21:41.238 --> 00:21:44.995 .86 here for inter rater variability.

NOTE Confidence: 0.932407768333333

00:21:44.995 --> 00:21:47.820 You know that's reasonably good,

NOTE Confidence: 0.932407768333333

00:21:47.820 --> 00:21:50.080 but something close to .2.

NOTE Confidence: 0.932407768333333

00:21:50.080 --> 00:21:52.000 That's absolutely terrible.

NOTE Confidence: 0.9206764325

00:21:54.570 --> 00:21:56.634 Alright, so that's created

NOTE Confidence: 0.9206764325

00:21:56.634 --> 00:21:58.698 an opportunity for us.

NOTE Confidence: 0.9206764325

00:21:58.700 --> 00:22:00.916 In terms of pathologists

NOTE Confidence: 0.9206764325

00:22:00.916 --> 00:22:03.034 because which PDL went antibody,

NOTE Confidence: 0.9206764325

00:22:03.034 --> 00:22:04.989 there's actually many out there.

NOTE Confidence: 0.9206764325

00:22:04.990 --> 00:22:06.157 What's staining pattern?

NOTE Confidence: 0.9206764325

00:22:06.157 --> 00:22:09.435 Is it tumor cells or is it inflammatory

NOTE Confidence: 0.9206764325

00:22:09.435 --> 00:22:12.959 cells and and then a cut off?

NOTE Confidence: 0.9206764325

00:22:12.959 --> 00:22:15.674 Even changes between the different.

NOTE Confidence: 0.822175775

00:22:18.070 --> 00:22:21.717 The different stains and then how many

NOTE Confidence: 0.822175775

00:22:21.717 --> 00:22:23.310 pathologists do we need to agree?

NOTE Confidence: 0.822175775

00:22:23.310 --> 00:22:25.986 We've never even even considered this.

NOTE Confidence: 0.842606672727273

00:22:28.060 --> 00:22:31.476 So Doctor Robert and I have been

NOTE Confidence: 0.842606672727273

00:22:31.476 --> 00:22:34.511 fortunate enough to be to to spearhead

NOTE Confidence: 0.842606672727273

00:22:34.511 --> 00:22:38.770 an effort to look at ways to improve PDL.

NOTE Confidence: 0.842606672727273

00:22:38.770 --> 00:22:41.385 1, staining, evaluation and what

NOTE Confidence: 0.842606672727273

00:22:41.385 --> 00:22:44.000 we've developed is an international

NOTE Confidence: 0.842606672727273

00:22:44.080 --> 00:22:48.670 collaboration looking at PDL 1 staining.

NOTE Confidence: 0.842606672727273

00:22:48.670 --> 00:22:51.246 And the the goal here is to

NOTE Confidence: 0.842606672727273

00:22:51.246 --> 00:22:53.530 measure how well we can agree.

NOTE Confidence: 0.842606672727273

00:22:53.530 --> 00:22:54.646 I've got a hint for you.

NOTE Confidence: 0.842606672727273

00:22:54.650 --> 00:22:57.160 We don't agree very well.

NOTE Confidence: 0.842606672727273

00:22:57.160 --> 00:22:58.696 And then more importantly,

NOTE Confidence: 0.842606672727273

00:22:58.696 --> 00:23:01.818 how can we do better and what digital

NOTE Confidence: 0.842606672727273

00:23:01.818 --> 00:23:04.394 systems may be able to help us?

NOTE Confidence: 0.842606672727273

00:23:04.400 --> 00:23:06.675 So that's something I wish I could

NOTE Confidence: 0.842606672727273

00:23:06.675 --> 00:23:08.920 share with you a little bit more,

NOTE Confidence: 0.842606672727273

00:23:08.920 --> 00:23:11.454 but we're in the process of of

NOTE Confidence: 0.842606672727273

00:23:11.454 --> 00:23:13.339 of putting together that data,

NOTE Confidence: 0.842606672727273

00:23:13.340 --> 00:23:17.039 but I promise you that it will be very

NOTE Confidence: 0.842606672727273

00:23:17.039 --> 00:23:19.805 revealing in that we really need to

NOTE Confidence: 0.842606672727273

00:23:19.805 --> 00:23:22.860 do better in order to help patients.

NOTE Confidence: 0.842606672727273

00:23:22.860 --> 00:23:25.458 OK, So what about the development

NOTE Confidence: 0.842606672727273

00:23:25.458 --> 00:23:27.190 of of of biomarkers?

NOTE Confidence: 0.842606672727273

00:23:27.190 --> 00:23:31.152 So it turns out that mismatch repair

NOTE Confidence: 0.842606672727273

00:23:31.152 --> 00:23:33.764 deficiency MMR proteins or MSI?

NOTE Confidence: 0.842606672727273

00:23:33.764 --> 00:23:34.786 You know,

NOTE Confidence: 0.842606672727273

00:23:34.790 --> 00:23:39.060 by PCR is a really important marker.

NOTE Confidence: 0.842606672727273

00:23:39.060 --> 00:23:44.415 A biomarker in terms of immune therapy,

NOTE Confidence: 0.842606672727273

00:23:44.420 --> 00:23:47.143 so I would like to invoke this

NOTE Confidence: 0.842606672727273

00:23:47.143 --> 00:23:48.310 individual Margaret Fuller.

NOTE Confidence: 0.842606672727273

00:23:48.310 --> 00:23:50.475 She was a transcendentalist female

NOTE Confidence: 0.842606672727273

00:23:50.475 --> 00:23:53.430 author who wrote this very important.

NOTE Confidence: 0.842606672727273

00:23:53.430 --> 00:23:53.964 Book.

NOTE Confidence: 0.842606672727273

00:23:53.964 --> 00:23:57.168 And what I wish to highlight

NOTE Confidence: 0.842606672727273

00:23:57.168 --> 00:23:59.819 out of this book is.

NOTE Confidence: 0.842606672727273

00:23:59.820 --> 00:24:02.670 Nature provides exceptions to every rule.

NOTE Confidence: 0.826563254

00:24:04.680 --> 00:24:08.628 And that's not how we generally

NOTE Confidence: 0.826563254

00:24:08.628 --> 00:24:11.260 think about cancer therapy.

NOTE Confidence: 0.826563254

00:24:11.260 --> 00:24:14.214 So what I want you is young,

NOTE Confidence: 0.826563254

00:24:14.220 --> 00:24:16.940 possibly physician scientists is.

NOTE Confidence: 0.826563254

00:24:16.940 --> 00:24:20.340 Study the exceptions and I'm

NOTE Confidence: 0.826563254

00:24:20.340 --> 00:24:23.220 gonna show you exactly why.

NOTE Confidence: 0.826563254

00:24:23.220 --> 00:24:24.306 So pharmaceutical companies

NOTE Confidence: 0.826563254

00:24:24.306 --> 00:24:26.478 have a very top down approach.

NOTE Confidence: 0.826563254

00:24:26.480 --> 00:24:30.908 They would love it if 100% of patients got

NOTE Confidence: 0.826563254

00:24:30.908 --> 00:24:34.608 a treatment and 10% of them responded.

NOTE Confidence: 0.826563254

00:24:34.608 --> 00:24:37.576 Because 100% of them need to be treated,

NOTE Confidence: 0.826563254

00:24:37.580 --> 00:24:39.248 but what I'm encouraging

NOTE Confidence: 0.826563254

00:24:39.248 --> 00:24:42.316 you to think about is not.

NOTE Confidence: 0.826563254

00:24:42.316 --> 00:24:45.806 That 90% that didn't respond,

NOTE Confidence: 0.826563254

00:24:45.810 --> 00:24:48.194 but actually thinking about

NOTE Confidence: 0.826563254

00:24:48.194 --> 00:24:52.786 the 1% or 10% that did respond.

NOTE Confidence: 0.826563254

00:24:52.790 --> 00:24:55.859 So the thinking is is very upside down here.

NOTE Confidence: 0.889750823913044

00:24:57.970 --> 00:25:00.518 As pathologists, what we want to think

NOTE Confidence: 0.889750823913044

00:25:00.518 --> 00:25:03.965 about is we apply a therapy and if there's

NOTE Confidence: 0.889750823913044

00:25:03.965 --> 00:25:06.578 one responder we need to drill down.

NOTE Confidence: 0.878597683333333

00:25:09.350 --> 00:25:11.405 And focus on that responder

NOTE Confidence: 0.878597683333333

00:25:11.405 --> 00:25:13.049 and figure out why.

NOTE Confidence: 0.878597683333333

00:25:13.050 --> 00:25:15.723 And I'm going to tell you exactly why here.

NOTE Confidence: 0.878597683333333

00:25:15.730 --> 00:25:18.007 So if I had a dollar for every time

NOTE Confidence: 0.878597683333333

00:25:18.007 --> 00:25:20.527 I heard this, well since immune

NOTE Confidence: 0.878597683333333

00:25:20.527 --> 00:25:22.922 based cancer therapy doesn't work

NOTE Confidence: 0.878597683333333

00:25:22.922 --> 00:25:25.848 for colon cancer so very early on.

NOTE Confidence: 0.878597683333333

00:25:25.850 --> 00:25:26.969 In my career.

NOTE Confidence: 0.932593613333333

00:25:30.110 --> 00:25:32.798 Immunotherapy didn't work for colon cancer.

NOTE Confidence: 0.9424099425

00:25:35.080 --> 00:25:37.280 And and that goes all the way back.

NOTE Confidence: 0.9424099425

00:25:37.280 --> 00:25:39.233 Look at look at the years on this here.

NOTE Confidence: 0.9424099425

00:25:39.240 --> 00:25:43.320 This was 2006, 2009.

NOTE Confidence: 0.9424099425

00:25:43.320 --> 00:25:45.896 In which we did a phase one again,

NOTE Confidence: 0.9424099425

00:25:45.900 --> 00:25:49.940 this is safety. Study.

NOTE Confidence: 0.9424099425

00:25:49.940 --> 00:25:54.708 And that was conducted here at Johns Hopkins.

NOTE Confidence: 0.9424099425

00:25:54.710 --> 00:25:56.628 And you can see that the the

NOTE Confidence: 0.9424099425

00:25:56.628 --> 00:25:58.250 cancers that are listed here.

NOTE Confidence: 0.9424099425

00:25:58.250 --> 00:26:03.164 So Melanoma, lung cancer, renal cell cancer.

NOTE Confidence: 0.9424099425

00:26:03.170 --> 00:26:04.430 You know what? These are?

NOTE Confidence: 0.9424099425

00:26:04.430 --> 00:26:06.950 All immune based cancer therapies.

NOTE Confidence: 0.9424099425

00:26:06.950 --> 00:26:09.110 They kind of tend to respond.

NOTE Confidence: 0.9424099425

00:26:09.110 --> 00:26:11.102 In fact, one in four patients

NOTE Confidence: 0.9424099425

00:26:11.102 --> 00:26:13.040 did respond to this therapy.

NOTE Confidence: 0.9424099425

00:26:13.040 --> 00:26:16.568 Again, this was a safety trial.

NOTE Confidence: 0.9424099425

00:26:16.570 --> 00:26:18.166 We are focusing on, you know,

NOTE Confidence: 0.9424099425

00:26:18.170 --> 00:26:21.649 can patients tolerate this and suddenly in

NOTE Confidence: 0.9424099425

00:26:21.649 --> 00:26:26.374 this 2006 study we're talking about response.

NOTE Confidence: 0.9424099425

00:26:26.374 --> 00:26:29.016 This was crazy. And then.

NOTE Confidence: 0.9424099425

37

00:26:29.016 --> 00:26:30.868 The interesting thing is,

NOTE Confidence: 0.9424099425

00:26:30.870 --> 00:26:33.993 as I was hearing the chorus of well colon

NOTE Confidence: 0.9424099425

00:26:33.993 --> 00:26:36.867 cancer doesn't respond to immune therapy.

NOTE Confidence: 0.9424099425

00:26:36.870 --> 00:26:38.976 There were 14 patients who were

NOTE Confidence: 0.9424099425

00:26:38.976 --> 00:26:41.200 who were enrolled on this study,

NOTE Confidence: 0.9424099425

00:26:41.200 --> 00:26:43.908 and you know what?

NOTE Confidence: 0.9424099425

00:26:43.910 --> 00:26:45.548 It wasn't hard to find them right.

NOTE Confidence: 0.9424099425

00:26:45.550 --> 00:26:48.105 'cause colon cancer is among the most

NOTE Confidence: 0.9424099425

00:26:48.105 --> 00:26:51.347 common cancers and the take home was yeah,

NOTE Confidence: 0.9424099425

00:26:51.350 --> 00:26:54.395 you treated 14 patients with immune therapy.

NOTE Confidence: 0.9424099425

00:26:54.400 --> 00:26:56.974 Nobody is responding.

NOTE Confidence: 0.9424099425

00:26:56.974 --> 00:27:00.406 It clearly doesn't work.

NOTE Confidence: 0.9424099425

00:27:00.410 --> 00:27:02.302 Well, not so fast.

NOTE Confidence: 0.9424099425

00:27:02.302 --> 00:27:06.642 So it turns out that one patient did

NOTE Confidence: 0.9424099425

00:27:06.642 --> 00:27:09.648 respond and that patients Histology

NOTE Confidence: 0.9424099425

00:27:09.648 --> 00:27:13.110 ended up under my microscope and

38

NOTE Confidence: 0.9424099425

00:27:13.207 --> 00:27:15.897 it looked exactly like this.

NOTE Confidence: 0.9424099425

00:27:15.900 --> 00:27:18.546 And in fact, if any of you are are

NOTE Confidence: 0.9424099425

00:27:18.546 --> 00:27:20.219 familiar with Johns Hopkins,

NOTE Confidence: 0.9424099425

00:27:20.220 --> 00:27:23.196 it actually looked exactly like this.

NOTE Confidence: 0.9424099425

00:27:23.200 --> 00:27:25.896 So we were at one of these multi

NOTE Confidence: 0.9424099425

00:27:25.896 --> 00:27:27.889 headed scopes and Doctor Pardo,

NOTE Confidence: 0.9424099425

00:27:27.890 --> 00:27:29.620 a very well known tumor,

NOTE Confidence: 0.9424099425

00:27:29.620 --> 00:27:30.051 rheumatologist.

NOTE Confidence: 0.9424099425

00:27:30.051 --> 00:27:31.344 Here I was.

NOTE Confidence: 0.9424099425

00:27:31.344 --> 00:27:35.612 I was at this scope here or the head of

NOTE Confidence: 0.9424099425

00:27:35.612 --> 00:27:38.793 the scope and doctor Janice Tower was at

NOTE Confidence: 0.9424099425

00:27:38.793 --> 00:27:42.380 this scope and we looked underneath the

NOTE Confidence: 0.9424099425

00:27:42.380 --> 00:27:46.679 microscope at the one of 14 patients.

NOTE Confidence: 0.9424099425

00:27:46.680 --> 00:27:48.815 Who did respond to therapy

NOTE Confidence: 0.9424099425

00:27:48.815 --> 00:27:51.420 and this is what we saw.

NOTE Confidence: 0.9424099425

00:27:51.420 --> 00:27:53.752 This is the Histology,

NOTE Confidence: 0.9424099425

00:27:53.752 --> 00:27:56.084 typical Histology of mismatch

NOTE Confidence: 0.9424099425

00:27:56.084 --> 00:27:58.870 repair deficiency right all it's

NOTE Confidence: 0.9424099425

00:27:58.870 --> 00:28:00.914 almost medullary in quality.

NOTE Confidence: 0.9424099425

00:28:00.920 --> 00:28:04.388 There's a bunch of tumor infiltrating

NOTE Confidence: 0.9424099425

00:28:04.388 --> 00:28:06.786 lymphocytes. And you know what?

NOTE Confidence: 0.9424099425

00:28:06.786 --> 00:28:08.602 It's not surprising that

NOTE Confidence: 0.9424099425

00:28:08.602 --> 00:28:10.410 this patient responded.

NOTE Confidence: 0.9424099425

00:28:10.410 --> 00:28:13.097 To anti PD one therapy. Why?

NOTE Confidence: 0.9424099425

00:28:13.097 --> 00:28:15.732 Because everything is in place

NOTE Confidence: 0.9424099425

00:28:15.732 --> 00:28:19.378 and I'm I'll go through here and

NOTE Confidence: 0.9424099425

00:28:19.378 --> 00:28:22.710 and and and and map this out.

NOTE Confidence: 0.9424099425

00:28:22.710 --> 00:28:23.778 Mismatch repair deficiency.

NOTE Confidence: 0.9424099425

00:28:23.778 --> 00:28:26.270 They have a lot of antigens because

NOTE Confidence: 0.9424099425

00:28:26.330 --> 00:28:27.968 they have a lot of mutations.

NOTE Confidence: 0.9424099425

00:28:27.970 --> 00:28:29.494 How many mutations?

NOTE Confidence: 0.9424099425

00:28:29.494 --> 00:28:31.136 A lot right?

NOTE Confidence: 0.9424099425

00:28:31.136 --> 00:28:34.266 So here's a graph showing

NOTE Confidence: 0.9424099425

00:28:34.266 --> 00:28:37.250 the the frequency of of.

NOTE Confidence: 0.9424099425

00:28:37.250 --> 00:28:39.605 Of mutations and even in

NOTE Confidence: 0.9424099425

00:28:39.605 --> 00:28:41.489 something like a mutation,

NOTE Confidence: 0.9424099425

00:28:41.490 --> 00:28:44.170 associated cancer even MSI

NOTE Confidence: 0.9424099425

00:28:44.170 --> 00:28:47.520 here is orders of magnitude

NOTE Confidence: 0.9424099425

00:28:47.520 --> 00:28:50.568 greater in terms of antigens.

NOTE Confidence: 0.9424099425

00:28:50.570 --> 00:28:52.460 You know the way I think about

NOTE Confidence: 0.9424099425

00:28:52.460 --> 00:28:54.398 it is every one of these antigens

NOTE Confidence: 0.9424099425

00:28:54.398 --> 00:28:56.499 is is is is kind of like a.

NOTE Confidence: 0.941377794666667

00:28:58.550 --> 00:29:00.926 Is kind of like a ticket to Lynn to

NOTE Confidence: 0.941377794666667

00:29:00.926 --> 00:29:03.228 win the lottery and these people.

NOTE Confidence: 0.941377794666667

00:29:03.230 --> 00:29:06.350 These people have thousands of tickets.

NOTE Confidence: 0.941377794666667

00:29:06.350 --> 00:29:08.156 They also have lots of lymphocytes.

NOTE Confidence: 0.941377794666667

00:29:08.160 --> 00:29:08.628 Lymphocytes.

NOTE Confidence: 0.941377794666667

00:29:08.628 --> 00:29:11.436 We've known that every GI pathologist

NOTE Confidence: 0.941377794666667

00:29:11.436 --> 00:29:14.308 known knows that we actually went in,

NOTE Confidence: 0.941377794666667

00:29:14.310 --> 00:29:16.266 and our laboratory and measured it.

NOTE Confidence: 0.941377794666667

00:29:16.270 --> 00:29:18.586 We measured it in the in,

NOTE Confidence: 0.941377794666667

00:29:18.590 --> 00:29:21.502 in the tumor cells at the interface

NOTE Confidence: 0.941377794666667

00:29:21.502 --> 00:29:24.557 between the tumor cells and the and the.

NOTE Confidence: 0.862700343333333

00:29:26.620 --> 00:29:28.930 Are immune cells and this was work

NOTE Confidence: 0.862700343333333

00:29:28.930 --> 00:29:31.508 of a fellow and and junior faculty

NOTE Confidence: 0.862700343333333

00:29:31.508 --> 00:29:34.046 member at the time, and we were

NOTE Confidence: 0.862700343333333

00:29:34.046 --> 00:29:36.740 able to count them and guess what?

NOTE Confidence: 0.862700343333333

00:29:36.740 --> 00:29:39.516 It's not a surprise people with

NOTE Confidence: 0.862700343333333

00:29:39.516 --> 00:29:42.056 MSI or mismatch repair deficiency.

NOTE Confidence: 0.862700343333333

00:29:42.060 --> 00:29:44.490 They have more tumor infiltrating

NOTE Confidence: 0.862700343333333

00:29:44.490 --> 00:29:46.700 lymphocytes. Well, what about PDL one?

NOTE Confidence: 0.862700343333333

00:29:46.700 --> 00:29:50.004 Well, we were in the process of measuring

NOTE Confidence: 0.862700343333333

00:29:50.004 --> 00:29:53.640 PD L1 in solid tumors like this.

NOTE Confidence: 0.862700343333333

00:29:53.640 --> 00:29:58.174 Gastric cancer here. And what? Doctor.

NOTE Confidence: 0.862700343333333

00:29:58.174 --> 00:30:03.427 Thompson and Basharat T here found was

NOTE Confidence: 0.862700343333333

00:30:03.427 --> 00:30:05.996 that there's a lot of expression of

NOTE Confidence: 0.862700343333333

00:30:06.000 --> 00:30:10.800 PD L1 at the tumor infiltrate edge.

NOTE Confidence: 0.862700343333333

00:30:10.800 --> 00:30:13.264 The interesting thing is it's actually

NOTE Confidence: 0.862700343333333

00:30:13.264 --> 00:30:15.780 not on the tumor cells which are up here.

NOTE Confidence: 0.862700343333333

00:30:15.780 --> 00:30:17.772 It's actually at these immune cells

NOTE Confidence: 0.862700343333333

00:30:17.772 --> 00:30:20.378 and then we went and quantified this

NOTE Confidence: 0.862700343333333

00:30:20.380 --> 00:30:23.628 with Doctor Cruz lossa and by G here.

NOTE Confidence: 0.934975242857143

00:30:25.650 --> 00:30:27.568 Everybody that I've shown by the way,

NOTE Confidence: 0.934975242857143

00:30:27.570 --> 00:30:29.990 just as a as a as an aside here everybody

NOTE Confidence: 0.934975242857143

00:30:30.057 --> 00:30:31.971 that I've shown who's who's rotated

NOTE Confidence: 0.934975242857143

00:30:31.971 --> 00:30:34.378 through the lab or worked in the lab.

NOTE Confidence: 0.934975242857143

00:30:34.380 --> 00:30:36.040 They're all faculty members.

NOTE Confidence: 0.934975242857143

00:30:36.040 --> 00:30:38.942 So if you know if you're not even interested

NOTE Confidence: 0.934975242857143

00:30:38.942 --> 00:30:40.642 in tumor immunology, but you want to,

NOTE Confidence: 0.934975242857143

00:30:40.642 --> 00:30:42.230 you want to become a faculty member.

NOTE Confidence: 0.934975242857143

00:30:42.230 --> 00:30:43.654 Just study tumor immunology.

NOTE Confidence: 0.934975242857143

00:30:43.654 --> 00:30:45.790 The odds are in your favor,

NOTE Confidence: 0.934975242857143

00:30:45.790 --> 00:30:50.038 so in the end, you know it's obvious.

NOTE Confidence: 0.934975242857143

00:30:50.040 --> 00:30:51.012 Mismatch repair.

NOTE Confidence: 0.934975242857143

00:30:51.012 --> 00:30:54.414 Deficient cancers have a lot of antigens.

NOTE Confidence: 0.934975242857143

00:30:54.420 --> 00:30:56.436 They have a lot of lymphocytes and

NOTE Confidence: 0.934975242857143

00:30:56.436 --> 00:30:58.987 they have a lot of PDL one expression.

NOTE Confidence: 0.934975242857143

00:30:58.990 --> 00:31:01.475 So I'm going to show you this.

NOTE Confidence: 0.934975242857143

00:31:01.480 --> 00:31:03.656 Particular publication here looking

NOTE Confidence: 0.934975242857143

00:31:03.656 --> 00:31:06.920 at PD1 blockade in the setting

NOTE Confidence: 0.934975242857143

00:31:07.006 --> 00:31:09.478 of mismatch repair deficiency.

NOTE Confidence: 0.934975242857143

00:31:09.480 --> 00:31:13.140 There's 10 pathologists on this manual.

NOTE Confidence: 0.09579292

00:31:15.160 --> 00:31:17.030 And somebody please mute who's

44

NOTE Confidence: 0.09579292

00:31:17.030 --> 00:31:18.910 ever talking neuter phone.

NOTE Confidence: 0.642456304

00:31:19.700 --> 00:31:21.770 Somebody is somebody talking. So

NOTE Confidence: 0.589385754

00:31:22.600 --> 00:31:26.803 this study was presented in 2015

NOTE Confidence: 0.589385754

00:31:26.803 --> 00:31:29.470 and one what they collected

NOTE Confidence: 0.787986258

00:31:29.480 --> 00:31:33.290 were mismatch repair. Deficient cancers.

NOTE Confidence: 0.813022387333333

00:31:35.400 --> 00:31:38.291 About 25 of each. They treated them

NOTE Confidence: 0.813022387333333

00:31:38.291 --> 00:31:41.908 with PD one and it's no surprise that.

NOTE Confidence: 0.9050253675

00:31:44.910 --> 00:31:46.350 They responded well.

NOTE Confidence: 0.9050253675

00:31:46.350 --> 00:31:49.356 They were responded super well and

NOTE Confidence: 0.9050253675

00:31:49.356 --> 00:31:52.386 the thing that really catapulted

NOTE Confidence: 0.9050253675

00:31:52.386 --> 00:31:56.520 this particular finding was that.

NOTE Confidence: 0.9050253675

00:31:56.520 --> 00:31:59.170 The response rate here 62

NOTE Confidence: 0.9050253675

00:31:59.170 --> 00:32:01.915 versus 60 or 92 versus 70.

NOTE Confidence: 0.9050253675

00:32:01.915 --> 00:32:05.320 It didn't matter if they were colon cancers.

NOTE Confidence: 0.9050253675

00:32:05.320 --> 00:32:07.780 What mattered?

NOTE Confidence: 0.9050253675

00:32:07.780 --> 00:32:09.490 Was that they were mismatched

00:32:09.490 --> 00:32:10.516 for pair deficient,

00:32:10.520 --> 00:32:13.640 so suddenly now we move forward,

00:32:13.640 --> 00:32:15.340 it's not mismatch repair,

00:32:15.340 --> 00:32:16.615 deficient colon cancer,

00:32:16.620 --> 00:32:18.272 it's mismatch repair, deficient,

00:32:18.272 --> 00:32:22.208 any cancer, and that quickly catapulted.

00:32:22.210 --> 00:32:26.170 Monk ologists at at at at Johns Hopkins.

00:32:26.170 --> 00:32:30.158 Doctor Lee and Doctor Diaz to put

00:32:30.158 --> 00:32:33.347 together a study in which the

00:32:33.347 --> 00:32:35.743 enrollment criteria was mismatch

00:32:35.743 --> 00:32:39.089 repair deficiency or MSI instability.

00:32:39.090 --> 00:32:40.920 However you wish to call

00:32:40.920 --> 00:32:42.750 it in any tumor type.

00:32:42.750 --> 00:32:44.334 This is crazy.

00:32:44.334 --> 00:32:48.807 We never thought that this would ever, ever.

NOTE Confidence: 0.9050253675

00:32:48.807 --> 00:32:54.246 B. Away we enrolled criteria patients right?

NOTE Confidence: 0.9050253675

00:32:54.250 --> 00:32:55.660 If you have a colon cancer,

NOTE Confidence: 0.9050253675

00:32:55.660 --> 00:32:56.684 you get one treatment.

NOTE Confidence: 0.9050253675

00:32:56.684 --> 00:32:58.220 If you have a pancreatic cancer,

NOTE Confidence: 0.9050253675

00:32:58.220 --> 00:33:00.740 you get a different treatment.

NOTE Confidence: 0.9050253675

00:33:00.740 --> 00:33:04.496 This was based on molecular diagnosis

NOTE Confidence: 0.9050253675

00:33:04.500 --> 00:33:08.060 and you know what it goes even crazier.

NOTE Confidence: 0.9050253675

00:33:08.060 --> 00:33:10.170 Because the FDA approved it.

NOTE Confidence: 0.89959647

00:33:12.510 --> 00:33:16.150 Now I have sat with the FDA

NOTE Confidence: 0.89959647

00:33:16.150 --> 00:33:19.290 for prolonged periods of time.

NOTE Confidence: 0.89959647

00:33:19.290 --> 00:33:23.526 They are not very exciting people.

NOTE Confidence: 0.89959647

00:33:23.530 --> 00:33:27.324 And the fact that they approved a

NOTE Confidence: 0.89959647

00:33:27.324 --> 00:33:29.178 therapy independent of Histology

NOTE Confidence: 0.89959647

00:33:29.178 --> 00:33:32.230 First off has never been done before,

NOTE Confidence: 0.89959647

00:33:32.230 --> 00:33:34.070 so that's worth mentioning.

NOTE Confidence: 0.89959647

00:33:34.070 --> 00:33:37.341 But the fact that they approved a

NOTE Confidence: 0.89959647

00:33:37.341 --> 00:33:39.621 treatment independent of Histology,

NOTE Confidence: 0.89959647

00:33:39.621 --> 00:33:44.590 and based on a non FDA approved test.

NOTE Confidence: 0.89959647

00:33:44.590 --> 00:33:47.330 Are you kidding me?

NOTE Confidence: 0.89959647

00:33:47.330 --> 00:33:51.354 But yet it's the standard of care today.

NOTE Confidence: 0.89959647

00:33:51.360 --> 00:33:53.740 And it all came back.

NOTE Confidence: 0.89959647

00:33:53.740 --> 00:33:59.990 To the fact that we were. Looking for.

NOTE Confidence: 0.89959647

00:33:59.990 --> 00:34:03.270 Patients who did respond.

NOTE Confidence: 0.89959647

00:34:03.270 --> 00:34:06.126 In a setting of patients who.

NOTE Confidence: 0.89959647

00:34:06.130 --> 00:34:07.918 Largely didn't respond.

NOTE Confidence: 0.898454395

00:34:10.500 --> 00:34:13.852 OK, so the thing that happens to me

NOTE Confidence: 0.898454395

00:34:13.852 --> 00:34:17.002 most and it is probably happening

NOTE Confidence: 0.898454395

00:34:17.002 --> 00:34:20.320 to doctor Shelper and Doctor Rim,

NOTE Confidence: 0.898454395

00:34:20.320 --> 00:34:23.520 is let's find more biomarkers.

NOTE Confidence: 0.898454395

00:34:23.520 --> 00:34:27.055 You guys are the pathologist tissue is

NOTE Confidence: 0.898454395

00:34:27.055 --> 00:34:29.620 important. Let's find more biomarkers.

NOTE Confidence: 0.898454395

00:34:29.620 --> 00:34:32.710 So how do we find more?

NOTE Confidence: 0.898454395

00:34:32.710 --> 00:34:37.410 File markers. So.

NOTE Confidence: 0.898454395

00:34:37.410 --> 00:34:40.290 Anyone who walks in my office.

NOTE Confidence: 0.898454395

00:34:40.290 --> 00:34:42.166 The first thing that they hear is

NOTE Confidence: 0.898454395

00:34:42.166 --> 00:34:43.610 there's no substitute for quality,

NOTE Confidence: 0.898454395

00:34:43.610 --> 00:34:48.394 and that's true in terms of cancer biology,

NOTE Confidence: 0.898454395

00:34:48.400 --> 00:34:53.370 and it's really a science of corollary.

NOTE Confidence: 0.898454395

00:34:53.370 --> 00:34:54.550 And you know, for me,

NOTE Confidence: 0.898454395

00:34:54.550 --> 00:34:56.030 how do you cure cancer?

NOTE Confidence: 0.898454395

00:34:56.030 --> 00:34:58.915 You make high accurate or

NOTE Confidence: 0.898454395

00:34:58.915 --> 00:35:01.040 highly accurate measurements.

NOTE Confidence: 0.8996276075

00:35:04.320 --> 00:35:07.295 And the emphasis here on

NOTE Confidence: 0.8996276075

00:35:07.295 --> 00:35:09.080 accurate and measurements.

NOTE Confidence: 0.8996276075

00:35:09.080 --> 00:35:11.048 Well then it brings up the

NOTE Confidence: 0.8996276075

00:35:11.048 --> 00:35:12.550 question how many measurements?

NOTE Confidence: 0.8996276075

00:35:12.550 --> 00:35:16.320 Do we need to make hundreds of measurements?

NOTE Confidence: 0.8996276075

00:35:16.320 --> 00:35:16.948 Four measurements,

NOTE Confidence: 0.8996276075

00:35:16.948 --> 00:35:19.859 you know we have that issue in front of us.

NOTE Confidence: 0.8996276075

00:35:19.860 --> 00:35:21.336 What are we going to do?

NOTE Confidence: 0.8996276075

00:35:21.340 --> 00:35:23.538 And that was the subject of a

NOTE Confidence: 0.8996276075

00:35:23.538 --> 00:35:25.848 beautiful paper done by one of our

NOTE Confidence: 0.8996276075

00:35:25.848 --> 00:35:27.762 graduate students here Steve Lu.

NOTE Confidence: 0.8996276075

00:35:27.762 --> 00:35:30.588 And what I'm showing you is

NOTE Confidence: 0.8996276075

00:35:30.588 --> 00:35:33.408 the receiver operator curve for

NOTE Confidence: 0.8996276075

00:35:33.408 --> 00:35:35.698 a number of different tests.

NOTE Confidence: 0.8996276075

00:35:35.700 --> 00:35:38.372 And for those of you who might not

NOTE Confidence: 0.8996276075

00:35:38.372 --> 00:35:40.708 be familiar with a narrow C curve,

NOTE Confidence: 0.8996276075

00:35:40.710 --> 00:35:43.825 the closer you get to this one.

NOTE Confidence: 0.8996276075

00:35:43.830 --> 00:35:47.250 The better so the green line

NOTE Confidence: 0.8996276075

00:35:47.250 --> 00:35:49.770 is better than the dashed line.

NOTE Confidence: 0.8996276075

00:35:49.770 --> 00:35:53.081 To put it simply. OK,

NOTE Confidence: 0.8996276075

00:35:53.081 --> 00:35:56.098 So what do these different lines represent?

NOTE Confidence: 0.8996276075

00:35:56.100 --> 00:35:59.517 And so this is the, UM.

NOTE Confidence: 0.8996276075

00:35:59.517 --> 00:36:03.416 This is a meta analysis in which

NOTE Confidence: 0.8996276075

00:36:03.416 --> 00:36:07.080 Steve Lew collected 55 studies

NOTE Confidence: 0.8996276075

00:36:07.080 --> 00:36:09.210 from 10 different tumor types,

NOTE Confidence: 0.8996276075

00:36:09.210 --> 00:36:11.370 encompassing over 8000 patients.

NOTE Confidence: 0.8996276075

00:36:11.370 --> 00:36:14.610 So this is about as comprehensive

NOTE Confidence: 0.8996276075

00:36:14.692 --> 00:36:17.456 as we could get in in 2019,

NOTE Confidence: 0.8996276075

00:36:17.456 --> 00:36:21.640 and what was determined.

NOTE Confidence: 0.8996276075

00:36:21.640 --> 00:36:25.940 Four response was either PDL.

NOTE Confidence: 0.8996276075

00:36:25.940 --> 00:36:29.124 One expression by immunohistochemistry,

NOTE Confidence: 0.8996276075

00:36:29.124 --> 00:36:32.308 that's the blue line.

NOTE Confidence: 0.8996276075

00:36:32.310 --> 00:36:34.590 Total mutational burden.

NOTE Confidence: 0.8996276075

00:36:34.590 --> 00:36:37.438 So that's you know the number

NOTE Confidence: 0.8996276075

00:36:37.438 --> 00:36:39.098 of mutations in a genome.

NOTE Confidence: 0.8996276075

00:36:39.100 --> 00:36:43.486 That's the red line. And then.

NOTE Confidence: 0.8996276075

00:36:43.490 --> 00:36:45.850 The expression of RNA markers.

NOTE Confidence: 0.8996276075

00:36:45.850 --> 00:36:48.070 Generally these are inflammatory markers.

NOTE Confidence: 0.8996276075

00:36:48.070 --> 00:36:50.074 That's the yellow wine.

NOTE Confidence: 0.8996276075

00:36:50.074 --> 00:36:53.080 And then in the green line.

NOTE Confidence: 0.8996276075

00:36:53.080 --> 00:36:56.335 Which is showing the best performance here?

NOTE Confidence: 0.8996276075

00:36:56.340 --> 00:37:01.750 All we needed. Was a minimum of two.

NOTE Confidence: 0.8996276075

00:37:01.750 --> 00:37:03.878 Emphasis on 2 markers.

NOTE Confidence: 0.943972611428571

00:37:06.250 --> 00:37:09.770 And you can see the significant shift in

NOTE Confidence: 0.943972611428571

00:37:09.770 --> 00:37:16.310 the arosi curve here with as few as two.

NOTE Confidence: 0.943972611428571

00:37:16.310 --> 00:37:18.260 Immunohistochemistry markers.

NOTE Confidence: 0.924478722

00:37:21.090 --> 00:37:23.338 So based on that,

NOTE Confidence: 0.924478722

00:37:23.338 --> 00:37:26.932 on those types of findings and in

NOTE Confidence: 0.924478722

00:37:26.932 --> 00:37:28.708 a lot of the work that we've done,

NOTE Confidence: 0.924478722

00:37:28.710 --> 00:37:31.938 Doctor Janice Taube and I were

NOTE Confidence: 0.924478722

00:37:31.938 --> 00:37:34.769 were charged with setting up the

NOTE Confidence: 0.924478722

00:37:34.770 --> 00:37:37.254 tumor and microenvironment core.

NOTE Confidence: 0.924478722

00:37:37.254 --> 00:37:43.819 We have a very experienced lab manager here.

NOTE Confidence: 0.924478722

00:37:43.820 --> 00:37:46.868 It was set up through the Bloomberg Kimmel

NOTE Confidence: 0.924478722

00:37:46.868 --> 00:37:51.560 Institute for Immune based Cancer therapy.

NOTE Confidence: 0.924478722

00:37:51.560 --> 00:37:53.660 Essentially it's a Cancer Center resource.

NOTE Confidence: 0.924478722

00:37:53.660 --> 00:37:56.700 Here the idea is that we would help

NOTE Confidence: 0.924478722

00:37:56.700 --> 00:37:59.748 you measure tumor markers in the

NOTE Confidence: 0.924478722

00:37:59.748 --> 00:38:02.498 tumor microenvironment and our current

NOTE Confidence: 0.924478722

00:38:02.498 --> 00:38:04.997 holdings are are explained here.

NOTE Confidence: 0.924478722

00:38:05.000 --> 00:38:07.598 We we offer hundreds of stains,

NOTE Confidence: 0.924478722

00:38:07.600 --> 00:38:10.720 some of which we can do in two color and

NOTE Confidence: 0.924478722

00:38:10.799 --> 00:38:14.309 some of which we can do in in multiple color.

NOTE Confidence: 0.924478722

00:38:14.310 --> 00:38:19.198 We have a lot of machines in this

NOTE Confidence: 0.924478722

00:38:19.198 --> 00:38:21.868 particular laboratory that we run.

NOTE Confidence: 0.924478722

00:38:21.870 --> 00:38:25.791 We have 4. Our scanning machines.

NOTE Confidence: 0.924478722

00:38:25.791 --> 00:38:28.376 We have two auto stainers.

NOTE Confidence: 0.924478722

00:38:28.380 --> 00:38:31.398 We have an optical scanner and

NOTE Confidence: 0.924478722

00:38:31.398 --> 00:38:33.410 a laser microdissection scope,

NOTE Confidence: 0.924478722

00:38:33.410 --> 00:38:36.238 so that's to say you know we're

NOTE Confidence: 0.924478722

00:38:36.238 --> 00:38:38.214 we're we're equipped as anyone

NOTE Confidence: 0.924478722

00:38:38.214 --> 00:38:40.950 would expect us to be in order to,

NOTE Confidence: 0.924478722

00:38:40.950 --> 00:38:43.414 you know, perform investigations

NOTE Confidence: 0.924478722

00:38:43.414 --> 00:38:45.878 into the tumor microenvironment,

NOTE Confidence: 0.924478722

00:38:45.880 --> 00:38:47.644 and you can see this is what

NOTE Confidence: 0.924478722

00:38:47.644 --> 00:38:48.940 we're able to produce.

NOTE Confidence: 0.924478722

00:38:48.940 --> 00:38:49.854 And again,

NOTE Confidence: 0.924478722

00:38:49.854 --> 00:38:52.722 Doctor Shelper and and RIM have really

NOTE Confidence: 0.924478722

00:38:52.722 --> 00:38:54.759 been leading the way in terms of.

NOTE Confidence: 0.924478722

00:38:54.760 --> 00:38:56.518 Multi color immunofluorescence,

NOTE Confidence: 0.924478722

00:38:56.518 --> 00:39:00.594 which is what we see here now.

NOTE Confidence: 0.924478722

00:39:00.594 --> 00:39:02.810 The interesting thing is.

NOTE Confidence: 0.924478722

00:39:02.810 --> 00:39:08.711 That when we broke down the the steps

NOTE Confidence: 0.924478722

00:39:08.711 --> 00:39:14.406 of evaluating us a slide that's been

NOTE Confidence: 0.924478722

00:39:14.406 --> 00:39:16.779 staying with immunofluorescence.

NOTE Confidence: 0.924478722

00:39:16.780 --> 00:39:19.222 Janice and I found out there's

NOTE Confidence: 0.924478722

00:39:19.222 --> 00:39:20.850 a lot of errors.

NOTE Confidence: 0.924478722

00:39:20.850 --> 00:39:24.485 And those errors make evaluation

NOTE Confidence: 0.924478722

00:39:24.485 --> 00:39:26.666 very very problematic.

NOTE Confidence: 0.924478722

00:39:26.670 --> 00:39:30.842 So I'm summarizing the steps of of

NOTE Confidence: 0.924478722

00:39:30.842 --> 00:39:34.489 staining something with multiple markers.

NOTE Confidence: 0.924478722

00:39:34.490 --> 00:39:39.158 And and summarizing the errors here.

NOTE Confidence: 0.924478722

00:39:39.160 --> 00:39:42.664 Such that the image acquisition off

NOTE Confidence: 0.924478722

00:39:42.664 --> 00:39:46.072 of the microscope it was it turned

NOTE Confidence: 0.924478722

00:39:46.072 --> 00:39:49.149 out that the spherical you know sort

NOTE Confidence: 0.924478722

00:39:49.149 --> 00:39:52.705 of band or aperture of the objectives

NOTE Confidence: 0.924478722

00:39:52.705 --> 00:39:55.574 was contributing almost to a two fold

NOTE Confidence: 0.924478722

00:39:55.574 --> 00:39:57.760 error in in in image acquisition.

NOTE Confidence: 0.924478722

00:39:57.760 --> 00:39:58.180 Well,

NOTE Confidence: 0.924478722

00:39:58.180 --> 00:40:01.540 it's really hard to be sure what you're

NOTE Confidence: 0.924478722

00:40:01.613 --> 00:40:04.504 measuring when there's a two fold error.

NOTE Confidence: 0.924478722

00:40:04.510 --> 00:40:07.678 And again we systematically.

NOTE Confidence: 0.924478722

00:40:07.680 --> 00:40:11.194 Went through and and looked at these

NOTE Confidence: 0.924478722

00:40:11.194 --> 00:40:14.864 different errors the the method of

NOTE Confidence: 0.924478722

00:40:14.864 --> 00:40:18.194 immunofluorescence is is indicated here.

NOTE Confidence: 0.924478722

00:40:18.200 --> 00:40:24.100 It's a. It's a TSA method, it's actually a.

NOTE Confidence: 0.924478722

00:40:24.100 --> 00:40:27.440 It's a covalent bond.

NOTE Confidence: 0.924478722

00:40:27.440 --> 00:40:28.432 Such that.

NOTE Confidence: 0.924478722

00:40:28.432 --> 00:40:31.408 When the two antibodies are present,

NOTE Confidence: 0.924478722

00:40:31.410 --> 00:40:33.614 so this could be a CD3 antibody

NOTE Confidence: 0.924478722

00:40:33.614 --> 00:40:36.626 and this would be an antibody

NOTE Confidence: 0.924478722

00:40:36.626 --> 00:40:39.090 to detect this antibody.

NOTE Confidence: 0.924478722

00:40:39.090 --> 00:40:43.668 In the presence of horseradish peroxidase.

NOTE Confidence: 0.924478722

00:40:43.670 --> 00:40:47.990 This tyramide becomes inactive and

NOTE Confidence: 0.924478722

00:40:47.990 --> 00:40:52.310 becomes active and covalently links

NOTE Confidence: 0.924478722

00:40:52.442 --> 00:40:55.298 with the proteins that are nearby.

NOTE Confidence: 0.924478722

00:40:55.298 --> 00:40:59.479 This is what allows us to do reciprocal.

NOTE Confidence: 0.893013185833333

00:41:02.880 --> 00:41:05.328 Antibody staining because these

NOTE Confidence: 0.893013185833333

00:41:05.328 --> 00:41:09.000 antibodies are then rinsed off while

NOTE Confidence: 0.893013185833333

00:41:09.090 --> 00:41:14.178 their covalent binding is in place.

NOTE Confidence: 0.893013185833333

00:41:14.180 --> 00:41:19.112 Uh, it's not easy to to acquire these images.

NOTE Confidence: 0.893013185833333

00:41:19.120 --> 00:41:21.712 What I'm showing you here is

NOTE Confidence: 0.893013185833333

00:41:21.712 --> 00:41:23.960 a typical lung cancer case.

NOTE Confidence: 0.893013185833333

00:41:23.960 --> 00:41:28.027 Each square is a high power field.

NOTE Confidence: 0.893013185833333

00:41:28.030 --> 00:41:31.366 Each each cancer then would be

NOTE Confidence: 0.893013185833333

00:41:31.366 --> 00:41:35.254 represented by over a 1000 fields

NOTE Confidence: 0.893013185833333

00:41:35.254 --> 00:41:39.630 which which is 75 gigabytes of data.

NOTE Confidence: 0.893013185833333

00:41:39.630 --> 00:41:41.980 That's a lot of data.

NOTE Confidence: 0.893013185833333

00:41:41.980 --> 00:41:44.938 For one patient.

NOTE Confidence: 0.893013185833333

00:41:44.940 --> 00:41:46.490 So Janice and I were,

NOTE Confidence: 0.893013185833333

00:41:46.490 --> 00:41:49.920 as pathologists were quickly overwhelmed

NOTE Confidence: 0.893013185833333

00:41:49.920 --> 00:41:53.722 and we were so fortunate by Doctor

NOTE Confidence: 0.893013185833333

00:41:53.722 --> 00:41:58.874 Jaffe to be pointed in the direction.

NOTE Confidence: 0.893013185833333

00:41:58.880 --> 00:42:03.017 Of Doctor Alex Szalay who helped us

NOTE Confidence: 0.893013185833333

00:42:03.017 --> 00:42:06.400 develop essentially the Astro pathology

NOTE Confidence: 0.893013185833333

00:42:06.400 --> 00:42:09.400 platform and the idea is that Doctor Salay.

NOTE Confidence: 0.893013185833333

00:42:09.400 --> 00:42:14.174 Here he is an expert in establishing

NOTE Confidence: 0.893013185833333

00:42:14.180 --> 00:42:16.668 the database that's responsible

NOTE Confidence: 0.893013185833333

00:42:16.668 --> 00:42:19.778 for imaging the entire sky.

NOTE Confidence: 0.893013185833333

00:42:19.780 --> 00:42:22.650 Not your pretty daunting idea here and

NOTE Confidence: 0.893013185833333

00:42:22.650 --> 00:42:25.145 then what Doctor Salay quickly realized

NOTE Confidence: 0.893013185833333

00:42:25.145 --> 00:42:28.959 is that what Janice and I were trying to do.

NOTE Confidence: 0.893013185833333

00:42:28.960 --> 00:42:30.748 On the microscopic level,

NOTE Confidence: 0.893013185833333

00:42:30.748 --> 00:42:34.454 was really exactly what he had done at

NOTE Confidence: 0.893013185833333

00:42:34.454 --> 00:42:36.809 the macroscopic level in establishing

NOTE Confidence: 0.893013185833333

00:42:36.809 --> 00:42:39.818 the the Sloan Digital Sky server,

NOTE Confidence: 0.893013185833333

00:42:39.820 --> 00:42:41.738 and if you've never done this before,

NOTE Confidence: 0.893013185833333

00:42:41.740 --> 00:42:42.901 it's super cool.

NOTE Confidence: 0.893013185833333

00:42:42.901 --> 00:42:45.223 You don't have to be in

NOTE Confidence: 0.893013185833333

00:42:45.223 --> 00:42:46.599 astronomer or anything,

NOTE Confidence: 0.893013185833333

00:42:46.600 --> 00:42:49.312 you can just log in as a regular

NOTE Confidence: 0.893013185833333

00:42:49.312 --> 00:42:51.820 you know interested scientist,

NOTE Confidence: 0.893013185833333

00:42:51.820 --> 00:42:55.719 person and and look at the sky.

NOTE Confidence: 0.893013185833333

00:42:55.720 --> 00:42:56.929 And in fact,

NOTE Confidence: 0.893013185833333

00:42:56.929 --> 00:42:59.750 there have been very high level publications.

NOTE Confidence: 0.893013185833333

00:42:59.750 --> 00:43:02.565 Nature level publications that have

NOTE Confidence: 0.893013185833333

00:43:02.565 --> 00:43:07.068 come out of. You know, sort of.

NOTE Confidence: 0.893013185833333

00:43:07.070 --> 00:43:11.138 Public scientists going into this database

NOTE Confidence: 0.893013185833333

00:43:11.138 --> 00:43:14.532 that doctor Slate helped establish

NOTE Confidence: 0.893013185833333

00:43:14.532 --> 00:43:19.940 and and and finding things in a straw.

NOTE Confidence: 0.893013185833333

00:43:19.940 --> 00:43:21.974 In the night sky that we

NOTE Confidence: 0.893013185833333

00:43:21.974 --> 00:43:23.330 didn't even know existed.

NOTE Confidence: 0.893013185833333

00:43:23.330 --> 00:43:27.690 So probably after the telescope.

NOTE Confidence: 0.893013185833333

00:43:27.690 --> 00:43:33.210 This is the most important piece of.

NOTE Confidence: 0.893013185833333

00:43:33.210 --> 00:43:36.332 Technology that we've had to look into

NOTE Confidence: 0.893013185833333

00:43:36.332 --> 00:43:40.223 the skies and we again had just been so

NOTE Confidence: 0.893013185833333

00:43:40.223 --> 00:43:43.139 so fortunate that this individual doctor

NOTE Confidence: 0.893013185833333

00:43:43.139 --> 00:43:46.673 Salay was interested in our problems.

NOTE Confidence: 0.893013185833333

00:43:46.680 --> 00:43:48.618 And again, I don't think it's

NOTE Confidence: 0.893013185833333

00:43:48.620 --> 00:43:51.590 too complicated to think of.

NOTE Confidence: 0.893013185833333

00:43:51.590 --> 00:43:54.390 Microscopes and telescopes are just

NOTE Confidence: 0.893013185833333

00:43:54.390 --> 00:43:59.758 sort of the same problem, inverted.

NOTE Confidence: 0.893013185833333

00:43:59.760 --> 00:44:04.056 So that led to this publication.

NOTE Confidence: 0.893013185833333

00:44:04.060 --> 00:44:06.540 Where we described the method.

NOTE Confidence: 0.893013185833333

00:44:06.540 --> 00:44:08.226 Now let let let's just step

NOTE Confidence: 0.893013185833333

00:44:08.226 --> 00:44:09.730 back for a second here.

NOTE Confidence: 0.893013185833333

00:44:09.730 --> 00:44:13.700 This is essentially a method describing.

NOTE Confidence: 0.917711923333333

00:44:15.760 --> 00:44:18.718 How to interrogate in multiple colors?

NOTE Confidence: 0.917711923333333

00:44:18.720 --> 00:44:20.995 Oh it was only seven or eight

NOTE Confidence: 0.917711923333333

00:44:20.995 --> 00:44:23.030 colors in into human tissue and

NOTE Confidence: 0.917711923333333

00:44:23.030 --> 00:44:25.780 it ended up with a high impact.

NOTE Confidence: 0.917711923333333

00:44:25.780 --> 00:44:29.850 You know publication, I think.

NOTE Confidence: 0.917711923333333

00:44:29.850 --> 00:44:32.628 That's really a testament to the

NOTE Confidence: 0.917711923333333

00:44:32.628 --> 00:44:35.259 fact of how difficult this is.

NOTE Confidence: 0.917711923333333

00:44:35.260 --> 00:44:38.277 What did we do in this paper?

NOTE Confidence: 0.917711923333333

00:44:38.280 --> 00:44:40.620 We looked at metastatic melanomas

NOTE Confidence: 0.917711923333333

00:44:40.620 --> 00:44:42.492 and found predictive biomarkers.

NOTE Confidence: 0.917711923333333

00:44:42.500 --> 00:44:45.510 The discovery cohort came out of Johns

NOTE Confidence: 0.917711923333333

00:44:45.510 --> 00:44:48.478 Hopkins in the validation cohort was

NOTE Confidence: 0.917711923333333

00:44:48.478 --> 00:44:51.670 so graciously provided by Doctor Rim.

NOTE Confidence: 0.917711923333333

00:44:51.670 --> 00:44:54.950 What? What was the what was the magic?

NOTE Confidence: 0.892539366

00:44:57.460 --> 00:45:00.300 It was, it was cells that you and

NOTE Confidence: 0.892539366

00:45:00.300 --> 00:45:03.102 I as tumor immunologists or even

NOTE Confidence: 0.892539366

00:45:03.102 --> 00:45:05.194 as pathologists would predict.

NOTE Confidence: 0.892539366

00:45:05.200 --> 00:45:08.368 It's you know PDL, one expression

NOTE Confidence: 0.892539366

00:45:08.368 --> 00:45:11.849 Fox P3 expression CD 8 expression.

NOTE Confidence: 0.892539366

00:45:11.850 --> 00:45:14.378 You know things that we know are important.

NOTE Confidence: 0.892539366

00:45:14.380 --> 00:45:18.916 These are the the the predictive biomarkers.

NOTE Confidence: 0.892539366

00:45:18.920 --> 00:45:23.424 Alright, so how can we improve upon multi

NOTE Confidence: 0.892539366

00:45:23.424 --> 00:45:26.499 marker detection and cancer tissues?

NOTE Confidence: 0.892539366

00:45:26.500 --> 00:45:30.469 So we're exploring adding more markers in,

NOTE Confidence: 0.892539366

00:45:30.470 --> 00:45:33.422 but I don't actually think that is the key.

NOTE Confidence: 0.892539366

00:45:33.430 --> 00:45:37.294 Using a codex of.

NOTE Confidence: 0.892539366

00:45:37.294 --> 00:45:42.950 Method there's also RNA based methods.

NOTE Confidence: 0.892539366

00:45:42.950 --> 00:45:44.894 Let's just get back down to you know,

NOTE Confidence: 0.892539366

00:45:44.900 --> 00:45:47.672 I've been doing this for over a decade now.

NOTE Confidence: 0.892539366

00:45:47.680 --> 00:45:49.776 And and here's my thoughts on on really

NOTE Confidence: 0.892539366

00:45:49.776 --> 00:45:51.899 how to find predictive biomarkers.

NOTE Confidence: 0.892539366

00:45:51.900 --> 00:45:55.519 First off, there's no substitute for quality.

NOTE Confidence: 0.892539366

00:45:55.520 --> 00:45:56.978 If you don't know what you're

NOTE Confidence: 0.892539366

00:45:56.978 --> 00:45:58.220 measuring or there's too much,

NOTE Confidence: 0.892539366

00:45:58.220 --> 00:46:00.278 you know error and what you're measuring,

NOTE Confidence: 0.892539366

00:46:00.280 --> 00:46:01.780 you're just looking at noise.

NOTE Confidence: 0.892539366

00:46:01.780 --> 00:46:04.900 It's easy to generate noisy signals,

NOTE Confidence: 0.892539366

00:46:04.900 --> 00:46:07.480 but it's difficult to, you know,

NOTE Confidence: 0.892539366

00:46:07.480 --> 00:46:10.120 sort through that noise.

NOTE Confidence: 0.892539366

00:46:10.120 --> 00:46:12.760 Don't overthink the analysis.

NOTE Confidence: 0.892539366

00:46:12.760 --> 00:46:15.100 We need T cells and we need B cells

NOTE Confidence: 0.892539366

00:46:15.100 --> 00:46:18.750 to make immune based, you know.

NOTE Confidence: 0.892539366

00:46:18.750 --> 00:46:20.535 Cancer therapies that's sort of

NOTE Confidence: 0.892539366

00:46:20.535 --> 00:46:22.550 what they're what they're aimed at.

NOTE Confidence: 0.925175462222222

63

00:46:24.610 --> 00:46:28.650 I think we should focus on on spatial

00:46:28.650 --> 00:46:31.300 relationships and that's described or or

00:46:31.300 --> 00:46:34.640 or demonstrated here in the bottom figure.

00:46:34.640 --> 00:46:36.579 So what I'm showing you here is

00:46:36.579 --> 00:46:38.700 a tumor cell that's in white and

00:46:38.700 --> 00:46:40.940 the T or B cells. I don't know.

00:46:40.940 --> 00:46:43.544 Pick your favorite are are the yellow

00:46:43.544 --> 00:46:47.290 dots here and something tells me.

00:46:47.290 --> 00:46:51.520 That the image on the right.

00:46:51.520 --> 00:46:56.758 With T or B cells surrounding the tumor cell.

00:46:56.760 --> 00:47:00.694 He's probably more indicative of a tumor

00:47:00.694 --> 00:47:04.498 immune response than the one over here yet.

00:47:04.500 --> 00:47:05.844 By simple density,

00:47:05.844 --> 00:47:09.470 we would report out the same numbers here.

00:47:09.470 --> 00:47:11.475 So I think the spatial

00:47:11.475 --> 00:47:12.678 relationships which interestingly

NOTE Confidence: 0.88613685

00:47:15.060 --> 00:47:17.370 we're not part of this.

NOTE Confidence: 0.88613685

00:47:17.370 --> 00:47:20.730 Publication this was simply a density.

NOTE Confidence: 0.88613685

00:47:20.730 --> 00:47:23.410 Publication so I think spatial

NOTE Confidence: 0.88613685

00:47:23.410 --> 00:47:25.554 relationships are very important.

NOTE Confidence: 0.88613685

00:47:25.560 --> 00:47:27.963 The other thing is have a validation plan it.

NOTE Confidence: 0.88613685

00:47:27.970 --> 00:47:30.805 There's no sense in in in measuring

NOTE Confidence: 0.88613685

00:47:30.805 --> 00:47:34.760 a bunch of markers that you can't

NOTE Confidence: 0.88613685

00:47:34.760 --> 00:47:37.802 secondarily validate like you know

NOTE Confidence: 0.88613685

00:47:37.802 --> 00:47:40.257 that that's called doing science

NOTE Confidence: 0.88613685

00:47:40.257 --> 00:47:42.379 without having a hypothesis.

NOTE Confidence: 0.925333669375

00:47:44.510 --> 00:47:47.534 And I think I think finding low frequency

NOTE Confidence: 0.925333669375

00:47:47.534 --> 00:47:50.258 markers at this stage is not the key.

NOTE Confidence: 0.925333669375

00:47:50.260 --> 00:47:52.815 Uhm, there's not some super

NOTE Confidence: 0.925333669375

00:47:52.815 --> 00:47:55.370 secret cell that's hiding deep

NOTE Confidence: 0.925333669375

00:47:55.461 --> 00:47:57.926 deep in these tumor tissues.

NOTE Confidence: 0.925333669375

00:47:57.930 --> 00:47:59.170 Like it's CD three,

NOTE Confidence: 0.925333669375

00:47:59.170 --> 00:48:01.870 it's CD 8 and it's the relationship of

NOTE Confidence: 0.925333669375

00:48:01.870 --> 00:48:05.460 those CD3 and CD8 cells to the tumor cells.

NOTE Confidence: 0.925333669375

00:48:05.460 --> 00:48:08.520 So I'll I'll wrap up here

NOTE Confidence: 0.925333669375

00:48:08.520 --> 00:48:10.050 with some conclusions.

NOTE Confidence: 0.925333669375

00:48:10.050 --> 00:48:12.180 You find cancer biomarkers by looking

NOTE Confidence: 0.925333669375

00:48:12.180 --> 00:48:14.629 in cancer tissue that should be great.

NOTE Confidence: 0.925333669375

00:48:14.630 --> 00:48:16.943 That should be great news to all of us.

NOTE Confidence: 0.925333669375

00:48:16.950 --> 00:48:18.062 As pathologists,

NOTE Confidence: 0.925333669375

00:48:18.062 --> 00:48:21.398 we can improve upon the evaluation

NOTE Confidence: 0.925333669375

00:48:21.398 --> 00:48:24.428 of PDL one as a biomarker,

NOTE Confidence: 0.925333669375

00:48:24.430 --> 00:48:25.714 and there are a lot of

NOTE Confidence: 0.925333669375

00:48:25.714 --> 00:48:27.020 efforts out there to do that.

NOTE Confidence: 0.928935013125

00:48:29.480 --> 00:48:31.460 Look for rare responders.

NOTE Confidence: 0.928935013125

00:48:31.460 --> 00:48:33.935 They those are individuals that

NOTE Confidence: 0.928935013125

00:48:33.935 --> 00:48:36.882 are really trying to tell you

NOTE Confidence: 0.928935013125

00:48:36.882 --> 00:48:39.404 something important and you know,

NOTE Confidence: 0.928935013125

00:48:39.404 --> 00:48:42.990 in our case here they were MSI.

NOTE Confidence: 0.928935013125

00:48:42.990 --> 00:48:45.790 Trust me, nobody wanted to fund this.

NOTE Confidence: 0.928935013125

00:48:45.790 --> 00:48:48.840 Nobody was interested in this.

NOTE Confidence: 0.928935013125

00:48:48.840 --> 00:48:50.950 Nobody, despite the fact that

NOTE Confidence: 0.928935013125

00:48:50.950 --> 00:48:53.060 we were standing there saying

NOTE Confidence: 0.928935013125

00:48:53.137 --> 00:48:55.497 these are MSI associated cancers.

NOTE Confidence: 0.928935013125

00:48:55.500 --> 00:48:57.420 So you really need to

NOTE Confidence: 0.928935013125

00:48:57.420 --> 00:48:58.956 make your argument here.

NOTE Confidence: 0.928935013125

00:48:58.960 --> 00:49:02.446 Focus on the people who do respond.

NOTE Confidence: 0.928935013125

00:49:02.450 --> 00:49:05.012 And then I think high quality analysis

NOTE Confidence: 0.928935013125

00:49:05.012 --> 00:49:07.364 are important and you're all very

NOTE Confidence: 0.928935013125

00:49:07.364 --> 00:49:09.329 lucky to have individuals again,

NOTE Confidence: 0.928935013125

00:49:09.330 --> 00:49:12.142 like Doctor Rim and Shelper who are

NOTE Confidence: 0.928935013125

00:49:12.142 --> 00:49:14.147 interested in making high quality.

NOTE Confidence: 0.928935013125

67

00:49:14.150 --> 00:49:16.126 You know tissue biomarkers.

00:49:16.126 --> 00:49:17.608 I'll end here.

00:49:17.610 --> 00:49:22.490 It's impossible to do this all in isolation.

00:49:22.490 --> 00:49:25.538 I tried to point out the

00:49:25.538 --> 00:49:28.140 key people along the way.

00:49:28.140 --> 00:49:29.967 And and those in and and many

00:49:29.967 --> 00:49:32.004 more of the individuals who work

00:49:32.004 --> 00:49:34.374 in my laboratory or who have

00:49:34.374 --> 00:49:36.053 collaborated with me over the

00:49:36.053 --> 00:49:37.573 years are are listed here.

00:49:37.580 --> 00:49:39.440 And I'm gonna stop right there.

00:49:39.440 --> 00:49:41.966 And thank goodness because I'm exhausted.

00:49:45.510 --> 00:49:50.190 Thank you Bob for that really,

00:49:50.190 --> 00:49:53.490 really elegant and and sort of.

00:49:53.490 --> 00:49:56.619 Focusing on very high points and meticulous

00:49:56.619 --> 00:49:59.467 points of quality that we might not

NOTE Confidence: 0.867304281666667

00:49:59.467 --> 00:50:01.980 always here in talks about Peter one

NOTE Confidence: 0.867304281666667

00:50:01.980 --> 00:50:04.164 another biomarkers and I'm I'm, you know,

NOTE Confidence: 0.867304281666667

00:50:04.164 --> 00:50:05.718 there's a silent applause going on,

NOTE Confidence: 0.867304281666667

00:50:05.720 --> 00:50:07.700 which is so missed in zoom,

NOTE Confidence: 0.867304281666667

00:50:07.700 --> 00:50:09.296 but it's definitely happening.

NOTE Confidence: 0.867304281666667

00:50:09.296 --> 00:50:12.270 We have a few minutes for questions

NOTE Confidence: 0.867304281666667

00:50:12.270 --> 00:50:13.994 and please, since I can't see,

NOTE Confidence: 0.867304281666667

00:50:13.994 --> 00:50:15.779 I don't know if you wanna stop your share.

NOTE Confidence: 0.867304281666667

00:50:15.780 --> 00:50:17.949 Or maybe you want to keep it on 'cause

NOTE Confidence: 0.867304281666667

00:50:17.949 --> 00:50:20.117 people might want to go back to slides so,

NOTE Confidence: 0.867304281666667

00:50:20.120 --> 00:50:22.235 but please just speak out

NOTE Confidence: 0.867304281666667

00:50:22.235 --> 00:50:23.504 with your questions.

NOTE Confidence: 0.867304281666667

00:50:23.510 --> 00:50:24.890 And I'll start with one just

NOTE Confidence: 0.867304281666667

00:50:24.890 --> 00:50:26.290 to get the ball rolling.

NOTE Confidence: 0.867304281666667

00:50:26.290 --> 00:50:27.775 I actually have two things

NOTE Confidence: 0.867304281666667

00:50:27.775 --> 00:50:28.963 I wanted to discuss,

NOTE Confidence: 0.867304281666667

00:50:28.970 --> 00:50:30.986 but one is I'm just gonna start with.

NOTE Confidence: 0.867304281666667

00:50:30.990 --> 00:50:34.068 I was really intrigued by and

NOTE Confidence: 0.867304281666667

00:50:34.068 --> 00:50:36.958 thank you for talking about.

NOTE Confidence: 0.867304281666667

00:50:36.960 --> 00:50:40.912 You had a slide on errors in Multiplex

NOTE Confidence: 0.867304281666667

00:50:40.912 --> 00:50:43.007 immunofluorescence and you showed

NOTE Confidence: 0.867304281666667

00:50:43.007 --> 00:50:44.900 multiple steps along the way where

NOTE Confidence: 0.867304281666667

00:50:44.900 --> 00:50:46.780 you found errors and I'm curious.

NOTE Confidence: 0.867304281666667

00:50:46.780 --> 00:50:48.425 I wonder if you can say just

NOTE Confidence: 0.867304281666667

00:50:48.425 --> 00:50:49.460 a minute about that.

NOTE Confidence: 0.867304281666667

00:50:49.460 --> 00:50:51.581 How did you detect the errors and

NOTE Confidence: 0.867304281666667

00:50:51.581 --> 00:50:54.117 did are you able to fix the errors?

NOTE Confidence: 0.867304281666667

00:50:54.120 --> 00:50:55.705 And is this something that

NOTE Confidence: 0.867304281666667

00:50:55.705 --> 00:50:57.290 everyone who's publishing in this

NOTE Confidence: 0.867304281666667

00:50:57.352 --> 00:50:58.727 or are they as meticulous?

NOTE Confidence: 0.867304281666667

00:50:58.730 --> 00:51:00.764 You know they doing this careful

NOTE Confidence: 0.867304281666667

00:51:00.764 --> 00:51:02.120 detection that you're doing?

NOTE Confidence: 0.867304281666667

00:51:02.120 --> 00:51:03.254 Can you just talk a little

NOTE Confidence: 0.867304281666667

00:51:03.254 --> 00:51:04.010 bit more about this?

NOTE Confidence: 0.703333485

00:51:04.180 --> 00:51:06.976 Yeah, sure great great question so.

NOTE Confidence: 0.703333485

00:51:06.980 --> 00:51:09.479 Some you know, Janice and I are

NOTE Confidence: 0.703333485

00:51:09.479 --> 00:51:10.890 ultimately were pathologists, and,

NOTE Confidence: 0.703333485

00:51:10.890 --> 00:51:13.950 you know, for us what we would do is

NOTE Confidence: 0.703333485

00:51:14.039 --> 00:51:16.481 everything had to be referenced back

NOTE Confidence: 0.703333485

00:51:16.481 --> 00:51:20.017 to a a brown state or an IHC state.

NOTE Confidence: 0.703333485

00:51:20.020 --> 00:51:23.266 So anything that we were doing,

NOTE Confidence: 0.703333485

00:51:23.270 --> 00:51:25.314 whether it's digital image

NOTE Confidence: 0.703333485

00:51:25.314 --> 00:51:27.358 analysis or image acquisition,

NOTE Confidence: 0.703333485

00:51:27.360 --> 00:51:29.560 they were always put against

NOTE Confidence: 0.703333485

00:51:29.560 --> 00:51:32.636 the gold standard and the gold

NOTE Confidence: 0.703333485

00:51:32.636 --> 00:51:35.018 standard was immunohistochemistry.

NOTE Confidence: 0.703333485

00:51:35.020 --> 00:51:36.581 So that's kind of how we were

NOTE Confidence: 0.703333485

00:51:36.581 --> 00:51:39.070 able to go back and say, oh look.

NOTE Confidence: 0.703333485

00:51:39.070 --> 00:51:42.675 The the the images are not being

NOTE Confidence: 0.703333485

00:51:42.675 --> 00:51:46.328 acquired in a in a flat manner, or.

NOTE Confidence: 0.703333485

00:51:46.328 --> 00:51:51.000 There is over acquisition of cells in it,

NOTE Confidence: 0.703333485

00:51:51.000 --> 00:51:53.440 you know, and any reasonable observer

NOTE Confidence: 0.703333485

00:51:53.440 --> 00:51:55.900 learned weren't deemed to be positive,

NOTE Confidence: 0.703333485

00:51:55.900 --> 00:52:01.110 you know? In the end, you know.

NOTE Confidence: 0.703333485

00:52:01.110 --> 00:52:02.746 That's a science paper,

NOTE Confidence: 0.703333485

00:52:02.746 --> 00:52:05.200 and it's a methods paper which

NOTE Confidence: 0.703333485

00:52:05.283 --> 00:52:07.192 is not super common. Right?

NOTE Confidence: 0.703333485

00:52:07.192 --> 00:52:10.328 Like when we when we were putting this

NOTE Confidence: 0.703333485

00:52:10.328 --> 00:52:12.252 together, a lot of people said, oh,

NOTE Confidence: 0.703333485

00:52:12.252 --> 00:52:15.388 you know that that's just a methods paper.

NOTE Confidence: 0.703333485

00:52:15.390 --> 00:52:17.086 But but I think.

NOTE Confidence: 0.703333485

00:52:17.086 --> 00:52:20.190 I think it's recognized how difficult it is.

NOTE Confidence: 0.703333485

00:52:20.190 --> 00:52:22.814 It took us five years to do it.

NOTE Confidence: 0.703333485

00:52:22.820 --> 00:52:24.864 To to kind of sort out the

NOTE Confidence: 0.703333485

00:52:24.864 --> 00:52:26.170 errors at each step.

NOTE Confidence: 0.775529412

00:52:28.520 --> 00:52:32.400 And and then it is. This are those

NOTE Confidence: 0.775529412

00:52:32.400 --> 00:52:35.545 errors likely to be possible in

NOTE Confidence: 0.775529412

00:52:35.545 --> 00:52:37.570 in anyone doing Multiplex IF.

NOTE Confidence: 0.890308219090909

00:52:39.040 --> 00:52:40.444 If you use our,

NOTE Confidence: 0.890308219090909

00:52:40.444 --> 00:52:42.550 if you use the same technologies

NOTE Confidence: 0.890308219090909

00:52:42.624 --> 00:52:46.318 which is akoya Biosystems, yeah.

NOTE Confidence: 0.890308219090909

00:52:46.320 --> 00:52:48.360 That you know they're the good.

NOTE Confidence: 0.890308219090909

00:52:48.360 --> 00:52:49.416 The good thing is,

NOTE Confidence: 0.890308219090909

00:52:49.416 --> 00:52:51.000 once we figure out the errors,

NOTE Confidence: 0.890308219090909

00:52:51.000 --> 00:52:55.300 we can send you the code that will fix them.

NOTE Confidence: 0.890308219090909

00:52:55.300 --> 00:52:57.799 You know it's you know if a

NOTE Confidence: 0.890308219090909

00:52:57.799 --> 00:53:01.017 if a if an objective is not.

NOTE Confidence: 0.890308219090909

00:53:01.020 --> 00:53:03.580 Perfectly round or perfectly

NOTE Confidence: 0.890308219090909

00:53:03.580 --> 00:53:06.372 flat in acquiring there,

NOTE Confidence: 0.890308219090909

00:53:06.372 --> 00:53:09.860 there are easy easy.

NOTE Confidence: 0.890308219090909

00:53:09.860 --> 00:53:11.967 As a non computer person there are

NOTE Confidence: 0.890308219090909

00:53:11.967 --> 00:53:14.210 easier ways to to fix that, so yeah,

NOTE Confidence: 0.933879728947368

00:53:14.720 --> 00:53:17.224 well as you say we have experts here

NOTE Confidence: 0.933879728947368

00:53:17.224 --> 00:53:19.982 and some of them may be on the the

NOTE Confidence: 0.933879728947368

00:53:19.982 --> 00:53:21.790 grand rounds so I'm sure they can.

NOTE Confidence: 0.933879728947368

00:53:21.790 --> 00:53:23.400 They can speak to this as well,

NOTE Confidence: 0.933879728947368

00:53:23.400 --> 00:53:24.664 'cause they're excellent pay.

NOTE Confidence: 0.933879728947368

00:53:24.664 --> 00:53:26.800 I see you have your hand up.

NOTE Confidence: 0.933879728947368

00:53:26.800 --> 00:53:29.030 Go ahead and then Dave who's done

NOTE Confidence: 0.17803928

00:53:30.510 --> 00:53:32.608 this? Can you hear me?

NOTE Confidence: 0.17803928

00:53:32.608 --> 00:53:34.110 Yes, OK thank you.

NOTE Confidence: 0.17803928

00:53:34.110 --> 00:53:35.522 Thanks for the excellent talk.

NOTE Confidence: 0.17803928

00:53:35.522 --> 00:53:36.875 I enjoy a lot so I have

NOTE Confidence: 0.17803928

00:53:36.875 --> 00:53:39.626 a question about the MSI.

NOTE Confidence: 0.17803928

00:53:39.626 --> 00:53:42.140 NMR question about the

NOTE Confidence: 0.17803928

00:53:42.310 --> 00:53:45.090 testing at your site. Do

NOTE Confidence: 0.811466046666667

00:53:45.100 --> 00:53:45.859 you run both

NOTE Confidence: 0.61337328

00:53:45.870 --> 00:53:47.705 tests in molecular or

NOTE Confidence: 0.61337328

00:53:47.705 --> 00:53:49.320 immunohistochemistry? Or you

NOTE Confidence: 0.824607733333333

00:53:49.330 --> 00:53:50.539 select just one?

NOTE Confidence: 0.817652181428571

00:53:50.770 --> 00:53:52.630 Yeah, great question.

NOTE Confidence: 0.817652181428571

00:53:52.630 --> 00:53:55.924 It's probably after is PDL 1A.

NOTE Confidence: 0.817652181428571

00:53:55.924 --> 00:53:56.738 Good biomarker,

NOTE Confidence: 0.817652181428571

00:53:56.738 --> 00:53:59.510 it's which MSI should I or Mr?

NOTE Confidence: 0.817652181428571

00:53:59.510 --> 00:54:01.267 Should I be testing so you know,

NOTE Confidence: 0.817652181428571

00:54:01.270 --> 00:54:02.084 Doctor Vogelstein,

NOTE Confidence: 0.817652181428571

00:54:02.084 --> 00:54:04.526 you know one of our most

NOTE Confidence: 0.817652181428571

00:54:04.526 --> 00:54:06.540 eminent cancer biologists here.

NOTE Confidence: 0.817652181428571

00:54:06.540 --> 00:54:10.005 You know he was really instrumental and.

NOTE Confidence: 0.817652181428571

00:54:10.010 --> 00:54:12.124 You know, in in in figuring out

NOTE Confidence: 0.817652181428571

00:54:12.124 --> 00:54:14.378 the MSI along with Stan Hamilton,

NOTE Confidence: 0.817652181428571

00:54:14.380 --> 00:54:16.054 another GI pathologist,

NOTE Confidence: 0.817652181428571

00:54:16.054 --> 00:54:19.024 I see Dave Pat Jane is on and

NOTE Confidence: 0.817652181428571

00:54:19.024 --> 00:54:21.400 a few other GI pathologists.

NOTE Confidence: 0.77250135

00:54:23.570 --> 00:54:27.140 We're very much a PCR based system.

NOTE Confidence: 0.9170975575

00:54:29.700 --> 00:54:32.820 I do believe that if a

NOTE Confidence: 0.9170975575

00:54:32.820 --> 00:54:36.064 patient is Ms is PCR negative,

NOTE Confidence: 0.9170975575

00:54:36.064 --> 00:54:39.917 it's probably reasonable to go back and

NOTE Confidence: 0.9170975575

00:54:39.917 --> 00:54:43.477 and do a stain for MMR just because.

NOTE Confidence: 0.9170975575

00:54:43.480 --> 00:54:45.790 You're almost talking about a

NOTE Confidence: 0.9170975575

00:54:45.790 --> 00:54:49.098 cure in 50 to 70% of patients.

NOTE Confidence: 0.9170975575

00:54:49.098 --> 00:54:52.500 And and I don't think we can.

NOTE Confidence: 0.9170975575

00:54:52.500 --> 00:54:54.918 I don't think we can miss.

NOTE Confidence: 0.9170975575

00:54:54.920 --> 00:54:55.970 Potential cure.

NOTE Confidence: 0.9170975575

00:54:55.970 --> 00:55:00.193 I do believe that the performance of of

NOTE Confidence: 0.9170975575

00:55:00.193 --> 00:55:04.537 PCR and MMR testing are about the same,

NOTE Confidence: 0.9170975575

00:55:04.540 --> 00:55:08.425 but they both have their their weaknesses.

NOTE Confidence: 0.9170975575

00:55:08.430 --> 00:55:10.248 Thanks for that.

NOTE Confidence: 0.9170975575

00:55:10.250 --> 00:55:13.276 Our notion so actually

NOTE Confidence: 0.9170975575

00:55:13.276 --> 00:55:14.770 hear different services

NOTE Confidence: 0.76637685

00:55:14.780 --> 00:55:17.918 actually approach differently.

NOTE Confidence: 0.76637685

00:55:17.920 --> 00:55:20.300 GI service using them are

NOTE Confidence: 0.76637685

00:55:20.300 --> 00:55:21.682 sold at giant service.

NOTE Confidence: 0.76637685

00:55:21.682 --> 00:55:24.214 Yeah, exactly what you just said.

NOTE Confidence: 0.76637685

00:55:24.220 --> 00:55:26.510 I think our geologist they

NOTE Confidence: 0.907877583333333

00:55:26.520 --> 00:55:28.153 don't want to miss a single patient

NOTE Confidence: 0.907877583333333

00:55:28.153 --> 00:55:30.660 so we know very well you know

NOTE Confidence: 0.907877583333333

00:55:30.660 --> 00:55:33.260 the some of the MSI high tumors

NOTE Confidence: 0.907877583333333

00:55:33.260 --> 00:55:34.620 may turn out to be a memory.

NOTE Confidence: 0.907877583333333

00:55:34.620 --> 00:55:36.385 You know, you know if you you

00:55:36.385 --> 00:55:37.666 know can be normal. Yeah,

00:55:37.666 --> 00:55:39.900 and it seems like it happens the same way.

00:55:39.900 --> 00:55:41.500 That's why I think now in

00:55:41.500 --> 00:55:43.813 the answer is here we do.

00:55:43.813 --> 00:55:46.678 Simultaneous testing for both methods.

00:55:46.680 --> 00:55:48.090 So with the sense to

00:55:48.100 --> 00:55:50.132 capture. All possible patients?

00:55:50.132 --> 00:55:52.385 Yeah, especially, especially since you know

00:55:52.385 --> 00:55:55.848 it has to do with the turnover of the cells.

00:55:55.850 --> 00:55:58.646 You know baseline and you know

00:55:58.646 --> 00:56:01.452 you wanna get it. Oncologist mad.

00:56:01.452 --> 00:56:05.710 Tell him that you know MSI PCR or MMR.

00:56:05.710 --> 00:56:08.668 You know HC hasn't really been.

00:56:08.670 --> 00:56:11.010 I mean none of its FDA approved number one,

00:56:11.010 --> 00:56:13.386 but it's never really been vetted

NOTE Confidence: 0.699944976

00:56:13.390 --> 00:56:15.664 on all of these different tissues

NOTE Confidence: 0.699944976

00:56:15.664 --> 00:56:18.198 yet we're doing it all the time.

NOTE Confidence: 0.699944976

00:56:18.200 --> 00:56:20.170 You know that'll make their brain melt, so

NOTE Confidence: 0.880001658571429

00:56:20.200 --> 00:56:22.720 I just wanna go to David you,

NOTE Confidence: 0.880001658571429

00:56:22.720 --> 00:56:25.078 you did a show us yourself did you one?

NOTE Confidence: 0.880001658571429

00:56:25.080 --> 00:56:26.970 Then I see curtain Uma Dave please

NOTE Confidence: 0.880001658571429

00:56:26.970 --> 00:56:28.430 go ahead. If you had a comment

NOTE Confidence: 0.732839242

00:56:28.860 --> 00:56:30.650 I just wanted to follow

NOTE Confidence: 0.867592148

00:56:30.660 --> 00:56:32.980 up with your concerns about.

NOTE Confidence: 0.867592148

00:56:32.980 --> 00:56:34.969 Standardization of quantitative

NOTE Confidence: 0.867592148

00:56:34.970 --> 00:56:37.646 fluorescence and bobs showing of

NOTE Confidence: 0.867592148

00:56:37.646 --> 00:56:39.316 the problems with each one and

NOTE Confidence: 0.867592148

00:56:39.316 --> 00:56:40.737 and comment about the MITRE study

NOTE Confidence: 0.867592148

00:56:40.737 --> 00:56:42.039 which is actually being led by

NOTE Confidence: 0.867592148

00:56:42.040 --> 00:56:43.980 Janice Bob's colleague at Hopkins,

NOTE Confidence: 0.867592148

00:56:43.980 --> 00:56:45.939 which is a standardization study

NOTE Confidence: 0.867592148

00:56:45.940 --> 00:56:47.080 of quantitative fluorescence,

NOTE Confidence: 0.867592148

00:56:47.080 --> 00:56:49.240 and I think that will address that

NOTE Confidence: 0.867592148

00:56:49.240 --> 00:56:51.020 question that you asked Marie exactly,

NOTE Confidence: 0.867592148

00:56:51.020 --> 00:56:54.980 but as the minor one study was where

NOTE Confidence: 0.867592148

00:56:54.980 --> 00:56:56.340 the data analysis was all done

NOTE Confidence: 0.85955112

00:56:56.350 --> 00:56:57.390 at one site and the

NOTE Confidence: 0.8277683815

00:56:57.460 --> 00:56:59.322 scanning was done at 6 sites might

NOTE Confidence: 0.8277683815

00:56:59.322 --> 00:57:01.353 or two study will have the scanning

NOTE Confidence: 0.8277683815

00:57:01.353 --> 00:57:03.117 and analysis done at 6 sites.

NOTE Confidence: 0.8277683815

00:57:03.120 --> 00:57:04.848 And that will answer your question,

NOTE Confidence: 0.8277683815

00:57:04.850 --> 00:57:06.482 and Bob will probably participate in

NOTE Confidence: 0.8277683815

00:57:06.482 --> 00:57:07.966 that since it's being led by Janice.

NOTE Confidence: 0.947677992222222

00:57:08.940 --> 00:57:10.818 Well, I have complete faith in

NOTE Confidence: 0.947677992222222

00:57:10.818 --> 00:57:13.110 our unit here, that's for sure.

NOTE Confidence: 0.947677992222222

00:57:13.110 --> 00:57:15.928 Thank you. I see Kurt and and then Uma.

NOTE Confidence: 0.4913397

00:57:18.060 --> 00:57:19.508 OK, then can you hear

NOTE Confidence: 0.66188515

00:57:19.520 --> 00:57:21.776 me? Yes, Yep we can hear it.

NOTE Confidence: 0.66188515

00:57:21.776 --> 00:57:23.088 So when one thing we

NOTE Confidence: 0.835620506666667

00:57:23.120 --> 00:57:25.640 touch on before Bob and I think

NOTE Confidence: 0.835620506666667

00:57:25.640 --> 00:57:27.340 it's becoming more and more relevant

NOTE Confidence: 0.835620506666667

00:57:27.340 --> 00:57:30.340 is the rapid shrinkage in and

NOTE Confidence: 0.835620506666667

00:57:30.340 --> 00:57:32.340 sometimes the disappearance of

NOTE Confidence: 0.835620506666667

00:57:32.431 --> 00:57:35.048 tissue samples in the eminent role

NOTE Confidence: 0.835620506666667

00:57:35.048 --> 00:57:37.220 of circulating toward DNA to call.

NOTE Confidence: 0.835620506666667

00:57:37.220 --> 00:57:39.630 You know, Microsoft instability status,

NOTE Confidence: 0.835620506666667

00:57:39.630 --> 00:57:41.350 TMB and other things?

NOTE Confidence: 0.835620506666667

00:57:41.350 --> 00:57:44.520 How do you foresee some of these

NOTE Confidence: 0.835620506666667

00:57:44.520 --> 00:57:46.470 immune biology or immune biomarkers?

NOTE Confidence: 0.835620506666667

00:57:46.470 --> 00:57:48.460 Adapting to circulating tumor DNA?

NOTE Confidence: 0.835620506666667

00:57:48.460 --> 00:57:49.970 Do you think that something?

NOTE Confidence: 0.835620506666667

00:57:49.970 --> 00:57:52.146 That we'll pair will and and how to,

NOTE Confidence: 0.835620506666667

00:57:52.150 --> 00:57:54.813 you know, marry with our usual, you know,

NOTE Confidence: 0.835620506666667

00:57:54.813 --> 00:57:56.919 diagnostic operation that is tissue based.

NOTE Confidence: 0.894526018823529

00:57:57.700 --> 00:58:00.016 Yeah, that that's a great question

NOTE Confidence: 0.894526018823529

00:58:00.016 --> 00:58:02.420 because you know not not every

NOTE Confidence: 0.894526018823529

00:58:02.420 --> 00:58:04.375 patient is biopsy able right?

NOTE Confidence: 0.894526018823529

00:58:04.380 --> 00:58:06.700 I mean, we we we kind of wish they were,

NOTE Confidence: 0.894526018823529

00:58:06.700 --> 00:58:09.010 but it's it's not. And you know,

NOTE Confidence: 0.894526018823529

00:58:09.010 --> 00:58:10.746 I you know I would like to see.

NOTE Confidence: 0.894526018823529

00:58:10.750 --> 00:58:13.207 I would like to see a study of just

NOTE Confidence: 0.894526018823529

00:58:13.207 --> 00:58:15.085 immune cell activation, right?

NOTE Confidence: 0.894526018823529

00:58:15.085 --> 00:58:19.458 Like like someone who gets CMV if you can't

NOTE Confidence: 0.894526018823529

00:58:19.458 --> 00:58:22.496 measure CMV like can you just tell that

NOTE Confidence: 0.894526018823529

00:58:22.496 --> 00:58:25.169 their immune system is activating right?

NOTE Confidence: 0.894526018823529

00:58:25.170 --> 00:58:27.258 And and I kind of think that the

NOTE Confidence: 0.894526018823529

00:58:27.258 --> 00:58:29.809 same might be true. Then you know,

00:58:29.809 --> 00:58:32.767 for for tumor immunologists it's just.

00:58:32.770 --> 00:58:35.850 Hey we gave PDL one is the

00:58:35.850 --> 00:58:37.194 patient's immune system activating?

00:58:37.194 --> 00:58:38.330 You know, I don't.

00:58:38.330 --> 00:58:39.710 I don't know what that entails,

00:58:39.710 --> 00:58:43.062 but you know is there a way to

00:58:43.062 --> 00:58:45.172 to not relatively non invasively

00:58:45.172 --> 00:58:47.716 you know with a blood sample?

00:58:50.820 --> 00:58:52.768 Measure that because again,

00:58:52.768 --> 00:58:54.229 not every patient.

00:58:54.230 --> 00:58:55.718 You know we're pathologists,

00:58:55.718 --> 00:58:56.834 we love tissue.

00:58:56.840 --> 00:58:59.408 I just told you how awesome tissue is,

00:58:59.410 --> 00:59:01.540 but it's not always available,

00:59:01.540 --> 00:59:02.989 so I I'm not sure if I

00:59:02.989 --> 00:59:03.610 answered your question.

NOTE Confidence: 0.6602848342

00:59:03.700 --> 00:59:05.595 Are you currently testing MSI

NOTE Confidence: 0.6602848342

00:59:05.595 --> 00:59:09.610 status by city DNA at Hopkins now?

NOTE Confidence: 0.83644130875

00:59:09.610 --> 00:59:12.568 Even I haven't seen that outside

NOTE Confidence: 0.83644130875

00:59:12.568 --> 00:59:14.370 of research. OK, thank you.

NOTE Confidence: 0.755808556666667

00:59:15.400 --> 00:59:17.800 Uma yeah thank you Doctor Andrews.

NOTE Confidence: 0.755808556666667

00:59:17.800 --> 00:59:19.000 That is a wonderful talk.

NOTE Confidence: 0.755808556666667

00:59:19.000 --> 00:59:21.245 My question was on heterogeneity

NOTE Confidence: 0.755808556666667

00:59:21.245 --> 00:59:25.587 in a study I did with 100 plus you

NOTE Confidence: 0.755808556666667

00:59:25.587 --> 00:59:28.082 know cervical and anal cancers.

NOTE Confidence: 0.755808556666667

00:59:28.090 --> 00:59:30.170 95% were heterogeneous in their

NOTE Confidence: 0.755808556666667

00:59:30.170 --> 00:59:32.250 staining with Foo side dead

NOTE Confidence: 0.755808556666667

00:59:32.324 --> 00:59:34.369 negative tofu side with 100%.

NOTE Confidence: 0.755808556666667

00:59:34.370 --> 00:59:36.360 So for an individual patient,

NOTE Confidence: 0.755808556666667

00:59:36.360 --> 00:59:37.854 is it going to be a luck of the

NOTE Confidence: 0.755808556666667

00:59:37.854 --> 00:59:40.386 draw when you have cut off someone

NOTE Confidence: 0.755808556666667

00:59:40.386 --> 00:59:42.210 and 10 how much should they be?

NOTE Confidence: 0.755808556666667

00:59:42.210 --> 00:59:43.624 You know what will be the guideline?

NOTE Confidence: 0.755808556666667

00:59:43.630 --> 00:59:44.550 What are your thoughts on

NOTE Confidence: 0.821191961666667

00:59:44.560 --> 00:59:47.998 that? Yeah, yeah, that's that's really.

NOTE Confidence: 0.821191961666667

00:59:48.000 --> 00:59:49.500 That's really important, right?

NOTE Confidence: 0.821191961666667

00:59:49.500 --> 00:59:52.809 I kind of think it's like one of these

NOTE Confidence: 0.821191961666667

00:59:52.809 --> 00:59:55.585 things where if it's positive we learn

NOTE Confidence: 0.821191961666667

00:59:55.585 --> 00:59:57.822 something, but if it's negative.

NOTE Confidence: 0.821191961666667

00:59:57.822 --> 01:00:00.674 We didn't really learn anything and and

NOTE Confidence: 0.821191961666667

01:00:00.674 --> 01:00:03.407 and I think that you know that's where we

NOTE Confidence: 0.821191961666667

01:00:03.407 --> 01:00:05.689 need to help our immunologists or our.

NOTE Confidence: 0.821191961666667

01:00:05.690 --> 01:00:08.510 I'm sorry our oncologists to say.

NOTE Confidence: 0.821191961666667

01:00:08.510 --> 01:00:10.180 You know, a negative result

NOTE Confidence: 0.821191961666667

01:00:10.180 --> 01:00:11.850 shouldn't really dissuade you here,

NOTE Confidence: 0.821191961666667

01:00:11.850 --> 01:00:14.834 but we're a long way from that. And yeah,

NOTE Confidence: 0.821191961666667

01:00:14.834 --> 01:00:17.928 any any look at heterogeneity and I,

NOTE Confidence: 0.821191961666667

01:00:17.930 --> 01:00:20.030 I know Kurt and I talked about.

NOTE Confidence: 0.821191961666667

01:00:20.030 --> 01:00:22.295 You know, some actually mathematical

NOTE Confidence: 0.821191961666667

01:00:22.295 --> 01:00:24.107 models of of heterogeneity.

NOTE Confidence: 0.821191961666667

01:00:24.110 --> 01:00:25.520 I think it's all important.

NOTE Confidence: 0.95912945

01:00:27.290 --> 01:00:28.080 Thank you.

NOTE Confidence: 0.8776301

01:00:31.740 --> 01:00:33.790 Other questions.

NOTE Confidence: 0.8776301

01:00:33.790 --> 01:00:35.326 And I'll, I'll I'll ask my last one,

NOTE Confidence: 0.8776301

01:00:35.330 --> 01:00:38.558 which just pivots off of Kurt's

NOTE Confidence: 0.8776301

01:00:38.558 --> 01:00:41.101 comment about a circulating tumor.

NOTE Confidence: 0.8776301

01:00:41.101 --> 01:00:43.056 You looking for markers and

NOTE Confidence: 0.8776301

01:00:43.056 --> 01:00:44.229 circulating tumor cells.

NOTE Confidence: 0.8776301

01:00:44.230 --> 01:00:47.218 And so I was just going to ask the

NOTE Confidence: 0.8776301

01:00:47.218 --> 01:00:49.414 classic question, what's next?

NOTE Confidence: 0.8776301

01:00:49.414 --> 01:00:52.606 What is the future of this?

NOTE Confidence: 0.8776301

01:00:52.610 --> 01:00:54.248 Especially since relying

NOTE Confidence: 0.8776301

01:00:54.248 --> 01:00:57.524 on MMR is is is easy.

NOTE Confidence: 0.8776301

01:00:57.530 --> 01:00:58.325 Staying pretty easy,

NOTE Confidence: 0.8776301

01:00:58.325 --> 01:00:59.650 stain to read but PDL.

NOTE Confidence: 0.8776301

01:00:59.650 --> 01:01:02.058 One has challenges and and then there

NOTE Confidence: 0.8776301

01:01:02.058 --> 01:01:04.268 are just things deeper than this.

NOTE Confidence: 0.8776301

01:01:04.270 --> 01:01:07.339 That Kurt and Dave and you are working on

NOTE Confidence: 0.8776301

01:01:07.339 --> 01:01:10.277 that are deeper than than just PDL one.

NOTE Confidence: 0.8776301

01:01:10.280 --> 01:01:13.061 So how far are we from getting to a

NOTE Confidence: 0.8776301

01:01:13.061 --> 01:01:15.569 blood test talking about not being

NOTE Confidence: 0.76912665

01:01:16.010 --> 01:01:18.542 people? My talk about blood tests

NOTE Confidence: 0.76912665

01:01:18.542 --> 01:01:21.441 'cause I you know, I don't know that

NOTE Confidence: 0.76912665

01:01:21.441 --> 01:01:23.369 you know I was talking with Kurt a

NOTE Confidence: 0.76912665

01:01:23.369 --> 01:01:25.295 little bit earlier as like you know I.

NOTE Confidence: 0.76912665

01:01:25.300 --> 01:01:28.170 I would like to see some CD 8 cells and

NOTE Confidence: 0.76912665

01:01:28.247 --> 01:01:30.657 some CD 20 cells in a tumor. Right?

NOTE Confidence: 0.76912665

01:01:30.657 --> 01:01:33.086 Like are they close to the tumor?

NOTE Confidence: 0.76912665

01:01:33.090 --> 01:01:34.574 Are they not close to the tumor,

NOTE Confidence: 0.76912665

01:01:34.580 --> 01:01:36.328 or are they present?

NOTE Confidence: 0.76912665

01:01:36.328 --> 01:01:38.513 Are they not present like?

NOTE Confidence: 0.76912665

01:01:38.520 --> 01:01:41.160 I I think I think we have so many basic

NOTE Confidence: 0.76912665

01:01:41.228 --> 01:01:43.340 things that we could be measuring

NOTE Confidence: 0.76912665

01:01:43.340 --> 01:01:45.893 here and and we're all and and I'm

NOTE Confidence: 0.76912665

01:01:45.893 --> 01:01:47.930 not blaming anyone on the call here,

NOTE Confidence: 0.76912665

01:01:47.930 --> 01:01:50.132 but we're all like can you

NOTE Confidence: 0.76912665

01:01:50.132 --> 01:01:52.534 do 4000 markers right?

NOTE Confidence: 0.76912665

01:01:52.534 --> 01:01:54.594 Like and you know,

NOTE Confidence: 0.76912665

01:01:54.594 --> 01:01:56.706 I bet you we could spitball

NOTE Confidence: 0.76912665

01:01:56.710 --> 01:01:58.940 four or five important markers.

NOTE Confidence: 0.84490356

01:02:01.310 --> 01:02:04.410 So yeah, dhanpat, sorry.

NOTE Confidence: 0.67826491

01:02:04.420 --> 01:02:05.659 I think we are all your time.

NOTE Confidence: 0.67826491

01:02:05.660 --> 01:02:07.004 I was in the liver tumor board

88

NOTE Confidence: 0.67826491

01:02:07.004 --> 01:02:08.620 so I had to attend something.

NOTE Confidence: 0.67826491

01:02:08.620 --> 01:02:12.256 Great. Talk Bob. Nice seeing you.

NOTE Confidence: 0.67826491

01:02:12.260 --> 01:02:14.228 I have a question which is sort of

NOTE Confidence: 0.67826491

01:02:14.228 --> 01:02:15.363 follow-up question to what Doctor

NOTE Confidence: 0.67826491

01:02:15.363 --> 01:02:17.180 Who was asking and I want to clarify.

NOTE Confidence: 0.67826491

01:02:17.180 --> 01:02:19.182 So I understand that you guys do

NOTE Confidence: 0.67826491

01:02:19.182 --> 01:02:21.437 only the MSI as the starting test,

NOTE Confidence: 0.67826491

01:02:21.440 --> 01:02:23.717 but you don't do them are to begin with.

NOTE Confidence: 0.67826491

01:02:23.720 --> 01:02:25.820 Is that correct or you do both?

NOTE Confidence: 0.67826491

01:02:25.820 --> 01:02:26.430 We

NOTE Confidence: 0.806754705714286

01:02:26.560 --> 01:02:30.844 we tend to heavily rely on MSI.

NOTE Confidence: 0.740395450666666

01:02:31.470 --> 01:02:34.512 I see the issue I think is I think

NOTE Confidence: 0.740395450666666

01:02:34.512 --> 01:02:37.187 what Doctor Who was asking was,

NOTE Confidence: 0.740395450666666

01:02:37.190 --> 01:02:38.235 you know whether do both

NOTE Confidence: 0.740395450666666

01:02:38.235 --> 01:02:39.670 or do you only one person?

NOTE Confidence: 0.740395450666666

01:02:39.670 --> 01:02:41.680 As I understand, most of those

NOTE Confidence: 0.740395450666666

01:02:41.680 --> 01:02:43.979 centers do either one of the tests

NOTE Confidence: 0.740395450666666

01:02:43.979 --> 01:02:46.051 and what you said is correct that

NOTE Confidence: 0.740395450666666

01:02:46.060 --> 01:02:48.044 none of the tests will ever be 100%.

NOTE Confidence: 0.740395450666666

01:02:48.050 --> 01:02:50.234 Like many other things that we do

NOTE Confidence: 0.740395450666666

01:02:50.234 --> 01:02:52.724 and you always accept the yeah Greer

NOTE Confidence: 0.740395450666666

01:02:52.724 --> 01:02:55.098 false positive or false negative you

NOTE Confidence: 0.740395450666666

01:02:55.098 --> 01:02:57.428 get with each test is like how many

NOTE Confidence: 0.740395450666666

01:02:57.428 --> 01:02:59.820 blocks will you stay in for PDL one

NOTE Confidence: 0.740395450666666

01:02:59.889 --> 01:03:02.199 or a given case you end somewhere.

NOTE Confidence: 0.740395450666666

01:03:02.200 --> 01:03:04.736 So, and I think a lot of people

NOTE Confidence: 0.740395450666666

01:03:04.736 --> 01:03:07.739 tend to go with DNA mismatch repair,

NOTE Confidence: 0.740395450666666

01:03:07.740 --> 01:03:10.918 yet see for two reasons that the

NOTE Confidence: 0.740395450666666

01:03:10.918 --> 01:03:12.732 sensitivity is basically almost

NOTE Confidence: 0.740395450666666

01:03:12.732 --> 01:03:14.196 as close to MSI.

NOTE Confidence: 0.740395450666666

01:03:14.200 --> 01:03:18.368 But in addition also identifies the germ

01:03:18.368 --> 01:03:20.032 line defect that one should be looking for.

01:03:20.040 --> 01:03:22.116 If you're screening for is syndrome,

01:03:22.120 --> 01:03:23.660 so there is added advantage.

01:03:23.660 --> 01:03:24.648 But I I agree.

01:03:24.648 --> 01:03:26.723 I mean there are pitfalls of each methods

01:03:26.723 --> 01:03:29.190 and you will miss a few no matter what.

01:03:30.320 --> 01:03:33.728 Yeah, yes, we're we're on the same page.

01:03:33.730 --> 01:03:35.280 You know, I you know,

01:03:35.280 --> 01:03:38.300 sometimes with a limited biopsy,

01:03:38.300 --> 01:03:39.340 you don't really know if

01:03:39.340 --> 01:03:40.380 you're getting that you know.

01:03:40.380 --> 01:03:42.690 Are you really getting the cancer DNA,

01:03:42.690 --> 01:03:45.236 but with an IHC you can, you know?

01:03:45.236 --> 01:03:46.508 Clearly see whether it's

01:03:46.508 --> 01:03:48.310 the cancer or not. So yeah.

01:03:50.800 --> 01:03:53.883 Oh, I'm sorry. Joanna, and then

NOTE Confidence: 0.906385

01:03:53.883 --> 01:03:55.598 I think Jeff might. I don't know,

NOTE Confidence: 0.843827189333333

01:03:55.650 --> 01:03:56.966 or I I actually.

NOTE Confidence: 0.843827189333333

01:03:56.966 --> 01:03:58.611 I like this discussion that

NOTE Confidence: 0.843827189333333

01:03:58.611 --> 01:04:00.759 people have been having about MRI,

NOTE Confidence: 0.843827189333333

01:04:00.760 --> 01:04:02.802 HC versus MSI PCR.

NOTE Confidence: 0.843827189333333

01:04:02.802 --> 01:04:05.154 I think we don't really need to

NOTE Confidence: 0.843827189333333

01:04:05.154 --> 01:04:07.688 worry about which method is better,

NOTE Confidence: 0.843827189333333

01:04:07.690 --> 01:04:09.922 but I do think that we need to understand

NOTE Confidence: 0.843827189333333

01:04:09.922 --> 01:04:11.670 what information each method provides

NOTE Confidence: 0.843827189333333

01:04:11.670 --> 01:04:13.836 and why each method was developed.

NOTE Confidence: 0.843827189333333

01:04:13.840 --> 01:04:15.508 And also I really liked your

NOTE Confidence: 0.843827189333333

01:04:15.508 --> 01:04:17.164 comment towards the end of your

NOTE Confidence: 0.843827189333333

01:04:17.164 --> 01:04:18.782 talk where you said we're doing

NOTE Confidence: 0.843827189333333

01:04:18.782 --> 01:04:20.646 MSI testing on all of these tumors.

NOTE Confidence: 0.843827189333333

01:04:20.650 --> 01:04:22.169 MRI HD on all of these tumors

NOTE Confidence: 0.843827189333333

01:04:22.169 --> 01:04:23.370 now because of treatment.

NOTE Confidence: 0.843827189333333

01:04:23.370 --> 01:04:25.464 Options and we really don't know.

NOTE Confidence: 0.843827189333333

01:04:25.464 --> 01:04:27.680 What you know? How?

NOTE Confidence: 0.843827189333333

01:04:27.680 --> 01:04:29.640 How this how these MRI,

NOTE Confidence: 0.843827189333333

01:04:29.640 --> 01:04:31.745 HC behave and tumors outside

NOTE Confidence: 0.843827189333333

01:04:31.745 --> 01:04:33.429 of endometrial and colorectal

NOTE Confidence: 0.843827189333333

01:04:33.429 --> 01:04:35.734 cancer to the same extent that we

NOTE Confidence: 0.843827189333333

01:04:35.734 --> 01:04:37.369 understand in those original pores.

NOTE Confidence: 0.843827189333333

01:04:37.370 --> 01:04:39.320 And I think you know,

NOTE Confidence: 0.843827189333333

01:04:39.320 --> 01:04:42.640 I think doing doing MSI PCR in

NOTE Confidence: 0.843827189333333

01:04:42.640 --> 01:04:44.089 addition like is not really a

NOTE Confidence: 0.843827189333333

01:04:44.089 --> 01:04:45.823 problem for those cases where it

NOTE Confidence: 0.843827189333333

01:04:45.823 --> 01:04:47.499 is really important for treatment.

NOTE Confidence: 0.843827189333333

01:04:47.500 --> 01:04:49.213 So I think we just need to really

NOTE Confidence: 0.843827189333333

01:04:49.213 --> 01:04:51.401 keep in mind why are we doing this

NOTE Confidence: 0.843827189333333

01:04:51.401 --> 01:04:53.480 task right now at this very moment?

NOTE Confidence: 0.843827189333333

01:04:53.480 --> 01:04:54.698 What is the purpose of it?

NOTE Confidence: 0.843827189333333

01:04:54.700 --> 01:04:55.960 Is it for lynching of screening?

NOTE Confidence: 0.843827189333333

01:04:55.960 --> 01:04:58.618 Is it? For. Ms for treatment?

NOTE Confidence: 0.843827189333333

01:04:58.620 --> 01:05:00.411 Or is it for both and then we really

NOTE Confidence: 0.843827189333333

01:05:00.411 --> 01:05:02.185 need to sort of be cognizant that

NOTE Confidence: 0.843827189333333

01:05:02.185 --> 01:05:03.682 what information we get out of

NOTE Confidence: 0.843827189333333

01:05:03.682 --> 01:05:05.194 it and how it's gonna be helpful.

NOTE Confidence: 0.843827189333333

01:05:05.200 --> 01:05:05.881 So I I,

NOTE Confidence: 0.843827189333333

01:05:05.881 --> 01:05:07.470 I really liked your summary and your

NOTE Confidence: 0.843827189333333

01:05:07.531 --> 01:05:09.239 and and the fact that you brought

NOTE Confidence: 0.648720738571428

01:05:09.250 --> 01:05:10.944 up my side. Yeah, I think we're,

NOTE Confidence: 0.648720738571428

01:05:10.950 --> 01:05:13.116 you know we're speaking the same,

NOTE Confidence: 0.648720738571428

01:05:13.120 --> 01:05:14.638 the same language and you know

NOTE Confidence: 0.648720738571428

01:05:14.638 --> 01:05:16.547 I'm I'm I'm on a few of these,

NOTE Confidence: 0.648720738571428

01:05:16.550 --> 01:05:18.896 you know like advisory boards and

NOTE Confidence: 0.648720738571428

01:05:18.896 --> 01:05:20.848 you start telling oncologists that

NOTE Confidence: 0.648720738571428

01:05:20.848 --> 01:05:23.074 none of these tests have been valid.

NOTE Confidence: 0.648720738571428

01:05:23.080 --> 01:05:25.432 I mean number one not nothing is FDA

NOTE Confidence: 0.648720738571428

01:05:25.432 --> 01:05:27.496 approved but they haven't been validated

NOTE Confidence: 0.648720738571428

01:05:27.496 --> 01:05:29.620 in other cancers and they just.

NOTE Confidence: 0.648720738571428

01:05:29.620 --> 01:05:34.070 Their their mind is. Dissolves.

NOTE Confidence: 0.648720738571428

01:05:34.070 --> 01:05:36.418 Just one, there's a limitation.

NOTE Confidence: 0.839877227142857

01:05:37.020 --> 01:05:37.736 I have a question.

NOTE Confidence: 0.839877227142857

01:05:37.736 --> 01:05:39.728 I want to go back to leave in the middle

NOTE Confidence: 0.839877227142857

01:05:39.728 --> 01:05:41.400 so I might have missed some things,

NOTE Confidence: 0.839877227142857

01:05:41.400 --> 01:05:43.596 but I'm gonna go back to a point you

NOTE Confidence: 0.839877227142857

01:05:43.596 --> 01:05:45.780 made early on about the negative

NOTE Confidence: 0.839877227142857

01:05:45.780 --> 01:05:48.216 predictive value of absence of

NOTE Confidence: 0.839877227142857

01:05:48.216 --> 01:05:53.120 ligands or PDL one PD one in tumors.

NOTE Confidence: 0.839877227142857

01:05:53.120 --> 01:05:55.064 What is the thinking about

NOTE Confidence: 0.839877227142857

01:05:55.064 --> 01:05:57.800 those patients who respond?

01:05:57.800 --> 01:06:00.836 When they have no detectable antigen,

01:06:00.840 --> 01:06:01.956 no detectable PDL want.

01:06:01.956 --> 01:06:03.630 Is it that the test is

01:06:03.699 --> 01:06:05.219 insufficiently sensitive?

01:06:05.220 --> 01:06:06.728 That doesn't explain at all,

01:06:06.728 --> 01:06:07.760 I don't think.

01:06:07.760 --> 01:06:09.846 And is it a matter of these

01:06:09.846 --> 01:06:11.650 other factors that they had high

01:06:11.650 --> 01:06:13.234 mutation rates but nevertheless

01:06:13.234 --> 01:06:16.089 had low PDL one so that compensates

01:06:16.089 --> 01:06:18.495 for the absence of PDL one?

01:06:18.500 --> 01:06:19.880 What's understood about the

01:06:19.880 --> 01:06:21.260 biology of these responders?

01:06:21.260 --> 01:06:22.082 Who were PDL?

01:06:22.082 --> 01:06:22.630 One negative?

NOTE Confidence: 0.88970232

01:06:23.440 --> 01:06:24.819 Yeah, I mean I think number one,

NOTE Confidence: 0.88970232

01:06:24.820 --> 01:06:25.780 it's just you know it.

NOTE Confidence: 0.88970232

01:06:25.780 --> 01:06:27.424 It is a concern that it's

NOTE Confidence: 0.88970232

01:06:27.424 --> 01:06:28.548 a sampling issue, right?

NOTE Confidence: 0.88970232

01:06:28.548 --> 01:06:30.932 We have a tiny piece of a large

NOTE Confidence: 0.88970232

01:06:30.932 --> 01:06:32.829 tumor and the second thing would

NOTE Confidence: 0.88970232

01:06:32.829 --> 01:06:35.239 be you know if the TMB is high.

NOTE Confidence: 0.88970232

01:06:35.240 --> 01:06:37.748 There's not an oncologist who won't.

NOTE Confidence: 0.88970232

01:06:37.750 --> 01:06:39.130 Go for, you know,

NOTE Confidence: 0.88970232

01:06:39.130 --> 01:06:41.200 won't treat those types of patients.

NOTE Confidence: 0.912442395

01:06:44.240 --> 01:06:45.416 So I you know, I don't.

NOTE Confidence: 0.912442395

01:06:45.420 --> 01:06:47.892 I don't think we have detailed

NOTE Confidence: 0.912442395

01:06:47.892 --> 01:06:50.094 answers about I, I'm actually.

NOTE Confidence: 0.912442395

01:06:50.094 --> 01:06:52.384 I'm actually more interested in

NOTE Confidence: 0.912442395

01:06:52.384 --> 01:06:55.241 the people who are PD L1 positive

NOTE Confidence: 0.912442395

01:06:55.241 --> 01:06:57.600 who don't respond or or design

NOTE Confidence: 0.912442395

01:06:57.600 --> 01:06:59.690 positive who don't respond right.

NOTE Confidence: 0.734132044

01:06:59.700 --> 01:07:01.170 Everybody is interested in those,

NOTE Confidence: 0.734132044

01:07:01.170 --> 01:07:03.906 but I think that there might be value in

NOTE Confidence: 0.734132044

01:07:03.906 --> 01:07:06.838 the ones who are the atypical responders.

NOTE Confidence: 0.734132044

01:07:06.840 --> 01:07:09.724 Yeah, yeah, the drug has the drugs

NOTE Confidence: 0.734132044

01:07:09.724 --> 01:07:12.810 I assume are incredibly specific.

NOTE Confidence: 0.734132044

01:07:12.810 --> 01:07:16.840 It's not that they're often responses.

NOTE Confidence: 0.734132044

01:07:16.840 --> 01:07:18.200 Sorry, can I come in on that quickly?

NOTE Confidence: 0.734132044

01:07:18.200 --> 01:07:19.694 No, go ahead, Kurt, yes.

NOTE Confidence: 0.734132044

01:07:19.694 --> 01:07:22.206 So so there is a story published a

NOTE Confidence: 0.734132044

01:07:22.206 --> 01:07:24.915 couple of papers showing that PDL one

NOTE Confidence: 0.734132044

01:07:24.915 --> 01:07:27.656 can get glycosylated and when it gets

NOTE Confidence: 0.734132044

01:07:27.656 --> 01:07:30.020 glycosylated antibodies may not recognize it.

NOTE Confidence: 0.734132044

01:07:30.020 --> 01:07:32.397 So that's at least one direct

NOTE Confidence: 0.734132044

01:07:32.397 --> 01:07:34.482 biological ground by which patients

98

NOTE Confidence: 0.734132044

01:07:34.482 --> 01:07:36.869 may be false negative for PD L1.

NOTE Confidence: 0.734132044

01:07:36.870 --> 01:07:38.775 I could explain why some

NOTE Confidence: 0.734132044

01:07:38.775 --> 01:07:39.918 negative cases respond.

NOTE Confidence: 0.734132044

01:07:39.920 --> 01:07:42.572 That's one thing that's been sort

NOTE Confidence: 0.734132044

01:07:42.572 --> 01:07:45.136 of well established and and this is

NOTE Confidence: 0.734132044

01:07:45.136 --> 01:07:46.990 a work from Indy Anderson Group.

NOTE Confidence: 0.734132044

01:07:46.990 --> 01:07:49.496 And then the second layer is that

NOTE Confidence: 0.734132044

01:07:49.496 --> 01:07:51.600 tumor mutational burden and PDL one

NOTE Confidence: 0.734132044

01:07:51.600 --> 01:07:53.526 are not correlated in most tumors.

NOTE Confidence: 0.734132044

01:07:53.530 --> 01:07:55.274 So to your point it is likely that

NOTE Confidence: 0.734132044

01:07:55.274 --> 01:07:57.187 some of those period one negatives may

NOTE Confidence: 0.734132044

01:07:57.187 --> 01:07:59.212 actually be TNB high and that could

NOTE Confidence: 0.734132044

01:07:59.212 --> 01:08:01.109 be the driver of a clinical benefit.

NOTE Confidence: 0.734132044

01:08:01.110 --> 01:08:04.142 So it could be you know around those

NOTE Confidence: 0.734132044

01:08:04.142 --> 01:08:07.566 topics and in some unknown things for sure.

NOTE Confidence: 0.734132044

01:08:07.570 --> 01:08:10.340 But presumably response has to

NOTE Confidence: 0.734132044

01:08:10.340 --> 01:08:13.110 be through the PDL 1.

NOTE Confidence: 0.734132044

01:08:13.110 --> 01:08:17.400 PD One you know circuit because.

NOTE Confidence: 0.734132044

01:08:17.400 --> 01:08:19.255 That's what's with the drug works, right?

NOTE Confidence: 0.734132044

01:08:19.255 --> 01:08:21.280 That's the part I'm doing.

NOTE Confidence: 0.734132044

01:08:21.280 --> 01:08:22.200 There may be other things,

NOTE Confidence: 0.734132044

01:08:22.200 --> 01:08:22.450 yeah?

NOTE Confidence: 0.93305248

01:08:24.790 --> 01:08:26.020 OK thanks.

NOTE Confidence: 0.89665085

01:08:29.410 --> 01:08:31.201 Great, great discussion. Well,

NOTE Confidence: 0.89665085

01:08:31.201 --> 01:08:33.943 if there are no further questions,

NOTE Confidence: 0.852467273333333

01:08:33.950 --> 01:08:36.274 we're 10 minutes over which I always

NOTE Confidence: 0.852467273333333

01:08:36.274 --> 01:08:38.470 love because it means that this

NOTE Confidence: 0.852467273333333

01:08:38.470 --> 01:08:40.350 is really an interesting topic.

NOTE Confidence: 0.852467273333333

01:08:40.350 --> 01:08:42.766 I want to thank you Bob for spending

NOTE Confidence: 0.852467273333333

01:08:42.766 --> 01:08:45.016 time with us today and for meeting

NOTE Confidence: 0.852467273333333

01:08:45.016 --> 01:08:47.190 with several of us this morning.

NOTE Confidence: 0.852467273333333

01:08:47.190 --> 01:08:49.505 It's been a real pleasure

NOTE Confidence: 0.852467273333333

01:08:49.505 --> 01:08:51.910 and an education as well.

NOTE Confidence: 0.852467273333333

01:08:51.910 --> 01:08:54.335 Congratulations on your wonderful work.

NOTE Confidence: 0.850953952222222

01:08:54.780 --> 01:08:57.076 Thanks for the invite and all the

NOTE Confidence: 0.850953952222222

01:08:57.076 --> 01:08:59.996 time this. Yeah. With everyone,

NOTE Confidence: 0.850953952222222

01:08:59.996 --> 01:09:03.030 thank you. Bye bye OK bye.