WEBVTT

NOTE duration:"01:04:52"

NOTE recognizability:0.780

NOTE language:en-us

NOTE Confidence: 0.675779826666667

00:00:00.000 --> 00:00:02.823 2 grand rounds.

NOTE Confidence: 0.675779826666667

00:00:02.823 --> 00:00:05.646 Virtually yet again.

NOTE Confidence: 0.675779826666667

00:00:05.650 --> 00:00:10.300 And we have two speakers today.

NOTE Confidence: 0.675779826666667

00:00:10.300 --> 00:00:12.288 Doctor Michael Lippman and

NOTE Confidence: 0.675779826666667

00:00:12.288 --> 00:00:13.779 Doctor Carlos Fernandez,

NOTE Confidence: 0.675779826666667

00:00:13.780 --> 00:00:15.652 Hernando and Doctor Leibman,

NOTE Confidence: 0.675779826666667

00:00:15.652 --> 00:00:18.856 is gonna be first and let me

NOTE Confidence: 0.675779826666667

00:00:18.856 --> 00:00:22.010 just briefly introduce him.

NOTE Confidence: 0.675779826666667

00:00:22.010 --> 00:00:25.370 So Michael Liebman is an assistant

NOTE Confidence: 0.675779826666667

00:00:25.370 --> 00:00:28.994 professor of Urology and takes care of

NOTE Confidence: 0.675779826666667

00:00:28.994 --> 00:00:32.700 the full range of patients with Gu cancers.

NOTE Confidence: 0.675779826666667

00:00:32.700 --> 00:00:34.675 He graduated from Cornell University

NOTE Confidence: 0.675779826666667

00:00:34.675 --> 00:00:37.137 and received his medical degree from

NOTE Confidence: 0.675779826666667

00:00:37.137 --> 00:00:39.567 the University of Maryland in Baltimore,

NOTE Confidence: 0.675779826666667

00:00:39.570 --> 00:00:41.830 completing his general surgery and

NOTE Confidence: 0.675779826666667

00:00:41.830 --> 00:00:44.459 urology at Mount Sinai before moving

NOTE Confidence: 0.675779826666667

00:00:44.459 --> 00:00:46.827 on to UCSF where he did it two

NOTE Confidence: 0.675779826666667

00:00:46.827 --> 00:00:48.966 year urologic Oncology fellowship.

NOTE Confidence: 0.675779826666667

00:00:48.966 --> 00:00:53.347 He was recruited to Yale in 2016

NOTE Confidence: 0.675779826666667

00:00:53.347 --> 00:00:56.882 specializing in urologic oncology with

NOTE Confidence: 0.675779826666667

00:00:56.882 --> 00:01:01.320 an appointment at Yale and at the VA.

NOTE Confidence: 0.675779826666667

00:01:01.320 --> 00:01:04.519 His research has largely focused on risk

NOTE Confidence: 0.675779826666667

00:01:04.519 --> 00:01:07.280 stratification and and clinical outcomes,

NOTE Confidence: 0.675779826666667

00:01:07.280 --> 00:01:09.702 and he is widely published and today

NOTE Confidence: 0.675779826666667

00:01:09.702 --> 00:01:12.976 is going to talk to us about Ken new

NOTE Confidence: 0.675779826666667

00:01:12.976 --> 00:01:15.073 risk assessment tools for prostate

NOTE Confidence: 0.675779826666667

00:01:15.073 --> 00:01:17.958 cancer deliver better patient outcomes.

NOTE Confidence: 0.675779826666667

00:01:17.960 --> 00:01:18.682 Michael welcome,

NOTE Confidence: 0.675779826666667

00:01:18.682 --> 00:01:20.126 thank you very much.

NOTE Confidence: 0.929726411818182

00:01:20.630 --> 00:01:22.905 Well, thanks so much for the warm

NOTE Confidence: 0.929726411818182

00:01:22.905 --> 00:01:24.530 introduction and good afternoon,

NOTE Confidence: 0.929726411818182

00:01:24.530 --> 00:01:26.706 so I'm happy to speak about this question.

NOTE Confidence: 0.929726411818182

00:01:26.710 --> 00:01:30.490 Can new risk assessment technologies for

NOTE Confidence: 0.929726411818182

00:01:30.490 --> 00:01:33.990 prostate cancer deliver better outcomes?

NOTE Confidence: 0.929726411818182

00:01:33.990 --> 00:01:36.358 I have no disclosures,

NOTE Confidence: 0.929726411818182

00:01:36.360 --> 00:01:39.078 so I'm a urologist whose interest,

NOTE Confidence: 0.929726411818182

00:01:39.080 --> 00:01:39.772 as mentioned,

NOTE Confidence: 0.929726411818182

00:01:39.772 --> 00:01:41.848 are really focused on urologic cancer,

NOTE Confidence: 0.929726411818182

00:01:41.850 --> 00:01:42.879 specifically prostate cancer,

NOTE Confidence: 0.929726411818182

00:01:42.879 --> 00:01:44.937 and this has fueled my interest

NOTE Confidence: 0.929726411818182

00:01:44.937 --> 00:01:46.480 in understanding how technology

NOTE Confidence: 0.929726411818182

00:01:46.480 --> 00:01:48.390 is aimed at decision making,

NOTE Confidence: 0.929726411818182

00:01:48.390 --> 00:01:50.448 are used in men with prostate cancer,

NOTE Confidence: 0.929726411818182

00:01:50.450 --> 00:01:52.754 a disease with a high burden

NOTE Confidence: 0.929726411818182

00:01:52.754 --> 00:01:53.906 of decisional conflict.

NOTE Confidence: 0.929726411818182

00:01:53.910 --> 00:01:54.242 Specifically,

NOTE Confidence: 0.929726411818182

00:01:54.242 --> 00:01:55.902 I'm interested in learning how

NOTE Confidence: 0.929726411818182

00:01:55.902 --> 00:01:57.852 they're being used whether or not

NOTE Confidence: 0.929726411818182

00:01:57.852 --> 00:01:59.287 they're meeting their intended goal,

NOTE Confidence: 0.929726411818182

00:01:59.290 --> 00:02:01.330 and how they can be optimized.

NOTE Confidence: 0.929726411818182

00:02:01.330 --> 00:02:03.304 So the overarching goal of this

NOTE Confidence: 0.929726411818182

00:02:03.304 --> 00:02:05.564 work is to improve how we screen

NOTE Confidence: 0.929726411818182

00:02:05.564 --> 00:02:07.594 for how we diagnose and how we

NOTE Confidence: 0.929726411818182

00:02:07.662 --> 00:02:09.967 manage early stage prostate cancer.

NOTE Confidence: 0.929726411818182

00:02:09.970 --> 00:02:12.292 So in my time I want to cover the

NOTE Confidence: 0.929726411818182

00:02:12.292 --> 00:02:14.059 rationale for active surveillance,

NOTE Confidence: 0.929726411818182

00:02:14.060 --> 00:02:16.070 the why and how of it,

NOTE Confidence: 0.929726411818182

00:02:16.070 --> 00:02:17.687 and then talk about a series of

NOTE Confidence: 0.929726411818182

00:02:17.687 --> 00:02:19.569 advances in the past decade that have

NOTE Confidence: 0.929726411818182

00:02:19.569 --> 00:02:21.279 been undertaken to help increase the

4

NOTE Confidence: 0.929726411818182

00:02:21.328 --> 00:02:22.948 precision of active surveillance,

NOTE Confidence: 0.929726411818182

00:02:22.950 --> 00:02:26.208 focusing on prostate MRI and tissue

NOTE Confidence: 0.929726411818182

00:02:26.208 --> 00:02:28.380 based gene expression signatures.

NOTE Confidence: 0.929726411818182

00:02:28.380 --> 00:02:30.096 And then talk about our work.

NOTE Confidence: 0.929726411818182

00:02:30.100 --> 00:02:32.554 Looking at real-world uptake and studies

NOTE Confidence: 0.929726411818182

00:02:32.554 --> 00:02:34.900 to estimate the effectiveness of testing.

NOTE Confidence: 0.929726411818182

00:02:34.900 --> 00:02:35.578 And lastly,

NOTE Confidence: 0.929726411818182

00:02:35.578 --> 00:02:37.951 take a close look at the question

NOTE Confidence: 0.929726411818182

00:02:37.951 --> 00:02:40.521 of the equity of the dissemination

NOTE Confidence: 0.929726411818182

00:02:40.521 --> 00:02:42.676 of new risk assessment tools.

NOTE Confidence: 0.929726411818182

00:02:42.680 --> 00:02:45.024 I want to start with a patient example.

NOTE Confidence: 0.929726411818182

00:02:45.030 --> 00:02:47.046 A common scenario that we see in the clinic.

NOTE Confidence: 0.929726411818182

00:02:47.050 --> 00:02:49.510 A gentleman referred for an elevated

NOTE Confidence: 0.929726411818182

00:02:49.510 --> 00:02:52.170 PSA to 8.1 on routine screening.

NOTE Confidence: 0.929726411818182

00:02:52.170 --> 00:02:53.550 He has diabetes,

NOTE Confidence: 0.929726411818182

00:02:53.550 --> 00:02:54.732 hypertension, hyperlipidemia.

NOTE Confidence: 0.929726411818182

00:02:54.732 --> 00:02:57.687 His father had localized prostate

NOTE Confidence: 0.929726411818182

00:02:57.687 --> 00:03:00.430 cancer but lived his mid 90s.

NOTE Confidence: 0.929726411818182

00:03:00.430 --> 00:03:02.686 He has a prostate biopsy showing

NOTE Confidence: 0.929726411818182

00:03:02.686 --> 00:03:05.790 three corps police in $3 + 3$ or grade

NOTE Confidence: 0.929726411818182

00:03:05.790 --> 00:03:07.703 Group One prostate cancer and has

NOTE Confidence: 0.929726411818182

00:03:07.703 --> 00:03:10.175 come to see us for a second opinion.

NOTE Confidence: 0.929726411818182

00:03:10.180 --> 00:03:11.724 Based on standard clinical

NOTE Confidence: 0.929726411818182

00:03:11.724 --> 00:03:12.496 risk stratification,

NOTE Confidence: 0.929726411818182

00:03:12.500 --> 00:03:14.420 he falls in this green category.

NOTE Confidence: 0.929726411818182

00:03:14.420 --> 00:03:19.470 The low risk or very low risk criteria.

NOTE Confidence: 0.929726411818182

00:03:19.470 --> 00:03:20.950 So this patient is presented

NOTE Confidence: 0.929726411818182

00:03:20.950 --> 00:03:22.430 with a few different options.

NOTE Confidence: 0.929726411818182

00:03:22.430 --> 00:03:24.798 He can have surgery to remove his prostate,

NOTE Confidence: 0.929726411818182

00:03:24.800 --> 00:03:26.284 and that's what that's what I do.

NOTE Confidence: 0.929726411818182

00:03:26.290 --> 00:03:28.210 He can have radiation treatment

NOTE Confidence: 0.929726411818182

00:03:28.210 --> 00:03:30.130 to his prostate or monitoring

NOTE Confidence: 0.929726411818182

00:03:30.194 --> 00:03:32.018 known as active surveillance.

NOTE Confidence: 0.929726411818182

00:03:32.020 --> 00:03:33.651 His inclination is to be monitored and

NOTE Confidence: 0.929726411818182

00:03:33.651 --> 00:03:35.458 not be treated for his prostate cancer.

NOTE Confidence: 0.929726411818182

00:03:35.460 --> 00:03:37.614 He knows people who've had treatment

NOTE Confidence: 0.929726411818182

00:03:37.614 --> 00:03:39.690 and didn't like what he heard.

NOTE Confidence: 0.929726411818182

00:03:39.690 --> 00:03:40.878 So understandably has many

NOTE Confidence: 0.929726411818182

00:03:40.878 --> 00:03:42.066 questions about his options.

NOTE Confidence: 0.929726411818182

00:03:42.070 --> 00:03:43.420 How risky are the treatments?

NOTE Confidence: 0.929726411818182

00:03:43.420 --> 00:03:45.274 How might they affect his quality

NOTE Confidence: 0.929726411818182

00:03:45.274 --> 00:03:46.912 of life and particularly his

NOTE Confidence: 0.929726411818182

00:03:46.912 --> 00:03:48.276 urinary and sexual function?

NOTE Confidence: 0.929726411818182

00:03:48.280 --> 00:03:49.764 And what are the risks if he

NOTE Confidence: 0.929726411818182

00:03:49.764 --> 00:03:50.400 does active surveillance?

NOTE Confidence: 0.929726411818182

00:03:50.400 --> 00:03:51.400 Can the cancer spread?

NOTE Confidence: 0.92475964

00:03:53.510 --> 00:03:55.220 Our index patient is not alone.

NOTE Confidence: 0.92475964

00:03:55.220 --> 00:03:57.326 Prostate cancer is the most commonly

NOTE Confidence: 0.92475964

00:03:57.326 --> 00:03:59.189 diagnosed non skin cancer in men,

NOTE Confidence: 0.92475964

00:03:59.190 --> 00:04:01.646 accounting for nearly 270,000

NOTE Confidence: 0.92475964

00:04:01.646 --> 00:04:04.790 diagnosis estimated in 2022.

NOTE Confidence: 0.92475964

00:04:04.790 --> 00:04:06.226 And although the incidence,

NOTE Confidence: 0.92475964

00:04:06.226 --> 00:04:08.021 the ratio of incidents to

NOTE Confidence: 0.92475964

00:04:08.021 --> 00:04:09.469 mortality is heavily skewed,

NOTE Confidence: 0.92475964

00:04:09.470 --> 00:04:11.468 prostate cancer is still the second

NOTE Confidence: 0.92475964

00:04:11.468 --> 00:04:13.708 leading cause of cancer death in males,

NOTE Confidence: 0.92475964

00:04:13.710 --> 00:04:15.816 and this finding reflects both the

NOTE Confidence: 0.92475964

00:04:15.816 --> 00:04:17.220 wide heterogeneity of prostate

NOTE Confidence: 0.92475964

00:04:17.282 --> 00:04:19.312 cancer with some cancers bearing

NOTE Confidence: 0.92475964

00:04:19.312 --> 00:04:20.530 highly aggressive features,

NOTE Confidence: 0.92475964

00:04:20.530 --> 00:04:22.280 while others demonstrate an indolent

NOTE Confidence: 0.92475964

00:04:22.280 --> 00:04:24.987 course and may never be capable of

NOTE Confidence: 0.92475964

00:04:24.987 --> 00:04:26.775 metastasis or regional progression.

NOTE Confidence: 0.92903303

00:04:29.170 --> 00:04:31.704 For patients with low risk prostate cancer,

NOTE Confidence: 0.92903303

00:04:31.710 --> 00:04:32.790 such as our patient,

NOTE Confidence: 0.92903303

00:04:32.790 --> 00:04:34.140 we're fortunate that a vast

NOTE Confidence: 0.92903303

00:04:34.140 --> 00:04:35.450 amount of data has matured.

NOTE Confidence: 0.92903303

00:04:35.450 --> 00:04:37.840 Regarding the safety and long

NOTE Confidence: 0.92903303

00:04:37.840 --> 00:04:39.752 term outcomes of surveillance.

NOTE Confidence: 0.92903303

00:04:39.760 --> 00:04:41.148 And by active surveillance,

NOTE Confidence: 0.92903303

00:04:41.148 --> 00:04:43.230 I'm referring to the careful process

NOTE Confidence: 0.92903303

00:04:43.289 --> 00:04:44.914 of monitoring low risk prostate

NOTE Confidence: 0.92903303

00:04:44.914 --> 00:04:46.980 cancer with the intention of providing

NOTE Confidence: 0.92903303

00:04:46.980 --> 00:04:49.260 curative local treatment in the future.

NOTE Confidence: 0.92903303

00:04:49.260 --> 00:04:51.900 If progression is identified.

NOTE Confidence: 0.92903303

00:04:51.900 --> 00:04:53.952 It is the preferred management for

NOTE Confidence: 0.92903303

00:04:53.952 --> 00:04:56.404 very low risk and low risk prostate

NOTE Confidence: 0.92903303

00:04:56.404 --> 00:04:58.645 cancer by the NCCN and in longitudinal

NOTE Confidence: 0.92903303

00:04:58.645 --> 00:05:00.880 studies it is safe with less than 1%

NOTE Confidence: 0.92903303

00:05:00.880 --> 00:05:03.118 risk of mortality within 10 years,

NOTE Confidence: 0.92903303

00:05:03.120 --> 00:05:05.160 and it's effective at preserving

NOTE Confidence: 0.92903303

00:05:05.160 --> 00:05:07.690 long term quality of life.

NOTE Confidence: 0.92903303

00:05:07.690 --> 00:05:10.112 The monitoring that we refer to commonly

NOTE Confidence: 0.92903303

00:05:10.112 --> 00:05:11.830 involves periodic PSA monitoring,

NOTE Confidence: 0.92903303

00:05:11.830 --> 00:05:14.990 monitoring, prostate biopsy and imaging,

NOTE Confidence: 0.92903303

00:05:14.990 --> 00:05:17.960 including prostate MRI.

NOTE Confidence: 0.92903303

00:05:17.960 --> 00:05:20.116 How strong is the data for surveillance

NOTE Confidence: 0.92903303

00:05:20.120 --> 00:05:22.235 in this randomized trial published

NOTE Confidence: 0.92903303

00:05:22.235 --> 00:05:25.593 in 2016 from the UK of nearly 1500

NOTE Confidence: 0.92903303

00:05:25.593 --> 00:05:28.180 patients randomized to receive surgery,

NOTE Confidence: 0.92903303

00:05:28.180 --> 00:05:28.591 radiotherapy,

NOTE Confidence: 0.92903303

00:05:28.591 --> 00:05:30.646 or active monitoring for low

NOTE Confidence: 0.92903303

00:05:30.646 --> 00:05:31.879 risk prostate cancer,

NOTE Confidence: 0.92903303

00:05:31.880 --> 00:05:33.704 or the 10 year overall survival

NOTE Confidence: 0.92903303

00:05:33.704 --> 00:05:36.420 is nearly 100% in all groups

NOTE Confidence: 0.92903303

00:05:36.420 --> 00:05:38.220 without significant differences.

NOTE Confidence: 0.92903303

00:05:38.220 --> 00:05:40.055 These striking findings cement the

NOTE Confidence: 0.92903303

00:05:40.055 --> 00:05:41.890 long term safety of surveillance

NOTE Confidence: 0.92903303

00:05:41.950 --> 00:05:43.540 and its centrality in efforts

NOTE Confidence: 0.92903303

00:05:43.540 --> 00:05:45.580 to push back against decades of

NOTE Confidence: 0.92903303

00:05:45.580 --> 00:05:47.156 overtreatment of prostate cancer.

NOTE Confidence: 0.930988486363636

00:05:49.350 --> 00:05:50.742 As part of this work and as part

NOTE Confidence: 0.930988486363636

00:05:50.742 --> 00:05:52.320 of this mission, we've undertaken

NOTE Confidence: 0.930988486363636

00:05:52.320 --> 00:05:53.980 formative qualitative interviews to

NOTE Confidence: 0.930988486363636

00:05:53.980 --> 00:05:56.573 gain insights about the perspectives of

NOTE Confidence: 0.930988486363636

00:05:56.573 --> 00:05:58.758 patients diagnosed with prostate cancer.

NOTE Confidence: 0.930988486363636

00:05:58.760 --> 00:06:00.200 We spoke with patients recently

NOTE Confidence: 0.930988486363636

00:06:00.200 --> 00:06:02.000 diagnosed with low risk prostate cancer.

NOTE Confidence: 0.930988486363636

00:06:02.000 --> 00:06:04.562 To get a deeper sense about

NOTE Confidence: 0.930988486363636

00:06:04.562 --> 00:06:05.416 their experiences.

NOTE Confidence: 0.930988486363636

00:06:05.420 --> 00:06:06.880 And one patient poignantly told

NOTE Confidence: 0.930988486363636

00:06:06.880 --> 00:06:08.759 us it was very emotional for me.

NOTE Confidence: 0.930988486363636

00:06:08.760 --> 00:06:10.216 My first doctor told me that I

NOTE Confidence: 0.930988486363636

00:06:10.216 --> 00:06:11.870 needed to have surgery or radiation,

NOTE Confidence: 0.930988486363636

00:06:11.870 --> 00:06:13.600 just very matter of fact.

NOTE Confidence: 0.930988486363636

00:06:13.600 --> 00:06:14.896 After I heard the word cancer,

NOTE Confidence: 0.930988486363636

00:06:14.900 --> 00:06:15.776 I didn't know what to say.

NOTE Confidence: 0.930988486363636

00:06:15.780 --> 00:06:16.568 I just went blank.

NOTE Confidence: 0.870210902

00:06:18.610 --> 00:06:20.870 And another patient encapsulated it.

NOTE Confidence: 0.870210902

00:06:20.870 --> 00:06:22.820 Quite simply, I wanted to understand

NOTE Confidence: 0.870210902

00:06:22.820 --> 00:06:24.678 the reasons behind why my cancer

NOTE Confidence: 0.870210902

00:06:24.678 --> 00:06:26.166 was low risk or high risk,

NOTE Confidence: 0.870210902

00:06:26.170 --> 00:06:27.098 and why active surveillance

NOTE Confidence: 0.870210902

00:06:27.098 --> 00:06:28.258 could be reasonable for me.

NOTE Confidence: 0.9314563725

00:06:30.440 --> 00:06:32.036 So when faced with a diagnosis

NOTE Confidence: 0.9314563725

00:06:32.036 --> 00:06:34.199 that many of us consider indolent,

NOTE Confidence: 0.9314563725

00:06:34.200 --> 00:06:35.825 patients frequently feel that their

NOTE Confidence: 0.9314563725

00:06:35.825 --> 00:06:37.874 life has been upended and sometimes

NOTE Confidence: 0.9314563725

00:06:37.874 --> 00:06:40.064 don't feel supported by their doctors.

NOTE Confidence: 0.9314563725

00:06:40.070 --> 00:06:41.003 In any circumstance,

NOTE Confidence: 0.9314563725

00:06:41.003 --> 00:06:42.869 the word cancer evokes very strong

NOTE Confidence: 0.9314563725

00:06:42.869 --> 00:06:44.917 and intense emotions and clinicians,

NOTE Confidence: 0.9314563725

00:06:44.920 --> 00:06:47.228 including us, are very

NOTE Confidence: 0.9314563725

00:06:47.228 --> 00:06:49.536 frequently unaware or unprepared.

NOTE Confidence: 0.9314563725

00:06:49.540 --> 00:06:50.224 And most notably,

NOTE Confidence: 0.9314563725

00:06:50.224 --> 00:06:51.820 many of our patients want to be

NOTE Confidence: 0.9314563725

00:06:51.868 --> 00:06:53.378 well informed about their cancer

NOTE Confidence: 0.9314563725

00:06:53.378 --> 00:06:54.888 diagnosis and management to feel

NOTE Confidence: 0.9314563725

00:06:54.940 --> 00:06:56.360 agency in their decision making

NOTE Confidence: 0.9314563725

00:06:56.360 --> 00:06:57.780 and assess their choices from

NOTE Confidence: 0.9314563725

00:06:57.780 --> 00:06:59.860 a variety of vantage points.

NOTE Confidence: 0.9314563725

00:06:59.860 --> 00:07:01.358 And it's this last point that we

NOTE Confidence: 0.9314563725

00:07:01.358 --> 00:07:02.738 really want to focus on today,

NOTE Confidence: 0.9314563725

00:07:02.740 --> 00:07:04.356 particularly the emergence of

NOTE Confidence: 0.9314563725

00:07:04.356 --> 00:07:05.972 precision diagnostic tools that

NOTE Confidence: 0.9314563725

00:07:05.972 --> 00:07:08.624 seek to deliver on the goal of

NOTE Confidence: 0.9314563725

00:07:08.624 --> 00:07:10.052 enhanced risk stratification and

NOTE Confidence: 0.9314563725

00:07:10.052 --> 00:07:12.192 begin to unpack how their news is

NOTE Confidence: 0.9314563725

00:07:12.192 --> 00:07:13.910 is delivering on this promise.

NOTE Confidence: 0.931398748181818

00:07:16.700 --> 00:07:19.106 So although we commonly distill prostate

NOTE Confidence: 0.931398748181818

00:07:19.106 --> 00:07:21.380 cancer into clinical risk groupings,

NOTE Confidence: 0.931398748181818

00:07:21.380 --> 00:07:23.684 the disease is in fact quite varied both in

NOTE Confidence: 0.931398748181818

00:07:23.684 --> 00:07:25.816 terms of its biology and clinical course,

NOTE Confidence: 0.931398748181818

00:07:25.820 --> 00:07:27.468 and I want to take a few minutes

NOTE Confidence: 0.931398748181818

00:07:27.468 --> 00:07:29.422 to also explain why A1 size fits

NOTE Confidence: 0.931398748181818

00:07:29.422 --> 00:07:30.912 all approach for prostate cancer.

NOTE Confidence: 0.931398748181818

00:07:30.920 --> 00:07:33.559 Even low risk prostate cancer may still

NOTE Confidence: 0.931398748181818

00:07:33.559 --> 00:07:35.890 be too inflexible and not optimally

NOTE Confidence: 0.931398748181818

00:07:35.890 --> 00:07:38.152 meet the needs of our patients

NOTE Confidence: 0.931398748181818

00:07:38.152 --> 00:07:40.119 enrolled in active surveillance.

NOTE Confidence: 0.931398748181818

00:07:40.120 --> 00:07:41.814 So I showed you earlier at the

NOTE Confidence: 0.931398748181818

00:07:41.814 --> 00:07:43.459 excellent data from the PROTECT study,

NOTE Confidence: 0.931398748181818

00:07:43.460 --> 00:07:45.620 which randomized patients to observation,

NOTE Confidence: 0.931398748181818

00:07:45.620 --> 00:07:46.922 radiation or monitoring.

NOTE Confidence: 0.931398748181818

00:07:46.922 --> 00:07:49.518 I'm sorry, observation, radiation or surgery.

NOTE Confidence: 0.931398748181818

00:07:49.518 --> 00:07:52.230 In this study, patients did not

NOTE Confidence: 0.931398748181818

00:07:52.230 --> 00:07:53.640 receive intensive monitoring,

NOTE Confidence: 0.931398748181818

00:07:53.640 --> 00:07:55.644 but rather we only followed at

NOTE Confidence: 0.931398748181818

00:07:55.644 --> 00:07:57.380 arms length with PSA monitoring

NOTE Confidence: 0.931398748181818

00:07:57.380 --> 00:07:59.718 and only had further work up if

NOTE Confidence: 0.931398748181818

00:07:59.718 --> 00:08:01.629 they had overt progression.

NOTE Confidence: 0.931398748181818

00:08:01.630 --> 00:08:02.780 This is pretty different from

NOTE Confidence: 0.931398748181818

00:08:02.780 --> 00:08:03.930 how we do things today.

NOTE Confidence: 0.931398748181818

00:08:03.930 --> 00:08:05.530 There is no MRI.

NOTE Confidence: 0.931398748181818

00:08:05.530 --> 00:08:07.530 There were no men mandated

NOTE Confidence: 0.931398748181818

00:08:07.530 --> 00:08:08.650 confirmatory biopsies,

NOTE Confidence: 0.931398748181818

00:08:08.650 --> 00:08:10.115 and although the overall survival

NOTE Confidence: 0.931398748181818

00:08:10.115 --> 00:08:11.910 at 10 years was quite good,

NOTE Confidence: 0.931398748181818

00:08:11.910 --> 00:08:13.914 there were beginning to see significantly

NOTE Confidence: 0.931398748181818

00:08:13.914 --> 00:08:16.116 higher risks of local progression and

NOTE Confidence: 0.931398748181818

00:08:16.116 --> 00:08:18.126 metastatic progression in this group,

NOTE Confidence: 0.931398748181818

00:08:18.130 --> 00:08:20.560 likely due to misclassification and

NOTE Confidence: 0.931398748181818

00:08:20.560 --> 00:08:22.990 therefore this data highlights the

NOTE Confidence: 0.931398748181818

00:08:23.061 --> 00:08:25.036 extent to which active monitoring

NOTE Confidence: 0.931398748181818

00:08:25.036 --> 00:08:27.011 must in fact be active.

NOTE Confidence: 0.931398748181818

00:08:27.020 --> 00:08:29.252 But just how good are are we at

NOTE Confidence: 0.931398748181818

00:08:29.252 --> 00:08:31.180 predicting boost disease is going to

NOTE Confidence: 0.931398748181818

00:08:31.180 --> 00:08:33.136 progress overtime and whose will not

NOTE Confidence: 0.931398748181818

00:08:33.140 --> 00:08:35.492 our best clinical models based on

NOTE Confidence: 0.931398748181818

00:08:35.492 --> 00:08:38.057 PSA Gleason score and stage actually

NOTE Confidence: 0.931398748181818

00:08:38.057 --> 00:08:40.372 performed quite model only modestly

NOTE Confidence: 0.931398748181818

00:08:40.372 --> 00:08:43.575 with C indices ranging from .52 to 0.7?

NOTE Confidence: 0.931398748181818

00:08:43.575 --> 00:08:45.345 So we're really not meeting the

NOTE Confidence: 0.931398748181818

00:08:45.345 --> 00:08:47.368 mark yet and has significant ground

NOTE Confidence: 0.931398748181818

00:08:47.368 --> 00:08:49.650 to cover in guiding our patients.

NOTE Confidence: 0.880488586363636

00:08:52.070 --> 00:08:53.402 The questions that we want to

NOTE Confidence: 0.880488586363636

00:08:53.402 --> 00:08:54.770 know are actually very practical.

NOTE Confidence: 0.880488586363636

00:08:54.770 --> 00:08:57.283 For example, how likely is a patient

NOTE Confidence: 0.880488586363636

00:08:57.283 --> 00:08:59.450 cancer to spread if not treated,

NOTE Confidence: 0.880488586363636

00:08:59.450 --> 00:09:01.910 how often will monitoring be needed

NOTE Confidence: 0.880488586363636

00:09:01.910 --> 00:09:04.648 and can treatment be given in time?

NOTE Confidence: 0.880488586363636

00:09:04.650 --> 00:09:06.568 Due to a very high prevalence of

NOTE Confidence: 0.880488586363636

00:09:06.568 --> 00:09:08.183 prostate cancer and it's desperate

NOTE Confidence: 0.880488586363636

00:09:08.183 --> 00:09:09.659 and it's decisional burden,

NOTE Confidence: 0.880488586363636

00:09:09.660 --> 00:09:11.870 there's perhaps equally important need

NOTE Confidence: 0.880488586363636

00:09:11.870 --> 00:09:14.080 to present this information coherently

NOTE Confidence: 0.880488586363636

00:09:14.144 --> 00:09:16.433 to our patients and enable them to

NOTE Confidence: 0.880488586363636

00:09:16.433 --> 00:09:18.426 make optimal decisions and also live

NOTE Confidence: 0.880488586363636

00:09:18.426 --> 00:09:20.322 for years with their diagnosis and

NOTE Confidence: 0.880488586363636

00:09:20.322 --> 00:09:22.008 manage the associated uncertainty.

NOTE Confidence: 0.892628519615385

00:09:24.720 --> 00:09:26.796 Several new tests have been developed

NOTE Confidence: 0.892628519615385

00:09:26.796 --> 00:09:29.142 and are now commercially integrated to

NOTE Confidence: 0.892628519615385

00:09:29.142 --> 00:09:31.402 improve prognostication for patients with

NOTE Confidence: 0.892628519615385

00:09:31.402 --> 00:09:33.253 localized prostate cancer considering

NOTE Confidence: 0.892628519615385

00:09:33.253 --> 00:09:35.438 or enrolled on active surveillance.

NOTE Confidence: 0.892628519615385

00:09:35.440 --> 00:09:37.360 These tests are all biopsy based.

NOTE Confidence: 0.892628519615385

00:09:37.360 --> 00:09:39.495 M RNA expression signatures that

NOTE Confidence: 0.892628519615385

00:09:39.495 --> 00:09:41.203 measure genes highly associated

NOTE Confidence: 0.892628519615385

00:09:41.203 --> 00:09:43.238 with prostate cancer outcomes.

NOTE Confidence: 0.892628519615385

00:09:43.240 --> 00:09:45.280 The decipher genomic classifier

NOTE Confidence: 0.892628519615385

00:09:45.280 --> 00:09:48.820 generates a score ranging from zero to

NOTE Confidence: 0.892628519615385

00:09:48.820 --> 00:09:51.620 1 from microarray analysis of 22 genes.

NOTE Confidence: 0.892628519615385

00:09:51.620 --> 00:09:53.924 The uncle Type DX test measures

NOTE Confidence: 0.892628519615385

00:09:53.924 --> 00:09:56.733 the expression level of 12 genes

NOTE Confidence: 0.892628519615385

00:09:56.733 --> 00:09:58.533 reflecting androgen signaling

NOTE Confidence: 0.892628519615385

00:09:58.533 --> 00:10:00.333 cellular organization proliferation

NOTE Confidence: 0.892628519615385

00:10:00.333 --> 00:10:02.870 and stromal response pathways.

NOTE Confidence: 0.892628519615385

00:10:02.870 --> 00:10:05.397 And lastly, the Polaris signature is a

NOTE Confidence: 0.892628519615385

00:10:05.397 --> 00:10:07.254 cell cycle progression score calculated

NOTE Confidence: 0.892628519615385

00:10:07.254 --> 00:10:10.094 based on the expression levels of 31 genes.

NOTE Confidence: 0.892628519615385

00:10:10.100 --> 00:10:12.110 Each of these tests yields discrete

NOTE Confidence: 0.892628519615385

00:10:12.110 --> 00:10:13.450 predictions about cancer risk,

NOTE Confidence: 0.892628519615385

00:10:13.450 --> 00:10:14.258 including recommendations

NOTE Confidence: 0.892628519615385

00:10:14.258 --> 00:10:15.470 for clinical management.

NOTE Confidence: 0.891811376

00:10:18.990 --> 00:10:21.468 So all of these tests are independently

NOTE Confidence: 0.891811376

00:10:21.468 --> 00:10:23.499 provide prognostic value compared to the

NOTE Confidence: 0.891811376

00:10:23.499 --> 00:10:25.627 standard of care variables such as PSA,

NOTE Confidence: 0.891811376

00:10:25.630 --> 00:10:28.480 Gleason, score, and clinical stage.

NOTE Confidence: 0.891811376

00:10:28.480 --> 00:10:30.608 The disciple classifier is now the best

NOTE Confidence: 0.891811376

00:10:30.608 --> 00:10:33.004 studied and has been validated as both

NOTE Confidence: 0.891811376

00:10:33.004 --> 00:10:34.784 a prognostic and predictive marker.

NOTE Confidence: 0.891811376

00:10:34.790 --> 00:10:37.010 In one retrospective study where

NOTE Confidence: 0.891811376

00:10:37.010 --> 00:10:39.230 the decipher scores were calculated

NOTE Confidence: 0.891811376

00:10:39.299 --> 00:10:41.389 based on archival FFP specimens,

NOTE Confidence: 0.891811376

00:10:41.390 --> 00:10:43.290 patients in the highest group

NOTE Confidence: 0.891811376

00:10:43.290 --> 00:10:45.190 faced substantially greater risk of

NOTE Confidence: 0.891811376

00:10:45.256 --> 00:10:47.540 metastatic progression after treatment.

NOTE Confidence: 0.891811376

00:10:47.540 --> 00:10:49.532 However, a key point is that each of

NOTE Confidence: 0.891811376

00:10:49.532 --> 00:10:51.398 these tests have been studied only

NOTE Confidence: 0.891811376

00:10:51.398 --> 00:10:53.033 in retrospective cohorts of patients

NOTE Confidence: 0.891811376

00:10:53.033 --> 00:10:54.929 who have previously been treated,

NOTE Confidence: 0.891811376

00:10:54.930 --> 00:10:56.445 and comparatively little is known

NOTE Confidence: 0.891811376

00:10:56.445 --> 00:10:58.355 about their real-world use or the

NOTE Confidence: 0.891811376

00:10:58.355 --> 00:11:00.080 decisions that arise following testing.

NOTE Confidence: 0.90124940125

00:11:02.580 --> 00:11:04.200 The other major advancement

NOTE Confidence: 0.90124940125

00:11:04.200 --> 00:11:05.820 has been prostate MRI,

NOTE Confidence: 0.90124940125

00:11:05.820 --> 00:11:08.660 something that Yale is truly a leader in.

NOTE Confidence: 0.90124940125

00:11:08.660 --> 00:11:11.678 So high resolution prostate MRI affords

NOTE Confidence: 0.90124940125

00:11:11.678 --> 00:11:14.247 reliable identification of prostate cancer

NOTE Confidence: 0.90124940125

00:11:14.247 --> 00:11:17.175 and facilitates directed or fusion biopsies.

NOTE Confidence: 0.90124940125

00:11:17.180 --> 00:11:21.218 It also substantially improves local staging.

NOTE Confidence: 0.90124940125

00:11:21.220 --> 00:11:22.280 And it's now the standard

NOTE Confidence: 0.90124940125

00:11:22.280 --> 00:11:23.340 of care in many countries,

NOTE Confidence: 0.90124940125

00:11:23.340 --> 00:11:24.920 including the in the UK,

NOTE Confidence: 0.90124940125

00:11:24.920 --> 00:11:26.516 where it's performed almost

NOTE Confidence: 0.90124940125

00:11:26.516 --> 00:11:28.511 universally in patients with known

NOTE Confidence: 0.90124940125

00:11:28.511 --> 00:11:30.569 or suspected prostate cancer.

NOTE Confidence: 0.90124940125

00:11:30.570 --> 00:11:32.302 And actually, at Yale,

NOTE Confidence: 0.90124940125

00:11:32.302 --> 00:11:34.900 in undertaking in the majority of

NOTE Confidence: 0.90124940125

00:11:34.981 --> 00:11:37.686 patients in our diagnostic process.

NOTE Confidence: 0.90124940125

00:11:37.690 --> 00:11:40.007 In one randomized trial of 500 patients,

NOTE Confidence: 0.90124940125

00:11:40.010 --> 00:11:42.386 MRI led to increased detection of

NOTE Confidence: 0.90124940125

00:11:42.386 --> 00:11:43.970 clinically significant prostate cancer,

NOTE Confidence: 0.90124940125

00:11:43.970 --> 00:11:45.560 and in fact, and actually less

NOTE Confidence: 0.90124940125

00:11:45.560 --> 00:11:47.030 detection of low grade cancer.

NOTE Confidence: 0.90124940125

00:11:47.030 --> 00:11:48.948 So here's the breakdown that we can

NOTE Confidence: 0.90124940125

00:11:48.948 --> 00:11:51.098 see in this chart over here that

NOTE Confidence: 0.90124940125

00:11:51.098 --> 00:11:52.988 the majority of patients who have

NOTE Confidence: 0.90124940125

00:11:53.055 --> 00:11:55.717 a high suspicion lesion on MRI are

NOTE Confidence: 0.90124940125

00:11:55.717 --> 00:11:57.912 found to have clinically clinically

NOTE Confidence: 0.90124940125

00:11:57.912 --> 00:12:00.160 significant or high grade cancer.

NOTE Confidence: 0.90124940125

00:12:00.160 --> 00:12:01.825 Versus quite low on patients

NOTE Confidence: 0.90124940125

00:12:01.825 --> 00:12:03.490 who have a lower suspicion.

NOTE Confidence: 0.92813383

00:12:07.370 --> 00:12:08.898 So based on improvements

NOTE Confidence: 0.92813383

00:12:08.898 --> 00:12:10.044 in diagnostic accuracy,

NOTE Confidence: 0.92813383

00:12:10.050 --> 00:12:12.745 it's been assumed that the routine use

NOTE Confidence: 0.92813383

00:12:12.745 --> 00:12:15.689 of prostate MRI will also enhance the

NOTE Confidence: 0.92813383

00:12:15.689 --> 00:12:18.257 use and safety of active surveillance.

NOTE Confidence: 0.92813383

00:12:18.260 --> 00:12:20.129 So in light of a major shift

NOTE Confidence: 0.92813383

00:12:20.129 --> 00:12:21.400 in the acceptance uptake,

NOTE Confidence: 0.92813383

00:12:21.400 --> 00:12:23.038 there is a pressing need to understand

NOTE Confidence: 0.92813383

00:12:23.038 --> 00:12:24.740 how these two new forms of testing,

NOTE Confidence: 0.92813383

00:12:24.740 --> 00:12:26.300 genomic testing and prostate

NOTE Confidence: 0.92813383

00:12:26.300 --> 00:12:28.250 MRI have impacted its practice.

NOTE Confidence: 0.925548484545455

00:12:30.710 --> 00:12:32.852 Use of active surveillance has increased

NOTE Confidence: 0.925548484545455

00:12:32.852 --> 00:12:34.690 significantly within the past decade.

NOTE Confidence: 0.925548484545455

00:12:34.690 --> 00:12:36.522 Between 2010 and 2015,

NOTE Confidence: 0.925548484545455

00:12:36.522 --> 00:12:39.873 data from SEER indicates that the rates

NOTE Confidence: 0.925548484545455

00:12:39.873 --> 00:12:44.530 have increased from 14.5 percent 2010 to

NOTE Confidence: 0.925548484545455

00:12:44.530 --> 00:12:48.628 42.1% in 2015 among low risk patients.

NOTE Confidence: 0.925548484545455

00:12:48.630 --> 00:12:51.216 But it's also worth noting how

NOTE Confidence: 0.925548484545455

00:12:51.216 --> 00:12:52.940 substantially practice patterns differ

NOTE Confidence: 0.925548484545455

00:12:53.003 --> 00:12:55.606 for prostate cancer by geography in

NOTE Confidence: 0.925548484545455

00:12:55.606 --> 00:12:57.966 this elegant study recently published,

NOTE Confidence: 0.925548484545455

00:12:57.970 --> 00:12:59.650 the authors contrasted changes

NOTE Confidence: 0.925548484545455

00:12:59.650 --> 00:13:01.330 in active surveillance use,

NOTE Confidence: 0.925548484545455

00:13:01.330 --> 00:13:03.666 which are these yellow bars on the right

NOTE Confidence: 0.925548484545455

00:13:03.666 --> 00:13:05.725 by sea region, and so Connecticut.

NOTE Confidence: 0.925548484545455

00:13:05.725 --> 00:13:07.025 We're doing quite well,

NOTE Confidence: 0.925548484545455

00:13:07.030 --> 00:13:09.046 but we really see how market the

NOTE Confidence: 0.925548484545455

00:13:09.046 --> 00:13:11.160 differences are between, for example,

NOTE Confidence: 0.925548484545455

00:13:11.160 --> 00:13:13.660 Connecticut and Greater Georgia.

NOTE Confidence: 0.925548484545455

00:13:13.660 --> 00:13:16.474 Showing that although changes appear to be.

NOTE Confidence: 0.925548484545455

00:13:16.480 --> 00:13:16.815 Continuing,

NOTE Confidence: 0.925548484545455

00:13:16.815 --> 00:13:18.825 there's also a really a substantial

NOTE Confidence: 0.925548484545455

00:13:18.825 --> 00:13:19.830 amount of heterogeneity.

NOTE Confidence: 0.927587596956522

00:13:22.530 --> 00:13:24.672 So it's within this context that we

NOTE Confidence: 0.927587596956522

00:13:24.672 --> 00:13:27.138 aim to evaluate the uptake of risk

NOTE Confidence: 0.927587596956522

00:13:27.138 --> 00:13:28.998 assessment tools with a particular

NOTE Confidence: 0.927587596956522

00:13:28.998 --> 00:13:31.050 emphasis on regional considerations,

NOTE Confidence: 0.927587596956522

00:13:31.050 --> 00:13:32.898 and in this analysis we focus

NOTE Confidence: 0.927587596956522

00:13:32.898 --> 00:13:34.130 on hospital referral regions,

NOTE Confidence: 0.927587596956522

00:13:34.130 --> 00:13:35.990 which are Regional Health care markets.

NOTE Confidence: 0.927587596956522

00:13:35.990 --> 00:13:38.000 Patricia Re medical care that

NOTE Confidence: 0.927587596956522

00:13:38.000 --> 00:13:40.010 have previously been defined and

NOTE Confidence: 0.927587596956522

00:13:40.075 --> 00:13:41.707 used to characterize variation

NOTE Confidence: 0.927587596956522

00:13:41.707 --> 00:13:44.155 in the intensity of health care.

NOTE Confidence: 0.927587596956522

00:13:44.160 --> 00:13:45.954 So we first sought to understand

NOTE Confidence: 0.927587596956522

00:13:45.954 --> 00:13:48.150 the use of prostate MRI and using

NOTE Confidence: 0.927587596956522

00:13:48.150 --> 00:13:49.305 Deidentified administrative claims

NOTE Confidence: 0.927587596956522

00:13:49.305 --> 00:13:51.230 from Blue Cross Blue Shield.

NOTE Confidence: 0.927587596956522

00:13:51.230 --> 00:13:53.726 We characterize the use of prostate

NOTE Confidence: 0.927587596956522

00:13:53.726 --> 00:13:55.953 MRI among beneficiaries who have

NOTE Confidence: 0.927587596956522

00:13:55.953 --> 00:13:58.428 recently diagnosed with prostate cancer.

NOTE Confidence: 0.927587596956522

00:13:58.430 --> 00:14:01.237 And we found that overall use of

NOTE Confidence: 0.927587596956522

00:14:01.237 --> 00:14:02.790 prostate cancer increased from

NOTE Confidence: 0.927587596956522

00:14:02.790 --> 00:14:06.070 7.2% among patients diagnosed in

NOTE Confidence: 0.927587596956522

00:14:06.070 --> 00:14:12.307 2012 to 16.7% in 2018 and 2019.

NOTE Confidence: 0.927587596956522

00:14:12.310 --> 00:14:12.702 However,

NOTE Confidence: 0.927587596956522

00:14:12.702 --> 00:14:15.054 it's clear that the vast variation

NOTE Confidence: 0.927587596956522

00:14:15.054 --> 00:14:17.121 by region continues to be a

NOTE Confidence: 0.927587596956522

00:14:17.121 --> 00:14:18.687 dominant theme in certain areas,

NOTE Confidence: 0.927587596956522

00:14:18.687 --> 00:14:21.060 such as the Northeast and HRR in

NOTE Confidence: 0.927587596956522

00:14:21.131 --> 00:14:23.369 Connecticut are high users of Mr.

NOTE Confidence: 0.927587596956522

00:14:23.370 --> 00:14:26.730 As our parts of the Mid Atlantic where,

NOTE Confidence: 0.927587596956522

00:14:26.730 --> 00:14:28.400 whereas others show minimal use.

NOTE Confidence: 0.83584552125

00:14:31.790 --> 00:14:33.800 And genomic testing presents an

NOTE Confidence: 0.83584552125

00:14:33.800 --> 00:14:35.006 interesting distinction because,

NOTE Confidence: 0.83584552125

00:14:35.010 --> 00:14:36.314 in contrast to MRI,

NOTE Confidence: 0.83584552125

00:14:36.314 --> 00:14:38.270 which has been available for years

NOTE Confidence: 0.83584552125

00:14:38.337 --> 00:14:40.027 but only rose in popularity,

NOTE Confidence: 0.83584552125

00:14:40.030 --> 00:14:42.430 slowly genomic testing has become approved

NOTE Confidence: 0.83584552125

00:14:42.430 --> 00:14:44.974 and reimbursed by payers at roughly all

NOTE Confidence: 0.83584552125

00:14:44.974 --> 00:14:49.229 at the same time beginning in 2013 and 2014.

NOTE Confidence: 0.83584552125

00:14:49.230 --> 00:14:51.186 Another consideration is that testing is

NOTE Confidence: 0.83584552125

00:14:51.186 --> 00:14:53.200 also performed at remote laboratories,

NOTE Confidence: 0.83584552125

00:14:53.200 --> 00:14:55.072 so complex local infrastructure

NOTE Confidence: 0.83584552125

00:14:55.072 --> 00:14:56.944 is generally not needed.

NOTE Confidence: 0.83584552125

00:14:56.950 --> 00:14:58.996 And these tests are very much

NOTE Confidence: 0.83584552125

00:14:58.996 --> 00:15:00.360 discretionary at the discretion

NOTE Confidence: 0.83584552125

00:15:00.415 --> 00:15:02.257 of the position of the physician.

NOTE Confidence: 0.83584552125

00:15:02.260 --> 00:15:04.416 So to answer the question about uptake,

NOTE Confidence: 0.83584552125

00:15:04.420 --> 00:15:06.520 we evaluated trends and testing

NOTE Confidence: 0.83584552125

00:15:06.520 --> 00:15:08.620 at the HRR level again.

NOTE Confidence: 0.83584552125

00:15:08.620 --> 00:15:10.440 In addition to evaluating the

NOTE Confidence: 0.83584552125

00:15:10.440 --> 00:15:11.896 presence of regional variation,

NOTE Confidence: 0.83584552125

00:15:11.900 --> 00:15:14.260 we sought to also understand

NOTE Confidence: 0.83584552125

00:15:14.260 --> 00:15:15.676 similarities among regions,

NOTE Confidence: 0.83584552125

00:15:15.680 --> 00:15:18.128 and we use something called group

NOTE Confidence: 0.83584552125

00:15:18.128 --> 00:15:20.250 based trajectory modeling perform of

NOTE Confidence: 0.83584552125

00:15:20.250 --> 00:15:22.355 finite mixture modeling to identify

NOTE Confidence: 0.83584552125

00:15:22.355 --> 00:15:24.039 shared phenotypes of adoption.

NOTE Confidence: 0.83584552125

00:15:24.040 --> 00:15:26.479 So to just to say it's simply the big

NOTE Confidence: 0.83584552125

00:15:26.479 --> 00:15:29.167 picture goal here is to understand how

NOTE Confidence: 0.83584552125

00:15:29.167 --> 00:15:31.207 regional patterns cluster together and

NOTE Confidence: 0.83584552125

00:15:31.207 --> 00:15:32.847 help understand what characteristics

NOTE Confidence: 0.83584552125

00:15:32.847 --> 00:15:34.897 they might share in common.

NOTE Confidence: 0.83584552125

00:15:34.900 --> 00:15:36.034 Using this approach,

NOTE Confidence: 0.83584552125

00:15:36.034 --> 00:15:37.924 we uncovered 5 distinct regional

NOTE Confidence: 0.83584552125

00:15:37.924 --> 00:15:39.270 clusters of adoption.

NOTE Confidence: 0.83584552125

00:15:39.270 --> 00:15:41.881 We can think of these as the

NOTE Confidence: 0.83584552125

00:15:41.881 --> 00:15:43.000 rapid adopters red.

NOTE Confidence: 0.83584552125

00:15:43.000 --> 00:15:46.104 Be slow or minimal adopters in the bottom

NOTE Confidence: 0.83584552125

00:15:46.104 --> 00:15:49.385 and those that sort of land in the middle.

NOTE Confidence: 0.83584552125

00:15:49.390 --> 00:15:51.405 Clusters of regions with the

NOTE Confidence: 0.83584552125

00:15:51.405 --> 00:15:53.017 largest expansion of genomic

NOTE Confidence: 0.83584552125

00:15:53.017 --> 00:15:55.123 testing had hired median incomes

NOTE Confidence: 0.83584552125

00:15:55.123 --> 00:15:56.763 and higher education levels,

NOTE Confidence: 0.83584552125

00:15:56.770 --> 00:15:59.325 and we did not notably find any

NOTE Confidence: 0.83584552125

00:15:59.325 --> 00:16:00.928 significant differences by race

NOTE Confidence: 0.83584552125

00:16:00.928 --> 00:16:02.904 provider density or historical

NOTE Confidence: 0.83584552125

00:16:02.904 --> 00:16:05.639 use of surgery or radiation.

NOTE Confidence: 0.83584552125

00:16:05.640 --> 00:16:07.554 And these these findings are important

NOTE Confidence: 0.83584552125

00:16:07.554 --> 00:16:09.571 because they provide the first indication

NOTE Confidence: 0.83584552125

00:16:09.571 --> 00:16:11.635 of the extent to which discretionary

NOTE Confidence: 0.83584552125

00:16:11.635 --> 00:16:13.120 testing varies geographically and

NOTE Confidence: 0.83584552125

00:16:13.120 --> 00:16:14.600 also proposes shared conditions

NOTE Confidence: 0.83584552125

00:16:14.600 --> 00:16:16.908 that may be associated with testing

NOTE Confidence: 0.83584552125

00:16:16.908 --> 00:16:18.978 and from a practical perspective,

NOTE Confidence: 0.83584552125

00:16:18.980 --> 00:16:20.190 this work also reveals potential

NOTE Confidence: 0.83584552125

00:16:20.190 --> 00:16:21.880 gaps in how we are applying.

NOTE Confidence: 0.83584552125

00:16:21.880 --> 00:16:23.696 Testing and get can give us a better

NOTE Confidence: 0.83584552125

00:16:23.696 --> 00:16:25.780 sense of the need for consistency in

NOTE Confidence: 0.83584552125

00:16:25.780 --> 00:16:27.350 our guidelines and care practices.

NOTE Confidence: 0.951970950714286

00:16:30.390 --> 00:16:31.900 So understanding that the clinical

NOTE Confidence: 0.951970950714286

00:16:31.900 --> 00:16:33.108 landscape is changing with

NOTE Confidence: 0.951970950714286

00:16:33.108 --> 00:16:34.618 the integration of new tools,

NOTE Confidence: 0.951970950714286

00:16:34.620 --> 00:16:36.654 we also wanted to understand the

NOTE Confidence: 0.951970950714286

00:16:36.654 --> 00:16:38.926 relation of taste testing to actual

NOTE Confidence: 0.951970950714286

00:16:38.926 --> 00:16:41.056 clinical management received by patients.

NOTE Confidence: 0.951970950714286

00:16:41.060 --> 00:16:42.845 But doing this experimentally is

NOTE Confidence: 0.951970950714286

00:16:42.845 --> 00:16:44.630 actually is difficult in observation.

NOTE Confidence: 0.951970950714286

00:16:44.630 --> 00:16:46.766 ULL data, given the absence of

NOTE Confidence: 0.951970950714286

00:16:46.766 --> 00:16:48.190 granular clinical information and

NOTE Confidence: 0.951970950714286

00:16:48.253 --> 00:16:49.869 the absence of randomization,

NOTE Confidence: 0.951970950714286

00:16:49.870 --> 00:16:52.022 a common theme in this work is seeking

NOTE Confidence: 0.951970950714286

00:16:52.022 --> 00:16:54.049 therefore to understand and account for.

NOTE Confidence: 0.951970950714286

00:16:54.050 --> 00:16:56.054 These unmeasured bias is associated with

NOTE Confidence: 0.951970950714286

00:16:56.054 --> 00:16:58.826 who gets a test and doesn't get a test.

NOTE Confidence: 0.951970950714286

00:16:58.830 --> 00:17:00.630 And this investigation may be

NOTE Confidence: 0.951970950714286

00:17:00.630 --> 00:17:02.430 increasingly valuable given the number

NOTE Confidence: 0.951970950714286

00:17:02.488 --> 00:17:04.450 of auxiliary services in cancer care,

NOTE Confidence: 0.951970950714286

00:17:04.450 --> 00:17:06.988 including many like MRI and genomics,

NOTE Confidence: 0.951970950714286

00:17:06.990 --> 00:17:10.252 whose clinical efficacy has not and may

NOTE Confidence: 0.951970950714286

00:17:10.252 --> 00:17:13.507 never be evaluated in a randomized trial.

NOTE Confidence: 0.951970950714286

00:17:13.510 --> 00:17:15.148 So we first sought to address

NOTE Confidence: 0.951970950714286

00:17:15.148 --> 00:17:16.690 this question of the association

NOTE Confidence: 0.951970950714286

00:17:16.690 --> 00:17:19.048 between prostate MRI use and initial

NOTE Confidence: 0.951970950714286

00:17:19.048 --> 00:17:20.670 management for prostate cancer.

NOTE Confidence: 0.951970950714286

00:17:20.670 --> 00:17:21.464 Answer Medicare.

NOTE Confidence: 0.951970950714286

00:17:21.464 --> 00:17:23.449 After identifying a cohort of

NOTE Confidence: 0.951970950714286

00:17:23.449 --> 00:17:25.580 patients with low risk prostate

NOTE Confidence: 0.951970950714286

00:17:25.580 --> 00:17:27.320 cancer by clinical criteria,

NOTE Confidence: 0.951970950714286

00:17:27.320 --> 00:17:29.290 we examine the association between

NOTE Confidence: 0.951970950714286

00:17:29.290 --> 00:17:32.291 receipt of a prostate MRI and initial

NOTE Confidence: 0.951970950714286

00:17:32.291 --> 00:17:34.215 observation for prostate cancer.

NOTE Confidence: 0.951970950714286

00:17:34.220 --> 00:17:36.760 And assess the association using

NOTE Confidence: 0.951970950714286

00:17:36.760 --> 00:17:38.284 conventional logistic regression

NOTE Confidence: 0.951970950714286

00:17:38.284 --> 00:17:40.319 and propensity score matching.

NOTE Confidence: 0.951970950714286

00:17:40.320 --> 00:17:41.661 In these analysis,

NOTE Confidence: 0.951970950714286

00:17:41.661 --> 00:17:44.343 we consistently found a strong association

NOTE Confidence: 0.951970950714286

00:17:44.343 --> 00:17:46.442 between MRI use and and observation

NOTE Confidence: 0.951970950714286

00:17:46.442 --> 00:17:48.809 with an odds ratio of nearly two.

NOTE Confidence: 0.909013288125

00:17:52.050 --> 00:17:53.955 Taking advantage of the substantial

NOTE Confidence: 0.909013288125

00:17:53.955 --> 00:17:55.860 of the substantial regional variation

NOTE Confidence: 0.909013288125

00:17:55.919 --> 00:17:57.539 that we saw in earlier studies,

NOTE Confidence: 0.909013288125

00:17:57.540 --> 00:18:00.263 we wanted to study whether a region's

NOTE Confidence: 0.909013288125

00:18:00.263 --> 00:18:02.786 adoption of prostate MRI genomic testing

NOTE Confidence: 0.909013288125

00:18:02.786 --> 00:18:05.360 was also associated with changes in

NOTE Confidence: 0.909013288125

00:18:05.360 --> 00:18:07.940 clinical management for prostate cancer.

NOTE Confidence: 0.909013288125

00:18:07.940 --> 00:18:10.405 To do this, we identified over 65,000

NOTE Confidence: 0.909013288125

00:18:10.405 --> 00:18:12.230 patients with prostate cancer and

NOTE Confidence: 0.909013288125

00:18:12.230 --> 00:18:14.497 Blue Cross Blue Shield and assess

NOTE Confidence: 0.909013288125

00:18:14.497 --> 00:18:16.352 both individual and regional adoption

NOTE Confidence: 0.909013288125

00:18:16.352 --> 00:18:18.690 of prostate MRI and genomic testing.

NOTE Confidence: 0.909013288125

00:18:18.690 --> 00:18:21.245 And we sought to test the hypothesis

NOTE Confidence: 0.909013288125

00:18:21.245 --> 00:18:23.460 that regions with high levels of

NOTE Confidence: 0.909013288125

00:18:23.460 --> 00:18:26.476 uptake of MRI and genomic testing had

NOTE Confidence: 0.909013288125

00:18:26.476 --> 00:18:28.656 greater changes favoring observation

NOTE Confidence: 0.909013288125

00:18:28.656 --> 00:18:31.400 versus treatment for prostate cancer.

NOTE Confidence: 0.909013288125

00:18:31.400 --> 00:18:33.591 And what we found was that those

NOTE Confidence: 0.909013288125

00:18:33.591 --> 00:18:35.745 eight hours in the highest quartile

NOTE Confidence: 0.909013288125

00:18:35.745 --> 00:18:37.269 of adoption of MRI,

NOTE Confidence: 0.909013288125

00:18:37.270 --> 00:18:39.468 or associated with a four point 1%

NOTE Confidence: 0.909013288125

00:18:39.470 --> 00:18:42.370 increase in observation versus treatment

NOTE Confidence: 0.909013288125

00:18:42.370 --> 00:18:44.128 and those in the highest quartile.

NOTE Confidence: 0.909013288125

00:18:44.130 --> 00:18:45.714 Genomic testing were associated

NOTE Confidence: 0.909013288125

00:18:45.714 --> 00:18:49.070 with a 2.5% adjusted increase in

NOTE Confidence: 0.909013288125

00:18:49.070 --> 00:18:51.630 observation versus definitive treatment.

NOTE Confidence: 0.909013288125

00:18:51.630 --> 00:18:53.295 So the way I think to look at this

NOTE Confidence: 0.909013288125

00:18:53.295 --> 00:18:54.930 is that these findings suggest

NOTE Confidence: 0.909013288125

00:18:54.930 --> 00:18:56.330 alignment between a regions.

NOTE Confidence: 0.909013288125

00:18:56.330 --> 00:18:58.400 Use of a new risk stratification

NOTE Confidence: 0.909013288125

00:18:58.400 --> 00:19:00.264 technique occurring at the extremes

NOTE Confidence: 0.909013288125

00:19:00.264 --> 00:19:01.948 and changes in observation,

NOTE Confidence: 0.909013288125

00:19:01.950 --> 00:19:02.854 ULL management.

NOTE Confidence: 0.909013288125

00:19:02.854 --> 00:19:03.306 However,

NOTE Confidence: 0.909013288125

00:19:03.306 --> 00:19:05.566 owing to the limitations of

NOTE Confidence: 0.909013288125

00:19:05.566 --> 00:19:07.400 this ecological study design,

NOTE Confidence: 0.909013288125

00:19:07.400 --> 00:19:09.488 we're very careful not to directly

NOTE Confidence: 0.909013288125

00:19:09.488 --> 00:19:11.380 extrapolate these to patient effects,

NOTE Confidence: 0.909013288125

00:19:11.380 --> 00:19:13.543 but I think the consistency of these

NOTE Confidence: 0.909013288125

00:19:13.543 --> 00:19:14.849 associations and the practical

NOTE Confidence: 0.909013288125

00:19:14.849 --> 00:19:16.769 observation that there seems to be

NOTE Confidence: 0.909013288125

00:19:16.769 --> 00:19:18.781 a certain type or inclination of

NOTE Confidence: 0.909013288125

00:19:18.781 --> 00:19:20.767 institutions or providers who are much

NOTE Confidence: 0.909013288125

00:19:20.767 --> 00:19:22.936 more invested in the idea of surveillance,

NOTE Confidence: 0.909013288125

00:19:22.940 --> 00:19:25.028 suggests that these two may go hand in hand.

NOTE Confidence: 0.9532116

00:19:28.920 --> 00:19:30.992 Another major focus of our work has

NOTE Confidence: 0.9532116

00:19:30.992 --> 00:19:33.090 been to understand the experiences that

NOTE Confidence: 0.9532116

00:19:33.090 --> 00:19:35.010 patients with prostate cancer have.

NOTE Confidence: 0.9532116

00:19:35.010 --> 00:19:37.800 When using these patient facing tools.

NOTE Confidence: 0.9532116

00:19:37.800 --> 00:19:40.155 Through in-depth interviews, we've also

NOTE Confidence: 0.9532116

00:19:40.155 --> 00:19:42.510 specifically focused on this point.

NOTE Confidence: 0.9532116

00:19:42.510 --> 00:19:43.645 And would speak and when

NOTE Confidence: 0.9532116

00:19:43.645 --> 00:19:44.326 speaking with patients,

NOTE Confidence: 0.9532116

00:19:44.330 --> 00:19:46.586 the responses are really quite humbling

NOTE Confidence: 0.9532116

00:19:46.586 --> 00:19:48.990 and often clarifying in their insight.

NOTE Confidence: 0.9532116

00:19:48.990 --> 00:19:50.436 Patients say, often say things like

NOTE Confidence: 0.9532116

00:19:50.436 --> 00:19:52.310 the more data you can get the better,

NOTE Confidence: 0.9532116

00:19:52.310 --> 00:19:53.890 especially if it's noninvasive,

NOTE Confidence: 0.9532116

00:19:53.890 --> 00:19:56.260 like an MRI or genomic test.

NOTE Confidence: 0.9532116

00:19:56.260 --> 00:19:57.700 But they also expressed uncertainty.

NOTE Confidence: 0.9532116

00:19:57.700 --> 00:20:00.420 I wasn't really sure about the genetic thing,

NOTE Confidence: 0.9532116

00:20:00.420 --> 00:20:02.764 and we also hear very frank answers about

NOTE Confidence: 0.9532116

00:20:02.764 --> 00:20:04.437 the experiences of going through it.

NOTE Confidence: 0.9532116

00:20:04.440 --> 00:20:06.560 The MRI was loud and I couldn't breathe.

NOTE Confidence: 0.9532116

00:20:06.560 --> 00:20:08.904 No one told me about it and I

NOTE Confidence: 0.9532116

00:20:08.904 --> 00:20:10.549 wish I knew before.

NOTE Confidence: 0.9532116

00:20:10.550 --> 00:20:12.982 So many patients seem to express this sort

NOTE Confidence: 0.9532116

00:20:12.982 --> 00:20:15.436 of maximalist approach when it comes to

NOTE Confidence: 0.9532116

00:20:15.436 --> 00:20:17.226 information about their prostate cancer.

NOTE Confidence: 0.9532116

00:20:17.230 --> 00:20:17.450 However,

NOTE Confidence: 0.9532116

00:20:17.450 --> 00:20:19.430 we also have to realize that in the quest

NOTE Confidence: 0.9532116

00:20:19.476 --> 00:20:21.366 to deliver as much information as possible,

NOTE Confidence: 0.9532116

00:20:21.370 --> 00:20:23.050 we often fall short,

NOTE Confidence: 0.9532116

00:20:23.050 --> 00:20:25.150 especially when it comes to

NOTE Confidence: 0.9532116

00:20:25.150 --> 00:20:27.069 explaining complex predictions.

NOTE Confidence: 0.9532116

00:20:27.070 --> 00:20:28.638 Iterative testing is also

NOTE Confidence: 0.9532116

00:20:28.638 --> 00:20:29.814 not without downsides,

NOTE Confidence: 0.9532116

00:20:29.820 --> 00:20:31.398 as even small low risk procedures

NOTE Confidence: 0.9532116

00:20:31.398 --> 00:20:33.058 can be challenging for patients over

NOTE Confidence: 0.9532116

00:20:33.058 --> 00:20:34.714 the long course of their disease.

NOTE Confidence: 0.907213545333333

00:20:36.760 --> 00:20:38.938 And lastly, as we make strides in the science

NOTE Confidence: 0.907213545333333

00:20:38.938 --> 00:20:41.157 and clinical implementation of these tools,

NOTE Confidence: 0.907213545333333

00:20:41.160 --> 00:20:43.772 it's also vital to ask, are we ensuring

NOTE Confidence: 0.907213545333333

00:20:43.772 --> 00:20:46.196 that access to testing is equitable?

NOTE Confidence: 0.907213545333333

00:20:46.200 --> 00:20:49.020 Or are we perhaps widening gulfs?

NOTE Confidence: 0.907213545333333

00:20:49.020 --> 00:20:49.926 This is particularly

NOTE Confidence: 0.907213545333333

00:20:49.926 --> 00:20:51.134 relevant in prostate cancer,

NOTE Confidence: 0.907213545333333

00:20:51.140 --> 00:20:52.940 where there are entrenched racial

NOTE Confidence: 0.907213545333333

00:20:52.940 --> 00:20:54.020 disparities in diagnosis,

NOTE Confidence: 0.907213545333333

00:20:54.020 --> 00:20:54.920 treatment, and outcome.

NOTE Confidence: 0.907213545333333

00:20:54.920 --> 00:20:56.720 Black men with prostate cancer in

NOTE Confidence: 0.907213545333333

00:20:56.720 --> 00:20:58.524 the United States are more likely

NOTE Confidence: 0.907213545333333

00:20:58.524 --> 00:21:00.358 to be diagnosed with prostate cancer

NOTE Confidence: 0.907213545333333

00:21:00.358 --> 00:21:01.998 less likely to receive guideline,

NOTE Confidence: 0.907213545333333

00:21:02.000 --> 00:21:03.632 concordant care and experience.

NOTE Confidence: 0.907213545333333

00:21:03.632 --> 00:21:06.080 A nearly two fold greater risk

NOTE Confidence: 0.907213545333333

00:21:06.152 --> 00:21:07.800 of prostate cancer death.

NOTE Confidence: 0.907213545333333

00:21:07.800 --> 00:21:09.835 One mechanism through which differences

NOTE Confidence: 0.907213545333333

00:21:09.835 --> 00:21:12.334 in outcome might occur is less

NOTE Confidence: 0.907213545333333

00:21:12.334 --> 00:21:14.704 access and less use of diagnostic

NOTE Confidence: 0.907213545333333

00:21:14.704 --> 00:21:16.864 technologies involved in the timely

NOTE Confidence: 0.907213545333333

00:21:16.864 --> 00:21:19.144 detection of potentially lethal cancers.

NOTE Confidence: 0.907213545333333

00:21:19.150 --> 00:21:20.714 In our earliest work,

NOTE Confidence: 0.907213545333333

00:21:20.714 --> 00:21:22.278 we identified substantially lower

NOTE Confidence: 0.907213545333333

00:21:22.278 --> 00:21:23.949 use of prostate MRI,

NOTE Confidence: 0.907213545333333

00:21:23.950 --> 00:21:26.670 even adjusting for clinical characteristics

NOTE Confidence: 0.907213545333333

00:21:26.670 --> 00:21:29.390 among black versus white patients.

NOTE Confidence: 0.907213545333333

00:21:29.390 --> 00:21:32.270 38% lower odds of prostate MRI

NOTE Confidence: 0.907213545333333

00:21:32.270 --> 00:21:35.318 use in in in patients with low

NOTE Confidence: 0.907213545333333

00:21:35.318 --> 00:21:37.176 risk prostate cancer and although

NOTE Confidence: 0.907213545333333

00:21:37.176 --> 00:21:38.468 there are stark disparities,

NOTE Confidence: 0.907213545333333

00:21:38.470 --> 00:21:40.130 there are also very market

NOTE Confidence: 0.907213545333333

00:21:40.130 --> 00:21:41.126 differences by region.

NOTE Confidence: 0.907213545333333

00:21:41.130 --> 00:21:42.288 So, for example,

NOTE Confidence: 0.907213545333333

00:21:42.288 --> 00:21:44.604 in the Los Angeles City Registry,

NOTE Confidence: 0.907213545333333

00:21:44.610 --> 00:21:47.418 15% of patients of black patients

NOTE Confidence: 0.907213545333333

00:21:47.418 --> 00:21:49.686 with prostate cancer received an

NOTE Confidence: 0.907213545333333

00:21:49.686 --> 00:21:51.794 MRI versus 28% of white patients.

NOTE Confidence: 0.907213545333333

00:21:51.794 --> 00:21:54.910 We do see also disparities in Connecticut.

NOTE Confidence: 0.907213545333333

00:21:54.910 --> 00:21:57.269 But this is contrasted by some regions

NOTE Confidence: 0.907213545333333

00:21:57.269 --> 00:21:59.554 where things are relatively equal and

NOTE Confidence: 0.907213545333333

00:21:59.554 --> 00:22:01.966 Atlanta rates were at approximately 9%

NOTE Confidence: 0.907213545333333

00:22:01.970 --> 00:22:05.936 for black patients and white patients.

NOTE Confidence: 0.907213545333333

00:22:05.940 --> 00:22:07.510 So despite a growing recognition

NOTE Confidence: 0.907213545333333

00:22:07.510 --> 00:22:09.080 of the existence and pervasiveness

NOTE Confidence: 0.907213545333333

00:22:09.134 --> 00:22:10.118 of these disparities,

NOTE Confidence: 0.907213545333333

00:22:10.120 --> 00:22:12.836 little is known about the root causes.

NOTE Confidence: 0.907213545333333

00:22:12.840 --> 00:22:15.484 And recently we aim to under to

NOTE Confidence: 0.907213545333333

00:22:15.484 --> 00:22:17.304 identify factors that might underlie

NOTE Confidence: 0.907213545333333

00:22:17.304 --> 00:22:19.828 this disparity in the use of prostate

NOTE Confidence: 0.907213545333333

00:22:19.828 --> 00:22:21.832 MRI using a technique known as

NOTE Confidence: 0.907213545333333

00:22:21.832 --> 00:22:23.569 mediation analysis to breakdown the

NOTE Confidence: 0.907213545333333

00:22:23.569 --> 00:22:25.985 total effect of a patient race on

NOTE Confidence: 0.907213545333333

00:22:25.985 --> 00:22:28.415 their likelihood of receiving an MRI.

NOTE Confidence: 0.907213545333333

00:22:28.420 --> 00:22:30.130 And essentially what we're trying to

NOTE Confidence: 0.907213545333333

00:22:30.130 --> 00:22:32.227 do is explain where does this 38%

NOTE Confidence: 0.907213545333333

00:22:32.227 --> 00:22:35.356 difference come from, and to do this,

NOTE Confidence: 0.907213545333333

00:22:35.360 --> 00:22:37.212 we proposed a model.

NOTE Confidence: 0.907213545333333

00:22:37.212 --> 00:22:39.527 Through which the observed disparity

NOTE Confidence: 0.907213545333333

00:22:39.527 --> 00:22:42.143 may be explained by clinical

NOTE Confidence: 0.907213545333333

00:22:42.143 --> 00:22:43.422 mediators candidate mediators.

NOTE Confidence: 0.907213545333333

00:22:43.422 --> 00:22:45.708 In this sort of exist as

NOTE Confidence: 0.907213545333333

00:22:45.708 --> 00:22:46.470 intervening variables.

NOTE Confidence: 0.907213545333333

00:22:46.470 --> 00:22:48.864 Those might be explained by clinical factors,

NOTE Confidence: 0.907213545333333

00:22:48.870 --> 00:22:50.619 socioeconomic status, geography,

NOTE Confidence: 0.907213545333333

00:22:50.619 --> 00:22:52.368 and structural racism.

NOTE Confidence: 0.900814584

00:22:57.330 --> 00:22:59.470 Using multiple additive regression trees,

NOTE Confidence: 0.900814584

00:22:59.470 --> 00:23:02.207 a tool of for predictive data mining,

NOTE Confidence: 0.900814584

00:23:02.210 --> 00:23:04.610 we perform mediation analysis to

NOTE Confidence: 0.900814584

00:23:04.610 --> 00:23:06.530 decompose these known disparities

NOTE Confidence: 0.900814584

00:23:06.530 --> 00:23:08.910 into their potential components.

NOTE Confidence: 0.900814584

00:23:08.910 --> 00:23:10.086 Using this approach,

NOTE Confidence: 0.900814584

00:23:10.086 --> 00:23:12.046 we estimated that variation in

NOTE Confidence: 0.900814584

00:23:12.046 --> 00:23:14.231 region accounted for 24% of the

NOTE Confidence: 0.900814584

00:23:14.231 --> 00:23:16.166 of the observed affective race,

NOTE Confidence: 0.900814584

00:23:16.170 --> 00:23:18.318 19% to residential segregation,

NOTE Confidence: 0.900814584

00:23:18.318 --> 00:23:21.003 a manifestation of structural racism,

NOTE Confidence: 0.900814584

00:23:21.010 --> 00:23:22.962 19% to socioeconomic status.

NOTE Confidence: 0.900814584

00:23:22.962 --> 00:23:25.311 And 11% to dual eligibility.

NOTE Confidence: 0.900814584

00:23:25.311 --> 00:23:28.510 A marker for low income or disability.

NOTE Confidence: 0.900814584

00:23:28.510 --> 00:23:29.658 And to our knowledge,

NOTE Confidence: 0.900814584

00:23:29.658 --> 00:23:31.380 these with the first analysis to

NOTE Confidence: 0.900814584

00:23:31.441 --> 00:23:32.623 propose upstream contributors

NOTE Confidence: 0.900814584

00:23:32.623 --> 00:23:34.593 to inequalities in access to

NOTE Confidence: 0.900814584

00:23:34.593 --> 00:23:36.130 prostate cancer technologies,

NOTE Confidence: 0.900814584

00:23:36.130 --> 00:23:37.840 and we're hopeful that these results

NOTE Confidence: 0.900814584

00:23:37.840 --> 00:23:39.618 can help inform multi level efforts

NOTE Confidence: 0.900814584

00:23:39.618 --> 00:23:41.382 to improve equitable access and the

NOTE Confidence: 0.900814584

00:23:41.382 --> 00:23:43.045 quality of diagnostic cancer imaging

NOTE Confidence: 0.900814584

00:23:43.045 --> 00:23:45.418 beginning with efforts in our own backyard.

NOTE Confidence: 0.945461002727273

00:23:47.850 --> 00:23:49.770 So I want to start concluding here by

NOTE Confidence: 0.945461002727273

00:23:49.770 --> 00:23:51.763 saying that the way that we manage low

NOTE Confidence: 0.945461002727273

00:23:51.763 --> 00:23:53.629 risk prostate cancer is changing rapidly.

NOTE Confidence: 0.945461002727273

00:23:53.630 --> 00:23:55.359 One major change that we may see

NOTE Confidence: 0.945461002727273

00:23:55.359 --> 00:23:57.406 in the future is fewer diagnosis of

NOTE Confidence: 0.945461002727273

00:23:57.406 --> 00:23:58.966 low risk prostate cancer through

NOTE Confidence: 0.945461002727273

00:23:58.966 --> 00:24:01.286 the use of use of refined pre biopsy

NOTE Confidence: 0.945461002727273

00:24:01.286 --> 00:24:03.636 decision tools such as prostate MRI

NOTE Confidence: 0.945461002727273

00:24:03.636 --> 00:24:06.146 and other biomarkers with better

NOTE Confidence: 0.945461002727273

00:24:06.146 --> 00:24:08.638 specificity for high risk disease.

NOTE Confidence: 0.945461002727273

00:24:08.640 --> 00:24:10.356 But among patients with prostate cancer,

NOTE Confidence: 0.945461002727273

00:24:10.360 --> 00:24:12.445 we've also identified gaps in

NOTE Confidence: 0.945461002727273

00:24:12.445 --> 00:24:14.530 access comprehension and support for

NOTE Confidence: 0.945461002727273

00:24:14.601 --> 00:24:16.877 patients undergoing complex testing.

NOTE Confidence: 0.945461002727273

00:24:16.880 --> 00:24:17.964 To close this gap,

NOTE Confidence: 0.945461002727273

00:24:17.964 --> 00:24:19.590 I think that multifaceted efforts are

NOTE Confidence: 0.945461002727273

00:24:19.644 --> 00:24:21.330 needed to help improve the consistency

NOTE Confidence: 0.945461002727273

00:24:21.330 --> 00:24:23.278 and quality of care that we deliver,

NOTE Confidence: 0.945461002727273

00:24:23.280 --> 00:24:25.232 and this is going to be a clear

NOTE Confidence: 0.945461002727273

00:24:25.232 --> 00:24:27.367 focus of ours in the years to come.

NOTE Confidence: 0.945461002727273

00:24:27.370 --> 00:24:29.236 There are also clear opportunities to

NOTE Confidence: 0.945461002727273

00:24:29.236 --> 00:24:31.304 improve the quality of our predictions

NOTE Confidence: 0.945461002727273

00:24:31.304 --> 00:24:32.840 by leveraging institutional and

NOTE Confidence: 0.945461002727273

00:24:32.840 --> 00:24:35.092 national data sources such as baseline

NOTE Confidence: 0.945461002727273

00:24:35.092 --> 00:24:36.420 genomic and imaging characteristics

NOTE Confidence: 0.945461002727273

00:24:36.420 --> 00:24:38.430 to refine how we predict risk.

NOTE Confidence: 0.945461002727273

00:24:38.430 --> 00:24:40.810 So I think it's likely that we'll

NOTE Confidence: 0.945461002727273

00:24:40.810 --> 00:24:43.693 look back at these snapshots of gene

NOTE Confidence: 0.945461002727273

00:24:43.693 --> 00:24:45.341 expression as pretty antiquated

NOTE Confidence: 0.945461002727273

00:24:45.412 --> 00:24:46.460 relatively soon.

NOTE Confidence: 0.945461002727273

00:24:46.460 --> 00:24:46.942 And lastly,

NOTE Confidence: 0.945461002727273

00:24:46.942 --> 00:24:48.388 I think there's a great progress

NOTE Confidence: 0.945461002727273

00:24:48.388 --> 00:24:50.098 in the form of advanced imaging,

NOTE Confidence: 0.945461002727273

00:24:50.100 --> 00:24:52.555 including pet tracers with high

NOTE Confidence: 0.945461002727273

00:24:52.555 --> 00:24:54.519 sensitivity and specificity for

NOTE Confidence: 0.945461002727273

00:24:54.519 --> 00:24:56.890 prostate cancer that will soon likely

NOTE Confidence: 0.945461002727273

00:24:56.890 --> 00:24:59.660 be part of our diagnosis and tracking.

NOTE Confidence: 0.945461002727273

00:24:59.660 --> 00:25:01.548 So I want to stop there and conclude

NOTE Confidence: 0.945461002727273

00:25:01.548 --> 00:25:03.093 by saying that new technologies

NOTE Confidence: 0.945461002727273

00:25:03.093 --> 00:25:04.788 have been deployed to increased

NOTE Confidence: 0.945461002727273

00:25:04.788 --> 00:25:06.753 precision in the management of low

NOTE Confidence: 0.945461002727273

00:25:06.753 --> 00:25:08.096 risk prostate cancer patients.

NOTE Confidence: 0.945461002727273

00:25:08.096 --> 00:25:11.008 When you speak to them clearly value

NOTE Confidence: 0.945461002727273

00:25:11.008 --> 00:25:13.416 information about their cancer in one

NOTE Confidence: 0.945461002727273

00:25:13.416 --> 00:25:15.678 agency in the decision making process.

NOTE Confidence: 0.945461002727273

00:25:15.680 --> 00:25:17.882 Genomic testing and prostate MRI are

NOTE Confidence: 0.945461002727273

00:25:17.882 --> 00:25:20.250 associated with increased use of observation,

NOTE Confidence: 0.945461002727273

00:25:20.250 --> 00:25:22.194 but Kohl's relationship is

NOTE Confidence: 0.945461002727273

00:25:22.194 --> 00:25:24.138 still not clearly defined.

NOTE Confidence: 0.945461002727273

00:25:24.140 --> 00:25:24.580 And lastly,

NOTE Confidence: 0.945461002727273

00:25:24.580 --> 00:25:26.120 as we make strides in the science,

NOTE Confidence: 0.945461002727273

00:25:26.120 --> 00:25:28.255 we need to sharpen our attention to

NOTE Confidence: 0.945461002727273

00:25:28.255 --> 00:25:30.588 disparities in access that may in fact

NOTE Confidence: 0.945461002727273

00:25:30.588 --> 00:25:32.283 widen racial and geographic disparities.

NOTE Confidence: 0.957587904545455

00:25:34.730 --> 00:25:36.128 And I just want to say

NOTE Confidence: 0.957587904545455

00:25:36.128 --> 00:25:37.410 thank you for your time.

NOTE Confidence: 0.957587904545455

00:25:37.410 --> 00:25:39.954 I'm incredibly grateful to my wonderful

NOTE Confidence: 0.957587904545455

00:25:39.954 --> 00:25:41.590 mentors at the Yale Copper Center,

NOTE Confidence: 0.957587904545455

00:25:41.590 --> 00:25:42.970 particularly Kerry Gross.

NOTE Confidence: 0.957587904545455

00:25:42.970 --> 00:25:45.270 Shelmet Mott have been instrumental

NOTE Confidence: 0.957587904545455

00:25:45.270 --> 00:25:46.870 in developing this work.

NOTE Confidence: 0.957587904545455

00:25:46.870 --> 00:25:48.575 Extremely grateful to my colleagues

NOTE Confidence: 0.957587904545455

00:25:48.575 --> 00:25:50.280 in the Department of Neurology

NOTE Confidence: 0.957587904545455

00:25:50.338 --> 00:25:51.886 and the Yale Cancer Center has

NOTE Confidence: 0.957587904545455

00:25:51.886 --> 00:25:53.041 also been generous supporters

NOTE Confidence: 0.957587904545455

00:25:53.041 --> 00:25:54.526 of this work as well.

NOTE Confidence: 0.957587904545455

00:25:54.530 --> 00:25:54.940 Thank you.

NOTE Confidence: 0.931496585454546

00:25:56.820 --> 00:25:58.400 Thanks very much, Michael.

NOTE Confidence: 0.931496585454546

00:25:58.400 --> 00:26:00.770 If people have questions if they

NOTE Confidence: 0.931496585454546

00:26:00.839 --> 00:26:04.505 can put it in the chat and I'll

NOTE Confidence: 0.931496585454546

00:26:04.505 --> 00:26:06.985 I'll ask a question while we're

NOTE Confidence: 0.931496585454546

00:26:06.985 --> 00:26:09.420 waiting to see what people have.

NOTE Confidence: 0.931496585454546

00:26:09.420 --> 00:26:15.516 So is getting an MRI in it of itself

NOTE Confidence: 0.931496585454546

00:26:15.520 --> 00:26:17.206 something that leads to better care

NOTE Confidence: 0.931496585454546

00:26:17.206 --> 00:26:19.731 or is it a marker of doctors who

NOTE Confidence: 0.931496585454546

00:26:19.731 --> 00:26:21.741 provide a different kind of care?

NOTE Confidence: 0.743726158

00:26:22.750 --> 00:26:24.210 Yeah, it it's that's really.

NOTE Confidence: 0.743726158

00:26:24.210 --> 00:26:25.386 I think that the main question

NOTE Confidence: 0.743726158

00:26:25.386 --> 00:26:26.170 we're wrestling with it.

NOTE Confidence: 0.743726158

00:26:26.170 --> 00:26:28.026 It probably is a little bit of both.

NOTE Confidence: 0.743726158

00:26:28.030 --> 00:26:29.591 I mean, I think that the MRI

NOTE Confidence: 0.743726158

00:26:29.591 --> 00:26:31.193 you know if MRI is not even

NOTE Confidence: 0.743726158

00:26:31.193 --> 00:26:32.780 on the on the table for you,

NOTE Confidence: 0.743726158

00:26:32.780 --> 00:26:34.810 you're probably receiving one type of care.

NOTE Confidence: 0.743726158

00:26:34.810 --> 00:26:36.430 But I think but you know,

NOTE Confidence: 0.743726158

00:26:36.430 --> 00:26:38.565 with these very powerful tools you can,

NOTE Confidence: 0.743726158

00:26:38.570 --> 00:26:39.365 we can make.

NOTE Confidence: 0.743726158

00:26:39.365 --> 00:26:41.573 We can go in the wrong direction very

NOTE Confidence: 0.743726158

00:26:41.573 --> 00:26:43.925 easily because all of a sudden you have.

NOTE Confidence: 0.743726158

00:26:43.930 --> 00:26:46.016 A vast amount of data and one

NOTE Confidence: 0.743726158

00:26:46.016 --> 00:26:48.052 potential concern is that we may

NOTE Confidence: 0.743726158

00:26:48.052 --> 00:26:49.484 overestimate risk because we're

NOTE Confidence: 0.743726158

00:26:49.484 --> 00:26:52.027 finding you know things that we never

NOTE Confidence: 0.743726158

00:26:52.027 --> 00:26:53.782 found before and then therefore,

NOTE Confidence: 0.743726158

00:26:53.790 --> 00:26:56.190 patients veer off the path of

NOTE Confidence: 0.743726158

00:26:56.190 --> 00:26:57.790 surveillance because you've technically

NOTE Confidence: 0.743726158

00:26:57.850 --> 00:26:59.955 have found something that you had

NOTE Confidence: 0.743726158

00:26:59.955 --> 00:27:02.160 to work very hard to look for.

NOTE Confidence: 0.743726158

00:27:02.160 --> 00:27:02.530 Sure,

NOTE Confidence: 0.845781166

00:27:02.770 --> 00:27:05.880 thanks, and there's a question.

00:27:05.880 --> 00:27:08.484 Can you talk a little bit about

00:27:08.484 --> 00:27:11.351 what we're doing as an organization

00:27:11.351 --> 00:27:13.019 to minimize disparities?

00:27:13.020 --> 00:27:14.995 And I'll I'll focus this

00:27:14.995 --> 00:27:16.575 specifically on prostate cancer,

00:27:16.580 --> 00:27:17.810 although it wasn't written that way.

00:27:18.400 --> 00:27:19.480 Well, yeah, thank you. I mean,

00:27:19.480 --> 00:27:21.392 I think that you know the first step

00:27:21.392 --> 00:27:23.340 really is kind of understanding this,

00:27:23.340 --> 00:27:24.838 and I think that this when we

00:27:24.838 --> 00:27:26.397 you know we're so excited about

00:27:26.397 --> 00:27:27.832 the technology and we're only

00:27:27.832 --> 00:27:29.439 beginning to ask these questions.

00:27:29.440 --> 00:27:30.352 So it starts.

00:27:30.352 --> 00:27:32.480 I think with just very basic quality

00:27:32.543 --> 00:27:35.129 improvement efforts and we have an

NOTE Confidence: 0.815031256666667

00:27:35.129 --> 00:27:36.853 outstanding quality improvement team

NOTE Confidence: 0.815031256666667

00:27:36.923 --> 00:27:39.401 within the Department of Urology that's

NOTE Confidence: 0.815031256666667

00:27:39.401 --> 00:27:41.291 focused specifically on this question.

NOTE Confidence: 0.815031256666667

00:27:41.291 --> 00:27:43.370 And so I think that will be part of.

NOTE Confidence: 0.815031256666667

00:27:43.370 --> 00:27:44.489 Are you know?

NOTE Confidence: 0.815031256666667

00:27:44.489 --> 00:27:45.981 Interim reporting and quality

NOTE Confidence: 0.815031256666667

00:27:45.981 --> 00:27:48.319 improvement process to make sure that

NOTE Confidence: 0.815031256666667

00:27:48.319 --> 00:27:50.244 we are not disproportionately offering

NOTE Confidence: 0.815031256666667

00:27:50.244 --> 00:27:52.088 these services to certain groups?

NOTE Confidence: 0.888547425909091

00:27:53.340 --> 00:27:55.716 And and finally, so what's going

NOTE Confidence: 0.888547425909091

00:27:55.716 --> 00:27:58.111 on in California and Atlanta that

NOTE Confidence: 0.888547425909091

00:27:58.111 --> 00:28:00.673 that that we don't see the same

NOTE Confidence: 0.888547425909091

00:28:00.673 --> 00:28:03.578 kind of disparities? Any any clue?

NOTE Confidence: 0.897721886666667

00:28:04.750 --> 00:28:05.986 I, I think that I mean,

NOTE Confidence: 0.897721886666667

00:28:05.990 --> 00:28:07.970 that's really where I think that

NOTE Confidence: 0.897721886666667

00:28:07.970 --> 00:28:09.870 that you know major centers.

NOTE Confidence: 0.897721886666667

00:28:09.870 --> 00:28:11.424 You know it's this MRI and

NOTE Confidence: 0.897721886666667

00:28:11.424 --> 00:28:12.460 genomic testing are really

NOTE Confidence: 0.897721886666667

00:28:12.517 --> 00:28:13.889 an early adopter phenomenon.

NOTE Confidence: 0.897721886666667

00:28:13.890 --> 00:28:15.696 So I think we have a

NOTE Confidence: 0.897721886666667

00:28:15.696 --> 00:28:16.298 disproportionate influence.

NOTE Confidence: 0.897721886666667

00:28:16.300 --> 00:28:18.328 I think that in Los Angeles,

NOTE Confidence: 0.897721886666667

00:28:18.330 --> 00:28:20.005 certain medical centers probably also

NOTE Confidence: 0.897721886666667

00:28:20.005 --> 00:28:21.345 have a disproportionate influence,

NOTE Confidence: 0.897721886666667

00:28:21.350 --> 00:28:23.870 so all the more reason to be

NOTE Confidence: 0.897721886666667

00:28:23.870 --> 00:28:25.535 very circumspect and proactive

NOTE Confidence: 0.897721886666667

00:28:25.535 --> 00:28:28.580 in in when we roll the when

NOTE Confidence: 0.897721886666667

00:28:28.666 --> 00:28:30.716 we roll these things out.

NOTE Confidence: 0.897721886666667

00:28:30.720 --> 00:28:31.150 Great,

NOTE Confidence: 0.7774961625

00:28:31.890 --> 00:28:33.213 well, I think we're going to move

NOTE Confidence: 0.7774961625

00:28:33.213 --> 00:28:34.640 on to our next speaker, Michael.

NOTE Confidence: 0.7774961625

00:28:34.640 --> 00:28:35.600 Thank you very much.

NOTE Confidence: 0.7774961625

00:28:35.600 --> 00:28:39.010 It was really great. Thank you.

NOTE Confidence: 0.7774961625

00:28:39.010 --> 00:28:43.295 So our next speaker is

NOTE Confidence: 0.7774961625

00:28:43.295 --> 00:28:45.866 Carlos Fernandez Fernando,

NOTE Confidence: 0.7774961625

00:28:45.870 --> 00:28:49.167 who is the Anthony and Brady Professor

NOTE Confidence: 0.7774961625

00:28:49.167 --> 00:28:51.678 of Comparative medicine and pathology.

NOTE Confidence: 0.7774961625

00:28:51.678 --> 00:28:53.874 He studied biochemistry and

NOTE Confidence: 0.7774961625

00:28:53.874 --> 00:28:57.060 molecular biology at the University,

NOTE Confidence: 0.7774961625

00:28:57.060 --> 00:28:59.008 Dodge Autonoma of Madrid,

NOTE Confidence: 0.7774961625

00:28:59.008 --> 00:29:01.930 and received his PhD at Hospital,

NOTE Confidence: 0.7774961625

00:29:01.930 --> 00:29:05.310 Vermont in Madrid as well.

NOTE Confidence: 0.7774961625

00:29:05.310 --> 00:29:07.625 He did his postdoctoral work

NOTE Confidence: 0.7774961625

00:29:07.625 --> 00:29:09.014 with Doctor William.

NOTE Confidence: 0.7774961625

00:29:09.020 --> 00:29:10.948 Tessa here at Yale.

NOTE Confidence: 0.7774961625

00:29:10.948 --> 00:29:12.876 His first position was

NOTE Confidence: 0.7774961625

00:29:12.876 --> 00:29:14.818 faculty position was at NYU,

NOTE Confidence: 0.7774961625

00:29:14.820 --> 00:29:18.558 and then he returned to Yale where

NOTE Confidence: 0.7774961625

00:29:18.558 --> 00:29:21.474 his research seeks to identify novel

NOTE Confidence: 0.7774961625

00:29:21.474 --> 00:29:24.549 mechanisms by which cholesterol and

NOTE Confidence: 0.7774961625

00:29:24.549 --> 00:29:27.900 lipoprotein metabolism are regulated

NOTE Confidence: 0.7774961625

00:29:27.900 --> 00:29:30.652 and without further comments,

NOTE Confidence: 0.7774961625

00:29:30.652 --> 00:29:33.260 I'm going to turn this over to Carlos.

NOTE Confidence: 0.81487696

00:29:47.710 --> 00:29:49.030 You're still on mute.

NOTE Confidence: 0.8595668

00:30:00.030 --> 00:30:03.156 OK, now I see this working well

NOTE Confidence: 0.822809175555556

00:30:03.790 --> 00:30:05.350 so we can't see your slides

NOTE Confidence: 0.822809175555556

00:30:05.350 --> 00:30:06.598 at this month. Now we can

NOTE Confidence: 0.8334467725

00:30:07.250 --> 00:30:10.698 OK. Thanks very much.

NOTE Confidence: 0.8334467725

00:30:10.700 --> 00:30:13.388 I really appreciate the invitation for

NOTE Confidence: 0.8334467725

00:30:13.388 --> 00:30:15.660 for giving the presentation today.

NOTE Confidence: 0.8334467725

00:30:15.660 --> 00:30:17.604 Let me put this in full skin, uhm?

NOTE Confidence: 0.8334467725

00:30:17.604 --> 00:30:21.015 As as you mentioned, I'm not a.

NOTE Confidence: 0.8334467725

00:30:21.015 --> 00:30:23.325 I didn't never study much about

NOTE Confidence: 0.8334467725

00:30:23.325 --> 00:30:25.980 two more biology or counselor.

NOTE Confidence: 0.8334467725

00:30:25.980 --> 00:30:28.682 I did my PhD in biochemistry back

NOTE Confidence: 0.8334467725

00:30:28.682 --> 00:30:32.150 in Madrid and at that time I was

NOTE Confidence: 0.8334467725

00:30:32.150 --> 00:30:34.370 interested to study how cholesterol

NOTE Confidence: 0.8334467725

00:30:34.455 --> 00:30:37.500 metabolism and other lipids regulated

NOTE Confidence: 0.8334467725

00:30:37.500 --> 00:30:41.160 leukemia cell proliferation.

NOTE Confidence: 0.8334467725

00:30:41.160 --> 00:30:43.797 Since then here I moved to the field of

NOTE Confidence: 0.8334467725

00:30:43.797 --> 00:30:45.841 vascular biology for many years until,

NOTE Confidence: 0.8334467725

00:30:45.841 --> 00:30:47.887 like about four years ago I

NOTE Confidence: 0.8334467725

00:30:47.887 --> 00:30:49.820 get a very incredible,

NOTE Confidence: 0.8334467725

00:30:49.820 --> 00:30:52.418 talented student come into my lap.

NOTE Confidence: 0.8334467725

00:30:52.420 --> 00:30:55.500 To do that, PSD.

NOTE Confidence: 0.8334467725

00:30:55.500 --> 00:30:56.914 As I do always with the people

NOTE Confidence: 0.8334467725

00:30:56.914 --> 00:30:58.518 who has this passion for science,

00:30:58.520 --> 00:31:00.560 I ask them whether it is the product

00:31:00.560 --> 00:31:02.500 they want to do it and then he told me

00:31:02.500 --> 00:31:03.780 that he was very interested in deep.

00:31:03.780 --> 00:31:06.444 It's like he wanted to do something related

00:31:06.444 --> 00:31:08.960 to two more biology and immunology.

00:31:08.960 --> 00:31:11.680 And then we came up with this project

00:31:11.680 --> 00:31:13.660 because has something related to

00:31:13.660 --> 00:31:16.523 lipids and also it's a problem related

00:31:16.601 --> 00:31:19.876 to counter that is is based in the

00:31:19.876 --> 00:31:23.530 however city or lipid metabolism, Dr.

00:31:23.530 --> 00:31:26.480 Local phenomena using a mouse.

00:31:26.480 --> 00:31:27.407 Of the disease.

00:31:27.407 --> 00:31:29.261 Then I wouldn't guys like to

00:31:29.261 --> 00:31:31.190 get full credit to Jonathan,

00:31:31.190 --> 00:31:32.670 who actually wears the person.

00:31:32.670 --> 00:31:34.870 The driving force here.

NOTE Confidence: 0.8334467725

00:31:34.870 --> 00:31:37.522 Who did this work? Why?

NOTE Confidence: 0.8334467725

00:31:37.522 --> 00:31:38.878 Why this tumor?

NOTE Confidence: 0.8334467725

00:31:38.878 --> 00:31:41.590 Why we were interested in a

NOTE Confidence: 0.8334467725

00:31:41.687 --> 00:31:44.419 particular carcinoma as this?

NOTE Confidence: 0.8334467725

00:31:44.420 --> 00:31:45.186 No more,

NOTE Confidence: 0.8334467725

00:31:45.186 --> 00:31:48.060 he said he became more prevalent right now,

NOTE Confidence: 0.8334467725

00:31:48.060 --> 00:31:49.400 particularly with the situation

NOTE Confidence: 0.8334467725

00:31:49.400 --> 00:31:51.288 that we are with this crisis.

NOTE Confidence: 0.8334467725

00:31:51.288 --> 00:31:52.632 So overeating and obesity

NOTE Confidence: 0.8334467725

00:31:52.632 --> 00:31:54.758 and type 2 diabetes that is,

NOTE Confidence: 0.8334467725

00:31:54.760 --> 00:31:57.220 having in all the Western societies.

NOTE Confidence: 0.8334467725

00:31:57.220 --> 00:31:59.278 Then, as you probably are aware,

NOTE Confidence: 0.8334467725

00:31:59.280 --> 00:32:01.898 about 30% of the population in the

NOTE Confidence: 0.8334467725

00:32:01.898 --> 00:32:03.734 United States that accumulates large

NOTE Confidence: 0.8334467725

00:32:03.734 --> 00:32:05.876 amount of neutral lipids in the

NOTE Confidence: 0.8334467725

00:32:05.876 --> 00:32:08.805 liver and cause this pathology called

NOTE Confidence: 0.8334467725

00:32:08.805 --> 00:32:10.857 non-alcoholic fatty liver disease

NOTE Confidence: 0.8334467725

00:32:10.857 --> 00:32:14.216 that is quite prevalent from this situation.

NOTE Confidence: 0.8334467725

00:32:14.216 --> 00:32:18.242 We saw that about 25% of the people

NOTE Confidence: 0.8334467725

00:32:18.242 --> 00:32:21.380 that has Nathalie our transition to

NOTE Confidence: 0.8334467725

00:32:21.484 --> 00:32:25.040 an estate of nasty is non alcoholic.

NOTE Confidence: 0.8334467725

00:32:25.040 --> 00:32:26.495 Like that is,

NOTE Confidence: 0.8334467725

00:32:26.495 --> 00:32:28.920 which is characterized for the

NOTE Confidence: 0.8334467725

00:32:28.920 --> 00:32:30.428 cyclonic inflammation that occurs

NOTE Confidence: 0.8334467725

00:32:30.428 --> 00:32:34.668 in the liver and the fibrosis.

NOTE Confidence: 0.8334467725

00:32:34.670 --> 00:32:37.366 As well as by the damage and turnover

NOTE Confidence: 0.8334467725

00:32:37.366 --> 00:32:40.027 that happened in this particular situation,

NOTE Confidence: 0.8334467725

00:32:40.030 --> 00:32:41.870 then this is kind of a chronic disease,

NOTE Confidence: 0.8334467725

00:32:41.870 --> 00:32:44.486 but in about 5% of the patients they

NOTE Confidence: 0.8334467725

00:32:44.486 --> 00:32:47.040 are able to transition to develop.

NOTE Confidence: 0.581718573333333

00:32:49.480 --> 00:32:51.622 This is actually a pretty bad kind

NOTE Confidence: 0.581718573333333

00:32:51.622 --> 00:32:53.674 of concert, since the survival

NOTE Confidence: 0.581718573333333

00:32:53.674 --> 00:32:56.542 rate is pretty low in general.

NOTE Confidence: 0.581718573333333

00:32:56.550 --> 00:32:58.998 Then when we set up the

NOTE Confidence: 0.581718573333333

00:32:58.998 --> 00:33:01.450 idea for for his thesis,

NOTE Confidence: 0.581718573333333

00:33:01.450 --> 00:33:03.592 we were actually looking at that

NOTE Confidence: 0.581718573333333

00:33:03.592 --> 00:33:05.737 time for developing and noble mouse

NOTE Confidence: 0.581718573333333

00:33:05.737 --> 00:33:08.012 models to start exist and also to

NOTE Confidence: 0.581718573333333

00:33:08.012 --> 00:33:09.909 apply novel technologies that they

NOTE Confidence: 0.581718573333333

00:33:09.909 --> 00:33:12.165 start coming out at that time.

NOTE Confidence: 0.581718573333333

00:33:12.170 --> 00:33:14.150 We try to investigate the molecular

NOTE Confidence: 0.581718573333333

00:33:14.150 --> 00:33:16.330 level where what could be the driver.

NOTE Confidence: 0.581718573333333

00:33:16.330 --> 00:33:19.842 So the formation of the catalog in a

NOTE Confidence: 0.581718573333333

00:33:19.842 --> 00:33:22.428 model of obesity driving tumor formation.

NOTE Confidence: 0.581718573333333

00:33:22.430 --> 00:33:24.738 Uhm? Around that time,

NOTE Confidence: 0.581718573333333

00:33:24.738 --> 00:33:27.623 the group from Matthias Eichenwald,

NOTE Confidence: 0.581718573333333

00:33:27.630 --> 00:33:30.290 airing in the Cancer Research

NOTE Confidence: 0.581718573333333

00:33:30.290 --> 00:33:31.886 Center in Heidelberg,

NOTE Confidence: 0.581718573333333

00:33:31.890 --> 00:33:35.160 published this novel model of obesity,

NOTE Confidence: 0.581718573333333

00:33:35.160 --> 00:33:38.404 driving part of local phenomena that was

NOTE Confidence: 0.581718573333333

00:33:38.404 --> 00:33:42.360 based in feeding the mice without killing,

NOTE Confidence: 0.581718573333333

00:33:42.360 --> 00:33:44.800 defeating high fat diet.

NOTE Confidence: 0.581718573333333

00:33:44.800 --> 00:33:47.418 In the upper panel you see a

NOTE Confidence: 0.581718573333333

00:33:47.420 --> 00:33:49.580 number of papers that this group

NOTE Confidence: 0.581718573333333

00:33:49.580 --> 00:33:51.916 publishes recently using this.

NOTE Confidence: 0.581718573333333

00:33:51.916 --> 00:33:54.836 This model of the disease.

NOTE Confidence: 0.581718573333333

00:33:54.840 --> 00:33:55.448 It's a,

NOTE Confidence: 0.581718573333333

00:33:55.448 --> 00:33:58.540 it's a pretty good model in in our opinion,

NOTE Confidence: 0.581718573333333

00:33:58.540 --> 00:33:59.118 because, uh,

NOTE Confidence: 0.581718573333333

00:33:59.118 --> 00:34:01.141 the mice develop all the features that

NOTE Confidence: 0.581718573333333

00:34:01.141 --> 00:34:03.136 help the people that develop obesity,

NOTE Confidence: 0.581718573333333

00:34:03.140 --> 00:34:06.308 type 2 diabetes and ended up having this

NOTE Confidence: 0.581718573333333

00:34:06.308 --> 00:34:09.970 issue that is increasing body weight,

NOTE Confidence: 0.581718573333333

00:34:09.970 --> 00:34:12.800 type 2 diabetes, insulin resistance,

NOTE Confidence: 0.581718573333333

00:34:12.800 --> 00:34:16.275 and eventually none of them.

NOTE Confidence: 0.581718573333333

00:34:16.280 --> 00:34:17.063 But you know,

NOTE Confidence: 0.581718573333333

00:34:17.063 --> 00:34:18.368 substantial amount of mice develop.

NOTE Confidence: 0.6054106485

00:34:20.580 --> 00:34:22.484 This is one of the benefits of the

NOTE Confidence: 0.6054106485

00:34:22.484 --> 00:34:24.153 model that the capital quite well

NOTE Confidence: 0.6054106485

00:34:24.153 --> 00:34:25.863 did not have any human disease.

NOTE Confidence: 0.6054106485

00:34:25.870 --> 00:34:27.364 The downside of the model is

NOTE Confidence: 0.6054106485

00:34:27.364 --> 00:34:29.270 not not all the mice developed,

NOTE Confidence: 0.6054106485

00:34:29.270 --> 00:34:30.894 but of local phenomena only on a

NOTE Confidence: 0.6054106485

00:34:30.894 --> 00:34:32.662 small fraction of mice, around 20%

NOTE Confidence: 0.6054106485

00:34:32.662 --> 00:34:35.826 of the mice and develop the disease.

NOTE Confidence: 0.6054106485

00:34:35.826 --> 00:34:39.140 In 12 months we were unable

NOTE Confidence: 0.6054106485

00:34:39.140 --> 00:34:41.580 to reproduce this high.

NOTE Confidence: 0.6054106485

00:34:41.580 --> 00:34:42.302 Incidence of.

NOTE Confidence: 0.6054106485

00:34:42.302 --> 00:34:45.190 In my mind we have to extend our

NOTE Confidence: 0.6054106485

00:34:45.270 --> 00:34:47.860 studies to 15 months to see that.

NOTE Confidence: 0.6054106485

00:34:47.860 --> 00:34:50.905 And one of the first thing that

NOTE Confidence: 0.6054106485

00:34:50.905 --> 00:34:53.994 we did was to fed the blocks

NOTE Confidence: 0.6054106485

00:34:53.994 --> 00:34:56.666 is miles for about 20 months.

NOTE Confidence: 0.6054106485

00:34:56.666 --> 00:34:59.078 With the this calling the fishing

NOTE Confidence: 0.6054106485

00:34:59.078 --> 00:35:01.532 Haifa diet and we sacrifice this

NOTE Confidence: 0.6054106485

00:35:01.532 --> 00:35:03.507 my son different time points

NOTE Confidence: 0.6054106485

00:35:03.510 --> 00:35:05.295 three months and states that

NOTE Confidence: 0.6054106485

00:35:05.295 --> 00:35:07.080 is considered to have NFLD.

NOTE Confidence: 0.6054106485

00:35:07.080 --> 00:35:09.817 Six months the NASA state and then

NOTE Confidence: 0.6054106485

00:35:09.817 --> 00:35:12.991 we were waiting on the 15 months to

NOTE Confidence: 0.6054106485

00:35:12.991 --> 00:35:15.619 study the formation of tumors in mice.

NOTE Confidence: 0.6054106485

00:35:15.620 --> 00:35:18.042 These are in police data from the

NOTE Confidence: 0.6054106485

00:35:18.042 --> 00:35:20.571 the war from from Jonathan and and

NOTE Confidence: 0.6054106485

00:35:20.571 --> 00:35:23.300 this is in the upper left corner.

NOTE Confidence: 0.6054106485

00:35:23.300 --> 00:35:25.848 You see the loyal to experiments that

NOTE Confidence: 0.6054106485

00:35:25.848 --> 00:35:28.785 we did here and all the analysis that

NOTE Confidence: 0.6054106485

00:35:28.785 --> 00:35:31.954 we did in every day and in every time

NOTE Confidence: 0.6054106485

00:35:31.954 --> 00:35:33.986 point I'm going to show you only a

NOTE Confidence: 0.6054106485

00:35:33.986 --> 00:35:36.435 few data about the this the whole study.

NOTE Confidence: 0.6054106485

00:35:36.440 --> 00:35:39.092 But then we actually collect

NOTE Confidence: 0.6054106485

00:35:39.092 --> 00:35:41.252 issues at three six 12115 months

NOTE Confidence: 0.6054106485

00:35:41.252 --> 00:35:42.656 to do lipidomic analysis.

NOTE Confidence: 0.6054106485

00:35:42.660 --> 00:35:44.268 Public functionary sequence

NOTE Confidence: 0.6054106485

00:35:44.268 --> 00:35:45.768 in single sequencing.

NOTE Confidence: 0.6054106485

00:35:45.768 --> 00:35:47.480 Oregon municipal Chemistry not

NOTE Confidence: 0.6054106485

00:35:47.480 --> 00:35:50.051 only for delivery but also for

NOTE Confidence: 0.6054106485

00:35:50.051 --> 00:35:52.211 other tissues and also we track

NOTE Confidence: 0.6054106485

00:35:52.211 --> 00:35:54.144 the glucosamine stasis and lipid

NOTE Confidence: 0.6054106485

00:35:54.144 --> 00:35:55.716 metabolism every time point.

NOTE Confidence: 0.6054106485

00:35:55.720 --> 00:35:56.760 As you can see here,

NOTE Confidence: 0.6054106485

00:35:56.760 --> 00:35:58.188 when you start feeling this match

NOTE Confidence: 0.6054106485

00:35:58.188 --> 00:35:59.529 with Pauline defeating high fat diet,

NOTE Confidence: 0.6054106485

00:35:59.530 --> 00:36:01.612 this might gain significantly amount of

NOTE Confidence: 0.6054106485

00:36:01.612 --> 00:36:03.800 body weight and disappears very early on.

NOTE Confidence: 0.6054106485

00:36:03.800 --> 00:36:05.956 After putting the mice in this diet

NOTE Confidence: 0.6054106485

00:36:05.960 --> 00:36:09.182 and the increasing body weight is

NOTE Confidence: 0.6054106485

00:36:09.182 --> 00:36:10.950 accounting because the increasing

NOTE Confidence: 0.6054106485

00:36:10.950 --> 00:36:14.030 pad mass and the lean mass in

NOTE Confidence: 0.6054106485

00:36:14.030 --> 00:36:15.956 the masses similar during the

NOTE Confidence: 0.6054106485

00:36:15.956 --> 00:36:18.532 feeding time but the fat mass is

NOTE Confidence: 0.6054106485

00:36:18.532 --> 00:36:20.333 significantly increased up on high

NOTE Confidence: 0.6054106485

00:36:20.333 --> 00:36:22.824 fat diet feeding and these mice in

NOTE Confidence: 0.6054106485

00:36:22.824 --> 00:36:25.020 in addition to half obesity that

NOTE Confidence: 0.6054106485

00:36:25.094 --> 00:36:27.509 develop significant dyslipidemia.

NOTE Confidence: 0.6054106485

00:36:27.510 --> 00:36:29.590 Down in the lower panels.

NOTE Confidence: 0.6054106485

00:36:29.590 --> 00:36:32.544 So in the high levels of cholesterol

NOTE Confidence: 0.6054106485

00:36:32.544 --> 00:36:34.697 interpolation that are in significant

NOTE Confidence: 0.6054106485

00:36:34.697 --> 00:36:37.139 increase in the later time points

NOTE Confidence: 0.6054106485

00:36:37.139 --> 00:36:39.566 and this increase in cholesterol

NOTE Confidence: 0.6054106485

00:36:39.566 --> 00:36:41.610 correspond to an increase.

NOTE Confidence: 0.6054106485

00:36:41.610 --> 00:36:43.975 Circulating levels of LDL lipoproteins

NOTE Confidence: 0.6054106485

00:36:43.975 --> 00:36:46.880 and stone in the middle panel.

NOTE Confidence: 0.6054106485

00:36:46.880 --> 00:36:49.466 We also perform GTIT assets to

NOTE Confidence: 0.6054106485

00:36:49.466 --> 00:36:51.840 demonstrate that this mass has

NOTE Confidence: 0.6054106485

00:36:51.840 --> 00:36:54.136 insistent and glucose intolerance,

NOTE Confidence: 0.6054106485

00:36:54.140 --> 00:36:56.340 and I'll show you here.

NOTE Confidence: 0.6054106485

00:36:56.340 --> 00:36:56.705 Also,

NOTE Confidence: 0.6054106485

00:36:56.705 --> 00:36:58.895 the fasting glucose in these mice

NOTE Confidence: 0.6054106485

00:36:58.895 --> 00:37:01.559 aspects are also significantly elevated.

NOTE Confidence: 0.6054106485

00:37:01.560 --> 00:37:03.864 Then we have a model that developed

NOTE Confidence: 0.6054106485

00:37:03.864 --> 00:37:05.908 the three stages of the disease and

NOTE Confidence: 0.6054106485

00:37:05.908 --> 00:37:08.015 also recapitulated quite well on the

NOTE Confidence: 0.6054106485

00:37:08.015 --> 00:37:09.770 metabolic alteration that is found

NOTE Confidence: 0.6054106485

00:37:09.825 --> 00:37:11.737 in in in in people with obesity and.

NOTE Confidence: 0.6054106485

00:37:11.740 --> 00:37:14.458 Anti two diabetes.

NOTE Confidence: 0.6054106485

00:37:14.460 --> 00:37:16.480 Then we also perform Mr.

NOTE Confidence: 0.6054106485

00:37:16.480 --> 00:37:19.651 Local analysis in in these mice and

NOTE Confidence: 0.6054106485

00:37:19.651 --> 00:37:21.652 Carter is well what's going on.

NOTE Confidence: 0.6054106485

00:37:21.652 --> 00:37:22.936 And as you can see here,

NOTE Confidence: 0.6054106485

00:37:22.940 --> 00:37:24.988 this might develop significant

NOTE Confidence: 0.6054106485

00:37:24.988 --> 00:37:26.524 accumulation of lipids.

NOTE Confidence: 0.6054106485

00:37:26.530 --> 00:37:28.318 You see the ballooning also there

NOTE Confidence: 0.6054106485

00:37:28.318 --> 00:37:30.286 in after three months and six months

NOTE Confidence: 0.6054106485

00:37:30.286 --> 00:37:31.952 in high point diet and also a

NOTE Confidence: 0.619640191333333

00:37:32.016 --> 00:37:33.936 significant fibrosis and damaging the liver

NOTE Confidence: 0.619640191333333

00:37:33.936 --> 00:37:37.532 as shown in the right panel by standing

NOTE Confidence: 0.619640191333333

00:37:37.532 --> 00:37:41.000 with serious right is most developed.

NOTE Confidence: 0.619640191333333

00:37:41.000 --> 00:37:43.280 Fibrosis early on as well,

NOTE Confidence: 0.619640191333333

00:37:43.280 --> 00:37:47.306 and the formation of fibrosis is

NOTE Confidence: 0.619640191333333

00:37:47.306 --> 00:37:50.548 also correlated with a significant

NOTE Confidence: 0.619640191333333

00:37:50.548 --> 00:37:52.474 increase in inflammation.

NOTE Confidence: 0.619640191333333

00:37:52.480 --> 00:37:54.928 So in the analysis and the flow cytometry

NOTE Confidence: 0.619640191333333

00:37:54.928 --> 00:37:56.560 analysis, or in the lower panel,

NOTE Confidence: 0.619640191333333

00:37:56.560 --> 00:37:58.205 I'm analyzing the 3:45 positive

NOTE Confidence: 0.619640191333333

00:37:58.205 --> 00:38:00.724 cells in the liver as well as

NOTE Confidence: 0.619640191333333

00:38:00.724 --> 00:38:02.340 neutrophils and also monocytes,

NOTE Confidence: 0.619640191333333

00:38:02.340 --> 00:38:04.890 and Cooper feels as well.

NOTE Confidence: 0.619640191333333

00:38:04.890 --> 00:38:08.218 Then one other result that we found here.

NOTE Confidence: 0.619640191333333

00:38:08.220 --> 00:38:12.576 We notice that after 12 months,

NOTE Confidence: 0.619640191333333

00:38:12.580 --> 00:38:14.332 efficiency of the of the the

00:38:14.332 --> 00:38:15.941 people of the development of

00:38:15.941 --> 00:38:17.457 commercial was quite restricted.

00:38:17.460 --> 00:38:19.816 We found seven of the 39 mice

00:38:19.816 --> 00:38:22.324 developed tumors and all of these

00:38:22.324 --> 00:38:25.330 correlate with the more or less with

00:38:25.330 --> 00:38:27.420 the simulating alpha fetal protein

00:38:27.499 --> 00:38:30.037 levels in circulation of the mice.

00:38:30.040 --> 00:38:32.990 As you can see in the in the 15 months group.

00:38:35.540 --> 00:38:38.235 The incidence of the two more simply

00:38:38.235 --> 00:38:40.810 significantly many of the money the mice

00:38:40.810 --> 00:38:42.980 around 50% of the mice develop tumors,

00:38:42.980 --> 00:38:44.558 and also they feel levels are

00:38:44.558 --> 00:38:46.470 very hot in the right panels you

00:38:46.470 --> 00:38:47.850 can see a representative image,

00:38:47.850 --> 00:38:49.722 so the kind of tumors that you observed

00:38:49.722 --> 00:38:51.906 in in this mouse model of the disease.

NOTE Confidence: 0.81696308

00:38:54.600 --> 00:38:56.060 Then we asked two questions

NOTE Confidence: 0.81696308

00:38:56.060 --> 00:38:58.126 and I'm going to be kind of.

NOTE Confidence: 0.81696308

00:38:58.126 --> 00:39:00.247 I'm going to sumarize all all all

NOTE Confidence: 0.81696308

00:39:00.247 --> 00:39:02.516 the other we have here, I mean.

NOTE Confidence: 0.81696308

00:39:02.516 --> 00:39:04.424 Happy to share more when next.

NOTE Confidence: 0.81696308

00:39:04.430 --> 00:39:07.220 I know you guys it can send us emails we can.

NOTE Confidence: 0.81696308

00:39:07.220 --> 00:39:08.879 We can meet with all of you

NOTE Confidence: 0.81696308

00:39:08.879 --> 00:39:10.360 and you know so with you.

NOTE Confidence: 0.81696308

00:39:10.360 --> 00:39:14.658 But the the two key aspects that

NOTE Confidence: 0.81696308

00:39:14.660 --> 00:39:16.459 you're not gonna want to address here,

NOTE Confidence: 0.81696308

00:39:16.460 --> 00:39:18.248 we're still first delineated,

NOTE Confidence: 0.81696308

00:39:18.248 --> 00:39:21.549 the metabolic changes that occurs in a party.

NOTE Confidence: 0.81696308

00:39:21.550 --> 00:39:23.145 They progress toward the Council

NOTE Confidence: 0.81696308

00:39:23.145 --> 00:39:25.329 felt I'm going to show you some.

NOTE Confidence: 0.81696308

00:39:25.330 --> 00:39:27.598 You know fewer slides about that.

NOTE Confidence: 0.81696308

00:39:27.600 --> 00:39:29.544 And the second part of the talk I'm

NOTE Confidence: 0.81696308

00:39:29.544 --> 00:39:31.668 going to focus a little bit more

NOTE Confidence: 0.81696308

00:39:31.668 --> 00:39:33.243 is about identification or novel.

NOTE Confidence: 0.81696308

00:39:33.250 --> 00:39:35.646 Potential targets that are

NOTE Confidence: 0.81696308

00:39:35.646 --> 00:39:38.641 associated in the development of

NOTE Confidence: 0.81696308

00:39:38.641 --> 00:39:42.009 the disease in this mouse model.

NOTE Confidence: 0.81696308

00:39:42.010 --> 00:39:44.100 Particularly in this protein fatty

NOTE Confidence: 0.81696308

00:39:44.100 --> 00:39:46.190 acid binding protein five that,

NOTE Confidence: 0.81696308

00:39:46.190 --> 00:39:47.870 as I will tell you in a minute,

NOTE Confidence: 0.81696308

00:39:47.870 --> 00:39:50.096 is a protein that is important not

NOTE Confidence: 0.81696308

00:39:50.096 --> 00:39:52.130 only in regulating lipid metabolism.

NOTE Confidence: 0.81696308

00:39:52.130 --> 00:39:54.680 Also preparation.

NOTE Confidence: 0.81696308

00:39:54.680 --> 00:39:56.396 Regulation of the suppression

NOTE Confidence: 0.81696308

00:39:56.396 --> 00:39:58.541 of this protein has been

NOTE Confidence: 0.81696308

00:39:58.541 --> 00:40:00.229 associated not only in liver.

NOTE Confidence: 0.722093108

00:40:02.360 --> 00:40:05.000 Humans, but also as a highly

NOTE Confidence: 0.722093108

00:40:05.000 --> 00:40:06.760 associated with prostate tumors,

NOTE Confidence: 0.722093108

00:40:06.760 --> 00:40:09.920 as engaging with the 1st.

NOTE Confidence: 0.722093108

00:40:09.920 --> 00:40:11.789 And part of the the first talk

NOTE Confidence: 0.722093108

00:40:11.789 --> 00:40:13.858 of the in the meeting today.

NOTE Confidence: 0.722093108

00:40:13.860 --> 00:40:15.615 Then if I will be 5 is highly elevated,

NOTE Confidence: 0.722093108

00:40:15.620 --> 00:40:16.475 doesn't prostate tumors,

NOTE Confidence: 0.722093108

00:40:16.475 --> 00:40:18.470 and there are a number of groups,

NOTE Confidence: 0.722093108

00:40:18.470 --> 00:40:19.787 particularly were collaborators

NOTE Confidence: 0.722093108

00:40:19.787 --> 00:40:21.982 that are looking at selling

NOTE Confidence: 0.722093108

00:40:21.982 --> 00:40:23.780 the efficacy of everything.

NOTE Confidence: 0.722093108

00:40:23.780 --> 00:40:26.370 In treating prostate cancer.

NOTE Confidence: 0.5618215964

00:40:28.940 --> 00:40:32.670 Then this is a cartoon. That's true.

NOTE Confidence: 0.5618215964

00:40:32.670 --> 00:40:35.330 Marissa little bit the.

NOTE Confidence: 0.5618215964

00:40:35.330 --> 00:40:37.650 The son of the first experiment we did,

NOTE Confidence: 0.5618215964

00:40:37.650 --> 00:40:40.656 we, we took a pentag here the 10 the

00:40:40.656 --> 00:40:43.758 the single cell RNA transcriptomics.

00:40:43.760 --> 00:40:46.434 Fight change in the pattern of gene

00:40:46.434 --> 00:40:48.857 expression not only in the patio sites but

00:40:48.857 --> 00:40:51.677 also in in the non parenchymal health,

00:40:51.680 --> 00:40:53.280 particularly in both illegal sales.

00:40:53.280 --> 00:40:55.779 Only minute sales.

00:40:55.780 --> 00:40:57.778 And then we will turn to look into it.

00:40:57.780 --> 00:41:00.321 Where where are the changes that occurs

00:41:00.321 --> 00:41:03.434 in the the tumor progression and how this

00:41:03.434 --> 00:41:05.829 has been associated with the disease?

00:41:05.830 --> 00:41:08.518 Then with the support of the

00:41:08.518 --> 00:41:10.310 liver center here ideal,

00:41:10.310 --> 00:41:12.795 we were able to isolate this quite

00:41:12.795 --> 00:41:15.978 well and and you're not on set up a

00:41:15.978 --> 00:41:18.168 very good protocol for keep this high

00:41:18.168 --> 00:41:20.100 school Bible on these cells and try

NOTE Confidence: 0.5618215964

00:41:20.161 --> 00:41:22.093 to isolate these cells as soon as

NOTE Confidence: 0.5618215964

00:41:22.093 --> 00:41:24.527 possible just to avoid any kind of a

NOTE Confidence: 0.5618215964

00:41:24.527 --> 00:41:26.072 target effect giving their solution.

NOTE Confidence: 0.5618215964

00:41:26.080 --> 00:41:26.621 Process.

NOTE Confidence: 0.5618215964

00:41:26.621 --> 00:41:29.867 Then we did the analysis in

NOTE Confidence: 0.5618215964

00:41:29.867 --> 00:41:32.430 different stages here and here.

NOTE Confidence: 0.5618215964

00:41:32.430 --> 00:41:35.010 You have couple of humor plots.

NOTE Confidence: 0.5618215964

00:41:35.010 --> 00:41:38.776 Then in the left plot the thing

NOTE Confidence: 0.5618215964

00:41:38.776 --> 00:41:42.447 that you see here is all the single

NOTE Confidence: 0.5618215964

00:41:42.447 --> 00:41:44.601 events thereby shown by dots that

NOTE Confidence: 0.5618215964

00:41:44.601 --> 00:41:46.558 corresponding are grouped in different

NOTE Confidence: 0.5618215964

00:41:46.558 --> 00:41:48.473 colors that correspond with the

NOTE Confidence: 0.5618215964

00:41:48.473 --> 00:41:49.835 different cellular populations that

NOTE Confidence: 0.5618215964

00:41:49.835 --> 00:41:54.060 you all share in the in the livers.

NOTE Confidence: 0.5618215964

00:41:54.060 --> 00:41:57.008 Then here are input.

NOTE Confidence: 0.5618215964

00:41:57.010 --> 00:41:58.910 Five different for different groups.

NOTE Confidence: 0.5618215964

00:41:58.910 --> 00:42:01.409 One of them is the mice that

NOTE Confidence: 0.5618215964

00:42:01.409 --> 00:42:03.662 are filled with the child diet.

NOTE Confidence: 0.5618215964

00:42:03.662 --> 00:42:07.070 Then they might that they were filled with

NOTE Confidence: 0.5618215964

00:42:07.153 --> 00:42:10.260 the five fat diet with low AFP expression.

NOTE Confidence: 0.5618215964

00:42:10.260 --> 00:42:13.080 Then others would have high FPS

NOTE Confidence: 0.5618215964

00:42:13.080 --> 00:42:15.935 present and then we also input

NOTE Confidence: 0.5618215964

00:42:15.935 --> 00:42:18.020 directly the DDST carcinoma here.

NOTE Confidence: 0.5618215964

00:42:18.020 --> 00:42:20.620 Then you can see here how all these

NOTE Confidence: 0.5618215964

00:42:20.687 --> 00:42:23.865 sales group quite well and in the in the

NOTE Confidence: 0.5618215964

00:42:23.865 --> 00:42:26.998 right panel that in that you see now is.

NOTE Confidence: 0.5618215964

00:42:27.000 --> 00:42:29.418 How the diverse populations can be

NOTE Confidence: 0.5618215964

00:42:29.418 --> 00:42:32.062 clustered and based in the differential

NOTE Confidence: 0.5618215964

00:42:32.062 --> 00:42:34.462 gene expression and different stages

NOTE Confidence: 0.5618215964

00:42:34.462 --> 00:42:37.124 from mice that are affecting child

NOTE Confidence: 0.5618215964

00:42:37.124 --> 00:42:39.410 idea with versus mice that are

NOTE Confidence: 0.5618215964

00:42:39.410 --> 00:42:42.560 fed with this calling deficient.

NOTE Confidence: 0.5618215964

00:42:42.560 --> 00:42:44.415 Then you see there the the path

NOTE Confidence: 0.5618215964

00:42:44.415 --> 00:42:46.087 aside and the concepts and cluster

NOTE Confidence: 0.5618215964

00:42:46.087 --> 00:42:48.520 and that is in the in the red box.

NOTE Confidence: 0.5618215964

00:42:48.520 --> 00:42:50.360 And as you can see here by the

NOTE Confidence: 0.5618215964

00:42:50.360 --> 00:42:52.409 color you can see how the population

NOTE Confidence: 0.5618215964

00:42:52.409 --> 00:42:53.633 shifted to the right.

NOTE Confidence: 0.5618215964

00:42:53.640 --> 00:42:57.160 Since you had the 1st in in normal

NOTE Confidence: 0.5618215964

00:42:57.160 --> 00:43:00.024 diet and how they transition to these

NOTE Confidence: 0.5618215964

00:43:00.024 --> 00:43:02.064 cancer cells that are highlighted

NOTE Confidence: 0.5618215964

00:43:02.064 --> 00:43:03.336 in the purple.

NOTE Confidence: 0.5618215964

00:43:03.336 --> 00:43:06.320 These are the purple dots in the

NOTE Confidence: 0.5618215964

00:43:06.320 --> 00:43:09.296 path aside group correspond to the

NOTE Confidence: 0.5618215964

00:43:09.296 --> 00:43:12.038 the cancer cells also within the two

NOTE Confidence: 0.5618215964

00:43:12.038 --> 00:43:14.627 more you see. Highly abundant also.

NOTE Confidence: 0.5618215964

00:43:14.627 --> 00:43:18.221 The details suspected that is also

NOTE Confidence: 0.5618215964

00:43:18.221 --> 00:43:19.940 in this plot.

NOTE Confidence: 0.5618215964

00:43:19.940 --> 00:43:21.806 Then doing this kind of analysis,

NOTE Confidence: 0.5618215964

00:43:21.810 --> 00:43:23.700 you can infer all the information

NOTE Confidence: 0.5618215964

00:43:23.700 --> 00:43:25.781 coming from all the gene expression

NOTE Confidence: 0.5618215964

00:43:25.781 --> 00:43:27.742 for every single event during

NOTE Confidence: 0.5618215964

00:43:27.742 --> 00:43:29.902 the transition from the side.

NOTE Confidence: 0.5618215964

00:43:29.902 --> 00:43:32.366 The healthy side do the content fell

NOTE Confidence: 0.5618215964

00:43:32.370 --> 00:43:34.770 and you can do this kind of analysis

NOTE Confidence: 0.5618215964

00:43:34.770 --> 00:43:37.028 called silver time that can tell you

NOTE Confidence: 0.5618215964

00:43:37.028 --> 00:43:38.995 how these cells can transition from

NOTE Confidence: 0.5618215964

00:43:38.995 --> 00:43:41.180 the healthy to the contact stage.

NOTE Confidence: 0.724906122

00:43:45.130 --> 00:43:46.090 Then this is the nicest.

NOTE Confidence: 0.724906122

00:43:46.090 --> 00:43:47.440 Save the time that you're not

NOTE Confidence: 0.724906122

00:43:47.440 --> 00:43:48.810 funded and you can see here.

NOTE Confidence: 0.724906122

00:43:48.810 --> 00:43:51.210 You can actually Coop at this quite

NOTE Confidence: 0.724906122

00:43:51.210 --> 00:43:53.130 well in the trajectories that instills

NOTE Confidence: 0.724906122

00:43:53.130 --> 00:43:54.989 come followed in the cellar time,

NOTE Confidence: 0.724906122

00:43:54.990 --> 00:43:57.566 and can group is also very well in

NOTE Confidence: 0.724906122

00:43:57.566 --> 00:43:59.890 the violent plug in the right panel

NOTE Confidence: 0.724906122

00:43:59.890 --> 00:44:02.482 you can see here probably better

NOTE Confidence: 0.724906122

00:44:02.482 --> 00:44:05.108 where the IPA or the pathways that

NOTE Confidence: 0.724906122

00:44:05.108 --> 00:44:07.100 appears to be deregulated in the

NOTE Confidence: 0.724906122

00:44:07.165 --> 00:44:09.607 process of the converting this healthy,

NOTE Confidence: 0.724906122

00:44:09.610 --> 00:44:13.118 but aside to two more two more

NOTE Confidence: 0.724906122

00:44:13.118 --> 00:44:15.200 two more cells.

NOTE Confidence: 0.724906122

00:44:15.200 --> 00:44:17.815 One of these boys are

NOTE Confidence: 0.724906122

00:44:17.815 --> 00:44:19.166 now under investigation.

NOTE Confidence: 0.724906122

00:44:19.166 --> 00:44:21.644 I'm going to talk about this.

NOTE Confidence: 0.724906122

00:44:21.650 --> 00:44:22.799 Like binding protein,

NOTE Confidence: 0.724906122

00:44:22.799 --> 00:44:25.097 but also we did metabolic analysis

NOTE Confidence: 0.724906122

00:44:25.097 --> 00:44:26.635 here in collaboration with

NOTE Confidence: 0.724906122

00:44:26.635 --> 00:44:28.819 Rachel Berry and follow up very

NOTE Confidence: 0.724906122

00:44:28.819 --> 00:44:30.628 well on these findings but.

NOTE Confidence: 0.724906122

00:44:30.630 --> 00:44:32.723 Things that you can see here is

NOTE Confidence: 0.724906122

00:44:32.723 --> 00:44:35.174 that there is a number of bad ways

NOTE Confidence: 0.724906122

00:44:35.174 --> 00:44:37.436 that appears to be regulated during

NOTE Confidence: 0.724906122

00:44:37.436 --> 00:44:39.435 the transition from the healthy to

NOTE Confidence: 0.724906122

00:44:39.435 --> 00:44:42.180 the malignant L and including the

NOTE Confidence: 0.724906122

00:44:42.180 --> 00:44:44.140 lipid oxidation understand toxic

NOTE Confidence: 0.724906122

00:44:44.140 --> 00:44:46.200 radical and then you have also

NOTE Confidence: 0.724906122

00:44:46.200 --> 00:44:47.770 significant and in regulation of

NOTE Confidence: 0.724906122

00:44:47.828 --> 00:44:49.768 further progress as people lipids,

NOTE Confidence: 0.724906122

00:44:49.770 --> 00:44:52.930 including the importance of transport.

NOTE Confidence: 0.724906122

00:44:52.930 --> 00:44:54.694 Then the the molecule I'm going

NOTE Confidence: 0.724906122

00:44:54.694 --> 00:44:56.290 to tell you about today,

NOTE Confidence: 0.724906122

00:44:56.290 --> 00:44:57.820 fatty acid binding protein actually

NOTE Confidence: 0.724906122

00:44:57.820 --> 00:44:59.870 play an important role in this pathway.

NOTE Confidence: 0.724906122

00:44:59.870 --> 00:45:01.950 So I want to show you why this

NOTE Confidence: 0.724906122

00:45:01.950 --> 00:45:04.478 could be very relevant.

NOTE Confidence: 0.724906122

00:45:04.480 --> 00:45:06.768 One of the question when when you do

NOTE Confidence: 0.724906122

00:45:06.768 --> 00:45:08.833 single task to mix now we are trying

NOTE Confidence: 0.724906122

00:45:08.833 --> 00:45:10.260 to do a special transcriptomics

NOTE Confidence: 0.724906122

00:45:10.260 --> 00:45:12.295 to see where I'm located.

NOTE Confidence: 0.724906122

00:45:12.300 --> 00:45:17.230 These cells within the tumor and how.

NOTE Confidence: 0.724906122

00:45:17.230 --> 00:45:20.429 How even is this pressing of the

NOTE Confidence: 0.724906122

00:45:20.429 --> 00:45:22.879 these genes across the tumors?

NOTE Confidence: 0.724906122

00:45:22.880 --> 00:45:24.872 This is decent ongoing war with

NOTE Confidence: 0.724906122

00:45:24.872 --> 00:45:26.480 the collection with sticking one.

NOTE Confidence: 0.724906122

00:45:26.480 --> 00:45:28.552 One of the things that we did in

NOTE Confidence: 0.724906122

00:45:28.552 --> 00:45:30.332 parallel in another different study

NOTE Confidence: 0.724906122

00:45:30.332 --> 00:45:32.332 that the Inmaculada Root Maldonado

NOTE Confidence: 0.724906122

00:45:32.332 --> 00:45:34.548 help help in this this world is

NOTE Confidence: 0.724906122

00:45:34.548 --> 00:45:35.988 trying to develop another mouse

NOTE Confidence: 0.724906122

00:45:35.988 --> 00:45:37.740 model here that is a rainbow.

NOTE Confidence: 0.724906122

00:45:37.740 --> 00:45:41.499 Mice that allow you to study more

NOTE Confidence: 0.724906122

00:45:41.499 --> 00:45:44.145 clonality this this mouse model that

NOTE Confidence: 0.724906122

00:45:44.145 --> 00:45:46.818 thing that does is randomly labeled

NOTE Confidence: 0.724906122

00:45:46.818 --> 00:45:50.276 the patio sites in three different colors.

NOTE Confidence: 0.724906122

00:45:50.280 --> 00:45:53.408 As you can see in the center pictures.

NOTE Confidence: 0.724906122

00:45:53.410 --> 00:45:55.030 These are the control mice and

NOTE Confidence: 0.724906122

00:45:55.030 --> 00:45:57.408 then you can see here where is the

NOTE Confidence: 0.724906122

00:45:57.408 --> 00:45:59.268 random distribution of all the paper

NOTE Confidence: 0.724906122

00:45:59.328 --> 00:46:01.188 cites in the three different colors

NOTE Confidence: 0.724906122

00:46:01.188 --> 00:46:03.855 and in green color are stain and

NOTE Confidence: 0.724906122

00:46:03.855 --> 00:46:06.705 the cells that are non epicycles.

NOTE Confidence: 0.724906122

00:46:06.710 --> 00:46:12.060 This correspond to the endothelial cells.

NOTE Confidence: 0.724906122

00:46:12.060 --> 00:46:13.956 And the mother was quite well to study.

NOTE Confidence: 0.724906122

00:46:13.960 --> 00:46:15.344 Regeneration is something I'm

NOTE Confidence: 0.724906122

00:46:15.344 --> 00:46:17.074 not going to touch today,

NOTE Confidence: 0.724906122

00:46:17.080 --> 00:46:20.692 but here in the right panel you see in

NOTE Confidence: 0.724906122

00:46:20.692 --> 00:46:23.716 a model of liver injury that treatment

NOTE Confidence: 0.724906122

00:46:23.716 --> 00:46:27.057 with carbon tetrachloride that induce death.

NOTE Confidence: 0.724906122

00:46:27.057 --> 00:46:29.139 And then you can start regeneration.

NOTE Confidence: 0.724906122

00:46:29.140 --> 00:46:31.678 You can see how you see a very nice

NOTE Confidence: 0.724906122

00:46:31.678 --> 00:46:34.147 clonal expansion of some of the

NOTE Confidence: 0.724906122

00:46:34.147 --> 00:46:35.839 existing apotheosized to develop

NOTE Confidence: 0.724906122

00:46:35.839 --> 00:46:38.217 these patches in different colors.

NOTE Confidence: 0.724906122

00:46:38.220 --> 00:46:39.893 Then we also employ in this same

NOTE Confidence: 0.724906122

00:46:39.893 --> 00:46:41.502 model to see where we actually

NOTE Confidence: 0.724906122

00:46:41.502 --> 00:46:43.441 happen in the context of aging and

NOTE Confidence: 0.724906122

00:46:43.496 --> 00:46:45.380 the context and situation where we

NOTE Confidence: 0.724906122

00:46:45.380 --> 00:46:47.240 have a chronic metabolic damage.

NOTE Confidence: 0.724906122

00:46:47.240 --> 00:46:49.640 What's happened with naphthalene,

NOTE Confidence: 0.724906122

00:46:49.640 --> 00:46:51.716 and this is actually very interesting,

NOTE Confidence: 0.724906122

00:46:51.720 --> 00:46:52.720 as you can see here,

NOTE Confidence: 0.667202877047619

00:46:52.720 --> 00:46:54.911 because even in US you see their

NOTE Confidence: 0.667202877047619

00:46:54.911 --> 00:46:56.897 selection on some specific clones that

NOTE Confidence: 0.667202877047619

00:46:56.897 --> 00:46:59.620 occurs in the liver in the left panel,

NOTE Confidence: 0.667202877047619

00:46:59.620 --> 00:47:01.126 and this is probably because you

NOTE Confidence: 0.667202877047619

00:47:01.126 --> 00:47:02.800 have this damage and regeneration.

NOTE Confidence: 0.667202877047619

00:47:02.800 --> 00:47:04.620 Delivery is a very interesting

NOTE Confidence: 0.667202877047619

00:47:04.620 --> 00:47:06.076 organ to study that.

NOTE Confidence: 0.667202877047619

00:47:06.080 --> 00:47:08.768 And you can see also accumulation of fat

NOTE Confidence: 0.667202877047619

00:47:08.768 --> 00:47:11.399 here with showing this like dark spot.

NOTE Confidence: 0.667202877047619

00:47:11.400 --> 00:47:14.240 But why I want to why I want to illustrate

NOTE Confidence: 0.667202877047619

00:47:14.312 --> 00:47:17.360 you this model and why it's very interesting.

NOTE Confidence: 0.667202877047619

00:47:17.360 --> 00:47:19.064 This model is because you can

NOTE Confidence: 0.667202877047619

00:47:19.064 --> 00:47:20.200 actually start to mortality.

NOTE Confidence: 0.667202877047619

00:47:20.200 --> 00:47:22.420 Then you can not only see.

NOTE Confidence: 0.667202877047619

00:47:22.420 --> 00:47:24.076 Diversity of two more sales by

NOTE Confidence: 0.667202877047619

00:47:24.076 --> 00:47:25.760 single seller and just get to me.

NOTE Confidence: 0.667202877047619

00:47:25.760 --> 00:47:27.725 But you can actually interrogate

NOTE Confidence: 0.667202877047619

00:47:27.725 --> 00:47:29.794 whether the two more unit for one

NOTE Confidence: 0.667202877047619

00:47:29.794 --> 00:47:32.000 cell that expanding a single clone of

NOTE Confidence: 0.667202877047619

00:47:32.000 --> 00:47:34.058 is coming from two different clones.

NOTE Confidence: 0.667202877047619

00:47:34.060 --> 00:47:36.204 And the thing that we are seeing now

NOTE Confidence: 0.667202877047619

00:47:36.204 --> 00:47:38.260 is preliminary is that many of these

NOTE Confidence: 0.667202877047619

00:47:38.260 --> 00:47:39.780 two more oligoclonal or monoclonal.

NOTE Confidence: 0.667202877047619

00:47:39.780 --> 00:47:41.656 This is the right you can see

NOTE Confidence: 0.667202877047619

00:47:41.656 --> 00:47:43.677 only two cells or maybe 2 patches

NOTE Confidence: 0.667202877047619

00:47:43.677 --> 00:47:45.399 and only in blue and yellow,

NOTE Confidence: 0.667202877047619

00:47:45.400 --> 00:47:48.298 suggesting that some of this too much

NOTE Confidence: 0.667202877047619

00:47:48.298 --> 00:47:50.498 pressure originated one or two cells.

84

00:47:50.500 --> 00:47:53.464 Doug knows the kissing status and

00:47:53.464 --> 00:47:55.440 started providing status started

00:47:55.522 --> 00:47:57.916 the United two more so in there.

00:47:57.920 --> 00:48:01.907 And we're using these kind of tools to map.

00:48:01.910 --> 00:48:05.010 The the molecular mechanism how?

00:48:05.010 --> 00:48:07.689 How diet induce?

00:48:07.690 --> 00:48:09.626 Obviously this is actually a very nice model.

00:48:09.630 --> 00:48:11.470 Also to study metastasis.

00:48:11.470 --> 00:48:13.770 The model can do it.

00:48:13.770 --> 00:48:16.052 You can actually track all this Cape

00:48:16.052 --> 00:48:18.036 and track those cells in different

00:48:18.036 --> 00:48:20.595 colors to see where the mass is being

00:48:20.595 --> 00:48:22.618 caused by the tumor's oriented in

00:48:22.618 --> 00:48:25.250 blue color or unity in jello color.

00:48:25.250 --> 00:48:27.743 And then this can be a stand and be

00:48:27.743 --> 00:48:30.328 using for other kind of tumors as well.

NOTE Confidence: 0.667202877047619

00:48:30.330 --> 00:48:32.130 Then one other thing that we're

NOTE Confidence: 0.667202877047619

00:48:32.130 --> 00:48:34.131 trying to look here is OK where

NOTE Confidence: 0.667202877047619

00:48:34.131 --> 00:48:35.734 you know this could be important.

NOTE Confidence: 0.667202877047619

00:48:35.734 --> 00:48:36.886 That may drive this,

NOTE Confidence: 0.667202877047619

00:48:36.890 --> 00:48:39.170 and this is when we identify 55

NOTE Confidence: 0.667202877047619

00:48:39.170 --> 00:48:41.890 then then in the in the left panel.

NOTE Confidence: 0.667202877047619

00:48:41.890 --> 00:48:43.038 This is uhm again.

NOTE Confidence: 0.667202877047619

00:48:43.038 --> 00:48:45.134 So in the suppression of alpha fetal

NOTE Confidence: 0.667202877047619

00:48:45.134 --> 00:48:47.346 protein and this is a totally restricted

NOTE Confidence: 0.667202877047619

00:48:47.346 --> 00:48:49.649 in most of all the content cells

NOTE Confidence: 0.667202877047619

00:48:49.649 --> 00:48:51.753 that is not actually expressed in

NOTE Confidence: 0.667202877047619

00:48:51.753 --> 00:48:54.658 this adult in the adult hepatocytes.

NOTE Confidence: 0.667202877047619

00:48:54.658 --> 00:48:57.286 Then if I will be 5,

NOTE Confidence: 0.667202877047619

00:48:57.290 --> 00:48:59.618 it's identified here as a very.

NOTE Confidence: 0.667202877047619

00:48:59.620 --> 00:49:01.414 You know remarkable and very specific

NOTE Confidence: 0.667202877047619

00:49:01.414 --> 00:49:03.741 for this tumour cells and and you can

NOTE Confidence: 0.667202877047619

00:49:03.741 --> 00:49:05.660 actually interpret this in the cellar time,

NOTE Confidence: 0.667202877047619

00:49:05.660 --> 00:49:07.028 if I will be 5 here.

NOTE Confidence: 0.667202877047619

00:49:07.030 --> 00:49:08.997 When you import the seller time and

NOTE Confidence: 0.667202877047619

00:49:08.997 --> 00:49:11.251 put here the events in different colors

NOTE Confidence: 0.667202877047619

00:49:11.251 --> 00:49:13.760 again in these dots corresponds to

NOTE Confidence: 0.667202877047619

00:49:13.760 --> 00:49:17.240 the patricide in different diets and

NOTE Confidence: 0.667202877047619

00:49:17.240 --> 00:49:20.299 coming from from different animals with low,

NOTE Confidence: 0.667202877047619

00:49:20.300 --> 00:49:23.135 high or directly from the Patella carcinoma.

NOTE Confidence: 0.667202877047619

00:49:23.140 --> 00:49:25.165 And you can see here that the

NOTE Confidence: 0.667202877047619

00:49:25.165 --> 00:49:27.475 expression of every five in healthy

NOTE Confidence: 0.667202877047619

00:49:27.475 --> 00:49:29.968 liver is pretty much nothing over.

NOTE Confidence: 0.667202877047619

00:49:29.970 --> 00:49:30.741 Very lowest price,

NOTE Confidence: 0.667202877047619

00:49:30.741 --> 00:49:32.909 but then they start to be highly suppressed

NOTE Confidence: 0.667202877047619

00:49:32.909 --> 00:49:34.811 when when the match start developing

NOTE Confidence: 0.667202877047619

00:49:34.811 --> 00:49:37.028 tumors which is actually there came out.

NOTE Confidence: 0.667202877047619

00:49:37.030 --> 00:49:39.262 Very interesting for us because if you want

NOTE Confidence: 0.667202877047619

00:49:39.262 --> 00:49:41.508 to target something or silence something,

NOTE Confidence: 0.667202877047619

00:49:41.510 --> 00:49:42.638 it's better to silence

NOTE Confidence: 0.667202877047619

00:49:42.638 --> 00:49:44.330 something in the liver that is

NOTE Confidence: 0.80565626

00:49:44.386 --> 00:49:46.086 not expressing a healthy tissue.

NOTE Confidence: 0.80565626

00:49:46.090 --> 00:49:48.295 Then you should expect a very low

NOTE Confidence: 0.80565626

00:49:48.295 --> 00:49:51.451 or non non off target effect or

NOTE Confidence: 0.80565626

00:49:51.451 --> 00:49:53.050 the therapeutical intervention.

NOTE Confidence: 0.80565626

00:49:53.050 --> 00:49:54.891 That is something is by expressing the

NOTE Confidence: 0.80565626

00:49:54.891 --> 00:49:56.995 liver and maybe you are messing around

NOTE Confidence: 0.80565626

00:49:56.995 --> 00:49:58.575 with another different function that

NOTE Confidence: 0.80565626

00:49:58.575 --> 00:50:00.408 could be important for other things.

NOTE Confidence: 0.80565626

00:50:00.410 --> 00:50:02.666 And This is why it was very interesting

NOTE Confidence: 0.80565626

00:50:02.666 --> 00:50:04.830 for us to follow at this target.

NOTE Confidence: 0.80565626

00:50:04.830 --> 00:50:06.435 Then then Jonathan went ahead

NOTE Confidence: 0.80565626

00:50:06.435 --> 00:50:08.962 here and try to identify also buy

NOTE Confidence: 0.80565626

00:50:08.962 --> 00:50:10.670 monistat demonstrate expression of

NOTE Confidence: 0.80565626

00:50:10.670 --> 00:50:13.260 F 55 in in in tomorrow's theses

NOTE Confidence: 0.80565626

00:50:13.260 --> 00:50:15.356 animals committee analysis so in very

NOTE Confidence: 0.80565626

00:50:15.356 --> 00:50:17.186 clearly here in the green color.

NOTE Confidence: 0.80565626

00:50:17.190 --> 00:50:19.556 The highest president of 85 and again

NOTE Confidence: 0.80565626

00:50:19.556 --> 00:50:21.507 highly restricted to 2 more when

NOTE Confidence: 0.80565626

00:50:21.507 --> 00:50:23.253 you compare with a healthy agent.

NOTE Confidence: 0.80565626

00:50:23.260 --> 00:50:25.732 Healthy liver in the in the lower in

NOTE Confidence: 0.80565626

00:50:25.732 --> 00:50:29.529 the lower panel and again this this.

NOTE Confidence: 0.80565626

00:50:29.530 --> 00:50:31.206 It's pretty much whistle,

NOTE Confidence: 0.80565626

00:50:31.206 --> 00:50:33.301 so corroborated by Western blot

NOTE Confidence: 0.80565626

00:50:33.301 --> 00:50:35.000 analysis in the right place.

NOTE Confidence: 0.80565626

00:50:35.000 --> 00:50:36.010 As I mentioned to you,

NOTE Confidence: 0.80565626

00:50:36.010 --> 00:50:37.984 and this was very exciting and now

NOTE Confidence: 0.80565626

00:50:37.984 --> 00:50:40.386 when you go to the human teeth that

NOTE Confidence: 0.80565626

00:50:40.386 --> 00:50:44.690 you can see that but you know not only

NOTE Confidence: 0.80565626

00:50:44.690 --> 00:50:48.320 my mentioned before so caustic content.

NOTE Confidence: 0.80565626

00:50:48.320 --> 00:50:49.451 Has high levels.

NOTE Confidence: 0.80565626

00:50:49.451 --> 00:50:52.060 I think that's enough and not

NOTE Confidence: 0.80565626

00:50:52.060 --> 00:50:54.260 only is very elevated,

NOTE Confidence: 0.80565626

00:50:54.260 --> 00:50:57.442 but also the overall survival of

NOTE Confidence: 0.80565626

00:50:57.442 --> 00:51:00.394 the persons with phenomenal at fast,

NOTE Confidence: 0.80565626

00:51:00.400 --> 00:51:02.105 high levels of advice significantly

NOTE Confidence: 0.80565626

00:51:02.105 --> 00:51:03.810 diminished with those that have

NOTE Confidence: 0.80565626

00:51:03.866 --> 00:51:04.630 low expression.

NOTE Confidence: 0.669405791875

00:51:07.400 --> 00:51:10.217 Then then well, what is 55 doing and then

NOTE Confidence: 0.669405791875

00:51:10.217 --> 00:51:12.718 when you start to see the territory?

NOTE Confidence: 0.669405791875

00:51:12.720 --> 00:51:16.972 I'm not only in the context of the cancer,

NOTE Confidence: 0.669405791875

00:51:16.972 --> 00:51:18.676 feel like another field,

NOTE Confidence: 0.669405791875

00:51:18.680 --> 00:51:20.824 you see that you know we have as

NOTE Confidence: 0.669405791875

00:51:20.824 --> 00:51:22.983 many scenes and it's not clear still

NOTE Confidence: 0.669405791875

00:51:22.983 --> 00:51:25.260 is the mechanism of action that can

NOTE Confidence: 0.669405791875

00:51:25.260 --> 00:51:27.228 have passed in the tumor pressing.

NOTE Confidence: 0.669405791875

00:51:27.230 --> 00:51:29.610 Then I tell you be 5 and the renal name

NOTE Confidence: 0.669405791875

00:51:29.677 --> 00:51:32.221 was given like SVP 5 because it's highly

NOTE Confidence: 0.669405791875

00:51:32.221 --> 00:51:34.584 abundant in the epidermis is highly

NOTE Confidence: 0.669405791875

00:51:34.584 --> 00:51:37.230 expressed. Their win was was found.

NOTE Confidence: 0.669405791875

00:51:37.230 --> 00:51:39.678 Uhm, has been associated with multiple

NOTE Confidence: 0.669405791875

00:51:39.678 --> 00:51:40.990 tumors, as I mentioned to you.

NOTE Confidence: 0.669405791875

00:51:40.990 --> 00:51:43.909 Long trusted and then the mechanism faction

NOTE Confidence: 0.669405791875

00:51:43.909 --> 00:51:47.548 that has been ascribed or if it be 5 is,

NOTE Confidence: 0.669405791875

00:51:47.550 --> 00:51:49.965 there are several one of them that

NOTE Confidence: 0.669405791875

00:51:49.965 --> 00:51:51.850 there probably is the most established

NOTE Confidence: 0.669405791875

00:51:51.850 --> 00:51:54.688 is that the F B5 is a little chop

NOTE Confidence: 0.669405791875

00:51:54.688 --> 00:51:56.536 around that binds to this party.

NOTE Confidence: 0.545212474428572

00:51:58.550 --> 00:52:00.242 Particularly by Mary got it appears

NOTE Confidence: 0.545212474428572

00:52:00.242 --> 00:52:03.079 to be a very potent Liam for that and

NOTE Confidence: 0.545212474428572

00:52:03.079 --> 00:52:05.538 activate the people better then and then

NOTE Confidence: 0.545212474428572

00:52:05.538 --> 00:52:07.788 regulate fatty acid synthesis and storage,

NOTE Confidence: 0.545212474428572

00:52:07.790 --> 00:52:10.926 but also regulates a lot preparation as well.

NOTE Confidence: 0.545212474428572

00:52:10.930 --> 00:52:12.906 There were also a number of other papers,

NOTE Confidence: 0.545212474428572

00:52:12.910 --> 00:52:14.498 particularly in San Fran,

NOTE Confidence: 0.545212474428572

00:52:14.498 --> 00:52:17.458 and it appears that they studied the role

NOTE Confidence: 0.545212474428572

00:52:17.458 --> 00:52:19.852 of T cells die actually discovered at

NOTE Confidence: 0.545212474428572

00:52:19.852 --> 00:52:22.890 55 is actually a mitochondrial protein.

NOTE Confidence: 0.545212474428572

00:52:22.890 --> 00:52:24.810 There that maybe the transfer of

NOTE Confidence: 0.545212474428572

00:52:24.810 --> 00:52:27.520 fatty acids and it's important for the

NOTE Confidence: 0.545212474428572

00:52:27.520 --> 00:52:29.790 Christian morphology in the mitochondrion,

NOTE Confidence: 0.545212474428572

00:52:29.790 --> 00:52:31.760 also controlling the fatty oxidation.

NOTE Confidence: 0.545212474428572

00:52:31.760 --> 00:52:32.876 Please dance as well.

NOTE Confidence: 0.545212474428572

00:52:32.876 --> 00:52:34.906 And also there were a number of

00:52:34.906 --> 00:52:36.070 other papers out there.

00:52:36.070 --> 00:52:39.094 Point out that 55 can control

00:52:39.094 --> 00:52:42.350 actually ER and maybe content and

00:52:42.350 --> 00:52:44.550 therefore control translation control.

00:52:44.550 --> 00:52:46.525 Also the activation of standard

00:52:46.525 --> 00:52:48.500 transcription factor that resides in

00:52:48.566 --> 00:52:50.718 the ER and also may regulate as well.

00:52:50.720 --> 00:52:54.577 The ER stress in in these cells.

00:52:54.580 --> 00:52:58.528 Then then we have generated the

00:52:58.530 --> 00:53:00.105 conditional local mass model that

00:53:00.105 --> 00:53:02.748 now are on the diet we we don't know.

00:53:02.750 --> 00:53:05.072 We we're looking forward for the

00:53:05.072 --> 00:53:05.846 genetic model,

00:53:05.850 --> 00:53:08.978 but in the meantime we call out my

00:53:08.978 --> 00:53:11.441 Martin Passando Gemma who got a

00:53:11.441 --> 00:53:13.835 multimillion ground with a group in

NOTE Confidence: 0.545212474428572

00:53:13.918 --> 00:53:16.853 Cold Spring Harbor to use the fighting

NOTE Confidence: 0.545212474428572

00:53:16.853 --> 00:53:20.168 hitters for treating prostate contact.

NOTE Confidence: 0.545212474428572

00:53:20.170 --> 00:53:22.459 Main character is so nice in the

NOTE Confidence: 0.545212474428572

00:53:22.459 --> 00:53:24.880 left the doctor organized the chair.

NOTE Confidence: 0.545212474428572

00:53:24.880 --> 00:53:28.054 Of that chemistry and they developed

NOTE Confidence: 0.545212474428572

00:53:28.054 --> 00:53:30.511 those specific incubators for 75.

NOTE Confidence: 0.545212474428572

00:53:30.511 --> 00:53:33.195 Then we call them Adam, basing the size.

NOTE Confidence: 0.545212474428572

00:53:33.195 --> 00:53:35.470 Large amount of this indicator for us

NOTE Confidence: 0.545212474428572

00:53:35.536 --> 00:53:38.330 for treating the HTC in this model.

NOTE Confidence: 0.545212474428572

00:53:38.330 --> 00:53:40.754 Then the thing that we did here is

NOTE Confidence: 0.545212474428572

00:53:40.754 --> 00:53:42.740 treating blacks eat mice with the

NOTE Confidence: 0.545212474428572

00:53:42.740 --> 00:53:44.708 high fat diet calling defeating diet

NOTE Confidence: 0.545212474428572

00:53:44.770 --> 00:53:45.619 for 12 months,

NOTE Confidence: 0.545212474428572

00:53:45.620 --> 00:53:47.654 then inject the inhibitor and then

NOTE Confidence: 0.545212474428572

00:53:47.654 --> 00:53:50.194 track the two more progression for the

NOTE Confidence: 0.545212474428572

00:53:50.194 --> 00:53:54.820 next demo and evaluate also potential tumor.

NOTE Confidence: 0.545212474428572

00:53:54.820 --> 00:53:58.276 And this is a data that was really incredible

NOTE Confidence: 0.545212474428572

00:53:58.276 --> 00:54:01.208 for us because the the data was stunning.

NOTE Confidence: 0.545212474428572

00:54:01.208 --> 00:54:01.904 I mean,

NOTE Confidence: 0.545212474428572

00:54:01.904 --> 00:54:04.795 we we we were not expecting such

NOTE Confidence: 0.545212474428572

00:54:04.795 --> 00:54:08.119 as a nice outcome in this model.

NOTE Confidence: 0.545212474428572

00:54:08.120 --> 00:54:09.864 The thing that you see here is that

NOTE Confidence: 0.545212474428572

00:54:09.864 --> 00:54:11.922 when you leave the mice to progress

NOTE Confidence: 0.545212474428572

00:54:11.922 --> 00:54:13.487 without treating or vehicle treated,

NOTE Confidence: 0.545212474428572

00:54:13.490 --> 00:54:15.618 you see that again we were able to

NOTE Confidence: 0.545212474428572

00:54:15.618 --> 00:54:17.477 reproduce the data we saw previously.

NOTE Confidence: 0.545212474428572

00:54:17.480 --> 00:54:20.680 That about 50% of the mice developed tumors.

NOTE Confidence: 0.545212474428572

00:54:20.680 --> 00:54:23.950 But when you treat these mice.

NOTE Confidence: 0.545212474428572

00:54:23.950 --> 00:54:26.421 For the last three months and keeping

NOTE Confidence: 0.545212474428572

00:54:26.421 --> 00:54:29.850 the mice and I do see that the two more

NOTE Confidence: 0.545212474428572

00:54:29.850 --> 00:54:31.690 incidents in significantly reviews

NOTE Confidence: 0.545212474428572

00:54:31.690 --> 00:54:34.726 which we only observe only 6 of 20.

NOTE Confidence: 0.545212474428572

00:54:34.730 --> 00:54:35.555 Did not work.

NOTE Confidence: 0.545212474428572

00:54:35.555 --> 00:54:37.480 Even more remarkable is when we actually

NOTE Confidence: 0.545212474428572

00:54:37.531 --> 00:54:39.667 measure that replating anything this nice.

NOTE Confidence: 0.545212474428572

00:54:39.670 --> 00:54:40.114 Yeah,

NOTE Confidence: 0.545212474428572

00:54:40.114 --> 00:54:41.890 you can see that.

NOTE Confidence: 0.545212474428572

00:54:41.890 --> 00:54:45.422 There you see levels increase in the

NOTE Confidence: 0.545212474428572

00:54:45.422 --> 00:54:47.366 mice that progress towards the disease,

NOTE Confidence: 0.545212474428572

00:54:47.370 --> 00:54:50.610 but those miles adapted with the.

NOTE Confidence: 0.545212474428572

00:54:50.610 --> 00:54:54.306 Incubator not only you stop the progression,

NOTE Confidence: 0.545212474428572

00:54:54.306 --> 00:54:56.308 but you see also a regulation of

NOTE Confidence: 0.545212474428572

00:54:56.308 --> 00:54:56.850 these bodies.

NOTE Confidence: 0.545212474428572

00:54:56.850 --> 00:54:59.866 Then this telling us that this

NOTE Confidence: 0.545212474428572

00:54:59.866 --> 00:55:02.746 track price not only preventing

NOTE Confidence: 0.545212474428572

00:55:02.750 --> 00:55:05.870 but it's only private private from

NOTE Confidence: 0.545212474428572

00:55:05.870 --> 00:55:07.526 something that we had to study.

NOTE Confidence: 0.545212474428572

00:55:07.530 --> 00:55:09.840 We had to do further studies with

NOTE Confidence: 0.545212474428572

00:55:09.840 --> 00:55:13.236 imaging and use my miles to to

NOTE Confidence: 0.797661448

00:55:13.240 --> 00:55:16.240 make this as a conclusion.

NOTE Confidence: 0.797661448

00:55:16.240 --> 00:55:19.417 Then you Nathan did a number of studies here,

NOTE Confidence: 0.797661448

00:55:19.420 --> 00:55:21.695 and this summarizing 3 or 4 slides.

NOTE Confidence: 0.797661448

00:55:21.700 --> 00:55:24.400 But this is the pathway analysis

NOTE Confidence: 0.797661448

00:55:24.400 --> 00:55:27.930 that he did in this tumor cells.

NOTE Confidence: 0.797661448

00:55:27.930 --> 00:55:30.079 This is coming also from the single

NOTE Confidence: 0.797661448

00:55:30.079 --> 00:55:31.459 cell RNA transcriptomics as well.

NOTE Confidence: 0.797661448

00:55:31.460 --> 00:55:34.658 Then this is actually restricted to.

NOTE Confidence: 0.797661448

00:55:34.660 --> 00:55:38.531 The the other side within the the phenomena.

NOTE Confidence: 0.797661448

00:55:38.531 --> 00:55:41.128 But things that you can see again is.

NOTE Confidence: 0.797661448

00:55:41.128 --> 00:55:45.032 You see also that the suppression of these

NOTE Confidence: 0.797661448

00:55:45.040 --> 00:55:46.937 five you see an increase in pressure.

NOTE Confidence: 0.797661448

00:55:46.940 --> 00:55:48.684 Someone living metabolism Bedok

NOTE Confidence: 0.797661448

00:55:48.684 --> 00:55:51.690 sedation things that you sit down in

NOTE Confidence: 0.797661448

00:55:51.690 --> 00:55:54.194 the model you start to see higher here.

NOTE Confidence: 0.797661448

00:55:54.200 --> 00:55:58.780 Uhm? He's also a number of.

NOTE Confidence: 0.797661448

00:55:58.780 --> 00:56:01.676 And all that analysis in in human cells.

NOTE Confidence: 0.797661448

00:56:01.680 --> 00:56:05.290 Then this is the the study that he did in

NOTE Confidence: 0.797661448

00:56:05.387 --> 00:56:08.968 in age who is 7 human local cinema line.

NOTE Confidence: 0.797661448

00:56:08.968 --> 00:56:14.158 And try to go even induce you know deeper

NOTE Confidence: 0.797661448

00:56:14.158 --> 00:56:17.650 study here where he treat with inhibitor.

NOTE Confidence: 0.797661448

00:56:17.650 --> 00:56:20.648 These tales for 48 hours and they are

NOTE Confidence: 0.797661448

00:56:20.648 --> 00:56:23.088 not sequencing analysis and again.

NOTE Confidence: 0.797661448

00:56:23.090 --> 00:56:25.449 He found many pathways that it was

NOTE Confidence: 0.797661448

00:56:25.449 --> 00:56:27.876 being out there and one of them that

NOTE Confidence: 0.797661448

00:56:27.876 --> 00:56:30.130 was remarkable clear is that they are

NOTE Confidence: 0.797661448

00:56:30.130 --> 00:56:32.809 stress and I'm going to show you some

NOTE Confidence: 0.797661448

00:56:32.809 --> 00:56:34.429 data regarding that thing appears

00:56:34.429 --> 00:56:36.142 to be significantly up regulated

00:56:36.142 --> 00:56:40.340 in my city with the the typing.

00:56:40.340 --> 00:56:43.176 Then for the Penguin analysis, the the data.

00:56:43.176 --> 00:56:45.528 These data suggest that this incubator

00:56:45.528 --> 00:56:47.823 influence or regulate the pool of

00:56:47.823 --> 00:56:49.658 industrial loan chain fatty acids.

00:56:49.660 --> 00:56:52.495 We are now doing a bit American

00:56:52.495 --> 00:56:55.032 alloces and those tumors and also

00:56:55.032 --> 00:56:56.680 that induced lipid peroxidation

00:56:56.680 --> 00:56:58.328 and free radical accumulation.

00:56:58.330 --> 00:56:59.555 Jonathan follow up is I'm

00:56:59.555 --> 00:57:00.780 going to show you another,

00:57:00.780 --> 00:57:03.020 but he has also data in these cells,

00:57:03.020 --> 00:57:05.456 proving that at the biochemical level

00:57:05.460 --> 00:57:07.224 and also so very clear data showing

00:57:07.224 --> 00:57:08.792 that the oxidative stress also in

NOTE Confidence: 0.797661448

00:57:08.792 --> 00:57:10.316 the US here stressing these tales.

NOTE Confidence: 0.797661448

00:57:10.320 --> 00:57:10.745 Unluckily,

NOTE Confidence: 0.797661448

00:57:10.745 --> 00:57:13.720 this induced cell death in this match.

NOTE Confidence: 0.797661448

00:57:13.720 --> 00:57:16.254 In there in these two more cells.

NOTE Confidence: 0.797661448

00:57:16.260 --> 00:57:19.100 This is the heat map from scientist pathways.

NOTE Confidence: 0.797661448

00:57:19.100 --> 00:57:22.592 You can see that the pair UTR padway being

NOTE Confidence: 0.797661448

00:57:22.592 --> 00:57:24.831 significantly unregulated in the mice.

NOTE Confidence: 0.797661448

00:57:24.831 --> 00:57:26.179 And just to finish,

NOTE Confidence: 0.797661448

00:57:26.180 --> 00:57:28.782 because I'm running out of time, yes,

NOTE Confidence: 0.797661448

00:57:28.782 --> 00:57:32.226 the last couple of slides this is.

NOTE Confidence: 0.797661448

00:57:32.230 --> 00:57:34.414 An example of some of the experiments

NOTE Confidence: 0.797661448

00:57:34.414 --> 00:57:35.350 he did here,

NOTE Confidence: 0.797661448

00:57:35.350 --> 00:57:38.972 and when we did with the cells and she

NOTE Confidence: 0.797661448

00:57:38.972 --> 00:57:41.450 very nicely over with very bad way.

NOTE Confidence: 0.797661448

00:57:41.450 --> 00:57:42.614 And not only that,

00:57:42.614 --> 00:57:44.682 but when he did also understanding here

00:57:44.682 --> 00:57:46.826 with PIE and also an accident to track.

00:57:46.830 --> 00:57:51.398 I felt better so that their treatment with

00:57:51.398 --> 00:57:55.365 the SP FY103 in DSL data higher dose.

00:57:55.370 --> 00:57:55.676 Obviously,

00:57:55.676 --> 00:57:57.818 one thing that we're really must looking

00:57:57.818 --> 00:58:00.446 for ways to the data with the genetic

00:58:00.446 --> 00:58:02.450 model that we're developing right now,

00:58:02.450 --> 00:58:04.550 we know that this inhibitor,

00:58:04.550 --> 00:58:06.335 despite you know they show a high

00:58:06.335 --> 00:58:07.444 efficacy and how specificity

00:58:07.444 --> 00:58:09.160 of inhibitor we know that they

00:58:09.160 --> 00:58:10.888 can have some after that fact,

00:58:10.890 --> 00:58:13.098 and we're trying to combine this with the

00:58:13.098 --> 00:58:15.190 genomic data just to demonstrate the role.

00:58:15.190 --> 00:58:17.914 Sucky role of fighting into more

NOTE Confidence: 0.797661448

00:58:17.914 --> 00:58:19.690 pressing then this is a little

NOTE Confidence: 0.797661448

00:58:19.690 --> 00:58:21.626 bit the summary of this of this

NOTE Confidence: 0.797661448

00:58:21.626 --> 00:58:23.294 work I'm doing so many things,

NOTE Confidence: 0.63618844

00:58:23.300 --> 00:58:25.793 but the thing that we. Trump

NOTE Confidence: 0.63618844

00:58:25.793 --> 00:58:27.958 carries that the suppression of.

NOTE Confidence: 0.4711104252

00:58:30.050 --> 00:58:33.210 Mr accumulation of fatty acid.

NOTE Confidence: 0.4711104252

00:58:33.210 --> 00:58:35.454 Resulting in increasing years, just new

NOTE Confidence: 0.4711104252

00:58:35.454 --> 00:58:37.858 Paris Ponce leading to Apple classes.

NOTE Confidence: 0.4711104252

00:58:37.858 --> 00:58:41.706 This is only like 50% on the part of

NOTE Confidence: 0.4711104252

00:58:41.706 --> 00:58:44.615 the story because the thing that he

NOTE Confidence: 0.4711104252

00:58:44.615 --> 00:58:47.345 Jonathan also observed here is that

NOTE Confidence: 0.4711104252

00:58:47.350 --> 00:58:50.570 not only the inhibitor has a very

NOTE Confidence: 0.4711104252

00:58:50.570 --> 00:58:54.020 important effect controlling the.

NOTE Confidence: 0.4711104252

00:58:54.020 --> 00:58:56.245 And the cancer cell metabolism

NOTE Confidence: 0.4711104252

00:58:56.245 --> 00:58:58.470 reducing this year stress and

NOTE Confidence: 0.4711104252

00:58:58.546 --> 00:59:00.986 and dependent apoptosis in in.

NOTE Confidence: 0.4711104252

00:59:00.986 --> 00:59:03.446 Directly related to other side,

NOTE Confidence: 0.4711104252

00:59:03.450 --> 00:59:05.515 but also he found a very interesting

NOTE Confidence: 0.4711104252

00:59:05.515 --> 00:59:07.639 wire in the two Micron violent.

NOTE Confidence: 0.4711104252

00:59:07.640 --> 00:59:09.053 In these tumors.

NOTE Confidence: 0.4711104252

00:59:09.053 --> 00:59:13.890 One thing that was very clear for the single.

NOTE Confidence: 0.4711104252

00:59:13.890 --> 00:59:17.826 Analysis is that that would be 5 positive.

NOTE Confidence: 0.4711104252

00:59:17.830 --> 00:59:20.248 Macrophage has more kind of and

NOTE Confidence: 0.4711104252

00:59:20.248 --> 00:59:22.737 inflammatory terms and then when you

NOTE Confidence: 0.4711104252

00:59:22.737 --> 00:59:25.143 actually suppress this you leave more.

NOTE Confidence: 0.4711104252

00:59:25.150 --> 00:59:27.382 The formation of 19 presentation failed

NOTE Confidence: 0.4711104252

00:59:27.382 --> 00:59:29.919 that they stimulate more T cells and this.

NOTE Confidence: 0.646646158235294

00:59:32.540 --> 00:59:34.092 Activation have working activity

NOTE Confidence: 0.646646158235294

00:59:34.092 --> 00:59:36.828 on these two more cells and then

NOTE Confidence: 0.646646158235294

00:59:36.828 --> 00:59:38.880 we we think that this inhibitor,

NOTE Confidence: 0.646646158235294

00:59:38.880 --> 00:59:40.300 which is actually very interesting,

NOTE Confidence: 0.646646158235294

00:59:40.300 --> 00:59:41.820 is working in different ways,

NOTE Confidence: 0.646646158235294

00:59:41.820 --> 00:59:44.550 not only reacting in the counterfoils.

NOTE Confidence: 0.646646158235294

00:59:44.550 --> 00:59:48.033 But those show acting at the in the two

NOTE Confidence: 0.646646158235294

00:59:48.033 --> 00:59:51.679 more microenvironment at the level of the

NOTE Confidence: 0.646646158235294

00:59:51.680 --> 00:59:54.356 immune response within the two months.

NOTE Confidence: 0.646646158235294

00:59:54.360 --> 00:59:56.592 Then with this I would like to to

NOTE Confidence: 0.646646158235294

00:59:56.592 --> 00:59:58.419 finish the presentation again.

NOTE Confidence: 0.646646158235294

00:59:58.420 --> 00:59:59.920 I put them in capital letter.

NOTE Confidence: 0.646646158235294

00:59:59.920 --> 01:00:02.720 Jonathan served all the credit for this work.

NOTE Confidence: 0.646646158235294

01:00:02.720 --> 01:00:05.904 He took the challenge to do it and.

NOTE Confidence: 0.646646158235294

01:00:05.910 --> 01:00:08.610 Did many models to study this

NOTE Confidence: 0.646646158235294

01:00:08.610 --> 01:00:10.410 and employing novel technology,

NOTE Confidence: 0.646646158235294

01:00:10.410 --> 01:00:12.797 then then he really did the the

NOTE Confidence: 0.646646158235294

01:00:12.797 --> 01:00:14.873 person who decided credit for this

NOTE Confidence: 0.646646158235294

01:00:14.873 --> 01:00:16.798 work and also my laboratory has

NOTE Confidence: 0.646646158235294

01:00:16.798 --> 01:00:18.383 been actively collaborating all the

NOTE Confidence: 0.646646158235294

01:00:18.383 --> 01:00:21.570 time with the laboratory Suarez.

NOTE Confidence: 0.646646158235294

01:00:21.570 --> 01:00:23.634 I would like to thank so Steven and

NOTE Confidence: 0.646646158235294

01:00:23.634 --> 01:00:25.791 you Meow who are helping us with

NOTE Confidence: 0.646646158235294

01:00:25.791 --> 01:00:27.644 the Murphy's technology to map out

NOTE Confidence: 0.646646158235294

01:00:27.644 --> 01:00:30.045 the special task atomic level with

NOTE Confidence: 0.646646158235294

01:00:30.045 --> 01:00:32.240 this happening in these tumors.

NOTE Confidence: 0.646646158235294

01:00:32.240 --> 01:00:35.150 Also Rachel Berry City than

NOTE Confidence: 0.646646158235294

01:00:35.150 --> 01:00:36.314 unbelievable work.

NOTE Confidence: 0.646646158235294

01:00:36.320 --> 01:00:38.500 Stop trying to show that I'm doing

NOTE Confidence: 0.646646158235294

01:00:38.500 --> 01:00:40.400 the metabolic analysis that happen

NOTE Confidence: 0.646646158235294

01:00:40.400 --> 01:00:42.541 within these tumors with this pinned

NOTE Confidence: 0.646646158235294

01:00:42.541 --> 01:00:44.501 analysis that is doing in her lab

NOTE Confidence: 0.646646158235294

01:00:44.501 --> 01:00:46.720 is fantastic collaboration and also

NOTE Confidence: 0.646646158235294

01:00:46.720 --> 01:00:50.264 marketing Stony Brook for providing

NOTE Confidence: 0.646646158235294

01:00:50.264 --> 01:00:53.162 not only inhibitor but also the FTP

01:00:53.162 --> 01:00:55.237 Firefox miles that they developed

01:00:55.237 --> 01:00:57.960 in the laboratory and with this

01:00:57.960 --> 01:00:59.439 habit technique question.

01:00:59.440 --> 01:00:59.670 So

01:00:59.680 --> 01:01:01.400 thank you very much, Carlos.

01:01:01.400 --> 01:01:03.338 We're a little short on time,

01:01:03.340 --> 01:01:05.979 but there are a couple of questions

01:01:05.979 --> 01:01:09.000 in and why don't we get to those?

01:01:09.000 --> 01:01:11.457 So the first is based on your mouse model.

01:01:11.460 --> 01:01:13.722 Do you have any explanation why

01:01:13.722 --> 01:01:16.277 Nash related liver cancer is less

01:01:16.277 --> 01:01:18.221 responsive to tyrosine kinase

01:01:18.221 --> 01:01:19.679 inhibitors or immunotherapy?

01:01:19.680 --> 01:01:21.400 Then viral related patterns

01:01:21.400 --> 01:01:22.690 cited against her.

NOTE Confidence: 0.803543863333334

01:01:23.720 --> 01:01:25.028 Well, I think it's a great.

NOTE Confidence: 0.803543863333334

01:01:25.030 --> 01:01:26.200 I think it's a great question

NOTE Confidence: 0.803543863333334

01:01:26.200 --> 01:01:27.688 and I think we will take note

NOTE Confidence: 0.803543863333334

01:01:27.688 --> 01:01:29.014 of that because I didn't know.

NOTE Confidence: 0.803543863333334

01:01:29.020 --> 01:01:31.432 But the thing that we see is a very

NOTE Confidence: 0.803543863333334

01:01:31.432 --> 01:01:33.560 strong component in the muni response

NOTE Confidence: 0.803543863333334

01:01:33.560 --> 01:01:35.990 in these tumors with high fat diet,

NOTE Confidence: 0.803543863333334

01:01:35.990 --> 01:01:38.018 we don't think that they discuss

NOTE Confidence: 0.803543863333334

01:01:38.018 --> 01:01:39.987 actually with with Jonathan is to

NOTE Confidence: 0.803543863333334

01:01:39.987 --> 01:01:41.919 look into the other data from Michael,

NOTE Confidence: 0.803543863333334

01:01:41.920 --> 01:01:44.476 Karen and others that use models

NOTE Confidence: 0.803543863333334

01:01:44.476 --> 01:01:46.596 of cathedral in induced coma

NOTE Confidence: 0.803543863333334

01:01:46.596 --> 01:01:48.260 and just to compare,

NOTE Confidence: 0.803543863333334

01:01:48.260 --> 01:01:51.669 where are the immune landscape in these

NOTE Confidence: 0.803543863333334

01:01:51.669 --> 01:01:55.088 tumors compared with the high fidelity user?

NOTE Confidence: 0.803543863333334

01:01:55.090 --> 01:01:57.267 Then, and this is a great question,

NOTE Confidence: 0.803543863333334

01:01:57.270 --> 01:02:01.715 then about the map kinase we got.

NOTE Confidence: 0.803543863333334

01:02:01.720 --> 01:02:05.280 We got a pilot grants here at the L

NOTE Confidence: 0.803543863333334

01:02:05.280 --> 01:02:07.492 and we partner with Anthony Bennett

NOTE Confidence: 0.803543863333334

01:02:07.492 --> 01:02:10.054 who actually work in mechanics and then

NOTE Confidence: 0.803543863333334

01:02:10.054 --> 01:02:13.129 we are looking in this pilot for the

NOTE Confidence: 0.803543863333334

01:02:13.129 --> 01:02:14.900 transition between novelty and mass,

NOTE Confidence: 0.803543863333334

01:02:14.900 --> 01:02:16.440 but the part of the things that

NOTE Confidence: 0.803543863333334

01:02:16.440 --> 01:02:17.993 they are going to study is with

NOTE Confidence: 0.803543863333334

01:02:17.993 --> 01:02:19.550 issues that we have in this nice.

NOTE Confidence: 0.803543863333334

01:02:19.550 --> 01:02:21.538 We're going to look how all these

NOTE Confidence: 0.803543863333334

01:02:21.538 --> 01:02:23.182 mechanics activity is being affected

NOTE Confidence: 0.803543863333334

01:02:23.182 --> 01:02:25.017 during the transition of friendliness

NOTE Confidence: 0.803543863333334

01:02:25.017 --> 01:02:26.560 and potentially in the cinema,

NOTE Confidence: 0.803543863333334

01:02:26.560 --> 01:02:27.940 but both both are great questions

NOTE Confidence: 0.803543863333334

01:02:27.940 --> 01:02:29.469 and we are looking into that.

NOTE Confidence: 0.636165254444444

01:02:30.160 --> 01:02:33.715 And in that question was from her to Chow,

NOTE Confidence: 0.636165254444444

01:02:33.720 --> 01:02:36.776 and this is from Claire Flannery great talk.

NOTE Confidence: 0.636165254444444

01:02:36.780 --> 01:02:39.522 Thank you. We're experiments for HTC

NOTE Confidence: 0.636165254444444

01:02:39.522 --> 01:02:41.790 development done in female mice.

NOTE Confidence: 0.636165254444444

01:02:41.790 --> 01:02:44.598 If so, were there any difference in HTC

NOTE Confidence: 0.636165254444444

01:02:44.598 --> 01:02:46.749 development time relative to male mice?

NOTE Confidence: 0.618185414

01:02:47.280 --> 01:02:48.522 Well, great question also and I

NOTE Confidence: 0.618185414

01:02:48.522 --> 01:02:49.944 think and I think it's a great

NOTE Confidence: 0.618185414

01:02:49.944 --> 01:02:51.066 question because you know today

NOTE Confidence: 0.618185414

01:02:51.066 --> 01:02:52.518 that the user not granted NIH.

NOTE Confidence: 0.618185414

01:02:52.520 --> 01:02:54.080 You have to have both. Then.

NOTE Confidence: 0.865495698571429

01:02:55.380 --> 01:02:56.486 Then I want to point out that

NOTE Confidence: 0.786601756428571

01:02:56.500 --> 01:02:58.215 we did this experiment with with money

NOTE Confidence: 0.786601756428571

01:02:58.215 --> 01:03:00.178 that it was not supported by grants.

NOTE Confidence: 0.786601756428571

01:03:00.180 --> 01:03:01.800 And obviously I mean you can.

NOTE Confidence: 0.786601756428571

01:03:01.800 --> 01:03:03.520 You can analyze the standard.

NOTE Confidence: 0.786601756428571

01:03:03.520 --> 01:03:04.940 The study take two years,

NOTE Confidence: 0.786601756428571

01:03:04.940 --> 01:03:07.685 but I'm going to be short in the answer.

NOTE Confidence: 0.786601756428571

01:03:07.690 --> 01:03:09.300 We need only in males,

NOTE Confidence: 0.786601756428571

01:03:09.300 --> 01:03:11.040 but will be extremely interesting

NOTE Confidence: 0.786601756428571

01:03:11.040 --> 01:03:12.780 to do in females then.

NOTE Confidence: 0.786601756428571

01:03:12.780 --> 01:03:14.876 Then we did some experiments in female there.

NOTE Confidence: 0.786601756428571

01:03:14.880 --> 01:03:16.710 Rainbow studies were done in females

NOTE Confidence: 0.786601756428571

01:03:16.710 --> 01:03:19.241 and the two more incidents actually in

NOTE Confidence: 0.786601756428571

01:03:19.241 --> 01:03:21.737 females are significantly lower than males.

NOTE Confidence: 0.786601756428571

01:03:21.740 --> 01:03:24.305 OK, then you have to wait even like two

NOTE Confidence: 0.786601756428571

01:03:24.305 --> 01:03:26.612 years in high fat diet and the tumor

NOTE Confidence: 0.786601756428571

01:03:26.612 --> 01:03:29.390 extent is not the thing that you see in then.

NOTE Confidence: 0.786601756428571

01:03:29.390 --> 01:03:31.130 It's difference in male and females.

NOTE Confidence: 0.786601756428571

01:03:31.130 --> 01:03:34.603 This has been shown this in modern cinema.

NOTE Confidence: 0.786601756428571

01:03:34.603 --> 01:03:36.660 In mice I I know, I know,

01:03:36.660 --> 01:03:38.375 much aware about the literature in human,

01:03:38.380 --> 01:03:40.900 I should be more aware now after I

01:03:40.900 --> 01:03:43.252 sent him again, I will read more,

01:03:43.252 --> 01:03:46.750 but but at least in mouse models OK?

01:03:46.750 --> 01:03:50.224 Because being shown that in in in the in

01:03:50.224 --> 01:03:53.471 other models the females asked happen

01:03:53.471 --> 01:03:56.727 here develop significantly as less tumors,

01:03:56.727 --> 01:04:00.066 and this has been associated in part

01:04:00.070 --> 01:04:02.968 to the adipose tissue production of

01:04:02.968 --> 01:04:05.450 adiponectin and another or modes.

01:04:05.450 --> 01:04:07.226 Then it's not clear whether this

01:04:07.226 --> 01:04:08.410 is translated to human,

01:04:08.410 --> 01:04:10.601 but looks at all the depots that

01:04:10.601 --> 01:04:12.645 are different fat depots that are

01:04:12.645 --> 01:04:14.761 different in male and female appears

01:04:14.761 --> 01:04:17.107 to be affecting the hormone secretion.

NOTE Confidence: 0.786601756428571

01:04:17.110 --> 01:04:19.590 It has an impact on the tumor formation,

NOTE Confidence: 0.786601756428571

01:04:19.590 --> 01:04:20.714 at least in mice.

NOTE Confidence: 0.786601756428571

01:04:20.714 --> 01:04:23.210 Then then it's a great question we should do.

NOTE Confidence: 0.786601756428571

01:04:23.210 --> 01:04:25.149 We have the rainbow Maes was done

NOTE Confidence: 0.786601756428571

01:04:25.149 --> 01:04:27.218 in females and This is why I tell

NOTE Confidence: 0.786601756428571

01:04:27.218 --> 01:04:29.077 you that in this model the two

NOTE Confidence: 0.786601756428571

01:04:29.077 --> 01:04:30.742 more incidences is less, but yes,

NOTE Confidence: 0.786601756428571

01:04:30.742 --> 01:04:32.038 I mean we should actually try

NOTE Confidence: 0.786601756428571

01:04:32.038 --> 01:04:33.009 to do them more,

NOTE Confidence: 0.786601756428571

01:04:33.010 --> 01:04:33.260 yeah?

NOTE Confidence: 0.845287186

01:04:34.090 --> 01:04:35.240 Well, there are other questions,

NOTE Confidence: 0.845287186

01:04:35.240 --> 01:04:36.703 but I think we're gonna have to

NOTE Confidence: 0.845287186

01:04:36.703 --> 01:04:38.030 end because it's five after one.

NOTE Confidence: 0.63971587

01:04:38.280 --> 01:04:40.416 You guys can send me by my email.

NOTE Confidence: 0.63971587

01:04:40.420 --> 01:04:42.048 Yeah, thank you. Yeah

NOTE Confidence: 0.755850848

01:04:42.460 --> 01:04:43.870 thanks thanks so much thanks.

NOTE Confidence: 0.755850848

01:04:43.870 --> 01:04:45.660 Thanks to thank you Carlos.

NOTE Confidence: 0.755850848

01:04:45.660 --> 01:04:47.928 And thanks to both of our speakers.

NOTE Confidence: 0.755850848

01:04:47.930 --> 01:04:48.930 See you all next week.