WEBVTT

NOTE duration:"00:58:47"

NOTE recognizability:0.803

NOTE language:en-us

NOTE Confidence: 0.896058158181818

00:00:00.000 --> 00:00:02.440 Good afternoon everyone. Welcome to

NOTE Confidence: 0.896058158181818

00:00:02.440 --> 00:00:05.500 the Yale Cancer Center grand rounds.

NOTE Confidence: 0.896058158181818

00:00:05.500 --> 00:00:08.391 Today we have two fantastic speakers both

NOTE Confidence: 0.896058158181818

00:00:08.391 --> 00:00:11.440 who are in the developmental therapeutics

NOTE Confidence: 0.896058158181818

00:00:11.440 --> 00:00:14.884 program of the Yale Cancer Center.

NOTE Confidence: 0.896058158181818

00:00:14.890 --> 00:00:16.348 And why don't we get started?

NOTE Confidence: 0.896058158181818

00:00:16.350 --> 00:00:18.086 I'm delighted to introduce

NOTE Confidence: 0.896058158181818

00:00:18.086 --> 00:00:19.388 Doctor James Farrell,

NOTE Confidence: 0.896058158181818

00:00:19.390 --> 00:00:21.630 who is a professor of medicine in

NOTE Confidence: 0.896058158181818

00:00:21.630 --> 00:00:23.970 the director of the Yale Center

NOTE Confidence: 0.896058158181818

00:00:23.970 --> 00:00:25.278 for Pancreatic Diseases.

NOTE Confidence: 0.896058158181818

00:00:25.280 --> 00:00:27.168 He's an internationally recognized,

NOTE Confidence: 0.896058158181818

00:00:27.168 --> 00:00:29.056 expert and pancreatic disease

NOTE Confidence: 0.896058158181818

00:00:29.056 --> 00:00:30.308 treatment and research,

NOTE Confidence: 0.896058158181818

00:00:30.308 --> 00:00:33.031 and is known for his development of

NOTE Confidence: 0.896058158181818

00:00:33.031 --> 00:00:34.904 personalized therapy approaches for

NOTE Confidence: 0.896058158181818

00:00:34.904 --> 00:00:37.259 pancreatic cancer and early detection

NOTE Confidence: 0.896058158181818

00:00:37.259 --> 00:00:39.400 biomarkers for pancreatic cancer.

NOTE Confidence: 0.896058158181818

00:00:39.400 --> 00:00:41.200 He received his medical medical

NOTE Confidence: 0.896058158181818

00:00:41.200 --> 00:00:42.640 degree from University College

NOTE Confidence: 0.896058158181818

00:00:42.640 --> 00:00:44.187 Dublin and completed internal

NOTE Confidence: 0.896058158181818

00:00:44.187 --> 00:00:46.077 medicine training at Johns Hopkins.

NOTE Confidence: 0.896058158181818

00:00:46.080 --> 00:00:48.120 And a gastroenterology fellowship

NOTE Confidence: 0.896058158181818

00:00:48.120 --> 00:00:51.186 at MGH and Harvard Medical School.

NOTE Confidence: 0.896058158181818

00:00:51.186 --> 00:00:53.692 He then completed advanced Therapeutic

NOTE Confidence: 0.896058158181818

00:00:53.692 --> 00:00:55.684 Endoscopy fellowship training at

NOTE Confidence: 0.896058158181818

00:00:55.684 --> 00:00:58.220 mass General and Brigham and Women's,

NOTE Confidence: 0.896058158181818

00:00:58.220 --> 00:00:59.795 in addition to his clinical

NOTE Confidence: 0.896058158181818

00:00:59.795 --> 00:01:01.055 practice and pancreatic disease

NOTE Confidence: 0.896058158181818

00:01:01.055 --> 00:01:02.679 and interventional endoscopy.

NOTE Confidence: 0.896058158181818

00:01:02.680 --> 00:01:05.194 His clinical research has focused on

NOTE Confidence: 0.896058158181818

00:01:05.194 --> 00:01:07.380 early detection of pancreatic cancer,

NOTE Confidence: 0.896058158181818

00:01:07.380 --> 00:01:09.030 including studying pancreatitis,

NOTE Confidence: 0.896058158181818

00:01:09.030 --> 00:01:12.330 high risk individuals and pancreatic cysts.

NOTE Confidence: 0.896058158181818

00:01:12.330 --> 00:01:14.520 His translational research includes the

NOTE Confidence: 0.896058158181818

00:01:14.520 --> 00:01:16.272 development of personalized therapy.

NOTE Confidence: 0.896058158181818

00:01:16.280 --> 00:01:18.056 Approaches for pancreatic cancer

NOTE Confidence: 0.896058158181818

00:01:18.056 --> 00:01:20.276 and the evaluation of biomarkers

NOTE Confidence: 0.896058158181818

00:01:20.276 --> 00:01:22.009 and pancreatic disease.

NOTE Confidence: 0.896058158181818

00:01:22.010 --> 00:01:24.110 Delighted to turn it over to you

NOTE Confidence: 0.896058158181818

00:01:24.110 --> 00:01:25.664 Doctor Farrell and look forward

NOTE Confidence: 0.896058158181818

00:01:25.664 --> 00:01:27.722 to hearing what you have to say.

NOTE Confidence: 0.896058158181818

00:01:27.730 --> 00:01:28.710 Thank you.

NOTE Confidence: 0.638810976

00:01:29.390 --> 00:01:32.650 Thanks everyone and good afternoon.

NOTE Confidence: 0.638810976

00:01:32.650 --> 00:01:33.530 Thanks for the invitation.

NOTE Confidence: 0.638810976

00:01:33.530 --> 00:01:34.630 So we're going to talk

NOTE Confidence: 0.638810976

00:01:34.630 --> 00:01:35.620 about pancreatic cancer,

NOTE Confidence: 0.638810976

00:01:35.620 --> 00:01:38.710 early detection prevention this morning.

NOTE Confidence: 0.638810976

00:01:38.710 --> 00:01:40.702 It really is going to be an overview

NOTE Confidence: 0.638810976

00:01:40.702 --> 00:01:42.517 in the time allotted and kind

NOTE Confidence: 0.638810976

00:01:42.517 --> 00:01:44.395 of emphasizing some of the work

NOTE Confidence: 0.638810976

00:01:44.458 --> 00:01:46.198 that we've been involved with.

NOTE Confidence: 0.638810976

00:01:46.200 --> 00:01:48.270 Disclosures.

NOTE Confidence: 0.638810976

00:01:48.270 --> 00:01:49.674 So when you think about pancreatic

NOTE Confidence: 0.638810976

00:01:49.674 --> 00:01:51.449 cancer in terms of overall incidence,

NOTE Confidence: 0.638810976

00:01:51.450 --> 00:01:53.200 it's actually low down in the list,

NOTE Confidence: 0.638810976

00:01:53.200 --> 00:01:55.132 and maybe sometimes doesn't get as

NOTE Confidence: 0.638810976

00:01:55.132 --> 00:01:56.762 much prominence as other cancers

NOTE Confidence: 0.638810976

00:01:56.762 --> 00:01:58.764 such as prostate or lung or colon.

NOTE Confidence: 0.638810976

00:01:58.770 --> 00:02:00.786 But when you look at cancer related deaths,

NOTE Confidence: 0.638810976

00:02:00.790 --> 00:02:01.810 it jumps up the list,

NOTE Confidence: 0.638810976

00:02:01.810 --> 00:02:03.805 and it's probably around the

NOTE Confidence: 0.638810976

00:02:03.805 --> 00:02:05.800 third or fourth most common

NOTE Confidence: 0.638810976

00:02:05.872 --> 00:02:08.007 cause of cancer related death.

NOTE Confidence: 0.638810976

00:02:08.010 --> 00:02:09.306 So in 2022,

NOTE Confidence: 0.638810976

00:02:09.306 --> 00:02:11.466 it's estimated there'll be about

NOTE Confidence: 0.638810976

00:02:11.470 --> 00:02:13.750 62,000 cases and just under 50,000

NOTE Confidence: 0.638810976

00:02:13.750 --> 00:02:16.787 deaths related to it and has long been

NOTE Confidence: 0.638810976

00:02:16.787 --> 00:02:19.570 predicted and certainly on its way by 2030,

NOTE Confidence: 0.638810976

00:02:19.570 --> 00:02:22.034 it's expected to be the second most

NOTE Confidence: 0.638810976

00:02:22.034 --> 00:02:25.469 common cause for cancer related death.

NOTE Confidence: 0.638810976

00:02:25.470 --> 00:02:27.036 It also needs to be emphasized.

NOTE Confidence: 0.638810976

00:02:27.040 --> 00:02:28.180 The fact that yes,

NOTE Confidence: 0.638810976

00:02:28.180 --> 00:02:29.320 there have been improvements

NOTE Confidence: 0.638810976

00:02:29.320 --> 00:02:31.154 in the management and treatment

NOTE Confidence: 0.638810976

00:02:31.154 --> 00:02:32.366 of pancreatic cancer,

NOTE Confidence: 0.638810976

00:02:32.370 --> 00:02:32.842 but really,

NOTE Confidence: 0.638810976

00:02:32.842 --> 00:02:33.786 they have fallen short,

NOTE Confidence: 0.638810976

00:02:33.790 --> 00:02:35.186 although progress still continues

NOTE Confidence: 0.638810976

00:02:35.186 --> 00:02:37.630 to be made and just emphasizing the

NOTE Confidence: 0.638810976

00:02:37.630 --> 00:02:39.660 need for a better and improved early

NOTE Confidence: 0.638810976

00:02:39.660 --> 00:02:41.589 detection for this particular disease.

NOTE Confidence: 0.638810976

00:02:41.590 --> 00:02:44.020 If we're hoping to improve

NOTE Confidence: 0.638810976

00:02:44.020 --> 00:02:45.478 the overall survival.

NOTE Confidence: 0.638810976

00:02:45.480 --> 00:02:45.794 Now,

NOTE Confidence: 0.638810976

00:02:45.794 --> 00:02:47.678 there has been tremendous progress in

NOTE Confidence: 0.638810976

00:02:47.678 --> 00:02:49.880 the world of understanding cancer,

NOTE Confidence: 0.638810976

00:02:49.880 --> 00:02:51.524 biology of pancreatic cancer.

NOTE Confidence: 0.638810976

00:02:51.524 --> 00:02:52.757 Along the bottom,

NOTE Confidence: 0.638810976

00:02:52.760 --> 00:02:55.004 here is a normal progression through

NOTE Confidence: 0.638810976

00:02:55.004 --> 00:02:57.338 low grade and high grade dysplasia

NOTE Confidence: 0.638810976

00:02:57.338 --> 00:03:00.005 or so called pen and lesions to

NOTE Confidence: 0.638810976

00:03:00.005 --> 00:03:02.708 invasive pancreatic ductal adenocarcinoma.

NOTE Confidence: 0.638810976

00:03:02.710 --> 00:03:05.010 It always typically starts with

NOTE Confidence: 0.638810976

00:03:05.010 --> 00:03:07.310 the activation of an oncogene,

NOTE Confidence: 0.638810976

00:03:07.310 --> 00:03:09.220 and then it's been several

NOTE Confidence: 0.638810976

00:03:09.220 --> 00:03:10.748 well known characterized tumor

NOTE Confidence: 0.638810976

00:03:10.748 --> 00:03:12.039 suppressor gene mutations,

NOTE Confidence: 0.638810976

00:03:12.040 --> 00:03:15.670 including P53 and SMAD 4.

NOTE Confidence: 0.638810976

00:03:15.670 --> 00:03:17.740 It's also worth noticing that related

NOTE Confidence: 0.638810976

00:03:17.740 --> 00:03:20.469 to this is another entity of the

NOTE Confidence: 0.638810976

00:03:20.469 --> 00:03:22.599 pancreas called Ipmn or introductive

NOTE Confidence: 0.638810976

00:03:22.599 --> 00:03:24.070 papillary mucinous neoplasm.

NOTE Confidence: 0.638810976

00:03:24.070 --> 00:03:26.555 It also goes through a similar sequence,

NOTE Confidence: 0.638810976

00:03:26.560 --> 00:03:29.040 resulting in an invasive neoplasm

NOTE Confidence: 0.638810976

00:03:29.040 --> 00:03:31.410 with similar mutations, such as in K.

NOTE Confidence: 0.638810976

00:03:31.410 --> 00:03:32.920 Ras, but also some unique ones.

NOTE Confidence: 0.638810976

00:03:32.920 --> 00:03:35.935 Which is Gina Genas uncle

NOTE Confidence: 0.638810976

00:03:35.935 --> 00:03:37.744 Gene observation activation,

NOTE Confidence: 0.638810976

00:03:37.750 --> 00:03:39.507 but it's very hard to talk about.

NOTE Confidence: 0.89824665625

00:03:42.840 --> 00:03:44.688 Carcinoma without without talking

NOTE Confidence: 0.89824665625

00:03:44.688 --> 00:03:48.710 about the other disease of ipmn.

NOTE Confidence: 0.89824665625

00:03:48.710 --> 00:03:50.095 It's also worth making the

NOTE Confidence: 0.89824665625

00:03:50.095 --> 00:03:51.203 point that this progression,

NOTE Confidence: 0.89824665625

00:03:51.210 --> 00:03:53.106 we think from the initial K.

NOTE Confidence: 0.89824665625

00:03:53.110 --> 00:03:55.318 Ras mutation to the time of

NOTE Confidence: 0.89824665625

00:03:55.318 --> 00:03:56.790 let's say metastatic cancer,

NOTE Confidence: 0.89824665625

00:03:56.790 --> 00:03:58.855 is probably of the region

NOTE Confidence: 0.89824665625

00:03:58.855 --> 00:04:01.549 of of about 11 years or so.

NOTE Confidence: 0.89824665625

00:04:01.550 --> 00:04:03.470 And so this number is debatable.

NOTE Confidence: 0.89824665625

00:04:03.470 --> 00:04:05.454 But basically it's a long time for us

NOTE Confidence: 0.89824665625

00:04:05.454 --> 00:04:07.496 to try and intervene and understand

NOTE Confidence: 0.89824665625

00:04:07.496 --> 00:04:09.728 what's going on during this sequence.

NOTE Confidence: 0.89824665625

00:04:09.730 --> 00:04:11.945 However, it's also worth noting

NOTE Confidence: 0.89824665625

00:04:11.945 --> 00:04:14.682 that in its early stages and pre

NOTE Confidence: 0.89824665625

00:04:14.682 --> 00:04:16.210 invasive stages with pannin,

NOTE Confidence: 0.89824665625

00:04:16.210 --> 00:04:17.690 it typically can't be seen.

NOTE Confidence: 0.89824665625

00:04:17.690 --> 00:04:18.160 Radiologically,

NOTE Confidence: 0.89824665625

00:04:18.160 --> 00:04:21.450 when an early stage cancer does arise,

NOTE Confidence: 0.89824665625

00:04:21.450 --> 00:04:24.558 this can be seen by radiologic imaging,

NOTE Confidence: 0.89824665625

00:04:24.560 --> 00:04:26.919 but in the time required to go

NOTE Confidence: 0.89824665625

00:04:26.919 --> 00:04:29.029 from an early stage, resectable,

NOTE Confidence: 0.89824665625

00:04:29.029 --> 00:04:31.265 surgically manageable pancreatic cancer

NOTE Confidence: 0.89824665625

00:04:31.265 --> 00:04:34.386 to an advanced metastatic stage can

NOTE Confidence: 0.89824665625

00:04:34.386 --> 00:04:37.330 be as short as one to 1 1/2 years, and so.

NOTE Confidence: 0.89824665625

00:04:37.330 --> 00:04:38.290 At that point,

NOTE Confidence: 0.89824665625

00:04:38.290 --> 00:04:40.040 the clock does start ticking.

NOTE Confidence: 0.89824665625

00:04:40.040 --> 00:04:42.839 And it brings up the issue of missed cancers,

NOTE Confidence: 0.89824665625

00:04:42.840 --> 00:04:43.764 interval cancers,

NOTE Confidence: 0.89824665625

00:04:43.764 --> 00:04:46.998 cancers that may be seen on imaging

NOTE Confidence: 0.89824665625

00:04:46.998 --> 00:04:50.175 with more advanced uses of of imaging.

NOTE Confidence: 0.89824665625

00:04:50.180 --> 00:04:52.628 Now there's no shortage of biomarker

NOTE Confidence: 0.89824665625

00:04:52.628 --> 00:04:54.740 signatures for early pancreatic cancer.

NOTE Confidence: 0.89824665625

00:04:54.740 --> 00:04:57.620 This is just a selection of of some of these,

NOTE Confidence: 0.89824665625

00:04:57.620 --> 00:05:00.124 and they all have very promising

NOTE Confidence: 0.89824665625

00:05:00.124 --> 00:05:03.500 operating characteristics or AUC.

NOTE Confidence: 0.89824665625

00:05:03.500 --> 00:05:05.612 So in the top left is a salivary

NOTE Confidence: 0.89824665625

00:05:05.612 --> 00:05:08.309 based 4 gene panel of RNA that we

NOTE Confidence: 0.89824665625

00:05:08.309 --> 00:05:10.172 worked with again comparing non

NOTE Confidence: 0.89824665625

00:05:10.172 --> 00:05:12.152 cancers to patients with cancers

NOTE Confidence: 0.89824665625

00:05:12.152 --> 00:05:16.818 with a very respectable AUC of .97.

NOTE Confidence: 0.89824665625

00:05:16.820 --> 00:05:19.557 Below is a work of Anoop Sharma.

NOTE Confidence: 0.89824665625

00:05:19.560 --> 00:05:21.930 He said who Jim looking at?

NOTE Confidence: 0.89824665625

00:05:21.930 --> 00:05:23.055 DNA methylation markers?

NOTE Confidence: 0.89824665625

00:05:23.055 --> 00:05:25.680 And this is a particular 4 gene

NOTE Confidence: 0.89824665625

00:05:25.753 --> 00:05:27.898 cell free DNA methylation panel,

NOTE Confidence: 0.89824665625

00:05:27.900 --> 00:05:31.687 again with very respectable AU C curves.

NOTE Confidence: 0.89824665625

00:05:31.690 --> 00:05:33.466 We've kind of come to the age in

NOTE Confidence: 0.89824665625

00:05:33.470 --> 00:05:36.186 2022 where we now have the beginning

NOTE Confidence: 0.89824665625

00:05:36.186 --> 00:05:37.860 of commercially available panels,

NOTE Confidence: 0.89824665625

00:05:37.860 --> 00:05:40.686 not just for cancer in general,

NOTE Confidence: 0.89824665625

00:05:40.690 --> 00:05:42.139 so you have heard of GRAIL and

NOTE Confidence: 0.89824665625

00:05:42.139 --> 00:05:43.349 you've heard of cancer seek,

NOTE Confidence: 0.89824665625

00:05:43.350 --> 00:05:46.310 but now Innovia has an imray pan candy,

NOTE Confidence: 0.89824665625

00:05:46.310 --> 00:05:48.765 which is an antibody panel

NOTE Confidence: 0.89824665625

00:05:48.765 --> 00:05:50.729 specifically for pancreatic cancer,

NOTE Confidence: 0.89824665625

00:05:50.730 --> 00:05:53.376 and in the studies to date at

NOTE Confidence: 0.89824665625

00:05:53.376 --> 00:05:55.721 least shows very promising AUC's

NOTE Confidence: 0.89824665625

00:05:55.721 --> 00:05:57.245 for the differentiation between

NOTE Confidence: 0.89824665625

00:05:57.245 --> 00:05:59.150 early stage cancer and control.

NOTE Confidence: 0.89824665625

00:05:59.150 --> 00:05:59.957 And in fact,

NOTE Confidence: 0.89824665625

00:05:59.957 --> 00:06:01.302 this is being currently tested

NOTE Confidence: 0.89824665625

00:06:01.302 --> 00:06:02.459 in a high risk.

NOTE Confidence: 0.89824665625

00:06:02.460 --> 00:06:04.450 Population the Pantheon One study

NOTE Confidence: 0.89824665625

00:06:04.450 --> 00:06:06.440 in which we're involved with

NOTE Confidence: 0.89824665625

00:06:06.506 --> 00:06:08.690 results of which will be out soon.

NOTE Confidence: 0.89824665625

00:06:08.690 --> 00:06:10.240 But the problem is yes,

NOTE Confidence: 0.89824665625

00:06:10.240 --> 00:06:11.760 there are all these great

NOTE Confidence: 0.89824665625

00:06:11.760 --> 00:06:12.368 biomarker signatures,

NOTE Confidence: 0.89824665625

00:06:12.370 --> 00:06:14.218 but they're not being applied or can't

NOTE Confidence: 0.89824665625

00:06:14.218 --> 00:06:16.229 be applied to the general population.

NOTE Confidence: 0.89824665625

00:06:16.230 --> 00:06:18.921 And this has to do with an issue of

NOTE Confidence: 0.89824665625

00:06:18.921 --> 00:06:20.660 mathematics and the 1.6 lifetime risk,

NOTE Confidence: 0.89824665625

00:06:20.660 --> 00:06:21.590 and the low,

NOTE Confidence: 0.89824665625

00:06:21.590 --> 00:06:23.153 relatively low prevalence

NOTE Confidence: 0.89824665625

00:06:23.153 --> 00:06:24.716 of pancreatic cancer.

NOTE Confidence: 0.89824665625

00:06:24.720 --> 00:06:26.936 What that means is that even with a

NOTE Confidence: 0.89824665625

00:06:26.936 --> 00:06:29.280 very good sensitivity and specificity,

NOTE Confidence: 0.89824665625

00:06:29.280 --> 00:06:31.266 whereas you have a very high

NOTE Confidence: 0.89824665625

00:06:31.266 --> 00:06:32.259 negative predictive value,

NOTE Confidence: 0.89824665625

00:06:32.260 --> 00:06:34.285 you have a very low

NOTE Confidence: 0.89824665625

00:06:34.285 --> 00:06:35.500 positive predictive value.

NOTE Confidence: 0.89824665625

00:06:35.500 --> 00:06:37.720 And even as you increase the

NOTE Confidence: 0.89824665625

00:06:37.720 --> 00:06:39.669 sensitivity and specificity of these

NOTE Confidence: 0.89824665625

00:06:39.669 --> 00:06:41.659 tests in the general population,

NOTE Confidence: 0.89824665625

00:06:41.660 --> 00:06:43.164 the positive predictive value

NOTE Confidence: 0.89824665625

00:06:43.164 --> 00:06:45.760 only gets as good as about 20%.

NOTE Confidence: 0.89824665625

00:06:45.760 --> 00:06:47.792 And what that means is that most of

NOTE Confidence: 0.89824665625

00:06:47.792 --> 00:06:49.541 the positive tests that you're going

NOTE Confidence: 0.89824665625

00:06:49.541 --> 00:06:51.317 to see in the general population

NOTE Confidence: 0.892557816785714

00:06:51.377 --> 00:06:53.545 will turn out to be false positive tests,

NOTE Confidence: 0.892557816785714

00:06:53.550 --> 00:06:55.258 and this is one of the major

NOTE Confidence: 0.892557816785714

00:06:55.258 --> 00:06:56.510 reasons why we haven't.

NOTE Confidence: 0.892557816785714

00:06:56.510 --> 00:06:58.796 Unraveled general population

NOTE Confidence: 0.892557816785714

00:06:58.796 --> 00:07:00.320 screening currently.

NOTE Confidence: 0.892557816785714

00:07:00.320 --> 00:07:01.280 So as a result of that,

NOTE Confidence: 0.892557816785714

00:07:01.280 --> 00:07:03.120 we tend to focus on high risk groups

NOTE Confidence: 0.892557816785714

00:07:03.120 --> 00:07:05.147 and the three big high risk groups

NOTE Confidence: 0.892557816785714

00:07:05.147 --> 00:07:06.662 which are these enriched groups

NOTE Confidence: 0.892557816785714

00:07:06.716 --> 00:07:08.846 that increase the prevalence of the

NOTE Confidence: 0.892557816785714

00:07:08.846 --> 00:07:10.266 chances of developing pancreatic

NOTE Confidence: 0.892557816785714

00:07:10.270 --> 00:07:12.960 cancer include new onset diabetes.

NOTE Confidence: 0.892557816785714

00:07:12.960 --> 00:07:14.381 And I'm not going to go spend

NOTE Confidence: 0.892557816785714

00:07:14.381 --> 00:07:15.699 too much time on this today.

NOTE Confidence: 0.892557816785714

00:07:15.700 --> 00:07:16.150 Shiraz Shari,

NOTE Confidence: 0.892557816785714

00:07:16.150 --> 00:07:18.365 who's kind of a leader in this area, spoke.

NOTE Confidence: 0.892557816785714

00:07:18.365 --> 00:07:20.440 Very passionate about this subject.

NOTE Confidence: 0.892557816785714

00:07:20.440 --> 00:07:22.318 Here at Yale several weeks back,

NOTE Confidence: 0.892557816785714

00:07:22.320 --> 00:07:23.770 but diabetes interplays with everything

NOTE Confidence: 0.892557816785714

00:07:23.770 --> 00:07:26.100 that we talk about with pancreatic system,

NOTE Confidence: 0.892557816785714

00:07:26.100 --> 00:07:27.470 family history.

NOTE Confidence: 0.892557816785714

00:07:27.470 --> 00:07:30.360 The other two high risk groups.

NOTE Confidence: 0.824197183333333

00:07:30.360 --> 00:07:30.888 So what about

NOTE Confidence: 0.67844358

00:07:30.900 --> 00:07:31.692 pancreatic cysts?

NOTE Confidence: 0.67844358

00:07:31.692 --> 00:07:33.544 So pancreatic cysts, and specifically

NOTE Confidence: 0.67844358

00:07:33.544 --> 00:07:35.868 a type of cyst called an ipmn,

NOTE Confidence: 0.67844358

00:07:35.870 --> 00:07:38.118 are incredibly common findings,

NOTE Confidence: 0.67844358

00:07:38.118 --> 00:07:40.237 incidentally, found typically on

NOTE Confidence: 0.67844358

00:07:40.237 --> 00:07:43.870 CT scans or Mris of the abdomen.

NOTE Confidence: 0.67844358

00:07:43.870 --> 00:07:46.798 We use a variety of imaging

NOTE Confidence: 0.67844358

00:07:46.798 --> 00:07:49.370 features of these incidental cysts,

NOTE Confidence: 0.67844358

00:07:49.370 --> 00:07:50.860 such as high risk stigmata,

NOTE Confidence: 0.67844358

00:07:50.860 --> 00:07:53.009 are they associated with jaundice or amass.

NOTE Confidence: 0.67844358

00:07:53.010 --> 00:07:54.586 Is the pancreatic duct,

NOTE Confidence: 0.67844358

00:07:54.586 --> 00:07:55.768 for example dilated,

NOTE Confidence: 0.67844358

00:07:55.770 --> 00:07:56.790 are worrisome features?

NOTE Confidence: 0.67844358

00:07:56.790 --> 00:07:58.150 Is there a nodule?

NOTE Confidence: 0.67844358

00:07:58.150 --> 00:07:59.760 Is there an intermediate ductal

NOTE Confidence: 0.67844358

00:07:59.760 --> 00:08:02.063 dilation of the main pancreatic duct is

NOTE Confidence: 0.67844358

00:08:02.063 --> 00:08:03.668 assessed greater than 3 centimeters?

NOTE Confidence: 0.67844358

00:08:03.670 --> 00:08:05.290 Is there a change in caliber?

NOTE Confidence: 0.67844358

00:08:05.290 --> 00:08:08.970 Is a cyst getting rapidly bigger over time?

NOTE Confidence: 0.67844358

00:08:08.970 --> 00:08:11.658 So we use these imaging features to try

NOTE Confidence: 0.67844358

00:08:11.658 --> 00:08:14.416 and better understand what's the risk of?

NOTE Confidence: 0.67844358

00:08:14.420 --> 00:08:18.170 This particular IP man having cancer,

NOTE Confidence: 0.67844358

00:08:18.170 --> 00:08:20.456 and so we think that overall

NOTE Confidence: 0.67844358

00:08:20.456 --> 00:08:23.160 there's a 1% chance per year of

NOTE Confidence: 0.67844358

00:08:23.160 --> 00:08:25.110 these IP amends developing cancer,

NOTE Confidence: 0.67844358

00:08:25.110 --> 00:08:26.510 and when we look at the imaging,

NOTE Confidence: 0.67844358

00:08:26.510 --> 00:08:28.512 one of the first questions that we

NOTE Confidence: 0.67844358

00:08:28.512 --> 00:08:31.151 end up trying to sort out is should

NOTE Confidence: 0.67844358

00:08:31.151 --> 00:08:33.016 these patients undergo surgery and so

NOTE Confidence: 0.67844358

00:08:33.016 --> 00:08:34.717 we use a combination of the imaging.

NOTE Confidence: 0.67844358

00:08:34.720 --> 00:08:37.628 But even with our best imaging in 2022,

NOTE Confidence: 0.67844358

00:08:37.628 --> 00:08:39.776 it's likely that anywhere in the

NOTE Confidence: 0.67844358

00:08:39.776 --> 00:08:42.666 region of about 60% of patients are

NOTE Confidence: 0.67844358

00:08:42.666 --> 00:08:44.028 undergoing unnecessary surgery,

NOTE Confidence: 0.67844358

00:08:44.030 --> 00:08:46.450 meaning that we are resecting

NOTE Confidence: 0.67844358

00:08:46.450 --> 00:08:47.922 low grade dysplastic lesions,

NOTE Confidence: 0.67844358

00:08:47.922 --> 00:08:49.762 not the high grade dysplastic,

NOTE Confidence: 0.67844358

00:08:49.770 --> 00:08:51.720 not the invasive cancer patients

NOTE Confidence: 0.67844358

00:08:51.720 --> 00:08:54.070 that we're really trying to find.

NOTE Confidence: 0.67844358

00:08:54.070 --> 00:08:56.294 And so this kind of begs for an

NOTE Confidence: 0.67844358

00:08:56.294 --> 00:08:57.924 improvement in this particular area

NOTE Confidence: 0.67844358

00:08:57.924 --> 00:09:00.290 and one particular area has been in

NOTE Confidence: 0.67844358

00:09:00.355 --> 00:09:02.406 looking at the role of cyst fluid,

NOTE Confidence: 0.67844358

00:09:02.410 --> 00:09:04.909 and so we have the ability with

NOTE Confidence: 0.67844358

00:09:04.909 --> 00:09:06.683 endoscopic ultrasound to pass a

NOTE Confidence: 0.67844358

00:09:06.683 --> 00:09:08.591 camera down into the stomach and

NOTE Confidence: 0.67844358

00:09:08.591 --> 00:09:10.640 sample the fluid in these cysts.

NOTE Confidence: 0.67844358

00:09:10.640 --> 00:09:12.453 And this can be very helpful for

NOTE Confidence: 0.67844358

00:09:12.453 --> 00:09:13.868 making the diagnosis of the cyst.

NOTE Confidence: 0.67844358

00:09:13.870 --> 00:09:16.166 Like is it an ipmn or some other

NOTE Confidence: 0.67844358

00:09:16.166 --> 00:09:17.750 type of precancerous?

NOTE Confidence: 0.67844358

00:09:17.750 --> 00:09:19.150 But it also has the ability for

NOTE Confidence: 0.67844358

00:09:19.150 --> 00:09:20.812 us to look at, for example,

NOTE Confidence: 0.67844358

00:09:20.812 --> 00:09:21.674 methylation markers,

NOTE Confidence: 0.67844358

00:09:21.674 --> 00:09:24.440 and this is very promising 2 panel

NOTE Confidence: 0.67844358

00:09:24.440 --> 00:09:26.575 marker that has a very good high

NOTE Confidence: 0.67844358

00:09:26.575 --> 00:09:28.250 operating characteristics for separating

NOTE Confidence: 0.67844358

00:09:28.250 --> 00:09:30.420 out low grade dysplastic system

NOTE Confidence: 0.67844358

00:09:30.420 --> 00:09:32.999 which we don't want to operate on

NOTE Confidence: 0.67844358

00:09:32.999 --> 00:09:35.172 and high grade dysplastic and cancer cells.

NOTE Confidence: 0.67844358

00:09:35.172 --> 00:09:37.260 So expect to hear more in time about

NOTE Confidence: 0.67844358

00:09:37.315 --> 00:09:39.037 these particular markers and SIS fluid

NOTE Confidence: 0.67844358

00:09:39.037 --> 00:09:41.259 as well as other even protein based

NOTE Confidence: 0.67844358

00:09:41.259 --> 00:09:42.954 markers in this particular field.

NOTE Confidence: 0.744730942222222

00:09:45.170 --> 00:09:47.210 The other issue with pancreatic

NOTE Confidence: 0.744730942222222

00:09:47.210 --> 00:09:48.842 cysts relates to surveillance,

NOTE Confidence: 0.744730942222222

00:09:48.850 --> 00:09:51.901 and so as we get better at deciding which

NOTE Confidence: 0.744730942222222

00:09:51.901 --> 00:09:54.068 patients shouldn't undergo surgery,

NOTE Confidence: 0.744730942222222

00:09:54.070 --> 00:09:56.471 it'll become obvious to people that the

NOTE Confidence: 0.744730942222222

00:09:56.471 --> 00:09:59.096 vast majority of these patients with I PMN

NOTE Confidence: 0.744730942222222

00:09:59.100 --> 00:10:01.290 nothing really happens them dramatically.

NOTE Confidence: 0.744730942222222

00:10:01.290 --> 00:10:02.955 Over time, they might get

NOTE Confidence: 0.744730942222222

00:10:02.955 --> 00:10:04.287 a little bit bigger.

NOTE Confidence: 0.744730942222222

00:10:04.290 --> 00:10:06.226 They're duct might get a little bit bigger,

NOTE Confidence: 0.744730942222222

00:10:06.230 --> 00:10:08.924 but their chances of developing cancer

NOTE Confidence: 0.744730942222222

00:10:08.924 --> 00:10:11.050 requiring surgery is incredibly low,

NOTE Confidence: 0.744730942222222

00:10:11.050 --> 00:10:12.988 but we're obliged to follow them,

NOTE Confidence: 0.744730942222222

00:10:12.990 --> 00:10:13.896 especially younger patients,

NOTE Confidence: 0.744730942222222

00:10:13.896 --> 00:10:15.708 because we're telling them your cyst.

NOTE Confidence: 0.744730942222222

00:10:15.710 --> 00:10:18.470 As a risk of developing cancer.

NOTE Confidence: 0.744730942222222

00:10:18.470 --> 00:10:20.479 And in that, the field of surveillance

NOTE Confidence: 0.744730942222222

00:10:20.479 --> 00:10:22.469 has really become a very complex issue,

NOTE Confidence: 0.744730942222222

00:10:22.470 --> 00:10:24.095 primarily because there's a lot

NOTE Confidence: 0.744730942222222

00:10:24.095 --> 00:10:25.070 of cysts involved,

NOTE Confidence: 0.744730942222222

00:10:25.070 --> 00:10:26.841 so it's estimated at about 6 million

NOTE Confidence: 0.744730942222222

00:10:26.841 --> 00:10:28.369 people in the United States.

NOTE Confidence: 0.744730942222222

00:10:28.370 --> 00:10:30.866 At least have some form of pancreatic cyst,

NOTE Confidence: 0.744730942222222

00:10:30.870 --> 00:10:32.352 and it's brought up questions of

NOTE Confidence: 0.744730942222222

00:10:32.352 --> 00:10:33.762 when should we stop surveying

NOTE Confidence: 0.744730942222222

00:10:33.762 --> 00:10:35.587 patients that have pancreatic cysts?

NOTE Confidence: 0.744730942222222

00:10:35.590 --> 00:10:36.846 Is there an age?

NOTE Confidence: 0.744730942222222

00:10:36.846 --> 00:10:38.730 Are there Co morbidities that we

NOTE Confidence: 0.744730942222222

00:10:38.803 --> 00:10:41.309 should say outweigh the risk of cancer?

NOTE Confidence: 0.744730942222222

00:10:41.310 --> 00:10:42.913 Is there any way of tailoring or

NOTE Confidence: 0.744730942222222

00:10:42.913 --> 00:10:44.743 having kind of a frank discussion with

NOTE Confidence: 0.744730942222222

00:10:44.743 --> 00:10:46.723 patients to kind of educate them on

NOTE Confidence: 0.744730942222222

00:10:46.723 --> 00:10:48.475 who needs surveillance and who doesn't?

NOTE Confidence: 0.744730942222222

00:10:48.480 --> 00:10:50.454 And is there any progress we could

NOTE Confidence: 0.744730942222222

00:10:50.454 --> 00:10:52.677 make in the realm of understanding

NOTE Confidence: 0.744730942222222

00:10:52.677 --> 00:10:54.429 the biology of progression?

NOTE Confidence: 0.744730942222222

00:10:54.430 --> 00:10:57.067 So we know for a fact that says do

NOTE Confidence: 0.744730942222222

00:10:57.067 --> 00:10:59.455 change at some says do change over

NOTE Confidence: 0.744730942222222

00:10:59.455 --> 00:11:01.778 time and some cysts will change

NOTE Confidence: 0.744730942222222

00:11:01.778 --> 00:11:04.028 even after periods of stability.

NOTE Confidence: 0.744730942222222

00:11:04.030 --> 00:11:05.006 On the flip side,

NOTE Confidence: 0.744730942222222

00:11:05.006 --> 00:11:06.226 we also know that stability,

NOTE Confidence: 0.744730942222222

00:11:06.230 --> 00:11:07.690 especially for small cyst,

NOTE Confidence: 0.744730942222222

00:11:07.690 --> 00:11:10.566 is a good hallmark, or it's not great,

NOTE Confidence: 0.744730942222222

00:11:10.566 --> 00:11:12.336 but it's a good hallmark.

NOTE Confidence: 0.744730942222222

00:11:12.340 --> 00:11:12.604 Nonetheless,

NOTE Confidence: 0.744730942222222

00:11:12.604 --> 00:11:14.452 in a variety of guidelines that are

NOTE Confidence: 0.744730942222222

00:11:14.452 --> 00:11:16.206 out there to help us understand who

NOTE Confidence: 0.744730942222222

00:11:16.206 --> 00:11:18.029 we should be following who we should be,

NOTE Confidence: 0.744730942222222

00:11:18.030 --> 00:11:20.870 stopping surveillance on the American

NOTE Confidence: 0.744730942222222

00:11:20.870 --> 00:11:22.574 Gastroenterology Association has

NOTE Confidence: 0.744730942222222

00:11:22.574 --> 00:11:25.214 made the recommendation that after

NOTE Confidence: 0.744730942222222

00:11:25.214 --> 00:11:27.908 five years of CIS stability that

NOTE Confidence: 0.744730942222222

00:11:27.908 --> 00:11:29.448 you should stop surveillance and

NOTE Confidence: 0.744730942222222

00:11:29.448 --> 00:11:31.459 this actually has been quite a

NOTE Confidence: 0.744730942222222

00:11:31.459 --> 00:11:34.160 controversial recommendation.

NOTE Confidence: 0.744730942222222

00:11:34.160 --> 00:11:36.428 I could choda one of the physicians

NOTE Confidence: 0.744730942222222

00:11:36.428 --> 00:11:38.401 in our research group had the

NOTE Confidence: 0.744730942222222

00:11:38.401 --> 00:11:40.578 ability to look at about 18 studies

NOTE Confidence: 0.744730942222222

00:11:40.648 --> 00:11:42.778 with over 10,000 patients followed

NOTE Confidence: 0.744730942222222

00:11:42.778 --> 00:11:44.908 for almost 60,000 patient years.

NOTE Confidence: 0.744730942222222

00:11:44.910 --> 00:11:46.998 And I could look at in these studies

NOTE Confidence: 0.744730942222222

00:11:46.998 --> 00:11:49.455 that have now long term follow up for

NOTE Confidence: 0.744730942222222

00:11:49.455 --> 00:11:51.449 patients with otherwise low risk IP men.

NOTE Confidence: 0.744730942222222

00:11:51.450 --> 00:11:53.472 So patients that we would typically

NOTE Confidence: 0.744730942222222

00:11:53.472 --> 00:11:55.129 just be following and he was

NOTE Confidence: 0.744730942222222

00:11:55.129 --> 00:11:56.194 able to notice that yeah,

NOTE Confidence: 0.744730942222222

00:11:56.200 --> 00:11:58.570 after five years or so,

NOTE Confidence: 0.744730942222222

00:11:58.570 --> 00:12:01.822 the risks of them developing progression

NOTE Confidence: 0.744730942222222

00:12:01.822 --> 00:12:05.462 is probably around 3% per year and the

NOTE Confidence: 0.744730942222222

00:12:05.462 --> 00:12:08.457 risk of them developing a cancer or an

NOTE Confidence: 0.744730942222222

00:12:08.457 --> 00:12:10.864 advanced lesion is about 1% per year.

NOTE Confidence: 0.744730942222222

00:12:10.864 --> 00:12:12.766 And when he looked at the

NOTE Confidence: 0.744730942222222

00:12:12.766 --> 00:12:14.080 subgroup of patients,

NOTE Confidence: 0.744730942222222

00:12:14.080 --> 00:12:16.536 so patients who were stable for five years,

NOTE Confidence: 0.744730942222222

00:12:16.540 --> 00:12:18.324 so this would be the group that we

NOTE Confidence: 0.744730942222222

00:12:18.324 --> 00:12:19.718 would typically talk about stopping.

NOTE Confidence: 0.744730942222222

00:12:19.720 --> 00:12:22.674 There's still a .2% risk per year

NOTE Confidence: 0.744730942222222

00:12:22.674 --> 00:12:25.120 of developing cancer long-term out,

NOTE Confidence: 0.744730942222222

00:12:25.120 --> 00:12:27.360 so we don't think that there's enough

NOTE Confidence: 0.744730942222222

00:12:27.360 --> 00:12:29.579 evidence right now to really be

NOTE Confidence: 0.744730942222222

00:12:29.579 --> 00:12:31.179 talking about stopping surveillance.

NOTE Confidence: 0.744730942222222

00:12:31.180 --> 00:12:33.100 What we do know is that there are

NOTE Confidence: 0.744730942222222

00:12:33.100 --> 00:12:34.886 subgroups of patients who we should

NOTE Confidence: 0.744730942222222

00:12:34.886 --> 00:12:36.764 be probably having a more intelligent

NOTE Confidence: 0.884782320454546

00:12:36.820 --> 00:12:37.760 conversation with,

NOTE Confidence: 0.884782320454546

00:12:37.760 --> 00:12:40.380 and particularly patients who

NOTE Confidence: 0.884782320454546

00:12:40.380 --> 00:12:42.345 have significant comorbidities.

NOTE Confidence: 0.884782320454546

00:12:42.350 --> 00:12:46.830 We had the ability to look at.

NOTE Confidence: 0.884782320454546

00:12:46.830 --> 00:12:48.695 440 patients that we were

NOTE Confidence: 0.884782320454546

00:12:48.695 --> 00:12:50.910 actively surveying at Yale over a

NOTE Confidence: 0.884782320454546

00:12:50.910 --> 00:12:52.856 period of about 56 months or so,

NOTE Confidence: 0.884782320454546

00:12:52.860 --> 00:12:55.860 and in that group of patients,

NOTE Confidence: 0.884782320454546

00:12:55.860 --> 00:12:57.087 44 patients died,

NOTE Confidence: 0.884782320454546

00:12:57.087 --> 00:12:59.541 but the vast majority of deaths

NOTE Confidence: 0.884782320454546

00:12:59.541 --> 00:13:02.793 on follow-up were not related to

NOTE Confidence: 0.884782320454546

00:13:02.793 --> 00:13:04.737 pancreatic disease, and in fact,

NOTE Confidence: 0.884782320454546

00:13:04.737 --> 00:13:07.175 when we took a cut off of a

NOTE Confidence: 0.884782320454546

00:13:07.175 --> 00:13:08.819 comorbidity index of four.

NOTE Confidence: 0.884782320454546

00:13:08.820 --> 00:13:11.106 So an index that takes in

NOTE Confidence: 0.884782320454546

00:13:11.106 --> 00:13:13.174 cardiac renal pulmonary issues to

NOTE Confidence: 0.884782320454546

00:13:13.174 --> 00:13:15.078 determine long term comorbidity,

NOTE Confidence: 0.884782320454546

00:13:15.080 --> 00:13:16.508 a cutoff of four.

NOTE Confidence: 0.884782320454546

00:13:16.508 --> 00:13:18.293 It's very good at predicting

NOTE Confidence: 0.884782320454546

00:13:18.293 --> 00:13:20.059 long term comorbidities,

NOTE Confidence: 0.884782320454546

00:13:20.060 --> 00:13:22.270 not related to pancreatic cancer,

NOTE Confidence: 0.884782320454546

00:13:22.270 --> 00:13:24.580 and so now we're beginning to have

NOTE Confidence: 0.884782320454546

00:13:24.580 --> 00:13:26.040 these discussions with patients

NOTE Confidence: 0.884782320454546

00:13:26.040 --> 00:13:28.070 based on their overall prognosis,

NOTE Confidence: 0.884782320454546

00:13:28.070 --> 00:13:30.435 not just focusing specifically on

NOTE Confidence: 0.884782320454546

00:13:30.435 --> 00:13:33.590 the issue related to their pancreas.

NOTE Confidence: 0.884782320454546

00:13:33.590 --> 00:13:36.264 This very useful tool that's now available.

NOTE Confidence: 0.884782320454546

00:13:36.270 --> 00:13:38.763 We actually have it on our high risk website.

NOTE Confidence: 0.884782320454546

00:13:38.770 --> 00:13:42.568 The PCD website is a validated

NOTE Confidence: 0.884782320454546

00:13:42.568 --> 00:13:45.586 tool that was initiated and

NOTE Confidence: 0.884782320454546

00:13:45.586 --> 00:13:47.818 validated in both Dutch,

NOTE Confidence: 0.884782320454546

00:13:47.820 --> 00:13:49.734 Italian and several US sites for

NOTE Confidence: 0.884782320454546

00:13:49.734 --> 00:13:51.939 looking at both the five year and

NOTE Confidence: 0.884782320454546

00:13:51.939 --> 00:13:53.955 the three year and five year risk

NOTE Confidence: 0.884782320454546

00:13:54.023 --> 00:13:56.047 of developing worrisome features.

NOTE Confidence: 0.884782320454546

00:13:56.050 --> 00:13:57.646 A high risk of matter if you

NOTE Confidence: 0.884782320454546

00:13:57.646 --> 00:13:59.380 have a a low risk branch.

NOTE Confidence: 0.884782320454546

00:13:59.380 --> 00:14:01.270 Strict IP men so you you as a patient

NOTE Confidence: 0.884782320454546

00:14:01.270 --> 00:14:03.030 are able to go on to the website.

NOTE Confidence: 0.884782320454546

00:14:03.030 --> 00:14:04.270 You're able to put in.

NOTE Confidence: 0.884782320454546

00:14:04.270 --> 00:14:05.440 The size of your cyst,

NOTE Confidence: 0.884782320454546

00:14:05.440 --> 00:14:06.086 for example.

NOTE Confidence: 0.884782320454546

00:14:06.086 --> 00:14:07.701 There's some other parameters like

NOTE Confidence: 0.884782320454546

00:14:07.701 --> 00:14:09.499 smoking is your SIS multifocal,

NOTE Confidence: 0.884782320454546

00:14:09.500 --> 00:14:11.756 and it's able to give you a pictorial

NOTE Confidence: 0.884782320454546

00:14:11.756 --> 00:14:13.607 representation of your risk of the

NOTE Confidence: 0.884782320454546

00:14:13.607 --> 00:14:14.839 cyst developing into worrisome

NOTE Confidence: 0.884782320454546

00:14:14.839 --> 00:14:16.430 features and high risk matters,

NOTE Confidence: 0.884782320454546

00:14:16.430 --> 00:14:18.584 so this is very helpful in

NOTE Confidence: 0.884782320454546

00:14:18.584 --> 00:14:20.020 discussions with patients overall

NOTE Confidence: 0.884782320454546

00:14:20.083 --> 00:14:22.021 and ultimately we would like to

NOTE Confidence: 0.884782320454546

00:14:22.021 --> 00:14:24.382 get greater numbers to to be able

NOTE Confidence: 0.884782320454546

00:14:24.382 --> 00:14:26.057 to calculate individual risk of

NOTE Confidence: 0.884782320454546

00:14:26.057 --> 00:14:29.570 developing an advanced neoplasia.

NOTE Confidence: 0.884782320454546

00:14:29.570 --> 00:14:31.570 But I think a key issue is also

NOTE Confidence: 0.884782320454546

00:14:31.570 --> 00:14:33.591 trying to understand at a molecular

NOTE Confidence: 0.884782320454546

00:14:33.591 --> 00:14:35.416 level what makes some sense

NOTE Confidence: 0.884782320454546

00:14:35.416 --> 00:14:37.070 stable for periods of time.

NOTE Confidence: 0.884782320454546

00:14:37.070 --> 00:14:38.730 What makes certain IP amends

NOTE Confidence: 0.884782320454546

00:14:38.730 --> 00:14:40.792 decide that they want to take

NOTE Confidence: 0.884782320454546

00:14:40.792 --> 00:14:42.820 off after five years and develop

NOTE Confidence: 0.884782320454546

00:14:42.820 --> 00:14:44.590 into an invasive malignancy?

NOTE Confidence: 0.884782320454546

00:14:44.590 --> 00:14:47.407 And to this end there was a need to

NOTE Confidence: 0.884782320454546

00:14:47.407 --> 00:14:49.637 understand IP mensys progression more.

NOTE Confidence: 0.884782320454546

00:14:49.640 --> 00:14:50.212 To date,

NOTE Confidence: 0.884782320454546

00:14:50.212 --> 00:14:51.928 there have been some limited data

NOTE Confidence: 0.884782320454546

00:14:51.928 --> 00:14:54.141 and the use of organoids derive

NOTE Confidence: 0.884782320454546

00:14:54.141 --> 00:14:55.721 some surgical resection specimens

NOTE Confidence: 0.884782320454546

00:14:55.721 --> 00:14:57.737 so patients who have gone to

NOTE Confidence: 0.884782320454546

00:14:57.737 --> 00:14:59.197 the operating room and people

NOTE Confidence: 0.884782320454546

00:14:59.197 --> 00:15:01.680 have been able to develop ipmn

NOTE Confidence: 0.884782320454546

00:15:01.680 --> 00:15:03.432 organoids for additional study.

NOTE Confidence: 0.884782320454546

00:15:03.440 --> 00:15:05.210 We've taken a slightly different approach.

NOTE Confidence: 0.884782320454546

00:15:05.210 --> 00:15:06.536 We were actually interested in the

NOTE Confidence: 0.884782320454546

00:15:06.536 --> 00:15:08.040 groups of patients that were surveying,

NOTE Confidence: 0.884782320454546

00:15:08.040 --> 00:15:10.576 so patients who do not go for surgery

NOTE Confidence: 0.884782320454546

00:15:10.580 --> 00:15:12.800 and using again endoscopic ultrasound.

NOTE Confidence: 0.884782320454546

00:15:12.800 --> 00:15:14.640 We've been sampling the fluid

NOTE Confidence: 0.884782320454546

00:15:14.640 --> 00:15:16.480 from these pancreatic cysts and

NOTE Confidence: 0.884782320454546

00:15:16.547 --> 00:15:18.419 generating organoid structures.

NOTE Confidence: 0.884782320454546

00:15:18.420 --> 00:15:20.380 This is very preliminary data,

NOTE Confidence: 0.884782320454546

00:15:20.380 --> 00:15:22.312 and these are some of the images

NOTE Confidence: 0.884782320454546

00:15:22.312 --> 00:15:23.966 that we are identifying similar

NOTE Confidence: 0.884782320454546

00:15:23.966 --> 00:15:26.605 to what we would see in organoids.

NOTE Confidence: 0.884782320454546

00:15:26.610 --> 00:15:29.508 To date we have studied 9

NOTE Confidence: 0.884782320454546

00:15:29.508 --> 00:15:31.440 patients with presumed ipms.

NOTE Confidence: 0.884782320454546

00:15:31.440 --> 00:15:32.766 They're all growing,

NOTE Confidence: 0.884782320454546

00:15:32.766 --> 00:15:34.976 they're all growing exceptionally slow,

NOTE Confidence: 0.884782320454546

00:15:34.980 --> 00:15:35.925 but we've been able to

NOTE Confidence: 0.884782320454546

00:15:35.925 --> 00:15:37.120 passage some of them as well,

NOTE Confidence: 0.884782320454546

00:15:37.120 --> 00:15:38.992 so this is a an interesting

NOTE Confidence: 0.884782320454546

00:15:38.992 --> 00:15:40.860 development to allow us to study.

NOTE Confidence: 0.80779545

00:15:40.860 --> 00:15:43.164 I PM and progression to maybe

NOTE Confidence: 0.80779545

00:15:43.164 --> 00:15:44.700 tailor approaches for individuals,

NOTE Confidence: 0.80779545

00:15:44.700 --> 00:15:47.070 and maybe offer interventions such

NOTE Confidence: 0.80779545

00:15:47.070 --> 00:15:50.699 as chemoprevention, so stay tuned.

NOTE Confidence: 0.80779545

00:15:50.700 --> 00:15:54.864 Now the other large area within the risk

NOTE Confidence: 0.80779545

00:15:54.864 --> 00:15:56.698 or the high risk of pancreatic cancer

NOTE Confidence: 0.80779545

00:15:56.698 --> 00:15:58.678 is your hereditary susceptibility,

NOTE Confidence: 0.80779545

00:15:58.680 --> 00:16:00.924 or your inherited risk of developing

NOTE Confidence: 0.80779545

00:16:00.924 --> 00:16:02.041 cancer pancreatic cancer raw,

NOTE Confidence: 0.80779545

00:16:02.041 --> 00:16:04.195 but we think that maybe about 10% of

NOTE Confidence: 0.80779545

00:16:04.195 --> 00:16:07.170 all pancreatic cancers are at risk for

NOTE Confidence: 0.80779545

00:16:07.170 --> 00:16:09.598 developing cancer based on a family history,

NOTE Confidence: 0.80779545

00:16:09.600 --> 00:16:11.637 and there's a variety of guidelines that

NOTE Confidence: 0.80779545

00:16:11.637 --> 00:16:13.170 we've been involved with specifically

NOTE Confidence: 0.80779545

00:16:13.170 --> 00:16:15.000 the CAPS guidelines to help us

NOTE Confidence: 0.80779545

00:16:15.000 --> 00:16:16.769 understand who we should be surveying

NOTE Confidence: 0.80779545

00:16:16.769 --> 00:16:18.425 and who we shouldn't be surveying.

NOTE Confidence: 0.80779545

00:16:18.430 --> 00:16:19.834 And very Simply put,

NOTE Confidence: 0.80779545

00:16:19.834 --> 00:16:21.940 there's a high risk group that

NOTE Confidence: 0.80779545

00:16:22.017 --> 00:16:24.747 carries a very high lifetime risk

NOTE Confidence: 0.80779545

00:16:24.747 --> 00:16:26.567 of developing pancreatic cancer.

NOTE Confidence: 0.80779545

00:16:26.570 --> 00:16:28.734 It includes individuals with

NOTE Confidence: 0.80779545

00:16:28.734 --> 00:16:31.439 mutations and P-16 puts YAGERS,

NOTE Confidence: 0.80779545

00:16:31.440 --> 00:16:32.925 but also individuals who have

NOTE Confidence: 0.80779545

00:16:32.925 --> 00:16:34.787 a family history with three or

NOTE Confidence: 0.80779545

00:16:34.787 --> 00:16:36.079 four first degree relatives.

NOTE Confidence: 0.80779545

00:16:36.080 --> 00:16:38.528 So these people are at a higher risk

NOTE Confidence: 0.80779545

00:16:38.528 --> 00:16:40.949 without a known genetic abnormality.

NOTE Confidence: 0.80779545

00:16:40.950 --> 00:16:42.686 There's also a low to moderate risk that

NOTE Confidence: 0.80779545

00:16:42.686 --> 00:16:44.187 includes genes that you're familiar with,

NOTE Confidence: 0.80779545

00:16:44.190 --> 00:16:45.550 such as Braca one bracket,

NOTE Confidence: 0.80779545

00:16:45.550 --> 00:16:47.435 two other DNA repair genes

NOTE Confidence: 0.80779545

00:16:47.435 --> 00:16:49.320 like Paul V2 and ATM,

NOTE Confidence: 0.80779545

00:16:49.320 --> 00:16:51.792 but also again in there is a family

NOTE Confidence: 0.80779545

00:16:51.792 --> 00:16:54.334 risk of two first degree relatives

NOTE Confidence: 0.80779545

00:16:54.334 --> 00:16:56.649 and that carries a significant,

NOTE Confidence: 0.80779545

00:16:56.650 --> 00:16:58.512 albeit low risk than those that have

NOTE Confidence: 0.80779545

00:16:58.512 --> 00:17:00.458 three first three relatives with no

NOTE Confidence: 0.80779545

00:17:00.458 --> 00:17:02.278 abnormality identifiable in the germline.

NOTE Confidence: 0.895210255555555

00:17:04.480 --> 00:17:05.690 To take care of these

NOTE Confidence: 0.895210255555555

00:17:05.690 --> 00:17:06.658 individuals several years back,

NOTE Confidence: 0.895210255555555

00:17:06.660 --> 00:17:08.459 we set up a pancreatic cancer early

NOTE Confidence: 0.895210255555555

00:17:08.459 --> 00:17:10.109 detection clinic at Yale through smile

NOTE Confidence: 0.895210255555555

00:17:10.109 --> 00:17:12.041 through the general support of Smile and

NOTE Confidence: 0.895210255555555

00:17:12.088 --> 00:17:13.817 Javier Loras group and in this group.

NOTE Confidence: 0.895210255555555

00:17:13.820 --> 00:17:16.340 Currently we're following about 185 patients,

NOTE Confidence: 0.895210255555555

00:17:16.340 --> 00:17:18.716 most of them in protocol who are at high

NOTE Confidence: 0.895210255555555

00:17:18.716 --> 00:17:20.917 risk of developing pancreatic cancer,

NOTE Confidence: 0.895210255555555

00:17:20.920 --> 00:17:22.774 and again, you can see this from this group.

NOTE Confidence: 0.895210255555555

00:17:22.780 --> 00:17:25.384 The the majority of patients are actually

NOTE Confidence: 0.895210255555555

00:17:25.384 --> 00:17:27.789 individuals who have a strong family history

NOTE Confidence: 0.895210255555555

00:17:27.789 --> 00:17:30.410 but do not have any genetic abnormality.

NOTE Confidence: 0.895210255555555

00:17:30.410 --> 00:17:32.586 One of the original studies that was done

NOTE Confidence: 0.895210255555555

00:17:32.586 --> 00:17:34.924 in this area was that what's called the

NOTE Confidence: 0.895210255555555

00:17:34.924 --> 00:17:37.070 Caps three study and these patients are

NOTE Confidence: 0.895210255555555

00:17:37.070 --> 00:17:39.754 typically imaged with a variety of CT scans.

NOTE Confidence: 0.895210255555555

00:17:39.754 --> 00:17:41.770 Mris and endoscopic ultrasounds,

NOTE Confidence: 0.895210255555555

00:17:41.770 --> 00:17:44.668 and a small percentage of them will have an

NOTE Confidence: 0.895210255555555

00:17:44.668 --> 00:17:46.990 abnormality that requires surgical resection.

NOTE Confidence: 0.895210255555555

00:17:46.990 --> 00:17:49.546 So in Caps 3, for example,

NOTE Confidence: 0.895210255555555

00:17:49.550 --> 00:17:52.398 225 patients were enrolled.

NOTE Confidence: 0.895210255555555

00:17:52.400 --> 00:17:54.140 Umm?

NOTE Confidence: 0.895210255555555

00:17:54.140 --> 00:17:55.976 A total of 216 were ultimately

NOTE Confidence: 0.895210255555555

00:17:55.976 --> 00:17:57.882 studied and the majority of these

NOTE Confidence: 0.895210255555555

00:17:57.882 --> 00:17:59.760 are the time were familial patients.

NOTE Confidence: 0.895210255555555

00:17:59.760 --> 00:18:02.840 This is a multicenter study.

NOTE Confidence: 0.895210255555555

00:18:02.840 --> 00:18:04.020 For the majority of patients,

NOTE Confidence: 0.895210255555555

00:18:04.020 --> 00:18:05.408 no abnormality was identified,

NOTE Confidence: 0.895210255555555

00:18:05.408 --> 00:18:08.668 but you can see that for some of these

NOTE Confidence: 0.895210255555555

00:18:08.668 --> 00:18:10.894 patients had a dilated pancreatic duct.

NOTE Confidence: 0.895210255555555

00:18:10.900 --> 00:18:14.176 For example, a cyst, probably an ipmn,

NOTE Confidence: 0.895210255555555

00:18:14.180 --> 00:18:15.670 and a small percentage ended

NOTE Confidence: 0.895210255555555

00:18:15.670 --> 00:18:17.160 up having a solid lesion.

NOTE Confidence: 0.895210255555555

00:18:17.160 --> 00:18:18.004 In total,

NOTE Confidence: 0.895210255555555

00:18:18.004 --> 00:18:19.692 five of these patients

NOTE Confidence: 0.895210255555555

00:18:19.692 --> 00:18:20.958 underwent surgical resection,

NOTE Confidence: 0.895210255555555

00:18:20.960 --> 00:18:23.158 2 of them had high grade dysplasia,

NOTE Confidence: 0.895210255555555

00:18:23.160 --> 00:18:25.044 and three of them had low

NOTE Confidence: 0.895210255555555

00:18:25.044 --> 00:18:26.700 grade dysplasia IP and then,

NOTE Confidence: 0.895210255555555

00:18:26.700 --> 00:18:28.611 although all five of them ended up

NOTE Confidence: 0.895210255555555

00:18:28.611 --> 00:18:30.253 with having either an intermediate

NOTE Confidence: 0.895210255555555

00:18:30.253 --> 00:18:32.168 or high grade dysplastic completion.

NOTE Confidence: 0.895210255555555

00:18:32.170 --> 00:18:35.327 In the form of a panel lesion.

NOTE Confidence: 0.895210255555555

00:18:35.330 --> 00:18:37.430 Very interesting data from these CAP studies.

NOTE Confidence: 0.895210255555555

00:18:37.430 --> 00:18:40.370 In fact has been the ability to

NOTE Confidence: 0.895210255555555

00:18:40.370 --> 00:18:42.488 collect pancreatic juice and what's

NOTE Confidence: 0.895210255555555

00:18:42.488 --> 00:18:44.633 been noticed in individuals who

NOTE Confidence: 0.895210255555555

00:18:44.633 --> 00:18:45.920 subsequently developed established

NOTE Confidence: 0.895210255555555

00:18:45.979 --> 00:18:47.789 pancreatic Dr Latner carcinoma is

NOTE Confidence: 0.895210255555555

00:18:47.789 --> 00:18:49.931 that investigators were able to go

NOTE Confidence: 0.895210255555555

00:18:49.931 --> 00:18:51.842 back and look at the pancreatic juice

NOTE Confidence: 0.895210255555555

00:18:51.842 --> 00:18:54.400 of these individuals at a time when

NOTE Confidence: 0.895210255555555

00:18:54.400 --> 00:18:56.410 they had no radiologic abnormality.

NOTE Confidence: 0.895210255555555

00:18:56.410 --> 00:18:58.552 And they were able to identify

NOTE Confidence: 0.895210255555555

00:18:58.552 --> 00:19:00.724 either combinations of P53 mutations

NOTE Confidence: 0.895210255555555

00:19:00.724 --> 00:19:04.006 or P60 mutations long before a

NOTE Confidence: 0.895210255555555

00:19:04.006 --> 00:19:06.409 radiologic abnormality was identified.

NOTE Confidence: 0.895210255555555

00:19:06.410 --> 00:19:09.362 So this is another direction to go in

NOTE Confidence: 0.895210255555555

00:19:09.362 --> 00:19:12.437 in terms of surveying these patients.

NOTE Confidence: 0.895210255555555

00:19:12.440 --> 00:19:15.080 The initial results of the Caps five study,

NOTE Confidence: 0.895210255555555

00:19:15.080 --> 00:19:17.320 which is a much larger multicenter study,

NOTE Confidence: 0.895210255555555

00:19:17.320 --> 00:19:19.938 which Yale was part have just been

NOTE Confidence: 0.895210255555555

00:19:19.938 --> 00:19:22.760 accepted for publication in in JCO in

NOTE Confidence: 0.895210255555555

00:19:22.760 --> 00:19:27.780 Caps 5 almost 1500 patients were studied.

NOTE Confidence: 0.895210255555555

00:19:27.780 --> 00:19:30.588 A total of nine screen detected

NOTE Confidence: 0.895210255555555

00:19:30.588 --> 00:19:32.460 pancreatic cancers were identified,

NOTE Confidence: 0.895210255555555

00:19:32.460 --> 00:19:34.450 of which eight were resectable

NOTE Confidence: 0.895210255555555

00:19:34.450 --> 00:19:36.760 and seven at a stage 1A,

NOTE Confidence: 0.895210255555555

00:19:36.760 --> 00:19:38.672 and when you put that together with some

NOTE Confidence: 0.895210255555555

00:19:38.672 --> 00:19:40.737 of the high grade dysplastic lesions,

NOTE Confidence: 0.895210255555555

00:19:40.740 --> 00:19:42.744 well over 50% of the patients

NOTE Confidence: 0.895210255555555

00:19:42.744 --> 00:19:44.971 enrolled in these studies had an

NOTE Confidence: 0.895210255555555

00:19:44.971 --> 00:19:47.036 achievement of what's called a

NOTE Confidence: 0.895210255555555

00:19:47.036 --> 00:19:48.275 successful goals surveillance.

NOTE Confidence: 0.895210255555555

00:19:48.280 --> 00:19:50.758 So we identified either an early stage

NOTE Confidence: 0.895210255555555

00:19:50.758 --> 00:19:53.947 cancer or a high grade dysplastic lesion.

NOTE Confidence: 0.895210255555555

00:19:53.950 --> 00:19:55.912 When all the patients from the

NOTE Confidence: 0.895210255555555

00:19:55.912 --> 00:19:57.796 caps one through five study

NOTE Confidence: 0.895210255555555

00:19:57.796 --> 00:19:59.308 were amalgamated together,

NOTE Confidence: 0.895210255555555

00:19:59.310 --> 00:20:01.739 what we were able to demonstrate was

NOTE Confidence: 0.895210255555555

00:20:01.739 --> 00:20:04.186 that those patients who were diagnosed

NOTE Confidence: 0.895210255555555

00:20:04.186 --> 00:20:06.416 during a surveillance protocol with

NOTE Confidence: 0.895210255555555

00:20:06.416 --> 00:20:08.718 pancreatic cancer had a much higher

NOTE Confidence: 0.895210255555555

00:20:08.718 --> 00:20:10.728 median survival than those that were

NOTE Confidence: 0.849172274

00:20:10.730 --> 00:20:13.150 diagnosed outside of surveillance protocol,

NOTE Confidence: 0.849172274

00:20:13.150 --> 00:20:16.420 showing some form of survival benefit

NOTE Confidence: 0.849172274

00:20:16.420 --> 00:20:19.680 within this within this initiative.

NOTE Confidence: 0.849172274

00:20:19.680 --> 00:20:20.920 Anca Chotto you know.

NOTE Confidence: 0.849172274

00:20:20.920 --> 00:20:22.745 Again, being very productive went and

NOTE Confidence: 0.849172274

00:20:22.745 --> 00:20:24.689 looked at some of these surveillance

NOTE Confidence: 0.849172274

00:20:24.689 --> 00:20:26.514 studies that were done more

NOTE Confidence: 0.849172274

00:20:26.514 --> 00:20:28.600 concerned about what was happening.

NOTE Confidence: 0.849172274

00:20:28.600 --> 00:20:30.280 Not so much when patients were

NOTE Confidence: 0.849172274

00:20:30.280 --> 00:20:31.749 initially enrolled, but as they

NOTE Confidence: 0.849172274

00:20:31.749 --> 00:20:33.870 were followed over a period of time.

NOTE Confidence: 0.849172274

00:20:33.870 --> 00:20:36.622 He took 13 of the most recent studies

NOTE Confidence: 0.849172274

00:20:36.622 --> 00:20:39.361 and what he noted was that in 53

NOTE Confidence: 0.849172274

00:20:39.361 --> 00:20:41.716 patients that were identified with

NOTE Confidence: 0.849172274

00:20:41.716 --> 00:20:43.129 pancreatic ductal adenocarcinoma.

NOTE Confidence: 0.849172274

00:20:43.130 --> 00:20:46.308 In these 13 odd studies or so.

NOTE Confidence: 0.849172274

00:20:46.310 --> 00:20:50.094 Whereas 22 patients or 41% had goals of

NOTE Confidence: 0.849172274

00:20:50.094 --> 00:20:52.182 surveillance achieved so in early cancer,

NOTE Confidence: 0.849172274

00:20:52.190 --> 00:20:53.810 a high grade dysplastic,

NOTE Confidence: 0.849172274

00:20:53.810 --> 00:20:55.025 a very worrisome,

NOTE Confidence: 0.849172274

00:20:55.030 --> 00:20:58.286 almost 60% of patients had an advanced Lee.

NOTE Confidence: 0.849172274

00:20:58.290 --> 00:21:00.925 A more advanced lesion including

NOTE Confidence: 0.849172274

00:21:00.925 --> 00:21:01.979 metastatic lesions.

NOTE Confidence: 0.849172274

00:21:01.980 --> 00:21:03.676 He tried to look at some of the

NOTE Confidence: 0.849172274

00:21:03.676 --> 00:21:05.168 factors that might be associated

NOTE Confidence: 0.849172274

00:21:05.168 --> 00:21:06.858 with these late stage presentations.

NOTE Confidence: 0.849172274

00:21:06.860 --> 00:21:09.050 It had nothing to do with

NOTE Confidence: 0.849172274

00:21:09.050 --> 00:21:09.780 surveillance modality,

NOTE Confidence: 0.849172274

00:21:09.780 --> 00:21:11.092 a baseline imaging abnormality,

NOTE Confidence: 0.849172274

00:21:11.092 --> 00:21:13.060 even the presence or absence of

NOTE Confidence: 0.849172274

00:21:13.117 --> 00:21:14.158 a germline mutation.

NOTE Confidence: 0.849172274

00:21:14.160 --> 00:21:16.428 A lot of the patients who presented

NOTE Confidence: 0.849172274

00:21:16.428 --> 00:21:17.400 were actually asymptomatic.

NOTE Confidence: 0.849172274

00:21:17.400 --> 00:21:20.136 We were able to look at the timing of

NOTE Confidence: 0.849172274

00:21:20.136 --> 00:21:22.088 preceding imaging and most patients

NOTE Confidence: 0.849172274

00:21:22.088 --> 00:21:24.063 had a normal preceding image.

NOTE Confidence: 0.849172274

00:21:24.070 --> 00:21:25.525 There was some questions about

NOTE Confidence: 0.849172274

00:21:25.525 --> 00:21:27.578 diagnostic errors in the in the limited

NOTE Confidence: 0.849172274

00:21:27.578 --> 00:21:29.475 data that was available and there was

NOTE Confidence: 0.849172274

00:21:29.475 --> 00:21:31.409 some issue of surveillance adherence.

NOTE Confidence: 0.849172274

00:21:31.410 --> 00:21:33.760 In some of this data.

NOTE Confidence: 0.849172274

00:21:33.760 --> 00:21:35.524 And what this leads into is kind

NOTE Confidence: 0.849172274

00:21:35.524 --> 00:21:36.978 of a growing conversation about

NOTE Confidence: 0.849172274

00:21:36.978 --> 00:21:38.578 how we can do better.

NOTE Confidence: 0.849172274

00:21:38.580 --> 00:21:40.344 You're going to see more and more

NOTE Confidence: 0.849172274

00:21:40.344 --> 00:21:41.863 of these types of studies in

NOTE Confidence: 0.849172274

00:21:41.863 --> 00:21:43.515 the next couple of years or so.

NOTE Confidence: 0.849172274

00:21:43.520 --> 00:21:45.488 This is the initial study that

NOTE Confidence: 0.849172274

00:21:45.488 --> 00:21:46.472 proved this point.

NOTE Confidence: 0.849172274

00:21:46.480 --> 00:21:49.224 These are patients who had a diagnosis

NOTE Confidence: 0.849172274

00:21:49.224 --> 00:21:51.800 of pancreatic ductil adenocarcinoma made,

NOTE Confidence: 0.849172274

00:21:51.800 --> 00:21:53.641 and when we when they went back

NOTE Confidence: 0.849172274

00:21:53.641 --> 00:21:54.859 over a year or so,

NOTE Confidence: 0.849172274

00:21:54.860 --> 00:21:57.332 it was said that the pancreatic

NOTE Confidence: 0.849172274

00:21:57.332 --> 00:21:58.980 cancer could be identified.

NOTE Confidence: 0.849172274

00:21:58.980 --> 00:22:03.032 So a variety of of methods were

NOTE Confidence: 0.849172274

00:22:03.032 --> 00:22:05.210 looked at in these individuals.

NOTE Confidence: 0.849172274

00:22:05.210 --> 00:22:07.842 But issue is with to do with issues

NOTE Confidence: 0.849172274

00:22:07.842 --> 00:22:09.724 relating to abnormalities that were

NOTE Confidence: 0.849172274

00:22:09.724 --> 00:22:11.764 identified on imaging that could

NOTE Confidence: 0.849172274

00:22:11.764 --> 00:22:14.527 be seen and maybe radiomics or some

NOTE Confidence: 0.849172274

00:22:14.527 --> 00:22:17.050 other feature could help figure that out.

NOTE Confidence: 0.849172274

00:22:17.050 --> 00:22:18.286 I think it's important to say,

NOTE Confidence: 0.849172274

00:22:18.290 --> 00:22:19.859 just to summarize,

NOTE Confidence: 0.849172274

00:22:19.860 --> 00:22:20.360 I'm sorry.

NOTE Confidence: 0.768032867538461

00:22:29.520 --> 00:22:32.058 That the the stage of pancreatic

NOTE Confidence: 0.768032867538461

00:22:32.058 --> 00:22:35.419 cancer at an early stage is improving,

NOTE Confidence: 0.768032867538461

00:22:35.420 --> 00:22:37.144 especially in younger populations,

NOTE Confidence: 0.768032867538461

00:22:37.144 --> 00:22:39.299 and the overall survival related

NOTE Confidence: 0.768032867538461

00:22:39.299 --> 00:22:41.835 to early stage pancreatic cancer is

NOTE Confidence: 0.768032867538461

00:22:41.835 --> 00:22:44.620 increased from about 44% in 2004.

NOTE Confidence: 0.768032867538461

00:22:44.620 --> 00:22:46.700 And now getting closer

NOTE Confidence: 0.768032867538461

00:22:46.700 --> 00:22:49.330 to about just over 80%.

NOTE Confidence: 0.768032867538461

00:22:49.330 --> 00:22:52.025 This is unclear why this is happening,

NOTE Confidence: 0.768032867538461

00:22:52.030 --> 00:22:53.530 but may be related to increased

NOTE Confidence: 0.768032867538461

00:22:53.530 --> 00:22:54.530 use of abdominal imaging,

NOTE Confidence: 0.768032867538461

00:22:54.530 --> 00:22:55.900 and perhaps some of the

NOTE Confidence: 0.768032867538461

00:22:55.900 --> 00:22:56.448 surveillance programs.

NOTE Confidence: 0.768032867538461

00:22:56.450 --> 00:22:59.018 So we're beginning to gather some

NOTE Confidence: 0.768032867538461

00:22:59.018 --> 00:23:01.565 information about the benefit of both

NOTE Confidence: 0.768032867538461

00:23:01.565 --> 00:23:03.857 the surveillance programs as well as.

NOTE Confidence: 0.768032867538461

00:23:03.860 --> 00:23:06.188 As well as.

NOTE Confidence: 0.768032867538461

00:23:06.190 --> 00:23:08.565 Are the outcomes related to

NOTE Confidence: 0.768032867538461

00:23:08.565 --> 00:23:09.990 those surveillance programs?

NOTE Confidence: 0.768032867538461

00:23:09.990 --> 00:23:11.196 And I'll leave you with this.

NOTE Confidence: 0.768032867538461

00:23:11.200 --> 00:23:12.680 Notice something to kind of

NOTE Confidence: 0.768032867538461

00:23:12.680 --> 00:23:14.160 look forward within the CAPS

NOTE Confidence: 0.768032867538461

00:23:14.220 --> 00:23:15.810 cohort of patients at Hopkins.

NOTE Confidence: 0.768032867538461

00:23:15.810 --> 00:23:18.575 Currently there is now open a mutant

NOTE Confidence: 0.768032867538461

00:23:18.575 --> 00:23:21.167 Karas targeted vaccine for patients at

NOTE Confidence: 0.768032867538461

00:23:21.167 --> 00:23:23.387 risk of developing pancreatic cancer.

NOTE Confidence: 0.768032867538461

00:23:23.390 --> 00:23:26.099 This is a phase one study that

NOTE Confidence: 0.768032867538461

00:23:26.099 --> 00:23:27.260 requires multiple intramuscular

NOTE Confidence: 0.768032867538461

00:23:27.327 --> 00:23:29.385 injections over a period of time.

NOTE Confidence: 0.768032867538461

00:23:29.390 --> 00:23:31.440 The initial outcome is for

NOTE Confidence: 0.768032867538461

00:23:31.440 --> 00:23:32.670 safety and tolerability,

NOTE Confidence: 0.768032867538461

00:23:32.670 --> 00:23:35.622 but they are going to look at changes in

NOTE Confidence: 0.768032867538461

00:23:35.622 --> 00:23:39.578 K Ras specific CD8 and CD4T cells at 2.

NOTE Confidence: 0.768032867538461

00:23:39.578 --> 00:23:41.566 And that four years.

NOTE Confidence: 0.768032867538461

00:23:41.570 --> 00:23:43.551 I'm also interested to know that modern

NOTE Confidence: 0.768032867538461

00:23:43.551 --> 00:23:45.929 it does have an M RNA based KRAS target.

NOTE Confidence: 0.768032867538461

00:23:45.930 --> 00:23:47.850 These are typically being

NOTE Confidence: 0.768032867538461

00:23:47.850 --> 00:23:50.250 used in in oncology trials,

NOTE Confidence: 0.768032867538461

00:23:50.250 --> 00:23:52.092 but may actually have a role

NOTE Confidence: 0.768032867538461

00:23:52.092 --> 00:23:54.342 in the high risk population to

NOTE Confidence: 0.768032867538461

00:23:54.342 --> 00:23:56.727 ultimately prevent and the the

NOTE Confidence: 0.768032867538461

00:23:56.727 --> 00:23:58.710 development of pancreatic cancer.

NOTE Confidence: 0.768032867538461

00:23:58.710 --> 00:24:00.003 So in summary,

NOTE Confidence: 0.768032867538461

00:24:00.003 --> 00:24:02.589 therefore just looking at the time.

NOTE Confidence: 0.768032867538461

00:24:02.590 --> 00:24:04.690 We currently are not performing

NOTE Confidence: 0.768032867538461

00:24:04.690 --> 00:24:06.790 screening in the general population.

NOTE Confidence: 0.768032867538461

00:24:06.790 --> 00:24:08.869 We are focusing on high risk groups,

NOTE Confidence: 0.768032867538461

00:24:08.870 --> 00:24:10.222 such as pancreatic cysts.

NOTE Confidence: 0.768032867538461

00:24:10.222 --> 00:24:11.912 Although we're trying to get

NOTE Confidence: 0.768032867538461

00:24:11.912 --> 00:24:13.528 better at surgical selection,

NOTE Confidence: 0.768032867538461

00:24:13.530 --> 00:24:15.582 but also get better at tailoring

NOTE Confidence: 0.768032867538461

00:24:15.582 --> 00:24:17.320 individuals who should be surveyed

NOTE Confidence: 0.768032867538461

00:24:17.320 --> 00:24:19.186 and those that should not be

NOTE Confidence: 0.768032867538461

00:24:19.190 --> 00:24:21.075 with respect to the familial

NOTE Confidence: 0.768032867538461

00:24:21.075 --> 00:24:22.583 pancreatic cancer cohort patients,

NOTE Confidence: 0.768032867538461

00:24:22.590 --> 00:24:25.047 we're getting better at documenting some of

NOTE Confidence: 0.768032867538461

00:24:25.047 --> 00:24:27.158 the outcomes associated with these studies.

NOTE Confidence: 0.768032867538461

00:24:27.160 --> 00:24:27.612 Really,

NOTE Confidence: 0.768032867538461

00:24:27.612 --> 00:24:29.872 with the view to improving

NOTE Confidence: 0.768032867538461

00:24:29.872 --> 00:24:31.680 those outcomes long term.

NOTE Confidence: 0.768032867538461

00:24:31.680 --> 00:24:33.928 And I think you'll hear more about nuance.

NOTE Confidence: 0.768032867538461

00:24:33.930 --> 00:24:34.660 Set diabetes.

NOTE Confidence: 0.768032867538461

00:24:34.660 --> 00:24:36.485 It certainly plays a role.

NOTE Confidence: 0.768032867538461

00:24:36.490 --> 00:24:37.375 And it it.

NOTE Confidence: 0.768032867538461

00:24:37.375 --> 00:24:38.850 It helps us stratify our

NOTE Confidence: 0.768032867538461

00:24:38.850 --> 00:24:40.469 patients with pancreatic cysts

NOTE Confidence: 0.768032867538461

00:24:40.469 --> 00:24:42.397 and familial pancreatic cancer.

NOTE Confidence: 0.768032867538461

00:24:42.400 --> 00:24:44.128 And I would use this talk just to say

NOTE Confidence: 0.768032867538461

00:24:44.128 --> 00:24:45.941 that there are plenty of opportunities

NOTE Confidence: 0.768032867538461

00:24:45.941 --> 00:24:47.516 within our group for collaboration,

NOTE Confidence: 0.768032867538461

00:24:47.520 --> 00:24:49.760 for additional biomarker developed

NOTE Confidence: 0.768032867538461

00:24:49.760 --> 00:24:51.440 development and validation,

NOTE Confidence: 0.768032867538461

00:24:51.440 --> 00:24:54.268 but also in the realm of imaging.

NOTE Confidence: 0.768032867538461

00:24:54.270 --> 00:24:55.677 And just to say that really it

NOTE Confidence: 0.768032867538461

00:24:55.677 --> 00:24:57.259 takes a group of people to try

NOTE Confidence: 0.768032867538461

00:24:57.259 --> 00:24:58.424 and keep these studies going.

NOTE Confidence: 0.768032867538461

00:24:58.430 --> 00:25:00.678 This is a picture of Ankit who's been

NOTE Confidence: 0.768032867538461

00:25:00.678 --> 00:25:01.869 incredibly productive and helpful.

NOTE Confidence: 0.768032867538461

00:25:01.870 --> 00:25:03.814 Getting our group up and running by there.

NOTE Confidence: 0.768032867538461

00:25:03.820 --> 00:25:05.755 Several other individuals such as

NOTE Confidence: 0.768032867538461

00:25:05.755 --> 00:25:08.048 Scott and disease and Ling helping

NOTE Confidence: 0.768032867538461

00:25:08.048 --> 00:25:10.368 on the the steady side as well as

NOTE Confidence: 0.768032867538461

00:25:10.368 --> 00:25:12.467 our really close and productive

NOTE Confidence: 0.768032867538461

00:25:12.470 --> 00:25:13.535 collaboration with Doctor,

NOTE Confidence: 0.768032867538461

00:25:13.535 --> 00:25:15.310 Hutch, and Doctor Sharma's lab.

NOTE Confidence: 0.768032867538461

00:25:15.310 --> 00:25:15.780 Thank you.

NOTE Confidence: 0.8289154475

00:25:17.610 --> 00:25:19.071 Wonderful doctor Farrell.

NOTE Confidence: 0.8289154475

00:25:19.071 --> 00:25:21.506 Thank you so much for

NOTE Confidence: 0.8289154475

00:25:21.506 --> 00:25:23.720 that really nice overview.

NOTE Confidence: 0.8289154475

00:25:23.720 --> 00:25:25.936 I don't see any questions in the chat,

NOTE Confidence: 0.8289154475

00:25:25.940 --> 00:25:27.347 but if if there are those watching

NOTE Confidence: 0.8289154475

00:25:27.347 --> 00:25:29.612 who have a question, please type it

NOTE Confidence: 0.8289154475

00:25:29.612 --> 00:25:32.820 in and I'll make sure to ask it.

NOTE Confidence: 0.8289154475

00:25:32.820 --> 00:25:34.080 I have a question for you,

NOTE Confidence: 0.8289154475

00:25:34.080 --> 00:25:35.907 so it I'm thinking about the sort

NOTE Confidence: 0.8289154475

00:25:35.907 --> 00:25:38.312 of the root cause of the increased

NOTE Confidence: 0.8289154475

00:25:38.312 --> 00:25:39.876 incidence in pancreatic cancer.

NOTE Confidence: 0.8289154475

00:25:39.880 --> 00:25:41.865 Because we we're seeing an

NOTE Confidence: 0.8289154475

00:25:41.865 --> 00:25:43.056 increase incidence nationally,

NOTE Confidence: 0.8289154475

00:25:43.060 --> 00:25:44.957 but also in the state of Connecticut,

NOTE Confidence: 0.8289154475

00:25:44.960 --> 00:25:45.430 correct?

NOTE Confidence: 0.8289154475

00:25:45.430 --> 00:25:48.720 And so it's either I can't remember

NOTE Confidence: 0.8289154475

00:25:48.720 --> 00:25:52.155 what you said the the number of

NOTE Confidence: 0.8289154475

00:25:52.155 --> 00:25:53.942 pancreatic says of the population

NOTE Confidence: 0.8289154475

00:25:53.942 --> 00:25:55.038 that have pancreatic cysts.

NOTE Confidence: 0.8289154475

00:25:55.040 --> 00:25:55.446 It was.

NOTE Confidence: 0.8289154475

00:25:55.446 --> 00:25:56.664 It seemed like a quite large

NOTE Confidence: 0.70906171075

00:25:56.680 --> 00:25:57.730 number, typically 6,000,000,

NOTE Confidence: 0.70906171075

00:25:57.730 --> 00:25:59.480 is a number that's quoted.

NOTE Confidence: 0.70906171075

00:25:59.480 --> 00:26:01.256 Yeah, if you would do extrapolation

NOTE Confidence: 0.70906171075

00:26:01.256 --> 00:26:03.090 from imaging studies and extrapolate.

NOTE Confidence: 0.70906171075

00:26:03.090 --> 00:26:05.538 Up to to the general population,

NOTE Confidence: 0.838665882631579

00:26:05.740 --> 00:26:08.988 so are we seeing an increase in the

NOTE Confidence: 0.838665882631579

00:26:08.988 --> 00:26:12.886 instance of cysts or is it diabetes and

NOTE Confidence: 0.838665882631579

00:26:12.886 --> 00:26:15.143 therefore with diabetes? Is it obesity?

NOTE Confidence: 0.838665882631579

00:26:15.143 --> 00:26:17.843 So what do you think is the root cause

NOTE Confidence: 0.838665882631579

00:26:17.843 --> 00:26:19.599 driving this increased incidence?

NOTE Confidence: 0.720397675384615

00:26:20.970 --> 00:26:23.270 There's different explanations given for

NOTE Confidence: 0.720397675384615

00:26:23.270 --> 00:26:25.110 the different increases specifically

NOTE Confidence: 0.720397675384615

00:26:25.110 --> 00:26:27.508 for pancreatic ductil adenocarcinoma.

NOTE Confidence: 0.720397675384615

00:26:27.510 --> 00:26:29.120 It's felt that it's also

NOTE Confidence: 0.720397675384615

00:26:29.120 --> 00:26:30.730 related to an aging population,

NOTE Confidence: 0.720397675384615

00:26:30.730 --> 00:26:32.410 so as the population ages,

NOTE Confidence: 0.720397675384615

00:26:32.410 --> 00:26:34.240 that's driving up the overall incidence

NOTE Confidence: 0.720397675384615

00:26:34.240 --> 00:26:36.106 of it, so that's one explanation,

NOTE Confidence: 0.720397675384615

00:26:36.106 --> 00:26:38.338 but for sure there are other issues

NOTE Confidence: 0.720397675384615

00:26:38.338 --> 00:26:40.333 with it and so issues related to.

NOTE Confidence: 0.841007631666667

00:26:42.520 --> 00:26:44.310 Like you know, metabolic explanations

NOTE Confidence: 0.841007631666667

00:26:44.310 --> 00:26:47.090 and obesity would be one one explanation.

NOTE Confidence: 0.841007631666667

00:26:47.090 --> 00:26:49.434 Trying to link that then to pancreatic cysts.

NOTE Confidence: 0.841007631666667

00:26:49.440 --> 00:26:51.536 The reason for the large volume of cysts

NOTE Confidence: 0.841007631666667

00:26:51.536 --> 00:26:53.059 are perception that there are more.

NOTE Confidence: 0.841007631666667

00:26:53.060 --> 00:26:54.254 This is really to just do

NOTE Confidence: 0.841007631666667

00:26:54.254 --> 00:26:55.490 with the use of imaging.

NOTE Confidence: 0.841007631666667

00:26:55.490 --> 00:26:57.898 So the prevalent use of MRI scans

NOTE Confidence: 0.841007631666667

00:26:57.898 --> 00:27:00.240 CT scans has really been driving

NOTE Confidence: 0.841007631666667

00:27:00.240 --> 00:27:02.295 why we see more assists.

NOTE Confidence: 0.841007631666667

00:27:02.300 --> 00:27:03.515 Also, imaging scans are getting

NOTE Confidence: 0.841007631666667

00:27:03.515 --> 00:27:05.389 better so we can see 3 millimeter,

NOTE Confidence: 0.841007631666667

00:27:05.390 --> 00:27:07.155 says 2 millimeter cysts on

NOTE Confidence: 0.841007631666667

00:27:07.155 --> 00:27:08.567 MRI scans done routinely.

NOTE Confidence: 0.841007631666667

00:27:08.570 --> 00:27:10.302 Now the question is.

NOTE Confidence: 0.841007631666667

00:27:10.302 --> 00:27:12.900 Can finding those cysts be converted

NOTE Confidence: 0.841007631666667

00:27:12.983 --> 00:27:15.353 to a better early detection strategy

NOTE Confidence: 0.841007631666667

00:27:15.353 --> 00:27:18.690 for ipms the OR for pancreatic cancer?

NOTE Confidence: 0.841007631666667

00:27:18.690 --> 00:27:22.078 The issue is that maybe those cysts

NOTE Confidence: 0.841007631666667

00:27:22.078 --> 00:27:25.230 account for 1015% of the total volume

NOTE Confidence: 0.841007631666667

00:27:25.230 --> 00:27:26.974 of pancreatic ductal adenocarcinoma.

NOTE Confidence: 0.87344297

00:27:28.510 --> 00:27:30.138 OK, thank you David.

NOTE Confidence: 0.87344297

00:27:30.138 --> 00:27:31.766 RIM had a question.

NOTE Confidence: 0.87344297

00:27:31.770 --> 00:27:33.430 Stage ones went from 40,

NOTE Confidence: 0.87344297

00:27:33.430 --> 00:27:35.150 some to 80 some percent.

NOTE Confidence: 0.87344297

00:27:35.150 --> 00:27:37.586 Survival is that due to greater

NOTE Confidence: 0.87344297

00:27:37.586 --> 00:27:40.291 diagnosis in stage one and have

NOTE Confidence: 0.87344297

00:27:40.291 --> 00:27:42.295 high stage diagnosis decreased.

NOTE Confidence: 0.843321582173913

00:27:43.850 --> 00:27:46.714 So this this phenomenon is from is from

NOTE Confidence: 0.843321582173913

00:27:46.714 --> 00:27:49.618 SEER data and all the positive glowing

NOTE Confidence: 0.843321582173913

00:27:49.618 --> 00:27:52.689 phenomena has been related to stage one a.

NOTE Confidence: 0.843321582173913

00:27:52.690 --> 00:27:55.426 So it has been the increase in incidence,

NOTE Confidence: 0.843321582173913

00:27:55.430 --> 00:27:57.415 the increase in survival associated

NOTE Confidence: 0.843321582173913

00:27:57.415 --> 00:28:00.834 with stage one as the decrease in age of

NOTE Confidence: 0.843321582173913

00:28:00.834 --> 00:28:03.649 diagnosis and it's not seen in the other.

NOTE Confidence: 0.843321582173913

00:28:03.650 --> 00:28:05.974 The other stages it's not even seen

NOTE Confidence: 0.843321582173913

00:28:05.974 --> 00:28:08.570 in stage twos and for sure it's not

NOTE Confidence: 0.843321582173913

00:28:08.570 --> 00:28:10.150 being seen and advanced stages.

NOTE Confidence: 0.843321582173913

00:28:10.150 --> 00:28:11.800 So there's something going on

NOTE Confidence: 0.843321582173913

00:28:11.800 --> 00:28:13.819 and so it's pure speculation.

NOTE Confidence: 0.843321582173913

00:28:13.820 --> 00:28:15.852 Whether it's related to the fact that people

NOTE Confidence: 0.843321582173913

00:28:15.852 --> 00:28:17.900 are more worried about pancreatic cysts,

NOTE Confidence: 0.843321582173913

00:28:17.900 --> 00:28:19.245 you know our surveillance programs

NOTE Confidence: 0.843321582173913

00:28:19.245 --> 00:28:20.590 in high risk individuals that

NOTE Confidence: 0.843321582173913

00:28:20.638 --> 00:28:21.858 count for certain population,

NOTE Confidence: 0.843321582173913

00:28:21.860 --> 00:28:23.477 but I'm not sure they account for

NOTE Confidence: 0.843321582173913

00:28:23.477 --> 00:28:24.788 all that population to switch it,

NOTE Confidence: 0.843321582173913

00:28:24.790 --> 00:28:26.010 so there's something going

NOTE Confidence: 0.843321582173913

00:28:26.010 --> 00:28:26.925 on that's changing,

NOTE Confidence: 0.843321582173913

00:28:26.930 --> 00:28:29.954 but it's it's a unique facet of stage one,

NOTE Confidence: 0.843321582173913

00:28:29.960 --> 00:28:32.135 as rather than the global

NOTE Confidence: 0.843321582173913

00:28:32.135 --> 00:28:34.310 numbers in in pancreatic cancer,

NOTE Confidence: 0.846203750833333

00:28:35.100 --> 00:28:37.956 and then with that year period of

NOTE Confidence: 0.846203750833333

00:28:37.956 --> 00:28:40.300 stage one progressing to metastatic,

NOTE Confidence: 0.846203750833333

00:28:40.300 --> 00:28:44.269 that's probably explaining in 2030 being the.

NOTE Confidence: 0.846203750833333

00:28:44.270 --> 00:28:46.486 Second, cancer mortality related

NOTE Confidence: 0.846203750833333

00:28:46.486 --> 00:28:48.780 to pancreatic cancer, correct?

NOTE Confidence: 0.877657457777778

00:28:49.010 --> 00:28:49.950 I think that's true,

NOTE Confidence: 0.877657457777778

00:28:49.950 --> 00:28:51.360 and I think also because there

NOTE Confidence: 0.877657457777778

00:28:51.414 --> 00:28:52.730 have been some significant

NOTE Confidence: 0.877657457777778

00:28:52.730 --> 00:28:54.311 improvements in other cancers, right?

NOTE Confidence: 0.877657457777778

00:28:54.311 --> 00:28:55.877 So you're seeing you know they're

NOTE Confidence: 0.877657457777778

00:28:55.877 --> 00:28:57.252 being slow improvements and having

NOTE Confidence: 0.877657457777778

00:28:57.252 --> 00:28:58.617 some improvements in the therapeutic

NOTE Confidence: 0.877657457777778

00:28:58.617 --> 00:28:59.770 side for pancreatic cancer.

NOTE Confidence: 0.877657457777778

00:28:59.770 --> 00:29:01.541 But you know, we really need to

NOTE Confidence: 0.877657457777778

00:29:01.541 --> 00:29:03.677 make a real dent for the early

NOTE Confidence: 0.877657457777778

00:29:03.677 --> 00:29:04.865 detection to really kind of begin

NOTE Confidence: 0.877657457777778

00:29:04.865 --> 00:29:06.179 to move that needle a bit better.

NOTE Confidence: 0.805596353684211

00:29:06.810 --> 00:29:08.712 And then the last question from

NOTE Confidence: 0.805596353684211

00:29:08.712 --> 00:29:11.185 Rosa is there also an increase of

NOTE Confidence: 0.805596353684211

00:29:11.185 --> 00:29:13.465 incidence in patients with young onset?

NOTE Confidence: 0.805596353684211

00:29:13.470 --> 00:29:14.580 And I believe you just.

NOTE Confidence: 0.805596353684211

00:29:14.580 --> 00:29:16.536 They said that in answering David's

NOTE Confidence: 0.311486117666667

00:29:16.820 --> 00:29:20.329 question, the age of the age of the

NOTE Confidence: 0.311486117666667

00:29:20.329 --> 00:29:23.160 diagnosis for the stage 1A's is going down,

NOTE Confidence: 0.311486117666667

00:29:23.160 --> 00:29:24.924 not for the other councils but for

NOTE Confidence: 0.311486117666667

00:29:24.924 --> 00:29:26.920 the other stages, but the stage one

NOTE Confidence: 0.311486117666667

00:29:26.920 --> 00:29:28.780 age of diagnosis has gone down.

NOTE Confidence: 0.311486117666667

00:29:28.780 --> 00:29:32.080 There are data about the overall decrease in

NOTE Confidence: 0.311486117666667

00:29:32.080 --> 00:29:34.250 the age of diagnosis of pancreatic cancer,

NOTE Confidence: 0.311486117666667

00:29:34.250 --> 00:29:35.993 and it may in fact be associated

NOTE Confidence: 0.311486117666667

00:29:35.993 --> 00:29:37.315 with slightly different types of

NOTE Confidence: 0.311486117666667

00:29:37.315 --> 00:29:38.625 genotypes and molecular profiling and

NOTE Confidence: 0.311486117666667

00:29:38.625 --> 00:29:40.510 some of that data has been kind of

NOTE Confidence: 0.311486117666667

00:29:40.510 --> 00:29:42.284 presented here at Yale in the past,

NOTE Confidence: 0.311486117666667

00:29:42.284 --> 00:29:43.732 so certainly focusing in

NOTE Confidence: 0.311486117666667

00:29:43.732 --> 00:29:45.180 on the younger population,

NOTE Confidence: 0.311486117666667

00:29:45.180 --> 00:29:46.830 hearing about a younger population.

NOTE Confidence: 0.311486117666667

00:29:46.830 --> 00:29:47.844 With pancreatic cancer,

NOTE Confidence: 0.311486117666667

00:29:47.844 --> 00:29:49.534 which is certainly very concerning.

NOTE Confidence: 0.862206432

00:29:50.450 --> 00:29:52.030 Well, thank you so much.

NOTE Confidence: 0.862206432

00:29:52.030 --> 00:29:54.186 It'd be great to to continue our

NOTE Confidence: 0.862206432

00:29:54.186 --> 00:29:56.208 our work here with the focus

NOTE Confidence: 0.862206432

00:29:56.208 --> 00:29:58.260 on Connecticut and how we can

NOTE Confidence: 0.862206432

00:29:58.260 --> 00:30:00.277 really improve upon the lower

NOTE Confidence: 0.862206432

00:30:00.277 --> 00:30:02.287 the incidence and or mortality.

NOTE Confidence: 0.862206432

00:30:02.290 --> 00:30:04.150 So thank you so much.

NOTE Confidence: 0.862206432

00:30:04.150 --> 00:30:05.548 Thanks very much.

NOTE Confidence: 0.862206432

00:30:05.550 --> 00:30:08.035 OK, if you can stop sharing and

NOTE Confidence: 0.862206432

00:30:08.035 --> 00:30:11.072 I'm now I'm delighted to introduce

NOTE Confidence: 0.862206432

00:30:11.072 --> 00:30:13.050 Doctor Bacillus Vessella who

NOTE Confidence: 0.862206432

00:30:13.050 --> 00:30:15.210 is chair of our Department of

NOTE Confidence: 0.862206432

00:30:15.210 --> 00:30:16.638 Environmental Health Sciences in

NOTE Confidence: 0.862206432

00:30:16.638 --> 00:30:18.570 the Yale School of Public Health.

NOTE Confidence: 0.862206432

00:30:18.570 --> 00:30:20.880 He's also the Susan Dwight Bliss

NOTE Confidence: 0.862206432

00:30:20.880 --> 00:30:22.420 professor of epidemiology and

NOTE Confidence: 0.862206432

00:30:22.489 --> 00:30:24.117 of ophthalmology and visual

NOTE Confidence: 0.862206432

00:30:24.117 --> 00:30:26.152 science and of the environment.

NOTE Confidence: 0.862206432

00:30:26.160 --> 00:30:28.458 He received his bachelors in Chemistry

NOTE Confidence: 0.862206432

00:30:28.458 --> 00:30:30.450 and PhD in biochemical pharmacology

NOTE Confidence: 0.862206432

00:30:30.450 --> 00:30:32.425 from the University of Ioannina

NOTE Confidence: 0.862206432

00:30:32.425 --> 00:30:35.456 in Greece and then he trained in

NOTE Confidence: 0.862206432

00:30:35.456 --> 00:30:36.836 gene environment interactions,

NOTE Confidence: 0.862206432

00:30:36.840 --> 00:30:38.920 molecular toxicology and pharmacogenetics

NOTE Confidence: 0.862206432

00:30:38.920 --> 00:30:41.520 at the Department of Environmental

NOTE Confidence: 0.862206432

00:30:41.520 --> 00:30:44.025 Health in the College of Medicine

NOTE Confidence: 0.862206432

00:30:44.025 --> 00:30:45.557 at University of Cincinnati.

NOTE Confidence: 0.862206432

00:30:45.560 --> 00:30:47.956 He's established an internationally

NOTE Confidence: 0.862206432

00:30:47.956 --> 00:30:49.753 recognized research program

NOTE Confidence: 0.862206432

00:30:49.753 --> 00:30:52.271 that's been continuously funded by

NOTE Confidence: 0.862206432

00:30:52.271 --> 00:30:54.708 NIH since 1997 and his research

NOTE Confidence: 0.862206432

00:30:54.708 --> 00:30:56.496 interests include the etiology.

NOTE Confidence: 0.862206432

00:30:56.500 --> 00:30:58.300 The molecular mechanisms of

NOTE Confidence: 0.862206432

00:30:58.300 --> 00:30:59.650 environmentally induced human

NOTE Confidence: 0.862206432

00:30:59.650 --> 00:31:01.930 disease such as liver disease,

NOTE Confidence: 0.862206432

00:31:01.930 --> 00:31:03.625 obesity and diabetes,

NOTE Confidence: 0.862206432

00:31:03.625 --> 00:31:05.320 cancer and neurogenic

NOTE Confidence: 0.862206432

00:31:05.320 --> 00:31:06.450 neurodegenerative diseases.

NOTE Confidence: 0.862206432

00:31:06.450 --> 00:31:08.502 His laboratory uses state of the

NOTE Confidence: 0.862206432

00:31:08.502 --> 00:31:09.870 art integrated approaches that

NOTE Confidence: 0.862206432

00:31:09.929 --> 00:31:11.666 include metabolomics, lipidomics,

NOTE Confidence: 0.862206432

00:31:11.666 --> 00:31:14.050 expoza, omics tissue imaging,

NOTE Confidence: 0.862206432

00:31:14.050 --> 00:31:14.668 mass spec,

NOTE Confidence: 0.862206432

00:31:14.668 --> 00:31:16.522 deep learning as well as human

NOTE Confidence: 0.862206432

00:31:16.522 --> 00:31:18.286 cohorts and genetically engineered

NOTE Confidence: 0.862206432

00:31:18.286 --> 00:31:21.344 mouse models and we are delighted

NOTE Confidence: 0.862206432

00:31:21.344 --> 00:31:24.006 to have him here today to talk

NOTE Confidence: 0.862206432

00:31:24.006 --> 00:31:26.666 specifically about alcohol and cancer.

NOTE Confidence: 0.862206432

00:31:26.670 --> 00:31:27.840 Thank you Vasilis.

NOTE Confidence: 0.594001571666667

00:31:28.070 --> 00:31:29.990 Thank you many days my microphone.

NOTE Confidence: 0.594001571666667

00:31:29.990 --> 00:31:31.730 Yes, my microphone is on.

NOTE Confidence: 0.594001571666667

00:31:31.730 --> 00:31:33.588 Thank you very much for your nice work

NOTE Confidence: 0.594001571666667

00:31:33.590 --> 00:31:36.788 and thanks also James for pointing

NOTE Confidence: 0.594001571666667

00:31:36.788 --> 00:31:40.940 out our T 32 who has helped on the

NOTE Confidence: 0.594001571666667

00:31:40.940 --> 00:31:43.530 studies before before I start mine I

NOTE Confidence: 0.594001571666667

00:31:43.606 --> 00:31:46.502 also want to address a little bit of

NOTE Confidence: 0.594001571666667

00:31:46.502 --> 00:31:49.293 the question of Melinda your question

NOTE Confidence: 0.594001571666667

00:31:49.293 --> 00:31:51.773 regarding the increasing density of

NOTE Confidence: 0.594001571666667

00:31:51.773 --> 00:31:54.274 cancer lately one of the things that

NOTE Confidence: 0.594001571666667

00:31:54.274 --> 00:31:57.249 I would like to point out is we have.

NOTE Confidence: 0.594001571666667

00:31:57.250 --> 00:32:00.250 Some increases in environmental exposures,

NOTE Confidence: 0.594001571666667

00:32:00.250 --> 00:32:03.410 especially for the perfluorinated compounds,

NOTE Confidence: 0.594001571666667

00:32:03.410 --> 00:32:05.815 namely PFAS, which may have

NOTE Confidence: 0.594001571666667

00:32:05.815 --> 00:32:09.190 contributed in all all kind of tumors.

NOTE Confidence: 0.594001571666667

00:32:09.190 --> 00:32:11.719 I wish we should have a round table another

NOTE Confidence: 0.594001571666667

00:32:11.719 --> 00:32:14.106 time to discuss about all these factors.

NOTE Confidence: 0.594001571666667

00:32:14.110 --> 00:32:17.332 So today what I'm going to talk to you

NOTE Confidence: 0.594001571666667

00:32:17.332 --> 00:32:20.272 about it is molecular mechanisms of

NOTE Confidence: 0.594001571666667

00:32:20.272 --> 00:32:23.882 alcohol and cancer, and so we have.

NOTE Confidence: 0.594001571666667

00:32:23.882 --> 00:32:27.294 We have edited 3 books on alcohol.

NOTE Confidence: 0.594001571666667

00:32:27.294 --> 00:32:29.968 You cancer and one special issue on

NOTE Confidence: 0.594001571666667

00:32:29.968 --> 00:32:32.750 chemical biological interactions which

NOTE Confidence: 0.594001571666667

00:32:32.750 --> 00:32:37.180 was based on my third international

NOTE Confidence: 0.594001571666667

00:32:37.180 --> 00:32:38.940 conference on alcohol and cancer,

NOTE Confidence: 0.594001571666667

00:32:38.940 --> 00:32:42.377 which we held it here in Newport.

NOTE Confidence: 0.594001571666667

00:32:42.380 --> 00:32:45.915 A couple of just before the COVID

NOTE Confidence: 0.594001571666667

00:32:45.920 --> 00:32:47.120 As a matter of fact,

NOTE Confidence: 0.594001571666667

00:32:47.120 --> 00:32:50.228 we just received a note from

NOTE Confidence: 0.830666932

00:32:51.020 --> 00:32:53.827 from Springer that our books doing so

NOTE Confidence: 0.830666932

00:32:53.827 --> 00:32:56.887 good and alcohol and cancer and they want

NOTE Confidence: 0.924430438

00:32:56.900 --> 00:32:59.776 us to write another one very much.

NOTE Confidence: 0.924430438

00:32:59.776 --> 00:33:04.595 But we will see. So I have all there

NOTE Confidence: 0.924430438

00:33:04.595 --> 00:33:07.224 is this association between alcohol

NOTE Confidence: 0.924430438

00:33:07.224 --> 00:33:10.606 and cancer and it's actually, you know,

NOTE Confidence: 0.924430438

00:33:10.606 --> 00:33:12.760 there is epidemiological evidence that

NOTE Confidence: 0.924430438

00:33:12.760 --> 00:33:15.990 is kind or is convincing that alcohol.

NOTE Confidence: 0.924430438

00:33:15.990 --> 00:33:17.878 Is associated with several

NOTE Confidence: 0.924430438

00:33:17.878 --> 00:33:19.355 cancers listed in here.

NOTE Confidence: 0.924430438

00:33:19.355 --> 00:33:21.712 Mouth fighting, slurring, esophagus,

NOTE Confidence: 0.924430438

00:33:21.712 --> 00:33:26.430 colon and breast for women and you

NOTE Confidence: 0.924430438

00:33:26.535 --> 00:33:28.842 know there is some more breast and

NOTE Confidence: 0.924430438

00:33:28.842 --> 00:33:31.610 liver based on IRC and there is a

NOTE Confidence: 0.924430438

00:33:31.692 --> 00:33:34.634 probable liver and colorectal for women.

NOTE Confidence: 0.924430438

00:33:34.634 --> 00:33:37.470 One of the things that I have not

NOTE Confidence: 0.924430438

00:33:37.470 --> 00:33:39.295 included in this presentation though

NOTE Confidence: 0.924430438

00:33:39.295 --> 00:33:41.867 and I have to say that as well they

NOTE Confidence: 0.924430438

00:33:41.867 --> 00:33:44.086 have been epidemiological studies which

NOTE Confidence: 0.924430438

00:33:44.086 --> 00:33:46.776 indicates that alcohol in sometimes.

NOTE Confidence: 0.924430438

00:33:46.780 --> 00:33:51.223 Is a positive factor in preventing alcohol,

NOTE Confidence: 0.924430438

00:33:51.223 --> 00:33:55.640 so I I don't have time to go with that.

NOTE Confidence: 0.924430438

00:33:55.640 --> 00:33:58.097 I'm gonna stick with the mechanisms today.

NOTE Confidence: 0.924430438

00:33:58.100 --> 00:34:00.464 Molecular mechanisms of the

NOTE Confidence: 0.924430438

00:34:00.464 --> 00:34:02.237 alcohol induced cancer.

NOTE Confidence: 0.924430438

00:34:02.240 --> 00:34:04.904 So let me before we go to that.

NOTE Confidence: 0.924430438

00:34:04.910 --> 00:34:07.556 And since we're talking about epidemiology

NOTE Confidence: 0.924430438

00:34:07.556 --> 00:34:11.655 is I want to tell you the categories of

NOTE Confidence: 0.924430438

00:34:11.655 --> 00:34:13.990 association between alcohol consumption and

NOTE Confidence: 0.924430438

00:34:14.059 --> 00:34:17.120 cancer and there is first case is sufficient.

NOTE Confidence: 0.924430438

00:34:17.120 --> 00:34:19.430 Evidence of a causal association,

NOTE Confidence: 0.924430438

00:34:19.430 --> 00:34:23.160 which is the case for every every study.

NOTE Confidence: 0.924430438

00:34:23.160 --> 00:34:24.975 There is sufficient

NOTE Confidence: 0.924430438

00:34:24.975 --> 00:34:27.395 evidence of an association.

NOTE Confidence: 0.924430438

00:34:27.400 --> 00:34:30.405 There is limited and suggestive

NOTE Confidence: 0.924430438

00:34:30.405 --> 00:34:32.208 evidence of unappreciation.

NOTE Confidence: 0.924430438

00:34:32.210 --> 00:34:35.195 Inadequate or insufficient to determine

NOTE Confidence: 0.924430438

00:34:35.195 --> 00:34:37.583 whether an association exists.

NOTE Confidence: 0.924430438

00:34:37.590 --> 00:34:39.513 Limited and suggestive.

NOTE Confidence: 0.924430438

00:34:39.513 --> 00:34:42.718 Evidence to of no association.

NOTE Confidence: 0.924430438

00:34:42.720 --> 00:34:46.336 This has been described very well in a

NOTE Confidence: 0.924430438

00:34:46.336 --> 00:34:51.170 paper by our junior faculty just walach.

NOTE Confidence: 0.924430438

00:34:51.170 --> 00:34:54.850 It was in in 2020 in the International

NOTE Confidence: 0.924430438

00:34:54.850 --> 00:34:57.090 Journal of Epidemiology,

NOTE Confidence: 0.924430438

00:34:57.090 --> 00:34:59.370 and this is worth reading it.

NOTE Confidence: 0.924430438

00:34:59.370 --> 00:35:02.136 One of the problems with alcohol.

NOTE Confidence: 0.924430438

00:35:02.140 --> 00:35:04.040 Based.

NOTE Confidence: 0.924430438

00:35:04.040 --> 00:35:08.158 Epidemiological studies is most of the

NOTE Confidence: 0.924430438

00:35:08.158 --> 00:35:10.192 studies are based on a questionnaire

NOTE Confidence: 0.924430438

00:35:10.192 --> 00:35:12.473 and rather than having clinical data

NOTE Confidence: 0.924430438

00:35:12.473 --> 00:35:14.771 in terms of the alcohol consumption

NOTE Confidence: 0.924430438

00:35:14.780 --> 00:35:16.508 and we know there are certain

NOTE Confidence: 0.924430438

00:35:16.510 --> 00:35:18.890 biases that could really interfere

NOTE Confidence: 0.924430438

00:35:18.890 --> 00:35:21.092 with the outcome of the studies,

NOTE Confidence: 0.924430438

00:35:21.092 --> 00:35:22.940 and this is most of the time

NOTE Confidence: 0.924430438

00:35:23.000 --> 00:35:24.080 people really are.

NOTE Confidence: 0.924430438

00:35:24.080 --> 00:35:25.880 You know, don't tell the truth.

NOTE Confidence: 0.924430438

00:35:25.880 --> 00:35:27.296 So answering the question,

NOTE Confidence: 0.924430438

00:35:27.296 --> 00:35:30.050 how many drinks you have there per week?

NOTE Confidence: 0.924430438

00:35:30.050 --> 00:35:31.022 Well maybe 1,

NOTE Confidence: 0.924430438

00:35:31.022 --> 00:35:33.999 maybe you know and could be just a bottle.

NOTE Confidence: 0.924430438

00:35:34.000 --> 00:35:37.748 Of of of of Hard Liquor per week.

NOTE Confidence: 0.924430438

00:35:37.750 --> 00:35:40.426 So this may create some problems,

NOTE Confidence: 0.924430438

00:35:40.430 --> 00:35:42.766 and this is what I'm trying to introduce.

NOTE Confidence: 0.924430438

00:35:42.770 --> 00:35:45.290 A new term which called the ALCOM,

NOTE Confidence: 0.924430438

00:35:45.290 --> 00:35:48.058 which is a panel of markets that could

NOTE Confidence: 0.924430438

00:35:48.058 --> 00:35:50.640 indicate what is your alcohol consumption

NOTE Confidence: 0.924430438

00:35:50.640 --> 00:35:53.210 throughout the years of your life.

NOTE Confidence: 0.924430438

00:35:53.210 --> 00:35:59.155 So in December 2020 I I was involved

NOTE Confidence: 0.924430438

00:35:59.155 --> 00:36:02.990 in an NCI workshop that we presented.

NOTE Confidence: 0.924430438

00:36:02.990 --> 00:36:04.610 You know the existing.

NOTE Confidence: 0.924430438

00:36:04.610 --> 00:36:06.095 Knowledge and everything.

NOTE Confidence: 0.924430438

00:36:06.095 --> 00:36:09.065 Evidence and gaps across the cancer

NOTE Confidence: 0.924430438

00:36:09.065 --> 00:36:11.936 continuum regarding the alcohol and cancer.

NOTE Confidence: 0.924430438

00:36:11.940 --> 00:36:16.268 So we have looked at from epidemiology to

NOTE Confidence: 0.924430438

00:36:16.270 --> 00:36:19.499 and biology of the alcohol and cancer risk.

NOTE Confidence: 0.924430438

00:36:19.500 --> 00:36:22.748 What needs to be addressed and how

NOTE Confidence: 0.924430438

00:36:22.748 --> 00:36:25.827 we can really work in preventing

NOTE Confidence: 0.924430438

00:36:25.827 --> 00:36:28.772 you know this alcohol consumption

NOTE Confidence: 0.924430438

00:36:28.772 --> 00:36:31.448 that could lead to cancer.

NOTE Confidence: 0.924430438

00:36:31.450 --> 00:36:31.793 Again,

NOTE Confidence: 0.924430438

00:36:31.793 --> 00:36:35.570 this is a readily available to everybody.

NOTE Confidence: 0.924430438

00:36:35.570 --> 00:36:37.815 And I'm going to go directly

NOTE Confidence: 0.924430438

00:36:37.815 --> 00:36:38.790 to the mechanism,

NOTE Confidence: 0.924430438

00:36:38.790 --> 00:36:41.870 so I've been working with alcohol metabolism

NOTE Confidence: 0.924430438

00:36:41.870 --> 00:36:44.958 since day one of my graduate studies,

NOTE Confidence: 0.943816495714286

00:36:44.970 --> 00:36:48.470 and that was the metabolism of alcohol,

NOTE Confidence: 0.943816495714286

00:36:48.470 --> 00:36:50.996 which actually is involved is been.

NOTE Confidence: 0.7181348

00:36:53.590 --> 00:36:57.090 Consider it as the mechanism of inducing

NOTE Confidence: 0.7181348

00:36:57.090 --> 00:36:59.748 cancer so your alcohol, your ethanol,

NOTE Confidence: 0.7181348

00:36:59.748 --> 00:37:02.293 is metabolized by alcohol dehydrogenases

NOTE Confidence: 0.7181348

00:37:02.293 --> 00:37:05.370 to an aldehyde which is a powerful.

NOTE Confidence: 0.7181348

00:37:05.370 --> 00:37:06.675 You know it's an aldehydes

NOTE Confidence: 0.7181348

00:37:06.675 --> 00:37:07.458 and an electrophile,

NOTE Confidence: 0.7181348

00:37:07.460 --> 00:37:10.142 which is capable of interacting with

NOTE Confidence: 0.7181348

00:37:10.142 --> 00:37:13.710 DNA and protein and forming adducts and,

NOTE Confidence: 0.7181348

00:37:13.710 --> 00:37:17.710 and this is a very important molecule in

NOTE Confidence: 0.7181348

00:37:17.710 --> 00:37:20.880 here, so ethanol can also be metabolized

NOTE Confidence: 0.7181348

00:37:20.880 --> 00:37:23.550 by catalase and also by cytochrome P.

NOTE Confidence: 0.7181348

00:37:23.550 --> 00:37:26.082 The 50s, mostly cytochrome P452 you

NOTE Confidence: 0.7181348

00:37:26.082 --> 00:37:29.725 want and to a lesser extent by 182.

NOTE Confidence: 0.7181348

00:37:29.725 --> 00:37:32.635 What happens during the ethanol metabolism.

NOTE Confidence: 0.7181348

00:37:32.640 --> 00:37:33.496 P4, fifties.

NOTE Confidence: 0.7181348

00:37:33.496 --> 00:37:35.636 You have generation of reactive

NOTE Confidence: 0.7181348

00:37:35.636 --> 00:37:36.492 oxygen species.

NOTE Confidence: 0.7181348

00:37:36.500 --> 00:37:38.685 You have glutathione depletion which

NOTE Confidence: 0.7181348

00:37:38.685 --> 00:37:40.840 leads to oxidative stress and as

NOTE Confidence: 0.7181348

00:37:40.840 --> 00:37:43.681 you will see later on we have the

NOTE Confidence: 0.7181348

00:37:43.681 --> 00:37:45.811 formation of further aldehydes namely

NOTE Confidence: 0.7181348

00:37:45.811 --> 00:37:48.098 4 hydroxy nonenal and malondialdehyde

NOTE Confidence: 0.7181348

00:37:48.098 --> 00:37:50.433 which are further capable of

NOTE Confidence: 0.7181348

00:37:50.433 --> 00:37:54.470 causing DNA and protein adducts so.

NOTE Confidence: 0.7181348

00:37:54.470 --> 00:37:57.206 Ald H2 is the major enzyme

NOTE Confidence: 0.7181348

00:37:57.206 --> 00:37:58.574 which metabolizes acetaldehyde.

NOTE Confidence: 0.7181348

00:37:58.580 --> 00:38:00.770 The major product of ethanol,

NOTE Confidence: 0.7181348

00:38:00.770 --> 00:38:03.650 and it is converted to acetate and then

NOTE Confidence: 0.7181348

00:38:03.650 --> 00:38:07.010 from the acetate can go to kettle coenzyme,

NOTE Confidence: 0.7181348

00:38:07.010 --> 00:38:09.614 which can be used as a building

NOTE Confidence: 0.7181348

00:38:09.614 --> 00:38:11.340 biomolecule for a lot of.

NOTE Confidence: 0.781828214

00:38:13.350 --> 00:38:15.650 Cells, including the cancer cell,

NOTE Confidence: 0.781828214

00:38:15.650 --> 00:38:16.472 that's another story.

NOTE Confidence: 0.781828214

00:38:16.472 --> 00:38:19.330 We don't have the time to go over that today,

NOTE Confidence: 0.781828214

00:38:19.330 --> 00:38:22.055 so as you can see, the other heads and the

NOTE Confidence: 0.781828214

00:38:22.055 --> 00:38:24.210 reactive oxygen species are very important.

NOTE Confidence: 0.781828214

00:38:24.210 --> 00:38:26.586 My lab is focusing in all aldehyde metabolism

NOTE Confidence: 0.781828214

00:38:26.586 --> 00:38:28.730 and I'll show you a little bit more.

NOTE Confidence: 0.781828214

00:38:28.730 --> 00:38:31.152 But we also looking at the LDH

NOTE Confidence: 0.781828214

00:38:31.152 --> 00:38:34.826 2 and a LDH 1V1 and a LDH 1A1.

NOTE Confidence: 0.781828214

00:38:34.826 --> 00:38:36.941 This is aldehyde dehydrogenase enzymes

NOTE Confidence: 0.781828214

00:38:36.941 --> 00:38:39.577 which they take us at aldehyde and

NOTE Confidence: 0.781828214

00:38:39.577 --> 00:38:40.976 convert it to acetate.

NOTE Confidence: 0.781828214

00:38:40.976 --> 00:38:43.960 So again you can see for the risk.

NOTE Confidence: 0.781828214

00:38:43.960 --> 00:38:46.990 Factors in terms of alcohol drinking

NOTE Confidence: 0.781828214

00:38:46.990 --> 00:38:49.588 as mentioned earlier there is aids,

NOTE Confidence: 0.781828214

00:38:49.590 --> 00:38:51.198 the personal history,

NOTE Confidence: 0.781828214

00:38:51.198 --> 00:38:54.422 family history, race and also diet,

NOTE Confidence: 0.781828214

00:38:54.422 --> 00:38:55.930 physical activity, obesity,

NOTE Confidence: 0.781828214

00:38:55.930 --> 00:38:57.650 smoking and alcohol use.

NOTE Confidence: 0.781828214

00:38:57.650 --> 00:39:00.989 As Melinda and James were mentioning above.

NOTE Confidence: 0.781828214

00:39:00.990 --> 00:39:03.546 So what Mike what we're doing in my lab

NOTE Confidence: 0.781828214

00:39:03.546 --> 00:39:06.330 is and I have a center funded by the NAA

NOTE Confidence: 0.781828214

00:39:06.330 --> 00:39:09.178 as we have all you can see here is this.

NOTE Confidence: 0.781828214

00:39:09.180 --> 00:39:11.024 The ethanol metabolism and

NOTE Confidence: 0.781828214

00:39:11.024 --> 00:39:12.407 also glutathione metabolism.

NOTE Confidence: 0.781828214

00:39:12.410 --> 00:39:15.248 They the synthesis of your major.

NOTE Confidence: 0.781828214

00:39:15.250 --> 00:39:17.740 Antioxidant of your system here and

NOTE Confidence: 0.781828214

00:39:17.740 --> 00:39:21.159 what you can see on those red letters.

NOTE Confidence: 0.781828214

00:39:21.160 --> 00:39:23.710 Are the enzymes involved in these

NOTE Confidence: 0.781828214

00:39:23.710 --> 00:39:25.915 pathways and we have single and

NOTE Confidence: 0.781828214

00:39:25.915 --> 00:39:28.240 double knockouts of all these enzymes

NOTE Confidence: 0.781828214

00:39:28.240 --> 00:39:30.662 which are involved in the eye in

NOTE Confidence: 0.781828214

00:39:30.662 --> 00:39:32.469 the ethanol metabolism and the

NOTE Confidence: 0.781828214

00:39:32.469 --> 00:39:34.229 interplay and essentially trying to

NOTE Confidence: 0.781828214

00:39:34.229 --> 00:39:36.970 clear up the reactive oxygen species

NOTE Confidence: 0.781828214

00:39:36.970 --> 00:39:39.126 generated and protecting yourselves.

NOTE Confidence: 0.781828214

00:39:39.130 --> 00:39:42.674 So we just published a review in cancers

NOTE Confidence: 0.781828214

00:39:42.674 --> 00:39:45.488 on molecular mechanisms of alcohol.

NOTE Confidence: 0.781828214

00:39:45.490 --> 00:39:47.430 And yours.

NOTE Confidence: 0.781828214

00:39:47.430 --> 00:39:49.212 Colorectal cancer so this is one

NOTE Confidence: 0.781828214

00:39:49.212 --> 00:39:51.606 of the area that my lab has been

NOTE Confidence: 0.781828214

00:39:51.606 --> 00:39:53.316 focusing for a number of years.

NOTE Confidence: 0.781828214

00:39:53.320 --> 00:39:55.742 We had EU one which I'm planning

NOTE Confidence: 0.781828214

00:39:55.742 --> 00:39:58.753 to go for the renewal as well and

NOTE Confidence: 0.781828214

00:39:58.753 --> 00:40:01.591 essentially again you can see that

NOTE Confidence: 0.781828214

00:40:01.591 --> 00:40:03.871 ethanol metabolism is involved in

NOTE Confidence: 0.781828214

00:40:03.871 --> 00:40:06.580 here and we have what I described

NOTE Confidence: 0.781828214

00:40:06.580 --> 00:40:09.018 you before the pathways here.

NOTE Confidence: 0.781828214

00:40:09.020 --> 00:40:11.009 But one of the things I want to tell

NOTE Confidence: 0.781828214

00:40:11.009 --> 00:40:14.788 you is the ethanol per se is not only

NOTE Confidence: 0.781828214

00:40:14.788 --> 00:40:17.574 metabolized by cytochrome P452 one,

NOTE Confidence: 0.781828214

00:40:17.574 --> 00:40:18.241 but.

NOTE Confidence: 0.781828214

00:40:18.241 --> 00:40:20.909 Constantly induces increases the

NOTE Confidence: 0.781828214

00:40:20.909 --> 00:40:23.670 levels of cytochrome P452E1 why?

NOTE Confidence: 0.781828214

00:40:23.670 --> 00:40:24.810 This is important?

NOTE Confidence: 0.781828214

00:40:24.810 --> 00:40:28.363 Because 2 E one it can metabolize

NOTE Confidence: 0.781828214

00:40:28.363 --> 00:40:30.828 the processing loggens into the

NOTE Confidence: 0.781828214

00:40:30.828 --> 00:40:33.705 carcinogens and that is very important

NOTE Confidence: 0.781828214

00:40:33.705 --> 00:40:36.610 and other area of the cytochrome P.

NOTE Confidence: 0.781828214

00:40:36.610 --> 00:40:39.053 For the two one it can increase

NOTE Confidence: 0.781828214

00:40:39.053 --> 00:40:40.860 the cell proliferation and also

NOTE Confidence: 0.781828214

00:40:40.860 --> 00:40:42.918 as we discussed it can create

NOTE Confidence: 0.781828214

00:40:42.918 --> 00:40:44.450 reactive boxes and species.

NOTE Confidence: 0.781828214

00:40:44.450 --> 00:40:46.415 The other is the important

NOTE Confidence: 0.781828214

00:40:46.415 --> 00:40:47.987 roles of both sides.

NOTE Confidence: 0.781828214

00:40:47.990 --> 00:40:50.489 From P452 you are and also you

NOTE Confidence: 0.781828214

00:40:50.489 --> 00:40:52.296 know the aldehyde dehydrogenases

NOTE Confidence: 0.781828214

00:40:52.296 --> 00:40:54.916 in retinoic acid homeostasis,

NOTE Confidence: 0.781828214

00:40:54.920 --> 00:40:57.020 which they been also involved

NOTE Confidence: 0.781828214

00:40:57.020 --> 00:40:59.120 in the the whole process.

NOTE Confidence: 0.781828214

00:40:59.120 --> 00:41:01.495 Another important issue here is

NOTE Confidence: 0.781828214

00:41:01.495 --> 00:41:04.479 the ratio between NADH and NAD

NOTE Confidence: 0.781828214

00:41:04.479 --> 00:41:07.099 which is completely changed based

NOTE Confidence: 0.781828214

00:41:07.099 --> 00:41:09.195 on the ethanol metabolism.

NOTE Confidence: 0.781828214

00:41:09.200 --> 00:41:11.480 Another area which ethanol could

NOTE Confidence: 0.781828214

00:41:11.480 --> 00:41:14.300 affect is the one carbon metabolism

NOTE Confidence: 0.781828214

00:41:14.300 --> 00:41:17.244 and that has effects on the DNA

NOTE Confidence: 0.781828214

00:41:17.244 --> 00:41:18.808 methylation which can really.

NOTE Confidence: 0.781828214

00:41:18.810 --> 00:41:20.170 Umm?

NOTE Confidence: 0.781828214

00:41:20.170 --> 00:41:21.418 Give a lot of.

NOTE Confidence: 0.83555562

00:41:23.510 --> 00:41:25.795 Changes in DNA methylation associated

NOTE Confidence: 0.83555562

00:41:25.795 --> 00:41:27.750 with cancer, as I told you before,

NOTE Confidence: 0.83555562

00:41:27.750 --> 00:41:32.403 I get there may can be used as macromolecule

NOTE Confidence: 0.83555562

00:41:32.403 --> 00:41:34.236 biosynthesis including including

NOTE Confidence: 0.83555562

00:41:34.236 --> 00:41:37.484 in the cancer cells we have a lot.

NOTE Confidence: 0.83555562

00:41:37.490 --> 00:41:38.785 I don't have the time to go,

NOTE Confidence: 0.83555562

00:41:38.790 --> 00:41:40.518 I just want to give you a brief

NOTE Confidence: 0.83555562

00:41:40.518 --> 00:41:41.809 overview of what's going on.

NOTE Confidence: 0.83555562

00:41:41.810 --> 00:41:43.346 So one of the major thing.

NOTE Confidence: 0.83555562

00:41:43.350 --> 00:41:46.086 So here if we can focus is you

NOTE Confidence: 0.83555562

00:41:46.086 --> 00:41:48.710 have the the adduct formation,

NOTE Confidence: 0.83555562

00:41:48.710 --> 00:41:50.520 the DNA and the proteins.

NOTE Confidence: 0.83555562

00:41:50.520 --> 00:41:51.714 I'm just going to show you

NOTE Confidence: 0.83555562

00:41:51.714 --> 00:41:52.730 some examples of the DNA.

NOTE Confidence: 0.83555562

00:41:52.730 --> 00:41:55.115 And we're gonna talk about

NOTE Confidence: 0.83555562

00:41:55.115 --> 00:41:57.500 some the inflammation as well,

NOTE Confidence: 0.83555562

00:41:57.500 --> 00:42:00.080 and we're gonna go from there.

NOTE Confidence: 0.83555562

00:42:00.080 --> 00:42:01.890 So what happened with the

NOTE Confidence: 0.83555562

00:42:01.890 --> 00:42:03.700 acetaldehyde and also the other

NOTE Confidence: 0.83555562

00:42:03.764 --> 00:42:06.049 aldehyde generating the DNA attacks?

NOTE Confidence: 0.83555562

00:42:06.050 --> 00:42:08.696 So these aldehydes are both in electrophiles,

NOTE Confidence: 0.83555562

00:42:08.700 --> 00:42:09.848 they can interact with

NOTE Confidence: 0.732048920444444

00:42:09.860 --> 00:42:11.415 bases of the DNA, and

NOTE Confidence: 0.732048920444444

00:42:11.415 --> 00:42:12.830 they can form others. And

NOTE Confidence: 0.819997891111111

00:42:12.840 --> 00:42:15.168 these adducts then they they are

NOTE Confidence: 0.819997891111111

00:42:15.168 --> 00:42:17.150 responsible for causing mutations

NOTE Confidence: 0.819997891111111

00:42:17.150 --> 00:42:20.320 into your into your transcripts.

NOTE Confidence: 0.819997891111111

00:42:20.320 --> 00:42:22.760 And I said aldehyde by.

NOTE Confidence: 0.819997891111111

00:42:22.760 --> 00:42:24.810 Also interact with various amounts.

NOTE Confidence: 0.819997891111111

00:42:24.810 --> 00:42:27.785 Can give a crotonaldehyde and

NOTE Confidence: 0.819997891111111

00:42:27.785 --> 00:42:30.165 this also conform further.

NOTE Confidence: 0.819997891111111

00:42:30.170 --> 00:42:31.820 Adducts in here at the same

NOTE Confidence: 0.819997891111111

00:42:31.820 --> 00:42:34.110 time as I mentioned before,

NOTE Confidence: 0.819997891111111

00:42:34.110 --> 00:42:36.936 you also have an increased lipid

NOTE Confidence: 0.819997891111111

00:42:36.936 --> 00:42:38.349 peroxidation from acetaldehyde,

NOTE Confidence: 0.819997891111111

00:42:38.350 --> 00:42:41.199 which is due to the glutathione depletion

NOTE Confidence: 0.819997891111111

00:42:41.199 --> 00:42:43.650 which generates further aldehydes for

NOTE Confidence: 0.819997891111111

00:42:43.650 --> 00:42:46.464 hydroxyzine on and all, and so on.

NOTE Confidence: 0.819997891111111

00:42:46.464 --> 00:42:48.270 So you have another type of the

NOTE Confidence: 0.819997891111111

00:42:48.332 --> 00:42:49.867 ethanol the the shock should

NOTE Confidence: 0.819997891111111

00:42:49.867 --> 00:42:51.730 go on Guana sitting here.

NOTE Confidence: 0.819997891111111

00:42:51.730 --> 00:42:52.970 Another type of attack.

NOTE Confidence: 0.819997891111111

00:42:52.970 --> 00:42:55.924 So it is very well documented that

NOTE Confidence: 0.819997891111111

00:42:55.924 --> 00:42:58.670 both acetaldehyde per se or the

NOTE Confidence: 0.819997891111111

00:42:58.670 --> 00:43:00.520 byproduct atheists that can interact

NOTE Confidence: 0.819997891111111

00:43:00.520 --> 00:43:02.960 with DNA that can cause addicts,

NOTE Confidence: 0.819997891111111

00:43:02.960 --> 00:43:04.682 and these others can lead to mutations

NOTE Confidence: 0.819997891111111

00:43:04.682 --> 00:43:06.299 and they can cause the cancer.

NOTE Confidence: 0.819997891111111

00:43:06.300 --> 00:43:07.620 This is a causative effect,

NOTE Confidence: 0.819997891111111

00:43:07.620 --> 00:43:13.361 and this is what helped to establish and put.

NOTE Confidence: 0.819997891111111

00:43:13.361 --> 00:43:15.134 That the goodbyes,

NOTE Confidence: 0.819997891111111

00:43:15.134 --> 00:43:18.680 as ethanol as a cancer agent.

NOTE Confidence: 0.819997891111111

00:43:18.680 --> 00:43:21.370 Another area I am not going to go

NOTE Confidence: 0.819997891111111

00:43:21.370 --> 00:43:23.806 on this aspects in here what I want

NOTE Confidence: 0.819997891111111

00:43:23.806 --> 00:43:25.934 to tell you is that ethanol also

NOTE Confidence: 0.819997891111111

00:43:26.006 --> 00:43:28.321 can induce inflammation and changes

NOTE Confidence: 0.819997891111111

00:43:28.321 --> 00:43:30.636 in the cytokines and chemokines

NOTE Confidence: 0.819997891111111

00:43:30.640 --> 00:43:32.803 and then they can have a various

NOTE Confidence: 0.819997891111111

00:43:32.803 --> 00:43:34.970 effects into all the signaling which

NOTE Confidence: 0.819997891111111

00:43:34.970 --> 00:43:37.316 essentially they can affect the DNA

NOTE Confidence: 0.819997891111111

00:43:37.316 --> 00:43:39.479 repair mechanisms into the system.

NOTE Confidence: 0.819997891111111

00:43:39.480 --> 00:43:41.820 So the importance this is less

NOTE Confidence: 0.819997891111111

00:43:41.820 --> 00:43:44.478 studied but this is an area that.

NOTE Confidence: 0.819997891111111

00:43:44.480 --> 00:43:47.900 We should emphasize and as a matter of fact,

NOTE Confidence: 0.819997891111111

00:43:47.900 --> 00:43:49.760 you know, this is what I'm going to tell you.

NOTE Confidence: 0.819997891111111

00:43:49.760 --> 00:43:51.356 What we're planning to do in here,

NOTE Confidence: 0.819997891111111

00:43:51.360 --> 00:43:53.260 but you know, again,

NOTE Confidence: 0.819997891111111

00:43:53.260 --> 00:43:56.797 it is a pathway that ethanol could

NOTE Confidence: 0.819997891111111

00:43:56.797 --> 00:43:58.900 affect all these pathways in here,

NOTE Confidence: 0.819997891111111

00:43:58.900 --> 00:44:00.540 including the DNA damage,

NOTE Confidence: 0.819997891111111

00:44:00.540 --> 00:44:01.770 and you know,

NOTE Confidence: 0.819997891111111

00:44:01.770 --> 00:44:04.022 and essentially having the more

NOTE Confidence: 0.819997891111111

00:44:04.022 --> 00:44:05.180 further mutations.

NOTE Confidence: 0.85150081

00:44:06.190 --> 00:44:07.178 So one of the

NOTE Confidence: 0.829125251789474

00:44:07.190 --> 00:44:09.717 areas that I am planning to expand

NOTE Confidence: 0.829125251789474

00:44:09.717 --> 00:44:11.878 is the immuno metabolism and

NOTE Confidence: 0.829125251789474

00:44:11.878 --> 00:44:14.884 this is the interplay between the

NOTE Confidence: 0.829125251789474

00:44:14.884 --> 00:44:16.425 monological and metabolic processes.

NOTE Confidence: 0.829125251789474

00:44:16.425 --> 00:44:19.307 And as a matter of fact we have

NOTE Confidence: 0.829125251789474

00:44:19.307 --> 00:44:21.701 published several papers on the role

NOTE Confidence: 0.829125251789474

00:44:21.701 --> 00:44:24.092 of glutathione in the control of

NOTE Confidence: 0.829125251789474

00:44:24.092 --> 00:44:26.342 the T cell and macrophage fashions.

NOTE Confidence: 0.829125251789474

00:44:26.350 --> 00:44:29.871 But essentially again you can see the

NOTE Confidence: 0.829125251789474

00:44:29.871 --> 00:44:32.315 mitochondrial metabolism here and how

NOTE Confidence: 0.829125251789474

00:44:32.315 --> 00:44:34.455 the ethanol metabolism can interfere

NOTE Confidence: 0.829125251789474

00:44:34.455 --> 00:44:37.317 with that in terms of the cancer.

NOTE Confidence: 0.829125251789474

00:44:37.320 --> 00:44:41.000 Incidents. As I told you before,

NOTE Confidence: 0.829125251789474

00:44:41.000 --> 00:44:42.380 the ethanol can also.

NOTE Confidence: 0.829125251789474

00:44:42.380 --> 00:44:45.120 I mean, alcohol can also affect the

NOTE Confidence: 0.829125251789474

00:44:45.120 --> 00:44:47.170 one carbon metabolism and ethanol

NOTE Confidence: 0.829125251789474

00:44:47.240 --> 00:44:49.256 can block the absorption of the

NOTE Confidence: 0.829125251789474

00:44:49.256 --> 00:44:51.409 folic acid and can interfere with

NOTE Confidence: 0.829125251789474

00:44:51.409 --> 00:44:53.623 all the the folate and cycle,

NOTE Confidence: 0.829125251789474

00:44:53.630 --> 00:44:55.930 and the methionine cycle which

NOTE Confidence: 0.829125251789474

00:44:55.930 --> 00:44:59.282 eventually and as you can see here

NOTE Confidence: 0.829125251789474

00:44:59.282 --> 00:45:02.186 in very stages through the either

NOTE Confidence: 0.829125251789474

00:45:02.186 --> 00:45:04.537 interacting with proteins and you

NOTE Confidence: 0.829125251789474

00:45:04.537 --> 00:45:06.806 know forming adducts or interacting

NOTE Confidence: 0.829125251789474

00:45:06.806 --> 00:45:09.560 with pathways or absorption or stuff.

NOTE Confidence: 0.829125251789474

00:45:09.560 --> 00:45:09.977 Essentially,

NOTE Confidence: 0.829125251789474

00:45:09.977 --> 00:45:12.479 we have a DNA hypermethylation which

NOTE Confidence: 0.829125251789474

00:45:12.479 --> 00:45:14.539 can be associated with cancer.

NOTE Confidence: 0.829125251789474

00:45:14.540 --> 00:45:15.542 And of course,

NOTE Confidence: 0.829125251789474

00:45:15.542 --> 00:45:17.546 you know that's the other pathway

NOTE Confidence: 0.829125251789474

00:45:17.546 --> 00:45:19.628 that you know by interfering

NOTE Confidence: 0.829125251789474

00:45:19.628 --> 00:45:21.813 with the one carbon metabolism,

NOTE Confidence: 0.829125251789474

00:45:21.820 --> 00:45:23.878 you can have decreased through the thione,

NOTE Confidence: 0.829125251789474

00:45:23.880 --> 00:45:27.391 which really you know gives

NOTE Confidence: 0.829125251789474

00:45:27.391 --> 00:45:28.819 rise to oxidative stress,

NOTE Confidence: 0.829125251789474

00:45:28.820 --> 00:45:31.424 which is a result of reactive

NOTE Confidence: 0.829125251789474

00:45:31.424 --> 00:45:33.744 oxygen species generated by the

NOTE Confidence: 0.829125251789474

00:45:33.744 --> 00:45:35.834 cytochrome P-450 metabolism of

NOTE Confidence: 0.829125251789474

00:45:35.834 --> 00:45:39.593 the P42 and taking a break here.

NOTE Confidence: 0.829125251789474

00:45:39.600 --> 00:45:41.637 What I wanted to tell you is,

NOTE Confidence: 0.829125251789474

00:45:41.640 --> 00:45:44.440 in the slide before here

NOTE Confidence: 0.829125251789474

00:45:44.440 --> 00:45:45.712 is the broker synonyms.

NOTE Confidence: 0.829125251789474

00:45:45.712 --> 00:45:47.620 We have a lot of Procter

NOTE Confidence: 0.829125251789474

00:45:47.690 --> 00:45:49.680 synonyms exposed in our lives,

NOTE Confidence: 0.829125251789474

00:45:49.680 --> 00:45:52.065 so if alcohol induces the

NOTE Confidence: 0.829125251789474

00:45:52.065 --> 00:45:53.893 site from P452 you want,

NOTE Confidence: 0.829125251789474

00:45:53.893 --> 00:45:55.348 then we have increased levels

NOTE Confidence: 0.829125251789474

00:45:55.348 --> 00:45:56.740 of the two you want.

NOTE Confidence: 0.829125251789474

00:45:56.740 --> 00:45:59.526 So I've been exposed to dimethyl nitrosamine,

NOTE Confidence: 0.829125251789474

00:45:59.526 --> 00:46:02.417 for example the nitrosamines or the P.

NOTE Confidence: 0.829125251789474

00:46:02.420 --> 00:46:03.198 Fashion everything.

NOTE Confidence: 0.829125251789474

00:46:03.198 --> 00:46:05.921 Then you can have a further activation

NOTE Confidence: 0.829125251789474

00:46:05.921 --> 00:46:08.360 of this carcinogens and you can

NOTE Confidence: 0.829125251789474

00:46:08.360 --> 00:46:10.340 have this generation of reactive.

NOTE Confidence: 0.829125251789474

00:46:10.340 --> 00:46:13.427 Which is in species and further mutation.

NOTE Confidence: 0.829125251789474

00:46:13.430 --> 00:46:14.966 I'm gonna end up very quick.

NOTE Confidence: 0.904692338571429

00:46:15.350 --> 00:46:17.527 I'm gonna talk. I'm not gonna spend

NOTE Confidence: 0.904692338571429

00:46:17.530 --> 00:46:20.175 my time you all know the incidence of

NOTE Confidence: 0.904692338571429

00:46:20.175 --> 00:46:22.790 the colon cancer and what is going on.

NOTE Confidence: 0.904692338571429

00:46:22.790 --> 00:46:26.048 But my lab has been focusing on the colon

NOTE Confidence: 0.904692338571429

00:46:26.050 --> 00:46:30.022 cancer and alcohol metabolism we have.

NOTE Confidence: 0.904692338571429

00:46:30.022 --> 00:46:32.303 We were the first to clone the

NOTE Confidence: 0.904692338571429

00:46:32.303 --> 00:46:34.220 secondary enzyme. If you remember,

NOTE Confidence: 0.466815214111111

00:46:34.230 --> 00:46:36.366 said aldehyde is metabolized

NOTE Confidence: 0.466815214111111

00:46:36.366 --> 00:46:39.036 to acetate by the aldehyde.

NOTE Confidence: 0.466815214111111

00:46:39.040 --> 00:46:41.048 Progenesis Ald. Stew is

NOTE Confidence: 0.865842128333333

00:46:41.060 --> 00:46:43.388 the major enzyme, but we did

NOTE Confidence: 0.794094442857143

00:46:43.400 --> 00:46:46.454 found we cloned this enzyme and

NOTE Confidence: 0.794094442857143

00:46:46.454 --> 00:46:48.935 mitochondrial enzyme which is very

NOTE Confidence: 0.794094442857143

00:46:48.935 --> 00:46:51.580 similar to a LH2 and we cloned it.

NOTE Confidence: 0.794094442857143

00:46:51.580 --> 00:46:53.695 We expressed it throughout the

NOTE Confidence: 0.794094442857143

00:46:53.695 --> 00:46:55.802 years we made beautiful antibodies.

NOTE Confidence: 0.794094442857143

00:46:55.802 --> 00:46:59.316 We made the cover pages of several

NOTE Confidence: 0.794094442857143

00:46:59.316 --> 00:47:01.523 journals and we found that

NOTE Confidence: 0.794094442857143

00:47:01.523 --> 00:47:03.428 first of all that metabolizes

NOTE Confidence: 0.794094442857143

00:47:03.428 --> 00:47:05.438 acetaldehyde with very high affinity,

NOTE Confidence: 0.794094442857143

00:47:05.440 --> 00:47:08.212 which is makes it as equal as a LD.

NOTE Confidence: 0.794094442857143

00:47:08.220 --> 00:47:10.710 It's too in terms of clearing.

NOTE Confidence: 0.794094442857143

00:47:10.710 --> 00:47:13.706 The acetaldehyde but also what we found

NOTE Confidence: 0.794094442857143

00:47:13.706 --> 00:47:17.014 out is this enzyme is also involved

NOTE Confidence: 0.794094442857143

00:47:17.014 --> 00:47:19.434 into the retinoic acid metabolism,

NOTE Confidence: 0.794094442857143

00:47:19.434 --> 00:47:21.370 which is very important.

NOTE Confidence: 0.794094442857143

00:47:21.370 --> 00:47:24.000 So one of the things in early

NOTE Confidence: 0.794094442857143

00:47:24.000 --> 00:47:28.470 we found out that aldh 1B1 is a

NOTE Confidence: 0.794094442857143

00:47:28.470 --> 00:47:30.470 potential biomarker for colon cancer,

NOTE Confidence: 0.794094442857143

00:47:30.470 --> 00:47:32.138 so we have screened several

NOTE Confidence: 0.794094442857143

00:47:32.138 --> 00:47:34.730 several panels of humors,

NOTE Confidence: 0.794094442857143

00:47:34.730 --> 00:47:36.765 and we found that especially

NOTE Confidence: 0.794094442857143

00:47:36.765 --> 00:47:37.986 for colon cancer,

NOTE Confidence: 0.794094442857143

00:47:37.990 --> 00:47:40.840 every single column cancer sample.

NOTE Confidence: 0.794094442857143

00:47:40.840 --> 00:47:43.020 But we have tested.

NOTE Confidence: 0.794094442857143

00:47:43.020 --> 00:47:48.028 It really expresses AL H1B1

NOTE Confidence: 0.903634888

00:47:46.450 --> 00:47:48.020 at the very high level, very

NOTE Confidence: 0.849234321333333

00:47:48.030 --> 00:47:50.350 high level and which we didn't see it

NOTE Confidence: 0.849234321333333

00:47:50.350 --> 00:47:52.806 in long breast on ovary or anything.

NOTE Confidence: 0.849234321333333

00:47:52.810 --> 00:47:55.048 And it was especially this it

NOTE Confidence: 0.849234321333333

00:47:55.048 --> 00:47:57.660 was not a LH1A1, it was a L

NOTE Confidence: 0.849234321333333

00:47:57.660 --> 00:47:59.860 H1B1 and this has to do also.

NOTE Confidence: 0.849234321333333

00:47:59.860 --> 00:48:01.540 You know with the colony

NOTE Confidence: 0.849234321333333

00:48:01.540 --> 00:48:02.884 formation and everything else.

NOTE Confidence: 0.849234321333333

00:48:02.890 --> 00:48:06.410 So we also in addition to colon cancer.

NOTE Confidence: 0.849234321333333

00:48:06.410 --> 00:48:09.626 We have also found out that

NOTE Confidence: 0.849234321333333

00:48:09.630 --> 00:48:11.328 ADH 1B1 plays a really big.

NOTE Confidence: 0.849234321333333

00:48:11.330 --> 00:48:12.694 Call in pancreatic cancer.

NOTE Confidence: 0.849234321333333

00:48:12.694 --> 00:48:14.399 Trying to make a connection

NOTE Confidence: 0.849234321333333

00:48:14.400 --> 00:48:17.160 with James talk earlier on,

NOTE Confidence: 0.849234321333333

00:48:17.160 --> 00:48:22.084 so this is the AL H1B1 and then you can

NOTE Confidence: 0.849234321333333

00:48:22.084 --> 00:48:24.329 series really high expression of this

NOTE Confidence: 0.849234321333333

00:48:24.329 --> 00:48:26.354 in the pancreatic Andrew carcinoma.

NOTE Confidence: 0.849234321333333

00:48:26.354 --> 00:48:29.840 So one of the things that actually

NOTE Confidence: 0.849234321333333

00:48:29.926 --> 00:48:31.880 you can use that as a prognostic

NOTE Confidence: 0.849234321333333

00:48:31.880 --> 00:48:33.863 market is you can take the tumor

NOTE Confidence: 0.849234321333333

00:48:33.863 --> 00:48:36.700 and then you can really isolate aldh

NOTE Confidence: 0.849234321333333

00:48:36.700 --> 00:48:39.700 positive and aldh negative sales,

NOTE Confidence: 0.849234321333333

00:48:39.700 --> 00:48:41.596 and then you can put them in culture.

NOTE Confidence: 0.849234321333333

00:48:41.600 --> 00:48:43.136 As you can see,

NOTE Confidence: 0.849234321333333

00:48:43.136 --> 00:48:45.440 if aldehyde hydrogenase is not present,

NOTE Confidence: 0.849234321333333

00:48:45.440 --> 00:48:46.965 you have very small formation

NOTE Confidence: 0.849234321333333

00:48:46.965 --> 00:48:47.880 of the colonies,

NOTE Confidence: 0.849234321333333

00:48:47.880 --> 00:48:50.379 but if they LDH positive you have

NOTE Confidence: 0.849234321333333

00:48:50.379 --> 00:48:52.960 really have seen the tumor formation.

NOTE Confidence: 0.849234321333333

00:48:52.960 --> 00:48:56.520 So for somehow this a LDH is involved

NOTE Confidence: 0.849234321333333

00:48:56.520 --> 00:48:58.902 in the tumor proliferation initiation.

NOTE Confidence: 0.849234321333333

00:48:58.902 --> 00:49:02.430 I don't know we're still looking at the

NOTE Confidence: 0.849234321333333

00:49:02.507 --> 00:49:05.426 role of this throughout either through the.

NOTE Confidence: 0.849234321333333

00:49:05.430 --> 00:49:06.756 DNA repair mechanisms,

NOTE Confidence: 0.849234321333333

00:49:06.756 --> 00:49:08.524 or through retinoic acid.

NOTE Confidence: 0.849234321333333

00:49:08.530 --> 00:49:09.390 It's an active area,

NOTE Confidence: 0.849234321333333

00:49:09.390 --> 00:49:12.960 so we have several papers on the

NOTE Confidence: 0.849234321333333

00:49:12.960 --> 00:49:15.210 how the Ald H1B1 could be that,

NOTE Confidence: 0.849234321333333

00:49:15.210 --> 00:49:17.810 and we found out that can be

NOTE Confidence: 0.849234321333333

00:49:17.810 --> 00:49:20.130 modulating the wind better.

NOTE Confidence: 0.849234321333333

00:49:20.130 --> 00:49:24.366 Catherine Pathway and the the also

NOTE Confidence: 0.849234321333333

00:49:24.370 --> 00:49:26.950 P1K they get signaling pathway,

NOTE Confidence: 0.849234321333333

00:49:26.950 --> 00:49:28.120 but the most important thing,

NOTE Confidence: 0.849234321333333

00:49:28.120 --> 00:49:30.480 and this is a work that we have

NOTE Confidence: 0.849234321333333

00:49:30.480 --> 00:49:33.647 done and we have identified that it

NOTE Confidence: 0.849234321333333

00:49:33.647 --> 00:49:35.647 is immunohistochemical market for.

NOTE Confidence: 0.849234321333333

00:49:35.650 --> 00:49:36.100 Further,

NOTE Confidence: 0.849234321333333

00:49:36.100 --> 00:49:38.800 for colorectal cancers and we look

NOTE Confidence: 0.849234321333333

00:49:38.800 --> 00:49:41.812 at that and several several samples

NOTE Confidence: 0.849234321333333

00:49:41.812 --> 00:49:43.816 and including some comparisons

NOTE Confidence: 0.849234321333333

00:49:43.816 --> 00:49:46.919 that we have done here at Yale.

NOTE Confidence: 0.849234321333333

00:49:46.920 --> 00:49:50.035 So it's a very strong market for that.

NOTE Confidence: 0.849234321333333

00:49:50.035 --> 00:49:51.510 And whereas as I said,

NOTE Confidence: 0.849234321333333

00:49:51.510 --> 00:49:54.510 we're still looking on what is going on.

NOTE Confidence: 0.849234321333333

00:49:54.510 --> 00:49:57.228 So one of the ways that we have trying

NOTE Confidence: 0.849234321333333

00:49:57.228 --> 00:50:00.397 to address the role of this is we

NOTE Confidence: 0.849234321333333

00:50:00.397 --> 00:50:02.410 have generated specific knockouts,

NOTE Confidence: 0.849234321333333

00:50:02.410 --> 00:50:05.539 so it's a tissue specific inducible knockout.

NOTE Confidence: 0.849234321333333

00:50:05.540 --> 00:50:07.425 The triple knockout mice show

NOTE Confidence: 0.849234321333333

00:50:07.425 --> 00:50:08.933 the APC mean mice.

NOTE Confidence: 0.849234321333333

00:50:08.940 --> 00:50:13.119 We know that the they are forming,

NOTE Confidence: 0.849234321333333

00:50:13.120 --> 00:50:13.490 they're

NOTE Confidence: 0.784147056086957

00:50:13.500 --> 00:50:14.703 forming many cancers.

NOTE Confidence: 0.784147056086957

00:50:14.703 --> 00:50:17.510 So anyway to make time is running

NOTE Confidence: 0.784147056086957

00:50:17.586 --> 00:50:19.770 we have generated a triple knockout

NOTE Confidence: 0.784147056086957

00:50:19.770 --> 00:50:22.618 of this with a PC and everything.

NOTE Confidence: 0.784147056086957

00:50:22.620 --> 00:50:26.027 So this mice we have found out that

NOTE Confidence: 0.784147056086957

00:50:26.027 --> 00:50:28.306 this is the ASPCA knockout and this

NOTE Confidence: 0.784147056086957

00:50:28.306 --> 00:50:30.610 is the well typed knockout mice

NOTE Confidence: 0.849208734

00:50:31.140 --> 00:50:32.640 and this is the experiment.

NOTE Confidence: 0.849208734

00:50:32.640 --> 00:50:34.098 This is how we generate it.

NOTE Confidence: 0.849208734

00:50:34.100 --> 00:50:35.630 It was a painful process.

NOTE Confidence: 0.849208734

00:50:35.630 --> 00:50:38.850 Triple knockout is not an easy way to do it,

NOTE Confidence: 0.849208734

00:50:38.850 --> 00:50:40.439 but the way that you're doing that

NOTE Confidence: 0.849208734

00:50:40.439 --> 00:50:42.169 is you have an industrial model,

NOTE Confidence: 0.849208734

00:50:42.170 --> 00:50:44.258 you you treat them with tamoxifen,

NOTE Confidence: 0.849208734

00:50:44.260 --> 00:50:46.708 you delete the gene and then you can

NOTE Confidence: 0.849208734

00:50:46.708 --> 00:50:48.767 further figure out of what's going on.

NOTE Confidence: 0.849208734

00:50:48.770 --> 00:50:51.770 So we did not find anything

NOTE Confidence: 0.849208734

00:50:51.770 --> 00:50:53.770 any difference in the.

NOTE Confidence: 0.849208734

00:50:53.770 --> 00:50:56.650 Vehicle treated mice and also in

NOTE Confidence: 0.849208734

00:50:56.650 --> 00:50:58.710 the tamoxifen treated groups at

NOTE Confidence: 0.849208734

00:50:58.789 --> 00:51:01.039 the numbers were not evident in

NOTE Confidence: 0.849208734

00:51:01.039 --> 00:51:03.430 jejunum or ileum in these mice.

NOTE Confidence: 0.849208734

00:51:03.430 --> 00:51:06.490 However, we did find the

NOTE Confidence: 0.849208734

00:51:06.490 --> 00:51:08.326 carcinoma colorectal adenomas,

NOTE Confidence: 0.849208734

00:51:08.330 --> 00:51:11.432 which in the knockout developed significant

NOTE Confidence: 0.849208734

00:51:11.432 --> 00:51:15.149 loan numbers of the macro and enormous.

NOTE Confidence: 0.849208734

00:51:15.150 --> 00:51:17.691 And there was a significant reduction in

NOTE Confidence: 0.849208734

00:51:17.691 --> 00:51:19.750 the total macroadenomas in the knockout.

NOTE Confidence: 0.849208734

00:51:19.750 --> 00:51:22.246 So, when we knockout the gene

NOTE Confidence: 0.849208734

00:51:22.246 --> 00:51:23.910 in a model that.

NOTE Confidence: 0.849208734

00:51:23.910 --> 00:51:25.150 Induces

NOTE Confidence: 0.677699724444444

00:51:27.310 --> 00:51:32.134 colorectal and the normas, uh it is the gene.

NOTE Confidence: 0.677699724444444

00:51:32.140 --> 00:51:34.065 If you knock out the aldehyde progenesis

NOTE Confidence: 0.677699724444444

00:51:34.065 --> 00:51:36.147 you reduce you can see that you reduce.

NOTE Confidence: 0.677699724444444

00:51:36.150 --> 00:51:40.176 So this confirms our initial studies

NOTE Confidence: 0.677699724444444

00:51:40.176 --> 00:51:44.426 that the ALDH 1B1 it is involved in the

NOTE Confidence: 0.677699724444444

00:51:44.426 --> 00:51:47.789 development of under cellular carcinomas.

NOTE Confidence: 0.677699724444444

00:51:47.790 --> 00:51:50.814 And we have been trying to to dissect

NOTE Confidence: 0.677699724444444

00:51:50.814 --> 00:51:54.410 more more involvement of this gene and we

NOTE Confidence: 0.677699724444444

00:51:54.410 --> 00:51:57.602 didn't see any difference at the P53 level.

NOTE Confidence: 0.677699724444444

00:51:57.602 --> 00:52:00.770 But we did see a decreased expression of

NOTE Confidence: 0.677699724444444

00:52:00.848 --> 00:52:05.738 the beta catenin in the knockout, a LH now

NOTE Confidence: 0.677699724444444

00:52:05.738 --> 00:52:10.750 beta catenin knockout for beta catenin.

NOTE Confidence: 0.677699724444444

00:52:10.750 --> 00:52:12.760 Expression which you know that Becca

NOTE Confidence: 0.677699724444444

00:52:12.760 --> 00:52:14.881 took Catenin is plays an important

NOTE Confidence: 0.677699724444444

00:52:14.881 --> 00:52:16.309 role in the development.

NOTE Confidence: 0.677699724444444

00:52:16.310 --> 00:52:18.851 All colon carcinoma.

NOTE Confidence: 0.677699724444444

00:52:18.851 --> 00:52:25.005 So the expression of of 191 could be used as

NOTE Confidence: 0.677699724444444

00:52:25.005 --> 00:52:27.528 a novel biomarker in identified colorectal

NOTE Confidence: 0.677699724444444

00:52:27.528 --> 00:52:30.690 cancers and also in pancreatic cancers.

NOTE Confidence: 0.677699724444444

00:52:30.690 --> 00:52:33.020 The Althe knocked down because

NOTE Confidence: 0.677699724444444

00:52:33.020 --> 00:52:35.350 the dramatic reduction of humor,

NOTE Confidence: 0.677699724444444

00:52:35.350 --> 00:52:38.115 growth, and loss of function of APC,

NOTE Confidence: 0.677699724444444

00:52:38.120 --> 00:52:39.125 and options of.

NOTE Confidence: 0.677699724444444

00:52:39.125 --> 00:52:41.910 Maybe it's trying to be 1 reduces the

NOTE Confidence: 0.677699724444444

00:52:41.910 --> 00:52:44.220 column adenoma and in turn delays

NOTE Confidence: 0.677699724444444

00:52:44.220 --> 00:52:46.176 that emerged in the progression

NOTE Confidence: 0.677699724444444

00:52:46.176 --> 00:52:48.920 of cancer in that to that effect.

NOTE Confidence: 0.677699724444444

00:52:48.920 --> 00:52:50.540 I have collaborated with.

NOTE Confidence: 0.783430214736842

00:52:52.670 --> 00:52:55.640 And cuts and we have developed

NOTE Confidence: 0.783430214736842

00:52:55.640 --> 00:52:58.234 special specific inhibitors of the

NOTE Confidence: 0.783430214736842

00:52:58.234 --> 00:53:00.362 aldehyde dehydrogenases that could

NOTE Confidence: 0.783430214736842

00:53:00.362 --> 00:53:03.538 be used for delaying the expression,

NOTE Confidence: 0.783430214736842

00:53:03.538 --> 00:53:06.158 delaying the progression of the

NOTE Confidence: 0.783430214736842

00:53:06.158 --> 00:53:11.080 tumor once it's been detected so.

NOTE Confidence: 0.783430214736842

00:53:11.080 --> 00:53:13.458 It looks like the Ald H1B1 is a

NOTE Confidence: 0.783430214736842

00:53:13.458 --> 00:53:16.020 key player in this carcinogenesis,

NOTE Confidence: 0.783430214736842

00:53:16.020 --> 00:53:19.154 so if I can go back a little bit on

NOTE Confidence: 0.783430214736842

00:53:19.154 --> 00:53:21.518 the molecular mechanisms to conclude my

NOTE Confidence: 0.783430214736842

00:53:21.518 --> 00:53:24.210 studies in here and the the directions

NOTE Confidence: 0.783430214736842

00:53:24.210 --> 00:53:26.894 is the alcohol metabolism is a key

NOTE Confidence: 0.783430214736842

00:53:26.894 --> 00:53:29.159 player through the cytochrome P-450,

NOTE Confidence: 0.783430214736842

00:53:29.160 --> 00:53:31.044 or through the aldehydes

NOTE Confidence: 0.783430214736842

00:53:31.044 --> 00:53:33.399 generated in here and then.

NOTE Confidence: 0.783430214736842

00:53:33.400 --> 00:53:36.193 You have also the changes in the

NOTE Confidence: 0.783430214736842

00:53:36.193 --> 00:53:39.194 NADH NADH ratio, which we can have

NOTE Confidence: 0.783430214736842

00:53:39.194 --> 00:53:40.998 also have epigenetic modifications.

NOTE Confidence: 0.783430214736842

00:53:41.000 --> 00:53:42.564 Remember reactive oxygen species.

NOTE Confidence: 0.783430214736842

00:53:42.564 --> 00:53:44.519 They can cause the inflammation

NOTE Confidence: 0.783430214736842

00:53:44.519 --> 00:53:46.028 that can lead to cancer.

NOTE Confidence: 0.783430214736842

00:53:46.030 --> 00:53:47.322 In addition to that,

NOTE Confidence: 0.783430214736842

00:53:47.322 --> 00:53:48.744 you also, as mentioned,

NOTE Confidence: 0.783430214736842

00:53:48.744 --> 00:53:50.679 this is very important here.

NOTE Confidence: 0.783430214736842

00:53:50.680 --> 00:53:53.335 This is especially with increased

NOTE Confidence: 0.783430214736842

00:53:53.335 --> 00:53:55.990 exposure to environmental casino egens

NOTE Confidence: 0.783430214736842

00:53:56.072 --> 00:53:58.672 the high levels of the two one they

NOTE Confidence: 0.783430214736842

00:53:58.672 --> 00:54:01.388 can lead to DNA damage segmentation.

NOTE Confidence: 0.783430214736842

00:54:01.390 --> 00:54:03.170 Then they can cause cancer.

NOTE Confidence: 0.783430214736842

00:54:03.170 --> 00:54:05.802 And of course you know the DNA repair

NOTE Confidence: 0.783430214736842

00:54:05.802 --> 00:54:08.418 can be also be affected by both the

NOTE Confidence: 0.783430214736842

00:54:08.418 --> 00:54:11.018 two U one and also the alcohol.

NOTE Confidence: 0.783430214736842

00:54:11.020 --> 00:54:14.188 Double so a very important process in here,

NOTE Confidence: 0.783430214736842

00:54:14.190 --> 00:54:16.054 and this is where we're focusing as well.

NOTE Confidence: 0.783430214736842

00:54:16.060 --> 00:54:21.485 Is how ethanol metabolism could the could.

NOTE Confidence: 0.783430214736842

00:54:21.490 --> 00:54:23.548 Have a defect in the day DNA

NOTE Confidence: 0.783430214736842

00:54:23.548 --> 00:54:25.807 repair as well and as I mentioned,

NOTE Confidence: 0.783430214736842

00:54:25.810 --> 00:54:28.930 also you know we have the one carbon

NOTE Confidence: 0.783430214736842

00:54:28.930 --> 00:54:31.010 metabolism and DNA methylation.

NOTE Confidence: 0.783430214736842

00:54:31.010 --> 00:54:34.079 I didn't have time to go on your micro

NOTE Confidence: 0.783430214736842

00:54:34.079 --> 00:54:36.935 RNA in here but also I did mention

NOTE Confidence: 0.783430214736842

00:54:36.935 --> 00:54:38.810 the crosstalk between these pathways.

NOTE Confidence: 0.783430214736842

00:54:38.810 --> 00:54:40.874 The alcohol and the immune system

NOTE Confidence: 0.783430214736842

00:54:40.874 --> 00:54:43.394 which eventually they can end up in

NOTE Confidence: 0.783430214736842

00:54:43.394 --> 00:54:44.477 causing epigenetic modifications

NOTE Confidence: 0.783430214736842

00:54:44.477 --> 00:54:46.630 that they can cause the cancer.

NOTE Confidence: 0.783430214736842

00:54:46.630 --> 00:54:48.961 This is a slide that the best

NOTE Confidence: 0.783430214736842

00:54:48.961 --> 00:54:51.300 slide that I've seen in terms of.

NOTE Confidence: 0.783430214736842

00:54:51.300 --> 00:54:55.186 Mark concluding all the effects of

NOTE Confidence: 0.783430214736842

00:54:55.186 --> 00:54:57.040 the alcohol in terms of the cancer,

NOTE Confidence: 0.783430214736842

00:54:57.040 --> 00:54:59.609 and this was from the former director

NOTE Confidence: 0.783430214736842

00:54:59.609 --> 00:55:02.178 of the metabolism of the NAIA SAMSARIC,

NOTE Confidence: 0.783430214736842

00:55:02.180 --> 00:55:04.434 who is a very good friend and

NOTE Confidence: 0.783430214736842

00:55:04.434 --> 00:55:05.400 colleague of mine,

NOTE Confidence: 0.783430214736842

00:55:05.400 --> 00:55:08.740 and I want to tell you this slide is I'm,

NOTE Confidence: 0.783430214736842

00:55:08.740 --> 00:55:10.558 you know, a little bit sad,

NOTE Confidence: 0.783430214736842

00:55:10.560 --> 00:55:12.985 but my next fifth international

NOTE Confidence: 0.783430214736842

00:55:12.985 --> 00:55:15.410 conference on alcohol and cancer

NOTE Confidence: 0.783430214736842

00:55:15.494 --> 00:55:18.159 was going to be in in Greece 2021.

NOTE Confidence: 0.783430214736842

00:55:18.159 --> 00:55:20.324 Unfortunately with the COVID we

NOTE Confidence: 0.783430214736842

00:55:20.324 --> 00:55:23.398 have to move it ahead and probably.

NOTE Confidence: 0.783430214736842

00:55:23.400 --> 00:55:24.870 It's not gonna be 2022.

NOTE Confidence: 0.783430214736842

00:55:24.870 --> 00:55:25.818 It's gonna be probably

NOTE Confidence: 0.8762074775

00:55:26.530 --> 00:55:31.118 2023 and I expect to see quite a few of our

NOTE Confidence: 0.755934514

00:55:31.270 --> 00:55:33.500 Yale colleagues here. Thank you,

NOTE Confidence: 0.755934514

00:55:33.500 --> 00:55:35.000 Melinda. I'm going to stop and

NOTE Confidence: 0.755934514

00:55:35.000 --> 00:55:37.340 get some time for questions. Thank

NOTE Confidence: 0.8018645196

00:55:37.350 --> 00:55:38.002 you vicellous.

NOTE Confidence: 0.8018645196

00:55:38.002 --> 00:55:40.610 Count me in on a trip to Greece.

NOTE Confidence: 0.8018645196

00:55:40.610 --> 00:55:42.695 I know you just returned

NOTE Confidence: 0.8018645196

00:55:42.695 --> 00:55:44.363 and I wasn't invited.

NOTE Confidence: 0.8018645196

00:55:44.370 --> 00:55:47.328 Anyway to the topic at hand.

NOTE Confidence: 0.8018645196

00:55:47.330 --> 00:55:49.213 I was intrigued at the beginning of

NOTE Confidence: 0.8018645196

00:55:49.213 --> 00:55:51.326 your talk when you were talking about

NOTE Confidence: 0.8018645196

00:55:51.326 --> 00:55:53.580 measurement error and the fact that often.

NOTE Confidence: 0.8018645196

00:55:53.580 --> 00:55:55.750 We measure alcohol intake through

NOTE Confidence: 0.8018645196

00:55:55.750 --> 00:55:57.920 questionnaire and we know there's

NOTE Confidence: 0.8018645196

00:55:57.989 --> 00:56:00.394 a lot of misclassification with

NOTE Confidence: 0.8018645196

00:56:00.394 --> 00:56:02.222 that underreporting, perhaps,

NOTE Confidence: 0.8018645196

00:56:02.222 --> 00:56:05.670 and then that misclassification

NOTE Confidence: 0.8018645196

00:56:05.670 --> 00:56:08.064 really attenuates the, say,

NOTE Confidence: 0.8018645196

00:56:08.064 --> 00:56:10.056 the hazard ratio to the null.

NOTE Confidence: 0.8018645196

00:56:10.060 --> 00:56:12.472 So in reality the impact of

NOTE Confidence: 0.8018645196

00:56:12.472 --> 00:56:14.687 alcohol on cancer is probably

NOTE Confidence: 0.8018645196

00:56:14.687 --> 00:56:17.777 even higher than noted in studies,

NOTE Confidence: 0.8018645196

00:56:17.780 --> 00:56:19.685 but you then mentioned what

NOTE Confidence: 0.8018645196

00:56:19.685 --> 00:56:22.038 do you call an alcohol zone

NOTE Confidence: 0.8018645196

00:56:22.038 --> 00:56:24.258 or something of a channel of.

NOTE Confidence: 0.8018645196

00:56:24.260 --> 00:56:26.395 Can you can you discuss that briefly?

NOTE Confidence: 0.8018645196

00:56:26.400 --> 00:56:28.200 A little bit more So what

NOTE Confidence: 0.602545503333333

00:56:28.200 --> 00:56:31.395 we you see. Also show me this term

NOTE Confidence: 0.602545503333333

00:56:31.395 --> 00:56:33.358 similar to the Exposome and I'm

NOTE Confidence: 0.602545503333333

00:56:33.358 --> 00:56:35.518 trying to pattern actually this word,

NOTE Confidence: 0.602545503333333

00:56:35.520 --> 00:56:37.561 so I'm trying to figure out

NOTE Confidence: 0.602545503333333

00:56:37.561 --> 00:56:40.966 through animal studies and human

NOTE Confidence: 0.602545503333333

00:56:40.966 --> 00:56:44.960 studies how I can define a.

NOTE Confidence: 0.602545503333333

00:56:44.960 --> 00:56:49.624 Motif of changes that you can utilize

NOTE Confidence: 0.602545503333333

00:56:49.624 --> 00:56:52.868 by looking at the blood and finally

NOTE Confidence: 0.602545503333333

00:56:52.868 --> 00:56:56.820 modeling it to how much alcohol the one

NOTE Confidence: 0.602545503333333

00:56:56.926 --> 00:57:00.416 person has consumed during lifetime.

NOTE Confidence: 0.602545503333333

00:57:00.420 --> 00:57:02.220 This is not an easy task.

NOTE Confidence: 0.602545503333333

00:57:02.220 --> 00:57:05.188 OK, so because one of The thing is

NOTE Confidence: 0.602545503333333

00:57:05.188 --> 00:57:07.905 remember you can drink alcohol and then

NOTE Confidence: 0.602545503333333

00:57:07.905 --> 00:57:11.380 even if you measure a few of the enzymes,

NOTE Confidence: 0.602545503333333

00:57:11.380 --> 00:57:12.990 you're a pathic enzymes if you have.

NOTE Confidence: 0.602545503333333

00:57:12.990 --> 00:57:15.276 If you have abstinence of alcohol.

NOTE Confidence: 0.602545503333333

00:57:15.280 --> 00:57:17.982 Delivery cover so you don't know to

NOTE Confidence: 0.602545503333333

00:57:17.982 --> 00:57:20.329 how much alcohol you have drunk,

NOTE Confidence: 0.602545503333333

00:57:20.330 --> 00:57:22.618 So what we're trying to do is we're

NOTE Confidence: 0.602545503333333

00:57:22.618 --> 00:57:25.779 trying to have a a more educated.

NOTE Confidence: 0.8334116085

00:57:27.890 --> 00:57:29.926 Measurement of determining how

NOTE Confidence: 0.8334116085

00:57:29.926 --> 00:57:32.980 much alcohol a person have done

NOTE Confidence: 0.8334116085

00:57:33.068 --> 00:57:35.533 throughout life and the same

NOTE Confidence: 0.8334116085

00:57:35.533 --> 00:57:37.998 thing as the explosion concept.

NOTE Confidence: 0.8334116085

00:57:38.000 --> 00:57:39.476 As I said, it's not easy,

NOTE Confidence: 0.8334116085

00:57:39.480 --> 00:57:40.929 but we're trying to do that and

NOTE Confidence: 0.8334116085

00:57:40.929 --> 00:57:42.341 we're trying to do with animal

NOTE Confidence: 0.8334116085

00:57:42.341 --> 00:57:43.835 studies and also with human studies.

NOTE Confidence: 0.8334116085

00:57:43.840 --> 00:57:45.954 This is one of the of the

NOTE Confidence: 0.8334116085

00:57:45.954 --> 00:57:47.660 ways that it can help.

NOTE Confidence: 0.8334116085

00:57:47.660 --> 00:57:50.705 Really, the epidemiology to assess you

NOTE Confidence: 0.8334116085

00:57:50.705 --> 00:57:53.120 know the causal effects of alcohol because

NOTE Confidence: 0.8334116085

00:57:53.120 --> 00:57:55.720 they this is another area of big debate.

NOTE Confidence: 0.8334116085

00:57:55.720 --> 00:57:57.058 Melinda, as you know, you know,

NOTE Confidence: 0.8334116085

00:57:57.060 --> 00:57:58.719 there was a couple of years ago

NOTE Confidence: 0.8334116085

00:57:58.719 --> 00:58:00.601 there was one paper from New Zealand

NOTE Confidence: 0.8334116085

00:58:00.601 --> 00:58:02.275 and it's saying all the women,

NOTE Confidence: 0.8334116085

00:58:02.280 --> 00:58:05.094 even if they have one one drink.

NOTE Confidence: 0.8334116085

00:58:05.100 --> 00:58:07.578 Per year they can develop colon,

NOTE Confidence: 0.8334116085

00:58:07.580 --> 00:58:10.012 I mean breast cancer and if you look

NOTE Confidence: 0.8334116085

00:58:10.012 --> 00:58:12.477 at really of these studies they were,

NOTE Confidence: 0.8334116085

00:58:12.480 --> 00:58:13.320 you know,

NOTE Confidence: 0.8334116085

00:58:13.320 --> 00:58:15.366 based everything on on on,

NOTE Confidence: 0.8334116085

00:58:15.366 --> 00:58:16.938 on just the questioners.

NOTE Confidence: 0.8334116085

00:58:16.940 --> 00:58:18.172 And as I said,

NOTE Confidence: 0.8334116085

00:58:18.172 --> 00:58:20.808 this is not the accurate measure to do this.

NOTE Confidence: 0.884046335

00:58:22.600 --> 00:58:24.016 Yeah, yes, I agree.

NOTE Confidence: 0.884046335

00:58:24.016 --> 00:58:26.518 So much work to be done. Well.

NOTE Confidence: 0.884046335

00:58:26.518 --> 00:58:29.164 Thank you so much to both of

NOTE Confidence: 0.884046335

00:58:29.164 --> 00:58:31.730 our speakers today and if others

NOTE Confidence: 0.884046335

00:58:31.730 --> 00:58:33.880 who tuned in have questions,

NOTE Confidence: 0.884046335

00:58:33.880 --> 00:58:36.536 I'm sure you can reach out to both

NOTE Confidence: 0.884046335

00:58:36.536 --> 00:58:39.100 our speakers via email and hopefully

NOTE Confidence: 0.884046335

00:58:39.100 --> 00:58:41.380 there will be some collaborations.

NOTE Confidence: 0.884046335

00:58:41.380 --> 00:58:43.858 Initiated from today's talk. Thank you.

NOTE Confidence: 0.884046335

00:58:43.860 --> 00:58:46.100 Both have a great rest of the day.

NOTE Confidence: 0.884046335

00:58:46.100 --> 00:58:47.000 Thank you.