WEBVTT

NOTE duration: ”00:54:10.808”

NOTE Confidence: 0.93056357

00:00:00.160 --> 00:00:01.540 This this dynamic duo,

NOTE Confidence: 0.976598

00:00:01.920 --> 00:00:02.879 that are gonna be giving

NOTE Confidence: 0.976598

00:00:02.879 --> 00:00:04.000 us grand rounds today. It's

NOTE Confidence: 0.976598

00:00:04.000 --> 00:00:05.540 my proud privilege to introduce

NOTE Confidence: 0.976598

00:00:05.600 --> 00:00:07.520 doctor Khan. Doctor Saj Khan

NOTE Confidence: 0.976598

00:00:07.520 --> 00:00:08.960 is our section chief of,

NOTE Confidence: 0.9289166

00:00:09.679 --> 00:00:11.780 HBB mixed tumors. He's a

NOTE Confidence: 0.9289166

00:00:11.920 --> 00:00:12.980 wonderful clinician,

NOTE Confidence: 0.9812702

00:00:13.759 --> 00:00:15.540 and an incredible researcher.

NOTE Confidence: 0.9802991

00:00:16.185 --> 00:00:17.465 We've known each other for

NOTE Confidence: 0.9802991

00:00:17.465 --> 00:00:19.465 over a decade. He finished

NOTE Confidence: 0.9802991

00:00:19.465 --> 00:00:20.744 his fellowship at the University

NOTE Confidence: 0.9802991

00:00:20.744 --> 00:00:22.345 of Chicago, and we tried

NOTE Confidence: 0.9802991

00:00:22.345 --> 00:00:23.545 recruiting him when I was

NOTE Confidence: 0.9802991

00:00:23.545 --> 00:00:24.505 at my first job, and

NOTE Confidence: 0.9802991

00:00:24.505 --> 00:00:25.544 now I have the proud

NOTE Confidence: 0.9802991

00:00:25.544 --> 00:00:27.085 privilege of working with him.

NOTE Confidence: 0.99888206

00:00:27.785 --> 00:00:29.145 His science has been focused

NOTE Confidence: 0.99888206

00:00:29.145 --> 00:00:30.125 a lot on the

NOTE Confidence: 0.9917296

00:00:30.600 --> 00:00:32.140 underpinnings of liver metastases,

NOTE Confidence: 0.96213096

00:00:32.440 --> 00:00:33.479 which you'll hear a little

NOTE Confidence: 0.96213096

00:00:33.479 --> 00:00:34.760 bit about, but also about

NOTE Confidence: 0.96213096

00:00:34.760 --> 00:00:36.840 other things, including, biomarkers or

NOTE Confidence: 0.96213096

00:00:36.840 --> 00:00:37.820 pancreas cancer.

NOTE Confidence: 0.94945574

00:00:39.080 --> 00:00:40.760 And then with him is

NOTE Confidence: 0.94945574

00:00:40.760 --> 00:00:41.659 doctor Johnson.

NOTE Confidence: 0.9806732

00:00:42.360 --> 00:00:43.800 Together, they have won numerous

NOTE Confidence: 0.9806732

00:00:43.800 --> 00:00:46.114 awards, numerous NIH peer funded

NOTE Confidence: 0.9806732

00:00:46.114 --> 00:00:46.614 grants,

NOTE Confidence: 0.91889954

00:00:47.555 --> 00:00:49.175 and I think, exemplify

NOTE Confidence: 0.99195415

00:00:49.555 --> 00:00:51.155 how team science works. Doctor

NOTE Confidence: 0.99195415

00:00:51.155 --> 00:00:53.315 Johnson did her PhD in

NOTE Confidence: 0.99195415

00:00:53.315 --> 00:00:54.995 analytical chemistry, which I didn't

NOTE Confidence: 0.99195415

00:00:54.995 --> 00:00:55.815 know you did,

NOTE Confidence: 0.9784944

00:00:56.275 --> 00:00:57.555 at the Imperial College of

NOTE Confidence: 0.9784944

00:00:57.555 --> 00:00:58.754 London, which is one of

NOTE Confidence: 0.9784944

00:00:58.754 --> 00:00:59.895 the premier schools,

NOTE Confidence: 0.82386565

00:01:00.670 --> 00:01:01.890 and she is now,

NOTE Confidence: 0.91876066

00:01:02.590 --> 00:01:03.629 held a position as an

NOTE Confidence: 0.91876066

00:01:03.629 --> 00:01:05.390 associate professor at the School

NOTE Confidence: 0.91876066

00:01:05.390 --> 00:01:06.930 of Public Health in epidemiology.

NOTE Confidence: 0.9571822

00:01:08.270 --> 00:01:09.229 Together, I think both of

NOTE Confidence: 0.9571822

00:01:09.229 --> 00:01:10.049 them have explored,

NOTE Confidence: 0.9981847

00:01:10.350 --> 00:01:11.250 tumor metabolites

NOTE Confidence: 0.8057092

00:01:11.709 --> 00:01:13.330 and genetic differences,

NOTE Confidence: 0.9681794

00:01:13.950 --> 00:01:15.170 around liver metastases,

NOTE Confidence: 0.9857397

00:01:16.135 --> 00:01:17.174 and they'll share some of

NOTE Confidence: 0.9857397

00:01:17.174 --> 00:01:18.455 their journey about the team

NOTE Confidence: 0.9857397

00:01:18.455 --> 00:01:19.595 science as well as,

NOTE Confidence: 0.9527682

00:01:20.694 --> 00:01:21.895 perhaps a little bit about

NOTE Confidence: 0.9527682

00:01:21.895 --> 00:01:22.715 liver metastases.

NOTE Confidence: 0.9426057

00:01:23.015 --> 00:01:24.715 So welcome, Saj and Caroline.

NOTE Confidence: 0.958753

00:01:39.900 --> 00:01:40.780 Hey. Well, thank you very

NOTE Confidence: 0.958753

00:01:40.780 --> 00:01:42.460 much, for the introduction. And

NOTE Confidence: 0.958753

00:01:42.460 --> 00:01:43.660 we'd also like to thank

NOTE Confidence: 0.958753

00:01:43.660 --> 00:01:44.955 the Yale Cancer Center for

NOTE Confidence: 0.958753

00:01:44.955 --> 00:01:45.994 inviting us to give a

NOTE Confidence: 0.958753

00:01:45.994 --> 00:01:47.134 talk today about

NOTE Confidence: 0.96359617

00:01:47.595 --> 00:01:49.595 our collaborative team science work,

NOTE Confidence: 0.96359617

00:01:49.835 --> 00:01:51.854 specifically looking at sex disparities

NOTE Confidence: 0.96359617

00:01:51.994 --> 00:01:52.655 in cancer.

NOTE Confidence: 0.9545739

00:01:53.354 --> 00:01:54.715 So as mentioned, I'm from

NOTE Confidence: 0.9545739

00:01:54.715 --> 00:01:55.994 the School of Public Health.

NOTE Confidence: 0.9545739

00:01:56.395 --> 00:01:57.435 I'm in the Department of

NOTE Confidence: 0.9545739

00:01:57.435 --> 00:01:59.354 Environmental Health Sciences, and doctor

NOTE Confidence: 0.9545739

00:01:59.354 --> 00:01:59.854 Khan

NOTE Confidence: 0.9762397

00:02:00.210 --> 00:02:01.650 is in, the Department of

NOTE Confidence: 0.9762397

00:02:01.650 --> 00:02:02.930 Surgery at Yale School of

NOTE Confidence: 0.9762397

00:02:02.930 --> 00:02:04.210 Medicine. And we've been working

NOTE Confidence: 0.9762397

00:02:04.210 --> 00:02:05.650 together for over nine years

NOTE Confidence: 0.9762397

00:02:05.650 --> 00:02:06.150 now.

NOTE Confidence: 0.978056

00:02:06.610 --> 00:02:07.890 So over the next forty

NOTE Confidence: 0.978056

00:02:07.890 --> 00:02:08.630 five minutes,

NOTE Confidence: 0.94269

00:02:09.250 --> 00:02:10.690 Sajhi is going to start

NOTE Confidence: 0.94269

00:02:10.690 --> 00:02:12.930 our presentation by introducing some

NOTE Confidence: 0.94269

00:02:12.930 --> 00:02:14.450 of the background to sex

NOTE Confidence: 0.94269

00:02:14.450 --> 00:02:14.950 disparities

NOTE Confidence: 0.99674916

00:02:15.250 --> 00:02:15.750 in

NOTE Confidence: 0.9795308

00:02:16.145 --> 00:02:17.985 both, basic research and also

NOTE Confidence: 0.9795308

00:02:17.985 --> 00:02:19.584 clinical research. And then we're

NOTE Confidence: 0.9795308

00:02:19.584 --> 00:02:21.345 gonna, take turns talking about

NOTE Confidence: 0.9795308

00:02:21.345 --> 00:02:23.044 some of our collaborative research,

NOTE Confidence: 0.9925948

00:02:23.425 --> 00:02:24.944 which is mostly in the

NOTE Confidence: 0.9925948

00:02:24.944 --> 00:02:25.985 area of looking at the

NOTE Confidence: 0.9925948

00:02:25.985 --> 00:02:27.044 role of asparagine

NOTE Confidence: 0.9864408

00:02:27.504 --> 00:02:29.504 in colorectal cancer for female

NOTE Confidence: 0.9864408

00:02:29.504 --> 00:02:30.940 patients. And then we'll end

NOTE Confidence: 0.9864408

00:02:30.940 --> 00:02:32.400 talking about some of our,

NOTE Confidence: 0.99937963

00:02:32.940 --> 00:02:33.840 future directions.

NOTE Confidence: 0.99972856

00:02:34.139 --> 00:02:34.880 Thank you.

NOTE Confidence: 0.9898908

00:02:40.620 --> 00:02:41.599 Okay. So

NOTE Confidence: 0.97405446

00:02:43.465 --> 00:02:45.144 so thanks again for, for

NOTE Confidence: 0.97405446

00:02:45.144 --> 00:02:46.264 the opportunity to speak. Thanks,

NOTE Confidence: 0.97405446

00:02:46.264 --> 00:02:47.305 Kieran, for that very nice

NOTE Confidence: 0.97405446

00:02:47.305 --> 00:02:47.805 introduction.

NOTE Confidence: 0.9613871

00:02:49.305 --> 00:02:50.264 You know, cancer is the

NOTE Confidence: 0.9613871

00:02:50.264 --> 00:02:51.944 second leading cause of deaths

NOTE Confidence: 0.9613871

00:02:51.944 --> 00:02:52.444 worldwide.

NOTE Confidence: 0.98613244

00:02:54.185 --> 00:02:55.704 About ten million people each

NOTE Confidence: 0.98613244

00:02:55.704 --> 00:02:56.105 year,

NOTE Confidence: 0.999152

00:02:56.504 --> 00:02:58.025 die of cancer across the

NOTE Confidence: 0.999152

00:02:58.025 --> 00:02:58.525 globe.

NOTE Confidence: 0.88532895

00:02:59.180 --> 00:02:59.680 Cancers,

NOTE Confidence: 0.98188865

00:03:00.300 --> 00:03:02.220 affects people of, every walk

NOTE Confidence: 0.98188865

00:03:02.220 --> 00:03:03.740 of life. It affects,

NOTE Confidence: 0.99327415

00:03:04.139 --> 00:03:05.200 females and males,

NOTE Confidence: 0.9892479

00:03:05.580 --> 00:03:07.100 and there's no race or

NOTE Confidence: 0.9892479

00:03:07.100 --> 00:03:08.700 ethnic background in the world

NOTE Confidence: 0.9892479

00:03:08.700 --> 00:03:09.980 that's immune to the development

NOTE Confidence: 0.9892479

00:03:09.980 --> 00:03:10.639 of cancer.

NOTE Confidence: 0.9927053

00:03:13.985 --> 00:03:15.025 Cancer is not just a

NOTE Confidence: 0.9927053

00:03:15.025 --> 00:03:16.465 global problem, but it is

NOTE Confidence: 0.9927053

00:03:16.465 --> 00:03:17.665 a local problem here in

NOTE Confidence: 0.9927053

00:03:17.665 --> 00:03:19.345 Connecticut for women and for

NOTE Confidence: 0.9927053

00:03:19.345 --> 00:03:19.845 men.

NOTE Confidence: 0.9964356

00:03:20.385 --> 00:03:21.585 Here are examples of three

NOTE Confidence: 0.9964356

00:03:21.585 --> 00:03:23.025 patients I've operated on over

NOTE Confidence: 0.9964356

00:03:23.025 --> 00:03:23.745 the last twelve and a

NOTE Confidence: 0.9964356

00:03:23.745 --> 00:03:24.945 half years at Yale throughout

NOTE Confidence: 0.9964356

00:03:24.945 --> 00:03:25.905 the health system. We have

NOTE Confidence: 0.9964356

00:03:25.905 --> 00:03:27.044 a large health system.

NOTE Confidence: 0.97784317

00:03:27.819 --> 00:03:29.180 The left picture is a

NOTE Confidence: 0.97784317

00:03:29.180 --> 00:03:30.540 patient of a seventy year

NOTE Confidence: 0.97784317

00:03:30.540 --> 00:03:32.060 old male with colorectal cancer

NOTE Confidence: 0.97784317

00:03:32.060 --> 00:03:33.500 liver metastases who I did

NOTE Confidence: 0.97784317

00:03:33.500 --> 00:03:34.939 a right hepatectomy on years

NOTE Confidence: 0.97784317

00:03:34.939 --> 00:03:35.439 ago.

NOTE Confidence: 0.9965633

00:03:35.980 --> 00:03:37.260 In the center is a

NOTE Confidence: 0.9965633

00:03:37.260 --> 00:03:38.540 seventy five year old female,

NOTE Confidence: 0.9395487

00:03:39.615 --> 00:03:40.415 who had a diagnosis of

NOTE Confidence: 0.9395487

00:03:40.415 --> 00:03:41.475 pancreas adenocarcinoma,

NOTE Confidence: 0.92211026

00:03:41.935 --> 00:03:42.735 who I did a WIPA

NOTE Confidence: 0.92211026

00:03:42.735 --> 00:03:44.035 on several years ago.

NOTE Confidence: 0.9881103

00:03:44.335 --> 00:03:45.295 And on the right is

NOTE Confidence: 0.9881103

00:03:45.295 --> 00:03:46.255 a seventy one year old

NOTE Confidence: 0.9881103

00:03:46.255 --> 00:03:47.775 female who had a gastric

NOTE Confidence: 0.9881103

00:03:47.855 --> 00:03:48.355 gastrointestinal

NOTE Confidence: 0.9961735

00:03:48.655 --> 00:03:49.555 stromal tumor,

NOTE Confidence: 0.9051582

00:03:50.015 --> 00:03:51.375 a giant one for which

NOTE Confidence: 0.9051582

00:03:51.375 --> 00:03:52.675 we did a a gastrectomy

NOTE Confidence: 0.97984827

00:03:52.975 --> 00:03:54.035 and a distal pancreatectomy.

NOTE Confidence: 0.98306614

00:03:57.610 --> 00:03:58.730 Here are some gross and

NOTE Confidence: 0.98306614

00:03:58.730 --> 00:03:59.230 microscopic

NOTE Confidence: 0.99654055

00:03:59.530 --> 00:04:00.890 pictures of patients who underwent

NOTE Confidence: 0.99654055

00:04:01.129 --> 00:04:02.650 who underwent of a patient

NOTE Confidence: 0.99654055

00:04:02.650 --> 00:04:04.010 who underwent a colectomy for

NOTE Confidence: 0.99654055

00:04:04.010 --> 00:04:04.989 colon adenocarcinoma.

NOTE Confidence: 0.9209858

00:04:06.170 --> 00:04:07.769 The pictures were nicely prepared

NOTE Confidence: 0.9209858

00:04:07.769 --> 00:04:09.129 for by doctor Zuchin Zhang

NOTE Confidence: 0.9209858

00:04:09.129 --> 00:04:10.430 from our department of pathology.

NOTE Confidence: 0.99496

00:04:10.965 --> 00:04:12.004 On the top left, you

NOTE Confidence: 0.99496

00:04:12.004 --> 00:04:13.364 can see a picture of,

NOTE Confidence: 0.9930323

00:04:13.685 --> 00:04:14.644 a gross picture of the

NOTE Confidence: 0.9930323

00:04:14.644 --> 00:04:16.104 ascending colon adenocarcinoma.

NOTE Confidence: 0.94669247

00:04:16.964 --> 00:04:17.845 And on the bottom and

NOTE Confidence: 0.94669247

00:04:17.845 --> 00:04:18.645 the right, you can see

NOTE Confidence: 0.94669247

00:04:18.645 --> 00:04:20.404 beautiful histology pictures of a

NOTE Confidence: 0.94669247

00:04:20.404 --> 00:04:21.464 lymph node metastasis

NOTE Confidence: 0.99722373

00:04:22.005 --> 00:04:23.385 and full thickness invasion.

NOTE Confidence: 0.98500746

00:04:30.339 --> 00:04:31.380 Here are the ten leading

NOTE Confidence: 0.98500746

00:04:31.380 --> 00:04:33.240 causes of new cancer diagnoses

NOTE Confidence: 0.98500746

00:04:33.300 --> 00:04:34.420 in the United States and

NOTE Confidence: 0.98500746

00:04:34.420 --> 00:04:35.300 the ten leading cause of

NOTE Confidence: 0.98500746

00:04:35.300 --> 00:04:36.420 cancer deaths in the United

NOTE Confidence: 0.98500746

00:04:36.420 --> 00:04:37.960 States in females and males.

NOTE Confidence: 0.9462796

00:04:38.544 --> 00:04:39.345 What I do want you

NOTE Confidence: 0.9462796

00:04:39.345 --> 00:04:40.384 to notice that even for

NOTE Confidence: 0.9462796

00:04:40.384 --> 00:04:41.044 the nonreproductive

NOTE Confidence: 0.99897647

00:04:41.425 --> 00:04:41.925 cancers,

NOTE Confidence: 0.9944321

00:04:42.305 --> 00:04:43.044 the incidence,

NOTE Confidence: 0.9654398

00:04:44.145 --> 00:04:45.285 is not equivalent.

NOTE Confidence: 0.9835726

00:04:45.664 --> 00:04:46.705 So it's something we'll get

NOTE Confidence: 0.9835726

00:04:46.705 --> 00:04:47.504 back to a little bit

NOTE Confidence: 0.9835726

00:04:47.504 --> 00:04:48.645 later in this talk.

NOTE Confidence: 0.99984664

00:04:49.585 --> 00:04:50.625 And the reason for that

NOTE Confidence: 0.99984664

00:04:50.625 --> 00:04:52.250 is because sex and gender

NOTE Confidence: 0.99984664

00:04:52.310 --> 00:04:53.669 have a major influence on

NOTE Confidence: 0.99984664

00:04:53.669 --> 00:04:54.490 human health.

NOTE Confidence: 0.9833984

00:04:55.190 --> 00:04:57.270 Generally speaking, sex refers to

NOTE Confidence: 0.9833984

00:04:57.270 --> 00:04:59.110 the biological characteristics of an

NOTE Confidence: 0.9833984

00:04:59.110 --> 00:04:59.610 individual,

NOTE Confidence: 0.99039537

00:04:59.990 --> 00:05:01.349 while gender refers to the

NOTE Confidence: 0.99039537

00:05:01.349 --> 00:05:01.849 sociocultural

NOTE Confidence: 0.99458694

00:05:02.629 --> 00:05:04.629 roles and sexual identity of

NOTE Confidence: 0.99458694

00:05:04.629 --> 00:05:05.289 an individual.

NOTE Confidence: 0.95922637

00:05:05.835 --> 00:05:06.795 So the perp for the

NOTE Confidence: 0.95922637

00:05:06.795 --> 00:05:08.175 purposes of this talk,

NOTE Confidence: 0.98862064

00:05:08.955 --> 00:05:10.154 Carol and I are gonna

NOTE Confidence: 0.98862064

00:05:10.154 --> 00:05:10.955 focus on the sex of

NOTE Confidence: 0.98862064

00:05:10.955 --> 00:05:12.735 an individual, and we'll interchangeably

NOTE Confidence: 0.98862064

00:05:12.955 --> 00:05:14.154 use the words female and

NOTE Confidence: 0.98862064

00:05:14.154 --> 00:05:14.654 women,

NOTE Confidence: 0.96280247

00:05:15.355 --> 00:05:16.955 males and men, when discussing

NOTE Confidence: 0.96280247

00:05:16.955 --> 00:05:18.175 the individual sexes.

NOTE Confidence: 0.9761674

00:05:19.970 --> 00:05:21.650 There are differences which exist

NOTE Confidence: 0.9761674

00:05:21.650 --> 00:05:23.089 between sexes in regards to

NOTE Confidence: 0.9761674

00:05:23.089 --> 00:05:23.990 disease development,

NOTE Confidence: 0.97682196

00:05:24.370 --> 00:05:26.770 diagnosis, treatment response, which are

NOTE Confidence: 0.97682196

00:05:26.770 --> 00:05:28.529 rooted in genetic differences between

NOTE Confidence: 0.97682196

00:05:28.529 --> 00:05:29.509 women and men.

NOTE Confidence: 0.98829806

00:05:29.810 --> 00:05:31.250 And understanding the effect of

NOTE Confidence: 0.98829806

00:05:31.250 --> 00:05:33.029 sex as a biological variable

NOTE Confidence: 0.99981946

00:05:33.445 --> 00:05:34.645 will improve the health of

NOTE Confidence: 0.99981946

00:05:34.645 --> 00:05:35.705 women and men

NOTE Confidence: 0.9996149

00:05:36.085 --> 00:05:37.145 across the globe.

NOTE Confidence: 0.9860863

00:05:39.125 --> 00:05:40.565 Unfortunately, there's been a global

NOTE Confidence: 0.9860863

00:05:40.565 --> 00:05:42.485 bias and historical neglect of

NOTE Confidence: 0.9860863

00:05:42.485 --> 00:05:43.785 studying sex as a biological

NOTE Confidence: 0.9860863

00:05:43.925 --> 00:05:45.285 variable in both basic and

NOTE Confidence: 0.9860863

00:05:45.285 --> 00:05:46.265 clinical research,

NOTE Confidence: 0.99989176

00:05:46.725 --> 00:05:47.625 over the years.

NOTE Confidence: 0.9986847

00:05:48.710 --> 00:05:50.790 In biomedical research, females are

NOTE Confidence: 0.9986847

00:05:50.790 --> 00:05:51.290 underrepresented

NOTE Confidence: 0.97813606

00:05:51.590 --> 00:05:53.450 in clinical trials and research,

NOTE Confidence: 0.98321545

00:05:54.150 --> 00:05:56.310 and, biological sex has long

NOTE Confidence: 0.98321545

00:05:56.310 --> 00:05:57.910 been ignored in sciences, and

NOTE Confidence: 0.98321545

00:05:57.910 --> 00:05:59.370 male animals have been predominantly

NOTE Confidence: 0.98321545

00:05:59.510 --> 00:06:00.010 used.

NOTE Confidence: 0.970942

00:06:00.310 --> 00:06:01.485 So So the majority of

NOTE Confidence: 0.970942

00:06:01.485 --> 00:06:01.985 research,

NOTE Confidence: 0.9994782

00:06:03.005 --> 00:06:04.285 in our world has been

NOTE Confidence: 0.9994782

00:06:04.285 --> 00:06:05.904 heavily biased towards men.

NOTE Confidence: 0.9385814

00:06:09.085 --> 00:06:10.764 The neglect of research where

NOTE Confidence: 0.9385814

00:06:10.764 --> 00:06:11.805 sex is considered as a

NOTE Confidence: 0.9385814

00:06:11.805 --> 00:06:14.340 biological variable includes cancer research,

NOTE Confidence: 0.9385814

00:06:14.340 --> 00:06:15.380 and we're here at a

NOTE Confidence: 0.9385814

00:06:15.380 --> 00:06:16.680 premier cancer center,

NOTE Confidence: 0.9872088

00:06:17.060 --> 00:06:18.100 and this is something that

NOTE Confidence: 0.9872088

00:06:18.100 --> 00:06:19.140 we wanna focus a bit

NOTE Confidence: 0.9872088

00:06:19.140 --> 00:06:20.440 more of this talk on.

NOTE Confidence: 0.9959975

00:06:21.060 --> 00:06:22.580 Sex disparities are evident in

NOTE Confidence: 0.9959975

00:06:22.580 --> 00:06:23.080 nonreproductive

NOTE Confidence: 0.94662064

00:06:23.460 --> 00:06:24.900 cancers as the incidence of

NOTE Confidence: 0.94662064

00:06:24.900 --> 00:06:25.400 mortality,

NOTE Confidence: 0.96451956

00:06:26.100 --> 00:06:27.460 are higher in males compared

NOTE Confidence: 0.96451956

00:06:27.460 --> 00:06:28.040 to females.

NOTE Confidence: 0.97958964

00:06:28.815 --> 00:06:30.654 And, unfortunately, sex disparities are

NOTE Confidence: 0.97958964

00:06:30.654 --> 00:06:32.514 poorly understood at a molecular

NOTE Confidence: 0.97958964

00:06:32.574 --> 00:06:33.074 level.

NOTE Confidence: 0.98720264

00:06:33.535 --> 00:06:34.975 This includes the impact which

NOTE Confidence: 0.98720264

00:06:34.975 --> 00:06:37.074 sex plays on genetic differences,

NOTE Confidence: 0.9943537

00:06:37.854 --> 00:06:39.074 epigenetic alterations,

NOTE Confidence: 0.9997633

00:06:39.535 --> 00:06:40.595 and sex hormones.

NOTE Confidence: 0.9823774

00:06:41.669 --> 00:06:44.389 Furthermore, there's emerging research, which

NOTE Confidence: 0.9823774

00:06:44.389 --> 00:06:45.509 reveals that x and y

NOTE Confidence: 0.9823774

00:06:45.509 --> 00:06:47.350 genes encode for regulators of

NOTE Confidence: 0.9823774

00:06:47.350 --> 00:06:47.850 metabolism,

NOTE Confidence: 0.9977182

00:06:48.470 --> 00:06:48.970 immunity,

NOTE Confidence: 0.997135

00:06:49.430 --> 00:06:50.490 and tumor suppression.

NOTE Confidence: 0.9731111

00:06:54.604 --> 00:06:55.884 There are sex disparities that

NOTE Confidence: 0.9731111

00:06:55.884 --> 00:06:57.005 are evident in the major

NOTE Confidence: 0.9731111

00:06:57.005 --> 00:06:58.044 types of treatment we offer

NOTE Confidence: 0.9731111

00:06:58.044 --> 00:06:59.645 for our patients here. We

NOTE Confidence: 0.9731111

00:06:59.645 --> 00:07:00.845 have doctor Traga, who's a

NOTE Confidence: 0.9731111

00:07:00.845 --> 00:07:02.285 surgical oncologist. So when we

NOTE Confidence: 0.9731111

00:07:02.285 --> 00:07:04.065 look at cancer surgery performed,

NOTE Confidence: 0.9731111

00:07:04.365 --> 00:07:06.445 lung cancer surgery, believe it

NOTE Confidence: 0.9731111

00:07:06.445 --> 00:07:08.365 or not, for, female patients

NOTE Confidence: 0.9731111

00:07:08.365 --> 00:07:09.480 actually lead to a better

NOTE Confidence: 0.9731111

00:07:09.480 --> 00:07:10.600 are associated with a better

NOTE Confidence: 0.9731111

00:07:10.600 --> 00:07:11.100 survival

NOTE Confidence: 0.9558854

00:07:11.400 --> 00:07:12.920 and less likely experience of

NOTE Confidence: 0.9558854

00:07:12.920 --> 00:07:14.840 sepsis complications suggesting that there

NOTE Confidence: 0.9558854

00:07:14.840 --> 00:07:15.420 may be,

NOTE Confidence: 0.99972

00:07:15.960 --> 00:07:17.340 differences in the biology

NOTE Confidence: 0.9555371

00:07:17.640 --> 00:07:18.760 of a female with a

NOTE Confidence: 0.9555371

00:07:18.760 --> 00:07:20.060 male even from surgery.

NOTE Confidence: 0.9971569

00:07:20.520 --> 00:07:22.600 Radiation treatment for esophagus squamous

NOTE Confidence: 0.9971569

00:07:22.600 --> 00:07:23.800 cell carcinoma has a better

NOTE Confidence: 0.9971569

00:07:23.800 --> 00:07:25.215 survival for females compared to

NOTE Confidence: 0.9971569

00:07:25.215 --> 00:07:25.715 males.

NOTE Confidence: 0.97296786

00:07:26.574 --> 00:07:28.175 And for systemic therapies, and

NOTE Confidence: 0.97296786

00:07:28.175 --> 00:07:28.974 we have a lot of,

NOTE Confidence: 0.97296786

00:07:29.215 --> 00:07:30.655 medical oncologists on the Zoom

NOTE Confidence: 0.97296786

00:07:30.655 --> 00:07:32.254 and on the audience, multiple

NOTE Confidence: 0.97296786

00:07:32.254 --> 00:07:34.014 chemotherapy regimens are associated with

NOTE Confidence: 0.97296786

00:07:34.014 --> 00:07:35.955 the longer survival for esophagus

NOTE Confidence: 0.97296786

00:07:36.014 --> 00:07:36.514 cancer,

NOTE Confidence: 0.9716537

00:07:36.895 --> 00:07:38.414 stomach cancer, non small cell

NOTE Confidence: 0.9716537

00:07:38.414 --> 00:07:39.634 lung cancer, and glioblastoma

NOTE Confidence: 0.987609

00:07:40.094 --> 00:07:40.920 for females.

NOTE Confidence: 0.9701294

00:07:41.540 --> 00:07:43.720 EGFR inhibitors, the targeted drugs,

NOTE Confidence: 0.9701294

00:07:43.780 --> 00:07:45.140 lead to longer survival for

NOTE Confidence: 0.9701294

00:07:45.140 --> 00:07:45.640 females.

NOTE Confidence: 0.9377935

00:07:47.060 --> 00:07:49.060 And interestingly, immune therapies for

NOTE Confidence: 0.9377935

00:07:49.060 --> 00:07:50.520 non small cell lung cancer

NOTE Confidence: 0.9377935

00:07:50.660 --> 00:07:52.100 lead to longer survival for

NOTE Confidence: 0.9377935

00:07:52.100 --> 00:07:54.120 females, but actually for males

NOTE Confidence: 0.9377935

00:07:54.325 --> 00:07:55.205 that get into,

NOTE Confidence: 0.9166564

00:07:55.605 --> 00:07:56.105 IO,

NOTE Confidence: 0.9852066

00:07:56.725 --> 00:07:58.325 they have longer survivals for,

NOTE Confidence: 0.9852066

00:07:58.725 --> 00:07:59.925 again, implying that there's a

NOTE Confidence: 0.9852066

00:07:59.925 --> 00:08:00.985 difference in the biology,

NOTE Confidence: 0.9634479

00:08:01.685 --> 00:08:03.625 of, female and male cancers.

NOTE Confidence: 0.98556846

00:08:05.765 --> 00:08:07.045 There are multiple examples of

NOTE Confidence: 0.98556846

00:08:07.045 --> 00:08:08.725 sex not being considered in

NOTE Confidence: 0.98556846

00:08:08.725 --> 00:08:09.225 preclinical

NOTE Confidence: 0.9968815

00:08:09.685 --> 00:08:11.120 research settings as well.

NOTE Confidence: 0.9901062

00:08:11.500 --> 00:08:13.500 In cancer cell lines, there

NOTE Confidence: 0.9901062

00:08:13.500 --> 00:08:14.380 are, believe it or not,

NOTE Confidence: 0.9901062

00:08:14.380 --> 00:08:15.680 greater stocks of nonreproductive

NOTE Confidence: 0.95009434

00:08:16.140 --> 00:08:17.660 male cell lines compared compared

NOTE Confidence: 0.95009434

00:08:17.660 --> 00:08:19.040 to female cell lines.

NOTE Confidence: 0.9594067

00:08:20.060 --> 00:08:21.980 Single sex analyses fail to

NOTE Confidence: 0.9594067

00:08:21.980 --> 00:08:23.840 consider male and female responses.

NOTE Confidence: 0.996116

00:08:25.185 --> 00:08:26.385 Many studies just show an

NOTE Confidence: 0.996116

00:08:26.385 --> 00:08:28.145 averaging of responses across the

NOTE Confidence: 0.996116

00:08:28.145 --> 00:08:29.365 models for both sexes.

NOTE Confidence: 0.9959104

00:08:30.465 --> 00:08:31.745 When one looks very carefully

NOTE Confidence: 0.9959104

00:08:31.745 --> 00:08:33.425 at cell culture media, the

NOTE Confidence: 0.9959104

00:08:33.425 --> 00:08:34.945 serum of the calf fetus

NOTE Confidence: 0.9959104

00:08:34.945 --> 00:08:36.304 is sometimes mixed with male

NOTE Confidence: 0.9959104

00:08:36.304 --> 00:08:37.445 and female derived,

NOTE Confidence: 0.92948806

00:08:38.304 --> 00:08:39.525 organism organs

NOTE Confidence: 0.9706864

00:08:39.900 --> 00:08:41.020 and more often is not

NOTE Confidence: 0.9706864

00:08:41.020 --> 00:08:41.520 scrutinized.

NOTE Confidence: 0.97840375

00:08:42.380 --> 00:08:43.740 There's a mismatch of cell

NOTE Confidence: 0.97840375

00:08:43.740 --> 00:08:45.520 culture media with cultured cells.

NOTE Confidence: 0.9839856

00:08:46.300 --> 00:08:48.000 And finally, with mouse models,

NOTE Confidence: 0.9839856

00:08:48.059 --> 00:08:49.020 you know, there are also

NOTE Confidence: 0.9839856

00:08:49.020 --> 00:08:51.280 problems. Cancer drugs are often

NOTE Confidence: 0.9839856

00:08:51.580 --> 00:08:52.640 tested in premenopausal

NOTE Confidence: 0.9006506

00:08:53.020 --> 00:08:54.220 mice where the majority of

NOTE Confidence: 0.9006506

00:08:54.220 --> 00:08:55.280 cancers diagnosed,

NOTE Confidence: 0.9770438

00:08:55.845 --> 00:08:57.304 in females are postmenopausal,

NOTE Confidence: 0.92552644

00:08:58.245 --> 00:08:58.904 of age.

NOTE Confidence: 0.97968036

00:08:59.285 --> 00:09:00.404 And there are, of course,

NOTE Confidence: 0.97968036

00:09:00.404 --> 00:09:02.324 financial considerations. We're in constrained

NOTE Confidence: 0.97968036

00:09:02.324 --> 00:09:03.845 times with our financial budgets

NOTE Confidence: 0.97968036

00:09:03.845 --> 00:09:04.644 right now for a lot

NOTE Confidence: 0.97968036

00:09:04.644 --> 00:09:05.385 of our research,

NOTE Confidence: 0.9995074

00:09:05.764 --> 00:09:06.725 and a lot of that

NOTE Confidence: 0.9995074

00:09:06.725 --> 00:09:07.545 leads investigators

NOTE Confidence: 0.92246807

00:09:07.925 --> 00:09:08.165 to,

NOTE Confidence: 0.9961578

00:09:09.520 --> 00:09:11.040 favoring single sex studies in

NOTE Confidence: 0.9961578

00:09:11.040 --> 00:09:12.980 younger mice for financial considerations.

NOTE Confidence: 0.9985545

00:09:15.360 --> 00:09:16.480 As you can imagine, if

NOTE Confidence: 0.9985545

00:09:16.480 --> 00:09:17.440 there's a problem with the

NOTE Confidence: 0.9985545

00:09:17.440 --> 00:09:18.960 basic science, it translates into

NOTE Confidence: 0.9985545

00:09:18.960 --> 00:09:20.420 clinical trials as well.

NOTE Confidence: 0.99814415

00:09:21.125 --> 00:09:22.804 Women have lower enrollment in

NOTE Confidence: 0.99814415

00:09:22.804 --> 00:09:24.644 colorectal cancer and lung cancer

NOTE Confidence: 0.99814415

00:09:24.644 --> 00:09:26.105 trials compared to males.

NOTE Confidence: 0.99802834

00:09:26.644 --> 00:09:27.625 Women are underrepresented

NOTE Confidence: 0.9118927

00:09:28.084 --> 00:09:30.725 in, IO, or immune therapy

NOTE Confidence: 0.9118927

00:09:30.725 --> 00:09:31.225 trials.

NOTE Confidence: 0.9256198

00:09:31.845 --> 00:09:33.764 In a study, that looked

NOTE Confidence: 0.9256198

00:09:33.764 --> 00:09:35.365 at clinical trials and FDA

NOTE Confidence: 0.9256198

00:09:35.365 --> 00:09:37.620 approved modern anticancer drugs,

NOTE Confidence: 0.99176216

00:09:37.920 --> 00:09:39.440 fifty percent of the studies

NOTE Confidence: 0.99176216

00:09:39.440 --> 00:09:40.480 did not report the drug

NOTE Confidence: 0.99176216

00:09:40.480 --> 00:09:41.220 and efficacy,

NOTE Confidence: 0.9891224

00:09:41.840 --> 00:09:43.220 of these drugs in females.

NOTE Confidence: 0.97895855

00:09:43.840 --> 00:09:45.520 And women are also known

NOTE Confidence: 0.97895855

00:09:45.520 --> 00:09:47.040 to be underrepresented in these

NOTE Confidence: 0.97895855

00:09:47.040 --> 00:09:48.480 trials, and this is most

NOTE Confidence: 0.97895855

00:09:48.480 --> 00:09:49.679 this is most pronounced in

NOTE Confidence: 0.97895855

00:09:49.679 --> 00:09:50.500 GI cancer

NOTE Confidence: 0.9963064

00:09:50.895 --> 00:09:52.335 clinical trials, lung cancer, and

NOTE Confidence: 0.9963064

00:09:52.335 --> 00:09:53.395 leukemia trials.

NOTE Confidence: 0.9991582

00:09:56.735 --> 00:09:58.115 Despite these challenges,

NOTE Confidence: 0.9691571

00:09:58.815 --> 00:09:59.455 which we've,

NOTE Confidence: 0.9748409

00:09:59.935 --> 00:10:01.615 mentioned, you know, there are

NOTE Confidence: 0.9748409

00:10:01.615 --> 00:10:04.040 some ongoing efforts which believes

NOTE Confidence: 0.9748409

00:10:04.100 --> 00:10:05.779 that which provide hope that

NOTE Confidence: 0.9748409

00:10:05.779 --> 00:10:06.820 things will get better in

NOTE Confidence: 0.9748409

00:10:06.820 --> 00:10:07.400 the future,

NOTE Confidence: 0.96455014

00:10:07.779 --> 00:10:08.820 and more sex is gonna

NOTE Confidence: 0.96455014

00:10:08.820 --> 00:10:09.960 be looked at as biological

NOTE Confidence: 0.96455014

00:10:10.020 --> 00:10:11.640 variable in scientific research.

NOTE Confidence: 0.9722313

00:10:12.740 --> 00:10:13.940 There have been efforts made

NOTE Confidence: 0.9722313

00:10:13.940 --> 00:10:15.380 to include females and males

NOTE Confidence: 0.9722313

00:10:15.380 --> 00:10:17.540 in cells, tissues, animals, and

NOTE Confidence: 0.9722313

00:10:17.540 --> 00:10:18.040 humans.

NOTE Confidence: 0.9227047

00:10:18.825 --> 00:10:20.184 And, notably, there have been

NOTE Confidence: 0.9227047

00:10:20.184 --> 00:10:21.945 some important policy changes made

NOTE Confidence: 0.9227047

00:10:21.945 --> 00:10:22.985 in the last twenty six

NOTE Confidence: 0.9227047

00:10:22.985 --> 00:10:24.985 years, which are helping helping

NOTE Confidence: 0.9227047

00:10:24.985 --> 00:10:25.725 helping move,

NOTE Confidence: 0.99776334

00:10:26.905 --> 00:10:28.365 biomedical research forward.

NOTE Confidence: 0.966172

00:10:28.825 --> 00:10:29.865 In two thousand and one,

NOTE Confidence: 0.966172

00:10:29.865 --> 00:10:31.085 the Institute of Medicine

NOTE Confidence: 0.98605293

00:10:31.465 --> 00:10:32.825 convened a think tank that

NOTE Confidence: 0.98605293

00:10:32.825 --> 00:10:34.525 concluded that sufficient evidence

NOTE Confidence: 0.9907885

00:10:35.040 --> 00:10:36.320 existed, which shows that there's

NOTE Confidence: 0.9907885

00:10:36.320 --> 00:10:38.240 biological differences of women and

NOTE Confidence: 0.9907885

00:10:38.240 --> 00:10:40.240 men that influence treatment and

NOTE Confidence: 0.9907885

00:10:40.240 --> 00:10:41.300 prevention strategies.

NOTE Confidence: 0.9924079

00:10:42.720 --> 00:10:44.080 In two thousand and seven,

NOTE Confidence: 0.9924079

00:10:44.080 --> 00:10:45.380 the World Health Organization

NOTE Confidence: 0.95914954

00:10:46.080 --> 00:10:48.019 passed resolution to urge researchers

NOTE Confidence: 0.95914954

00:10:48.160 --> 00:10:49.519 to split their data according

NOTE Confidence: 0.95914954

00:10:49.519 --> 00:10:50.179 to sex

NOTE Confidence: 0.99108094

00:10:50.995 --> 00:10:52.995 and include gender analysis when

NOTE Confidence: 0.99108094

00:10:52.995 --> 00:10:53.495 appropriate.

NOTE Confidence: 0.9762971

00:10:54.915 --> 00:10:56.274 In two thousand eleven, the

NOTE Confidence: 0.9762971

00:10:56.274 --> 00:10:57.975 Canadian Institutes of Health,

NOTE Confidence: 0.99732864

00:10:58.514 --> 00:11:00.615 expected research applicants to integrate

NOTE Confidence: 0.99732864

00:11:00.675 --> 00:11:01.654 sex and gender,

NOTE Confidence: 0.99129254

00:11:02.355 --> 00:11:04.190 into their research design. To

NOTE Confidence: 0.99129254

00:11:04.190 --> 00:11:05.390 show an example of progress

NOTE Confidence: 0.99129254

00:11:05.390 --> 00:11:06.670 from two thousand eleven to

NOTE Confidence: 0.99129254

00:11:06.670 --> 00:11:08.110 two thousand and twenty two,

NOTE Confidence: 0.99129254

00:11:08.110 --> 00:11:09.390 the research proposal for the

NOTE Confidence: 0.99129254

00:11:09.390 --> 00:11:11.390 Canadian Institute of Health Research

NOTE Confidence: 0.99129254

00:11:11.390 --> 00:11:12.910 increased from twenty two percent

NOTE Confidence: 0.99129254

00:11:12.910 --> 00:11:14.050 to eighty three percent.

NOTE Confidence: 0.9639644

00:11:15.470 --> 00:11:16.990 In nineteen ninety three, the

NOTE Confidence: 0.9639644

00:11:16.990 --> 00:11:19.015 NIH Revitalization Act required the

NOTE Confidence: 0.9639644

00:11:19.015 --> 00:11:20.395 inclusion of women in NIH,

NOTE Confidence: 0.95872045

00:11:21.815 --> 00:11:24.455 funded clinical research. Unfortunately, many

NOTE Confidence: 0.95872045

00:11:24.455 --> 00:11:26.375 researchers did not, follow this

NOTE Confidence: 0.95872045

00:11:26.375 --> 00:11:27.895 recommendation, and sometimes it takes

NOTE Confidence: 0.95872045

00:11:27.895 --> 00:11:28.934 a nudge and sometimes you

NOTE Confidence: 0.95872045

00:11:28.934 --> 00:11:29.895 have to bring back good

NOTE Confidence: 0.95872045

00:11:29.895 --> 00:11:31.675 ideas. And in two thousand

NOTE Confidence: 0.95872045

00:11:31.735 --> 00:11:32.714 sixteen, the NIH

NOTE Confidence: 0.9769157

00:11:33.269 --> 00:11:35.190 passed the Century Cures Act

NOTE Confidence: 0.9769157

00:11:35.190 --> 00:11:36.490 that called for the inclusion

NOTE Confidence: 0.9769157

00:11:36.550 --> 00:11:38.070 of male and female sexes

NOTE Confidence: 0.9769157

00:11:38.070 --> 00:11:39.829 in studies involving cells, tissues,

NOTE Confidence: 0.9769157

00:11:39.829 --> 00:11:40.490 and animals.

NOTE Confidence: 0.96447706

00:11:41.110 --> 00:11:42.170 And most recently,

NOTE Confidence: 0.9501993

00:11:42.550 --> 00:11:43.910 during the Biden administration, the

NOTE Confidence: 0.9501993

00:11:43.910 --> 00:11:45.350 White House initiative on women's

NOTE Confidence: 0.9501993

00:11:45.350 --> 00:11:46.809 health research called to improve

NOTE Confidence: 0.9501993

00:11:46.985 --> 00:11:48.845 women's health research by prioritizing

NOTE Confidence: 0.9501993

00:11:48.985 --> 00:11:49.485 investments

NOTE Confidence: 0.9610466

00:11:49.945 --> 00:11:50.265 in,

NOTE Confidence: 0.93223125

00:11:50.985 --> 00:11:51.965 women's health research.

NOTE Confidence: 0.9364519

00:12:00.690 --> 00:12:01.910 Let's see here.

NOTE Confidence: 0.996611

00:12:04.050 --> 00:12:04.550 Okay.

NOTE Confidence: 0.952216

00:12:07.250 --> 00:12:09.010 So, so, hopefully, so far,

NOTE Confidence: 0.952216

00:12:09.010 --> 00:12:10.309 we've convinced you that,

NOTE Confidence: 0.9817716

00:12:11.090 --> 00:12:12.390 studying sex as a biological

NOTE Confidence: 0.9817716

00:12:12.450 --> 00:12:13.890 variable is an important thing

NOTE Confidence: 0.9817716

00:12:13.890 --> 00:12:14.850 to do, and it's gonna

NOTE Confidence: 0.9817716

00:12:14.850 --> 00:12:15.975 improve cancer outcomes.

NOTE Confidence: 0.9996316

00:12:16.454 --> 00:12:17.095 But how do you go

NOTE Confidence: 0.9996316

00:12:17.095 --> 00:12:17.595 about

NOTE Confidence: 0.9648859

00:12:17.975 --> 00:12:19.175 performing this kind of impactful

NOTE Confidence: 0.9648859

00:12:19.175 --> 00:12:19.675 research?

NOTE Confidence: 0.9831029

00:12:20.054 --> 00:12:21.334 Sometimes when one starts a

NOTE Confidence: 0.9831029

00:12:21.334 --> 00:12:22.235 research project,

NOTE Confidence: 0.99135274

00:12:22.934 --> 00:12:23.815 it can seem like a

NOTE Confidence: 0.99135274

00:12:23.815 --> 00:12:25.334 long windy road. You don't

NOTE Confidence: 0.99135274

00:12:25.334 --> 00:12:26.295 know where to start. You

NOTE Confidence: 0.99135274

00:12:26.295 --> 00:12:27.334 don't know where the the

NOTE Confidence: 0.99135274

00:12:27.334 --> 00:12:28.214 goal line is. You don't

NOTE Confidence: 0.99135274

00:12:28.214 --> 00:12:28.934 know where the end is.

NOTE Confidence: 0.99135274

00:12:28.934 --> 00:12:29.894 So so how do you

NOTE Confidence: 0.99135274

00:12:29.894 --> 00:12:31.014 get go about doing the

NOTE Confidence: 0.99135274

00:12:31.014 --> 00:12:31.514 research?

NOTE Confidence: 0.97655547

00:12:32.399 --> 00:12:33.679 So for one, no one

NOTE Confidence: 0.97655547

00:12:33.679 --> 00:12:34.899 can walk the road anymore,

NOTE Confidence: 0.99977714

00:12:35.360 --> 00:12:35.860 alone.

NOTE Confidence: 0.9834546

00:12:36.480 --> 00:12:37.220 The NIH,

NOTE Confidence: 0.9957239

00:12:37.679 --> 00:12:39.540 has realized that scientific problems,

NOTE Confidence: 0.98104465

00:12:39.920 --> 00:12:41.279 become more challenging given the

NOTE Confidence: 0.98104465

00:12:41.279 --> 00:12:43.360 vast amount of information, technologies,

NOTE Confidence: 0.98104465

00:12:43.360 --> 00:12:44.640 and resources that are ever

NOTE Confidence: 0.98104465

00:12:44.640 --> 00:12:45.140 present,

NOTE Confidence: 0.97308946

00:12:45.565 --> 00:12:46.525 and we're seeing this more

NOTE Confidence: 0.97308946

00:12:46.525 --> 00:12:47.645 and more exponentially in the

NOTE Confidence: 0.97308946

00:12:47.645 --> 00:12:48.845 last one or two years

NOTE Confidence: 0.97308946

00:12:48.845 --> 00:12:49.585 with AI.

NOTE Confidence: 0.980357

00:12:50.125 --> 00:12:51.165 The increase in number of

NOTE Confidence: 0.980357

00:12:51.165 --> 00:12:53.105 publications in science and engineering

NOTE Confidence: 0.9902498

00:12:53.565 --> 00:12:53.805 is

NOTE Confidence: 0.99073344

00:12:54.605 --> 00:12:56.465 with multiple authors is increasing

NOTE Confidence: 0.99073344

00:12:56.525 --> 00:12:57.025 exponentially.

NOTE Confidence: 0.96199465

00:12:59.209 --> 00:13:00.510 So in order to tackle,

NOTE Confidence: 0.9825824

00:13:01.130 --> 00:13:02.809 complex problems, the team science

NOTE Confidence: 0.9825824

00:13:02.809 --> 00:13:04.490 approach is the answer. And

NOTE Confidence: 0.9825824

00:13:04.490 --> 00:13:05.529 in order to understand this,

NOTE Confidence: 0.9825824

00:13:05.529 --> 00:13:06.329 we would first like to

NOTE Confidence: 0.9825824

00:13:06.329 --> 00:13:08.329 define what team science exactly

NOTE Confidence: 0.9825824

00:13:08.329 --> 00:13:08.829 is.

NOTE Confidence: 0.9626654

00:13:09.769 --> 00:13:11.149 Team science is a collaborative

NOTE Confidence: 0.9626654

00:13:11.290 --> 00:13:12.750 effort to address a scientific

NOTE Confidence: 0.9626654

00:13:12.889 --> 00:13:13.389 challenge,

NOTE Confidence: 0.9977355

00:13:13.995 --> 00:13:15.675 by leveraging experts in different

NOTE Confidence: 0.9977355

00:13:15.675 --> 00:13:16.175 fields,

NOTE Confidence: 0.9745695

00:13:17.035 --> 00:13:18.554 who need a compelling clinically

NOTE Confidence: 0.9745695

00:13:18.554 --> 00:13:20.735 driven research question to start.

NOTE Confidence: 0.9665993

00:13:21.515 --> 00:13:22.895 The tree the team,

NOTE Confidence: 0.98316264

00:13:23.275 --> 00:13:25.275 is comprised of, individuals that

NOTE Confidence: 0.98316264

00:13:25.275 --> 00:13:26.815 address a clinically focused

NOTE Confidence: 0.9986472

00:13:27.149 --> 00:13:28.050 research project.

NOTE Confidence: 0.9890573

00:13:28.589 --> 00:13:30.209 They are comprised of members

NOTE Confidence: 0.9890573

00:13:30.429 --> 00:13:31.649 with training and expertise,

NOTE Confidence: 0.91625434

00:13:32.509 --> 00:13:34.209 from multiple scientific disciplines.

NOTE Confidence: 0.99353963

00:13:34.829 --> 00:13:36.110 The team works together to

NOTE Confidence: 0.99353963

00:13:36.110 --> 00:13:37.089 combine and integrate,

NOTE Confidence: 0.8437634

00:13:37.550 --> 00:13:39.329 different knowledge skills perspectives,

NOTE Confidence: 0.95720273

00:13:39.790 --> 00:13:40.929 from different fields.

NOTE Confidence: 0.93904734

00:13:41.470 --> 00:13:42.449 And this approach,

NOTE Confidence: 0.9965866

00:13:43.605 --> 00:13:45.605 enables for medical and scientific

NOTE Confidence: 0.9965866

00:13:45.605 --> 00:13:47.684 communities to solve complex problems

NOTE Confidence: 0.9965866

00:13:47.684 --> 00:13:49.304 and help, people worldwide.

NOTE Confidence: 0.98699886

00:13:51.445 --> 00:13:52.645 To apply a team science

NOTE Confidence: 0.98699886

00:13:52.645 --> 00:13:54.165 approach, first, one needs to

NOTE Confidence: 0.98699886

00:13:54.165 --> 00:13:55.900 assemble a team. So the

NOTE Confidence: 0.98699886

00:13:55.900 --> 00:13:57.340 research question should drive who

NOTE Confidence: 0.98699886

00:13:57.340 --> 00:13:58.220 the members of the team

NOTE Confidence: 0.98699886

00:13:58.220 --> 00:13:59.340 should be. So to use

NOTE Confidence: 0.98699886

00:13:59.340 --> 00:14:00.700 a sports analogy, I I

NOTE Confidence: 0.98699886

00:14:00.700 --> 00:14:02.320 enjoy baseball and basketball.

NOTE Confidence: 0.92045665

00:14:03.179 --> 00:14:05.020 So, you know, we're the

NOTE Confidence: 0.92045665

00:14:05.020 --> 00:14:06.620 March Madness is underway right

NOTE Confidence: 0.92045665

00:14:06.620 --> 00:14:07.760 now. So,

NOTE Confidence: 0.97841454

00:14:08.385 --> 00:14:09.665 so in order for, you

NOTE Confidence: 0.97841454

00:14:09.665 --> 00:14:11.184 know, the Yukon women's team

NOTE Confidence: 0.97841454

00:14:11.184 --> 00:14:12.945 to win another championship, every

NOTE Confidence: 0.97841454

00:14:12.945 --> 00:14:13.985 member of the team doesn't

NOTE Confidence: 0.97841454

00:14:13.985 --> 00:14:14.705 need to be a three

NOTE Confidence: 0.97841454

00:14:14.705 --> 00:14:15.825 point shooter. You need a

NOTE Confidence: 0.97841454

00:14:15.825 --> 00:14:17.025 well balanced team with good

NOTE Confidence: 0.97841454

00:14:17.025 --> 00:14:18.245 defenders, good rebounders,

NOTE Confidence: 0.9479873

00:14:18.705 --> 00:14:19.905 a good point guard, so

NOTE Confidence: 0.9479873

00:14:19.905 --> 00:14:21.285 it's a well balanced team.

NOTE Confidence: 0.9479873

00:14:21.480 --> 00:14:22.600 To win a World Series

NOTE Confidence: 0.9479873

00:14:22.600 --> 00:14:24.360 in baseball so Caroline is

NOTE Confidence: 0.9479873

00:14:24.360 --> 00:14:25.639 a Red Sox fan. I'm

NOTE Confidence: 0.9479873

00:14:25.639 --> 00:14:26.760 a Yankees fan, but we

NOTE Confidence: 0.9479873

00:14:26.760 --> 00:14:27.660 still get along.

NOTE Confidence: 0.9802642

00:14:28.360 --> 00:14:30.040 But every player can't be

NOTE Confidence: 0.9802642

00:14:30.040 --> 00:14:31.240 a Derek Jeter. Every player

NOTE Confidence: 0.9802642

00:14:31.240 --> 00:14:32.199 can't be a Mookie Betts.

NOTE Confidence: 0.9802642

00:14:32.199 --> 00:14:33.079 You need a well rounded

NOTE Confidence: 0.9802642

00:14:33.079 --> 00:14:34.699 team of good pitchers, defenders,

NOTE Confidence: 0.96327114

00:14:35.945 --> 00:14:36.445 batters,

NOTE Confidence: 0.9261896

00:14:36.905 --> 00:14:37.785 in order to win a

NOTE Confidence: 0.9261896

00:14:37.785 --> 00:14:38.525 world series.

NOTE Confidence: 0.9872269

00:14:39.945 --> 00:14:41.785 And finally, you know, one

NOTE Confidence: 0.9872269

00:14:41.785 --> 00:14:43.065 needs to identify the right

NOTE Confidence: 0.9872269

00:14:43.065 --> 00:14:44.205 people for the team.

NOTE Confidence: 0.979533

00:14:44.985 --> 00:14:46.345 Generally speaking, here's a solid

NOTE Confidence: 0.979533

00:14:46.345 --> 00:14:47.705 component of what Caroline and

NOTE Confidence: 0.979533

00:14:47.705 --> 00:14:48.585 I have used over the

NOTE Confidence: 0.979533

00:14:48.585 --> 00:14:49.945 last, you know, nine years

NOTE Confidence: 0.979533

00:14:49.945 --> 00:14:50.845 for our team.

NOTE Confidence: 0.81744564

00:14:51.730 --> 00:14:52.230 So,

NOTE Confidence: 0.9971035

00:14:53.090 --> 00:14:53.970 you know, you need good

NOTE Confidence: 0.9971035

00:14:53.970 --> 00:14:55.030 collaborators, biostatisticians,

NOTE Confidence: 0.931969

00:14:56.450 --> 00:14:57.730 students and pre docs who

NOTE Confidence: 0.931969

00:14:57.730 --> 00:14:59.090 are passionate about the research

NOTE Confidence: 0.931969

00:14:59.090 --> 00:15:00.290 project that the PIs are

NOTE Confidence: 0.931969

00:15:00.290 --> 00:15:02.130 interested in, good mentorship and

NOTE Confidence: 0.931969

00:15:02.130 --> 00:15:03.810 advisorship. We both feel strongly

NOTE Confidence: 0.931969

00:15:03.810 --> 00:15:04.550 about mentorship.

NOTE Confidence: 0.9897622

00:15:04.985 --> 00:15:06.525 Good lab staff that's supportive,

NOTE Confidence: 0.94919014

00:15:07.225 --> 00:15:08.825 and good postdocs in creating

NOTE Confidence: 0.94919014

00:15:08.825 --> 00:15:09.725 a good environment.

NOTE Confidence: 0.97101516

00:15:11.625 --> 00:15:13.245 Doctor Johnson and I both,

NOTE Confidence: 0.9883689

00:15:13.705 --> 00:15:15.225 have individual labs at the

NOTE Confidence: 0.9883689

00:15:15.225 --> 00:15:16.825 Yale School of Public Health

NOTE Confidence: 0.9883689

00:15:16.825 --> 00:15:17.705 and the Yale School of

NOTE Confidence: 0.9883689

00:15:17.705 --> 00:15:19.560 Medicine where we create synergy

NOTE Confidence: 0.9883689

00:15:19.560 --> 00:15:20.779 in our research projects,

NOTE Confidence: 0.91376966

00:15:21.399 --> 00:15:22.519 from the team members so

NOTE Confidence: 0.91376966

00:15:22.519 --> 00:15:23.180 the intellectual,

NOTE Confidence: 0.96982485

00:15:24.200 --> 00:15:25.480 sum is far greater than

NOTE Confidence: 0.96982485

00:15:25.480 --> 00:15:27.160 the individuals. So the intellectual

NOTE Confidence: 0.96982485

00:15:27.160 --> 00:15:28.040 sum is greater than the

NOTE Confidence: 0.96982485

00:15:28.040 --> 00:15:29.980 individuals. So so we strongly

NOTE Confidence: 0.96982485

00:15:30.040 --> 00:15:31.399 advocate for a team science

NOTE Confidence: 0.96982485

00:15:31.399 --> 00:15:31.899 approach,

NOTE Confidence: 0.9573521

00:15:32.454 --> 00:15:34.214 and together, our labs study

NOTE Confidence: 0.9573521

00:15:34.214 --> 00:15:36.295 how metabolism and biological sex

NOTE Confidence: 0.9573521

00:15:36.295 --> 00:15:37.975 influence colorectal cancer and patient

NOTE Confidence: 0.9573521

00:15:37.975 --> 00:15:38.475 outcomes.

NOTE Confidence: 0.9943048

00:15:40.055 --> 00:15:41.735 Our team science approach has

NOTE Confidence: 0.9943048

00:15:41.735 --> 00:15:43.175 resulted in science, which is

NOTE Confidence: 0.9943048

00:15:43.175 --> 00:15:44.454 moving the field forward by

NOTE Confidence: 0.9943048

00:15:44.454 --> 00:15:45.675 tackling GI cancers.

NOTE Confidence: 0.99192303

00:15:47.010 --> 00:15:48.209 Our approach has led to

NOTE Confidence: 0.99192303

00:15:48.209 --> 00:15:50.050 multiple high impact publications over

NOTE Confidence: 0.99192303

00:15:50.050 --> 00:15:50.769 the last nine,

NOTE Confidence: 0.95713997

00:15:51.410 --> 00:15:52.769 less than nine years in

NOTE Confidence: 0.95713997

00:15:52.769 --> 00:15:54.050 addition to millions of dollars

NOTE Confidence: 0.95713997

00:15:54.050 --> 00:15:55.250 of funding from the NIH,

NOTE Confidence: 0.95713997

00:15:55.250 --> 00:15:56.529 which has has enabled us

NOTE Confidence: 0.95713997

00:15:56.529 --> 00:15:58.370 to contribute to society's understanding

NOTE Confidence: 0.95713997

00:15:58.370 --> 00:15:59.385 of GI cancers

NOTE Confidence: 0.9945953

00:15:59.865 --> 00:16:02.025 both globally globally and locally

NOTE Confidence: 0.9945953

00:16:02.025 --> 00:16:03.005 here in New England.

NOTE Confidence: 0.96957904

00:16:04.185 --> 00:16:05.065 I'm gonna turn it over

NOTE Confidence: 0.96957904

00:16:05.065 --> 00:16:05.965 to doctor Johnson.

NOTE Confidence: 0.9256122

00:16:07.305 --> 00:16:08.585 Thank you, Saj. So,

NOTE Confidence: 0.99457586

00:16:09.145 --> 00:16:10.425 I'm now gonna be discussing

NOTE Confidence: 0.99457586

00:16:10.425 --> 00:16:12.025 some of our collaborative research

NOTE Confidence: 0.99457586

00:16:12.025 --> 00:16:13.405 that has used metabolomics

NOTE Confidence: 0.9905054

00:16:13.820 --> 00:16:15.440 to identify sex specific

NOTE Confidence: 0.9977806

00:16:15.899 --> 00:16:17.760 metabolism in colorectal cancer.

NOTE Confidence: 0.9855846

00:16:19.100 --> 00:16:20.060 So I'd first like to

NOTE Confidence: 0.9855846

00:16:20.060 --> 00:16:21.820 start by explaining why it's

NOTE Confidence: 0.9855846

00:16:21.820 --> 00:16:23.420 important to understand the diversity

NOTE Confidence: 0.9855846

00:16:23.420 --> 00:16:25.100 and functions of metabolites in

NOTE Confidence: 0.9855846

00:16:25.100 --> 00:16:25.600 cancer.

NOTE Confidence: 0.9596243

00:16:26.334 --> 00:16:28.255 Well, metabolites and actually metabolic

NOTE Confidence: 0.9596243

00:16:28.255 --> 00:16:29.935 rewiring can actually help the

NOTE Confidence: 0.9596243

00:16:29.935 --> 00:16:30.435 transition

NOTE Confidence: 0.9900074

00:16:30.894 --> 00:16:32.175 from a primary tumor to

NOTE Confidence: 0.9900074

00:16:32.175 --> 00:16:33.615 a metastasis. So you see

NOTE Confidence: 0.9900074

00:16:33.615 --> 00:16:34.755 here on this diagram

NOTE Confidence: 0.88461614

00:16:35.214 --> 00:16:36.575 that actually the production of

NOTE Confidence: 0.88461614

00:16:36.575 --> 00:16:38.515 acidic metabolites like lactate

NOTE Confidence: 0.9058327

00:16:38.990 --> 00:16:40.350 can help the the primary

NOTE Confidence: 0.9058327

00:16:40.350 --> 00:16:41.970 tumor cells undergo interversation

NOTE Confidence: 0.9981028

00:16:42.430 --> 00:16:43.230 into the,

NOTE Confidence: 0.9986706

00:16:43.790 --> 00:16:45.009 circulatory system.

NOTE Confidence: 0.97540754

00:16:45.790 --> 00:16:46.750 Once the tumor cells are

NOTE Confidence: 0.97540754

00:16:46.750 --> 00:16:48.430 in the circulatory system, they

NOTE Confidence: 0.97540754

00:16:48.430 --> 00:16:49.709 actually undergo a high amount

NOTE Confidence: 0.97540754

00:16:49.709 --> 00:16:51.595 of oxidative stress. So the

NOTE Confidence: 0.97540754

00:16:51.595 --> 00:16:53.035 cells ramp up their production

NOTE Confidence: 0.97540754

00:16:53.035 --> 00:16:54.815 of glutathione and NADPH

NOTE Confidence: 0.9992192

00:16:55.195 --> 00:16:55.855 to survive.

NOTE Confidence: 0.9645828

00:16:56.475 --> 00:16:57.995 Once they reach their new

NOTE Confidence: 0.9645828

00:16:57.995 --> 00:16:59.355 seeded sites, such as the

NOTE Confidence: 0.9645828

00:16:59.355 --> 00:17:00.715 liver or the lung, the

NOTE Confidence: 0.9645828

00:17:00.715 --> 00:17:01.595 cells are actually in a

NOTE Confidence: 0.9645828

00:17:01.595 --> 00:17:02.415 state of dormancy

NOTE Confidence: 0.9177392

00:17:02.795 --> 00:17:03.995 because this is a completely

NOTE Confidence: 0.9177392

00:17:03.995 --> 00:17:04.494 new,

NOTE Confidence: 0.89717513

00:17:04.795 --> 00:17:05.295 microenvironment,

NOTE Confidence: 0.9981964

00:17:05.675 --> 00:17:07.170 different nutrients present there.

NOTE Confidence: 0.9771444

00:17:07.730 --> 00:17:08.770 Then they start to ramp

NOTE Confidence: 0.9771444

00:17:08.770 --> 00:17:11.010 up their anabolic metabolism, producing

NOTE Confidence: 0.9771444

00:17:11.010 --> 00:17:12.930 more metabolites and also nucleic

NOTE Confidence: 0.9771444

00:17:12.930 --> 00:17:14.369 acids and proteins and lipids

NOTE Confidence: 0.9771444

00:17:14.369 --> 00:17:15.730 to grow in the new

NOTE Confidence: 0.9771444

00:17:15.730 --> 00:17:17.090 organ. So you can see

NOTE Confidence: 0.9771444

00:17:17.090 --> 00:17:18.850 there are many bottlenecks along

NOTE Confidence: 0.9771444

00:17:18.850 --> 00:17:20.369 this cascade that can actually

NOTE Confidence: 0.9771444

00:17:20.369 --> 00:17:21.109 be targeted,

NOTE Confidence: 0.99651814

00:17:21.805 --> 00:17:23.085 by using by looking at

NOTE Confidence: 0.99651814

00:17:23.085 --> 00:17:25.505 metabolites and targeting metabolites to

NOTE Confidence: 0.99651814

00:17:25.645 --> 00:17:26.625 improve prognosis.

NOTE Confidence: 0.98749435

00:17:29.325 --> 00:17:30.285 But, you know, we came

NOTE Confidence: 0.98749435

00:17:30.285 --> 00:17:31.905 to think about sex differences

NOTE Confidence: 0.98749435

00:17:31.965 --> 00:17:33.484 in metabolism because there is

NOTE Confidence: 0.98749435

00:17:33.484 --> 00:17:35.325 this fundamental fact that nearly

NOTE Confidence: 0.98749435

00:17:35.325 --> 00:17:36.950 all aspects of metabolism do

NOTE Confidence: 0.98749435

00:17:36.950 --> 00:17:38.330 show this sexual dimorphism.

NOTE Confidence: 0.9897038

00:17:39.190 --> 00:17:40.869 So even eighty years ago,

NOTE Confidence: 0.9897038

00:17:40.869 --> 00:17:42.230 the first paper that really

NOTE Confidence: 0.9897038

00:17:42.230 --> 00:17:43.910 showed this was, come from

NOTE Confidence: 0.9897038

00:17:43.910 --> 00:17:45.850 Marseille, and this professor noted

NOTE Confidence: 0.85691774

00:17:46.150 --> 00:17:47.609 differences in fact deposition.

NOTE Confidence: 0.99915123

00:17:47.990 --> 00:17:48.869 So this is a quote

NOTE Confidence: 0.99915123

00:17:48.869 --> 00:17:49.770 from his paper

NOTE Confidence: 0.93731886

00:17:53.005 --> 00:17:54.684 man's fat mass, though she

NOTE Confidence: 0.93731886

00:17:54.684 --> 00:17:56.044 is as often obese as

NOTE Confidence: 0.93731886

00:17:56.044 --> 00:17:57.484 a man or fatter, she's

NOTE Confidence: 0.93731886

00:17:57.484 --> 00:17:58.225 very nice,

NOTE Confidence: 0.95221937

00:17:58.765 --> 00:18:00.205 she dies less often from

NOTE Confidence: 0.95221937

00:18:00.205 --> 00:18:02.385 the metabolic complications of obesity.

NOTE Confidence: 0.9459202

00:18:02.970 --> 00:18:04.490 So women resist the loss

NOTE Confidence: 0.9459202

00:18:04.490 --> 00:18:06.169 of body energy stores while

NOTE Confidence: 0.9459202

00:18:06.169 --> 00:18:08.350 men mobilize energy stores promptly.

NOTE Confidence: 0.995121

00:18:08.970 --> 00:18:09.770 And you can see this

NOTE Confidence: 0.995121

00:18:09.770 --> 00:18:10.890 quite clearly if you look

NOTE Confidence: 0.995121

00:18:10.890 --> 00:18:12.830 at carbohydrate and lipid metabolism

NOTE Confidence: 0.95915717

00:18:13.130 --> 00:18:14.570 at rest and exercise and

NOTE Confidence: 0.95915717

00:18:14.570 --> 00:18:16.090 the differences between men and

NOTE Confidence: 0.95915717

00:18:16.090 --> 00:18:18.785 women. So during rest, females

NOTE Confidence: 0.95915717

00:18:18.785 --> 00:18:20.225 tend to incorporate free fatty

NOTE Confidence: 0.95915717

00:18:20.225 --> 00:18:21.285 acids into triglycerides

NOTE Confidence: 0.9446044

00:18:21.665 --> 00:18:23.185 to store fat. And then

NOTE Confidence: 0.9446044

00:18:23.185 --> 00:18:25.185 in exercise, they preferentially use

NOTE Confidence: 0.9446044

00:18:25.185 --> 00:18:26.945 these, lipids as a fuse

NOTE Confidence: 0.9446044

00:18:27.025 --> 00:18:27.765 fuel source.

NOTE Confidence: 0.9580432

00:18:28.145 --> 00:18:29.425 Whereas for males, at rest,

NOTE Confidence: 0.9580432

00:18:29.425 --> 00:18:30.785 they tend to oxidize these

NOTE Confidence: 0.9580432

00:18:30.785 --> 00:18:32.725 free fatty acids. And during

NOTE Confidence: 0.9580432

00:18:32.840 --> 00:18:34.780 exercise, they preferentially use carbohydrates

NOTE Confidence: 0.9580432

00:18:35.080 --> 00:18:36.040 of a as a fuel

NOTE Confidence: 0.9580432

00:18:36.040 --> 00:18:37.720 fuel source. So this is

NOTE Confidence: 0.9580432

00:18:37.720 --> 00:18:39.240 just one example of how

NOTE Confidence: 0.9580432

00:18:39.240 --> 00:18:40.520 there are sex differences in

NOTE Confidence: 0.9580432

00:18:40.520 --> 00:18:42.119 metabolism, but it obviously goes

NOTE Confidence: 0.9580432

00:18:42.119 --> 00:18:43.900 much more broader than this.

NOTE Confidence: 0.96592784

00:18:45.705 --> 00:18:46.984 And, there was a review

NOTE Confidence: 0.96592784

00:18:46.984 --> 00:18:48.184 paper out about five years

NOTE Confidence: 0.96592784

00:18:48.184 --> 00:18:49.625 ago, which collated a lot

NOTE Confidence: 0.96592784

00:18:49.625 --> 00:18:51.304 of, studies that has seen

NOTE Confidence: 0.96592784

00:18:51.304 --> 00:18:52.984 the same effect in cancer

NOTE Confidence: 0.96592784

00:18:52.984 --> 00:18:55.065 cells between differences between males

NOTE Confidence: 0.96592784

00:18:55.065 --> 00:18:55.804 and females.

NOTE Confidence: 0.97747797

00:18:56.345 --> 00:18:57.625 So highlighted here in the

NOTE Confidence: 0.97747797

00:18:57.625 --> 00:18:59.225 green are is a metabolic

NOTE Confidence: 0.97747797

00:18:59.225 --> 00:19:01.130 pathway that's preferentially used

NOTE Confidence: 0.9847622

00:19:01.670 --> 00:19:03.050 by cancer cells in males,

NOTE Confidence: 0.9847622

00:19:03.190 --> 00:19:05.030 and in purple is a

NOTE Confidence: 0.9847622

00:19:05.030 --> 00:19:06.790 pathway that's used preferentially by

NOTE Confidence: 0.9847622

00:19:06.790 --> 00:19:08.010 cancer cells in females.

NOTE Confidence: 0.9814649

00:19:08.390 --> 00:19:09.510 So you can see glucose

NOTE Confidence: 0.9814649

00:19:09.510 --> 00:19:11.590 is converted into pyruvate and

NOTE Confidence: 0.9814649

00:19:11.590 --> 00:19:13.130 lactate in males preferentially.

NOTE Confidence: 0.9932653

00:19:13.765 --> 00:19:15.465 But for females, the intermediates

NOTE Confidence: 0.9932653

00:19:15.525 --> 00:19:16.184 in glycolysis

NOTE Confidence: 0.98882294

00:19:16.484 --> 00:19:17.845 actually get shunted through to

NOTE Confidence: 0.98882294

00:19:17.845 --> 00:19:19.465 the pentose phosphate pathway

NOTE Confidence: 0.86815804

00:19:19.924 --> 00:19:21.145 and to generate NADPH,

NOTE Confidence: 0.92628855

00:19:21.924 --> 00:19:23.304 and are used as metabolic

NOTE Confidence: 0.92628855

00:19:23.445 --> 00:19:24.645 building blocks as well in

NOTE Confidence: 0.92628855

00:19:24.645 --> 00:19:25.145 metabolites.

NOTE Confidence: 0.97914433

00:19:25.619 --> 00:19:26.580 So you can see even

NOTE Confidence: 0.97914433

00:19:26.580 --> 00:19:28.359 in these core metabolic pathways,

NOTE Confidence: 0.97914433

00:19:28.420 --> 00:19:29.940 there really are profound sex

NOTE Confidence: 0.97914433

00:19:29.940 --> 00:19:30.440 differences.

NOTE Confidence: 0.9525142

00:19:32.820 --> 00:19:33.619 And then if we look

NOTE Confidence: 0.9525142

00:19:33.619 --> 00:19:35.540 at colorectal cancer, as doctor

NOTE Confidence: 0.9525142

00:19:35.540 --> 00:19:36.900 Khan mentioned, there are sex

NOTE Confidence: 0.9525142

00:19:36.900 --> 00:19:38.680 differences in incidence of mortality,

NOTE Confidence: 0.9584182

00:19:39.234 --> 00:19:40.195 where males tend to have

NOTE Confidence: 0.9584182

00:19:40.195 --> 00:19:41.654 a higher incidence of mortality

NOTE Confidence: 0.9584182

00:19:41.715 --> 00:19:42.695 of this disease.

NOTE Confidence: 0.9501306

00:19:43.075 --> 00:19:44.434 But actually, new studies coming

NOTE Confidence: 0.9501306

00:19:44.434 --> 00:19:45.794 out from IARC just in

NOTE Confidence: 0.9501306

00:19:45.794 --> 00:19:46.835 the past year have seen

NOTE Confidence: 0.9501306

00:19:46.835 --> 00:19:48.294 that for early onset colorectal

NOTE Confidence: 0.9501306

00:19:48.355 --> 00:19:48.855 cancer

NOTE Confidence: 0.96425784

00:19:49.234 --> 00:19:50.534 in the UK and Australia,

NOTE Confidence: 0.96425784

00:19:50.595 --> 00:19:51.955 it's almost at parity now

NOTE Confidence: 0.96425784

00:19:51.955 --> 00:19:53.315 for men and women, which

NOTE Confidence: 0.96425784

00:19:53.315 --> 00:19:54.970 is very interesting as this

NOTE Confidence: 0.96425784

00:19:54.970 --> 00:19:56.009 may this must be some

NOTE Confidence: 0.96425784

00:19:56.009 --> 00:19:57.769 sort of environmental factor that's

NOTE Confidence: 0.96425784

00:19:57.769 --> 00:19:58.669 driving this.

NOTE Confidence: 0.9858746

00:19:59.049 --> 00:19:59.769 But if we look at

NOTE Confidence: 0.9858746

00:19:59.769 --> 00:20:01.049 the colorectal, we can see

NOTE Confidence: 0.9858746

00:20:01.049 --> 00:20:02.649 here that it's typically divided

NOTE Confidence: 0.9858746

00:20:02.649 --> 00:20:03.850 into these two parts, the

NOTE Confidence: 0.9858746

00:20:03.850 --> 00:20:04.809 right side and the left

NOTE Confidence: 0.9858746

00:20:04.809 --> 00:20:06.090 side. And you can see

NOTE Confidence: 0.9858746

00:20:06.090 --> 00:20:07.289 just how different they are

NOTE Confidence: 0.9858746

00:20:07.289 --> 00:20:08.509 in terms of the frequency

NOTE Confidence: 0.9858746

00:20:08.649 --> 00:20:09.950 of molecular features.

NOTE Confidence: 0.9868655

00:20:10.375 --> 00:20:11.494 So on the right side,

NOTE Confidence: 0.9868655

00:20:11.494 --> 00:20:13.095 highlighted here in green, you

NOTE Confidence: 0.9868655

00:20:13.095 --> 00:20:14.215 tend to have more,

NOTE Confidence: 0.7294563

00:20:14.695 --> 00:20:15.674 CpG islemethylated

NOTE Confidence: 0.9661398

00:20:15.975 --> 00:20:16.475 phenotype,

NOTE Confidence: 0.9503382

00:20:17.815 --> 00:20:19.575 more BRAF mutations, and more

NOTE Confidence: 0.9503382

00:20:19.575 --> 00:20:21.515 KRAS mutations in these tumors.

NOTE Confidence: 0.985066

00:20:21.895 --> 00:20:23.015 Whereas those tumors on the

NOTE Confidence: 0.985066

00:20:23.015 --> 00:20:24.135 left side tend to have

NOTE Confidence: 0.985066

00:20:24.135 --> 00:20:25.350 more p fifty three and

NOTE Confidence: 0.985066

00:20:25.350 --> 00:20:26.330 APC mutations.

NOTE Confidence: 0.9994728

00:20:27.430 --> 00:20:27.930 Importantly,

NOTE Confidence: 0.9848919

00:20:28.390 --> 00:20:29.670 women tend to develop more

NOTE Confidence: 0.9848919

00:20:29.670 --> 00:20:30.950 right sided cancers than left

NOTE Confidence: 0.9848919

00:20:30.950 --> 00:20:32.790 sided cancers, whereas it's the

NOTE Confidence: 0.9848919

00:20:32.790 --> 00:20:33.930 opposite for males.

NOTE Confidence: 0.9707147

00:20:34.550 --> 00:20:36.310 Another important fact is that

NOTE Confidence: 0.9707147

00:20:36.310 --> 00:20:37.750 a right sided patient tends

NOTE Confidence: 0.9707147

00:20:37.750 --> 00:20:39.369 to have overall worse prognosis

NOTE Confidence: 0.9707147

00:20:39.645 --> 00:20:41.425 than a left sided colorectal

NOTE Confidence: 0.9707147

00:20:41.565 --> 00:20:43.085 cancer patient. And this is

NOTE Confidence: 0.9707147

00:20:43.085 --> 00:20:44.605 even after studies have adjusted

NOTE Confidence: 0.9707147

00:20:44.605 --> 00:20:45.565 for things such as,

NOTE Confidence: 0.9244139

00:20:46.205 --> 00:20:48.205 therapy use when the stage

NOTE Confidence: 0.9244139

00:20:48.205 --> 00:20:49.345 of the cancer diagnosis

NOTE Confidence: 0.9313843

00:20:49.965 --> 00:20:51.005 and also the type of

NOTE Confidence: 0.9313843

00:20:51.005 --> 00:20:51.505 screening.

NOTE Confidence: 0.9922702

00:20:52.200 --> 00:20:53.240 So you can see just,

NOTE Confidence: 0.9922702

00:20:53.480 --> 00:20:54.859 the differences along

NOTE Confidence: 0.99501336

00:20:55.240 --> 00:20:55.899 the colorectum,

NOTE Confidence: 0.999794

00:20:56.440 --> 00:20:57.659 for males and females.

NOTE Confidence: 0.9646926

00:20:58.119 --> 00:20:59.480 So then we had, the

NOTE Confidence: 0.9646926

00:20:59.480 --> 00:21:01.899 question if sex differences exist

NOTE Confidence: 0.9646926

00:21:02.039 --> 00:21:03.639 in where tumors occur within

NOTE Confidence: 0.9646926

00:21:03.639 --> 00:21:05.179 the colorectum, could metabolism

NOTE Confidence: 0.99641246

00:21:05.480 --> 00:21:07.179 also differ in these tumors?

NOTE Confidence: 0.9077598

00:21:08.804 --> 00:21:10.404 So the first collaborative study

NOTE Confidence: 0.9077598

00:21:10.404 --> 00:21:11.605 that we did, was with

NOTE Confidence: 0.9077598

00:21:11.605 --> 00:21:12.885 Yatzi San, who was a

NOTE Confidence: 0.9077598

00:21:12.885 --> 00:21:14.404 Miles per hour student and

NOTE Confidence: 0.9077598

00:21:14.404 --> 00:21:15.845 Doctor. Mironova, who was a

NOTE Confidence: 0.9077598

00:21:15.845 --> 00:21:16.345 resident,

NOTE Confidence: 0.9731454

00:21:16.725 --> 00:21:17.924 and they looked at publicly

NOTE Confidence: 0.9731454

00:21:17.924 --> 00:21:19.445 available data. So we went

NOTE Confidence: 0.9731454

00:21:19.445 --> 00:21:20.265 to NCBI's

NOTE Confidence: 0.69603634

00:21:21.044 --> 00:21:21.544 GEO

NOTE Confidence: 0.9718379

00:21:21.890 --> 00:21:23.090 and we found five gene

NOTE Confidence: 0.9718379

00:21:23.090 --> 00:21:25.410 expression datasets, which had information

NOTE Confidence: 0.9718379

00:21:25.410 --> 00:21:27.250 for colorectal cancer patients and

NOTE Confidence: 0.9718379

00:21:27.250 --> 00:21:28.210 also the sex of the

NOTE Confidence: 0.9718379

00:21:28.210 --> 00:21:28.710 patient

NOTE Confidence: 0.9804948

00:21:29.170 --> 00:21:30.610 and where the tumor occurred

NOTE Confidence: 0.9804948

00:21:30.610 --> 00:21:31.590 within the colorectum.

NOTE Confidence: 0.9982921

00:21:32.130 --> 00:21:32.930 And what you can see

NOTE Confidence: 0.9982921

00:21:32.930 --> 00:21:34.130 here is just a,

NOTE Confidence: 0.90869015

00:21:34.610 --> 00:21:37.030 diagram of principal components analyses.

NOTE Confidence: 0.959487

00:21:37.684 --> 00:21:38.804 So basically each one of

NOTE Confidence: 0.959487

00:21:38.804 --> 00:21:40.484 these dots represents a gene

NOTE Confidence: 0.959487

00:21:40.484 --> 00:21:40.984 expression

NOTE Confidence: 0.9828436

00:21:41.525 --> 00:21:42.565 profile for one of these

NOTE Confidence: 0.9828436

00:21:42.565 --> 00:21:43.065 tumors.

NOTE Confidence: 0.9867939

00:21:43.684 --> 00:21:45.044 And when the dots are

NOTE Confidence: 0.9867939

00:21:45.044 --> 00:21:46.244 sort of more closely clustered

NOTE Confidence: 0.9867939

00:21:46.244 --> 00:21:47.445 together, it means they're more

NOTE Confidence: 0.9867939

00:21:47.445 --> 00:21:48.885 similar in their gene expression

NOTE Confidence: 0.9867939

00:21:48.885 --> 00:21:49.385 profile.

NOTE Confidence: 0.98962784

00:21:50.165 --> 00:21:51.365 So the figure on the

NOTE Confidence: 0.98962784

00:21:51.365 --> 00:21:51.845 left,

NOTE Confidence: 0.9996532

00:21:52.244 --> 00:21:52.744 shows

NOTE Confidence: 0.9765403

00:21:53.050 --> 00:21:54.810 differences in gene expression between

NOTE Confidence: 0.9765403

00:21:54.810 --> 00:21:55.690 the right side and the

NOTE Confidence: 0.9765403

00:21:55.690 --> 00:21:57.630 left sided tumors for women,

NOTE Confidence: 0.9952082

00:21:58.010 --> 00:21:59.210 and the figure in b

NOTE Confidence: 0.9952082

00:21:59.210 --> 00:22:00.890 shows the differences between men

NOTE Confidence: 0.9952082

00:22:00.890 --> 00:22:02.410 and women for right sided

NOTE Confidence: 0.9952082

00:22:02.410 --> 00:22:02.910 cancers.

NOTE Confidence: 0.97744423

00:22:03.290 --> 00:22:04.170 So you can see just

NOTE Confidence: 0.97744423

00:22:04.170 --> 00:22:05.530 how different even the gene

NOTE Confidence: 0.97744423

00:22:05.530 --> 00:22:07.050 expression at the gene expression

NOTE Confidence: 0.97744423

00:22:07.050 --> 00:22:07.930 level these,

NOTE Confidence: 0.9994759

00:22:08.925 --> 00:22:09.425 these

NOTE Confidence: 0.9861239

00:22:09.885 --> 00:22:10.385 are.

NOTE Confidence: 0.9230734

00:22:10.765 --> 00:22:12.045 We then model this gene

NOTE Confidence: 0.9230734

00:22:12.045 --> 00:22:13.185 expression data,

NOTE Confidence: 0.91270894

00:22:13.565 --> 00:22:15.345 using a tool called MetaCore

NOTE Confidence: 0.89683294

00:22:15.805 --> 00:22:17.505 and with help from Rolando,

NOTE Confidence: 0.54822224

00:22:18.205 --> 00:22:18.705 Garciemilian

NOTE Confidence: 0.92619556

00:22:19.085 --> 00:22:20.605 at the the Yale Medical

NOTE Confidence: 0.92619556

00:22:20.605 --> 00:22:21.105 Library.

NOTE Confidence: 0.9622911

00:22:21.980 --> 00:22:23.020 And what we found was

NOTE Confidence: 0.9622911

00:22:23.020 --> 00:22:24.300 five pathways that seem to

NOTE Confidence: 0.9622911

00:22:24.300 --> 00:22:25.740 be enriched in women that

NOTE Confidence: 0.9622911

00:22:25.740 --> 00:22:27.520 had right sided colorectal cancer.

NOTE Confidence: 0.9906784

00:22:27.820 --> 00:22:28.780 So this is just one

NOTE Confidence: 0.9906784

00:22:28.780 --> 00:22:29.900 of them here, and it's

NOTE Confidence: 0.9906784

00:22:29.900 --> 00:22:32.460 the carbohydrate responsive element binding

NOTE Confidence: 0.9906784

00:22:32.460 --> 00:22:33.359 protein pathway.

NOTE Confidence: 0.99688834

00:22:34.484 --> 00:22:34.885 And it basically shows that

NOTE Confidence: 0.99688834

00:22:34.885 --> 00:22:36.484 these genes work together to

NOTE Confidence: 0.99688834

00:22:36.484 --> 00:22:36.984 regulate

NOTE Confidence: 0.83826256

00:22:37.285 --> 00:22:38.905 protein kinase a signaling,

NOTE Confidence: 0.9342838

00:22:39.285 --> 00:22:41.145 also AMPK and GPCRs.

NOTE Confidence: 0.91084135

00:22:41.525 --> 00:22:42.725 And we've seen the same

NOTE Confidence: 0.91084135

00:22:42.725 --> 00:22:43.845 effect actually in more of

NOTE Confidence: 0.91084135

00:22:43.845 --> 00:22:45.945 our studies now, doing metabolomics.

NOTE Confidence: 0.9986843

00:22:46.325 --> 00:22:48.025 So we have replicated this.

NOTE Confidence: 0.95746017

00:22:50.760 --> 00:22:51.720 So now I'd like to

NOTE Confidence: 0.95746017

00:22:51.720 --> 00:22:53.240 move on to, our sort

NOTE Confidence: 0.95746017

00:22:53.240 --> 00:22:54.700 of metabolomics analysis.

NOTE Confidence: 0.98691773

00:22:55.080 --> 00:22:56.440 So we decided to,

NOTE Confidence: 0.96895635

00:22:57.000 --> 00:22:58.519 design this study to investigate

NOTE Confidence: 0.96895635

00:22:58.519 --> 00:23:00.279 sex differences in metabolism in

NOTE Confidence: 0.96895635

00:23:00.279 --> 00:23:01.905 tissues from the colorectal cancer

NOTE Confidence: 0.96895635

00:23:01.905 --> 00:23:02.405 patients.

NOTE Confidence: 0.9177009

00:23:02.705 --> 00:23:03.905 And doctor Khan and I

NOTE Confidence: 0.9177009

00:23:03.905 --> 00:23:06.145 collaborated with doctor Patty Patey,

NOTE Confidence: 0.9177009

00:23:06.145 --> 00:23:08.005 rather, at Memorial Sloan Kettering

NOTE Confidence: 0.9177009

00:23:08.065 --> 00:23:08.965 Cancer Center.

NOTE Confidence: 0.9659454

00:23:09.505 --> 00:23:10.805 But in the nineteen nineties,

NOTE Confidence: 0.9659454

00:23:10.945 --> 00:23:12.785 he collected tumor tissues and

NOTE Confidence: 0.9659454

00:23:12.785 --> 00:23:13.525 normal tissues

NOTE Confidence: 0.95491236

00:23:13.930 --> 00:23:15.770 and also liver metastases and

NOTE Confidence: 0.95491236

00:23:15.770 --> 00:23:17.609 normal liver from over seven

NOTE Confidence: 0.95491236

00:23:17.609 --> 00:23:19.150 hundred and sixty two cases.

NOTE Confidence: 0.95755166

00:23:20.570 --> 00:23:22.010 The tumors are actually taken

NOTE Confidence: 0.95755166

00:23:22.010 --> 00:23:23.210 in the OR and then

NOTE Confidence: 0.95755166

00:23:23.210 --> 00:23:24.570 snap frozen and put in

NOTE Confidence: 0.95755166

00:23:24.570 --> 00:23:25.869 the minus eighty freezer.

NOTE Confidence: 0.99553794

00:23:26.170 --> 00:23:27.369 So they're really perfect for

NOTE Confidence: 0.99553794

00:23:27.369 --> 00:23:28.109 mass spectrometry

NOTE Confidence: 0.76868707

00:23:28.410 --> 00:23:28.910 analysis.

NOTE Confidence: 0.9725074

00:23:30.465 --> 00:23:31.825 In twenty eighteen, we were

NOTE Confidence: 0.9725074

00:23:31.825 --> 00:23:33.025 lucky to receive a r

NOTE Confidence: 0.9725074

00:23:33.025 --> 00:23:34.865 twenty one grant, which enabled

NOTE Confidence: 0.9725074

00:23:34.865 --> 00:23:36.385 us to hire somebody to

NOTE Confidence: 0.9725074

00:23:36.385 --> 00:23:37.765 go to the medical vault

NOTE Confidence: 0.9725074

00:23:38.065 --> 00:23:40.005 at Sloan Kettering and transpose

NOTE Confidence: 0.9725074

00:23:40.065 --> 00:23:41.345 all of the medical records

NOTE Confidence: 0.9725074

00:23:41.345 --> 00:23:42.705 for the seven hundred and

NOTE Confidence: 0.9725074

00:23:42.705 --> 00:23:44.290 sixty two patients. So we

NOTE Confidence: 0.9725074

00:23:44.290 --> 00:23:45.190 then had information

NOTE Confidence: 0.99923146

00:23:45.570 --> 00:23:47.270 more information about these patients,

NOTE Confidence: 0.90687346

00:23:47.890 --> 00:23:49.810 including their out outcomes. So

NOTE Confidence: 0.90687346

00:23:49.810 --> 00:23:51.510 it's very valuable resource.

NOTE Confidence: 0.98958796

00:23:52.609 --> 00:23:53.810 So for our first study,

NOTE Confidence: 0.98958796

00:23:53.810 --> 00:23:54.770 we wanted to keep it

NOTE Confidence: 0.98958796

00:23:54.770 --> 00:23:56.130 very clean. So we just

NOTE Confidence: 0.98958796

00:23:56.130 --> 00:23:57.410 looked at stage one to

NOTE Confidence: 0.98958796

00:23:57.410 --> 00:23:57.810 three,

NOTE Confidence: 0.9985148

00:23:58.290 --> 00:23:58.790 cases.

NOTE Confidence: 0.9676467

00:23:59.355 --> 00:24:00.315 At the time, we didn't

NOTE Confidence: 0.9676467

00:24:00.315 --> 00:24:01.434 know if the stage four

NOTE Confidence: 0.9676467

00:24:01.434 --> 00:24:02.955 cases had been treated with

NOTE Confidence: 0.9676467

00:24:02.955 --> 00:24:03.455 chemotherapy

NOTE Confidence: 0.9807767

00:24:03.755 --> 00:24:05.195 beforehand, which could change the

NOTE Confidence: 0.9807767

00:24:05.195 --> 00:24:05.695 metabolism.

NOTE Confidence: 0.99531823

00:24:06.475 --> 00:24:07.275 And we just looked at

NOTE Confidence: 0.99531823

00:24:07.275 --> 00:24:08.315 the left and the right

NOTE Confidence: 0.99531823

00:24:08.315 --> 00:24:09.535 sided cases.

NOTE Confidence: 0.9764442

00:24:09.994 --> 00:24:10.955 So we had a hundred

NOTE Confidence: 0.9764442

00:24:10.955 --> 00:24:13.195 and two, tissues from males

NOTE Confidence: 0.9764442

00:24:13.195 --> 00:24:14.734 and ninety five from females,

NOTE Confidence: 0.9854757

00:24:15.035 --> 00:24:16.049 and then we also had

NOTE Confidence: 0.9854757

00:24:16.049 --> 00:24:17.990 about thirty nine normal mucosa.

NOTE Confidence: 0.95373756

00:24:21.010 --> 00:24:22.869 So doctors Kai and Retre,

NOTE Confidence: 0.95373756

00:24:23.090 --> 00:24:24.770 back in twenty eighteen, performed

NOTE Confidence: 0.95373756

00:24:24.770 --> 00:24:26.869 the untargeted metabolomic analysis.

NOTE Confidence: 0.91394573

00:24:27.424 --> 00:24:28.544 And basically what we did

NOTE Confidence: 0.91394573

00:24:28.544 --> 00:24:30.865 was extracted the tissues for

NOTE Confidence: 0.91394573

00:24:30.865 --> 00:24:31.365 metabolites,

NOTE Confidence: 0.9070395

00:24:31.905 --> 00:24:32.865 and then we ran them

NOTE Confidence: 0.9070395

00:24:32.865 --> 00:24:34.784 through our LC QTof,

NOTE Confidence: 0.969404

00:24:35.105 --> 00:24:35.845 mass spectrometry

NOTE Confidence: 0.99037147

00:24:36.225 --> 00:24:36.725 system.

NOTE Confidence: 0.95340186

00:24:37.025 --> 00:24:38.465 And this system allows us

NOTE Confidence: 0.95340186

00:24:38.465 --> 00:24:39.765 to look in an unbiased

NOTE Confidence: 0.95340186

00:24:39.984 --> 00:24:42.010 manner at everything that's present

NOTE Confidence: 0.95340186

00:24:42.010 --> 00:24:43.530 within these tumor tissues that

NOTE Confidence: 0.95340186

00:24:43.530 --> 00:24:45.369 is below basically twelve hundred

NOTE Confidence: 0.95340186

00:24:45.369 --> 00:24:47.230 daltons, all these low molecular

NOTE Confidence: 0.95340186

00:24:47.290 --> 00:24:48.590 weight, metabolites.

NOTE Confidence: 0.9902397

00:24:49.369 --> 00:24:50.570 So in our analysis, we

NOTE Confidence: 0.9902397

00:24:50.570 --> 00:24:51.690 can look at about forty

NOTE Confidence: 0.9902397

00:24:51.690 --> 00:24:53.150 thousand different features.

NOTE Confidence: 0.96696365

00:24:54.145 --> 00:24:55.605 In our lab, we have

NOTE Confidence: 0.96696365

00:24:55.665 --> 00:24:57.905 a database now that's comprised

NOTE Confidence: 0.96696365

00:24:57.905 --> 00:24:59.345 of one thousand standards, so

NOTE Confidence: 0.96696365

00:24:59.345 --> 00:25:01.025 we're able to directly match

NOTE Confidence: 0.96696365

00:25:01.025 --> 00:25:02.725 these features to the standards.

NOTE Confidence: 0.98770636

00:25:03.265 --> 00:25:04.545 And then we performed a

NOTE Confidence: 0.98770636

00:25:04.545 --> 00:25:06.145 statistical analysis, and then we

NOTE Confidence: 0.98770636

00:25:06.145 --> 00:25:06.865 looked to see if any

NOTE Confidence: 0.98770636

00:25:06.865 --> 00:25:08.645 of these metabolites were prognostic

NOTE Confidence: 0.98770636

00:25:08.865 --> 00:25:09.605 by sex.

NOTE Confidence: 0.95632696

00:25:10.679 --> 00:25:12.539 So, actually, our initial analysis

NOTE Confidence: 0.95632696

00:25:12.679 --> 00:25:13.320 showed us,

NOTE Confidence: 0.9647386

00:25:14.119 --> 00:25:15.320 similar findings to what I

NOTE Confidence: 0.9647386

00:25:15.320 --> 00:25:16.280 showed you in that figure

NOTE Confidence: 0.9647386

00:25:16.280 --> 00:25:17.480 before where we saw that

NOTE Confidence: 0.9647386

00:25:17.480 --> 00:25:19.240 male tumors for males tended

NOTE Confidence: 0.9647386

00:25:19.240 --> 00:25:19.880 to have sort of a

NOTE Confidence: 0.9647386

00:25:19.880 --> 00:25:21.100 high production of lactate,

NOTE Confidence: 0.9584524

00:25:21.400 --> 00:25:22.760 whereas for females, it seemed

NOTE Confidence: 0.9584524

00:25:22.760 --> 00:25:24.255 that, glucose was shunted into

NOTE Confidence: 0.9584524

00:25:24.255 --> 00:25:25.795 the pentose phosphate pathway,

NOTE Confidence: 0.8807886

00:25:26.734 --> 00:25:27.875 and produce NADPH.

NOTE Confidence: 0.97745514

00:25:28.895 --> 00:25:30.195 But there was one pathway

NOTE Confidence: 0.97745514

00:25:30.255 --> 00:25:31.455 that really stood out to

NOTE Confidence: 0.97745514

00:25:31.455 --> 00:25:32.575 us, and that was the,

NOTE Confidence: 0.97745514

00:25:32.895 --> 00:25:34.595 asparagine metabolic pathway,

NOTE Confidence: 0.9734541

00:25:35.295 --> 00:25:36.755 where in female patients,

NOTE Confidence: 0.98801297

00:25:37.170 --> 00:25:38.390 we could see that asparagine

NOTE Confidence: 0.98801297

00:25:38.450 --> 00:25:39.570 was produced at a high

NOTE Confidence: 0.98801297

00:25:39.570 --> 00:25:41.090 amount in stage one, two,

NOTE Confidence: 0.98801297

00:25:41.090 --> 00:25:41.990 and three tissues.

NOTE Confidence: 0.9816385

00:25:42.530 --> 00:25:43.490 So this is just a

NOTE Confidence: 0.9816385

00:25:43.490 --> 00:25:44.930 diagram here of the abundance

NOTE Confidence: 0.9816385

00:25:44.930 --> 00:25:46.450 of asparagine in the normal

NOTE Confidence: 0.9816385

00:25:46.450 --> 00:25:47.730 tissues and then the stage

NOTE Confidence: 0.9816385

00:25:47.730 --> 00:25:48.710 one, two, and three

NOTE Confidence: 0.966618

00:25:49.054 --> 00:25:50.655 for males and females. So

NOTE Confidence: 0.966618

00:25:50.655 --> 00:25:51.535 you can see for male

NOTE Confidence: 0.966618

00:25:51.535 --> 00:25:52.815 tissues that it was only

NOTE Confidence: 0.966618

00:25:52.815 --> 00:25:54.275 at stage three that asparagine

NOTE Confidence: 0.966618

00:25:54.494 --> 00:25:55.875 was significantly increased.

NOTE Confidence: 0.9488118

00:25:57.375 --> 00:25:58.895 Around the same time, we

NOTE Confidence: 0.9488118

00:25:58.895 --> 00:26:00.914 saw this paper from UCLA,

NOTE Confidence: 0.9900505

00:26:01.470 --> 00:26:02.850 and they noted that asparagine

NOTE Confidence: 0.9900505

00:26:02.909 --> 00:26:04.350 could actually be used when

NOTE Confidence: 0.9900505

00:26:04.350 --> 00:26:06.210 the tumor tissues are nutrient

NOTE Confidence: 0.9900505

00:26:06.270 --> 00:26:07.470 deplete and need to keep

NOTE Confidence: 0.9900505

00:26:07.470 --> 00:26:09.090 growing. And what asparagine

NOTE Confidence: 0.85892826

00:26:09.390 --> 00:26:10.850 does, it helps increase,

NOTE Confidence: 0.9679637

00:26:11.309 --> 00:26:13.409 mTOR and also protein synthesis

NOTE Confidence: 0.9679637

00:26:13.630 --> 00:26:14.770 and nucleotide synthesis.

NOTE Confidence: 0.98374635

00:26:15.265 --> 00:26:16.304 And it can actually,

NOTE Confidence: 0.9983165

00:26:16.785 --> 00:26:18.544 also increase the uptake of

NOTE Confidence: 0.9983165

00:26:18.544 --> 00:26:19.984 serine and threonine to help

NOTE Confidence: 0.9983165

00:26:19.984 --> 00:26:20.804 tumor growth.

NOTE Confidence: 0.95058537

00:26:21.105 --> 00:26:22.645 So we measured these metabolites,

NOTE Confidence: 0.95051193

00:26:23.265 --> 00:26:24.544 and again, we saw that

NOTE Confidence: 0.95051193

00:26:24.544 --> 00:26:25.445 they were increased,

NOTE Confidence: 0.97145236

00:26:25.744 --> 00:26:27.105 only really in the female

NOTE Confidence: 0.97145236

00:26:27.105 --> 00:26:28.544 tumors at stage one to

NOTE Confidence: 0.97145236

00:26:28.544 --> 00:26:30.059 three. So this sort of

NOTE Confidence: 0.97145236

00:26:30.059 --> 00:26:31.760 helped us develop our hypothesis

NOTE Confidence: 0.97145236

00:26:31.820 --> 00:26:33.260 that, you know, asparagine could

NOTE Confidence: 0.97145236

00:26:33.260 --> 00:26:34.780 be very important. And here

NOTE Confidence: 0.97145236

00:26:34.780 --> 00:26:35.900 you can see here that

NOTE Confidence: 0.97145236

00:26:35.900 --> 00:26:37.900 asparagine, anthranine, and serine are

NOTE Confidence: 0.97145236

00:26:37.900 --> 00:26:39.600 positively correlated as well.

NOTE Confidence: 0.99702996

00:26:40.220 --> 00:26:41.500 So this suggested to us

NOTE Confidence: 0.99702996

00:26:41.500 --> 00:26:43.595 that asparagine increases in tumors

NOTE Confidence: 0.99702996

00:26:43.595 --> 00:26:45.115 from female patients to drive

NOTE Confidence: 0.99702996

00:26:45.115 --> 00:26:47.455 growth under nutrient deplete conditions.

NOTE Confidence: 0.95325

00:26:49.675 --> 00:26:51.375 So asparagine is a nonessential

NOTE Confidence: 0.95325

00:26:51.595 --> 00:26:52.795 amino acid, so it can

NOTE Confidence: 0.95325

00:26:52.795 --> 00:26:53.994 actually be derived from the

NOTE Confidence: 0.95325

00:26:53.994 --> 00:26:55.675 diet. But the tumor cells

NOTE Confidence: 0.95325

00:26:55.675 --> 00:26:57.435 can produce it themselves through

NOTE Confidence: 0.95325

00:26:57.435 --> 00:26:59.410 this, for Asparte and through

NOTE Confidence: 0.95325

00:26:59.410 --> 00:27:00.950 this asparagine synthetase,

NOTE Confidence: 0.9252875

00:27:01.890 --> 00:27:02.390 reaction,

NOTE Confidence: 0.9497126

00:27:02.690 --> 00:27:05.010 which require requires glutamine and

NOTE Confidence: 0.9497126

00:27:05.010 --> 00:27:05.510 ATP.

NOTE Confidence: 0.91604066

00:27:06.450 --> 00:27:07.990 So we went to TCGA

NOTE Confidence: 0.91604066

00:27:08.210 --> 00:27:09.110 and the CoEDGE,

NOTE Confidence: 0.9585977

00:27:09.904 --> 00:27:11.024 resource, and we looked at

NOTE Confidence: 0.9585977

00:27:11.024 --> 00:27:13.105 ASNS expression in females and

NOTE Confidence: 0.9585977

00:27:13.105 --> 00:27:13.605 males.

NOTE Confidence: 0.9462989

00:27:14.065 --> 00:27:15.024 And we saw that if

NOTE Confidence: 0.9462989

00:27:15.024 --> 00:27:16.625 a female patient had high

NOTE Confidence: 0.9462989

00:27:16.625 --> 00:27:18.385 ASNS expression, they had a

NOTE Confidence: 0.9462989

00:27:18.385 --> 00:27:20.144 poor outcome compared to or

NOTE Confidence: 0.9462989

00:27:20.144 --> 00:27:21.505 five year over so honestly,

NOTE Confidence: 0.9462989

00:27:21.505 --> 00:27:22.544 not five years. It's longer

NOTE Confidence: 0.9462989

00:27:22.544 --> 00:27:23.205 than that. Sorry.

NOTE Confidence: 0.9889183

00:27:23.585 --> 00:27:24.804 They had a poor outcome

NOTE Confidence: 0.9127347

00:27:25.320 --> 00:27:26.679 compared to those that had

NOTE Confidence: 0.9127347

00:27:26.679 --> 00:27:28.460 low medium ASNS expression.

NOTE Confidence: 0.9526653

00:27:29.240 --> 00:27:30.440 Whereas for males, there was

NOTE Confidence: 0.9526653

00:27:30.440 --> 00:27:31.980 no, difference whatsoever.

NOTE Confidence: 0.96251816

00:27:34.039 --> 00:27:35.240 So in summary for this

NOTE Confidence: 0.96251816

00:27:35.240 --> 00:27:36.779 section, we see that differences

NOTE Confidence: 0.96251816

00:27:36.840 --> 00:27:38.220 exist in tumor metabolites

NOTE Confidence: 0.9312805

00:27:38.600 --> 00:27:40.059 between females and males,

NOTE Confidence: 0.9431179

00:27:40.894 --> 00:27:41.934 That stage one to three

NOTE Confidence: 0.9431179

00:27:41.934 --> 00:27:43.875 tumors from females have elevated

NOTE Confidence: 0.9431179

00:27:43.934 --> 00:27:44.434 asparagine

NOTE Confidence: 0.8400469

00:27:44.734 --> 00:27:46.095 that could drive cancer growth

NOTE Confidence: 0.8400469

00:27:46.095 --> 00:27:47.715 during nutrient to complete conditions.

NOTE Confidence: 0.95769596

00:27:48.494 --> 00:27:49.475 And then overexpression

NOTE Confidence: 0.9512753

00:27:49.855 --> 00:27:51.615 of ASNS in TCGA is

NOTE Confidence: 0.9512753

00:27:51.615 --> 00:27:54.180 prognostic for females only. So

NOTE Confidence: 0.9512753

00:27:54.180 --> 00:27:55.220 I'm gonna turn the next

NOTE Confidence: 0.9512753

00:27:55.220 --> 00:27:56.360 section to such.

NOTE Confidence: 0.9930951

00:27:59.300 --> 00:28:00.420 So the next question we

NOTE Confidence: 0.9930951

00:28:00.420 --> 00:28:01.619 wanted to ask is, is

NOTE Confidence: 0.9930951

00:28:01.619 --> 00:28:03.320 there a link between colorectal

NOTE Confidence: 0.9930951

00:28:03.460 --> 00:28:04.920 cancer tumor metabolites

NOTE Confidence: 0.99774164

00:28:05.220 --> 00:28:07.460 and prognosis when stratified by

NOTE Confidence: 0.99774164

00:28:07.460 --> 00:28:07.960 sex?

NOTE Confidence: 0.95724297

00:28:10.055 --> 00:28:11.335 We used the same biobank

NOTE Confidence: 0.95724297

00:28:11.335 --> 00:28:12.935 that doctor Johnson had mentioned

NOTE Confidence: 0.95724297

00:28:12.935 --> 00:28:15.175 and evaluated individual metabolites for

NOTE Confidence: 0.95724297

00:28:15.175 --> 00:28:15.675 prognosis.

NOTE Confidence: 0.9257343

00:28:16.455 --> 00:28:17.355 In a multivariate

NOTE Confidence: 0.8870401

00:28:17.895 --> 00:28:19.494 in in the multivariable Cox

NOTE Confidence: 0.8870401

00:28:19.494 --> 00:28:19.994 proportional,

NOTE Confidence: 0.93466306

00:28:21.510 --> 00:28:23.350 hazard model where we controlled

NOTE Confidence: 0.93466306

00:28:23.350 --> 00:28:25.930 for clinical factors and established

NOTE Confidence: 0.93466306

00:28:25.990 --> 00:28:26.490 colorectal

NOTE Confidence: 0.9675707

00:28:26.950 --> 00:28:28.869 genes, such as MSI high

NOTE Confidence: 0.9675707

00:28:28.869 --> 00:28:29.369 status,

NOTE Confidence: 0.9923339

00:28:29.670 --> 00:28:30.170 BRAF,

NOTE Confidence: 0.8520436

00:28:30.550 --> 00:28:31.050 KRAS,

NOTE Confidence: 0.9235471

00:28:31.350 --> 00:28:33.030 we found that the eighteen

NOTE Confidence: 0.9235471

00:28:33.030 --> 00:28:33.850 listed metabolites

NOTE Confidence: 0.97252464

00:28:34.310 --> 00:28:36.135 on this slide were associated

NOTE Confidence: 0.97252464

00:28:36.135 --> 00:28:37.494 with prognosis in a self

NOTE Confidence: 0.97252464

00:28:37.494 --> 00:28:38.475 specific manner.

NOTE Confidence: 0.9803265

00:28:39.495 --> 00:28:41.275 Specifically, we found that asparagine,

NOTE Confidence: 0.9621498

00:28:42.375 --> 00:28:43.675 on the top in yellow,

NOTE Confidence: 0.9621498

00:28:43.735 --> 00:28:44.635 and serine,

NOTE Confidence: 0.963072

00:28:44.935 --> 00:28:46.395 in the middle in blue,

NOTE Confidence: 0.92112637

00:28:46.775 --> 00:28:48.135 were associated with a poorer

NOTE Confidence: 0.92112637

00:28:48.135 --> 00:28:49.835 five year survival in females,

NOTE Confidence: 0.9723306

00:28:50.500 --> 00:28:52.020 whereas the same metabolites were

NOTE Confidence: 0.9723306

00:28:52.020 --> 00:28:53.720 associated with a better survival

NOTE Confidence: 0.9947045

00:28:54.020 --> 00:28:54.760 for males.

NOTE Confidence: 0.99919426

00:28:55.539 --> 00:28:56.039 Furthermore,

NOTE Confidence: 0.9346761

00:28:56.340 --> 00:28:56.840 succinate,

NOTE Confidence: 0.9935751

00:28:57.460 --> 00:28:58.900 was associated with a favorable

NOTE Confidence: 0.9935751

00:28:58.900 --> 00:29:00.419 survival in females and a

NOTE Confidence: 0.9935751

00:29:00.419 --> 00:29:01.880 worse survival for males.

NOTE Confidence: 0.9975322

00:29:04.915 --> 00:29:06.515 We next tested for sex

NOTE Confidence: 0.9975322

00:29:06.515 --> 00:29:08.835 specific associations after adjusting for

NOTE Confidence: 0.9975322

00:29:08.835 --> 00:29:10.535 the same clinical and pathologic

NOTE Confidence: 0.9975322

00:29:10.755 --> 00:29:11.255 variables,

NOTE Confidence: 0.973121

00:29:11.795 --> 00:29:12.675 which I mentioned in the

NOTE Confidence: 0.973121

00:29:12.675 --> 00:29:14.195 last slide, with a specific

NOTE Confidence: 0.973121

00:29:14.195 --> 00:29:16.055 focus on the asparagine synthesis

NOTE Confidence: 0.973121

00:29:16.115 --> 00:29:16.615 pathway.

NOTE Confidence: 0.9853441

00:29:17.660 --> 00:29:19.760 Asparagine abundance was very significantly

NOTE Confidence: 0.9853441

00:29:19.980 --> 00:29:22.380 associated with poor survival and

NOTE Confidence: 0.9853441

00:29:22.380 --> 00:29:23.980 poor recurrence free survival for

NOTE Confidence: 0.9853441

00:29:23.980 --> 00:29:24.480 females,

NOTE Confidence: 0.902398

00:29:25.100 --> 00:29:26.620 whereas it was associated with

NOTE Confidence: 0.902398

00:29:26.620 --> 00:29:28.400 the favorable survival for males.

NOTE Confidence: 0.9564418

00:29:29.100 --> 00:29:30.434 So females had a a

NOTE Confidence: 0.9564418

00:29:30.434 --> 00:29:31.794 hazard ratio of six point

NOTE Confidence: 0.9564418

00:29:31.794 --> 00:29:33.014 three nine for overall

NOTE Confidence: 0.9841638

00:29:33.315 --> 00:29:34.455 death with overexpression

NOTE Confidence: 0.9943689

00:29:34.755 --> 00:29:35.575 of asparagine.

NOTE Confidence: 0.93601894

00:29:37.955 --> 00:29:39.875 We then, performed a COX

NOTE Confidence: 0.93601894

00:29:39.875 --> 00:29:41.634 survival analysis looking at the

NOTE Confidence: 0.93601894

00:29:41.634 --> 00:29:42.774 asparagine levels.

NOTE Confidence: 0.9891816

00:29:43.530 --> 00:29:45.450 High expression of asparagine, shown

NOTE Confidence: 0.9891816

00:29:45.450 --> 00:29:46.190 in blue,

NOTE Confidence: 0.9375061

00:29:46.810 --> 00:29:48.250 on these Kaplan Meier curves

NOTE Confidence: 0.9375061

00:29:48.250 --> 00:29:50.270 had a worse overall survival

NOTE Confidence: 0.9808677

00:29:50.570 --> 00:29:52.090 and a worse recurrence free

NOTE Confidence: 0.9808677

00:29:52.090 --> 00:29:52.590 survival,

NOTE Confidence: 0.9890772

00:29:53.850 --> 00:29:55.450 compared to low asparagine levels,

NOTE Confidence: 0.9890772

00:29:55.450 --> 00:29:56.570 which are shown in red,

NOTE Confidence: 0.9890772

00:29:56.570 --> 00:29:57.690 and this finding was only

NOTE Confidence: 0.9890772

00:29:57.690 --> 00:29:59.070 found in female patients.

NOTE Confidence: 0.9962388

00:29:59.554 --> 00:30:01.235 In males in male patients,

NOTE Confidence: 0.97295886

00:30:01.955 --> 00:30:03.395 asparagine actually was not associated

NOTE Confidence: 0.97295886

00:30:03.395 --> 00:30:04.835 with survival at all. So

NOTE Confidence: 0.97295886

00:30:04.835 --> 00:30:05.875 just to summarize a bit,

NOTE Confidence: 0.97295886

00:30:05.875 --> 00:30:07.554 so Caroline had mentioned about

NOTE Confidence: 0.97295886

00:30:07.554 --> 00:30:09.174 ASNS. This is the asparagine

NOTE Confidence: 0.97295886

00:30:09.395 --> 00:30:10.455 metabolite, so,

NOTE Confidence: 0.93265396

00:30:11.075 --> 00:30:12.035 the story is starting to

NOTE Confidence: 0.93265396

00:30:12.035 --> 00:30:13.815 build. So in summary,

NOTE Confidence: 0.98778254

00:30:16.360 --> 00:30:17.660 sex specific differences

NOTE Confidence: 0.9950695

00:30:18.040 --> 00:30:20.200 exist between individual metabolites and

NOTE Confidence: 0.9950695

00:30:20.200 --> 00:30:20.700 prognosis.

NOTE Confidence: 0.96717805

00:30:22.680 --> 00:30:24.520 Asparagine metabolism is linked to

NOTE Confidence: 0.96717805

00:30:24.520 --> 00:30:25.980 poor survival in females.

NOTE Confidence: 0.82062024

00:30:27.835 --> 00:30:28.955 And that we talked about

NOTE Confidence: 0.82062024

00:30:28.955 --> 00:30:31.294 asparagine metabolite abundance, being,

NOTE Confidence: 0.97936344

00:30:31.835 --> 00:30:32.735 being the case.

NOTE Confidence: 0.93950784

00:30:33.755 --> 00:30:35.835 Serum metabolite abundance is linked

NOTE Confidence: 0.93950784

00:30:35.835 --> 00:30:37.375 to poor survival in males.

NOTE Confidence: 0.92157716

00:30:39.515 --> 00:30:41.135 Caroline's gonna take over each.

NOTE Confidence: 0.91800064

00:30:43.230 --> 00:30:44.030 So, yeah, so now we

NOTE Confidence: 0.91800064

00:30:44.030 --> 00:30:45.070 turned our research to look

NOTE Confidence: 0.91800064

00:30:45.070 --> 00:30:46.750 at the functional effect of

NOTE Confidence: 0.91800064

00:30:46.750 --> 00:30:47.970 ASNS and Asparagine

NOTE Confidence: 0.99615705

00:30:48.430 --> 00:30:50.050 on colorectal cancer metabolism.

NOTE Confidence: 0.91473913

00:30:50.990 --> 00:30:52.030 So this work has been

NOTE Confidence: 0.91473913

00:30:52.030 --> 00:30:54.190 primarily read, led by doctor

NOTE Confidence: 0.91473913

00:30:54.190 --> 00:30:55.010 Ola Aladelacun,

NOTE Confidence: 0.96376705

00:30:56.405 --> 00:30:57.525 And he's been looking at

NOTE Confidence: 0.96376705

00:30:57.525 --> 00:30:58.664 the role of the ASNS

NOTE Confidence: 0.96376705

00:30:58.804 --> 00:31:00.885 gene and also asparagine in

NOTE Confidence: 0.96376705

00:31:00.885 --> 00:31:01.385 driving

NOTE Confidence: 0.9742824

00:31:01.765 --> 00:31:03.044 cancer growth in in vitro

NOTE Confidence: 0.9742824

00:31:03.044 --> 00:31:04.265 and in vivo models.

NOTE Confidence: 0.94781286

00:31:04.725 --> 00:31:06.005 So the first first thing

NOTE Confidence: 0.94781286

00:31:06.005 --> 00:31:07.465 that we did was knockout

NOTE Confidence: 0.94781286

00:31:07.605 --> 00:31:09.845 ASNS in a colorectal cancer

NOTE Confidence: 0.94781286

00:31:09.845 --> 00:31:11.710 cell line. So HCT one

NOTE Confidence: 0.94781286

00:31:11.710 --> 00:31:12.990 one six is a male

NOTE Confidence: 0.94781286

00:31:12.990 --> 00:31:14.190 cell line. And you can

NOTE Confidence: 0.94781286

00:31:14.190 --> 00:31:15.490 see here from this diagram

NOTE Confidence: 0.94781286

00:31:15.630 --> 00:31:16.370 at the top,

NOTE Confidence: 0.99092245

00:31:17.309 --> 00:31:18.850 the two cell lines there,

NOTE Confidence: 0.9654062

00:31:19.630 --> 00:31:21.390 are cultured without sparigene in

NOTE Confidence: 0.9654062

00:31:21.390 --> 00:31:22.590 the media. And you can

NOTE Confidence: 0.9654062

00:31:22.590 --> 00:31:24.289 see how knockout of ASNS,

NOTE Confidence: 0.97680604

00:31:25.070 --> 00:31:26.205 really affects the way these

NOTE Confidence: 0.97680604

00:31:26.205 --> 00:31:27.325 spheroids grow. They have a

NOTE Confidence: 0.97680604

00:31:27.325 --> 00:31:28.544 really hard time growing.

NOTE Confidence: 0.9849105

00:31:28.845 --> 00:31:30.225 But if we add asparagine

NOTE Confidence: 0.9849105

00:31:30.365 --> 00:31:31.485 back into the media, you

NOTE Confidence: 0.9849105

00:31:31.485 --> 00:31:32.605 can see it actually does

NOTE Confidence: 0.9849105

00:31:32.605 --> 00:31:34.525 rescue cell growth. So this

NOTE Confidence: 0.9849105

00:31:34.525 --> 00:31:35.645 just shows for this cell

NOTE Confidence: 0.9849105

00:31:35.645 --> 00:31:37.345 line that ASNS and asparagine

NOTE Confidence: 0.9849105

00:31:37.565 --> 00:31:39.025 are important to maintain,

NOTE Confidence: 0.99961346

00:31:39.885 --> 00:31:41.184 the growth of the cancer.

NOTE Confidence: 0.97235906

00:31:42.580 --> 00:31:43.779 We then took these cell

NOTE Confidence: 0.97235906

00:31:43.779 --> 00:31:45.240 lines and did a subcutaneous

NOTE Confidence: 0.97235906

00:31:45.539 --> 00:31:46.039 xenograft,

NOTE Confidence: 0.9832577

00:31:46.820 --> 00:31:47.320 experiment

NOTE Confidence: 0.98434836

00:31:47.620 --> 00:31:48.519 using immunocompromised

NOTE Confidence: 0.9983194

00:31:49.220 --> 00:31:50.580 mice. This was done in

NOTE Confidence: 0.9983194

00:31:50.580 --> 00:31:51.080 collaboration

NOTE Confidence: 0.87679464

00:31:51.380 --> 00:31:52.840 with the Center for Precision

NOTE Confidence: 0.8571023

00:31:53.539 --> 00:31:54.405 Modeling Core.

NOTE Confidence: 0.99422944

00:31:54.885 --> 00:31:56.085 So we had ten mice

NOTE Confidence: 0.99422944

00:31:56.085 --> 00:31:57.865 per group, males and females

NOTE Confidence: 0.94091004

00:31:58.325 --> 00:31:59.865 inoculated with the ASNS,

NOTE Confidence: 0.98565406

00:32:00.325 --> 00:32:02.565 wild type or, knockout cell

NOTE Confidence: 0.98565406

00:32:02.565 --> 00:32:03.845 line, and then they were

NOTE Confidence: 0.98565406

00:32:03.845 --> 00:32:05.545 grown for about three weeks.

NOTE Confidence: 0.98565406

00:32:05.845 --> 00:32:06.725 So we looked at the

NOTE Confidence: 0.98565406

00:32:06.725 --> 00:32:08.520 growth kinetics and also the

NOTE Confidence: 0.98565406

00:32:08.520 --> 00:32:10.040 metabolomics of the tumors as

NOTE Confidence: 0.98565406

00:32:10.040 --> 00:32:10.540 well.

NOTE Confidence: 0.9863632

00:32:11.960 --> 00:32:13.160 So the diagram on the

NOTE Confidence: 0.9863632

00:32:13.160 --> 00:32:14.700 left shows you the asparagine

NOTE Confidence: 0.9863632

00:32:14.840 --> 00:32:15.340 abundance,

NOTE Confidence: 0.9989345

00:32:15.800 --> 00:32:16.860 within the tumors.

NOTE Confidence: 0.98207325

00:32:17.720 --> 00:32:19.000 You can see that in

NOTE Confidence: 0.98207325

00:32:19.000 --> 00:32:20.380 green, these are the knockout

NOTE Confidence: 0.98207325

00:32:20.524 --> 00:32:21.644 cell lines that were grown

NOTE Confidence: 0.98207325

00:32:21.644 --> 00:32:22.524 in the mice, and you

NOTE Confidence: 0.98207325

00:32:22.524 --> 00:32:23.804 can see they do produce

NOTE Confidence: 0.98207325

00:32:23.804 --> 00:32:24.705 less asparagine

NOTE Confidence: 0.99202335

00:32:25.085 --> 00:32:26.524 than the wild type cell

NOTE Confidence: 0.99202335

00:32:26.524 --> 00:32:27.804 line. But the difference is

NOTE Confidence: 0.99202335

00:32:27.804 --> 00:32:29.005 about the same for both

NOTE Confidence: 0.99202335

00:32:29.005 --> 00:32:29.985 males and females.

NOTE Confidence: 0.99662477

00:32:30.605 --> 00:32:31.644 When we look at tumor

NOTE Confidence: 0.99662477

00:32:31.644 --> 00:32:32.144 volume,

NOTE Confidence: 0.997928

00:32:32.445 --> 00:32:33.825 we can see that the,

NOTE Confidence: 0.99227667

00:32:34.284 --> 00:32:35.565 the tumors that grow in

NOTE Confidence: 0.99227667

00:32:35.565 --> 00:32:36.225 the males

NOTE Confidence: 0.99524564

00:32:36.660 --> 00:32:37.940 grow the fastest, but the

NOTE Confidence: 0.99524564

00:32:37.940 --> 00:32:39.460 knockout does have an effect

NOTE Confidence: 0.99524564

00:32:39.460 --> 00:32:40.740 on how these tumors grow.

NOTE Confidence: 0.99524564

00:32:40.740 --> 00:32:42.040 They grow a lot slower.

NOTE Confidence: 0.9734495

00:32:42.500 --> 00:32:43.300 And and then for the

NOTE Confidence: 0.9734495

00:32:43.300 --> 00:32:44.820 female, the cell lines, they

NOTE Confidence: 0.9734495

00:32:44.820 --> 00:32:45.940 both grow slower in the

NOTE Confidence: 0.9734495

00:32:45.940 --> 00:32:47.400 females compared to the males,

NOTE Confidence: 0.9734495

00:32:47.460 --> 00:32:48.580 but the knockout has the

NOTE Confidence: 0.9734495

00:32:48.580 --> 00:32:49.960 slowest tumor growth.

NOTE Confidence: 0.99449927

00:32:50.945 --> 00:32:52.645 But our next question was,

NOTE Confidence: 0.99449927

00:32:52.785 --> 00:32:53.585 you know, what is the

NOTE Confidence: 0.99449927

00:32:53.585 --> 00:32:55.445 effect of asparagine supplementation?

NOTE Confidence: 0.98195076

00:32:55.985 --> 00:32:57.185 So thinking about this in

NOTE Confidence: 0.98195076

00:32:57.185 --> 00:32:58.565 terms of we find asparagine

NOTE Confidence: 0.98195076

00:32:58.625 --> 00:32:59.905 readily in our diet and

NOTE Confidence: 0.98195076

00:32:59.905 --> 00:33:00.945 can be produced by the

NOTE Confidence: 0.98195076

00:33:00.945 --> 00:33:02.245 microbiome as well.

NOTE Confidence: 0.9446088

00:33:03.169 --> 00:33:04.230 So we took the ASNS

NOTE Confidence: 0.9446088

00:33:04.529 --> 00:33:05.250 wild type,

NOTE Confidence: 0.9710169

00:33:05.730 --> 00:33:06.770 cell lines and did a

NOTE Confidence: 0.9710169

00:33:06.770 --> 00:33:07.909 xenograft again,

NOTE Confidence: 0.94715554

00:33:08.450 --> 00:33:09.890 in the males and females

NOTE Confidence: 0.94715554

00:33:09.890 --> 00:33:11.010 and gave the mice an

NOTE Confidence: 0.94715554

00:33:11.010 --> 00:33:12.690 IP injection of one or

NOTE Confidence: 0.94715554

00:33:12.690 --> 00:33:14.070 ten MPK asparagine

NOTE Confidence: 0.96817577

00:33:14.610 --> 00:33:15.890 about every three to seven

NOTE Confidence: 0.96817577

00:33:15.890 --> 00:33:18.205 days and, let these tumors

NOTE Confidence: 0.96817577

00:33:18.205 --> 00:33:19.325 grow again for about three

NOTE Confidence: 0.96817577

00:33:19.325 --> 00:33:19.825 weeks.

NOTE Confidence: 0.9637061

00:33:20.445 --> 00:33:21.325 So you can see in

NOTE Confidence: 0.9637061

00:33:21.325 --> 00:33:23.085 the in the males, the

NOTE Confidence: 0.9637061

00:33:23.085 --> 00:33:25.165 asparagine did slightly increase tumor

NOTE Confidence: 0.9637061

00:33:25.165 --> 00:33:26.605 volume at the earlier stages,

NOTE Confidence: 0.9637061

00:33:26.605 --> 00:33:27.265 but ultimately

NOTE Confidence: 0.96326554

00:33:27.645 --> 00:33:28.365 at the end of three

NOTE Confidence: 0.96326554

00:33:28.365 --> 00:33:29.725 weeks, the tumor volume was

NOTE Confidence: 0.96326554

00:33:29.725 --> 00:33:30.545 about the same.

NOTE Confidence: 0.9958297

00:33:31.180 --> 00:33:32.620 But surprising to us,

NOTE Confidence: 0.9645498

00:33:32.940 --> 00:33:34.780 we saw that Asparagine actually

NOTE Confidence: 0.9645498

00:33:34.780 --> 00:33:36.540 decreased tumor growth in the

NOTE Confidence: 0.9645498

00:33:36.540 --> 00:33:38.060 female mice, which was opposite

NOTE Confidence: 0.9645498

00:33:38.060 --> 00:33:39.340 to our hypothesis. But I

NOTE Confidence: 0.9645498

00:33:39.340 --> 00:33:40.220 like it when that happens

NOTE Confidence: 0.9645498

00:33:40.220 --> 00:33:41.180 because it leads to new

NOTE Confidence: 0.9645498

00:33:41.180 --> 00:33:41.680 questions

NOTE Confidence: 0.90266067

00:33:42.220 --> 00:33:43.120 and new findings.

NOTE Confidence: 0.92476577

00:33:43.585 --> 00:33:44.625 So one thing we thought

NOTE Confidence: 0.92476577

00:33:44.625 --> 00:33:46.005 is that perhaps the asparagine

NOTE Confidence: 0.9663235

00:33:46.305 --> 00:33:47.665 being present in the in

NOTE Confidence: 0.9663235

00:33:47.665 --> 00:33:48.865 the female mice is having

NOTE Confidence: 0.9663235

00:33:48.865 --> 00:33:50.625 a negative feedback on the

NOTE Confidence: 0.9663235

00:33:50.625 --> 00:33:52.065 production of asparagine in the

NOTE Confidence: 0.9663235

00:33:52.065 --> 00:33:53.505 tumor and maybe knocking you

NOTE Confidence: 0.9663235

00:33:53.505 --> 00:33:55.105 know, decreasing the expression of

NOTE Confidence: 0.9663235

00:33:55.105 --> 00:33:55.605 ASNS.

NOTE Confidence: 0.97828245

00:33:56.625 --> 00:33:57.679 So we looked at ASNS

NOTE Confidence: 0.97828245

00:33:57.899 --> 00:33:59.760 expression in the tumor tissues,

NOTE Confidence: 0.97828245

00:34:00.059 --> 00:34:00.860 and we saw that it

NOTE Confidence: 0.97828245

00:34:00.860 --> 00:34:02.700 was indeed decreased only in

NOTE Confidence: 0.97828245

00:34:02.700 --> 00:34:04.460 the female tumors, and it

NOTE Confidence: 0.97828245

00:34:04.460 --> 00:34:05.899 wasn't changed in the male

NOTE Confidence: 0.97828245

00:34:05.899 --> 00:34:07.840 tumors after asparagine supplementation.

NOTE Confidence: 0.9798036

00:34:09.225 --> 00:34:10.445 We then looked at asparagine

NOTE Confidence: 0.9798036

00:34:10.585 --> 00:34:12.025 and aspartate levels in the

NOTE Confidence: 0.9798036

00:34:12.025 --> 00:34:13.385 tumors, and we could see

NOTE Confidence: 0.9798036

00:34:13.385 --> 00:34:14.425 that for both the males

NOTE Confidence: 0.9798036

00:34:14.425 --> 00:34:15.545 and the females that were

NOTE Confidence: 0.9798036

00:34:15.545 --> 00:34:15.945 given,

NOTE Confidence: 0.9791608

00:34:16.345 --> 00:34:17.565 exogenous asparagine,

NOTE Confidence: 0.99163234

00:34:18.025 --> 00:34:19.865 asparagine levels did increase within

NOTE Confidence: 0.99163234

00:34:19.865 --> 00:34:20.525 the tumors.

NOTE Confidence: 0.9825709

00:34:21.140 --> 00:34:22.340 And then surprising to us,

NOTE Confidence: 0.9825709

00:34:22.340 --> 00:34:24.020 we saw that aspartate was

NOTE Confidence: 0.9825709

00:34:24.020 --> 00:34:25.860 decreased in the female tumors

NOTE Confidence: 0.9825709

00:34:25.860 --> 00:34:26.360 only

NOTE Confidence: 0.92336047

00:34:26.739 --> 00:34:28.040 that were given asparagine.

NOTE Confidence: 0.98737544

00:34:28.500 --> 00:34:30.040 So aspartate is a substrate

NOTE Confidence: 0.98737544

00:34:30.100 --> 00:34:31.160 for this reaction.

NOTE Confidence: 0.98414356

00:34:31.860 --> 00:34:33.780 So aspartate actually requires a

NOTE Confidence: 0.98414356

00:34:33.780 --> 00:34:35.380 transporter to be brought into

NOTE Confidence: 0.98414356

00:34:35.380 --> 00:34:36.015 the cell,

NOTE Confidence: 0.9646218

00:34:36.575 --> 00:34:38.275 the cancer cell, whereas asparagine

NOTE Confidence: 0.9646218

00:34:38.414 --> 00:34:39.614 can use a transporter or

NOTE Confidence: 0.9646218

00:34:39.614 --> 00:34:40.515 it can passively

NOTE Confidence: 0.99913496

00:34:40.815 --> 00:34:41.315 diffuse.

NOTE Confidence: 0.96698856

00:34:41.855 --> 00:34:43.375 So we looked at the

NOTE Confidence: 0.96698856

00:34:43.375 --> 00:34:45.474 transporter SLC one a three,

NOTE Confidence: 0.96698856

00:34:45.694 --> 00:34:46.894 and we saw again that

NOTE Confidence: 0.96698856

00:34:46.894 --> 00:34:47.954 this was significantly

NOTE Confidence: 0.99285734

00:34:48.335 --> 00:34:50.015 decreased in the female mice

NOTE Confidence: 0.99285734

00:34:50.015 --> 00:34:51.234 that received asparagine,

NOTE Confidence: 0.9709137

00:34:51.535 --> 00:34:52.299 but but it was actually

NOTE Confidence: 0.9709137

00:34:52.299 --> 00:34:53.819 increased in the male mice.

NOTE Confidence: 0.9709137

00:34:53.819 --> 00:34:54.859 You can just see how

NOTE Confidence: 0.9709137

00:34:54.859 --> 00:34:56.299 different these are between the

NOTE Confidence: 0.9709137

00:34:56.299 --> 00:34:57.819 mouse models just by sex

NOTE Confidence: 0.9709137

00:34:57.819 --> 00:34:58.559 of the mouse.

NOTE Confidence: 0.97062474

00:34:59.900 --> 00:35:01.760 So de novo asparagine production

NOTE Confidence: 0.97062474

00:35:01.819 --> 00:35:03.420 decreased in the female tumors

NOTE Confidence: 0.97062474

00:35:03.420 --> 00:35:04.914 only. So I'll just talk

NOTE Confidence: 0.97062474

00:35:04.914 --> 00:35:06.454 about sort of the hormonal

NOTE Confidence: 0.97062474

00:35:06.594 --> 00:35:07.714 changes that we saw as

NOTE Confidence: 0.97062474

00:35:07.714 --> 00:35:09.234 well in these mice that

NOTE Confidence: 0.97062474

00:35:09.234 --> 00:35:09.974 had asparagine

NOTE Confidence: 0.9918463

00:35:10.835 --> 00:35:11.335 supplemented.

NOTE Confidence: 0.99647796

00:35:11.954 --> 00:35:13.255 So we measured estradiol

NOTE Confidence: 0.90730935

00:35:13.555 --> 00:35:15.174 just using a serum estradiol

NOTE Confidence: 0.90730935

00:35:15.395 --> 00:35:16.375 using ELISA.

NOTE Confidence: 0.9475696

00:35:16.940 --> 00:35:18.140 And what we found was

NOTE Confidence: 0.9475696

00:35:18.140 --> 00:35:19.500 surprising to us again was

NOTE Confidence: 0.9475696

00:35:19.500 --> 00:35:20.780 that when the mice received

NOTE Confidence: 0.9475696

00:35:20.780 --> 00:35:21.280 asparagine,

NOTE Confidence: 0.99156886

00:35:21.980 --> 00:35:23.900 it's actually increased estradiol levels

NOTE Confidence: 0.99156886

00:35:23.900 --> 00:35:24.940 in the serum of the

NOTE Confidence: 0.99156886

00:35:24.940 --> 00:35:26.940 female mice, but it decreased

NOTE Confidence: 0.99156886

00:35:26.940 --> 00:35:28.540 estradiol levels in the serum

NOTE Confidence: 0.99156886

00:35:28.540 --> 00:35:29.680 of the male mice.

NOTE Confidence: 0.9769461

00:35:30.105 --> 00:35:31.465 So we didn't unfortunately have

NOTE Confidence: 0.9769461

00:35:31.465 --> 00:35:32.985 the ovaries from these,

NOTE Confidence: 0.98198056

00:35:33.545 --> 00:35:34.744 from these mice, but we

NOTE Confidence: 0.98198056

00:35:34.744 --> 00:35:36.525 did look at aromatase expression

NOTE Confidence: 0.98198056

00:35:36.665 --> 00:35:37.485 in the tumors.

NOTE Confidence: 0.98712337

00:35:37.945 --> 00:35:39.145 And we found as well

NOTE Confidence: 0.98712337

00:35:39.145 --> 00:35:41.485 that asparagine actually increased aromatase

NOTE Confidence: 0.98712337

00:35:41.625 --> 00:35:43.225 expression in the tumors themselves

NOTE Confidence: 0.98712337

00:35:43.225 --> 00:35:44.744 from female mice, but there

NOTE Confidence: 0.98712337

00:35:44.744 --> 00:35:45.869 was no effect in the

NOTE Confidence: 0.98712337

00:35:45.869 --> 00:35:46.369 males.

NOTE Confidence: 0.9816224

00:35:46.670 --> 00:35:48.109 And this is interesting because

NOTE Confidence: 0.9816224

00:35:48.109 --> 00:35:49.549 estradiol is a known anti

NOTE Confidence: 0.9816224

00:35:49.549 --> 00:35:51.869 proliferative for colorectal cancer and

NOTE Confidence: 0.9816224

00:35:51.869 --> 00:35:53.309 does provide protection for women

NOTE Confidence: 0.9816224

00:35:53.309 --> 00:35:55.309 against colorectal cancer. So this

NOTE Confidence: 0.9816224

00:35:55.309 --> 00:35:57.170 increase in estradiol and aromatase

NOTE Confidence: 0.9816224

00:35:57.390 --> 00:35:58.210 could be potentially

NOTE Confidence: 0.99640626

00:35:59.125 --> 00:36:00.565 having that sort of effect

NOTE Confidence: 0.99640626

00:36:00.565 --> 00:36:02.344 on decreasing the tumor growth.

NOTE Confidence: 0.991995

00:36:03.525 --> 00:36:04.485 We then looked at the

NOTE Confidence: 0.991995

00:36:04.485 --> 00:36:06.245 estrogen receptors, and we found

NOTE Confidence: 0.991995

00:36:06.245 --> 00:36:08.105 no difference in estrogen receptor

NOTE Confidence: 0.991995

00:36:08.245 --> 00:36:09.864 beta or alpha expression.

NOTE Confidence: 0.9589945

00:36:10.485 --> 00:36:11.685 So we looked at Gepa,

NOTE Confidence: 0.9589945

00:36:11.685 --> 00:36:12.425 which is

NOTE Confidence: 0.96191365

00:36:13.150 --> 00:36:14.830 a membrane bound and very

NOTE Confidence: 0.96191365

00:36:14.830 --> 00:36:16.770 nutrient sensitive estrogen receptor.

NOTE Confidence: 0.9830137

00:36:17.310 --> 00:36:18.270 And what we found was

NOTE Confidence: 0.9830137

00:36:18.270 --> 00:36:19.390 that this actually did change

NOTE Confidence: 0.9830137

00:36:19.390 --> 00:36:20.750 in expression in response to

NOTE Confidence: 0.9830137

00:36:20.750 --> 00:36:21.250 asparagine

NOTE Confidence: 0.8524084

00:36:21.950 --> 00:36:22.610 being supplemented.

NOTE Confidence: 0.83953536

00:36:23.150 --> 00:36:24.989 So it's significantly decreasing the

NOTE Confidence: 0.83953536

00:36:24.989 --> 00:36:26.750 females and again increasing the

NOTE Confidence: 0.83953536

00:36:26.750 --> 00:36:27.250 males.

NOTE Confidence: 0.9594888

00:36:28.344 --> 00:36:29.725 So we did some further

NOTE Confidence: 0.9594888

00:36:29.785 --> 00:36:31.465 investigations into the link between

NOTE Confidence: 0.9594888

00:36:31.465 --> 00:36:32.685 GPRA and ASNS,

NOTE Confidence: 0.996121

00:36:33.225 --> 00:36:34.265 and we see they're actually

NOTE Confidence: 0.996121

00:36:34.265 --> 00:36:35.305 linked to each other through

NOTE Confidence: 0.996121

00:36:35.305 --> 00:36:37.565 this integrated stress response pathway,

NOTE Confidence: 0.996121

00:36:37.864 --> 00:36:39.545 which is typically activated as

NOTE Confidence: 0.996121

00:36:39.545 --> 00:36:40.950 well under nutrient stress.

NOTE Confidence: 0.99154943

00:36:41.430 --> 00:36:42.550 So you may recognize some

NOTE Confidence: 0.99154943

00:36:42.550 --> 00:36:43.190 of these,

NOTE Confidence: 0.92495126

00:36:43.670 --> 00:36:44.790 molecules here if you work

NOTE Confidence: 0.92495126

00:36:44.790 --> 00:36:46.070 in this area, but we

NOTE Confidence: 0.92495126

00:36:46.070 --> 00:36:47.589 could see that downstream of

NOTE Confidence: 0.92495126

00:36:47.589 --> 00:36:48.650 of GPO signaling,

NOTE Confidence: 0.9937043

00:36:48.950 --> 00:36:50.010 we have AMPK

NOTE Confidence: 0.83566356

00:36:50.310 --> 00:36:51.430 and we have p r

NOTE Confidence: 0.83566356

00:36:51.430 --> 00:36:52.650 three k and mTOR

NOTE Confidence: 0.9809503

00:36:53.175 --> 00:36:54.155 and also ASNS.

NOTE Confidence: 0.97246087

00:36:54.855 --> 00:36:56.055 So in our models, we

NOTE Confidence: 0.97246087

00:36:56.055 --> 00:36:57.175 see that in the females,

NOTE Confidence: 0.97246087

00:36:57.175 --> 00:36:58.475 when we give them asparagine,

NOTE Confidence: 0.97246087

00:36:58.614 --> 00:36:59.495 this has a knock on

NOTE Confidence: 0.97246087

00:36:59.495 --> 00:37:01.415 effect of decreasing this pathway

NOTE Confidence: 0.97246087

00:37:01.415 --> 00:37:03.415 and decreasing tumor growth. But

NOTE Confidence: 0.97246087

00:37:03.415 --> 00:37:04.455 in the males, it appears

NOTE Confidence: 0.97246087

00:37:04.455 --> 00:37:05.915 to be an opposite effect.

NOTE Confidence: 0.89053136

00:37:07.980 --> 00:37:09.660 In another study, led by

NOTE Confidence: 0.89053136

00:37:09.660 --> 00:37:11.820 Lingan Liu from, CDE at

NOTE Confidence: 0.89053136

00:37:11.820 --> 00:37:12.320 YSPH,

NOTE Confidence: 0.8197624

00:37:13.100 --> 00:37:14.219 he looked at G Pro

NOTE Confidence: 0.8197624

00:37:14.219 --> 00:37:14.719 expression

NOTE Confidence: 0.9912565

00:37:15.020 --> 00:37:15.840 in TCGA

NOTE Confidence: 0.9720789

00:37:16.380 --> 00:37:17.820 again. And what we saw

NOTE Confidence: 0.9720789

00:37:17.820 --> 00:37:18.940 was that at the advanced

NOTE Confidence: 0.9720789

00:37:18.940 --> 00:37:20.540 stages of tumor growth, so

NOTE Confidence: 0.9720789

00:37:20.540 --> 00:37:22.080 at stage three and four,

NOTE Confidence: 0.93637407

00:37:22.505 --> 00:37:23.405 female patients,

NOTE Confidence: 0.9545079

00:37:24.185 --> 00:37:25.945 with high GPRA expression have

NOTE Confidence: 0.9545079

00:37:25.945 --> 00:37:27.545 a poor outcome compared to

NOTE Confidence: 0.9545079

00:37:27.545 --> 00:37:28.285 low expression

NOTE Confidence: 0.9491962

00:37:28.665 --> 00:37:29.625 where we don't see that

NOTE Confidence: 0.9491962

00:37:29.625 --> 00:37:30.985 effect for males and we

NOTE Confidence: 0.9491962

00:37:30.985 --> 00:37:32.025 don't see that effect in

NOTE Confidence: 0.9491962

00:37:32.025 --> 00:37:33.805 the early stages as well.

NOTE Confidence: 0.96493685

00:37:35.910 --> 00:37:37.190 So I just wanna mention

NOTE Confidence: 0.96493685

00:37:37.190 --> 00:37:38.630 in two slides a resource

NOTE Confidence: 0.96493685

00:37:38.630 --> 00:37:39.910 that might also be useful

NOTE Confidence: 0.96493685

00:37:39.910 --> 00:37:41.930 for Yale Cancer Center members.

NOTE Confidence: 0.99272794

00:37:42.390 --> 00:37:43.750 So within this space, we

NOTE Confidence: 0.99272794

00:37:43.750 --> 00:37:45.109 were also wondering what the

NOTE Confidence: 0.99272794

00:37:45.109 --> 00:37:46.869 scale of sex disparities in

NOTE Confidence: 0.99272794

00:37:46.869 --> 00:37:48.010 cancers are.

NOTE Confidence: 0.91431195

00:37:48.344 --> 00:37:49.224 So I have this very

NOTE Confidence: 0.91431195

00:37:49.224 --> 00:37:51.224 talented PhD student, Shiny Shen,

NOTE Confidence: 0.91431195

00:37:51.224 --> 00:37:52.744 who should be graduating soon.

NOTE Confidence: 0.91431195

00:37:52.744 --> 00:37:54.505 She's commented by both me

NOTE Confidence: 0.91431195

00:37:54.505 --> 00:37:56.105 and Saaj, and she wanted

NOTE Confidence: 0.91431195

00:37:56.105 --> 00:37:57.945 to understand what really is

NOTE Confidence: 0.91431195

00:37:57.945 --> 00:37:59.244 the scale of these differences.

NOTE Confidence: 0.91431195

00:37:59.385 --> 00:38:00.605 So what are the molecular

NOTE Confidence: 0.91431195

00:38:00.665 --> 00:38:01.165 differences,

NOTE Confidence: 0.95737696

00:38:02.000 --> 00:38:04.640 potential therapeutic efficacy and adverse

NOTE Confidence: 0.95737696

00:38:04.640 --> 00:38:05.140 responses,

NOTE Confidence: 0.97410274

00:38:05.760 --> 00:38:07.440 and also some environmental factors

NOTE Confidence: 0.97410274

00:38:07.440 --> 00:38:08.880 that could affect risk, such

NOTE Confidence: 0.97410274

00:38:08.880 --> 00:38:10.719 as different exposures and the

NOTE Confidence: 0.97410274

00:38:10.719 --> 00:38:11.219 microbiome.

NOTE Confidence: 0.9966096

00:38:11.920 --> 00:38:12.960 But when she looked in

NOTE Confidence: 0.9966096

00:38:12.960 --> 00:38:14.400 the literature, she found this

NOTE Confidence: 0.9966096

00:38:14.400 --> 00:38:14.900 information

NOTE Confidence: 0.87152255

00:38:15.280 --> 00:38:16.099 very disparate,

NOTE Confidence: 0.9925275

00:38:16.405 --> 00:38:17.365 and there were no real

NOTE Confidence: 0.9925275

00:38:17.365 --> 00:38:19.225 databases that held this information.

NOTE Confidence: 0.9759908

00:38:19.765 --> 00:38:20.485 And if there was a

NOTE Confidence: 0.9759908

00:38:20.485 --> 00:38:21.685 database, it was quite old

NOTE Confidence: 0.9759908

00:38:21.685 --> 00:38:23.045 or didn't really have everything

NOTE Confidence: 0.9759908

00:38:23.045 --> 00:38:23.625 in there.

NOTE Confidence: 0.9563378

00:38:23.925 --> 00:38:25.205 So she decided to make

NOTE Confidence: 0.9563378

00:38:25.205 --> 00:38:26.805 her own database, which is

NOTE Confidence: 0.9563378

00:38:26.805 --> 00:38:28.025 called Onco Sexome.

NOTE Confidence: 0.98093605

00:38:28.645 --> 00:38:29.685 And what she's done is

NOTE Confidence: 0.98093605

00:38:29.685 --> 00:38:31.340 amass all of the sex

NOTE Confidence: 0.98093605

00:38:31.340 --> 00:38:32.540 differences that she could find

NOTE Confidence: 0.98093605

00:38:32.540 --> 00:38:34.239 on seventy one different cancers.

NOTE Confidence: 0.98991096

00:38:34.940 --> 00:38:36.219 So we have four domains

NOTE Confidence: 0.98991096

00:38:36.219 --> 00:38:37.260 here. I can't talk about

NOTE Confidence: 0.98991096

00:38:37.260 --> 00:38:38.380 it in detail because of

NOTE Confidence: 0.98991096

00:38:38.380 --> 00:38:40.620 time, but basically we have,

NOTE Confidence: 0.9551863

00:38:41.020 --> 00:38:42.620 sex differences on over two

NOTE Confidence: 0.9551863

00:38:42.620 --> 00:38:45.265 thousand drugs, the anticancer drugs,

NOTE Confidence: 0.9551863

00:38:45.405 --> 00:38:46.625 in terms of pharmacokinetics,

NOTE Confidence: 0.955247

00:38:47.325 --> 00:38:49.405 adverse responses, side effects. You

NOTE Confidence: 0.955247

00:38:49.405 --> 00:38:50.605 know, throughout we see with

NOTE Confidence: 0.955247

00:38:50.605 --> 00:38:52.285 five Fluorouracil, it has poor

NOTE Confidence: 0.955247

00:38:52.285 --> 00:38:53.805 efficacy and more side effects

NOTE Confidence: 0.955247

00:38:53.805 --> 00:38:55.565 for females with colorectal cancer.

NOTE Confidence: 0.955247

00:38:55.565 --> 00:38:56.845 That's just one finding from

NOTE Confidence: 0.955247

00:38:56.845 --> 00:38:57.345 this.

NOTE Confidence: 0.9635956

00:38:58.920 --> 00:39:00.200 Over three hundred and sixty

NOTE Confidence: 0.9635956

00:39:00.200 --> 00:39:01.719 risk factors using data from

NOTE Confidence: 0.9635956

00:39:01.719 --> 00:39:02.219 IARC,

NOTE Confidence: 0.9977241

00:39:02.760 --> 00:39:04.380 and then nearly twelve thousand

NOTE Confidence: 0.9977241

00:39:04.440 --> 00:39:06.599 different molecular differences in terms

NOTE Confidence: 0.9977241

00:39:06.599 --> 00:39:08.460 of genes, immune cells,

NOTE Confidence: 0.8839794

00:39:09.800 --> 00:39:11.420 hormones, and proteins.

NOTE Confidence: 0.9223757

00:39:12.215 --> 00:39:13.975 And then nearly fifteen hundred

NOTE Confidence: 0.9223757

00:39:13.975 --> 00:39:15.895 different microbes that are changing

NOTE Confidence: 0.9223757

00:39:15.895 --> 00:39:16.614 their risk,

NOTE Confidence: 0.9956952

00:39:17.015 --> 00:39:18.535 for different types of cancers.

NOTE Confidence: 0.9956952

00:39:18.535 --> 00:39:19.495 So if you're working in

NOTE Confidence: 0.9956952

00:39:19.495 --> 00:39:20.235 this area,

NOTE Confidence: 0.95214087

00:39:20.614 --> 00:39:22.055 I'd encourage you to check

NOTE Confidence: 0.95214087

00:39:22.055 --> 00:39:22.715 it out.

NOTE Confidence: 0.9833541

00:39:23.895 --> 00:39:25.035 So just to summarize,

NOTE Confidence: 0.96084046

00:39:26.480 --> 00:39:27.359 we do see in our

NOTE Confidence: 0.96084046

00:39:27.359 --> 00:39:29.440 studies that ASNS knockout slows

NOTE Confidence: 0.96084046

00:39:29.440 --> 00:39:31.359 tumor growth and decreases tumor

NOTE Confidence: 0.96084046

00:39:31.359 --> 00:39:32.420 asparagine levels.

NOTE Confidence: 0.99126554

00:39:33.039 --> 00:39:34.099 Asparagine supplementation

NOTE Confidence: 0.9680479

00:39:34.480 --> 00:39:36.319 has this differential effect on

NOTE Confidence: 0.9680479

00:39:36.319 --> 00:39:38.579 CRC tumors that express ASNS,

NOTE Confidence: 0.9061513

00:39:39.665 --> 00:39:41.265 and GPO signaling could be

NOTE Confidence: 0.9061513

00:39:41.265 --> 00:39:42.325 driving these differences,

NOTE Confidence: 0.98395604

00:39:43.025 --> 00:39:44.385 where high GPO is actually

NOTE Confidence: 0.98395604

00:39:44.385 --> 00:39:45.744 linked to poor outcomes for

NOTE Confidence: 0.98395604

00:39:45.744 --> 00:39:47.685 advanced stage females only.

NOTE Confidence: 0.8955059

00:39:48.065 --> 00:39:49.744 So I'm gonna have, Serge

NOTE Confidence: 0.8955059

00:39:49.744 --> 00:39:50.805 wrap up the last.

NOTE Confidence: 0.93812436

00:39:55.480 --> 00:39:56.920 The team science approach for

NOTE Confidence: 0.93812436

00:39:56.920 --> 00:39:58.440 the Johnson and Khan Labs

NOTE Confidence: 0.93812436

00:39:58.440 --> 00:39:59.640 for nearly a decade has

NOTE Confidence: 0.93812436

00:39:59.640 --> 00:40:01.099 generated a lot of exciting

NOTE Confidence: 0.93812436

00:40:01.160 --> 00:40:01.660 findings,

NOTE Confidence: 0.99946105

00:40:01.960 --> 00:40:03.160 but we continue to build

NOTE Confidence: 0.99946105

00:40:03.160 --> 00:40:04.380 what we've done together.

NOTE Confidence: 0.9538114

00:40:05.105 --> 00:40:06.305 As part of our current

NOTE Confidence: 0.9538114

00:40:06.305 --> 00:40:07.424 r o one, our labs

NOTE Confidence: 0.9538114

00:40:07.424 --> 00:40:08.704 are looking at sex specific

NOTE Confidence: 0.9538114

00:40:08.704 --> 00:40:10.724 clinical factors which regulate asparagin

NOTE Confidence: 0.9538114

00:40:10.785 --> 00:40:13.285 metabolism in colorectal cancer patients.

NOTE Confidence: 0.9967776

00:40:14.145 --> 00:40:15.344 We are building a well

NOTE Confidence: 0.9967776

00:40:15.344 --> 00:40:16.964 annotated clinical database.

NOTE Confidence: 0.95039874

00:40:17.870 --> 00:40:19.570 Jean, who's in my lab,

NOTE Confidence: 0.96300596

00:40:20.110 --> 00:40:21.390 is working on this where

NOTE Confidence: 0.96300596

00:40:21.390 --> 00:40:23.550 he's building a robust database

NOTE Confidence: 0.96300596

00:40:23.550 --> 00:40:24.910 of patients with stage three

NOTE Confidence: 0.96300596

00:40:24.910 --> 00:40:27.150 colon cancer, stage four colon

NOTE Confidence: 0.96300596

00:40:27.150 --> 00:40:28.989 cancer, stage four colon cancer,

NOTE Confidence: 0.96300596

00:40:28.989 --> 00:40:29.810 liver metastases,

NOTE Confidence: 0.9986531

00:40:30.565 --> 00:40:31.385 and he is

NOTE Confidence: 0.9009376

00:40:31.925 --> 00:40:33.305 developing tissue microarrays,

NOTE Confidence: 0.9336769

00:40:34.405 --> 00:40:35.525 and he's about to start

NOTE Confidence: 0.9336769

00:40:35.525 --> 00:40:37.445 to doing spatial transcriptomics experiments

NOTE Confidence: 0.9336769

00:40:37.445 --> 00:40:39.145 and RNA sequencing experiments

NOTE Confidence: 0.97386444

00:40:39.525 --> 00:40:40.645 on the tumor blocks to

NOTE Confidence: 0.97386444

00:40:40.645 --> 00:40:42.265 better characterize the asparagine

NOTE Confidence: 0.98400694

00:40:42.725 --> 00:40:44.185 and the estrogen pathways.

NOTE Confidence: 0.9802277

00:40:45.239 --> 00:40:46.280 At the same time, we're

NOTE Confidence: 0.9802277

00:40:46.280 --> 00:40:48.600 also prospectively collecting tumors and

NOTE Confidence: 0.9802277

00:40:48.600 --> 00:40:50.620 stool from patients in collaborations

NOTE Confidence: 0.9802277

00:40:50.680 --> 00:40:52.680 with our wonderful colorectal colleagues

NOTE Confidence: 0.9802277

00:40:52.680 --> 00:40:53.880 at the Yale New Haven

NOTE Confidence: 0.9802277

00:40:53.880 --> 00:40:55.719 Hospital, Bridgeport Hospital. Again, we

NOTE Confidence: 0.9802277

00:40:55.719 --> 00:40:56.920 have a great health system

NOTE Confidence: 0.9802277

00:40:56.920 --> 00:40:58.520 here, so two different sites

NOTE Confidence: 0.9802277

00:40:58.520 --> 00:40:59.260 of surgeons,

NOTE Confidence: 0.976258

00:40:59.744 --> 00:41:01.505 have are helping us, crew

NOTE Confidence: 0.976258

00:41:01.505 --> 00:41:02.805 some of our patients here.

NOTE Confidence: 0.9296355

00:41:03.184 --> 00:41:04.964 And finally, we're closely collaborating

NOTE Confidence: 0.9296355

00:41:05.105 --> 00:41:06.864 with doctor Juthen Roper, who's

NOTE Confidence: 0.9296355

00:41:06.864 --> 00:41:07.525 a gastroenterologist

NOTE Confidence: 0.9966842

00:41:07.825 --> 00:41:09.184 at Duke University and has

NOTE Confidence: 0.9966842

00:41:09.184 --> 00:41:10.384 been a wonderful partner for

NOTE Confidence: 0.9966842

00:41:10.384 --> 00:41:11.444 Caroline and I.

NOTE Confidence: 0.964102

00:41:12.680 --> 00:41:14.120 Through our collaboration with doctor

NOTE Confidence: 0.964102

00:41:14.120 --> 00:41:14.620 Roper,

NOTE Confidence: 0.99335885

00:41:15.160 --> 00:41:16.540 we're using an orthotopic

NOTE Confidence: 0.9263807

00:41:16.840 --> 00:41:18.380 mouse model using

NOTE Confidence: 0.92192936

00:41:18.680 --> 00:41:19.739 CRISPR edited

NOTE Confidence: 0.9686458

00:41:20.040 --> 00:41:22.360 ASNS edited cells to better

NOTE Confidence: 0.9686458

00:41:22.360 --> 00:41:22.860 recapitulate

NOTE Confidence: 0.999722

00:41:23.160 --> 00:41:24.380 the metabolic changes

NOTE Confidence: 0.9900244

00:41:24.680 --> 00:41:26.280 in the colorectal cancer during

NOTE Confidence: 0.9900244

00:41:26.280 --> 00:41:28.224 cancer development and the progression

NOTE Confidence: 0.9900244

00:41:28.224 --> 00:41:29.984 towards liver metastasis, which is

NOTE Confidence: 0.9900244

00:41:29.984 --> 00:41:31.364 a great model to study

NOTE Confidence: 0.9900244

00:41:31.425 --> 00:41:32.945 our, stage three and stage

NOTE Confidence: 0.9900244

00:41:32.945 --> 00:41:34.325 four colorectal cancer.

NOTE Confidence: 0.9381725

00:41:36.785 --> 00:41:38.244 In addition to our RO1,

NOTE Confidence: 0.9908987

00:41:38.705 --> 00:41:39.785 we are building on some

NOTE Confidence: 0.9908987

00:41:39.785 --> 00:41:41.105 of the additional high impact

NOTE Confidence: 0.9908987

00:41:41.105 --> 00:41:42.500 work, that we've done, some

NOTE Confidence: 0.9908987

00:41:42.500 --> 00:41:43.800 of which is already published,

NOTE Confidence: 0.9971068

00:41:44.260 --> 00:41:45.140 and some of which is

NOTE Confidence: 0.9971068

00:41:45.140 --> 00:41:46.099 based on one of our

NOTE Confidence: 0.9971068

00:41:46.099 --> 00:41:46.599 R21s

NOTE Confidence: 0.9334688

00:41:47.219 --> 00:41:48.200 on social disadvantages

NOTE Confidence: 0.9775118

00:41:49.140 --> 00:41:50.739 and patient outcomes, which are

NOTE Confidence: 0.9775118

00:41:50.739 --> 00:41:52.020 linked to increased deaths in

NOTE Confidence: 0.9775118

00:41:52.020 --> 00:41:54.200 African Americans with colorectal cancer,

NOTE Confidence: 0.933166

00:41:54.500 --> 00:41:55.320 and the microbiome.

NOTE Confidence: 0.9487497

00:41:56.265 --> 00:41:57.385 We continue to use the

NOTE Confidence: 0.9487497

00:41:57.385 --> 00:41:58.825 National Cancer Database. I see

NOTE Confidence: 0.9487497

00:41:58.825 --> 00:41:59.944 Wafa here in the audience.

NOTE Confidence: 0.9487497

00:41:59.944 --> 00:42:00.905 She's another member of our

NOTE Confidence: 0.9487497

00:42:00.905 --> 00:42:01.944 lab who's working on that

NOTE Confidence: 0.9487497

00:42:01.944 --> 00:42:03.065 right now in the All

NOTE Confidence: 0.9487497

00:42:03.065 --> 00:42:04.744 of Us database, which, Sam

NOTE Confidence: 0.9487497

00:42:04.744 --> 00:42:05.944 Butinski, who's one of our

NOTE Confidence: 0.9487497

00:42:05.944 --> 00:42:07.224 former surgical who's a current

NOTE Confidence: 0.9487497

00:42:07.224 --> 00:42:08.744 surgical resident, was in the

NOTE Confidence: 0.9487497

00:42:08.744 --> 00:42:09.210 lab,

NOTE Confidence: 0.9958765

00:42:09.690 --> 00:42:11.050 has been using to examine

NOTE Confidence: 0.9958765

00:42:11.050 --> 00:42:12.650 risk factors and barriers to

NOTE Confidence: 0.9958765

00:42:12.650 --> 00:42:14.010 GI cancer care and the

NOTE Confidence: 0.9958765

00:42:14.010 --> 00:42:14.510 well-being.

NOTE Confidence: 0.98578805

00:42:15.130 --> 00:42:16.570 And finally, our labs have

NOTE Confidence: 0.98578805

00:42:16.570 --> 00:42:17.310 also shown,

NOTE Confidence: 0.93821865

00:42:17.930 --> 00:42:19.690 through the work of, Montana

NOTE Confidence: 0.93821865

00:42:19.690 --> 00:42:21.530 Morris, who's actually a research

NOTE Confidence: 0.93821865

00:42:21.530 --> 00:42:22.969 fellow at University of Pennsylvania,

NOTE Confidence: 0.93821865

00:42:22.969 --> 00:42:24.954 and Doctor Abhishek Jain, who

NOTE Confidence: 0.93821865

00:42:24.954 --> 00:42:25.594 is a member of the

NOTE Confidence: 0.93821865

00:42:25.594 --> 00:42:26.795 Johnson Lab, who is now

NOTE Confidence: 0.93821865

00:42:26.795 --> 00:42:28.335 a faculty at SUNY Albany,

NOTE Confidence: 0.93821865

00:42:28.395 --> 00:42:29.515 have shown that there and

NOTE Confidence: 0.93821865

00:42:29.515 --> 00:42:30.795 they've shown that there's clear

NOTE Confidence: 0.93821865

00:42:30.795 --> 00:42:31.295 metabolic

NOTE Confidence: 0.99957854

00:42:31.594 --> 00:42:32.094 heterogeneity

NOTE Confidence: 0.9720095

00:42:32.635 --> 00:42:34.415 on colon cancer liver metastases,

NOTE Confidence: 0.94901246

00:42:35.194 --> 00:42:36.075 based on the site of

NOTE Confidence: 0.94901246

00:42:36.075 --> 00:42:37.194 the primary tumor of the

NOTE Confidence: 0.94901246

00:42:37.194 --> 00:42:38.515 sidedness, the right sided versus

NOTE Confidence: 0.94901246

00:42:38.515 --> 00:42:39.675 the left side going to

NOTE Confidence: 0.94901246

00:42:39.675 --> 00:42:41.739 one of Caroline's earlier slides.

NOTE Confidence: 0.8719573

00:42:42.760 --> 00:42:43.820 So in conclusion,

NOTE Confidence: 0.993117

00:42:44.359 --> 00:42:45.739 studying sex as a biological

NOTE Confidence: 0.993117

00:42:45.880 --> 00:42:47.400 variable is important in the

NOTE Confidence: 0.993117

00:42:47.400 --> 00:42:49.020 pursuit towards precision medicine.

NOTE Confidence: 0.9684404

00:42:51.160 --> 00:42:52.200 All the work presented by

NOTE Confidence: 0.9684404

00:42:52.200 --> 00:42:53.640 doctor Johnson and I, however,

NOTE Confidence: 0.9684404

00:42:53.640 --> 00:42:55.099 is clearly a team effort.

NOTE Confidence: 0.9684404

00:42:55.275 --> 00:42:56.795 So here's our acknowledgment slide,

NOTE Confidence: 0.9684404

00:42:56.795 --> 00:42:57.755 and it shows the current

NOTE Confidence: 0.9684404

00:42:57.755 --> 00:42:58.795 members of each of our

NOTE Confidence: 0.9684404

00:42:58.795 --> 00:43:00.395 labs, and it acknowledges the

NOTE Confidence: 0.9684404

00:43:00.395 --> 00:43:01.835 many previous members who we

NOTE Confidence: 0.9684404

00:43:01.835 --> 00:43:03.295 have been fortunate to mentor.

NOTE Confidence: 0.9653355

00:43:04.075 --> 00:43:05.614 We have had wonderful collaborations

NOTE Confidence: 0.9653355

00:43:05.674 --> 00:43:06.714 at Yale, both at the

NOTE Confidence: 0.9653355

00:43:06.714 --> 00:43:07.994 School of Public Health and

NOTE Confidence: 0.9653355

00:43:07.994 --> 00:43:09.355 the School of Medicine across

NOTE Confidence: 0.9653355

00:43:09.355 --> 00:43:10.335 multiple departments,

NOTE Confidence: 0.9994907

00:43:10.660 --> 00:43:12.020 and some of those individuals

NOTE Confidence: 0.9994907

00:43:12.020 --> 00:43:12.920 are listed here.

NOTE Confidence: 0.94626045

00:43:13.460 --> 00:43:14.739 Across the United States, we're

NOTE Confidence: 0.94626045

00:43:14.739 --> 00:43:16.200 fortunate to have great collaborations

NOTE Confidence: 0.94626045

00:43:16.260 --> 00:43:17.700 with doctor Jatin Roper at

NOTE Confidence: 0.94626045

00:43:17.700 --> 00:43:19.620 Duke University and, doctor Philip

NOTE Confidence: 0.94626045

00:43:19.620 --> 00:43:21.060 Pady at Memorial Sloan Kettering

NOTE Confidence: 0.94626045

00:43:21.060 --> 00:43:21.960 Cancer Center.

NOTE Confidence: 0.9960851

00:43:22.340 --> 00:43:23.380 So we thank you for

NOTE Confidence: 0.9960851

00:43:23.380 --> 00:43:24.500 your time, and the floor

NOTE Confidence: 0.9960851

00:43:24.500 --> 00:43:25.719 is open for questions.

NOTE Confidence: 0.9769714

00:43:26.935 --> 00:43:27.994 Thank you very much.

NOTE Confidence: 0.79899395

00:43:37.094 --> 00:43:38.315 I think there's some microphones

NOTE Confidence: 0.79899395

00:43:38.375 --> 00:43:40.155 here of, being with Mozart.

NOTE Confidence: 0.9885864

00:43:50.390 --> 00:43:51.670 That was a great talk.

NOTE Confidence: 0.9885864

00:43:51.670 --> 00:43:52.730 Thank you very much.

NOTE Confidence: 0.9637282

00:43:54.094 --> 00:43:55.535 In one of the slides,

NOTE Confidence: 0.9637282

00:43:55.535 --> 00:43:56.835 you mentioned that there

NOTE Confidence: 0.9978851

00:43:57.535 --> 00:43:58.994 were seven hundred and something

NOTE Confidence: 0.98970425

00:43:59.694 --> 00:44:01.635 specimens from the Sloan Kettering

NOTE Confidence: 0.97528976

00:44:02.255 --> 00:44:03.934 database over a thirty year

NOTE Confidence: 0.97528976

00:44:03.934 --> 00:44:05.694 period or something. It doesn't

NOTE Confidence: 0.97528976

00:44:05.694 --> 00:44:06.895 seem like very many. So

NOTE Confidence: 0.97528976

00:44:06.895 --> 00:44:08.390 did you have to choose

NOTE Confidence: 0.97528976

00:44:08.390 --> 00:44:10.870 different specimens, or how how

NOTE Confidence: 0.97528976

00:44:10.870 --> 00:44:11.989 come there were only seven

NOTE Confidence: 0.97528976

00:44:11.989 --> 00:44:12.969 hundred and sixty?

NOTE Confidence: 0.89855057

00:44:13.750 --> 00:44:14.870 Yeah. Do you want me

NOTE Confidence: 0.89855057

00:44:14.870 --> 00:44:15.670 to answer that? I don't

NOTE Confidence: 0.89855057

00:44:15.670 --> 00:44:16.550 know the answer to that.

NOTE Confidence: 0.89855057

00:44:16.550 --> 00:44:17.050 Okay.

NOTE Confidence: 0.95508707

00:44:18.150 --> 00:44:19.510 You know, that was developed

NOTE Confidence: 0.95508707

00:44:19.510 --> 00:44:20.870 over it's it it just

NOTE Confidence: 0.95508707

00:44:20.870 --> 00:44:22.185 shows how much hard work

NOTE Confidence: 0.95508707

00:44:22.185 --> 00:44:23.305 was to get to those

NOTE Confidence: 0.95508707

00:44:23.305 --> 00:44:24.585 seven hundred sixty two. So

NOTE Confidence: 0.95508707

00:44:24.585 --> 00:44:25.485 those were accrued,

NOTE Confidence: 0.98924446

00:44:26.185 --> 00:44:27.625 for, you know, about fifteen

NOTE Confidence: 0.98924446

00:44:27.625 --> 00:44:28.605 years or so,

NOTE Confidence: 0.9918337

00:44:28.905 --> 00:44:29.705 and part of it when

NOTE Confidence: 0.9918337

00:44:29.705 --> 00:44:30.745 I was a research fellow

NOTE Confidence: 0.9918337

00:44:30.745 --> 00:44:32.825 in, at Memorial Sloan Kettering.

NOTE Confidence: 0.9918337

00:44:32.825 --> 00:44:33.325 And

NOTE Confidence: 0.9978315

00:44:33.945 --> 00:44:35.325 but, you know,

NOTE Confidence: 0.9903696

00:44:35.705 --> 00:44:36.585 I think some of it

NOTE Confidence: 0.9903696

00:44:36.585 --> 00:44:38.020 came down to some being

NOTE Confidence: 0.9903696

00:44:38.020 --> 00:44:39.960 practical about certain things, about

NOTE Confidence: 0.9903696

00:44:40.100 --> 00:44:41.300 what time the tumor was

NOTE Confidence: 0.9903696

00:44:41.300 --> 00:44:42.740 removed in the operating room

NOTE Confidence: 0.9903696

00:44:42.740 --> 00:44:43.780 and who was around that

NOTE Confidence: 0.9903696

00:44:43.780 --> 00:44:44.280 day,

NOTE Confidence: 0.9456104

00:44:45.140 --> 00:44:46.500 because these had to be

NOTE Confidence: 0.9456104

00:44:46.500 --> 00:44:48.500 captured and snap frozen and,

NOTE Confidence: 0.9456104

00:44:48.980 --> 00:44:50.260 prepared freshly so they could

NOTE Confidence: 0.9456104

00:44:50.260 --> 00:44:51.880 be used for subsequent analyses.

NOTE Confidence: 0.9456104

00:44:51.940 --> 00:44:52.020 But,

NOTE Confidence: 0.9971116

00:44:53.255 --> 00:44:55.015 but, it's it's actually one

NOTE Confidence: 0.9971116

00:44:55.015 --> 00:44:56.155 of the largest biorepositories

NOTE Confidence: 0.9809454

00:44:57.094 --> 00:44:57.835 in the world.

NOTE Confidence: 0.9773646

00:44:58.455 --> 00:45:00.295 So, but it did you

NOTE Confidence: 0.9773646

00:45:00.295 --> 00:45:01.415 know, ideally, we would have

NOTE Confidence: 0.9773646

00:45:01.415 --> 00:45:02.135 had more, but I think,

NOTE Confidence: 0.9773646

00:45:02.135 --> 00:45:03.495 you know, seven hundred sixty

NOTE Confidence: 0.9773646

00:45:03.495 --> 00:45:04.855 two is, but those are

NOTE Confidence: 0.9773646

00:45:04.855 --> 00:45:05.735 all of the cases from

NOTE Confidence: 0.9773646

00:45:05.735 --> 00:45:06.315 the biorepository.

NOTE Confidence: 0.9280071

00:45:15.060 --> 00:45:15.560 Yeah.

NOTE Confidence: 0.99184024

00:45:19.380 --> 00:45:20.760 Thank you for the presentation.

NOTE Confidence: 0.94378614

00:45:21.540 --> 00:45:22.100 Did you,

NOTE Confidence: 0.8881928

00:45:23.325 --> 00:45:24.945 assess the the immunostatice

NOTE Confidence: 0.91586

00:45:26.844 --> 00:45:27.825 of your patients?

NOTE Confidence: 0.8787646

00:45:28.445 --> 00:45:29.984 Particular, for instance,

NOTE Confidence: 0.8906498

00:45:30.445 --> 00:45:30.945 cytokine,

NOTE Confidence: 0.9035448

00:45:31.325 --> 00:45:31.825 chemokine,

NOTE Confidence: 0.9778756

00:45:33.005 --> 00:45:33.744 those parameters.

NOTE Confidence: 0.99548256

00:45:34.925 --> 00:45:36.864 That's one. Number two,

NOTE Confidence: 0.9754653

00:45:37.539 --> 00:45:39.400 you're you're talking about

NOTE Confidence: 0.7870941

00:45:39.859 --> 00:45:41.859 the difference of the, aging

NOTE Confidence: 0.7870941

00:45:41.859 --> 00:45:42.359 process,

NOTE Confidence: 0.69784683

00:45:43.460 --> 00:45:44.200 a sex

NOTE Confidence: 0.67622083

00:45:45.619 --> 00:45:46.119 and,

NOTE Confidence: 0.979756

00:45:46.660 --> 00:45:47.859 among the patient with

NOTE Confidence: 0.74305195

00:45:49.140 --> 00:45:50.519 how about the print

NOTE Confidence: 0.9918585

00:45:51.335 --> 00:45:52.875 the picture of aging

NOTE Confidence: 0.7620716

00:45:54.214 --> 00:45:55.194 in other age

NOTE Confidence: 0.8740737

00:45:56.135 --> 00:45:57.194 into the picture,

NOTE Confidence: 0.92884874

00:45:57.894 --> 00:45:59.894 and then relate that to

NOTE Confidence: 0.92884874

00:45:59.894 --> 00:46:00.394 the

NOTE Confidence: 0.9061276

00:46:00.694 --> 00:46:01.594 sex hormone?

NOTE Confidence: 0.86420554

00:46:03.760 --> 00:46:04.640 Yeah. So that there are

NOTE Confidence: 0.86420554

00:46:04.640 --> 00:46:05.620 two great questions.

NOTE Confidence: 0.9730244

00:46:06.320 --> 00:46:07.840 For the immune status, we

NOTE Confidence: 0.9730244

00:46:07.840 --> 00:46:09.120 haven't looked at that, but

NOTE Confidence: 0.9730244

00:46:09.120 --> 00:46:10.239 I think that's something that

NOTE Confidence: 0.9730244

00:46:10.239 --> 00:46:11.280 we can look at with

NOTE Confidence: 0.9730244

00:46:11.280 --> 00:46:12.980 the micro rate, the

NOTE Confidence: 0.8443471

00:46:13.840 --> 00:46:15.860 TMAs rather that we're developing

NOTE Confidence: 0.9983773

00:46:16.160 --> 00:46:16.980 in the lab.

NOTE Confidence: 0.9875481

00:46:17.895 --> 00:46:19.335 In terms of age, so

NOTE Confidence: 0.9875481

00:46:19.335 --> 00:46:21.415 our studies primarily have focused

NOTE Confidence: 0.9875481

00:46:21.415 --> 00:46:22.155 on individuals

NOTE Confidence: 0.9820768

00:46:22.455 --> 00:46:23.575 over fifty five. So I

NOTE Confidence: 0.9820768

00:46:23.575 --> 00:46:25.015 think they're fifty five to

NOTE Confidence: 0.9820768

00:46:25.015 --> 00:46:26.795 eighteen. There probably is some,

NOTE Confidence: 0.9820768

00:46:27.015 --> 00:46:28.475 you know, range within

NOTE Confidence: 0.979684

00:46:28.775 --> 00:46:30.135 that age group as well

NOTE Confidence: 0.979684

00:46:30.135 --> 00:46:31.755 in terms of the metabolites.

NOTE Confidence: 0.9952445

00:46:32.550 --> 00:46:33.989 For the prognostic work, we

NOTE Confidence: 0.9952445

00:46:33.989 --> 00:46:34.489 do

NOTE Confidence: 0.96957123

00:46:34.870 --> 00:46:36.310 adjust for age to take

NOTE Confidence: 0.96957123

00:46:36.310 --> 00:46:37.290 that into account,

NOTE Confidence: 0.99731547

00:46:37.590 --> 00:46:38.710 but we have started some

NOTE Confidence: 0.99731547

00:46:38.710 --> 00:46:39.450 new studies,

NOTE Confidence: 0.9869741

00:46:39.989 --> 00:46:41.350 last year on early onset

NOTE Confidence: 0.9869741

00:46:41.350 --> 00:46:43.530 colorectal cancer. So for patients

NOTE Confidence: 0.9869741

00:46:43.670 --> 00:46:45.050 under the age of fifty,

NOTE Confidence: 0.9869741

00:46:45.325 --> 00:46:46.445 We had a paper out

NOTE Confidence: 0.9869741

00:46:46.445 --> 00:46:48.205 earlier this year with that

NOTE Confidence: 0.9869741

00:46:48.205 --> 00:46:48.705 data.

NOTE Confidence: 0.9870621

00:46:49.405 --> 00:46:50.285 We don't have a huge

NOTE Confidence: 0.9870621

00:46:50.285 --> 00:46:52.285 number of cases, so we

NOTE Confidence: 0.9870621

00:46:52.285 --> 00:46:54.305 didn't stratify by sex initially.

NOTE Confidence: 0.9860852

00:46:54.605 --> 00:46:55.805 I think there's about fifty

NOTE Confidence: 0.9860852

00:46:55.805 --> 00:46:57.885 cases for early onset, but

NOTE Confidence: 0.9860852

00:46:57.885 --> 00:46:59.085 we do see some, you

NOTE Confidence: 0.9860852

00:46:59.085 --> 00:47:01.469 know, striking differences compared to

NOTE Confidence: 0.9860852

00:47:01.469 --> 00:47:02.210 late onset.

NOTE Confidence: 0.98929065

00:47:02.910 --> 00:47:03.790 But we have a study

NOTE Confidence: 0.98929065

00:47:03.790 --> 00:47:04.670 right now where we are

NOTE Confidence: 0.98929065

00:47:04.670 --> 00:47:06.210 looking at early onset.

NOTE Confidence: 0.9127761

00:47:06.590 --> 00:47:07.330 We found

NOTE Confidence: 0.97273576

00:47:07.790 --> 00:47:09.469 actually, Asparagine doesn't seem to

NOTE Confidence: 0.97273576

00:47:09.469 --> 00:47:10.670 be coming up as an

NOTE Confidence: 0.97273576

00:47:10.670 --> 00:47:12.510 important pathway for the early

NOTE Confidence: 0.97273576

00:47:12.510 --> 00:47:13.870 onset, but we have,

NOTE Confidence: 0.96893847

00:47:15.005 --> 00:47:17.025 also found data in collaboration

NOTE Confidence: 0.96893847

00:47:17.085 --> 00:47:19.165 with other individuals to validate

NOTE Confidence: 0.96893847

00:47:19.165 --> 00:47:20.205 that work even though it's,

NOTE Confidence: 0.96893847

00:47:20.205 --> 00:47:20.945 like, smaller

NOTE Confidence: 0.96523696

00:47:21.405 --> 00:47:23.245 sample sizes. So, yeah, it's

NOTE Confidence: 0.96523696

00:47:23.245 --> 00:47:23.745 definitely

NOTE Confidence: 0.9391522

00:47:24.045 --> 00:47:25.165 an important thing to look

NOTE Confidence: 0.9391522

00:47:25.165 --> 00:47:26.525 at. And in our in

NOTE Confidence: 0.9391522

00:47:26.525 --> 00:47:27.167 our current collections,

NOTE Confidence: 0.85633177

00:47:29.170 --> 00:47:30.370 Yale, we are looking at

NOTE Confidence: 0.85633177

00:47:30.370 --> 00:47:32.550 things such as, oral contraceptive

NOTE Confidence: 0.85633177

00:47:32.690 --> 00:47:33.190 use,

NOTE Confidence: 0.96665543

00:47:33.730 --> 00:47:35.430 HRT use, and,

NOTE Confidence: 0.9774876

00:47:36.690 --> 00:47:37.190 anything

NOTE Confidence: 0.92988217

00:47:37.969 --> 00:47:38.950 else. Oophorectomy.

NOTE Confidence: 0.9877596

00:47:39.810 --> 00:47:40.310 Oophorectomy

NOTE Confidence: 0.91231006

00:47:40.610 --> 00:47:41.810 as well and things like

NOTE Confidence: 0.91231006

00:47:41.810 --> 00:47:42.290 that. So

NOTE Confidence: 0.9565237

00:47:48.675 --> 00:47:49.175 yep.

NOTE Confidence: 0.8723536

00:47:51.315 --> 00:47:52.455 Since you did

NOTE Confidence: 0.8835154

00:47:53.395 --> 00:47:53.895 metabolomics

NOTE Confidence: 0.705103

00:47:54.849 --> 00:47:56.950 and also renate the asparagin

NOTE Confidence: 0.705103

00:47:57.170 --> 00:47:57.670 sensitivities

NOTE Confidence: 0.6913487

00:47:58.050 --> 00:47:59.670 may play clear on there.

NOTE Confidence: 0.99845916

00:48:01.010 --> 00:48:02.369 Did you ever look into

NOTE Confidence: 0.99845916

00:48:02.369 --> 00:48:03.109 the possibility

NOTE Confidence: 0.76740587

00:48:03.650 --> 00:48:04.790 actually asparagin,

NOTE Confidence: 0.977376

00:48:06.609 --> 00:48:07.109 over

NOTE Confidence: 0.8171959

00:48:07.410 --> 00:48:07.910 aspartate

NOTE Confidence: 0.99128485

00:48:08.964 --> 00:48:09.464 ratio

NOTE Confidence: 0.8645668

00:48:10.885 --> 00:48:11.785 as a perimeter.

NOTE Confidence: 0.87811726

00:48:12.805 --> 00:48:14.325 Maybe you'll find the more

NOTE Confidence: 0.87811726

00:48:14.325 --> 00:48:14.825 significance,

NOTE Confidence: 0.99814475

00:48:15.684 --> 00:48:16.184 more

NOTE Confidence: 0.93744683

00:48:16.484 --> 00:48:18.885 drastic difference there using the

NOTE Confidence: 0.93744683

00:48:18.885 --> 00:48:21.125 ratio and relating that to

NOTE Confidence: 0.93744683

00:48:21.285 --> 00:48:22.425 in the in the plasma.

NOTE Confidence: 0.9989847

00:48:23.210 --> 00:48:24.670 That's just one suggestion.

NOTE Confidence: 0.99878335

00:48:25.609 --> 00:48:26.589 Another is

NOTE Confidence: 0.921306

00:48:27.529 --> 00:48:29.769 the we actually intend to

NOTE Confidence: 0.921306

00:48:29.769 --> 00:48:31.309 assess the in the pancreatic

NOTE Confidence: 0.921306

00:48:31.529 --> 00:48:32.029 cancer's

NOTE Confidence: 0.85644644

00:48:32.650 --> 00:48:33.150 situation.

NOTE Confidence: 0.88606024

00:48:34.410 --> 00:48:36.029 The cytokine, chemokine

NOTE Confidence: 0.9480458

00:48:37.049 --> 00:48:37.549 profile

NOTE Confidence: 0.9186454

00:48:38.375 --> 00:48:39.575 of the patient on the

NOTE Confidence: 0.9186454

00:48:39.575 --> 00:48:40.075 different

NOTE Confidence: 0.99038565

00:48:40.935 --> 00:48:41.435 treatment.

NOTE Confidence: 0.99339944

00:48:42.135 --> 00:48:43.575 So if you're interested, you

NOTE Confidence: 0.99339944

00:48:43.575 --> 00:48:44.614 can come to us. We

NOTE Confidence: 0.99339944

00:48:44.614 --> 00:48:45.114 use

NOTE Confidence: 0.9195333

00:48:45.655 --> 00:48:47.994 the beads to evaluate that.

NOTE Confidence: 0.9195333

00:48:48.214 --> 00:48:49.655 Okay. At least the more

NOTE Confidence: 0.9195333

00:48:49.655 --> 00:48:50.395 than ten

NOTE Confidence: 0.9175285

00:48:50.700 --> 00:48:51.920 cytokine, chemokine.

NOTE Confidence: 0.9643522

00:48:52.300 --> 00:48:54.140 Mhmm. Perhaps we can help

NOTE Confidence: 0.9643522

00:48:54.140 --> 00:48:55.500 you on some of those

NOTE Confidence: 0.9643522

00:48:55.500 --> 00:48:56.780 aspects. Thank you. I think

NOTE Confidence: 0.9643522

00:48:56.780 --> 00:48:57.580 it's very generous.

NOTE Confidence: 0.9742709

00:48:58.219 --> 00:48:59.020 Yeah. I think with the

NOTE Confidence: 0.9742709

00:48:59.020 --> 00:49:00.219 ratio, it's a little bit

NOTE Confidence: 0.9742709

00:49:00.219 --> 00:49:01.119 tricky because

NOTE Confidence: 0.95983005

00:49:01.420 --> 00:49:03.094 asparagine can come like, if

NOTE Confidence: 0.95983005

00:49:03.094 --> 00:49:03.815 we're looking at,

NOTE Confidence: 0.997424

00:49:04.214 --> 00:49:06.614 clinical samples, asparagine can come

NOTE Confidence: 0.997424

00:49:06.614 --> 00:49:08.315 from the diet as well

NOTE Confidence: 0.9526497

00:49:08.694 --> 00:49:11.434 and also from microbial production.

NOTE Confidence: 0.9731709

00:49:13.255 --> 00:49:14.934 So we have some studies

NOTE Confidence: 0.9731709

00:49:14.934 --> 00:49:16.474 planned in the mouse models,

NOTE Confidence: 0.9731709

00:49:16.535 --> 00:49:17.755 actually, where we're

NOTE Confidence: 0.9679557

00:49:19.390 --> 00:49:20.750 going to be or we

NOTE Confidence: 0.9679557

00:49:20.750 --> 00:49:21.790 currently have a study where

NOTE Confidence: 0.9679557

00:49:21.790 --> 00:49:23.310 we're knocking out ASNS in

NOTE Confidence: 0.9679557

00:49:23.310 --> 00:49:25.390 a bacterial cell line with

NOTE Confidence: 0.9679557

00:49:25.390 --> 00:49:26.670 Andy Goodman's lab. So we're

NOTE Confidence: 0.9679557

00:49:26.670 --> 00:49:27.630 going to see what effect

NOTE Confidence: 0.9679557

00:49:27.630 --> 00:49:28.510 that might have on the

NOTE Confidence: 0.9679557

00:49:28.510 --> 00:49:29.950 tumor and then also modulate

NOTE Confidence: 0.9679557

00:49:29.950 --> 00:49:30.610 the diet.

NOTE Confidence: 0.9733114

00:49:31.790 --> 00:49:32.989 So yeah. But that's a

NOTE Confidence: 0.9733114

00:49:32.989 --> 00:49:34.210 good idea. Thanks.

NOTE Confidence: 0.98170435

00:49:34.725 --> 00:49:36.005 I mean, I I think

NOTE Confidence: 0.98170435

00:49:36.005 --> 00:49:37.685 that's phenomenal. You know, obviously,

NOTE Confidence: 0.98170435

00:49:37.685 --> 00:49:39.525 it's a wonderful work over

NOTE Confidence: 0.98170435

00:49:39.525 --> 00:49:40.985 a decade for all the

NOTE Confidence: 0.98170435

00:49:41.045 --> 00:49:42.165 the samples that have been

NOTE Confidence: 0.98170435

00:49:42.165 --> 00:49:43.445 collected, the science that has

NOTE Confidence: 0.98170435

00:49:43.445 --> 00:49:44.185 come forth.

NOTE Confidence: 0.9872651

00:49:44.485 --> 00:49:45.285 I think one of the

NOTE Confidence: 0.9872651

00:49:45.285 --> 00:49:46.965 challenges for metabolomics is, of

NOTE Confidence: 0.9872651

00:49:46.965 --> 00:49:47.285 course, the,

NOTE Confidence: 0.96534485

00:49:48.965 --> 00:49:50.030 you know, there's so many

NOTE Confidence: 0.96534485

00:49:50.030 --> 00:49:51.570 variables to adjust for,

NOTE Confidence: 0.97901917

00:49:52.190 --> 00:49:54.130 including, say, genomics, including,

NOTE Confidence: 0.9608254

00:49:54.750 --> 00:49:55.810 you know, the dietary

NOTE Confidence: 0.93180484

00:49:56.910 --> 00:49:58.450 concerns, immune modulation.

NOTE Confidence: 0.9552803

00:50:00.590 --> 00:50:01.710 And and I think also

NOTE Confidence: 0.9552803

00:50:01.710 --> 00:50:03.170 this field of functional metabolomics

NOTE Confidence: 0.9552803

00:50:03.390 --> 00:50:03.950 of, like, how do you

NOTE Confidence: 0.9552803

00:50:03.950 --> 00:50:05.094 actually look at, you know,

NOTE Confidence: 0.9552803

00:50:05.094 --> 00:50:05.594 maybe,

NOTE Confidence: 0.9949115

00:50:06.295 --> 00:50:07.655 labeling some of these molecules

NOTE Confidence: 0.9949115

00:50:07.655 --> 00:50:08.614 and seeing if they're coming

NOTE Confidence: 0.9949115

00:50:08.614 --> 00:50:09.435 up in this.

NOTE Confidence: 0.9885011

00:50:10.055 --> 00:50:10.935 So, you know, I I

NOTE Confidence: 0.9885011

00:50:10.935 --> 00:50:12.295 I sense that you're thinking

NOTE Confidence: 0.9885011

00:50:12.295 --> 00:50:13.655 about animal models as your

NOTE Confidence: 0.9885011

00:50:13.655 --> 00:50:15.175 next step to to confirm

NOTE Confidence: 0.9885011

00:50:15.175 --> 00:50:16.614 your work. But how are

NOTE Confidence: 0.9885011

00:50:16.614 --> 00:50:17.495 you going to account for

NOTE Confidence: 0.9885011

00:50:17.495 --> 00:50:19.370 all this heterogeneity that's that's

NOTE Confidence: 0.9885011

00:50:19.370 --> 00:50:21.210 involved in thinking about colon

NOTE Confidence: 0.9885011

00:50:21.210 --> 00:50:22.730 cancers in general? You know?

NOTE Confidence: 0.9885011

00:50:22.730 --> 00:50:23.930 Because I think diet is

NOTE Confidence: 0.9885011

00:50:23.930 --> 00:50:26.030 different, and your CMS subclasses

NOTE Confidence: 0.9885011

00:50:26.170 --> 00:50:27.370 are different. So what are

NOTE Confidence: 0.9885011

00:50:27.370 --> 00:50:28.489 what are your guys' thoughts

NOTE Confidence: 0.9885011

00:50:28.489 --> 00:50:29.870 on how to address that?

NOTE Confidence: 0.5075389

00:50:30.489 --> 00:50:30.989 Try.

NOTE Confidence: 0.96249837

00:50:31.625 --> 00:50:32.665 Yeah. So that that's a

NOTE Confidence: 0.96249837

00:50:32.665 --> 00:50:34.025 great question, Kieran. So,

NOTE Confidence: 0.9849513

00:50:34.585 --> 00:50:36.125 so that's what we're, you

NOTE Confidence: 0.9849513

00:50:36.265 --> 00:50:37.625 know, working on right now

NOTE Confidence: 0.9849513

00:50:37.625 --> 00:50:38.585 to figure out,

NOTE Confidence: 0.98901325

00:50:39.305 --> 00:50:41.065 because there are different areas

NOTE Confidence: 0.98901325

00:50:41.065 --> 00:50:42.025 that could explain some of

NOTE Confidence: 0.98901325

00:50:42.025 --> 00:50:43.065 our findings in regards to

NOTE Confidence: 0.98901325

00:50:43.065 --> 00:50:44.344 asparagine. And the question is,

NOTE Confidence: 0.98901325

00:50:44.344 --> 00:50:45.305 is it inherent to the

NOTE Confidence: 0.98901325

00:50:45.305 --> 00:50:46.684 tumor in and of itself,

NOTE Confidence: 0.9954396

00:50:47.570 --> 00:50:48.469 which is where,

NOTE Confidence: 0.9502779

00:50:49.010 --> 00:50:50.450 the spheroid and the organoid

NOTE Confidence: 0.9502779

00:50:50.450 --> 00:50:52.070 model is becomes very useful.

NOTE Confidence: 0.9502779

00:50:52.290 --> 00:50:53.510 Is it coming from,

NOTE Confidence: 0.9947231

00:50:54.210 --> 00:50:54.950 the diet?

NOTE Confidence: 0.97394246

00:50:55.489 --> 00:50:57.330 So, hence, the animal model

NOTE Confidence: 0.97394246

00:50:57.330 --> 00:50:58.130 that we have, we can

NOTE Confidence: 0.97394246

00:50:58.130 --> 00:50:59.489 adjust the asparagine in the

NOTE Confidence: 0.97394246

00:50:59.489 --> 00:51:00.530 chow. But in addition to

NOTE Confidence: 0.97394246

00:51:00.530 --> 00:51:02.515 that, we're prospectively collecting,

NOTE Confidence: 0.99943686

00:51:03.295 --> 00:51:05.075 a questionnaire for our patients

NOTE Confidence: 0.9684721

00:51:05.455 --> 00:51:06.575 to see what their dietary

NOTE Confidence: 0.9684721

00:51:06.575 --> 00:51:08.095 intake may be representative of

NOTE Confidence: 0.9684721

00:51:08.095 --> 00:51:09.135 asparagine two to see if

NOTE Confidence: 0.9684721

00:51:09.135 --> 00:51:10.355 it's coming from the environment

NOTE Confidence: 0.9684721

00:51:10.415 --> 00:51:12.175 or the diet. And, the

NOTE Confidence: 0.9684721

00:51:12.175 --> 00:51:13.375 work that Caroline mentioned with

NOTE Confidence: 0.9684721

00:51:13.375 --> 00:51:14.195 Andy Goodman,

NOTE Confidence: 0.96875584

00:51:14.530 --> 00:51:15.570 there's a very good,

NOTE Confidence: 0.98864686

00:51:16.050 --> 00:51:17.570 mouse model that's being used,

NOTE Confidence: 0.9818219

00:51:18.050 --> 00:51:19.110 to look if the microbiome

NOTE Confidence: 0.9818219

00:51:19.250 --> 00:51:20.130 might be driving some of

NOTE Confidence: 0.9818219

00:51:20.130 --> 00:51:21.330 those findings as well too.

NOTE Confidence: 0.9818219

00:51:21.330 --> 00:51:23.250 So I think, you know,

NOTE Confidence: 0.9818219

00:51:23.250 --> 00:51:24.530 to answer the question, stay

NOTE Confidence: 0.9818219

00:51:24.530 --> 00:51:25.570 tuned. Hopefully, in a few

NOTE Confidence: 0.9818219

00:51:25.570 --> 00:51:26.770 years, we'll have some, more

NOTE Confidence: 0.9818219

00:51:26.770 --> 00:51:28.480 specific answers to that.

NOTE Confidence: 0.8728718

00:51:31.145 --> 00:51:31.724 Of course.

NOTE Confidence: 0.97778493

00:51:32.344 --> 00:51:34.025 I think the problem of

NOTE Confidence: 0.97778493

00:51:34.025 --> 00:51:35.005 current approach

NOTE Confidence: 0.9690467

00:51:35.864 --> 00:51:37.244 is too much reductionist

NOTE Confidence: 0.99806386

00:51:37.625 --> 00:51:38.125 approach.

NOTE Confidence: 0.9991398

00:51:39.224 --> 00:51:40.445 You have to consider

NOTE Confidence: 0.99762374

00:51:41.065 --> 00:51:42.045 system biology

NOTE Confidence: 0.9990663

00:51:42.344 --> 00:51:42.844 approach.

NOTE Confidence: 0.8996283

00:51:43.859 --> 00:51:45.059 So when you look at

NOTE Confidence: 0.8996283

00:51:45.059 --> 00:51:46.119 the those marker

NOTE Confidence: 0.8490071

00:51:47.059 --> 00:51:48.339 and then you're looking for

NOTE Confidence: 0.8490071

00:51:48.339 --> 00:51:50.119 the parameter in the plasma,

NOTE Confidence: 0.9963319

00:51:51.299 --> 00:51:52.900 so if you focus just

NOTE Confidence: 0.9963319

00:51:52.900 --> 00:51:53.640 on bacteria

NOTE Confidence: 0.9463972

00:51:54.980 --> 00:51:56.440 or just on the

NOTE Confidence: 0.7828814

00:51:56.895 --> 00:51:58.915 nutrition status may not be.

NOTE Confidence: 0.8918027

00:51:59.295 --> 00:52:00.735 You are looking the overall

NOTE Confidence: 0.8918027

00:52:00.735 --> 00:52:01.235 pictures.

NOTE Confidence: 0.68614405

00:52:02.175 --> 00:52:02.415 And,

NOTE Confidence: 0.95497286

00:52:02.975 --> 00:52:04.655 using the AI system, I

NOTE Confidence: 0.95497286

00:52:04.655 --> 00:52:05.775 think it's going to be

NOTE Confidence: 0.95497286

00:52:05.775 --> 00:52:06.275 discussed,

NOTE Confidence: 0.91722167

00:52:07.055 --> 00:52:08.594 you may end up with

NOTE Confidence: 0.91722167

00:52:08.655 --> 00:52:09.395 a surprising,

NOTE Confidence: 0.8872936

00:52:14.910 --> 00:52:16.210 more surprising results.

NOTE Confidence: 0.96435356

00:52:16.910 --> 00:52:18.210 That's what we did.

NOTE Confidence: 0.9191246

00:52:18.830 --> 00:52:20.350 We actually didn't do too

NOTE Confidence: 0.9191246

00:52:20.350 --> 00:52:21.570 many colon patients.

NOTE Confidence: 0.9199647

00:52:22.565 --> 00:52:24.025 In our clinic trial,

NOTE Confidence: 0.9197749

00:52:24.645 --> 00:52:25.845 we can predict that,

NOTE Confidence: 0.85561466

00:52:26.885 --> 00:52:27.864 we use metabolomics

NOTE Confidence: 0.8203509

00:52:29.125 --> 00:52:31.465 and cytokine chemokine profile,

NOTE Confidence: 0.8822077

00:52:32.405 --> 00:52:34.345 just this two parameter ink.

NOTE Confidence: 0.8822077

00:52:34.580 --> 00:52:36.100 For each patient, we're showing

NOTE Confidence: 0.8822077

00:52:36.100 --> 00:52:37.300 a deal with more than

NOTE Confidence: 0.8822077

00:52:37.300 --> 00:52:38.760 one hundred data points.

NOTE Confidence: 0.94953185

00:52:39.460 --> 00:52:40.660 Well, we have to use

NOTE Confidence: 0.94953185

00:52:40.660 --> 00:52:42.600 the statistics. This is with

NOTE Confidence: 0.78881764

00:52:46.580 --> 00:52:47.080 collaboration.

NOTE Confidence: 0.7764164

00:52:47.805 --> 00:52:48.765 We end up with the

NOTE Confidence: 0.7764164

00:52:48.765 --> 00:52:50.704 only three parameter can predict

NOTE Confidence: 0.81420076

00:52:51.405 --> 00:52:53.565 whether the patient that's a

NOTE Confidence: 0.81420076

00:52:53.645 --> 00:52:54.864 with limit patient,

NOTE Confidence: 0.6130192

00:52:55.885 --> 00:52:56.704 well, response,

NOTE Confidence: 0.9980772

00:52:57.484 --> 00:52:58.385 to the chemotherapy

NOTE Confidence: 0.865388

00:52:59.005 --> 00:52:59.744 or not.

NOTE Confidence: 0.7593032

00:53:00.364 --> 00:53:00.844 And,

NOTE Confidence: 0.8999677

00:53:01.869 --> 00:53:03.150 if in the first two

NOTE Confidence: 0.8999677

00:53:03.150 --> 00:53:03.650 cycles.

NOTE Confidence: 0.771691

00:53:04.349 --> 00:53:05.710 So then just make a

NOTE Confidence: 0.771691

00:53:05.710 --> 00:53:06.210 point.

NOTE Confidence: 0.9690912

00:53:06.910 --> 00:53:09.170 Consider using system biology

NOTE Confidence: 0.8312291

00:53:09.469 --> 00:53:10.369 working together

NOTE Confidence: 0.652914

00:53:11.230 --> 00:53:12.050 with your,

NOTE Confidence: 0.8328412

00:53:13.710 --> 00:53:14.670 with with with the if

NOTE Confidence: 0.8328412

00:53:14.670 --> 00:53:15.170 you'd,

NOTE Confidence: 0.937999

00:53:15.630 --> 00:53:16.690 with with your

NOTE Confidence: 0.84820384

00:53:18.114 --> 00:53:18.614 statistician.

NOTE Confidence: 0.91556346

00:53:19.555 --> 00:53:20.935 They are really powerful

NOTE Confidence: 0.8049804

00:53:21.635 --> 00:53:23.575 tool to explore those complicated

NOTE Confidence: 0.8798084

00:53:24.835 --> 00:53:26.375 issues you brought in.

NOTE Confidence: 0.9490204

00:53:27.875 --> 00:53:29.975 Yeah. Thanks. Very good point.

NOTE Confidence: 0.9490204

00:53:30.195 --> 00:53:31.510 You know, the challenge sometimes,

NOTE Confidence: 0.9490204

00:53:31.510 --> 00:53:32.309 I think, with using the

NOTE Confidence: 0.9490204

00:53:32.309 --> 00:53:33.690 systems approach is, again,

NOTE Confidence: 0.808169

00:53:33.989 --> 00:53:34.730 it can,

NOTE Confidence: 0.9840761

00:53:35.510 --> 00:53:36.630 you're not sure what the

NOTE Confidence: 0.9840761

00:53:36.630 --> 00:53:38.390 effect of where the variable

NOTE Confidence: 0.9840761

00:53:38.390 --> 00:53:40.489 is driving the the biological

NOTE Confidence: 0.9840761

00:53:40.549 --> 00:53:41.589 findings. So that's why we're

NOTE Confidence: 0.9840761

00:53:41.589 --> 00:53:42.630 trying to keep it simple

NOTE Confidence: 0.9840761

00:53:42.630 --> 00:53:44.010 and focus on the microbiome,

NOTE Confidence: 0.99935

00:53:44.735 --> 00:53:45.395 the diet,

NOTE Confidence: 0.99659294

00:53:45.695 --> 00:53:46.355 and then

NOTE Confidence: 0.89165336

00:53:46.815 --> 00:53:48.015 the the cancer cells in

NOTE Confidence: 0.89165336

00:53:48.015 --> 00:53:49.295 and of itself. But,

NOTE Confidence: 0.9748517

00:53:49.614 --> 00:53:50.575 but, yeah, I think,

NOTE Confidence: 0.99804443

00:53:51.055 --> 00:53:52.015 very good points that you

NOTE Confidence: 0.99804443

00:53:52.015 --> 00:53:52.675 bring up.

NOTE Confidence: 0.9803167

00:53:53.455 --> 00:53:54.575 Well, I think it's about

NOTE Confidence: 0.9803167

00:53:54.575 --> 00:53:56.255 time right now. Doctor Khan

NOTE Confidence: 0.9803167

00:53:56.255 --> 00:53:57.695 and doctor Johnson are available

NOTE Confidence: 0.9803167

00:53:57.695 --> 00:53:58.950 by email. If you have

NOTE Confidence: 0.9803167

00:53:59.030 --> 00:54:00.630 questions or you wanna collaborate

NOTE Confidence: 0.9803167

00:54:00.630 --> 00:54:02.230 or wanna access the seven

NOTE Confidence: 0.9803167

00:54:02.230 --> 00:54:03.930 hundred and ninety two patient,

NOTE Confidence: 0.91537

00:54:04.230 --> 00:54:04.730 databank.

NOTE Confidence: 0.9914005

00:54:05.589 --> 00:54:06.550 But thank you very much.

NOTE Confidence: 0.9914005

00:54:06.550 --> 00:54:07.829 It was a wonderful talk.

NOTE Confidence: 0.9914005

00:54:07.829 --> 00:54:08.730 Thank you both.

NOTE Confidence: 0.83966696

00:54:09.589 --> 00:54:10.089 Yes.