## WEBVTT

 $00:00:00.000 \longrightarrow 00:00:02.490$  Support for Yale Cancer Answers

NOTE Confidence: 0.85496736

 $00:00:02.490 \longrightarrow 00:00:04.980$  comes from AstraZeneca, dedicated

NOTE Confidence: 0.85496736

 $00:00:05.057 \longrightarrow 00:00:07.432$  to advancing options and providing

NOTE Confidence: 0.85496736

 $00:00:07.432 \longrightarrow 00:00:10.420$  hope for people living with cancer.

NOTE Confidence: 0.85496736

 $00{:}00{:}10.420 \dashrightarrow 00{:}00{:}14.380$  More information at a strazeneca-us.com.

NOTE Confidence: 0.85496736

 $00:00:14.380 \longrightarrow 00:00:16.522$  Welcome to Yale Cancer Answers with

NOTE Confidence: 0.85496736

00:00:16.522 --> 00:00:18.929 your host doctor Anees Chagpar.

NOTE Confidence: 0.85496736

 $00:00:18.930 \longrightarrow 00:00:20.810$  Yale Cancer Answers features the

NOTE Confidence: 0.85496736

00:00:20.810 --> 00:00:23.111 latest information on cancer care by

NOTE Confidence: 0.85496736

 $00{:}00{:}23.111 \dashrightarrow 00{:}00{:}24.567$  welcoming on cologists and specialists

NOTE Confidence: 0.85496736

 $00:00:24.567 \longrightarrow 00:00:27.019$  who are on the forefront of the

NOTE Confidence: 0.85496736

 $00:00:27.019 \longrightarrow 00:00:28.723$  battle to fight cancer. This week,

NOTE Confidence: 0.85496736

 $00{:}00{:}28.730 \dashrightarrow 00{:}00{:}30.455$  it's a conversation about genetic

NOTE Confidence: 0.85496736

 $00:00:30.455 \longrightarrow 00:00:32.180$  and environmental influences in colon

NOTE Confidence: 0.85496736

 $00:00:32.230 \longrightarrow 00:00:33.980$  cancer with Doctor Caroline Johnson.

 $00:00:33.980 \longrightarrow 00:00:35.960$  Doctor Johnson is assistant professor

NOTE Confidence: 0.85496736

 $00{:}00{:}35.960 {\:{\circ}{\circ}{\circ}}>00{:}00{:}38.341$  of Epidemiology in the Department of

NOTE Confidence: 0.85496736

 $00{:}00{:}38.341 \dashrightarrow 00{:}00{:}40.041$  Environmental Health Sciences at the

NOTE Confidence: 0.85496736

 $00:00:40.041 \longrightarrow 00:00:42.367$  Yale School of Public Health and Doctor

NOTE Confidence: 0.85496736

00:00:42.367 --> 00:00:44.474 Chagpar is a professor of surgical

NOTE Confidence: 0.85496736

 $00:00:44.480 \longrightarrow 00:00:46.930$  oncology at the Yale School of Medicine.

NOTE Confidence: 0.87317926

00:00:48.260 --> 00:00:50.204 Caroline you can

NOTE Confidence: 0.87317926

 $00:00:50.204 \longrightarrow 00:00:52.634$  start off by telling us

NOTE Confidence: 0.87317926

 $00{:}00{:}52.640 \dashrightarrow 00{:}00{:}55.568$  a little bit about your research?

NOTE Confidence: 0.87317926

 $00:00:55.570 \longrightarrow 00:00:58.486$  I use a technology called metabolomics

NOTE Confidence: 0.87317926

NOTE Confidence: 0.87317926

 $00:01:00.922 \longrightarrow 00:01:03.838$  in metabolism that affect colon cancer,

NOTE Confidence: 0.87317926

 $00:01:03.840 \longrightarrow 00:01:05.301$  development progression and

NOTE Confidence: 0.87317926

 $00{:}01{:}05.301 \dashrightarrow 00{:}01{:}07.249$  even response to the rapeutics.

NOTE Confidence: 0.87317926

 $00:01:07.250 \longrightarrow 00:01:10.165$  So particularly in my research

NOTE Confidence: 0.87317926

 $00{:}01{:}10.165 \dashrightarrow 00{:}01{:}12.497$  I'm interested in examining

 $00:01:12.500 \longrightarrow 00:01:15.002$  metabolism in patients that develop tumors

NOTE Confidence: 0.87317926

 $00{:}01{:}15.002 \dashrightarrow 00{:}01{:}18.406$  that occur on the right side of the colon,

NOTE Confidence: 0.87317926

 $00:01:18.410 \longrightarrow 00:01:21.443$  so that is the area of the colon between

NOTE Confidence: 0.87317926

 $00:01:21.443 \longrightarrow 00:01:24.259$  the appendix and slightly up from

NOTE Confidence: 0.87317926

 $00:01:24.259 \longrightarrow 00:01:27.470$  there in the rectum and ascending colon,

NOTE Confidence: 0.87317926

 $00:01:27.470 \longrightarrow 00:01:29.948$  because those patients have the poorest

NOTE Confidence: 0.87317926

 $00:01:29.948 \longrightarrow 00:01:32.855$  survival and what we've seen in the

NOTE Confidence: 0.87317926

 $00:01:32.855 \longrightarrow 00:01:34.825$  literature is actually female patients

NOTE Confidence: 0.87317926

 $00:01:34.825 \longrightarrow 00:01:37.122$  have much higher incidence of tumors

NOTE Confidence: 0.87317926

 $00:01:37.122 \longrightarrow 00:01:40.230$  that occur in this region of the colon,

NOTE Confidence: 0.87317926

 $00:01:40.230 \longrightarrow 00:01:43.050$  so we've been using

NOTE Confidence: 0.87317926

 $00:01:43.050 \longrightarrow 00:01:44.975$  metabolomics to get a

NOTE Confidence: 0.87317926

 $00{:}01{:}44.975 \dashrightarrow 00{:}01{:}46.515$  better understanding of the

NOTE Confidence: 0.87317926

00:01:46.515 --> 00:01:47.929 metabolism of these tumors.

NOTE Confidence: 0.87317926

 $00:01:47.930 \longrightarrow 00:01:50.180$  So maybe we can stop there

 $00:01:50.180 \longrightarrow 00:01:52.952$  for a second and just kind of dig a

NOTE Confidence: 0.8275753

 $00:01:52.952 \longrightarrow 00:01:55.438$  little bit deeper into what exactly

NOTE Confidence: 0.8275753

 $00:01:55.438 \longrightarrow 00:01:58.050$  metabolomics is and how that works.

 $00:01:59.930 \longrightarrow 00:02:02.810$  It's the study of all the small

NOTE Confidence: 0.8275753

 $00:02:02.810 \longrightarrow 00:02:04.925$  molecules that are present within a

NOTE Confidence: 0.8275753

 $00:02:04.925 \longrightarrow 00:02:07.820$  sample so we can take a biological sample

NOTE Confidence: 0.8275753

00:02:07.820 --> 00:02:11.180 from a patient such as a blood sample,

NOTE Confidence: 0.8275753

 $00:02:11.180 \longrightarrow 00:02:14.260$  or even a tumor tissue,

NOTE Confidence: 0.8275753

 $00:02:14.260 \longrightarrow 00:02:17.356$  and we can analyze it in an agnostic manner.

NOTE Confidence: 0.8275753

 $00:02:17.360 \longrightarrow 00:02:19.663$  So we examine basically all the different

NOTE Confidence: 0.8275753

 $00{:}02{:}19.663 \dashrightarrow 00{:}02{:}21.771$  levels of all the small molecules

NOTE Confidence: 0.8275753

 $00:02:21.771 \longrightarrow 00:02:23.883$  that might be within that sample

 $00:02:27.680 \longrightarrow 00:02:29.738$  and this is similar to genomics

NOTE Confidence: 0.8275753

 $00:02:29.738 \longrightarrow 00:02:30.424$  or transcriptomics.

NOTE Confidence: 0.8275753

 $00:02:30.430 \longrightarrow 00:02:32.150$  So small molecules are basically

NOTE Confidence: 0.8275753

 $00{:}02{:}32.150 \dashrightarrow 00{:}02{:}33.870$  metabolites that are within our

NOTE Confidence: 0.8275753

 $00:02:33.932 \longrightarrow 00:02:35.834$  bodies that come from the processing

00:02:35.834 --> 00:02:37.650 of things like dietary products,

NOTE Confidence: 0.8275753

 $00:02:37.650 \longrightarrow 00:02:39.660$  and they produce vital components

NOTE Confidence: 0.8275753

 $00:02:39.660 \longrightarrow 00:02:41.670$  that are needed for our bodies

NOTE Confidence: 0.8275753

00:02:41.670 --> 00:02:43.554 for different biological processes,

NOTE Confidence: 0.8275753

 $00:02:43.554 \longrightarrow 00:02:45.909$  such as growth and healing,

NOTE Confidence: 0.8275753

 $00:02:45.910 \longrightarrow 00:02:47.323$  immune responses, energy,

NOTE Confidence: 0.8275753

 $00:02:47.323 \longrightarrow 00:02:48.736$  and even sleep,

NOTE Confidence: 0.8275753

 $00:02:48.740 \longrightarrow 00:02:51.800$  so metabolomic analysis can also

NOTE Confidence: 0.8275753

 $00:02:51.800 \longrightarrow 00:02:53.924$  really show us about the metabolism

NOTE Confidence: 0.8275753

 $00:02:53.924 \longrightarrow 00:02:56.300$  of an individual and it can

NOTE Confidence: 0.8275753

 $00:02:56.300 \longrightarrow 00:02:58.379$  also show us metabolism of things

NOTE Confidence: 0.8275753

 $00{:}02{:}58.448 \dashrightarrow 00{:}03{:}00.144$  like environmental chemicals and

NOTE Confidence: 0.8275753

 $00:03:00.144 \longrightarrow 00:03:02.688$  drugs as well within an individual

NOTE Confidence: 0.8275753

 $00:03:02.690 \longrightarrow 00:03:04.628$  and that could

NOTE Confidence: 0.8275753

 $00:03:04.628 \longrightarrow 00:03:07.198$  be produced by the bacteria or even

 $00:03:07.198 \longrightarrow 00:03:09.218$  the microbiome within an individual.

NOTE Confidence: 0.8275753

 $00{:}03{:}09.220 \dashrightarrow 00{:}03{:}11.675$  And this technology is particularly

NOTE Confidence: 0.8275753

 $00:03:11.675 \longrightarrow 00:03:12.657$  important for cancer

NOTE Confidence: 0.8275753

00:03:12.660 --> 00:03:14.706 because we know that metabolites

NOTE Confidence: 0.8275753

 $00:03:14.706 \longrightarrow 00:03:17.495$  can affect how a tumor grows as tumor

NOTE Confidence: 0.8275753

 $00:03:17.495 \longrightarrow 00:03:20.113$  cells need nutrients and energy and the

NOTE Confidence: 0.8275753

 $00:03:20.113 \longrightarrow 00:03:22.157$  tumors themselves produce metabolites.

NOTE Confidence: 0.8275753

00:03:22.160 --> 00:03:23.890 So metabolomics can really provide

NOTE Confidence: 0.8275753

 $00{:}03{:}23.890 \mathrel{--}{>} 00{:}03{:}26.093$  us great insight into how an

NOTE Confidence: 0.8275753

 $00:03:26.093 \longrightarrow 00:03:27.323$  individual produces metabolites

NOTE Confidence: 0.8275753

 $00{:}03{:}27.323 \dashrightarrow 00{:}03{:}29.373$  and how this might propagate

NOTE Confidence: 0.8275753

 $00:03:29.380 \longrightarrow 00:03:30.900$  tumor growth as well.

NOTE Confidence: 0.8275753

 $00:03:30.900 \longrightarrow 00:03:32.040$  So basically you're

NOTE Confidence: 0.83694094

 $00:03:32.040 \longrightarrow 00:03:34.448$  kind of looking at all of these

NOTE Confidence: 0.83694094

 $00:03:34.448 \longrightarrow 00:03:36.407$  metabolites to gain some insight

NOTE Confidence: 0.83694094

 $00:03:36.407 \longrightarrow 00:03:38.115$  into these colon cancers.

 $00:03:38.120 \longrightarrow 00:03:40.318$  Tell us what sample you used to

NOTE Confidence: 0.83694094

 $00:03:40.318 \longrightarrow 00:03:42.680$  to look at these metabolites.

NOTE Confidence: 0.83694094

 $00:03:42.680 \longrightarrow 00:03:44.972$  One can imagine that there may

NOTE Confidence: 0.83694094

 $00:03:44.972 \longrightarrow 00:03:47.330$  be many options that you would

NOTE Confidence: 0.83694094

 $00:03:47.330 \longrightarrow 00:03:49.885$  have whether it's looking at the stool

NOTE Confidence: 0.83694094

 $00:03:49.885 \longrightarrow 00:03:52.679$  or whether it's looking at tumor tissue,

NOTE Confidence: 0.83694094

 $00:03:52.680 \longrightarrow 00:03:54.966$  or whether it's looking at blood.

NOTE Confidence: 0.83694094

 $00:03:54.970 \longrightarrow 00:03:58.026$  So what exactly do you do to try

NOTE Confidence: 0.84392136

 $00:03:58.030 \longrightarrow 00:03:59.554$  to gain this insight?

NOTE Confidence: 0.84392136

 $00:03:59.554 \longrightarrow 00:04:02.561$  That's a really good question,

NOTE Confidence: 0.84392136

 $00:04:02.561 \longrightarrow 00:04:05.130$  basically we can take anything, we can

NOTE Confidence: 0.84392136

00:04:05.207 --> 00:04:07.958 take a blood sample or stool sample,

NOTE Confidence: 0.84392136

 $00:04:07.960 \longrightarrow 00:04:09.344$  or a tumor tissue,

NOTE Confidence: 0.84392136

 $00:04:09.344 \longrightarrow 00:04:12.160$  and we can obtain these from patients,

NOTE Confidence: 0.84392136

 $00:04:12.160 \longrightarrow 00:04:14.736$  and we can extract all the different

 $00:04:14.736 \longrightarrow 00:04:17.578$  metabolites out of these biological samples.

NOTE Confidence: 0.84392136

 $00{:}04{:}17.580 \dashrightarrow 00{:}04{:}21.010$  And what we end up with is sort of a mixture

NOTE Confidence: 0.84392136

 $00:04:21.099 \longrightarrow 00:04:24.267$  of anywhere from maybe 3000 up to you

NOTE Confidence: 0.84392136

 $00:04:24.267 \longrightarrow 00:04:27.363$  know 10 to 20,000 different molecules

NOTE Confidence: 0.84392136

 $00:04:27.363 \longrightarrow 00:04:30.687$  that could be present within this

NOTE Confidence: 0.84392136

 $00{:}04{:}30.690 \dashrightarrow 00{:}04{:}33.306$  sample within my research so far,

NOTE Confidence: 0.84392136

 $00:04:33.310 \longrightarrow 00:04:35.058$  we have primarily examined

NOTE Confidence: 0.84392136

00:04:35.058 --> 00:04:36.806 tumor tissues from patients,

NOTE Confidence: 0.84392136

 $00:04:36.810 \longrightarrow 00:04:39.175$  so with collaborations with

NOTE Confidence: 0.84392136

 $00:04:39.175 \longrightarrow 00:04:41.540$  both Sloan Kettering Cancer Center

NOTE Confidence: 0.84392136

00:04:41.616 --> 00:04:43.800 and also Yale Cancer Center,

NOTE Confidence: 0.84392136

 $00:04:43.800 \longrightarrow 00:04:45.120$  we obtained over

NOTE Confidence: 0.84392136

 $00:04:45.120 \longrightarrow 00:04:47.320$  200 tumor tissues from patients

NOTE Confidence: 0.84392136

 $00:04:47.320 \longrightarrow 00:04:49.897$  where these tumors had been obtained

NOTE Confidence: 0.84392136

00:04:49.897 --> 00:04:52.877 during surgery and we were able to

NOTE Confidence: 0.84392136

 $00:04:52.877 \longrightarrow 00:04:55.739$  analyze these tissues to examine which

 $00:04:55.739 \longrightarrow 00:04:58.439$  metabolites were present and how they

NOTE Confidence: 0.84392136

 $00:04:58.439 \longrightarrow 00:05:00.554$  were different between different patients.

NOTE Confidence: 0.84392136

 $00:05:00.560 \longrightarrow 00:05:02.936$  So how they were different between

NOTE Confidence: 0.84392136

 $00:05:02.936 \longrightarrow 00:05:05.968$  both women and men and from patients

NOTE Confidence: 0.84392136

 $00{:}05{:}05{:}05{:}068 \dashrightarrow 00{:}05{:}08.248$  with right sided colorectal cancer

NOTE Confidence: 0.84392136

 $00:05:08.248 \longrightarrow 00:05:11.260$  and also from tumors that occurred in

NOTE Confidence: 0.84392136

 $00:05:11.260 \longrightarrow 00:05:14.126$  other regions of the colon as well?

00:05:14.550 --> 00:05:18.294 And if all of these patients had cancer,

NOTE Confidence: 0.8549831

 $00{:}05{:}18.300 \dashrightarrow 00{:}05{:}20.784$  one would imagine that you're

NOTE Confidence: 0.8549831

 $00:05:20.784 \longrightarrow 00:05:23.038$  really looking at the metabolomic

NOTE Confidence: 0.8549831

 $00{:}05{:}23.038 \dashrightarrow 00{:}05{:}26.134$  profile of tumors in these patients

NOTE Confidence: 0.8549831

 $00:05:26.140 \longrightarrow 00:05:28.828$  is that different than what you

NOTE Confidence: 0.8549831

 $00:05:28.828 \longrightarrow 00:05:31.210$  would expect in normal colon?

NOTE Confidence: 0.8549831

 $00:05:31.210 \longrightarrow 00:05:33.450$  So are there some metabolites

NOTE Confidence: 0.8549831

 $00:05:33.450 \longrightarrow 00:05:36.243$  that you would expect only in

NOTE Confidence: 0.8549831

 $00:05:36.243 \longrightarrow 00:05:38.578$  tumors versus in healthy tissue?

 $00:05:38.580 \longrightarrow 00:05:39.969$  Yeah, that's

NOTE Confidence: 0.8328215

 $00:05:39.970 \longrightarrow 00:05:44.119$  a great question, so we know that

NOTE Confidence: 0.8328215

00:05:44.120 --> 00:05:48.184 tumors have very sort of increased

NOTE Confidence: 0.8328215

 $00:05:48.190 \longrightarrow 00:05:51.710$  rapid growth, so we tend to see metabolites

NOTE Confidence: 0.8328215

 $00:05:51.710 \longrightarrow 00:05:55.612$  linked to energy metabolism and sort of

NOTE Confidence: 0.8328215

 $00:05:55.612 \longrightarrow 00:05:58.504$  making those or encouraging those building

NOTE Confidence: 0.8328215

 $00:05:58.504 \longrightarrow 00:06:02.267$  blocks to be built to build new cells so

NOTE Confidence: 0.8328215

 $00:06:02.267 \longrightarrow 00:06:05.570$  we know there's a lot of what they call

NOTE Confidence: 0.8328215

 $00:06:05.660 \longrightarrow 00:06:08.220$  metabolic rewiring that happens within

NOTE Confidence: 0.8328215

 $00{:}06{:}08.220 \dashrightarrow 00{:}06{:}12.070$  a tumor compared to a normal tissue.

NOTE Confidence: 0.8328215

00:06:12.070 --> 00:06:14.040 Andwithin my research,

NOTE Confidence: 0.8328215

 $00:06:14.040 \longrightarrow 00:06:17.368$  we were really interested in looking at the

NOTE Confidence: 0.8328215

 $00{:}06{:}17.368 \dashrightarrow 00{:}06{:}19.996$  tumors themselves and how they differed

NOTE Confidence: 0.8328215

 $00:06:19.996 \longrightarrow 00:06:22.576$  between male and female patients because

NOTE Confidence: 0.8328215

 $00:06:22.580 \longrightarrow 00:06:24.590$  what is quite interesting about

 $00:06:24.590 \longrightarrow 00:06:26.640$  colorectal cancer and all cancers,

NOTE Confidence: 0.8328215

 $00:06:26.640 \longrightarrow 00:06:28.668$  they tend to have a higher

NOTE Confidence: 0.8328215

00:06:28.668 --> 00:06:30.020 incidence in male patients,

NOTE Confidence: 0.8328215

 $00:06:30.020 \longrightarrow 00:06:32.309$  but what we see is that in

NOTE Confidence: 0.8328215

 $00:06:32.309 \longrightarrow 00:06:34.410$  the right side of the colon,

NOTE Confidence: 0.8328215

 $00:06:34.410 \longrightarrow 00:06:37.754$  women tend to have this higher incidence, so

NOTE Confidence: 0.8328215

 $00:06:37.760 \longrightarrow 00:06:40.539$  we wanted to see what was different

NOTE Confidence: 0.8328215

 $00:06:40.539 \longrightarrow 00:06:42.571$  metabolically about these tumors that

NOTE Confidence: 0.8328215

00:06:42.571 --> 00:06:45.259 occur specifically in in women with right

NOTE Confidence: 0.8328215

 $00:06:45.259 \longrightarrow 00:06:47.707$  sided colorectal cancer and what we saw

NOTE Confidence: 0.8328215

 $00:06:47.707 \longrightarrow 00:06:50.378$  was that they had this very different

NOTE Confidence: 0.8328215

 $00:06:50.378 \longrightarrow 00:06:53.054$  metabolic profile where they tended to

NOTE Confidence: 0.8328215

00:06:53.060 --> 00:06:54.656 generate energy differently

NOTE Confidence: 0.8328215

 $00{:}06{:}54.656 \dashrightarrow 00{:}06{:}57.050$  and they use one metabolites where

NOTE Confidence: 0.8328215

00:06:57.113 --> 00:06:59.228 they produce one metabolite school,

NOTE Confidence: 0.8328215

 $00{:}06{:}59.230 \dashrightarrow 00{:}07{:}01.588$  disparaging that seemed to be much

 $00:07:01.588 \longrightarrow 00:07:04.082$  higher within this set of patients

NOTE Confidence: 0.8328215

 $00{:}07{:}04.082 \dashrightarrow 00{:}07{:}06.620$  than compared to male patients that had

NOTE Confidence: 0.8328215

 $00:07:06.620 \longrightarrow 00:07:08.432$  right sided colon cancer,

NOTE Confidence: 0.8328215

00:07:08.432 --> 00:07:11.150 and also patients that had tumors

NOTE Confidence: 0.8328215

 $00:07:11.229 \longrightarrow 00:07:13.609$  in the other side of the colon.

NOTE Confidence: 0.8328215

 $00:07:13.610 \longrightarrow 00:07:16.454$  So we've really gone after this

NOTE Confidence: 0.8328215

00:07:16.454 --> 00:07:18.350 metabolic pathway to understand

NOTE Confidence: 0.8328215

 $00:07:18.350 \longrightarrow 00:07:21.262$  more about this side of metabolism and

NOTE Confidence: 0.8328215

 $00{:}07{:}21.262 \dashrightarrow 00{:}07{:}24.248$  potentially how it could in the future

NOTE Confidence: 0.8328215

 $00:07:24.248 \longrightarrow 00:07:26.328$  be potentially targeted for perhaps

NOTE Confidence: 0.8328215

00:07:26.328 --> 00:07:29.077 a precision medicine approach for

NOTE Confidence: 0.84086907

 $00:07:29.080 \longrightarrow 00:07:30.740$  these groups of patients.

NOTE Confidence: 0.84086907

00:07:30.740 --> 00:07:32.815 That's interesting that

NOTE Confidence: 0.84086907

00:07:32.815 --> 00:07:35.659 women have a metabolite that

NOTE Confidence: 0.84086907

 $00:07:35.659 \longrightarrow 00:07:38.014$  processes energy differently than men.

 $00:07:39.804 \longrightarrow 00:07:43.388$  I just wonder when I think about

 $00:07:43.388 \longrightarrow 00:07:46.509$  Asparagine I started thinking about

NOTE Confidence: 0.84086907

 $00{:}07{:}48.493 \dashrightarrow 00{:}07{:}53.120$  nucleic acids and amino acids

NOTE Confidence: 0.84086907

 $00:07:53.242 \longrightarrow 00:07:57.136$  that form the building blocks of

NOTE Confidence: 0.84086907

 $00:07:57.136 \longrightarrow 00:08:01.409$  cells and whether these could be

NOTE Confidence: 0.84086907

 $00{:}08{:}01.409 \dashrightarrow 00{:}08{:}05.289$  manipulated based on dietary factors,

NOTE Confidence: 0.84086907

 $00:08:05.290 \longrightarrow 00:08:06.610$  for example.

NOTE Confidence: 0.84086907

 $00:08:06.610 \longrightarrow 00:08:12.970$  So when we think about how cells use energy,

NOTE Confidence: 0.84086907

 $00:08:12.970 \longrightarrow 00:08:14.785$  sometimes that may be

NOTE Confidence: 0.84086907

00:08:14.785 --> 00:08:19.020 mediated in part by people's dietary intake,

NOTE Confidence: 0.84086907

 $00:08:19.020 \longrightarrow 00:08:21.785$  did you look at that as a

NOTE Confidence: 0.84086907

00:08:21.785 --> 00:08:23.623 potential difference in male

NOTE Confidence: 0.84086907

 $00:08:23.623 \longrightarrow 00:08:25.318$  versus female patients?

 $00:08:25.770 \longrightarrow 00:08:27.120$  Within our cohort

NOTE Confidence: 0.8287141

00:08:27.120 --> 00:08:29.820 we didn't have information on diet,

NOTE Confidence: 0.8287141

 $00:08:29.820 \longrightarrow 00:08:32.058$  but that's very much something that

NOTE Confidence: 0.8287141

 $00:08:32.058 \longrightarrow 00:08:34.758$  would be useful to have something

00:08:34.758 --> 00:08:37.018 like a food frequency questionnaire,

NOTE Confidence: 0.8287141

 $00{:}08{:}37.020 \dashrightarrow 00{:}08{:}38.820$  which is sometimes collected

NOTE Confidence: 0.8287141

 $00:08:38.820 \longrightarrow 00:08:41.070$  for different biobanks

NOTE Confidence: 0.8287141

 $00:08:41.070 \longrightarrow 00:08:43.317$  and in different cohorts.

NOTE Confidence: 0.8287141

00:08:43.320 --> 00:08:46.881 Yes, exactly I think it's

NOTE Confidence: 0.8287141

 $00:08:46.881 \longrightarrow 00:08:48.629$  really important here,

NOTE Confidence: 0.8287141

00:08:48.630 --> 00:08:52.014 but I think Asparagine does come from

NOTE Confidence: 0.8287141

00:08:52.014 --> 00:08:54.427 many many different dietary sources

NOTE Confidence: 0.8287141

 $00:08:54.427 \longrightarrow 00:08:58.380$  and it actually has been seen

NOTE Confidence: 0.8287141

 $00:08:58.380 \longrightarrow 00:09:00.936$  to be produced potentially,

NOTE Confidence: 0.8287141

 $00:09:00.940 \longrightarrow 00:09:02.806$  or metabolize by the microbiome as

NOTE Confidence: 0.8287141

 $00:09:02.806 \longrightarrow 00:09:05.470$  well and it can be produced internally

NOTE Confidence: 0.8287141

 $00{:}09{:}05.470 \dashrightarrow 00{:}09{:}07.725$  through your own biochemical processing

NOTE Confidence: 0.8287141

 $00{:}09{:}07.725 \dashrightarrow 00{:}09{:}10.296$  of other metabolites through an

NOTE Confidence: 0.8287141

 $00:09:10.296 \longrightarrow 00:09:12.436$  enzyme called Asparagine synthetase.

00:09:12.440 --> 00:09:13.290 So, biologically,

NOTE Confidence: 0.8287141

 $00{:}09{:}13.290 \dashrightarrow 00{:}09{:}16.265$  it can come from your internal processing,

NOTE Confidence: 0.8287141

 $00:09:16.270 \longrightarrow 00:09:19.678$  but it can also come from dietary sources,

NOTE Confidence: 0.8287141

 $00:09:19.680 \longrightarrow 00:09:22.230$  and it can come from microbial

NOTE Confidence: 0.8287141

 $00:09:22.230 \longrightarrow 00:09:23.505$  processing as well.

NOTE Confidence: 0.8287141

 $00:09:23.510 \longrightarrow 00:09:26.012$  So, as with many metabolites that

NOTE Confidence: 0.8287141

 $00:09:26.012 \longrightarrow 00:09:28.300$  are present within

NOTE Confidence: 0.8287141

 $00:09:28.300 \longrightarrow 00:09:31.316$  tumors and also present within the colon,

NOTE Confidence: 0.8287141

 $00{:}09{:}31.320 \dashrightarrow 00{:}09{:}33.854$  we always have to take into account

NOTE Confidence: 0.8287141

 $00:09:33.854 \longrightarrow 00:09:35.392$  all these different biological

NOTE Confidence: 0.8287141

 $00:09:35.392 \longrightarrow 00:09:38.094$  sources of where they can come from.

NOTE Confidence: 0.8287141

 $00:09:38.100 \longrightarrow 00:09:40.356$  So we can either

NOTE Confidence: 0.8287141

00:09:40.360 --> 00:09:42.999 manipulate them and try and sort of,

NOTE Confidence: 0.8287141

 $00:09:43.000 \longrightarrow 00:09:44.131$  potentially

NOTE Confidence: 0.8287141

00:09:44.131 --> 00:09:46.393 reduce the effects of the disease,

NOTE Confidence: 0.8287141

 $00:09:46.400 \longrightarrow 00:09:47.904$  or improve the rapeutic response.  $00:09:48.280 \longrightarrow 00:09:49.040$  And it seems

NOTE Confidence: 0.8555086

 $00:09:49.040 \longrightarrow 00:09:50.845$  to be so multifactorial when

NOTE Confidence: 0.8555086

 $00:09:50.845 \longrightarrow 00:09:53.115$  you think about where all of

NOTE Confidence: 0.8555086

 $00:09:53.115 \longrightarrow 00:09:55.065$  these metabolites can come from,

NOTE Confidence: 0.8555086

 $00:09:55.070 \longrightarrow 00:09:57.566$  and all of the different processes

NOTE Confidence: 0.8555086

 $00:09:57.566 \longrightarrow 00:09:59.987$  that could be going on

NOTE Confidence: 0.8555086

 $00:09:59.987 \longrightarrow 00:10:02.222$  both within normal cells as

NOTE Confidence: 0.8555086

 $00:10:02.222 \longrightarrow 00:10:04.580$  well as within cancer cells,

NOTE Confidence: 0.8555086

 $00:10:04.580 \longrightarrow 00:10:06.368$  which raises the question,

 $00:10:07.710 \longrightarrow 00:10:10.380$  do women normally have more of

NOTE Confidence: 0.8555086

 $00{:}10{:}10.380 \dashrightarrow 00{:}10{:}12.160$  this metabolite even outside

NOTE Confidence: 0.8555086

 $00:10:12.235 \longrightarrow 00:10:13.967$  of their colon cancers?

 $00:10:14.860 \longrightarrow 00:10:19.364$  I think in this context what we've begun to see

NOTE Confidence: 0.89197695

 $00:10:19.370 \dashrightarrow 00:10:22.156$  is that As paragine might be increased in

NOTE Confidence: 0.89197695

 $00:10:22.156 \longrightarrow 00:10:24.740$  these patients because these tumors may be

NOTE Confidence: 0.89197695

 $00:10:24.740 \longrightarrow 00:10:27.407$  what we call nutrient deplete and this is

NOTE Confidence: 0.89197695

 $00:10:27.407 \longrightarrow 00:10:29.895$  something that we still have to look into,

 $00:10:29.900 \longrightarrow 00:10:32.006$  so we can't really confirm this,

NOTE Confidence: 0.89197695

 $00:10:32.010 \longrightarrow 00:10:34.110$  but just from our metabolomic studies,

NOTE Confidence: 0.89197695

 $00:10:34.110 \longrightarrow 00:10:36.216$  it seems to be indicating this.

NOTE Confidence: 0.89197695

 $00:10:36.220 \longrightarrow 00:10:38.733$  And this is maybe due to differences

NOTE Confidence: 0.89197695

 $00:10:38.733 \longrightarrow 00:10:40.779$  in blood supply to the tumor,

NOTE Confidence: 0.89197695

 $00:10:40.780 \longrightarrow 00:10:41.833$  or something else.

NOTE Confidence: 0.89197695

 $00:10:41.833 \longrightarrow 00:10:43.943$  Less oxygen

NOTE Confidence: 0.89197695

 $00{:}10{:}43.943 \dashrightarrow 00{:}10{:}46.400$  that might be getting to the tumor.

NOTE Confidence: 0.89197695

 $00:10:46.400 \longrightarrow 00:10:48.871$  And when we look at the other

NOTE Confidence: 0.89197695

00:10:48.871 --> 00:10:50.669 processes that are going on

NOTE Confidence: 0.89197695

 $00{:}10{:}50.670 \dashrightarrow 00{:}10{:}53.337$  within these samples we see

NOTE Confidence: 0.89197695

00:10:53.337 --> 00:10:55.734 that the generation of other energy

NOTE Confidence: 0.89197695

 $00{:}10{:}55.734 \dashrightarrow 00{:}10{:}58.092$  metabolites is different as well,

NOTE Confidence: 0.89197695

 $00:10:58.100 \longrightarrow 00:11:00.330$  which could be indicating that

NOTE Confidence: 0.89197695

 $00:11:00.330 \longrightarrow 00:11:02.560$  there could be something particular

 $00:11:02.629 \longrightarrow 00:11:04.735$  about how these tumors might be

NOTE Confidence: 0.89197695

 $00{:}11{:}04.735 \dashrightarrow 00{:}11{:}07.090$  growing in this area of the colon.

NOTE Confidence: 0.89197695

 $00:11:07.090 \longrightarrow 00:11:09.890$  So at the moment we don't have normal

NOTE Confidence: 0.89197695

00:11:09.890 --> 00:11:12.179 colon tissues from from individuals,

NOTE Confidence: 0.89197695

 $00:11:12.180 \longrightarrow 00:11:15.050$  but that's something that we do want

NOTE Confidence: 0.89197695

 $00:11:15.050 \longrightarrow 00:11:18.625$  to look at to see if

NOTE Confidence: 0.89197695

 $00:11:18.625 \longrightarrow 00:11:21.268$  the patients that do not have

NOTE Confidence: 0.89197695

 $00:11:21.270 \longrightarrow 00:11:24.926$  colon cancer, if the colon tissues have these

NOTE Confidence: 0.89197695

 $00:11:24.930 \longrightarrow 00:11:27.275$  different metabolites that

NOTE Confidence: 0.89197695

00:11:27.275 --> 00:11:30.410 could be different between men and women,

NOTE Confidence: 0.89197695

 $00:11:32.700 \longrightarrow 00:11:35.436$  and could affect the development of these tumors.

NOTE Confidence: 0.8281183

 $00:11:35.440 \longrightarrow 00:11:38.639$  You kind of wonder as

NOTE Confidence: 0.8281183

 $00:11:38.639 \longrightarrow 00:11:41.839$  well whether this is cause or effect.

NOTE Confidence: 0.8281183

 $00:11:41.840 \longrightarrow 00:11:44.952$  So in other words, is it that you

NOTE Confidence: 0.8281183

00:11:44.952 --> 00:11:48.230 had a tumor which was growing,

NOTE Confidence: 0.8281183

 $00:11:48.230 \longrightarrow 00:11:50.278$  which then caused this

00:11:50.278 --> 00:11:51.814 altered metabolomic profile,

NOTE Confidence: 0.8281183

 $00:11:51.820 \longrightarrow 00:11:54.492$  or was it that you had some other

NOTE Confidence: 0.8281183

00:11:54.492 --> 00:11:57.047 processes that were going on that

NOTE Confidence: 0.8281183

00:11:57.047 --> 00:11:58.859 altered your metabolomic profile,

NOTE Confidence: 0.8281183

 $00:11:58.860 \longrightarrow 00:12:01.200$  which then spurred on the cancer?

NOTE Confidence: 0.8281183

00:12:01.200 --> 00:12:04.328 Did you gain any insight into that question?

NOTE Confidence: 0.9122841

00:12:05.860 --> 00:12:09.940 I think it's probably more of the latter.

NOTE Confidence: 0.9122841

 $00:12:09.940 \longrightarrow 00:12:13.510$  We see that Asparagine

NOTE Confidence: 0.9122841

 $00:12:13.510 \longrightarrow 00:12:15.550$  is produced internally.

NOTE Confidence: 0.9122841

00:12:15.550 --> 00:12:18.100 As I mentioned through this

NOTE Confidence: 0.9122841

 $00{:}12{:}18.100 \dashrightarrow 00{:}12{:}19.630$  enzyme as paragine synthetase,

NOTE Confidence: 0.9122841

 $00:12:19.630 \longrightarrow 00:12:23.291$  and this enzyme is controlled somewhat by

NOTE Confidence: 0.9122841

 $00{:}12{:}23.291 \dashrightarrow 00{:}12{:}26.767$  another gene mutation of aging mutant Kras,

NOTE Confidence: 0.9122841

 $00:12:26.770 \longrightarrow 00:12:31.530$  so it could be that these tumors

NOTE Confidence: 0.9122841

 $00:12:31.530 \longrightarrow 00:12:33.847$  have this oncogene and it could

 $00:12:33.847 \longrightarrow 00:12:36.009$  be affecting these metabolites,

NOTE Confidence: 0.9122841

00:12:36.010 --> 00:12:39.358 so it could be an effect that we're seeing,

NOTE Confidence: 0.9122841

 $00:12:39.360 \longrightarrow 00:12:41.598$  but it is probably a combination

NOTE Confidence: 0.9122841

 $00:12:41.598 \longrightarrow 00:12:43.836$  of many things, that includes this

NOTE Confidence: 0.9122841

00:12:43.836 --> 00:12:45.696 potential mutation to this gene.

NOTE Confidence: 0.9122841

 $00:12:45.700 \longrightarrow 00:12:48.150$  But also it could be the way

NOTE Confidence: 0.9122841

 $00:12:48.150 \longrightarrow 00:12:50.180$  that the tumor is growing

NOTE Confidence: 0.9122841

 $00:12:50.180 \longrightarrow 00:12:51.870$  as I mentioned within the

NOTE Confidence: 0.9122841

 $00:12:51.870 \longrightarrow 00:12:54.280$  colon as well and all together,

NOTE Confidence: 0.9122841

 $00:12:54.280 \longrightarrow 00:12:56.428$  all these different processes are

NOTE Confidence: 0.9122841

 $00{:}12{:}56.428 \dashrightarrow 00{:}12{:}58.760$  causing this effect of this increase

NOTE Confidence: 0.9122841

 $00{:}12{:}58.760 \dashrightarrow 00{:}13{:}01.916$  in Asparagine that seem to help

NOTE Confidence: 0.9122841

 $00:13:01.920 \longrightarrow 00:13:03.866$  propagate the tumor when it

NOTE Confidence: 0.9122841

 $00:13:03.866 \longrightarrow 00:13:05.766$  might be under these stress

NOTE Confidence: 0.9122841

 $00{:}13{:}05.766 \dashrightarrow 00{:}13{:}08.104$  conditions where it's not able to obtain

NOTE Confidence: 0.9122841

00:13:08.110 --> 00:13:10.200 nutrients in a normal fashion,

 $00:13:10.200 \longrightarrow 00:13:13.119$  so I think this is what

NOTE Confidence: 0.9122841

 $00:13:13.119 \longrightarrow 00:13:14.370$  could be happening.

NOTE Confidence: 0.9122841

 $00:13:14.370 \longrightarrow 00:13:17.275$  And also as I mentioned as well,

NOTE Confidence: 0.9122841

00:13:17.280 --> 00:13:19.440 this combination of the microbiome

NOTE Confidence: 0.9122841

 $00:13:19.440 \longrightarrow 00:13:22.060$  present as well within the colon

NOTE Confidence: 0.9122841

 $00:13:22.060 \longrightarrow 00:13:24.364$  that could be affecting how this

NOTE Confidence: 0.8519883

00:13:24.370 --> 00:13:26.460 metabolite is being processed.

00:13:29.016 --> 00:13:31.050 And it's an interesting puzzle to

NOTE Confidence: 0.8519883

 $00:13:31.050 \longrightarrow 00:13:33.310$  think about how metabolomics works

NOTE Confidence: 0.8519883

 $00:13:33.310 \longrightarrow 00:13:36.049$  along with genetic mutations and so on

NOTE Confidence: 0.8519883

 $00{:}13{:}36.050 \dashrightarrow 00{:}13{:}38.738$  when we think about colon cancer.

NOTE Confidence: 0.8519883

 $00{:}13{:}38.740 \dashrightarrow 00{:}13{:}40.954$  We're going to take a short

NOTE Confidence: 0.8519883

 $00:13:40.954 \longrightarrow 00:13:43.060$  break for a medical minute.

NOTE Confidence: 0.8519883

00:13:43.060 --> 00:13:45.406 Please stay tuned to learn more

NOTE Confidence: 0.8519883

00:13:45.406 --> 00:13:46.970 about genetic and environmental

NOTE Confidence: 0.8519883

00:13:47.035 --> 00:13:48.960 influences in colon cancer with

00:13:48.960 --> 00:13:50.920 my guest Doctor Caroline Johnson.

NOTE Confidence: 0.85478395

 $00:13:50.920 \longrightarrow 00:13:53.060$  Support for Yale Cancer Answers

NOTE Confidence: 0.85478395

 $00:13:53.060 \longrightarrow 00:13:55.617$  comes from AstraZeneca, working to

NOTE Confidence: 0.85478395

00:13:55.617 --> 00:13:57.997 eliminate cancer as a cause of death.

NOTE Confidence: 0.85478395

 $00{:}13{:}58.000 \dashrightarrow 00{:}14{:}01.528$  Learn more at a strazeneca-us.com.

NOTE Confidence: 0.85478395

 $00:14:01.530 \longrightarrow 00:14:03.360$  This is a medical minute

NOTE Confidence: 0.85478395

 $00:14:03.360 \longrightarrow 00:14:05.190$  about head and neck cancers,

NOTE Confidence: 0.85478395

 $00{:}14{:}05.190 \dashrightarrow 00{:}14{:}07.434$  although the percentage of oral in

NOTE Confidence: 0.85478395

00:14:07.434 --> 00:14:09.702 head and neck cancer patients in

NOTE Confidence: 0.85478395

00:14:09.702 --> 00:14:11.790 the United States is only about

NOTE Confidence: 0.85478395

 $00:14:11.790 \longrightarrow 00:14:13.712$  5% of all diagnosed cancers,

NOTE Confidence: 0.85478395

 $00:14:13.712 \longrightarrow 00:14:15.677$  there are challenging side effects

NOTE Confidence: 0.85478395

 $00{:}14{:}15.677 \dashrightarrow 00{:}14{:}17.102$  associated with these types

NOTE Confidence: 0.85478395

 $00:14:17.102 \longrightarrow 00:14:18.727$  of cancer and their treatment.

NOTE Confidence: 0.85478395

 $00:14:18.730 \longrightarrow 00:14:20.326$  Clinical trials are currently

00:14:20.326 --> 00:14:22.321 underway to test innovative new

NOTE Confidence: 0.85478395

 $00{:}14{:}22.321 \dashrightarrow 00{:}14{:}24.218$  treatments for head and neck cancers,

NOTE Confidence: 0.85478395

 $00:14:24.220 \longrightarrow 00:14:26.200$  and in many cases less radical

NOTE Confidence: 0.85478395

00:14:26.200 --> 00:14:28.610 surgeries are able to preserve nerves,

NOTE Confidence: 0.85478395

00:14:28.610 --> 00:14:30.806 arteries and muscles in the neck,

NOTE Confidence: 0.85478395

 $00:14:30.810 \longrightarrow 00:14:32.450$  enabling patients to move,

NOTE Confidence: 0.85478395

 $00:14:32.450 \longrightarrow 00:14:34.912$  speak, breathe and eat normally

NOTE Confidence: 0.85478395

 $00:14:34.912 \longrightarrow 00:14:35.938$  after surgery.

NOTE Confidence: 0.85478395

00:14:35.940 --> 00:14:37.992 More information is available

NOTE Confidence: 0.85478395

 $00:14:37.992 \longrightarrow 00:14:39.018$  at yalecancercenter.org.

NOTE Confidence: 0.85478395

 $00:14:39.020 \longrightarrow 00:14:42.098$  You're listening to Connecticut Public Radio.

NOTE Confidence: 0.84102845

 $00:14:43.280 \longrightarrow 00:14:45.578$  Welcome back to Yale cancer answers.

NOTE Confidence: 0.84102845

 $00:14:45.580 \longrightarrow 00:14:48.180$  This is doctor Anees Chagpar and I'm

NOTE Confidence: 0.84102845

00:14:48.180 --> 00:14:50.487 joined to night by my guest doctor

NOTE Confidence: 0.84102845

 $00:14:50.487 \longrightarrow 00:14:52.472$  Caroline Johnson and we're talking about

NOTE Confidence: 0.84102845

 $00:14:52.472 \longrightarrow 00:14:54.599$  genetic and environmental influences in

00:14:54.599 --> 00:14:57.440 colon cancer and right before the break,

NOTE Confidence: 0.84102845

 $00{:}14{:}57.440 \dashrightarrow 00{:}14{:}59.480$  Caroline was telling us about her

NOTE Confidence: 0.84102845

00:14:59.480 --> 00:15:01.330 studies looking at metabolomics.

NOTE Confidence: 0.84102845

 $00:15:01.330 \longrightarrow 00:15:03.628$  That is to say the study

NOTE Confidence: 0.84102845

 $00:15:03.628 \longrightarrow 00:15:04.777$  of different metabolites.

NOTE Confidence: 0.84102845

 $00:15:04.780 \longrightarrow 00:15:06.316$  Looking at gender differences

NOTE Confidence: 0.84102845

 $00:15:06.316 \longrightarrow 00:15:08.236$  in right sided colon cancer.

NOTE Confidence: 0.84102845

 $00:15:08.240 \dashrightarrow 00:15:10.879$  So Caroline, I wanted to dig into

NOTE Confidence: 0.84102845

 $00:15:10.879 \longrightarrow 00:15:13.870$  that a little bit more because we

NOTE Confidence: 0.84102845

 $00{:}15{:}13.870 \dashrightarrow 00{:}15{:}16.095$  started to talk about whether

NOTE Confidence: 0.84102845

 $00{:}15{:}16.100 \dashrightarrow 00{:}15{:}18.510$  these metabolomic changes

NOTE Confidence: 0.84102845

 $00:15:18.510 \longrightarrow 00:15:21.853$  are what drives the colon cancer or

NOTE Confidence: 0.84102845

 $00{:}15{:}21.853 \dashrightarrow 00{:}15{:}24.403$  whether the colon cancer is what

NOTE Confidence: 0.84102845

00:15:24.403 --> 00:15:26.949 drives the metabolomic changes,

NOTE Confidence: 0.84102845

 $00:15:26.950 \longrightarrow 00:15:30.106$  and you had mentioned that the

 $00:15:30.106 \longrightarrow 00:15:33.185$  metabolomic changes may be in part

NOTE Confidence: 0.84102845

00:15:33.185 --> 00:15:35.813 related to mutations in KRas,

NOTE Confidence: 0.84102845

 $00{:}15{:}35.820 \dashrightarrow 00{:}15{:}39.708$  but we know that Kras and oncogenes

NOTE Confidence: 0.84102845

00:15:39.708 --> 00:15:43.217 may spur on cancers as well.

NOTE Confidence: 0.84102845

 $00:15:43.220 \longrightarrow 00:15:46.268$  I wonder whether these two processes

NOTE Confidence: 0.84102845

 $00:15:46.270 \longrightarrow 00:15:48.690$  are independent of each other.

NOTE Confidence: 0.84102845

 $00:15:48.690 \longrightarrow 00:15:50.326$  That is to say,

NOTE Confidence: 0.84102845

 $00:15:50.326 \longrightarrow 00:15:52.780$  Kras causes metabolomic changes and

NOTE Confidence: 0.84102845

 $00{:}15{:}52.864 \operatorname{{\scriptsize -->}} 00{:}15{:}55.499$  also causes separately tumor development

NOTE Confidence: 0.84102845

 $00:15:55.499 \longrightarrow 00:15:58.850$  or whether these are Interrelated.

NOTE Confidence: 0.84102845

 $00:15:58.850 \longrightarrow 00:16:02.238$  Do you have any sense on that?

NOTE Confidence: 0.8153747

 $00{:}16{:}03.350 \dashrightarrow 00{:}16{:}06.830$  I think they are interrelated and the

NOTE Confidence: 0.8153747

 $00:16:06.830 \longrightarrow 00:16:09.674$  findings that we have seen

NOTE Confidence: 0.8153747

 $00:16:09.674 \longrightarrow 00:16:12.266$  linking Mutant Kras and Asparagine

NOTE Confidence: 0.8153747

 $00:16:12.266 \longrightarrow 00:16:15.529$  have been seen in other cancers as well.

NOTE Confidence: 0.8153747

 $00:16:15.530 \longrightarrow 00:16:18.666$  So you know the mutant carriers is very

 $00:16:18.666 \longrightarrow 00:16:22.248$  common in pancreatic cancers and there is a

NOTE Confidence: 0.8153747

 $00:16:22.250 \longrightarrow 00:16:24.770$  clinical trial right now

NOTE Confidence: 0.8153747

 $00:16:24.770 \longrightarrow 00:16:26.860$  actually that I saw yesterday

NOTE Confidence: 0.8153747

 $00:16:26.860 \longrightarrow 00:16:28.532$  for targeting Asparagine by

NOTE Confidence: 0.8153747

 $00:16:28.532 \longrightarrow 00:16:30.649$  using a drug

NOTE Confidence: 0.8153747

 $00:16:30.650 \longrightarrow 00:16:33.674$  along with other first line chemo.

 $00:16:36.360 \longrightarrow 00:16:39.370$  So we do know that the mutant

NOTE Confidence: 0.8153747

 $00:16:39.370 \longrightarrow 00:16:41.260$  Kras does regulate other

NOTE Confidence: 0.8153747

00:16:41.260 --> 00:16:43.360 genes and signaling pathways that

NOTE Confidence: 0.8153747

 $00:16:43.360 \longrightarrow 00:16:45.040$  does affect Asparagine production.

NOTE Confidence: 0.8153747

 $00:16:45.040 \longrightarrow 00:16:48.064$  So I think it's probably a case of mutant

NOTE Confidence: 0.8153747

 $00{:}16{:}48.064 \dashrightarrow 00{:}16{:}50.498$  Kras affecting Asparagine levels.

NOTE Confidence: 0.8153747

 $00:16:50.500 \longrightarrow 00:16:53.440$  But of course, as I mentioned before,

NOTE Confidence: 0.8153747

 $00:16:53.440 \longrightarrow 00:16:56.380$  asparagine can be modulated by other sources,

NOTE Confidence: 0.8153747

 $00:16:59.320 \longrightarrow 00:17:01.840$  and also from the microbiome,

NOTE Confidence: 0.8153747

 $00:17:01.840 \longrightarrow 00:17:04.944$  and we have analyzed the microbiome from some

 $00:17:04.944 \longrightarrow 00:17:08.557$  of the tumors from the right sided patients.

NOTE Confidence: 0.8153747

 $00:17:08.560 \longrightarrow 00:17:11.500$  So from both men and women,

NOTE Confidence: 0.8153747

 $00:17:11.500 \longrightarrow 00:17:13.700$  and we have a sense that

NOTE Confidence: 0.8153747

 $00:17:13.700 \longrightarrow 00:17:16.507$  there is some microbiota

NOTE Confidence: 0.8153747

 $00:17:16.507 \longrightarrow 00:17:18.722$  that are correlated with asparagine

NOTE Confidence: 0.8153747

 $00:17:18.722 \longrightarrow 00:17:21.963$  levels only in the female patients.

NOTE Confidence: 0.8153747

 $00:17:21.970 \longrightarrow 00:17:25.008$  So we do believe there is a

NOTE Confidence: 0.8153747

00:17:25.880 --> 00:17:27.185 multifactorial effect

NOTE Confidence: 0.8153747

00:17:27.185 --> 00:17:28.490 on a sparagine production

NOTE Confidence: 0.8153747

 $00:17:28.490 \longrightarrow 00:17:30.974$  that could be itself propagating

NOTE Confidence: 0.8153747

 $00:17:30.974 \longrightarrow 00:17:33.637$  the tumors as well by giving

NOTE Confidence: 0.8153747

00:17:33.637 --> 00:17:35.020 them more nutrients,

NOTE Confidence: 0.8153747

 $00{:}17{:}35.020 \dashrightarrow 00{:}17{:}37.702$  we know that Asparagine can increase

NOTE Confidence: 0.8153747

 $00:17:37.702 \longrightarrow 00:17:41.305$  the uptake of other amino acids and can

NOTE Confidence: 0.8153747

 $00{:}17{:}41.305 \dashrightarrow 00{:}17{:}44.370$  affect other processes such as even

00:17:44.370 --> 00:17:45.573 polymetabolite

NOTE Confidence: 0.8153747

00:17:45.573 --> 00:17:47.177 production or autophagy,

NOTE Confidence: 0.8153747

 $00:17:47.180 \longrightarrow 00:17:49.180$  another process is like that.

NOTE Confidence: 0.8153747

 $00:17:49.180 \longrightarrow 00:17:52.388$  So I believe this is

NOTE Confidence: 0.8153747

 $00:17:52.390 \longrightarrow 00:17:54.400$  very wide combined effect.

NOTE Confidence: 0.8153747

 $00{:}17{:}54.400 \dashrightarrow 00{:}17{:}56.595$  And really the technology metabolomics

NOTE Confidence: 0.8153747

 $00:17:56.595 \longrightarrow 00:17:59.919$  has allowed us to get an insight into

NOTE Confidence: 0.8153747

 $00:17:59.919 \longrightarrow 00:18:02.820$  this because we can not only

NOTE Confidence: 0.8153747

 $00{:}18{:}02.820 \dashrightarrow 00{:}18{:}03.750$ analyze Asparagine,

NOTE Confidence: 0.8153747

 $00:18:03.750 \longrightarrow 00:18:06.540$  we can analyze all the other

NOTE Confidence: 0.8153747

 $00:18:06.540 \longrightarrow 00:18:08.179$  metabolites that could be

NOTE Confidence: 0.8153747

 $00:18:08.180 \longrightarrow 00:18:10.190$  affected by asparagine levels as well,

NOTE Confidence: 0.8153747

 $00:18:10.190 \longrightarrow 00:18:12.535$  it could be affected by mutant Kras

NOTE Confidence: 0.8153747

 $00:18:12.540 \longrightarrow 00:18:14.144$  so it really is

NOTE Confidence: 0.8153747

00:18:14.144 --> 00:18:17.765 a wider scope or a magnifying

NOTE Confidence: 0.8153747

 $00{:}18{:}17.765 \dashrightarrow 00{:}18{:}21.119$  glass really into looking more into

 $00:18:21.120 \longrightarrow 00:18:23.004$  how these pathways are regulated

NOTE Confidence: 0.8153747

 $00{:}18{:}23.004 \dashrightarrow 00{:}18{:}25.359$  by both genes and metabolites.

NOTE Confidence: 0.7731498

 $00:18:26.040 \longrightarrow 00:18:28.416$  Have you found a difference in

NOTE Confidence: 0.7731498

 $00{:}18{:}28.416 \dashrightarrow 00{:}18{:}30.537$  As paragine between men and

NOTE Confidence: 0.7731498

00:18:30.537 --> 00:18:32.357 women who are Kras negative?

NOTE Confidence: 0.7731498

 $00:18:32.360 \longrightarrow 00:18:34.580$  That is to say, they don't

NOTE Confidence: 0.7731498

 $00:18:34.580 \longrightarrow 00:18:36.990$  have a Kras mutation.

NOTE Confidence: 0.7731498

 $00:18:36.990 \longrightarrow 00:18:39.660$  I wonder whether

NOTE Confidence: 0.7731498

 $00:18:39.660 \longrightarrow 00:18:41.950$  these two are directly linked,

NOTE Confidence: 0.7731498

 $00:18:41.950 \longrightarrow 00:18:43.321$  so for example,

NOTE Confidence: 0.7731498

 $00:18:43.321 \longrightarrow 00:18:46.520$  women may have more Kras mutations,

NOTE Confidence: 0.7731498

00:18:46.520 --> 00:18:48.998 and therefore you may be seeing

NOTE Confidence: 0.7731498

00:18:48.998 --> 00:18:50.237 these metabolomic differences

NOTE Confidence: 0.7731498

00:18:50.237 --> 00:18:52.755 or whether these are really

NOTE Confidence: 0.7731498

 $00:18:52.755 \longrightarrow 00:18:54.279$  separate processes altogether?

 $00:18:56.230 \longrightarrow 00:19:01.410$  We haven't looked at that specifically

 $00:19:04.586 \longrightarrow 00:19:07.909$  but what we have done is we've

NOTE Confidence: 0.86162424

 $00:19:07.910 \longrightarrow 00:19:09.940$  looked at survival, and actually

NOTE Confidence: 0.86162424

 $00:19:09.940 \longrightarrow 00:19:12.200$  there's many different

NOTE Confidence: 0.86162424

 $00{:}19{:}12.200 \dashrightarrow 00{:}19{:}14.008$  publicly available data sources

NOTE Confidence: 0.86162424

 $00{:}19{:}14.008 \dashrightarrow 00{:}19{:}17.039$  that we can look at to look at gene

NOTE Confidence: 0.86162424

 $00:19:17.039 \longrightarrow 00:19:19.268$  expression and also patient survival.

NOTE Confidence: 0.86162424

 $00:19:19.270 \longrightarrow 00:19:21.496$  So we looked at mutant Kras

NOTE Confidence: 0.86162424

00:19:21.496 --> 00:19:24.149 we looked at asparagine synthetase

NOTE Confidence: 0.86162424

 $00:19:24.150 \longrightarrow 00:19:27.430$  and we saw that patients with these

NOTE Confidence: 0.86162424

 $00{:}19{:}27.430 \dashrightarrow 00{:}19{:}30.421$  genes had much poorer survival if

NOTE Confidence: 0.86162424

00:19:30.421 --> 00:19:34.010 they were female and they had a right sided

NOTE Confidence: 0.86162424

 $00:19:34.010 \longrightarrow 00:19:35.786$  tumor so we compared,

NOTE Confidence: 0.86162424

00:19:35.790 --> 00:19:37.560 the Kras mutant to the Kras

NOTE Confidence: 0.86162424

 $00:19:37.560 \longrightarrow 00:19:39.261$  wild type, and it was again

NOTE Confidence: 0.86162424

 $00:19:39.261 \longrightarrow 00:19:41.110$  in these different resources

00:19:41.110 --> 00:19:43.206 we saw that it was always the female

NOTE Confidence: 0.86162424

 $00:19:43.206 \longrightarrow 00:19:44.772$  patients of right sided colon

NOTE Confidence: 0.86162424

 $00:19:44.772 \longrightarrow 00:19:46.740$  cancer that had the poorer survival,

NOTE Confidence: 0.86162424

 $00:19:46.740 \longrightarrow 00:19:48.220$  and we looked at asparagine

NOTE Confidence: 0.86162424

 $00:19:48.220 \longrightarrow 00:19:49.700$  levels within our own cohorts.

NOTE Confidence: 0.86162424

 $00:19:49.700 \longrightarrow 00:19:52.004$  And we looked at the survival data because

NOTE Confidence: 0.86162424

 $00:19:52.004 \longrightarrow 00:19:54.430$  our tumors were collected in the 1990s,

NOTE Confidence: 0.86162424

 $00:19:54.430 \longrightarrow 00:19:56.327$  so we were able to follow up

NOTE Confidence: 0.86162424

 $00{:}19{:}56.327 \dashrightarrow 00{:}19{:}57.990$  with survival of the patients.

NOTE Confidence: 0.86162424

 $00:19:57.990 \longrightarrow 00:20:00.237$  And we saw that it was again,

NOTE Confidence: 0.86162424

 $00:20:00.240 \longrightarrow 00:20:01.046$  the women with

NOTE Confidence: 0.86162424

 $00:20:01.046 \longrightarrow 00:20:03.061$  right sided tumors

NOTE Confidence: 0.86162424

00:20:03.061 --> 00:20:05.030 that had poor survival,

NOTE Confidence: 0.86162424

 $00:20:05.030 \longrightarrow 00:20:07.232$  and increased risk of recurrence if

NOTE Confidence: 0.86162424

 $00:20:07.232 \longrightarrow 00:20:09.200$  they had high asparagine levels.

NOTE Confidence: 0.85799515

 $00:20:11.080 \longrightarrow 00:20:13.320$  Interesting and did you

 $00:20:13.320 \longrightarrow 00:20:15.110$  look at whether these as paragine

NOTE Confidence: 0.85799515

 $00{:}20{:}15.110 \dashrightarrow 00{:}20{:}17.396$  levels were higher in tumors that

NOTE Confidence: 0.85799515

 $00{:}20{:}17.396 \dashrightarrow 00{:}20{:}20.093$  were larger versus smaller, or was it

NOTE Confidence: 0.85799515

 $00:20:20.093 \longrightarrow 00:20:22.019$  if you looked at two tumors

NOTE Confidence: 0.85799515

 $00:20:22.019 \longrightarrow 00:20:24.029$  that were identical in terms

NOTE Confidence: 0.85799515

00:20:24.029 --> 00:20:26.447 of their size and their grade,

NOTE Confidence: 0.85799515

 $00:20:26.450 \longrightarrow 00:20:28.280$  and the level of invasion

NOTE Confidence: 0.85799515

 $00:20:28.280 \longrightarrow 00:20:30.110$  and their lymph node status,

NOTE Confidence: 0.85799515

 $00:20:30.110 \longrightarrow 00:20:31.694$  and all of the other markers

NOTE Confidence: 0.85799515

 $00:20:31.694 \longrightarrow 00:20:33.756$  that we look at for prognosis

NOTE Confidence: 0.85799515

 $00{:}20{:}33.756 \dashrightarrow 00{:}20{:}35.648$  was a sparagine independently

NOTE Confidence: 0.85799515

00:20:35.648 --> 00:20:37.430 associated with prognosis?

NOTE Confidence: 0.85799515

 $00:20:37.430 \longrightarrow 00:20:40.034$  We didn't have the size of the tumors

NOTE Confidence: 0.85799515

 $00:20:40.034 \longrightarrow 00:20:42.140$  to sort of understand that,

NOTE Confidence: 0.85799515

 $00:20:42.140 \longrightarrow 00:20:44.120$  but that's a very good question.

 $00:20:44.120 \longrightarrow 00:20:46.860$  What we did was we we had a very small

NOTE Confidence: 0.85799515

 $00{:}20{:}46.941 \dashrightarrow 00{:}20{:}49.395$  amount of tumor from each patient,

NOTE Confidence: 0.85799515

 $00:20:49.400 \longrightarrow 00:20:52.000$  but it was the same size for each

NOTE Confidence: 0.85799515

 $00:20:52.000 \longrightarrow 00:20:54.349$  patient that the biopsy that we had.

NOTE Confidence: 0.85799515

 $00:20:54.350 \longrightarrow 00:20:56.660$  So we compared between those biopsy sizes.

NOTE Confidence: 0.85799515

 $00:20:56.660 \longrightarrow 00:20:59.388$  But we did take into account things like

NOTE Confidence: 0.85799515

 $00{:}20{:}59.388 \rightarrow 00{:}21{:}02.062$  the stage of the patient and we saw

NOTE Confidence: 0.85799515

00:21:02.062 --> 00:21:04.579 across the board that it was stage one,

NOTE Confidence: 0.85799515

 $00{:}21{:}04.580 \dashrightarrow 00{:}21{:}07.226$  stage two and three that had

NOTE Confidence: 0.85799515

 $00:21:07.230 \longrightarrow 00:21:09.974$  high levels of asparagine in the

NOTE Confidence: 0.85799515

 $00{:}21{:}09.974 \dashrightarrow 00{:}21{:}13.309$  women with right sided colon cancer,

NOTE Confidence: 0.85799515

 $00:21:13.310 \longrightarrow 00:21:15.212$  but for men they didn't have

NOTE Confidence: 0.85799515

00:21:15.212 --> 00:21:17.041 these high levels of asparagine

NOTE Confidence: 0.85799515

 $00{:}21{:}17.041 \dashrightarrow 00{:}21{:}19.009$  at these different stages,

NOTE Confidence: 0.85799515

 $00:21:19.010 \longrightarrow 00:21:22.430$  so it tended to be mostly in the

NOTE Confidence: 0.83655167

 $00:21:22.430 \longrightarrow 00:21:23.570$  women again.

00:21:23.570 --> 00:21:26.230 And so when you looked at prognosis,

NOTE Confidence: 0.83655167

 $00{:}21{:}26.230 \dashrightarrow 00{:}21{:}28.722$  did you look at it and found that

NOTE Confidence: 0.83655167

 $00:21:28.722 \longrightarrow 00:21:30.789$  asparagine was correlated with prognosis?

NOTE Confidence: 0.83655167

 $00:21:30.790 \longrightarrow 00:21:32.310$  Was that independent of

NOTE Confidence: 0.83655167

 $00:21:32.310 \longrightarrow 00:21:33.830$  their stage at presentation?

NOTE Confidence: 0.77925295

 $00:21:34.530 \longrightarrow 00:21:39.438$  Yes, it seems to be

NOTE Confidence: 0.77925295

 $00:21:39.440 \longrightarrow 00:21:41.170$  independent of stages

NOTE Confidence: 0.77925295

 $00:21:41.170 \longrightarrow 00:21:42.900$  as paragine levels within the tumors.

NOTE Confidence: 0.77925295

 $00:21:42.900 \longrightarrow 00:21:44.804$  So what we really want to do

NOTE Confidence: 0.77925295

 $00:21:44.804 \longrightarrow 00:21:47.109$  next is we want to obtain blood

NOTE Confidence: 0.77925295

 $00{:}21{:}47.109 \dashrightarrow 00{:}21{:}49.233$  samples from patients to see if

NOTE Confidence: 0.77925295

 $00:21:49.302 \longrightarrow 00:21:51.547$  we can measure as paragine levels.

NOTE Confidence: 0.77925295

 $00:21:51.550 \longrightarrow 00:21:53.825$  And if this could be potentially a

NOTE Confidence: 0.77925295

 $00:21:53.825 \longrightarrow 00:21:56.048$  biomarker as well for these patients.

NOTE Confidence: 0.77925295

 $00:21:56.050 \longrightarrow 00:21:57.952$  So that's something that we want

 $00:21:57.952 \longrightarrow 00:22:00.200$  to validate in a larger cohort.

NOTE Confidence: 0.77925295

 $00{:}22{:}00.200 \dashrightarrow 00{:}22{:}01.860$  That's something we're looking into

NOTE Confidence: 0.77925295

00:22:01.860 --> 00:22:04.010 right now to collect these samples. 00:22:05.003 --> 00:22:06.989 When we were talking about cause

NOTE Confidence: 0.8433062

 $00:22:06.989 \longrightarrow 00:22:09.546$  versus effect, it really gets to

NOTE Confidence: 0.8433062

00:22:09.546 --> 00:22:12.144 your next steps, right?

NOTE Confidence: 0.8433062

 $00:22:12.144 \longrightarrow 00:22:14.688$  So if we think that

NOTE Confidence: 0.8433062

00:22:14.688 --> 00:22:16.899 asparagine is really an effect,

NOTE Confidence: 0.8433062

 $00:22:16.900 \longrightarrow 00:22:20.196$  in other words, you have a tumor that

NOTE Confidence: 0.8433062

 $00{:}22{:}20.196 \dashrightarrow 00{:}22{:}23.378$  then causes a sparagine levels to go up,

NOTE Confidence: 0.8433062

 $00:22:23.380 \longrightarrow 00:22:25.540$  such that those as paragine levels

NOTE Confidence: 0.8433062

00:22:25.540 --> 00:22:27.268 are predictive of prognosis,

NOTE Confidence: 0.8433062

00:22:27.270 --> 00:22:28.566 certainly thinking about,

NOTE Confidence: 0.8433062

 $00:22:28.566 \longrightarrow 00:22:31.590$  can we use this as a biomarker,

NOTE Confidence: 0.8433062

 $00:22:31.590 \longrightarrow 00:22:35.542$  especially if it can be found in something

NOTE Confidence: 0.8433062

 $00:22:35.542 \longrightarrow 00:22:39.644$  simple like a blood sample or a stool sample,

 $00:22:39.650 \longrightarrow 00:22:40.946$  might be helpful.

NOTE Confidence: 0.8433062

 $00:22:40.946 \longrightarrow 00:22:42.674$  On the other hand,

NOTE Confidence: 0.8433062

00:22:42.680 --> 00:22:47.010 if we think about it being more of a cause,

NOTE Confidence: 0.8433062

 $00:22:47.010 \longrightarrow 00:22:48.466$  that is to say,

NOTE Confidence: 0.8433062

 $00:22:48.466 \longrightarrow 00:22:52.209$  if you have high levels of asparagine that

NOTE Confidence: 0.8433062

 $00:22:52.210 \longrightarrow 00:22:54.982$  then sets off a cascade that leads

NOTE Confidence: 0.8433062

00:22:54.982 --> 00:22:57.838 to worse tumors and worse prognosis,

NOTE Confidence: 0.8433062

 $00:22:57.840 \longrightarrow 00:22:59.750$  then the concept might shift

NOTE Confidence: 0.8433062

 $00:22:59.750 \longrightarrow 00:23:02.600$  not only to be a biomarker,

NOTE Confidence: 0.8433062

 $00:23:02.600 \longrightarrow 00:23:05.198$  but to really think about

NOTE Confidence: 0.8433062

 $00:23:05.198 \longrightarrow 00:23:06.930$  this as a therapeutic target.

NOTE Confidence: 0.8433062

 $00:23:06.930 \longrightarrow 00:23:11.320$  So where where do you kind of come down on

NOTE Confidence: 0.8433062

 $00:23:11.320 \longrightarrow 00:23:13.728$  your next steps with regards to that?

NOTE Confidence: 0.8060469

 $00{:}23{:}14.510 \dashrightarrow 00{:}23{:}16.958$  That's a really good question.

NOTE Confidence: 0.8060469

 $00:23:16.960 \longrightarrow 00:23:18.990$  We are currently designing

NOTE Confidence: 0.8060469

 $00:23:18.990 \longrightarrow 00:23:21.899$  studies to look at the effect of

00:23:21.899 --> 00:23:24.299 asparagine on tumor growth.

00:23:25.928 --> 00:23:27.963 Providing a different cell line,

NOTE Confidence: 0.8060469

 $00{:}23{:}27.970 \dashrightarrow 00{:}23{:}30.322$  and animal models as paragine to see

NOTE Confidence: 0.8060469

00:23:30.322 --> 00:23:32.870 if it does propagate tumor growth.

NOTE Confidence: 0.8060469

 $00:23:32.870 \longrightarrow 00:23:35.516$  There was a study

NOTE Confidence: 0.8060469

 $00:23:35.516 \longrightarrow 00:23:38.142$  out in Nature a couple of

NOTE Confidence: 0.8060469

 $00:23:38.142 \longrightarrow 00:23:40.841$  years ago where they in a different

NOTE Confidence: 0.8060469

00:23:40.841 --> 00:23:44.285 cancer model, in a breast cancer model,

NOTE Confidence: 0.8060469

 $00:23:44.290 \longrightarrow 00:23:44.950$  they fed mice

NOTE Confidence: 0.8060469

 $00:23:44.950 \longrightarrow 00:23:46.930$  asparagine in their diet and

NOTE Confidence: 0.8060469

 $00:23:46.930 \longrightarrow 00:23:49.257$  they saw that it actually caused

NOTE Confidence: 0.8060469

00:23:49.257 --> 00:23:51.262 the primary tumor to metastasize.

NOTE Confidence: 0.8060469

 $00{:}23{:}51.270 \dashrightarrow 00{:}23{:}53.580$  So there's been a number of studies

NOTE Confidence: 0.8060469

 $00:23:53.580 \longrightarrow 00:23:55.725$  that have looked into asparagine and

NOTE Confidence: 0.8060469

 $00:23:55.725 \longrightarrow 00:23:58.770$  have seen that it can propagate tumor growth.

NOTE Confidence: 0.8060469

 $00:23:58.770 \longrightarrow 00:24:03.070$  So we had we have a study that has been

00:24:03.070 --> 00:24:05.164 funded by the American Cancer Society

NOTE Confidence: 0.8060469

 $00:24:05.164 \longrightarrow 00:24:07.968$  where we will be looking at the effect

NOTE Confidence: 0.8060469

 $00:24:07.968 \longrightarrow 00:24:10.554$  of both the gene that produces

NOTE Confidence: 0.8060469

 $00:24:10.554 \longrightarrow 00:24:12.570$  asparagine so asparagine synthetase,

NOTE Confidence: 0.8060469

 $00:24:12.570 \longrightarrow 00:24:15.258$  and we've developed some cell lines where

NOTE Confidence: 0.8060469

00:24:15.258 --> 00:24:18.269 we have the knockout of this gene,

NOTE Confidence: 0.8060469

 $00:24:18.270 \longrightarrow 00:24:22.050$  and we will be

NOTE Confidence: 0.8060469

 $00:24:22.050 \longrightarrow 00:24:24.966$  injecting this

NOTE Confidence: 0.8060469

 $00:24:24.966 \longrightarrow 00:24:28.383$  into mice and also to feed them

NOTE Confidence: 0.8060469

 $00:24:28.383 \longrightarrow 00:24:31.596$  asparagine to see if it will actually

NOTE Confidence: 0.8060469

 $00:24:31.687 \longrightarrow 00:24:34.900$  affect tumor growth so

NOTE Confidence: 0.8060469

 $00:24:34.900 \longrightarrow 00:24:37.024$  hopefully in the future

NOTE Confidence: 0.8060469

 $00{:}24{:}37.024 \dashrightarrow 00{:}24{:}39.641$  down the line we can sort of test

NOTE Confidence: 0.8060469

 $00:24:39.641 \longrightarrow 00:24:42.284$  to see if any of the asparagine

NOTE Confidence: 0.8060469

 $00:24:42.284 \longrightarrow 00:24:44.509$  reducing drugs

 $00:24:44.509 \longrightarrow 00:24:47.310$  could be used as a therapeutic

NOTE Confidence: 0.8060469

 $00{:}24{:}47.310 \dashrightarrow 00{:}24{:}49.135$  to reduce a sparagine levels

NOTE Confidence: 0.8060469

00:24:49.140 --> 00:24:51.326 in colon cancer patients, potentially.

00:24:52.060 --> 00:24:54.980 iI's so interesting when you talk about that

NOTE Confidence: 0.80210626

 $00:24:54.980 \longrightarrow 00:24:57.318$  study in breast cancer where feeding

NOTE Confidence: 0.80210626

 $00:24:57.318 \longrightarrow 00:24:59.720$  as paragine led to increased metastasis.

NOTE Confidence: 0.80210626

 $00:24:59.720 \longrightarrow 00:25:02.443$  One of the obvious questions I'm sure

NOTE Confidence: 0.80210626

 $00:25:02.443 \longrightarrow 00:25:05.797$  all of our listeners want to know is

NOTE Confidence: 0.80210626

 $00:25:05.800 \longrightarrow 00:25:10.128$  what foods out there are high in asparagine?

NOTE Confidence: 0.8389733

 $00:25:11.370 \longrightarrow 00:25:13.055$  That's something

NOTE Confidence: 0.8389733

 $00:25:13.055 \longrightarrow 00:25:14.740$  we're looking into as well.

NOTE Confidence: 0.8389733

00:25:14.740 --> 00:25:17.764 As with any sort of food source,

NOTE Confidence: 0.8389733

 $00:25:17.770 \longrightarrow 00:25:19.455$  there are many different components

NOTE Confidence: 0.8389733

 $00{:}25{:}19.455 \dashrightarrow 00{:}25{:}21.448$  within a

NOTE Confidence: 0.8389733

00:25:21.448 --> 00:25:23.893 vegetable or within

NOTE Confidence: 0.8389733

 $00:25:23.893 \longrightarrow 00:25:26.734$  anything that you eat.

 $00:25:29.300 \longrightarrow 00:25:32.630$  I think if it was going to be given

 $00:25:32.630 \longrightarrow 00:25:36.050$  as a the rapeutic

NOTE Confidence: 0.8389733

 $00:25:36.050 \longrightarrow 00:25:38.946 \text{ I don't know if diet is}$ 

NOTE Confidence: 0.8389733

 $00{:}25{:}38.946 \to 00{:}25{:}41.736$  really the best way to approach it.

NOTE Confidence: 0.8389733

00:25:41.740 --> 00:25:44.008 It could be better to potentially

NOTE Confidence: 0.8389733

00:25:44.008 --> 00:25:45.142 try and reduce

NOTE Confidence: 0.8351811

 $00:25:45.150 \longrightarrow 00:25:46.320$  asparagine levels,

NOTE Confidence: 0.8351811

 $00:25:46.320 \longrightarrow 00:25:49.492$  and that's what I mean as using

NOTE Confidence: 0.8351811

 $00:25:49.492 \longrightarrow 00:25:52.075$  it as a preventative measure

NOTE Confidence: 0.8351811

00:25:52.075 --> 00:25:54.342 so encouraging people to eat less

NOTE Confidence: 0.8351811

 $00:25:54.342 \longrightarrow 00:25:56.520$  foods that are high in as paragine.

NOTE Confidence: 0.8351811

00:25:56.520 --> 00:25:58.415 Which brings us to the

NOTE Confidence: 0.8351811

 $00:25:58.415 \longrightarrow 00:26:00.310$  question which foods are those?

00:26:03.770 --> 00:26:06.038 At the moment we don't really know

NOTE Confidence: 0.80393267

 $00:26:06.038 \longrightarrow 00:26:08.538$  which foods have high asparagine levels.

NOTE Confidence: 0.80393267

 $00:26:08.540 \longrightarrow 00:26:10.532$  That's something that we

NOTE Confidence: 0.80393267

 $00{:}26{:}10.532 \longrightarrow 00{:}26{:}13.333$  would need to look into 'cause you know

00:26:13.333 --> 00:26:15.439 each food product does contain many

NOTE Confidence: 0.80393267

 $00{:}26{:}15.507 \dashrightarrow 00{:}26{:}18.075$  different amino acids and other products,

NOTE Confidence: 0.80393267

 $00:26:18.080 \longrightarrow 00:26:20.564$  and it tends to be some food products that

NOTE Confidence: 0.80393267

 $00:26:20.564 \longrightarrow 00:26:23.260$  may have higher asparagine levels have

NOTE Confidence: 0.80393267

 $00:26:23.260 \longrightarrow 00:26:25.790$  other beneficial properties.

NOTE Confidence: 0.8334635

 $00:26:28.050 \longrightarrow 00:26:29.838$  Yeah, that's a

NOTE Confidence: 0.8334635

00:26:29.838 --> 00:26:31.179 really interesting point,

NOTE Confidence: 0.8334635

 $00:26:31.180 \longrightarrow 00:26:33.286$  but I think that perhaps

NOTE Confidence: 0.8334635

 $00:26:33.286 \longrightarrow 00:26:35.839$  targeting maybe

NOTE Confidence: 0.8334635

 $00{:}26{:}35.839 \dashrightarrow 00{:}26{:}37.975$  a the rapeutic standpoint from

NOTE Confidence: 0.8334635

 $00{:}26{:}37.975 \dashrightarrow 00{:}26{:}40.111$  using something like as paragine.

NOTE Confidence: 0.8334635

00:26:40.120 --> 00:26:42.796 AIDS might perhaps be more effective,

NOTE Confidence: 0.8334635

 $00:26:42.800 \longrightarrow 00:26:45.458$  but definitely the diet would be

NOTE Confidence: 0.8334635

 $00:26:45.458 \longrightarrow 00:26:47.753$  something that would be useful

NOTE Confidence: 0.8334635

 $00:26:47.753 \longrightarrow 00:26:50.399$  to look into for these patients.

00:26:50.400 --> 00:26:53.034 Yeah, because they kind of wonder

NOTE Confidence: 0.8334635

 $00{:}26{:}53.034 \dashrightarrow 00{:}26{:}54.790$  whether women just naturally

NOTE Confidence: 0.8334635

 $00:26:54.865 \longrightarrow 00:26:56.817$  gravitate towards eating foods

NOTE Confidence: 0.8334635

00:26:56.817 --> 00:26:59.257 that are higher in asparagine

NOTE Confidence: 0.8334635

 $00:26:59.260 \longrightarrow 00:27:02.506$  or whether they process those

NOTE Confidence: 0.8334635

00:27:02.506 --> 00:27:06.299 differently such that they end up with

NOTE Confidence: 0.8334635

 $00:27:06.299 \longrightarrow 00:27:09.365$  higher levels of asparagine versus men,

NOTE Confidence: 0.8334635

 $00:27:09.370 \longrightarrow 00:27:12.278$  and so understanding how

NOTE Confidence: 0.8334635

 $00{:}27{:}12.278 \dashrightarrow 00{:}27{:}15.186$  they metabolize those foods

NOTE Confidence: 0.8334635

 $00:27:15.190 \longrightarrow 00:27:17.962$  might play a role, but can you

NOTE Confidence: 0.8334635

 $00{:}27{:}17.962 \dashrightarrow 00{:}27{:}21.367$  comment that in looking at the

NOTE Confidence: 0.8334635

 $00:27:21.367 \longrightarrow 00:27:23.887$  enzymes that breakdown asparagine and

NOTE Confidence: 0.8334635

 $00:27:23.887 \longrightarrow 00:27:26.747$  also those that increase asparagine,

NOTE Confidence: 0.8334635

 $00:27:26.750 \longrightarrow 00:27:29.878$  did you find a difference between men and

NOTE Confidence: 0.8334635

 $00:27:29.878 \longrightarrow 00:27:33.168$  women in terms of their natural enzymes?

NOTE Confidence: 0.8334635

 $00:27:33.170 \longrightarrow 00:27:35.726$  Even outside of the cancer patient?

 $00:27:35.730 \longrightarrow 00:27:37.450$  We haven't looked at

NOTE Confidence: 0.82178473

 $00{:}27{:}37.450 \dashrightarrow 00{:}27{:}39.590$  the expression levels of those,

NOTE Confidence: 0.82178473

 $00:27:39.590 \longrightarrow 00:27:42.579$  but that's a really interesting point.

NOTE Confidence: 0.82178473

 $00:27:42.580 \longrightarrow 00:27:45.639$  We do know that the asparagine synthetase

NOTE Confidence: 0.82178473

 $00{:}27{:}45.640 \dashrightarrow 00{:}27{:}47.986$  is associated with poor survival

NOTE Confidence: 0.82178473

 $00:27:47.990 \longrightarrow 00:27:50.646$  if it's a higher expression only in

NOTE Confidence: 0.82178473

 $00:27:50.646 \longrightarrow 00:27:53.479$  women with right sided colorectal cancer.

NOTE Confidence: 0.82178473

 $00{:}27{:}53.480 \dashrightarrow 00{:}27{:}55.872$  But I think also having a

NOTE Confidence: 0.82178473

 $00:27:55.872 \longrightarrow 00:27:58.031$  look more deeply at the microbiome

NOTE Confidence: 0.82178473

00:27:58.031 --> 00:28:00.835 because we know that there are many

NOTE Confidence: 0.82178473

00:28:00.835 --> 00:28:03.280 species within the microbiome that

NOTE Confidence: 0.82178473

 $00{:}28{:}03.280 \dashrightarrow 00{:}28{:}05.236$  can also metabolize a sparagine.

NOTE Confidence: 0.82178473

00:28:05.240 --> 00:28:07.200 This could be, you know,

NOTE Confidence: 0.82178473

 $00:28:07.200 \longrightarrow 00:28:08.768$  another the rapeutic that

NOTE Confidence: 0.82178473

 $00:28:08.768 \longrightarrow 00:28:10.728$  could be explored as well,

 $00:28:10.730 \longrightarrow 00:28:13.166$  and I think having a

NOTE Confidence: 0.82178473

00:28:13.166 --> 00:28:15.649 more in depth look at

NOTE Confidence: 0.82178473

 $00:28:15.650 \longrightarrow 00:28:17.530$  the microbiome that could be

NOTE Confidence: 0.82178473

 $00:28:17.530 \longrightarrow 00:28:19.842$  present within the stool sample or

NOTE Confidence: 0.82178473

 $00:28:19.842 \longrightarrow 00:28:21.687$  within the tissue samples within

NOTE Confidence: 0.82178473

00:28:21.687 --> 00:28:23.860 patients is also really important.

 $00:28:25.030 \longrightarrow 00:28:27.196$  The other question

NOTE Confidence: 0.83346504

 $00:28:27.196 \longrightarrow 00:28:29.946$  that comes to mind is while your

NOTE Confidence: 0.83346504

 $00:28:29.946 \longrightarrow 00:28:32.406$  research is really focused on the

NOTE Confidence: 0.83346504

00:28:32.406 --> 00:28:34.418 differences between men and women,

NOTE Confidence: 0.83346504

 $00:28:34.420 \longrightarrow 00:28:36.430$  one wonders, especially when you

NOTE Confidence: 0.83346504

 $00{:}28{:}36.430 \dashrightarrow 00{:}28{:}38.877$  think about the potential role for

NOTE Confidence: 0.83346504

 $00:28:38.877 \longrightarrow 00:28:41.067$  as paragine in mediating prognosis.

NOTE Confidence: 0.83346504

 $00{:}28{:}41.070 \dashrightarrow 00{:}28{:}43.597$  I'm going back to that study

NOTE Confidence: 0.83346504

 $00{:}28{:}43.597 \dashrightarrow 00{:}28{:}46.607$  that you said was published in Nature

NOTE Confidence: 0.83346504

 $00:28:46.610 \longrightarrow 00:28:49.426$  in the breast cancer model,

 $00:28:49.430 \longrightarrow 00:28:51.548$  whether if you look at

NOTE Confidence: 0.83346504

 $00:28:51.548 \longrightarrow 00:28:52.960$  men with colon cancers,

NOTE Confidence: 0.83346504

 $00:28:52.960 \longrightarrow 00:28:54.675$  whether men with higher levels

NOTE Confidence: 0.83346504

00:28:54.675 --> 00:28:56.814 of a sparagine do worse than men

NOTE Confidence: 0.83346504

00:28:56.814 --> 00:28:58.609 with lower levels of asparagine

NOTE Confidence: 0.83346504

 $00:28:58.610 \longrightarrow 00:29:00.380$  have you looked at that?

NOTE Confidence: 0.83346504

 $00:29:00.380 \longrightarrow 00:29:02.140$  We have and it doesn't

NOTE Confidence: 0.85276526

 $00:29:02.140 \longrightarrow 00:29:03.910$  seem to be the case,

NOTE Confidence: 0.85276526

 $00:29:03.910 \longrightarrow 00:29:06.781$  so it seems to be sort of what we've

NOTE Confidence: 0.85276526

 $00:29:06.781 \longrightarrow 00:29:09.906$  seen is the opposite way round.

NOTE Confidence: 0.85276526

 $00{:}29{:}09.910 \dashrightarrow 00{:}29{:}11.752$  The with you for male patient

NOTE Confidence: 0.85276526

 $00:29:11.752 \longrightarrow 00:29:13.790$  has higher levels of disparaging.

NOTE Confidence: 0.85276526

 $00:29:13.790 \longrightarrow 00:29:15.560$  They tend to do better.

NOTE Confidence: 0.85276526

 $00:29:15.560 \longrightarrow 00:29:18.176$  So it's really perplexing

NOTE Confidence: 0.85276526

00:29:18.180 --> 00:29:19.044 Interesting, you know,

NOTE Confidence: 0.85276526

00:29:19.044 --> 00:29:20.196 and it's really fascinating,

00:29:20.200 --> 00:29:21.904 so it's something that you know

NOTE Confidence: 0.85276526

 $00{:}29{:}21.904 \dashrightarrow 00{:}29{:}23.388$  where we're looking into within

NOTE Confidence: 0.85276526

00:29:23.388 --> 00:29:24.828 my lab in different models,

NOTE Confidence: 0.85276526

 $00:29:24.830 \longrightarrow 00:29:26.558$  so hopefully we'll get

NOTE Confidence: 0.85276526

 $00{:}29{:}26.560 \dashrightarrow 00{:}29{:}28.702$  better insight into this in the

NOTE Confidence: 0.85276526

 $00:29:28.702 \longrightarrow 00:29:30.610$  the next couple of years or so.

NOTE Confidence: 0.8815004

00:29:31.290 --> 00:29:33.215 Doctor Caroline Johnson is assistant

NOTE Confidence: 0.8815004

 $00:29:33.215 \longrightarrow 00:29:35.564$  professor of Epidemiology in the Department

NOTE Confidence: 0.8815004

 $00:29:35.564 \longrightarrow 00:29:37.379$  of Environmental Health Sciences at

NOTE Confidence: 0.8815004

 $00{:}29{:}37.379 \dashrightarrow 00{:}29{:}39.670$  the Yale School of Public Health.

NOTE Confidence: 0.8815004

 $00:29:39.670 \longrightarrow 00:29:41.202$  If you have questions,

NOTE Confidence: 0.8815004

 $00{:}29{:}41.202 \dashrightarrow 00{:}29{:}42.734$  the address is canceranswers@yale.edu

NOTE Confidence: 0.8815004

 $00:29:42.734 \longrightarrow 00:29:44.843$  and past editions of the program

NOTE Confidence: 0.8815004

00:29:44.843 --> 00:29:46.775 are available in audio and written

NOTE Confidence: 0.8815004

 $00:29:46.830 \longrightarrow 00:29:48.438$  form at yalecancercenter.org.

 $00{:}29{:}48.440 {\:{\circ}{\circ}{\circ}}>00{:}29{:}51.216$  We hope you'll join us next week to

NOTE Confidence: 0.8815004

 $00{:}29{:}51.216 \dashrightarrow 00{:}29{:}53.925$  learn more about the fight against

NOTE Confidence: 0.8815004

 $00{:}29{:}53.925 \dashrightarrow 00{:}29{:}56.823$  cancer here on Connecticut Public Radio.