WEBVTT

00:00:00.000 --> 00:00:03.186 Funding for Yale Cancer Answers is NOTE Confidence: 0.9380176 00:00:03.186 --> 00:00:06.200 provided by Smilow Cancer Hospital. NOTE Confidence: 0.9380176 00:00:06.200 --> 00:00:08.400 Welcome to Yale Cancer Answers NOTE Confidence: 0.9380176 $00:00:08.400 \rightarrow 00:00:10.160$ with Doctor Anees Chappar. NOTE Confidence: 0.9380176 00:00:10.160 --> 00:00:11.656 Yale Cancer Answers features NOTE Confidence: 0.9380176 00:00:11.656 --> 00:00:13.526 the latest information on cancer NOTE Confidence: 0.9380176 $00:00:13.526 \rightarrow 00:00:15.430$ care by welcoming oncologists and NOTE Confidence: 0.9380176 $00:00:15.430 \rightarrow 00:00:17.638$ specialists who are on the forefront NOTE Confidence: 0.9380176 $00:00:17.699 \longrightarrow 00:00:19.397$ of the battle to fight cancer. NOTE Confidence: 0.9380176 $00:00:19.400 \rightarrow 00:00:21.752$ This week it's a conversation about new NOTE Confidence: 0.9380176 $00:00:21.752 \rightarrow 00:00:24.026$ research into the early detection of NOTE Confidence: 0.9380176 $00:00:24.026 \rightarrow 00:00:26.426$ ovarian cancer with Doctor Stacy Malaker. NOTE Confidence: 0.9380176 00:00:26.430 --> 00:00:28.434 Dr. Malaker is an assistant professor NOTE Confidence: 0.9380176 00:00:28.434 --> 00:00:30.238 in the Department of Chemistry NOTE Confidence: 0.9380176 $00:00:30.238 \rightarrow 00:00:32.084$ at Yale University, and Dr. NOTE Confidence: 0.9380176

00:00:32.084 --> 00:00:33.926 Chagpar is a professor of Surgical

NOTE Confidence: 0.9380176

 $00:00:33.926 \rightarrow 00:00:36.188$ oncology at the Yale School of Medicine.

NOTE Confidence: 0.92948914

00:00:37.390 --> 00:00:39.084 So, Stacy, maybe we can start off

NOTE Confidence: 0.92948914

 $00:00:39.084 \rightarrow 00:00:41.048$ by you telling us a little bit more

NOTE Confidence: 0.92948914

 $00:00:41.048 \longrightarrow 00:00:42.789$ about yourself and what it is you do.

NOTE Confidence: 0.92948914

 $00{:}00{:}43.870 \dashrightarrow 00{:}00{:}46.685$ I got my PhD at the University of Virginia NOTE Confidence: 0.92948914

 $00{:}00{:}46.685 \dashrightarrow 00{:}00{:}49.793$ where I was in the lab of Professor

NOTE Confidence: 0.92948914

 $00:00:49.793 \longrightarrow 00:00:53.032$ Donald Hunt and he is one of

NOTE Confidence: 0.92948914

 $00{:}00{:}53.032 \dashrightarrow 00{:}00{:}55.078$ the founding fathers of biological mass

NOTE Confidence: 0.92948914

 $00{:}00{:}55{.}078 \dashrightarrow 00{:}00{:}57{.}766$ spectrometry and mass spec is kind

NOTE Confidence: 0.92948914

 $00{:}00{:}57.766 \dashrightarrow 00{:}01{:}00.415$ of what I do or what I'm known for.

NOTE Confidence: 0.92948914

 $00:01:00.420 \longrightarrow 00:01:03.280$ And then I did my postdoc in the

NOTE Confidence: 0.92948914

 $00{:}01{:}03.361 \dashrightarrow 00{:}01{:}06.396$ the lab of Carolyn Bertozzi, who just

NOTE Confidence: 0.92948914

 $00:01:06.396 \rightarrow 00:01:09.812$ recently won the Nobel Prize in Chemistry.

NOTE Confidence: 0.92948914

 $00:01:09.820 \rightarrow 00:01:13.008$ And there I got really interested in

NOTE Confidence: 0.92948914

00:01:13.008 --> 00:01:16.580 a class of of proteins called mucins

- NOTE Confidence: 0.92948914
- $00:01:16.580 \longrightarrow 00:01:19.408$ which have tons and tons of sugar

 $00:01:19.408 \longrightarrow 00:01:20.620$ units on them.

NOTE Confidence: 0.92948914

 $00{:}01{:}20.620 \dashrightarrow 00{:}01{:}22.336$ And so I spent

NOTE Confidence: 0.92948914

 $00:01:22.340 \rightarrow 00:01:24.180$ five years there researching those.

NOTE Confidence: 0.92948914

00:01:24.180 --> 00:01:27.260 And so now in my own laboratory,

NOTE Confidence: 0.92948914

 $00:01:27.260 \longrightarrow 00:01:30.152$ I combine the expertise of the

NOTE Confidence: 0.92948914

 $00:01:30.152 \dashrightarrow 00:01:32.636$ instrumentation or the mass spec

NOTE Confidence: 0.92948914

 $00:01:32.636 \rightarrow 00:01:35.414$ and the sugars or glycobiology

NOTE Confidence: 0.92948914

 $00:01:35.420 \longrightarrow 00:01:37.436$ and we do something

NOTE Confidence: 0.92948914

00:01:37.436 --> 00:01:38.300 that's called glycoproteomics,

NOTE Confidence: 0.92948914

 $00:01:38.300 \longrightarrow 00:01:40.036$ which is studying sugars

NOTE Confidence: 0.92948914

 $00{:}01{:}40.036 \dashrightarrow 00{:}01{:}41.338$ that modify proteins.

NOTE Confidence: 0.9306428

 $00:01:41.580 \longrightarrow 00:01:43.848$ So now everybody wants to know, what

NOTE Confidence: 0.9306428

 $00{:}01{:}43.848 \dashrightarrow 00{:}01{:}46.815$ does any of this have to do with cancer?

NOTE Confidence: 0.9366184

 $00:01:47.920 \longrightarrow 00:01:50.110$ Sure. So sugars are altered in

 $00:01:50.110 \rightarrow 00:01:51.990$ pretty much every disease that's

NOTE Confidence: 0.9366184

 $00{:}01{:}51{.}990 \dashrightarrow 00{:}01{:}54{.}078$ ever been studied and

NOTE Confidence: 0.9366184

00:01:54.080 --> 00:01:55.436 primarily in cancer,

NOTE Confidence: 0.9366184

00:01:55.436 --> 00:01:57.696 but also other diseases like

NOTE Confidence: 0.9366184

 $00:01:57.696 \longrightarrow 00:01:59.826$ inflammatory bowel disease or cystic

NOTE Confidence: 0.9366184

00:01:59.826 --> 00:02:01.788 fibrosis or even heart disease.

NOTE Confidence: 0.9366184

 $00:02:01.788 \longrightarrow 00:02:04.164$ And so we try to monopolize

NOTE Confidence: 0.9366184

 $00:02:04.164 \longrightarrow 00:02:07.115$ on those changes in the sugar

NOTE Confidence: 0.9366184

 $00{:}02{:}07{.}115 \dashrightarrow 00{:}02{:}09{.}224$ structures to identify

NOTE Confidence: 0.9366184

 $00:02:09.224 \rightarrow 00:02:10.472$ new biomarkers or potential

NOTE Confidence: 0.9366184

 $00:02:10.472 \longrightarrow 00:02:11.720$ the rapeutics.

NOTE Confidence: 0.9366184

00:02:12.960 --> 00:02:15.935 Tell us more about your

NOTE Confidence: 0.9366184

 $00:02:15.935 \rightarrow 00:02:18.086$ research in particular, what are you

NOTE Confidence: 0.9366184

 $00:02:18.086 \rightarrow 00:02:20.130$ looking at and how might this make

NOTE Confidence: 0.9366184

 $00:02:20.194 \longrightarrow 00:02:22.366$ a difference to people with cancer?

NOTE Confidence: 0.934648

 $00:02:23.490 \longrightarrow 00:02:26.850$ Sure, this project in

- NOTE Confidence: 0.934648
- 00:02:26.850 --> 00:02:29.090 particular regarding ovarian cancer,

 $00:02:29.090 \longrightarrow 00:02:32.420$ right now more than 70% of women

NOTE Confidence: 0.934648

 $00:02:32.420 \longrightarrow 00:02:34.120$ are diagnosed with ovarian

NOTE Confidence: 0.934648

 $00:02:34.120 \rightarrow 00:02:35.804$ cancer in the late stages,

NOTE Confidence: 0.934648

 $00:02:35.804 \longrightarrow 00:02:38.558$ so stage 3 or stage 4 and the five

NOTE Confidence: 0.934648

 $00{:}02{:}38.558 \dashrightarrow 00{:}02{:}40.778$ year survival rate for women diagnosed

NOTE Confidence: 0.934648

 $00:02:40.778 \dashrightarrow 00:02:43.049$ in those stages is really poor.

NOTE Confidence: 0.934648

 $00{:}02{:}43.050 \dashrightarrow 00{:}02{:}45.170$ It's less than 20%.

NOTE Confidence: 0.934648

 $00{:}02{:}45{.}170 \dashrightarrow 00{:}02{:}47{.}685$ Now if ovarian cancer is caught in

NOTE Confidence: 0.934648

00:02:47.685 --> 00:02:49.590 early stages like stage 1 or two,

NOTE Confidence: 0.934648

 $00:02:49.590 \dashrightarrow 00:02:52.026$ that five year survival rate goes up to 95%.

NOTE Confidence: 0.934648

 $00{:}02{:}52{.}026 \dashrightarrow 00{:}02{:}53{.}958$ But the problem is that we don't

NOTE Confidence: 0.934648

 $00:02:53.958 \longrightarrow 00:02:55.784$ have a really good biomarker

NOTE Confidence: 0.934648

 $00:02:55.784 \longrightarrow 00:02:57.789$ for ovarian cancer right now.

NOTE Confidence: 0.934648

 $00:02:57.790 \rightarrow 00:03:00.238$ Right now what is currently used

 $00:03:00.238 \rightarrow 00:03:02.251$ is something that's called CA-125

NOTE Confidence: 0.934648

 $00{:}03{:}02{.}251 \dashrightarrow 00{:}03{:}04{.}918$ and CA-125 happens to be one of

NOTE Confidence: 0.934648

 $00{:}03{:}04{.}918 \dashrightarrow 00{:}03{:}07{.}107$ those muc in type proteins that

NOTE Confidence: 0.934648

 $00{:}03{:}07{.}107 \dashrightarrow 00{:}03{:}09{.}347$ I was talking about earlier.

NOTE Confidence: 0.934648

 $00:03:09.350 \longrightarrow 00:03:11.343$ And so it's this really,

NOTE Confidence: 0.934648

00:03:11.343 --> 00:03:12.908 really huge protein that's decorated

NOTE Confidence: 0.934648

 $00:03:12.908 \dashrightarrow 00:03:15.190$ by tons and tons and tons of sugars.

NOTE Confidence: 0.934648

 $00:03:15.190 \dashrightarrow 00:03:18.700$ And so 80% of its mass is actually sugar

NOTE Confidence: 0.934648

 $00{:}03{:}18.700 \dashrightarrow 00{:}03{:}22.484$ units as opposed to the protein backbone.

NOTE Confidence: 0.934648

 $00:03:22.490 \longrightarrow 00:03:26.362$ Again, the sugar units

NOTE Confidence: 0.934648

 $00:03:26.362 \rightarrow 00:03:29.322$ are perpetually disordered in cancer

NOTE Confidence: 0.934648

00:03:29.322 --> 00:03:33.210 yet when doctors are detecting the CA-125,

NOTE Confidence: 0.934648

 $00:03:33.210 \rightarrow 00:03:35.360$ they're usually only detecting the

NOTE Confidence: 0.934648

 $00:03:35.360 \rightarrow 00:03:37.510$ unmodified regions of the protein.

NOTE Confidence: 0.934648

 $00{:}03{:}37{.}510 \dashrightarrow 00{:}03{:}40{.}331$ And so we want to identify altered

NOTE Confidence: 0.934648

00:03:40.331 - > 00:03:43.030 sugar units on this huge protein

- NOTE Confidence: 0.934648
- 00:03:43.030 00:03:45.870 to ideally detect cancer earlier.

00:03:45.870 - 00:03:48.318 So that if we can do that and identify

NOTE Confidence: 0.934648

 $00:03:48.318 \rightarrow 00:03:49.658$ something that's changed early

NOTE Confidence: 0.934648

 $00:03:49.658 \longrightarrow 00:03:51.662$ on in the progression of cancer,

NOTE Confidence: 0.934648

 $00:03:51.670 \dashrightarrow 00:03:54.166$ then we could ostensibly develop a

NOTE Confidence: 0.934648

 $00:03:54.166 \rightarrow 00:03:56.989$ better biomarker and early stage detection.

NOTE Confidence: 0.9350412

00:03:58.070 --> 00:04:01.146 Yeah, I think

NOTE Confidence: 0.9350412

 $00:04:01.146 \longrightarrow 00:04:03.210$ the problem though is

NOTE Confidence: 0.9350412

 $00:04:03.210 \longrightarrow 00:04:05.274$ that for ovarian cancer,

NOTE Confidence: 0.9350412

 $00:04:05.280 \longrightarrow 00:04:07.720$ it's not incredibly common.

NOTE Confidence: 0.9350412

 $00{:}04{:}07.720 \dashrightarrow 00{:}04{:}09.757$ You're quite right, when it is diagnosed,

NOTE Confidence: 0.9350412

 $00{:}04{:}09{.}760 \dashrightarrow 00{:}04{:}11{.}460$ it's diagnosed late because we

NOTE Confidence: 0.9350412

 $00{:}04{:}11.460 \dashrightarrow 00{:}04{:}13.160$ don't have a screening test.

NOTE Confidence: 0.9350412

 $00{:}04{:}13.160 \dashrightarrow 00{:}04{:}16.198$ But one of the questions always is,

NOTE Confidence: 0.9350412

 $00:04:16.200 \longrightarrow 00:04:18.380$ you know, are there blood

 $00:04:18.380 \longrightarrow 00:04:20.560$ tests for detection of cancer?

NOTE Confidence: 0.9350412

 $00:04:20.560 \longrightarrow 00:04:22.756$ Are there blood tests for screening?

NOTE Confidence: 0.9350412

 $00{:}04{:}22.760 \dashrightarrow 00{:}04{:}25.476$ And while CA-125 is a biomarker that NOTE Confidence: 0.9350412

 $00{:}04{:}25{.}476 \dashrightarrow 00{:}04{:}29{.}128$ might be used to help doctors in terms

NOTE Confidence: 0.9350412

 $00{:}04{:}29{.}128 \dashrightarrow 00{:}04{:}31{.}533$ of monitoring progression of disease,

NOTE Confidence: 0.9350412

 $00{:}04{:}31{.}540 \dashrightarrow 00{:}04{:}34{.}340$ it's really not a wides pread

NOTE Confidence: 0.9350412

 $00:04:34.340 \rightarrow 00:04:37.140$ screening tool like for example,

NOTE Confidence: 0.9350412

 $00:04:37.140 \longrightarrow 00:04:39.036$ a colaguard would be or

NOTE Confidence: 0.9350412

00:04:39.036 --> 00:04:40.300 a mammogram would be.

NOTE Confidence: 0.9350412

 $00:04:40.300 \rightarrow 00:04:42.939$ So is your research trying to look

NOTE Confidence: 0.9350412

 $00{:}04{:}42{.}939 \dashrightarrow 00{:}04{:}45{.}260$ at these altered sugar moieties,

NOTE Confidence: 0.9350412

 $00:04:45.260 \rightarrow 00:04:47.780$ really trying to find a screening modality?

NOTE Confidence: 0.9350412

 $00{:}04{:}47{.}780 \dashrightarrow 00{:}04{:}48{.}896$ And if so,

NOTE Confidence: 0.9350412

 $00:04:48.896 \longrightarrow 00:04:50.756$ would that be administered on

NOTE Confidence: 0.9350412

 $00{:}04{:}50.756 \dashrightarrow 00{:}04{:}52.760$ a population basis like to all

NOTE Confidence: 0.9350412

 $00:04:52.760 \longrightarrow 00:04:55.007$ women or would it be for women

- NOTE Confidence: 0.9350412
- $00:04:55.007 \rightarrow 00:04:57.419$ who are particularly at high risk?
- NOTE Confidence: 0.9268508
- $00{:}04{:}58{.}540 \dashrightarrow 00{:}05{:}00{.}654$ So that's a great question and I
- NOTE Confidence: 0.9268508
- $00:05:00.654 \rightarrow 00:05:02.820$ think that as a basic scientist,
- NOTE Confidence: 0.9268508
- 00:05:02.820 --> 00:05:05.660 I can only say that I'm
- NOTE Confidence: 0.9268508
- $00:05:05.660 \longrightarrow 00:05:07.346$ hopeful that we'll be able
- NOTE Confidence: 0.9268508
- $00:05:07.346 \longrightarrow 00:05:08.782$ to identify something that has
- NOTE Confidence: 0.9268508
- $00:05:08.782 \longrightarrow 00:05:10.057$ changed early on in cancer.
- NOTE Confidence: 0.9268508
- $00:05:10.060 \rightarrow 00:05:13.580$ So we're using serum from high risk patients,
- NOTE Confidence: 0.9268508
- $00{:}05{:}13.580 \dashrightarrow 00{:}05{:}17.048$ some of whom developed ovarian cancer.
- NOTE Confidence: 0.9268508
- $00{:}05{:}17.050 \dashrightarrow 00{:}05{:}18.986$ And so the idea would be that we
- NOTE Confidence: 0.9268508
- $00:05:18.986 \rightarrow 00:05:20.502$ do identify something that could
- NOTE Confidence: 0.9268508
- $00:05:20.502 \rightarrow 00:05:22.446$ be used as a screening modality,
- NOTE Confidence: 0.9268508
- $00:05:22.450 \rightarrow 00:05:24.442$ but I don't want to make any early
- NOTE Confidence: 0.9268508
- $00{:}05{:}24{.}442 \dashrightarrow 00{:}05{:}26{.}010$ promises since we haven't actually,
- NOTE Confidence: 0.9268508
- $00:05:26.010 \rightarrow 00:05:27.930$ you know, identified anything quite yet.
- NOTE Confidence: 0.93441564

- 00:05:28.210 --> 00:05:29.715 Tell us a little bit
- NOTE Confidence: 0.93441564
- $00{:}05{:}29{.}715$ --> $00{:}05{:}30{.}810$ more about your project.
- NOTE Confidence: 0.93441564
- 00:05:30.810 -> 00:05:32.736 I mean, when you say you're
- NOTE Confidence: 0.93441564
- 00:05:32.736 --> 00:05:34.490 looking at high risk women,
- NOTE Confidence: 0.93441564
- $00:05:34.490 \dashrightarrow 00:05:37.208$ you tell us more about who those women are.
- NOTE Confidence: 0.93441564
- $00{:}05{:}37{.}210 \dashrightarrow 00{:}05{:}39{.}964$ And the concept that you kind of laid out,
- NOTE Confidence: 0.93441564
- 00:05:39.970 --> 00:05:41.490 if I've understood it correctly,
- NOTE Confidence: 0.93441564
- $00:05:41.490 \longrightarrow 00:05:42.890$ is that you're looking
- NOTE Confidence: 0.93441564
- $00{:}05{:}42.890 \dashrightarrow 00{:}05{:}44.290$ at these high-risk women.
- NOTE Confidence: 0.93441564
- $00:05:44.290 \rightarrow 00:05:47.220$ You're taking blood samples from
- NOTE Confidence: 0.93441564
- $00{:}05{:}47.220 \dashrightarrow 00{:}05{:}49.615$ them and comparing those of them
- NOTE Confidence: 0.93441564
- $00:05:49.615 \longrightarrow 00:05:51.958$ who went on to truly develop
- NOTE Confidence: 0.93441564
- 00:05:51.958 --> 00:05:54.730 ovarian cancer to those who didn't?
- NOTE Confidence: 0.93441564
- $00:05:54.730 \longrightarrow 00:05:56.370$ Is that right?
- NOTE Confidence: 0.928521
- $00{:}05{:}56{.}370 \dashrightarrow 00{:}05{:}57{.}930$ That's basically correct.
- NOTE Confidence: 0.928521
- $00:05:57.930 \longrightarrow 00:06:01.570$ So we have access to approximately 4000

- NOTE Confidence: 0.928521
- 00:06:01.650 --> 00:06:04.370 serum samples from high-risk women.

 $00:06:04.370 \longrightarrow 00:06:05.855$ These are women that have

NOTE Confidence: 0.928521

00:06:05.855 --> 00:06:07.496 been diagnosed with the BRCA,

NOTE Confidence: 0.928521

 $00{:}06{:}07{.}496 \dashrightarrow 00{:}06{:}09{.}280$ one or two mutations.

NOTE Confidence: 0.928521

 $00:06:09.280 \rightarrow 00:06:12.836$ So from the point of genetic diagnosis,

NOTE Confidence: 0.928521

 $00:06:12.840 \dashrightarrow 00:06:15.759$ you know throughout the years many,

NOTE Confidence: 0.928521

 $00:06:15.760 \rightarrow 00:06:17.315$ many samples have been collected

NOTE Confidence: 0.928521

 $00:06:17.315 \longrightarrow 00:06:18.559$ from these various women.

NOTE Confidence: 0.928521

 $00:06:18.560 \longrightarrow 00:06:21.185$ And so to kind of develop our

NOTE Confidence: 0.928521

 $00:06:21.185 \dashrightarrow 00:06:23.164$ technology we're using women that

NOTE Confidence: 0.928521

 $00:06:23.164 \rightarrow 00:06:25.109$ have not actually been diagnosed

NOTE Confidence: 0.928521

 $00{:}06{:}25{.}109 \dashrightarrow 00{:}06{:}27{.}800$ just to be able to identify the

NOTE Confidence: 0.928521

00:06:27.800 --> 00:06:29.905 CA-125 modifications or sugar units

NOTE Confidence: 0.928521

 $00{:}06{:}29{.}905 \dashrightarrow 00{:}06{:}32{.}493$ and then we'd basically be given

NOTE Confidence: 0.928521

00:06:32.493 --> 00:06:34.533 a blinded sample and hopefully

00:06:34.533 - > 00:06:36.596 identify those biomarkers

NOTE Confidence: 0.928521

 $00{:}06{:}36{.}596 \dashrightarrow 00{:}06{:}39{.}476$ or what have you that could indicate

NOTE Confidence: 0.928521

 $00:06:39.476 \dashrightarrow 00:06:42.010$ cancer versus non cancerous samples. NOTE Confidence: 0.91922235

 $00{:}06{:}42.770 \dashrightarrow 00{:}06{:}46.970$ And so that sounds really interesting NOTE Confidence: 0.91922235

 $00{:}06{:}46{.}970 \dashrightarrow 00{:}06{:}49{.}730$ when we think about BRC A1 and two

NOTE Confidence: 0.91922235

 $00:06:49.730 \longrightarrow 00:06:52.255$ often times we think not only of

NOTE Confidence: 0.91922235

00:06:52.255 --> 00:06:54.520 ovarian cancer but also of breast

NOTE Confidence: 0.91922235

 $00{:}06{:}54{.}520 \dashrightarrow 00{:}06{:}57{.}125$ cancer and one of the questions that

NOTE Confidence: 0.91922235

 $00{:}06{:}57{.}125 \dashrightarrow 00{:}07{:}00{.}565$ is often asked is, is there a

NOTE Confidence: 0.91922235

 $00{:}07{:}00.565 \dashrightarrow 00{:}07{:}03.369$ blood test for breast cancer as well.

NOTE Confidence: 0.91922235

 $00{:}07{:}03.370 \dashrightarrow 00{:}07{:}05.520$ You mentioned earlier that the

NOTE Confidence: 0.91922235

00:07:05.520 --> 00:07:08.454 sugar moieties tend to be, you know,

NOTE Confidence: 0.91922235

 $00{:}07{:}08.454 \dashrightarrow 00{:}07{:}10.414$ involved or disrupted or altered

NOTE Confidence: 0.91922235

 $00:07:10.414 \longrightarrow 00:07:12.589$ in a variety of processes.

NOTE Confidence: 0.91922235

 $00:07:12.590 \longrightarrow 00:07:14.510$ Do you think that your technology

NOTE Confidence: 0.91922235

 $00:07:14.510 \longrightarrow 00:07:17.141$ might have a role to play in breast

00:07:17.141 -> 00:07:19.061 cancer as well as ovarian cancer?

NOTE Confidence: 0.91922235

 $00{:}07{:}19{.}070$ --> $00{:}07{:}21{.}632$ Or is it really something specific about

NOTE Confidence: 0.91922235

 $00:07:21.632 \rightarrow 00:07:23.828$ ovarian cancer that you're looking at?

NOTE Confidence: 0.93097055

 $00:07:24.510 \rightarrow 00:07:27.149$ It's pretty much any epithelial cancer,

NOTE Confidence: 0.93097055

 $00:07:27.150 \longrightarrow 00:07:29.035$ you know, has these altered

NOTE Confidence: 0.93097055

 $00{:}07{:}29{.}035 \dashrightarrow 00{:}07{:}30{.}994$ muc in structures and so

NOTE Confidence: 0.93097055

 $00:07:30.994 \longrightarrow 00:07:35.390$ CA-125 is known as Mucin 16 or Mach 16.

NOTE Confidence: 0.93097055

 $00:07:35.390 \rightarrow 00:07:38.742$ Mucin one or Mach one is dysregulated or

NOTE Confidence: 0.93097055

 $00{:}07{:}38{.}742 \dashrightarrow 00{:}07{:}41{.}557$ upregulated in over 90% of breast carcinomas.

NOTE Confidence: 0.93097055

 $00:07:41.557 \rightarrow 00:07:44.131$ So this could ostensibly be extended

NOTE Confidence: 0.93097055

 $00:07:44.131 \longrightarrow 00:07:46.158$ to other cancers.

NOTE Confidence: 0.93097055

00:07:46.158 --> 00:07:48.224 Pancreatic cancer is another one that

NOTE Confidence: 0.93097055

 $00{:}07{:}48.224 \dashrightarrow 00{:}07{:}50.065$ would be really interesting to look at.

NOTE Confidence: 0.93097055

 $00{:}07{:}50{.}070 \dashrightarrow 00{:}07{:}52{.}326$ Pretty much any epithelial cancer is

NOTE Confidence: 0.93097055

 $00:07:52.326 \rightarrow 00:07:53.830$ associated with dysregulated mucins.

 $00:07:54.830 \rightarrow 00:07:58.350$ And so presumably in this population

NOTE Confidence: 0.93529564

 $00{:}07{:}58.350 \dashrightarrow 00{:}08{:}02.287$ of BRCA one and two gene mutation carriers,

NOTE Confidence: 0.93529564

 $00:08:02.290 \longrightarrow 00:08:05.134$ you'd be able to see not only the

NOTE Confidence: 0.93529564

 $00{:}08{:}05{.}134 \dashrightarrow 00{:}08{:}07{.}102$ comparison between those who developed

NOTE Confidence: 0.93529564

 $00:08:07.102 \rightarrow 00:08:09.810$ ovarian cancer and those who did not,

NOTE Confidence: 0.93529564

00:08:09.810 --> 00:08:11.987 but also those who developed breast cancer NOTE Confidence: 0.93529564

 $00{:}08{:}11{.}987 \dashrightarrow 00{:}08{:}14{.}114$ or in fact pancreatic cancer because

NOTE Confidence: 0.93529564

 $00:08:14.114 \dashrightarrow 00:08:16.746$ that's another cancer that tends to be

NOTE Confidence: 0.93529564

00:08:16.808 --> 00:08:18.970 associated with those mutations, right? NOTE Confidence: 0.93121064

00:08:19.410 --> 00:08:21.622 Yeah, absolutely. I would have to talk NOTE Confidence: 0.93121064

 $00{:}08{:}21.622 \dashrightarrow 00{:}08{:}23.740$ to my collaborators to see how many NOTE Confidence: 0.93121064

 $00:08:23.740 \longrightarrow 00:08:25.408$ of these women actually did develop

NOTE Confidence: 0.93121064

 $00{:}08{:}25{.}465 \dashrightarrow 00{:}08{:}27{.}210$ breast and or pancreatic cancer.

NOTE Confidence: 0.93121064

 $00{:}08{:}27{.}210 \dashrightarrow 00{:}08{:}28{.}645$ But that could be done.

NOTE Confidence: 0.93182003

 $00{:}08{:}29{.}600 \dashrightarrow 00{:}08{:}32{.}048$ So you know one of the things when we

NOTE Confidence: 0.93182003

 $00:08:32.048 \rightarrow 00:08:34.477$ think about that kind of an experiment,

- NOTE Confidence: 0.93182003
- $00:08:34.480 \longrightarrow 00:08:35.775$ one would think that time

 $00{:}08{:}35{.}775 \dashrightarrow 00{:}08{:}37{.}280$ has something to do with it,

NOTE Confidence: 0.93182003

 $00:08:37.280 \longrightarrow 00:08:41.072$ right that it takes time to develop

NOTE Confidence: 0.93182003

00:08:41.072 -> 00:08:43.837 these alterations in the protein

NOTE Confidence: 0.93182003

 $00{:}08{:}43.837 \dashrightarrow 00{:}08{:}46.435$ structure or in the sugar structure

NOTE Confidence: 0.93182003

 $00:08:46.440 \longrightarrow 00:08:48.358$ and it takes time to develop cancer.

NOTE Confidence: 0.93182003

 $00:08:48.360 \dashrightarrow 00:08:53.328$ So have you found any correlation

NOTE Confidence: 0.93182003

 $00:08:53.328 \longrightarrow 00:08:56.520$ between the the timing of things,

NOTE Confidence: 0.93182003

 $00{:}08{:}56{.}520 \dashrightarrow 00{:}08{:}59{.}131$ I mean presumably if some body just gets

NOTE Confidence: 0.93182003

 $00:08:59.131 \dashrightarrow 00:09:02.856$ a blood sample today and you know

NOTE Confidence: 0.93182003

00:09:02.856 --> 00:09:05.187 and then isn't followed for very long,

NOTE Confidence: 0.93182003

 $00{:}09{:}05{.}190 \dashrightarrow 00{:}09{:}07{.}188$ you may not find an association.

NOTE Confidence: 0.9339164

 $00:09:08.350 \rightarrow 00:09:10.445$ Yeah, that's a really great point.

NOTE Confidence: 0.9339164

00:09:10.445 --> 00:09:12.790 And you know this is we're very,

NOTE Confidence: 0.9339164

 $00{:}09{:}12.790 \dashrightarrow 00{:}09{:}14.750$ very, very early on in this project.

 $00:09:14.750 \longrightarrow 00:09:17.190$ It was just awarded a few months ago.

NOTE Confidence: 0.9339164

00:09:17.190 --> 00:09:19.254 And so I anticipate we will

NOTE Confidence: 0.9339164

 $00:09:19.254 \dashrightarrow 00:09:21.030$ actually see changes over time.

NOTE Confidence: 0.9339164

00:09:21.030 --> 00:09:22.986 But because again

NOTE Confidence: 0.9339164

 $00:09:22.986 \longrightarrow 00:09:24.677$ we haven't actually done much

NOTE Confidence: 0.9339164

 $00:09:24.677 \longrightarrow 00:09:26.267$ of the research quite yet,

NOTE Confidence: 0.9339164

 $00:09:26.270 \longrightarrow 00:09:27.827$ I can't give you a straight answer to that.

NOTE Confidence: 0.9314148

 $00:09:28.310 \longrightarrow 00:09:32.896$ But of these 4000 women,

NOTE Confidence: 0.9314148

 $00:09:32.896 \rightarrow 00:09:36.794$ are you kind of looking at these women

NOTE Confidence: 0.9314148

00:09:36.794 --> 00:09:40.224 going forward as well or is this kind of NOTE Confidence: 0.9314148

 $00{:}09{:}40{.}224$ --> $00{:}09{:}42{.}606$ a deidentified mass sample that you've NOTE Confidence: $0{.}9314148$

 $00:09:42.606 \rightarrow 00:09:45.602$ got where you've got some clinical

NOTE Confidence: 0.9314148

 $00{:}09{:}45{.}602 \dashrightarrow 00{:}09{:}48{.}085$ correlation data and would have to

NOTE Confidence: 0.9314148

 $00{:}09{:}48.085 \dashrightarrow 00{:}09{:}50.762$ use covariates to see whether a

NOTE Confidence: 0.9314148

 $00:09:50.762 \dashrightarrow 00:09:52.389$ relationship existed. Fo example,

NOTE Confidence: 0.9314148

 $00:09:52.389 \rightarrow 00:09:54.147$ looking at age as a surrogate.

- NOTE Confidence: 0.9352205
- 00:09:55.610 --> 00:09:57.050 OK. So just to clarify,

00:09:57.050 --> 00:09:58.494 it's not 4000 women,

NOTE Confidence: 0.9352205

 $00:09:58.494 \rightarrow 00:10:00.660$ it's 4000 samples that have been

NOTE Confidence: 0.9352205

 $00{:}10{:}00{.}729 \dashrightarrow 00{:}10{:}02{.}969$ collected from I think 50 to 100

NOTE Confidence: 0.9352205

 $00:10:02.969 \rightarrow 00:10:05.089$ women over the course of their life.

NOTE Confidence: 0.9352205

 $00{:}10{:}07{.}890 \dashrightarrow 00{:}10{:}09{.}265$ I see, so then you're comparing samples

NOTE Confidence: 0.9352205

 $00:10:09.265 \longrightarrow 00:10:10.970$ as you go along in time.

NOTE Confidence: 0.9352205

 $00:10:10.970 \longrightarrow 00:10:14.102$ So there might be out of the

NOTE Confidence: 0.9352205

 $00{:}10{:}14.102 \dashrightarrow 00{:}10{:}17.690$ 4000, say 100 people,

NOTE Confidence: 0.9352205

 $00:10:17.690 \longrightarrow 00:10:19.888$ then that would be like 40 time

NOTE Confidence: 0.9352205

00:10:19.888 --> 00:10:21.609 points per person on average,

NOTE Confidence: 0.9352205

 $00{:}10{:}21.850 \dashrightarrow 00{:}10{:}22.770$ something like that.

NOTE Confidence: 0.94081473

 $00:10:24.060 \rightarrow 00:10:25.544$ So then that's very cool, right,

NOTE Confidence: 0.94081473

 $00{:}10{:}25{.}544 \dashrightarrow 00{:}10{:}27{.}488$ because then you could see whether

NOTE Confidence: 0.94081473

 $00:10:27.488 \longrightarrow 00:10:29.720$ these people are

- $00:10:29.720 \longrightarrow 00:10:32.380$ acquiring these mutations.
- NOTE Confidence: 0.94081473
- $00{:}10{:}32{.}380 \dashrightarrow 00{:}10{:}35{.}430$ Exactly, exactly.
- NOTE Confidence: 0.94081473
- $00{:}10{:}35{.}430 \dashrightarrow 00{:}10{:}37{.}970$ So now that makes a lot more
- NOTE Confidence: 0.94081473
- $00:10:37.970 \rightarrow 00:10:40.455$ sense because now you can actually see,
- NOTE Confidence: 0.94081473
- $00{:}10{:}40.460 \dashrightarrow 00{:}10{:}43.228$ you know, how long does it take for
- NOTE Confidence: 0.94081473
- $00{:}10{:}43.228 \dashrightarrow 00{:}10{:}45.933$ people to develop these alterations and
- NOTE Confidence: 0.94081473
- $00:10:45.933 \rightarrow 00:10:49.380$ do these alterations once they do occur,
- NOTE Confidence: 0.94081473
- $00:10:49.380 \rightarrow 00:10:53.324$ how quickly or not do people develop cancer?
- NOTE Confidence: 0.94081473
- $00{:}10{:}53{.}330 \dashrightarrow 00{:}10{:}54{.}968$ Is that kind of the idea?
- NOTE Confidence: 0.94081473
- $00:10:54.970 \longrightarrow 00:10:56.410$ Yes, precisely.
- NOTE Confidence: 0.94081473
- $00:10:56.410 \longrightarrow 00:10:57.874$ Yeah, that's very cool.
- NOTE Confidence: 0.94081473
- $00:10:57.874 \longrightarrow 00:10:59.610$ So tell us a little bit more.
- NOTE Confidence: 0.94081473
- 00:10:59.610 --> 00:11:01.170 I realized that this is
- NOTE Confidence: 0.94081473
- $00:11:01.170 \longrightarrow 00:11:03.170$ a fresh project,
- NOTE Confidence: 0.94081473
- 00:11:03.170 --> 00:11:05.690 hot off the presses, just awarded.
- NOTE Confidence: 0.94081473
- 00:11:05.690 00:11:07.573 Tell us about some of the research

- NOTE Confidence: 0.94081473
- $00:11:07.573 \longrightarrow 00:11:09.650$ that kind of led up to this award.
- NOTE Confidence: 0.94081473
- $00:11:09.650 \longrightarrow 00:11:12.368$ What have you found in your
- NOTE Confidence: 0.94081473
- $00:11:12.368 \longrightarrow 00:11:13.727$ more earlier studies?
- NOTE Confidence: 0.924282204
- $00{:}11{:}15.690 \dashrightarrow 00{:}11{:}18.510$ When I was a post doc,
- NOTE Confidence: 0.924282204
- $00{:}11{:}18.510 \dashrightarrow 00{:}11{:}21.079$ when we do mass spectrometry we
- NOTE Confidence: 0.924282204
- 00:11:21.079 $\operatorname{-->}$ 00:11:24.161 usually take a protein and we digest
- NOTE Confidence: 0.924282204
- $00:11:24.161 \longrightarrow 00:11:26.903$ it using enzymes into short peptides
- NOTE Confidence: 0.924282204
- $00{:}11{:}26{.}903 \dashrightarrow 00{:}11{:}30{.}065$ and then you know we basically blast
- NOTE Confidence: 0.924282204
- $00{:}11{:}30.065 \dashrightarrow 00{:}11{:}32.825$ those apart by bombarding them
- NOTE Confidence: 0.924282204
- $00:11:32.825 \rightarrow 00:11:35.444$ with gas molecules and/or radical
- NOTE Confidence: 0.924282204
- $00:11:35.444 \rightarrow 00:11:37.796$ anions and by the way that they
- NOTE Confidence: 0.924282204
- 00:11:37.796 --> 00:11:40.216 fall apart we can kind of piece back
- NOTE Confidence: 0.924282204
- $00:11:40.216 \dashrightarrow 00:11:42.210$ what was present there previously.
- NOTE Confidence: 0.924282204
- $00{:}11{:}42.210 \dashrightarrow 00{:}11{:}43.930$ But one of the problems with these really,
- NOTE Confidence: 0.924282204
- 00:11:43.930 --> 00:11:45.830 really densely like oscillated proteins
- NOTE Confidence: 0.924282204

 $00:11:45.830 \longrightarrow 00:11:48.074$ or you know sugar modified proteins

NOTE Confidence: 0.924282204

 $00:11:48.074 \rightarrow 00:11:50.290$ is that they can't be chopped up by

NOTE Confidence: 0.924282204

 $00{:}11{:}50{.}290$ --> $00{:}11{:}52{.}527$ the normal enzymes that we would use. NOTE Confidence: 0.924282204

 $00:11:52.530 \rightarrow 00:11:55.806$ And so when I was in my postdoc I

NOTE Confidence: 0.924282204

 $00{:}11{:}55{.}806 \dashrightarrow 00{:}11{:}57{.}810$ characterized a series of enzymes that

NOTE Confidence: 0.924282204

 $00{:}11{:}57{.}810$ --> $00{:}12{:}00{.}248$ we call mucine ases that are actually able NOTE Confidence: 0.924282204

 $00{:}12{:}00{.}248 \dashrightarrow 00{:}12{:}02{.}810$ to create short segments of the protein

NOTE Confidence: 0.924282204

 $00{:}12{:}02{.}810 \dashrightarrow 00{:}12{:}05{.}448$ that are amenable to mass spec analysis.

NOTE Confidence: 0.924282204

 $00{:}12{:}05{.}450 \dashrightarrow 00{:}12{:}07{.}515$ So before we couldn't look at these

NOTE Confidence: 0.924282204

 $00:12:07.515 \rightarrow 00:12:10.170$ at all by my instrumentation method,

NOTE Confidence: 0.924282204

 $00:12:10.170 \rightarrow 00:12:12.242$ but now we can actually get pieces and NOTE Confidence: 0.924282204

 $00{:}12{:}12{.}242 \dashrightarrow 00{:}12{:}14{.}580$ see them in the in the mass spectrometer.

NOTE Confidence: 0.93528324

 $00:12:14.740 \longrightarrow 00:12:17.511$ So why is that important?

NOTE Confidence: 0.93528324

 $00:12:17.511 \rightarrow 00:12:20.430$ Why is looking at these with mass

NOTE Confidence: 0.93528324

 $00{:}12{:}20.529 \dashrightarrow 00{:}12{:}22.415$ spec so important as opposed to

NOTE Confidence: 0.93528324

 $00:12:22.415 \rightarrow 00:12:24.620$ looking at them with other techniques?

 $00:12:24.620 \longrightarrow 00:12:26.040$ Or are there no other

NOTE Confidence: 0.93528324

 $00:12:26.040 \longrightarrow 00:12:27.460$ techniques to look at them?

NOTE Confidence: 0.93528324

00:12:28.380 --> 00:12:32.068 I mean, you could potentially

NOTE Confidence: 0.93528324

 $00{:}12{:}32{.}068 \dashrightarrow 00{:}12{:}36{.}450$ use staining techniques, or NOTE Confidence: $0{.}93528324$

 $00:12:36.450 \longrightarrow 00:12:38.430$ certain other techniques.

NOTE Confidence: 0.93528324

 $00:12:38.430 \longrightarrow 00:12:39.470$ I'm not saying that mass

NOTE Confidence: 0.93528324

 $00:12:39.470 \longrightarrow 00:12:40.510$ spec is the only technique.

NOTE Confidence: 0.93528324

00:12:40.510 --> 00:12:43.667 However, in my opinion,

NOTE Confidence: 0.93528324

 $00:12:43.670 \rightarrow 00:12:45.070$ and of course I'm biased,

NOTE Confidence: 0.93528324

 $00:12:45.070 \rightarrow 00:12:47.401$ it's the best way of actually digging

NOTE Confidence: 0.93528324

 $00:12:47.401 \rightarrow 00:12:49.711$ into what sugar structures are modifying

NOTE Confidence: 0.93528324

 $00{:}12{:}49{.}711 \dashrightarrow 00{:}12{:}52{.}189$ what amino acids in what patterns.

NOTE Confidence: 0.93528324

 $00:12:52.190 \longrightarrow 00:12:54.006$ And you're not going to get that molecular

NOTE Confidence: 0.93528324

 $00:12:54.006 \rightarrow 00:12:55.707$ level of detail using other methods.

NOTE Confidence: 0.9232246

 $00:12:57.280 \longrightarrow 00:13:00.112$ So one of the things

00:13:00.112 $\operatorname{-->}$ 00:13:02.513 that you did before embarking on

NOTE Confidence: 0.9232246

00:13:02.513 --> 00:13:05.384 this was to figure out how you

NOTE Confidence: 0.9232246

 $00{:}13{:}05{.}384 \dashrightarrow 00{:}13{:}07{.}604$ could actually use mass spec to NOTE Confidence: 0.9232246

 $00:13:07.604 \longrightarrow 00:13:10.025$ look at at these sugar moieties

NOTE Confidence: 0.9232246

 $00:13:10.025 \rightarrow 00:13:12.200$ in these proteins going forward.

NOTE Confidence: 0.9232246

00:13:12.760 --> 00:13:14.596 Precisely, yes. And so my lab,

NOTE Confidence: 0.9232246

00:13:14.600 --> 00:13:16.796 you know, I have kind of two arms in

NOTE Confidence: 0.9232246

00:13:16.796 --> 00:13:19.872 my laboratory, one being, you know,

NOTE Confidence: 0.9232246

00:13:19.872 --> 00:13:21.426 instrumentation development and

NOTE Confidence: 0.9232246

 $00{:}13{:}21.426 \dashrightarrow 00{:}13{:}24.038$ method development so that we can

NOTE Confidence: 0.9232246

00:13:24.038 --> 00:13:25.966 better see these altered sugar

NOTE Confidence: 0.9232246

 $00{:}13{:}25{.}966$ --> $00{:}13{:}27{.}858$ structures and various diseases.

NOTE Confidence: 0.9232246

 $00:13:27.860 \longrightarrow 00:13:30.276$ And then another arm where we study

NOTE Confidence: 0.9232246

 $00:13:30.276 \rightarrow 00:13:32.060$ the biological role of the altered,

NOTE Confidence: 0.9232246

 $00:13:32.060 \longrightarrow 00:13:34.220$ glycosylation patterns in

NOTE Confidence: 0.9232246

 $00:13:34.220 \longrightarrow 00:13:35.540$ cellular systems.

- NOTE Confidence: 0.9379816
- 00:13:36.220 --> 00:13:37.966 Fantastic. Well, we're going to take
- NOTE Confidence: 0.9379816
- 00:13:37.966 --> 00:13:40.099 a short break for a medical minute,
- NOTE Confidence: 0.9379816
- $00:13:40.100 \longrightarrow 00:13:41.840$ but please stay tuned to learn
- NOTE Confidence: 0.9379816
- $00:13:41.840 \longrightarrow 00:13:43.407$ more about the early detection
- NOTE Confidence: 0.9379816
- 00:13:43.407 -> 00:13:45.459 of ovarian cancer with my guest,
- NOTE Confidence: 0.9379816
- 00:13:45.460 --> 00:13:46.900 Doctor Stacy Malaker.
- NOTE Confidence: 0.9379816
- 00:13:47.500 --> 00:13:49.545 Funding for Yale Cancer Answers
- NOTE Confidence: 0.9379816
- 00:13:49.545 --> 00:13:51.590 comes from Smilow Cancer Hospital,
- NOTE Confidence: 0.9379816
- $00{:}13{:}51{.}590 \dashrightarrow 00{:}13{:}53{.}782$ where their Oncodermatology program
- NOTE Confidence: 0.9379816
- 00:13:53.782 --> 00:13:55.426 treats dermatologic concerns,
- NOTE Confidence: 0.9379816
- 00:13:55.430 --> 00:13:57.435 including very dry skin, itching,
- NOTE Confidence: 0.9379816
- $00{:}13{:}57{.}435 \dashrightarrow 00{:}13{:}59{.}440$ and skin changes that arise as
- NOTE Confidence: 0.9379816
- $00{:}13{:}59{.}514 \dashrightarrow 00{:}14{:}01{.}590$ side effects from chemotherapy.
- NOTE Confidence: 0.9379816
- 00:14:01.590 --> 00:14:05.590 Smilowcancerhospital.org.
- NOTE Confidence: 0.9379816
- 00:14:05.590 --> 00:14:07.486 The American Cancer Society
- NOTE Confidence: 0.9379816

- $00:14:07.486 \rightarrow 00:14:09.590$ estimates that over 200,000 cases
- NOTE Confidence: 0.9379816
- 00:14:09.590 --> 00:14:11.290 of Melanoma will be diagnosed
- NOTE Confidence: 0.9379816
- 00:14:11.290 --> 00:14:13.389 in the United States this year,
- NOTE Confidence: 0.9379816
- $00:14:13.390 \rightarrow 00:14:16.659$ with over 1000 patients in Connecticut alone.
- NOTE Confidence: 0.9379816
- $00{:}14{:}16.660 \dashrightarrow 00{:}14{:}18.830$ While Melanoma accounts for only
- NOTE Confidence: 0.9379816
- $00:14:18.830 \longrightarrow 00:14:21.308$ about 1% of skin cancer cases,
- NOTE Confidence: 0.9379816
- $00{:}14{:}21{.}308 \dashrightarrow 00{:}14{:}24{.}340$ it causes the most skin cancer deaths,
- NOTE Confidence: 0.9379816
- $00:14:24.340 \rightarrow 00:14:25.744$ but when detected early,
- NOTE Confidence: 0.9379816
- $00:14:25.744 \rightarrow 00:14:28.420$ it is easily treated and highly curable.
- NOTE Confidence: 0.9379816
- $00:14:28.420 \rightarrow 00:14:30.448$ Clinical trials are currently
- NOTE Confidence: 0.9379816
- $00:14:30.448 \longrightarrow 00:14:32.476$ underway at federally designated
- NOTE Confidence: 0.9379816
- 00:14:32.476 --> 00:14:34.226 comprehensive Cancer centers such
- NOTE Confidence: 0.9379816
- 00:14:34.226 --> 00:14:36.578 as Yale Cancer Center and Smilow
- NOTE Confidence: 0.9379816
- 00:14:36.578 --> 00:14:38.685 Cancer Hospital to test innovative
- NOTE Confidence: 0.9379816
- 00:14:38.685 --> 00:14:40.393 new treatments for Melanoma.
- NOTE Confidence: 0.9379816
- $00:14:40.400 \rightarrow 00:14:42.560$ The goal of the Specialized Programs

- NOTE Confidence: 0.9379816
- $00:14:42.560 \longrightarrow 00:14:44.709$ of Research Excellence in Skin Cancer
- NOTE Confidence: 0.9379816
- 00:14:44.709 --> 00:14:46.659 grant is to better understand the
- NOTE Confidence: 0.9379816
- $00:14:46.659 \rightarrow 00:14:49.024$ biology of skin cancer with a focus
- NOTE Confidence: 0.9379816
- $00:14:49.024 \rightarrow 00:14:51.166$ on discovering targets that will lead
- NOTE Confidence: 0.9379816
- $00:14:51.166 \longrightarrow 00:14:53.596$ to improve diagnosis and treatment.
- NOTE Confidence: 0.9379816
- $00:14:53.600 \dashrightarrow 00:14:56.032$ More information is available
- NOTE Confidence: 0.9379816
- $00:14:56.032 \rightarrow 00:14:57.062$ at yalecancercenter.org.
- NOTE Confidence: 0.9379816
- $00{:}14{:}57{.}062 \dashrightarrow 00{:}14{:}59{.}594$ You're listening to Connecticut Public Radio.
- NOTE Confidence: 0.93090713
- $00{:}15{:}01.760 \dashrightarrow 00{:}15{:}03.960$ Welcome back to Yale Cancer Answers.
- NOTE Confidence: 0.93090713
- 00:15:03.960 --> 00:15:05.560 This is Dr. Anees Chagpar,
- NOTE Confidence: 0.93090713
- 00:15:05.560 --> 00:15:07.582 and I'm joined tonight by my
- NOTE Confidence: 0.93090713
- 00:15:07.582 --> 00:15:09.054 guest doctor Stacy Malaker.
- NOTE Confidence: 0.93090713
- $00{:}15{:}09{.}054 \dashrightarrow 00{:}15{:}10{.}944$ We're talking about the early
- NOTE Confidence: 0.93090713
- 00:15:10.944 --> 00:15:12.640 detection of ovarian cancer.
- NOTE Confidence: 0.93090713
- 00:15:12.640 --> 00:15:13.960 As all of you know,
- NOTE Confidence: 0.93090713

 $00:15:13.960 \longrightarrow 00:15:15.910$ this has been widely talked

NOTE Confidence: 0.93090713

 $00:15:15.910 \longrightarrow 00:15:18.332$ about as the silent cancer and

NOTE Confidence: 0.93090713

 $00:15:18.332 \longrightarrow 00:15:20.317$ the cancer that whispers.

NOTE Confidence: 0.93090713

00:15:20.320 --> 00:15:22.992 And Stacy in her lab is trying to

NOTE Confidence: 0.93090713

 $00:15:22.992 \longrightarrow 00:15:25.557$ figure out whether we can actually,

NOTE Confidence: 0.93090713

 $00:15:25.560 \longrightarrow 00:15:27.680$ well, make ovarian cancer speak

NOTE Confidence: 0.93090713

 $00{:}15{:}27.680 \dashrightarrow 00{:}15{:}30.295$ a little bit more loudly by

NOTE Confidence: 0.93090713

 $00:15:30.295 \longrightarrow 00:15:32.770$ looking at sugar molecules and

NOTE Confidence: 0.93090713

 $00{:}15{:}32.770 \dashrightarrow 00{:}15{:}35.520$ how they're disrupted or altered.

NOTE Confidence: 0.93090713

 $00{:}15{:}35{.}520 \dashrightarrow 00{:}15{:}37{.}116$ And Stacy, right before the break,

NOTE Confidence: 0.93090713

 $00{:}15{:}37{.}120 \dashrightarrow 00{:}15{:}39{.}451$ one of the things that you were

NOTE Confidence: 0.93090713

 $00{:}15{:}39{.}451 \dashrightarrow 00{:}15{:}41{.}916$ talking about is that in the work

NOTE Confidence: 0.93090713

 $00{:}15{:}41{.}916 \dashrightarrow 00{:}15{:}44{.}148$ up to your current project which

NOTE Confidence: 0.93090713

 $00{:}15{:}44{.}148 \dashrightarrow 00{:}15{:}46{.}480$ is looking at how these alterations

NOTE Confidence: 0.93090713

 $00{:}15{:}46{.}480 \dashrightarrow 00{:}15{:}49{.}176$ over time are changing and how that

NOTE Confidence: 0.93090713

 $00:15:49.176 \longrightarrow 00:15:51.352$ might affect people with a BRCA 1 or 2

- NOTE Confidence: 0.93090713
- $00{:}15{:}51{.}352 \dashrightarrow 00{:}15{:}54{.}390$ mutation both in the
- NOTE Confidence: 0.93090713
- $00{:}15{:}54{.}390 \dashrightarrow 00{:}15{:}55{.}710$ development of ovarian cancer
- NOTE Confidence: 0.93090713
- 00:15:55.710 --> 00:15:57.280 your primary of interest,
- NOTE Confidence: 0.93090713
- $00{:}15{:}57{.}280 \dashrightarrow 00{:}15{:}58{.}944$ but also other cancers.
- NOTE Confidence: 0.93090713
- $00{:}15{:}58{.}944 \dashrightarrow 00{:}16{:}01{.}861$ One of the things that your lab
- NOTE Confidence: 0.93090713
- $00:16:01.861 \longrightarrow 00:16:04.470$ did was to really look at how
- NOTE Confidence: 0.93090713
- 00:16:04.470 --> 00:16:07.370 you can use mass spectrometry
- NOTE Confidence: 0.93090713
- $00:16:07.370 \longrightarrow 00:16:10.690$ to look at these alterations,
- NOTE Confidence: 0.93090713
- $00:16:10.690 \rightarrow 00:16:13.810$ which is something that you really
- NOTE Confidence: 0.93090713
- $00{:}16{:}13.810 \dashrightarrow 00{:}16{:}17.538$ couldn't do otherwise and you couldn't
- NOTE Confidence: 0.93090713
- $00:16:17.538 \rightarrow 00:16:20.610$ do and look at at the molecular
- NOTE Confidence: 0.93090713
- $00{:}16{:}20.610 \dashrightarrow 00{:}16{:}22.210$ level with mass spectrometry.
- NOTE Confidence: 0.93090713
- $00:16:22.210 \rightarrow 00:16:25.730$ So I guess the other question that I have is,
- $00:16:26.002 \longrightarrow 00:16:27.906$ can you tell us a little bit
- NOTE Confidence: 0.93090713
- $00:16:27.906 \longrightarrow 00:16:29.529$ more about this technology?
- NOTE Confidence: 0.93090713
- 00:16:29.530 --> 00:16:32.029 I mean presumably if you can now

- NOTE Confidence: 0.93090713
- $00:16:32.029 \longrightarrow 00:16:34.885$ look at the sugar moieties and as
- NOTE Confidence: 0.93090713
- 00:16:34.885 $\operatorname{-->}$ 00:16:37.868 you said before the break that these
- NOTE Confidence: 0.93090713
- $00{:}16{:}37.868 \dashrightarrow 00{:}16{:}40.442$ alterations are seen in not just
- NOTE Confidence: 0.93090713
- $00:16:40.442 \rightarrow 00:16:43.608$ cancer but a variety of other diseases.
- NOTE Confidence: 0.93090713
- $00:16:43.610 \longrightarrow 00:16:47.486$ How is this being utilized now
- NOTE Confidence: 0.93090713
- $00:16:47.490 \longrightarrow 00:16:50.535$ in terms of of looking at other
- NOTE Confidence: 0.93090713
- $00:16:50.535 \rightarrow 00:16:52.730$ cancers and other diseases?
- NOTE Confidence: 0.93090713
- 00:16:52.730 --> 00:16:54.926 I mean, how do you see this moving forward?
- NOTE Confidence: 0.92526495
- $00{:}16{:}56{.}330 \dashrightarrow 00{:}16{:}58{.}346$ Yeah, I mean, the world
- NOTE Confidence: 0.92526495
- $00:16:58.346 \longrightarrow 00:16:59.690$ is our oyster really.
- NOTE Confidence: 0.92526495
- $00{:}16{:}59{.}690 \dashrightarrow 00{:}17{:}01{.}524$ We have this is 1 project of
- NOTE Confidence: 0.92526495
- $00{:}17{:}01{.}524 \dashrightarrow 00{:}17{:}03{.}529$ of many in my lab right now.
- NOTE Confidence: 0.92526495
- $00{:}17{:}03.530 \dashrightarrow 00{:}17{:}06.754$ We're looking at cardiovascular disease.
- NOTE Confidence: 0.92526495
- $00{:}17{:}06{.}754 \dashrightarrow 00{:}17{:}08{.}170$ We're looking at
- NOTE Confidence: 0.92526495
- $00{:}17{:}08{.}170 \dashrightarrow 00{:}17{:}09{.}490$ breast cancer,
- NOTE Confidence: 0.92526495

 $00:17:09.490 \longrightarrow 00:17:12.400$ but in a different fashion.

NOTE Confidence: 0.92526495

 $00{:}17{:}12{.}400 \dashrightarrow 00{:}17{:}14{.}885$ And we also look at changes in

NOTE Confidence: 0.92526495

 $00{:}17{:}14.885 \dashrightarrow 00{:}17{:}16.692$ intestinal linings and stress and

NOTE Confidence: 0.92526495

 $00:17:16.692 \dashrightarrow 00:17:19.037$ depression and so on and so forth.

NOTE Confidence: 0.92526495

 $00:17:19.040 \longrightarrow 00:17:21.158$ And so we're really trying to

NOTE Confidence: 0.92526495

 $00{:}17{:}21{.}158$ --> $00{:}17{:}22{.}570$ monopolize on these developments NOTE Confidence: 0.92526495

 $00:17:22.631 \longrightarrow 00:17:24.941$ that we've made in order to study

NOTE Confidence: 0.92526495

 $00:17:24.941 \longrightarrow 00:17:26.612$ altered sugar structures in a

NOTE Confidence: 0.92526495

 $00{:}17{:}26.612 \dashrightarrow 00{:}17{:}28.157$ whole host of different diseases.

NOTE Confidence: 0.93757594

 $00{:}17{:}29{.}520 \dashrightarrow 00{:}17{:}32{.}184$ And so tell us a little bit more about,

NOTE Confidence: 0.93757594

 $00:17:32.190 \longrightarrow 00:17:34.190$ you know, these sugar moieties.

NOTE Confidence: 0.93757594

 $00{:}17{:}34{.}190 \dashrightarrow 00{:}17{:}36{.}734$ I mean, I know that you became very NOTE Confidence: 0.93757594

NOTE Confidence: 0.95757594

00:17:36.734 --> 00:17:38.963 interested in these during your postdoc

NOTE Confidence: 0.93757594

 $00{:}17{:}38{.}963 \dashrightarrow 00{:}17{:}41{.}255$ working with a Nobel Prize winner

NOTE Confidence: 0.93757594

 $00:17:41.328 \longrightarrow 00:17:43.470$ whose lab really looked at these,

NOTE Confidence: 0.93757594

 $00:17:43.470 \longrightarrow 00:17:46.070$ these molecules. But you know,

 $00:17:46.070 \longrightarrow 00:17:49.490$ these days I think a lot of people think

NOTE Confidence: 0.93757594

00:17:49.490 --> 00:17:52.436 about cancer from the perspective of

NOTE Confidence: 0.93757594

 $00{:}17{:}52{.}436$ --> $00{:}17{:}56{.}733$ genetics and they think about it from the NOTE Confidence: 0.93757594

 $00:17:56.733 \rightarrow 00:17:59.045$ perspective of environmental factors.

NOTE Confidence: 0.93757594

 $00{:}17{:}59{.}050 \dashrightarrow 00{:}18{:}01{.}703$ But we really don't think about how

NOTE Confidence: 0.93757594

 $00{:}18{:}01.703 \dashrightarrow 00{:}18{:}04.528$ these two things affect sugars.

NOTE Confidence: 0.93757594

 $00:18:04.530 \longrightarrow 00:18:06.778$ So can you tell us a little bit

NOTE Confidence: 0.93757594

 $00{:}18{:}06.778 \dashrightarrow 00{:}18{:}08.253$ more about those interactions

NOTE Confidence: 0.93757594

 $00:18:08.253 \longrightarrow 00:18:10.767$ and how prevalent they are?

NOTE Confidence: 0.93757594

00:18:10.770 --> 00:18:13.087 I mean, do you really think that

NOTE Confidence: 0.93757594

 $00{:}18{:}13.087 \dashrightarrow 00{:}18{:}15.517$ by looking at these sugar muleides

NOTE Confidence: 0.93757594

00:18:15.517 --> 00:18:18.186 that we might actually, you know,

NOTE Confidence: 0.93757594

00:18:18.186 --> 00:18:21.182 kind of unlock a portion of cancer

NOTE Confidence: 0.93757594

 $00{:}18{:}21{.}182 \dashrightarrow 00{:}18{:}23{.}805$ biology that had heretofore been

NOTE Confidence: 0.93757594

 $00:18:23.805 \rightarrow 00:18:26.967$ largely well overlooked to some degree? NOTE Confidence: 0.9343778

- 00:18:28.090 --> 00:18:28.890 Yeah, absolutely.
- NOTE Confidence: 0.9343778
- 00:18:28.890 --> 00:18:31.874 I think that sugar structures,
- NOTE Confidence: 0.9343778
- 00:18:31.874 --> 00:18:33.626 sugar structures, excuse me,
- NOTE Confidence: 0.9343778
- $00:18:33.626 \rightarrow 00:18:35.766$ are extremely difficult to study.
- NOTE Confidence: 0.9343778
- 00:18:35.770 --> 00:18:37.978 One of the issues is that
- NOTE Confidence: 0.9343778
- 00:18:37.978 --> 00:18:39.450 you just mentioned genetics,
- NOTE Confidence: 0.9343778
- $00:18:39.450 \longrightarrow 00:18:41.090$ glycobiology or the sugar
- NOTE Confidence: 0.9343778
- 00:18:41.090 --> 00:18:42.730 structures are not templated,
- NOTE Confidence: 0.9343778
- $00{:}18{:}42.730 \dashrightarrow 00{:}18{:}45.298$ meaning that there are 200 different
- NOTE Confidence: 0.9343778
- $00:18:45.298 \longrightarrow 00:18:47.648$ enzymes that build these sugar
- NOTE Confidence: 0.9343778
- $00:18:47.648 \longrightarrow 00:18:49.848$ structures on the surface of our cells.
- NOTE Confidence: 0.9343778
- 00:18:49.850 --> 00:18:51.600 And so you can't necessarily
- NOTE Confidence: 0.9343778
- $00:18:51.600 \rightarrow 00:18:53.760$ look at changes in those enzyme
- NOTE Confidence: 0.9343778
- $00:18:53.760 \longrightarrow 00:18:55.818$ levels via genetics in order to
- NOTE Confidence: 0.9343778
- 00:18:55.818 --> 00:18:57.623 build back up what's possibly
- NOTE Confidence: 0.9343778
- $00:18:57.623 \rightarrow 00:19:00.087$ going to be on the cell surface.

- NOTE Confidence: 0.9343778
- $00:19:00.090 \rightarrow 00:19:01.608$ And so because of that it's
- 00:19:02.404 --> 00:19:04.786 much more difficult to study and
- NOTE Confidence: 0.9343778
- 00:19:04.786 --> 00:19:07.688 so it's lagged behind in you know,
- NOTE Confidence: 0.9343778
- $00:19:07.690 \rightarrow 00:19:11.365$ in comparison to more general fields like
- NOTE Confidence: 0.9343778
- 00:19:11.365 --> 00:19:14.089 genomics or transcriptomics or proteomics.
- NOTE Confidence: 0.9343778
- $00{:}19{:}14.090 \dashrightarrow 00{:}19{:}15.286$ And so
- NOTE Confidence: 0.9343778
- $00:19:15.286 \longrightarrow 00:19:17.424$ we really want to monopolize on these
- NOTE Confidence: 0.9343778
- $00:19:17.424 \longrightarrow 00:19:19.391$ changes in order to break open a
- NOTE Confidence: 0.9343778
- $00{:}19{:}19{.}391 \dashrightarrow 00{:}19{:}21{.}368$ whole new area of cancer biology.
- NOTE Confidence: 0.9391263
- $00{:}19{:}22{.}130 \dashrightarrow 00{:}19{:}25{.}522$ I mean, do you think that there's an
- NOTE Confidence: 0.9391263
- 00:19:25.522 --> 00:19:28.509 interplay between genomics and
- NOTE Confidence: 0.9391263
- $00:19:28.509 \rightarrow 00:19:30.648$ these sugar structures?
- NOTE Confidence: 0.9391263
- $00:19:30.650 \longrightarrow 00:19:33.426$ Or do you think that these are two
- NOTE Confidence: 0.9391263
- $00:19:33.426 \longrightarrow 00:19:35.924$ separate issues that they cause or
- NOTE Confidence: 0.9391263
- $00:19:35.924 \rightarrow 00:19:38.084$ are affected by cancer independently?
- NOTE Confidence: 0.9391263
- 00:19:38.090 --> 00:19:38.970 In other words, I mean,

 $00:19:38.970 \longrightarrow 00:19:40.512$ do you think that these two

NOTE Confidence: 0.9391263

 $00:19:40.512 \longrightarrow 00:19:41.970$ play together or not really?

NOTE Confidence: 0.933372370000001

 $00:19:42.450 \longrightarrow 00:19:43.570$ Oh, they definitely do.

NOTE Confidence: 0.933372370000001

 $00{:}19{:}43.570 \dashrightarrow 00{:}19{:}45.942$ It's just that you can't look at enzyme

NOTE Confidence: 0.933372370000001

 $00:19:45.942 \rightarrow 00:19:47.844$ changes and then immediately know how

NOTE Confidence: 0.933372370000001

 $00{:}19{:}47.844 \dashrightarrow 00{:}19{:}49.912$ that's going to change the sugar

NOTE Confidence: 0.933372370000001

 $00{:}19{:}49{.}912 \dashrightarrow 00{:}19{:}52{.}066$ structures on the outside of the cell.

NOTE Confidence: 0.933372370000001

 $00:19:52.066 \rightarrow 00:19:55.042$ But you can kind of gain hypothesis by

NOTE Confidence: 0.933372370000001

 $00{:}19{:}55{.}042 \dashrightarrow 00{:}19{:}57{.}450$ looking at changes in the enzyme levels.

NOTE Confidence: 0.933372370000001

 $00:19:57.450 \longrightarrow 00:20:00.450$ So if for instance,

NOTE Confidence: 0.933372370000001

 $00{:}20{:}00{.}450 \dashrightarrow 00{:}20{:}02{.}005$ there's a capping structure called

NOTE Confidence: 0.933372370000001

 $00{:}20{:}02{.}005 \dashrightarrow 00{:}20{:}04.674$ sialic acid and you can look at the sial

NOTE Confidence: 0.933372370000001

 $00{:}20{:}04.674 \dashrightarrow 00{:}20{:}06.740$ transferases and if those are up or down

NOTE Confidence: 0.933372370000001

 $00{:}20{:}06{.}740 \dashrightarrow 00{:}20{:}08{.}498$ you could then gather that your

NOTE Confidence: 0.933372370000001

 $00{:}20{:}08{.}498 \dashrightarrow 00{:}20{:}10{.}593$ structures will have more or less of a

 $00:20:10.593 \rightarrow 00:20:12.460$ certain type of that sugar structure,

NOTE Confidence: 0.933372370000001

00:20:12.460 --> 00:20:14.272 but it won't tell you exactly

NOTE Confidence: 0.933372370000001

 $00:20:14.272 \longrightarrow 00:20:15.178$ what it's modifying.

NOTE Confidence: 0.933372370000001

 $00:20:15.180 \longrightarrow 00:20:16.979$ So what protein it's on or

NOTE Confidence: 0.933372370000001

 $00:20:16.979 \longrightarrow 00:20:18.684$ it won't tell you exactly what

NOTE Confidence: 0.933372370000001

 $00:20:18.684 \rightarrow 00:20:20.430$ type of sugar structure it's

NOTE Confidence: 0.933372370000001

 $00{:}20{:}20{.}430 \dashrightarrow 00{:}20{:}22{.}099$ on and so on and so forth.

NOTE Confidence: 0.92736816

 $00:20:22.660 \longrightarrow 00:20:25.188$ And so going back to

NOTE Confidence: 0.92736816

 $00{:}20{:}25.188 \dashrightarrow 00{:}20{:}27.570$ the project for which you were just

NOTE Confidence: 0.92736816

 $00:20:27.570 \rightarrow 00:20:29.708$ awarded a grant where you're looking

NOTE Confidence: 0.92736816

 $00{:}20{:}29{.}708 \dashrightarrow 00{:}20{:}32{.}392$ at these BRCA mutation carriers,

NOTE Confidence: 0.92736816

 $00:20:32.392 \rightarrow 00:20:36.090$ is it possible that BRCA in and of itself,

NOTE Confidence: 0.92736816

00:20:36.090 --> 00:20:41.090 I mean we know BRCA as being a gene which

NOTE Confidence: 0.92736816

 $00:20:41.090 \rightarrow 00:20:44.210$ is largely responsible for DNA repair.

NOTE Confidence: 0.92736816

 $00:20:44.210 \rightarrow 00:20:47.207$ And so when you get a mutation in that,

NOTE Confidence: 0.92736816

 $00:20:47.210 \longrightarrow 00:20:50.275$ it's difficult to correct those

- NOTE Confidence: 0.92736816
- $00:20:50.275 \rightarrow 00:20:52.702$ mistakes that your DNA may have and

 $00:20:52.702 \longrightarrow 00:20:54.940$ the thinking is that

NOTE Confidence: 0.92736816

 $00:20:54.940 \longrightarrow 00:20:57.187$ really leads to the higher risk of

NOTE Confidence: 0.92736816

 $00:20:57.260 \rightarrow 00:20:59.690$ developing a variety of malignancies.

NOTE Confidence: 0.92736816

 $00{:}20{:}59{.}690 \dashrightarrow 00{:}21{:}03{.}452$ So if genetics and these altered

NOTE Confidence: 0.92736816

00:21:03.452 --> 00:21:05.960 sugar structures are related,

NOTE Confidence: 0.92736816

 $00:21:05.960 \longrightarrow 00:21:08.046$ do you think that

NOTE Confidence: 0.92736816

 $00{:}21{:}08.046 \dashrightarrow 00{:}21{:}10.790$ BRCA might be doing something to the sugar

NOTE Confidence: 0.92736816

 $00:21:10.863 \rightarrow 00:21:13.439$ structures and are you looking at that?

NOTE Confidence: 0.92736816

 $00:21:13.440 \longrightarrow 00:21:14.416$ For example,

NOTE Confidence: 0.92736816

 $00{:}21{:}14.416 \dashrightarrow 00{:}21{:}17.506$ are you comparing BRCA carriers to

NOTE Confidence: 0.92736816

00:21:17.506 --> 00:21:20.396 people who are not BRCA carriers

NOTE Confidence: 0.92736816

 $00{:}21{:}20{.}396 \dashrightarrow 00{:}21{:}22{.}186$ and seeing whether there's a

NOTE Confidence: 0.92736816

00:21:22.186 --> 00:21:23.870 difference in terms of

NOTE Confidence: 0.92736816

 $00{:}21{:}23.870 \dashrightarrow 00{:}21{:}25.590$ these sugar structures between

 $00:21:25.590 \rightarrow 00:21:26.880$ these two populations?

NOTE Confidence: 0.92099065

 $00:21:27.760 \rightarrow 00:21:29.080$ That's not something that we're currently

NOTE Confidence: 0.92099065

00:21:29.080 --> 00:21:31.880 looking at simply because we

NOTE Confidence: 0.92099065

 $00:21:31.880 \rightarrow 00:21:34.896$ only have access to these BRCA1 and 2 samples.

 $00:21:37.372 \rightarrow 00:21:40.276$ But we could ostensibly look at healthy,

NOTE Confidence: 0.92099065

00:21:40.280 --> 00:21:42.080 you know, healthy samples or healthy

NOTE Confidence: 0.92099065

 $00{:}21{:}42.080 \dashrightarrow 00{:}21{:}44.160$ patient serum in order to compare them.

NOTE Confidence: 0.92099065

 $00:21:44.160 \longrightarrow 00:21:45.678$ So definitely something we could do,

NOTE Confidence: 0.92099065

 $00:21:45.680 \longrightarrow 00:21:46.600$ but not something that's

NOTE Confidence: 0.92099065

 $00:21:46.600 \longrightarrow 00:21:49.480$ currently on our docket.

NOTE Confidence: 0.92099065

 $00{:}21{:}49{.}480 \dashrightarrow 00{:}21{:}51{.}209$ And then the other thing that I

NOTE Confidence: 0.92099065

 $00:21:51.209 \rightarrow 00:21:53.291$ kind of wonder about is one of the

NOTE Confidence: 0.92099065

00:21:53.291 --> 00:21:54.800 questions I always get asked is,

NOTE Confidence: 0.92099065

00:21:54.800 --> 00:21:57.596 well, why did I get cancer?

NOTE Confidence: 0.92099065

 $00:21:57.600 \longrightarrow 00:22:00.016$ Can you tell us a little bit more

NOTE Confidence: 0.92099065

 $00:22:00.016 \longrightarrow 00:22:02.112$ about whether you think that

 $00:22:02.112 \rightarrow 00:22:04.352$ having these altered sugar moides NOTE Confidence: 0.92099065 $00{:}22{:}04.352 \dashrightarrow 00{:}22{:}06.678$ might have something to do with NOTE Confidence: 0.92099065 00:22:06.680 --> 00:22:09.000 people's risk of developing cancer? NOTE Confidence: 0.92099065 $00:22:09.000 \rightarrow 00:22:10.720$ And secondary to that, NOTE Confidence: 0.92099065 $00:22:10.720 \longrightarrow 00:22:13.300$ why do people have these alterations NOTE Confidence: 0.92099065 00:22:13.373 - 00:22:15.558 in these sugar moides anyways? NOTE Confidence: 0.92099065 $00:22:15.560 \longrightarrow 00:22:17.440$ I mean what causes that? NOTE Confidence: 0.8961784 00:22:17.680 --> 00:22:19.399 Again, that's a very, NOTE Confidence: 0.8961784 $00{:}22{:}19{.}399 \dashrightarrow 00{:}22{:}21{.}118$ very loaded question. NOTE Confidence: 0.8961784 $00:22:21.120 \longrightarrow 00:22:22.560$ So what was the first part NOTE Confidence: 0.8961784 $00:22:22.560 \longrightarrow 00:22:23.600$ of the question? NOTE Confidence: 0.8961784 $00{:}22{:}23.640 \dashrightarrow 00{:}22{:}26.270$ Could these altered sugar Moides NOTE Confidence: 0.8961784 $00:22:26.270 \longrightarrow 00:22:28.692$ be part of the explanation of why NOTE Confidence: 0.8961784 00:22:28.692 --> 00:22:30.645 some people develop cancer even NOTE Confidence: 0.8961784 $00:22:30.645 \rightarrow 00:22:32.745$ though they did everything right? NOTE Confidence: 0.934395 00:22:33.030 --> 00:22:36.960 Sure. So I mean there are many,

- NOTE Confidence: 0.934395
- $00:22:36.960 \rightarrow 00:22:38.670$ many possible answers to that question,

 $00:22:38.670 \longrightarrow 00:22:40.080$ but I'll probably lean into the

NOTE Confidence: 0.934395

 $00{:}22{:}40.080 \dashrightarrow 00{:}22{:}41.750$ one that I'm most familiar with.

NOTE Confidence: 0.934395

00:22:41.750 --> 00:22:43.755 So you know, cancer immunotherapies

NOTE Confidence: 0.934395

 $00{:}22{:}43.755 \dashrightarrow 00{:}22{:}46.541$ are the the new pillar of

NOTE Confidence: 0.934395

 $00{:}22{:}46.541 \dashrightarrow 00{:}22{:}48.665$ treatment as I'm sure you're aware.

NOTE Confidence: 0.934395

 $00{:}22{:}48.670 \dashrightarrow 00{:}22{:}50.325$ And so altered sugar structures

NOTE Confidence: 0.934395

 $00:22:50.325 \longrightarrow 00:22:52.763$ are a way that cancer cells can

NOTE Confidence: 0.934395

 $00{:}22{:}52{.}763 \dashrightarrow 00{:}22{:}54{.}899$ actually avoid the immune system and

NOTE Confidence: 0.934395

 $00:22:54.899 \longrightarrow 00:22:57.212$ the immune system is really key in

NOTE Confidence: 0.934395

 $00:22:57.212 \longrightarrow 00:22:59.640$ getting rid of cells that have become

NOTE Confidence: 0.934395

 $00{:}22{:}59.640 \dashrightarrow 00{:}23{:}02.310$ transformed or cancerous.

NOTE Confidence: 0.934395

 $00{:}23{:}02{.}310 \dashrightarrow 00{:}23{:}04{.}326$ And so there's this really fine-tuned

NOTE Confidence: 0.934395

00:23:04.326 --> 00:23:06.308 balance there where you want your

NOTE Confidence: 0.934395

 $00{:}23{:}06{.}308 \dashrightarrow 00{:}23{:}08{.}030$ immune system to be active and

 $00:23:08.030 \longrightarrow 00:23:09.708$ killing off these cancer cells.

NOTE Confidence: 0.934395

 $00{:}23{:}09{.}710 \dashrightarrow 00{:}23{:}11{.}822$ Now the sugar moieties can actually

NOTE Confidence: 0.934395

 $00{:}23{:}11{.}822 \dashrightarrow 00{:}23{:}14{.}356$ act as a mechanism to shield the

NOTE Confidence: 0.934395

 $00{:}23{:}14.356 \dashrightarrow 00{:}23{:}16.116$ cancer cell from immune cells

NOTE Confidence: 0.934395

 $00:23:16.116 \rightarrow 00:23:18.257$ that would normally kill it off.

NOTE Confidence: 0.934395

 $00:23:18.260 \longrightarrow 00:23:19.252$ For instance,

NOTE Confidence: 0.934395

 $00{:}23{:}19{.}252 \dashrightarrow 00{:}23{:}22{.}948$ my lab studies what's called a checkpoint

NOTE Confidence: 0.934395

 $00:23:22.948 \longrightarrow 00:23:24.932$ inhibitor where when that

NOTE Confidence: 0.934395

00:23:24.932 --> 00:23:27.080 checkpoint inhibitor is bound to one

NOTE Confidence: 0.934395

 $00:23:27.148 \longrightarrow 00:23:29.578$ of its ligands through sugar structures,

NOTE Confidence: 0.934395

 $00{:}23{:}29{.}580 \dashrightarrow 00{:}23{:}31{.}980$ it shuts down T cell function.

NOTE Confidence: 0.934395

 $00{:}23{:}31{.}980 \dashrightarrow 00{:}23{:}35{.}244$ And it's so important that antibodies

NOTE Confidence: 0.934395

 $00:23:35.244 \rightarrow 00:23:37.788$ that block that interaction are currently

NOTE Confidence: 0.934395

 $00:23:37.788 \rightarrow 00:23:39.749$ being investigated in the clinic.

NOTE Confidence: 0.934395

 $00{:}23{:}39{.}750 \dashrightarrow 00{:}23{:}41{.}822$ And so we're trying to again monopolize

NOTE Confidence: 0.934395

 $00:23:41.822 \longrightarrow 00:23:43.473$ on the altered sugar structures

- NOTE Confidence: 0.934395
- $00:23:43.473 \longrightarrow 00:23:45.228$ in order to potentially develop

00:23:45.228 --> 00:23:47.110 a better cancer immuno
therapy.

NOTE Confidence: 0.934395

 $00{:}23{:}47{.}110 \dashrightarrow 00{:}23{:}49{.}162$ But basically kind of summarizing that

NOTE Confidence: 0.934395

00:23:49.162 --> 00:23:51.567 is that these sugar moieties can serve

NOTE Confidence: 0.934395

00:23:51.567 --> 00:23:53.835 to shut down various types of immune

NOTE Confidence: 0.934395

 $00{:}23{:}53{.}903 \dashrightarrow 00{:}23{:}56{.}255$ cells which then allow the tumor cells

NOTE Confidence: 0.934395

00:23:56.255 --> 00:23:58.503 to proliferate and become

NOTE Confidence: 0.934395

 $00{:}23{:}58{.}503 \dashrightarrow 00{:}24{:}01{.}389$ a solid tumor or various cancers.

NOTE Confidence: 0.9340521

 $00:24:02.430 \longrightarrow 00:24:06.502$ So why do some people get these

NOTE Confidence: 0.9340521

 $00{:}24{:}06{.}502 \dashrightarrow 00{:}24{:}08{.}757$ altered sugar moieties that can

NOTE Confidence: 0.9340521

 $00:24:08.757 \rightarrow 00:24:11.049$ essentially shut down your immune

NOTE Confidence: 0.9340521

 $00{:}24{:}11.049 \dashrightarrow 00{:}24{:}13.748$ system or at least its ability to

NOTE Confidence: 0.9340521

 $00:24:13.748 \rightarrow 00:24:16.319$ detect cancer and other people don't?

NOTE Confidence: 0.9340521

 $00{:}24{:}16{.}320 \dashrightarrow 00{:}24{:}19{.}600$ I mean, are there factors that drive that?

NOTE Confidence: 0.9340521

00:24:19.600 --> 00:24:21.196 You know, some people might be wondering,

 $00:24:21.200 \longrightarrow 00:24:22.943$ is it the sugar that I'm eating

NOTE Confidence: 0.9340521

 $00:24:22.943 \longrightarrow 00:24:24.998$ or is it how I metabolize it?

NOTE Confidence: 0.9340521

00:24:25.000 --> 00:24:26.780 Or is it, you know, diabetes?

NOTE Confidence: 0.9340521

00:24:26.780 --> 00:24:30.200 Or is it something to do with my genetics?

NOTE Confidence: 0.9360402

 $00{:}24{:}31{.}210 \dashrightarrow 00{:}24{:}32{.}554$ Yeah. So I mean that's a great question

NOTE Confidence: 0.9360402

 $00{:}24{:}32{.}554 \dashrightarrow 00{:}24{:}33{.}890$ that I don't have the answer for.

NOTE Confidence: 0.9360402

 $00:24:33.890 \longrightarrow 00:24:35.530$ I will specify that the

NOTE Confidence: 0.9360402

00:24:35.530 - 00:24:37.364 sugars that you're eating are very,

NOTE Confidence: 0.9360402

 $00{:}24{:}37{.}370 \dashrightarrow 00{:}24{:}38{.}970$ very, very different than the

NOTE Confidence: 0.9360402

 $00:24:38.970 \longrightarrow 00:24:40.250$ sugars I'm talking about.

NOTE Confidence: 0.9360402

 $00{:}24{:}40{.}250 \dashrightarrow 00{:}24{:}42{.}140$ I mean, essentially they can get

NOTE Confidence: 0.9360402

 $00:24:42.140 \longrightarrow 00:24:44.043$ metabolized and turned into the sugar

NOTE Confidence: 0.9360402

 $00{:}24{:}44.043 \dashrightarrow 00{:}24{:}46.087$ structures that are on the cell surface.

NOTE Confidence: 0.9360402

00:24:46.090 --> 00:24:47.776 But I'm not looking at glucose

NOTE Confidence: 0.9360402

 $00:24:47.776 \longrightarrow 00:24:49.489$ or sucrose or anything like that.

NOTE Confidence: 0.9360402

 $00:24:49.490 \rightarrow 00:24:51.330$ These are very different structures.

- NOTE Confidence: 0.9360402
- $00:24:52.530 \longrightarrow 00:24:53.698$ And so, you know,
- NOTE Confidence: 0.9360402
- 00:24:53.698 00:24:56.529 I think a lot of people may be asking,
- NOTE Confidence: 0.9360402
- $00{:}24{:}56{.}530 \dashrightarrow 00{:}25{:}00{.}606$ especially now that the WHO is
- NOTE Confidence: 0.9360402
- 00:25:00.606 00:25:02.971 coming out with their statement
- NOTE Confidence: 0.9360402
- $00{:}25{:}02{.}971 \dashrightarrow 00{:}25{:}05{.}495$ against some artificial sweeteners of
- NOTE Confidence: 0.9360402
- $00:25:05.495 \rightarrow 00:25:08.573$ thinking that they may be carcinogenic.
- NOTE Confidence: 0.9360402
- $00{:}25{:}08{.}580 \dashrightarrow 00{:}25{:}11{.}928$ Do do those have anything to do with the
- NOTE Confidence: 0.9360402
- $00:25:11.928 \rightarrow 00:25:15.216$ sugar moieties that you're talking about?
- NOTE Confidence: 0.9360402
- 00:25:15.220 --> 00:25:18.739 I don't know, my understanding
- NOTE Confidence: 0.9337291
- $00:25:18.740 \longrightarrow 00:25:20.284$ for those those altered
- NOTE Confidence: 0.9337291
- $00:25:20.284 \longrightarrow 00:25:22.214$ sugar moieties that are in,
- NOTE Confidence: 0.9337291
- $00{:}25{:}22{.}220 \dashrightarrow 00{:}25{:}23{.}920$ you know artificial sweeteners and
- NOTE Confidence: 0.9337291
- $00{:}25{:}23{.}920 \dashrightarrow 00{:}25{:}25{.}938$ so on is that they can't be broken
- NOTE Confidence: 0.9337291
- 00:25:25.938 --> 00:25:27.329 down or metabolized in the same
- NOTE Confidence: 0.9337291
- $00{:}25{:}27{.}329 \dashrightarrow 00{:}25{:}28{.}673$ way that normal sugars would be.
- NOTE Confidence: 0.9337291

 $00:25:28.680 \rightarrow 00:25:31.277$ But that is just what I understand.

NOTE Confidence: 0.9337291

 $00{:}25{:}31{.}280 \dashrightarrow 00{:}25{:}34{.}080$ I have not studied up on that too much.

NOTE Confidence: 0.92916805

 $00:25:35.120 \longrightarrow 00:25:39.440$ So for the alterations

NOTE Confidence: 0.92916805

 $00:25:39.440 \longrightarrow 00:25:42.518$ of sugar moties, I mean the

NOTE Confidence: 0.92916805

 $00:25:42.518 \longrightarrow 00:25:44.354$ the truth of the matter is,

NOTE Confidence: 0.92916805

 $00{:}25{:}44{.}360 \dashrightarrow 00{:}25{:}46{.}166$ that at least the research

NOTE Confidence: 0.92916805

 $00:25:46.166 \longrightarrow 00:25:47.680$ that you've done so far,

NOTE Confidence: 0.92916805

 $00:25:47.680 \rightarrow 00:25:52.108$ your hypothesis is that these alterations

NOTE Confidence: 0.92916805

 $00{:}25{:}52{.}110 \dashrightarrow 00{:}25{:}54{.}504$ have a role to play in cancer,

NOTE Confidence: 0.92916805

00:25:54.510 --> 00:25:57.385 whether it's the immune system

NOTE Confidence: 0.92916805

00:25:57.385 --> 00:26:00.264 evading cancers or you know,

NOTE Confidence: 0.92916805

 $00{:}26{:}00{.}264 \dashrightarrow 00{:}26{:}03{.}149$ increasing risk or whatever.

NOTE Confidence: 0.92916805

00:26:03.150 --> 00:26:05.257 Do we know of any risk factors

NOTE Confidence: 0.92916805

00:26:05.257 --> 00:26:07.140 that make people more susceptible

NOTE Confidence: 0.92916805

 $00:26:07.140 \longrightarrow 00:26:09.425$ to having altered sugar moieties,

NOTE Confidence: 0.92916805

 $00:26:09.430 \longrightarrow 00:26:10.750$ the ones that you're studying?

- NOTE Confidence: 0.9343979
- $00:26:12.310 \longrightarrow 00:26:15.390$ I mean not that I'm aware of.

00:26:15.390 --> 00:26:17.118 I think that if you did

NOTE Confidence: 0.9343979

 $00:26:17.118 \longrightarrow 00:26:17.982$ genetic studies again,

NOTE Confidence: 0.9343979

 $00:26:17.990 \rightarrow 00:26:20.395$ you could probably create hypothesis

NOTE Confidence: 0.9343979

 $00:26:20.395 \longrightarrow 00:26:22.319$ and individuals regarding different

NOTE Confidence: 0.9343979

 $00:26:22.319 \rightarrow 00:26:24.665$ enzymes that are up or down regulated.

NOTE Confidence: 0.9343979

00:26:24.670 --> 00:26:26.506 But as far as I'm aware,

NOTE Confidence: 0.9343979

 $00:26:26.510 \longrightarrow 00:26:29.102$ there's not anything like a

NOTE Confidence: 0.9343979

 $00:26:29.102 \longrightarrow 00:26:30.582$ BRCA1 that would definitely

NOTE Confidence: 0.9343979

 $00:26:30.582 \longrightarrow 00:26:32.548$ indicate that you're going to have

NOTE Confidence: 0.9343979

 $00{:}26{:}32{.}548 \dashrightarrow 00{:}26{:}33{.}908$ these altered sugar structures.

NOTE Confidence: 0.93575597

00:26:34.990 --> 00:26:37.926 And my perception is from your

NOTE Confidence: 0.93575597

00:26:37.926 --> 00:26:40.029 description of your earlier study,

NOTE Confidence: 0.93575597

 $00{:}26{:}40.030 \dashrightarrow 00{:}26{:}42.214$ is that it's not like you're born

NOTE Confidence: 0.93575597

 $00:26:42.214 \rightarrow 00:26:44.110$ with these altered sugar moieties,

- $00:26:44.110 \longrightarrow 00:26:46.306$ it's that they develop over time.
- NOTE Confidence: 0.93575597
- $00:26:46.310 \longrightarrow 00:26:47.818$ Is that right?
- NOTE Confidence: 0.9361285
- 00:26:47.820 -> 00:26:49.737 I mean it would be kind of similar to,
- NOTE Confidence: 0.9361285
- $00:26:49.740 \longrightarrow 00:26:52.035$ you know, genetic mutations that
- NOTE Confidence: 0.9361285
- $00{:}26{:}52.035 \dashrightarrow 00{:}26{:}55.420$ accumulate over time in cancer cells.
- NOTE Confidence: 0.9361285
- $00{:}26{:}55{.}420 \dashrightarrow 00{:}26{:}57{.}742$ And again,
- NOTE Confidence: 0.9361285
- $00:26:57.742 \rightarrow 00:26:59.308$ you were asking if genetics and
- NOTE Confidence: 0.9361285
- $00:26:59.308 \rightarrow 00:27:00.980$ altered sugar structures are related.
- NOTE Confidence: 0.9361285
- 00:27:00.980 --> 00:27:02.780 If you acquire many,
- NOTE Confidence: 0.9361285
- 00:27:02.780 --> 00:27:05.300 many genetic mutations over time,
- NOTE Confidence: 0.9361285
- $00:27:05.300 \longrightarrow 00:27:07.340$ you tend to develop cancer.
- NOTE Confidence: 0.9361285
- 00:27:07.340 --> 00:27:09.734 Similarly, you would also
- NOTE Confidence: 0.9361285
- $00:27:09.734 \rightarrow 00:27:11.734$ mutate these various glycan structures
- NOTE Confidence: 0.9361285
- $00:27:11.734 \rightarrow 00:27:14.100$ on the surface of cells.
- NOTE Confidence: 0.9316189
- $00{:}27{:}15{.}270 \dashrightarrow 00{:}27{:}18{.}086$ And so it sounds like there's a lot
- NOTE Confidence: 0.9316189
- 00:27:18.086 --> 00:27:20.757 going on in your laboratory both

 $00:27:20.757 \longrightarrow 00:27:23.886$ on the kind of developing the

NOTE Confidence: 0.9316189

 $00{:}27{:}23.886 \dashrightarrow 00{:}27{:}26.402$ methodologies as well as in terms of

NOTE Confidence: 0.9316189

 $00{:}27{:}26{.}402 \dashrightarrow 00{:}27{:}28{.}346$ looking at the actual clinical impact

NOTE Confidence: 0.9316189

 $00:27:28.346 \longrightarrow 00:27:30.547$ of these altered sugar moieties.

NOTE Confidence: 0.9316189

00:27:30.550 --> 00:27:33.022 Looking forward, what projects are you

NOTE Confidence: 0.9316189

00:27:33.022 --> 00:27:35.658 most excited about and what do you

NOTE Confidence: 0.9316189

 $00{:}27{:}35.658 \dashrightarrow 00{:}27{:}38.115$ think we can expect to hear about in

NOTE Confidence: 0.9316189

 $00:27:38.115 \rightarrow 00:27:40.428$ the next year or two or five or 10?

NOTE Confidence: 0.93945575

00:27:42.030 --> 00:27:45.140 Oh gosh, my students listen to this and

NOTE Confidence: 0.93945575

 $00:27:45.140 \longrightarrow 00:27:46.989$ I won't say their individual projects.

NOTE Confidence: 0.93945575

 $00{:}27{:}46{.}990 \dashrightarrow 00{:}27{:}48{.}826$ I don't want to pick favorites.

NOTE Confidence: 0.93945575

00:27:48.830 --> 00:27:50.710 Obviously I'm very excited about

NOTE Confidence: 0.93945575

 $00:27:50.710 \longrightarrow 00:27:52.590$ this ovarian cancer project simply

NOTE Confidence: 0.93945575

00:27:52.650 --> 00:27:54.460 because I think that, you know,

NOTE Confidence: 0.93945575

00:27:54.460 --> 00:27:56.980 CA-125 is really a black box of information

 $00{:}27{:}57{.}044 \dashrightarrow 00{:}27{:}59{.}276$ that I think we can monopolize on to

NOTE Confidence: 0.93945575

 $00:27:59.276 \longrightarrow 00:28:01.390$ develop an improved diagnostic tool.

NOTE Confidence: 0.93945575

00:28:01.390 --> 00:28:03.855 And it's a somewhat selfish project

NOTE Confidence: 0.93945575

 $00{:}28{:}03{.}855 \dashrightarrow 00{:}28{:}07{.}349$ because I am a BRCA 2 carrier.

NOTE Confidence: 0.93945575

 $00{:}28{:}07{.}350 \dashrightarrow 00{:}28{:}09{.}996$ So I would like to identify ovarian

NOTE Confidence: 0.93945575

 $00{:}28{:}09{.}996 \dashrightarrow 00{:}28{:}12{.}364$ cancer earlier for my own self

NOTE Confidence: 0.93945575

 $00:28:12.364 \longrightarrow 00:28:14.885$ and family in in addition to all

NOTE Confidence: 0.93945575

 $00:28:14.885 \longrightarrow 00:28:17.630$ of the women that are at risk.

NOTE Confidence: 0.93945575

00:28:17.630 --> 00:28:19.150 But I also, you know,

NOTE Confidence: 0.93945575

 $00{:}28{:}19{.}150 \dashrightarrow 00{:}28{:}21{.}790$ I love all of my projects equally in my lab,

NOTE Confidence: 0.93945575

 $00{:}28{:}21.790 \dashrightarrow 00{:}28{:}23.794$ and I'm really excited about the

NOTE Confidence: 0.93945575

 $00:28:23.794 \rightarrow 00:28:25.430$ instrumentation developments that we have,

NOTE Confidence: 0.93945575

 $00{:}28{:}25{.}430 \dashrightarrow 00{:}28{:}27{.}908$ as well as really cracking open

NOTE Confidence: 0.93945575

 $00:28:27.910 \longrightarrow 00:28:30.270$ all of the biological underlying

NOTE Confidence: 0.93945575

 $00{:}28{:}30{.}270 \dashrightarrow 00{:}28{:}31{.}749$ of altered glycosylation.

NOTE Confidence: 0.9326976

00:28:32.590 --> 00:28:34.882 Doctor Stacy Malaker is an assistant

- NOTE Confidence: 0.9326976
- $00:28:34.882 \rightarrow 00:28:36.845$ professor in the Department of

00:28:36.845 --> 00:28:38.349 Chemistry at Yale University.

NOTE Confidence: 0.9326976

 $00{:}28{:}38{.}350 \dashrightarrow 00{:}28{:}40{.}528$ If you have questions, the address

NOTE Confidence: 0.9326976

 $00{:}28{:}40{.}528 \dashrightarrow 00{:}28{:}42{.}909$ is Cancer Answers at Yale dot Edu.

NOTE Confidence: 0.9326976

 $00{:}28{:}42{.}910 \dashrightarrow 00{:}28{:}45{.}334$ And past editions of the program

NOTE Confidence: 0.9326976

 $00{:}28{:}45{.}334 \dashrightarrow 00{:}28{:}47{.}730$ are available in audio and written

NOTE Confidence: 0.9326976

 $00:28:47.730 \longrightarrow 00:28:48.746$ form at yalecancercenter.org.

NOTE Confidence: 0.9326976

00:28:48.746 --> 00:28:51.274 We hope you'll join us next week to

NOTE Confidence: 0.9326976

 $00{:}28{:}51{.}274 \dashrightarrow 00{:}28{:}53{.}199$ learn more about the fight against

NOTE Confidence: 0.9326976

 $00{:}28{:}53{.}199 \dashrightarrow 00{:}28{:}55{.}110$ cancer here on Connecticut Public Radio.

NOTE Confidence: 0.9326976

 $00{:}28{:}55{.}110 \dashrightarrow 00{:}28{:}57{.}618$ Funding for Yale Cancer Answers is

NOTE Confidence: 0.9326976

 $00{:}28{:}57.618 \dashrightarrow 00{:}29{:}00.000$ provided by Smilow Cancer Hospital.