WEBVTT

00:00:00.000 --> 00:00:03.054 Funding for Yale Cancer Answers is NOTE Confidence: 0.926819506363636 $00{:}00{:}03.054 \dashrightarrow 00{:}00{:}05.960$ provided by Smilow Cancer Hospital. NOTE Confidence: 0.926819506363636 00:00:05.960 --> 00:00:08.160 Welcome to Yale Cancer Answers NOTE Confidence: 0.926819506363636 $00:00:08.160 \longrightarrow 00:00:09.920$ with doctor Anees Chappar. NOTE Confidence: 0.926819506363636 $00:00:09.920 \longrightarrow 00:00:11.696$ Yale Cancer Answers features the NOTE Confidence: 0.926819506363636 $00:00:11.696 \rightarrow 00:00:13.516$ latest information on cancer care NOTE Confidence: 0.926819506363636 00:00:13.516 --> 00:00:15.053 by welcoming oncologists and NOTE Confidence: 0.926819506363636 $00:00:15.053 \rightarrow 00:00:17.273$ specialists who are on the forefront NOTE Confidence: 0.926819506363636 $00{:}00{:}17{.}273 \dashrightarrow 00{:}00{:}19{.}237$ of the battle to fight cancer. NOTE Confidence: 0.926819506363636 $00:00:19.240 \rightarrow 00:00:21.585$ This week it's a conversation about new NOTE Confidence: 0.926819506363636 $00:00:21.585 \rightarrow 00:00:23.950$ research into cell mutations and cancer NOTE Confidence: 0.926819506363636 $00:00:23.950 \rightarrow 00:00:26.115$ therapies with Doctor Jeffrey Townsend. NOTE Confidence: 0.926819506363636 $00:00:26.120 \longrightarrow 00:00:28.694$ Dr. Townsend is the Elihu Professor NOTE Confidence: 0.926819506363636 $00{:}00{:}28.694 \dashrightarrow 00{:}00{:}30.850$ of Biostatistics and professor of NOTE Confidence: 0.926819506363636 $00:00:30.850 \rightarrow 00:00:32.330$ ecology and evolutionary biology NOTE Confidence: 0.926819506363636

00:00:32.330 --> 00:00:34.840 at the Yale School of Medicine,

NOTE Confidence: 0.926819506363636

 $00{:}00{:}34.840 \dashrightarrow 00{:}00{:}37.000$ where Doctor Chagpar is a professor

NOTE Confidence: 0.926819506363636

00:00:37.000 --> 00:00:38.080 of surgical oncology.

NOTE Confidence: 0.960570288333333

00:00:39.000 - 00:00:40.790 So maybe we can start off, Jeff,

NOTE Confidence: 0.960570288333333

 $00:00:40.790 \longrightarrow 00:00:42.630$ by you telling us a little bit more

NOTE Confidence: 0.960570288333333

 $00:00:42.630 \rightarrow 00:00:44.436$ about yourself and what it is you do.

NOTE Confidence: 0.909610674285714

00:00:45.560 --> 00:00:48.675 I'm in the Biostatistics department at Yale,

NOTE Confidence: 0.909610674285714

 $00{:}00{:}48.680 \dashrightarrow 00{:}00{:}51.200$ but I'm perhaps the most biological

NOTE Confidence: 0.909610674285714

 $00:00:51.200 \rightarrow 00:00:52.840$ of the members of the department

NOTE Confidence: 0.909610674285714

 $00:00:52.840 \rightarrow 00:00:55.358$ in that all my degrees are biology

NOTE Confidence: 0.909610674285714

 $00{:}00{:}55{.}358 \dashrightarrow 00{:}00{:}58{.}120$ and what I work on is large scale

NOTE Confidence: 0.909610674285714

 $00:00:58.120 \longrightarrow 00:01:01.384$ genomic data sets about the genomic

NOTE Confidence: 0.909610674285714

 $00:01:01.384 \rightarrow 00:01:04.224$ mutations that change tumors and

NOTE Confidence: 0.909610674285714

 $00{:}01{:}04.224 \dashrightarrow 00{:}01{:}08.255$ what leads to tumors and also the

NOTE Confidence: 0.909610674285714

 $00:01:08.255 \rightarrow 00:01:10.491$ exogenous and endogenous factors

NOTE Confidence: 0.909610674285714

 $00:01:10.491 \dashrightarrow 00:01:12.720$ that make us come down with cancer.

- NOTE Confidence: 0.800123712727273
- 00:01:13.880 --> 00:01:15.665 So let's dive into
- NOTE Confidence: 0.800123712727273
- $00{:}01{:}15.665 \dashrightarrow 00{:}01{:}17.960$ that a little bit more.
- NOTE Confidence: 0.800123712727273
- 00:01:17.960 --> 00:01:19.760 Many of our listeners may know
- NOTE Confidence: 0.800123712727273
- $00:01:19.760 \longrightarrow 00:01:21.200$ about what the genome is.
- NOTE Confidence: 0.800123712727273
- $00:01:21.200 \longrightarrow 00:01:23.550$ Basically the conglomeration
- NOTE Confidence: 0.800123712727273
- $00:01:23.550 \longrightarrow 00:01:27.117$ of DNA that makes us who we are.
- NOTE Confidence: 0.800123712727273
- $00{:}01{:}27.120 \dashrightarrow 00{:}01{:}29.640$ But tell us a little bit more
- NOTE Confidence: 0.800123712727273
- $00:01:29.640 \longrightarrow 00:01:31.627$ about genomics and the
- NOTE Confidence: 0.800123712727273
- $00:01:31.627 \longrightarrow 00:01:33.279$ study of these mutations.
- NOTE Confidence: 0.92987426
- 00:01:33.840 --> 00:01:35.502 Yeah, I think the thing that's
- NOTE Confidence: 0.92987426
- $00:01:35.502 \longrightarrow 00:01:37.069$ important to understand about the work
- NOTE Confidence: 0.92987426
- $00{:}01{:}37{.}069 \dashrightarrow 00{:}01{:}38{.}693$ that we do is that we're working on
- NOTE Confidence: 0.92987426
- $00{:}01{:}38.746 \dashrightarrow 00{:}01{:}40.316$ what are called somatic mutations.
- NOTE Confidence: 0.92987426
- $00{:}01{:}40{.}320 \dashrightarrow 00{:}01{:}42{.}222$ So not what you inherited from
- NOTE Confidence: 0.92987426
- $00:01:42.222 \rightarrow 00:01:44.320$ your mother or from your father,
- NOTE Confidence: 0.92987426

 $00:01:44.320 \longrightarrow 00:01:45.945$ but rather the mutations that

NOTE Confidence: 0.92987426

00:01:45.945 --> 00:01:48.007 occur in your body during the

NOTE Confidence: 0.92987426

00:01:48.007 - 00:01:49.519 time that you're developing.

NOTE Confidence: 0.92987426

 $00{:}01{:}49{.}520 \dashrightarrow 00{:}01{:}51{.}368$ These are the kinds of mutations

NOTE Confidence: 0.92987426

 $00{:}01{:}51{.}368 \dashrightarrow 00{:}01{:}53{.}235$ that people talk about trying to

NOTE Confidence: 0.92987426

 $00:01:53.235 \dashrightarrow 00:01:55.237$ avoid by not smoking or not being NOTE Confidence: 0.92987426

 $00:01:55.237 \rightarrow 00:01:56.756$ exposed to too much UV light.

NOTE Confidence: 0.92987426

 $00{:}01{:}56{.}760 \dashrightarrow 00{:}01{:}59{.}432$ So we look at those kinds of mutations

NOTE Confidence: 0.92987426

 $00{:}01{:}59{.}432 \dashrightarrow 00{:}02{:}01{.}108$ that accumulate during your lifetime

NOTE Confidence: 0.92987426

 $00{:}02{:}01{.}108 \dashrightarrow 00{:}02{:}03{.}712$ and then lead to cancer on top of

NOTE Confidence: 0.92987426

 $00{:}02{:}03.712 \dashrightarrow 00{:}02{:}05.372$ all the germline variation that

NOTE Confidence: 0.92987426

 $00{:}02{:}05{.}372 \dashrightarrow 00{:}02{:}07{.}160$ you have coming from your parents.

NOTE Confidence: 0.915732384583333

 $00{:}02{:}08{.}160 \dashrightarrow 00{:}02{:}10{.}680$ And so tell us more about kind of

NOTE Confidence: 0.915732384583333

 $00:02:10.680 \longrightarrow 00:02:13.412$ how that works and how you

NOTE Confidence: 0.915732384583333

 $00{:}02{:}13.412 \dashrightarrow 00{:}02{:}15.437$ discover these mutations and

NOTE Confidence: 0.915732384583333

 $00:02:15.514 \rightarrow 00:02:18.130$ how you actually define that these

 $00:02:18.130 \rightarrow 00:02:20.355$ particular mutations have an impact

NOTE Confidence: 0.915732384583333

 $00:02:20.355 \longrightarrow 00:02:23.160$ in terms of cancer generation.

NOTE Confidence: 0.942250608571429

00:02:23.960 - 00:02:26.426 This is a really, really important

NOTE Confidence: 0.942250608571429

 $00:02:26.426 \rightarrow 00:02:28.372$ topic since the human genome,

NOTE Confidence: 0.942250608571429

 $00:02:28.372 \rightarrow 00:02:30.287$ we've developed lots of technologies

NOTE Confidence: 0.942250608571429

 $00:02:30.287 \dashrightarrow 00:02:32.436$ that allow us to sequence genomes,

NOTE Confidence: 0.942250608571429

 $00:02:32.440 \longrightarrow 00:02:34.330$ including the genomes of tumor tissue

NOTE Confidence: 0.942250608571429

 $00:02:34.330 \rightarrow 00:02:36.439$ as opposed to your normal tissue.

NOTE Confidence: 0.942250608571429

 $00:02:36.440 \rightarrow 00:02:39.226$ And by comparing that tumor tissue sequence

NOTE Confidence: 0.942250608571429

 $00:02:39.226 \rightarrow 00:02:42.214$ to the sequence we see from your blood

NOTE Confidence: 0.942250608571429

 $00:02:42.214 \rightarrow 00:02:44.480$ or from some normal adjacent tissue,

NOTE Confidence: 0.942250608571429

 $00{:}02{:}44.480 \dashrightarrow 00{:}02{:}47.238$ we can uncover all the genetic mutations

NOTE Confidence: 0.942250608571429

 $00{:}02{:}47.238 \dashrightarrow 00{:}02{:}49.736$ that are specific to the tumor and

NOTE Confidence: 0.942250608571429

 $00:02:49.736 \dashrightarrow 00:02:52.359$ aren't natural to the rest of your body.

NOTE Confidence: 0.942250608571429

 $00:02:52.360 \rightarrow 00:02:56.554$ And those mutations tend to be of two kinds.

 $00{:}02{:}56{.}560 \dashrightarrow 00{:}02{:}58{.}723$ Some are just mutations that just happen

NOTE Confidence: 0.942250608571429

 $00{:}02{:}58{.}723 \dashrightarrow 00{:}03{:}00{.}819$ to have happened and don't really lead

NOTE Confidence: 0.942250608571429

 $00{:}03{:}00{.}819 \dashrightarrow 00{:}03{:}03{.}079$ to cancer and other ones lead to cancer.

NOTE Confidence: 0.942250608571429

 $00:03:03.080 \rightarrow 00:03:05.545$ And so differentiating between those

NOTE Confidence: 0.942250608571429

 $00{:}03{:}05{.}545 \dashrightarrow 00{:}03{:}08{.}840$ two can be done by just looking at the

NOTE Confidence: 0.942250608571429

00:03:08.840 --> 00:03:11.199 frequencies that certain mutations occur NOTE Confidence: 0.942250608571429

 $00:03:11.200 \rightarrow 00:03:13.310$ and understanding what the underlying

NOTE Confidence: 0.942250608571429

 $00:03:13.310 \rightarrow 00:03:16.119$ rate at which those mutations occur are.

NOTE Confidence: 0.942250608571429

 $00:03:16.120 \rightarrow 00:03:18.997$ And by combining those two factors together,

NOTE Confidence: 0.942250608571429

 $00{:}03{:}19{.}000 \dashrightarrow 00{:}03{:}21{.}688$ we can get a quantitative estimate of

NOTE Confidence: 0.942250608571429

 $00:03:21.688 \dashrightarrow 00:03:24.907$ exactly how much of the cancer is being

NOTE Confidence: 0.942250608571429

 $00:03:24.907 \rightarrow 00:03:27.759$ caused by particular mutations in the genome.

NOTE Confidence: 0.942250608571429

 $00{:}03{:}27.760 \dashrightarrow 00{:}03{:}29.452$ So I'm very excited about research

NOTE Confidence: 0.942250608571429

 $00:03:29.452 \longrightarrow 00:03:31.754$ we're doing that allows us to take that

NOTE Confidence: 0.942250608571429

 $00:03:31.754 \rightarrow 00:03:33.159$ quantitative estimate and do things.

NOTE Confidence: 0.942250608571429

 $00:03:33.160 \rightarrow 00:03:34.679$ This is very preliminary at this point,

- NOTE Confidence: 0.942250608571429
- $00:03:34.680 \rightarrow 00:03:37.067$ but like actually assess in an individual
- NOTE Confidence: 0.942250608571429
- $00{:}03{:}37{.}067 \dashrightarrow 00{:}03{:}39{.}677$ why did that person get their cancer.
- NOTE Confidence: 0.942250608571429
- 00:03:39.680 --> 00:03:40.771 And it's not just saying, Oh,
- NOTE Confidence: 0.942250608571429
- $00:03:40.771 \longrightarrow 00:03:41.062$ well,
- NOTE Confidence: 0.942250608571429
- $00:03:41.062 \rightarrow 00:03:43.099$ we know smoking causes cancer or we
- NOTE Confidence: 0.942250608571429
- 00:03:43.099 --> 00:03:45.080 know UV light can cause Melanoma,
- NOTE Confidence: 0.942250608571429
- $00:03:45.080 \rightarrow 00:03:46.814$ but actually looking at the individual
- NOTE Confidence: 0.942250608571429
- $00:03:46.814 \rightarrow 00:03:48.280$ and saying, in your case,
- NOTE Confidence: 0.942250608571429
- $00:03:48.280 \longrightarrow 00:03:50.120$ why did that cancer arise?
- NOTE Confidence: 0.9420589186666667
- $00:03:51.320 \longrightarrow 00:03:53.903$ So tell us more about the study
- NOTE Confidence: 0.9420589186666667
- $00:03:53.903 \rightarrow 00:03:56.668$ itself because I can imagine that
- NOTE Confidence: 0.9420589186666667
- $00{:}03{:}56{.}668 \dashrightarrow 00{:}04{:}00{.}320$ as you look at these mutations and
- NOTE Confidence: 0.9420589186666667
- $00:04:00.320 \longrightarrow 00:04:02.632$ when you compare tumor DNA to
- NOTE Confidence: 0.9420589186666667
- $00{:}04{:}02.632 \dashrightarrow 00{:}04{:}05.040$ normal DNA that there are more mutations.
- NOTE Confidence: 0.9420589186666667
- $00:04:05.040 \longrightarrow 00:04:07.544$ You might be able to say, OK
- NOTE Confidence: 0.9420589186666667

 $00:04:07.544 \longrightarrow 00:04:10.232$ there are more mutations and

NOTE Confidence: 0.9420589186666667

 $00:04:10.232 \rightarrow 00:04:12.680$ hypothesize that those more mutations

NOTE Confidence: 0.9420589186666667

 $00:04:12.680 \longrightarrow 00:04:15.554$ are what actually caused the cancer.

NOTE Confidence: 0.9420589186666667

 $00:04:15.560 \rightarrow 00:04:18.356$ But causation and association are different.

NOTE Confidence: 0.9420589186666667

 $00:04:18.360 \longrightarrow 00:04:21.756$ So how did you establish that?

NOTE Confidence: 0.9420589186666667

 $00{:}04{:}21.760 \dashrightarrow 00{:}04{:}24.360$ And what is the long term impact of

NOTE Confidence: 0.9420589186666667

 $00:04:24.360 \longrightarrow 00:04:27.353$ being able to define in a particular

NOTE Confidence: 0.9420589186666667

 $00{:}04{:}27.353 \dashrightarrow 00{:}04{:}29.618$ individual what mutations cause their

NOTE Confidence: 0.9420589186666667

 $00:04:29.691 \rightarrow 00:04:32.235$ cancer? Because once they have cancer,

NOTE Confidence: 0.9420589186666667

 $00:04:32.240 \longrightarrow 00:04:34.116$ isn't it kind of like a fait accompli, or

NOTE Confidence: 0.9420589186666667

 $00{:}04{:}37{.}477 \dashrightarrow 00{:}04{:}40{.}111$ does defining those mutations actually

NOTE Confidence: 0.9420589186666667

 $00:04:40.111 \rightarrow 00:04:43.280$ have an impact then on how they're treated?

NOTE Confidence: 0.919434170769231

00:04:43.800 --> 00:04:46.600 Yeah. So first, in terms of defining

NOTE Confidence: 0.919434170769231

 $00:04:46.600 \rightarrow 00:04:49.158$ which mutations are leading to cancer,

NOTE Confidence: 0.919434170769231

 $00:04:49.160 \longrightarrow 00:04:50.472$ what's important to understand

NOTE Confidence: 0.919434170769231

 $00:04:50.472 \rightarrow 00:04:52.112$ is that there are very,

 $00:04:52.120 \rightarrow 00:04:54.658$ very different rates of mutation for

NOTE Confidence: 0.919434170769231

 $00:04:54.658 \rightarrow 00:04:56.880$ different sites within your genome.

NOTE Confidence: 0.919434170769231

 $00{:}04{:}56.880 \dashrightarrow 00{:}04{:}59.302$ Some parts of the genome are much

NOTE Confidence: 0.919434170769231

 $00:04:59.302 \longrightarrow 00:05:01.188$ more exposed just because of the

NOTE Confidence: 0.919434170769231

 $00:05:01.188 \rightarrow 00:05:02.673$ way the genome replicates and

NOTE Confidence: 0.919434170769231

 $00:05:02.673 \rightarrow 00:05:04.082$ things like that, than others.

NOTE Confidence: 0.919434170769231

 $00:05:04.082 \longrightarrow 00:05:06.170$ And so what we have to do is

NOTE Confidence: 0.919434170769231

 $00:05:06.242 \longrightarrow 00:05:07.837$ estimate how likely every site

NOTE Confidence: 0.919434170769231

 $00:05:07.837 \rightarrow 00:05:10.200$ in the genome is to be mutated.

NOTE Confidence: 0.919434170769231

 $00:05:10.200 \longrightarrow 00:05:11.472$ And then from that look at

NOTE Confidence: 0.919434170769231

 $00:05:11.472 \rightarrow 00:05:12.320$ the tumors and say,

NOTE Confidence: 0.919434170769231

 $00{:}05{:}12.320 \dashrightarrow 00{:}05{:}14.864$ do we see that frequency of mutation in

NOTE Confidence: 0.919434170769231

 $00:05:14.864 \rightarrow 00:05:17.317$ the tumor or do we see it more often?

NOTE Confidence: 0.919434170769231

 $00{:}05{:}17{.}320 \dashrightarrow 00{:}05{:}19{.}360$ And if it's more often,

NOTE Confidence: 0.919434170769231

 $00{:}05{:}19{.}360 \dashrightarrow 00{:}05{:}21{.}285$ then it must be leading to tumors

 $00:05:21.285 \rightarrow 00:05:22.978$ because that's what we're sequencing and

NOTE Confidence: 0.919434170769231

 $00{:}05{:}22.978 \dashrightarrow 00{:}05{:}25.600$ seeing more of it there than we would expect.

NOTE Confidence: 0.919434170769231

 $00{:}05{:}25{.}600 \dashrightarrow 00{:}05{:}27{.}230$ So that's how we differentiate

NOTE Confidence: 0.919434170769231

 $00:05:27.230 \longrightarrow 00:05:28.860$ those ones that are causing

NOTE Confidence: 0.919434170769231

 $00:05:28.923 \longrightarrow 00:05:30.580$ cancer from those that aren't.

NOTE Confidence: 0.919434170769231

 $00:05:30.580 \rightarrow 00:05:32.680$ And then why is it important?

NOTE Confidence: 0.919434170769231

00:05:32.680 --> 00:05:32.905 Well,

NOTE Confidence: 0.919434170769231

 $00{:}05{:}32{.}905 \dashrightarrow 00{:}05{:}34{.}480$ in addition to sort of the question

NOTE Confidence: 0.919434170769231

00:05:34.480 --> 00:05:36.160 that I introduced originally,

NOTE Confidence: 0.919434170769231

00:05:36.160 - 00:05:37.760 like trying to understand

NOTE Confidence: 0.919434170769231

 $00:05:37.760 \longrightarrow 00:05:39.360$ why individuals get cancer.

NOTE Confidence: 0.919434170769231

 $00{:}05{:}39{.}360 \dashrightarrow 00{:}05{:}41{.}528$ Cancer continues to evolve.

NOTE Confidence: 0.919434170769231

00:05:41.528 --> 00:05:44.172 It's not just a

NOTE Confidence: 0.919434170769231

 $00:05:44.172 \longrightarrow 00:05:45.437$ static thing that you have,

NOTE Confidence: 0.919434170769231

 $00{:}05{:}45{.}440 \dashrightarrow 00{:}05{:}47{.}480$ but it actually changes

NOTE Confidence: 0.919434170769231

 $00:05:47.480 \longrightarrow 00:05:49.520$ over time in individuals.

 $00:05:49.520 \rightarrow 00:05:53.500$ If you come in and you have a tumor removed,

NOTE Confidence: 0.919434170769231

 $00:05:53.500 \rightarrow 00:05:54.880$ but you have recurrence,

NOTE Confidence: 0.919434170769231

 $00:05:54.880 \longrightarrow 00:05:56.798$ then one of the things that the

NOTE Confidence: 0.919434170769231

 $00:05:56.800 \rightarrow 00:05:58.630$ physicians are charged with doing is

NOTE Confidence: 0.919434170769231

 $00:05:58.630 \rightarrow 00:06:00.600$ trying to understand why that recurrence

NOTE Confidence: 0.919434170769231

 $00{:}06{:}00{.}600 \dashrightarrow 00{:}06{:}02{.}330$ occurred and trying to negotiate

NOTE Confidence: 0.919434170769231

 $00:06:02.330 \dashrightarrow 00:06:04.120$ around the evolution of that tumor.

NOTE Confidence: 0.919434170769231

 $00:06:04.120 \longrightarrow 00:06:06.654$ So the tools that have just been

NOTE Confidence: 0.919434170769231

 $00:06:06.654 \rightarrow 00:06:09.146$ released now that we've been using

NOTE Confidence: 0.919434170769231

 $00{:}06{:}09{.}146 \dashrightarrow 00{:}06{:}11.356$ allow one to understand what

NOTE Confidence: 0.919434170769231

 $00:06:11.356 \rightarrow 00:06:13.480$ that trajectory of evolution is.

NOTE Confidence: 0.919434170769231

 $00{:}06{:}13.480 \dashrightarrow 00{:}06{:}14.380$ In other words,

NOTE Confidence: 0.919434170769231

 $00:06:14.380 \rightarrow 00:06:16.480$ you're at this state right now genetically,

NOTE Confidence: 0.919434170769231

 $00{:}06{:}16.480 \dashrightarrow 00{:}06{:}18.412$ but what's the next genetic change

NOTE Confidence: 0.919434170769231

 $00{:}06{:}18{.}412 \dashrightarrow 00{:}06{:}20{.}467$ likely to be in a probabilistic

 $00:06:20.467 \longrightarrow 00:06:22.555$ way and what's the next one

NOTE Confidence: 0.919434170769231

 $00{:}06{:}22.555 \dashrightarrow 00{:}06{:}24.158$ after that likely to be?

NOTE Confidence: 0.919434170769231

 $00:06:24.160 \longrightarrow 00:06:25.768$ And it's the first time we've

NOTE Confidence: 0.919434170769231

 $00:06:25.768 \longrightarrow 00:06:27.803$ really been able to

NOTE Confidence: 0.919434170769231

 $00{:}06{:}27.803 \dashrightarrow 00{:}06{:}29.609$ characterize that in terms of a

NOTE Confidence: 0.919434170769231

 $00:06:29.609 \rightarrow 00:06:31.437$ trajectory of change where we

NOTE Confidence: 0.919434170769231

 $00:06:31.437 \longrightarrow 00:06:32.905$ understand quantitatively how much

NOTE Confidence: 0.919434170769231

 $00{:}06{:}32{.}905 \dashrightarrow 00{:}06{:}34{.}879$ each mutation is increasing the

NOTE Confidence: 0.919434170769231

 $00{:}06{:}34.879 \dashrightarrow 00{:}06{:}37.357$ survival and proliferation of these cells.

NOTE Confidence: 0.661824508

 $00:06:38.600 \longrightarrow 00:06:39.976$ So, that's interesting.

NOTE Confidence: 0.661824508

 $00:06:39.976 \longrightarrow 00:06:42.620$ How exactly do you do

NOTE Confidence: 0.661824508

 $00:06:42.620 \longrightarrow 00:06:45.566$ that in terms of defining, OK,

NOTE Confidence: 0.661824508

 $00:06:45.566 \rightarrow 00:06:49.420$ this mutation caused your cancer and

NOTE Confidence: 0.661824508

 $00:06:49.420 \longrightarrow 00:06:53.140$ probabilistically you have an X percent

NOTE Confidence: 0.661824508

 $00:06:53.140 \rightarrow 00:06:55.860$ probability of getting a recurrence.

NOTE Confidence: 0.661824508

 $00:06:55.860 \rightarrow 00:06:58.870$ Tell us more about if that's really

 $00:06:58.870 \longrightarrow 00:07:01.436$ what you can do in an individual

NOTE Confidence: 0.661824508

 $00:07:01.436 \longrightarrow 00:07:03.848$ way and how exactly you

NOTE Confidence: 0.661824508

 $00:07:03.848 \longrightarrow 00:07:06.238$ come up with that probability.

NOTE Confidence: 0.947071578571429

00:07:06.680 --> 00:07:08.276 Right. So what we work with,

NOTE Confidence: 0.947071578571429

 $00{:}07{:}08.280 \dashrightarrow 00{:}07{:}10.176$ as typical with these kinds

NOTE Confidence: 0.947071578571429

 $00:07:10.176 \longrightarrow 00:07:11.440$ of studies, is population.

NOTE Confidence: 0.947071578571429

 $00:07:11.440 \longrightarrow 00:07:12.835$ So we don't know necessarily

NOTE Confidence: 0.947071578571429

 $00:07:12.835 \longrightarrow 00:07:14.230$ for an individual what their

NOTE Confidence: 0.947071578571429

 $00:07:14.279 \longrightarrow 00:07:15.599$ next change is going to be.

NOTE Confidence: 0.947071578571429

00:07:15.600 --> 00:07:18.160 But what we can do is look at lots of tumors,

NOTE Confidence: 0.947071578571429

 $00:07:18.160 \longrightarrow 00:07:19.885$ see which changes have occurred

NOTE Confidence: 0.947071578571429

00:07:19.885 --> 00:07:22.371 and in some sense order them in

NOTE Confidence: 0.947071578571429

 $00{:}07{:}22.371 \dashrightarrow 00{:}07{:}24.455$ individual tumors and then say, oh,

NOTE Confidence: 0.947071578571429

 $00{:}07{:}24.455 \dashrightarrow 00{:}07{:}26.800$ given where you are on this trajectory,

NOTE Confidence: 0.947071578571429

 $00:07:26.800 \longrightarrow 00:07:29.796$ what's the next mutation likely to be?

00:07:31.480 --> 00:07:34.800 And so I can imagine that for

NOTE Confidence: 0.888861823333333

00:07:34.800 --> 00:07:37.200 people who may be listening,

NOTE Confidence: 0.888861823333333

 $00:07:37.200 \rightarrow 00:07:38.598$ they may be saying to themselves,

NOTE Confidence: 0.888861823333333

00:07:38.600 --> 00:07:40.842 well, that's great. You know,

NOTE Confidence: 0.888861823333333

 $00:07:40.842 \longrightarrow 00:07:43.250$ you can give me an estimate of what

NOTE Confidence: 0.888861823333333

 $00:07:43.326 \rightarrow 00:07:45.517$ my next mutation is going to be.

NOTE Confidence: 0.888861823333333

 $00{:}07{:}45{.}520$ --> $00{:}07{:}47{.}810$ Has there been work to kind of say, well,

NOTE Confidence: 0.888861823333333

 $00:07:47.810 \rightarrow 00:07:50.120$ how do we prevent that from happening?

NOTE Confidence: 0.888861823333333

00:07:50.120 --> 00:07:52.318 How do we prevent your next recurrence? NOTE Confidence: 0.885301267777778

00:07:52.600 --> 00:07:54.364 Yeah, that's what we're working on

NOTE Confidence: 0.88530126777778

 $00{:}07{:}54{.}364 \dashrightarrow 00{:}07{:}56{.}632$ right now with this approach is to

NOTE Confidence: 0.88530126777778

00:07:56.632 $-\!>$ 00:07:58.690 better understand and better line up

NOTE Confidence: 0.88530126777778

 $00{:}07{:}58.690 \dashrightarrow 00{:}08{:}00.656$ essentially what we know about these

NOTE Confidence: 0.88530126777778

 $00:08:00.656 \rightarrow 00:08:02.800$ genetic changes and how they occur,

NOTE Confidence: 0.88530126777778

 $00{:}08{:}02{.}800 \dashrightarrow 00{:}08{:}04{.}970$ what order they occur with the

NOTE Confidence: 0.88530126777778

 $00:08:04.970 \longrightarrow 00:08:06.595$ kinds of precision medicines that

 $00:08:06.595 \rightarrow 00:08:08.909$ are now being developed at a more

NOTE Confidence: 0.88530126777778

00:08:08.909 --> 00:08:10.504 breakneck pace through

NOTE Confidence: 0.88530126777778

 $00:08:10.504 \longrightarrow 00:08:12.468$ the great research that's

NOTE Confidence: 0.88530126777778

 $00:08:12.468 \rightarrow 00:08:14.838$ happening here at Yale and elsewhere.

NOTE Confidence: 0.88530126777778

 $00:08:14.840 \longrightarrow 00:08:17.624$ And the point is that all of those

NOTE Confidence: 0.88530126777778

 $00{:}08{:}17.624 \dashrightarrow 00{:}08{:}19.380$ different precision treatments can

NOTE Confidence: 0.88530126777778

 $00:08:19.380 \longrightarrow 00:08:21.080$ be marshaled in different ways.

NOTE Confidence: 0.88530126777778

 $00:08:21.080 \rightarrow 00:08:22.893$ And it's getting more and more complex

NOTE Confidence: 0.88530126777778

 $00:08:22.893 \rightarrow 00:08:25.172$ to sort of think through how to treat

NOTE Confidence: 0.88530126777778

 $00:08:25.172 \longrightarrow 00:08:27.304$ an individual when they have this sort

NOTE Confidence: 0.88530126777778

 $00:08:27.304 \rightarrow 00:08:29.170$ of evolving cancer that is evolving

NOTE Confidence: 0.88530126777778

 $00:08:29.170 \dashrightarrow 00:08:30.706$ resistance to different the rapies.

NOTE Confidence: 0.88530126777778

 $00{:}08{:}30{.}706 \dashrightarrow 00{:}08{:}34{.}330$ And so hopefully what we can do with

NOTE Confidence: 0.88530126777778

 $00{:}08{:}34{.}417 \dashrightarrow 00{:}08{:}36{.}979$ our genetic trajectories is to inform

NOTE Confidence: 0.88530126777778

 $00{:}08{:}36{.}979 \dashrightarrow 00{:}08{:}39{.}440$ for a patient's decision making and

00:08:39.440 --> 00:08:41.320 for a physician's decision making

NOTE Confidence: 0.88530126777778

 $00{:}08{:}41.320 \dashrightarrow 00{:}08{:}43.840$ about the next the rapy that must be

NOTE Confidence: 0.88530126777778

 $00{:}08{:}43{.}840 \dashrightarrow 00{:}08{:}46{.}480$ prescribed to someone who has cancer.

NOTE Confidence: 0.88530126777778

 $00:08:46.480 \longrightarrow 00:08:48.643$ What would be the best trajectory to

NOTE Confidence: 0.88530126777778

 $00{:}08{:}48.643 \dashrightarrow 00{:}08{:}51.117$ occupy in terms of the genetic evolution?

NOTE Confidence: 0.88530126777778

 $00:08:51.120 \longrightarrow 00:08:53.808$ And are there ways we can corner the NOTE Confidence: 0.885301267777778

 $00{:}08{:}53.808 \dashrightarrow 00{:}08{:}55.895$ cancer essentially so it can't evolve

NOTE Confidence: 0.88530126777778

 $00:08:55.895 \rightarrow 00:08:57.911$ resistance and lead to a recurrence?

NOTE Confidence: 0.8220461

00:08:59.440 $\operatorname{-->}$ 00:09:03.879 So kind of trying to treat to the

NOTE Confidence: 0.8220461

 $00:09:03.879 \dashrightarrow 00:09:06.950$ cancer currently in a way that they NOTE Confidence: 0.8220461

 $00:09:06.950 \longrightarrow 00:09:09.420$ then don't mutate according to the NOTE Confidence: 0.8220461

 $00:09:09.420 \dashrightarrow 00:09:11.036$ trajectory that you've hypothesized

NOTE Confidence: 0.8220461

 $00:09:11.036 \longrightarrow 00:09:12.718$ that they otherwise would?

NOTE Confidence: 0.970087248571428

 $00:09:13.120 \longrightarrow 00:09:14.026$ That's exactly right.

NOTE Confidence: 0.970087248571428

 $00:09:14.026 \rightarrow 00:09:16.140$ Let me give you an example from

NOTE Confidence: 0.970087248571428

 $00:09:16.140 \longrightarrow 00:09:18.906$ other work that we did which

00:09:18.906 - 00:09:21.438 was looking at EGFR therapy.

NOTE Confidence: 0.970087248571428

 $00:09:21.440 \longrightarrow 00:09:23.701$ This is an irlatinib therapy that is

NOTE Confidence: 0.970087248571428

00:09:23.701 -> 00:09:25.640 not actually given currently,

NOTE Confidence: 0.970087248571428

 $00{:}09{:}25.640 \dashrightarrow 00{:}09{:}28.216$ but when we looked at

00:09:30.200 --> 00:09:32.120 irlatinib therapy,

NOTE Confidence: 0.970087248571428

 $00{:}09{:}32.120 \dashrightarrow 00{:}09{:}34.500$ one of the things that we noticed

NOTE Confidence: 0.970087248571428

 $00:09:34.500 \rightarrow 00:09:36.263$ was that cisplatin therapy which

NOTE Confidence: 0.970087248571428

 $00:09:36.263 \longrightarrow 00:09:38.267$ is often given in the context

NOTE Confidence: 0.970087248571428

00:09:38.267 --> 00:09:40.680 of EGFR driven lung cancer can

NOTE Confidence: 0.970087248571428

 $00{:}09{:}40.680 \dashrightarrow 00{:}09{:}42.775$ actually lead to the underlying

NOTE Confidence: 0.970087248571428

 $00:09:42.775 \dashrightarrow 00:09:45.220$ mutations that give you resistance,

NOTE Confidence: 0.970087248571428

 $00:09:45.220 \longrightarrow 00:09:47.240$ give the tumor resistance

NOTE Confidence: 0.970087248571428

 $00:09:47.240 \longrightarrow 00:09:48.960$ to erlatinib therapy.

 $00:09:49.261 \dashrightarrow 00:09:51.067$ So that's an example where you

NOTE Confidence: 0.970087248571428

 $00{:}09{:}51{.}067 \dashrightarrow 00{:}09{:}52{.}914$ wouldn't want to order the

NOTE Confidence: 0.970087248571428

 $00:09:52.914 \rightarrow 00:09:54.240$ particular treatments cisplatin

 $00:09:54.240 \rightarrow 00:09:56.450$ and then erlatinib because you're

NOTE Confidence: 0.970087248571428

 $00{:}09{:}56.518 \dashrightarrow 00{:}09{:}57.958$ basically creating the genetic

NOTE Confidence: 0.970087248571428

 $00{:}09{:}57{.}958 \dashrightarrow 00{:}10{:}00{.}118$ variation in the tumor so that

NOTE Confidence: 0.970087248571428

 $00:10:00.120 \longrightarrow 00:10:01.920$ it can evolve resistance very

NOTE Confidence: 0.970087248571428

 $00:10:01.920 \longrightarrow 00:10:04.320$ quickly once you give the therapy.

NOTE Confidence: 0.9553902

 $00:10:05.880 \longrightarrow 00:10:09.438$ And so as we think about

NOTE Confidence: 0.9553902

 $00:10:09.438 \longrightarrow 00:10:12.815$ the idea that you may be able to

NOTE Confidence: 0.9553902

 $00{:}10{:}12.815 \dashrightarrow 00{:}10{:}15.060$ understand better how tumors evolve

NOTE Confidence: 0.9553902

 $00{:}10{:}15{.}060 \dashrightarrow 00{:}10{:}18{.}044$ in terms of their genetic mutations

NOTE Confidence: 0.9553902

00:10:18.044 --> 00:10:22.096 which can kind of bypass some of our

NOTE Confidence: 0.9553902

 $00{:}10{:}22.096 \dashrightarrow 00{:}10{:}24.640$ the rapies and cause resistance.

NOTE Confidence: 0.9553902

 $00:10:24.640 \longrightarrow 00:10:27.331$ One can only think about how do

NOTE Confidence: 0.9553902

 $00{:}10{:}27{.}331 \dashrightarrow 00{:}10{:}30{.}278$ you take this into the preventative arena.

NOTE Confidence: 0.9553902

00:10:30.280 --> 00:10:32.038 So if we know, for example,

NOTE Confidence: 0.9553902

 $00{:}10{:}32.040 \dashrightarrow 00{:}10{:}35.148$ that UV light causes certain mutations

NOTE Confidence: 0.9553902

 $00:10:35.148 \rightarrow 00:10:38.120$ or smoking causes certain mutations,

- NOTE Confidence: 0.9553902
- $00:10:38.120 \longrightarrow 00:10:41.432$ is there a way to use the information
- NOTE Confidence: 0.9553902
- $00{:}10{:}41{.}432 \dashrightarrow 00{:}10{:}44{.}257$ that you have been able to garner
- NOTE Confidence: 0.9553902
- $00{:}10{:}44.257 \dashrightarrow 00{:}10{:}46.896$ so far to think about whether there
- NOTE Confidence: 0.9553902
- $00:10:46.896 \rightarrow 00:10:48.545$ are preventative treatments that
- NOTE Confidence: 0.9553902
- $00:10:48.545 \rightarrow 00:10:51.035$ can actually stop the mutations from
- NOTE Confidence: 0.9553902
- $00:10:51.035 \rightarrow 00:10:53.437$ occurring in the 1st place that
- NOTE Confidence: 0.9553902
- $00:10:53.437 \rightarrow 00:10:55.317$ give people their initial cancers?
- NOTE Confidence: 0.921425496842105
- $00{:}10{:}56{.}280 \dashrightarrow 00{:}10{:}58{.}100$ As a member of the School of Public Health as
- NOTE Confidence: 0.921425496842105
- $00{:}10{:}58{.}140 \dashrightarrow 00{:}10{:}59{.}913$ well as a member of Yale Cancer Center,
- NOTE Confidence: 0.921425496842105
- $00:10:59.920 \longrightarrow 00:11:01.678$ I think about prevention a lot.
- NOTE Confidence: 0.921425496842105
- 00:11:01.680 --> 00:11:04.168 And one of the things that I'm really
- NOTE Confidence: 0.921425496842105
- $00{:}11{:}04{.}168 \dashrightarrow 00{:}11{:}07{.}040$ hopeful we can do is to use the methods
- NOTE Confidence: 0.921425496842105
- $00{:}11{:}07{.}040 \dashrightarrow 00{:}11{:}09{.}196$ that we've designed to better characterize
- NOTE Confidence: 0.921425496842105
- $00{:}11{:}09{.}196 \dashrightarrow 00{:}11{:}12{.}234$ what has led to cancer in individual cases,
- NOTE Confidence: 0.921425496842105
- $00:11:12.234 \rightarrow 00:11:15.066$ to give more information to patients
- NOTE Confidence: 0.921425496842105

 $00:11:15.066 \rightarrow 00:11:18.110$ so that they can share it with their loved

NOTE Confidence: 0.921425496842105

 $00{:}11{:}18{.}110 \dashrightarrow 00{:}11{:}20{.}875$ ones and the ones that they care about.

NOTE Confidence: 0.921425496842105

 $00{:}11{:}20.880 \dashrightarrow 00{:}11{:}22.224$ And so if they find out

NOTE Confidence: 0.921425496842105

 $00:11:22.224 \rightarrow 00:11:23.504$ that their cancer was, say,

NOTE Confidence: 0.921425496842105

00:11:23.504 --> 00:11:25.424 caused by smoking or caused

NOTE Confidence: 0.921425496842105

 $00:11:25.424 \rightarrow 00:11:26.960$ by UV light exposure,

NOTE Confidence: 0.921425496842105

 $00:11:26.960 \longrightarrow 00:11:29.200$ those individuals who are close to them

NOTE Confidence: 0.921425496842105

 $00{:}11{:}29{.}200 \dashrightarrow 00{:}11{:}31{.}445$ can know some of these risk factors

NOTE Confidence: 0.921425496842105

 $00{:}11{:}31{.}445 \dashrightarrow 00{:}11{:}34{.}080$ that affected them and led to their cancer.

NOTE Confidence: 0.921425496842105

 $00{:}11{:}34.080 \dashrightarrow 00{:}11{:}36.621$ And hopefully that kind of peer education

NOTE Confidence: 0.921425496842105

 $00{:}11{:}36.621 \dashrightarrow 00{:}11{:}39.720$ I think can play a role in helping to

NOTE Confidence: 0.921425496842105

 $00:11:39.720 \rightarrow 00:11:42.320$ prevent many of these exogenous factors,

NOTE Confidence: 0.921425496842105

 $00:11:42.320 \rightarrow 00:11:44.342$ these factors outside of the body

NOTE Confidence: 0.921425496842105

 $00:11:44.342 \longrightarrow 00:11:46.240$ that can lead to cancer.

NOTE Confidence: 0.871707711428572

00:11:47.400 --> 00:11:49.556 Yeah,

NOTE Confidence: 0.871707711428572

 $00:11:49.560 \rightarrow 00:11:53.396$ I hope that most people know that

 $00:11:53.396 \rightarrow 00:11:55.762$ smoking leads to cancer and UV

NOTE Confidence: 0.871707711428572

 $00:11:55.762 \rightarrow 00:11:58.364$ light leads to cancer and there

NOTE Confidence: 0.871707711428572

 $00:11:58.364 \rightarrow 00:12:00.440$ is good public awareness of that.

NOTE Confidence: 0.871707711428572

 $00:12:00.440 \rightarrow 00:12:03.919$ What I'm kind of thinking about is

NOTE Confidence: 0.871707711428572

 $00{:}12{:}03{.}920 \dashrightarrow 00{:}12{:}07{.}350$ if you're doing work that looks at

NOTE Confidence: 0.871707711428572

 $00:12:07.350 \longrightarrow 00:12:10.134$ how these exogenous factors can

NOTE Confidence: 0.871707711428572

 $00:12:10.134 \rightarrow 00:12:13.418$ actually change the genomic profile

NOTE Confidence: 0.871707711428572

 $00:12:13.418 \rightarrow 00:12:16.390$ that causes cancers and understand

NOTE Confidence: 0.871707711428572

 $00:12:16.390 \longrightarrow 00:12:18.665$ the trajectory by which those

NOTE Confidence: 0.871707711428572

00:12:18.665 --> 00:12:20.800 cancers have further mutations,

NOTE Confidence: 0.871707711428572

 $00:12:20.800 \longrightarrow 00:12:22.876$ is there a way to prevent

NOTE Confidence: 0.871707711428572

 $00:12:22.876 \longrightarrow 00:12:23.914$ the initial mutation?

NOTE Confidence: 0.871707711428572

 $00:12:23.920 \longrightarrow 00:12:25.720$ So for example,

NOTE Confidence: 0.871707711428572

 $00{:}12{:}25{.}720 \dashrightarrow 00{:}12{:}28{.}564$ one could imagine that just like

NOTE Confidence: 0.871707711428572

 $00{:}12{:}28{.}564 \dashrightarrow 00{:}12{:}31{.}558$ you have drugs that can kind of

 $00:12:31.560 \longrightarrow 00:12:34.680$ direct cancers into either for

NOTE Confidence: 0.871707711428572

00:12:34.680 --> 00:12:37.080 causing more resistance or less

NOTE Confidence: 0.871707711428572

 $00:12:37.080 \rightarrow 00:12:39.765$ resistance to further the rapies

NOTE Confidence: 0.871707711428572

 $00:12:39.765 \longrightarrow 00:12:42.640$ and there are further mutations.

NOTE Confidence: 0.871707711428572

 $00:12:42.640 \longrightarrow 00:12:44.516$ I could imagine that you could have,

NOTE Confidence: 0.871707711428572

00:12:44.520 --> 00:12:46.920 you know what a sunscreen that

NOTE Confidence: 0.871707711428572

 $00:12:46.920 \longrightarrow 00:12:50.304$ would prevent the UV light from

NOTE Confidence: 0.871707711428572

 $00:12:50.304 \longrightarrow 00:12:53.392$ causing certain mutations or an

NOTE Confidence: 0.871707711428572

 $00:12:53.392 \rightarrow 00:12:57.456$ inhaler that might prevent cigarette

NOTE Confidence: 0.871707711428572

 $00:12:57.456 \longrightarrow 00:13:00.400$ smoke from causing mutations.

00:13:00.723 --> 00:13:04.200 Just a thought to kind of think about,

NOTE Confidence: 0.871707711428572

 $00:13:04.200 \longrightarrow 00:13:06.223$ but we have to take a quick

NOTE Confidence: 0.871707711428572

 $00{:}13{:}06{.}223 \dashrightarrow 00{:}13{:}08{.}279$ break for a medical minute,

NOTE Confidence: 0.871707711428572

 $00{:}13{:}08{.}280 \dashrightarrow 00{:}13{:}09{.}765$ so we'll pick up the

NOTE Confidence: 0.871707711428572

 $00{:}13{:}09{.}765 \dashrightarrow 00{:}13{:}10{.}953$ conversation right after that.

NOTE Confidence: 0.871707711428572

00:13:10.960 --> 00:13:13.256 Please stay tuned to learn more about

 $00:13:13.256 \rightarrow 00:13:15.078$ tracking cancer cells with my guest,

NOTE Confidence: 0.871707711428572

00:13:15.080 --> 00:13:16.439 Doctor Jeffrey Townsend.

NOTE Confidence: 0.901923601111111

 $00{:}13{:}17.040 \dashrightarrow 00{:}13{:}19.440$ Funding for Yale Cancer Answers comes

NOTE Confidence: 0.901923601111111

 $00:13:19.440 \longrightarrow 00:13:21.530$ from Smilow Cancer Hospital where

NOTE Confidence: 0.901923601111111

 $00{:}13{:}21{.}530 \dashrightarrow 00{:}13{:}23{.}625$ the lung cancer screening program

NOTE Confidence: 0.901923601111111

 $00{:}13{:}23.625 \dashrightarrow 00{:}13{:}26.120$ provides screening to those at risk

NOTE Confidence: 0.901923601111111

 $00:13:26.120 \rightarrow 00:13:27.995$ for lung cancer and individualized

NOTE Confidence: 0.901923601111111

 $00:13:28.000 \rightarrow 00:13:30.640$ state-of-the-art evaluation of lung nodules.

NOTE Confidence: 0.901923601111111

 $00{:}13{:}30{.}640$ --> $00{:}13{:}35{.}800$ To learn more, visit smilowcancerhospital.org.

NOTE Confidence: 0.901923601111111

 $00{:}13{:}35{.}800 \dashrightarrow 00{:}13{:}37{.}642$ Genetic testing can be useful for

NOTE Confidence: 0.901923601111111

 $00{:}13{:}37.642 \dashrightarrow 00{:}13{:}39.453$ people with certain types of cancer

NOTE Confidence: 0.901923601111111

 $00{:}13{:}39{.}453 \dashrightarrow 00{:}13{:}41{.}280$ that seem to run in their families.

NOTE Confidence: 0.901923601111111

 $00{:}13{:}41{.}280 \dashrightarrow 00{:}13{:}43{.}175$ Genetic counseling is a process

NOTE Confidence: 0.901923601111111

 $00{:}13{:}43.175 \dashrightarrow 00{:}13{:}45.070$ that includes collecting a detailed

NOTE Confidence: 0.901923601111111

00:13:45.133 --> 00:13:46.717 personal and family history,

NOTE Confidence: 0.901923601111111

00:13:46.720 --> 00:13:48.064 a risk assessment,

 $00:13:48.064 \rightarrow 00:13:51.200$ and a discussion of genetic testing options.

NOTE Confidence: 0.901923601111111

00:13:51.200 --> 00:13:53.826 Only about 5 to 10% of all cancers

NOTE Confidence: 0.901923601111111

 $00:13:53.826 \rightarrow 00:13:55.536$ are inherited and genetic testing

NOTE Confidence: 0.901923601111111

 $00:13:55.536 \rightarrow 00:13:57.838$ is not recommended for everyone.

NOTE Confidence: 0.901923601111111

 $00:13:57.840 \rightarrow 00:14:00.216$ Individuals who have a personal and

NOTE Confidence: 0.90192360111111

 $00:14:00.216 \longrightarrow 00:14:02.324$ or family history that includes

NOTE Confidence: 0.901923601111111

 $00:14:02.324 \rightarrow 00:14:04.599$ cancer at unusually early ages,

NOTE Confidence: 0.901923601111111

 $00:14:04.600 \rightarrow 00:14:06.568$ multiple relatives on the same side

NOTE Confidence: 0.901923601111111

 $00:14:06.568 \rightarrow 00:14:08.918$ of the family with the same cancer,

NOTE Confidence: 0.901923601111111

00:14:08.920 --> 00:14:11.580 more than one diagnosis of cancer in

NOTE Confidence: 0.901923601111111

 $00:14:11.580 \longrightarrow 00:14:13.522$ the same individual, rare cancers,

NOTE Confidence: 0.901923601111111

 $00{:}14{:}13.522 \dashrightarrow 00{:}14{:}16.329$ or family history of a known altered

NOTE Confidence: 0.901923601111111

 $00{:}14{:}16{.}329 \dashrightarrow 00{:}14{:}18{.}840$ cancer predisposing gene could be

NOTE Confidence: 0.901923601111111

 $00{:}14{:}18{.}840 \dashrightarrow 00{:}14{:}20{.}880$ candidates for genetic testing.

NOTE Confidence: 0.901923601111111

 $00{:}14{:}20{.}880 \dashrightarrow 00{:}14{:}22{.}955$ Resources for genetic counseling and

00:14:22.955 --> 00:14:25.030 testing are available at federally

NOTE Confidence: 0.901923601111111

00:14:25.097 --> 00:14:26.327 designated comprehensive cancer

NOTE Confidence: 0.901923601111111

 $00{:}14{:}26{.}327 \dashrightarrow 00{:}14{:}28{.}787$ centers such as Yale Cancer Center

NOTE Confidence: 0.901923601111111

00:14:28.787 --> 00:14:30.720 and Smilow Cancer Hospital.

NOTE Confidence: 0.901923601111111

00:14:30.720 --> 00:14:33.120 More information is available

NOTE Confidence: 0.901923601111111

 $00:14:33.120 \longrightarrow 00:14:34.148$ at yale cancercenter.org.

NOTE Confidence: 0.901923601111111

 $00{:}14{:}34{.}148 \dashrightarrow 00{:}14{:}36{.}716$ You're listening to Connecticut Public Radio.

NOTE Confidence: 0.95390486

 $00:14:37.400 \rightarrow 00:14:39.476$ Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.95390486

 $00:14:39.480 \longrightarrow 00:14:41.080$ This is Doctor Anees Chagpar

NOTE Confidence: 0.95390486

 $00{:}14{:}41.080 \dashrightarrow 00{:}14{:}43.320$ and I'm joined to night by my guest,

NOTE Confidence: 0.95390486

00:14:43.320 --> 00:14:44.766 Doctor Jeffrey Townsend.

NOTE Confidence: 0.95390486

 $00{:}14{:}44.766 \dashrightarrow 00{:}14{:}47.658$ We're talking about his work looking

NOTE Confidence: 0.95390486

 $00{:}14{:}47.658 \dashrightarrow 00{:}14{:}50.512$ at mutations and how these mutations

NOTE Confidence: 0.95390486

 $00:14:50.512 \rightarrow 00:14:53.792$ can influence each other in a way

NOTE Confidence: 0.95390486

 $00{:}14{:}53.792 \dashrightarrow 00{:}14{:}55.600$ that affects cancer evolution.

NOTE Confidence: 0.95390486

00:14:55.600 --> 00:14:58.064 And to that end, you know, Jeff,

- NOTE Confidence: 0.95390486
- $00:14:58.064 \rightarrow 00:15:00.192$ maybe you can talk a little bit
- NOTE Confidence: 0.95390486
- 00:15:00.192 --> 00:15:02.064 more about the actual techniques of
- NOTE Confidence: 0.95390486
- $00:15:02.064 \rightarrow 00:15:03.960$ the work that you've been doing.
- NOTE Confidence: 0.95390486
- 00:15:03.960 --> 00:15:05.178 And you know,
- NOTE Confidence: 0.95390486
- $00{:}15{:}05{.}178 \dashrightarrow 00{:}15{:}07{.}614$ whether it's that you have found
- NOTE Confidence: 0.95390486
- $00{:}15{:}07.614 \dashrightarrow 00{:}15{:}10.331$ that there's just one mutation that
- NOTE Confidence: 0.95390486
- $00{:}15{:}10.331 \dashrightarrow 00{:}15{:}13.600$ occurs that kind of leads to a
- NOTE Confidence: 0.95390486
- $00:15:13.600 \longrightarrow 00:15:16.388$ series of steps that then cause
- NOTE Confidence: 0.95390486
- $00{:}15{:}16.388 \dashrightarrow 00{:}15{:}18.752$ cancer and recurrence or whether
- NOTE Confidence: 0.95390486
- $00:15:18.752 \rightarrow 00:15:20.800$ there's actually multiple mutations.
- NOTE Confidence: 0.95390486
- 00:15:20.800 --> 00:15:22.960 And if you only have one,
- NOTE Confidence: 0.95390486
- $00{:}15{:}22{.}960 \dashrightarrow 00{:}15{:}24{.}916$ it may not lead to anything.
- NOTE Confidence: 0.95390486
- $00:15:24.920 \longrightarrow 00:15:27.600$ And so maybe disrupting the
- NOTE Confidence: 0.95390486
- $00{:}15{:}27.600 \dashrightarrow 00{:}15{:}29.744$ interactions between these mutations
- NOTE Confidence: 0.95390486
- $00:15:29.744 \rightarrow 00:15:31.758$ actually has a role to play.
- NOTE Confidence: 0.95390486

 $00:15:31.760 \longrightarrow 00:15:33.041$ Can you can you talk a little

NOTE Confidence: 0.95390486

 $00:15:33.041 \longrightarrow 00:15:33.840$ bit more about that?

NOTE Confidence: 0.9677077866666667

 $00:15:34.360 \longrightarrow 00:15:36.328$ Absolutely. Let me give a little

NOTE Confidence: 0.9677077866666667

 $00:15:36.328 \rightarrow 00:15:38.720$ bit of context, which is over the

NOTE Confidence: 0.9677077866666667

 $00{:}15{:}38{.}720 \dashrightarrow 00{:}15{:}41{.}280$ past decade or even a little more,

NOTE Confidence: 0.9677077866666667

 $00{:}15{:}41{.}280 \dashrightarrow 00{:}15{:}42{.}720$ there's been a very,

NOTE Confidence: 0.9677077866666667

 $00:15:42.720 \longrightarrow 00:15:44.160$ very concentrated effort

NOTE Confidence: 0.9677077866666667

 $00{:}15{:}44{.}160 \dashrightarrow 00{:}15{:}47{.}240$ to find these mutations that underlie cancer.

NOTE Confidence: 0.9677077866666667

 $00{:}15{:}47{.}240 \dashrightarrow 00{:}15{:}48{.}716$ And many groups are doing it,

NOTE Confidence: 0.9677077866666667

 $00:15:48.720 \longrightarrow 00:15:50.118$ not just mine, of course.

NOTE Confidence: 0.9677077866666667

 $00{:}15{:}50{.}120 \dashrightarrow 00{:}15{:}53{.}080$ And and have been for many years now,

NOTE Confidence: 0.9677077866666667

 $00:15:53.080 \rightarrow 00:15:54.520$ as I said, almost a decade.

NOTE Confidence: 0.9677077866666667

 $00{:}15{:}54{.}520 \dashrightarrow 00{:}15{:}57{.}130$ So that effort has largely focused

NOTE Confidence: 0.9677077866666667

 $00:15:57.130 \longrightarrow 00:15:59.332$ on the identification or the

NOTE Confidence: 0.9677077866666667

00:15:59.332 --> 00:16:01.595 discovery of gene naming, oh,

NOTE Confidence: 0.9677077866666667

 $00:16:01.595 \rightarrow 00:16:04.080$ this gene is actually relevant to cancer,

- NOTE Confidence: 0.9677077866666667
- $00:16:04.080 \rightarrow 00:16:05.676$ or that gene is relevant to cancer,
- NOTE Confidence: 0.9677077866666667
- $00:16:05.680 \longrightarrow 00:16:07.600$ or this gene is not.
- NOTE Confidence: 0.9677077866666667
- 00:16:07.600 00:16:09.896 And one of the things that my
- NOTE Confidence: 0.9677077866666667
- 00:16:09.896 --> 00:16:11.723 group specialized in was not to
- NOTE Confidence: 0.9677077866666667
- $00:16:11.723 \longrightarrow 00:16:13.822$ look at it as just like, oh,
- NOTE Confidence: 0.9677077866666667
- $00{:}16{:}13.822 \dashrightarrow 00{:}16{:}16.238$ cancer causing a driver of cancer or a
- NOTE Confidence: 0.9677077866666667
- $00:16:16.238 \rightarrow 00:16:18.516$ passenger that doesn't really cause cancer,
- NOTE Confidence: 0.9677077866666667
- 00:16:18.520 --> 00:16:20.840 but quantifying how much each
- NOTE Confidence: 0.9677077866666667
- $00{:}16{:}20.840 \dashrightarrow 00{:}16{:}23.160$ mutation is contributing to cancer.
- NOTE Confidence: 0.9677077866666667
- $00{:}16{:}23.160 \dashrightarrow 00{:}16{:}26.136$ And the way that sort of came about
- NOTE Confidence: 0.9677077866666667
- $00:16:26.136 \rightarrow 00:16:27.897$ scientifically is many people worked
- NOTE Confidence: 0.9677077866666667
- $00{:}16{:}27{.}897 \dashrightarrow 00{:}16{:}30{.}270$ on looking at how frequently you
- NOTE Confidence: 0.9677077866666667
- $00{:}16{:}30{.}338 \dashrightarrow 00{:}16{:}33{.}456$ saw a given mutation in the genome in a
- NOTE Confidence: 0.9677077866666667
- $00{:}16{:}33.456 \dashrightarrow 00{:}16{:}36.693$ tumor compared to in normal situations.
- NOTE Confidence: 0.9677077866666667
- $00{:}16{:}36{.}693 \dashrightarrow 00{:}16{:}40{.}982$ And then what we did is better understand NOTE Confidence: 0.9677077866666667

 $00:16:40.982 \rightarrow 00:16:42.946$ the underlying mutational variation

NOTE Confidence: 0.9677077866666667

 $00{:}16{:}42.946 \dashrightarrow 00{:}16{:}46.373$ from site to a site that allows us to

NOTE Confidence: 0.9677077866666667

00:16:46.373 --> 00:16:48.452 quantify how much more a certain

NOTE Confidence: 0.9677077866666667

 $00:16:48.452 \rightarrow 00:16:50.874$ mutation is causing cancer than say another.

NOTE Confidence: 0.9677077866666667

 $00{:}16{:}50{.}880 \dashrightarrow 00{:}16{:}52{.}595$ That quantification enables a more

NOTE Confidence: 0.9677077866666667

 $00{:}16{:}52{.}595 \dashrightarrow 00{:}16{:}54{.}959$ nuanced view that is not just like,

NOTE Confidence: 0.9677077866666667

00:16:54.960 --> 00:16:55.333 oh,

NOTE Confidence: 0.9677077866666667

 $00:16:55.333 \longrightarrow 00:16:57.198$ this is the driver mutation

NOTE Confidence: 0.9677077866666667

00:16:57.198 --> 00:16:58.317 causing your cancer.

NOTE Confidence: 0.9677077866666667

 $00:16:58.320 \longrightarrow 00:16:59.776$ And that's the only thing we need

NOTE Confidence: 0.9677077866666667

00:16:59.776 --> 00:17:00.400 to know about,

NOTE Confidence: 0.9677077866666667

 $00{:}17{:}00{.}400 \dashrightarrow 00{:}17{:}02{.}904$ but rather as I said

NOTE Confidence: 0.9677077866666667

 $00:17:02.904 \rightarrow 00:17:05.222$ earlier in this discussion,

NOTE Confidence: 0.9677077866666667

 $00:17:05.222 \rightarrow 00:17:07.392$ what the trajectory of changes

NOTE Confidence: 0.9677077866666667

 $00{:}17{:}07{.}392 \dashrightarrow 00{:}17{:}10{.}500$ are and how each one changes your

NOTE Confidence: 0.9677077866666667

 $00:17:10.500 \rightarrow 00:17:13.800$ prospects going forward with cancer.

- NOTE Confidence: 0.9677077866666667
- $00:17:13.800 \longrightarrow 00:17:15.984$ And the key division there is
- NOTE Confidence: 0.9677077866666667
- $00:17:15.984 \rightarrow 00:17:18.119$ between two forces which we ended
- NOTE Confidence: 0.9677077866666667
- 00:17:18.119 --> 00:17:20.240 up talking about near the end of
- NOTE Confidence: 0.9677077866666667
- $00:17:20.240 \longrightarrow 00:17:22.800$ the our previous talk which is
- $00{:}17{:}25{.}000 \dashrightarrow 00{:}17{:}27{.}280$ there's the underlying mutations that happen.
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}27.280 \dashrightarrow 00{:}17{:}28.875$ What causes those mutations happen
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}28.875 \dashrightarrow 00{:}17{:}31.197$ and on the other hand there's the
- NOTE Confidence: 0.9677077866666667
- $00:17:31.197 \longrightarrow 00:17:33.183$ selection or the fact that
- NOTE Confidence: 0.9677077866666667
- 00:17:33.183 --> 00:17:34.988 those mutations may increase the
- NOTE Confidence: 0.9677077866666667
- $00:17:34.988 \rightarrow 00:17:37.154$ proliferation or the survival of cancer.
- NOTE Confidence: 0.9677077866666667
- $00:17:37.160 \longrightarrow 00:17:37.736$ Of course,
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}37{.}736 \dashrightarrow 00{:}17{:}39{.}464$ we don't want cancer to proliferate
- NOTE Confidence: 0.9677077866666667
- $00:17:39.464 \longrightarrow 00:17:40.040$ and survive.
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}40.040 \dashrightarrow 00{:}17{:}42.640$ And so the prospect for whether or not,
- NOTE Confidence: 0.9677077866666667
- $00:17:42.640 \longrightarrow 00:17:43.055$ say,
- NOTE Confidence: 0.9677077866666667
- $00:17:43.055 \longrightarrow 00:17:45.960$ a given drug that you're on is

- NOTE Confidence: 0.9677077866666667
- 00:17:45.960 --> 00:17:48.059 under development may or may not
- NOTE Confidence: 0.9677077866666667
- $00:17:48.059 \longrightarrow 00:17:49.690$ help a patient if it's targeted
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}49.690 \dashrightarrow 00{:}17{:}50.754$ at a specific driver
- NOTE Confidence: 0.9677077866666667
- $00:17:50.760 \rightarrow 00:17:52.128$ mutation is basically proportional
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}52{.}128 \dashrightarrow 00{:}17{:}54{.}695$ to how much it makes that cancer
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}54.695 \dashrightarrow 00{:}17{:}56.519$ cell survivor proliferate better.
- NOTE Confidence: 0.9677077866666667
- $00{:}17{:}56{.}520 \dashrightarrow 00{:}17{:}59{.}090$ So this quantitative measure that
- NOTE Confidence: 0.9677077866666667
- $00:17:59.090 \rightarrow 00:18:01.740$ we're taking actually tells us the
- NOTE Confidence: 0.9677077866666667
- $00:18:01.740 \longrightarrow 00:18:03.980$ prospects for how powerful a
- NOTE Confidence: 0.9677077866666667
- 00:18:03.980 --> 00:18:06.460 prospective drug could possibly
- NOTE Confidence: 0.9677077866666667
- $00:18:06.460 \rightarrow 00:18:09.460$ be if it completely abrogates the
- NOTE Confidence: 0.9677077866666667
- $00:18:09.460 \longrightarrow 00:18:11.840$ function of the mutated protein.
- NOTE Confidence: 0.9677077866666667
- 00:18:11.840 --> 00:18:13.842 And then what we've moved on to
- NOTE Confidence: 0.9677077866666667
- $00:18:13.842 \rightarrow 00:18:16.179$ doing is not just quantifying for
- NOTE Confidence: 0.9677077866666667
- $00{:}18{:}16{.}179 \dashrightarrow 00{:}18{:}18{.}524$ each individual mutation just what
- NOTE Confidence: 0.9677077866666667

 $00:18:18.524 \rightarrow 00:18:20.485$ the quantitative benefit to the

NOTE Confidence: 0.9677077866666667

00:18:20.485 --> 00:18:22.399 cancer cell is or the detriment

NOTE Confidence: 0.9677077866666667

 $00:18:22.399 \rightarrow 00:18:25.000$ to the patient obviously,

NOTE Confidence: 0.9677077866666667

 $00:18:25.000 \rightarrow 00:18:27.440$ but quantifying how that benefit

NOTE Confidence: 0.9677077866666667

 $00{:}18{:}27{.}440 \dashrightarrow 00{:}18{:}29{.}880$ or detriment changes with other

NOTE Confidence: 0.9677077866666667

 $00:18:29.962 \dashrightarrow 00:18:32.292$ mutations that also happening.

 $00:18:34.160 \longrightarrow 00:18:36.136$ So it's not just a simple change of

NOTE Confidence: 0.9677077866666667

 $00:18:36.136 \rightarrow 00:18:38.160$ a single gene that leads to cancer.

NOTE Confidence: 0.9677077866666667

 $00:18:38.160 \longrightarrow 00:18:39.159$ In most cases,

NOTE Confidence: 0.9677077866666667

 $00:18:39.159 \rightarrow 00:18:41.157$ it's usually a cascade of changes.

NOTE Confidence: 0.933962127272727

 $00:18:41.160 \rightarrow 00:18:44.401$ And how that cascade plays out determines

NOTE Confidence: 0.933962127272727

 $00:18:44.401 \rightarrow 00:18:47.432$ the time course of one's cancer journey.

NOTE Confidence: 0.933962127272727

 $00{:}18{:}47{.}432 \dashrightarrow 00{:}18{:}50{.}128$ And so the more we can better

NOTE Confidence: 0.933962127272727

 $00{:}18{:}50{.}128$ --> $00{:}18{:}52{.}758$ understand the genetics underlying that

NOTE Confidence: 0.933962127272727

 $00{:}18{:}52.758 \dashrightarrow 00{:}18{:}55.760$ journey from a molecular standpoint,

NOTE Confidence: 0.933962127272727

 $00{:}18{:}55{.}760 \dashrightarrow 00{:}18{:}58{.}196$ the better we can understand what the

00:18:58.200 --> 00:19:00.314 patient's journey is going to be and

NOTE Confidence: 0.933962127272727

 $00{:}19{:}00{.}314 \dashrightarrow 00{:}19{:}02{.}521$ treat that patient so that they can

NOTE Confidence: 0.933962127272727

 $00{:}19{:}02{.}521 \dashrightarrow 00{:}19{:}04{.}076$ receive the best outcome possible.

NOTE Confidence: 0.8127277016666667

 $00:19:05.520 \rightarrow 00:19:08.886$ You know, as you talk about these

NOTE Confidence: 0.8127277016666667

 $00{:}19{:}08.886 \dashrightarrow 00{:}19{:}12.123$ cancers and the mutations and

NOTE Confidence: 0.8127277016666667

00:19:12.123
 $\operatorname{-->}$ 00:19:14.138 how these mutations ultimately

NOTE Confidence: 0.812727701666667

 $00{:}19{:}14.138 \dashrightarrow 00{:}19{:}17.048$ lead to cancer and how you're able to

NOTE Confidence: 0.812727701666667

 $00:19:17.048 \rightarrow 00:19:19.540$ use kind of these mathematical models

NOTE Confidence: 0.8127277016666667

 $00{:}19{:}19{.}540 \dashrightarrow 00{:}19{:}23{.}320$ to predict the trajectory.

NOTE Confidence: 0.8127277016666667

00:19:23.320 --> 00:19:26.519 I started thinking about cancer in the

NOTE Confidence: 0.8127277016666667

 $00{:}19{:}26.519 \dashrightarrow 00{:}19{:}29.552$ context of the human environment

NOTE Confidence: 0.8127277016666667

 $00:19:29.552 \rightarrow 00:19:33.380$ in which they are and how different

NOTE Confidence: 0.8127277016666667

 $00:19:33.380 \longrightarrow 00:19:36.920$ that can be in every individual.

NOTE Confidence: 0.812727701666667

 $00{:}19{:}36{.}920 \dashrightarrow 00{:}19{:}39{.}902$ So we know for example that your

NOTE Confidence: 0.812727701666667

00:19:39.902 --> 00:19:43.307 immune system plays a role in terms of

NOTE Confidence: 0.8127277016666667

 $00:19:43.307 \rightarrow 00:19:46.670$ identifying cells that are thought to

- NOTE Confidence: 0.8127277016666667
- $00:19:46.670 \rightarrow 00:19:50.579$ be quote foreign or mutated including
- NOTE Confidence: 0.8127277016666667
- $00{:}19{:}50{.}579 \dashrightarrow 00{:}19{:}54{.}121$ cancer cells and how cancer cells
- NOTE Confidence: 0.8127277016666667
- $00{:}19{:}54{.}121 \dashrightarrow 00{:}19{:}57{.}390$ have started to develop a kind of
- NOTE Confidence: 0.8127277016666667
- $00:19:57.488 \longrightarrow 00:20:00.476$ evasion of the immune system.
- NOTE Confidence: 0.8127277016666667
- $00{:}20{:}00{.}480 \dashrightarrow 00{:}20{:}03{.}448$ And so can you talk a little bit
- NOTE Confidence: 0.812727701666667
- $00:20:03.448 \longrightarrow 00:20:05.744$ about how your mathematical models
- NOTE Confidence: 0.812727701666667
- $00:20:05.744 \longrightarrow 00:20:09.655$ kind of factor in the host in
- NOTE Confidence: 0.8127277016666667
- $00:20:09.655 \longrightarrow 00:20:12.815$ terms of the interplay of its
- NOTE Confidence: 0.812727701666667
- $00:20:12.815 \rightarrow 00:20:14.640$ ability to identify these mutations
- NOTE Confidence: 0.812727701666667
- $00:20:14.640 \longrightarrow 00:20:17.197$ and get rid of them versus not?
- NOTE Confidence: 0.865158184285714
- 00:20:18.160 --> 00:20:20.330 A recent graduate student
- NOTE Confidence: 0.865158184285714
- $00{:}20{:}20{.}330 \dashrightarrow 00{:}20{:}22{.}700$ in my laboratory who's now an assistant
- NOTE Confidence: 0.865158184285714
- 00:20:22.700 --> 00:20:25.240 professor at the University of Rhode Island,
- NOTE Confidence: 0.865158184285714
- $00{:}20{:}25{.}240 \dashrightarrow 00{:}20{:}27{.}334$ Nick Fisk did some very interesting
- NOTE Confidence: 0.865158184285714
- $00:20:27.334 \rightarrow 00:20:29.839$ work that is still pre publication.
- NOTE Confidence: 0.865158184285714

 $00:20:29.840 \rightarrow 00:20:32.531$ But I'm happy to talk about it here where

NOTE Confidence: 0.865158184285714

 $00:20:32.531 \longrightarrow 00:20:35.280$ we were able to actually look at

NOTE Confidence: 0.865158184285714

 $00{:}20{:}35{.}280 \dashrightarrow 00{:}20{:}37{.}611$ the increase in selection or the amount

NOTE Confidence: 0.865158184285714

 $00{:}20{:}37.611 \dashrightarrow 00{:}20{:}40.202$ that it benefits cancer or hurts cancer

NOTE Confidence: 0.865158184285714

 $00{:}20{:}40{.}202 \dashrightarrow 00{:}20{:}42{.}117$ to have these particular mutations.

NOTE Confidence: 0.865158184285714

 $00{:}20{:}42.120 \dashrightarrow 00{:}20{:}44.780$ And we could show a correlation between

NOTE Confidence: 0.865158184285714

 $00:20:44.780 \rightarrow 00:20:47.598$ the immune system or the microenvironment,

NOTE Confidence: 0.865158184285714

 $00:20:47.600 \rightarrow 00:20:50.108$ how that that microenvironment is responding

NOTE Confidence: 0.865158184285714

 $00{:}20{:}50{.}108 \dashrightarrow 00{:}20{:}52{.}440$ and these selection coefficients themselves.

NOTE Confidence: 0.865158184285714

 $00{:}20{:}52{.}440 \dashrightarrow 00{:}20{:}55{.}446$ So in other words the more the immune

NOTE Confidence: 0.865158184285714

 $00{:}20{:}55{.}446 \dashrightarrow 00{:}20{:}58{.}449$ system could grab on to a particular

NOTE Confidence: 0.865158184285714

 $00{:}20{:}58{.}449 \dashrightarrow 00{:}21{:}01{.}492$ mutation that identifies cancer as

NOTE Confidence: 0.865158184285714

 $00:21:01.492 \longrightarrow 00:21:04.040$ problematic,

NOTE Confidence: 0.865158184285714

 $00:21:04.040 \longrightarrow 00:21:06.525$ the more we could see the active

NOTE Confidence: 0.865158184285714

 $00{:}21{:}06{.}525 \dashrightarrow 00{:}21{:}08{.}153$ selection against that particular

NOTE Confidence: 0.865158184285714

 $00:21:08.153 \longrightarrow 00:21:10.117$ mutation in the individual.

 $00:21:10.120 \rightarrow 00:21:12.968$ So at the same time as we're thinking

NOTE Confidence: 0.865158184285714

 $00{:}21{:}12{.}968 \dashrightarrow 00{:}21{:}15{.}363$ about these selection coefficients or

NOTE Confidence: 0.865158184285714

00:21:15.363 - 00:21:17.655 these benefits or detriments,

NOTE Confidence: 0.865158184285714

 $00:21:17.655 \rightarrow 00:21:19.275$ benefits of the cells,

NOTE Confidence: 0.865158184285714

00:21:19.280 --> 00:21:20.924 detriments of the patient,

NOTE Confidence: 0.865158184285714

 $00:21:20.924 \longrightarrow 00:21:22.157$ of the cancer,

NOTE Confidence: 0.865158184285714

 $00:21:22.160 \longrightarrow 00:21:24.827$ we can actually look at how that

NOTE Confidence: 0.865158184285714

 $00:21:24.827 \longrightarrow 00:21:26.702$ interaction is playing into the

NOTE Confidence: 0.865158184285714

 $00{:}21{:}26.702 \dashrightarrow 00{:}21{:}28.612$ particular mutations that spread or

NOTE Confidence: 0.865158184285714

 $00:21:28.612 \longrightarrow 00:21:31.000$ don't spread within the cancer cells.

NOTE Confidence: 0.865158184285714

 $00:21:31.000 \rightarrow 00:21:32.596$ And that interaction is a really,

NOTE Confidence: 0.865158184285714

 $00:21:32.600 \rightarrow 00:21:35.155$ really key thing to understand for many

NOTE Confidence: 0.865158184285714

00:21:35.155 --> 00:21:37.279 different therapies that are being developed

00:21:39.608 --> 00:21:41.499 in immunotherapy areas,

NOTE Confidence: 0.865158184285714

 $00:21:41.499 \rightarrow 00:21:43.872$ which is of course a very promising

NOTE Confidence: 0.865158184285714

 $00:21:43.872 \rightarrow 00:21:46.158$ area right now in cancer treatment.

 $00:21:46.446 \longrightarrow 00:21:48.734$ So hopefully what we can do is to

NOTE Confidence: 0.865158184285714

 $00{:}21{:}48.734 \dashrightarrow 00{:}21{:}51.052$ use those same kinds of measurements

NOTE Confidence: 0.865158184285714

 $00:21:51.052 \longrightarrow 00:21:53.529$ of how much this allows cells

NOTE Confidence: 0.865158184285714

 $00:21:53.529 \rightarrow 00:21:55.317$ to proliferate or survive,

NOTE Confidence: 0.865158184285714

 $00:21:55.320 \longrightarrow 00:21:57.580$ to better understand which immunotherapies

NOTE Confidence: 0.865158184285714

 $00{:}21{:}57{.}580 \dashrightarrow 00{:}22{:}00{.}222$ are actually going to serve patients

NOTE Confidence: 0.865158184285714

 $00:22:00.222 \longrightarrow 00:22:03.278$ to a better level as well.

NOTE Confidence: 0.865158184285714

00:22:03.280 --> 00:22:05.518 All of these methods, you know,

NOTE Confidence: 0.865158184285714

 $00:22:05.520 \longrightarrow 00:22:08.080$ depend on mathematics.

NOTE Confidence: 0.865158184285714

00:22:08.080 --> 00:22:09.640 Of course,

NOTE Confidence: 0.865158184285714

 $00:22:09.640 \longrightarrow 00:22:11.500$ like any of this sort

NOTE Confidence: 0.865158184285714

00:22:11.500 --> 00:22:12.120 of bioinformatics,

NOTE Confidence: 0.865158184285714

 $00:22:12.120 \longrightarrow 00:22:14.238$ relies on a lot of algorithms.

NOTE Confidence: 0.865158184285714

 $00:22:14.240 \rightarrow 00:22:16.040$ But my collaborator for this most

NOTE Confidence: 0.865158184285714

 $00:22:16.040 \rightarrow 00:22:18.205$ recent work looking at the epistasis

NOTE Confidence: 0.865158184285714

00:22:18.205 -> 00:22:19.558 between different mutations,

- NOTE Confidence: 0.865158184285714
- 00:22:19.560 --> 00:22:22.959 Jorge Alfaro Morello,
- NOTE Confidence: 0.865158184285714
- $00:22:22.960 \rightarrow 00:22:26.116$ is actually a mathematician by training.
- NOTE Confidence: 0.865158184285714
- 00:22:26.120 --> 00:22:27.360 I'm a biologist by training, and
- NOTE Confidence: 0.865158184285714
- 00:22:27.360 --> 00:22:29.436 used a lot of mathematics myself
- NOTE Confidence: 0.865158184285714
- $00:22:29.440 \longrightarrow 00:22:31.573$ in much of my work and early on
- NOTE Confidence: 0.865158184285714
- $00{:}22{:}31{.}573 \dashrightarrow 00{:}22{:}33{.}885$ in the development of this most
- NOTE Confidence: 0.865158184285714
- 00:22:33.885 --> 00:22:35.706 recent work I sat down and
- NOTE Confidence: 0.865158184285714
- 00:22:35.706 --> 00:22:37.660 was like OK I really need to look
- NOTE Confidence: 0.865158184285714
- 00:22:37.660 --> 00:22:39.364 not just at individual mutations in
- NOTE Confidence: 0.865158184285714
- $00:22:39.419 \rightarrow 00:22:41.409$ individual genes as working completely
- NOTE Confidence: 0.865158184285714
- $00:22:41.409 \rightarrow 00:22:43.001$ independently from everything else
- NOTE Confidence: 0.865158184285714
- $00{:}22{:}43.001 \dashrightarrow 00{:}22{:}45.344$ but as in a pair wise way looking at
- NOTE Confidence: 0.865158184285714
- $00:22:45.344 \rightarrow 00:22:48.040$ how this gene interacts with this other genes.
- NOTE Confidence: 0.865158184285714
- $00{:}22{:}48.040 \dashrightarrow 00{:}22{:}50.105$ Fortunately I was able to do a little
- NOTE Confidence: 0.865158184285714
- $00{:}22{:}50{.}105 \dashrightarrow 00{:}22{:}51{.}861$ bit of mathematics that solved that
- NOTE Confidence: 0.865158184285714

00:22:51.861 -> 00:22:53.472 pair wise case and was very proud

NOTE Confidence: 0.865158184285714

 $00{:}22{:}53.472 \dashrightarrow 00{:}22{:}54.880$ of myself for doing that but

NOTE Confidence: 0.865158184285714

 $00{:}22{:}54{.}880 \dashrightarrow 00{:}22{:}56{.}944$ I ran into a roadblock when I tried

NOTE Confidence: 0.865158184285714

 $00:22:56.944 \rightarrow 00:22:59.200$ to look at not just one interaction,

NOTE Confidence: 0.865158184285714

 $00:22:59.200 \rightarrow 00:23:00.760$ 1 gene interacting with another,

NOTE Confidence: 0.865158184285714

00:23:00.760 --> 00:23:01.810 but you know,

NOTE Confidence: 0.865158184285714

 $00:23:01.810 \longrightarrow 00:23:03.910$ how about those two genes

NOTE Confidence: 0.865158184285714

 $00:23:03.910 \rightarrow 00:23:05.480$ interacting with a third gene?

NOTE Confidence: 0.865158184285714

00:23:05.480 --> 00:23:07.237 It starts getting more and more complicated,

NOTE Confidence: 0.865158184285714

 $00{:}23{:}07{.}240 \dashrightarrow 00{:}23{:}08{.}698$ the mathematics that we have to

NOTE Confidence: 0.865158184285714

 $00{:}23{:}08.698 \dashrightarrow 00{:}23{:}10.520$ use to solve that kind of problem.

NOTE Confidence: 0.865158184285714

00:23:10.520 --> 00:23:13.436 And so I worked with Jorge Alfaro Amarillo,

NOTE Confidence: 0.865158184285714

 $00{:}23{:}13.440 \dashrightarrow 00{:}23{:}16.394$ who's a research scientist here at Yale,

NOTE Confidence: 0.865158184285714

 $00:23:16.400 \longrightarrow 00:23:20.036$ and he was able to solve it for

NOTE Confidence: 0.917909043636364

00:23:20.040 --> 00:23:21.870 3-4, even 5 different mutations

NOTE Confidence: 0.917909043636364

00:23:21.870 -> 00:23:24.080 and even more given enough data.

- NOTE Confidence: 0.917909043636364
- $00:23:24.080 \longrightarrow 00:23:26.390$ So, we're able to now better
- NOTE Confidence: 0.917909043636364
- $00{:}23{:}26{.}390 \dashrightarrow 00{:}23{:}28{.}598$ understand how all of these genes
- NOTE Confidence: 0.917909043636364
- $00:23:28.598 \rightarrow 00:23:30.513$ are interacting with each other
- NOTE Confidence: 0.917909043636364
- $00:23:30.513 \rightarrow 00:23:32.799$ during that time course of cancer.
- NOTE Confidence: 0.917909043636364
- $00:23:32.800 \longrightarrow 00:23:34.525$ And that understanding I think
- NOTE Confidence: 0.917909043636364
- 00:23:34.525 --> 00:23:36.640 is going to be critical toward
- NOTE Confidence: 0.917909043636364
- $00:23:36.640 \longrightarrow 00:23:37.830$ the most powerful precision
- NOTE Confidence: 0.917909043636364
- $00:23:37.830 \longrightarrow 00:23:39.755$ medicine we can do in the future.
- NOTE Confidence: 0.81374020875
- $00{:}23{:}40{.}960 \dashrightarrow 00{:}23{:}44{.}720$ So Jeff, you used a term earlier which
- NOTE Confidence: 0.81374020875
- $00:23:44.720 \longrightarrow 00:23:46.720$ many of us may not be familiar with.
- NOTE Confidence: 0.81374020875
- $00:23:46.720 \longrightarrow 00:23:48.680$ What exactly is epistasis?
- NOTE Confidence: 0.6408106525
- 00:23:49.440 --> 00:23:52.174 Yeah you may have remembered
- NOTE Confidence: 0.6408106525
- $00:23:52.174 \rightarrow 00:23:53.709$ something from like high school
- NOTE Confidence: 0.6408106525
- $00{:}23{:}53.709 \dashrightarrow 00{:}23{:}55.643$ genetics or when you learned
- NOTE Confidence: 0.6408106525
- $00{:}23{:}55{.}643 \dashrightarrow 00{:}23{:}57{.}736$ about the peas and the pods and how
- NOTE Confidence: 0.6408106525

 $00:23:57.736 \longrightarrow 00:23:59.251$ they're different colors and

NOTE Confidence: 0.6408106525

 $00{:}23{:}59{.}251 \dashrightarrow 00{:}24{:}00{.}916$ stuff and there's something called

NOTE Confidence: 0.6408106525

 $00:24:00.916 \longrightarrow 00:24:03.184$ epistasis and what it

NOTE Confidence: 0.6408106525

 $00:24:03.184 \rightarrow 00:24:05.448$ means is just 1 gene is affecting

NOTE Confidence: 0.6408106525

 $00:24:05.448 \rightarrow 00:24:07.918$ what you see in the other genes.

NOTE Confidence: 0.6408106525

 $00{:}24{:}07{.}920 \dashrightarrow 00{:}24{:}10{.}531$ So it means that you don't necessarily

NOTE Confidence: 0.6408106525

00:24:10.531 --> 00:24:12.702 get your segregation of three to

NOTE Confidence: 0.6408106525

 $00:24:12.702 \longrightarrow 00:24:15.133$ one or 9:00 to 3:00 to 3:00 to 1:00 if

NOTE Confidence: 0.6408106525

00:24:15.133 --> 00:24:16.792 you remember your high school genetics

NOTE Confidence: 0.6408106525

 $00{:}24{:}16.792 \dashrightarrow 00{:}24{:}18.742$ that you expect because there's some

NOTE Confidence: 0.6408106525

 $00{:}24{:}18.742 \dashrightarrow 00{:}24{:}21.155$ other gene affecting that segregation.

NOTE Confidence: 0.6408106525

00:24:21.155 --> 00:24:24.080 So epistasis is just a

NOTE Confidence: 0.6408106525

 $00:24:24.080 \longrightarrow 00:24:25.410$ complicated word for

NOTE Confidence: 0.6408106525

 $00{:}24{:}25{.}410 \dashrightarrow 00{:}24{:}26{.}474$ a fairly simple phenomenon,

NOTE Confidence: 0.6408106525

 $00{:}24{:}26{.}480 \dashrightarrow 00{:}24{:}27{.}520$ which is just that

NOTE Confidence: 0.6408106525

 $00:24:27.520 \rightarrow 00:24:31.559$ it matters what genetic context you're in.

- NOTE Confidence: 0.6408106525
- 00:24:31.560 --> 00:24:35.320 Meaning if you have Gene A in a certain form,

00:24:35.320 --> 00:24:37.000 then that's going to change how

NOTE Confidence: 0.6408106525

00:24:37.000 --> 00:24:39.340 Gene B is going to act or how Gene

NOTE Confidence: 0.6408106525

 $00:24:39.340 \rightarrow 00:24:41.160$ B is going to impact something.

NOTE Confidence: 0.6408106525

 $00:24:41.160 \rightarrow 00:24:43.080$ And in the particular case we're looking at,

NOTE Confidence: 0.6408106525

 $00{:}24{:}43.080 \dashrightarrow 00{:}24{:}46.568$ what we're concerned is how much is gene

NOTE Confidence: 0.6408106525

 $00{:}24{:}46.568 \dashrightarrow 00{:}24{:}48.976$ A contributing to cancer in general.

NOTE Confidence: 0.6408106525

 $00{:}24{:}48{.}976 \dashrightarrow 00{:}24{:}51{.}920$ And then the other complication

NOTE Confidence: 0.6408106525

00:24:51.991 --> 00:24:54.322 that's driven by epistasis is

NOTE Confidence: 0.6408106525

 $00{:}24{:}54{.}322 \dashrightarrow 00{:}24{:}57{.}199$ what if we have Gene B mutated first,

NOTE Confidence: 0.6408106525

00:24:57.200 --> 00:24:59.600 how much will A contribute then?

NOTE Confidence: 0.6408106525

 $00{:}24{:}59{.}600 \dashrightarrow 00{:}25{:}01{.}483$ And in some cases if you have

NOTE Confidence: 0.6408106525

00:25:01.483 --> 00:25:02.720 Gene B mutated first,

NOTE Confidence: 0.6408106525

 $00{:}25{:}02{.}720 \dashrightarrow 00{:}25{:}04{.}995$ Gene A won't contribute anything to cancer.

NOTE Confidence: 0.6408106525

 $00{:}25{:}05{.}000 \dashrightarrow 00{:}25{:}06{.}782$ And in other cases if you

00:25:06.782 --> 00:25:08.440 have Gene B mutated first,

NOTE Confidence: 0.6408106525

 $00{:}25{:}08{.}440 \dashrightarrow 00{:}25{:}11{.}114$ Gene A contributes much more to cancer.

NOTE Confidence: 0.6408106525

 $00:25:11.120 \rightarrow 00:25:13.556$ And so understanding that is really key.

NOTE Confidence: 0.6408106525

00:25:13.560 --> 00:25:14.613 So for instance,

NOTE Confidence: 0.6408106525

 $00{:}25{:}14.613 \dashrightarrow 00{:}25{:}17.070$ if I were to try to treat

NOTE Confidence: 0.6408106525

00:25:17.158 --> 00:25:19.918 patients who have gene A mutated,

NOTE Confidence: 0.6408106525

 $00:25:19.920 \rightarrow 00:25:22.240$ depending on which of those cases it was,

NOTE Confidence: 0.6408106525

 $00:25:22.240 \longrightarrow 00:25:24.130$ it might really make a big

NOTE Confidence: 0.6408106525

 $00{:}25{:}24{.}130 \dashrightarrow 00{:}25{:}25{.}888$ difference to whether that the rapy

NOTE Confidence: 0.6408106525

 $00:25:25.888 \dashrightarrow 00:25:27.430$ might actually be beneficial.

NOTE Confidence: 0.6408106525

 $00:25:27.430 \longrightarrow 00:25:31.057$ And so this is actually a tool in part for

NOTE Confidence: 0.6408106525

 $00:25:31.057 \rightarrow 00:25:33.673$ identifying biomarkers that mean

NOTE Confidence: 0.6408106525

 $00:25:33.680 \rightarrow 00:25:35.396$ therapy towards this gene might work,

NOTE Confidence: 0.6408106525

 $00{:}25{:}35{.}400 \dashrightarrow 00{:}25{:}37{.}128$ but we need to know about this other

NOTE Confidence: 0.6408106525

 $00:25:37.128 \longrightarrow 00:25:38.797$ gene to know whether it'll work.

NOTE Confidence: 0.926403539411765

 $00:25:39.880 \longrightarrow 00:25:42.895$ It kind of almost makes

- NOTE Confidence: 0.926403539411765
- $00:25:42.895 \rightarrow 00:25:45.785$ me think that if you could identify
- NOTE Confidence: 0.926403539411765
- $00{:}25{:}45.785 \dashrightarrow 00{:}25{:}48.798$ that mutations in gene A cause cancer.
- NOTE Confidence: 0.926403539411765
- 00:25:48.800 --> 00:25:51.680 But if you have mutation in Gene B,
- NOTE Confidence: 0.926403539411765
- $00:25:51.680 \rightarrow 00:25:55.055$ then mutations in gene A will not lead to
- NOTE Confidence: 0.926403539411765
- $00{:}25{:}55{.}055 \dashrightarrow 00{:}25{:}58{.}435$ the development of a full blown cancer.
- NOTE Confidence: 0.926403539411765
- $00{:}25{:}58{.}440 \dashrightarrow 00{:}26{:}00{.}845$ That you could potentially develop
- NOTE Confidence: 0.926403539411765
- 00:26:00.845 --> 00:26:03.250 a screening tool for patients
- NOTE Confidence: 0.926403539411765
- $00:26:03.326 \longrightarrow 00:26:05.276$ who have gene A mutations.
- NOTE Confidence: 0.926403539411765
- 00:26:05.280 --> 00:26:06.840 And in those patients,
- NOTE Confidence: 0.926403539411765
- $00:26:06.840 \longrightarrow 00:26:10.122$ you might be able to create a cellular
- NOTE Confidence: 0.926403539411765
- $00:26:10.122 \rightarrow 00:26:13.554$ therapy where you induce mutation in gene B,
- NOTE Confidence: 0.926403539411765
- $00{:}26{:}13.560 \dashrightarrow 00{:}26{:}16.130$ which then turns off the
- NOTE Confidence: 0.926403539411765
- $00{:}26{:}16.130 \dashrightarrow 00{:}26{:}18.440$ effect of mutations in Gene A.
- NOTE Confidence: 0.926403539411765
- $00:26:18.440 \rightarrow 00:26:21.480$ Is that kind of where you're going with this?
- NOTE Confidence: 0.890548633636364
- $00{:}26{:}21.600 \dashrightarrow 00{:}26{:}23.115$ Certainly with enough data we
- NOTE Confidence: 0.890548633636364

 $00:26:23.115 \longrightarrow 00:26:24.960$ can get at questions like that.

NOTE Confidence: 0.890548633636364

 $00:26:24.960 \longrightarrow 00:26:26.496$ Right now, it's a little hard

NOTE Confidence: 0.890548633636364

 $00:26:26.496 \longrightarrow 00:26:28.546$ for us to understand the sort of

NOTE Confidence: 0.890548633636364

 $00:26:28.546 \rightarrow 00:26:29.834$ negative interactions very well.

NOTE Confidence: 0.890548633636364

 $00:26:29.840 \longrightarrow 00:26:31.465$ We mostly understand the positive

NOTE Confidence: 0.890548633636364

 $00:26:31.465 \longrightarrow 00:26:32.383$ interactions

NOTE Confidence: 0.890548633636364

00:26:32.383 --> 00:26:34.487 but I think as we get more and

NOTE Confidence: 0.890548633636364

 $00{:}26{:}34{.}487 \dashrightarrow 00{:}26{:}36{.}360$ more data and it is

NOTE Confidence: 0.890548633636364

 $00:26:36.360 \rightarrow 00:26:38.635$ churning out even every six months,

NOTE Confidence: 0.890548633636364

 $00{:}26{:}38.640 \dashrightarrow 00{:}26{:}40.728$ I sort of look back at how much data

NOTE Confidence: 0.890548633636364

 $00{:}26{:}40.728 \dashrightarrow 00{:}26{:}42.800$ we have on each different cancer

NOTE Confidence: 0.890548633636364

 $00:26:42.800 \longrightarrow 00:26:44.580$ and the amount it's increasing

NOTE Confidence: 0.890548633636364

 $00:26:44.649 \rightarrow 00:26:46.344$ is just astounding and wonderful

NOTE Confidence: 0.890548633636364

 $00:26:46.344 \longrightarrow 00:26:48.039$ for our kind of science.

NOTE Confidence: 0.890548633636364

 $00:26:48.040 \longrightarrow 00:26:49.114$ So I think in time we're

NOTE Confidence: 0.890548633636364

 $00:26:49.114 \rightarrow 00:26:50.320$ going to be able to get at

- NOTE Confidence: 0.890548633636364
- $00:26:50.320 \longrightarrow 00:26:52.020$ questions like that where we'll
- NOTE Confidence: 0.890548633636364
- $00:26:52.020 \longrightarrow 00:26:54.512$ be able to say look, if you get
- NOTE Confidence: 0.890548633636364
- $00:26:54.512 \longrightarrow 00:26:57.239$ rid of the function of this gene,
- NOTE Confidence: 0.890548633636364
- $00:26:57.240 \longrightarrow 00:26:58.812$ then this other gene won't have
- NOTE Confidence: 0.890548633636364
- $00{:}26{:}58.812 \dashrightarrow 00{:}27{:}00.759$ the impact that it would otherwise.
- NOTE Confidence: 0.890548633636364
- $00:27:00.760 \longrightarrow 00:27:01.840$ And that may be a really,
- NOTE Confidence: 0.890548633636364
- $00:27:01.840 \longrightarrow 00:27:02.288$ really,
- NOTE Confidence: 0.890548633636364
- 00:27:02.288 --> 00:27:04.528 really beneficial way to sort
- NOTE Confidence: 0.890548633636364
- $00{:}27{:}04{.}528 \dashrightarrow 00{:}27{:}06{.}320$ of guide our the rapeutic
- NOTE Confidence: 0.890548633636364
- 00:27:06.320 --> 00:27:07.679 discovery.
- NOTE Confidence: 0.889439312857143
- $00:27:08.640 \longrightarrow 00:27:11.720$ So thinking about the future,
- NOTE Confidence: 0.889439312857143
- 00:27:11.720 --> 00:27:13.498 what things are you working on now
- NOTE Confidence: 0.889439312857143
- $00:27:13.498 \longrightarrow 00:27:15.093$ and what things are you really
- NOTE Confidence: 0.889439312857143
- $00{:}27{:}15.093 \dashrightarrow 00{:}27{:}16.647$ excited about in terms of where
- NOTE Confidence: 0.889439312857143
- $00:27:16.647 \rightarrow 00:27:18.440$ this field is going in the future?
- NOTE Confidence: 0.835882066363636

- $00:27:19.040 \longrightarrow 00:27:21.336$ As is typical in
- NOTE Confidence: 0.835882066363636
- $00:27:21.336 \longrightarrow 00:27:23.566$ science in my group, we tend to
- NOTE Confidence: 0.835882066363636
- $00:27:23.566 \longrightarrow 00:27:26.063$ use the tools that we have
- NOTE Confidence: 0.835882066363636
- $00:27:26.063 \rightarrow 00:27:27.918$ available which are somewhat unique,
- NOTE Confidence: 0.835882066363636
- $00{:}27{:}27{.}920 \dashrightarrow 00{:}27{:}30{.}896$ but to address the things that can be
- NOTE Confidence: 0.835882066363636
- $00{:}27{:}30.896 \dashrightarrow 00{:}27{:}32.520$ addressed before the things that are much,
- NOTE Confidence: 0.835882066363636
- $00:27:32.520 \longrightarrow 00:27:33.576$ much harder to address.
- NOTE Confidence: 0.835882066363636
- 00:27:33.576 --> 00:27:35.556 And what we focused on mostly
- NOTE Confidence: 0.835882066363636
- $00{:}27{:}35{.}556 \dashrightarrow 00{:}27{:}37{.}251$ are these individual changes in
- NOTE Confidence: 0.835882066363636
- 00:27:37.251 --> 00:27:39.111 individual base pairs of the DNA
- NOTE Confidence: 0.835882066363636
- $00{:}27{:}39{.}111 \dashrightarrow 00{:}27{:}40{.}879$ that lead to a change in an amino
- NOTE Confidence: 0.835882066363636
- $00:27:40.880 \longrightarrow 00:27:43.808$ acid and then cause proteins to
- NOTE Confidence: 0.835882066363636
- $00:27:43.808 \longrightarrow 00:27:47.240$ function in ways that lead to cancer.
- NOTE Confidence: 0.835882066363636
- $00{:}27{:}47{.}240 \dashrightarrow 00{:}27{:}49{.}360$ But there's a a whole suite of other
- NOTE Confidence: 0.835882066363636
- $00:27:49.360 \rightarrow 00:27:51.554$ kinds of changes that occur that are
- NOTE Confidence: 0.835882066363636
- $00:27:51.554 \rightarrow 00:27:53.799$ well known to be important to cancer.

- NOTE Confidence: 0.835882066363636
- $00:27:53.800 \longrightarrow 00:27:55.030$ So for instance,
- NOTE Confidence: 0.835882066363636
- $00:27:55.030 \longrightarrow 00:27:57.080$ in addition to the typical,
- NOTE Confidence: 0.835882066363636
- 00:27:57.080 -> 00:27:59.397 you know, base pair change in DNA
- NOTE Confidence: 0.835882066363636
- 00:27:59.397 00:28:01.799 that leads to amino acid changes,
- NOTE Confidence: 0.835882066363636
- $00:28:01.800 \rightarrow 00:28:04.116$ you can have something called methylation,
- NOTE Confidence: 0.835882066363636
- $00:28:04.120 \longrightarrow 00:28:06.164$ which it means those base pairs get
- NOTE Confidence: 0.835882066363636
- $00:28:06.164 \rightarrow 00:28:08.272$ sort of tagged with this methyl group
- NOTE Confidence: 0.835882066363636
- $00{:}28{:}08{.}272 \dashrightarrow 00{:}28{:}10{.}791$ and it means that the those genes that
- NOTE Confidence: 0.835882066363636
- $00:28:10.791 \longrightarrow 00:28:12.897$ have that methylation are either not
- NOTE Confidence: 0.835882066363636
- $00:28:12.897 \rightarrow 00:28:14.920$ expressed or in some cases are expressed.
- NOTE Confidence: 0.835882066363636
- $00:28:14.920 \longrightarrow 00:28:16.960$ It depends on exactly the context.
- NOTE Confidence: 0.835882066363636
- $00{:}28{:}16.960 \dashrightarrow 00{:}28{:}18.320$ But that methylation process is
- NOTE Confidence: 0.835882066363636
- $00:28:18.320 \longrightarrow 00:28:20.080$ known to be relevant to cancer,
- NOTE Confidence: 0.835882066363636
- $00{:}28{:}20.080 \dashrightarrow 00{:}28{:}21.720$ and so understanding how those
- NOTE Confidence: 0.835882066363636
- $00:28:21.720 \rightarrow 00:28:23.360$ contribute to cell proliferation and
- NOTE Confidence: 0.835882066363636

 $00:28:23.415 \longrightarrow 00:28:25.403$ survival in the same depth that we

NOTE Confidence: 0.835882066363636

 $00:28:25.403 \rightarrow 00:28:26.580$ understand these single nucleotide

NOTE Confidence: 0.835882066363636

 $00{:}28{:}26{.}580 \dashrightarrow 00{:}28{:}28{.}756$ mutations is a major goal in our group.

NOTE Confidence: 0.896837555909091

00:28:29.200 --> 00:28:31.816 Doctor Jeffrey Townsend is the Eliu

NOTE Confidence: 0.896837555909091

 $00{:}28{:}31{.}816 \dashrightarrow 00{:}28{:}34{.}052$ Professor of Biostatistics and professor

NOTE Confidence: 0.896837555909091

00:28:34.052 --> 00:28:36.167 of Ecology and Evolutionary biology

NOTE Confidence: 0.896837555909091

 $00{:}28{:}36{.}167 \dashrightarrow 00{:}28{:}38{.}719$ at the Yale School of Medicine.

NOTE Confidence: 0.896837555909091

 $00:28:38.720 \longrightarrow 00:28:40.776$ If you have questions,

NOTE Confidence: 0.896837555909091

 $00:28:40.776 \rightarrow 00:28:42.777$ the address is canceranswers@yale.edu,

NOTE Confidence: 0.896837555909091

 $00{:}28{:}42.777 \dashrightarrow 00{:}28{:}45.519$ and past editions of the program

NOTE Confidence: 0.896837555909091

 $00{:}28{:}45{.}519 \dashrightarrow 00{:}28{:}47{.}893$ are available in audio and written

NOTE Confidence: 0.896837555909091

 $00:28:47.893 \rightarrow 00:28:48.828$ form at yalecancercenter.org.

NOTE Confidence: 0.896837555909091

 $00:28:48.828 \longrightarrow 00:28:51.292$ We hope you'll join us next week to

NOTE Confidence: 0.896837555909091

 $00:28:51.292 \rightarrow 00:28:53.177$ learn more about the fight against

NOTE Confidence: 0.896837555909091

 $00{:}28{:}53.177 \dashrightarrow 00{:}28{:}55.040$ cancer here on Connecticut Public Radio.

NOTE Confidence: 0.896837555909091

 $00:28:55.040 \rightarrow 00:28:57.584$ Funding for Yale Cancer Answers is

00:28:57.584 --> 00:29:00.000 provided by Smilow Cancer Hospital.