WEBVTT

00:00:00.000 --> 00:00:03.054 Funding for Yale Cancer Answers is

NOTE Confidence: 0.926819506363636

00:00:03.054 --> 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 --> 00:00:09.920 with doctor Anees Chagpar.

NOTE Confidence: 0.926819506363636

00:00:09.920 --> 00:00:11.696 Yale Cancer Answers features the

NOTE Confidence: 0.926819506363636

00:00:11.696 --> 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 --> 00:00:17.273 specialists who are on the forefront

NOTE Confidence: 0.926819506363636

00:00:17.273 --> 00:00:19.237 of the battle to fight cancer.

NOTE Confidence: 0.926819506363636

00:00:19.240 --> 00:00:21.585 This week it's a conversation about new

NOTE Confidence: 0.926819506363636

00:00:21.585 --> 00:00:23.950 research into cell mutations and cancer

NOTE Confidence: 0.926819506363636

00:00:23.950 --> 00:00:26.115 therapies with Doctor Jeffrey Townsend.

NOTE Confidence: 0.926819506363636

00:00:26.120 --> 00:00:28.694 Dr. Townsend is the Elihu Professor

NOTE Confidence: 0.926819506363636

00:00:28.694 --> 00:00:30.850 of Biostatistics and professor of

NOTE Confidence: 0.926819506363636

00:00:30.850 --> 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 --> 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 --> 00:00:42.630 by you telling us a little bit more

NOTE Confidence: 0.960570288333333

00:00:42.630 --> 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 --> 00:00:51.200 but I'm perhaps the most biological

NOTE Confidence: 0.909610674285714

00:00:51.200 --> 00:00:52.840 of the members of the department

NOTE Confidence: 0.909610674285714

00:00:52.840 --> 00:00:55.358 in that all my degrees are biology

NOTE Confidence: 0.909610674285714

00:00:55.358 --> 00:00:58.120 and what I work on is large scale

NOTE Confidence: 0.909610674285714

00:00:58.120 --> 00:01:01.384 genomic data sets about the genomic

NOTE Confidence: 0.909610674285714

00:01:01.384 --> 00:01:04.224 mutations that change tumors and

NOTE Confidence: 0.909610674285714

00:01:04.224 --> 00:01:08.255 what leads to tumors and also the

NOTE Confidence: 0.909610674285714

00:01:08.255 --> 00:01:10.491 exogenous and endogenous factors

NOTE Confidence: 0.909610674285714

00:01:10.491 --> 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 --> 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 --> 00:01:21.200 about what the genome is.

NOTE Confidence: 0.800123712727273

00:01:21.200 --> 00:01:23.550 Basically the conglomeration

NOTE Confidence: 0.800123712727273

00:01:23.550 --> 00:01:27.117 of DNA that makes us who we are.

NOTE Confidence: 0.800123712727273

00:01:27.120 --> 00:01:29.640 But tell us a little bit more

NOTE Confidence: 0.800123712727273

00:01:29.640 --> 00:01:31.627 about genomics and the

NOTE Confidence: 0.800123712727273

00:01:31.627 --> 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 --> 00:01:37.069 important to understand about the work

NOTE Confidence: 0.92987426

00:01:37.069 --> 00:01:38.693 that we do is that we're working on

NOTE Confidence: 0.92987426

00:01:38.746 --> 00:01:40.316 what are called somatic mutations.

NOTE Confidence: 0.92987426

00:01:40.320 --> 00:01:42.222 So not what you inherited from

NOTE Confidence: 0.92987426

00:01:42.222 --> 00:01:44.320 your mother or from your father,

NOTE Confidence: 0.92987426

00:01:44.320 --> 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 --> 00:01:51.368 These are the kinds of mutations

NOTE Confidence: 0.92987426

00:01:51.368 --> 00:01:53.235 that people talk about trying to

NOTE Confidence: 0.92987426

00:01:53.235 --> 00:01:55.237 avoid by not smoking or not being

NOTE Confidence: 0.92987426

00:01:55.237 --> 00:01:56.756 exposed to too much UV light.

NOTE Confidence: 0.92987426

00:01:56.760 --> 00:01:59.432 So we look at those kinds of mutations

NOTE Confidence: 0.92987426

00:01:59.432 --> 00:02:01.108 that accumulate during your lifetime

NOTE Confidence: 0.92987426

00:02:01.108 --> 00:02:03.712 and then lead to cancer on top of

NOTE Confidence: 0.92987426

00:02:03.712 --> 00:02:05.372 all the germline variation that

NOTE Confidence: 0.92987426

00:02:05.372 --> 00:02:07.160 you have coming from your parents.

NOTE Confidence: 0.915732384583333

00:02:08.160 --> 00:02:10.680 And so tell us more about kind of

NOTE Confidence: 0.915732384583333

00:02:10.680 --> 00:02:13.412 how that works and how you

NOTE Confidence: 0.915732384583333

00:02:13.412 --> 00:02:15.437 discover these mutations and

NOTE Confidence: 0.915732384583333

00:02:15.514 --> 00:02:18.130 how you actually define that these

NOTE Confidence: 0.915732384583333

00:02:18.130 --> 00:02:20.355 particular mutations have an impact

NOTE Confidence: 0.915732384583333

00:02:20.355 --> 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 --> 00:02:28.372 topic since the human genome,

NOTE Confidence: 0.942250608571429

00:02:28.372 --> 00:02:30.287 we've developed lots of technologies

NOTE Confidence: 0.942250608571429

00:02:30.287 --> 00:02:32.436 that allow us to sequence genomes,

NOTE Confidence: 0.942250608571429

00:02:32.440 --> 00:02:34.330 including the genomes of tumor tissue

NOTE Confidence: 0.942250608571429

00:02:34.330 --> 00:02:36.439 as opposed to your normal tissue.

NOTE Confidence: 0.942250608571429

00:02:36.440 --> 00:02:39.226 And by comparing that tumor tissue sequence

NOTE Confidence: 0.942250608571429

00:02:39.226 --> 00:02:42.214 to the sequence we see from your blood

NOTE Confidence: 0.942250608571429

00:02:42.214 --> 00:02:44.480 or from some normal adjacent tissue,

NOTE Confidence: 0.942250608571429

00:02:44.480 --> 00:02:47.238 we can uncover all the genetic mutations

NOTE Confidence: 0.942250608571429

00:02:47.238 --> 00:02:49.736 that are specific to the tumor and

NOTE Confidence: 0.942250608571429

00:02:49.736 --> 00:02:52.359 aren't natural to the rest of your body.

NOTE Confidence: 0.942250608571429

00:02:52.360 --> 00:02:56.554 And those mutations tend to be of two kinds.

NOTE Confidence: 0.942250608571429

00:02:56.560 --> 00:02:58.723 Some are just mutations that just happen

NOTE Confidence: 0.942250608571429

00:02:58.723 --> 00:03:00.819 to have happened and don't really lead

NOTE Confidence: 0.942250608571429

00:03:00.819 --> 00:03:03.079 to cancer and other ones lead to cancer.

NOTE Confidence: 0.942250608571429

00:03:03.080 --> 00:03:05.545 And so differentiating between those

NOTE Confidence: 0.942250608571429

00:03:05.545 --> 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 --> 00:03:13.310 and understanding what the underlying

NOTE Confidence: 0.942250608571429

00:03:13.310 --> 00:03:16.119 rate at which those mutations occur are.

NOTE Confidence: 0.942250608571429

00:03:16.120 --> 00:03:18.997 And by combining those two factors together,

NOTE Confidence: 0.942250608571429

00:03:19.000 --> 00:03:21.688 we can get a quantitative estimate of

NOTE Confidence: 0.942250608571429

00:03:21.688 --> 00:03:24.907 exactly how much of the cancer is being

NOTE Confidence: 0.942250608571429

00:03:24.907 --> 00:03:27.759 caused by particular mutations in the genome.

NOTE Confidence: 0.942250608571429

00:03:27.760 --> 00:03:29.452 So I'm very excited about research

NOTE Confidence: 0.942250608571429

00:03:29.452 --> 00:03:31.754 we're doing that allows us to take that

NOTE Confidence: 0.942250608571429

00:03:31.754 --> 00:03:33.159 quantitative estimate and do things.

NOTE Confidence: 0.942250608571429

00:03:33.160 --> 00:03:34.679 This is very preliminary at this point,

NOTE Confidence: 0.942250608571429

00:03:34.680 --> 00:03:37.067 but like actually assess in an individual

NOTE Confidence: 0.942250608571429

00:03:37.067 --> 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 --> 00:03:41.062 well,

NOTE Confidence: 0.942250608571429

00:03:41.062 --> 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 --> 00:03:46.814 but actually looking at the individual

NOTE Confidence: 0.942250608571429

00:03:46.814 --> 00:03:48.280 and saying, in your case,

NOTE Confidence: 0.942250608571429

00:03:48.280 --> 00:03:50.120 why did that cancer arise?

NOTE Confidence: 0.942058918666667

00:03:51.320 --> 00:03:53.903 So tell us more about the study

NOTE Confidence: 0.942058918666667

00:03:53.903 --> 00:03:56.668 itself because I can imagine that

NOTE Confidence: 0.942058918666667

00:03:56.668 --> 00:04:00.320 as you look at these mutations and

NOTE Confidence: 0.942058918666667

00:04:00.320 --> 00:04:02.632 when you compare tumor DNA to

NOTE Confidence: 0.942058918666667

00:04:02.632 --> 00:04:05.040 normal DNA that there are more mutations.

NOTE Confidence: 0.942058918666667

00:04:05.040 --> 00:04:07.544 You might be able to say, OK

NOTE Confidence: 0.942058918666667

00:04:07.544 --> 00:04:10.232 there are more mutations and

NOTE Confidence: 0.942058918666667

00:04:10.232 --> 00:04:12.680 hypothesize that those more mutations

NOTE Confidence: 0.942058918666667

00:04:12.680 --> 00:04:15.554 are what actually caused the cancer.

NOTE Confidence: 0.942058918666667

00:04:15.560 --> 00:04:18.356 But causation and association are different.

NOTE Confidence: 0.942058918666667

00:04:18.360 --> 00:04:21.756 So how did you establish that?

NOTE Confidence: 0.942058918666667

00:04:21.760 --> 00:04:24.360 And what is the long term impact of

NOTE Confidence: 0.942058918666667

00:04:24.360 --> 00:04:27.353 being able to define in a particular

NOTE Confidence: 0.942058918666667

00:04:27.353 --> 00:04:29.618 individual what mutations cause their

NOTE Confidence: 0.942058918666667

00:04:29.691 --> 00:04:32.235 cancer? Because once they have cancer,

NOTE Confidence: 0.942058918666667

00:04:32.240 --> 00:04:34.116 isn't it kind of like a fait accompli, or

NOTE Confidence: 0.942058918666667

00:04:37.477 --> 00:04:40.111 does defining those mutations actually

NOTE Confidence: 0.942058918666667

00:04:40.111 --> 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 --> 00:04:49.158 which mutations are leading to cancer,

NOTE Confidence: 0.919434170769231

00:04:49.160 --> 00:04:50.472 what's important to understand

NOTE Confidence: 0.919434170769231

00:04:50.472 --> 00:04:52.112 is that there are very,

NOTE Confidence: 0.919434170769231

00:04:52.120 --> 00:04:54.658 very different rates of mutation for

NOTE Confidence: 0.919434170769231

00:04:54.658 --> 00:04:56.880 different sites within your genome.

NOTE Confidence: 0.919434170769231

00:04:56.880 --> 00:04:59.302 Some parts of the genome are much

NOTE Confidence: 0.919434170769231

00:04:59.302 --> 00:05:01.188 more exposed just because of the

NOTE Confidence: 0.919434170769231

00:05:01.188 --> 00:05:02.673 way the genome replicates and

NOTE Confidence: 0.919434170769231

00:05:02.673 --> 00:05:04.082 things like that, than others.

NOTE Confidence: 0.919434170769231

00:05:04.082 --> 00:05:06.170 And so what we have to do is

NOTE Confidence: 0.919434170769231

00:05:06.242 --> 00:05:07.837 estimate how likely every site

NOTE Confidence: 0.919434170769231

00:05:07.837 --> 00:05:10.200 in the genome is to be mutated.

NOTE Confidence: 0.919434170769231

00:05:10.200 --> 00:05:11.472 And then from that look at

NOTE Confidence: 0.919434170769231

00:05:11.472 --> 00:05:12.320 the tumors and say,

NOTE Confidence: 0.919434170769231

00:05:12.320 --> 00:05:14.864 do we see that frequency of mutation in

NOTE Confidence: 0.919434170769231

00:05:14.864 --> 00:05:17.317 the tumor or do we see it more often?

NOTE Confidence: 0.919434170769231

00:05:17.320 --> 00:05:19.360 And if it's more often,

NOTE Confidence: 0.919434170769231

00:05:19.360 --> 00:05:21.285 then it must be leading to tumors

NOTE Confidence: 0.919434170769231

00:05:21.285 --> 00:05:22.978 because that's what we're sequencing and

NOTE Confidence: 0.919434170769231

00:05:22.978 --> 00:05:25.600 seeing more of it there than we would expect.

NOTE Confidence: 0.919434170769231

00:05:25.600 --> 00:05:27.230 So that's how we differentiate

NOTE Confidence: 0.919434170769231

00:05:27.230 --> 00:05:28.860 those ones that are causing

NOTE Confidence: 0.919434170769231

00:05:28.923 --> 00:05:30.580 cancer from those that aren't.

NOTE Confidence: 0.919434170769231

00:05:30.580 --> 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 --> 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 --> 00:05:39.360 why individuals get cancer.

NOTE Confidence: 0.919434170769231

00:05:39.360 --> 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 --> 00:05:45.437 static thing that you have,

NOTE Confidence: 0.919434170769231

00:05:45.440 --> 00:05:47.480 but it actually changes

NOTE Confidence: 0.919434170769231

00:05:47.480 --> 00:05:49.520 over time in individuals.

NOTE Confidence: 0.919434170769231

00:05:49.520 --> 00:05:53.500 If you come in and you have a tumor removed,

NOTE Confidence: 0.919434170769231

00:05:53.500 --> 00:05:54.880 but you have recurrence,

NOTE Confidence: 0.919434170769231

00:05:54.880 --> 00:05:56.798 then one of the things that the

NOTE Confidence: 0.919434170769231

00:05:56.800 --> 00:05:58.630 physicians are charged with doing is

NOTE Confidence: 0.919434170769231

00:05:58.630 --> 00:06:00.600 trying to understand why that recurrence

NOTE Confidence: 0.919434170769231

00:06:00.600 --> 00:06:02.330 occurred and trying to negotiate

NOTE Confidence: 0.919434170769231

00:06:02.330 --> 00:06:04.120 around the evolution of that tumor.

NOTE Confidence: 0.919434170769231

00:06:04.120 --> 00:06:06.654 So the tools that have just been

NOTE Confidence: 0.919434170769231

00:06:06.654 --> 00:06:09.146 released now that we've been using

NOTE Confidence: 0.919434170769231

00:06:09.146 --> 00:06:11.356 allow one to understand what

NOTE Confidence: 0.919434170769231

00:06:11.356 --> 00:06:13.480 that trajectory of evolution is.

NOTE Confidence: 0.919434170769231

00:06:13.480 --> 00:06:14.380 In other words,

NOTE Confidence: 0.919434170769231

00:06:14.380 --> 00:06:16.480 you're at this state right now genetically,

NOTE Confidence: 0.919434170769231

00:06:16.480 --> 00:06:18.412 but what's the next genetic change

NOTE Confidence: 0.919434170769231

00:06:18.412 --> 00:06:20.467 likely to be in a probabilistic

NOTE Confidence: 0.919434170769231

00:06:20.467 --> 00:06:22.555 way and what's the next one

NOTE Confidence: 0.919434170769231

00:06:22.555 --> 00:06:24.158 after that likely to be?

NOTE Confidence: 0.919434170769231

00:06:24.160 --> 00:06:25.768 And it's the first time we've

NOTE Confidence: 0.919434170769231

00:06:25.768 --> 00:06:27.803 really been able to

NOTE Confidence: 0.919434170769231

00:06:27.803 --> 00:06:29.609 characterize that in terms of a

NOTE Confidence: 0.919434170769231

00:06:29.609 --> 00:06:31.437 trajectory of change where we

NOTE Confidence: 0.919434170769231

00:06:31.437 --> 00:06:32.905 understand quantitatively how much

NOTE Confidence: 0.919434170769231

00:06:32.905 --> 00:06:34.879 each mutation is increasing the

NOTE Confidence: 0.919434170769231

00:06:34.879 --> 00:06:37.357 survival and proliferation of these cells.

NOTE Confidence: 0.661824508

00:06:38.600 --> 00:06:39.976 So, that's interesting.

NOTE Confidence: 0.661824508

00:06:39.976 --> 00:06:42.620 How exactly do you do

NOTE Confidence: 0.661824508

00:06:42.620 --> 00:06:45.566 that in terms of defining, OK,

NOTE Confidence: 0.661824508

00:06:45.566 --> 00:06:49.420 this mutation caused your cancer and

NOTE Confidence: 0.661824508

00:06:49.420 --> 00:06:53.140 probabilistically you have an X percent

NOTE Confidence: 0.661824508

00:06:53.140 --> 00:06:55.860 probability of getting a recurrence.

NOTE Confidence: 0.661824508

00:06:55.860 --> 00:06:58.870 Tell us more about if that's really

NOTE Confidence: 0.661824508

00:06:58.870 --> 00:07:01.436 what you can do in an individual

NOTE Confidence: 0.661824508

00:07:01.436 --> 00:07:03.848 way and how exactly you

NOTE Confidence: 0.661824508

00:07:03.848 --> 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 --> 00:07:10.176 as typical with these kinds

NOTE Confidence: 0.947071578571429

00:07:10.176 --> 00:07:11.440 of studies, is population.

NOTE Confidence: 0.947071578571429

00:07:11.440 --> 00:07:12.835 So we don't know necessarily

NOTE Confidence: 0.947071578571429

00:07:12.835 --> 00:07:14.230 for an individual what their

NOTE Confidence: 0.947071578571429

00:07:14.279 --> 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 --> 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 --> 00:07:24.455 individual tumors and then say, oh,

NOTE Confidence: 0.947071578571429

00:07:24.455 --> 00:07:26.800 given where you are on this trajectory,

NOTE Confidence: 0.947071578571429

00:07:26.800 --> 00:07:29.796 what's the next mutation likely to be?

NOTE Confidence: 0.888861823333333

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 --> 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 --> 00:07:43.250 you can give me an estimate of what

NOTE Confidence: 0.888861823333333

00:07:43.326 --> 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 --> 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: 0.885301267777778

00:07:54.364 --> 00:07:56.632 right now with this approach is to

NOTE Confidence: 0.885301267777778

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

NOTE Confidence: 0.885301267777778

00:07:58.690 --> 00:08:00.656 essentially what we know about these

NOTE Confidence: 0.885301267777778

00:08:00.656 --> 00:08:02.800 genetic changes and how they occur,

NOTE Confidence: 0.885301267777778

00:08:02.800 --> 00:08:04.970 what order they occur with the

NOTE Confidence: 0.885301267777778

00:08:04.970 --> 00:08:06.595 kinds of precision medicines that

NOTE Confidence: 0.885301267777778

00:08:06.595 --> 00:08:08.909 are now being developed at a more

NOTE Confidence: 0.885301267777778

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

NOTE Confidence: 0.885301267777778

00:08:10.504 --> 00:08:12.468 the great research that's

NOTE Confidence: 0.885301267777778

00:08:12.468 --> 00:08:14.838 happening here at Yale and elsewhere.

NOTE Confidence: 0.885301267777778

00:08:14.840 --> 00:08:17.624 And the point is that all of those

NOTE Confidence: 0.885301267777778

00:08:17.624 --> 00:08:19.380 different precision treatments can

NOTE Confidence: 0.885301267777778

00:08:19.380 --> 00:08:21.080 be marshaled in different ways.

NOTE Confidence: 0.885301267777778

00:08:21.080 --> 00:08:22.893 And it's getting more and more complex

NOTE Confidence: 0.885301267777778

00:08:22.893 --> 00:08:25.172 to sort of think through how to treat

NOTE Confidence: 0.885301267777778

00:08:25.172 --> 00:08:27.304 an individual when they have this sort

NOTE Confidence: 0.885301267777778

00:08:27.304 --> 00:08:29.170 of evolving cancer that is evolving

NOTE Confidence: 0.885301267777778

00:08:29.170 --> 00:08:30.706 resistance to different therapies.

NOTE Confidence: 0.885301267777778

00:08:30.706 --> 00:08:34.330 And so hopefully what we can do with

NOTE Confidence: 0.885301267777778

00:08:34.417 --> 00:08:36.979 our genetic trajectories is to inform

NOTE Confidence: 0.885301267777778

00:08:36.979 --> 00:08:39.440 for a patient's decision making and

NOTE Confidence: 0.885301267777778

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

NOTE Confidence: 0.885301267777778

00:08:41.320 --> 00:08:43.840 about the next therapy that must be

NOTE Confidence: 0.885301267777778

00:08:43.840 --> 00:08:46.480 prescribed to someone who has cancer.

NOTE Confidence: 0.885301267777778

00:08:46.480 --> 00:08:48.643 What would be the best trajectory to

NOTE Confidence: 0.885301267777778

00:08:48.643 --> 00:08:51.117 occupy in terms of the genetic evolution?

NOTE Confidence: 0.885301267777778

00:08:51.120 --> 00:08:53.808 And are there ways we can corner the

NOTE Confidence: 0.885301267777778

00:08:53.808 --> 00:08:55.895 cancer essentially so it can't evolve

NOTE Confidence: 0.885301267777778

00:08:55.895 --> 00:08:57.911 resistance and lead to a recurrence?

NOTE Confidence: 0.8220461

00:08:59.440 --> 00:09:03.879 So kind of trying to treat to the

NOTE Confidence: 0.8220461

00:09:03.879 --> 00:09:06.950 cancer currently in a way that they

NOTE Confidence: 0.8220461

00:09:06.950 --> 00:09:09.420 then don't mutate according to the

NOTE Confidence: 0.8220461

00:09:09.420 --> 00:09:11.036 trajectory that you've hypothesized

NOTE Confidence: 0.8220461

00:09:11.036 --> 00:09:12.718 that they otherwise would?

NOTE Confidence: 0.970087248571428

00:09:13.120 --> 00:09:14.026 That's exactly right.

NOTE Confidence: 0.970087248571428

00:09:14.026 --> 00:09:16.140 Let me give you an example from

NOTE Confidence: 0.970087248571428

00:09:16.140 --> 00:09:18.906 other work that we did which

NOTE Confidence: 0.970087248571428

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

NOTE Confidence: 0.970087248571428

00:09:21.440 --> 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 --> 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 --> 00:09:34.500 one of the things that we noticed

NOTE Confidence: 0.970087248571428

00:09:34.500 --> 00:09:36.263 was that cisplatin therapy which

NOTE Confidence: 0.970087248571428

00:09:36.263 --> 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 --> 00:09:42.775 actually lead to the underlying

NOTE Confidence: 0.970087248571428

00:09:42.775 --> 00:09:45.220 mutations that give you resistance,

NOTE Confidence: 0.970087248571428

00:09:45.220 --> 00:09:47.240 give the tumor resistance

NOTE Confidence: 0.970087248571428

00:09:47.240 --> 00:09:48.960 to erlatinib therapy.

00:09:49.261 --> 00:09:51.067 So that's an example where you

NOTE Confidence: 0.970087248571428

00:09:51.067 --> 00:09:52.914 wouldn't want to order the

NOTE Confidence: 0.970087248571428

00:09:52.914 --> 00:09:54.240 particular treatments cisplatin

NOTE Confidence: 0.970087248571428

00:09:54.240 --> 00:09:56.450 and then erlatinib because you're

NOTE Confidence: 0.970087248571428

00:09:56.518 --> 00:09:57.958 basically creating the genetic

NOTE Confidence: 0.970087248571428

00:09:57.958 --> 00:10:00.118 variation in the tumor so that

NOTE Confidence: 0.970087248571428

00:10:00.120 --> 00:10:01.920 it can evolve resistance very

NOTE Confidence: 0.970087248571428

00:10:01.920 --> 00:10:04.320 quickly once you give the therapy.

NOTE Confidence: 0.9553902

00:10:05.880 --> 00:10:09.438 And so as we think about

NOTE Confidence: 0.9553902

00:10:09.438 --> 00:10:12.815 the idea that you may be able to

NOTE Confidence: 0.9553902

00:10:12.815 --> 00:10:15.060 understand better how tumors evolve

NOTE Confidence: 0.9553902

00:10:15.060 --> 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 --> 00:10:24.640 therapies and cause resistance.

NOTE Confidence: 0.9553902

00:10:24.640 --> 00:10:27.331 One can only think about how do

NOTE Confidence: 0.9553902

00:10:27.331 --> 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 --> 00:10:35.148 that UV light causes certain mutations

NOTE Confidence: 0.9553902

00:10:35.148 --> 00:10:38.120 or smoking causes certain mutations,

NOTE Confidence: 0.9553902

00:10:38.120 --> 00:10:41.432 is there a way to use the information

NOTE Confidence: 0.9553902

00:10:41.432 --> 00:10:44.257 that you have been able to garner

NOTE Confidence: 0.9553902

00:10:44.257 --> 00:10:46.896 so far to think about whether there

NOTE Confidence: 0.9553902

00:10:46.896 --> 00:10:48.545 are preventative treatments that

NOTE Confidence: 0.9553902

00:10:48.545 --> 00:10:51.035 can actually stop the mutations from

NOTE Confidence: 0.9553902

00:10:51.035 --> 00:10:53.437 occurring in the 1st place that

NOTE Confidence: 0.9553902

00:10:53.437 --> 00:10:55.317 give people their initial cancers?

NOTE Confidence: 0.921425496842105

00:10:56.280 --> 00:10:58.100 As a member of the School of Public Health as

NOTE Confidence: 0.921425496842105

00:10:58.140 --> 00:10:59.913 well as a member of Yale Cancer Center,

NOTE Confidence: 0.921425496842105

00:10:59.920 --> 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 --> 00:11:07.040 hopeful we can do is to use the methods

NOTE Confidence: 0.921425496842105

00:11:07.040 --> 00:11:09.196 that we've designed to better characterize

NOTE Confidence: 0.921425496842105

00:11:09.196 --> 00:11:12.234 what has led to cancer in individual cases,

NOTE Confidence: 0.921425496842105

00:11:12.234 --> 00:11:15.066 to give more information to patients

NOTE Confidence: 0.921425496842105

00:11:15.066 --> 00:11:18.110 so that they can share it with their loved

NOTE Confidence: 0.921425496842105

00:11:18.110 --> 00:11:20.875 ones and the ones that they care about.

NOTE Confidence: 0.921425496842105

00:11:20.880 --> 00:11:22.224 And so if they find out

NOTE Confidence: 0.921425496842105

00:11:22.224 --> 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 --> 00:11:26.960 by UV light exposure,

NOTE Confidence: 0.921425496842105

00:11:26.960 --> 00:11:29.200 those individuals who are close to them

NOTE Confidence: 0.921425496842105

00:11:29.200 --> 00:11:31.445 can know some of these risk factors

NOTE Confidence: 0.921425496842105

00:11:31.445 --> 00:11:34.080 that affected them and led to their cancer.

NOTE Confidence: 0.921425496842105

00:11:34.080 --> 00:11:36.621 And hopefully that kind of peer education

NOTE Confidence: 0.921425496842105

00:11:36.621 --> 00:11:39.720 I think can play a role in helping to

NOTE Confidence: 0.921425496842105

00:11:39.720 --> 00:11:42.320 prevent many of these exogenous factors,

NOTE Confidence: 0.921425496842105

00:11:42.320 --> 00:11:44.342 these factors outside of the body

NOTE Confidence: 0.921425496842105

00:11:44.342 --> 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 --> 00:11:53.396 I hope that most people know that

NOTE Confidence: 0.871707711428572

00:11:53.396 --> 00:11:55.762 smoking leads to cancer and UV

NOTE Confidence: 0.871707711428572

00:11:55.762 --> 00:11:58.364 light leads to cancer and there

NOTE Confidence: 0.871707711428572

00:11:58.364 --> 00:12:00.440 is good public awareness of that.

NOTE Confidence: 0.871707711428572

00:12:00.440 --> 00:12:03.919 What I'm kind of thinking about is

NOTE Confidence: 0.871707711428572

00:12:03.920 --> 00:12:07.350 if you're doing work that looks at

NOTE Confidence: 0.871707711428572

00:12:07.350 --> 00:12:10.134 how these exogenous factors can

NOTE Confidence: 0.871707711428572

00:12:10.134 --> 00:12:13.418 actually change the genomic profile

NOTE Confidence: 0.871707711428572

00:12:13.418 --> 00:12:16.390 that causes cancers and understand

NOTE Confidence: 0.871707711428572

00:12:16.390 --> 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 --> 00:12:22.876 is there a way to prevent

NOTE Confidence: 0.871707711428572

00:12:22.876 --> 00:12:23.914 the initial mutation?

NOTE Confidence: 0.871707711428572

00:12:23.920 --> 00:12:25.720 So for example,

NOTE Confidence: 0.871707711428572

00:12:25.720 --> 00:12:28.564 one could imagine that just like

NOTE Confidence: 0.871707711428572

00:12:28.564 --> 00:12:31.558 you have drugs that can kind of

NOTE Confidence: 0.871707711428572

00:12:31.560 --> 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 --> 00:12:39.765 resistance to further therapies

NOTE Confidence: 0.871707711428572

00:12:39.765 --> 00:12:42.640 and there are further mutations.

NOTE Confidence: 0.871707711428572

00:12:42.640 --> 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 --> 00:12:50.304 would prevent the UV light from

NOTE Confidence: 0.871707711428572

00:12:50.304 --> 00:12:53.392 causing certain mutations or an

NOTE Confidence: 0.871707711428572

00:12:53.392 --> 00:12:57.456 inhaler that might prevent cigarette

NOTE Confidence: 0.871707711428572

00:12:57.456 --> 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 --> 00:13:06.223 but we have to take a quick

NOTE Confidence: 0.871707711428572

00:13:06.223 --> 00:13:08.279 break for a medical minute,

NOTE Confidence: 0.871707711428572

00:13:08.280 --> 00:13:09.765 so we'll pick up the

NOTE Confidence: 0.871707711428572

00:13:09.765 --> 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

NOTE Confidence: 0.871707711428572

00:13:13.256 --> 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 --> 00:13:19.440 Funding for Yale Cancer Answers comes

NOTE Confidence: 0.901923601111111

00:13:19.440 --> 00:13:21.530 from Smilow Cancer Hospital where

NOTE Confidence: 0.901923601111111

00:13:21.530 --> 00:13:23.625 the lung cancer screening program

NOTE Confidence: 0.901923601111111

00:13:23.625 --> 00:13:26.120 provides screening to those at risk

NOTE Confidence: 0.901923601111111

00:13:26.120 --> 00:13:27.995 for lung cancer and individualized

NOTE Confidence: 0.901923601111111

00:13:28.000 --> 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 --> 00:13:37.642 Genetic testing can be useful for

NOTE Confidence: 0.901923601111111

00:13:37.642 --> 00:13:39.453 people with certain types of cancer

NOTE Confidence: 0.901923601111111

00:13:39.453 --> 00:13:41.280 that seem to run in their families.

NOTE Confidence: 0.901923601111111

00:13:41.280 --> 00:13:43.175 Genetic counseling is a process

NOTE Confidence: 0.901923601111111

00:13:43.175 --> 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,

NOTE Confidence: 0.901923601111111

00:13:48.064 --> 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 --> 00:13:55.536 are inherited and genetic testing

NOTE Confidence: 0.901923601111111

00:13:55.536 --> 00:13:57.838 is not recommended for everyone.

NOTE Confidence: 0.901923601111111

00:13:57.840 --> 00:14:00.216 Individuals who have a personal and

NOTE Confidence: 0.901923601111111

00:14:00.216 --> 00:14:02.324 or family history that includes

NOTE Confidence: 0.901923601111111

00:14:02.324 --> 00:14:04.599 cancer at unusually early ages,

NOTE Confidence: 0.901923601111111

00:14:04.600 --> 00:14:06.568 multiple relatives on the same side

NOTE Confidence: 0.901923601111111

00:14:06.568 --> 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 --> 00:14:13.522 the same individual, rare cancers,

NOTE Confidence: 0.901923601111111

00:14:13.522 --> 00:14:16.329 or family history of a known altered

NOTE Confidence: 0.901923601111111

00:14:16.329 --> 00:14:18.840 cancer predisposing gene could be

NOTE Confidence: 0.901923601111111

00:14:18.840 --> 00:14:20.880 candidates for genetic testing.

NOTE Confidence: 0.901923601111111

00:14:20.880 --> 00:14:22.955 Resources for genetic counseling and

NOTE Confidence: 0.901923601111111

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 --> 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 --> 00:14:34.148 at yalecancercenter.org.

NOTE Confidence: 0.901923601111111

00:14:34.148 --> 00:14:36.716 You're listening to Connecticut Public Radio.

NOTE Confidence: 0.95390486

00:14:37.400 --> 00:14:39.476 Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.95390486

00:14:39.480 --> 00:14:41.080 This is Doctor Anees Chagpar

NOTE Confidence: 0.95390486

00:14:41.080 --> 00:14:43.320 and I'm joined tonight 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 --> 00:14:47.658 We're talking about his work looking

NOTE Confidence: 0.95390486

00:14:47.658 --> 00:14:50.512 at mutations and how these mutations

NOTE Confidence: 0.95390486

00:14:50.512 --> 00:14:53.792 can influence each other in a way

NOTE Confidence: 0.95390486

00:14:53.792 --> 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 --> 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 --> 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 --> 00:15:07.614 whether it's that you have found

NOTE Confidence: 0.95390486

00:15:07.614 --> 00:15:10.331 that there's just one mutation that

NOTE Confidence: 0.95390486

00:15:10.331 --> 00:15:13.600 occurs that kind of leads to a

NOTE Confidence: 0.95390486

00:15:13.600 --> 00:15:16.388 series of steps that then cause

NOTE Confidence: 0.95390486

00:15:16.388 --> 00:15:18.752 cancer and recurrence or whether

NOTE Confidence: 0.95390486

00:15:18.752 --> 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 --> 00:15:24.916 it may not lead to anything.

NOTE Confidence: 0.95390486

00:15:24.920 --> 00:15:27.600 And so maybe disrupting the

NOTE Confidence: 0.95390486

00:15:27.600 --> 00:15:29.744 interactions between these mutations

NOTE Confidence: 0.95390486

00:15:29.744 --> 00:15:31.758 actually has a role to play.

NOTE Confidence: 0.95390486

00:15:31.760 --> 00:15:33.041 Can you can you talk a little

NOTE Confidence: 0.95390486

00:15:33.041 --> 00:15:33.840 bit more about that?

NOTE Confidence: 0.967707786666667

00:15:34.360 --> 00:15:36.328 Absolutely. Let me give a little

NOTE Confidence: 0.967707786666667

00:15:36.328 --> 00:15:38.720 bit of context, which is over the

NOTE Confidence: 0.967707786666667

00:15:38.720 --> 00:15:41.280 past decade or even a little more,

NOTE Confidence: 0.967707786666667

00:15:41.280 --> 00:15:42.720 there's been a very,

NOTE Confidence: 0.967707786666667

00:15:42.720 --> 00:15:44.160 very concentrated effort

NOTE Confidence: 0.967707786666667

00:15:44.160 --> 00:15:47.240 to find these mutations that underlie cancer.

NOTE Confidence: 0.967707786666667

00:15:47.240 --> 00:15:48.716 And many groups are doing it,

NOTE Confidence: 0.967707786666667

00:15:48.720 --> 00:15:50.118 not just mine, of course.

NOTE Confidence: 0.967707786666667

00:15:50.120 --> 00:15:53.080 And and have been for many years now,

NOTE Confidence: 0.967707786666667

00:15:53.080 --> 00:15:54.520 as I said, almost a decade.

NOTE Confidence: 0.967707786666667

00:15:54.520 --> 00:15:57.130 So that effort has largely focused

NOTE Confidence: 0.967707786666667

00:15:57.130 --> 00:15:59.332 on the identification or the

NOTE Confidence: 0.967707786666667

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

NOTE Confidence: 0.967707786666667

00:16:01.595 --> 00:16:04.080 this gene is actually relevant to cancer,

NOTE Confidence: 0.967707786666667

00:16:04.080 --> 00:16:05.676 or that gene is relevant to cancer,

NOTE Confidence: 0.967707786666667

00:16:05.680 --> 00:16:07.600 or this gene is not.

NOTE Confidence: 0.967707786666667

00:16:07.600 --> 00:16:09.896 And one of the things that my

NOTE Confidence: 0.967707786666667

00:16:09.896 --> 00:16:11.723 group specialized in was not to

NOTE Confidence: 0.967707786666667

00:16:11.723 --> 00:16:13.822 look at it as just like, oh,

NOTE Confidence: 0.967707786666667

00:16:13.822 --> 00:16:16.238 cancer causing a driver of cancer or a

NOTE Confidence: 0.967707786666667

00:16:16.238 --> 00:16:18.516 passenger that doesn't really cause cancer,

NOTE Confidence: 0.967707786666667

00:16:18.520 --> 00:16:20.840 but quantifying how much each

NOTE Confidence: 0.967707786666667

00:16:20.840 --> 00:16:23.160 mutation is contributing to cancer.

NOTE Confidence: 0.967707786666667

00:16:23.160 --> 00:16:26.136 And the way that sort of came about

NOTE Confidence: 0.967707786666667

00:16:26.136 --> 00:16:27.897 scientifically is many people worked

NOTE Confidence: 0.967707786666667

00:16:27.897 --> 00:16:30.270 on looking at how frequently you

NOTE Confidence: 0.967707786666667

00:16:30.338 --> 00:16:33.456 saw a given mutation in the genome in a

NOTE Confidence: 0.967707786666667

00:16:33.456 --> 00:16:36.693 tumor compared to in normal situations.

NOTE Confidence: 0.967707786666667

00:16:36.693 --> 00:16:40.982 And then what we did is better understand

NOTE Confidence: 0.967707786666667

00:16:40.982 --> 00:16:42.946 the underlying mutational variation

NOTE Confidence: 0.967707786666667

00:16:42.946 --> 00:16:46.373 from site to a site that allows us to

NOTE Confidence: 0.967707786666667

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

NOTE Confidence: 0.967707786666667

00:16:48.452 --> 00:16:50.874 mutation is causing cancer than say another.

NOTE Confidence: 0.967707786666667

00:16:50.880 --> 00:16:52.595 That quantification enables a more

NOTE Confidence: 0.967707786666667

00:16:52.595 --> 00:16:54.959 nuanced view that is not just like,

NOTE Confidence: 0.967707786666667

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

NOTE Confidence: 0.967707786666667

00:16:55.333 --> 00:16:57.198 this is the driver mutation

NOTE Confidence: 0.967707786666667

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

NOTE Confidence: 0.967707786666667

00:16:58.320 --> 00:16:59.776 And that's the only thing we need

NOTE Confidence: 0.967707786666667

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

NOTE Confidence: 0.967707786666667

00:17:00.400 --> 00:17:02.904 but rather as I said

NOTE Confidence: 0.967707786666667

00:17:02.904 --> 00:17:05.222 earlier in this discussion,

NOTE Confidence: 0.967707786666667

00:17:05.222 --> 00:17:07.392 what the trajectory of changes

NOTE Confidence: 0.967707786666667

00:17:07.392 --> 00:17:10.500 are and how each one changes your

NOTE Confidence: 0.967707786666667

00:17:10.500 --> 00:17:13.800 prospects going forward with cancer.

NOTE Confidence: 0.967707786666667

00:17:13.800 --> 00:17:15.984 And the key division there is

NOTE Confidence: 0.967707786666667

00:17:15.984 --> 00:17:18.119 between two forces which we ended

NOTE Confidence: 0.967707786666667

00:17:18.119 --> 00:17:20.240 up talking about near the end of

NOTE Confidence: 0.967707786666667

00:17:20.240 --> 00:17:22.800 the our previous talk which is

00:17:25.000 --> 00:17:27.280 there's the underlying mutations that happen.

NOTE Confidence: 0.967707786666667

00:17:27.280 --> 00:17:28.875 What causes those mutations happen

NOTE Confidence: 0.967707786666667

00:17:28.875 --> 00:17:31.197 and on the other hand there's the

NOTE Confidence: 0.967707786666667

00:17:31.197 --> 00:17:33.183 selection or the fact that

NOTE Confidence: 0.967707786666667

00:17:33.183 --> 00:17:34.988 those mutations may increase the

NOTE Confidence: 0.967707786666667

00:17:34.988 --> 00:17:37.154 proliferation or the survival of cancer.

NOTE Confidence: 0.967707786666667

00:17:37.160 --> 00:17:37.736 Of course,

NOTE Confidence: 0.967707786666667

00:17:37.736 --> 00:17:39.464 we don't want cancer to proliferate

NOTE Confidence: 0.967707786666667

00:17:39.464 --> 00:17:40.040 and survive.

NOTE Confidence: 0.967707786666667

00:17:40.040 --> 00:17:42.640 And so the prospect for whether or not,

NOTE Confidence: 0.967707786666667

00:17:42.640 --> 00:17:43.055 say,

NOTE Confidence: 0.967707786666667

00:17:43.055 --> 00:17:45.960 a given drug that you're on is

NOTE Confidence: 0.967707786666667

00:17:45.960 --> 00:17:48.059 under development may or may not

NOTE Confidence: 0.967707786666667

00:17:48.059 --> 00:17:49.690 help a patient if it's targeted

NOTE Confidence: 0.967707786666667

00:17:49.690 --> 00:17:50.754 at a specific driver

NOTE Confidence: 0.967707786666667

00:17:50.760 --> 00:17:52.128 mutation is basically proportional

NOTE Confidence: 0.967707786666667

00:17:52.128 --> 00:17:54.695 to how much it makes that cancer

NOTE Confidence: 0.967707786666667

00:17:54.695 --> 00:17:56.519 cell survivor proliferate better.

NOTE Confidence: 0.967707786666667

00:17:56.520 --> 00:17:59.090 So this quantitative measure that

NOTE Confidence: 0.967707786666667

00:17:59.090 --> 00:18:01.740 we're taking actually tells us the

NOTE Confidence: 0.967707786666667

00:18:01.740 --> 00:18:03.980 prospects for how powerful a

NOTE Confidence: 0.967707786666667

00:18:03.980 --> 00:18:06.460 prospective drug could possibly

NOTE Confidence: 0.967707786666667

00:18:06.460 --> 00:18:09.460 be if it completely abrogates the

NOTE Confidence: 0.967707786666667

00:18:09.460 --> 00:18:11.840 function of the mutated protein.

NOTE Confidence: 0.967707786666667

00:18:11.840 --> 00:18:13.842 And then what we've moved on to

NOTE Confidence: 0.967707786666667

00:18:13.842 --> 00:18:16.179 doing is not just quantifying for

NOTE Confidence: 0.967707786666667

00:18:16.179 --> 00:18:18.524 each individual mutation just what

NOTE Confidence: 0.967707786666667

00:18:18.524 --> 00:18:20.485 the quantitative benefit to the

NOTE Confidence: 0.967707786666667

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

NOTE Confidence: 0.967707786666667

00:18:22.399 --> 00:18:25.000 to the patient obviously,

NOTE Confidence: 0.967707786666667

00:18:25.000 --> 00:18:27.440 but quantifying how that benefit

NOTE Confidence: 0.967707786666667

00:18:27.440 --> 00:18:29.880 or detriment changes with other

NOTE Confidence: 0.967707786666667

00:18:29.962 --> 00:18:32.292 mutations that also happening.

00:18:34.160 --> 00:18:36.136 So it's not just a simple change of

NOTE Confidence: 0.967707786666667

00:18:36.136 --> 00:18:38.160 a single gene that leads to cancer.

NOTE Confidence: 0.967707786666667

00:18:38.160 --> 00:18:39.159 In most cases,

NOTE Confidence: 0.967707786666667

00:18:39.159 --> 00:18:41.157 it's usually a cascade of changes.

NOTE Confidence: 0.933962127272727

00:18:41.160 --> 00:18:44.401 And how that cascade plays out determines

NOTE Confidence: 0.933962127272727

00:18:44.401 --> 00:18:47.432 the time course of one's cancer journey.

NOTE Confidence: 0.933962127272727

00:18:47.432 --> 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 --> 00:18:55.760 journey from a molecular standpoint,

NOTE Confidence: 0.933962127272727

00:18:55.760 --> 00:18:58.196 the better we can understand what the

NOTE Confidence: 0.933962127272727

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

NOTE Confidence: 0.933962127272727

00:19:00.314 --> 00:19:02.521 treat that patient so that they can

NOTE Confidence: 0.933962127272727

00:19:02.521 --> 00:19:04.076 receive the best outcome possible.

NOTE Confidence: 0.812727701666667

00:19:05.520 --> 00:19:08.886 You know, as you talk about these

NOTE Confidence: 0.812727701666667

00:19:08.886 --> 00:19:12.123 cancers and the mutations and

NOTE Confidence: 0.812727701666667

00:19:12.123 --> 00:19:14.138 how these mutations ultimately

NOTE Confidence: 0.812727701666667

00:19:14.138 --> 00:19:17.048 lead to cancer and how you're able to

NOTE Confidence: 0.812727701666667

00:19:17.048 --> 00:19:19.540 use kind of these mathematical models

NOTE Confidence: 0.812727701666667

00:19:19.540 --> 00:19:23.320 to predict the trajectory.

NOTE Confidence: 0.812727701666667

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

NOTE Confidence: 0.812727701666667

00:19:26.519 --> 00:19:29.552 context of the human environment

NOTE Confidence: 0.812727701666667

00:19:29.552 --> 00:19:33.380 in which they are and how different

NOTE Confidence: 0.812727701666667

00:19:33.380 --> 00:19:36.920 that can be in every individual.

NOTE Confidence: 0.812727701666667

00:19:36.920 --> 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: 0.812727701666667

00:19:43.307 --> 00:19:46.670 identifying cells that are thought to

NOTE Confidence: 0.812727701666667

00:19:46.670 --> 00:19:50.579 be quote foreign or mutated including

NOTE Confidence: 0.812727701666667

00:19:50.579 --> 00:19:54.121 cancer cells and how cancer cells

NOTE Confidence: 0.812727701666667

00:19:54.121 --> 00:19:57.390 have started to develop a kind of

NOTE Confidence: 0.812727701666667

00:19:57.488 --> 00:20:00.476 evasion of the immune system.

NOTE Confidence: 0.812727701666667

00:20:00.480 --> 00:20:03.448 And so can you talk a little bit

NOTE Confidence: 0.812727701666667

00:20:03.448 --> 00:20:05.744 about how your mathematical models

NOTE Confidence: 0.812727701666667

00:20:05.744 --> 00:20:09.655 kind of factor in the host in

NOTE Confidence: 0.812727701666667

00:20:09.655 --> 00:20:12.815 terms of the interplay of its

NOTE Confidence: 0.812727701666667

00:20:12.815 --> 00:20:14.640 ability to identify these mutations

NOTE Confidence: 0.812727701666667

00:20:14.640 --> 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 --> 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 --> 00:20:27.334 Nick Fisk did some very interesting

NOTE Confidence: 0.865158184285714

00:20:27.334 --> 00:20:29.839 work that is still pre publication.

NOTE Confidence: 0.865158184285714

00:20:29.840 --> 00:20:32.531 But I'm happy to talk about it here where

NOTE Confidence: 0.865158184285714

00:20:32.531 --> 00:20:35.280 we were able to actually look at

NOTE Confidence: 0.865158184285714

00:20:35.280 --> 00:20:37.611 the increase in selection or the amount

NOTE Confidence: 0.865158184285714

00:20:37.611 --> 00:20:40.202 that it benefits cancer or hurts cancer

NOTE Confidence: 0.865158184285714

00:20:40.202 --> 00:20:42.117 to have these particular mutations.

NOTE Confidence: 0.865158184285714

00:20:42.120 --> 00:20:44.780 And we could show a correlation between

NOTE Confidence: 0.865158184285714

00:20:44.780 --> 00:20:47.598 the immune system or the microenvironment,

NOTE Confidence: 0.865158184285714

00:20:47.600 --> 00:20:50.108 how that that microenvironment is responding

NOTE Confidence: 0.865158184285714

00:20:50.108 --> 00:20:52.440 and these selection coefficients themselves.

NOTE Confidence: 0.865158184285714

00:20:52.440 --> 00:20:55.446 So in other words the more the immune

NOTE Confidence: 0.865158184285714

00:20:55.446 --> 00:20:58.449 system could grab on to a particular

NOTE Confidence: 0.865158184285714

00:20:58.449 --> 00:21:01.492 mutation that identifies cancer as

NOTE Confidence: 0.865158184285714

00:21:01.492 --> 00:21:04.040 problematic,

NOTE Confidence: 0.865158184285714

00:21:04.040 --> 00:21:06.525 the more we could see the active

NOTE Confidence: 0.865158184285714

00:21:06.525 --> 00:21:08.153 selection against that particular

NOTE Confidence: 0.865158184285714

00:21:08.153 --> 00:21:10.117 mutation in the individual.

NOTE Confidence: 0.865158184285714

00:21:10.120 --> 00:21:12.968 So at the same time as we're thinking

NOTE Confidence: 0.865158184285714

00:21:12.968 --> 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 --> 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 --> 00:21:22.157 of the cancer,

NOTE Confidence: 0.865158184285714

00:21:22.160 --> 00:21:24.827 we can actually look at how that

NOTE Confidence: 0.865158184285714

00:21:24.827 --> 00:21:26.702 interaction is playing into the

NOTE Confidence: 0.865158184285714

00:21:26.702 --> 00:21:28.612 particular mutations that spread or

NOTE Confidence: 0.865158184285714

00:21:28.612 --> 00:21:31.000 don't spread within the cancer cells.

NOTE Confidence: 0.865158184285714

00:21:31.000 --> 00:21:32.596 And that interaction is a really,

NOTE Confidence: 0.865158184285714

00:21:32.600 --> 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 --> 00:21:43.872 which is of course a very promising

NOTE Confidence: 0.865158184285714

00:21:43.872 --> 00:21:46.158 area right now in cancer treatment.

00:21:46.446 --> 00:21:48.734 So hopefully what we can do is to

NOTE Confidence: 0.865158184285714

00:21:48.734 --> 00:21:51.052 use those same kinds of measurements

NOTE Confidence: 0.865158184285714

00:21:51.052 --> 00:21:53.529 of how much this allows cells

NOTE Confidence: 0.865158184285714

00:21:53.529 --> 00:21:55.317 to proliferate or survive,

NOTE Confidence: 0.865158184285714

00:21:55.320 --> 00:21:57.580 to better understand which immunotherapies

NOTE Confidence: 0.865158184285714

00:21:57.580 --> 00:22:00.222 are actually going to serve patients

NOTE Confidence: 0.865158184285714

00:22:00.222 --> 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 --> 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 --> 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 --> 00:22:14.238 relies on a lot of algorithms.

NOTE Confidence: 0.865158184285714

00:22:14.240 --> 00:22:16.040 But my collaborator for this most

NOTE Confidence: 0.865158184285714

00:22:16.040 --> 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 --> 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 --> 00:22:31.573 in much of my work and early on

NOTE Confidence: 0.865158184285714

00:22:31.573 --> 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 --> 00:22:41.409 individual genes as working completely

NOTE Confidence: 0.865158184285714

00:22:41.409 --> 00:22:43.001 independently from everything else

NOTE Confidence: 0.865158184285714

00:22:43.001 --> 00:22:45.344 but as in a pair wise way looking at

NOTE Confidence: 0.865158184285714

00:22:45.344 --> 00:22:48.040 how this gene interacts with this other genes.

NOTE Confidence: 0.865158184285714

00:22:48.040 --> 00:22:50.105 Fortunately I was able to do a little

NOTE Confidence: 0.865158184285714

00:22:50.105 --> 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 --> 00:22:54.880 of myself for doing that but

NOTE Confidence: 0.865158184285714

00:22:54.880 --> 00:22:56.944 I ran into a roadblock when I tried

NOTE Confidence: 0.865158184285714

00:22:56.944 --> 00:22:59.200 to look at not just one interaction,

NOTE Confidence: 0.865158184285714

00:22:59.200 --> 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 --> 00:23:03.910 how about those two genes

NOTE Confidence: 0.865158184285714

00:23:03.910 --> 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 --> 00:23:08.698 the mathematics that we have to

NOTE Confidence: 0.865158184285714

00:23:08.698 --> 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 --> 00:23:16.394 who's a research scientist here at Yale,

NOTE Confidence: 0.865158184285714

00:23:16.400 --> 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 --> 00:23:26.390 So, we're able to now better

NOTE Confidence: 0.917909043636364

00:23:26.390 --> 00:23:28.598 understand how all of these genes

NOTE Confidence: 0.917909043636364

00:23:28.598 --> 00:23:30.513 are interacting with each other

NOTE Confidence: 0.917909043636364

00:23:30.513 --> 00:23:32.799 during that time course of cancer.

NOTE Confidence: 0.917909043636364

00:23:32.800 --> 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 --> 00:23:37.830 the most powerful precision

NOTE Confidence: 0.917909043636364

00:23:37.830 --> 00:23:39.755 medicine we can do in the future.

NOTE Confidence: 0.81374020875

00:23:40.960 --> 00:23:44.720 So Jeff, you used a term earlier which

NOTE Confidence: 0.81374020875

00:23:44.720 --> 00:23:46.720 many of us may not be familiar with.

NOTE Confidence: 0.81374020875

00:23:46.720 --> 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 --> 00:23:53.709 something from like high school

NOTE Confidence: 0.6408106525

00:23:53.709 --> 00:23:55.643 genetics or when you learned

NOTE Confidence: 0.6408106525

00:23:55.643 --> 00:23:57.736 about the peas and the pods and how

NOTE Confidence: 0.6408106525

00:23:57.736 --> 00:23:59.251 they're different colors and

NOTE Confidence: 0.6408106525

00:23:59.251 --> 00:24:00.916 stuff and there's something called

NOTE Confidence: 0.6408106525

00:24:00.916 --> 00:24:03.184 epistasis and what it

NOTE Confidence: 0.6408106525

00:24:03.184 --> 00:24:05.448 means is just 1 gene is affecting

NOTE Confidence: 0.6408106525

00:24:05.448 --> 00:24:07.918 what you see in the other genes.

NOTE Confidence: 0.6408106525

00:24:07.920 --> 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 --> 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 --> 00:24:18.742 that you expect because there's some

NOTE Confidence: 0.6408106525

00:24:18.742 --> 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 --> 00:24:25.410 complicated word for

NOTE Confidence: 0.6408106525

00:24:25.410 --> 00:24:26.474 a fairly simple phenomenon,

NOTE Confidence: 0.6408106525

00:24:26.480 --> 00:24:27.520 which is just that

NOTE Confidence: 0.6408106525

00:24:27.520 --> 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,

NOTE Confidence: 0.6408106525

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 --> 00:24:41.160 B is going to impact something.

NOTE Confidence: 0.6408106525

00:24:41.160 --> 00:24:43.080 And in the particular case we're looking at,

NOTE Confidence: 0.6408106525

00:24:43.080 --> 00:24:46.568 what we're concerned is how much is gene

NOTE Confidence: 0.6408106525

00:24:46.568 --> 00:24:48.976 A contributing to cancer in general.

NOTE Confidence: 0.6408106525

00:24:48.976 --> 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 --> 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 --> 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 --> 00:25:04.995 Gene A won't contribute anything to cancer.

NOTE Confidence: 0.6408106525

00:25:05.000 --> 00:25:06.782 And in other cases if you

NOTE Confidence: 0.6408106525

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

NOTE Confidence: 0.6408106525

00:25:08.440 --> 00:25:11.114 Gene A contributes much more to cancer.

NOTE Confidence: 0.6408106525

00:25:11.120 --> 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 --> 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 --> 00:25:22.240 depending on which of those cases it was,

NOTE Confidence: 0.6408106525

00:25:22.240 --> 00:25:24.130 it might really make a big

NOTE Confidence: 0.6408106525

00:25:24.130 --> 00:25:25.888 difference to whether that therapy

NOTE Confidence: 0.6408106525

00:25:25.888 --> 00:25:27.430 might actually be beneficial.

NOTE Confidence: 0.6408106525

00:25:27.430 --> 00:25:31.057 And so this is actually a tool in part for

NOTE Confidence: 0.6408106525

00:25:31.057 --> 00:25:33.673 identifying biomarkers that mean

NOTE Confidence: 0.6408106525

00:25:33.680 --> 00:25:35.396 therapy towards this gene might work,

NOTE Confidence: 0.6408106525

00:25:35.400 --> 00:25:37.128 but we need to know about this other

NOTE Confidence: 0.6408106525

00:25:37.128 --> 00:25:38.797 gene to know whether it'll work.

NOTE Confidence: 0.926403539411765

00:25:39.880 --> 00:25:42.895 It kind of almost makes

NOTE Confidence: 0.926403539411765

00:25:42.895 --> 00:25:45.785 me think that if you could identify

NOTE Confidence: 0.926403539411765

00:25:45.785 --> 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 --> 00:25:55.055 then mutations in gene A will not lead to

NOTE Confidence: 0.926403539411765

00:25:55.055 --> 00:25:58.435 the development of a full blown cancer.

NOTE Confidence: 0.926403539411765

00:25:58.440 --> 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 --> 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 --> 00:26:10.122 you might be able to create a cellular

NOTE Confidence: 0.926403539411765

00:26:10.122 --> 00:26:13.554 therapy where you induce mutation in gene B,

NOTE Confidence: 0.926403539411765

00:26:13.560 --> 00:26:16.130 which then turns off the

NOTE Confidence: 0.926403539411765

00:26:16.130 --> 00:26:18.440 effect of mutations in Gene A.

NOTE Confidence: 0.926403539411765

00:26:18.440 --> 00:26:21.480 Is that kind of where you're going with this?

NOTE Confidence: 0.890548633636364

00:26:21.600 --> 00:26:23.115 Certainly with enough data we

NOTE Confidence: 0.890548633636364

00:26:23.115 --> 00:26:24.960 can get at questions like that.

NOTE Confidence: 0.890548633636364

00:26:24.960 --> 00:26:26.496 Right now, it's a little hard

NOTE Confidence: 0.890548633636364

00:26:26.496 --> 00:26:28.546 for us to understand the sort of

NOTE Confidence: 0.890548633636364

00:26:28.546 --> 00:26:29.834 negative interactions very well.

NOTE Confidence: 0.890548633636364

00:26:29.840 --> 00:26:31.465 We mostly understand the positive

NOTE Confidence: 0.890548633636364

00:26:31.465 --> 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 --> 00:26:36.360 more data and it is

NOTE Confidence: 0.890548633636364

00:26:36.360 --> 00:26:38.635 churning out even every six months,

NOTE Confidence: 0.890548633636364

00:26:38.640 --> 00:26:40.728 I sort of look back at how much data

NOTE Confidence: 0.890548633636364

00:26:40.728 --> 00:26:42.800 we have on each different cancer

NOTE Confidence: 0.890548633636364

00:26:42.800 --> 00:26:44.580 and the amount it's increasing

NOTE Confidence: 0.890548633636364

00:26:44.649 --> 00:26:46.344 is just astounding and wonderful

NOTE Confidence: 0.890548633636364

00:26:46.344 --> 00:26:48.039 for our kind of science.

NOTE Confidence: 0.890548633636364

00:26:48.040 --> 00:26:49.114 So I think in time we're

NOTE Confidence: 0.890548633636364

00:26:49.114 --> 00:26:50.320 going to be able to get at

NOTE Confidence: 0.890548633636364

00:26:50.320 --> 00:26:52.020 questions like that where we'll

NOTE Confidence: 0.890548633636364

00:26:52.020 --> 00:26:54.512 be able to say look, if you get

NOTE Confidence: 0.890548633636364

00:26:54.512 --> 00:26:57.239 rid of the function of this gene,

NOTE Confidence: 0.890548633636364

00:26:57.240 --> 00:26:58.812 then this other gene won't have

NOTE Confidence: 0.890548633636364

00:26:58.812 --> 00:27:00.759 the impact that it would otherwise.

NOTE Confidence: 0.890548633636364

00:27:00.760 --> 00:27:01.840 And that may be a really,

NOTE Confidence: 0.890548633636364

00:27:01.840 --> 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 --> 00:27:06.320 of guide our therapeutic

NOTE Confidence: 0.890548633636364

00:27:06.320 --> 00:27:07.679 discovery.

NOTE Confidence: 0.889439312857143

00:27:08.640 --> 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 --> 00:27:15.093 and what things are you really

NOTE Confidence: 0.889439312857143

00:27:15.093 --> 00:27:16.647 excited about in terms of where

NOTE Confidence: 0.889439312857143

00:27:16.647 --> 00:27:18.440 this field is going in the future?

NOTE Confidence: 0.835882066363636

00:27:19.040 --> 00:27:21.336 As is typical in

NOTE Confidence: 0.835882066363636

00:27:21.336 --> 00:27:23.566 science in my group, we tend to

NOTE Confidence: 0.835882066363636

00:27:23.566 --> 00:27:26.063 use the tools that we have

NOTE Confidence: 0.835882066363636

00:27:26.063 --> 00:27:27.918 available which are somewhat unique,

NOTE Confidence: 0.835882066363636

00:27:27.920 --> 00:27:30.896 but to address the things that can be

NOTE Confidence: 0.835882066363636

00:27:30.896 --> 00:27:32.520 addressed before the things that are much,

NOTE Confidence: 0.835882066363636

00:27:32.520 --> 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 --> 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 --> 00:27:40.879 that lead to a change in an amino

NOTE Confidence: 0.835882066363636

00:27:40.880 --> 00:27:43.808 acid and then cause proteins to

NOTE Confidence: 0.835882066363636

00:27:43.808 --> 00:27:47.240 function in ways that lead to cancer.

NOTE Confidence: 0.835882066363636

00:27:47.240 --> 00:27:49.360 But there's a a whole suite of other

NOTE Confidence: 0.835882066363636

00:27:49.360 --> 00:27:51.554 kinds of changes that occur that are

NOTE Confidence: 0.835882066363636

00:27:51.554 --> 00:27:53.799 well known to be important to cancer.

NOTE Confidence: 0.835882066363636

00:27:53.800 --> 00:27:55.030 So for instance,

NOTE Confidence: 0.835882066363636

00:27:55.030 --> 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 --> 00:28:04.116 you can have something called methylation,

NOTE Confidence: 0.835882066363636

00:28:04.120 --> 00:28:06.164 which it means those base pairs get

NOTE Confidence: 0.835882066363636

00:28:06.164 --> 00:28:08.272 sort of tagged with this methyl group

NOTE Confidence: 0.835882066363636

00:28:08.272 --> 00:28:10.791 and it means that the those genes that

NOTE Confidence: 0.835882066363636

00:28:10.791 --> 00:28:12.897 have that methylation are either not

NOTE Confidence: 0.835882066363636

00:28:12.897 --> 00:28:14.920 expressed or in some cases are expressed.

NOTE Confidence: 0.835882066363636

00:28:14.920 --> 00:28:16.960 It depends on exactly the context.

NOTE Confidence: 0.835882066363636

00:28:16.960 --> 00:28:18.320 But that methylation process is

NOTE Confidence: 0.835882066363636

00:28:18.320 --> 00:28:20.080 known to be relevant to cancer,

NOTE Confidence: 0.835882066363636

00:28:20.080 --> 00:28:21.720 and so understanding how those

NOTE Confidence: 0.835882066363636

00:28:21.720 --> 00:28:23.360 contribute to cell proliferation and

NOTE Confidence: 0.835882066363636

00:28:23.415 --> 00:28:25.403 survival in the same depth that we

NOTE Confidence: 0.835882066363636

00:28:25.403 --> 00:28:26.580 understand these single nucleotide

NOTE Confidence: 0.835882066363636

00:28:26.580 --> 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 --> 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 --> 00:28:38.719 at the Yale School of Medicine.

NOTE Confidence: 0.896837555909091

00:28:38.720 --> 00:28:40.776 If you have questions,

NOTE Confidence: 0.896837555909091

00:28:40.776 --> 00:28:42.777 the address is canceranswers@yale.edu,

NOTE Confidence: 0.896837555909091

00:28:42.777 --> 00:28:45.519 and past editions of the program

NOTE Confidence: 0.896837555909091

00:28:45.519 --> 00:28:47.893 are available in audio and written

NOTE Confidence: 0.896837555909091

00:28:47.893 --> 00:28:48.828 form at yalecancercenter.org.

NOTE Confidence: 0.896837555909091

00:28:48.828 --> 00:28:51.292 We hope you'll join us next week to

NOTE Confidence: 0.896837555909091

00:28:51.292 --> 00:28:53.177 learn more about the fight against

NOTE Confidence: 0.896837555909091

00:28:53.177 --> 00:28:55.040 cancer here on Connecticut Public Radio.

NOTE Confidence: 0.896837555909091

00:28:55.040 --> 00:28:57.584 Funding for Yale Cancer Answers is

NOTE Confidence: 0.896837555909091

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