WEBVTT

00:00:00.000 --> 00:00:03.204 Funding for Yale Cancer Answers is

NOTE Confidence: 0.9416965

00:00:03.204 --> 00:00:06.240 provided by Smilow Cancer Hospital.

NOTE Confidence: 0.9416965

00:00:06.240 --> 00:00:08.440 Welcome to Yale Cancer Answers

NOTE Confidence: 0.9416965

00:00:08.440 --> 00:00:10.200 with Doctor Anees Chagpar.

NOTE Confidence: 0.9416965

00:00:10.200 --> 00:00:11.985 Yale Cancer Answers features the

NOTE Confidence: 0.9416965

00:00:11.985 --> 00:00:13.760 latest information on cancer care

NOTE Confidence: 0.9416965

00:00:13.760 --> 00:00:15.147 by welcoming oncologists and

NOTE Confidence: 0.9416965

00:00:15.147 --> 00:00:17.019 specialists who are on the forefront

NOTE Confidence: 0.9416965

00:00:17.019 --> 00:00:18.917 of the battle to fight cancer.

NOTE Confidence: 0.9416965

00:00:18.920 --> 00:00:21.160 This week it's a conversation about the

NOTE Confidence: 0.9416965

00:00:21.160 --> 00:00:22.875 role of breakthrough therapeutics in

NOTE Confidence: 0.9416965

00:00:22.875 --> 00:00:24.957 fighting cancer with Doctor Sidi Chen.

NOTE Confidence: 0.9416965

00:00:24.960 --> 00:00:26.510 Doctor Chen is an associate

NOTE Confidence: 0.9416965

00:00:26.510 --> 00:00:28.425 professor of genetics at the Yale

NOTE Confidence: 0.9416965

00:00:28.425 --> 00:00:29.950 School of Medicine where Dr.

NOTE Confidence: 0.9416965

00:00:29.950 --> 00:00:32.547 Chagpar as a professor of surgical oncology.

NOTE Confidence: 0.933137500000001

00:00:34.070 --> 00:00:36.464 Maybe we can start off by you

NOTE Confidence: 0.933137500000001

00:00:36.464 --> 00:00:38.500 telling us a little bit more about

NOTE Confidence: 0.933137500000001

00:00:38.500 --> 00:00:40.310 yourself and what it is you do.

NOTE Confidence: 0.9331375

00:00:40.910 --> 00:00:43.550 Yeah, sure. I'm a faculty member at Yale

00:00:45.656 --> 00:00:47.909 and a professor of genetics Genetics,

NOTE Confidence: 0.9331375

00:00:47.909 --> 00:00:49.869 Systems Biology Institute, and Yale Cancer Center.

NOTE Confidence: 0.9331375

00:00:49.870 --> 00:00:53.110 My role in the field is trying to

NOTE Confidence: 0.9331375

00:00:53.110 --> 00:00:55.779 understand the biological systems of

NOTE Confidence: 0.9331375

00:00:55.779 --> 00:00:58.302 cancer and the biological systems of the

NOTE Confidence: 0.9331375

00:00:58.302 --> 00:01:00.550 immune system of our cells and therefore

NOTE Confidence: 0.9331375

00:01:00.550 --> 00:01:02.530 leverage immune system to fight cancer.

NOTE Confidence: 0.9209762

00:01:03.130 --> 00:01:07.027 So I mean that all sounds very high tech

NOTE Confidence: 0.9209762

00:01:07.027 --> 00:01:10.607 and new and novel and exciting.

NOTE Confidence: 0.9209762

00:01:10.610 --> 00:01:12.610 Tell us more about

NOTE Confidence: 0.9209762

00:01:12.610 --> 00:01:14.024 how exactly that works.

NOTE Confidence: 0.9209762

00:01:14.024 --> 00:01:15.559 How did you get interested

NOTE Confidence: 0.9209762

00:01:15.559 --> 00:01:17.494 in the field and what

NOTE Confidence: 0.9209762

00:01:17.494 --> 00:01:19.404 exactly is your research doing?

NOTE Confidence: 0.9209762

00:01:20.010 --> 00:01:23.766 Sure. I'll be happy to elaborate.

NOTE Confidence: 0.9209762

00:01:23.770 --> 00:01:27.578 As you know, our own

NOTE Confidence: 0.9209762

00:01:27.578 --> 00:01:30.026 body consists of the many,

NOTE Confidence: 0.9209762

00:01:30.026 --> 00:01:31.250 many different organs.

NOTE Confidence: 0.9209762

00:01:31.250 --> 00:01:33.754 And the system that protect our own organs

NOTE Confidence: 0.9209762

00:01:33.754 --> 00:01:36.485 or our own health is the immune system.

NOTE Confidence: 0.9209762

00:01:36.490 --> 00:01:38.690 It's our own defense system.

NOTE Confidence: 0.9209762

00:01:38.690 --> 00:01:41.810 For example, if we get infected,

NOTE Confidence: 0.9209762

00:01:41.810 --> 00:01:45.290 we have cells that produce antibody,

NOTE Confidence: 0.9209762

00:01:45.290 --> 00:01:48.006 we have cells that clear the infection.

NOTE Confidence: 0.9209762

00:01:48.010 --> 00:01:50.470 Likewise for cancer,

NOTE Confidence: 0.9209762

00:01:50.470 --> 00:01:54.050 when a patient gets cancer and

NOTE Confidence: 0.9209762

00:01:54.050 --> 00:01:56.720 the first reaction of the body

NOTE Confidence: 0.9209762

00:01:56.720 --> 00:01:58.980 is the immune system trying to

NOTE Confidence: 0.9209762

00:01:58.980 --> 00:02:01.080 distinguish which is the cancer cell,

NOTE Confidence: 0.9209762

00:02:01.080 --> 00:02:03.840 which is our own healthy cells.

NOTE Confidence: 0.9209762

00:02:03.840 --> 00:02:05.640 But very often our system

NOTE Confidence: 0.9209762

00:02:05.640 --> 00:02:07.080 is fooled by cancer.

NOTE Confidence: 0.9209762

00:02:07.080 --> 00:02:08.900 The immune system cannot recognize

NOTE Confidence: 0.9209762

00:02:08.900 --> 00:02:11.382 cancer or cannot clear them and our

NOTE Confidence: 0.9209762

00:02:11.382 --> 00:02:13.037 research is trying to understand

NOTE Confidence: 0.9209762

00:02:13.037 --> 00:02:15.971 why is that the case and how we can

NOTE Confidence: 0.9209762

00:02:15.971 --> 00:02:17.922 educate the immune system or help

NOTE Confidence: 0.9209762

00:02:17.922 --> 00:02:21.238 the immune system to detect cancer

NOTE Confidence: 0.9209762

00:02:21.238 --> 00:02:24.815 better and equip them with the tools

NOTE Confidence: 0.9209762

00:02:24.815 --> 00:02:27.377 to fight cancer and clear cancer

NOTE Confidence: 0.9209762

00:02:27.377 --> 00:02:29.370 cells and restore our own health.

NOTE Confidence: 0.93518937

00:02:31.730 --> 00:02:33.780 You know that sounds a

NOTE Confidence: 0.93518937

00:02:33.780 --> 00:02:35.010 lot like immunotherapy,

NOTE Confidence: 0.93518937

00:02:35.010 --> 00:02:36.690 which is something that we've

NOTE Confidence: 0.93518937

00:02:36.690 --> 00:02:39.850 discussed on this show previously.

NOTE Confidence: 0.93518937

00:02:39.850 --> 00:02:41.578 How is your research either the

NOTE Confidence: 0.93518937

00:02:41.578 --> 00:02:43.050 same or different than that?

NOTE Confidence: 0.93518937

00:02:43.050 --> 00:02:45.090 I thought that immunotherapy

NOTE Confidence: 0.93518937

00:02:45.090 --> 00:02:46.722 is already being used.

NOTE Confidence: 0.93518937

00:02:46.730 --> 00:02:49.089 Is your work trying to extend that?

NOTE Confidence: 0.9396244

00:02:50.590 --> 00:02:52.336 You're absolutely right.

NOTE Confidence: 0.9396244

00:02:52.336 --> 00:02:54.664 Immunotherapy is the current

NOTE Confidence: 0.9396244

00:02:57.150 --> 00:02:59.802 major therapeutic for cancer.

NOTE Confidence: 0.9396244

00:02:59.802 --> 00:03:01.791 Immunotherapy involving immune

NOTE Confidence: 0.9396244

00:03:01.791 --> 00:03:04.324 checkpoint blockage has been

NOTE Confidence: 0.9396244

00:03:04.324 --> 00:03:07.066 approved by over 30 indications now.

NOTE Confidence: 0.9396244

00:03:07.070 --> 00:03:08.654 But unfortunately immunotherapy only

NOTE Confidence: 0.9396244

00:03:08.654 --> 00:03:11.630 works for a small fraction of patients,

NOTE Confidence: 0.9396244

00:03:11.630 --> 00:03:14.150 about 20 to 30% overall.

NOTE Confidence: 0.9396244

00:03:14.150 --> 00:03:15.866 Some cancer have a better response,

NOTE Confidence: 0.9396244

00:03:15.870 --> 00:03:20.238 some cancer have literally no responses.

NOTE Confidence: 0.9396244

00:03:20.240 --> 00:03:23.048 So our goal is to understand

NOTE Confidence: 0.9396244

00:03:23.048 --> 00:03:24.920 why some cancers respond,

NOTE Confidence: 0.9396244

00:03:24.920 --> 00:03:28.940 why some don't and then try to either

NOTE Confidence: 0.9396244

00:03:28.940 --> 00:03:33.000 help the cells to improve the

NOTE Confidence: 0.9396244

00:03:33.000 --> 00:03:35.547 immunotherapy response or on the other

NOTE Confidence: 0.9396244

00:03:35.547 --> 00:03:38.130 hand we're thinking why don't we just

NOTE Confidence: 0.9396244

00:03:38.205 --> 00:03:40.788 take the immune cells out and engineer

NOTE Confidence: 0.9396244

00:03:40.788 --> 00:03:43.520 them in the lab or in the factory

NOTE Confidence: 0.9396244

00:03:43.520 --> 00:03:45.515 and then give them back to the patient.

NOTE Confidence: 0.9396244

00:03:45.520 --> 00:03:48.004 That's what we call cell therapy

NOTE Confidence: 0.9396244

00:03:48.004 --> 00:03:49.246 or cellular immunotherapy,

NOTE Confidence: 0.9396244

00:03:49.250 --> 00:03:51.375 which is another type of

NOTE Confidence: 0.9396244

00:03:51.375 --> 00:03:52.650 major cancer immunotherapy.

NOTE Confidence: 0.9396244

00:03:52.650 --> 00:03:54.930 So unlike immune checkpoint blockade,

NOTE Confidence: 0.9396244

00:03:54.930 --> 00:03:59.074 I used to utilize a therapeutic antibody,

NOTE Confidence: 0.9396244

00:03:59.074 --> 00:04:01.346 cell therapy utilizes cells

NOTE Confidence: 0.9396244

00:04:01.346 --> 00:04:03.210 instead of compounds.

NOTE Confidence: 0.9176469

00:04:05.410 --> 00:04:07.746 So that's very interesting and I want to

NOTE Confidence: 0.9176469

00:04:07.746 --> 00:04:10.170 kind of discuss both of those angles.

NOTE Confidence: 0.9176469

00:04:10.170 --> 00:04:13.418 So the first is why is it that

NOTE Confidence: 0.9176469

00:04:13.418 --> 00:04:15.716 some cancers respond better

NOTE Confidence: 0.9176469

00:04:15.716 --> 00:04:18.488 to immunotherapy than others?

NOTE Confidence: 0.9176469

00:04:18.490 --> 00:04:20.930 We know that for example,

NOTE Confidence: 0.9176469

00:04:20.930 --> 00:04:23.202 there are some cancers,

NOTE Confidence: 0.9176469

00:04:23.202 --> 00:04:26.210 melanoma being one of the

NOTE Confidence: 0.9176469

00:04:26.210 --> 00:04:28.162 mainstays that's very

NOTE Confidence: 0.9176469

00:04:28.170 --> 00:04:30.602 receptive to immunotherapy and

NOTE Confidence: 0.9176469

00:04:30.602 --> 00:04:33.642 other cancers not so much.

NOTE Confidence: 0.9176469

00:04:33.650 --> 00:04:35.650 So what is it?

NOTE Confidence: 0.9176469

00:04:35.650 --> 00:04:38.650 Is it something about the cancer

NOTE Confidence: 0.9176469

00:04:38.762 --> 00:04:41.728 itself or is it the way that the

NOTE Confidence: 0.9176469

00:04:41.728 --> 00:04:43.438 cancer evades the immune system?

NOTE Confidence: 0.9176469

00:04:43.440 --> 00:04:46.268 Or is it just that the immune

NOTE Confidence: 0.9176469

00:04:46.268 --> 00:04:49.196 system is better able to fight

NOTE Confidence: 0.9176469

00:04:49.196 --> 00:04:51.356 cancers in particular organs?

NOTE Confidence: 0.9176469

00:04:51.360 --> 00:04:52.518 Why the difference?

NOTE Confidence: 0.9346789

00:04:53.760 --> 00:04:55.440 This is a billion dollar question,

NOTE Confidence: 0.9346789

00:04:55.440 --> 00:04:57.324 great question. In fact,

NOTE Confidence: 0.9346789

00:04:57.324 --> 00:04:59.679 the answer is very complicated.

NOTE Confidence: 0.9346789

00:04:59.680 --> 00:05:01.857 I don't think I can even address

NOTE Confidence: 0.9346789

00:05:01.857 --> 00:05:03.960 in half an hour or a year.

NOTE Confidence: 0.9346789

00:05:03.960 --> 00:05:07.360 So the reason,

NOTE Confidence: 0.9346789

00:05:07.360 --> 00:05:09.632 to put it short, cancer cells

NOTE Confidence: 0.9346789

00:05:09.632 --> 00:05:11.712 can evade the immune systems and attack

NOTE Confidence: 0.9346789

00:05:11.712 --> 00:05:13.798 and the immune cells sometimes

NOTE Confidence: 0.9346789

00:05:13.798 --> 00:05:16.084 it's weak or enabled to find

NOTE Confidence: 0.9346789

00:05:16.084 --> 00:05:18.120 cancer or eradicate cancer.

NOTE Confidence: 0.9346789

00:05:18.120 --> 00:05:19.280 So in order

NOTE Confidence: 0.92279476

00:05:21.360 --> 00:05:23.882 to help the immune system there are a

NOTE Confidence: 0.92279476

00:05:23.882 --> 00:05:26.054 lot of different ways, for example,

NOTE Confidence: 0.92279476

00:05:26.054 --> 00:05:27.854 using the monoclonal antibody to

NOTE Confidence: 0.92279476

00:05:27.854 --> 00:05:30.115 hit the brake that cancer uses to

NOTE Confidence: 0.926691493333333

00:05:32.360 --> 00:05:35.677 to put on cancer. For example PD1,

NOTE Confidence: 0.926691493333333

00:05:35.677 --> 00:05:37.813 PDL one therapy which is well known now

NOTE Confidence: 0.926691493333333

00:05:37.813 --> 00:05:40.167 I don't want to go too much into and

NOTE Confidence: 0.926691493333333

00:05:40.167 --> 00:05:42.383 on the other hand it could be there's

NOTE Confidence: 0.926691493333333

00:05:42.383 --> 00:05:45.037 not enough immune cells in the tumor

NOTE Confidence: 0.926691493333333

00:05:45.037 --> 00:05:47.016 micro environment or there's simply

NOTE Confidence: 0.926691493333333

00:05:47.016 --> 00:05:50.490 not enough T cells to clear the cancer.

NOTE Confidence: 0.926691493333333

00:05:50.490 --> 00:05:53.840 So that's why cell therapy

NOTE Confidence: 0.926691493333333

00:05:53.840 --> 00:05:55.850 provides another solution.

NOTE Confidence: 0.926691493333333

00:05:55.850 --> 00:05:58.629 You take the cells out from the

NOTE Confidence: 0.926691493333333

00:05:58.629 --> 00:06:01.534 patient and then you amplify them to

NOTE Confidence: 0.926691493333333

00:06:01.534 --> 00:06:03.358 billions and billions of cells and

NOTE Confidence: 0.926691493333333

00:06:03.358 --> 00:06:05.706 then you give it back to the patient.

NOTE Confidence: 0.926691493333333

00:06:05.710 --> 00:06:07.774 And in addition you can equip

NOTE Confidence: 0.926691493333333

00:06:07.774 --> 00:06:09.981 the cells because you already

NOTE Confidence: 0.926691493333333

00:06:09.981 --> 00:06:12.083 took them out, right.

NOTE Confidence: 0.926691493333333

00:06:12.083 --> 00:06:15.860 So now you can install things like

NOTE Confidence: 0.926691493333333

00:06:15.860 --> 00:06:18.590 chimeric antigen receptor or CAR T that

NOTE Confidence: 0.926691493333333

00:06:18.590 --> 00:06:21.052 can recognize specific cancer antigens

NOTE Confidence: 0.926691493333333

00:06:21.052 --> 00:06:23.998 to distinguish cancer from the healthy

NOTE Confidence: 0.926691493333333

00:06:23.998 --> 00:06:26.677 cells and you can amplify those cells

NOTE Confidence: 0.926691493333333

00:06:26.677 --> 00:06:28.290 to billions and billions of them

NOTE Confidence: 0.926691493333333

00:06:28.290 --> 00:06:30.149 and then give it back to patient.

NOTE Confidence: 0.926691493333333

00:06:30.150 --> 00:06:34.340 So this is a solution to

NOTE Confidence: 0.926691493333333

00:06:34.340 --> 00:06:37.380 amplify the immune system.

NOTE Confidence: 0.9260515

00:06:39.300 --> 00:06:41.322 So in that case, right,

NOTE Confidence: 0.9260515

00:06:41.322 --> 00:06:43.614 that seems to make sense.

NOTE Confidence: 0.9260515

00:06:43.620 --> 00:06:47.524 If you have a cancer and it has

NOTE Confidence: 0.9260515

00:06:47.524 --> 00:06:50.322 particular antigens on its surface and

NOTE Confidence: 0.9260515

00:06:50.322 --> 00:06:53.378 it's the job of the immune system to

NOTE Confidence: 0.9260515

00:06:53.378 --> 00:06:56.216 recognize things that shouldn't be there.

NOTE Confidence: 0.9260515

00:06:56.220 --> 00:06:58.920 And you can take out a

NOTE Confidence: 0.9260515

00:06:58.920 --> 00:07:00.720 patient's own immune cells,

NOTE Confidence: 0.9260515

00:07:00.720 --> 00:07:02.904 kind of engineer them so that

NOTE Confidence: 0.9260515

00:07:02.904 --> 00:07:04.360 they recognize those antigens,

NOTE Confidence: 0.9260515

00:07:04.360 --> 00:07:07.066 essentially give them a targeting

NOTE Confidence: 0.9260515

00:07:07.066 --> 00:07:10.524 system so that they can go after this

NOTE Confidence: 0.9260515

00:07:10.524 --> 00:07:13.685 cancer and then give them back to the

NOTE Confidence: 0.9260515

00:07:13.685 --> 00:07:17.278 patient in billions and billions of cells,

NOTE Confidence: 0.9260515

00:07:17.280 --> 00:07:19.645 essentially giving the immune system

NOTE Confidence: 0.9260515

00:07:19.645 --> 00:07:22.600 an unfair advantage over the cancer.

NOTE Confidence: 0.9260515

00:07:22.600 --> 00:07:24.216 Presumably that would help

NOTE Confidence: 0.9260515

00:07:24.216 --> 00:07:26.236 to wipe the cancer out.

NOTE Confidence: 0.9260515

00:07:26.240 --> 00:07:30.090 So #1 is, has that been tried?

NOTE Confidence: 0.9260515

00:07:30.090 --> 00:07:31.635 Does it work?

NOTE Confidence: 0.9260515

00:07:31.635 --> 00:07:34.210 And #2 if it does,

NOTE Confidence: 0.9260515

00:07:34.210 --> 00:07:36.247 why are we still talking about cancer?

NOTE Confidence: 0.9260515

00:07:36.250 --> 00:07:38.374 Wouldn't that be the fundamental answer

NOTE Confidence: 0.9260515

00:07:38.374 --> 00:07:40.570 that would kill off all cancers?

NOTE Confidence: 0.93521374

00:07:41.410 --> 00:07:42.902 Those are great questions.

NOTE Confidence: 0.93521374

00:07:42.902 --> 00:07:47.112 And #1, it has been approved

NOTE Confidence: 0.93521374

00:07:47.112 --> 00:07:49.154 for several different diseases,

NOTE Confidence: 0.93521374

00:07:49.154 --> 00:07:50.722 for example, leukemia,

NOTE Confidence: 0.93521374

00:07:50.722 --> 00:07:53.090 lymphoma, and multiple myeloma.

NOTE Confidence: 0.93521374

00:07:53.090 --> 00:07:56.765 And the FDA has approved six different cell

NOTE Confidence: 0.93521374

00:07:56.765 --> 00:07:58.638 therapies for treating these diseases.

NOTE Confidence: 0.93521374

00:07:58.638 --> 00:08:02.270 And in fact, the overall response

NOTE Confidence: 0.93521374

00:08:02.270 --> 00:08:05.450 for these cell therapies are amazing.

NOTE Confidence: 0.93521374

00:08:05.450 --> 00:08:08.768 And for example, in multiple myeloma,

NOTE Confidence: 0.93521374

00:08:08.770 --> 00:08:09.938 the overall response rate

NOTE Confidence: 0.93521374

00:08:09.938 --> 00:08:12.010 can be in the high 90% digit.

NOTE Confidence: 0.9355516

00:08:14.170 --> 00:08:16.840 But the challenge is that #1 the

NOTE Confidence: 0.9355516

00:08:16.840 --> 00:08:19.210 cancer still can still come back.

NOTE Confidence: 0.9355516

00:08:19.210 --> 00:08:21.730 They can become resistant to cell therapy.

NOTE Confidence: 0.9355516

00:08:21.730 --> 00:08:25.190 And #2 for solid tumors,

NOTE Confidence: 0.9355516

00:08:25.190 --> 00:08:26.243 not leukemia, lymphoma,

NOTE Confidence: 0.9355516

00:08:26.243 --> 00:08:28.349 those are what we call blood cancers.

NOTE Confidence: 0.9355516

00:08:28.350 --> 00:08:32.470 Solid tumors are for example a breast cancer,

NOTE Confidence: 0.9355516

00:08:32.470 --> 00:08:34.438 lung cancer, melanoma,

NOTE Confidence: 0.9355516

00:08:34.438 --> 00:08:36.736 pancreatic cancer, brain cancer.

NOTE Confidence: 0.9355516

00:08:36.736 --> 00:08:38.708 Those are solid tumors.

NOTE Confidence: 0.9355516

00:08:38.710 --> 00:08:40.774 They are more resistant to cell

NOTE Confidence: 0.9355516

00:08:40.774 --> 00:08:42.949 therapy for a number of reasons.

NOTE Confidence: 0.9355516

00:08:42.950 --> 00:08:43.566 For example,

NOTE Confidence: 0.9355516

00:08:43.566 --> 00:08:46.030 the cell can't get in the solid tumor,

NOTE Confidence: 0.9355516

00:08:46.030 --> 00:08:47.950 the cells can get in,

NOTE Confidence: 0.9355516

00:08:47.950 --> 00:08:49.950 but they fail to proliferate.

NOTE Confidence: 0.9355516

00:08:49.950 --> 00:08:52.314 They can't grow because the solid

NOTE Confidence: 0.9355516

00:08:52.314 --> 00:08:54.304 tumor micro environment is very

NOTE Confidence: 0.9355516

00:08:54.304 --> 00:08:56.356 hostile for the immune cells or

NOTE Confidence: 0.9355516

00:08:56.356 --> 00:08:58.959 the cells can get in and proliferate,

NOTE Confidence: 0.9355516

00:08:58.960 --> 00:09:00.600 but then they become exhausted,

NOTE Confidence: 0.9355516

00:09:00.600 --> 00:09:02.256 which means they're too tired of

NOTE Confidence: 0.9355516

00:09:02.256 --> 00:09:03.720 killing so many cancer cells.

NOTE Confidence: 0.9355516

00:09:03.720 --> 00:09:06.933 So there's still a lot of problems

NOTE Confidence: 0.9355516

00:09:06.933 --> 00:09:09.520 hindering the success of this type

NOTE Confidence: 0.9355516

00:09:09.520 --> 00:09:12.400 of cell therapy for curing cancer.

NOTE Confidence: 0.9355516

00:09:12.400 --> 00:09:14.688 That's why we are trying very hard to

NOTE Confidence: 0.9355516

00:09:14.688 --> 00:09:17.439 find new solutions to improve cell therapy.

NOTE Confidence: 0.938678

00:09:19.840 --> 00:09:22.904 So we don't have a magic bullet

NOTE Confidence: 0.938678

00:09:22.904 --> 00:09:25.584 although it sounds like we have

NOTE Confidence: 0.938678

00:09:25.584 --> 00:09:27.844 something very effective for the

NOTE Confidence: 0.938678

00:09:27.844 --> 00:09:29.934 the liquid tumors, the leukemias.

NOTE Confidence: 0.938678

00:09:29.934 --> 00:09:33.389 So tell us more about your work in terms

NOTE Confidence: 0.938678

00:09:33.389 --> 00:09:36.041 of how you optimize cellular therapy

NOTE Confidence: 0.938678

00:09:36.041 --> 00:09:38.700 for solid tumors because presumably when

NOTE Confidence: 0.938678

00:09:38.700 --> 00:09:41.995 most of us think about cancer we

NOTE Confidence: 0.938678

00:09:41.995 --> 00:09:44.480 tend to think about those solid tumors,

NOTE Confidence: 0.938678

00:09:44.480 --> 00:09:46.132 breast cancer, lung cancer,

NOTE Confidence: 0.938678

00:09:46.132 --> 00:09:48.278 colon cancer, prostate cancer,

NOTE Confidence: 0.938678

00:09:48.278 --> 00:09:49.596 pancreatic cancer.

NOTE Confidence: 0.938678

00:09:49.596 --> 00:09:55.107 And so it would be really nice if we had

NOTE Confidence: 0.938678

00:09:55.107 --> 00:09:58.578 a way for us to target these cancers

NOTE Confidence: 0.938678

00:09:58.578 --> 00:10:02.149 and eliminate them with high efficacy.

NOTE Confidence: 0.938678

00:10:02.150 --> 00:10:04.688 So what have you been trying and

NOTE Confidence: 0.938678

00:10:04.688 --> 00:10:07.343 how well or not has it been working?

NOTE Confidence: 0.92647344

00:10:09.230 --> 00:10:12.307 Another great question in fact when

NOTE Confidence: 0.92647344

00:10:12.307 --> 00:10:15.169 the cell therapy stopped working or

NOTE Confidence: 0.92647344

00:10:15.169 --> 00:10:18.802 didn't even start working, the few ways

NOTE Confidence: 0.92647344

00:10:18.802 --> 00:10:21.706 we can naturally think about it,

NOTE Confidence: 0.92647344

00:10:21.710 --> 00:10:23.590 imagine this is a car,

NOTE Confidence: 0.92647344

00:10:23.590 --> 00:10:26.680 well it is car kinematic antigen

NOTE Confidence: 0.92647344

00:10:26.680 --> 00:10:28.662 receptor but pun intended.

NOTE Confidence: 0.92647344

00:10:28.662 --> 00:10:32.846 So for a car, you can push the gas on you

NOTE Confidence: 0.92647344

00:10:32.846 --> 00:10:35.478 can release the brake or you can

NOTE Confidence: 0.92647344

00:10:35.478 --> 00:10:37.990 change the structure of the car.

NOTE Confidence: 0.92647344

00:10:37.990 --> 00:10:39.374 So there's three different

NOTE Confidence: 0.92647344

00:10:39.374 --> 00:10:43.230 ways to make it run faster.

NOTE Confidence: 0.92647344

00:10:43.230 --> 00:10:46.110 So in order to put the gas pedal on,

NOTE Confidence: 0.92647344

00:10:46.110 --> 00:10:51.808 we develop things we call a hyper

NOTE Confidence: 0.92647344

00:10:51.808 --> 00:10:57.208 boost or like functional booster or

NOTE Confidence: 0.92647344

00:10:57.208 --> 00:11:01.618 functional augmentation factors so that

NOTE Confidence: 0.92647344

00:11:01.618 --> 00:11:05.618 we can allow the T cells to kill better,

NOTE Confidence: 0.92647344

00:11:05.618 --> 00:11:09.962 become tireless and remember the cancer

NOTE Confidence: 0.92647344

00:11:09.962 --> 00:11:12.850 cells, but sometimes T cells can

NOTE Confidence: 0.92647344

00:11:12.850 --> 00:11:15.173 be blocked by cancer cells, right,

NOTE Confidence: 0.92647344

00:11:15.173 --> 00:11:18.077 cancer cells put those brakes on and we

NOTE Confidence: 0.92647344

00:11:18.077 --> 00:11:21.356 can use a thing called gene editing,

NOTE Confidence: 0.92647344

00:11:21.360 --> 00:11:24.195 or CRISPR that we hear about a

NOTE Confidence: 0.92647344

00:11:24.195 --> 00:11:27.176 lot to eliminate those brakes,

NOTE Confidence: 0.92647344

00:11:27.176 --> 00:11:30.396 those we call cellular checkpoints

NOTE Confidence: 0.92647344

00:11:30.400 --> 00:11:33.478 like PD1 but not exactly PD1.

NOTE Confidence: 0.92647344

00:11:33.480 --> 00:11:37.456 So you can remove or at least

NOTE Confidence: 0.92647344

00:11:37.456 --> 00:11:40.120 stampen those blocked or like the

NOTE Confidence: 0.92647344

00:11:40.209 --> 00:11:43.198 hurdles the T cell has to overcome.

NOTE Confidence: 0.92647344

00:11:43.200 --> 00:11:46.088 So that's another way of modifying the cells.

NOTE Confidence: 0.92647344

00:11:46.090 --> 00:11:47.294 And finally

NOTE Confidence: 0.92647344

00:11:47.294 --> 00:11:49.808 the newer way is that why don't we

NOTE Confidence: 0.92647344

00:11:49.808 --> 00:11:52.048 make the car shape a little better,

NOTE Confidence: 0.92647344

00:11:52.050 --> 00:11:55.072 so a little more smooth so they

NOTE Confidence: 0.92647344

00:11:55.072 --> 00:11:57.178 can run more smoothly and that's

NOTE Confidence: 0.92647344

00:11:57.178 --> 00:11:59.502 called the structural design of the

NOTE Confidence: 0.92647344

00:11:59.502 --> 00:12:02.086 car to make it run more smoothly.

NOTE Confidence: 0.92647344

00:12:02.090 --> 00:12:04.556 So we're doing all three different

NOTE Confidence: 0.92647344

00:12:04.556 --> 00:12:07.388 approaches and we published a few pieces

NOTE Confidence: 0.92647344

00:12:07.388 --> 00:12:11.606 for the the gas pedal and the brake.

NOTE Confidence: 0.92647344

00:12:11.610 --> 00:12:14.266 And the recent piece of work is a

NOTE Confidence: 0.92647344

00:12:14.266 --> 00:12:16.170 structural design of the car that

NOTE Confidence: 0.92647344

00:12:16.170 --> 00:12:19.083 makes the car work more tirelessly

NOTE Confidence: 0.92647344

00:12:19.083 --> 00:12:21.338 against cancer and avoid self

NOTE Confidence: 0.92647344

00:12:21.338 --> 00:12:23.637 destruction like avoid the crashes

NOTE Confidence: 0.92647344

00:12:23.637 --> 00:12:25.405 between the cars themselves.

NOTE Confidence: 0.9245574

00:12:27.250 --> 00:12:29.450 So I want to dig into each of

NOTE Confidence: 0.9245574

00:12:29.450 --> 00:12:31.887 those in a little bit more detail.

NOTE Confidence: 0.9245574

00:12:31.890 --> 00:12:34.648 And let's start with CAR T therapy,

NOTE Confidence: 0.9245574

00:12:34.650 --> 00:12:36.432 which is something that some of

NOTE Confidence: 0.9245574

00:12:36.432 --> 00:12:38.160 our audience might have heard of,

NOTE Confidence: 0.9245574

00:12:38.160 --> 00:12:40.554 but others might still be unaware of.

NOTE Confidence: 0.9245574

00:12:40.560 --> 00:12:43.170 Can you tell us a little bit more about

NOTE Confidence: 0.9245574

00:12:43.170 --> 00:12:45.840 what exactly that is and how that works?

NOTE Confidence: 0.9351585

00:12:46.400 --> 00:12:50.236 Yeah, sure. To take two steps back,

NOTE Confidence: 0.9351585

00:12:50.240 --> 00:12:53.942 CAR T therapy means chimeric

NOTE Confidence: 0.9351585

00:12:53.942 --> 00:12:56.997 antigen receptor T cell therapy.

NOTE Confidence: 0.9351585

00:12:57.000 --> 00:13:01.568 So T cells, sometimes they recognize cancer,

NOTE Confidence: 0.9351585

00:13:01.568 --> 00:13:03.164 sometimes they don't.

NOTE Confidence: 0.9351585

00:13:03.170 --> 00:13:05.722 And in order to make all the T

NOTE Confidence: 0.9351585

00:13:05.722 --> 00:13:07.725 cells recognize the cancer

NOTE Confidence: 0.9351585

00:13:07.725 --> 00:13:10.287 we want to target,

NOTE Confidence: 0.9351585

00:13:10.290 --> 00:13:12.110 we install chimeric endogen

NOTE Confidence: 0.9351585

00:13:12.110 --> 00:13:13.930 receptor on their surface.

NOTE Confidence: 0.9351585

00:13:13.930 --> 00:13:16.410 Those are CAR for short.

NOTE Confidence: 0.9351585

00:13:16.410 --> 00:13:18.447 So by putting those cars on their

NOTE Confidence: 0.9351585

00:13:18.447 --> 00:13:20.233 surface then every T cell can

NOTE Confidence: 0.9351585

00:13:20.233 --> 00:13:21.943 recognize those cancer cells and we

NOTE Confidence: 0.9351585

00:13:21.943 --> 00:13:23.970 hope they can kill the cancer cell.

NOTE Confidence: 0.9351585

00:13:23.970 --> 00:13:25.338 But sometimes they don't.

00:13:26.370 --> 00:13:28.488 That's why we're doing all this,

NOTE Confidence: 0.9351585

00:13:28.490 --> 00:13:30.970 the three different tricks,

NOTE Confidence: 0.9351585

00:13:30.970 --> 00:13:32.830 the gas pedal,

NOTE Confidence: 0.9351585

00:13:32.830 --> 00:13:34.576 hitting the brake, and changing the

NOTE Confidence: 0.9351585

00:13:34.576 --> 00:13:36.749 shape in order to make them better.

NOTE Confidence: 0.93413925

00:13:37.950 --> 00:13:40.750 OK, well, we're going to pick up this

NOTE Confidence: 0.93413925

00:13:40.750 --> 00:13:42.745 conversation right after we take a

NOTE Confidence: 0.93413925

00:13:42.745 --> 00:13:44.581 short break for a medical minute.

NOTE Confidence: 0.93413925

00:13:44.590 --> 00:13:46.810 Please stay tuned to learn more

NOTE Confidence: 0.93413925

00:13:46.810 --> 00:13:48.290 about breakthrough therapeutics and

NOTE Confidence: 0.93413925

00:13:48.349 --> 00:13:50.590 cancer with my guest, Dr. Sidi Chen.

NOTE Confidence: 0.93413925

00:13:51.110 --> 00:13:53.090 Funding for Yale Cancer Answers

NOTE Confidence: 0.93413925

00:13:53.090 --> 00:13:55.070 comes from Smilow Cancer Hospital,

NOTE Confidence: 0.93413925

00:13:55.070 --> 00:13:57.000 where their hematology program offers

NOTE Confidence: 0.93413925

00:13:57.000 --> 00:13:59.430 diagnosis and treatment of blood cancers,

NOTE Confidence: 0.93413925

00:13:59.430 --> 00:14:02.690 including lymphoma, leukemia, and myeloma.

NOTE Confidence: 0.93413925

00:14:02.690 --> 00:14:05.724 More at smilowcancerhospital.org or

NOTE Confidence: 0.93413925

00:14:05.724 --> 00:14:08.363 e-mail Cancer Answers at Yale dot Edu.

NOTE Confidence: 0.92270476

00:14:10.490 --> 00:14:12.374 Genetic testing can be useful for

NOTE Confidence: 0.92270476

00:14:12.374 --> 00:14:14.222 people with certain types of cancer

NOTE Confidence: 0.92270476

00:14:14.222 --> 00:14:16.084 that seem to run in their families.

NOTE Confidence: 0.92270476

00:14:16.090 --> 00:14:17.985 Genetic counseling is a process

NOTE Confidence: 0.92270476

00:14:17.985 --> 00:14:19.880 that includes collecting a detailed

NOTE Confidence: 0.92270476

00:14:19.943 --> 00:14:21.527 personal and family history,

NOTE Confidence: 0.92270476

00:14:21.530 --> 00:14:22.874 a risk assessment,

NOTE Confidence: 0.92270476

00:14:22.874 --> 00:14:26.010 and a discussion of genetic testing options.

NOTE Confidence: 0.92270476

00:14:26.010 --> 00:14:28.596 Only about 5 to 10% of all cancers

NOTE Confidence: 0.92270476

00:14:28.596 --> 00:14:30.306 are inherited and genetic testing

NOTE Confidence: 0.92270476

00:14:30.306 --> 00:14:32.618 is not recommended for everyone.

NOTE Confidence: 0.92270476

00:14:32.620 --> 00:14:34.585 Individuals who have a personal

NOTE Confidence: 0.92270476

00:14:34.585 --> 00:14:37.077 and or family history that includes

NOTE Confidence: 0.92270476

00:14:37.077 --> 00:14:39.337 cancer at unusually early ages,

NOTE Confidence: 0.92270476

00:14:39.340 --> 00:14:41.344 multiple relatives on the same side

NOTE Confidence: 0.92270476

00:14:41.344 --> 00:14:43.738 of the family with the same cancer,

NOTE Confidence: 0.92270476

00:14:43.740 --> 00:14:46.020 more than one diagnosis of cancer

NOTE Confidence: 0.92270476

00:14:46.020 --> 00:14:47.540 in the same individual,

NOTE Confidence: 0.92270476

00:14:47.540 --> 00:14:48.342 rare cancers,

NOTE Confidence: 0.92270476

00:14:48.342 --> 00:14:51.149 or family history of a known altered

NOTE Confidence: 0.92270476

00:14:51.149 --> 00:14:53.660 cancer predisposing gene could be

NOTE Confidence: 0.92270476

00:14:53.660 --> 00:14:55.700 candidates for genetic testing.

NOTE Confidence: 0.92270476

00:14:55.700 --> 00:14:57.705 Resources for genetic counseling and

NOTE Confidence: 0.92270476

00:14:57.705 --> 00:14:59.710 testing are available at federally

NOTE Confidence: 0.92270476

00:14:59.774 --> 00:15:01.427 designated comprehensive cancer

NOTE Confidence: 0.92270476

00:15:01.427 --> 00:15:03.760 centers such as Yale Cancer Center

NOTE Confidence: 0.92270476

00:15:03.760 --> 00:15:05.540 and Smilow Cancer Hospital.

NOTE Confidence: 0.92270476

00:15:05.540 --> 00:15:07.908 More information is available

NOTE Confidence: 0.92270476

00:15:07.908 --> 00:15:08.934 at yalecancercenter.org.

NOTE Confidence: 0.92270476

00:15:08.934 --> 00:15:11.538 You're listening to Connecticut Public Radio.

NOTE Confidence: 0.92193615

00:15:12.180 --> 00:15:14.298 Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.92193615

00:15:14.300 --> 00:15:15.900 This is Dr. Anees Chagpar,

NOTE Confidence: 0.92193615

00:15:15.900 --> 00:15:18.421 and I'm joined tonight by my guest, Dr.

NOTE Confidence: 0.92193615

00:15:18.421 --> 00:15:20.587 Sidi Chen. We're talking about the

NOTE Confidence: 0.92193615

00:15:20.587 --> 00:15:22.193 role of breakthrough therapeutics

NOTE Confidence: 0.92193615

00:15:22.193 --> 00:15:24.017 in fighting cancer.

NOTE Confidence: 0.92193615

00:15:24.020 --> 00:15:25.972 Right before the break,

NOTE Confidence: 0.92193615

00:15:25.972 --> 00:15:28.900 we were talking about this concept

NOTE Confidence: 0.92193615

00:15:28.991 --> 00:15:31.615 of the interplay between cancers in

NOTE Confidence: 0.92193615

00:15:31.615 --> 00:15:34.070 the immune system and essentially

NOTE Confidence: 0.92193615

00:15:34.151 --> 00:15:36.724 the fact that cancers try to get

NOTE Confidence: 0.92193615

00:15:36.724 --> 00:15:39.652 the upper hand on the immune system

NOTE Confidence: 0.92193615

00:15:39.652 --> 00:15:42.075 and do that with a number of tricks

NOTE Confidence: 0.92193615

00:15:42.075 --> 00:15:44.597 that try to evade the immune system.

NOTE Confidence: 0.92193615

00:15:44.600 --> 00:15:46.885 There's now been some therapeutics

NOTE Confidence: 0.92193615

00:15:46.885 --> 00:15:48.713 like CAR T therapy,

NOTE Confidence: 0.92193615

00:15:48.720 --> 00:15:53.040 which essentially tries to arm the T cells,

NOTE Confidence: 0.92193615

00:15:53.040 --> 00:15:55.512 those fighting cells that are in

NOTE Confidence: 0.92193615

00:15:55.512 --> 00:15:58.098 the immune system so that they can

NOTE Confidence: 0.92193615

00:15:58.098 --> 00:16:00.510 recognize these cancers and go after them.

NOTE Confidence: 0.92193615

00:16:00.510 --> 00:16:02.374 But even with that,

NOTE Confidence: 0.92193615

00:16:02.374 --> 00:16:04.704 not all cellular therapeutics or

NOTE Confidence: 0.92193615

00:16:04.704 --> 00:16:07.430 CAR T therapies are effective,

NOTE Confidence: 0.92193615

00:16:07.430 --> 00:16:10.374 particularly for solid tumors.

00:16:11.598 --> 00:16:14.038 Sidi, if I understand it correctly

NOTE Confidence: 0.92193615

00:16:14.038 --> 00:16:15.990 that being the case,

NOTE Confidence: 0.92193615

00:16:15.990 --> 00:16:19.080 you have 3 strategies really to

NOTE Confidence: 0.92193615

00:16:19.080 --> 00:16:21.547 try to make things better,

NOTE Confidence: 0.92193615

00:16:21.547 --> 00:16:24.421 give the immune system kind

NOTE Confidence: 0.92193615

00:16:24.421 --> 00:16:27.838 of an upper edge on these tumor cells.

NOTE Confidence: 0.92193615

00:16:27.840 --> 00:16:30.612 So the first one you talked about

NOTE Confidence: 0.92193615

00:16:30.612 --> 00:16:33.960 was kind of like giving

NOTE Confidence: 0.92193615

00:16:33.960 --> 00:16:37.200 the immune system a hyper boost.

NOTE Confidence: 0.92193615

00:16:37.200 --> 00:16:38.859 Can you talk a little bit more

NOTE Confidence: 0.92193615

00:16:38.859 --> 00:16:40.040 about what that entails?

NOTE Confidence: 0.92193615

00:16:40.040 --> 00:16:42.833 I mean is that simply making more

NOTE Confidence: 0.92193615

00:16:42.833 --> 00:16:46.518 of these T cells that are armed to

NOTE Confidence: 0.92193615

00:16:46.518 --> 00:16:48.796 recognize the cancer cells or

NOTE Confidence: 0.92193615

00:16:48.796 --> 00:16:51.540 do you try to engineer them in some

NOTE Confidence: 0.92193615

00:16:51.540 --> 00:16:53.640 way to make them more effective,

NOTE Confidence: 0.92193615

00:16:53.640 --> 00:16:56.496 make them be more able to

NOTE Confidence: 0.92193615

00:16:56.496 --> 00:16:58.400 get into solid tumors?

NOTE Confidence: 0.9253724

00:16:59.200 --> 00:17:02.240 The first strategy as we

NOTE Confidence: 0.9253724

00:17:04.320 --> 00:17:07.400 term as hyper boost is with an analogy

NOTE Confidence: 0.9253724

00:17:07.400 --> 00:17:11.077 to putting the gas pedal on the CAR.

NOTE Confidence: 0.9253724

00:17:11.080 --> 00:17:14.008 So we're trying to engineer the car so

NOTE Confidence: 0.9253724

00:17:14.008 --> 00:17:17.080 that the gas pedals are more efficient,

NOTE Confidence: 0.9253724

00:17:17.080 --> 00:17:19.366 like a more fuel efficient car.

NOTE Confidence: 0.9253724

00:17:19.370 --> 00:17:22.202 So as you know, T cells kill cancer

NOTE Confidence: 0.9253724

00:17:22.202 --> 00:17:25.556 cells by recognizing them and then

NOTE Confidence: 0.9253724

00:17:25.556 --> 00:17:28.541 produce cancer killing cytokines and

NOTE Confidence: 0.9253724

00:17:28.541 --> 00:17:31.247 all trigger the cell death signal.

NOTE Confidence: 0.9253724

00:17:31.250 --> 00:17:37.445 And our approach is trying to install

NOTE Confidence: 0.9253724

00:17:37.450 --> 00:17:41.804 the modification to our normal T cells,

NOTE Confidence: 0.9253724

00:17:41.810 --> 00:17:46.570 which often fail to kill cancer cells

NOTE Confidence: 0.9253724

00:17:46.570 --> 00:17:49.660 by equipping with these T cells

NOTE Confidence: 0.9253724

00:17:49.660 --> 00:17:52.214 better tools or better modifications.

NOTE Confidence: 0.9253724

00:17:52.214 --> 00:17:55.728 For example, in one of the scenarios,

NOTE Confidence: 0.9253724

00:17:55.730 --> 00:17:59.118 we're trying to see which of our

NOTE Confidence: 0.9253724

00:17:59.118 --> 00:18:01.794 own 20,000 genes when you install

NOTE Confidence: 0.9253724

00:18:01.794 --> 00:18:05.214 or overexpress on a T cell can help

NOTE Confidence: 0.9253724

00:18:05.214 --> 00:18:08.028 the T cells produce more cytokines

NOTE Confidence: 0.9253724

00:18:08.028 --> 00:18:10.050 to cure cancer cells.

NOTE Confidence: 0.9253724

00:18:10.050 --> 00:18:14.580 And we did a scanning of the 20,000 and then

NOTE Confidence: 0.9253724

00:18:14.686 --> 00:18:18.268 we found a few that are working very well.

NOTE Confidence: 0.9253724

00:18:18.270 --> 00:18:22.441 This is one of the examples that we can

NOTE Confidence: 0.9253724

00:18:22.441 --> 00:18:26.281 find the modification genes and hook you

NOTE Confidence: 0.9253724

00:18:26.281 --> 00:18:29.023 up with the chimeric endogen receptor.

NOTE Confidence: 0.9253724

00:18:29.030 --> 00:18:32.082 So now we have a substantially improved

NOTE Confidence: 0.9253724

00:18:32.082 --> 00:18:34.734 CAR T cells to fight cancer cells.

NOTE Confidence: 0.9253724

00:18:34.734 --> 00:18:36.750 This is approach number one.

NOTE Confidence: 0.9362019

00:18:37.230 --> 00:18:40.408 So just on that, if these T

NOTE Confidence: 0.9362019

00:18:40.408 --> 00:18:43.430 cells are making more cytokines,

NOTE Confidence: 0.9362019

00:18:43.430 --> 00:18:45.628 could that be problematic for some patients?

NOTE Confidence: 0.9362019

00:18:45.630 --> 00:18:49.235 I mean, we've just lived through the

NOTE Confidence: 0.9362019

00:18:49.235 --> 00:18:52.047 COVID-19 pandemic and one of the

NOTE Confidence: 0.9362019

00:18:52.047 --> 00:18:55.798 things that came up as a result of

NOTE Confidence: 0.9362019

00:18:55.798 --> 00:18:58.900 that experience was that we learned

NOTE Confidence: 0.9362019

00:18:58.900 --> 00:19:01.785 about things like cytokine storm.

NOTE Confidence: 0.9362019

00:19:01.790 --> 00:19:04.710 So is that a possibility?

NOTE Confidence: 0.9362019

00:19:04.710 --> 00:19:06.876 Is there any downside to having

NOTE Confidence: 0.9362019

00:19:06.876 --> 00:19:09.510 your T cells make more cytokines?

NOTE Confidence: 0.928788

00:19:10.230 --> 00:19:11.184 Yeah, of course.

NOTE Confidence: 0.928788

00:19:11.184 --> 00:19:12.774 This is a great point.

NOTE Confidence: 0.928788

00:19:12.780 --> 00:19:15.755 In fact, one of the major cell

NOTE Confidence: 0.928788

00:19:15.755 --> 00:19:18.199 therapy drawbacks is

NOTE Confidence: 0.928788

00:19:18.199 --> 00:19:19.819 cytokine release syndrome.

NOTE Confidence: 0.928788

00:19:19.820 --> 00:19:21.938 We certainly want to avoid that.

NOTE Confidence: 0.928788

00:19:21.940 --> 00:19:25.605 So it's a balance of how much cytokine

NOTE Confidence: 0.928788

00:19:25.605 --> 00:19:28.800 you want to produce by enabling T cell

NOTE Confidence: 0.928788

00:19:28.800 --> 00:19:31.584 to produce but not overdo it so that

NOTE Confidence: 0.928788

00:19:31.584 --> 00:19:34.499 you create the unwanted side effect.

NOTE Confidence: 0.928788

00:19:34.500 --> 00:19:36.663 So we're doing a lot of work

NOTE Confidence: 0.928788

00:19:36.663 --> 00:19:39.050 trying to find the balance

NOTE Confidence: 0.928788

00:19:39.050 --> 00:19:41.140 of efficacy versus toxicity. And

NOTE Confidence: 0.93611157

00:19:41.140 --> 00:19:44.161 that balance I mean is that, I don't know,

NOTE Confidence: 0.93611157

00:19:44.161 --> 00:19:45.883 I'm thinking that might be

NOTE Confidence: 0.93611157

00:19:45.883 --> 00:19:47.842 something that is very personal, right.

NOTE Confidence: 0.93611157

00:19:47.842 --> 00:19:50.614 That depends on the individual,

NOTE Confidence: 0.93611157

00:19:50.620 --> 00:19:51.950 it depends on how much

NOTE Confidence: 0.93611157

00:19:51.950 --> 00:19:53.014 cancer they might have,

NOTE Confidence: 0.93611157

00:19:53.020 --> 00:19:55.176 the type of cancer they might have.

NOTE Confidence: 0.93611157

00:19:55.180 --> 00:19:56.993 Is that right or is that balance

NOTE Confidence: 0.93611157

00:19:56.993 --> 00:19:59.299 going to be kind of a one size fits all?

NOTE Confidence: 0.9392858

00:19:59.980 --> 00:20:02.446 Yes and no. There are certainly patient

NOTE Confidence: 0.9392858

00:20:02.446 --> 00:20:05.258 to patient and disease to disease variations.

NOTE Confidence: 0.9392858

00:20:05.260 --> 00:20:07.732 But the T cells on the other hand

NOTE Confidence: 0.9392858

00:20:07.732 --> 00:20:11.060 can be modified so that they can be

NOTE Confidence: 0.9392858

00:20:11.060 --> 00:20:14.020 tuned to shift towards better cancer

NOTE Confidence: 0.9392858

00:20:14.020 --> 00:20:16.900 killing and not being too toxic.

NOTE Confidence: 0.9392858

00:20:16.900 --> 00:20:19.700 And the other approach we're talking

NOTE Confidence: 0.9392858

00:20:19.700 --> 00:20:22.060 about is modified indulgent genes

NOTE Confidence: 0.9392858

00:20:22.060 --> 00:20:25.180 so they can remember cancer better,

NOTE Confidence: 0.9392858

00:20:25.180 --> 00:20:27.304 so they last longer without having

NOTE Confidence: 0.9392858

00:20:27.304 --> 00:20:29.380 to produce too much cytokine.

NOTE Confidence: 0.93125427

00:20:29.670 --> 00:20:31.902 Yeah, So let's talk about

NOTE Confidence: 0.93125427

00:20:31.902 --> 00:20:33.390 the second strategy.

NOTE Confidence: 0.93125427

00:20:33.390 --> 00:20:35.340 So the second strategy you

NOTE Confidence: 0.93125427

00:20:35.340 --> 00:20:37.602 talked about was kind of hitting

NOTE Confidence: 0.93125427

00:20:37.602 --> 00:20:40.150 the brakes on the car.

NOTE Confidence: 0.93125427

00:20:40.150 --> 00:20:41.482 Help us to understand

NOTE Confidence: 0.93125427

00:20:41.482 --> 00:20:43.147 that piece a bit better.

NOTE Confidence: 0.93125427

00:20:43.350 --> 00:20:46.486 As you know we have 20,000 different

NOTE Confidence: 0.93125427

00:20:46.486 --> 00:20:49.342 genes and a lot of different proteins,

NOTE Confidence: 0.93125427

00:20:49.350 --> 00:20:52.300 some are suppressive because nature

NOTE Confidence: 0.93125427

00:20:52.300 --> 00:20:54.892 evolves so that our immune system

NOTE Confidence: 0.93125427

00:20:54.892 --> 00:20:57.567 is not always on so that the

NOTE Confidence: 0.93125427

00:20:57.567 --> 00:20:59.625 immune system keeps damaging the body.

NOTE Confidence: 0.93125427

00:20:59.630 --> 00:21:02.582 So in order to avoid that our body and

NOTE Confidence: 0.93125427

00:21:02.590 --> 00:21:05.662 billion years of evolution evolve the

NOTE Confidence: 0.93125427

00:21:05.662 --> 00:21:07.710 molecule that are immunosuppressive.

NOTE Confidence: 0.93125427

00:21:07.710 --> 00:21:09.666 For example, a PD1 PDL one,

NOTE Confidence: 0.93125427

00:21:09.670 --> 00:21:12.222 which is one of the most famous pathway

NOTE Confidence: 0.93125427

00:21:12.222 --> 00:21:14.774 and there are many others and some

NOTE Confidence: 0.93125427

00:21:14.774 --> 00:21:18.230 are on the surface like PD1 PDL 1,

NOTE Confidence: 0.93125427

00:21:18.230 --> 00:21:19.361 some are internal,

NOTE Confidence: 0.93125427

00:21:19.361 --> 00:21:22.000 like we call this cellular checkpoint or

NOTE Confidence: 0.93125427

00:21:22.070 --> 00:21:25.770 internal checkpoints and those genes hold

NOTE Confidence: 0.93125427

00:21:25.770 --> 00:21:30.608 the T cells back from being too active.

NOTE Confidence: 0.93125427

00:21:30.608 --> 00:21:33.628 But those genes sometimes create

NOTE Confidence: 0.93125427

00:21:33.628 --> 00:21:37.195 a hurdle to block the efficacy of

NOTE Confidence: 0.93125427

00:21:37.195 --> 00:21:40.488 the T cell therapy and we can use

NOTE Confidence: 0.93125427

00:21:40.488 --> 00:21:42.600 gene editing to modify or dampen

NOTE Confidence: 0.93125427

00:21:42.682 --> 00:21:44.936 those pathways so that we let the

NOTE Confidence: 0.93125427

00:21:44.936 --> 00:21:47.968 T cell be a little more active in

NOTE Confidence: 0.93125427

00:21:47.968 --> 00:21:50.251 getting an upper hand against cancer,

NOTE Confidence: 0.93125427

00:21:50.251 --> 00:21:51.997 wiping them out first and then

NOTE Confidence: 0.93125427

00:21:51.997 --> 00:21:53.400 we can turn it down.

NOTE Confidence: 0.93125427

00:21:53.400 --> 00:21:55.488 That's the hitting the brake strategy

NOTE Confidence: 0.93125427

00:21:55.488 --> 00:21:58.000 like you can release the brake and then

NOTE Confidence: 0.93125427

00:21:58.000 --> 00:22:00.187 when the T cells kill the cancer cell

NOTE Confidence: 0.93125427

00:22:00.187 --> 00:22:02.581 and then you can put a brake back on.

NOTE Confidence: 0.93125427

00:22:02.581 --> 00:22:03.736 So those are the strategies

NOTE Confidence: 0.93125427

00:22:03.736 --> 00:22:04.429 we're talking about.

NOTE Confidence: 0.9242995

00:22:05.230 --> 00:22:08.250 Sidi, I can see how you can

NOTE Confidence: 0.9242995

00:22:08.339 --> 00:22:11.444 combine those two initial strategies,

NOTE Confidence: 0.9242995

00:22:11.444 --> 00:22:14.746 making the T cells more

NOTE Confidence: 0.9242995

00:22:14.746 --> 00:22:17.844 effective in terms of releasing those

NOTE Confidence: 0.9242995

00:22:17.844 --> 00:22:20.894 cytokines that hyper boost strategy

NOTE Confidence: 0.9242995

00:22:20.894 --> 00:22:24.456 with this other strategy which kind

NOTE Confidence: 0.9242995

00:22:24.456 --> 00:22:27.522 of dampens their brake system

NOTE Confidence: 0.9242995

00:22:27.522 --> 00:22:31.254 and so you can create a kind of a

NOTE Confidence: 0.9242995

00:22:31.254 --> 00:22:33.621 more effective T cell to kill cancer

NOTE Confidence: 0.9242995

00:22:33.621 --> 00:22:36.372 cells but by combining those two

NOTE Confidence: 0.9242995

00:22:36.372 --> 00:22:39.547 you can kind of modulate the response.

NOTE Confidence: 0.9242995

00:22:39.550 --> 00:22:41.706 My question then is you know one

NOTE Confidence: 0.9242995

00:22:41.706 --> 00:22:43.659 would think that would need

NOTE Confidence: 0.9242995

00:22:43.659 --> 00:22:45.269 to be tempered over time.

NOTE Confidence: 0.9242995

00:22:45.270 --> 00:22:47.706 So for example you might say well

NOTE Confidence: 0.9242995

00:22:47.706 --> 00:22:50.818 we need to really go after and kill

NOTE Confidence: 0.9242995

00:22:50.818 --> 00:22:53.596 all the cancer cells full throttle

NOTE Confidence: 0.9242995

00:22:53.596 --> 00:22:56.123 initially and then we need to ease up

NOTE Confidence: 0.9242995

00:22:56.123 --> 00:22:58.860 a bit and start actually using

NOTE Confidence: 0.9242995

00:22:58.860 --> 00:23:01.891 that brake pedal that was there to

NOTE Confidence: 0.9242995

00:23:01.891 --> 00:23:04.033 alleviate some of the side effects

NOTE Confidence: 0.9242995

00:23:04.033 --> 00:23:07.500 that might come from an overabundance

NOTE Confidence: 0.9242995

00:23:07.500 --> 00:23:11.310 of cytokines or T cell response.

NOTE Confidence: 0.9242995

00:23:11.310 --> 00:23:14.607 So how do you do that with

NOTE Confidence: 0.9242995

00:23:14.607 --> 00:23:15.549 cellular therapeutics?

NOTE Confidence: 0.9242995

00:23:15.550 --> 00:23:18.628 My understanding of how cellular

NOTE Confidence: 0.9242995

00:23:18.628 --> 00:23:22.254 therapies work and granted my

NOTE Confidence: 0.9242995

00:23:22.254 --> 00:23:24.536 understanding is very pedestrian, is

NOTE Confidence: 0.9242995

00:23:24.536 --> 00:23:27.392 really that you take these cells out,

NOTE Confidence: 0.9242995

00:23:27.400 --> 00:23:28.965 you genetically engineer them and

NOTE Confidence: 0.9242995

00:23:28.965 --> 00:23:31.279 you give them back to the patient.

NOTE Confidence: 0.9242995

00:23:31.280 --> 00:23:34.808 So is there a need to tailor this

NOTE Confidence: 0.9242995

00:23:34.808 --> 00:23:38.752 over time to kind of give patients

NOTE Confidence: 0.9242995

00:23:38.752 --> 00:23:41.485 different sets of T cells with

NOTE Confidence: 0.9242995

00:23:41.485 --> 00:23:43.530 different either hyper boost or

NOTE Confidence: 0.9242995

00:23:43.614 --> 00:23:46.079 brake pedal capacity over time?

NOTE Confidence: 0.9313311

00:23:46.720 --> 00:23:48.960 This is another excellent question.

NOTE Confidence: 0.9313311

00:23:48.960 --> 00:23:51.680 In fact, by taking the T cells out,

NOTE Confidence: 0.9313311

00:23:51.680 --> 00:23:53.552 there are a lot of ways

NOTE Confidence: 0.9313311

00:23:53.552 --> 00:23:54.800 you can engineer them.

NOTE Confidence: 0.9313311

00:23:54.800 --> 00:23:57.116 So you can change the brake,

NOTE Confidence: 0.9313311

00:23:57.120 --> 00:23:58.480 put the gas pedal on,

NOTE Confidence: 0.9313311

00:23:58.480 --> 00:24:00.880 and in addition you can change the structure.

NOTE Confidence: 0.9313311

00:24:00.880 --> 00:24:03.365 You can also put in control elements

NOTE Confidence: 0.9313311

00:24:03.365 --> 00:24:05.520 so that you can wipe them out when

NOTE Confidence: 0.9313311

00:24:05.520 --> 00:24:07.550 you no longer need them. For example,

NOTE Confidence: 0.9313311

00:24:07.550 --> 00:24:10.988 if you put a queue switch in the T cells,

NOTE Confidence: 0.9313311

00:24:10.988 --> 00:24:12.473 let them do the job,

NOTE Confidence: 0.9313311

00:24:12.480 --> 00:24:14.560 and when the CAR T clear the cancer,

NOTE Confidence: 0.9313311

00:24:14.560 --> 00:24:16.352 you no longer need so much CAR

NOTE Confidence: 0.9313311

00:24:16.352 --> 00:24:18.079 T that could be problematic.

NOTE Confidence: 0.9313311

00:24:18.080 --> 00:24:22.132 Later on you can give the

NOTE Confidence: 0.9313311

00:24:22.132 --> 00:24:24.986 patient a small molecule

NOTE Confidence: 0.9313311

00:24:24.986 --> 00:24:27.472 that can turn on the Q switch so

NOTE Confidence: 0.9313311

00:24:27.472 --> 00:24:29.593 to eliminate the T cells later on.

NOTE Confidence: 0.9313311

00:24:29.600 --> 00:24:31.520 Those are some of the strategies

NOTE Confidence: 0.9313311

00:24:31.520 --> 00:24:35.902 and in addition we now create a

NOTE Confidence: 0.9313311

00:24:35.902 --> 00:24:38.309 new strategy by protein design

NOTE Confidence: 0.9313311

00:24:38.309 --> 00:24:40.990 by fusing a small piece of tail

NOTE Confidence: 0.9313311

00:24:41.073 --> 00:24:43.417 to the T cell so that they are

NOTE Confidence: 0.92892903

00:24:45.620 --> 00:24:47.126 more long lasting,

NOTE Confidence: 0.92892903

00:24:47.126 --> 00:24:49.134 they persist for longer.

NOTE Confidence: 0.92892903

00:24:49.140 --> 00:24:51.372 So those are the several different

NOTE Confidence: 0.92892903

00:24:51.372 --> 00:24:54.393 strategies we can utilize to make the

NOTE Confidence: 0.92892903

00:24:54.393 --> 00:24:57.459 T cell more sophisticated in order

NOTE Confidence: 0.92892903

00:24:57.460 --> 00:24:59.485 for us to utilize the T cell to

NOTE Confidence: 0.92892903

00:24:59.485 --> 00:25:01.015 treat cancer better without

NOTE Confidence: 0.92892903

00:25:01.015 --> 00:25:03.220 doing too much damage to the body,

NOTE Confidence: 0.93666536

00:25:04.350 --> 00:25:07.110 so that changing the structure

NOTE Confidence: 0.93666536

00:25:07.110 --> 00:25:08.390 to make them last longer.

NOTE Confidence: 0.93666536

00:25:08.390 --> 00:25:10.567 That sounds like that third strategy that

NOTE Confidence: 0.93666536

00:25:10.567 --> 00:25:12.947 you were talking about redesigning the car,

NOTE Confidence: 0.93666536

00:25:12.950 --> 00:25:16.190 is that right? Absolutely.

NOTE Confidence: 0.93666536

00:25:16.190 --> 00:25:19.070 And so again, I can see how many

NOTE Confidence: 0.93666536

00:25:19.070 --> 00:25:21.799 of these are complementary, right?

NOTE Confidence: 0.93666536

00:25:21.799 --> 00:25:24.431 You want the T cells to last longer

NOTE Confidence: 0.93666536

00:25:24.431 --> 00:25:26.630 and to maintain their memory.

NOTE Confidence: 0.93666536

00:25:26.630 --> 00:25:28.724 Presumably that could even have an

NOTE Confidence: 0.93666536

00:25:28.724 --> 00:25:31.509 impact in terms of reducing recurrence.

NOTE Confidence: 0.93666536

00:25:31.510 --> 00:25:33.785 So, you know, maybe the T cells

NOTE Confidence: 0.93666536

00:25:33.785 --> 00:25:35.920 wipe out your initial cancer,

NOTE Confidence: 0.93666536

00:25:35.920 --> 00:25:38.200 but you'll always have this

NOTE Confidence: 0.93666536

00:25:38.200 --> 00:25:39.720 residual risk of recurrence.

NOTE Confidence: 0.93666536

00:25:39.720 --> 00:25:42.411 And so if the T cells retain some memory

NOTE Confidence: 0.93666536

00:25:42.411 --> 00:25:45.160 and if enough of them are still around,

NOTE Confidence: 0.93666536

00:25:45.160 --> 00:25:47.450 then presumably they can monitor

NOTE Confidence: 0.93666536

00:25:47.450 --> 00:25:50.675 the situation and get rid of cancer

NOTE Confidence: 0.93666536

00:25:50.675 --> 00:25:53.231 cells early before they even become

NOTE Confidence: 0.93666536

00:25:53.231 --> 00:25:56.304 a cancer recurrence down the line.

NOTE Confidence: 0.93666536

00:25:56.304 --> 00:25:58.096 On the other hand,

NOTE Confidence: 0.93666536

00:25:58.100 --> 00:26:01.277 I do like the idea of the kill switch

NOTE Confidence: 0.93666536

00:26:01.277 --> 00:26:03.770 because we want to make sure that

NOTE Confidence: 0.93666536

00:26:03.770 --> 00:26:05.858 we're not having an overabundance

NOTE Confidence: 0.93666536

00:26:05.858 --> 00:26:08.188 of this cellular activity that

NOTE Confidence: 0.93666536

00:26:08.188 --> 00:26:10.538 could cause other side effects.

NOTE Confidence: 0.93666536

00:26:10.540 --> 00:26:13.760 So how do you kind of engineer

NOTE Confidence: 0.93666536

00:26:13.760 --> 00:26:15.140 this delicate balance?

NOTE Confidence: 0.93666536

00:26:15.140 --> 00:26:17.504 It's almost like a Symphony where

NOTE Confidence: 0.93666536

00:26:17.504 --> 00:26:19.992 you need certain parts of the

NOTE Confidence: 0.93666536

00:26:19.992 --> 00:26:22.072 orchestra playing at certain levels

NOTE Confidence: 0.93666536

00:26:22.072 --> 00:26:24.659 in certain times and not in others.

NOTE Confidence: 0.93507236

00:26:26.110 --> 00:26:27.902 That's a nice analogy.

NOTE Confidence: 0.93507236

00:26:27.902 --> 00:26:31.790 I like symphonies too and the

NOTE Confidence: 0.93507236

00:26:31.790 --> 00:26:34.850 balance between the persistence and

NOTE Confidence: 0.93507236

00:26:34.850 --> 00:26:37.910 the durability is absolutely the

NOTE Confidence: 0.93507236

00:26:37.910 --> 00:26:41.746 the goal for solid tumors.

NOTE Confidence: 0.93507236

00:26:41.750 --> 00:26:43.829 The problem is that they don't last

NOTE Confidence: 0.93507236

00:26:43.829 --> 00:26:45.715 long enough and or at least last

NOTE Confidence: 0.93507236

00:26:45.715 --> 00:26:47.750 long enough in the tumor environment.

NOTE Confidence: 0.93507236

00:26:47.750 --> 00:26:50.662 So by a new strategy we now

NOTE Confidence: 0.93507236

00:26:50.662 --> 00:26:53.139 call the protein fusion tail,

NOTE Confidence: 0.93507236

00:26:53.140 --> 00:26:55.716 we allow the T cell to be more

NOTE Confidence: 0.93507236

00:26:55.716 --> 00:26:57.732 memory like which means they

NOTE Confidence: 0.93507236

00:26:57.732 --> 00:27:00.312 can remember the cancer cells or

NOTE Confidence: 0.93507236

00:27:00.312 --> 00:27:02.740 cancer cells antigen for longer.

NOTE Confidence: 0.93507236

00:27:02.740 --> 00:27:04.492 And by doing so,

NOTE Confidence: 0.93507236

00:27:04.492 --> 00:27:07.120 we enable the T cell therapy

NOTE Confidence: 0.93507236

00:27:07.225 --> 00:27:09.180 to have more durable effect,

NOTE Confidence: 0.93507236

00:27:09.180 --> 00:27:11.820 suppress the cancer growth for longer,

NOTE Confidence: 0.93507236

00:27:11.820 --> 00:27:16.746 preventing the relapse and

NOTE Confidence: 0.93507236

00:27:16.746 --> 00:27:19.683 therefore prolonged survival benefit.

NOTE Confidence: 0.93507236

00:27:19.683 --> 00:27:21.838 So those are the strategies

NOTE Confidence: 0.93507236

00:27:21.838 --> 00:27:23.389 we're testing right now.

NOTE Confidence: 0.93813497

00:27:24.390 --> 00:27:26.346 In terms of testing these strategies,

NOTE Confidence: 0.93813497

00:27:26.350 --> 00:27:29.346 have these been taken into the clinic?

NOTE Confidence: 0.93813497

00:27:29.350 --> 00:27:31.762 Do we have human data on

NOTE Confidence: 0.93813497

00:27:31.762 --> 00:27:33.910 whether or not these work?

NOTE Confidence: 0.93813497

00:27:33.910 --> 00:27:35.355 Is this something that patients

NOTE Confidence: 0.93813497

00:27:35.355 --> 00:27:37.689 can go in and talk to their doctor

NOTE Confidence: 0.93813497

00:27:37.689 --> 00:27:39.628 about today or when do you think

NOTE Confidence: 0.93813497

00:27:39.691 --> 00:27:41.306 that might be the situation?

NOTE Confidence: 0.93813497

00:27:41.710 --> 00:27:45.478 For now, the FDA has approved 6 cell therapy

NOTE Confidence: 0.93813497

00:27:45.478 --> 00:27:48.574 products for the patients

NOTE Confidence: 0.93813497

00:27:48.574 --> 00:27:50.750 within those indications,

NOTE Confidence: 0.93813497

00:27:50.750 --> 00:27:53.822 the doctor will see if they fit the

NOTE Confidence: 0.93813497

00:27:53.822 --> 00:27:56.469 criteria to receive those therapies.

NOTE Confidence: 0.93813497

00:27:56.470 --> 00:27:58.150 But unfortunately for solid tumors,

NOTE Confidence: 0.93813497

00:27:58.150 --> 00:28:01.270 no cell therapy has been approved

NOTE Confidence: 0.93813497

00:28:01.270 --> 00:28:06.143 yet by the FDA and there are many,

NOTE Confidence: 0.93813497

00:28:06.143 --> 00:28:08.908 many clinical trials ongoing over

NOTE Confidence: 0.93813497

00:28:08.908 --> 00:28:11.964 1000 cell therapy clinical trials now

NOTE Confidence: 0.93813497

00:28:11.964 --> 00:28:15.200 and the patient can see if they are

NOTE Confidence: 0.93813497

00:28:15.200 --> 00:28:17.625 right for enrollment of the clinical trials.

NOTE Confidence: 0.93813497

00:28:17.630 --> 00:28:20.324 In the newer strategy we're talking

NOTE Confidence: 0.93813497

00:28:20.324 --> 00:28:23.064 about of course the goal is

NOTE Confidence: 0.93813497

00:28:23.064 --> 00:28:25.790 to balance efficacy to safety

NOTE Confidence: 0.93813497

00:28:25.790 --> 00:28:28.870 and hopefully this can become the

NOTE Confidence: 0.93813497

00:28:28.870 --> 00:28:30.470 clinical product in the future.

NOTE Confidence: 0.93813497

00:28:30.470 --> 00:28:32.336 But as of now they're not

NOTE Confidence: 0.93813497

00:28:32.336 --> 00:28:33.269 approved products yet.

NOTE Confidence: 0.9233917

00:28:33.830 --> 00:28:36.526 Doctor Sidi Chen is an associate professor of

NOTE Confidence: 0.9233917

00:28:36.526 --> 00:28:38.990 genetics at the Yale School of Medicine.

NOTE Confidence: 0.9233917

00:28:38.990 --> 00:28:41.114 If you have questions, the address

NOTE Confidence: 0.9233917

00:28:41.114 --> 00:28:43.439 is Cancer Answers at Yale dot Edu,

NOTE Confidence: 0.9233917

00:28:43.440 --> 00:28:45.690 and past editions of the program

NOTE Confidence: 0.9233917

00:28:45.690 --> 00:28:47.911 are available in audio and written

NOTE Confidence: 0.9233917

00:28:47.911 --> 00:28:48.857 form at yalecancercenter.org.

NOTE Confidence: 0.9233917

00:28:48.857 --> 00:28:51.233 We hope you'll join us next week to

NOTE Confidence: 0.9233917

00:28:51.233 --> 00:28:53.042 learn more about the fight against

NOTE Confidence: 0.9233917

00:28:53.042 --> 00:28:54.840 cancer here on Connecticut Public Radio.

NOTE Confidence: 0.9233917

00:28:54.840 --> 00:28:57.492 Funding for Yale Cancer Answers is

NOTE Confidence: 0.9233917

00:28:57.492 --> 00:29:00.000 provided by Smilow Cancer Hospital.