WEBVTT

00:00:00.000 --> 00:00:03.180 Funding for Yale Cancer Answers is

NOTE Confidence: 0.933020486363636

00:00:03.180 --> 00:00:06.200 provided by Smilow Cancer Hospital.

NOTE Confidence: 0.933020486363636

00:00:06.200 --> 00:00:08.330 Welcome to Yale Cancer Answers

NOTE Confidence: 0.933020486363636

00:00:08.330 --> 00:00:10.034 with Doctor Anees Chagpar.

NOTE Confidence: 0.933020486363636

00:00:10.040 --> 00:00:11.772 Yale Cancer Answers features the

NOTE Confidence: 0.933020486363636

00:00:11.772 --> 00:00:13.144 latest information on cancer

NOTE Confidence: 0.933020486363636

00:00:13.144 --> 00:00:14.933 care by welcoming oncologists and

NOTE Confidence: 0.933020486363636

00:00:14.933 --> 00:00:17.021 specialists who are on the forefront

NOTE Confidence: 0.933020486363636

00:00:17.021 --> 00:00:18.876 of the battle to fight cancer.

NOTE Confidence: 0.933020486363636

00:00:18.880 --> 00:00:21.322 This week it's a conversation about

NOTE Confidence: 0.933020486363636

00:00:21.322 --> 00:00:22.950 hematopathology and breast cancer

NOTE Confidence: 0.933020486363636

00:00:23.012 --> 00:00:24.957 research with Doctor Samuel Katz.

NOTE Confidence: 0.933020486363636

00:00:24.960 --> 00:00:27.158 Dr. Katz is an associate professor of

NOTE Confidence: 0.933020486363636

00:00:27.158 --> 00:00:29.559 pathology at the Yale School of Medicine,

NOTE Confidence: 0.933020486363636

00:00:29.560 --> 00:00:31.690 where Doctor Chagpar is a professor

NOTE Confidence: 0.933020486363636

00:00:31.690 --> 00:00:32.755 of surgical oncology.

NOTE Confidence: 0.91429116

00:00:34.160 --> 00:00:35.896 So Dr. Katz, maybe we can start off

NOTE Confidence: 0.91429116

00:00:35.896 --> 00:00:37.878 by you telling us a little bit more

NOTE Confidence: 0.91429116

00:00:37.878 --> 00:00:39.557 about yourself and what it is you do.

NOTE Confidence: 0.943964666363636

00:00:40.160 --> 00:00:42.506 I'm a physician scientist

NOTE Confidence: 0.943964666363636

00:00:42.506 --> 00:00:44.800 within the Department of Pathology.

NOTE Confidence: 0.943964666363636

00:00:44.800 --> 00:00:49.000 I split my time where I spend 20% on

NOTE Confidence: 0.943964666363636

00:00:49.000 --> 00:00:52.800 clinical service diagnosing blood cancers,

NOTE Confidence: 0.943964666363636

00:00:52.800 --> 00:00:53.943 leukemias, and lymphomas.

NOTE Confidence: 0.943964666363636

00:00:53.943 --> 00:00:56.960 But I spend the majority of my time

NOTE Confidence: 0.943964666363636

00:00:56.960 --> 00:01:00.032 running a basic research laboratory that

NOTE Confidence: 0.943964666363636

00:01:00.032 --> 00:01:03.279 focuses on questions of how cells die.

NOTE Confidence: 0.943964666363636

00:01:03.280 --> 00:01:05.380 And we approach it from two

NOTE Confidence: 0.943964666363636

00:01:05.380 --> 00:01:06.552 different standpoints.

NOTE Confidence: 0.943964666363636

00:01:06.552 --> 00:01:08.912 By the pathway within the

NOTE Confidence: 0.943964666363636

00:01:08.912 --> 00:01:11.559 cells that cause them to die,

NOTE Confidence: 0.943964666363636

00:01:11.560 --> 00:01:14.792 but also by a pathway external to

NOTE Confidence: 0.943964666363636

00:01:14.792 --> 00:01:16.840 the cells and how we can kill them.

NOTE Confidence: 0.943964666363636

00:01:16.840 --> 00:01:19.020 Because if we can manipulate

NOTE Confidence: 0.943964666363636

00:01:19.020 --> 00:01:21.200 the ability to kill cells,

NOTE Confidence: 0.943964666363636

00:01:21.200 --> 00:01:23.130 that could help in many

NOTE Confidence: 0.943964666363636

00:01:23.130 --> 00:01:24.674 different diseases like cancers.

00:01:28.560 --> 00:01:30.832 Tell us a little bit more about how

NOTE Confidence: 0.9663498725

00:01:30.832 --> 00:01:34.065 you came to work on breast

NOTE Confidence: 0.9663498725

00:01:34.065 --> 00:01:36.037 cancer as a hematopathologist.

NOTE Confidence: 0.9663498725

00:01:36.040 --> 00:01:38.476 You mentioned that in your clinical role,

NOTE Confidence: 0.9663498725

00:01:38.480 --> 00:01:41.276 you really focus on blood cancers.

NOTE Confidence: 0.9663498725

00:01:41.280 --> 00:01:43.584 So how do you get

NOTE Confidence: 0.9663498725

00:01:43.584 --> 00:01:45.638 into the breast cancer world?

NOTE Confidence: 0.907417529285714

00:01:46.160 --> 00:01:48.446 As a hematopathologist who

NOTE Confidence: 0.907417529285714

00:01:48.446 --> 00:01:51.480 focuses on the blood and the blood system,

NOTE Confidence: 0.907417529285714

00:01:51.480 --> 00:01:54.491 I got very interested in a

NOTE Confidence: 0.907417529285714

00:01:54.491 --> 00:01:56.957 particular cell type called a T cell.

NOTE Confidence: 0.907417529285714

00:01:56.960 --> 00:02:00.152 And T cells are important in our

NOTE Confidence: 0.907417529285714

00:02:00.152 --> 00:02:02.840 immune system to attack cells that

NOTE Confidence: 0.907417529285714

00:02:02.840 --> 00:02:05.480 have been infected with foreign agents.

NOTE Confidence: 0.907417529285714

00:02:05.480 --> 00:02:07.874 They're able to recognize the cells

NOTE Confidence: 0.907417529285714

00:02:07.874 --> 00:02:10.240 as being infected and kill them.

NOTE Confidence: 0.907417529285714

00:02:10.240 --> 00:02:12.928 And people have realized that they

NOTE Confidence: 0.907417529285714

00:02:12.928 --> 00:02:15.561 have such incredible ability to kill

NOTE Confidence: 0.907417529285714

00:02:15.561 --> 00:02:17.865 those infected cells that perhaps we

NOTE Confidence: 0.907417529285714

00:02:17.865 --> 00:02:20.600 can usurp that ability in order to

NOTE Confidence: 0.907417529285714

00:02:20.600 --> 00:02:23.120 attack other cells like cancer cells.

NOTE Confidence: 0.940223532631579

00:02:24.840 --> 00:02:26.632 And so tell us more about how this

NOTE Confidence: 0.940223532631579

00:02:26.632 --> 00:02:28.684 kind of works in breast cancer and

NOTE Confidence: 0.940223532631579

00:02:28.684 --> 00:02:32.760 more about your research.

NOTE Confidence: 0.891859650769231

00:02:32.760 --> 00:02:34.979 Sure, so in breast cancer there are

NOTE Confidence: 0.891859650769231

00:02:34.979 --> 00:02:37.119 many other types of cancers,

NOTE Confidence: 0.891859650769231

00:02:37.120 --> 00:02:40.716 there are proteins that are on

NOTE Confidence: 0.891859650769231

00:02:40.716 --> 00:02:43.560 the surface of the cell that are

NOTE Confidence: 0.891859650769231

00:02:43.560 --> 00:02:45.680 not present in normal cells.

NOTE Confidence: 0.891859650769231

00:02:45.680 --> 00:02:49.666 And so we have devised a protein that

NOTE Confidence: 0.891859650769231

00:02:49.666 --> 00:02:52.490 we can add into the T cells called

NOTE Confidence: 0.891859650769231

00:02:52.569 --> 00:02:55.197 a CAR or chimeric antigen receptor,

NOTE Confidence: 0.891859650769231

00:02:55.200 --> 00:02:58.088 thus making a CAR T cell that can

NOTE Confidence: 0.891859650769231

00:02:58.088 --> 00:02:59.750 recognize this aberrant protein

NOTE Confidence: 0.891859650769231

00:02:59.750 --> 00:03:02.324 on the breast cancer cell and

NOTE Confidence: 0.891859650769231

00:03:02.324 --> 00:03:05.133 direct the T cells killing ability

NOTE Confidence: 0.891859650769231

00:03:05.133 --> 00:03:07.473 towards that breast cancer cell.

NOTE Confidence: 0.915714538571429

00:03:09.320 --> 00:03:12.316 That sounds really fascinating.

NOTE Confidence: 0.915714538571429

00:03:12.320 --> 00:03:14.000 So tell us more about

NOTE Confidence: 0.915714538571429

00:03:14.000 --> 00:03:15.680 how CAR T therapy works.

NOTE Confidence: 0.915714538571429

00:03:15.680 --> 00:03:17.324 I know some of our listeners

NOTE Confidence: 0.915714538571429

00:03:17.324 --> 00:03:18.760 may be familiar with this,

NOTE Confidence: 0.915714538571429

00:03:18.760 --> 00:03:21.020 but many may not be. So, you know,

NOTE Confidence: 0.915714538571429

00:03:21.020 --> 00:03:23.400 how do you actually change these T

NOTE Confidence: 0.915714538571429

00:03:23.479 --> 00:03:25.945 cells to make them recognize these

NOTE Confidence: 0.915714538571429

00:03:25.945 --> 00:03:28.520 proteins on the surface of the cell?

NOTE Confidence: 0.915714538571429

00:03:28.520 --> 00:03:29.965 Because it sounds like essentially

NOTE Confidence: 0.915714538571429

00:03:29.965 --> 00:03:31.410 what you're doing is you're

NOTE Confidence: 0.915714538571429

00:03:31.460 --> 00:03:33.000 taking a patient's immune system,

NOTE Confidence: 0.915714538571429

00:03:33.000 --> 00:03:34.044 these T cells,

NOTE Confidence: 0.915714538571429

00:03:34.044 --> 00:03:36.848 and you're kind of giving them a GPS, a

NOTE Confidence: 0.915714538571429

00:03:36.848 --> 00:03:39.792 targeting system to say go after those cells,

NOTE Confidence: 0.915714538571429

00:03:39.800 --> 00:03:40.892 those cancer cells,

NOTE Confidence: 0.915714538571429

00:03:40.892 --> 00:03:43.076 but somehow you have to get

NOTE Confidence: 0.915714538571429

00:03:43.076 --> 00:03:45.156 the GPS into those T cells.

NOTE Confidence: 0.915714538571429

00:03:45.160 --> 00:03:46.636 How do you do that exactly?

NOTE Confidence: 0.948618271818182

00:03:47.040 --> 00:03:48.990 Absolutely. And so there's a

NOTE Confidence: 0.948618271818182

00:03:48.990 --> 00:03:51.240 number of ways in which to,

NOTE Confidence: 0.948618271818182

00:03:51.240 --> 00:03:54.880 as we say, reprogram those T cells.

NOTE Confidence: 0.948618271818182

00:03:54.880 --> 00:03:58.330 The most commonly used ones are

NOTE Confidence: 0.948618271818182

00:03:58.330 --> 00:04:00.488 viral approaches using retroviruses

NOTE Confidence: 0.948618271818182

00:04:00.488 --> 00:04:03.512 or lentiviruses where a piece of

NOTE Confidence: 0.948618271818182

00:04:03.512 --> 00:04:06.875 DNA and that virus will infect the

NOTE Confidence: 0.948618271818182

00:04:06.875 --> 00:04:09.620 cell and then integrate or become

NOTE Confidence: 0.948618271818182

00:04:09.620 --> 00:04:12.371 part of that cells genome or DNA

NOTE Confidence: 0.948618271818182

00:04:12.371 --> 00:04:15.000 and it will then express this new

NOTE Confidence: 0.948618271818182

00:04:15.000 --> 00:04:17.249 protein that we've made which we

NOTE Confidence: 0.948618271818182

00:04:17.249 --> 00:04:19.277 can discuss later called the CAR,

NOTE Confidence: 0.948618271818182

00:04:19.280 --> 00:04:22.480 the chimeric antigen receptor.

NOTE Confidence: 0.948618271818182

00:04:22.480 --> 00:04:25.891 Another way in which to do it,

NOTE Confidence: 0.948618271818182

00:04:25.891 --> 00:04:27.913 which is the approach we've taken

NOTE Confidence: 0.948618271818182

00:04:27.913 --> 00:04:30.436 and really came about because of

NOTE Confidence: 0.948618271818182

00:04:30.436 --> 00:04:32.648 some work by a senior professor here

NOTE Confidence: 0.948618271818182

00:04:32.648 --> 00:04:34.423 at Yale called Sherman Weissman.

NOTE Confidence: 0.948618271818182

00:04:34.423 --> 00:04:37.456 He kind of took me under his wing

NOTE Confidence: 0.948618271818182

00:04:37.456 --> 00:04:39.700 as a mentor in this approach where

NOTE Confidence: 0.948618271818182

00:04:39.700 --> 00:04:42.692 instead of using DNA, he was using RNA.

NOTE Confidence: 0.948618271818182

00:04:42.692 --> 00:04:46.511 And so we can take the T cells out

NOTE Confidence: 0.948618271818182

00:04:46.511 --> 00:04:49.164 of the patient and what we call

NOTE Confidence: 0.948618271818182

00:04:49.164 --> 00:04:51.012 Electroplate in order to give

NOTE Confidence: 0.948618271818182

00:04:51.012 --> 00:04:53.089 them kind of a little shock that

NOTE Confidence: 0.948618271818182

00:04:53.089 --> 00:04:54.920 gets the RNA into the cells.

NOTE Confidence: 0.948618271818182

00:04:54.920 --> 00:04:58.320 And this has a very high efficiency of

NOTE Confidence: 0.948618271818182

00:04:58.320 --> 00:05:01.200 being able to reprogram those cells

NOTE Confidence: 0.948618271818182

00:05:01.200 --> 00:05:03.636 using the RNA in this manner.

NOTE Confidence: 0.948618271818182

00:05:03.640 --> 00:05:06.475 But it also has a lot of other advantages,

NOTE Confidence: 0.948618271818182

00:05:06.480 --> 00:05:09.238 chief among them being safety in that

NOTE Confidence: 0.948618271818182

00:05:09.238 --> 00:05:11.997 when you put an RNA into a cell,

NOTE Confidence: 0.948618271818182

00:05:12.000 --> 00:05:14.142 it doesn't change the genome of all

NOTE Confidence: 0.948618271818182

00:05:14.142 --> 00:05:16.838 of the T cells that you're taking

NOTE Confidence: 0.948618271818182

00:05:16.838 --> 00:05:18.119 from the patients.

NOTE Confidence: 0.948618271818182

00:05:18.120 --> 00:05:20.906 It only makes that RNA which then

NOTE Confidence: 0.948618271818182

00:05:20.906 --> 00:05:23.198 makes that protein and after a

NOTE Confidence: 0.948618271818182

00:05:23.198 --> 00:05:25.238 period of time it goes away.

NOTE Confidence: 0.948618271818182

00:05:25.240 --> 00:05:27.920 And so there's an added safety to that

NOTE Confidence: 0.968561089047619

00:05:29.400 --> 00:05:32.438 and that also sounds like that would

NOTE Confidence: 0.968561089047619

00:05:32.438 --> 00:05:34.825 be particularly handy once the job

NOTE Confidence: 0.968561089047619

00:05:34.825 --> 00:05:37.560 of getting rid of this cancer is done

NOTE Confidence: 0.968561089047619

00:05:37.560 --> 00:05:39.436 that the cells go back to normal.

NOTE Confidence: 0.968561089047619

00:05:39.440 --> 00:05:42.064 So how long does it take for

NOTE Confidence: 0.968561089047619

00:05:42.064 --> 00:05:44.960 that RNA to disintegrate or go away?

NOTE Confidence: 0.9591094

00:05:45.560 --> 00:05:48.898 The RNA actually is very

NOTE Confidence: 0.9591094

00:05:48.898 --> 00:05:50.872 short lived, but the protein it

NOTE Confidence: 0.9591094

00:05:50.872 --> 00:05:53.247 makes can last a little longer and

NOTE Confidence: 0.9591094

00:05:53.247 --> 00:05:55.476 it really depends on the particular

NOTE Confidence: 0.9591094

00:05:55.476 --> 00:05:57.520 protein that you're making.

NOTE Confidence: 0.9591094

00:05:57.520 --> 00:05:59.718 But we see it in the order

NOTE Confidence: 0.9591094

00:05:59.718 --> 00:06:01.679 of about a week or so.

NOTE Confidence: 0.9591094

00:06:01.680 --> 00:06:04.200 So one could envision giving this

NOTE Confidence: 0.9591094

00:06:04.200 --> 00:06:06.943 therapy as a weekly type of basis

NOTE Confidence: 0.9591094

00:06:06.943 --> 00:06:09.481 where you're giving the cells that

NOTE Confidence: 0.9591094

00:06:09.481 --> 00:06:11.524 have been reprogrammed with RNA or

NOTE Confidence: 0.9591094

00:06:11.524 --> 00:06:15.320 in newer work that's still ongoing

NOTE Confidence: 0.9591094

00:06:15.320 --> 00:06:17.906 trying to actually deliver the RNA

NOTE Confidence: 0.9591094

00:06:17.906 --> 00:06:20.721 into the body without having to take

NOTE Confidence: 0.9591094

00:06:20.721 --> 00:06:23.040 out the T cells to reprogram them.

00:06:27.240 --> 00:06:30.677 It sounds like it really is intriguing,

NOTE Confidence: 0.824624856

00:06:30.680 --> 00:06:33.039 right, that you kind of give

NOTE Confidence: 0.824624856

00:06:33.039 --> 00:06:35.198 these T cells a little shock,

NOTE Confidence: 0.824624856

00:06:35.200 --> 00:06:38.120 give them an RNA to make a protein.

NOTE Confidence: 0.824624856

00:06:38.120 --> 00:06:41.659 That protein, that CAR protein goes

NOTE Confidence: 0.824624856

00:06:41.659 --> 00:06:44.592 and attacks these cancer cells in a

NOTE Confidence: 0.824624856

00:06:44.592 --> 00:06:46.912 very specific way because presumably

NOTE Confidence: 0.824624856

00:06:46.912 --> 00:06:49.708 this protein is found on cancer

NOTE Confidence: 0.824624856

00:06:49.708 --> 00:06:52.120 cells and not on normal cells.

NOTE Confidence: 0.824624856

00:06:52.120 --> 00:06:55.144 So where are we in terms of actually

NOTE Confidence: 0.824624856

00:06:55.144 --> 00:06:57.599 getting this into clinical trials?

NOTE Confidence: 0.94188564

00:06:58.200 --> 00:07:01.428 Yeah, so we're still in the

NOTE Confidence: 0.94188564

00:07:01.428 --> 00:07:03.640 early phases I'd say of doing this.

NOTE Confidence: 0.94188564

00:07:03.640 --> 00:07:06.480 There's a lot of work to be done

NOTE Confidence: 0.94188564

00:07:06.480 --> 00:07:09.480 to optimize the system overall

NOTE Confidence: 0.874222667333333

00:07:11.520 --> 00:07:14.082 and these include the things that improve

NOTE Confidence: 0.874222667333333

00:07:14.082 --> 00:07:16.556 the ability of the T cells to kill,

NOTE Confidence: 0.874222667333333

00:07:16.560 --> 00:07:21.775 to make sure that they don't get exhausted,

NOTE Confidence: 0.874222667333333

00:07:21.775 --> 00:07:25.240 to make sure that again,

NOTE Confidence: 0.874222667333333

00:07:25.240 --> 00:07:26.200 as we're saying,

NOTE Confidence: 0.874222667333333

00:07:26.200 --> 00:07:27.558 to really make sure that it's safe.

NOTE Confidence: 0.874222667333333

00:07:27.560 --> 00:07:29.912 We still have work to do in

NOTE Confidence: 0.874222667333333

00:07:29.912 --> 00:07:32.013 animal models before we can get

NOTE Confidence: 0.874222667333333

00:07:32.013 --> 00:07:33.718 it into the clinical sphere,

NOTE Confidence: 0.874222667333333

00:07:33.720 --> 00:07:35.640 but because of the RNA approach

NOTE Confidence: 0.874222667333333

00:07:35.640 --> 00:07:36.600 and the safety,

NOTE Confidence: 0.874222667333333

00:07:36.600 --> 00:07:39.450 we do think it is a easier transition

NOTE Confidence: 0.874222667333333

00:07:39.450 --> 00:07:41.800 to getting it into patients.

NOTE Confidence: 0.908580070769231

00:07:43.000 --> 00:07:45.268 And in terms of

NOTE Confidence: 0.908580070769231

00:07:45.268 --> 00:07:47.599 the safety and side effects,

NOTE Confidence: 0.908580070769231

00:07:47.600 --> 00:07:49.076 can you talk a little bit

NOTE Confidence: 0.908580070769231

00:07:49.076 --> 00:07:50.560 more about the side effects?

NOTE Confidence: 0.908580070769231

00:07:50.560 --> 00:07:52.835 I mean I would assume that this

NOTE Confidence: 0.908580070769231

00:07:52.835 --> 00:07:56.001 has a lot to do with whether these

NOTE Confidence: 0.908580070769231

00:07:56.001 --> 00:07:58.980 proteins are on normal cells in any

NOTE Confidence: 0.908580070769231

00:07:58.980 --> 00:08:01.759 capacity or whether they are really

NOTE Confidence: 0.908580070769231

00:08:01.760 --> 00:08:04.890 100% only on cancer cells and also

NOTE Confidence: 0.908580070769231

00:08:04.890 --> 00:08:07.440 revving up the the immune system.

NOTE Confidence: 0.908580070769231

00:08:07.440 --> 00:08:09.928 You may think that you might get some

NOTE Confidence: 0.908580070769231

00:08:09.928 --> 00:08:12.056 immune related side effects as these T

NOTE Confidence: 0.908580070769231

00:08:12.056 --> 00:08:14.080 cells go about doing their business.

NOTE Confidence: 0.942190673333334

00:08:14.280 --> 00:08:17.016 and so maybe it is best to

NOTE Confidence: 0.942190673333334

00:08:17.016 --> 00:08:19.534 take one step back and to say where

NOTE Confidence: 0.942190673333334

00:08:19.534 --> 00:08:22.235 the CAR T cells have been really

NOTE Confidence: 0.942190673333334

00:08:22.235 --> 00:08:24.791 successful to date in the clinic.

NOTE Confidence: 0.942190673333334

00:08:24.800 --> 00:08:28.400 And these have been against actually

NOTE Confidence: 0.942190673333334

00:08:28.400 --> 00:08:31.571 targets that are on B cell malignancies

NOTE Confidence: 0.942190673333334

00:08:31.571 --> 00:08:33.586 or leukemias and lymphomas.

NOTE Confidence: 0.942190673333334

00:08:33.586 --> 00:08:35.798 And they're going

NOTE Confidence: 0.942190673333334

00:08:35.798 --> 00:08:38.640 after a target called CD 19,

NOTE Confidence: 0.942190673333334

00:08:38.640 --> 00:08:41.916 which is expressed on the surface of

NOTE Confidence: 0.942190673333334

00:08:41.916 --> 00:08:46.039 those B cells and that really is unique to

NOTE Confidence: 0.942190673333334

00:08:46.040 --> 00:08:50.279 those cancer cells as well as normal B cells.

NOTE Confidence: 0.942190673333334

00:08:50.280 --> 00:08:52.256 And so when the CAR T cells are

NOTE Confidence: 0.942190673333334

00:08:52.256 --> 00:08:53.640 introduced to those patients,

NOTE Confidence: 0.942190673333334

00:08:53.640 --> 00:08:56.000 it does get rid of all their normal B cells,

NOTE Confidence: 0.942190673333334

00:08:56.000 --> 00:08:58.478 but patients are fine with that.

NOTE Confidence: 0.942190673333334

00:08:58.480 --> 00:08:59.376 You can

NOTE Confidence: 0.942190673333334

00:08:59.376 --> 00:09:02.512 live without our B cells.

NOTE Confidence: 0.942190673333334

00:09:02.520 --> 00:09:03.755 There are some side effects

NOTE Confidence: 0.942190673333334

00:09:03.755 --> 00:09:05.440 that are seen with that therapy.

NOTE Confidence: 0.942190673333334

00:09:05.440 --> 00:09:08.520 One is a called a cytokine release

NOTE Confidence: 0.942190673333334

00:09:08.520 --> 00:09:10.700 syndrome where because you're getting so

NOTE Confidence: 0.942190673333334

00:09:10.700 --> 00:09:13.160 much killing so quickly of the cancer,

NOTE Confidence: 0.942190673333334

00:09:13.160 --> 00:09:15.351 it releases a lot of the cytokines

NOTE Confidence: 0.942190673333334

00:09:15.351 --> 00:09:17.780 that leads to kind of like an

NOTE Confidence: 0.942190673333334

00:09:17.780 --> 00:09:19.555 immune storm within the patients.

NOTE Confidence: 0.942190673333334

00:09:19.560 --> 00:09:21.837 They feel very sick and you have to really

NOTE Confidence: 0.942190673333334

00:09:21.837 --> 00:09:24.000 watch them carefully within the hospital.

NOTE Confidence: 0.942190673333334

00:09:24.000 --> 00:09:27.115 And there's also been some less well

NOTE Confidence: 0.942190673333334

00:09:27.115 --> 00:09:31.200 understood neurological disorders

NOTE Confidence: 0.942190673333334

00:09:31.200 --> 00:09:34.038 that occur in some patients.

NOTE Confidence: 0.942190673333334

00:09:34.040 --> 00:09:36.044 And some people have hypothesized that

NOTE Confidence: 0.942190673333334

00:09:36.044 --> 00:09:38.662 that might be due to the fact that

NOTE Confidence: 0.942190673333334

00:09:38.662 --> 00:09:40.486 we've learned later that there's a

NOTE Confidence: 0.942190673333334

00:09:40.553 --> 00:09:42.849 cell type within the brain that has

NOTE Confidence: 0.942190673333334

00:09:42.849 --> 00:09:44.851 very low expression of this target.

NOTE Confidence: 0.942190673333334

00:09:44.851 --> 00:09:47.705 And so then that gets us back to

NOTE Confidence: 0.942190673333334

00:09:47.705 --> 00:09:50.177 breast cancer and solid tumors where

NOTE Confidence: 0.942190673333334

00:09:50.177 --> 00:09:52.667 there aren't as many great targets

NOTE Confidence: 0.942190673333334

00:09:52.667 --> 00:09:55.397 that we know of that are uniquely

NOTE Confidence: 0.942190673333334

00:09:55.400 --> 00:09:59.320 expressed on the surface of these cells.

NOTE Confidence: 0.942190673333334

00:09:59.320 --> 00:10:01.700 The one that we're going after actually

NOTE Confidence: 0.942190673333334

00:10:01.700 --> 00:10:04.617 turns out to be increased in more than

NOTE Confidence: 0.942190673333334

00:10:04.617 --> 00:10:06.980 half of triple negative breast cancers

NOTE Confidence: 0.942190673333334

00:10:06.980 --> 00:10:09.300 and its expression correlates with

NOTE Confidence: 0.942190673333334

00:10:09.300 --> 00:10:11.776 poor prognosis within these patients.

NOTE Confidence: 0.942190673333334

00:10:11.776 --> 00:10:15.472 There is some very low

NOTE Confidence: 0.942190673333334

00:10:15.472 --> 00:10:17.320 expression during development,

NOTE Confidence: 0.942190673333334

00:10:17.320 --> 00:10:20.680 but we have some reasons to believe

NOTE Confidence: 0.942190673333334

00:10:20.680 --> 00:10:23.645 that we can kind of thread the needle

NOTE Confidence: 0.942190673333334

00:10:23.645 --> 00:10:25.658 between this very high expression

NOTE Confidence: 0.942190673333334

00:10:25.658 --> 00:10:28.696 on the cancer and this perhaps low

NOTE Confidence: 0.942190673333334

00:10:28.696 --> 00:10:30.839 expression on some normal tissues.

NOTE Confidence: 0.891613291111111

00:10:31.920 --> 00:10:36.660 Yeah, I mean I think that in general for

NOTE Confidence: 0.891613291111111

00:10:36.660 --> 00:10:42.234 most cancer related drugs

NOTE Confidence: 0.891613291111111

00:10:42.240 --> 00:10:44.436 it's never completely black and white.

NOTE Confidence: 0.891613291111111

00:10:44.440 --> 00:10:47.366 Even chemotherapy we know we still use

NOTE Confidence: 0.891613291111111

00:10:47.366 --> 00:10:51.392 and it really is designed to attack

NOTE Confidence: 0.891613291111111

00:10:51.392 --> 00:10:54.680 rapidly growing cells and dividing cells.

NOTE Confidence: 0.891613291111111

00:10:54.680 --> 00:10:57.564 But you still get some normal cells

NOTE Confidence: 0.891613291111111

00:10:57.564 --> 00:11:00.240 that are also rapidly dividing

NOTE Confidence: 0.891613291111111

00:11:00.240 --> 00:11:01.680 like your hair for example,

NOTE Confidence: 0.891613291111111

00:11:01.680 --> 00:11:05.004 which is why many patients undergoing

NOTE Confidence: 0.891613291111111

00:11:05.004 --> 00:11:06.586 chemotherapy lose their hair.

NOTE Confidence: 0.891613291111111

00:11:06.586 --> 00:11:08.980 So it sounds like even if there

NOTE Confidence: 0.891613291111111

00:11:09.060 --> 00:11:11.560 was a potential differential there,

NOTE Confidence: 0.891613291111111

00:11:11.560 --> 00:11:13.672 it still might be really handy

NOTE Confidence: 0.891613291111111

00:11:13.672 --> 00:11:15.960 in terms of a therapy,

NOTE Confidence: 0.891613291111111

00:11:15.960 --> 00:11:18.792 especially if it was less toxic

NOTE Confidence: 0.891613291111111

00:11:18.792 --> 00:11:20.680 than our standard therapies,

NOTE Confidence: 0.891613291111111

00:11:20.680 --> 00:11:23.565 which for triple negative breast

NOTE Confidence: 0.891613291111111

00:11:23.565 --> 00:11:25.873 cancer are primarily chemotherapy.

NOTE Confidence: 0.891613291111111

00:11:25.880 --> 00:11:27.980 Now the other question that I have

NOTE Confidence: 0.891613291111111

00:11:27.980 --> 00:11:29.942 for you is in triple negative

NOTE Confidence: 0.891613291111111

00:11:29.942 --> 00:11:31.358 breast cancer in particular,

NOTE Confidence: 0.891613291111111

00:11:31.360 --> 00:11:36.170 we've seen that there are now therapies that

NOTE Confidence: 0.891613291111111

00:11:36.170 --> 00:11:38.840 are being used that are immunotherapies.

NOTE Confidence: 0.891613291111111

00:11:38.840 --> 00:11:41.525 So really therapies that are

NOTE Confidence: 0.891613291111111

00:11:41.525 --> 00:11:44.472 designed to unleash the immune system

NOTE Confidence: 0.891613291111111

00:11:44.472 --> 00:11:46.812 especially because some of these

NOTE Confidence: 0.891613291111111

00:11:46.812 --> 00:11:49.080 triple negative breast cancers,

NOTE Confidence: 0.891613291111111

00:11:49.080 --> 00:11:54.040 they tend to evade the immune system.

NOTE Confidence: 0.891613291111111

00:11:54.040 --> 00:11:57.861 So if that's the case, and this CAR

NOTE Confidence: 0.891613291111111

00:11:57.861 --> 00:12:00.543 T therapy is really designed to

NOTE Confidence: 0.891613291111111

00:12:00.543 --> 00:12:02.758 use the immune system,

NOTE Confidence: 0.891613291111111

00:12:02.760 --> 00:12:04.874 is it the idea that this would

NOTE Confidence: 0.891613291111111

00:12:04.874 --> 00:12:06.658 be paired with immunotherapies or

NOTE Confidence: 0.891613291111111

00:12:06.658 --> 00:12:09.076 are you thinking about a different

NOTE Confidence: 0.891613291111111

00:12:09.076 --> 00:12:10.960 way of attacking this?

NOTE Confidence: 0.927612363333333

00:12:11.520 --> 00:12:14.516 So I think there is a potential

NOTE Confidence: 0.927612363333333

00:12:14.516 --> 00:12:17.079 for testing the two together,

NOTE Confidence: 0.927612363333333

00:12:17.080 --> 00:12:19.294 but it is very different in

NOTE Confidence: 0.927612363333333

00:12:19.294 --> 00:12:21.600 the way these two different

NOTE Confidence: 0.927612363333333

00:12:21.600 --> 00:12:23.712 classes of immunotherapies work.

NOTE Confidence: 0.927612363333333

00:12:23.712 --> 00:12:26.880 So the ones that you're referring

NOTE Confidence: 0.927612363333333

00:12:26.960 --> 00:12:29.625 to, so-called checkpoint inhibitors,

NOTE Confidence: 0.927612363333333

00:12:29.625 --> 00:12:35.054 these are ones that rely on new

NOTE Confidence: 0.927612363333333

00:12:35.054 --> 00:12:37.124 antigens that are made within

NOTE Confidence: 0.927612363333333

00:12:37.124 --> 00:12:39.706 the cancer cell that are mutant

NOTE Confidence: 0.927612363333333

00:12:39.706 --> 00:12:42.238 and specific to the cancer cells.

NOTE Confidence: 0.927612363333333

00:12:42.240 --> 00:12:45.160 And they really are unique.

NOTE Confidence: 0.927612363333333

00:12:45.160 --> 00:12:47.680 The T cells use their native,

NOTE Confidence: 0.927612363333333

00:12:47.680 --> 00:12:50.630 their normal T cell receptors

NOTE Confidence: 0.927612363333333

00:12:50.630 --> 00:12:52.400 to recognize those.

NOTE Confidence: 0.927612363333333

00:12:52.400 --> 00:12:54.720 But there's a so-called break

NOTE Confidence: 0.927612363333333

00:12:54.720 --> 00:12:57.616 mechanism that prevents the T cell

NOTE Confidence: 0.927612363333333

00:12:57.616 --> 00:13:00.544 from killing and the immunocheckpoint

NOTE Confidence: 0.927612363333333

00:13:00.544 --> 00:13:03.262 inhibitors take away that break, the

NOTE Confidence: 0.927612363333333

00:13:03.262 --> 00:13:05.554 CAR that I've been talking about,

NOTE Confidence: 0.927612363333333

00:13:05.560 --> 00:13:07.272 these CAR T cells,

NOTE Confidence: 0.927612363333333

00:13:07.272 --> 00:13:10.512 this is a new protein that we've

NOTE Confidence: 0.927612363333333

00:13:10.512 --> 00:13:13.440 devised by taking pieces of various

NOTE Confidence: 0.927612363333333

00:13:13.533 --> 00:13:16.599 other parts of the T cell receptor

NOTE Confidence: 0.927612363333333

00:13:16.599 --> 00:13:19.095 and other antigen recognition domains

NOTE Confidence: 0.927612363333333

00:13:19.095 --> 00:13:22.377 and they recognize or we've designed

NOTE Confidence: 0.927612363333333

00:13:22.377 --> 00:13:27.640 this one to recognize a specific

NOTE Confidence: 0.927612363333333

00:13:27.640 --> 00:13:31.035 protein that's not mutated but wild type.

NOTE Confidence: 0.927612363333333

00:13:31.040 --> 00:13:36.370 And this then activates the CAR T

NOTE Confidence: 0.927612363333333

00:13:36.370 --> 00:13:39.315 cell rather than stopping the brake.

NOTE Confidence: 0.927612363333333

00:13:39.315 --> 00:13:42.010 I'd say it's more akin to pressing

NOTE Confidence: 0.927612363333333

00:13:42.087 --> 00:13:44.684 on the gas pedal when we have

NOTE Confidence: 0.927612363333333

00:13:44.684 --> 00:13:45.797 that specific protein.

00:13:46.200 --> 00:13:48.307 Well, we need to take a

NOTE Confidence: 0.932746633076923

00:13:48.307 --> 00:13:50.478 short break for a medical minute,

NOTE Confidence: 0.932746633076923

00:13:50.480 --> 00:13:52.552 but please stay tuned to learn more

NOTE Confidence: 0.932746633076923

00:13:52.552 --> 00:13:54.851 about the role of pathology and new

NOTE Confidence: 0.932746633076923

00:13:54.851 --> 00:13:56.873 research into a potential target for

NOTE Confidence: 0.932746633076923

00:13:56.940 --> 00:13:58.568 metastatic triple negative breast

NOTE Confidence: 0.932746633076923

00:13:58.568 --> 00:14:01.280 cancer with my guest, Doctor Sam Katz.

NOTE Confidence: 0.858522909259259

00:14:01.960 --> 00:14:04.240 Support for Yale Cancer Answers comes

NOTE Confidence: 0.858522909259259

00:14:04.240 --> 00:14:06.216 from Smilow Cancer Hospital where

NOTE Confidence: 0.858522909259259

00:14:06.216 --> 00:14:08.176 their Prostate and Urologic Cancers

NOTE Confidence: 0.858522909259259

00:14:08.176 --> 00:14:10.674 program provides a multispecialty team

NOTE Confidence: 0.858522909259259

00:14:10.674 --> 00:14:12.839 dedicated to managing the diagnosis,

NOTE Confidence: 0.858522909259259

00:14:12.840 --> 00:14:15.798 evaluation, and treatment of bladder cancer.

NOTE Confidence: 0.858522909259259

00:14:15.800 --> 00:14:19.880 Smilowcancerhospital.org.

NOTE Confidence: 0.858522909259259

00:14:19.880 --> 00:14:22.610 The American Cancer Society estimates that

NOTE Confidence: 0.858522909259259

00:14:22.610 --> 00:14:25.395 more than 65,000 Americans will be diagnosed

NOTE Confidence: 0.858522909259259

00:14:25.395 --> 00:14:27.959 with head and neck cancer this year,

NOTE Confidence: 0.858522909259259

00:14:27.960 --> 00:14:31.355 making up about 4% of all cancers

NOTE Confidence: 0.858522909259259

00:14:31.355 --> 00:14:33.004 diagnosed. When detected early,

NOTE Confidence: 0.858522909259259

00:14:33.004 --> 00:14:35.332 however, head and neck cancers are

NOTE Confidence: 0.858522909259259

00:14:35.332 --> 00:14:37.480 easily treated and highly curable.

NOTE Confidence: 0.858522909259259

00:14:37.480 --> 00:14:39.472 Clinical trials are currently

NOTE Confidence: 0.858522909259259

00:14:39.472 --> 00:14:41.464 underway at federally designated

NOTE Confidence: 0.858522909259259

00:14:41.464 --> 00:14:43.000 comprehensive cancer centers,

NOTE Confidence: 0.858522909259259

00:14:43.000 --> 00:14:44.940 such as Yale Cancer Center

NOTE Confidence: 0.858522909259259

00:14:44.940 --> 00:14:46.880 and Smilow Cancer Hospital,

NOTE Confidence: 0.858522909259259

00:14:46.880 --> 00:14:48.780 to test innovative new treatments

NOTE Confidence: 0.858522909259259

00:14:48.780 --> 00:14:50.680 for head and neck cancers.

NOTE Confidence: 0.858522909259259

00:14:50.680 --> 00:14:52.680 Yale Cancer Center was recently

NOTE Confidence: 0.858522909259259

00:14:52.680 --> 00:14:54.680 awarded grants from the National

NOTE Confidence: 0.858522909259259

00:14:54.743 --> 00:14:56.969 Institutes of Health to fund the Yale

NOTE Confidence: 0.858522909259259

00:14:56.969 --> 00:14:59.036 Head and Neck Cancer Specialized

NOTE Confidence: 0.858522909259259

00:14:59.036 --> 00:15:01.120 Program of Research Excellence,

NOTE Confidence: 0.858522909259259

00:15:01.120 --> 00:15:01.926 or SPORE,

NOTE Confidence: 0.858522909259259

00:15:01.926 --> 00:15:03.941 to address critical barriers to

NOTE Confidence: 0.858522909259259

00:15:03.941 --> 00:15:06.863 treatment of head and neck squamous cell

NOTE Confidence: 0.858522909259259

00:15:06.863 --> 00:15:09.323 carcinoma due to resistance to immune

NOTE Confidence: 0.858522909259259

00:15:09.395 --> 00:15:11.720 DNA damaging and targeted therapy.

NOTE Confidence: 0.858522909259259

00:15:11.720 --> 00:15:14.120 More information is available

NOTE Confidence: 0.858522909259259

00:15:14.120 --> 00:15:15.171 at yalecancercenter.org.

NOTE Confidence: 0.858522909259259

00:15:15.171 --> 00:15:17.877 You're listening to Connecticut Public Radio.

NOTE Confidence: 0.961839495

00:15:18.960 --> 00:15:21.120 Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.961839495

00:15:21.120 --> 00:15:23.046 This is Doctor Anees Chagpar and

NOTE Confidence: 0.961839495

00:15:23.046 --> 00:15:24.920 I'm joined tonight by my guest,

NOTE Confidence: 0.961839495

00:15:24.920 --> 00:15:26.078 Doctor Samuel Katz.

NOTE Confidence: 0.961839495

00:15:26.078 --> 00:15:28.780 We're talking about the role of pathology

NOTE Confidence: 0.961839495

00:15:28.849 --> 00:15:31.313 and some new research into CAR T cells,

NOTE Confidence: 0.961839495

00:15:31.320 --> 00:15:33.150 but now for a new indication

NOTE Confidence: 0.961839495

00:15:33.150 --> 00:15:34.370 and that's really metastatic

NOTE Confidence: 0.961839495

00:15:34.431 --> 00:15:36.039 triple negative breast cancer.

NOTE Confidence: 0.961839495

00:15:36.040 --> 00:15:36.712 So Doctor Katz,

NOTE Confidence: 0.961839495

00:15:36.712 --> 00:15:38.938 I want to go back to something you were

NOTE Confidence: 0.961839495

00:15:38.938 --> 00:15:40.438 mentioning right before the break,

NOTE Confidence: 0.961839495

00:15:40.440 --> 00:15:43.440 which is how traditional immunotherapies,

NOTE Confidence: 0.961839495

00:15:43.440 --> 00:15:45.360 these checkpoint inhibitors which

NOTE Confidence: 0.961839495

00:15:45.360 --> 00:15:48.682 we now use in triple negative breast

NOTE Confidence: 0.961839495

00:15:48.682 --> 00:15:51.188 cancer really kind of get rid of

NOTE Confidence: 0.961839495

00:15:51.188 --> 00:15:53.817 a brake as you phrased it in

NOTE Confidence: 0.961839495

00:15:53.817 --> 00:15:55.926 terms of T cell killing.

NOTE Confidence: 0.961839495

00:15:55.926 --> 00:15:58.584 Because we know that certain cancer

NOTE Confidence: 0.961839495

00:15:58.584 --> 00:16:00.448 cells, especially triple negative

NOTE Confidence: 0.961839495

00:16:00.448 --> 00:16:04.210 cancer cells, may kind of put a

NOTE Confidence: 0.961839495

00:16:04.210 --> 00:16:07.304 brake on those T cells to

NOTE Confidence: 0.961839495

00:16:07.304 --> 00:16:09.034 kill off these cancer cells.

NOTE Confidence: 0.961839495

00:16:09.040 --> 00:16:11.600 And so traditional immunotherapies

NOTE Confidence: 0.961839495

00:16:11.600 --> 00:16:15.666 will remove that brake your car T

NOTE Confidence: 0.961839495

00:16:15.666 --> 00:16:18.678 therapy is more like an accelerator

NOTE Confidence: 0.961839495

00:16:18.680 --> 00:16:22.480 finding a new target on these T

NOTE Confidence: 0.961839495

00:16:22.480 --> 00:16:26.240 cells to attack cancer

NOTE Confidence: 0.961839495

00:16:26.240 --> 00:16:28.240 cells in a different way.

NOTE Confidence: 0.961839495

00:16:28.240 --> 00:16:31.840 So kind of like putting on an accelerator.

NOTE Confidence: 0.961839495

00:16:31.840 --> 00:16:36.100 My question is how do those two work

NOTE Confidence: 0.961839495

00:16:36.100 --> 00:16:38.520 together or is there an interplay?

NOTE Confidence: 0.961839495

00:16:38.520 --> 00:16:39.592 Thinking about, you know,

NOTE Confidence: 0.961839495

00:16:39.592 --> 00:16:40.396 driving a car,

NOTE Confidence: 0.961839495

00:16:40.400 --> 00:16:42.848 if you step on the gas while you're

NOTE Confidence: 0.961839495

00:16:42.848 --> 00:16:44.278 still got a brake on,

NOTE Confidence: 0.961839495

00:16:44.280 --> 00:16:46.680 it generally doesn't work very well.

NOTE Confidence: 0.961839495

00:16:46.680 --> 00:16:48.552 Can you talk a little bit more about that?

NOTE Confidence: 0.967997546666667

00:16:48.880 --> 00:16:51.718 Absolutely. And I think that's why,

NOTE Confidence: 0.967997546666667

00:16:51.720 --> 00:16:53.840 as you kind of suggested,

NOTE Confidence: 0.967997546666667

00:16:53.840 --> 00:16:58.452 the combination of this might be very useful.

NOTE Confidence: 0.967997546666667

00:16:58.452 --> 00:17:01.985 Because while if you're just

NOTE Confidence: 0.967997546666667

00:17:01.985 --> 00:17:04.190 releasing your foot off the brake by

NOTE Confidence: 0.967997546666667

00:17:04.257 --> 00:17:06.357 using these checkpoint inhibitors,

NOTE Confidence: 0.967997546666667

00:17:06.360 --> 00:17:07.878 if you don't have something driving,

NOTE Confidence: 0.967997546666667

00:17:07.880 --> 00:17:09.485 if there isn't a mutant

NOTE Confidence: 0.967997546666667

00:17:09.485 --> 00:17:11.600 antigen for you to go after,

NOTE Confidence: 0.967997546666667

00:17:11.600 --> 00:17:13.280 then the car won't move forward,

NOTE Confidence: 0.967997546666667

00:17:13.280 --> 00:17:15.520 the T cell won't kill.

NOTE Confidence: 0.967997546666667

00:17:15.520 --> 00:17:16.878 On the other hand, like you said,

NOTE Confidence: 0.967997546666667

00:17:16.880 --> 00:17:19.840 if the CAR T cell is engineered so that it

NOTE Confidence: 0.967997546666667

00:17:19.910 --> 00:17:22.798 is always pressing on the gas pedal yet,

NOTE Confidence: 0.967997546666667

00:17:22.800 --> 00:17:23.920 it might try going forward.

NOTE Confidence: 0.967997546666667

00:17:23.920 --> 00:17:25.996 But if you have that brake

NOTE Confidence: 0.967997546666667

00:17:25.996 --> 00:17:27.840 present at the same time,

NOTE Confidence: 0.967997546666667

00:17:27.840 --> 00:17:30.199 then it's it won't be able to.

NOTE Confidence: 0.967997546666667

00:17:30.200 --> 00:17:32.366 But if you can manipulate the

NOTE Confidence: 0.967997546666667

00:17:32.366 --> 00:17:34.626 cell in ways that many people

NOTE Confidence: 0.967997546666667

00:17:34.626 --> 00:17:37.195 are, to kind of combine the two,

NOTE Confidence: 0.967997546666667

00:17:37.200 --> 00:17:39.620 then perhaps we could get

NOTE Confidence: 0.967997546666667

00:17:39.620 --> 00:17:42.040 the full benefit of this.

NOTE Confidence: 0.967997546666667

00:17:42.040 --> 00:17:45.600 I also want to bring up one other

NOTE Confidence: 0.967997546666667

00:17:45.600 --> 00:17:47.080 thing that you had

NOTE Confidence: 0.967997546666667

00:17:47.080 --> 00:17:48.744 mentioned before the break,

NOTE Confidence: 0.967997546666667

00:17:48.744 --> 00:17:51.240 which is kind of getting towards

NOTE Confidence: 0.967997546666667

00:17:51.309 --> 00:17:53.249 the difference between solid

NOTE Confidence: 0.967997546666667

00:17:53.249 --> 00:17:55.674 tumors like triple negative breast

NOTE Confidence: 0.967997546666667

00:17:55.674 --> 00:17:58.280 cancer and the blood tumors where

NOTE Confidence: 0.967997546666667

00:17:58.280 --> 00:18:01.040 CAR T's have worked so well.

NOTE Confidence: 0.967997546666667

00:18:01.040 --> 00:18:03.698 Solid tumors have remained a

NOTE Confidence: 0.967997546666667

00:18:03.698 --> 00:18:06.688 real challenge for the CAR T field

NOTE Confidence: 0.967997546666667

00:18:06.688 --> 00:18:08.956 to be able to work efficiently.

NOTE Confidence: 0.967997546666667

00:18:08.960 --> 00:18:11.660 And that's because they create

NOTE Confidence: 0.967997546666667

00:18:11.660 --> 00:18:14.096 this tumor microenvironment that

NOTE Confidence: 0.967997546666667

00:18:14.096 --> 00:18:16.624 kind of quells the T cell,

NOTE Confidence: 0.967997546666667

00:18:16.624 --> 00:18:19.476 some of which might be to increase the

NOTE Confidence: 0.967997546666667

00:18:19.476 --> 00:18:22.116 brake like we've been talking about.

NOTE Confidence: 0.967997546666667

00:18:22.120 --> 00:18:24.696 Another way is you can imagine that

NOTE Confidence: 0.967997546666667

00:18:24.696 --> 00:18:27.752 the car won't do so well if you're

NOTE Confidence: 0.967997546666667

00:18:27.752 --> 00:18:30.160 always pressing the gas pedal right.

NOTE Confidence: 0.967997546666667

00:18:30.160 --> 00:18:31.996 You'll run out of gas eventually.

NOTE Confidence: 0.967997546666667

00:18:32.000 --> 00:18:34.376 And a lot of the CAR T designs

NOTE Confidence: 0.967997546666667

00:18:34.376 --> 00:18:36.881 in the past have this problem

NOTE Confidence: 0.967997546666667

00:18:36.881 --> 00:18:39.166 where you're always pushing on

NOTE Confidence: 0.967997546666667

00:18:39.166 --> 00:18:41.717 the gas even when you're not,

NOTE Confidence: 0.967997546666667

00:18:41.720 --> 00:18:42.836 when you don't want it to,

NOTE Confidence: 0.967997546666667

00:18:42.840 --> 00:18:46.319 when you don't have that target in sight.

NOTE Confidence: 0.967997546666667

00:18:46.320 --> 00:18:46.664 Fortunately,

NOTE Confidence: 0.967997546666667

00:18:46.664 --> 00:18:49.760 some work in the lab by Po Han Chen,

NOTE Confidence: 0.967997546666667

00:18:49.760 --> 00:18:51.128 another physician scientist who's

NOTE Confidence: 0.967997546666667

00:18:51.128 --> 00:18:52.838 been working on this problem,

NOTE Confidence: 0.967997546666667

00:18:52.840 --> 00:18:54.597 came up with a new design towards

NOTE Confidence: 0.967997546666667

00:18:54.597 --> 00:18:56.854 our car to make it so that it only

NOTE Confidence: 0.967997546666667

00:18:56.854 --> 00:18:58.958 presses on the gas when we want it to.

NOTE Confidence: 0.966690460909091

00:19:00.400 --> 00:19:00.866 That's interesting.

NOTE Confidence: 0.966690460909091

00:19:00.866 --> 00:19:03.000 Can you tell us a bit more about that?

NOTE Confidence: 0.966690460909091

00:19:03.000 --> 00:19:05.634 I mean, one would think that

NOTE Confidence: 0.966690460909091

00:19:05.634 --> 00:19:08.160 if there wasn't a target,

NOTE Confidence: 0.966690460909091

00:19:08.160 --> 00:19:10.116 but the T cells really wouldn't

NOTE Confidence: 0.966690460909091

00:19:10.116 --> 00:19:12.099 have anything to go after and

NOTE Confidence: 0.966690460909091

00:19:12.099 --> 00:19:14.248 so they would just be kind of

NOTE Confidence: 0.966690460909091

00:19:14.248 --> 00:19:16.067 floating around looking for that

NOTE Confidence: 0.966690460909091

00:19:16.067 --> 00:19:17.877 target if it should appear.

NOTE Confidence: 0.966690460909091

00:19:17.880 --> 00:19:20.248 So how do you turn on and turn

NOTE Confidence: 0.966690460909091

00:19:20.248 --> 00:19:22.704 off these T cells so that they

NOTE Confidence: 0.966690460909091

00:19:22.704 --> 00:19:24.484 don't get overly active

NOTE Confidence: 0.966690460909091

00:19:24.561 --> 00:19:26.637 and exhausted as you put it?

NOTE Confidence: 0.971472152

00:19:26.880 --> 00:19:29.040 Yeah, that's a great question.

NOTE Confidence: 0.971472152

00:19:29.040 --> 00:19:30.840 And I think what we have to remember

NOTE Confidence: 0.971472152

00:19:30.840 --> 00:19:32.677 is when we're putting in this car,

NOTE Confidence: 0.971472152

00:19:32.680 --> 00:19:35.228 this chimeric antigen receptor,

NOTE Confidence: 0.971472152

00:19:35.228 --> 00:19:38.413 it's really a man made

NOTE Confidence: 0.971472152

00:19:38.413 --> 00:19:40.480 Frankenstein type molecule.

NOTE Confidence: 0.971472152

00:19:40.480 --> 00:19:44.176 It hasn't been engineered by nature over

NOTE Confidence: 0.971472152

00:19:44.176 --> 00:19:47.360 you know millions of years of evolution.

NOTE Confidence: 0.971472152

00:19:47.360 --> 00:19:49.369 It's something that we've come up with

NOTE Confidence: 0.971472152

00:19:49.369 --> 00:19:52.105 and made in the lab and so therefore

NOTE Confidence: 0.971472152

00:19:52.105 --> 00:19:53.915 it doesn't work necessarily perfectly.

NOTE Confidence: 0.971472152

00:19:53.920 --> 00:19:56.270 We've taken snippets of different

NOTE Confidence: 0.971472152

00:19:56.270 --> 00:19:59.433 proteins and put them together and a

NOTE Confidence: 0.971472152

00:19:59.433 --> 00:20:02.002 normal receptor that's on the cell will

NOTE Confidence: 0.971472152

00:20:02.002 --> 00:20:04.544 only single to have its downstream

NOTE Confidence: 0.971472152

00:20:04.544 --> 00:20:07.016 effects when it engages its target.

NOTE Confidence: 0.971472152

00:20:07.016 --> 00:20:08.520 But these

NOTE Confidence: 0.971472152

00:20:08.520 --> 00:20:10.640 CARs that we've made ourselves,

NOTE Confidence: 0.971472152

00:20:10.640 --> 00:20:12.600 they have a little leakiness to them,

NOTE Confidence: 0.971472152

00:20:12.600 --> 00:20:14.295 many of them.

NOTE Confidence: 0.971472152

00:20:14.295 --> 00:20:16.555 And that leads to

NOTE Confidence: 0.971472152

00:20:16.560 --> 00:20:18.160 what we call tonic singling,

NOTE Confidence: 0.971472152

00:20:18.160 --> 00:20:20.020 singling all the time or pressing

NOTE Confidence: 0.971472152

00:20:20.020 --> 00:20:22.120 on that gas pedal all the time.

NOTE Confidence: 0.971472152

00:20:22.120 --> 00:20:25.529 And Po Han has realized that one of

NOTE Confidence: 0.971472152

00:20:25.529 --> 00:20:28.086 those domains could be optimized

NOTE Confidence: 0.971472152

00:20:28.086 --> 00:20:30.596 to help reduce that issue.

NOTE Confidence: 0.971472152

00:20:30.600 --> 00:20:32.454 And I think that's going to

NOTE Confidence: 0.971472152

00:20:32.454 --> 00:20:34.515 be really critical for when we

NOTE Confidence: 0.971472152

00:20:34.515 --> 00:20:36.039 start targeting solid tumors.

NOTE Confidence: 0.836603688333333

00:20:37.080 --> 00:20:39.198 And so when you say optimized,

NOTE Confidence: 0.836603688333333

00:20:39.200 --> 00:20:42.400 do you mean like it's kind of got

NOTE Confidence: 0.836603688333333

00:20:42.400 --> 00:20:46.706 a way that it it learns when to

NOTE Confidence: 0.836603688333333

00:20:46.706 --> 00:20:48.477 turn on and when to turn off?

NOTE Confidence: 0.836603688333333

00:20:48.480 --> 00:20:50.930 Because presumably you want the thing to

NOTE Confidence: 0.836603688333333

00:20:50.930 --> 00:20:53.838 to turn on when there is that target,

NOTE Confidence: 0.836603688333333

00:20:53.840 --> 00:20:55.744 and you want it to go full speed

NOTE Confidence: 0.836603688333333

00:20:55.744 --> 00:20:57.240 ahead and kill that target.

NOTE Confidence: 0.836603688333333

00:20:57.240 --> 00:20:58.596 And when the target isn't there,

NOTE Confidence: 0.836603688333333

00:20:58.600 --> 00:21:00.210 well, then you want it to conserve

NOTE Confidence: 0.836603688333333

00:21:00.210 --> 00:21:01.798 its energy and lay low for a bit?

NOTE Confidence: 0.964970972

00:21:02.440 --> 00:21:06.096 So looking at the actual structure

NOTE Confidence: 0.964970972

00:21:06.096 --> 00:21:10.352 or the presumed structure of the molecule,

NOTE Confidence: 0.964970972

00:21:10.360 --> 00:21:13.904 we hypothesized that they

NOTE Confidence: 0.964970972

00:21:13.904 --> 00:21:16.378 might be coming together.

NOTE Confidence: 0.964970972

00:21:16.378 --> 00:21:18.123 So the singling usually occurs

NOTE Confidence: 0.964970972

00:21:18.123 --> 00:21:20.515 when you get more than one of

NOTE Confidence: 0.964970972

00:21:20.515 --> 00:21:21.795 these CARs coming together,

NOTE Confidence: 0.964970972

00:21:21.800 --> 00:21:23.720 being brought together and that's

NOTE Confidence: 0.964970972

00:21:23.720 --> 00:21:25.640 what happens when it engages

NOTE Confidence: 0.964970972

00:21:25.702 --> 00:21:27.556 its target on the other cells.

NOTE Confidence: 0.964970972

00:21:27.560 --> 00:21:30.920 And so by changing one of those domains

NOTE Confidence: 0.964970972

00:21:30.920 --> 00:21:34.769 that we thought was leading to that

NOTE Confidence: 0.964970972

00:21:34.769 --> 00:21:37.679 aggregation and that baseline single,

NOTE Confidence: 0.964970972

00:21:37.680 --> 00:21:40.431 we were able to decrease that baseline

NOTE Confidence: 0.964970972

00:21:40.431 --> 00:21:43.228 singling and make it so that it only

NOTE Confidence: 0.964970972

00:21:43.228 --> 00:21:45.250 signals when it really is being

NOTE Confidence: 0.964970972

00:21:45.250 --> 00:21:47.668 brought together by the antigen on

NOTE Confidence: 0.964970972

00:21:47.668 --> 00:21:50.426 the other cell and not when it's

NOTE Confidence: 0.964970972

00:21:50.426 --> 00:21:52.800 existing on its own in the T cell.

00:21:53.080 --> 00:21:55.280 The other question that I

NOTE Confidence: 0.889925321428571

00:21:55.280 --> 00:21:57.584 have for you is you mentioned that one

NOTE Confidence: 0.889925321428571

00:21:57.584 --> 00:22:00.028 of the things that makes solid tumors

NOTE Confidence: 0.889925321428571

00:22:00.028 --> 00:22:02.118 tricky is this tumor microenvironment.

NOTE Confidence: 0.889925321428571

00:22:02.120 --> 00:22:03.956 The fact that

NOTE Confidence: 0.889925321428571

00:22:03.960 --> 00:22:06.739 the cancers know how to make an

NOTE Confidence: 0.889925321428571

00:22:06.739 --> 00:22:08.355 environment around themselves that's

NOTE Confidence: 0.889925321428571

00:22:08.355 --> 00:22:10.503 very comfortable for the cancer cells

NOTE Confidence: 0.889925321428571

00:22:10.503 --> 00:22:13.048 to grow in and not so comfortable

NOTE Confidence: 0.889925321428571

00:22:13.048 --> 00:22:15.154 for anything else to kill them.

NOTE Confidence: 0.889925321428571

00:22:15.160 --> 00:22:18.430 But in thinking about CAR T

NOTE Confidence: 0.889925321428571

00:22:18.430 --> 00:22:20.640 therapy and blood cancers,

NOTE Confidence: 0.889925321428571

00:22:20.640 --> 00:22:23.440 you know when you think

NOTE Confidence: 0.889925321428571

00:22:23.440 --> 00:22:25.120 about metastatic disease,

NOTE Confidence: 0.889925321428571

00:22:25.120 --> 00:22:28.516 really there is potentially a way

NOTE Confidence: 0.889925321428571

00:22:28.516 --> 00:22:32.039 to think about solid tumors that

NOTE Confidence: 0.889925321428571

00:22:32.040 --> 00:22:34.399 maybe like a blood tumor in the

NOTE Confidence: 0.889925321428571

00:22:34.399 --> 00:22:36.423 sense that when they're metastatic

NOTE Confidence: 0.889925321428571

00:22:36.423 --> 00:22:39.692 you're really trying to get at the

NOTE Confidence: 0.889925321428571

00:22:39.692 --> 00:22:42.312 circulating tumor cells and

NOTE Confidence: 0.889925321428571

00:22:42.312 --> 00:22:44.392 the disease that isn't necessarily

NOTE Confidence: 0.889925321428571

00:22:44.400 --> 00:22:47.720 in a particular solid organ.

NOTE Confidence: 0.889925321428571

00:22:47.720 --> 00:22:49.876 Can you talk a little bit about that, is

00:22:50.800 --> 00:22:53.428 CAR T therapy particularly good

NOTE Confidence: 0.889925321428571

00:22:53.428 --> 00:22:55.762 for metastatic disease and

NOTE Confidence: 0.889925321428571

00:22:55.762 --> 00:22:58.277 reducing the circulating tumor burden?

NOTE Confidence: 0.96172436

00:22:58.600 --> 00:22:59.730 Yeah, absolutely.

NOTE Confidence: 0.96172436

00:22:59.730 --> 00:23:04.720 So as I was mentioning the CD 19

NOTE Confidence: 0.96172436

00:23:04.720 --> 00:23:08.971 CAR that targets B cell leukemias,

NOTE Confidence: 0.96172436

00:23:08.971 --> 00:23:11.439 that one works phenomenal.

NOTE Confidence: 0.96172436

00:23:11.440 --> 00:23:13.195 It doesn't have any of

NOTE Confidence: 0.96172436

00:23:13.200 --> 00:23:15.902 the tonic singling that we were just

NOTE Confidence: 0.96172436

00:23:15.902 --> 00:23:18.520 talking about it is a great target.

NOTE Confidence: 0.96172436

00:23:18.520 --> 00:23:21.299 It's all in the bloodstream and

NOTE Confidence: 0.96172436

00:23:21.299 --> 00:23:23.719 patients do very well with that.

NOTE Confidence: 0.96172436

00:23:23.720 --> 00:23:26.558 Just underneath that there are so-called

NOTE Confidence: 0.96172436

00:23:26.558 --> 00:23:29.878 B cell lymphomas which take up residence.

NOTE Confidence: 0.96172436

00:23:29.880 --> 00:23:32.080 They form more of a mass as opposed

NOTE Confidence: 0.96172436

00:23:32.080 --> 00:23:34.268 to just being circulating through

NOTE Confidence: 0.96172436

00:23:34.268 --> 00:23:36.452 the bloodstream that they also can

NOTE Confidence: 0.96172436

00:23:36.452 --> 00:23:39.074 use the CD 19 CAR and they do OK,

NOTE Confidence: 0.96172436

00:23:39.074 --> 00:23:41.198 not as well as the leukemias

NOTE Confidence: 0.96172436

00:23:41.198 --> 00:23:42.640 with that CD19 CAR,

NOTE Confidence: 0.96172436

00:23:42.640 --> 00:23:45.322 but still somewhat OK and part

NOTE Confidence: 0.96172436

00:23:45.322 --> 00:23:48.208 of that is probably this tumor

NOTE Confidence: 0.96172436

00:23:48.208 --> 00:23:50.800 microenvironment that's created there.

NOTE Confidence: 0.96172436

00:23:50.800 --> 00:23:53.712 Now one of the best reasons to use

NOTE Confidence: 0.96172436

00:23:53.712 --> 00:23:55.874 the T cell to deliver these

NOTE Confidence: 0.96172436

00:23:55.874 --> 00:23:59.026 CAR T cells is that the T cells seek

NOTE Confidence: 0.96172436

00:23:59.026 --> 00:24:00.906 out and destroy these metastases

NOTE Confidence: 0.96172436

00:24:00.979 --> 00:24:02.999 that are throughout the body.

NOTE Confidence: 0.96172436

00:24:03.000 --> 00:24:05.508 There are molecules that kind of

NOTE Confidence: 0.96172436

00:24:05.508 --> 00:24:08.603 tell them to look within these areas

NOTE Confidence: 0.96172436

00:24:08.603 --> 00:24:11.688 and it gets them places where other

NOTE Confidence: 0.96172436

00:24:11.688 --> 00:24:14.136 less smart drugs might not realize

NOTE Confidence: 0.96172436

00:24:14.136 --> 00:24:17.120 how to get to or where to go.

NOTE Confidence: 0.96172436

00:24:17.120 --> 00:24:20.095 And so improving CAR T cells ability

NOTE Confidence: 0.96172436

00:24:20.095 --> 00:24:23.320 to find these metastases is another

NOTE Confidence: 0.96172436

00:24:23.320 --> 00:24:25.800 active area of investigation.

NOTE Confidence: 0.96172436

00:24:25.800 --> 00:24:26.738 In fact,

NOTE Confidence: 0.96172436

00:24:26.738 --> 00:24:29.552 we have a collaboration with another

NOTE Confidence: 0.96172436

00:24:29.552 --> 00:24:31.777 senior professor John Morrow in

NOTE Confidence: 0.96172436

00:24:31.777 --> 00:24:34.584 determining ways of how we can improve

NOTE Confidence: 0.96172436

00:24:34.666 --> 00:24:36.997 the T cells ability to traffic

NOTE Confidence: 0.96172436

00:24:36.997 --> 00:24:39.280 to get to where they're going.

NOTE Confidence: 0.96172436

00:24:39.280 --> 00:24:41.080 And then once they're there,

NOTE Confidence: 0.96172436

00:24:41.080 --> 00:24:43.600 they have to then face this

NOTE Confidence: 0.96172436

00:24:43.600 --> 00:24:45.116 kind of a barrier,

NOTE Confidence: 0.96172436

00:24:45.116 --> 00:24:46.632 this impenetrable barrier that

NOTE Confidence: 0.96172436

00:24:46.632 --> 00:24:48.997 the tumor kind of forms this wall.

NOTE Confidence: 0.96172436

00:24:49.000 --> 00:24:51.121 And so there are other ways that

NOTE Confidence: 0.96172436

00:24:51.121 --> 00:24:53.074 people are designing to equip the T

NOTE Confidence: 0.96172436

00:24:53.074 --> 00:24:54.887 cells to kind of get through that

NOTE Confidence: 0.96172436

00:24:54.887 --> 00:24:56.840 barrier a little better.

NOTE Confidence: 0.904436884

00:24:57.680 --> 00:25:00.134 You know as you mentioned thinking

NOTE Confidence: 0.904436884

00:25:00.134 --> 00:25:02.396 about metastatic sites and so

NOTE Confidence: 0.904436884

00:25:02.396 --> 00:25:04.596 on and the ability for T cells

NOTE Confidence: 0.904436884

00:25:04.669 --> 00:25:07.054 potentially to navigate through these

NOTE Confidence: 0.904436884

00:25:07.054 --> 00:25:09.439 barriers better than other drugs.

NOTE Confidence: 0.904436884

00:25:09.440 --> 00:25:11.744 It makes you think about things

NOTE Confidence: 0.904436884

00:25:11.744 --> 00:25:13.749 that have been historically very

NOTE Confidence: 0.904436884

00:25:13.749 --> 00:25:16.131 difficult for us to treat with

NOTE Confidence: 0.904436884

00:25:16.131 --> 00:25:18.162 standard chemotherapy and that's kind

NOTE Confidence: 0.904436884

00:25:18.162 --> 00:25:20.466 of getting to brain metastases and

NOTE Confidence: 0.904436884

00:25:20.466 --> 00:25:22.680 getting past the blood brain barrier.

NOTE Confidence: 0.904436884

00:25:22.680 --> 00:25:24.480 But earlier before the break,

NOTE Confidence: 0.904436884

00:25:24.480 --> 00:25:28.500 you were talking about some neurotoxicity

NOTE Confidence: 0.904436884

00:25:28.500 --> 00:25:30.932 associated with these newer therapies.

NOTE Confidence: 0.904436884

00:25:30.932 --> 00:25:33.116 Can you talk a little bit

NOTE Confidence: 0.904436884

00:25:33.116 --> 00:25:35.038 about whether CAR T therapy,

NOTE Confidence: 0.904436884

00:25:35.040 --> 00:25:37.158 you envisage this really having a

NOTE Confidence: 0.904436884

00:25:37.158 --> 00:25:39.896 role to play in in brain metastases

NOTE Confidence: 0.904436884

00:25:39.896 --> 00:25:42.392 and how exactly that would work?

NOTE Confidence: 0.957833628

00:25:42.960 --> 00:25:46.240 Yeah, absolutely. So interestingly enough,

NOTE Confidence: 0.957833628

00:25:46.240 --> 00:25:49.624 some of those original patients that

NOTE Confidence: 0.957833628

00:25:49.624 --> 00:25:52.568 had leukemias or blood lymphomas wound

NOTE Confidence: 0.957833628

00:25:52.568 --> 00:25:55.064 up having disease within their brain

NOTE Confidence: 0.957833628

00:25:55.064 --> 00:25:57.971 and it was found that the CAR T cells

NOTE Confidence: 0.957833628

00:25:57.971 --> 00:26:00.563 were making were actually

NOTE Confidence: 0.957833628

00:26:00.563 --> 00:26:03.110 fighting off the disease that was there.

NOTE Confidence: 0.957833628

00:26:03.110 --> 00:26:05.315 So I think the potential is possible

NOTE Confidence: 0.957833628

00:26:05.320 --> 00:26:07.186 and it's not quite understood yet

NOTE Confidence: 0.957833628

00:26:07.186 --> 00:26:09.309 whether they were able to get in

NOTE Confidence: 0.957833628

00:26:09.309 --> 00:26:10.941 because the blood brain barrier that

NOTE Confidence: 0.957833628

00:26:10.941 --> 00:26:13.244 we talked about was disrupted a little

NOTE Confidence: 0.957833628

00:26:13.244 --> 00:26:15.254 bit because the disease was already

NOTE Confidence: 0.957833628

00:26:15.254 --> 00:26:17.683 there or whether the CAR T cells

NOTE Confidence: 0.957833628

00:26:17.683 --> 00:26:20.455 are able to even in a completely

NOTE Confidence: 0.957833628

00:26:20.455 --> 00:26:22.599 intact blood vein barrier get in.

NOTE Confidence: 0.957833628

00:26:22.600 --> 00:26:24.904 But I think there's certainly is

NOTE Confidence: 0.957833628

00:26:24.904 --> 00:26:27.289 the potential and there have been

NOTE Confidence: 0.957833628

00:26:27.289 --> 00:26:29.239 several studies since then trying

NOTE Confidence: 0.957833628

00:26:29.239 --> 00:26:31.050 to target not just hematopoietic

NOTE Confidence: 0.957833628

00:26:31.050 --> 00:26:33.080 tumors that make it to the brain,

NOTE Confidence: 0.957833628

00:26:33.080 --> 00:26:34.562 but also solid tumors that have

NOTE Confidence: 0.957833628

00:26:34.562 --> 00:26:36.360 made it to the brain as well.

NOTE Confidence: 0.957833628

00:26:36.360 --> 00:26:39.600 In addition to brain tumors themselves,

NOTE Confidence: 0.957833628

00:26:39.600 --> 00:26:41.637 where there are different CARs that people

NOTE Confidence: 0.957833628

00:26:41.637 --> 00:26:43.476 have been developing in order to do that.

NOTE Confidence: 0.957833628

00:26:43.480 --> 00:26:46.105 And there is some evidence of some

NOTE Confidence: 0.957833628

00:26:46.105 --> 00:26:48.799 efficacy still needs to be improved though.

NOTE Confidence: 0.6971146

00:26:49.320 --> 00:26:52.168 Yeah, you know the, it sounds like such

NOTE Confidence: 0.6971146

00:26:52.168 --> 00:26:54.880 a wonderful exciting new target,

NOTE Confidence: 0.6971146

00:26:54.880 --> 00:26:58.600 but I wonder about the downsides as well.

NOTE Confidence: 0.6971146

00:26:58.600 --> 00:27:01.096 So you know when we think about really

NOTE Confidence: 0.6971146

00:27:01.096 --> 00:27:03.631 turning on the immune system after having

NOTE Confidence: 0.6971146

00:27:03.631 --> 00:27:06.120 lived through the the COVID pandemic,

NOTE Confidence: 0.6971146

00:27:06.120 --> 00:27:08.888 many of us saw that there were some

NOTE Confidence: 0.6971146

00:27:08.888 --> 00:27:11.091 patients whose immune systems were turned

NOTE Confidence: 0.6971146

00:27:11.091 --> 00:27:14.400 on so much that you ended up with this

NOTE Confidence: 0.6971146

00:27:14.400 --> 00:27:17.280 immune storm and really that caused a

NOTE Confidence: 0.6971146

00:27:17.280 --> 00:27:19.986 lot of side effects for these patients.

NOTE Confidence: 0.6971146

00:27:19.986 --> 00:27:23.262 Would you expect the same kind

NOTE Confidence: 0.6971146

00:27:23.262 --> 00:27:25.584 of thing with CAR T therapy?

NOTE Confidence: 0.6971146

00:27:25.584 --> 00:27:28.209 I mean, it seems like it might be a

NOTE Confidence: 0.6971146

00:27:28.209 --> 00:27:30.360 balance between too much and too little.

NOTE Confidence: 0.6971146

00:27:30.360 --> 00:27:31.232 On the one hand,

NOTE Confidence: 0.6971146

00:27:31.232 --> 00:27:33.438 you don't want your T cells to get exhausted.

NOTE Confidence: 0.6971146

00:27:33.440 --> 00:27:36.152 On the other hand, you don't want them

NOTE Confidence: 0.6971146

00:27:36.152 --> 00:27:37.919 working too hard either,

NOTE Confidence: 0.6971146

00:27:37.920 --> 00:27:39.640 at the expense of toxicity.

NOTE Confidence: 0.904736560555556

00:27:40.080 --> 00:27:42.712 Absolutely. And this is one of the

NOTE Confidence: 0.904736560555556

00:27:42.712 --> 00:27:45.419 reasons why I really appreciate the

NOTE Confidence: 0.904736560555556

00:27:45.419 --> 00:27:48.400 wisdom of Sherman Weissman in devising

NOTE Confidence: 0.904736560555556

00:27:48.400 --> 00:27:51.280 and thinking about this RNA approach.

NOTE Confidence: 0.904736560555556

00:27:51.280 --> 00:27:54.752 So when you give a standard CAR therapy

NOTE Confidence: 0.904736560555556

00:27:54.752 --> 00:27:58.639 using the lentiviral type approach and DNA,

NOTE Confidence: 0.904736560555556

00:27:58.640 --> 00:28:01.055 you really don't have any control over

NOTE Confidence: 0.904736560555556

00:28:01.055 --> 00:28:04.160 those T cells and how much they proliferate,

NOTE Confidence: 0.904736560555556

00:28:04.160 --> 00:28:06.596 how long they stay around for,

NOTE Confidence: 0.904736560555556

00:28:06.600 --> 00:28:08.400 what kind of dosing you give.

NOTE Confidence: 0.904736560555556

00:28:08.400 --> 00:28:10.521 And if a patient winds up having

NOTE Confidence: 0.904736560555556

00:28:10.521 --> 00:28:12.360 some of these side effects,

NOTE Confidence: 0.904736560555556

00:28:12.360 --> 00:28:15.756 there's not much you can do.

NOTE Confidence: 0.904736560555556

00:28:15.760 --> 00:28:17.300 On the other hand,

NOTE Confidence: 0.904736560555556

00:28:17.300 --> 00:28:18.840 for the RNA approach,

NOTE Confidence: 0.904736560555556

00:28:18.840 --> 00:28:21.060 you can very precisely decide

NOTE Confidence: 0.904736560555556

00:28:21.060 --> 00:28:23.760 how much you're giving and when,

NOTE Confidence: 0.904736560555556

00:28:23.760 --> 00:28:26.014 and you can titrate that amount so

NOTE Confidence: 0.904736560555556

00:28:26.014 --> 00:28:28.990 that you can make it less if in order

NOTE Confidence: 0.904736560555556

00:28:28.990 --> 00:28:31.580 to not get into that territory where

NOTE Confidence: 0.904736560555556

00:28:31.662 --> 00:28:34.434 you get those types of side effects.

00:28:34.800 --> 00:28:37.285 Samuel Katz is an associate professor of

NOTE Confidence: 0.950761903571429

00:28:37.285 --> 00:28:39.917 pathology at the Yale School of Medicine.

NOTE Confidence: 0.950761903571429

00:28:39.920 --> 00:28:41.952 If you have questions,

NOTE Confidence: 0.950761903571429

00:28:41.952 --> 00:28:43.932 the address is canceranswers@yale.edu,

NOTE Confidence: 0.950761903571429

00:28:43.932 --> 00:28:46.644 and past additions of the program

NOTE Confidence: 0.950761903571429

00:28:46.644 --> 00:28:48.988 are available in audio and written

NOTE Confidence: 0.950761903571429

00:28:48.988 --> 00:28:49.892 form at yalecancercenter.org.

NOTE Confidence: 0.950761903571429

00:28:49.892 --> 00:28:52.520 We hope you'll join us next time to learn

NOTE Confidence: 0.950761903571429

00:28:52.570 --> 00:28:54.238 more about the fight against cancer.

NOTE Confidence: 0.950761903571429

00:28:54.240 --> 00:28:57.192 Funding for Yale Cancer Answers is

NOTE Confidence: 0.950761903571429

00:28:57.192 --> 00:29:00.000 provided by Smilow Cancer Hospital.