

WEBVTT

00:00:00.000 --> 00:00:02.148 Funding for Yale Cancer Answers is

NOTE Confidence: 0.807644968181818

00:00:02.148 --> 00:00:04.180 provided by Smilow Cancer Hospital.

NOTE Confidence: 0.735037619090909

00:00:06.680 --> 00:00:08.966 Welcome to Yale Cancer Answers with

NOTE Confidence: 0.735037619090909

00:00:08.966 --> 00:00:11.090 your host Doctor Anees Chagpar.

NOTE Confidence: 0.735037619090909

00:00:11.090 --> 00:00:12.925 Yale Cancer Answers features the

NOTE Confidence: 0.735037619090909

00:00:12.925 --> 00:00:15.184 latest information on cancer care by

NOTE Confidence: 0.735037619090909

00:00:15.184 --> 00:00:16.632 welcoming oncologists and specialists

NOTE Confidence: 0.735037619090909

00:00:16.632 --> 00:00:19.055 who are on the forefront of the

NOTE Confidence: 0.735037619090909

00:00:19.055 --> 00:00:20.946 battle to fight cancer. This week,

NOTE Confidence: 0.735037619090909

00:00:20.946 --> 00:00:23.274 it's a conversation about increasing an

NOTE Confidence: 0.735037619090909

00:00:23.274 --> 00:00:25.876 immune cells ability to target and kill

NOTE Confidence: 0.735037619090909

00:00:25.876 --> 00:00:28.010 cancer cells with Doctor Sidi Chen.

NOTE Confidence: 0.735037619090909

00:00:28.010 --> 00:00:30.201 Doctor Chen is an associate professor of

NOTE Confidence: 0.735037619090909

00:00:30.201 --> 00:00:32.549 genetics at the Yale School of Medicine,

NOTE Confidence: 0.735037619090909

00:00:32.550 --> 00:00:34.782 where Doctor Chagpar is a professor

NOTE Confidence: 0.735037619090909

00:00:34.782 --> 00:00:35.898 of surgical oncology.
NOTE Confidence: 0.888623945217391

00:00:37.160 --> 00:00:39.266 So Sidi maybe we can start off by you
NOTE Confidence: 0.888623945217391

00:00:39.266 --> 00:00:41.099 telling us a little bit more about
NOTE Confidence: 0.888623945217391

00:00:41.099 --> 00:00:42.730 yourself and what it is you do.
NOTE Confidence: 0.849436625

00:00:43.320 --> 00:00:46.264 So I'm a scientist by training and I
NOTE Confidence: 0.849436625

00:00:46.264 --> 00:00:49.917 got my PhD at the University of Chicago.
NOTE Confidence: 0.849436625

00:00:49.920 --> 00:00:53.436 I studied genetics and evolution and
NOTE Confidence: 0.849436625

00:00:53.436 --> 00:00:57.200 then I went to MIT studying cancer
NOTE Confidence: 0.849436625

00:00:57.200 --> 00:01:00.980 biology and that's when I got motivated
NOTE Confidence: 0.849436625

00:01:00.980 --> 00:01:03.745 to find future cures for cancer
NOTE Confidence: 0.849436625

00:01:03.745 --> 00:01:05.970 and benefit the broader population.
NOTE Confidence: 0.908014515

00:01:06.040 --> 00:01:07.270 So tell us a little bit.
NOTE Confidence: 0.908014515

00:01:07.270 --> 00:01:09.328 More about your research and how
NOTE Confidence: 0.908014515

00:01:09.328 --> 00:01:11.210 you're trying to cure cancer.
NOTE Confidence: 0.923294361666667

00:01:12.120 --> 00:01:14.124 I believe currently we are in
NOTE Confidence: 0.923294361666667

00:01:14.124 --> 00:01:16.819 a new era of cancer medicine.

NOTE Confidence: 0.923294361666667

00:01:16.820 --> 00:01:18.536 There are a number of new

NOTE Confidence: 0.923294361666667

00:01:18.536 --> 00:01:19.680 therapies on the horizon,

NOTE Confidence: 0.923294361666667

00:01:19.680 --> 00:01:22.588 including cancer immunotherapy,

NOTE Confidence: 0.923294361666667

00:01:22.588 --> 00:01:24.160 using immune checkpoints,

NOTE Confidence: 0.923294361666667

00:01:24.160 --> 00:01:26.800 and more recently on cell and gene therapy,

NOTE Confidence: 0.923294361666667

00:01:26.800 --> 00:01:29.600 and I think the future of medicine

NOTE Confidence: 0.923294361666667

00:01:29.600 --> 00:01:32.757 is the use of a variety of novel

NOTE Confidence: 0.923294361666667

00:01:32.760 --> 00:01:37.351 therapeutics for for the patients,

NOTE Confidence: 0.923294361666667

00:01:37.351 --> 00:01:39.536 and these novel therapeutics would

NOTE Confidence: 0.923294361666667

00:01:39.536 --> 00:01:42.528 have to be better than what we have.

NOTE Confidence: 0.923294361666667

00:01:42.530 --> 00:01:44.024 Today, for example,

NOTE Confidence: 0.923294361666667

00:01:44.024 --> 00:01:47.325 they have to overcome the disease

NOTE Confidence: 0.923294361666667

00:01:47.325 --> 00:01:52.155 resistance relapse and have to have

NOTE Confidence: 0.923294361666667

00:01:52.155 --> 00:01:56.496 better safety profiles and have more

NOTE Confidence: 0.923294361666667

00:01:56.496 --> 00:01:59.706 balanced efficacy and toxicity ratio.

NOTE Confidence: 0.923294361666667

00:01:59.710 --> 00:02:01.060 And I can keep going,
NOTE Confidence: 0.923294361666667

00:02:01.060 --> 00:02:03.436 but I think for our patients
NOTE Confidence: 0.923294361666667

00:02:03.436 --> 00:02:05.020 we need better jobs.
NOTE Confidence: 0.932714055454545

00:02:05.800 --> 00:02:07.702 Absolutely, I couldn't agree with you
NOTE Confidence: 0.932714055454545

00:02:07.702 --> 00:02:09.759 more tell us about your research and
NOTE Confidence: 0.932714055454545

00:02:09.759 --> 00:02:12.259 how you hope to do all of those things.
NOTE Confidence: 0.932714055454545

00:02:12.260 --> 00:02:14.770 I mean, certainly. I I,
NOTE Confidence: 0.932714055454545

00:02:14.770 --> 00:02:18.010 I think that those are all lofty goals.
NOTE Confidence: 0.932714055454545

00:02:18.010 --> 00:02:19.846 So how are you approaching this?
NOTE Confidence: 0.772538225555556

00:02:20.570 --> 00:02:23.729 Sure, I think no man can do it all.
NOTE Confidence: 0.772538225555556

00:02:23.730 --> 00:02:25.179 Neither can I.
NOTE Confidence: 0.772538225555556

00:02:25.179 --> 00:02:28.094 As a geneticist, I believe the
NOTE Confidence: 0.772538225555556

00:02:28.094 --> 00:02:30.534 true power of unbiased approach.
NOTE Confidence: 0.772538225555556

00:02:30.540 --> 00:02:33.836 All of us have the same genetic compositions.
NOTE Confidence: 0.772538225555556

00:02:33.840 --> 00:02:36.432 We all share the same genes in the genome.
NOTE Confidence: 0.772538225555556

00:02:36.440 --> 00:02:39.720 Of course there are variations.

NOTE Confidence: 0.772538225555556
00:02:39.720 --> 00:02:45.012 But my approach has been let
NOTE Confidence: 0.772538225555556
00:02:45.012 --> 00:02:48.036 nature tell us what is the right?
NOTE Confidence: 0.772538225555556
00:02:48.040 --> 00:02:50.204 Approach. Which means we.
NOTE Confidence: 0.772538225555556
00:02:50.204 --> 00:02:54.789 Tend to go brawl in survey the entire
NOTE Confidence: 0.772538225555556
00:02:54.789 --> 00:02:59.087 genome or survey full set of genetic
NOTE Confidence: 0.772538225555556
00:02:59.087 --> 00:03:01.787 composition to see which genes.
NOTE Confidence: 0.772538225555556
00:03:01.790 --> 00:03:04.694 If you take it out or if you
NOTE Confidence: 0.772538225555556
00:03:04.694 --> 00:03:07.702 turn it on would help our own
NOTE Confidence: 0.772538225555556
00:03:07.702 --> 00:03:10.167 selves fight cancer cells better.
NOTE Confidence: 0.772538225555556
00:03:10.170 --> 00:03:13.614 And we do so by performing unbiased
NOTE Confidence: 0.772538225555556
00:03:13.614 --> 00:03:16.059 genetic screens such as CRISPR,
NOTE Confidence: 0.772538225555556
00:03:16.060 --> 00:03:17.920 knockout, CRISPR activation screen
NOTE Confidence: 0.772538225555556
00:03:17.920 --> 00:03:20.710 to find the therapeutic target that
NOTE Confidence: 0.772538225555556
00:03:20.780 --> 00:03:23.036 can overcome some of the problems.
NOTE Confidence: 0.772538225555556
00:03:23.040 --> 00:03:25.044 I mentioned previously,
NOTE Confidence: 0.772538225555556

00:03:25.044 --> 00:03:26.380 for example,
NOTE Confidence: 0.772538225555556

00:03:26.380 --> 00:03:29.465 resistance to cancer killing or
NOTE Confidence: 0.772538225555556

00:03:29.465 --> 00:03:31.933 tumor infiltration or metabolism,
NOTE Confidence: 0.772538225555556

00:03:31.940 --> 00:03:35.951 and by doing these screens we will
NOTE Confidence: 0.772538225555556

00:03:35.951 --> 00:03:40.447 be able to see through a big pile
NOTE Confidence: 0.772538225555556

00:03:40.447 --> 00:03:43.950 of haystacks to find the small set
NOTE Confidence: 0.772538225555556

00:03:43.950 --> 00:03:47.660 of needles that allow us to improve
NOTE Confidence: 0.772538225555556

00:03:47.660 --> 00:03:50.096 the property of immune cells such
NOTE Confidence: 0.772538225555556

00:03:50.096 --> 00:03:52.763 as T cells and thereby intense.
NOTE Confidence: 0.772538225555556

00:03:52.763 --> 00:03:56.130 Of Therapeutic FC and reduce the toxicity.
NOTE Confidence: 0.854300536363636

00:03:56.240 --> 00:03:58.454 Delve a little bit more into
NOTE Confidence: 0.854300536363636

00:03:58.454 --> 00:04:00.240 the details of that CD.
NOTE Confidence: 0.854300536363636

00:04:00.240 --> 00:04:02.238 Tell us a little bit more
NOTE Confidence: 0.854300536363636

00:04:02.238 --> 00:04:04.676 about how you go through this
NOTE Confidence: 0.854300536363636

00:04:04.676 --> 00:04:07.226 haystack and find these needles.
NOTE Confidence: 0.854300536363636

00:04:07.230 --> 00:04:08.850 Defined for our audience

NOTE Confidence: 0.854300536363636

00:04:08.850 --> 00:04:10.470 what technologies you use.

NOTE Confidence: 0.854300536363636

00:04:10.470 --> 00:04:12.085 Not everybody might be aware

NOTE Confidence: 0.854300536363636

00:04:12.085 --> 00:04:13.700 of what exactly crisper is

NOTE Confidence: 0.854300536363636

00:04:13.763 --> 00:04:16.490 and how that works. Sure,

NOTE Confidence: 0.714286372

00:04:16.490 --> 00:04:18.870 let me slightly switch gears.

NOTE Confidence: 0.714286372

00:04:18.870 --> 00:04:21.792 CRISPR is not a technology from

NOTE Confidence: 0.714286372

00:04:21.792 --> 00:04:24.378 the gecko because it's actually

NOTE Confidence: 0.714286372

00:04:24.378 --> 00:04:27.624 an immune system of the bacteria.

NOTE Confidence: 0.714286372

00:04:27.630 --> 00:04:30.990 But then, as the human beings

NOTE Confidence: 0.714286372

00:04:30.990 --> 00:04:35.950 harness those tools, those natural.

NOTE Confidence: 0.714286372

00:04:35.950 --> 00:04:39.597 Component for fun bacteria to become genetic

NOTE Confidence: 0.714286372

00:04:39.597 --> 00:04:43.648 tools the beauty of CRISPR is that it can be.

NOTE Confidence: 0.714286372

00:04:43.650 --> 00:04:46.946 Very easy to use and can be precisely

NOTE Confidence: 0.714286372

00:04:46.946 --> 00:04:49.179 targeted and can be scalable.

NOTE Confidence: 0.714286372

00:04:49.180 --> 00:04:52.980 So what we are doing is to use CRISPR to

NOTE Confidence: 0.714286372

00:04:53.078 --> 00:04:56.876 manipulate the genes for the expression.
NOTE Confidence: 0.714286372

00:04:56.880 --> 00:05:00.640 For example, we can take out a gene,
NOTE Confidence: 0.714286372

00:05:00.640 --> 00:05:05.630 or we can turn on a gene and we can do so.
NOTE Confidence: 0.714286372

00:05:05.630 --> 00:05:10.394 Thousands or 10s of thousands at a time.
NOTE Confidence: 0.714286372

00:05:10.394 --> 00:05:11.530 For example,
NOTE Confidence: 0.714286372

00:05:11.530 --> 00:05:14.946 if there are 20,000 genes in our genome,
NOTE Confidence: 0.714286372

00:05:14.950 --> 00:05:18.898 we can turn. One at a time,
NOTE Confidence: 0.714286372

00:05:18.900 --> 00:05:20.988 but we do it all together.
NOTE Confidence: 0.714286372

00:05:20.990 --> 00:05:25.730 And it's like we enumerate each
NOTE Confidence: 0.714286372

00:05:25.730 --> 00:05:30.230 of the haystack and see by turning
NOTE Confidence: 0.714286372

00:05:30.230 --> 00:05:32.030 on each of the gene.
NOTE Confidence: 0.714286372

00:05:32.030 --> 00:05:34.326 Which genes would help our own cells
NOTE Confidence: 0.714286372

00:05:34.326 --> 00:05:35.310 kill cancer cell?
NOTE Confidence: 0.714286372

00:05:35.310 --> 00:05:35.760 Better?
NOTE Confidence: 0.714286372

00:05:35.760 --> 00:05:38.460 Because we're doing so many at
NOTE Confidence: 0.714286372

00:05:38.460 --> 00:05:41.489 once and the chances we finding

NOTE Confidence: 0.714286372

00:05:41.489 --> 00:05:44.663 those needles are much higher than.

NOTE Confidence: 0.714286372

00:05:44.670 --> 00:05:46.968 Than using a traditional one at

NOTE Confidence: 0.714286372

00:05:46.968 --> 00:05:48.117 a time approach.

NOTE Confidence: 0.924685739642857

00:05:48.250 --> 00:05:50.889 So you you start turning on these

NOTE Confidence: 0.924685739642857

00:05:50.889 --> 00:05:53.462 genes to figure out which ones are

NOTE Confidence: 0.924685739642857

00:05:53.462 --> 00:05:56.001 going to help you in your fight

NOTE Confidence: 0.924685739642857

00:05:56.001 --> 00:05:58.969 against cancer and which ones are not.

NOTE Confidence: 0.924685739642857

00:05:58.970 --> 00:06:01.146 One would think however,

NOTE Confidence: 0.924685739642857

00:06:01.146 --> 00:06:03.674 that still that's rather simplistic

NOTE Confidence: 0.924685739642857

00:06:03.674 --> 00:06:06.154 in terms of fighting cancers.

NOTE Confidence: 0.924685739642857

00:06:06.160 --> 00:06:09.624 So how do you figure out which genes

NOTE Confidence: 0.924685739642857

00:06:09.624 --> 00:06:12.348 are particularly relevant for which

NOTE Confidence: 0.924685739642857

00:06:12.348 --> 00:06:15.308 particular cancers or which particular?

NOTE Confidence: 0.924685739642857

00:06:15.310 --> 00:06:18.438 Drugs, or is it the fact that you

NOTE Confidence: 0.924685739642857

00:06:18.438 --> 00:06:20.735 know certain genes are ubiquitous

NOTE Confidence: 0.924685739642857

00:06:20.735 --> 00:06:24.067 in terms of their effect in cancer?
NOTE Confidence: 0.710511120769231

00:06:24.540 --> 00:06:26.852 Those are great questions.
NOTE Confidence: 0.710511120769231

00:06:26.852 --> 00:06:31.153 There are numerous ways to look to Rome
NOTE Confidence: 0.710511120769231

00:06:31.153 --> 00:06:33.410 and just take one of our recent study.
NOTE Confidence: 0.710511120769231

00:06:33.410 --> 00:06:36.744 For example, we are taking triple
NOTE Confidence: 0.710511120769231

00:06:36.744 --> 00:06:39.290 negative breast cancer cells and we
NOTE Confidence: 0.710511120769231

00:06:39.290 --> 00:06:42.582 also take T cells as the cell from our
NOTE Confidence: 0.710511120769231

00:06:42.582 --> 00:06:45.676 own bodies immune cells to fight them.
NOTE Confidence: 0.710511120769231

00:06:45.680 --> 00:06:48.632 And then we turn on the genes in
NOTE Confidence: 0.710511120769231

00:06:48.632 --> 00:06:51.729 T cells using CRISPR and then we
NOTE Confidence: 0.710511120769231

00:06:51.729 --> 00:06:54.410 measure the ability of T cells to
NOTE Confidence: 0.710511120769231

00:06:54.504 --> 00:06:57.660 kill and there's a becomes technical.
NOTE Confidence: 0.710511120769231

00:06:57.660 --> 00:07:00.640 There's an essay called Degranulation
NOTE Confidence: 0.710511120769231

00:07:00.640 --> 00:07:04.152 Assay which means we can see how fast
NOTE Confidence: 0.710511120769231

00:07:04.152 --> 00:07:07.200 these T cell degranulate meaning how
NOTE Confidence: 0.710511120769231

00:07:07.200 --> 00:07:11.169 fast they release the enzyme to kill

NOTE Confidence: 0.710511120769231
00:07:11.272 --> 00:07:14.488 cancer cells and by measuring the.
NOTE Confidence: 0.710511120769231
00:07:14.490 --> 00:07:14.911 Generation,
NOTE Confidence: 0.710511120769231
00:07:14.911 --> 00:07:17.858 which means the T cell killing ability.
NOTE Confidence: 0.710511120769231
00:07:17.860 --> 00:07:20.176 Uh, one gene at a time,
NOTE Confidence: 0.710511120769231
00:07:20.180 --> 00:07:24.162 but in a massive pair of manner we can
NOTE Confidence: 0.710511120769231
00:07:24.162 --> 00:07:28.929 exhaust the entire genome for every gene.
NOTE Confidence: 0.710511120769231
00:07:28.930 --> 00:07:33.718 T cells and then we can.
NOTE Confidence: 0.710511120769231
00:07:33.720 --> 00:07:35.793 Identify which genes?
NOTE Confidence: 0.710511120769231
00:07:35.793 --> 00:07:37.866 When they're activated,
NOTE Confidence: 0.710511120769231
00:07:37.870 --> 00:07:40.055 would enhance such an ability
NOTE Confidence: 0.710511120769231
00:07:40.055 --> 00:07:41.803 to kill cancer cells.
NOTE Confidence: 0.710511120769231
00:07:41.810 --> 00:07:44.580 And of course, this we.
NOTE Confidence: 0.710511120769231
00:07:44.580 --> 00:07:46.350 Initially perform in
NOTE Confidence: 0.710511120769231
00:07:46.350 --> 00:07:48.698 breast cancer cell killing,
NOTE Confidence: 0.710511120769231
00:07:48.698 --> 00:07:53.900 but then when we apply to other cancer types,
NOTE Confidence: 0.710511120769231

00:07:53.900 --> 00:07:56.276 we found this is also true
NOTE Confidence: 0.710511120769231

00:07:56.276 --> 00:07:58.810 because the gene is universal.
NOTE Confidence: 0.710511120769231

00:07:58.810 --> 00:08:01.318 And therefore the ability of T
NOTE Confidence: 0.710511120769231

00:08:01.318 --> 00:08:03.940 cells to cure cancer cells is
NOTE Confidence: 0.710511120769231

00:08:03.940 --> 00:08:06.190 controlled by the same gene,
NOTE Confidence: 0.710511120769231

00:08:06.190 --> 00:08:08.008 no matter it's getting a breast
NOTE Confidence: 0.710511120769231

00:08:08.008 --> 00:08:09.668 cancer cell or killing leukemia
NOTE Confidence: 0.710511120769231

00:08:09.668 --> 00:08:11.236 cell killing myeloma cell.
NOTE Confidence: 0.767815507142857

00:08:11.330 --> 00:08:14.240 I mean, it certainly sounds
NOTE Confidence: 0.767815507142857

00:08:14.240 --> 00:08:16.886 incredibly interesting, but one of
NOTE Confidence: 0.767815507142857

00:08:16.886 --> 00:08:20.330 the things that might be curious is.
NOTE Confidence: 0.767815507142857

00:08:20.330 --> 00:08:23.228 You know you're turning on these genes
NOTE Confidence: 0.767815507142857

00:08:23.228 --> 00:08:26.467 and and kind of using CRISPR technology
NOTE Confidence: 0.767815507142857

00:08:26.467 --> 00:08:29.990 to activate these genes within a T cell,
NOTE Confidence: 0.767815507142857

00:08:29.990 --> 00:08:33.950 but in a human how would
NOTE Confidence: 0.767815507142857

00:08:33.950 --> 00:08:36.590 you activate that gene?

NOTE Confidence: 0.767815507142857

00:08:36.590 --> 00:08:40.170 Or is there a way to turn on a

NOTE Confidence: 0.767815507142857

00:08:40.170 --> 00:08:43.600 particular genes in an in vivo system?

NOTE Confidence: 0.681392594

00:08:43.890 --> 00:08:46.210 Yeah, that's another great question.

NOTE Confidence: 0.681392594

00:08:46.210 --> 00:08:49.220 A cell therapy, by definition,

NOTE Confidence: 0.681392594

00:08:49.220 --> 00:08:53.329 is the usage of cells as therapeutics,

NOTE Confidence: 0.681392594

00:08:53.330 --> 00:08:57.320 and for many of you you might have heard of

NOTE Confidence: 0.681392594

00:08:57.416 --> 00:09:01.408 car keys or camera engine receptor T cells.

NOTE Confidence: 0.681392594

00:09:01.410 --> 00:09:05.162 That's one form of cell therapy and

NOTE Confidence: 0.681392594

00:09:05.162 --> 00:09:07.989 what Carti or other form of self therapy

NOTE Confidence: 0.681392594

00:09:07.989 --> 00:09:10.503 does is that it takes the cells from

NOTE Confidence: 0.681392594

00:09:10.503 --> 00:09:12.990 a patient or from a healthy donor,

NOTE Confidence: 0.681392594

00:09:12.990 --> 00:09:15.708 and then you can perform genetic

NOTE Confidence: 0.681392594

00:09:15.708 --> 00:09:17.520 engineering in those cells.

NOTE Confidence: 0.681392594

00:09:17.520 --> 00:09:19.900 For example, putting cameras and

NOTE Confidence: 0.681392594

00:09:19.900 --> 00:09:22.280 antigen receptors on the surface.

NOTE Confidence: 0.681392594

00:09:22.280 --> 00:09:25.350 Or like what we're doing?
NOTE Confidence: 0.681392594

00:09:25.350 --> 00:09:27.408 Enhance the expression or turn on
NOTE Confidence: 0.681392594

00:09:27.408 --> 00:09:29.890 the expression of a particular gene,
NOTE Confidence: 0.681392594

00:09:29.890 --> 00:09:32.968 and we can do it by demand by using
NOTE Confidence: 0.681392594

00:09:32.970 --> 00:09:37.750 genetic engineering or vector transgenes.
NOTE Confidence: 0.681392594

00:09:37.750 --> 00:09:41.362 So after we modify these genes
NOTE Confidence: 0.681392594

00:09:41.362 --> 00:09:43.810 in these T cells,
NOTE Confidence: 0.681392594

00:09:43.810 --> 00:09:47.145 the cells would become therapeutic
NOTE Confidence: 0.681392594

00:09:47.145 --> 00:09:51.523 candidate and those are the type of
NOTE Confidence: 0.681392594

00:09:51.523 --> 00:09:56.050 cells we can use to infuse back into.
NOTE Confidence: 0.681392594

00:09:56.050 --> 00:10:00.330 In our case, the animals to treat the.
NOTE Confidence: 0.681392594

00:10:00.330 --> 00:10:02.628 The cancer in those animal models.
NOTE Confidence: 0.681392594

00:10:02.630 --> 00:10:03.850 Of course, in the clinic,
NOTE Confidence: 0.681392594

00:10:03.850 --> 00:10:06.370 the proof of cell therapy,
NOTE Confidence: 0.681392594

00:10:06.370 --> 00:10:08.250 where the same process happened.
NOTE Confidence: 0.681392594

00:10:08.250 --> 00:10:10.126 The cells were taken out from patient.

NOTE Confidence: 0.681392594

00:10:10.130 --> 00:10:11.894 The genes have been modified and

NOTE Confidence: 0.681392594

00:10:11.894 --> 00:10:13.475 the cells have been reinfused

NOTE Confidence: 0.681392594

00:10:13.475 --> 00:10:15.557 into the patient to treat cancer.

NOTE Confidence: 0.7826723211

00:10:15.750 --> 00:10:17.700 Then one would think that

NOTE Confidence: 0.7826723211

00:10:17.700 --> 00:10:19.650 you would have some cells.

NOTE Confidence: 0.7826723211

00:10:19.650 --> 00:10:23.157 The native cells that are in the

NOTE Confidence: 0.7826723211

00:10:23.160 --> 00:10:25.295 patient's that are not quote

NOTE Confidence: 0.7826723211

00:10:25.295 --> 00:10:27.003 supercharged or or modified,

NOTE Confidence: 0.7826723211

00:10:27.010 --> 00:10:29.826 and you'd have some cells that

NOTE Confidence: 0.7826723211

00:10:29.826 --> 00:10:31.810 were the more therapeutic

NOTE Confidence: 0.7826723211

00:10:31.810 --> 00:10:34.290 cells that had been reinfused.

NOTE Confidence: 0.7826723211

00:10:34.290 --> 00:10:39.722 How do you get or is there a way to

NOTE Confidence: 0.7826723211

00:10:39.722 --> 00:10:43.730 get patients to make their own cells?

NOTE Confidence: 0.7826723211

00:10:43.730 --> 00:10:46.010 Have that supercharged ability

NOTE Confidence: 0.7826723211

00:10:46.010 --> 00:10:49.710 so that when these cells die,

NOTE Confidence: 0.7826723211

00:10:49.710 --> 00:10:53.958 there isn't a continued need to have

NOTE Confidence: 0.7826723211

00:10:53.958 --> 00:10:56.406 an infusion of these modified cells?

NOTE Confidence: 0.7826723211

00:10:56.410 --> 00:10:59.259 Or is that something that isn't done?

NOTE Confidence: 0.869608751666667

00:10:59.430 --> 00:11:01.680 A patient may not need the

NOTE Confidence: 0.869608751666667

00:11:01.680 --> 00:11:03.577 supercharged cells in the body

NOTE Confidence: 0.869608751666667

00:11:03.577 --> 00:11:05.845 for a very long period of time.

NOTE Confidence: 0.869608751666667

00:11:05.850 --> 00:11:09.035 And we to some degree we haven't

NOTE Confidence: 0.869608751666667

00:11:09.035 --> 00:11:11.409 done the clinical study yet,

NOTE Confidence: 0.869608751666667

00:11:11.410 --> 00:11:14.428 but to some degree we believe

NOTE Confidence: 0.869608751666667

00:11:14.430 --> 00:11:17.890 it may be important to.

NOTE Confidence: 0.869608751666667

00:11:17.890 --> 00:11:20.150 Let the cells finish the

NOTE Confidence: 0.869608751666667

00:11:20.150 --> 00:11:22.410 job and then be done.

NOTE Confidence: 0.869608751666667

00:11:22.410 --> 00:11:23.990 Because we don't want

NOTE Confidence: 0.869608751666667

00:11:23.990 --> 00:11:25.965 them to stick on forever.

NOTE Confidence: 0.869608751666667

00:11:25.970 --> 00:11:30.146 So I think some cells may

NOTE Confidence: 0.869608751666667

00:11:30.146 --> 00:11:33.426 be sufficient to kill the

NOTE Confidence: 0.869608751666667
00:11:33.426 --> 00:11:36.390 cancer cells and we're talking
NOTE Confidence: 0.869608751666667
00:11:36.390 --> 00:11:38.550 about the persistence issue,
NOTE Confidence: 0.869608751666667
00:11:38.550 --> 00:11:40.960 which is can be very long conversation, but.
NOTE Confidence: 0.7909189825
00:11:43.030 --> 00:11:45.604 The ideal situation would be we
NOTE Confidence: 0.7909189825
00:11:45.604 --> 00:11:48.109 infuse those cells into the body.
NOTE Confidence: 0.7909189825
00:11:48.110 --> 00:11:49.928 The cells kill off the cancer
NOTE Confidence: 0.7909189825
00:11:49.928 --> 00:11:51.530 and the cancer is gone,
NOTE Confidence: 0.7909189825
00:11:51.530 --> 00:11:53.644 and then the cells are gone too,
NOTE Confidence: 0.7909189825
00:11:53.650 --> 00:11:55.650 and then the patient is back to normal.
NOTE Confidence: 0.7909189825
00:11:55.650 --> 00:11:57.288 So that would be ideal situation.
NOTE Confidence: 0.7909189825
00:11:57.290 --> 00:11:59.018 But in the real clinic this is a
NOTE Confidence: 0.7909189825
00:11:59.018 --> 00:12:00.640 much more complicated than that.
NOTE Confidence: 0.921399686363636
00:12:00.990 --> 00:12:04.005 I mean, one of the things that we think
NOTE Confidence: 0.921399686363636
00:12:04.005 --> 00:12:06.674 about is recurrences or even patients
NOTE Confidence: 0.921399686363636
00:12:06.674 --> 00:12:10.370 who denovo are at an increased risk,
NOTE Confidence: 0.921399686363636

00:12:10.370 --> 00:12:13.394 and so when we think about the immune system.

NOTE Confidence: 0.921399686363636

00:12:13.400 --> 00:12:15.808 Not only does the immune system help

NOTE Confidence: 0.921399686363636

00:12:15.808 --> 00:12:18.440 us in terms of you know, clearing

NOTE Confidence: 0.921399686363636

00:12:18.440 --> 00:12:21.200 cancer cells or treating cancer cells,

NOTE Confidence: 0.921399686363636

00:12:21.200 --> 00:12:24.431 and so having these supercharged cells

NOTE Confidence: 0.921399686363636

00:12:24.431 --> 00:12:27.857 would be useful in that context,

NOTE Confidence: 0.921399686363636

00:12:27.860 --> 00:12:31.100 but they may also be relevant in terms

NOTE Confidence: 0.921399686363636

00:12:31.100 --> 00:12:33.779 of preventing cancers from occurring.

NOTE Confidence: 0.921399686363636

00:12:33.780 --> 00:12:38.448 At all, so in high risk individuals or in

NOTE Confidence: 0.921399686363636

00:12:38.448 --> 00:12:41.280 patients who are at high risk of recurrence,

NOTE Confidence: 0.921399686363636

00:12:41.280 --> 00:12:43.900 reducing the risk of recurrence.

NOTE Confidence: 0.921399686363636

00:12:43.900 --> 00:12:46.231 O has this kind of therapy been

NOTE Confidence: 0.921399686363636

00:12:46.231 --> 00:12:48.628 thought about in those two contexts?

NOTE Confidence: 0.636769154485714

00:12:49.890 --> 00:12:52.402 All you're absolutely right.

NOTE Confidence: 0.636769154485714

00:12:52.402 --> 00:12:54.286 In cancer treatment,

NOTE Confidence: 0.636769154485714

00:12:54.290 --> 00:12:58.182 there are many cases of relapse or

NOTE Confidence: 0.636769154485714

00:12:58.182 --> 00:13:00.518 resistance and therefore multiple

NOTE Confidence: 0.636769154485714

00:13:00.518 --> 00:13:03.486 dosing is often required or beneficial,

NOTE Confidence: 0.636769154485714

00:13:03.486 --> 00:13:05.781 and it's absolutely case by

NOTE Confidence: 0.636769154485714

00:13:05.781 --> 00:13:08.700 case in the clinic disease by

NOTE Confidence: 0.636769154485714

00:13:08.700 --> 00:13:10.608 disease indication by indication,

NOTE Confidence: 0.636769154485714

00:13:10.610 --> 00:13:13.553 and I think we are still early in the

NOTE Confidence: 0.636769154485714

00:13:13.553 --> 00:13:16.409 form of self therapy because currently

NOTE Confidence: 0.636769154485714

00:13:16.409 --> 00:13:19.799 self therapy infusion is only given once.

NOTE Confidence: 0.636769154485714

00:13:19.800 --> 00:13:22.855 And there have been clinical

NOTE Confidence: 0.636769154485714

00:13:22.855 --> 00:13:27.690 trials for multiple infusions, or.

NOTE Confidence: 0.636769154485714

00:13:27.690 --> 00:13:29.202 Use as prophylaxis,

NOTE Confidence: 0.636769154485714

00:13:29.202 --> 00:13:31.722 but those much earlier studies

NOTE Confidence: 0.636769154485714

00:13:31.722 --> 00:13:34.775 the approved drugs were given as a

NOTE Confidence: 0.636769154485714

00:13:34.775 --> 00:13:37.539 single infusion for most of the time.

NOTE Confidence: 0.879098026153846

00:13:37.970 --> 00:13:39.664 OK, well, we're going to take a

NOTE Confidence: 0.879098026153846

00:13:39.664 --> 00:13:41.320 short break for a medical minute.
NOTE Confidence: 0.879098026153846

00:13:41.320 --> 00:13:43.798 Please stay tuned to learn more about
NOTE Confidence: 0.879098026153846

00:13:43.798 --> 00:13:45.673 supercharged T cells fighting cancer
NOTE Confidence: 0.879098026153846

00:13:45.673 --> 00:13:47.810 with my guest doctor Sidi Chen.
NOTE Confidence: 0.820595695238095

00:13:48.500 --> 00:13:50.715 Funding for Yale Cancer Answers
NOTE Confidence: 0.820595695238095

00:13:50.715 --> 00:13:52.930 comes from Smilow Cancer Hospital
NOTE Confidence: 0.820595695238095

00:13:53.004 --> 00:13:55.014 hosting a smilow shares cancer
NOTE Confidence: 0.820595695238095

00:13:55.014 --> 00:13:57.440 Survivor Series June 8th and 15th.
NOTE Confidence: 0.820595695238095

00:13:57.440 --> 00:13:59.200 Register at Yale Cancer
NOTE Confidence: 0.820595695238095

00:13:59.200 --> 00:14:00.960 Center or email cancer.
NOTE Confidence: 0.820595695238095

00:14:00.960 --> 00:14:04.629 Answers at yale.edu.
NOTE Confidence: 0.820595695238095

00:14:04.630 --> 00:14:06.942 Breast cancer is one of the most common
NOTE Confidence: 0.820595695238095

00:14:06.942 --> 00:14:09.149 cancers in women in Connecticut alone,
NOTE Confidence: 0.820595695238095

00:14:09.150 --> 00:14:11.365 approximately 3500 women will be
NOTE Confidence: 0.820595695238095

00:14:11.365 --> 00:14:13.990 diagnosed with breast cancer this year,
NOTE Confidence: 0.820595695238095

00:14:13.990 --> 00:14:15.338 but there is hope,

NOTE Confidence: 0.820595695238095

00:14:15.338 --> 00:14:16.686 thanks to earlier detection,

NOTE Confidence: 0.820595695238095

00:14:16.690 --> 00:14:18.575 non invasive treatments and the

NOTE Confidence: 0.820595695238095

00:14:18.575 --> 00:14:20.083 development of novel therapies

NOTE Confidence: 0.820595695238095

00:14:20.083 --> 00:14:21.688 to fight breast cancer.

NOTE Confidence: 0.820595695238095

00:14:21.690 --> 00:14:23.515 Women should schedule a baseline

NOTE Confidence: 0.820595695238095

00:14:23.515 --> 00:14:25.730 mammogram beginning at age 40 or

NOTE Confidence: 0.820595695238095

00:14:25.730 --> 00:14:27.704 earlier if they have risk factors

NOTE Confidence: 0.820595695238095

00:14:27.704 --> 00:14:29.230 associated with the disease.

NOTE Confidence: 0.820595695238095

00:14:29.230 --> 00:14:30.938 With screening early detection

NOTE Confidence: 0.820595695238095

00:14:30.938 --> 00:14:32.646 and a healthy lifestyle,

NOTE Confidence: 0.820595695238095

00:14:32.650 --> 00:14:34.800 breast cancer can be defeated.

NOTE Confidence: 0.820595695238095

00:14:34.800 --> 00:14:36.760 Clinical trials are currently

NOTE Confidence: 0.820595695238095

00:14:36.760 --> 00:14:38.720 underway at federally designated

NOTE Confidence: 0.820595695238095

00:14:38.720 --> 00:14:40.404 Comprehensive cancer centers such

NOTE Confidence: 0.820595695238095

00:14:40.404 --> 00:14:42.637 as Yale Cancer Center and Smilow

NOTE Confidence: 0.820595695238095

00:14:42.637 --> 00:14:44.725 Cancer Hospital to make innovative
NOTE Confidence: 0.820595695238095

00:14:44.725 --> 00:14:46.860 new treatments available to patients.
NOTE Confidence: 0.820595695238095

00:14:46.860 --> 00:14:49.350 Digital breast tomosynthesis or 3D
NOTE Confidence: 0.820595695238095

00:14:49.350 --> 00:14:51.840 mammography is also transforming breast
NOTE Confidence: 0.820595695238095

00:14:51.913 --> 00:14:54.121 cancer screening by significantly
NOTE Confidence: 0.820595695238095

00:14:54.121 --> 00:14:55.777 reducing unnecessary procedures
NOTE Confidence: 0.820595695238095

00:14:55.777 --> 00:14:58.380 while picking up more cancers.
NOTE Confidence: 0.820595695238095

00:14:58.380 --> 00:15:01.300 More information is available at
NOTE Confidence: 0.820595695238095

00:15:01.300 --> 00:15:02.596 yalecancercenter.org you're listening
NOTE Confidence: 0.820595695238095

00:15:02.596 --> 00:15:04.324 to Connecticut Public Radio.
NOTE Confidence: 0.826012165

00:15:05.380 --> 00:15:07.498 Welcome back to Yale Cancer Answers.
NOTE Confidence: 0.826012165

00:15:07.500 --> 00:15:09.836 This is doctor Anees Chagpar and I'm joined
NOTE Confidence: 0.826012165

00:15:09.836 --> 00:15:12.122 tonight by my guest doctor Sidi Chen.
NOTE Confidence: 0.826012165

00:15:12.122 --> 00:15:14.077 We're learning about his research
NOTE Confidence: 0.826012165

00:15:14.077 --> 00:15:16.775 into using T cells to fight cancer
NOTE Confidence: 0.826012165

00:15:16.775 --> 00:15:19.775 cells and right before the break

NOTE Confidence: 0.826012165

00:15:19.775 --> 00:15:23.579 he was telling us about how you

NOTE Confidence: 0.826012165

00:15:23.579 --> 00:15:26.737 could use new technology to look

NOTE Confidence: 0.826012165

00:15:26.737 --> 00:15:29.839 for genes that may be particularly

NOTE Confidence: 0.826012165

00:15:29.839 --> 00:15:33.340 effective in terms of getting rid of

NOTE Confidence: 0.826012165

00:15:33.340 --> 00:15:35.665 cancer and then using CRISPR.

NOTE Confidence: 0.826012165

00:15:35.670 --> 00:15:38.345 Technology to activate these genes

NOTE Confidence: 0.826012165

00:15:38.345 --> 00:15:41.757 and potentially using it in cellular

NOTE Confidence: 0.826012165

00:15:41.757 --> 00:15:44.975 therapies in patients to treat cancers.

NOTE Confidence: 0.826012165

00:15:44.975 --> 00:15:48.488 You had mentioned that your work

NOTE Confidence: 0.826012165

00:15:48.488 --> 00:15:52.112 right now is is using largely animal models.

NOTE Confidence: 0.826012165

00:15:52.120 --> 00:15:53.758 Has this been tested in clinical

NOTE Confidence: 0.826012165

00:15:53.758 --> 00:15:55.524 trials or is that something that

NOTE Confidence: 0.826012165

00:15:55.524 --> 00:15:57.049 is coming down the Pike?

NOTE Confidence: 0.81172539

00:15:57.220 --> 00:15:58.390 Thank you for the question,

NOTE Confidence: 0.81172539

00:15:58.390 --> 00:16:01.981 and my lab is Preclinical Research lab

NOTE Confidence: 0.81172539

00:16:01.981 --> 00:16:05.690 and of course my goal is to discover.
NOTE Confidence: 0.81172539

00:16:05.690 --> 00:16:08.700 And. Understand the therapeutic targets
NOTE Confidence: 0.81172539

00:16:08.700 --> 00:16:12.867 and pathways and how it works to
NOTE Confidence: 0.81172539

00:16:12.867 --> 00:16:16.023 build the portfolio or the platform
NOTE Confidence: 0.81172539

00:16:16.023 --> 00:16:19.279 for future translational studies.
NOTE Confidence: 0.81172539

00:16:19.280 --> 00:16:22.730 We of course talking to different
NOTE Confidence: 0.81172539

00:16:22.730 --> 00:16:25.780 translational partners or potential partners
NOTE Confidence: 0.81172539

00:16:25.780 --> 00:16:29.238 to bring this further down into clinic.
NOTE Confidence: 0.81172539

00:16:29.240 --> 00:16:32.980 But this is a complicated
NOTE Confidence: 0.81172539

00:16:32.980 --> 00:16:36.720 process because cell therapy has.
NOTE Confidence: 0.81172539

00:16:36.720 --> 00:16:39.291 Complex manufacturing and
NOTE Confidence: 0.81172539

00:16:39.291 --> 00:16:43.576 complex regulatory path as well,
NOTE Confidence: 0.81172539

00:16:43.580 --> 00:16:46.340 so it's not as easy as some of
NOTE Confidence: 0.81172539

00:16:46.340 --> 00:16:47.560 the traditional drugs.
NOTE Confidence: 0.85183636

00:16:48.630 --> 00:16:50.616 Yeah, now you had mentioned that
NOTE Confidence: 0.85183636

00:16:50.616 --> 00:16:52.570 you had started your research.

NOTE Confidence: 0.85183636
00:16:52.570 --> 00:16:54.042 Really looking at triple
NOTE Confidence: 0.85183636
00:16:54.042 --> 00:16:55.146 negative breast cancers.
NOTE Confidence: 0.85183636
00:16:55.150 --> 00:16:57.670 So do you want to tell our audience
NOTE Confidence: 0.85183636
00:16:57.670 --> 00:16:59.781 a little bit about why you
NOTE Confidence: 0.85183636
00:16:59.781 --> 00:17:01.887 chose triple negative as a good
NOTE Confidence: 0.85183636
00:17:01.890 --> 00:17:03.948 cancer to look at to begin with?
NOTE Confidence: 0.707675987153846
00:17:05.410 --> 00:17:08.791 Yasur Alice, you are a much better
NOTE Confidence: 0.707675987153846
00:17:08.791 --> 00:17:12.020 expert than me on breast cancer.
NOTE Confidence: 0.707675987153846
00:17:12.020 --> 00:17:14.540 US we believed triple negative breast
NOTE Confidence: 0.707675987153846
00:17:14.540 --> 00:17:18.042 cancer is the type of breast cancer that
NOTE Confidence: 0.707675987153846
00:17:18.042 --> 00:17:20.652 there is no hormone targeted therapy
NOTE Confidence: 0.707675987153846
00:17:20.734 --> 00:17:23.464 which is very commonly used for the
NOTE Confidence: 0.707675987153846
00:17:23.464 --> 00:17:27.708 other types such as her two positive.
NOTE Confidence: 0.707675987153846
00:17:27.710 --> 00:17:32.617 So we believe we need to identify
NOTE Confidence: 0.707675987153846
00:17:32.617 --> 00:17:35.148 other novel therapeutic targets or
NOTE Confidence: 0.707675987153846

00:17:35.148 --> 00:17:36.976 therapeutic approaches to adjust
NOTE Confidence: 0.707675987153846

00:17:36.976 --> 00:17:39.370 the unmet need for this disease.
NOTE Confidence: 0.716402806

00:17:40.210 --> 00:17:43.410 Yeah, I think that's right, but I think so.
NOTE Confidence: 0.716402806

00:17:43.410 --> 00:17:46.195 Certainly you know we we on this show
NOTE Confidence: 0.716402806

00:17:46.195 --> 00:17:48.655 talk a lot about targeted therapies
NOTE Confidence: 0.716402806

00:17:48.655 --> 00:17:50.797 and triple negative by definition
NOTE Confidence: 0.716402806

00:17:50.797 --> 00:17:53.287 don't have a target as such.
NOTE Confidence: 0.716402806

00:17:53.290 --> 00:17:55.582 They certainly are not responsive to
NOTE Confidence: 0.716402806

00:17:55.582 --> 00:17:57.786 endocrine therapy, being ER, PR negative.
NOTE Confidence: 0.716402806

00:17:57.786 --> 00:18:00.270 And they're not responsive to her too.
NOTE Confidence: 0.716402806

00:18:00.270 --> 00:18:03.372 Targets given the fact that they
NOTE Confidence: 0.716402806

00:18:03.372 --> 00:18:06.130 don't express that receptor either.
NOTE Confidence: 0.716402806

00:18:06.130 --> 00:18:08.914 One of the interesting things about
NOTE Confidence: 0.716402806

00:18:08.914 --> 00:18:11.749 triple negative breast cancer is that
NOTE Confidence: 0.716402806

00:18:11.749 --> 00:18:14.449 we've found that these are potentially
NOTE Confidence: 0.716402806

00:18:14.449 --> 00:18:16.960 more immunogenic in in the sense that

NOTE Confidence: 0.716402806

00:18:16.960 --> 00:18:19.302 they tend to have more tea infiltrating

NOTE Confidence: 0.716402806

00:18:19.302 --> 00:18:22.109 lymphocytes when when you look at them,

NOTE Confidence: 0.716402806

00:18:22.110 --> 00:18:25.050 when people have looked at immunotherapies,

NOTE Confidence: 0.716402806

00:18:25.050 --> 00:18:27.080 they they tend to respond

NOTE Confidence: 0.716402806

00:18:27.080 --> 00:18:28.298 to immunotherapy so.

NOTE Confidence: 0.716402806

00:18:28.300 --> 00:18:29.300 You know,

NOTE Confidence: 0.716402806

00:18:29.300 --> 00:18:32.800 in thinking about these supercharged T cells.

NOTE Confidence: 0.716402806

00:18:32.800 --> 00:18:36.258 I wonder whether part of the rationale

NOTE Confidence: 0.716402806

00:18:36.258 --> 00:18:40.433 is to look at cancers that are

NOTE Confidence: 0.716402806

00:18:40.433 --> 00:18:43.600 particularly prime for immune regulation.

NOTE Confidence: 0.716402806

00:18:43.600 --> 00:18:47.380 Did that play into your thinking,

NOTE Confidence: 0.716402806

00:18:47.380 --> 00:18:48.700 and if so,

NOTE Confidence: 0.716402806

00:18:48.700 --> 00:18:50.900 will it affect which cancers

NOTE Confidence: 0.716402806

00:18:50.900 --> 00:18:54.844 you look at next in terms of the

NOTE Confidence: 0.716402806

00:18:54.844 --> 00:18:56.824 ability for these supercharged

NOTE Confidence: 0.716402806

00:18:56.918 --> 00:18:59.200 T cells to to battle cancer?
NOTE Confidence: 0.776930182857143

00:19:00.430 --> 00:19:02.858 Ohh yes, of course,
NOTE Confidence: 0.776930182857143

00:19:02.858 --> 00:19:04.679 you're absolutely right,
NOTE Confidence: 0.776930182857143

00:19:04.680 --> 00:19:08.250 the breast cancer have different subtypes,
NOTE Confidence: 0.776930182857143

00:19:08.250 --> 00:19:13.420 and even between different patients or
NOTE Confidence: 0.776930182857143

00:19:13.420 --> 00:19:17.598 different level of immune infiltration or
NOTE Confidence: 0.776930182857143

00:19:17.598 --> 00:19:21.468 the tumor microenvironment is complex issues.
NOTE Confidence: 0.776930182857143

00:19:21.470 --> 00:19:24.498 There are tumors without.
NOTE Confidence: 0.776930182857143

00:19:24.500 --> 00:19:27.447 Any or there would be very little
NOTE Confidence: 0.776930182857143

00:19:27.447 --> 00:19:29.979 infiltrating T cells that you cancer
NOTE Confidence: 0.776930182857143

00:19:29.979 --> 00:19:32.758 fighting cell and on the other hand
NOTE Confidence: 0.776930182857143

00:19:32.842 --> 00:19:35.440 there are tumors that are filled
NOTE Confidence: 0.776930182857143

00:19:35.440 --> 00:19:37.970 with immune cells and in order
NOTE Confidence: 0.776930182857143

00:19:37.970 --> 00:19:40.840 for T cells to kill cancer cells,
NOTE Confidence: 0.776930182857143

00:19:40.840 --> 00:19:44.285 you need T cell to get there to
NOTE Confidence: 0.776930182857143

00:19:44.285 --> 00:19:46.980 the right place before they can do

NOTE Confidence: 0.776930182857143
00:19:46.980 --> 00:19:50.259 their job and therefore we are also
NOTE Confidence: 0.776930182857143
00:19:50.259 --> 00:19:52.679 looking for a genetic components.
NOTE Confidence: 0.776930182857143
00:19:52.680 --> 00:19:55.420 That controls the process of
NOTE Confidence: 0.776930182857143
00:19:55.420 --> 00:19:56.516 tumor infiltration.
NOTE Confidence: 0.776930182857143
00:19:56.520 --> 00:19:57.900 Besides cancer killing,
NOTE Confidence: 0.776930182857143
00:19:57.900 --> 00:20:00.660 and in order to do so,
NOTE Confidence: 0.776930182857143
00:20:00.660 --> 00:20:03.978 we are adopting a similar approach,
NOTE Confidence: 0.776930182857143
00:20:03.980 --> 00:20:06.505 unbiased genetic screens and look
NOTE Confidence: 0.776930182857143
00:20:06.505 --> 00:20:09.492 for the genes when you either
NOTE Confidence: 0.776930182857143
00:20:09.492 --> 00:20:12.452 get rid of or when you turn on
NOTE Confidence: 0.776930182857143
00:20:12.460 --> 00:20:14.630 what helped the T cells get into
NOTE Confidence: 0.776930182857143
00:20:14.630 --> 00:20:16.420 the term micro environment,
NOTE Confidence: 0.776930182857143
00:20:16.420 --> 00:20:22.391 and I think that property can be cancelled.
NOTE Confidence: 0.776930182857143
00:20:22.391 --> 00:20:24.893 Specific or can be more universal
NOTE Confidence: 0.776930182857143
00:20:24.893 --> 00:20:27.641 like and what we have been doing now
NOTE Confidence: 0.776930182857143

00:20:27.641 --> 00:20:30.023 is use triple negative breast cancer
NOTE Confidence: 0.776930182857143

00:20:30.023 --> 00:20:33.075 as a starter model and then identify
NOTE Confidence: 0.776930182857143

00:20:33.157 --> 00:20:35.563 those genes to supercharge the T
NOTE Confidence: 0.776930182857143

00:20:35.563 --> 00:20:38.915 cells and then apply those findings
NOTE Confidence: 0.776930182857143

00:20:38.915 --> 00:20:41.271 into other disease indications
NOTE Confidence: 0.776930182857143

00:20:41.271 --> 00:20:44.670 such as other form of breast cancer
NOTE Confidence: 0.776930182857143

00:20:44.670 --> 00:20:46.772 or Melanoma or pancreatic cancer
NOTE Confidence: 0.776930182857143

00:20:46.772 --> 00:20:48.256 or other cancer types.
NOTE Confidence: 0.764187991818182

00:20:49.050 --> 00:20:51.180 So CD when you've started to
NOTE Confidence: 0.764187991818182

00:20:51.180 --> 00:20:53.270 look at these other cancers.
NOTE Confidence: 0.764187991818182

00:20:53.270 --> 00:20:56.035 Have you found that there's a difference
NOTE Confidence: 0.764187991818182

00:20:56.035 --> 00:21:00.570 in terms of the response of these?
NOTE Confidence: 0.764187991818182

00:21:00.570 --> 00:21:03.832 These supercharged T cells based on how
NOTE Confidence: 0.764187991818182

00:21:03.832 --> 00:21:06.670 immunogenic the cancer is in other words.
NOTE Confidence: 0.764187991818182

00:21:06.670 --> 00:21:09.064 If a cancer doesn't have a lot of tea,
NOTE Confidence: 0.764187991818182

00:21:09.070 --> 00:21:13.198 infiltrating lymphocytes say like a luminal,

NOTE Confidence: 0.764187991818182

00:21:13.200 --> 00:21:17.352 a breast cancer or or a cancer that

NOTE Confidence: 0.764187991818182

00:21:17.352 --> 00:21:19.725 really doesn't evade the immune

NOTE Confidence: 0.764187991818182

00:21:19.725 --> 00:21:21.950 system or isn't as immunogenic,

NOTE Confidence: 0.764187991818182

00:21:21.950 --> 00:21:24.883 it is the effect different in those

NOTE Confidence: 0.764187991818182

00:21:24.883 --> 00:21:27.009 populations in those cancers in

NOTE Confidence: 0.764187991818182

00:21:27.009 --> 00:21:29.781 those patients than it is in cancers

NOTE Confidence: 0.764187991818182

00:21:29.781 --> 00:21:32.953 where there are a lot of tumor

NOTE Confidence: 0.764187991818182

00:21:32.953 --> 00:21:34.749 infiltrating lymphocytes or cancers

NOTE Confidence: 0.764187991818182

00:21:34.750 --> 00:21:36.676 that we know are highly immunogenic.

NOTE Confidence: 0.660047903428571

00:21:37.930 --> 00:21:41.020 Oh, thank you for the question and let

NOTE Confidence: 0.660047903428571

00:21:41.020 --> 00:21:44.030 me declare that I'm not the clinician,

NOTE Confidence: 0.660047903428571

00:21:44.030 --> 00:21:46.496 so therefore I cannot comment on

NOTE Confidence: 0.660047903428571

00:21:46.496 --> 00:21:48.576 the patient side, but however,

NOTE Confidence: 0.660047903428571

00:21:48.576 --> 00:21:52.760 based on the tumor models we use in animals.

NOTE Confidence: 0.660047903428571

00:21:52.760 --> 00:21:56.496 There are certainly differences

NOTE Confidence: 0.660047903428571

00:21:56.496 --> 00:21:59.298 in commonalities between
NOTE Confidence: 0.660047903428571

00:21:59.298 --> 00:22:02.100 different disease models.
NOTE Confidence: 0.660047903428571

00:22:02.100 --> 00:22:06.335 You you find in cases where the
NOTE Confidence: 0.660047903428571

00:22:06.335 --> 00:22:09.354 genes regulating T cell cancer
NOTE Confidence: 0.660047903428571

00:22:09.354 --> 00:22:11.730 killing or cancer infiltration.
NOTE Confidence: 0.660047903428571

00:22:11.730 --> 00:22:16.250 Uh is specific for some type of cancer,
NOTE Confidence: 0.660047903428571

00:22:16.250 --> 00:22:19.186 but also there's a set of genes that
NOTE Confidence: 0.660047903428571

00:22:19.186 --> 00:22:22.187 are common to multiple type of cancers.
NOTE Confidence: 0.660047903428571

00:22:22.190 --> 00:22:25.076 When we're performing these T cell
NOTE Confidence: 0.660047903428571

00:22:25.076 --> 00:22:27.000 studies cell screening studies.
NOTE Confidence: 0.7948586

00:22:29.040 --> 00:22:35.628 And so. So have you looked at whether
NOTE Confidence: 0.7948586

00:22:35.628 --> 00:22:39.970 when you supercharged these T lymphocytes,
NOTE Confidence: 0.7948586

00:22:39.970 --> 00:22:42.280 whether there is a difference in
NOTE Confidence: 0.7948586

00:22:42.280 --> 00:22:44.636 terms of how effective they are
NOTE Confidence: 0.7948586

00:22:44.636 --> 00:22:46.862 in cancer killing when they are
NOTE Confidence: 0.7948586

00:22:46.862 --> 00:22:49.290 coupled with other forms of therapy,

NOTE Confidence: 0.7948586

00:22:49.290 --> 00:22:51.818 say immunotherapy or chemotherapy?

NOTE Confidence: 0.902767188181818

00:22:54.000 --> 00:22:55.268 That's a great question,

NOTE Confidence: 0.902767188181818

00:22:55.268 --> 00:22:57.440 and that's exactly what we're trying now,

NOTE Confidence: 0.902767188181818

00:22:57.440 --> 00:23:01.250 because as you know and.

NOTE Confidence: 0.902767188181818

00:23:01.250 --> 00:23:04.890 Most of the late stage cancer cannot be

NOTE Confidence: 0.902767188181818

00:23:04.890 --> 00:23:08.747 cured by a single form of therapeutics,

NOTE Confidence: 0.902767188181818

00:23:08.750 --> 00:23:11.948 and that's why having more options

NOTE Confidence: 0.902767188181818

00:23:11.950 --> 00:23:15.860 in more innovative therapeutics would

NOTE Confidence: 0.902767188181818

00:23:15.860 --> 00:23:20.790 allow us to have more choices for

NOTE Confidence: 0.902767188181818

00:23:20.790 --> 00:23:24.546 the patient to have multiple lines of

NOTE Confidence: 0.902767188181818

00:23:24.546 --> 00:23:26.816 therapy or have different combinations.

NOTE Confidence: 0.902767188181818

00:23:26.820 --> 00:23:29.240 And we are studying different

NOTE Confidence: 0.902767188181818

00:23:29.240 --> 00:23:31.176 combinations in our lab,

NOTE Confidence: 0.902767188181818

00:23:31.180 --> 00:23:34.075 including immune checkpoint,

NOTE Confidence: 0.902767188181818

00:23:34.075 --> 00:23:36.970 antibodies and chemotherapy,

NOTE Confidence: 0.902767188181818

00:23:36.970 --> 00:23:39.574 and cell therapy with or without
NOTE Confidence: 0.902767188181818

00:23:39.574 --> 00:23:42.379 supercharged T cells and gene therapy.
NOTE Confidence: 0.902767188181818

00:23:42.380 --> 00:23:43.458 So we.
NOTE Confidence: 0.902767188181818

00:23:43.458 --> 00:23:46.692 Looking forward to see the signal
NOTE Confidence: 0.902767188181818

00:23:46.692 --> 00:23:50.908 of $1 + 1$ greater than two or at
NOTE Confidence: 0.902767188181818

00:23:50.908 --> 00:23:54.600 least $1 + 1$ greater than one.
NOTE Confidence: 0.902767188181818

00:23:54.600 --> 00:23:56.685 In terms of therapeutic efficacy
NOTE Confidence: 0.902767188181818

00:23:56.685 --> 00:23:59.500 and hopefully in terms of toxicity,
NOTE Confidence: 0.902767188181818

00:23:59.500 --> 00:24:02.279 $1 + 1$ is smaller than one,
NOTE Confidence: 0.902767188181818

00:24:02.280 --> 00:24:04.330 or like at least not.
NOTE Confidence: 0.902767188181818

00:24:04.330 --> 00:24:08.068 Bah, too much greater than two.
NOTE Confidence: 0.902767188181818

00:24:08.070 --> 00:24:10.016 So this is always a hot balance.
NOTE Confidence: 0.835739395

00:24:11.230 --> 00:24:15.622 So CD, have you? Have you gotten any
NOTE Confidence: 0.835739395

00:24:15.622 --> 00:24:19.726 initial results on that in terms of
NOTE Confidence: 0.835739395

00:24:19.726 --> 00:24:22.070 understanding what combines well with
NOTE Confidence: 0.835739395

00:24:22.070 --> 00:24:24.710 supercharge T cells versus what doesn't?

NOTE Confidence: 0.812598600541667

00:24:26.080 --> 00:24:29.476 Yeah, we're still early in the

NOTE Confidence: 0.812598600541667

00:24:29.476 --> 00:24:33.050 game and our research is ongoing

NOTE Confidence: 0.812598600541667

00:24:33.050 --> 00:24:36.045 and with some initial observation

NOTE Confidence: 0.812598600541667

00:24:36.045 --> 00:24:40.128 is that if we combined it with.

NOTE Confidence: 0.812598600541667

00:24:40.130 --> 00:24:44.344 The gene therapy, or a major base?

NOTE Confidence: 0.812598600541667

00:24:44.350 --> 00:24:46.159 Imagine therapy because

NOTE Confidence: 0.812598600541667

00:24:46.159 --> 00:24:49.777 like one side of my study,

NOTE Confidence: 0.812598600541667

00:24:49.780 --> 00:24:54.410 is to heat up the immune system in the tumor.

NOTE Confidence: 0.812598600541667

00:24:54.410 --> 00:24:57.770 Like we have an approach called

NOTE Confidence: 0.812598600541667

00:24:57.770 --> 00:25:00.010 Multiplex activation of endogenous

NOTE Confidence: 0.812598600541667

00:25:00.098 --> 00:25:03.068 genes as chemotherapy called Meiji.

NOTE Confidence: 0.812598600541667

00:25:03.070 --> 00:25:05.830 And we found self therapy and

NOTE Confidence: 0.812598600541667

00:25:05.830 --> 00:25:10.709 Meiji can be combined in order to.

NOTE Confidence: 0.812598600541667

00:25:10.710 --> 00:25:12.890 Improve the therapeutic efficacy

NOTE Confidence: 0.812598600541667

00:25:12.890 --> 00:25:14.525 of one another.

NOTE Confidence: 0.812598600541667

00:25:14.530 --> 00:25:16.846 This is natural because what major
NOTE Confidence: 0.812598600541667

00:25:16.846 --> 00:25:19.926 does is to heat up the immune system
NOTE Confidence: 0.812598600541667

00:25:19.926 --> 00:25:22.650 so the cells get in easier and
NOTE Confidence: 0.812598600541667

00:25:22.650 --> 00:25:24.970 recognize the cancer cell better
NOTE Confidence: 0.812598600541667

00:25:24.970 --> 00:25:27.945 and then the software app is to
NOTE Confidence: 0.812598600541667

00:25:27.945 --> 00:25:30.489 actually providing the T cells itself,
NOTE Confidence: 0.812598600541667

00:25:30.490 --> 00:25:31.252 supercharged them,
NOTE Confidence: 0.812598600541667

00:25:31.252 --> 00:25:33.919 and then let them do the job
NOTE Confidence: 0.812598600541667

00:25:33.919 --> 00:25:35.759 to kill cancer cells.
NOTE Confidence: 0.812598600541667

00:25:35.760 --> 00:25:38.364 So I think naturally these work together.
NOTE Confidence: 0.812598600541667

00:25:38.370 --> 00:25:39.999 But of course there's a long way to go.
NOTE Confidence: 0.911094563

00:25:40.880 --> 00:25:41.975 So how does?
NOTE Confidence: 0.911094563

00:25:41.975 --> 00:25:44.530 Just take us back a little bit.
NOTE Confidence: 0.911094563

00:25:44.530 --> 00:25:46.540 How does gene therapy actually
NOTE Confidence: 0.911094563

00:25:46.540 --> 00:25:48.920 work in terms of the clinic?
NOTE Confidence: 0.911094563

00:25:48.920 --> 00:25:51.615 I mean is that using a vector

NOTE Confidence: 0.911094563

00:25:51.615 --> 00:25:53.964 that goes into your cells and

NOTE Confidence: 0.911094563

00:25:53.964 --> 00:25:56.804 and kind of does its own little

NOTE Confidence: 0.911094563

00:25:56.804 --> 00:25:59.031 crisper in vivo help our audience

NOTE Confidence: 0.911094563

00:25:59.031 --> 00:26:00.566 to understand how that works?

NOTE Confidence: 0.79288724

00:26:01.640 --> 00:26:03.720 Yeah, sure, uh, gene therapy

NOTE Confidence: 0.79288724

00:26:03.720 --> 00:26:06.360 for cancer is still very early,

NOTE Confidence: 0.79288724

00:26:06.360 --> 00:26:10.770 and currently there's very little.

NOTE Confidence: 0.79288724

00:26:10.770 --> 00:26:13.416 Approved shocks for gene therapy for cancer.

NOTE Confidence: 0.595707314

00:26:16.020 --> 00:26:19.350 Currently there are.

NOTE Confidence: 0.595707314

00:26:19.350 --> 00:26:22.380 A few examples, for example,

NOTE Confidence: 0.595707314

00:26:22.380 --> 00:26:25.992 are you can deliver the gene

NOTE Confidence: 0.595707314

00:26:25.992 --> 00:26:27.713 therapy product systemically,

NOTE Confidence: 0.595707314

00:26:27.713 --> 00:26:31.304 or you can deliver the gene therapy

NOTE Confidence: 0.595707314

00:26:31.304 --> 00:26:33.934 product directly into cancer and

NOTE Confidence: 0.595707314

00:26:33.934 --> 00:26:35.562 hopefully. Not just.

NOTE Confidence: 0.595707314

00:26:35.562 --> 00:26:39.489 Cheat the tumor you that you injected,
NOTE Confidence: 0.595707314

00:26:39.490 --> 00:26:42.400 but also create inflammatory response.
NOTE Confidence: 0.595707314

00:26:42.400 --> 00:26:44.070 That's going to be systemic,
NOTE Confidence: 0.595707314

00:26:44.070 --> 00:26:48.594 meaning it has an effect on
NOTE Confidence: 0.595707314

00:26:48.594 --> 00:26:51.450 the distance side.
NOTE Confidence: 0.927464998

00:26:53.830 --> 00:26:55.910 This sounds challenging, but not impossible,
NOTE Confidence: 0.927464998

00:26:55.910 --> 00:26:59.180 because our own bodies connected
NOTE Confidence: 0.927464998

00:26:59.180 --> 00:27:01.796 immune system is connected.
NOTE Confidence: 0.927464998

00:27:01.800 --> 00:27:04.313 So what we've been doing and trying
NOTE Confidence: 0.927464998

00:27:04.313 --> 00:27:08.050 to do is to try to use therapy to
NOTE Confidence: 0.890639105

00:27:10.210 --> 00:27:13.360 activate the immune system so
NOTE Confidence: 0.890639105

00:27:13.360 --> 00:27:15.626 that when it gets activated,
NOTE Confidence: 0.890639105

00:27:15.626 --> 00:27:18.080 it has the ability to chase
NOTE Confidence: 0.890639105

00:27:18.164 --> 00:27:19.928 down the cancer cells,
NOTE Confidence: 0.890639105

00:27:19.930 --> 00:27:22.366 not just from the tumor side,
NOTE Confidence: 0.890639105

00:27:22.370 --> 00:27:24.830 but also on the distant side.

NOTE Confidence: 0.890639105

00:27:24.830 --> 00:27:26.438 For example, the metastasis.

NOTE Confidence: 0.924701439

00:27:28.410 --> 00:27:31.200 So how exactly does gene therapy

NOTE Confidence: 0.924701439

00:27:31.200 --> 00:27:33.060 activate the immune system?

NOTE Confidence: 0.924701439

00:27:33.060 --> 00:27:36.378 Because so many of us have heard

NOTE Confidence: 0.924701439

00:27:36.378 --> 00:27:37.800 about checkpoint inhibitors.

NOTE Confidence: 0.924701439

00:27:37.800 --> 00:27:40.050 You told us a little bit

NOTE Confidence: 0.924701439

00:27:40.050 --> 00:27:41.175 about cellular therapy.

NOTE Confidence: 0.924701439

00:27:41.180 --> 00:27:44.781 Tell us how gene therapy kind

NOTE Confidence: 0.924701439

00:27:44.781 --> 00:27:47.189 of revs up the immune system as well.

NOTE Confidence: 0.796740372

00:27:48.770 --> 00:27:50.390 One of our earlier studies,

NOTE Confidence: 0.796740372

00:27:50.390 --> 00:27:52.970 we used CRISPR

NOTE Confidence: 0.796740372

00:27:52.970 --> 00:27:55.944 activation and again this is similar to

NOTE Confidence: 0.796740372

00:27:55.944 --> 00:27:58.681 what we do for supercharging T cells,

NOTE Confidence: 0.796740372

00:27:58.690 --> 00:28:01.819 but in this case we are promoting

NOTE Confidence: 0.796740372

00:28:01.819 --> 00:28:04.218 the expression of antigens because

NOTE Confidence: 0.796740372

00:28:04.218 --> 00:28:07.110 the cancer cells they don't want
NOTE Confidence: 0.796740372

00:28:07.110 --> 00:28:10.448 to be seen by the immune system.
NOTE Confidence: 0.796740372

00:28:10.450 --> 00:28:12.785 Therefore they downregulate what they
NOTE Confidence: 0.796740372

00:28:12.785 --> 00:28:15.120 could downregulate the expression of
NOTE Confidence: 0.796740372

00:28:15.186 --> 00:28:17.268 their own antigen on the surface.
NOTE Confidence: 0.796740372

00:28:17.270 --> 00:28:19.388 What we try to do is
NOTE Confidence: 0.796740372

00:28:19.390 --> 00:28:21.810 forced expression of those antigen
NOTE Confidence: 0.796740372

00:28:21.810 --> 00:28:24.230 to be hyperactivated or hyper
NOTE Confidence: 0.796740372

00:28:24.306 --> 00:28:27.072 Express and presented on the surface
NOTE Confidence: 0.796740372

00:28:27.072 --> 00:28:29.734 and therefore we're like setting a
NOTE Confidence: 0.796740372

00:28:29.734 --> 00:28:32.324 light on those cancer cells and let
NOTE Confidence: 0.796740372

00:28:32.324 --> 00:28:34.250 the immune system see them better.
NOTE Confidence: 0.860489190666667

00:28:34.680 --> 00:28:37.288 Doctor Sidi Chen is an associate professor of
NOTE Confidence: 0.860489190666667

00:28:37.288 --> 00:28:39.660 genetics at the Yale School of Medicine.
NOTE Confidence: 0.860489190666667

00:28:39.660 --> 00:28:43.118 If you have questions the address is
NOTE Confidence: 0.860489190666667

00:28:43.120 --> 00:28:44.572 canceranswers@yale.edu and past editions

NOTE Confidence: 0.860489190666667

00:28:44.572 --> 00:28:47.084 of the program are available in audio

NOTE Confidence: 0.860489190666667

00:28:47.084 --> 00:28:49.065 and written form at Yale Cancer Center.org

NOTE Confidence: 0.860489190666667

00:28:49.070 --> 00:28:51.054 We hope you'll join us next week

NOTE Confidence: 0.860489190666667

00:28:51.054 --> 00:28:53.310 to learn more about the fight against

NOTE Confidence: 0.860489190666667

00:28:53.310 --> 00:28:55.403 cancer here on Connecticut Public radio.

NOTE Confidence: 0.860489190666667

00:28:55.403 --> 00:28:57.353 Funding for Yale Cancer Answers is

NOTE Confidence: 0.860489190666667

00:28:57.353 --> 00:29:00.000 provided by Smilow Cancer Hospital.