WEBVTT

00:00:00.000 --> 00:00:02.460 Support for Yale Cancer Answers

NOTE Confidence: 0.8556536

00:00:02.460 --> 00:00:04.920 comes from AstraZeneca, dedicated

NOTE Confidence: 0.8556536

00:00:04.999 --> 00:00:07.344 to advancing options and providing

NOTE Confidence: 0.8556536

00:00:07.344 --> 00:00:10.300 hope for people living with cancer.

NOTE Confidence: 0.8556536

00:00:10.300 --> 00:00:14.060 More information at astrazeneca-us.com.

NOTE Confidence: 0.8556536

00:00:14.060 --> 00:00:16.040 Welcome to Yale Cancer Answers with

NOTE Confidence: 0.8556536

00:00:16.040 --> 00:00:18.572 your host doctor Anees Chagpar.

NOTE Confidence: 0.8556536

00:00:18.572 --> 00:00:20.492 Yale Cancer Answers features the

NOTE Confidence: 0.8556536

00:00:20.492 --> 00:00:22.832 latest information on cancer care by

NOTE Confidence: 0.8556536

00:00:22.832 --> 00:00:24.344 welcoming oncologists and specialists

NOTE Confidence: 0.8556536

00:00:24.344 --> 00:00:26.910 who are on the forefront of the

NOTE Confidence: 0.8556536

00:00:26.910 --> 00:00:29.150 battle to fight cancer. This week,

NOTE Confidence: 0.8556536

00:00:29.150 --> 00:00:31.298 it's a conversation about immunotherapies

NOTE Confidence: 0.8556536

00:00:31.298 --> 00:00:33.560 for cancer with Doctor Carla Rothlin.

NOTE Confidence: 0.8556536

00:00:33.560 --> 00:00:35.400 Doctor Rothlin is Dorys McConnell Duberg Professor

1

NOTE Confidence: 0.8556536

00:00:35.400 --> 00:00:36.920 of Immunobiology

NOTE Confidence: 0.8556536

00:00:36.920 --> 00:00:38.440 and professor of Pharmacology

NOTE Confidence: 0.8556536

00:00:38.440 --> 00:00:40.560 at the Yale School of Medicine,

NOTE Confidence: 0.8556536

00:00:40.560 --> 00:00:43.266 where Doctor Chagpar is a

NOTE Confidence: 0.8556536

00:00:43.266 --> 00:00:45.070 professor of surgical oncology.

00:00:45.450 --> 00:00:48.042 Carla, maybe we can start off by you telling

NOTE Confidence: 0.8592381

00:00:48.042 --> 00:00:50.708 us a little bit about yourself

NOTE Confidence: 0.8592381

00:00:50.710 --> 00:00:52.999 and what you do.

NOTE Confidence: 0.8592381

00:00:52.999 --> 00:00:55.624 I was born in Argentina

NOTE Confidence: 0.8592381

00:00:55.624 --> 00:00:58.840 and it is in Argentina where I did

NOTE Confidence: 0.8592381

00:00:58.840 --> 00:01:01.234 all my initial training in science.

NOTE Confidence: 0.8592381

00:01:01.240 --> 00:01:04.384 I studied biochemistry in pharmacy at the

NOTE Confidence: 0.8592381

00:01:04.384 --> 00:01:06.969 University of Buenos Aires and did

NOTE Confidence: 0.8592381

00:01:06.969 --> 00:01:09.890 my PhD at the University of Buenos Aires.

NOTE Confidence: 0.8592381

00:01:09.890 --> 00:01:10.642 And interestingly,

NOTE Confidence: 0.8592381

00:01:10.642 --> 00:01:13.650 it was in a very different area of research.

NOTE Confidence: 0.8592381

00:01:13.650 --> 00:01:16.150 My PhD was in Neuropharmacology.

NOTE Confidence: 0.8592381

00:01:16.150 --> 00:01:18.484 And then now almost 20 years

NOTE Confidence: 0.8592381

00:01:18.484 --> 00:01:21.808 ago I came to the United States.

NOTE Confidence: 0.8592381

00:01:21.810 --> 00:01:24.420 I came in particular to California

NOTE Confidence: 0.8592381

00:01:24.420 --> 00:01:26.160 to the Salk Institute,

NOTE Confidence: 0.8592381

00:01:26.160 --> 00:01:28.770 where I did my postdoctoral training,

NOTE Confidence: 0.8592381

00:01:28.770 --> 00:01:31.745 and it was there where I became

NOTE Confidence: 0.8592381

00:01:31.745 --> 00:01:34.414 fascinated by immunology and where I

NOTE Confidence: 0.8592381

00:01:34.414 --> 00:01:36.599 started to learn about immunology,

NOTE Confidence: 0.8592381

00:01:36.600 --> 00:01:39.240 and I know today we're going

NOTE Confidence: 0.8592381

00:01:39.240 --> 00:01:41.380 to talk more about it,

NOTE Confidence: 0.8592381

00:01:41.380 --> 00:01:43.585 and after doing my postdoc

NOTE Confidence: 0.8592381

00:01:43.585 --> 00:01:45.790 at the Salk Institute about

NOTE Confidence: 0.8592381

00:01:45.790 --> 00:01:48.950 12 years ago I moved to Yale,

NOTE Confidence: 0.8592381

00:01:48.950 --> 00:01:51.598 where I started my own lab and I'm

NOTE Confidence: 0.8592381

00:01:51.598 --> 00:01:53.713 at the Department of Immunobiology.

00:01:58.830 --> 00:02:01.434 I've had a wonderful time here and I'm very

NOTE Confidence: 0.8592381

00:02:01.434 --> 00:02:03.905 fortunate to have been able to

NOTE Confidence: 0.8592381

00:02:03.905 --> 00:02:05.540 start my lab at this

00:02:06.330 --> 00:02:07.120 wonderful University.

NOTE Confidence: 0.845423

00:02:07.120 --> 00:02:10.675 So tell us more about what your lab does

NOTE Confidence: 0.845423

00:02:10.680 --> 00:02:12.264 and what you study?

NOTE Confidence: 0.845423

00:02:12.264 --> 00:02:14.244 We are very interested in

NOTE Confidence: 0.845423

00:02:14.244 --> 00:02:16.059 understanding the immune response.

NOTE Confidence: 0.845423

00:02:16.060 --> 00:02:17.473 But in particular,

NOTE Confidence: 0.845423

00:02:17.473 --> 00:02:19.828 what we're interested in understanding

NOTE Confidence: 0.845423

00:02:19.828 --> 00:02:23.055 is what are the mechanisms that regulate

NOTE Confidence: 0.845423

00:02:23.055 --> 00:02:25.920 how much the immune response will be.

NOTE Confidence: 0.845423

00:02:25.920 --> 00:02:28.380 So how do you regulate the

NOTE Confidence: 0.845423

00:02:28.380 --> 00:02:30.840 magnitude of the immune response?

NOTE Confidence: 0.845423

00:02:30.840 --> 00:02:33.080 And also how long that

NOTE Confidence: 0.845423

00:02:33.080 --> 00:02:34.872 immune response will be?

NOTE Confidence: 0.845423

00:02:34.880 --> 00:02:37.120 How do you regulate the

NOTE Confidence: 0.845423

00:02:37.120 --> 00:02:39.360 duration of the immune response?

NOTE Confidence: 0.845423

00:02:39.360 --> 00:02:41.600 And as you can imagine,

NOTE Confidence: 0.845423

00:02:41.600 --> 00:02:43.875 understanding the regulation of the

NOTE Confidence: 0.845423

00:02:43.875 --> 00:02:46.150 magnitude and the duration has

NOTE Confidence: 0.845423

00:02:46.150 --> 00:02:47.335 tremendous implications every time.

NOTE Confidence: 0.845423

00:02:47.335 --> 00:02:49.705 They mean responses turn on,

NOTE Confidence: 0.845423

00:02:49.710 --> 00:02:52.594 so those are the

NOTE Confidence: 0.845423

00:02:52.594 --> 00:02:54.670 two fundamental features of the

NOTE Confidence: 0.845423

00:02:54.670 --> 00:02:56.575 immune response that our lab

NOTE Confidence: 0.845423

00:02:56.575 --> 00:02:58.030 centers around.

NOTE Confidence: 0.87366736

00:02:58.030 --> 00:03:00.312 Right now when we're in the

NOTE Confidence: 0.87366736

00:03:00.312 --> 00:03:02.815 middle of this covid pandemic and

NOTE Confidence: 0.87366736

00:03:02.815 --> 00:03:04.755 people are getting vaccinated,

NOTE Confidence: 0.87366736

00:03:04.760 --> 00:03:07.528 I think a lot of people are thinking

NOTE Confidence: 0.87366736

00:03:07.528 --> 00:03:09.894 about the immune response in terms

NOTE Confidence: 0.87366736

00:03:09.894 --> 00:03:12.804 of vaccines and how long that

NOTE Confidence: 0.87366736

00:03:12.804 --> 00:03:15.922 immunity from the vaccine will last.

NOTE Confidence: 0.87366736

00:03:15.922 --> 00:03:19.698 Has your lab thought about that?

NOTE Confidence: 0.87366736

00:03:19.700 --> 00:03:23.120 How do we gauge how

NOTE Confidence: 0.87366736

00:03:23.120 --> 00:03:26.350 long an immune response will last

NOTE Confidence: 0.87366736

00:03:26.350 --> 00:03:29.008 from a vaccine, for example?

NOTE Confidence: 0.8374453

00:03:29.010 --> 00:03:31.220 That's a very,

NOTE Confidence: 0.8374453

00:03:31.220 --> 00:03:32.483 very interesting question.

NOTE Confidence: 0.8374453

00:03:32.483 --> 00:03:35.430 When you think about the

NOTE Confidence: 0.8374453

00:03:35.506 --> 00:03:37.866 duration of the immune response,

NOTE Confidence: 0.8374453

00:03:37.870 --> 00:03:40.908 you would probably want to also think

NOTE Confidence: 0.8374453

00:03:40.908 --> 00:03:43.629 how the immune system is built.

NOTE Confidence: 0.8374453

00:03:43.630 --> 00:03:47.246 So it turns out that the immune system

NOTE Confidence: 0.8374453

00:03:47.250 --> 00:03:49.375 in mammals, and in humans,

NOTE Confidence: 0.8374453

00:03:49.375 --> 00:03:51.500 has two big divisions.

00:03:52.697 --> 00:03:56.021 One, which is called innate and we are all

NOTE Confidence: 0.8374453

00:03:56.021 --> 00:03:59.150 born with that type of immune response.

NOTE Confidence: 0.8374453

00:03:59.150 --> 00:04:02.130 And it's the very fast, quick response.

NOTE Confidence: 0.8374453

00:04:02.130 --> 00:04:05.105 And then there's another one which is

NOTE Confidence: 0.8374453

00:04:05.105 --> 00:04:08.079 called adaptive and that is more tailored,

NOTE Confidence: 0.8374453

00:04:08.080 --> 00:04:11.480 more specific to each of the pathogens that,

NOTE Confidence: 0.8374453

00:04:11.480 --> 00:04:12.344 for instance,

NOTE Confidence: 0.8374453

00:04:12.344 --> 00:04:14.936 we can encounter when we're thinking

NOTE Confidence: 0.8374453

00:04:14.936 --> 00:04:17.568 about the duration of the immune

NOTE Confidence: 0.8374453

00:04:17.568 --> 00:04:20.112 response in the context of vaccines.

NOTE Confidence: 0.8374453

00:04:20.120 --> 00:04:22.544 We are thinking that we really

NOTE Confidence: 0.8374453

00:04:22.544 --> 00:04:25.550 want to activate those cells of the

NOTE Confidence: 0.8374453

00:04:25.550 --> 00:04:27.725 adaptive immune system because they

NOTE Confidence: 0.8374453

00:04:27.725 --> 00:04:30.508 have the peculiarity that they can

NOTE Confidence: 0.8374453

00:04:30.508 --> 00:04:33.256 remember, they have memory and that

NOTE Confidence: 0.8374453

00:04:33.260 --> 00:04:35.450 is very important to understand.

00:04:35.862 --> 00:04:38.746 Our lab has focused primarily on trying

NOTE Confidence: 0.8374453

00:04:38.746 --> 00:04:40.989 to understand what regulates the

NOTE Confidence: 0.8374453

00:04:40.989 --> 00:04:43.677 duration of the more initial immune

NOTE Confidence: 0.8374453

00:04:43.677 --> 00:04:46.396 response of this innate immune response,

NOTE Confidence: 0.8374453

00:04:46.400 --> 00:04:49.190 and the reason why that is

NOTE Confidence: 0.8374453

00:04:49.190 --> 00:04:51.826 also very important is that

NOTE Confidence: 0.8374453

00:04:51.826 --> 00:04:54.065 a response is not so much

NOTE Confidence: 0.8374453

00:04:54.065 --> 00:04:56.442 directed to the pathogen to the

NOTE Confidence: 0.8374453

00:04:56.442 --> 00:04:58.827 microorganism that is infecting us.

NOTE Confidence: 0.8374453

00:04:58.830 --> 00:05:01.206 It can be broader and therefore

NOTE Confidence: 0.8374453

00:05:01.206 --> 00:05:03.296 can potentially have some

NOTE Confidence: 0.8374453

00:05:03.296 --> 00:05:04.598 adverse effects.

NOTE Confidence: 0.8374453

00:05:04.600 --> 00:05:05.378 For instance,

NOTE Confidence: 0.8374453

00:05:05.378 --> 00:05:07.323 inflammation forms part of this

NOTE Confidence: 0.8374453

00:05:07.323 --> 00:05:09.540 very first innate immune response,

NOTE Confidence: 0.8374453

00:05:09.540 --> 00:05:11.941 so we absolutely needed to get the

NOTE Confidence: 0.8374453

00:05:11.941 --> 00:05:14.381 system going to get the immune

NOTE Confidence: 0.8374453

00:05:14.381 --> 00:05:16.611 response going which is absolutely required

NOTE Confidence: 0.8374453

00:05:16.611 --> 00:05:19.020 for inducing this immune response,

NOTE Confidence: 0.8374453

00:05:19.020 --> 00:05:21.576 but it cannot go on forever.

NOTE Confidence: 0.8374453

00:05:21.580 --> 00:05:24.485 So our lab has really focused on

NOTE Confidence: 0.8374453

00:05:24.485 --> 00:05:26.844 trying to understand what dictates

NOTE Confidence: 0.8374453

00:05:26.844 --> 00:05:29.429 the duration of this initial

NOTE Confidence: 0.8374453

00:05:29.429 --> 00:05:30.980 innate immune response.

NOTE Confidence: 0.8374453

00:05:30.980 --> 00:05:31.920 So when

NOTE Confidence: 0.8592791

00:05:31.920 --> 00:05:35.210 you talk about the innate immune response,

NOTE Confidence: 0.8592791

00:05:35.210 --> 00:05:38.834 is that kind of like if somebody got

NOTE Confidence: 0.8592791

00:05:38.834 --> 00:05:41.320 infected with covid, whether they

NOTE Confidence: 0.8592791

00:05:41.320 --> 00:05:43.670 produce a response against that,

NOTE Confidence: 0.8592791

00:05:43.670 --> 00:05:46.799 or is that still more the

NOTE Confidence: 0.8592791

00:05:46.799 --> 00:05:49.354 other longer term response where

NOTE Confidence: 0.8592791

00:05:49.354 --> 00:05:52.040 you develop a memory?

NOTE Confidence: 0.8397811

00:05:52.040 --> 00:05:55.608 It's more the first type of response,

NOTE Confidence: 0.8397811

00:05:55.610 --> 00:05:58.850 so in our system, our

NOTE Confidence: 0.8397811

00:05:58.850 --> 00:06:02.629 immune system, is capable in that it can

NOTE Confidence: 0.8397811

00:06:02.629 --> 00:06:04.997 first recognize general changes.

NOTE Confidence: 0.8397811

00:06:04.997 --> 00:06:08.573 And let's say maybe we are infected just

NOTE Confidence: 0.8397811

00:06:08.573 --> 00:06:11.640 with a bacterial, with a virus, right?

NOTE Confidence: 0.8397811

00:06:11.640 --> 00:06:15.060 And it can detect that and the cells that

NOTE Confidence: 0.8397811

00:06:15.145 --> 00:06:17.959 are involved in detecting that initially

NOTE Confidence: 0.8397811

00:06:17.959 --> 00:06:21.538 are the source of this first response.

NOTE Confidence: 0.8397811

00:06:21.540 --> 00:06:23.288 This innate immune response.

NOTE Confidence: 0.8397811

00:06:23.288 --> 00:06:26.362 That can detect that we've been infected

NOTE Confidence: 0.8397811

00:06:26.362 --> 00:06:28.973 with a bacteria or with a virus.

NOTE Confidence: 0.8397811

00:06:28.980 --> 00:06:32.044 Or with the fungi or parasite.

NOTE Confidence: 0.8397811

00:06:32.050 --> 00:06:35.497 Now, as I was alluding to, there is this other

NOTE Confidence: 0.8397811

00:06:35.500 --> 00:06:37.420 more sophisticated adaptive immune response,

NOTE Confidence: 0.8397811

00:06:37.420 --> 00:06:40.080 and that takes a little bit longer

NOTE Confidence: 0.8397811

00:06:40.080 --> 00:06:42.438 to be triggered, is triggered by

NOTE Confidence: 0.8397811

00:06:42.438 --> 00:06:44.338 first the innate,

NOTE Confidence: 0.8397811

00:06:44.340 --> 00:06:46.260 and has that memory capacity.

NOTE Confidence: 0.8397811

00:06:46.260 --> 00:06:48.899 And what is beautiful also about this

NOTE Confidence: 0.8397811

00:06:48.899 --> 00:06:51.917 adaptive response is that it has the ability

NOTE Confidence: 0.8397811

00:06:51.917 --> 00:06:54.390 to distinguish which bacteria is infected.

NOTE Confidence: 0.8397811

00:06:54.390 --> 00:06:56.320 Or which viruses is infecting us.

NOTE Confidence: 0.8397811

00:06:56.320 --> 00:06:59.785 So just to take the example of a virus.

NOTE Confidence: 0.8397811

00:06:59.790 --> 00:07:00.560 For instance,

NOTE Confidence: 0.8397811

00:07:00.560 --> 00:07:02.100 our adaptive immune response

NOTE Confidence: 0.8397811

00:07:02.100 --> 00:07:04.040 to COVID-19 to SARS CoV2

NOTE Confidence: 0.8397811

00:07:04.040 --> 00:07:06.356 will be different than,

NOTE Confidence: 0.8397811

00:07:06.360 --> 00:07:07.737 for instance influenza.

NOTE Confidence: 0.8397811

00:07:07.737 --> 00:07:10.491 So the adaptive immune response can

NOTE Confidence: 0.8397811

00:07:10.491 --> 00:07:12.364 distinguish that and our lab focused

NOTE Confidence: 0.8397811

00:07:12.364 --> 00:07:14.782 more on the very first response that

NOTE Confidence: 0.8397811

00:07:14.782 --> 00:07:16.774 realizes that you have a virus,

NOTE Confidence: 0.8397811

00:07:16.780 --> 00:07:18.670 but maybe doesn't realize which

NOTE Confidence: 0.8397811

00:07:18.670 --> 00:07:20.560 viruses or realizes that you've

NOTE Confidence: 0.8397811

00:07:20.620 --> 00:07:22.180 been infected by bacteria,

NOTE Confidence: 0.8397811

00:07:22.180 --> 00:07:24.028 but doesn't really realize

NOTE Confidence: 0.8397811

00:07:24.028 --> 00:07:25.876 which type of bacteria.

NOTE Confidence: 0.8397811

00:07:25.880 --> 00:07:28.628 But this first response is fundamental

NOTE Confidence: 0.8397811

00:07:28.628 --> 00:07:31.133 and the very interesting aspect of

NOTE Confidence: 0.8397811

00:07:31.133 --> 00:07:33.517 it is that we are born with it.

NOTE Confidence: 0.8397811

00:07:33.520 --> 00:07:35.430 That's why it's called innate.

NOTE Confidence: 0.8397811

00:07:35.430 --> 00:07:38.097 So as soon as we are born,

NOTE Confidence: 0.8397811

00:07:38.100 --> 00:07:40.774 we are able to react to these

NOTE Confidence: 0.8397811

00:07:40.780 --> 00:07:41.914 microorganisms.

NOTE Confidence: 0.8397811

00:07:41.914 --> 00:07:44.980 And then as we are exposed to them,

NOTE Confidence: 0.8397811

00:07:44.980 --> 00:07:47.272 we are able to induce this

NOTE Confidence: 0.8397811

00:07:47.272 --> 00:07:48.418 adaptive immune response.

NOTE Confidence: 0.8397811

00:07:48.420 --> 00:07:49.521 This learned response,

NOTE Confidence: 0.8397811

00:07:49.521 --> 00:07:52.557 that is the one that then will confer

NOTE Confidence: 0.8397811

00:07:52.557 --> 00:07:55.287 memory and that will be more specific.

NOTE Confidence: 0.8575336

00:07:55.290 --> 00:07:58.027 Carla, when your lab studies

NOTE Confidence: 0.8575336

00:07:58.030 --> 00:07:59.782 this innate immune response,

NOTE Confidence: 0.8575336

00:07:59.782 --> 00:08:01.972 this initial response that hey,

NOTE Confidence: 0.8575336

00:08:01.980 --> 00:08:03.990 there's something foreign in my

NOTE Confidence: 0.8575336

00:08:03.990 --> 00:08:06.546 body and that will help trigger

NOTE Confidence: 0.8575336

00:08:06.546 --> 00:08:09.354 the more adaptive response you had

NOTE Confidence: 0.8575336

00:08:09.354 --> 00:08:11.639 mentioned that you're looking at,

NOTE Confidence: 0.8575336

00:08:11.640 --> 00:08:14.274 kind of the magnitude and the

NOTE Confidence: 0.8575336

00:08:14.274 --> 00:08:16.470 duration of that innate response,

NOTE Confidence: 0.8575336

00:08:16.470 --> 00:08:19.540 but it seems that the innate response

NOTE Confidence: 0.8575336

13

00:08:19.540 --> 00:08:22.476 is a little bit shorter than

NOTE Confidence: 0.8575336

00:08:22.476 --> 00:08:25.690 the longer term adaptive response.

NOTE Confidence: 0.8575336

00:08:25.690 --> 00:08:28.353 So how important is the magnitude

NOTE Confidence: 0.8575336

00:08:28.353 --> 00:08:30.608 and the duration of the

NOTE Confidence: 0.8575336

00:08:30.610 --> 00:08:33.658 innate response and why did you choose to

NOTE Confidence: 0.8538312

00:08:33.660 --> 00:08:35.560 look at that?

NOTE Confidence: 0.8538312

00:08:35.560 --> 00:08:37.470 That's absolutely a very important question.

NOTE Confidence: 0.8538312

00:08:37.470 --> 00:08:40.449 So of course my answer will be that it is

NOTE Confidence: 0.8538312

00:08:40.449 --> 00:08:43.556 very important and let me elaborate why.

NOTE Confidence: 0.8538312

00:08:43.560 --> 00:08:46.160 So in the field we have learned by

NOTE Confidence: 0.8538312

00:08:46.160 --> 00:08:49.017 the time we were starting to

NOTE Confidence: 0.8538312

00:08:49.017 --> 00:08:51.613 focus on trying to understand what

NOTE Confidence: 0.8538312

00:08:51.613 --> 00:08:53.850 regulates the magnitude and duration,

NOTE Confidence: 0.8538312

00:08:53.850 --> 00:08:55.760 we already knew a lot about

NOTE Confidence: 0.8538312

00:08:55.760 --> 00:08:58.040 what triggers this innate immune response.

NOTE Confidence: 0.8538312

00:08:58.040 --> 00:08:59.950 And that was fundamental, right?

NOTE Confidence: 0.8538312

00:08:59.950 --> 00:09:02.120 So we understood the rules

NOTE Confidence: 0.8538312

00:09:02.120 --> 00:09:04.232 by which thee immune response

NOTE Confidence: 0.8538312

00:09:04.232 --> 00:09:06.710 is engaged, but as I was saying,

NOTE Confidence: 0.8538312

00:09:06.710 --> 00:09:09.149 this is the very first response.

NOTE Confidence: 0.8538312

00:09:09.149 --> 00:09:11.701 It's the one that tells us all we

NOTE Confidence: 0.8538312

00:09:11.701 --> 00:09:14.437 have a bacteria or we have a virus

NOTE Confidence: 0.8538312

00:09:14.437 --> 00:09:16.291 but cannot really distinguish between

NOTE Confidence: 0.8538312

00:09:16.291 --> 00:09:19.411 the type of bacteria or the type of

NOTE Confidence: 0.8538312

00:09:19.420 --> 00:09:21.538 virus and therefore is very broad.

NOTE Confidence: 0.8538312

00:09:21.540 --> 00:09:24.179 It doesn't really help us to only

NOTE Confidence: 0.8538312

00:09:24.179 --> 00:09:26.611 attack the bacteria or the

NOTE Confidence: 0.8538312

00:09:26.611 --> 00:09:28.950 virus or the parasite and it also can't,

NOTE Confidence: 0.8538312

00:09:28.950 --> 00:09:31.414 when a function is triggered,

NOTE Confidence: 0.8538312

00:09:31.420 --> 00:09:32.572 it can also

NOTE Confidence: 0.8538312

00:09:32.572 --> 00:09:35.260 induce what you could call collateral

NOTE Confidence: 0.8538312

00:09:35.338 --> 00:09:38.234 damage and it can affect your own cells.

NOTE Confidence: 0.8538312

00:09:38.240 --> 00:09:40.683 The classical example is that inflammation is

NOTE Confidence: 0.8538312

00:09:40.683 --> 00:09:43.726 a key part of this innate immune response,

NOTE Confidence: 0.8538312

00:09:43.730 --> 00:09:45.560 and as you can imagine,

NOTE Confidence: 0.8538312

00:09:45.560 --> 00:09:47.385 inflammation can be very good

NOTE Confidence: 0.8538312

00:09:47.385 --> 00:09:48.845 to help eliminate pathogens,

NOTE Confidence: 0.8538312

00:09:48.850 --> 00:09:51.419 but can also affect our own body.

NOTE Confidence: 0.8538312

00:09:51.420 --> 00:09:54.428 So we absolutely need this response when you

NOTE Confidence: 0.8538312

00:09:54.428 --> 00:09:57.269 get injured or when you have an infection.

NOTE Confidence: 0.8538312

00:09:57.270 --> 00:10:00.334 But the problem is what happens if you

NOTE Confidence: 0.8538312

00:10:00.334 --> 00:10:03.175 react way too much or if you react forever,

00:10:03.518 --> 00:10:05.884 and so that became a key interest

NOTE Confidence: 0.8538312

00:10:05.884 --> 00:10:08.290 of our lab trying to understand

NOTE Confidence: 0.8538312

00:10:08.290 --> 00:10:09.946 what dictates how much

NOTE Confidence: 0.8538312

00:10:09.950 --> 00:10:12.958 you should respond so that you can attack

NOTE Confidence: 0.8538312

00:10:12.958 --> 00:10:15.555 the pathogen but not yourself and how

NOTE Confidence: 0.8538312

00:10:15.555 --> 00:10:18.166 long you should respond so that once

NOTE Confidence: 0.8538312

00:10:18.166 --> 00:10:20.464 you have eliminated the passage and

NOTE Confidence: 0.8538312

00:10:20.464 --> 00:10:23.110 you don't keep on reacting against

NOTE Confidence: 0.8538312

00:10:23.110 --> 00:10:25.735 something that is not there anymore.

NOTE Confidence: 0.8538312

00:10:25.740 --> 00:10:28.099 So over the years we have been

NOTE Confidence: 0.8538312

00:10:28.099 --> 00:10:30.446 able to identify key breaks of

NOTE Confidence: 0.8538312

00:10:30.446 --> 00:10:32.126 the innate immune response.

00:10:32.510 --> 00:10:35.338 Why did you choose to look at

NOTE Confidence: 0.86353021

00:10:35.338 --> 00:10:38.188 the innate response and why is the

NOTE Confidence: 0.86353021

00:10:38.188 --> 00:10:40.516 magnitude and duration of that so

NOTE Confidence: 0.86260635

00:10:40.520 --> 00:10:42.896 important?

NOTE Confidence: 0.86260635

00:10:42.900 --> 00:10:45.490 As I was alluding, we

NOTE Confidence: 0.86260635

00:10:45.574 --> 00:10:48.521 require this very first innate

NOTE Confidence: 0.86260635

00:10:48.521 --> 00:10:51.844 response and at the time we started

NOTE Confidence: 0.86260635

00:10:51.844 --> 00:10:54.314 to become interested in understanding

NOTE Confidence: 0.86260635

00:10:54.314 --> 00:10:57.012 the regulation of the magnitude and the

NOTE Confidence: 0.86260635

17

00:10:57.012 --> 00:10:59.579 duration of the innate immune response,

NOTE Confidence: 0.86260635

00:10:59.580 --> 00:11:02.358 we already knew quite a lot what

NOTE Confidence: 0.86260635

00:11:02.360 --> 00:11:04.340 triggers this innate immune response.

NOTE Confidence: 0.86260635

00:11:04.340 --> 00:11:06.450 So that was fundamental work

NOTE Confidence: 0.86260635

00:11:06.450 --> 00:11:08.560 that allows us to understand

NOTE Confidence: 0.86260635

00:11:08.560 --> 00:11:10.800 that you need this response,

NOTE Confidence: 0.86260635

00:11:10.800 --> 00:11:14.544 but if features of this response as I was

NOTE Confidence: 0.86260635

00:11:14.544 --> 00:11:17.965 saying before is that it is triggered when,

NOTE Confidence: 0.86260635

00:11:17.970 --> 00:11:20.265 for instance, you encounter bacteria

NOTE Confidence: 0.86260635

00:11:20.265 --> 00:11:23.340 or a virus or parasite or fungi.

NOTE Confidence: 0.86260635

00:11:23.340 --> 00:11:25.734 But it's pretty broad and therefore

NOTE Confidence: 0.86260635

00:11:25.734 --> 00:11:28.423 it not only reacts against the

NOTE Confidence: 0.86260635

00:11:28.423 --> 00:11:30.958 microorganism or the macroorganism,

NOTE Confidence: 0.86260635

00:11:30.960 --> 00:11:34.536 but it can also affect your own self.

NOTE Confidence: 0.86260635

00:11:34.540 --> 00:11:35.524 For instance,

NOTE Confidence: 0.86260635

00:11:35.524 --> 00:11:38.476 a classic aspect of the innate

18

NOTE Confidence: 0.86260635

00:11:38.476 --> 00:11:40.450 immune response is what we

NOTE Confidence: 0.86260635

00:11:40.450 --> 00:11:42.934 usually call inflammation and so you

NOTE Confidence: 0.86260635

00:11:42.934 --> 00:11:45.850 can imagine that if this very broad

NOTE Confidence: 0.86260635

00:11:45.850 --> 00:11:48.214 immune response is way too high,

NOTE Confidence: 0.86260635

00:11:48.220 --> 00:11:50.270 or if it lasts forever,

NOTE Confidence: 0.86260635

00:11:50.270 --> 00:11:52.604 it can really induce what

NOTE Confidence: 0.86260635

00:11:52.604 --> 00:11:54.770 is known as collateral damage.

NOTE Confidence: 0.86260635

00:11:54.770 --> 00:11:58.034 It can really start affecting your own body,

NOTE Confidence: 0.86260635

00:11:58.040 --> 00:12:00.630 the way the system is built

NOTE Confidence: 0.86260635

00:12:00.630 --> 00:12:03.601 is that you kind of turn

NOTE Confidence: 0.86260635

00:12:03.601 --> 00:12:05.806 on this initial fire

NOTE Confidence: 0.86260635

00:12:05.810 --> 00:12:09.074 that then allows the induction of the more

NOTE Confidence: 0.86260635

00:12:09.074 --> 00:12:10.959 sophisticated adaptive immune response.

NOTE Confidence: 0.86260635

00:12:10.960 --> 00:12:14.218 But then you need to put off this fire,

NOTE Confidence: 0.86260635

00:12:14.220 --> 00:12:16.405 and that's when these molecular

NOTE Confidence: 0.86260635

19

00:12:16.405 --> 00:12:18.590 mechanisms that regulate how big

NOTE Confidence: 0.86260635

00:12:18.668 --> 00:12:20.726 the fire will be and how long

NOTE Confidence: 0.86260635

00:12:20.726 --> 00:12:22.910 the fire will be come into play.

NOTE Confidence: 0.86260635

00:12:22.910 --> 00:12:25.082 And you can imagine that then

NOTE Confidence: 0.86260635

00:12:25.082 --> 00:12:26.530 they become very important.

NOTE Confidence: 0.86260635

00:12:26.530 --> 00:12:28.340 You really need to regulate

NOTE Confidence: 0.86260635

00:12:28.340 --> 00:12:30.150 how much and the duration,

NOTE Confidence: 0.86260635

00:12:30.150 --> 00:12:32.418 so that then you don't start affecting

NOTE Confidence: 0.86260635

00:12:32.418 --> 00:12:34.858 your own self and this is what could

NOTE Confidence: 0.86260635

00:12:34.858 --> 00:12:37.265 happen in some type of diseases such

NOTE Confidence: 0.86260635

00:12:37.265 --> 00:12:39.605 as chronic inflammatory diseases or

NOTE Confidence: 0.86260635

00:12:39.605 --> 00:12:41.834 autoimmune diseases where you start

NOTE Confidence: 0.86260635

00:12:41.834 --> 00:12:43.894 affecting your own self.

NOTE Confidence: 0.86260635

00:12:43.900 --> 00:12:45.148 And so as

NOTE Confidence: 0.87161815

00:12:45.150 --> 00:12:48.069 we think about the implications for cancer,

NOTE Confidence: 0.87161815

00:12:48.070 --> 00:12:50.410 I mean what you're describing makes

NOTE Confidence: 0.87161815

00:12:50.410 --> 00:12:53.069 me think about things like hepatitis,

NOTE Confidence: 0.87161815

00:12:53.070 --> 00:12:55.989 where you can have hepatitis,

NOTE Confidence: 0.87161815

00:12:55.990 --> 00:12:57.494 which then causes inflammation

NOTE Confidence: 0.87161815

00:12:57.494 --> 00:12:59.750 and fibrosis and sets you

NOTE Confidence: 0.87161815

00:12:59.821 --> 00:13:01.829 up for hepatocellular carcinoma.

NOTE Confidence: 0.87161815

00:13:01.830 --> 00:13:04.806 Is that kind of the area that then

NOTE Confidence: 0.87161815

00:13:04.806 --> 00:13:07.660 brought you to thinking about cancer?

NOTE Confidence: 0.87161815

00:13:07.660 --> 00:13:10.996 Or where does the cancer angle come in?

NOTE Confidence: 0.8880543

00:13:11.910 --> 00:13:15.070 Yeah, that's a very very good analogy.

NOTE Confidence: 0.8880543

00:13:15.070 --> 00:13:17.440 So it turns out that absolutely,

NOTE Confidence: 0.8880543

00:13:17.440 --> 00:13:18.126 you're right.

NOTE Confidence: 0.8880543

00:13:18.126 --> 00:13:20.184 You have situations where you have

NOTE Confidence: 0.8880543

00:13:20.184 --> 00:13:22.180 this very chronic inflammation.

NOTE Confidence: 0.8880543

00:13:22.180 --> 00:13:24.388 This persistent

NOTE Confidence: 0.8880543

00:13:24.388 --> 00:13:26.920 activation of this innate immune response,

NOTE Confidence: 0.8880543

00:13:26.920 --> 00:13:29.811 and we know that chronic inflammation can

NOTE Confidence: 0.8880543

00:13:29.811 --> 00:13:32.447 absolutely increase the risk of some cancers.

NOTE Confidence: 0.8880543

00:13:32.450 --> 00:13:34.820 But the answer is not just

NOTE Confidence: 0.8880543

00:13:34.820 --> 00:13:36.400 so black and white.

NOTE Confidence: 0.8880543

00:13:36.400 --> 00:13:39.096 So what we're starting to learn is that

NOTE Confidence: 0.8880543

00:13:39.096 --> 00:13:42.049 there are different types of inflammation.

NOTE Confidence: 0.8880543

00:13:42.050 --> 00:13:44.018 One like the one you described,

NOTE Confidence: 0.8880543

00:13:44.020 --> 00:13:45.670 very well known to increase

NOTE Confidence: 0.8880543

00:13:45.670 --> 00:13:46.990 the risk of cancers,

NOTE Confidence: 0.8880543

00:13:46.990 --> 00:13:48.630 but there are other potential

NOTE Confidence: 0.8880543

00:13:48.630 --> 00:13:49.614 types of inflammation,

NOTE Confidence: 0.8880543

00:13:49.620 --> 00:13:51.540 and this is actually the area

NOTE Confidence: 0.8880543

00:13:51.540 --> 00:13:53.240 of much

NOTE Confidence: 0.8880543

00:13:53.240 --> 00:13:55.208 ongoing investigation in the whole field.

NOTE Confidence: 0.8880543

00:13:55.210 --> 00:13:57.382 What are the different types of

NOTE Confidence: 0.8880543

00:13:57.382 --> 00:13:59.532 inflammation that you have in cancer

22

NOTE Confidence: 0.8880543

00:13:59.532 --> 00:14:01.758 and how do they contribute to the

NOTE Confidence: 0.8880543

00:14:01.758 --> 00:14:03.609 concern and the analogy that I

NOTE Confidence: 0.8880543

00:14:03.609 --> 00:14:05.678 would make is that let's say you

NOTE Confidence: 0.8880543

00:14:05.678 --> 00:14:07.771 sometimes want to induce a little bit

NOTE Confidence: 0.8880543

00:14:07.771 --> 00:14:10.539 of this fire to mount a good

NOTE Confidence: 0.8880543

00:14:10.539 --> 00:14:12.319 immune response against the cancer,

NOTE Confidence: 0.8880543

00:14:12.320 --> 00:14:14.616 but you don't want to use too

NOTE Confidence: 0.8880543

00:14:14.616 --> 00:14:16.040 much that

NOTE Confidence: 0.8880543

00:14:16.040 --> 00:14:17.156 may be detrimental,

NOTE Confidence: 0.8880543

00:14:17.156 --> 00:14:20.272 so we are still at the level of

NOTE Confidence: 0.8880543

00:14:20.272 --> 00:14:22.834 trying to understand what are the

NOTE Confidence: 0.8880543

00:14:22.834 --> 00:14:24.697 different types of inflammatory

NOTE Confidence: 0.8880543

00:14:24.697 --> 00:14:27.721 responses in cancer and how they

NOTE Confidence: 0.8880543

00:14:27.721 --> 00:14:30.449 contribute to mount a good immune

NOTE Confidence: 0.8880543

00:14:30.449 --> 00:14:32.867 response against cancer or how they

NOTE Confidence: 0.8880543

00:14:32.867 --> 00:14:35.399 might contribute to actually favor

NOTE Confidence: 0.86789036

00:14:35.400 --> 00:14:36.244 cancer progression.

NOTE Confidence: 0.86789036

00:14:36.244 --> 00:14:38.776 And so when you're

NOTE Confidence: 0.86789036

00:14:38.776 --> 00:14:41.059 talking about mounting an

NOTE Confidence: 0.86789036

00:14:41.059 --> 00:14:42.879 immune response against cancer,

NOTE Confidence: 0.86789036

00:14:42.880 --> 00:14:45.180 it reminds me of things

NOTE Confidence: 0.86789036

00:14:45.180 --> 00:14:46.560 like immunotherapy.

NOTE Confidence: 0.86789036

00:14:46.560 --> 00:14:48.877 As we think about cancers

NOTE Confidence: 0.86789036

00:14:48.877 --> 00:14:51.950 and when we think about immunotherapy,

NOTE Confidence: 0.86789036

00:14:51.950 --> 00:14:54.456 we often think about revving

NOTE Confidence: 0.86789036

00:14:54.456 --> 00:14:57.152 up that immune system because so many

NOTE Confidence: 0.86789036

00:14:57.152 --> 00:15:00.040 cancers can hide from the immune system.

NOTE Confidence: 0.86789036

00:15:00.040 --> 00:15:02.336 So I wonder whether part of your

NOTE Confidence: 0.86789036

00:15:02.336 --> 00:15:05.039 work has to do with immunotherapy.

NOTE Confidence: 0.86789036

00:15:05.040 --> 00:15:07.864 But first we have to take a quick

NOTE Confidence: 0.86789036

00:15:07.864 --> 00:15:10.049 break for a medical minute,

NOTE Confidence: 0.86789036

00:15:10.050 --> 00:15:12.801 so please stay tuned for more information

NOTE Confidence: 0.86789036

00:15:12.801 --> 00:15:14.410 about immunotherapy and cancer

NOTE Confidence: 0.86789036

00:15:14.410 --> 00:15:16.588 with my guest Doctor Carla Rothlin.

NOTE Confidence: 0.838625

00:15:17.110 --> 00:15:19.670 Support for Yale Cancer Answers

NOTE Confidence: 0.838625

00:15:19.670 --> 00:15:22.722 comes from AstraZeneca, working to

NOTE Confidence: 0.838625

00:15:22.722 --> 00:15:25.564 eliminate cancer as a cause of death.

NOTE Confidence: 0.838625

00:15:25.570 --> 00:15:29.190 Learn more at astrazeneca-us.com.

NOTE Confidence: 0.838625

00:15:29.190 --> 00:15:31.969 This is a medical minute about Melanoma.

NOTE Confidence: 0.838625

00:15:31.970 --> 00:15:33.955 While Melanoma accounts for only

NOTE Confidence: 0.838625

00:15:33.955 --> 00:15:36.194 about 4% of skin cancer cases,

NOTE Confidence: 0.838625

00:15:36.194 --> 00:15:38.360 it causes the most skin cancer

NOTE Confidence: 0.838625

00:15:38.433 --> 00:15:40.309 deaths when detected early,

NOTE Confidence: 0.838625

00:15:40.310 --> 00:15:41.894 however, Melanoma is easily

NOTE Confidence: 0.838625

00:15:41.894 --> 00:15:43.874 treated and highly curable.

NOTE Confidence: 0.838625

00:15:43.880 --> 00:15:46.160 Clinical trials are currently underway to test

NOTE Confidence: 0.838625

00:15:46.160 --> 00:15:48.250 innovative new treatments for Melanoma.

NOTE Confidence: 0.838625

00:15:48.250 --> 00:15:50.764 The goal of the specialized programs

NOTE Confidence: 0.838625

00:15:50.764 --> 00:15:53.243 of research excellence in skin cancer

NOTE Confidence: 0.838625

00:15:53.243 --> 00:15:55.798 or SPORE grant is to better understand

NOTE Confidence: 0.838625

00:15:55.798 --> 00:15:58.979 the biology of skin cancer with a focus

NOTE Confidence: 0.838625

00:15:58.979 --> 00:16:01.525 on discovering targets that will lead

NOTE Confidence: 0.838625

00:16:01.525 --> 00:16:03.800 to improved diagnosis and treatment.

NOTE Confidence: 0.838625

00:16:03.800 --> 00:16:05.884 More information is available

NOTE Confidence: 0.838625

00:16:05.884 --> 00:16:06.926 at yalecancercenter.org.

NOTE Confidence: 0.838625

00:16:06.930 --> 00:16:11.286 You're listening to Connecticut Public Radio.

NOTE Confidence: 0.838625

00:16:11.290 --> 00:16:11.660 Welcome

NOTE Confidence: 0.859347

00:16:11.660 --> 00:16:13.500 back to Yale Cancer Answers.

NOTE Confidence: 0.859347

00:16:13.500 --> 00:16:15.782 This is doctor Anees Chagpar

NOTE Confidence: 0.859347

00:16:15.782 --> 00:16:18.086 and I'm joined tonight by my

NOTE Confidence: 0.859347

00:16:18.086 --> 00:16:19.750 guest doctor Carla Rothlin.

NOTE Confidence: 0.859347

00:16:19.750 --> 00:16:21.210 We're talking about immunotherapy

NOTE Confidence: 0.859347

00:16:21.210 --> 00:16:23.800 for cancer and right before the break

NOTE Confidence: 0.859347

00:16:23.800 --> 00:16:26.152 Carla, you were telling us about

NOTE Confidence: 0.859347

00:16:26.152 --> 00:16:28.949 the work that goes on in your lab.

NOTE Confidence: 0.859347

00:16:28.950 --> 00:16:31.326 Really looking at the innate immune

NOTE Confidence: 0.859347

00:16:31.326 --> 00:16:33.601 response and the magnitude and duration

NOTE Confidence: 0.859347

00:16:33.601 --> 00:16:35.792 of that response and I wonder

NOTE Confidence: 0.859347

00:16:35.792 --> 00:16:38.149 how that really pertains to cancer.

NOTE Confidence: 0.859347

00:16:38.150 --> 00:16:39.990 And right before the break,

NOTE Confidence: 0.859347

00:16:39.990 --> 00:16:42.030 you mentioned that it's not

NOTE Confidence: 0.859347

00:16:42.030 --> 00:16:43.254 only thinking about

NOTE Confidence: 0.859347

00:16:43.260 --> 00:16:45.335 the inflammation and collateral

NOTE Confidence: 0.859347

00:16:45.335 --> 00:16:47.937 damage that can occur that may

NOTE Confidence: 0.859347

00:16:47.937 --> 00:16:49.757 predispose patients to cancer,

NOTE Confidence: 0.859347

00:16:49.760 --> 00:16:52.112 but it's also in looking at

NOTE Confidence: 0.859347

00:16:52.112 --> 00:16:54.258 the immune response that your

NOTE Confidence: 0.859347

00:16:54.258 --> 00:16:56.250 body mounts against cancers,

NOTE Confidence: 0.859347

00:16:56.250 --> 00:16:58.410 which makes me think more

NOTE Confidence: 0.859347

00:16:58.410 --> 00:16:59.274 about immunotherapy.

NOTE Confidence: 0.859347

00:16:59.280 --> 00:17:02.432 So can you talk a little bit about

NOTE Confidence: 0.859347

00:17:02.432 --> 00:17:05.692 how that works and what work you've

NOTE Confidence: 0.859347

00:17:05.692 --> 00:17:08.809 been doing in that regard in your lab?

00:17:10.040 --> 00:17:13.670 When we think about the immune response

NOTE Confidence: 0.87820375

00:17:13.670 --> 00:17:15.914 against cancer, I think it's very

NOTE Confidence: 0.87820375

00:17:15.914 --> 00:17:17.831 important to recognize that you

NOTE Confidence: 0.87820375

00:17:17.831 --> 00:17:19.611 know the immune response evolved

NOTE Confidence: 0.87820375

00:17:19.611 --> 00:17:21.710 to protect us against pathogens.

NOTE Confidence: 0.87820375

00:17:21.710 --> 00:17:24.918 So when we mount an immune response against

NOTE Confidence: 0.87820375

00:17:24.918 --> 00:17:27.457 something that has changed in our body,

NOTE Confidence: 0.87820375

00:17:27.460 --> 00:17:30.516 such as is the case of cancer cells,

NOTE Confidence: 0.87820375

00:17:30.520 --> 00:17:33.584 we're going to go through the same rules.

NOTE Confidence: 0.87820375

00:17:33.590 --> 00:17:36.646 So as I was saying at the beginning,

NOTE Confidence: 0.87820375

00:17:36.650 --> 00:17:39.044 the very first innate immune response

NOTE Confidence: 0.87820375

00:17:39.044 --> 00:17:41.054 is absolutely essential for allowing

NOTE Confidence: 0.87820375

00:17:41.054 --> 00:17:43.160 us to mount an immune response,

NOTE Confidence: 0.87820375

00:17:43.160 --> 00:17:45.600 for instance to a microorganism.

NOTE Confidence: 0.87820375

00:17:45.600 --> 00:17:48.197 And it turns out that of course

NOTE Confidence: 0.87820375

00:17:48.197 --> 00:17:51.122 is going to be essential to mount

NOTE Confidence: 0.87820375

00:17:51.122 --> 00:17:53.612 a good immune response to cancer.

NOTE Confidence: 0.87820375

00:17:53.612 --> 00:17:56.356 Now when we start analyzing the immune

NOTE Confidence: 0.87820375

00:17:56.356 --> 00:17:59.230 response that the body mounts against cancer,

NOTE Confidence: 0.87820375

00:17:59.230 --> 00:18:02.046 we realize that there are a fraction of

NOTE Confidence: 0.87820375

00:18:02.046 --> 00:18:04.928 patients in which the immune response has

NOTE Confidence: 0.87820375

00:18:04.928 --> 00:18:07.660 effectively occurred, and probably during the years,

NOTE Confidence: 0.87820375

00:18:07.660 --> 00:18:10.460 it has tried to control that cancer,

NOTE Confidence: 0.87820375

00:18:10.460 --> 00:18:13.638 and so in those patients in which

NOTE Confidence: 0.87820375

00:18:13.638 --> 00:18:16.029 the immune response has occurred

NOTE Confidence: 0.87820375

00:18:16.030 --> 00:18:18.782 it could be that maybe now the immune

NOTE Confidence: 0.87820375

00:18:18.782 --> 00:18:20.876 response is kind of tired,

NOTE Confidence: 0.87820375

00:18:20.876 --> 00:18:23.298 many people refer to it as exhausted,

NOTE Confidence: 0.87820375

00:18:23.300 --> 00:18:25.262 and what happens is that those

NOTE Confidence: 0.87820375

00:18:25.262 --> 00:18:27.100 cells that have the memory,

NOTE Confidence: 0.87820375

00:18:27.100 --> 00:18:29.470 those cells of the adaptive immune

NOTE Confidence: 0.87820375

00:18:29.470 --> 00:18:32.374 response that can really go and kill the

NOTE Confidence: 0.87820375

00:18:32.374 --> 00:18:34.961 cancer cell right as they would have done

NOTE Confidence: 0.87820375

00:18:34.961 --> 00:18:37.826 it if they were responding to a micronysm,

NOTE Confidence: 0.87820375

00:18:37.826 --> 00:18:40.248 now they're responding to a cancer cell.

NOTE Confidence: 0.87820375

00:18:40.250 --> 00:18:41.402 They can become tired,

NOTE Confidence: 0.87820375

00:18:41.402 --> 00:18:44.468 and so a large fraction of the current immunother-
apies

NOTE Confidence: 0.87820375

00:18:44.468 --> 00:18:46.598 are centered on reactivating those

00:18:47.024 --> 00:18:48.720 for instance T cells,

NOTE Confidence: 0.87820375

00:18:48.720 --> 00:18:51.688 adaptive immune cells that have become tired,

NOTE Confidence: 0.87820375

00:18:51.690 --> 00:18:54.096 and this has been absolutely revolutionary

NOTE Confidence: 0.87820375

00:18:54.096 --> 00:18:56.350 in the treatment of patients.

NOTE Confidence: 0.87820375

00:18:56.350 --> 00:18:58.898 So you can see how understanding the

NOTE Confidence: 0.87820375

00:18:58.898 --> 00:19:00.967 fundamentals of the immune response

NOTE Confidence: 0.87820375

00:19:00.967 --> 00:19:03.242 has translated into effective new

NOTE Confidence: 0.87820375

00:19:03.242 --> 00:19:05.260 therapies for cancer patients.

NOTE Confidence: 0.87820375

00:19:05.260 --> 00:19:08.508 But it turns out that not all the

NOTE Confidence: 0.87820375

00:19:08.508 --> 00:19:11.478 patients have been able to mount a

NOTE Confidence: 0.87820375

00:19:11.478 --> 00:19:14.160 good immune response to the tumor.

NOTE Confidence: 0.87820375

00:19:14.160 --> 00:19:15.468 In some patients,

NOTE Confidence: 0.87820375

00:19:15.468 --> 00:19:17.648 there are no T cells to reactivate.

NOTE Confidence: 0.87820375

00:19:17.650 --> 00:19:20.514 They never were activated in the 1st place,

NOTE Confidence: 0.87820375

00:19:20.520 --> 00:19:23.040 and that's where our thinking came in.

NOTE Confidence: 0.87820375

00:19:23.040 --> 00:19:25.546 That's where turning on this you know,

NOTE Confidence: 0.87820375

00:19:25.550 --> 00:19:26.814 fire not too big,

NOTE Confidence: 0.87820375

00:19:26.814 --> 00:19:29.141 but turning it on a little bit

NOTE Confidence: 0.87820375

00:19:29.141 --> 00:19:31.654 might allow us to really keep the

NOTE Confidence: 0.87820375

00:19:31.654 --> 00:19:33.810 immune response against the cancer.

NOTE Confidence: 0.87820375

00:19:33.810 --> 00:19:36.578 And so a lot of current efforts in

NOTE Confidence: 0.87820375

00:19:36.578 --> 00:19:38.469 immunotherapy are centered on this

NOTE Confidence: 0.87820375

00:19:38.470 --> 00:19:40.475 initial response because we

NOTE Confidence: 0.87820375

00:19:40.475 --> 00:19:42.826 realized that in some patients it

NOTE Confidence: 0.87820375

00:19:42.826 --> 00:19:44.604 might not have occured.

NOTE Confidence: 0.87820375

00:19:44.604 --> 00:19:47.676 And so we need to turn this on.

NOTE Confidence: 0.87820375

00:19:47.680 --> 00:19:50.606 Or in some patients it may also

NOTE Confidence: 0.87820375

00:19:50.606 --> 00:19:53.149 have gotten tired and we need to

NOTE Confidence: 0.8819662

00:19:53.150 --> 00:19:53.932 reactivate it.

NOTE Confidence: 0.8819662

00:19:53.932 --> 00:19:56.669 So how exactly do you do that?

NOTE Confidence: 0.8819662

00:19:56.670 --> 00:19:59.407 Because I think when I think about

NOTE Confidence: 0.8819662

00:19:59.407 --> 00:20:01.754 cancer cells, I really think about

NOTE Confidence: 0.8819662

00:20:01.754 --> 00:20:04.100 normal cells that have gone awry,

NOTE Confidence: 0.8819662

00:20:04.100 --> 00:20:07.232 and so is it, perhaps that the body,

32

NOTE Confidence: 0.8819662

00:20:07.232 --> 00:20:09.187 especially in low grade cancers,

NOTE Confidence: 0.8819662

00:20:09.190 --> 00:20:10.750 cancers that look very

NOTE Confidence: 0.8819662

00:20:10.750 --> 00:20:12.310 much like normal cells,

NOTE Confidence: 0.8819662

00:20:12.310 --> 00:20:15.117 but that are just a little bit

NOTE Confidence: 0.8819662

00:20:15.117 --> 00:20:17.817 deranged that the body may not

NOTE Confidence: 0.8819662

00:20:17.817 --> 00:20:20.167 recognize them as being foreign.

NOTE Confidence: 0.8819662

00:20:20.170 --> 00:20:22.548 And how do you kickstart that

NOTE Confidence: 0.8338091

00:20:22.550 --> 00:20:23.340 innate response?

NOTE Confidence: 0.8338091

00:20:23.340 --> 00:20:26.105 We're talking about this very early stage,

NOTE Confidence: 0.8338091

00:20:26.110 --> 00:20:28.300 where cells are changing from being

NOTE Confidence: 0.8338091

00:20:28.300 --> 00:20:30.631 normal to to abnormal right from

NOTE Confidence: 0.8338091

00:20:30.631 --> 00:20:32.243 this premalignant to malignant stages

NOTE Confidence: 0.8338091

00:20:32.243 --> 00:20:34.819 and again our immune system,

NOTE Confidence: 0.8338091

00:20:34.820 --> 00:20:37.166 the innate immune system is very

NOTE Confidence: 0.8338091

00:20:37.166 --> 00:20:39.570 sensitive to changes in the tissue.

NOTE Confidence: 0.8338091

00:20:39.570 --> 00:20:41.635 So instead of recognizing changes

NOTE Confidence: 0.8338091

00:20:41.635 --> 00:20:44.130 in terms of mutations that may

NOTE Confidence: 0.8338091

00:20:44.130 --> 00:20:46.307 have arised in that cancer,

NOTE Confidence: 0.8338091

00:20:46.307 --> 00:20:49.086 Which is something that is much more

NOTE Confidence: 0.8338091

00:20:49.086 --> 00:20:51.840 recognized by the adaptive immune system,

NOTE Confidence: 0.8338091

00:20:51.840 --> 00:20:54.018 they can recognize if there

NOTE Confidence: 0.8338091

00:20:54.018 --> 00:20:56.568 has been a change in that issue.

NOTE Confidence: 0.8338091

00:20:56.570 --> 00:20:58.760 If maybe some cells are not

NOTE Confidence: 0.8338091

00:20:58.760 --> 00:21:00.580 functioning in the right way,

NOTE Confidence: 0.8338091

00:21:00.580 --> 00:21:02.806 and so those are things that we're

NOTE Confidence: 0.8338091

00:21:02.806 --> 00:21:04.264 very interested in understanding

NOTE Confidence: 0.8338091

00:21:04.264 --> 00:21:06.040 at the molecular level,

NOTE Confidence: 0.8338091

00:21:06.040 --> 00:21:07.492 what leads the activation

NOTE Confidence: 0.8338091

00:21:07.492 --> 00:21:09.307 of these innate immune cells?

NOTE Confidence: 0.8338091

00:21:09.310 --> 00:21:11.865 And then what is it that maybe

NOTE Confidence: 0.8338091

00:21:11.865 --> 00:21:13.746 changes that may appear

NOTE Confidence: 0.8338091

00:21:13.746 --> 00:21:15.858 like a wound that might affect

00:21:17.316 --> 00:21:19.500 the biology of these innate immune cells.

NOTE Confidence: 0.8311302

00:21:19.500 --> 00:21:22.604 Can you give us some glimmer into

NOTE Confidence: 0.8311302

00:21:22.610 --> 00:21:25.424 what those mechanisms are of actually

NOTE Confidence: 0.8311302

00:21:25.424 --> 00:21:27.300 kickstarting that immune system,

NOTE Confidence: 0.8311302

00:21:27.300 --> 00:21:30.485 because many of the people who are

NOTE Confidence: 0.8311302

00:21:30.485 --> 00:21:33.867 listening to this show are are thinking,

NOTE Confidence: 0.8311302

00:21:33.870 --> 00:21:35.746 that's great. You're studying

NOTE Confidence: 0.8311302

00:21:35.746 --> 00:21:38.560 it at the basic science level.

NOTE Confidence: 0.8311302

00:21:38.560 --> 00:21:42.088 But really, where we are interested in

NOTE Confidence: 0.8311302

00:21:42.088 --> 00:21:45.760 going is how do we actually conquer

NOTE Confidence: 0.8311302

00:21:45.760 --> 00:21:49.540 cancer at a patient level and so

NOTE Confidence: 0.8311302

00:21:49.540 --> 00:21:52.252 can you give us a sense

NOTE Confidence: 0.8311302

00:21:52.252 --> 00:21:55.458 of what are kind of the molecular

NOTE Confidence: 0.8311302

00:21:55.458 --> 00:21:57.898 mechanisms that you're looking at

NOTE Confidence: 0.8311302

00:21:57.986 --> 00:22:00.534 and how might we change those

NOTE Confidence: 0.8311302

00:22:00.534 --> 00:22:03.238 so that for actual patients we can

NOTE Confidence: 0.8776264

00:22:03.240 --> 00:22:06.054 potentially use this to make a difference?

NOTE Confidence: 0.8776264

00:22:06.060 --> 00:22:08.550 Absolutely this is where

NOTE Confidence: 0.8776264

00:22:08.550 --> 00:22:10.807 again basic science comes in.

NOTE Confidence: 0.8776264

00:22:10.807 --> 00:22:13.570 And I think this is where we need

NOTE Confidence: 0.8776264

00:22:13.650 --> 00:22:16.138 to understand fundamental biology.

NOTE Confidence: 0.8776264

00:22:16.140 --> 00:22:19.650 So the approach that we take is trying to

NOTE Confidence: 0.8776264

00:22:19.650 --> 00:22:22.668 understand what triggers this first response.

NOTE Confidence: 0.8776264

00:22:22.670 --> 00:22:25.406 To do this, we make use of models,

NOTE Confidence: 0.8776264

00:22:25.410 --> 00:22:28.330 sometimes it is not so easy to

NOTE Confidence: 0.8776264

00:22:28.396 --> 00:22:31.245 study this directly initially in a patient,

NOTE Confidence: 0.8776264

00:22:31.250 --> 00:22:34.013 but we can take models where we can induce

NOTE Confidence: 0.8776264

00:22:34.013 --> 00:22:36.190 for instance the transformation of a

NOTE Confidence: 0.8776264

00:22:36.190 --> 00:22:39.106 cell or we can induce an infection and

NOTE Confidence: 0.8776264

00:22:39.106 --> 00:22:41.868 this is very important because as I said,

NOTE Confidence: 0.8776264

36

00:22:41.868 --> 00:22:44.164 the principles are going to be pretty

NOTE Confidence: 0.8776264

00:22:44.164 --> 00:22:46.492 much shared with the immune response to

NOTE Confidence: 0.8776264

00:22:46.492 --> 00:22:48.907 infection and so in these models which

NOTE Confidence: 0.8776264

00:22:48.907 --> 00:22:51.139 are in many occasions animal models,

NOTE Confidence: 0.8776264

00:22:51.140 --> 00:22:53.625 what we try to do is to

NOTE Confidence: 0.8776264

00:22:53.630 --> 00:22:56.998 try to detect how the cells of the

NOTE Confidence: 0.8776264

00:22:56.998 --> 00:22:59.350 innate immune system these first

NOTE Confidence: 0.8776264

00:22:59.350 --> 00:23:02.661 responders react to a cell that is

NOTE Confidence: 0.8776264

00:23:02.670 --> 00:23:05.160 changing either because there has

NOTE Confidence: 0.8776264

00:23:05.160 --> 00:23:07.610 been an infection and a wound or

NOTE Confidence: 0.8776264

00:23:07.610 --> 00:23:10.109 because it's has been mutated and so

NOTE Confidence: 0.8776264

00:23:10.109 --> 00:23:12.724 we do this with advanced techniques

NOTE Confidence: 0.8776264

00:23:12.724 --> 00:23:15.318 that allow us to understand what

NOTE Confidence: 0.8776264

00:23:15.318 --> 00:23:17.766 is changing in the immune cell.

NOTE Confidence: 0.8776264

00:23:17.770 --> 00:23:19.810 Now a very important aspect

NOTE Confidence: 0.8776264

00:23:19.810 --> 00:23:22.680 I think is to then try to go to

NOTE Confidence: 0.8776264

00:23:22.767 --> 00:23:25.437 patient samples and understand whether

NOTE Confidence: 0.8776264

00:23:25.437 --> 00:23:28.961 those features that we saw change in

NOTE Confidence: 0.8776264

00:23:28.961 --> 00:23:31.663 the context of an infection or in

NOTE Confidence: 0.8776264

00:23:31.663 --> 00:23:34.756 the context of a model of cancer

NOTE Confidence: 0.8776264

00:23:34.760 --> 00:23:36.312 in an animal model,

NOTE Confidence: 0.8776264

00:23:36.312 --> 00:23:39.086 are also detected in the context of

NOTE Confidence: 0.8776264

00:23:39.086 --> 00:23:41.648 a transformation of a cell and the

NOTE Confidence: 0.8776264

00:23:41.648 --> 00:23:43.948 response to this in the patient.

NOTE Confidence: 0.8776264

00:23:43.950 --> 00:23:46.421 So I think going from this very

NOTE Confidence: 0.8776264

00:23:46.421 --> 00:23:48.394 fundamental basic approaches to taking

NOTE Confidence: 0.8776264

00:23:48.394 --> 00:23:50.090 some translational approaches and

NOTE Confidence: 0.8776264

00:23:50.090 --> 00:23:52.556 trying to understand whether the same

NOTE Confidence: 0.8776264

00:23:52.556 --> 00:23:54.674 changes are observed is very important.

NOTE Confidence: 0.8776264

00:23:54.680 --> 00:23:55.562 But then again,

NOTE Confidence: 0.8776264

00:23:55.562 --> 00:23:58.595 I think we need to go back to the

NOTE Confidence: 0.8776264

00:23:58.595 --> 00:24:00.840 experimental models because once we

NOTE Confidence: 0.8776264

00:24:00.840 --> 00:24:03.100 understand what those changes are,

NOTE Confidence: 0.8776264

00:24:03.100 --> 00:24:04.448 we would like to

NOTE Confidence: 0.8776264

00:24:04.448 --> 00:24:06.133 intervene and modulate

NOTE Confidence: 0.8776264

00:24:06.133 --> 00:24:08.333 them so we can maybe turn on

NOTE Confidence: 0.8776264

00:24:08.333 --> 00:24:10.168 that fire a little bit more.

NOTE Confidence: 0.8776264

00:24:10.170 --> 00:24:11.868 Maybe induce that immune response a

NOTE Confidence: 0.8776264

00:24:11.868 --> 00:24:14.140 little bit more, and to do that again,

NOTE Confidence: 0.8776264

00:24:14.140 --> 00:24:16.128 we need to go to the model.

NOTE Confidence: 0.8776264

00:24:16.130 --> 00:24:18.746 So we start with the model, we validate

NOTE Confidence: 0.8776264

00:24:18.746 --> 00:24:20.849 and understand whether it is the same

NOTE Confidence: 0.8776264

00:24:20.849 --> 00:24:23.240 in a human setting and then we go back

NOTE Confidence: 0.8776264

00:24:23.240 --> 00:24:25.218 to the model to try to understand how

NOTE Confidence: 0.8776264

00:24:25.218 --> 00:24:27.490 we can change it to make it better.

NOTE Confidence: 0.8776264

00:24:27.490 --> 00:24:28.910 And it is this iterative type of

00:24:30.330 --> 00:24:31.890 experimental approach

NOTE Confidence: 0.8776264

00:24:31.890 --> 00:24:33.761 from the model to human samples

NOTE Confidence: 0.8776264

00:24:33.761 --> 00:24:35.279 to the model that has led

NOTE Confidence: 0.8776264

00:24:35.280 --> 00:24:37.566 to a lot of new ways to change the

NOTE Confidence: 0.8776264

00:24:37.566 --> 00:24:39.406 immune response and I am confident

NOTE Confidence: 0.8776264

00:24:39.406 --> 00:24:41.659 that we will allow us to understand

NOTE Confidence: 0.8776264

00:24:41.659 --> 00:24:44.004 what we need to change in those

NOTE Confidence: 0.8776264

00:24:44.004 --> 00:24:45.548 patients that have mounted an

NOTE Confidence: 0.8776264

00:24:45.548 --> 00:24:46.756 immune response to cancer.

NOTE Confidence: 0.892330049999999

00:24:47.620 --> 00:24:50.988 So tell us more about some of these

NOTE Confidence: 0.892330049999999

00:24:50.988 --> 00:24:53.376 interventions that you've tried and how

NOTE Confidence: 0.892330049999999

00:24:53.376 --> 00:24:56.945 they work in in the models and and what

NOTE Confidence: 0.892330049999999

00:24:56.945 --> 00:24:59.519 prospects there are to actually having

NOTE Confidence: 0.892330049999999

00:24:59.519 --> 00:25:01.594 the same intervention in patients.

NOTE Confidence: 0.892330049999999

00:25:03.650 --> 00:25:06.116 And then just as a second

NOTE Confidence: 0.892330049999999

00:25:06.116 --> 00:25:07.760 piece to that question,

NOTE Confidence: 0.892330049999999

00:25:07.760 --> 00:25:10.226 when you talked earlier

NOTE Confidence: 0.892330049999999

00:25:10.226 --> 00:25:11.870 about this collateral damage,

NOTE Confidence: 0.892330049999999

00:25:11.870 --> 00:25:13.925 you wonder about when you

NOTE Confidence: 0.892330049999999

00:25:13.925 --> 00:25:15.980 actually take that into patients.

NOTE Confidence: 0.892330049999999

00:25:15.980 --> 00:25:18.140 Whether there will be collateral

NOTE Confidence: 0.892330049999999

00:25:18.140 --> 00:25:19.885 damage as well as you

NOTE Confidence: 0.892330049999999

00:25:19.885 --> 00:25:21.630 continue to light that fire,

NOTE Confidence: 0.892330049999999

00:25:21.630 --> 00:25:23.285 or whether you've really gotten

NOTE Confidence: 0.892330049999999

00:25:23.285 --> 00:25:25.658 it down to the point where you

NOTE Confidence: 0.892330049999999

00:25:25.658 --> 00:25:27.283 can modulate that very well

NOTE Confidence: 0.892330049999999

00:25:27.283 --> 00:25:28.960 to limit that collateral

NOTE Confidence: 0.87653905

00:25:28.960 --> 00:25:30.320 damage.

NOTE Confidence: 0.87653905

00:25:30.320 --> 00:25:33.500 Let me give you this with an example.

NOTE Confidence: 0.87653905

00:25:33.500 --> 00:25:35.964 So as I said, we try to understand

NOTE Confidence: 0.87653905

00:25:35.964 --> 00:25:38.727 what are those ways to regulate right?

NOTE Confidence: 0.87653905

00:25:38.730 --> 00:25:40.130 The magnitude and duration.

NOTE Confidence: 0.87653905

00:25:40.130 --> 00:25:43.266 And again, we went from the animal models to

00:25:43.270 --> 00:25:45.353 some human samples.

00:25:45.353 --> 00:25:47.411 And in doing that we identified

00:25:47.411 --> 00:25:49.324 genes that encode for molecules

00:25:49.324 --> 00:25:50.960 that are those regulators.

00:25:50.960 --> 00:25:53.613 And some of those genes and then

00:25:53.613 --> 00:25:55.790 those proteins that are encoded by

00:25:55.790 --> 00:25:58.528 this gene are a key focus of our

00:25:58.528 --> 00:26:01.030 lab and they're called TAM receptors.

00:26:01.030 --> 00:26:02.895 Tyrosine kinase is the interesting

00:26:02.895 --> 00:26:05.323 aspect of this is, as I said,

00:26:05.323 --> 00:26:07.500 they are like the brakes of this

00:26:07.575 --> 00:26:09.763 innate immune response.

00:26:09.763 --> 00:26:13.947 And these proteins can be targeted by drugs.

00:26:14.419 --> 00:26:17.233 So these proteins are in

00:26:17.233 --> 00:26:19.933 innate immune cells and when you

NOTE Confidence: 0.87653905

00:26:19.933 --> 00:26:22.754 activate this protein it will act as

NOTE Confidence: 0.87653905

00:26:22.839 --> 00:26:25.716 a break of this innate immune cell.

NOTE Confidence: 0.87653905

00:26:25.720 --> 00:26:28.661 It will put down this fire.

NOTE Confidence: 0.87653905

00:26:28.661 --> 00:26:31.550 What we can do is we can work

NOTE Confidence: 0.87653905

00:26:31.642 --> 00:26:34.347 and develop molecules that inhibit

NOTE Confidence: 0.87653905

00:26:34.347 --> 00:26:37.052 the function of this protein.

NOTE Confidence: 0.87653905

00:26:37.060 --> 00:26:39.923 Or we can also generate animal models

NOTE Confidence: 0.87653905

00:26:39.923 --> 00:26:43.538 that do not even have this protein.

NOTE Confidence: 0.87653905

00:26:43.538 --> 00:26:46.562 And so what you would predict is that

NOTE Confidence: 0.87653905

00:26:46.562 --> 00:26:50.004 if you do not engage this break so well,

NOTE Confidence: 0.87653905

00:26:50.010 --> 00:26:52.206 you will mount a better fire,

00:26:52.561 --> 00:26:55.018 so we will be able to regulate

NOTE Confidence: 0.87653905

00:26:55.018 --> 00:26:56.970 the magnitude of this response,

NOTE Confidence: 0.87653905

00:26:56.970 --> 00:26:59.525 and so that's what we have discovered.

NOTE Confidence: 0.87653905

00:26:59.530 --> 00:27:01.726 And so going from the animal

NOTE Confidence: 0.87653905

00:27:01.726 --> 00:27:03.190 models to human cells,

NOTE Confidence: 0.87653905

00:27:03.190 --> 00:27:05.758 we now know that we can use small

NOTE Confidence: 0.87653905

00:27:05.758 --> 00:27:07.948 molecules that inhibit this proteins,

NOTE Confidence: 0.87653905

00:27:07.950 --> 00:27:10.140 and that allows a better fire.

NOTE Confidence: 0.87653905

00:27:10.140 --> 00:27:12.396 And we know that in animal

NOTE Confidence: 0.87653905

00:27:12.396 --> 00:27:13.900 models these can lead

NOTE Confidence: 0.87653905

00:27:13.900 --> 00:27:15.895 to the ability of these

NOTE Confidence: 0.87653905

00:27:15.895 --> 00:27:17.890 animals to mount a much

NOTE Confidence: 0.87653905

00:27:17.890 --> 00:27:19.890 better immune response against cancer.

NOTE Confidence: 0.87653905

00:27:19.890 --> 00:27:22.202 So we are actually right now at the

NOTE Confidence: 0.87653905

00:27:22.202 --> 00:27:24.808 process of starting to translate this

NOTE Confidence: 0.87653905

00:27:24.808 --> 00:27:26.768 into humans through investigator

NOTE Confidence: 0.87653905

00:27:26.768 --> 00:27:28.260 initiated clinical trials.

NOTE Confidence: 0.87653905

00:27:28.260 --> 00:27:29.860 Actually here right here

NOTE Confidence: 0.87653905

00:27:29.860 --> 00:27:31.860 at Yale Cancer Center,

NOTE Confidence: 0.87653905

00:27:31.860 --> 00:27:34.646 so we can try to understand whether

NOTE Confidence: 0.87653905

00:27:34.646 --> 00:27:37.440 these drugs, which we know are safe,

NOTE Confidence: 0.87653905

00:27:37.440 --> 00:27:40.761 can ignite just a little bit more

NOTE Confidence: 0.87653905

00:27:40.761 --> 00:27:44.219 this fire and you asked me the question,

00:27:44.790 --> 00:27:46.785 how do I ensure that

NOTE Confidence: 0.87653905

00:27:46.785 --> 00:27:49.286 it's not a big fire that

NOTE Confidence: 0.87653905

00:27:49.286 --> 00:27:50.718 will induce collateral damage?

NOTE Confidence: 0.87653905

00:27:50.720 --> 00:27:52.270 That's a very very important

NOTE Confidence: 0.87653905

00:27:52.270 --> 00:27:53.510 question to answer.

NOTE Confidence: 0.87653905

00:27:53.510 --> 00:27:55.370 I think that brings me back

NOTE Confidence: 0.87653905

00:27:55.370 --> 00:27:56.610 to my initial training,

NOTE Confidence: 0.87653905

00:27:56.610 --> 00:27:58.160 which was really in pharmacology,

NOTE Confidence: 0.87653905

00:27:58.160 --> 00:28:00.020 in Neuropharmacology, but I learned,

NOTE Confidence: 0.87653905

00:28:00.020 --> 00:28:01.880 I think a lot about pharmacology,

NOTE Confidence: 0.87653905

00:28:01.880 --> 00:28:03.782 and that's where drugs

NOTE Confidence: 0.87653905

00:28:03.782 --> 00:28:05.290 give you the ability to

00:28:05.810 --> 00:28:07.890 think a lot about the dose is the

NOTE Confidence: 0.87653905

00:28:07.951 --> 00:28:09.907 regimens, how you're

NOTE Confidence: 0.87653905

00:28:09.907 --> 00:28:12.730 going to try to modulate this in vivo

NOTE Confidence: 0.87653905

00:28:12.730 --> 00:28:14.280 and that becomes very important.

NOTE Confidence: 0.87653905

00:28:14.280 --> 00:28:16.230 So how much you would give

NOTE Confidence: 0.87653905

00:28:16.230 --> 00:28:17.830 of this drug may be

NOTE Confidence: 0.87653905

00:28:17.830 --> 00:28:19.774 whether you will deliver it just

NOTE Confidence: 0.87653905

00:28:19.774 --> 00:28:22.168 to the tumor site so you don't

NOTE Confidence: 0.87653905

00:28:22.168 --> 00:28:23.540 start a fire everywhere,

NOTE Confidence: 0.87653905

00:28:23.540 --> 00:28:25.490 and that's an aspect that will

NOTE Confidence: 0.87653905

00:28:25.490 --> 00:28:27.221 be very important into making

NOTE Confidence: 0.87653905

00:28:27.221 --> 00:28:29.755 sure that this can truly help the

NOTE Confidence: 0.87653905

00:28:29.755 --> 00:28:31.468 patients eliminate the cancer and

NOTE Confidence: 0.87653905

00:28:31.468 --> 00:28:33.617 not induce fires in places that we

NOTE Confidence: 0.849178

00:28:33.620 --> 00:28:34.628 don't want to.

NOTE Confidence: 0.85792613

00:28:35.290 --> 00:28:37.516 Doctor Carla Rothlin is Dorys McConnell Duberg
Professor

NOTE Confidence: 0.85792613

00:28:37.520 --> 00:28:39.060 of Immunobiology

NOTE Confidence: 0.85792613

00:28:39.060 --> 00:28:40.600 and professor of Pharmacology

NOTE Confidence: 0.85792613

00:28:40.600 --> 00:28:42.710 at the Yale School of Medicine.

NOTE Confidence: 0.85792613

00:28:42.710 --> 00:28:44.864 If you have questions the addresses

NOTE Confidence: 0.85792613

00:28:44.864 --> 00:28:46.683 cancer answers at yale.edu and

NOTE Confidence: 0.85792613

00:28:46.683 --> 00:28:48.597 past editions of the program are

NOTE Confidence: 0.85792613

00:28:48.597 --> 00:28:50.562 available in audio and written

NOTE Confidence: 0.85792613

00:28:50.562 --> 00:28:51.987 form at yalecancercenter.org.

NOTE Confidence: 0.85792613

00:28:51.990 --> 00:28:54.662 We hope you'll join us next week to

NOTE Confidence: 0.85792613

00:28:54.662 --> 00:28:57.276 learn more about the fight against

NOTE Confidence: 0.85792613

00:28:57.276 --> 00:29:00.072 cancer here on Connecticut Public Radio.