WEBVTT

00:00:00.000 --> 00:00:03.675 Funding for Yale Cancer Answers is provided

NOTE Confidence: 0.95843685

 $00:00:03.675 \dashrightarrow 00:00:07.619$ by Smilow Cancer Hospital and Astra Zeneca.

NOTE Confidence: 0.95843685

 $00:00:07.620 \longrightarrow 00:00:09.800$ Welcome to Yale Cancer Answers with

NOTE Confidence: 0.95843685

00:00:09.800 --> 00:00:12.379 your host doctor Anees Chappar.

NOTE Confidence: 0.95843685

00:00:12.380 --> 00:00:14.335 Yale Cancer Answers features the

NOTE Confidence: 0.95843685

 $00:00:14.335 \longrightarrow 00:00:16.735$ latest information on cancer care by

NOTE Confidence: 0.95843685

 $00:00:16.735 \longrightarrow 00:00:18.275$ welcoming oncologists and specialists

NOTE Confidence: 0.95843685

00:00:18.275 --> 00:00:20.852 who are on the forefront of the

NOTE Confidence: 0.95843685

 $00:00:20.852 \longrightarrow 00:00:22.628$ battle to fight cancer. This week,

NOTE Confidence: 0.95843685

 $00:00:22.630 \longrightarrow 00:00:25.143$ it's a conversation about the use of

NOTE Confidence: 0.95843685

 $00:00:25.143 \longrightarrow 00:00:27.388$ nanoparticles to treat skin cancer with

NOTE Confidence: 0.95843685

 $00:00:27.388 \dashrightarrow 00:00:29.950$ doctors Michael Girardi and W. Mark Salzman.

NOTE Confidence: 0.95843685

 $00{:}00{:}29.950 \dashrightarrow 00{:}00{:}32.068$ Doctor Girardi is a professor of

NOTE Confidence: 0.95843685

 $00{:}00{:}32.068 \dashrightarrow 00{:}00{:}34.291$ dermatology and Doctor Saltzman is a

NOTE Confidence: 0.95843685

00:00:34.291 --> 00:00:35.799 professor of biomedical engineering,

 $00:00:35.800 \longrightarrow 00:00:37.308$ Cellular and Molecular Physiology

NOTE Confidence: 0.95843685

 $00{:}00{:}37.308 \dashrightarrow 00{:}00{:}39.193$ and of Chemical Engineering at

NOTE Confidence: 0.95843685

00:00:39.193 --> 00:00:40.940 the Yale School of Medicine,

NOTE Confidence: 0.95843685

 $00:00:40.940 \longrightarrow 00:00:42.938$ where Doctor Chagpar is a

NOTE Confidence: 0.95843685

00:00:42.938 --> 00:00:44.270 professor of surgical oncology.

NOTE Confidence: 0.9887273

00:00:45.150 --> 00:00:47.467 So maybe we'll start off by having

NOTE Confidence: 0.9887273

 $00{:}00{:}47.467 \dashrightarrow 00{:}00{:}50.776$ both of you tell us a little bit about

NOTE Confidence: 0.9887273

 $00:00:50.776 \longrightarrow 00:00:52.850$ yourselves and what you do.

NOTE Confidence: 0.9887273

 $00{:}00{:}52.850 \dashrightarrow 00{:}00{:}55.650$ Mike, maybe I'll start with you.

NOTE Confidence: 0.9887273

00:00:55.650 --> 00:00:57.534 Sure, I run a research laboratory

NOTE Confidence: 0.9887273

00:00:57.534 --> 00:00:59.973 with a big focus on skin cancer

NOTE Confidence: 0.9887273

 $00:00:59.973 \longrightarrow 00:01:02.199$ development and strategies to try to

NOTE Confidence: 0.9887273

 $00:01:02.199 \longrightarrow 00:01:04.397$ prevent skin cancer formation and to treat it.

NOTE Confidence: 0.9887273

00:01:04.400 --> 00:01:06.850 And how about you, Mark?

NOTE Confidence: 0.9887273

 $00:01:06.850 \longrightarrow 00:01:09.058$ I'm a professor in the

NOTE Confidence: 0.9887273

00:01:09.058 --> 00:01:10.700 Department of Biomedical Engineering.

00:01:10.700 --> 00:01:12.826 My training is in chemical engineering,

NOTE Confidence: 0.9887273

00:01:12.826 --> 00:01:15.367 but for my research career and my

NOTE Confidence: 0.9887273

00:01:15.370 --> 00:01:16.902 teaching career I've mainly

NOTE Confidence: 0.9887273

00:01:16.902 --> 00:01:19.200 focused on how to apply principles

NOTE Confidence: 0.9887273

00:01:19.263 --> 00:01:20.907 from chemical engineering to

NOTE Confidence: 0.9887273

00:01:20.907 --> 00:01:22.962 make new products for medicine.

NOTE Confidence: 0.9891947

 $00:01:22.970 \longrightarrow 00:01:25.525$ This is such an

NOTE Confidence: 0.9891947

 $00{:}01{:}25.525 \dashrightarrow 00{:}01{:}27.069$ unusual marriage and something

NOTE Confidence: 0.9891947

 $00:01:27.069 \longrightarrow 00:01:29.673$ that I love about academia is that

NOTE Confidence: 0.9891947

 $00{:}01{:}29.673 \dashrightarrow 00{:}01{:}32.286$ we can take disciplines that are

NOTE Confidence: 0.9891947

 $00{:}01{:}32.286 \dashrightarrow 00{:}01{:}34.521$ truly disperate on the surface

NOTE Confidence: 0.9891947

00:01:34.521 --> 00:01:36.970 and make them collide and have

NOTE Confidence: 0.9891947

00:01:36.970 --> 00:01:38.570 really fascinating things happen.

 $00:01:40.570 \longrightarrow 00:01:43.506$ Mike, tell me a little bit more about

NOTE Confidence: 0.9891947

 $00:01:43.506 \longrightarrow 00:01:46.639$ how your research evolved and

NOTE Confidence: 0.9891947

 $00:01:46.640 \longrightarrow 00:01:48.650$ how you got to meet Mark?

 $00:01:48.650 \longrightarrow 00:01:51.998$ You know we have a really rich

NOTE Confidence: 0.98948395

 $00{:}01{:}51.998 \dashrightarrow 00{:}01{:}54.717$ environment for exchange of ideas and just

NOTE Confidence: 0.98948395

00:01:54.717 --> 00:01:57.638 a tremendous breadth of faculty that is

NOTE Confidence: 0.98948395

 $00:01:57.638 \longrightarrow 00:02:00.302$ very welcoming to folks getting together.

NOTE Confidence: 0.98948395

 $00{:}02{:}00.310 \dashrightarrow 00{:}02{:}01.842$ Discussing how different perspectives

NOTE Confidence: 0.98948395

 $00:02:01.842 \longrightarrow 00:02:04.730$ and takes on research can be combined.

NOTE Confidence: 0.98948395

 $00:02:04.730 \longrightarrow 00:02:07.250$ Mark and I have had a

NOTE Confidence: 0.98948395

 $00{:}02{:}07.250 \longrightarrow 00{:}02{:}10.465$ chance to see each other at various

NOTE Confidence: 0.98948395

 $00{:}02{:}10.465 \dashrightarrow 00{:}02{:}11.965$ meetings and conferences here

NOTE Confidence: 0.98948395

 $00:02:11.970 \longrightarrow 00:02:14.875$ on campus and to

NOTE Confidence: 0.98948395

 $00:02:14.875 \longrightarrow 00:02:16.839$ have discussions time to time

NOTE Confidence: 0.98948395

 $00:02:16.840 \longrightarrow 00:02:18.484$ over the years after these meetings

 $00:02:19.720 \longrightarrow 00:02:22.924$ and then we really hit it off on Mark's

NOTE Confidence: 0.98948395

00:02:22.924 --> 00:02:24.773 technology of using nanoparticles

NOTE Confidence: 0.98948395

 $00:02:24.773 \longrightarrow 00:02:27.133$ to deliver anti tumor agents.

00:02:28.187 --> 00:02:30.630 And a thought bomb went off in my

 $00:02:30.718 \longrightarrow 00:02:33.278$ head regarding all the potential

NOTE Confidence: 0.98948395

 $00{:}02{:}33.278 \dashrightarrow 00{:}02{:}36.279$ applications in the skin which is

NOTE Confidence: 0.98948395

 $00:02:36.279 \longrightarrow 00:02:38.778$ so accessible and such a burden on

NOTE Confidence: 0.98948395

 $00:02:38.778 \longrightarrow 00:02:41.798$ our society in terms of the

NOTE Confidence: 0.98948395

00:02:41.798 --> 00:02:45.184 number of skin cancers and the

NOTE Confidence: 0.98948395

00:02:45.184 --> 00:02:47.399 challenges in controlling these and treating them.

 $00:02:48.606 \longrightarrow 00:02:52.345$ And so I reached out to Mark after one

NOTE Confidence: 0.98948395

 $00:02:52.345 \longrightarrow 00:02:55.697$ of his talks and he was very receptive.

NOTE Confidence: 0.98948395

 $00{:}02{:}55.700 \dashrightarrow 00{:}02{:}58.584$ We had a wonderful meeting and

NOTE Confidence: 0.98948395

 $00:02:58.584 \longrightarrow 00:03:00.634$ brains torming session and that was

NOTE Confidence: 0.98948395

 $00:03:00.634 \longrightarrow 00:03:02.860$ several years ago and we've really

NOTE Confidence: 0.98948395

 $00:03:02.860 \longrightarrow 00:03:05.079$ grown with our possibilities and directions

 $00:03:06.490 \longrightarrow 00:03:08.565$ research-wise in putting

NOTE Confidence: 0.98948395

00:03:08.565 --> 00:03:09.810 our heads together.

NOTE Confidence: 0.988194

 $00:03:09.810 \longrightarrow 00:03:12.960$ Mark tell us a little bit more

NOTE Confidence: 0.988194

00:03:12.960 --> 00:03:16.348 about your research and this drug

NOTE Confidence: 0.988194

 $00:03:16.348 \longrightarrow 00:03:19.149$ delivery mechanism that you have and

 $00:03:19.150 \longrightarrow 00:03:22.069$ the talk that spurred everything on?

00:03:23.318 --> 00:03:25.814 I'll start back almost 30 years ago when I first

 $00{:}03{:}28.648 \dashrightarrow 00{:}03{:}30.829$ got interested in this field,

NOTE Confidence: 0.9861952

 $00:03:30.830 \longrightarrow 00:03:32.910$ we had discovered that

NOTE Confidence: 0.9861952

 $00:03:32.910 \longrightarrow 00:03:34.574$ there were some polymers,

NOTE Confidence: 0.9861952

 $00:03:34.580 \longrightarrow 00:03:35.828$ some polymer materials,

NOTE Confidence: 0.9861952

 $00:03:35.830 \longrightarrow 00:03:38.560$ plastics that one could implant in the

NOTE Confidence: 0.9861952

00:03:38.560 --> 00:03:42.089 skin or put in contact with human tissues,

NOTE Confidence: 0.9861952

 $00:03:42.090 \longrightarrow 00:03:44.170$ and they're very inert.

NOTE Confidence: 0.9861952

 $00:03:44.170 \longrightarrow 00:03:47.178$ And the key discovery was that you could

NOTE Confidence: 0.9861952

 $00:03:47.178 \longrightarrow 00:03:50.089$ combine these materials with drug molecules.

NOTE Confidence: 0.9861952

 $00{:}03{:}50.090 \dashrightarrow 00{:}03{:}52.610$ So that you could make such things

NOTE Confidence: 0.9861952

 $00:03:52.610 \longrightarrow 00:03:54.411$ like implants that you could

NOTE Confidence: 0.9861952

00:03:54.411 --> 00:03:56.577 place in contact with tissues or

NOTE Confidence: 0.9861952

 $00:03:56.577 \longrightarrow 00:03:58.774$ implant into tissues and they would

NOTE Confidence: 0.9861952

 $00:03:58.774 \longrightarrow 00:04:00.519$ slowly release the drug molecules

00:04:00.519 --> 00:04:02.689 that you had embedded into them,

NOTE Confidence: 0.9861952

 $00{:}04{:}02.690 \dashrightarrow 00{:}04{:}05.210$ and so that really started me on a

NOTE Confidence: 0.9861952

 $00:04:05.210 \longrightarrow 00:04:07.900$ path to thinking about how you could

NOTE Confidence: 0.9861952

 $00:04:07.900 \longrightarrow 00:04:10.250$ both expand the range of materials

NOTE Confidence: 0.9861952

00:04:10.250 --> 00:04:12.770 that you could use in this fashion,

NOTE Confidence: 0.9861952

 $00:04:12.770 \longrightarrow 00:04:13.850$ and more importantly,

NOTE Confidence: 0.9861952

00:04:13.850 --> 00:04:16.010 how you could marry this technology

NOTE Confidence: 0.9861952

 $00:04:16.010 \longrightarrow 00:04:17.450$ to treat different diseases.

NOTE Confidence: 0.9861952

 $00{:}04{:}17.450 \longrightarrow 00{:}04{:}20.450$ And we really focused a lot on cancer

NOTE Confidence: 0.9861952

 $00:04:20.450 \longrightarrow 00:04:22.988$ because of the potential to create

NOTE Confidence: 0.9861952

 $00{:}04{:}22.988 \dashrightarrow 00{:}04{:}25.607$ drug delivery systems that would be

NOTE Confidence: 0.9861952

 $00{:}04{:}25.607 \dashrightarrow 00{:}04{:}27.737$ more effective at treating cancer.

NOTE Confidence: 0.9861952

 $00{:}04{:}27.740 \dashrightarrow 00{:}04{:}30.804$ But at the same time would be safer

NOTE Confidence: 0.9861952

 $00:04:30.804 \longrightarrow 00:04:34.347$ and we could use the materials to sort

NOTE Confidence: 0.9861952

 $00:04:34.347 \longrightarrow 00:04:38.237$ of focus the drug action on the tumor

NOTE Confidence: 0.9861952

 $00:04:38.237 \longrightarrow 00:04:41.249$ cells rather than on normal tissue.

 $00:04:41.250 \longrightarrow 00:04:44.099$ And I think the possibilities for this

NOTE Confidence: 0.9861952

 $00{:}04{:}44.099 \dashrightarrow 00{:}04{:}46.278$ really expanded about 15 years ago,

NOTE Confidence: 0.9861952

 $00:04:46.280 \longrightarrow 00:04:48.210$ when we discovered you could

NOTE Confidence: 0.9861952

 $00:04:48.210 \longrightarrow 00:04:49.754$ make not only implants,

NOTE Confidence: 0.9861952

 $00:04:49.760 \longrightarrow 00:04:51.938$ but you could make tiny tiny

NOTE Confidence: 0.9861952

 $00:04:51.938 \longrightarrow 00:04:53.390$ particles of these polymer

NOTE Confidence: 0.9861952

00:04:53.457 --> 00:04:55.567 materials and anti cancer drugs.

NOTE Confidence: 0.9861952

 $00:04:55.570 \longrightarrow 00:04:57.868$ So we call those nanoparticles because

NOTE Confidence: 0.9861952

 $00:04:57.868 \longrightarrow 00:05:00.599$ their size is measured in the nanometers.

NOTE Confidence: 0.9861952

 $00:05:00.600 \longrightarrow 00:05:01.806$ They're very small,

NOTE Confidence: 0.9861952

 $00{:}05{:}01.806 \dashrightarrow 00{:}05{:}05.423$ so the particles that Mike and I have been

NOTE Confidence: 0.9861952

 $00:05:05.423 \longrightarrow 00:05:08.722$ using are about the same size as a virus.

NOTE Confidence: 0.9861952

 $00{:}05{:}08.722 \dashrightarrow 00{:}05{:}11.528$ So because they're so small you can

NOTE Confidence: 0.9861952

 $00:05:11.530 \longrightarrow 00:05:13.205$ administer them easily in a

NOTE Confidence: 0.9861952

00:05:13.205 --> 00:05:14.545 variety of different settings.

00:05:14.550 --> 00:05:17.238 You can inject them easily through a needle,

NOTE Confidence: 0.9861952

 $00:05:17.240 \longrightarrow 00:05:17.920$ for example.

NOTE Confidence: 0.9861952

 $00{:}05{:}17.920 \dashrightarrow 00{:}05{:}20.300$ Or you could suspend them in a

NOTE Confidence: 0.9861952

 $00:05:20.300 \longrightarrow 00:05:22.374$ solution and infuse them or apply

NOTE Confidence: 0.9861952

 $00:05:22.374 \longrightarrow 00:05:24.753$ them topically on the skin so that

NOTE Confidence: 0.9861952

00:05:24.753 --> 00:05:26.993 that gives you a lot of possibilities

NOTE Confidence: 0.9861952

 $00:05:26.993 \longrightarrow 00:05:29.095$ and thinking about how you're going

NOTE Confidence: 0.9861952

 $00:05:29.095 \longrightarrow 00:05:31.572$ to match this delivery system to the

NOTE Confidence: 0.9861952

 $00{:}05{:}31.572 \dashrightarrow 00{:}05{:}33.172$ particular tumor that you're trying

NOTE Confidence: 0.9861952

 $00:05:33.172 \longrightarrow 00:05:35.475$ to treat and the other thing about

NOTE Confidence: 0.9861952

 $00{:}05{:}35.475 \dashrightarrow 00{:}05{:}37.395$ being tiny tiny particles is that

NOTE Confidence: 0.9861952

 $00:05:37.400 \longrightarrow 00:05:39.416$ they're much smaller than tumor cells,

NOTE Confidence: 0.9861952

 $00:05:39.420 \longrightarrow 00:05:41.856$ and so they can actually enter into

NOTE Confidence: 0.9861952

 $00:05:41.860 \longrightarrow 00:05:43.936$ tumor cells and once

NOTE Confidence: 0.9861952

 $00:05:43.936 \longrightarrow 00:05:45.740$ they're in the tumor cell,

NOTE Confidence: 0.9861952

 $00:05:45.740 \longrightarrow 00:05:47.858$ they'll start releasing slowly their drug,

 $00:05:47.860 \longrightarrow 00:05:49.912$ and this allows the drug, the

NOTE Confidence: 0.9861952

 $00:05:49.912 \longrightarrow 00:05:52.429$ source of the drug, to be released

NOTE Confidence: 0.9861952

 $00:05:52.429 \longrightarrow 00:05:54.565$ very near its site of action,

NOTE Confidence: 0.9861952

 $00:05:54.570 \longrightarrow 00:05:56.760$ which for anti-cancer drugs is

NOTE Confidence: 0.9861952

 $00:05:56.760 \longrightarrow 00:05:59.160$ often in the nucleus of the cell,

NOTE Confidence: 0.9861952

00:05:59.160 --> 00:06:01.379 and so this gives you another level

NOTE Confidence: 0.9861952

 $00:06:01.379 \longrightarrow 00:06:03.927$ of control or design that you can

NOTE Confidence: 0.9861952

 $00:06:03.927 \longrightarrow 00:06:06.219$ introduce into the delivery system

 $00:06:06.892 \longrightarrow 00:06:09.244$ in order to match them most

NOTE Confidence: 0.9861952

 $00:06:09.244 \longrightarrow 00:06:10.738$ effectively to treat the particular

NOTE Confidence: 0.9861952

 $00{:}06{:}10.738 \dashrightarrow 00{:}06{:}12.563$ tumor that you're interested in.

NOTE Confidence: 0.9836517

 $00:06:12.930 \longrightarrow 00:06:15.786$ And so Mike, tell us more about

NOTE Confidence: 0.9836517

 $00:06:15.786 \longrightarrow 00:06:18.199$ the thought bomb that you had.

NOTE Confidence: 0.9836517

00:06:18.200 --> 00:06:20.090 You know, it certainly sounds

NOTE Confidence: 0.9836517

 $00:06:20.090 \longrightarrow 00:06:21.980$ like this technology that Mark

NOTE Confidence: 0.9836517

 $00:06:22.043 \longrightarrow 00:06:23.867$ has is incredibly innovative,

 $00:06:23.870 \longrightarrow 00:06:26.300$ but has so many possible applications.

NOTE Confidence: 0.9836517

 $00:06:26.300 \longrightarrow 00:06:29.404$ So how did you really think about its

NOTE Confidence: 0.9836517

 $00:06:29.404 \longrightarrow 00:06:32.370$ utility in terms of skin cancer?

NOTE Confidence: 0.9836517

00:06:32.370 --> 00:06:36.015 I took a broad approach at first.

NOTE Confidence: 0.9836517

 $00{:}06{:}36.020 \dashrightarrow 00{:}06{:}38.855$ As to the potential applications in the

NOTE Confidence: 0.9836517

 $00:06:38.855 \longrightarrow 00:06:41.252$ skin topical application, for example,

NOTE Confidence: 0.9836517

 $00:06:41.252 \longrightarrow 00:06:43.616$ to improve sunscreen performance.

NOTE Confidence: 0.9836517

 $00:06:43.620 \longrightarrow 00:06:46.062$ Injection into tumors to improve delivery

NOTE Confidence: 0.9836517

00:06:46.062 --> 00:06:48.809 of anti tumor agents to skin cancers,

NOTE Confidence: 0.9836517

 $00{:}06{:}48.810 \dashrightarrow 00{:}06{:}51.442$ but also about the potential to stimulate

NOTE Confidence: 0.9836517

00:06:51.442 --> 00:06:53.600 the immune system against cancer.

NOTE Confidence: 0.9836517

 $00{:}06{:}53.600 \rightarrow 00{:}06{:}55.192$ How these could facilitate

NOTE Confidence: 0.9836517

00:06:55.192 --> 00:06:56.784 delivery of those agents.

NOTE Confidence: 0.9836517

 $00:06:56.790 \longrightarrow 00:07:00.198$ Mark and I also talked about the various

NOTE Confidence: 0.9836517

 $00:07:00.198 \longrightarrow 00:07:02.332$ inflammatory diseases of the skin and

 $00:07:02.332 \longrightarrow 00:07:05.128$ how we might use agents that are anti

NOTE Confidence: 0.9836517

 $00{:}07{:}05.128 \dashrightarrow 00{:}07{:}07.398$ inflammatory and better deliver

NOTE Confidence: 0.9836517

 $00:07:07.398 \longrightarrow 00:07:09.604$ those agents and increase their performance,

NOTE Confidence: 0.9836517

 $00:07:09.604 \longrightarrow 00:07:11.714$ increase their safety so they're

NOTE Confidence: 0.9836517

 $00:07:11.714 \longrightarrow 00:07:13.391$ not necessarily impacting the

NOTE Confidence: 0.9836517

00:07:13.391 --> 00:07:14.459 overall immune system in a negative way.

 $00{:}07{:}16.260 \dashrightarrow 00{:}07{:}18.510$ and throughout the entire body,

NOTE Confidence: 0.9836517

 $00:07:18.510 \longrightarrow 00:07:20.760$ so it's about local delivery.

NOTE Confidence: 0.9836517

 $00:07:20.760 \longrightarrow 00:07:22.560$ It's about increasing drug

NOTE Confidence: 0.9836517

 $00:07:22.560 \longrightarrow 00:07:24.810$ availability in terms of cancer.

NOTE Confidence: 0.9836517

 $00:07:24.810 \longrightarrow 00:07:27.603$ We have a huge burden

NOTE Confidence: 0.9836517

 $00:07:27.603 \longrightarrow 00:07:29.760$ with basal cell carcinoma.

NOTE Confidence: 0.9836517

 $00{:}07{:}29.760 \dashrightarrow 00{:}07{:}32.378$ These are a huge number of cancers

NOTE Confidence: 0.9836517

 $00{:}07{:}32.378 \dashrightarrow 00{:}07{:}35.677$ across the the world that outnumber all

NOTE Confidence: 0.9836517

 $00{:}07{:}35.677 \dashrightarrow 00{:}07{:}38.302$ cancers combined in their occurrence,

NOTE Confidence: 0.9836517

 $00:07:38.310 \longrightarrow 00:07:41.460$ and often are treated by surgery or

 $00:07:41.460 \longrightarrow 00:07:44.508$ multiple surgeries on the same patient.

NOTE Confidence: 0.9836517

 $00{:}07{:}44.510 \dashrightarrow 00{:}07{:}46.315$ An individual can develop many

NOTE Confidence: 0.9836517

 $00:07:46.315 \longrightarrow 00:07:48.666$ of these over a lifetime if

NOTE Confidence: 0.9836517

 $00:07:48.666 \longrightarrow 00:07:50.558$ they are fair skinned and

NOTE Confidence: 0.9836517

 $00:07:50.560 \longrightarrow 00:07:52.570$ have a lot of sun exposure.

NOTE Confidence: 0.9836517

 $00:07:52.570 \longrightarrow 00:07:54.585$ There is squamous cell carcinoma which

NOTE Confidence: 0.9836517

 $00:07:54.585 \longrightarrow 00:07:56.600$ presents another set of problems.

NOTE Confidence: 0.9836517

 $00:07:56.600 \longrightarrow 00:07:59.018$ They can be numerous as well,

NOTE Confidence: 0.9836517

 $00{:}07{:}59.020 \to 00{:}08{:}01.972$ but they can also have a small chance

NOTE Confidence: 0.9836517

 $00:08:01.972 \longrightarrow 00:08:04.260$ of traveling throughout the body.

NOTE Confidence: 0.9836517

 $00:08:04.260 \longrightarrow 00:08:07.081$ They tend to be deeper as well.

00:08:10.696 --> 00:08:13.270 Melanoma not as common as basal

NOTE Confidence: 0.9836517

 $00{:}08{:}13.270 \dashrightarrow 00{:}08{:}15.500$ cell and squamous cell carcinoma.

NOTE Confidence: 0.9836517

00:08:15.500 --> 00:08:18.314 But a whole other set of problems si that

NOTE Confidence: 0.9836517

 $00:08:18.320 \longrightarrow 00:08:21.947$ this is a real killer of young people.

NOTE Confidence: 0.9836517

 $00:08:21.950 \longrightarrow 00:08:22.369$ Melanoma is

 $00:08:22.369 \longrightarrow 00:08:25.302$ something that has a very high risk

NOTE Confidence: 0.9836517

 $00{:}08{:}25.302 \dashrightarrow 00{:}08{:}27.334$ of metastasis after it obtains

NOTE Confidence: 0.9836517

 $00:08:27.334 \longrightarrow 00:08:29.199$ a certain level of depth.

NOTE Confidence: 0.9836517

 $00:08:29.200 \longrightarrow 00:08:30.190$ There are clear,

NOTE Confidence: 0.9836517

 $00:08:30.190 \longrightarrow 00:08:32.170$ unmet needs in some patients who

NOTE Confidence: 0.9836517

 $00:08:32.170 \longrightarrow 00:08:33.964$ have intermediate depth Melanoma

NOTE Confidence: 0.9836517

 $00{:}08{:}33.964 \dashrightarrow 00{:}08{:}35.832$ that has already metastasized

NOTE Confidence: 0.9836517

 $00:08:35.832 \longrightarrow 00:08:37.670$ to regional lymph nodes.

NOTE Confidence: 0.9836517

 $00{:}08{:}37.670 \dashrightarrow 00{:}08{:}40.286$ And there are challenges in treating

NOTE Confidence: 0.9836517

 $00:08:40.286 \longrightarrow 00:08:42.030$ these patients without necessarily

NOTE Confidence: 0.9836517

 $00{:}08{:}42.094 \dashrightarrow 00{:}08{:}44.560$ giving them something aggressive

NOTE Confidence: 0.9836517

 $00:08:44.560 \longrightarrow 00:08:46.204$ and systemically delivered.

NOTE Confidence: 0.9836517

00:08:46.210 --> 00:08:48.590 Chemotherapy to the entire body.

NOTE Confidence: 0.9836517

 $00:08:48.590 \longrightarrow 00:08:51.872$ So all of these potential challenges

NOTE Confidence: 0.9836517

 $00:08:51.872 \longrightarrow 00:08:55.285$ in the world of skin cancer

NOTE Confidence: 0.9836517

 $00:08:55.285 \longrightarrow 00:08:58.065$ have areas that could be

 $00:08:58.070 \longrightarrow 00:08:59.698$ potentially leveraged with this technology.

NOTE Confidence: 0.9836517

 $00:08:59.698 \longrightarrow 00:09:02.140$ Mark and I have

NOTE Confidence: 0.9836517

00:09:02.213 --> 00:09:04.698 been really trying to look at all

NOTE Confidence: 0.9836517

 $00:09:04.698 \longrightarrow 00:09:06.671$ of the possibilities and begin

NOTE Confidence: 0.9836517

 $00:09:06.671 \longrightarrow 00:09:08.351$ to develop research programs

NOTE Confidence: 0.9836517

 $00:09:08.351 \longrightarrow 00:09:10.440$ and strategies to address them.

NOTE Confidence: 0.98096687

00:09:10.440 --> 00:09:13.200 Mark, a couple

NOTE Confidence: 0.98096687

 $00{:}09{:}13.200 \dashrightarrow 00{:}09{:}15.773$ of things that struck me when

NOTE Confidence: 0.98096687

 $00{:}09{:}15.773 \dashrightarrow 00{:}09{:}18.018$ you were talking about this

NOTE Confidence: 0.98096687

 $00:09:18.020 \longrightarrow 00:09:20.678$ technology, one is that these

NOTE Confidence: 0.98096687

 $00{:}09{:}20.678 \longrightarrow 00{:}09{:}23.663$ nanoparticles are so small that they can

NOTE Confidence: 0.98096687

 $00:09:23.663 \longrightarrow 00:09:26.302$ actually be engulfed by the tumor

NOTE Confidence: 0.98096687

 $00{:}09{:}26.377 \dashrightarrow 00{:}09{:}29.037$ cell and have a mechanism of action

NOTE Confidence: 0.98096687

 $00:09:29.040 \longrightarrow 00:09:30.512$ at their nucleus, essentially,

NOTE Confidence: 0.98096687

 $00:09:30.512 \longrightarrow 00:09:31.616$ really targeted therapy,

 $00:09:31.620 \longrightarrow 00:09:34.580$ delivered to the source of the tumor.

NOTE Confidence: 0.98096687

 $00:09:34.580 \longrightarrow 00:09:36.420$ But my question there is,

NOTE Confidence: 0.98096687

 $00:09:36.420 \longrightarrow 00:09:38.270$ how targeted can it be?

NOTE Confidence: 0.98096687

 $00:09:38.270 \longrightarrow 00:09:40.825$ I mean can you make these

NOTE Confidence: 0.98096687

 $00:09:40.825 \longrightarrow 00:09:43.089$ nanoparticles such that the tumor cells

NOTE Confidence: 0.98096687

 $00:09:43.089 \longrightarrow 00:09:45.644$ and only the tumor cells engulf them?

NOTE Confidence: 0.98096687

 $00:09:45.650 \longrightarrow 00:09:47.122$ How does that work?

NOTE Confidence: 0.98096687

 $00:09:47.122 \longrightarrow 00:09:48.594$ That's a great question and I think

 $00:09:51.545 \longrightarrow 00:09:53.390$ there's several different aspects to that.

NOTE Confidence: 0.9840316

 $00{:}09{:}53.390 \dashrightarrow 00{:}09{:}56.141$ The one that we've been talking about

NOTE Confidence: 0.9840316

00:09:56.141 --> 00:09:59.049 so far and a major

NOTE Confidence: 0.9840316

 $00:09:59.050 \longrightarrow 00:10:01.255$ one that Mike and I have been

NOTE Confidence: 0.9840316

 $00:10:01.255 \longrightarrow 00:10:02.790$ exploring is to

NOTE Confidence: 0.9840316

 $00:10:02.790 \longrightarrow 00:10:04.560$ put the particles as close to

NOTE Confidence: 0.9840316

 $00{:}10{:}04.560 \dashrightarrow 00{:}10{:}06.298$ the tumor cells as possible.

NOTE Confidence: 0.9840316

00:10:06.300 --> 00:10:08.498 To physically target them,

 $00:10:08.500 \longrightarrow 00:10:10.390$ inject them into a tumor,

NOTE Confidence: 0.9840316

 $00:10:10.390 \longrightarrow 00:10:11.024$ for example.

NOTE Confidence: 0.9840316

00:10:12.926 --> 00:10:14.846 And that's possible with the skin cancers

NOTE Confidence: 0.9840316

00:10:14.846 --> 00:10:16.682 that Mike is mentioning,

NOTE Confidence: 0.9840316

00:10:16.690 --> 00:10:18.380 because they're so accessible,

NOTE Confidence: 0.9840316

 $00{:}10{:}18.380 \dashrightarrow 00{:}10{:}20.788$ they're on the surface of the skin,

NOTE Confidence: 0.9840316

 $00:10:20.790 \longrightarrow 00:10:23.286$ at least some of them are

NOTE Confidence: 0.9840316

00:10:23.286 --> 00:10:25.509 exclusively on the surface of the skin,

 $00:10:26.692 \longrightarrow 00:10:29.056$ and dermatologists are very comfortable with

NOTE Confidence: 0.9840316

 $00:10:29.060 \longrightarrow 00:10:30.880$ using needles to inject locally

NOTE Confidence: 0.9840316

 $00:10:30.880 \longrightarrow 00:10:33.103$ in the skin and they're very

NOTE Confidence: 0.9840316

 $00:10:33.103 \longrightarrow 00:10:34.758$ talented as well,

NOTE Confidence: 0.9840316

 $00:10:34.760 \longrightarrow 00:10:36.896$ and so that makes a

NOTE Confidence: 0.9840316

 $00{:}10{:}36.896 \dashrightarrow 00{:}10{:}38.320$ reasonable form of targeting.

NOTE Confidence: 0.9840316

00:10:38.320 --> 00:10:40.808 But you could also make it more

NOTE Confidence: 0.9840316

00:10:40.810 --> 00:10:42.790 targeted and one possible way to

00:10:42.790 --> 00:10:45.347 make it more targeted is to take

NOTE Confidence: 0.9840316

 $00{:}10{:}45.347 \dashrightarrow 00{:}10{:}46.911$ the nanoparticles and engineer

NOTE Confidence: 0.9840316

00:10:46.911 --> 00:10:48.639 the surface properties of them.

NOTE Confidence: 0.9840316

 $00:10:48.640 \longrightarrow 00:10:51.202$ And one of the aspects of the

NOTE Confidence: 0.9840316

00:10:51.202 --> 00:10:52.742 technology that we've exploited

NOTE Confidence: 0.9840316

 $00{:}10{:}52.742 \dashrightarrow 00{:}10{:}55.304$ in many of the projects that we

NOTE Confidence: 0.9840316

 $00{:}10{:}55.304 \dashrightarrow 00{:}10{:}57.540$ worked on is to make the particles

NOTE Confidence: 0.9840316

 $00:10:57.540 \longrightarrow 00:10:59.450$ themselves very sticky to proteins.

NOTE Confidence: 0.9840316

 $00:10:59.450 \longrightarrow 00:11:01.676$ Or tumor cells that have a lot

NOTE Confidence: 0.9840316

 $00{:}11{:}01.676 \dashrightarrow 00{:}11{:}03.689$ of proteins on their surface.

NOTE Confidence: 0.9840316

 $00{:}11{:}03.690 --> 00{:}11{:}05.940$ And so when you inject these

NOTE Confidence: 0.9840316

 $00:11:05.940 \longrightarrow 00:11:07.830$ sticky particles they will

NOTE Confidence: 0.9840316

 $00:11:07.830 \longrightarrow 00:11:10.028$ tend to be taken up by whatever

NOTE Confidence: 0.9840316

 $00:11:10.028 \longrightarrow 00:11:12.502$ cells are near the site where

NOTE Confidence: 0.9840316

 $00:11:12.502 \longrightarrow 00:11:14.661$ you've placed them and this

NOTE Confidence: 0.9840316

 $00{:}11{:}14.661 \dashrightarrow 00{:}11{:}17.328$ allows the vast majority of the

00:11:17.328 --> 00:11:20.038 particles to stay in a tumor if you

NOTE Confidence: 0.9840316

00:11:20.038 --> 00:11:22.400 inject them right into the skin tumor,

NOTE Confidence: 0.9840316

 $00:11:22.400 \longrightarrow 00:11:23.052$ for example.

NOTE Confidence: 0.9840316

00:11:23.052 --> 00:11:25.334 And so that's one one way to

NOTE Confidence: 0.9840316

 $00:11:25.334 \longrightarrow 00:11:27.623$ augment the targeting that local

NOTE Confidence: 0.9840316

 $00:11:27.623 \longrightarrow 00:11:29.519$ delivery naturally provides you.

NOTE Confidence: 0.9840316

00:11:29.520 --> 00:11:31.800 A second way would be to not just

NOTE Confidence: 0.9840316

 $00{:}11{:}31.800 \dashrightarrow 00{:}11{:}33.261$ use physical properties like

NOTE Confidence: 0.9840316

 $00:11:33.261 \longrightarrow 00:11:35.311$ stickiness of particles to make

NOTE Confidence: 0.9840316

 $00{:}11{:}35.311 \dashrightarrow 00{:}11{:}37.350$ them attractive to tumor cells,

NOTE Confidence: 0.9840316

 $00:11:37.350 \longrightarrow 00:11:39.130$ but to make them specifically

NOTE Confidence: 0.9840316

 $00:11:39.130 \longrightarrow 00:11:40.554$ adhesive to tumor cells.

NOTE Confidence: 0.9840316

 $00:11:40.560 \longrightarrow 00:11:41.684$ So in that case,

NOTE Confidence: 0.9840316

 $00:11:41.684 \longrightarrow 00:11:44.526$ if you knew that there was

NOTE Confidence: 0.9840316

00:11:44.526 --> 00:11:47.046 a protein on the tumor cell surface

 $00:11:47.127 \longrightarrow 00:11:49.593$ that was expressed very abundantly in

NOTE Confidence: 0.9840316

00:11:49.593 --> 00:11:52.624 the tumor cells and not in normal cells,

NOTE Confidence: 0.9840316

00:11:52.624 --> 00:11:54.354 you could put some chemicals

NOTE Confidence: 0.9840316

 $00:11:54.354 \longrightarrow 00:11:56.922$ that bind to that protein on the

NOTE Confidence: 0.9840316

 $00:11:56.922 \longrightarrow 00:11:58.358$ surface of the nanoparticle.

NOTE Confidence: 0.9840316

 $00:11:58.360 \longrightarrow 00:12:00.556$ So this might be an antibody.

NOTE Confidence: 0.9840316

 $00{:}12{:}00.560 \dashrightarrow 00{:}12{:}03.395$ Or an antibody fragment that

NOTE Confidence: 0.9840316

 $00:12:03.395 \longrightarrow 00:12:06.043$ is specific for that protein that's

NOTE Confidence: 0.9840316

 $00{:}12{:}06.043 \dashrightarrow 00{:}12{:}08.743$ highly enriched on the tumor cell.

NOTE Confidence: 0.9840316

 $00:12:08.750 \longrightarrow 00:12:11.336$ Then that gives you an additional

NOTE Confidence: 0.9840316

 $00:12:11.336 \longrightarrow 00:12:12.630$ level of targeting.

NOTE Confidence: 0.9840316

 $00:12:12.630 \longrightarrow 00:12:17.928$ And it's even possible to think about

NOTE Confidence: 0.9840316

 $00:12:17.930 \longrightarrow 00:12:20.114$ administering those highly

NOTE Confidence: 0.9840316

 $00:12:20.114 \longrightarrow 00:12:22.298$ targeted particles systemically and

NOTE Confidence: 0.9840316

00:12:22.298 --> 00:12:25.019 and asking them to find the tumor

NOTE Confidence: 0.9840316

00:12:25.019 --> 00:12:27.406 for you instead of you using the

 $00:12:27.406 \longrightarrow 00:12:29.686$ needle to find the tumor yourself.

NOTE Confidence: 0.9840316

 $00{:}12{:}29.690 \to 00{:}12{:}33.362$ And that's been a very active area of

NOTE Confidence: 0.9840316

00:12:33.362 --> 00:12:37.243 study over the past 10 to 15 years or so,

NOTE Confidence: 0.9840316

 $00:12:37.250 \longrightarrow 00:12:40.869$ and it turns out to be

NOTE Confidence: 0.9840316

 $00:12:40.870 \longrightarrow 00:12:42.575$ hard to achieve practically for

NOTE Confidence: 0.9840316

 $00:12:42.575 \longrightarrow 00:12:44.280$ reasons that we could discuss.

NOTE Confidence: 0.9840316

 $00:12:44.280 \longrightarrow 00:12:46.667$ But it's also a method of targeting.

NOTE Confidence: 0.98745333999999900:12:46.670 --> 00:12:48.542 I would like

NOTE Confidence: 0.987453339999999

 $00{:}12{:}48.542 \dashrightarrow 00{:}12{:}50.967$ to get into how exactly we target

NOTE Confidence: 0.987453339999999

 $00:12:50.967 \longrightarrow 00:12:53.187$ things and what are the challenges

NOTE Confidence: 0.987453339999999

 $00:12:53.187 \longrightarrow 00:12:55.189$ that are being faced in this

NOTE Confidence: 0.987453339999999

 $00:12:55.190 \longrightarrow 00:12:56.900$ really exciting area, but first

NOTE Confidence: 0.987453339999999

 $00{:}12{:}56.900 \dashrightarrow 00{:}12{:}59.393$ we need to take a short break

NOTE Confidence: 0.987453339999999

 $00:12:59.393 \longrightarrow 00:13:01.749$ for a medical minute, so please stay

NOTE Confidence: 0.987453339999999

 $00:13:01.749 \longrightarrow 00:13:03.981$ tuned to learn more about nanoparticles

 $00:13:03.981 \longrightarrow 00:13:06.447$ and skin tumors with my guests

NOTE Confidence: 0.987453339999999

 $00:13:06.450 \longrightarrow 00:13:07.130$ Doctor Michael Girardi and

 $00:13:08.490 \longrightarrow 00:13:09.170$ Doctor Mark Saltzman.

NOTE Confidence: 0.88316566

00:13:09.850 --> 00:13:12.445 Funding for Yale Cancer Answers

NOTE Confidence: 0.88316566

 $00:13:12.445 \longrightarrow 00:13:15.536$ comes from AstraZeneca, working to

NOTE Confidence: 0.88316566

00:13:15.536 --> 00:13:18.420 eliminate cancer as a cause of death.

NOTE Confidence: 0.88316566

00:13:18.420 --> 00:13:22.188 Learn more at astrazeneca-us.com.

NOTE Confidence: 0.88316566

 $00:13:22.190 \longrightarrow 00:13:24.340$ Over 230,000 Americans will be

NOTE Confidence: 0.88316566

 $00:13:24.340 \longrightarrow 00:13:26.490$ diagnosed with lung cancer this

NOTE Confidence: 0.88316566

 $00{:}13{:}26.565 \dashrightarrow 00{:}13{:}28.405$ year and in Connecticut alone

NOTE Confidence: 0.88316566

00:13:28.405 --> 00:13:31.010 there will be over 2700 new cases.

NOTE Confidence: 0.88316566

 $00:13:31.010 \longrightarrow 00:13:33.170$ More than 85% of lung cancer

NOTE Confidence: 0.88316566

 $00{:}13{:}33.170 \dashrightarrow 00{:}13{:}35.553$ diagnosis are related to smoking and

NOTE Confidence: 0.88316566

 $00{:}13{:}35.553 \dashrightarrow 00{:}13{:}38.163$ quitting even after decades of use

NOTE Confidence: 0.88316566

 $00:13:38.163 \longrightarrow 00:13:40.282$ can significantly reduce your risk

NOTE Confidence: 0.88316566

 $00:13:40.282 \longrightarrow 00:13:42.640$ of developing lung cancer. Each day,

00:13:42.640 --> 00:13:44.950 patients with lung cancer are surviving

NOTE Confidence: 0.88316566

 $00{:}13{:}44.950 \dashrightarrow 00{:}13{:}47.386$ thanks to increased access to advanced

NOTE Confidence: 0.88316566

 $00:13:47.386 \longrightarrow 00:13:49.058$ therapies and specialized care,

NOTE Confidence: 0.88316566

 $00:13:49.060 \longrightarrow 00:13:51.005$ new treatment options and surgical

NOTE Confidence: 0.88316566

 $00:13:51.005 \longrightarrow 00:13:53.590$ techniques are giving lung cancer survivors

NOTE Confidence: 0.88316566

 $00:13:53.590 \longrightarrow 00:13:56.766$ more hope than they have ever had before.

NOTE Confidence: 0.88316566

00:13:56.770 --> 00:13:58.350 Clinical trials are currently

NOTE Confidence: 0.88316566

 $00:13:58.350 \longrightarrow 00:13:59.930$ underway at federally designated

NOTE Confidence: 0.88316566

 $00{:}13{:}59.930 \dashrightarrow 00{:}14{:}01.150$ Comprehensive cancer centers,

NOTE Confidence: 0.88316566

 $00{:}14{:}01.150 \dashrightarrow 00{:}14{:}03.740$ such as the BATTLE II trial at

NOTE Confidence: 0.88316566

 $00{:}14{:}03.740 \dashrightarrow 00{:}14{:}05.644$ Yale Cancer Center and Smilow

NOTE Confidence: 0.88316566

 $00:14:05.644 \longrightarrow 00:14:08.136$ Cancer Hospital to learn if a drug

NOTE Confidence: 0.88316566

 $00{:}14{:}08.136 \dashrightarrow 00{:}14{:}10.826$ or combination of drugs based on

NOTE Confidence: 0.88316566

00:14:10.826 --> 00:14:13.086 personal biomarkers can help to

NOTE Confidence: 0.88316566

 $00:14:13.090 \longrightarrow 00:14:15.478$ control non small cell lung cancer.

NOTE Confidence: 0.88316566

 $00:14:15.480 \longrightarrow 00:14:17.530$ More information is available at

00:14:17.530 --> 00:14:18.760 yalecancercenter.org. You're listening

NOTE Confidence: 0.88316566

 $00:14:18.760 \longrightarrow 00:14:20.260$ to Connecticut Public Radio.

NOTE Confidence: 0.9704669

 $00:14:21.320 \longrightarrow 00:14:23.816$ Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.9704669

00:14:23.820 --> 00:14:26.664 This is Doctor Anees Chappar

NOTE Confidence: 0.9704669

 $00:14:26.664 \longrightarrow 00:14:29.338$ and I'm joined tonight by my guest doctor

NOTE Confidence: 0.9704669

 $00:14:29.338 \longrightarrow 00:14:32.140$ Michael Girardi and Doctor Mark Saltzman.

NOTE Confidence: 0.9704669

00:14:32.140 --> 00:14:34.580 We're talking about research looking

NOTE Confidence: 0.9704669

 $00:14:34.580 \longrightarrow 00:14:37.020$ into using nanoparticles to treat

NOTE Confidence: 0.9704669

00:14:37.090 --> 00:14:39.346 skin tumors and right before the

NOTE Confidence: 0.9704669

 $00:14:39.346 \longrightarrow 00:14:42.032$ break we were talking about how these

NOTE Confidence: 0.9704669

00:14:42.032 --> 00:14:44.615 nanoparticles are so small and how we

NOTE Confidence: 0.9704669

 $00:14:44.620 \longrightarrow 00:14:47.399$ can try to make them really attack

NOTE Confidence: 0.9704669

 $00:14:47.399 \longrightarrow 00:14:50.020$ tumor cells rather than normal cells.

NOTE Confidence: 0.9704669

 $00:14:50.020 \longrightarrow 00:14:52.720$ So Mike, Mark was

NOTE Confidence: 0.9704669

 $00:14:52.720 \longrightarrow 00:14:55.170$ talking about how

00:14:55.170 --> 00:14:57.860 we can make nanoparticles sticky.

NOTE Confidence: 0.9704669

 $00{:}14{:}57.860 \dashrightarrow 00{:}15{:}00.748$ We can try to get them in an

NOTE Confidence: 0.9704669

 $00:15:00.748 \longrightarrow 00:15:03.418$ area where these cancers exist.

NOTE Confidence: 0.9704669

 $00:15:03.420 \longrightarrow 00:15:07.263$ What have you explored in terms of

NOTE Confidence: 0.9704669

 $00:15:07.270 \longrightarrow 00:15:10.694$ trying to treat these skin cancers?

 $00:15:11.139 \longrightarrow 00:15:13.773$ What are the exciting

NOTE Confidence: 0.9704669

 $00:15:13.773 \longrightarrow 00:15:15.400$ developments and where are

NOTE Confidence: 0.9880927

 $00:15:15.400 \longrightarrow 00:15:17.112$ we with this research?

NOTE Confidence: 0.9880927

 $00:15:17.112 \longrightarrow 00:15:20.111$ So I think there's several features that

NOTE Confidence: 0.9880927

 $00:15:20.111 \longrightarrow 00:15:22.657$ we're really leveraging about the sticky

NOTE Confidence: 0.9880927

 $00:15:22.657 \longrightarrow 00:15:25.590$ type particles and these will bind to proteins.

NOTE Confidence: 0.9880927

00:15:25.590 --> 00:15:28.008 Any proteins they come in contact

NOTE Confidence: 0.9880927

 $00:15:28.008 \longrightarrow 00:15:30.429$ with but what's really special about the

NOTE Confidence: 0.9880927

00:15:30.430 --> 00:15:32.550 tumor microenvironment is that it's

NOTE Confidence: 0.9880927

 $00:15:32.550 \longrightarrow 00:15:35.099$ very protein rich tumor cells secrete

NOTE Confidence: 0.9880927

 $00:15:35.099 \longrightarrow 00:15:37.277$ a lot of proteins.

 $00:15:37.280 \longrightarrow 00:15:39.290$ They create their own matrix.

NOTE Confidence: 0.9880927

 $00:15:39.290 \longrightarrow 00:15:41.310$ This is helpful for them.

NOTE Confidence: 0.9880927

00:15:41.310 --> 00:15:44.874 We think they perceive it as such so they

NOTE Confidence: 0.9880927

 $00:15:44.874 \longrightarrow 00:15:48.969$ can grow so they can begin to want to travel

NOTE Confidence: 0.9880927

00:15:48.970 --> 00:15:52.186 if we personify the tumor cells that way,

NOTE Confidence: 0.9880927

 $00:15:52.190 \longrightarrow 00:15:54.062$ and so these particles

NOTE Confidence: 0.9880927

 $00:15:54.062 \longrightarrow 00:15:57.803$ will bind to both tumor matrix proteins and

NOTE Confidence: 0.9880927

00:15:57.803 --> 00:16:01.230 bind to the surface of the tumor cells,

NOTE Confidence: 0.9880927

 $00{:}16{:}01.230 \mathrel{--}{>} 00{:}16{:}03.738$ so this really not only gets

NOTE Confidence: 0.9880927

 $00:16:03.738 \longrightarrow 00:16:06.570$ the drugs into the tumor cells,

NOTE Confidence: 0.9880927

 $00:16:06.570 \longrightarrow 00:16:09.174$ but creates anti-tumor

NOTE Confidence: 0.9880927

 $00{:}16{:}09.174 \dashrightarrow 00{:}16{:}11.470$ agents all around the tumor.

NOTE Confidence: 0.9880927

 $00:16:11.470 \longrightarrow 00:16:14.445$ We think this is really important for

NOTE Confidence: 0.9880927

 $00{:}16{:}14.445 \dashrightarrow 00{:}16{:}17.699$ trying to target and eliminate the tumor.

NOTE Confidence: 0.9880927

00:16:17.700 --> 00:16:20.202 We also have worked on strategies

NOTE Confidence: 0.9880927

 $00{:}16{:}20.202 \dashrightarrow 00{:}16{:}22.994$ and how we deliver these tiny

00:16:22.994 --> 00:16:25.078 particles beyond the simple

NOTE Confidence: 0.9880927

 $00{:}16{:}25.080 \mathrel{--}{>} 00{:}16{:}26.728$ syringe and needle strategy,

NOTE Confidence: 0.9880927

 $00:16:26.728 \longrightarrow 00:16:28.376$ which is actually quite

NOTE Confidence: 0.9880927

 $00:16:28.376 \longrightarrow 00:16:30.159$ effective in and of itself.

NOTE Confidence: 0.9880927

 $00:16:30.160 \longrightarrow 00:16:32.506$ But for certain tumors,

NOTE Confidence: 0.9880927

 $00:16:32.510 \longrightarrow 00:16:33.254$ for example,

NOTE Confidence: 0.9880927

 $00:16:33.254 \longrightarrow 00:16:35.114$ ones that are more broad

NOTE Confidence: 0.9880927

 $00:16:35.114 \longrightarrow 00:16:37.199$ but thin and shallow,

NOTE Confidence: 0.9880927

 $00:16:37.200 \longrightarrow 00:16:39.155$ they can create surgical challenges

NOTE Confidence: 0.9880927

00:16:39.155 --> 00:16:42.714 to cut out a large piece of skin when

NOTE Confidence: 0.9880927

 $00:16:42.714 \longrightarrow 00:16:45.012$ something is really not that deep.

NOTE Confidence: 0.9880927

 $00{:}16{:}45.020 \dashrightarrow 00{:}16{:}47.533$ That lets us wonder if there is a

NOTE Confidence: 0.9880927

 $00:16:47.533 \longrightarrow 00:16:49.710$ way to deliver these agents,

NOTE Confidence: 0.9880927

 $00:16:49.710 \longrightarrow 00:16:52.056$ for example over a larger area,

NOTE Confidence: 0.9880927

 $00:16:52.060 \longrightarrow 00:16:56.300$ but not as deep and so Mark and I have

 $00:16:56.300 \longrightarrow 00:16:58.260$ explored strategies using what's called

NOTE Confidence: 0.9880927

 $00:16:58.260 \longrightarrow 00:17:00.560$ micro needling or micro needle pads,

NOTE Confidence: 0.9880927

 $00:17:00.560 \longrightarrow 00:17:02.495$ and so the particles might

NOTE Confidence: 0.9880927

 $00:17:02.495 \longrightarrow 00:17:04.430$ be loaded into these hollow

NOTE Confidence: 0.9880927

 $00:17:04.430 \longrightarrow 00:17:07.118$ very tiny needles and in

NOTE Confidence: 0.9880927

00:17:07.118 --> 00:17:10.116 many cases they can be made to be

NOTE Confidence: 0.9880927

00:17:10.116 --> 00:17:12.372 painless because they just don't

NOTE Confidence: 0.9880927

00:17:12.372 --> 00:17:15.221 get to the depth where they're going

NOTE Confidence: 0.9880927

 $00{:}17{:}15.221 \dashrightarrow 00{:}17{:}17.500$ to trigger the nerve endings and

NOTE Confidence: 0.9880927

 $00:17:17.500 \longrightarrow 00:17:20.165$ these pads could be applied and the

NOTE Confidence: 0.9880927

 $00:17:20.165 \longrightarrow 00:17:22.993$ particles can be delivered in that fashion.

NOTE Confidence: 0.9880927

 $00:17:23.000 \longrightarrow 00:17:25.280$ We've also looked at strategies where

NOTE Confidence: 0.9880927

 $00{:}17{:}25.280 \dashrightarrow 00{:}17{:}27.380$ we've accelerated fluid that contains

NOTE Confidence: 0.9880927

 $00:17:27.380 \longrightarrow 00:17:28.248$ the nanoparticles

NOTE Confidence: 0.9880927

 $00:17:28.248 \longrightarrow 00:17:31.720$ in a way that can push them with

NOTE Confidence: 0.9880927

 $00:17:31.805 \longrightarrow 00:17:34.559$ a high pressure system through the

 $00:17:34.559 \longrightarrow 00:17:37.872$ surface of the skin into a tumor

NOTE Confidence: 0.9880927

 $00:17:37.872 \longrightarrow 00:17:39.720$ and the surrounding area.

NOTE Confidence: 0.9880927

00:17:39.720 --> 00:17:43.376 Kind of like a high pressure micro waterjet,

NOTE Confidence: 0.9880927

 $00:17:43.380 \longrightarrow 00:17:46.355$ so we're really looking at ways that

NOTE Confidence: 0.9880927

 $00{:}17{:}46.355 \dashrightarrow 00{:}17{:}49.089$ we can empower health care providers

NOTE Confidence: 0.9880927

 $00:17:49.089 \longrightarrow 00:17:52.295$ to be able to use this technology

NOTE Confidence: 0.9880927

 $00:17:52.383 \longrightarrow 00:17:54.798$ to best serve their patients.

NOTE Confidence: 0.9880927

 $00:17:54.800 \longrightarrow 00:17:57.968$ But in a number of different

NOTE Confidence: 0.9880927

00:17:57.970 --> 00:18:00.170 tumor settings, different tumor types,

NOTE Confidence: 0.9880927

 $00:18:00.170 \longrightarrow 00:18:01.484$ different tumor sizes,

NOTE Confidence: 0.9880927

 $00:18:01.484 \longrightarrow 00:18:03.236$ and different tumor depths.

NOTE Confidence: 0.9880927

 $00:18:03.240 \longrightarrow 00:18:03.680$ That's

NOTE Confidence: 0.9852848

 $00:18:03.680 \longrightarrow 00:18:06.572$ really interesting, and I guess the

NOTE Confidence: 0.9852848

 $00:18:06.572 \longrightarrow 00:18:09.820$ other way to do this is,

NOTE Confidence: 0.9852848

 $00:18:09.820 \longrightarrow 00:18:12.900$ as you both were talking about earlier,

 $00:18:12.900 \longrightarrow 00:18:14.696$ was injecting this systemically.

NOTE Confidence: 0.9852848

 $00:18:14.696 \longrightarrow 00:18:18.297$ So I would think intravenously to try and

NOTE Confidence: 0.9852848

 $00:18:18.297 \longrightarrow 00:18:20.799$ hone these nanoparticles to their target

NOTE Confidence: 0.9852848

 $00:18:20.800 \longrightarrow 00:18:23.428$ whether it's an

NOTE Confidence: 0.9852848

 $00:18:23.428 \longrightarrow 00:18:26.241$ antibody or other mechanism to

NOTE Confidence: 0.9852848

 $00:18:26.241 \longrightarrow 00:18:29.133$ try to find these cancer cells

NOTE Confidence: 0.9852848

 $00:18:29.140 \longrightarrow 00:18:31.170$ and target them that way.

NOTE Confidence: 0.9852848

00:18:31.170 --> 00:18:33.190 Mark, you know another concept

NOTE Confidence: 0.9852848

00:18:33.190 --> 00:18:34.806 that you had mentioned,

NOTE Confidence: 0.9852848

 $00:18:34.810 \longrightarrow 00:18:37.770$ or I think Mike had mentioned before the

NOTE Confidence: 0.9852848

 $00{:}18{:}37.770 \dashrightarrow 00{:}18{:}40.268$ break was using nanoparticles to kind

NOTE Confidence: 0.9852848

 $00{:}18{:}40.268 \dashrightarrow 00{:}18{:}43.320$ of prime the immune system.

NOTE Confidence: 0.9852848

 $00:18:43.320 \longrightarrow 00:18:46.020$ Often on this show we're talking about

NOTE Confidence: 0.9852848

 $00:18:46.020 \longrightarrow 00:18:48.759$ immunotherapy and the fact that these

NOTE Confidence: 0.9852848

 $00:18:48.759 \longrightarrow 00:18:51.748$ cancers kind of evade the immune system

NOTE Confidence: 0.9852848

 $00{:}18{:}51.748 \dashrightarrow 00{:}18{:}54.821$ whose job it is really to get rid of

00:18:54.821 --> 00:18:57.900 things that we don't want in our body,

NOTE Confidence: 0.9852848

 $00:18:57.900 \longrightarrow 00:18:59.229$ whether it's infections,

NOTE Confidence: 0.9852848

 $00:18:59.229 \longrightarrow 00:19:01.887$ or whether it's tumor cells.

NOTE Confidence: 0.9852848

00:19:01.887 --> 00:19:04.489 Tell us a little bit more about

NOTE Confidence: 0.9852848

 $00:19:04.489 \longrightarrow 00:19:06.482$ how you can engineer nanoparticles

NOTE Confidence: 0.9852848

 $00:19:06.482 \longrightarrow 00:19:09.127$ to trigger the immune system,

NOTE Confidence: 0.9852848

00:19:09.130 --> 00:19:12.147 and how that's working in treating cancer?

NOTE Confidence: 0.93299675

 $00:19:13.890 \longrightarrow 00:19:15.606$ I'd be happy

NOTE Confidence: 0.93299675

00:19:15.606 --> 00:19:16.750 to start addressing that,

NOTE Confidence: 0.93299675

 $00:19:16.750 \longrightarrow 00:19:19.315$ but Mike is really the expert on that part,

NOTE Confidence: 0.93299675

00:19:19.320 --> 00:19:21.552 but so I'll talk about the parts that

NOTE Confidence: 0.93299675

 $00:19:21.552 \longrightarrow 00:19:23.899$ I know and maybe he can follow up.

 $00:19:26.190 \longrightarrow 00:19:27.936$ One of the interesting things about some

NOTE Confidence: 0.93299675

 $00:19:27.936 \longrightarrow 00:19:30.532$ of the cells of the immune system is

NOTE Confidence: 0.93299675

00:19:30.532 --> 00:19:32.242 that their naturally bagocytic

NOTE Confidence: 0.93299675

 $00{:}19{:}32.250 \dashrightarrow 00{:}19{:}35.028$ and part of their job is to take up

 $00{:}19{:}38.070 \dashrightarrow 00{:}19{:}39.478$ particles from the environment

NOTE Confidence: 0.93299675

00:19:39.478 --> 00:19:41.985 and to sample them to look for

NOTE Confidence: 0.93299675

00:19:41.985 --> 00:19:43.317 danger signals,

NOTE Confidence: 0.93299675

 $00:19:43.320 \longrightarrow 00:19:44.528$ and so you can

NOTE Confidence: 0.93299675

00:19:44.528 --> 00:19:46.340 exploit those cells by

NOTE Confidence: 0.93299675

 $00:19:46.411 \longrightarrow 00:19:48.351$ creating nanoparticles that look

NOTE Confidence: 0.93299675

 $00:19:48.351 \longrightarrow 00:19:50.703$ like the natural kinds of things

NOTE Confidence: 0.93299675

00:19:50.703 --> 00:19:53.118 that they would take up and ingest.

NOTE Confidence: 0.93299675

 $00:19:53.120 \longrightarrow 00:19:55.129$ And you can do that by controlling

NOTE Confidence: 0.93299675

 $00:19:55.129 \longrightarrow 00:19:57.406$ the size of the particle and by

NOTE Confidence: 0.93299675

 $00{:}19{:}57.406 \dashrightarrow 00{:}19{:}59.428$ controlling its surface to make it

NOTE Confidence: 0.93299675

 $00:19:59.495 \longrightarrow 00:20:01.967$ most attractive to those

NOTE Confidence: 0.93299675

 $00{:}20{:}01.967 \dashrightarrow 00{:}20{:}04.012$ macrophages or antigen presenting cells.

NOTE Confidence: 0.93299675

00:20:04.012 --> 00:20:05.188 But in addition,

NOTE Confidence: 0.93299675

 $00:20:05.188 \longrightarrow 00:20:07.148$ you could further

00:20:07.148 --> 00:20:09.068 augment the activity of those

NOTE Confidence: 0.93299675

 $00:20:09.070 \longrightarrow 00:20:11.744$ particles by putting in the kind

NOTE Confidence: 0.93299675

 $00:20:11.744 \longrightarrow 00:20:14.160$ of danger signals that they might

NOTE Confidence: 0.93299675

 $00:20:14.160 \longrightarrow 00:20:16.542$ find from a microorganism and that

NOTE Confidence: 0.93299675

 $00:20:16.542 \longrightarrow 00:20:19.247$ revs up their their immune activity.

NOTE Confidence: 0.93299675

00:20:19.250 --> 00:20:21.686 And so we've been exploring that

NOTE Confidence: 0.93299675

 $00:20:21.686 \longrightarrow 00:20:24.001$ and also exploring the idea

NOTE Confidence: 0.93299675

 $00:20:24.001 \longrightarrow 00:20:27.406$ that you could present these

NOTE Confidence: 0.93299675

 $00{:}20{:}27.410 \dashrightarrow 00{:}20{:}29.290$ signals to immune cells

NOTE Confidence: 0.93299675

 $00:20:29.290 \longrightarrow 00:20:31.590$ in a variety of different ways,

NOTE Confidence: 0.93299675

 $00{:}20{:}31.590 \dashrightarrow 00{:}20{:}33.490$ either by slowly releasing them,

NOTE Confidence: 0.93299675

 $00:20:33.490 \longrightarrow 00:20:35.836$ the concept we talked about before,

NOTE Confidence: 0.93299675

 $00:20:35.836 \longrightarrow 00:20:38.245$ or by presenting them in different

NOTE Confidence: 0.93299675

 $00:20:38.245 \longrightarrow 00:20:40.549$ fashions on the surface or the

NOTE Confidence: 0.93299675

00:20:40.549 --> 00:20:42.789 interior of the particle and looking

NOTE Confidence: 0.93299675

 $00:20:42.789 \longrightarrow 00:20:45.628$ to see if by changing the way that

 $00:20:45.628 \longrightarrow 00:20:47.842$ the particle is engineered with these

NOTE Confidence: 0.93299675

 $00{:}20{:}47.842 \to 00{:}20{:}50.587$ signals for the immune system,

NOTE Confidence: 0.93299675

 $00:20:50.590 \longrightarrow 00:20:51.682$ if that changes

NOTE Confidence: 0.93299675

00:20:51.682 --> 00:20:54.230 the speed or the aggressiveness

NOTE Confidence: 0.93299675

 $00:20:54.303 \longrightarrow 00:20:56.253$ that you can introduce into

NOTE Confidence: 0.93299675

 $00:20:56.253 \longrightarrow 00:20:57.423$ the immune response.

NOTE Confidence: 0.97866803

 $00:20:58.690 \longrightarrow 00:21:01.000$ So Mike, do you want to

NOTE Confidence: 0.97866803

 $00:21:01.000 \longrightarrow 00:21:03.430$ kind of pick up on that?

NOTE Confidence: 0.97866803

00:21:03.430 --> 00:21:05.692 I mean, oftentimes when we're thinking

NOTE Confidence: 0.97866803

 $00{:}21{:}05.692 \dashrightarrow 00{:}21{:}07.780$ about generating an immune response,

NOTE Confidence: 0.97866803

 $00:21:07.780 \longrightarrow 00:21:10.150$ we kind of talked about

NOTE Confidence: 0.97866803

 $00:21:10.150 \longrightarrow 00:21:11.730$ two kinds of systems.

 $00:21:13.206 \longrightarrow 00:21:16.070$ One that's a more generalized immune response,

NOTE Confidence: 0.97866803

 $00{:}21{:}16.070 \dashrightarrow 00{:}21{:}17.745$ and one that's more targeted.

NOTE Confidence: 0.97866803

00:21:17.745 --> 00:21:20.274 Talk a little bit about how you

NOTE Confidence: 0.97866803

00:21:20.274 --> 00:21:21.453 envision nanoparticles really

 $00:21:21.453 \longrightarrow 00:21:24.002$ working in terms of the immune

NOTE Confidence: 0.97866803

 $00{:}21{:}24.002 \dashrightarrow 00{:}21{:}25.550$ response against cancers.

NOTE Confidence: 0.98842096

00:21:26.510 --> 00:21:29.604 Yeah, I think it's a critical question.

NOTE Confidence: 0.98842096

 $00:21:29.610 \longrightarrow 00:21:32.592$ I think that cancer therapy today is

NOTE Confidence: 0.98842096

 $00:21:32.592 \longrightarrow 00:21:35.016$ about targeting the tumor and

NOTE Confidence: 0.98842096

 $00:21:35.016 \longrightarrow 00:21:37.287$ it's about manipulating the immune

NOTE Confidence: 0.98842096

 $00:21:37.287 \longrightarrow 00:21:39.969$ system to to maximize the effects

NOTE Confidence: 0.98842096

 $00{:}21{:}40.045 \dashrightarrow 00{:}21{:}42.460$ of the tumor targeting strategies.

NOTE Confidence: 0.98842096

00:21:42.460 --> 00:21:45.112 No cancer therapy can ignore today

NOTE Confidence: 0.98842096

 $00:21:45.112 \longrightarrow 00:21:48.048$ what's going on with the immune system.

NOTE Confidence: 0.98842096

 $00:21:48.048 \longrightarrow 00:21:50.364$ It's too powerful an ally in

NOTE Confidence: 0.98842096

 $00{:}21{:}50.364 \dashrightarrow 00{:}21{:}53.320$ the fight against the cancer and

NOTE Confidence: 0.98842096

 $00{:}21{:}53.320 \dashrightarrow 00{:}21{:}55.308$ there's obstacles to overcome,

NOTE Confidence: 0.98842096

00:21:55.310 --> 00:21:57.822 so let me explain.

NOTE Confidence: 0.98842096

 $00:21:57.822 \longrightarrow 00:22:01.590$ That first dichotomy is

 $00:22:01.590 \longrightarrow 00:22:04.602$ that we have evolved to recognize

NOTE Confidence: 0.98842096

 $00{:}22{:}04.602 --> 00{:}22{:}05.606 \ foreign \ substances,$

NOTE Confidence: 0.98842096

 $00:22:05.610 \longrightarrow 00:22:08.646$ including antigens on tumor cells

NOTE Confidence: 0.98842096

 $00:22:08.646 \longrightarrow 00:22:12.226$ and we can stimulate the heck out

NOTE Confidence: 0.98842096

00:22:12.226 --> 00:22:14.666 of that process through agents,

NOTE Confidence: 0.98842096

00:22:14.670 --> 00:22:17.730 as Mark has described, that might

NOTE Confidence: 0.98842096

00:22:17.730 --> 00:22:19.770 be considered dangerous signals,

NOTE Confidence: 0.98842096

00:22:19.851 --> 00:22:22.719 molecules that might be for example,

NOTE Confidence: 0.98842096

 $00{:}22{:}22.720 \dashrightarrow 00{:}22{:}25.230$ normally found on infectious agents,

NOTE Confidence: 0.98842096

 $00:22:25.230 \longrightarrow 00:22:28.236$ molecules that might be produced by

NOTE Confidence: 0.98842096

00:22:28.236 --> 00:22:31.918 our own cells when they have sensed

NOTE Confidence: 0.98842096

 $00:22:31.920 \longrightarrow 00:22:34.140$ that they are infected, for example.

NOTE Confidence: 0.98842096

 $00:22:34.140 \longrightarrow 00:22:36.868$ We can begin to try to trick

NOTE Confidence: 0.98842096

 $00:22:36.868 \longrightarrow 00:22:38.210$ the immune system

NOTE Confidence: 0.98842096

 $00:22:38.210 \longrightarrow 00:22:40.380$ in looking at the cancer cells in

NOTE Confidence: 0.98842096

 $00:22:40.380 \longrightarrow 00:22:43.491$ a way that makes them appear as if

 $00:22:43.491 \longrightarrow 00:22:45.601$ they're a foreign infection,

NOTE Confidence: 0.98842096

00:22:45.610 --> 00:22:47.460 whether that be viral resemblance

NOTE Confidence: 0.98842096

00:22:47.460 --> 00:22:49.310 or bacterial resemblance or others.

NOTE Confidence: 0.98842096

 $00:22:49.310 \longrightarrow 00:22:52.640$ And we can do that in a general way,

NOTE Confidence: 0.98842096

 $00:22:52.640 \longrightarrow 00:22:55.405$ and so those are common molecules that

NOTE Confidence: 0.98842096

00:22:55.405 --> 00:22:57.820 are found on a bunch of microorganisms,

NOTE Confidence: 0.98842096

 $00:22:57.820 \longrightarrow 00:23:00.450$ so we can just introduce those types

NOTE Confidence: 0.98842096

 $00:23:00.450 \longrightarrow 00:23:02.350$ of compounds into the nanoparticles.

NOTE Confidence: 0.98842096

 $00:23:02.350 \longrightarrow 00:23:04.690$ Then we can try to facilitate

NOTE Confidence: 0.98842096

 $00{:}23{:}04.690 \dashrightarrow 00{:}23{:}07.175$ how they're seen by the immune

NOTE Confidence: 0.98842096

 $00{:}23{:}07.175 \longrightarrow 00{:}23{:}09.683$ system in a more optimized way.

NOTE Confidence: 0.98842096

 $00:23:09.690 \longrightarrow 00:23:11.730$ In a more specific way,

NOTE Confidence: 0.98842096

00:23:11.730 --> 00:23:14.178 we might try to load what

NOTE Confidence: 0.98842096

 $00:23:14.178 \longrightarrow 00:23:15.810$ are called tumor antigens,

NOTE Confidence: 0.98842096

00:23:15.810 --> 00:23:18.228 so these might be real signatures

00:23:18.228 --> 00:23:20.709 on very specific types of cancers,

NOTE Confidence: 0.98842096

 $00:23:20.710 \longrightarrow 00:23:23.152$ and they may be even specific

NOTE Confidence: 0.98842096

 $00:23:23.152 \longrightarrow 00:23:24.373$ to each patient.

NOTE Confidence: 0.98842096

 $00:23:24.380 \longrightarrow 00:23:25.565$ In this way,

NOTE Confidence: 0.98842096

00:23:25.565 --> 00:23:27.935 we're trying to stimulate a very

NOTE Confidence: 0.98842096

 $00{:}23{:}27.935 \dashrightarrow 00{:}23{:}30.090$ directed killer T cell response.

NOTE Confidence: 0.98842096

 $00:23:30.090 \longrightarrow 00:23:33.036$ That's akin to a vaccine, for example.

NOTE Confidence: 0.98842096

00:23:33.036 --> 00:23:36.207 That you know is being discussed

NOTE Confidence: 0.98842096

 $00{:}23{:}36.207 \dashrightarrow 00{:}23{:}39.595$ these days for a bunch of other reasons,

NOTE Confidence: 0.98842096

 $00:23:39.600 \longrightarrow 00:23:42.680$ and so we can use nanoparticles to

NOTE Confidence: 0.98842096

 $00{:}23{:}42.680 \dashrightarrow 00{:}23{:}45.321$ develop anti tumor vaccines that

NOTE Confidence: 0.98842096

 $00:23:45.321 \longrightarrow 00:23:47.793$ could more specifically stimulate

NOTE Confidence: 0.98842096

 $00:23:47.793 \longrightarrow 00:23:49.647$ the immune system

 $00:23:53.000 \longrightarrow 00:23:54.908$ to attack the cancer.

NOTE Confidence: 0.98772454

00:23:57.240 --> 00:23:59.210 And on another consideration though,

NOTE Confidence: 0.98772454

 $00:23:59.210 \longrightarrow 00:24:02.138$ we have to realize that tumors evolve and

 $00:24:02.138 \longrightarrow 00:24:05.486$ grow to try to suppress the immune system.

NOTE Confidence: 0.98772454

 $00:24:05.490 \longrightarrow 00:24:07.848$ And this is a major major

NOTE Confidence: 0.98772454

 $00:24:07.848 \longrightarrow 00:24:09.420$ consideration in treating cancer,

NOTE Confidence: 0.98772454

00:24:09.420 --> 00:24:11.390 immune checkpoint inhibitors or something,

NOTE Confidence: 0.98772454

 $00:24:11.390 \longrightarrow 00:24:13.435$ for example, that are delivered

NOTE Confidence: 0.98772454

 $00{:}24{:}13.435 \dashrightarrow 00{:}24{:}16.320$ throughout the body to try to alleviate

NOTE Confidence: 0.98772454

 $00:24:16.320 \longrightarrow 00:24:18.606$ some of these controls that the

NOTE Confidence: 0.98772454

00:24:18.606 --> 00:24:21.209 tumor has put on the immune system.

NOTE Confidence: 0.98772454

 $00:24:21.210 \longrightarrow 00:24:24.052$ But we can also try to target

NOTE Confidence: 0.98772454

 $00:24:24.052 \longrightarrow 00:24:25.970$ that with nanoparticles locally.

NOTE Confidence: 0.98772454

 $00:24:25.970 \longrightarrow 00:24:28.802$ So for example, there are immune cells that

NOTE Confidence: 0.98772454

00:24:28.802 --> 00:24:31.790 try to suppress the antitumor effects,

NOTE Confidence: 0.98772454

 $00:24:31.790 \longrightarrow 00:24:35.820$ and these need to be

NOTE Confidence: 0.98772454

 $00:24:35.820 \longrightarrow 00:24:37.850$ dealt with in a way,

NOTE Confidence: 0.98772454

 $00:24:37.850 \longrightarrow 00:24:39.880$ especially at the tumor site,

NOTE Confidence: 0.98772454

 $00:24:39.880 \longrightarrow 00:24:42.292$ so that the tumor can become

 $00:24:42.292 \longrightarrow 00:24:45.158$ what we call hot and not cold.

NOTE Confidence: 0.98772454

 $00{:}24{:}45.160 \dashrightarrow 00{:}24{:}48.240$ Hot, meaning it can be recognized by the

NOTE Confidence: 0.98772454

 $00:24:48.240 \longrightarrow 00:24:50.439$ antitumor immune system more readily.

NOTE Confidence: 0.9774533

 $00:24:51.830 \longrightarrow 00:24:54.398$ And it sounds like

NOTE Confidence: 0.9774533

00:24:54.398 --> 00:24:56.307 you have so many possibilities

NOTE Confidence: 0.9774533

00:24:56.307 --> 00:24:59.079 in terms of how you can fashion

NOTE Confidence: 0.9774533

 $00:24:59.155 \longrightarrow 00:25:01.637$ these nanoparticles, so you can

NOTE Confidence: 0.9774533

 $00:25:01.637 \longrightarrow 00:25:03.940$ target the tumor on one

NOTE Confidence: 0.9774533

00:25:04.021 --> 00:25:06.281 side and potentially attract the

NOTE Confidence: 0.9774533

 $00{:}25{:}06.281 \dashrightarrow 00{:}25{:}09.025$ immune system on the other side

NOTE Confidence: 0.9774533

 $00:25:09.025 \longrightarrow 00:25:11.867$ and get these two systems in

NOTE Confidence: 0.9774533

 $00{:}25{:}11.867 \dashrightarrow 00{:}25{:}14.284$ close proximity to each other in

NOTE Confidence: 0.9774533

 $00{:}25{:}14.284 \dashrightarrow 00{:}25{:}16.289$ addition to delivering drugs.

NOTE Confidence: 0.9774533

00:25:16.290 --> 00:25:19.013 Now the other thing that you mentioned

NOTE Confidence: 0.9774533

 $00:25:19.013 \longrightarrow 00:25:21.950$ before the break was using nanoparticles

 $00:25:21.950 \longrightarrow 00:25:24.908$ relating to skin cancers,

NOTE Confidence: 0.9774533

 $00:25:24.910 \longrightarrow 00:25:27.868$ but more on the prevention side.

NOTE Confidence: 0.9774533

00:25:27.870 --> 00:25:30.936 So Mark talk a little bit about

NOTE Confidence: 0.9774533

 $00:25:30.936 \longrightarrow 00:25:32.920$ using nanoparticles to make

NOTE Confidence: 0.9774533

 $00:25:32.920 \longrightarrow 00:25:35.256$ sunscreens more effective.

NOTE Confidence: 0.9900481

 $00:25:36.340 \longrightarrow 00:25:39.080$ Yeah, I'd be happy to do that and that was one

of

NOTE Confidence: 0.9900481

 $00:25:39.150 \longrightarrow 00:25:42.110$ the first big projects that Mike and I

NOTE Confidence: 0.9900481

 $00{:}25{:}42.110 \dashrightarrow 00{:}25{:}44.836$ worked together on and it was quite successful.

NOTE Confidence: 0.9900481

 $00:25:44.840 \longrightarrow 00:25:48.240$ So the idea was that we NOTE Confidence:

0.9900481

 $00:25:48.240 \longrightarrow 00:25:50.739$ knew that we could make these

NOTE Confidence: 0.9900481

 $00:25:50.739 \longrightarrow 00:25:52.737$ nanoparticles that would adhere to tissues

NOTE Confidence: 0.9900481

00:25:52.737 --> 00:25:55.552 and we tested them to see if you just

NOTE Confidence: 0.9900481

 $00:25:55.552 \longrightarrow 00:25:57.760$ suspended these particles,

NOTE Confidence: 0.9900481

00:25:57.760 --> 00:26:00.273 these sticky particles and NOTE Confidence:

0.9900481

00:26:00.273 --> 00:26:03.581 you put that water on the skin would

NOTE Confidence: 0.9900481

 $00:26:03.581 \longrightarrow 00:26:06.270$ the particles adhere and in fact they did.

00:26:06.270 --> 00:26:08.998 And they adhered very strongly to the skin.

 $00:26:09.909 \longrightarrow 00:26:12.030$ You could put some particles on the

NOTE Confidence: 0.9900481

00:26:12.100 --> 00:26:14.396 skin and then you could wash the

NOTE Confidence: 0.9900481

 $00:26:14.396 \longrightarrow 00:26:16.204$ skin extensively and the particles

NOTE Confidence: 0.9900481

 $00:26:16.204 \longrightarrow 00:26:18.472$ would just stay there and resist

NOTE Confidence: 0.9900481

 $00:26:18.472 \longrightarrow 00:26:19.910$ removal with washing.

NOTE Confidence: 0.9900481

 $00:26:19.910 \longrightarrow 00:26:22.635$ And so we knew that there was something

NOTE Confidence: 0.9900481

 $00:26:22.635 \longrightarrow 00:26:23.999$ special about that technology,

NOTE Confidence: 0.9900481

 $00{:}26{:}24.000 \dashrightarrow 00{:}26{:}26{:}238$ because if you can apply something

NOTE Confidence: 0.9900481

 $00:26:26.238 \longrightarrow 00:26:28.388$ topically to the skin and it

NOTE Confidence: 0.9900481

 $00{:}26{:}28.388 \dashrightarrow 00{:}26{:}30.140$ stays there for a long time,

NOTE Confidence: 0.9900481

 $00:26:30.140 \longrightarrow 00:26:31.850$ that might have some value.

NOTE Confidence: 0.9900481

 $00:26:31.850 \longrightarrow 00:26:34.730$ And so in the second phase we learned that

NOTE Confidence: 0.9900481

 $00:26:34.799 \longrightarrow 00:26:37.619$ one could take common sunscreen ingredients

NOTE Confidence: 0.9900481

 $00:26:37.620 \longrightarrow 00:26:40.357$ and load them at very high levels

NOTE Confidence: 0.9900481

 $00:26:40.357 \longrightarrow 00:26:41.530$ inside these nanoparticles,

 $00:26:41.530 \longrightarrow 00:26:43.485$ so that the nanoparticle itself

NOTE Confidence: 0.9900481

 $00:26:43.485 \longrightarrow 00:26:45.050$ was 50 percent, 60%,

NOTE Confidence: 0.9900481

00:26:45.050 --> 00:26:47.000 sometimes even 70% sunscreen agent.

NOTE Confidence: 0.9900481

 $00:26:47.000 \longrightarrow 00:26:50.072$ And then if you apply those to the

NOTE Confidence: 0.9900481

00:26:50.072 --> 00:26:52.480 surface of the skin, they stuck.

NOTE Confidence: 0.9900481

00:26:52.480 --> 00:26:54.820 They don't penetrate into the skin.

NOTE Confidence: 0.9900481

 $00:26:54.820 \longrightarrow 00:26:57.170$ They don't wash off very easily,

NOTE Confidence: 0.9900481

 $00:26:57.170 \longrightarrow 00:27:00.296$ but they're sitting on the skin now in

NOTE Confidence: 0.9900481

 $00{:}27{:}00.296 \dashrightarrow 00{:}27{:}03.422$ a position to be between the skin and

NOTE Confidence: 0.9900481

 $00:27:03.422 \longrightarrow 00:27:06.550$ any ultraviolet light that falls on the skin,

NOTE Confidence: 0.9900481

 $00:27:06.550 \longrightarrow 00:27:08.580$ and so they could be

NOTE Confidence: 0.9900481

 $00:27:08.580 \longrightarrow 00:27:11.165$ very effective at screening that

NOTE Confidence: 0.9900481

 $00{:}27{:}11.165 \dashrightarrow 00{:}27{:}13.750$ ultraviolet light and absorbing

NOTE Confidence: 0.9900481

 $00:27:13.833 \longrightarrow 00:27:16.527$ it and blocking it without anything

NOTE Confidence: 0.9900481

00:27:16.527 --> 00:27:19.059 ever entering your body and they

 $00:27:19.059 \longrightarrow 00:27:21.362$ stay on there for a long time.

NOTE Confidence: 0.9900481

 $00{:}27{:}21.370 \longrightarrow 00{:}27{:}24.628$ And so we did a number of studies

NOTE Confidence: 0.9900481

 $00:27:24.628 \longrightarrow 00:27:27.754$ trying to understand how this works and

NOTE Confidence: 0.9900481

 $00:27:27.754 \longrightarrow 00:27:30.622$ trying to perfect it using combinations

NOTE Confidence: 0.9900481

 $00:27:30.622 \longrightarrow 00:27:34.101$ of sunscreens so that we could block

NOTE Confidence: 0.9900481

 $00:27:34.101 \longrightarrow 00:27:35.923$ all wavelengths of ultraviolet

NOTE Confidence: 0.9900481

00:27:35.923 --> 00:27:38.826 light and ultimately did a

NOTE Confidence: 0.9900481

 $00:27:38.826 \longrightarrow 00:27:41.098$ small pilot clinical trial

NOTE Confidence: 0.9900481

00:27:41.100 --> 00:27:43.767 here at Yale showing that

NOTE Confidence: 0.9900481

 $00:27:43.767 \longrightarrow 00:27:46.453$ indeed you could put these on the

NOTE Confidence: 0.9900481

 $00{:}27{:}46.453 \dashrightarrow 00{:}27{:}48.649$ surface of the skin of volunteers

NOTE Confidence: 0.9900481

 $00:27:48.731 \longrightarrow 00:27:51.447$ that they were completely safe and

NOTE Confidence: 0.9900481

 $00{:}27{:}51.447 \dashrightarrow 00{:}27{:}54.208$ Mike can talk about the details of

NOTE Confidence: 0.9900481

 $00{:}27{:}54.208 \dashrightarrow 00{:}27{:}57.030$ that and that they would perform just

NOTE Confidence: 0.9900481

 $00:27:57.030 \longrightarrow 00:27:59.550$ as well as the kinds of sunscreens

NOTE Confidence: 0.9900481

 $00:27:59.550 \longrightarrow 00:28:02.220$ that you can buy at the drugstore.

 $00:28:02.220 \longrightarrow 00:28:04.518$ So we're very excited about that

NOTE Confidence: 0.9900481

 $00:28:05.670 \longrightarrow 00:28:08.575$ and new ways

NOTE Confidence: 0.9900481

 $00:28:08.575 \longrightarrow 00:28:09.820$ to use technology

NOTE Confidence: 0.9900481

 $00:28:09.820 \longrightarrow 00:28:11.308$ to prevent skin cancer.

00:28:16.992 --> 00:28:19.375 And my grandparents all worked on

NOTE Confidence: 0.9900481

 $00{:}28{:}19.375 \dashrightarrow 00{:}28{:}21.748$ farms and so are very familiar with the

NOTE Confidence: 0.9900481

00:28:21.748 --> 00:28:24.000 devastating effects

NOTE Confidence: 0.9574797

 $00:28:24.000 \longrightarrow 00:28:26.370$ of skin cancer.

NOTE Confidence: 0.9574797

 $00{:}28{:}26.370 \dashrightarrow 00{:}28{:}28.335$ Doctor W. Mark Saltzman is a professor

NOTE Confidence: 0.9574797

 $00:28:28.335 \longrightarrow 00:28:29.514$ of biomedical engineering,

NOTE Confidence: 0.9574797

00:28:29.520 --> 00:28:31.256 cellular and molecular Physiology

NOTE Confidence: 0.9574797

 $00:28:31.256 \longrightarrow 00:28:32.992$ and of chemical engineering

NOTE Confidence: 0.9574797

 $00{:}28{:}32.992 \dashrightarrow 00{:}28{:}34.961$ and Doctor Michael Girardi is

NOTE Confidence: 0.9574797

00:28:34.961 --> 00:28:36.681 a professor of dermatology at

NOTE Confidence: 0.9574797

00:28:36.681 --> 00:28:38.578 the Yale School of Medicine.

NOTE Confidence: 0.9574797

 $00:28:38.580 \longrightarrow 00:28:41.130$ If you have questions the address

00:28:41.130 --> 00:28:41.980 is canceranswers@yale.edu.

NOTE Confidence: 0.9574797

 $00:28:41.980 \longrightarrow 00:28:43.750$ And past editions of the program

NOTE Confidence: 0.9574797

 $00{:}28{:}43.750 \dashrightarrow 00{:}28{:}45.868$ are available in audio and written

NOTE Confidence: 0.9574797

 $00:28:45.868 \longrightarrow 00:28:47.188$ form at yalecancercenter.org.

NOTE Confidence: 0.9574797

00:28:47.190 --> 00:28:49.430 We hope you'll join us next week to

NOTE Confidence: 0.9574797

 $00:28:49.430 \longrightarrow 00:28:51.583$ learn more about the fight against

NOTE Confidence: 0.9574797

 $00:28:51.583 \longrightarrow 00:28:53.498$ cancer here on Connecticut Public

NOTE Confidence: 0.9574797

 $00{:}28{:}53.498 \dashrightarrow 00{:}28{:}55.407$ radio funding for Yale Cancer

NOTE Confidence: 0.9574797

00:28:55.407 --> 00:28:57.232 Answers is provided by Smilow

NOTE Confidence: 0.9574797

 $00{:}28{:}57.232 \dashrightarrow 00{:}29{:}00.072$ Cancer Hospital and Astra Zeneca.