WEBVTT

NOTE duration:"00:56:38"

NOTE recognizability:0.834

NOTE language:en-us

NOTE Confidence: 0.735234785833333

00:00:00.000 --> 00:00:01.503 Actually, we're Ratna.

NOTE Confidence: 0.735234785833333

00:00:01.503 --> 00:00:04.008 Who is an outstanding scientist

NOTE Confidence: 0.735234785833333

00:00:04.008 --> 00:00:08.215 and a dear friend, and I'll give

NOTE Confidence: 0.735234785833333

00:00:08.215 --> 00:00:11.740 a little background about ashis.

NOTE Confidence: 0.735234785833333

00:00:11.740 --> 00:00:15.023 Current many titles and are where where

NOTE Confidence: 0.735234785833333

00:00:15.023 --> 00:00:17.728 she developed from as a scientist.

NOTE Confidence: 0.735234785833333

00:00:17.730 --> 00:00:20.314 So Ashley is the EV McCollum chair of

NOTE Confidence: 0.735234785833333

00:00:20.314 --> 00:00:22.175 Biochemistry and molecular biology at

NOTE Confidence: 0.735234785833333

00:00:22.175 --> 00:00:24.485 John Hopkins School of Public Health.

NOTE Confidence: 0.735234785833333

00:00:24.490 --> 00:00:26.218 She's also a Bloomberg

NOTE Confidence: 0.735234785833333

00:00:26.218 --> 00:00:27.514 Distinguished Professor Co,

NOTE Confidence: 0.735234785833333

00:00:27.520 --> 00:00:30.256 leader of the program and cancer

NOTE Confidence: 0.735234785833333

00:00:30.256 --> 00:00:32.658 invasion and metastasis at the

NOTE Confidence: 0.735234785833333

00:00:32.658 --> 00:00:34.638 Sidney Kimmel Cancer Center.

NOTE Confidence: 0.735234785833333

00:00:34.640 --> 00:00:36.901 And I had interacted also a lot

NOTE Confidence: 0.735234785833333

00:00:36.901 --> 00:00:38.980 with Ashley before joining Hopkins,

NOTE Confidence: 0.735234785833333

00:00:38.980 --> 00:00:41.020 where she was a named professor

NOTE Confidence: 0.735234785833333

00:00:41.020 --> 00:00:42.040 and a program.

NOTE Confidence: 0.735234785833333

00:00:42.040 --> 00:00:43.844 Leader at the Wistar

NOTE Confidence: 0.735234785833333

00:00:43.844 --> 00:00:45.625 Institute in Philadelphia, AH.

NOTE Confidence: 0.735234785833333

00:00:45.625 --> 00:00:48.175 She has a very international background,

NOTE Confidence: 0.735234785833333

00:00:48.180 --> 00:00:49.662 having been born in Sri Lanka

NOTE Confidence: 0.735234785833333

00:00:49.662 --> 00:00:51.420 and grown up in South Africa.

NOTE Confidence: 0.735234785833333

00:00:51.420 --> 00:00:53.100 I think a brother who lives in Scotland.

NOTE Confidence: 0.735234785833333

00:00:53.100 --> 00:00:55.032 Now she's just a very cool person

NOTE Confidence: 0.735234785833333

00:00:55.032 --> 00:00:56.874 with a great great background on

NOTE Confidence: 0.735234785833333

00:00:56.874 --> 00:00:59.496 great science and you know one of the

NOTE Confidence: 0.735234785833333

00:00:59.496 --> 00:01:01.512 things that I would really emphasize

NOTE Confidence: 0.735234785833333

00:01:01.512 --> 00:01:04.179 about Ashley is that there's been

NOTE Confidence: 0.735234785833333

00:01:04.179 --> 00:01:06.944 a real emphasis and appropriate

NOTE Confidence: 0.735234785833333

00:01:06.944 --> 00:01:10.752 emphasis on supporting junior faculty.

NOTE Confidence: 0.735234785833333

00:01:10.752 --> 00:01:17.386 A female faculty and fat and and scientists

NOTE Confidence: 0.735234785833333

00:01:17.386 --> 00:01:20.650 of color over the last few years.

NOTE Confidence: 0.735234785833333

00:01:20.650 --> 00:01:22.819 But I can say that I can think of

NOTE Confidence: 0.735234785833333

00:01:22.819 --> 00:01:25.153 pretty much no one who is more of an

NOTE Confidence: 0.735234785833333

00:01:25.153 --> 00:01:27.178 advocate for all of those areas over

NOTE Confidence: 0.735234785833333

00:01:27.178 --> 00:01:29.352 a decade ago already and has been

NOTE Confidence: 0.735234785833333

00:01:29.352 --> 00:01:31.879 tireless in her efforts and promoting that.

NOTE Confidence: 0.735234785833333

00:01:31.880 --> 00:01:33.658 And it's really great to see the

NOTE Confidence: 0.735234785833333

00:01:33.658 --> 00:01:35.485 rest of the world that slowly

NOTE Confidence: 0.735234785833333

00:01:35.485 --> 00:01:37.150 catching up on those fronts.

NOTE Confidence: 0.735234785833333

00:01:37.150 --> 00:01:38.596 And you know,

NOTE Confidence: 0.735234785833333

00:01:38.596 --> 00:01:40.970 it's a real great pleasure to hear.

NOTE Confidence: 0.735234785833333

00:01:40.970 --> 00:01:43.250 And I I know a fair amount about the science.

NOTE Confidence: 0.735234785833333

00:01:43.250 --> 00:01:44.060 She's going to talk about,

NOTE Confidence: 0.735234785833333

00:01:44.060 --> 00:01:46.310 but it's a really appropriate area,

NOTE Confidence: 0.735234785833333

00:01:46.310 --> 00:01:47.441 especially at Yale,

NOTE Confidence: 0.735234785833333

00:01:47.441 --> 00:01:49.326 where we're thinking about having

NOTE Confidence: 0.735234785833333

00:01:49.326 --> 00:01:51.862 a new aging center based in

NOTE Confidence: 0.735234785833333

00:01:51.862 --> 00:01:53.149 the pathology department,

NOTE Confidence: 0.735234785833333

00:01:53.150 --> 00:01:55.694 and I think she's going to be talking

NOTE Confidence: 0.735234785833333

00:01:55.694 --> 00:01:57.760 about age against the machine,

NOTE Confidence: 0.735234785833333

00:01:57.760 --> 00:01:59.860 how the aging microenvironment covers

NOTE Confidence: 0.735234785833333

00:01:59.860 --> 00:02:02.500 tumor progression and response to therapy.

NOTE Confidence: 0.735234785833333

00:02:02.500 --> 00:02:04.198 I was thinking of playing some

NOTE Confidence: 0.735234785833333

00:02:04.198 --> 00:02:06.106 Rage Against the machine in the

NOTE Confidence: 0.735234785833333

00:02:06.106 --> 00:02:07.546 background during the introduction,

NOTE Confidence: 0.735234785833333

00:02:07.550 --> 00:02:09.060 but I thought that's probably

NOTE Confidence: 0.735234785833333

00:02:09.060 --> 00:02:09.966 go horribly wrong,

NOTE Confidence: 0.735234785833333

00:02:09.970 --> 00:02:13.674 so you'll just have to imagine that and.

NOTE Confidence: 0.735234785833333

00:02:13.680 --> 00:02:13.992 Actually,

NOTE Confidence: 0.735234785833333

00:02:13.992 --> 00:02:15.864 it's a real pleasure having you

NOTE Confidence: 0.735234785833333

00:02:15.864 --> 00:02:18.159 be a yellow sport and skin cancer,

NOTE Confidence: 0.735234785833333

00:02:18.160 --> 00:02:20.000 Cancer Center ground round speaker.

NOTE Confidence: 0.735234785833333

00:02:20.000 --> 00:02:20.570 Thank

NOTE Confidence: 0.871201915

00:02:20.580 --> 00:02:22.764 you so much Marcus for that

NOTE Confidence: 0.871201915

00:02:22.764 --> 00:02:24.220 lovely and warm introduction.

NOTE Confidence: 0.871201915

00:02:24.220 --> 00:02:27.964 And yeah, the title appeals to a very

NOTE Confidence: 0.871201915

00:02:27.964 --> 00:02:30.460 specific demographic of people think so.

NOTE Confidence: 0.871201915

00:02:30.460 --> 00:02:31.916 Thank you so much.

NOTE Confidence: 0.871201915

00:02:31.916 --> 00:02:34.540 I'm delighted to be giving this talk,

NOTE Confidence: 0.871201915

00:02:34.540 --> 00:02:37.044 although I really do wish it was in

NOTE Confidence: 0.871201915

00:02:37.044 --> 00:02:39.680 person and I will be talking to you all.

NOTE Confidence: 0.871201915

00:02:39.680 --> 00:02:42.380 As Marcus said about our work in the aging

NOTE Confidence: 0.871201915

00:02:42.380 --> 00:02:43.807 microenvironment and how that governs.

NOTE Confidence: 0.871201915

00:02:43.810 --> 00:02:44.950 Response to therapy.

NOTE Confidence: 0.871201915

00:02:44.950 --> 00:02:47.610 So we've been so interested in aging

NOTE Confidence: 0.871201915

00:02:47.677 --> 00:02:49.795 as a driver of tumor progression

NOTE Confidence: 0.871201915

00:02:49.795 --> 00:02:52.849 because we know that it's one of the

NOTE Confidence: 0.871201915

00:02:52.849 --> 00:02:54.421 most significant prognostic factors

NOTE Confidence: 0.871201915

00:02:54.421 --> 00:02:56.629 for the development of cancers.

NOTE Confidence: 0.871201915

00:02:56.629 --> 00:02:59.940 So of all hundred people diagnosed with

NOTE Confidence: 0.871201915

00:03:00.024 --> 00:03:02.809 cancer, 89 of them will be age 50 or over.

NOTE Confidence: 0.871201915

00:03:02.810 --> 00:03:04.938 And of those that are diagnosed with

NOTE Confidence: 0.871201915

00:03:04.938 --> 00:03:07.337 cancer and die from this disease again,

NOTE Confidence: 0.871201915

00:03:07.340 --> 00:03:09.040 the largest percentage of them

NOTE Confidence: 0.871201915

00:03:09.040 --> 00:03:11.020 is over the age of 50,

NOTE Confidence: 0.871201915

00:03:11.020 --> 00:03:12.485 and so we've been trying

NOTE Confidence: 0.871201915

00:03:12.485 --> 00:03:13.950 to understand why that is.

NOTE Confidence: 0.871201915

00:03:13.950 --> 00:03:15.302 And why that happens?

NOTE Confidence: 0.871201915

00:03:15.302 --> 00:03:17.330 Obviously there are a lot of

NOTE Confidence: 0.871201915

00:03:17.406 --> 00:03:19.098 systemic factors that Dr.

NOTE Confidence: 0.871201915

00:03:19.100 --> 00:03:19.800 Tumor progression,

NOTE Confidence: 0.871201915

00:03:19.800 --> 00:03:21.550 but we've been super interested

NOTE Confidence: 0.871201915

00:03:21.550 --> 00:03:24.523 in what is happening in the local

NOTE Confidence: 0.871201915

00:03:24.523 --> 00:03:26.387 microenvironment specifically of Melanoma.

NOTE Confidence: 0.871201915

00:03:26.390 --> 00:03:28.136 But as I'll tell you later,

NOTE Confidence: 0.871201915

00:03:28.140 --> 00:03:31.158 we are expanding into other cancers,

NOTE Confidence: 0.871201915

00:03:31.160 --> 00:03:33.416 such as pancreatic cancer as well.

NOTE Confidence: 0.871201915

00:03:33.420 --> 00:03:35.716 So what we have seen in our studies

NOTE Confidence: 0.871201915

00:03:35.716 --> 00:03:38.179 is that there are significant changes

NOTE Confidence: 0.871201915

00:03:38.179 --> 00:03:40.903 that occur largely due to fibroblasts,

NOTE Confidence: 0.871201915

00:03:40.910 --> 00:03:42.558 and I'll tell you a bit more about

NOTE Confidence: 0.871201915

00:03:42.558 --> 00:03:44.348 that in a second and these changes.

NOTE Confidence: 0.871201915

00:03:44.350 --> 00:03:47.743 Can affect not only the way tumor cells grow,

NOTE Confidence: 0.871201915

00:03:47.750 --> 00:03:49.634 but the way endothelial cells grow

NOTE Confidence: 0.871201915

00:03:49.634 --> 00:03:52.495 into the tumor as well as a biophysical

NOTE Confidence: 0.871201915

00:03:52.495 --> 00:03:54.035 matrices around these tumors,

NOTE Confidence: 0.871201915

00:03:54.040 --> 00:03:56.835 allowing them to metastasize and

NOTE Confidence: 0.871201915

00:03:56.835 --> 00:03:59.630 invade more effectively with age.

NOTE Confidence: 0.871201915

00:03:59.630 --> 00:04:02.286 So a few years ago what we did,

NOTE Confidence: 0.871201915

00:04:02.290 --> 00:04:04.770 and this was a lot,

NOTE Confidence: 0.871201915

00:04:04.770 --> 00:04:07.538 this was a very collaborative piece of work,

NOTE Confidence: 0.871201915

00:04:07.540 --> 00:04:10.964 and Marcus was on this paper as well.

NOTE Confidence: 0.871201915

00:04:10.970 --> 00:04:12.895 The cell lines and resources that he's

NOTE Confidence: 0.871201915

00:04:12.895 --> 00:04:14.779 developed up and absolutely critical.

NOTE Confidence: 0.871201915

00:04:14.780 --> 00:04:17.348 Press and continue to be to this day,

NOTE Confidence: 0.871201915

00:04:17.350 --> 00:04:19.513 so we're very grateful for those and

NOTE Confidence: 0.871201915

00:04:19.513 --> 00:04:21.519 the reason that we looked at the

NOTE Confidence: 0.871201915

00:04:21.519 --> 00:04:23.588 skin was that we were very interested

NOTE Confidence: 0.871201915

00:04:23.588 --> 00:04:25.488 in the fibroblast themselves.

NOTE Confidence: 0.871201915

00:04:25.490 --> 00:04:28.066 Because fiberglass in the skin also in

NOTE Confidence: 0.871201915

00:04:28.066 --> 00:04:30.755 work out of Yale from Valentina Greco

NOTE Confidence: 0.871201915

00:04:30.755 --> 00:04:33.537 slab tend to age with the individual

NOTE Confidence: 0.871201915

00:04:33.537 --> 00:04:36.694 rather than undergo a lot of turnover,

NOTE Confidence: 0.871201915

00:04:36.700 --> 00:04:38.668 and we were very curious to know as

NOTE Confidence: 0.871201915

00:04:38.668 --> 00:04:40.819 the age what were the differences they

NOTE Confidence: 0.871201915

00:04:40.819 --> 00:04:43.266 were sick reading and how would they

NOTE Confidence: 0.871201915

00:04:43.266 --> 00:04:45.226 change in their physical environment.

NOTE Confidence: 0.871201915

00:04:45.230 --> 00:04:46.590 Because the Melanoma cell spends

NOTE Confidence: 0.871201915

00:04:46.590 --> 00:04:48.877 much of his life right here at the

NOTE Confidence: 0.871201915

00:04:48.877 --> 00:04:50.623 intersection of the epidermis and dermis,

NOTE Confidence: 0.871201915

00:04:50.630 --> 00:04:51.624 becoming invasive.

NOTE Confidence: 0.871201915

00:04:51.624 --> 00:04:55.103 So in order to recapitulate that work,

NOTE Confidence: 0.871201915

00:04:55.110 --> 00:04:57.245 what we did was to take skin

NOTE Confidence: 0.871201915

00:04:57.245 --> 00:04:59.220 fibroblasts from the upper inner arm.

NOTE Confidence: 0.871201915

00:04:59.220 --> 00:05:03.396 So intermittent sun exposure of individuals,

NOTE Confidence: 0.871201915

00:05:03.396 --> 00:05:05.848 healthy non Melanoma bearing

NOTE Confidence: 0.871201915

00:05:05.848 --> 00:05:09.460 individuals in their mid 20s to mid

NOTE Confidence: 0.871201915

00:05:09.460 --> 00:05:12.612 30s and then in there in the in the

NOTE Confidence: 0.871201915

00:05:12.612 --> 00:05:14.670 age where sort of Melanoma starts

NOTE Confidence: 0.871201915

00:05:14.750 --> 00:05:16.830 the incidence of Melanoma starts

NOTE Confidence: 0.871201915

00:05:16.830 --> 00:05:19.429 to skyrocket which is 55 to 65.

NOTE Confidence: 0.871201915

00:05:19.430 --> 00:05:21.202 We use those fibroblasts

NOTE Confidence: 0.871201915

00:05:21.202 --> 00:05:22.974 to create artificial skin.

NOTE Confidence: 0.871201915

00:05:22.980 --> 00:05:24.792 Which is a technique taught to

NOTE Confidence: 0.871201915

00:05:24.792 --> 00:05:26.000 us by our friend

NOTE Confidence: 0.8636394325

00:05:26.070 --> 00:05:29.638 Meinhardt Harlan and in doing that we were

NOTE Confidence: 0.8636394325

00:05:29.638 --> 00:05:33.855 able to see that when we mate reconstructs

NOTE Confidence: 0.8636394325

00:05:33.855 --> 00:05:36.352 with fibroblasts from young individuals

NOTE Confidence: 0.8636394325

00:05:36.352 --> 00:05:38.717 versus fiberglass from aged individuals,

NOTE Confidence: 0.8636394325

00:05:38.720 --> 00:05:40.385 those Melanoma cells would invade

NOTE Confidence: 0.8636394325

00:05:40.385 --> 00:05:42.507 far more rapidly in the fibroblasts

NOTE Confidence: 0.8636394325

00:05:42.507 --> 00:05:44.859 in the skin reconstructs made with

NOTE Confidence: 0.8636394325

00:05:44.859 --> 00:05:48.680 fiberglass from aged individuals now.

NOTE Confidence: 0.8636394325

00:05:48.680 --> 00:05:50.684 You know the only difference between

NOTE Confidence: 0.8636394325

00:05:50.684 --> 00:05:52.800 these these sets of skin reconstructs

NOTE Confidence: 0.8636394325

00:05:52.800 --> 00:05:54.948 is the age of the fibroblasts.

NOTE Confidence: 0.8636394325

00:05:54.950 --> 00:05:57.160 Everything else is the same,

NOTE Confidence: 0.8636394325

00:05:57.160 --> 00:05:59.295 so we wanted to know if we

NOTE Confidence: 0.8636394325

00:05:59.295 --> 00:06:00.760 could recapitulate that in vivo.

NOTE Confidence: 0.8636394325

00:06:00.760 --> 00:06:02.512 And as I mentioned,

NOTE Confidence: 0.8636394325

00:06:02.512 --> 00:06:05.568 Marcus along with Martin McMahon has made

NOTE Confidence: 0.8636394325

00:06:05.568 --> 00:06:09.000 the beer FP10 mouse model of Melanoma Marcus,

NOTE Confidence: 0.8636394325

00:06:09.000 --> 00:06:11.100 then backcrossed ease to see 57 black,

NOTE Confidence: 0.8636394325

00:06:11.100 --> 00:06:11.610 six mice,

NOTE Confidence: 0.8636394325

00:06:11.610 --> 00:06:13.395 and as I'm sure you all know,

NOTE Confidence: 0.8636394325

00:06:13.400 --> 00:06:16.118 created a series of cell lines.

NOTE Confidence: 0.8636394325

00:06:16.120 --> 00:06:17.434 The most of the experiments I'm

NOTE Confidence: 0.8636394325

00:06:17.434 --> 00:06:19.207 going to show you are from the young.

NOTE Confidence: 0.8636394325

00:06:19.210 --> 00:06:21.744 1.7 so line which we have taken

NOTE Confidence: 0.8636394325

00:06:21.744 --> 00:06:23.810 and then injected into either young

NOTE Confidence: 0.8636394325

00:06:23.810 --> 00:06:26.820 mice of 6 to 8 weeks of age or age.

NOTE Confidence: 0.8636394325

00:06:26.820 --> 00:06:29.140 Mice of 12 to 18 months of age,

NOTE Confidence: 0.8636394325

00:06:29.140 --> 00:06:31.828 depending on the experiments we're doing.

NOTE Confidence: 0.8636394325

00:06:31.830 --> 00:06:33.552 And what we saw was that actually

NOTE Confidence: 0.8636394325

00:06:33.552 --> 00:06:35.412 in the young mice to tumors grow

NOTE Confidence: 0.8636394325

00:06:35.412 --> 00:06:37.014 much faster and they grow much

NOTE Confidence: 0.8636394325

00:06:37.072 --> 00:06:38.566 more slowly in the age mice.

NOTE Confidence: 0.8636394325

00:06:38.570 --> 00:06:39.027 However,

NOTE Confidence: 0.8636394325

00:06:39.027 --> 00:06:41.769 they metastasized to the lung far

NOTE Confidence: 0.8636394325

00:06:41.769 --> 00:06:44.188 more effectively in the age mice

NOTE Confidence: 0.8636394325

00:06:44.188 --> 00:06:46.456 than they do in the young mice,

NOTE Confidence: 0.8636394325

00:06:46.460 --> 00:06:48.844 and so we wanted to better understand that,

NOTE Confidence: 0.8636394325

00:06:48.850 --> 00:06:49.813 and Mitchell Fain,

NOTE Confidence: 0.8636394325

00:06:49.813 --> 00:06:52.444 who is a postdoctoral fellow in my lab

NOTE Confidence: 0.8636394325

00:06:52.444 --> 00:06:54.980 of very talented postdoc Buffalo in my lab,

NOTE Confidence: 0.8636394325

00:06:54.980 --> 00:06:57.326 decided to do an experiment where

NOTE Confidence: 0.8636394325

00:06:57.326 --> 00:06:59.612 he ceded the young 1.7 cells

NOTE Confidence: 0.8636394325

00:06:59.612 --> 00:07:02.139 intradermally in the skin of the mice.

NOTE Confidence: 0.8636394325

00:07:02.140 --> 00:07:04.793 And then he allowed them to metastasize

NOTE Confidence: 0.8636394325

00:07:04.793 --> 00:07:07.178 overtime to the lungs of the mice

NOTE Confidence: 0.8636394325

00:07:07.180 --> 00:07:09.244 and at three weeks he took the lungs

NOTE Confidence: 0.8636394325

00:07:09.244 --> 00:07:11.408 of both the young and the age mice,

NOTE Confidence: 0.8636394325

00:07:11.410 --> 00:07:13.834 and he looked for his M cherry labeled

NOTE Confidence: 0.8636394325

00:07:13.834 --> 00:07:15.757 Melanoma cells and what he found was

NOTE Confidence: 0.8636394325

00:07:15.757 --> 00:07:17.879 that in both the young and aged mice,

NOTE Confidence: 0.8636394325

00:07:17.880 --> 00:07:20.672 there were these sort of single or maybe

NOTE Confidence: 0.8636394325

00:07:20.672 --> 00:07:23.248 double cell colonies all over the lung.

NOTE Confidence: 0.8636394325

00:07:23.250 --> 00:07:25.427 If he waited just a couple more

NOTE Confidence: 0.8636394325

00:07:25.427 --> 00:07:28.058 weeks and he did this at five weeks,

NOTE Confidence: 0.8636394325

00:07:28.060 --> 00:07:30.076 what he saw is that in the Yung Lung,

NOTE Confidence: 0.8636394325

00:07:30.080 --> 00:07:32.810 the colonies remained as he single cells.

NOTE Confidence: 0.8636394325

00:07:32.810 --> 00:07:33.986 They're much smaller qualities,

NOTE Confidence: 0.8636394325

00:07:33.986 --> 00:07:36.101 whereas in the age long they had

NOTE Confidence: 0.8636394325

00:07:36.101 --> 00:07:37.865 started to grow up quite dramatically,

NOTE Confidence: 0.8636394325

00:07:37.870 --> 00:07:40.313 and we could quantitate this over a

NOTE Confidence: 0.8636394325

00:07:40.313 --> 00:07:42.576 series of mice which wanted to know

NOTE Confidence: 0.8636394325

00:07:42.576 --> 00:07:44.400 what kind of role the fiberglass

NOTE Confidence: 0.8636394325

00:07:44.467 --> 00:07:45.787 played and all of this,

NOTE Confidence: 0.8636394325

00:07:45.790 --> 00:07:48.478 and so he took fibroblasts from the

NOTE Confidence: 0.8636394325

00:07:48.478 --> 00:07:51.128 Yung lung and from the age long,

NOTE Confidence: 0.8636394325

00:07:51.130 --> 00:07:54.070 and then he ceded GFP tagged Melanoma

NOTE Confidence: 0.8636394325

00:07:54.070 --> 00:07:56.470 cells in a 3D sandwich.

NOTE Confidence: 0.8636394325

00:07:56.470 --> 00:07:58.871 With these fibroblasts and what he saw

NOTE Confidence: 0.8636394325

00:07:58.871 --> 00:08:01.309 is that when he incubated Melanoma

NOTE Confidence: 0.8636394325

00:08:01.309 --> 00:08:03.539 cells with age long fiberglass.

NOTE Confidence: 0.8636394325

00:08:03.540 --> 00:08:05.485 They would proliferate far more

NOTE Confidence: 0.8636394325

00:08:05.485 --> 00:08:07.807 rapidly than when he ceded them

NOTE Confidence: 0.8636394325

00:08:07.807 --> 00:08:09.502 with Yung lung fibroblasts.

NOTE Confidence: 0.8636394325

00:08:09.502 --> 00:08:12.286 He then looked compared the growth

NOTE Confidence: 0.8636394325

00:08:12.286 --> 00:08:14.787 rates of the Melanoma cells with

NOTE Confidence: 0.8636394325

00:08:14.787 --> 00:08:17.480 lung fibroblast to that of the skin.

NOTE Confidence: 0.8636394325

00:08:17.480 --> 00:08:17.850 Sorry,

NOTE Confidence: 0.8636394325

00:08:17.850 --> 00:08:20.440 and he found that the age skin

NOTE Confidence: 0.8636394325

00:08:20.440 --> 00:08:22.104 fiberglass actually suppressed the

NOTE Confidence: 0.8636394325

00:08:22.104 --> 00:08:24.239 growth of these Melanoma cells,

NOTE Confidence: 0.902922965333333

00:08:24.240 --> 00:08:25.960 which we had seen before and which I

NOTE Confidence: 0.902922965333333

00:08:25.960 --> 00:08:27.468 just showed you in the mouse model.

NOTE Confidence: 0.902922965333333

00:08:27.470 --> 00:08:29.045 Whereas the young skin fibroblast

NOTE Confidence: 0.902922965333333

00:08:29.045 --> 00:08:31.770 promoted it and so we saw a distinct

NOTE Confidence: 0.902922965333333

00:08:31.770 --> 00:08:33.948 difference between the way the fiberglass.

NOTE Confidence: 0.902922965333333

00:08:33.950 --> 00:08:36.410 And these two different tissues behaved,

NOTE Confidence: 0.902922965333333

00:08:36.410 --> 00:08:39.987 which was sort of a very striking

NOTE Confidence: 0.902922965333333

00:08:39.987 --> 00:08:43.040 and eye opening thing for us.

NOTE Confidence: 0.902922965333333

00:08:43.040 --> 00:08:45.528 So Mitch then did proteomics on both the

NOTE Confidence: 0.902922965333333

00:08:45.528 --> 00:08:47.570 skin fibroblasts and the lung fibroblasts,

NOTE Confidence: 0.902922965333333

00:08:47.570 --> 00:08:49.514 comparing the age to the young

NOTE Confidence: 0.902922965333333

00:08:49.514 --> 00:08:52.219 in both cases and what he found

NOTE Confidence: 0.902922965333333

00:08:52.219 --> 00:08:53.995 was something quite interesting.

NOTE Confidence: 0.902922965333333

00:08:54.000 --> 00:08:56.640 He found that in aging skin there was

NOTE Confidence: 0.902922965333333

00:08:56.640 --> 00:08:59.261 a signature of fiberglass promoting a

NOTE Confidence: 0.902922965333333

00:08:59.261 --> 00:09:01.621 non canonical went signaling phenotype

NOTE Confidence: 0.902922965333333

00:09:01.621 --> 00:09:04.390 which included jeans like SFRP 2 serpin

NOTE Confidence: 0.78424883

00:09:06.680 --> 00:09:08.860 E2DK1158RR2 in the age long.

NOTE Confidence: 0.78424883

00:09:08.860 --> 00:09:10.642 However, he saw a signature that

NOTE Confidence: 0.78424883

00:09:10.642 --> 00:09:12.336 showed there was a promotion

NOTE Confidence: 0.78424883

00:09:12.336 --> 00:09:14.108 of Canonical went signaling.

NOTE Confidence: 0.78424883

00:09:14.110 --> 00:09:16.830 And what he would see is sometimes the

NOTE Confidence: 0.78424883

00:09:16.830 --> 00:09:19.080 same family members SFRP one and SFRP

NOTE Confidence: 0.78424883

00:09:19.080 --> 00:09:21.904 2 which we know to play very different

NOTE Confidence: 0.78424883

00:09:21.904 --> 00:09:24.552 roles and one signaling were the ones

NOTE Confidence: 0.78424883

00:09:24.552 --> 00:09:25.848 that were differentially expressed.

NOTE Confidence: 0.78424883

00:09:25.850 --> 00:09:27.474 And so I'll tell you a little

NOTE Confidence: 0.78424883

00:09:27.474 --> 00:09:29.019 bit more about these two guys.

NOTE Confidence: 0.78424883

00:09:29.020 --> 00:09:31.548 So we had shown a few years ago

NOTE Confidence: 0.78424883

00:09:31.548 --> 00:09:34.319 that age fiberglass decreed SFRP 2.

NOTE Confidence: 0.78424883

00:09:34.320 --> 00:09:35.770 And when they do that,

NOTE Confidence: 0.78424883

00:09:35.770 --> 00:09:37.990 they shut off beta catenin signaling.

NOTE Confidence: 0.78424883

00:09:37.990 --> 00:09:41.308 So SFRP 2 inhibits Canonical went signaling.

NOTE Confidence: 0.78424883

00:09:41.310 --> 00:09:45.126 And and in doing so decreases the

NOTE Confidence: 0.78424883

00:09:45.126 --> 00:09:47.667 ability of a Melanoma cell to react

NOTE Confidence: 0.78424883

00:09:47.667 --> 00:09:49.867 to the reactive oxygen species

NOTE Confidence: 0.78424883

00:09:49.867 --> 00:09:52.067 in the micro environment because

NOTE Confidence: 0.78424883

00:09:52.067 --> 00:09:54.503 it disables this basic vision and

NOTE Confidence: 0.78424883

00:09:54.503 --> 00:09:56.927 a nucleus repair gene AP one.

NOTE Confidence: 0.78424883

00:09:56.927 --> 00:09:58.915 Sorry for the inappropriate

NOTE Confidence: 0.78424883

00:09:58.915 --> 00:10:00.903 domination animation over here,

NOTE Confidence: 0.78424883

00:10:00.910 --> 00:10:03.967 we'll get to in a second, however, So what?

NOTE Confidence: 0.78424883

00:10:03.967 --> 00:10:06.181 That did was to decrease the

NOTE Confidence: 0.78424883

00:10:06.181 --> 00:10:07.968 proliferation of the Melanoma cells,

NOTE Confidence: 0.78424883

00:10:07.970 --> 00:10:10.120 but make them more invasive.

NOTE Confidence: 0.78424883

00:10:10.120 --> 00:10:10.443 However,

NOTE Confidence: 0.78424883

00:10:10.443 --> 00:10:13.350 when Mitch looks at SFRP one and he treats

NOTE Confidence: 0.78424883

00:10:13.419 --> 00:10:16.017 Melanoma cells with recombinant SFRP one,

NOTE Confidence: 0.78424883

00:10:16.020 --> 00:10:17.660 they increase their proliferation

NOTE Confidence: 0.78424883

00:10:17.660 --> 00:10:19.710 and they actually shut off.

NOTE Confidence: 0.78424883

00:10:19.710 --> 00:10:23.614 Noncanonical went signaling in what

NOTE Confidence: 0.78424883

00:10:23.614 --> 00:10:26.830 Mitch then did was to do an experiment

NOTE Confidence: 0.78424883

00:10:26.919 --> 00:10:29.628 in Vivo where he took age mice.

NOTE Confidence: 0.78424883

00:10:29.630 --> 00:10:31.424 He allowed three weeks for the

NOTE Confidence: 0.78424883

00:10:31.424 --> 00:10:32.980 initial dissemination of the tumor.

NOTE Confidence: 0.78424883

00:10:32.980 --> 00:10:35.440 As I showed you previously.

NOTE Confidence: 0.78424883

00:10:35.440 --> 00:10:37.006 And then once the tumor cells

NOTE Confidence: 0.78424883

00:10:37.006 --> 00:10:38.440 had seated in the lungs,

NOTE Confidence: 0.78424883

00:10:38.440 --> 00:10:41.745 he treated the mice with

NOTE Confidence: 0.78424883

00:10:41.745 --> 00:10:44.389 antibodies against SFRP one.

NOTE Confidence: 0.78424883

00:10:44.390 --> 00:10:46.329 So in the IgG control you see

NOTE Confidence: 0.78424883

00:10:46.329 --> 00:10:47.890 this outburst of metastases,

NOTE Confidence: 0.78424883

00:10:47.890 --> 00:10:49.540 as I showed you earlier.

NOTE Confidence: 0.78424883

00:10:49.540 --> 00:10:51.752 But in the mice that were treated

NOTE Confidence: 0.78424883

00:10:51.752 --> 00:10:53.984 with anti SFRP one you see that

NOTE Confidence: 0.78424883

00:10:53.984 --> 00:10:56.234 the cells that have seated in the

NOTE Confidence: 0.78424883

00:10:56.234 --> 00:10:58.406 lungs remain there as single cells

NOTE Confidence: 0.78424883

00:10:58.406 --> 00:11:00.535 which were super interesting to us.

NOTE Confidence: 0.78424883

00:11:00.535 --> 00:11:03.302 So the reason this was so interesting is

NOTE Confidence: 0.78424883

00:11:03.302 --> 00:11:05.903 we've been working for a while on this idea.

NOTE Confidence: 0.78424883

00:11:05.910 --> 00:11:08.154 Of what we call phenotype switching

NOTE Confidence: 0.78424883

00:11:08.154 --> 00:11:10.111 where we have canonical wind

NOTE Confidence: 0.78424883

00:11:10.111 --> 00:11:12.066 signaling that's driven by beta,

NOTE Confidence: 0.78424883

00:11:12.070 --> 00:11:14.770 catenin and Noncanonical went signaling,

NOTE Confidence: 0.78424883

00:11:14.770 --> 00:11:18.378 driven by went such as 158 and we

NOTE Confidence: 0.78424883

00:11:18.378 --> 00:11:20.874 had always associated the wind 5A

NOTE Confidence: 0.78424883

00:11:20.874 --> 00:11:24.067 phenotype with metastasis and and the

NOTE Confidence: 0.78424883

00:11:24.067 --> 00:11:26.762 beta catenin phenotype with proliferation.

NOTE Confidence: 0.78424883

00:11:26.770 --> 00:11:28.690 But what I'm going to tell you shows

NOTE Confidence: 0.78424883

00:11:28.690 --> 00:11:30.695 that we were not as sophisticated in

NOTE Confidence: 0.78424883

00:11:30.695 --> 00:11:32.769 our thinking as we should have been,

NOTE Confidence: 0.78424883

00:11:32.770 --> 00:11:36.025 and instead the roles are much more

NOTE Confidence: 0.78424883

00:11:36.025 --> 00:11:37.846 interchangeable. And much more complex.

NOTE Confidence: 0.78424883

00:11:37.846 --> 00:11:39.880 So important to note that when

NOTE Confidence: 0.78424883

00:11:39.945 --> 00:11:42.249 5/8 promotes an invasive but slow

NOTE Confidence: 0.78424883

00:11:42.249 --> 00:11:44.527 cycling phenotype and that led us

NOTE Confidence: 0.78424883

00:11:44.527 --> 00:11:46.561 to wonder whether these changes we

NOTE Confidence: 0.78424883

00:11:46.561 --> 00:11:49.092 were seeing in the young versus

NOTE Confidence: 0.78424883

00:11:49.092 --> 00:11:51.407 aged lung colonies have any.

NOTE Confidence: 0.78424883

00:11:51.410 --> 00:11:52.778 I'm sorry I don't know what's

NOTE Confidence: 0.78424883

00:11:52.778 --> 00:11:53.690 happening to my animation.

NOTE Confidence: 0.78424883

00:11:53.690 --> 00:11:56.298 Had any relation to dormancy and so we

NOTE Confidence: 0.78424883

00:11:56.298 --> 00:11:58.989 turned to our good friend Julio Gerike.

NOTE Confidence: 0.78424883

00:11:58.990 --> 00:12:00.208 So who's now?

NOTE Confidence: 0.78424883

00:12:00.208 --> 00:12:02.644 I just started an Institute of

NOTE Confidence: 0.78424883

00:12:02.644 --> 00:12:04.811 dormancy at the Albert Einstein

NOTE Confidence: 0.78424883

00:12:04.811 --> 00:12:07.337 College of Medicine in New York.

NOTE Confidence: 0.78424883

00:12:07.340 --> 00:12:10.098 And he is a world leader in

NOTE Confidence: 0.78424883

00:12:10.098 --> 00:12:11.280 understanding tumor dormancy,

NOTE Confidence: 0.78424883

00:12:11.280 --> 00:12:14.448 and he has these signatures of door machines.

NOTE Confidence: 0.78424883

00:12:14.450 --> 00:12:16.935 So what Mitch did was to look

NOTE Confidence: 0.78424883

00:12:16.935 --> 00:12:18.000 at the expression

NOTE Confidence: 0.878864957777778

00:12:18.081 --> 00:12:20.524 of these genes and win 5A high

NOTE Confidence: 0.878864957777778

00:12:20.524 --> 00:12:23.148 versus 15 LO cells and what he sees

NOTE Confidence: 0.878864957777778

00:12:23.148 --> 00:12:26.032 is that when 5A high cells carry

NOTE Confidence: 0.878864957777778

00:12:26.032 --> 00:12:28.317 very strong markers of dormancy.

NOTE Confidence: 0.878864957777778

00:12:28.320 --> 00:12:30.987 Whereas went five a low cells carry

NOTE Confidence: 0.878864957777778

00:12:30.987 --> 00:12:32.991 very high markers of proliferative

NOTE Confidence: 0.878864957777778

00:12:32.991 --> 00:12:36.151 cells and so much is question was does

NOTE Confidence: 0.878864957777778

00:12:36.227 --> 00:12:38.202 the aging microenvironment drive a

NOTE Confidence: 0.878864957777778

00:12:38.202 --> 00:12:42.130 switch from a win 5A high to win 58 low

NOTE Confidence: 0.878864957777778

00:12:42.130 --> 00:12:45.505 phenotype and in doing so Dr increased

NOTE Confidence: 0.878864957777778

00:12:45.505 --> 00:12:48.165 proliferation in Melanoma cells?

NOTE Confidence: 0.878864957777778

00:12:48.170 --> 00:12:50.070 So to answer this, UM,

NOTE Confidence: 0.878864957777778

00:12:50.070 --> 00:12:51.939 the first thing which did was to

NOTE Confidence: 0.878864957777778

00:12:51.939 --> 00:12:53.621 take Melanoma cells and expose them

NOTE Confidence: 0.878864957777778

00:12:53.621 --> 00:12:55.265 to the condition media of young.

NOTE Confidence: 0.878864957777778

00:12:55.270 --> 00:12:57.100 An age long fiberglass and what

NOTE Confidence: 0.878864957777778

00:12:57.100 --> 00:12:58.850 he sees is that indeed,

NOTE Confidence: 0.878864957777778

00:12:58.850 --> 00:13:00.700 in the same Melanoma cells

NOTE Confidence: 0.878864957777778

00:13:00.700 --> 00:13:02.550 exposed to age condition media.

NOTE Confidence: 0.878864957777778

00:13:02.550 --> 00:13:05.020 These are just three separate.

NOTE Confidence: 0.878864957777778

00:13:05.020 --> 00:13:06.976 These are the same Melanoma cells,

NOTE Confidence: 0.878864957777778

00:13:06.980 --> 00:13:10.810 three separate donor, fiberglass media.

NOTE Confidence: 0.878864957777778

00:13:10.810 --> 00:13:13.673 What Michelle was that the the markers

NOTE Confidence: 0.878864957777778

00:13:13.673 --> 00:13:16.373 of dormancy were decreased when he

NOTE Confidence: 0.878864957777778

00:13:16.373 --> 00:13:18.698 exposed Melanoma cells to these?

NOTE Confidence: 0.878864957777778

00:13:18.700 --> 00:13:20.896 Each condition media from the lung,

NOTE Confidence: 0.878864957777778

00:13:20.900 --> 00:13:23.225 whereas the markers of proliferation

NOTE Confidence: 0.878864957777778

00:13:23.225 --> 00:13:26.040 were increased in the Melanoma cells,

NOTE Confidence: 0.878864957777778

00:13:26.040 --> 00:13:28.488 the next thing he did was to look

NOTE Confidence: 0.878864957777778

00:13:28.488 --> 00:13:31.416 at 15-A specifically and to look at

NOTE Confidence: 0.878864957777778

00:13:31.416 --> 00:13:35.254 it in vivo and what he saw is that

NOTE Confidence: 0.878864957777778

00:13:35.254 --> 00:13:38.275 if he stained young and aged tumors

NOTE Confidence: 0.878864957777778

00:13:38.275 --> 00:13:41.967 for 15-A and Ki 67 in the lungs,

NOTE Confidence: 0.878864957777778

00:13:41.970 --> 00:13:43.608 so these are cells that he has

NOTE Confidence: 0.878864957777778

00:13:43.608 --> 00:13:45.610 implanted in the skin of the mice that

NOTE Confidence: 0.878864957777778

00:13:45.610 --> 00:13:47.160 have now metastasized to the lung.

NOTE Confidence: 0.878864957777778

00:13:47.160 --> 00:13:49.010 They're labeled with them cherry.

NOTE Confidence: 0.878864957777778

00:13:49.010 --> 00:13:49.799 In the absence,

NOTE Confidence: 0.878864957777778

00:13:49.799 --> 00:13:51.640 and this is just standing for and

NOTE Confidence: 0.878864957777778

00:13:51.699 --> 00:13:53.373 cherry showing you that there are

NOTE Confidence: 0.878864957777778

00:13:53.373 --> 00:13:55.276 far fewer cells in the yung lung

NOTE Confidence: 0.878864957777778

00:13:55.276 --> 00:13:56.970 than there are in the age long.

NOTE Confidence: 0.878864957777778

00:13:56.970 --> 00:13:59.202 And if he stains the the lungs for

NOTE Confidence: 0.878864957777778

00:13:59.202 --> 00:14:01.168 win 5/8 these large tumors that

NOTE Confidence: 0.878864957777778

00:14:01.168 --> 00:14:03.581 are growing out in the age long

NOTE Confidence: 0.878864957777778

00:14:03.581 --> 00:14:05.657 have much less went 5A staining

NOTE Confidence: 0.878864957777778

00:14:05.657 --> 00:14:07.976 than the tumors in the yung lung,

NOTE Confidence: 0.878864957777778

00:14:07.976 --> 00:14:10.231 and they're highly positive for Ki 67

NOTE Confidence: 0.878864957777778

00:14:10.231 --> 00:14:12.439 telling us that the wind 5A may be

NOTE Confidence: 0.878864957777778

00:14:12.439 --> 00:14:14.928 driving this dormant phenotype in the lung,

NOTE Confidence: 0.878864957777778

00:14:14.930 --> 00:14:17.246 which was super interesting to us.

NOTE Confidence: 0.878864957777778

00:14:17.250 --> 00:14:20.064 What Mitch did then was to manipulate.

NOTE Confidence: 0.878864957777778

00:14:20.070 --> 00:14:21.338 15A in these conditions,

NOTE Confidence: 0.878864957777778

00:14:21.338 --> 00:14:22.923 so he took young mice,

NOTE Confidence: 0.878864957777778

00:14:22.930 --> 00:14:23.527 UM,

NOTE Confidence: 0.878864957777778

00:14:23.527 --> 00:14:27.109 and he injected cells with an

NOTE Confidence: 0.878864957777778

00:14:27.109 --> 00:14:29.791 induced adops inducible went 5SH158,

NOTE Confidence: 0.878864957777778

00:14:29.791 --> 00:14:32.679 so he knocked 158 out of the Melanoma

NOTE Confidence: 0.878864957777778

00:14:32.679 --> 00:14:34.637 cells in the young mouse lungs

NOTE Confidence: 0.878864957777778

00:14:34.637 --> 00:14:37.229 and what he saw is if he did that

NOTE Confidence: 0.878864957777778

00:14:37.230 --> 00:14:39.967 very early on he could reduce the

NOTE Confidence: 0.878864957777778

00:14:39.967 --> 00:14:42.010 number of metastases altogether.

NOTE Confidence: 0.878864957777778

00:14:42.010 --> 00:14:44.008 But if he did that later,

NOTE Confidence: 0.878864957777778

00:14:44.010 --> 00:14:47.010 he could cause the metastases to grow out.

NOTE Confidence: 0.878864957777778

00:14:47.010 --> 00:14:48.540 If he did the opposite experiment

NOTE Confidence: 0.878864957777778

00:14:48.540 --> 00:14:49.970 where he took age mounts.

NOTE Confidence: 0.878864957777778

00:14:49.970 --> 00:14:52.910 Once and then he gave them went

NOTE Confidence: 0.878864957777778

00:14:52.910 --> 00:14:54.731 5/8 he could come.

NOTE Confidence: 0.878864957777778

00:14:54.731 --> 00:14:57.536 He could actually prevent these

NOTE Confidence: 0.878864957777778

00:14:57.536 --> 00:15:00.704 these tumors from growing out at day

NOTE Confidence: 0.878864957777778

00:15:00.704 --> 00:15:04.562 21 and and he could also if he if

NOTE Confidence: 0.878864957777778

00:15:04.562 --> 00:15:07.968 he induced the win 5A at day three.

NOTE Confidence: 0.878864957777778

00:15:07.970 --> 00:15:09.668 They had already started to get

NOTE Confidence: 0.878864957777778

00:15:09.668 --> 00:15:11.956 to the lungs but they again were

NOTE Confidence: 0.878864957777778

00:15:11.956 --> 00:15:13.408 prevented from growing out,

NOTE Confidence: 0.878864957777778

00:15:13.410 --> 00:15:15.300 so this was absolutely fascinating

NOTE Confidence: 0.878864957777778

00:15:15.300 --> 00:15:17.942 to us because it kind of changed

NOTE Confidence: 0.878864957777778

00:15:17.942 --> 00:15:20.308 our thinking of how when 5A was

NOTE Confidence: 0.878864957777778

00:15:20.308 --> 00:15:21.460 driving metastasis.

NOTE Confidence: 0.878864957777778

00:15:21.460 --> 00:15:23.938 And what we saw was that you

NOTE Confidence: 0.878864957777778

00:15:23.938 --> 00:15:25.000 know these Melanoma

NOTE Confidence: 0.878828765

00:15:25.077 --> 00:15:26.477 cells in the young.

NOTE Confidence: 0.878828765

00:15:26.480 --> 00:15:28.976 First of all, the tumors are much bigger

NOTE Confidence: 0.878828765

00:15:28.976 --> 00:15:31.598 in the young skin than the age skin,

NOTE Confidence: 0.878828765

00:15:31.600 --> 00:15:33.553 and so even though we might see

NOTE Confidence: 0.878828765

00:15:33.553 --> 00:15:35.619 similar rates of seating in the lung,

NOTE Confidence: 0.878828765

00:15:35.620 --> 00:15:38.308 we know that the rates of tumor cells

NOTE Confidence: 0.878828765

00:15:38.308 --> 00:15:40.840 leaving the age skin are higher than

NOTE Confidence: 0.878828765

00:15:40.840 --> 00:15:43.040 the rate sleeping the young skin.

NOTE Confidence: 0.878828765

00:15:43.040 --> 00:15:44.920 But once they get to the yung lung,

NOTE Confidence: 0.878828765

00:15:44.920 --> 00:15:48.644 the yung lung fibroblasts are are secreting

NOTE Confidence: 0.878828765

00:15:48.644 --> 00:15:51.983 factors that maintain the win 5A phenotype.

NOTE Confidence: 0.878828765

00:15:51.990 --> 00:15:54.531 And and retain those cells in this

NOTE Confidence: 0.878828765

00:15:54.531 --> 00:15:56.670 invasive but slow cycling state.

NOTE Confidence: 0.878828765

00:15:56.670 --> 00:15:58.230 However, in the age long,

NOTE Confidence: 0.878828765

00:15:58.230 --> 00:16:00.540 we're seeing that there is an

NOTE Confidence: 0.878828765

00:16:00.540 --> 00:16:02.876 increase of secretion of SFRP one,

NOTE Confidence: 0.878828765

00:16:02.876 --> 00:16:05.662 and that is maintaining that is allowing

NOTE Confidence: 0.878828765

00:16:05.662 --> 00:16:08.390 these cells to now lose that slow

NOTE Confidence: 0.878828765

00:16:08.390 --> 00:16:10.970 cycling state become more proliferative.

NOTE Confidence: 0.878828765

00:16:10.970 --> 00:16:12.970 These are also positive for

NOTE Confidence: 0.878828765

00:16:12.970 --> 00:16:15.130 beta catenin MITF and Mark one,

NOTE Confidence: 0.878828765

00:16:15.130 --> 00:16:17.616 and they're they're rapidly proliferating,

NOTE Confidence: 0.878828765

00:16:17.616 --> 00:16:20.626 and so really for us,

NOTE Confidence: 0.878828765

00:16:20.630 --> 00:16:22.482 where we had always thought of 15-A

NOTE Confidence: 0.878828765

00:16:22.482 --> 00:16:24.594 is simply a driver of metastasis.

NOTE Confidence: 0.878828765

00:16:24.600 --> 00:16:27.216 It's actually playing a much more

NOTE Confidence: 0.878828765

00:16:27.216 --> 00:16:29.454 complicated role and driving an

NOTE Confidence: 0.878828765

00:16:29.454 --> 00:16:31.564 invasive but then dormant tumor

NOTE Confidence: 0.878828765

00:16:31.564 --> 00:16:34.058 phenotype that requires a change for

NOTE Confidence: 0.878828765

00:16:34.058 --> 00:16:36.627 these cells to come out of dormancy.

NOTE Confidence: 0.878828765

00:16:36.630 --> 00:16:38.830 I will add that we've also seen changes

NOTE Confidence: 0.878828765

00:16:38.830 --> 00:16:40.524 in the immune microenvironment in

NOTE Confidence: 0.878828765

00:16:40.524 --> 00:16:43.037 both the young and each lung that

NOTE Confidence: 0.878828765

00:16:43.104 --> 00:16:44.929 are contributing to this outgrowth

NOTE Confidence: 0.878828765

00:16:44.929 --> 00:16:47.080 and lack of immune editing of

NOTE Confidence: 0.878828765

00:16:47.080 --> 00:16:51.020 these cells as they grow out so.

NOTE Confidence: 0.878828765

00:16:51.020 --> 00:16:51.563 Sorry,

NOTE Confidence: 0.878828765

00:16:51.563 --> 00:16:55.204 hold on a second so I've started to

NOTE Confidence: 0.878828765

00:16:55.204 --> 00:16:58.216 give you now a snapshot of the fact that

NOTE Confidence: 0.878828765

00:16:58.216 --> 00:17:00.574 Asian can drive metastasis of tumors,

NOTE Confidence: 0.878828765

00:17:00.580 --> 00:17:02.374 but we've been very interested in

NOTE Confidence: 0.878828765

00:17:02.374 --> 00:17:04.801 also all of the other things that

NOTE Confidence: 0.878828765

00:17:04.801 --> 00:17:06.746 the aging microenvironment can do

NOTE Confidence: 0.878828765

00:17:06.750 --> 00:17:09.340 from driving not only metastasis,

NOTE Confidence: 0.878828765

00:17:09.340 --> 00:17:11.626 and we'll talk a little bit more about this,

NOTE Confidence: 0.878828765

00:17:11.630 --> 00:17:13.780 but things like therapy resistance,

NOTE Confidence: 0.878828765

00:17:13.780 --> 00:17:14.726 angiogenesis, metabolism,

NOTE Confidence: 0.878828765

00:17:14.726 --> 00:17:17.091 and changes in the immune

NOTE Confidence: 0.878828765

00:17:17.091 --> 00:17:18.510 microenvironment as well,

NOTE Confidence: 0.878828765

00:17:18.510 --> 00:17:20.736 so I'll start with the angiogenesis story,

NOTE Confidence: 0.878828765

00:17:20.740 --> 00:17:21.884 which is a story.

NOTE Confidence: 0.878828765

00:17:21.884 --> 00:17:24.099 That was recently published out of our lab.

NOTE Confidence: 0.878828765

00:17:24.100 --> 00:17:26.186 I should mention that all the work

NOTE Confidence: 0.878828765

00:17:26.186 --> 00:17:28.921 I just showed you is of matches is

NOTE Confidence: 0.878828765

00:17:28.921 --> 00:17:30.691 completely unpublished at this time,

NOTE Confidence: 0.878828765

00:17:30.700 --> 00:17:32.919 and most of the slides I'll show

NOTE Confidence: 0.878828765

00:17:32.919 --> 00:17:35.120 you today are unpublished work,

NOTE Confidence: 0.878828765

00:17:35.120 --> 00:17:37.272 but I thought I'd give you some snapshots

NOTE Confidence: 0.878828765

00:17:37.272 --> 00:17:39.630 of some recently published work as well,

NOTE Confidence: 0.878828765

00:17:39.630 --> 00:17:42.969 so the tumors that we grow in age mice

NOTE Confidence: 0.878828765

00:17:42.969 --> 00:17:46.141 have far more angiogenesis if we stay

NOTE Confidence: 0.878828765

00:17:46.141 --> 00:17:49.944 in with either CD31 or even CD105,

NOTE Confidence: 0.878828765

00:17:49.944 --> 00:17:52.388 and when we take.

NOTE Confidence: 0.878828765

00:17:52.390 --> 00:17:55.434 Dermal massive dermal microvascular

NOTE Confidence: 0.878828765

00:17:55.434 --> 00:17:58.056 endothelial cells and we treat them

NOTE Confidence: 0.878828765

00:17:58.056 --> 00:18:00.727 with medium from young age fibroblasts.

NOTE Confidence: 0.878828765

00:18:00.730 --> 00:18:02.968 We see that those dermal microvascular

NOTE Confidence: 0.878828765

00:18:02.968 --> 00:18:05.329 endothelial cells will form networks when

NOTE Confidence: 0.878828765

00:18:05.329 --> 00:18:07.747 they're treated with age conditioned media,

NOTE Confidence: 0.878828765

00:18:07.750 --> 00:18:09.400 but not so much when they're

NOTE Confidence: 0.878828765

00:18:09.400 --> 00:18:10.225 treated with young,

NOTE Confidence: 0.878828765

00:18:10.230 --> 00:18:12.876 and we can quantitate this as well.

NOTE Confidence: 0.878828765

00:18:12.880 --> 00:18:13.212 And,

NOTE Confidence: 0.878828765

00:18:13.212 --> 00:18:14.872 and this was really mysterious

NOTE Confidence: 0.878828765

00:18:14.872 --> 00:18:17.290 to us because we needed that veg.

NOTE Confidence: 0.878828765

00:18:17.290 --> 00:18:19.852 F and its receptors were decreased

NOTE Confidence: 0.878828765

00:18:19.852 --> 00:18:20.706 during aging,

NOTE Confidence: 0.878828765

00:18:20.710 --> 00:18:22.456 and so it didn't make sense to us that.

NOTE Confidence: 0.878828765

00:18:22.460 --> 00:18:24.301 We were seeing a decrease in veg

NOTE Confidence: 0.878828765

00:18:24.301 --> 00:18:26.770 F But an increase in angiogenesis.

NOTE Confidence: 0.878828765

00:18:26.770 --> 00:18:27.130 However,

NOTE Confidence: 0.878828765

00:18:27.130 --> 00:18:29.650 we knew from our work with SFRP

NOTE Confidence: 0.878828765

00:18:29.650 --> 00:18:32.703 2 that SFRP 2 has been shown

NOTE Confidence: 0.878828765

00:18:32.703 --> 00:18:34.053 to stimulate angiogenesis

NOTE Confidence: 0.702781086666667

00:18:34.060 --> 00:18:37.258 via a went related signaling pathway.

NOTE Confidence: 0.702781086666667

00:18:37.260 --> 00:18:39.580 So when it keeps rearing its head again

NOTE Confidence: 0.702781086666667

00:18:39.580 --> 00:18:42.482 and we knew that if we if we treated

NOTE Confidence: 0.702781086666667

00:18:42.482 --> 00:18:44.947 mice with recombinant SFRP 2 we could

NOTE Confidence: 0.702781086666667

00:18:44.947 --> 00:18:47.101 increase their metastases of these cells.

NOTE Confidence: 0.702781086666667

00:18:47.110 --> 00:18:50.078 So Mitch, along with Brett Decker and

NOTE Confidence: 0.702781086666667

00:18:50.078 --> 00:18:53.288 among car decided to explore this further.

NOTE Confidence: 0.702781086666667

00:18:53.290 --> 00:18:55.018 And what they did was to

NOTE Confidence: 0.702781086666667

00:18:55.018 --> 00:18:56.170 take these endothelial cells,

NOTE Confidence: 0.702781086666667

00:18:56.170 --> 00:18:58.130 treat them with either recombinant

NOTE Confidence: 0.702781086666667

00:18:58.130 --> 00:19:00.090 SFRP 2 and young media,

NOTE Confidence: 0.702781086666667

00:19:00.090 --> 00:19:03.170 or I don't know why that keeps happening

NOTE Confidence: 0.702781086666667

00:19:03.170 --> 00:19:06.617 or an antibody against SFRP 2 in age

NOTE Confidence: 0.702781086666667

00:19:06.617 --> 00:19:09.462 media when they manipulated SFRP 2 they

NOTE Confidence: 0.702781086666667

00:19:09.462 --> 00:19:12.410 could show that when they increase it,

NOTE Confidence: 0.702781086666667

00:19:12.410 --> 00:19:14.360 these microvascular endothelial

NOTE Confidence: 0.702781086666667

00:19:14.360 --> 00:19:15.660 networks increase.

NOTE Confidence: 0.702781086666667

00:19:15.660 --> 00:19:17.550 If they decrease SFRP 2,

NOTE Confidence: 0.702781086666667

00:19:17.550 --> 00:19:20.147 they can disrupt the formation of networks.

NOTE Confidence: 0.702781086666667

00:19:20.150 --> 00:19:22.320 They also did this in vivo and

NOTE Confidence: 0.702781086666667

00:19:22.320 --> 00:19:24.010 showed exactly the same thing.

NOTE Confidence: 0.702781086666667

00:19:24.010 --> 00:19:26.481 If they give young mice recombinant SFRP

NOTE Confidence: 0.702781086666667

00:19:26.481 --> 00:19:29.249 2 they have a ton more angiogenesis,

NOTE Confidence: 0.702781086666667

00:19:29.250 --> 00:19:30.458 old myself, more angiogenesis.

NOTE Confidence: 0.702781086666667

00:19:30.458 --> 00:19:32.623 But if you treat with an antibody

NOTE Confidence: 0.702781086666667

00:19:32.623 --> 00:19:33.807 against so far P2,

NOTE Confidence: 0.702781086666667

00:19:33.810 --> 00:19:37.324 it decreases the number of blood vessels.

NOTE Confidence: 0.702781086666667

00:19:37.330 --> 00:19:39.460 And so when UM mentioned,

NOTE Confidence: 0.702781086666667

00:19:39.460 --> 00:19:41.756 his colleagues looked at Veg F and

NOTE Confidence: 0.702781086666667

00:19:41.756 --> 00:19:44.593 SFRP 2 what they found was that these

NOTE Confidence: 0.702781086666667

00:19:44.593 --> 00:19:47.450 young mice had very high levels of veg.

NOTE Confidence: 0.702781086666667

00:19:47.450 --> 00:19:51.390 F But the age tumors in aged mice did not.

NOTE Confidence: 0.702781086666667

00:19:51.390 --> 00:19:55.944 The opposite was true for SFRB 2 and so

NOTE Confidence: 0.702781086666667

00:19:55.950 --> 00:19:58.263 you know that led us to ask the question,

NOTE Confidence: 0.702781086666667

00:19:58.270 --> 00:20:00.170 what does that mean for

NOTE Confidence: 0.702781086666667

00:20:00.170 --> 00:20:00.930 antiangiogenic therapy?

NOTE Confidence: 0.702781086666667

00:20:00.930 --> 00:20:02.478 Because antiangiogenic therapy,

NOTE Confidence: 0.702781086666667

00:20:02.478 --> 00:20:05.600 of course, is designed against veg F.

NOTE Confidence: 0.702781086666667

00:20:05.600 --> 00:20:07.776 And so this this hinted to us that.

NOTE Confidence: 0.702781086666667

00:20:07.780 --> 00:20:09.188 Younger patients might benefit

NOTE Confidence: 0.702781086666667

00:20:09.188 --> 00:20:10.244 from this therapy,

NOTE Confidence: 0.702781086666667

00:20:10.250 --> 00:20:12.734 but certainly older patients who had

NOTE Confidence: 0.702781086666667

00:20:12.734 --> 00:20:15.071 highly angiogenic tumors that were not

NOTE Confidence: 0.702781086666667

00:20:15.071 --> 00:20:17.220 dependent on veg F may not benefit.

NOTE Confidence: 0.702781086666667

00:20:17.220 --> 00:20:18.550 So to answer that question,

NOTE Confidence: 0.702781086666667

00:20:18.550 --> 00:20:21.142 what we did was to turn to our colleagues

NOTE Confidence: 0.702781086666667

00:20:21.142 --> 00:20:23.236 Pecori and Mark Middleton in the UK,

NOTE Confidence: 0.702781086666667

00:20:23.240 --> 00:20:26.090 who had just conducted this large

NOTE Confidence: 0.702781086666667

00:20:26.090 --> 00:20:28.580 trial for Avastin and Melanoma where

NOTE Confidence: 0.702781086666667

00:20:28.580 --> 00:20:31.300 they had treated over 1300 patients,

NOTE Confidence: 0.702781086666667

00:20:31.300 --> 00:20:33.659 or their observation at the end of

NOTE Confidence: 0.702781086666667

00:20:33.659 --> 00:20:35.932 this trial was that overall there

NOTE Confidence: 0.702781086666667

00:20:35.932 --> 00:20:38.104 was no change or no response.

NOTE Confidence: 0.702781086666667

00:20:38.110 --> 00:20:38.998 To adbaston, however,

NOTE Confidence: 0.702781086666667

00:20:38.998 --> 00:20:41.440 we asked them to go back and re

NOTE Confidence: 0.702781086666667

00:20:41.440 --> 00:20:43.270 analyze their data and this time,

NOTE Confidence: 0.702781086666667

00:20:43.270 --> 00:20:46.078 stratified by age and when they do that.

NOTE Confidence: 0.702781086666667

00:20:46.080 --> 00:20:48.726 Sorry for the traffic outside my window,

NOTE Confidence: 0.702781086666667

00:20:48.730 --> 00:20:51.840 and when they do that.

NOTE Confidence: 0.702781086666667

00:20:51.840 --> 00:20:54.073 We see that patients under the age

NOTE Confidence: 0.702781086666667

00:20:54.073 --> 00:20:56.437 of 45 who receive Avastin actually

NOTE Confidence: 0.702781086666667

00:20:56.437 --> 00:20:58.657 do do better on Avastin,

NOTE Confidence: 0.702781086666667

00:20:58.660 --> 00:21:02.089 whereas those over the age of 6565

NOTE Confidence: 0.702781086666667

00:21:02.089 --> 00:21:04.303 and older really have no difference

NOTE Confidence: 0.702781086666667

00:21:04.303 --> 00:21:06.120 in their response to Boston.

NOTE Confidence: 0.702781086666667

00:21:06.120 --> 00:21:07.132 To sort of close,

NOTE Confidence: 0.702781086666667

00:21:07.132 --> 00:21:08.650 this loop would match them did

NOTE Confidence: 0.702781086666667

00:21:08.707 --> 00:21:10.077 was to take young animals.

NOTE Confidence: 0.702781086666667

00:21:10.080 --> 00:21:12.162 He treated them with an antibody

NOTE Confidence: 0.702781086666667

00:21:12.162 --> 00:21:14.992 against Veg F and then attempted to do

NOTE Confidence: 0.702781086666667

00:21:14.992 --> 00:21:17.392 that in the presence of high levels

NOTE Confidence: 0.702781086666667

00:21:17.392 --> 00:21:19.957 of SFRP 2 and so when he does that

NOTE Confidence: 0.702781086666667

00:21:19.960 --> 00:21:22.396 there is no change and no response.

NOTE Confidence: 0.702781086666667

00:21:22.400 --> 00:21:25.627 To the mouse equivalent of Avastin in

NOTE Confidence: 0.702781086666667

00:21:25.627 --> 00:21:29.278 tumors in which which have highest Fr P2,

NOTE Confidence: 0.702781086666667

00:21:29.280 --> 00:21:31.219 which may be the reason why we're

NOTE Confidence: 0.702781086666667

00:21:31.219 --> 00:21:32.805 not seeing older patients responding

NOTE Confidence: 0.702781086666667

00:21:32.805 --> 00:21:34.545 to this therapy as well.

NOTE Confidence: 0.702781086666667

00:21:34.550 --> 00:21:37.046 So one of the things that we learned

NOTE Confidence: 0.702781086666667

00:21:37.046 --> 00:21:39.301 from this study was that you know

NOTE Confidence: 0.702781086666667

00:21:39.301 --> 00:21:40.861 not only could SFRB to

NOTE Confidence: 0.854732552333333

00:21:40.931 --> 00:21:43.531 take over from Veg F as a driver

NOTE Confidence: 0.854732552333333

00:21:43.531 --> 00:21:45.062 of angiogenesis during aging,

NOTE Confidence: 0.854732552333333

00:21:45.062 --> 00:21:48.114 meaning that older patients you know we're

NOTE Confidence: 0.854732552333333

00:21:48.114 --> 00:21:50.912 unlikely to respond to Avastin the reviewers

NOTE Confidence: 0.854732552333333

00:21:50.912 --> 00:21:53.519 had actually asked us some questions.

NOTE Confidence: 0.854732552333333

00:21:53.520 --> 00:21:56.272 About the matrix and what was happening to

NOTE Confidence: 0.854732552333333

00:21:56.272 --> 00:21:58.359 the permeability of these blood vessels.

NOTE Confidence: 0.854732552333333

00:21:58.360 --> 00:22:00.916 And so, although we felt that it was out

NOTE Confidence: 0.854732552333333

00:22:00.916 --> 00:22:03.577 of the scope of that particular paper,

NOTE Confidence: 0.854732552333333

00:22:03.580 --> 00:22:06.004 it was a question that really intrigued us,

NOTE Confidence: 0.854732552333333

00:22:06.010 --> 00:22:09.111 and so are my graduate student Gloria

NOTE Confidence: 0.854732552333333

00:22:09.111 --> 00:22:11.569 Mareno decided to take this on.

NOTE Confidence: 0.854732552333333

00:22:11.570 --> 00:22:14.125 The reason we found this so interesting

NOTE Confidence: 0.854732552333333

00:22:14.125 --> 00:22:16.164 is because of a previous study

NOTE Confidence: 0.854732552333333

00:22:16.164 --> 00:22:19.140 from an car in my lab who had shown

NOTE Confidence: 0.854732552333333

00:22:19.140 --> 00:22:21.325 that collagen density is decreased

NOTE Confidence: 0.854732552333333

00:22:21.325 --> 00:22:23.520 during aging and that can happen.

NOTE Confidence: 0.854732552333333

00:22:23.520 --> 00:22:26.079 Whether it's in the presence of a tumor,

NOTE Confidence: 0.854732552333333

00:22:26.080 --> 00:22:28.627 or even altogether in the absence of a tumor,

NOTE Confidence: 0.854732552333333

00:22:28.630 --> 00:22:31.723 so this is just normal mouse skin from an 8

NOTE Confidence: 0.854732552333333

00:22:31.723 --> 00:22:34.169 week old compared to a 12 week old mouse,

NOTE Confidence: 0.854732552333333

00:22:34.170 --> 00:22:36.303 and I think you can see that the collagen

NOTE Confidence: 0.854732552333333

00:22:36.303 --> 00:22:38.124 looks dramatically different between the

NOTE Confidence: 0.854732552333333

00:22:38.124 --> 00:22:41.134 two and a man wanted to know what was

NOTE Confidence: 0.854732552333333

00:22:41.134 --> 00:22:43.540 driving these differences in collagen,

NOTE Confidence: 0.854732552333333

00:22:43.540 --> 00:22:45.100 she identified this protein,

NOTE Confidence: 0.854732552333333

00:22:45.100 --> 00:22:46.270 called happen one,

NOTE Confidence: 0.854732552333333

00:22:46.270 --> 00:22:48.412 which was actually the protein that

NOTE Confidence: 0.854732552333333

00:22:48.412 --> 00:22:50.228 was the most significantly increased

NOTE Confidence: 0.854732552333333

00:22:50.228 --> 00:22:51.520 in the young skin,

NOTE Confidence: 0.854732552333333

00:22:51.520 --> 00:22:53.395 fibroblast secret tone and happen

NOTE Confidence: 0.854732552333333

00:22:53.395 --> 00:22:55.910 one turns out to be a super.

NOTE Confidence: 0.854732552333333

00:22:55.910 --> 00:22:57.374 Interesting protein because it's

NOTE Confidence: 0.854732552333333

00:22:57.374 --> 00:22:59.204 the protein that knits together,

NOTE Confidence: 0.854732552333333

00:22:59.210 --> 00:23:03.458 the collagen and the elastin in the skin.

NOTE Confidence: 0.854732552333333

00:23:03.460 --> 00:23:05.164 And maintain sort of the integrity

NOTE Confidence: 0.854732552333333

00:23:05.164 --> 00:23:06.016 of the skin,

NOTE Confidence: 0.854732552333333

00:23:06.020 --> 00:23:07.903 so you know when you're young you

NOTE Confidence: 0.854732552333333

00:23:07.903 --> 00:23:09.410 have this lovely smooth skin.

NOTE Confidence: 0.854732552333333

00:23:09.410 --> 00:23:10.810 And as you age,

NOTE Confidence: 0.854732552333333

00:23:10.810 --> 00:23:12.210 those collagen and elastin

NOTE Confidence: 0.854732552333333

00:23:12.210 --> 00:23:12.910 pressings breakdown,

NOTE Confidence: 0.854732552333333

00:23:12.910 --> 00:23:16.390 and that's a little bit how wrinkles occur.

NOTE Confidence: 0.854732552333333

00:23:16.390 --> 00:23:18.442 And so I happen,

NOTE Confidence: 0.854732552333333

00:23:18.442 --> 00:23:21.520 one is responsible for stitching together

NOTE Confidence: 0.854732552333333

00:23:21.612 --> 00:23:25.237 hyaluronic acid to proteoglycan monomers.

NOTE Confidence: 0.854732552333333

00:23:25.240 --> 00:23:26.872 So I'm undecided to explore this

NOTE Confidence: 0.854732552333333

00:23:26.872 --> 00:23:29.077 and the first thing she did was to

NOTE Confidence: 0.854732552333333

00:23:29.077 --> 00:23:30.673 just simply injected into mouse skin

NOTE Confidence: 0.854732552333333

00:23:30.735 --> 00:23:32.447 and see what it did and she found

NOTE Confidence: 0.854732552333333

00:23:32.447 --> 00:23:35.225 that if she put it in H mouse skin

NOTE Confidence: 0.854732552333333

00:23:35.230 --> 00:23:38.576 she could she could re densify the

NOTE Confidence: 0.854732552333333

00:23:38.576 --> 00:23:41.847 collagen again in the age mouse skin.

NOTE Confidence: 0.854732552333333

00:23:41.850 --> 00:23:44.048 She wanted to know what that meant

NOTE Confidence: 0.854732552333333

00:23:44.048 --> 00:23:46.735 for the type of fibers that these

NOTE Confidence: 0.854732552333333

00:23:46.735 --> 00:23:48.407 fibroblasts were laying down,

NOTE Confidence: 0.854732552333333

00:23:48.410 --> 00:23:49.960 and the ECM networks there.

NOTE Confidence: 0.854732552333333

00:23:49.960 --> 00:23:52.151 It's just selling matrix and so we

NOTE Confidence: 0.854732552333333

00:23:52.151 --> 00:23:53.829 collaborated with my dear friend.

NOTE Confidence: 0.854732552333333

00:23:53.830 --> 00:23:57.006 It secure men at Fox Chase and a

NOTE Confidence: 0.854732552333333

00:23:57.006 --> 00:23:58.910 man seated fiberglass.

NOTE Confidence: 0.854732552333333

00:23:58.910 --> 00:24:00.926 And then what she did was to basically

NOTE Confidence: 0.854732552333333

00:24:00.926 --> 00:24:03.302 look at the matrix they left behind and

NOTE Confidence: 0.854732552333333

00:24:03.302 --> 00:24:05.611 look at the orientation of those fibers.

NOTE Confidence: 0.854732552333333

00:24:05.611 --> 00:24:07.446 And when she does that,

NOTE Confidence: 0.854732552333333

00:24:07.450 --> 00:24:09.298 she sees that with young fiberglass,

NOTE Confidence: 0.854732552333333

00:24:09.300 --> 00:24:12.018 fibers are oriented in multiple different.

NOTE Confidence: 0.854732552333333

00:24:12.020 --> 00:24:13.960 Directions and each direction

NOTE Confidence: 0.854732552333333

00:24:13.960 --> 00:24:15.900 is assigned a color,

NOTE Confidence: 0.854732552333333

00:24:15.900 --> 00:24:18.196 so you see this very colorful matrix.

NOTE Confidence: 0.854732552333333

00:24:18.200 --> 00:24:20.000 If she knocks down happen one

NOTE Confidence: 0.854732552333333

00:24:20.000 --> 00:24:20.900 in these fiberglass,

NOTE Confidence: 0.854732552333333

00:24:20.900 --> 00:24:23.063 she now sees that the the direction

NOTE Confidence: 0.854732552333333

00:24:23.063 --> 00:24:25.070 of the fibers is more aligned.

NOTE Confidence: 0.854732552333333

00:24:25.070 --> 00:24:27.090 Fewer colors means fewer directions

NOTE Confidence: 0.854732552333333

00:24:27.090 --> 00:24:29.590 of the fibers and issue reconstitutes

NOTE Confidence: 0.854732552333333

00:24:29.590 --> 00:24:32.014 us by adding back happened once

NOTE Confidence: 0.854732552333333

00:24:32.014 --> 00:24:34.876 you can start to increase the multi

NOTE Confidence: 0.854732552333333

00:24:34.876 --> 00:24:37.606 directionality of these fibers again

NOTE Confidence: 0.854732552333333

00:24:37.610 --> 00:24:39.302 we can do the opposite experiment

NOTE Confidence: 0.854732552333333

00:24:39.302 --> 00:24:42.030 in the age so you can see that the

NOTE Confidence: 0.854732552333333

00:24:42.030 --> 00:24:43.258 age fiberglass start out.

NOTE Confidence: 0.826827033636364

00:24:43.260 --> 00:24:45.690 Looking very linear and if we

NOTE Confidence: 0.826827033636364

00:24:45.690 --> 00:24:47.680 add in recombinant happen one,

NOTE Confidence: 0.826827033636364

00:24:47.680 --> 00:24:50.062 we can now increase the multi

NOTE Confidence: 0.826827033636364

00:24:50.062 --> 00:24:51.650 directionality of the fibers.

NOTE Confidence: 0.826827033636364

00:24:51.650 --> 00:24:53.312 If we first boiled it happened

NOTE Confidence: 0.826827033636364

00:24:53.312 --> 00:24:54.640 one before adding it in.

NOTE Confidence: 0.826827033636364

00:24:54.640 --> 00:24:55.728 It doesn't do that,

NOTE Confidence: 0.826827033636364

00:24:55.728 --> 00:24:57.851 so it tells us that it really

NOTE Confidence: 0.826827033636364

00:24:57.851 --> 00:24:59.956 requires to happen one activity.

NOTE Confidence: 0.826827033636364

00:24:59.960 --> 00:25:01.745 A man wanted to know what that

NOTE Confidence: 0.826827033636364

00:25:01.745 --> 00:25:03.239 meant for the invasion of

NOTE Confidence: 0.826827033636364

00:25:03.239 --> 00:25:04.899 the Melanoma cells in vitro,

NOTE Confidence: 0.826827033636364

00:25:04.900 --> 00:25:06.970 and so she looked at.

NOTE Confidence: 0.826827033636364

00:25:06.970 --> 00:25:08.960 She added in recombinant happen

NOTE Confidence: 0.826827033636364

00:25:08.960 --> 00:25:10.950 one into reconstructs made with

NOTE Confidence: 0.826827033636364

00:25:11.020 --> 00:25:12.480 aged fibroblasts and showed

NOTE Confidence: 0.826827033636364

00:25:12.480 --> 00:25:14.305 that when she does that,

NOTE Confidence: 0.826827033636364

00:25:14.310 --> 00:25:16.956 there no longer is able to invade

NOTE Confidence: 0.826827033636364

00:25:16.956 --> 00:25:19.099 as effectively into the membrane.

NOTE Confidence: 0.826827033636364

00:25:19.100 --> 00:25:21.316 If she does the opposite where she depletes,

NOTE Confidence: 0.826827033636364

00:25:21.320 --> 00:25:23.492 happen one in the fibroblast before

NOTE Confidence: 0.826827033636364

00:25:23.492 --> 00:25:24.940 making reconstructs with them,

NOTE Confidence: 0.826827033636364

00:25:24.940 --> 00:25:27.232 they increase their ability

NOTE Confidence: 0.826827033636364

00:25:27.232 --> 00:25:30.097 to invade into the membrane.

NOTE Confidence: 0.826827033636364

00:25:30.100 --> 00:25:33.026 If we do this experiment in vivo,

NOTE Confidence: 0.826827033636364

00:25:33.030 --> 00:25:35.346 where we treat the primary tumor

NOTE Confidence: 0.826827033636364

00:25:35.346 --> 00:25:37.950 with japlan one in the age mice,

NOTE Confidence: 0.826827033636364

00:25:37.950 --> 00:25:40.862 we no longer see their these cells

NOTE Confidence: 0.826827033636364

00:25:40.862 --> 00:25:43.232 able to metastasize to the lungs

NOTE Confidence: 0.826827033636364

00:25:43.232 --> 00:25:45.661 in the age mouse versus C versus

NOTE Confidence: 0.826827033636364

00:25:45.738 --> 00:25:47.923 those mice treated with Kaplan

NOTE Confidence: 0.826827033636364

00:25:47.923 --> 00:25:50.772 one and and so we were super

NOTE Confidence: 0.826827033636364

00:25:50.772 --> 00:25:53.283 excited by those data and even

NOTE Confidence: 0.826827033636364

00:25:53.283 --> 00:25:56.132 more so when in a parallel study.

NOTE Confidence: 0.826827033636364

00:25:56.140 --> 00:25:56.716 Brett Becker,

NOTE Confidence: 0.826827033636364

00:25:56.716 --> 00:25:59.020 who is a visiting clinician to the lab,

NOTE Confidence: 0.826827033636364

00:25:59.020 --> 00:26:00.384 showed that happen one.

NOTE Confidence: 0.826827033636364

00:26:00.384 --> 00:26:03.319 Played a role not only in the metastasis

NOTE Confidence: 0.826827033636364

00:26:03.319 --> 00:26:06.182 of these cells from the primary tumor,

NOTE Confidence: 0.826827033636364

00:26:06.190 --> 00:26:08.416 but also the japlan one played a

NOTE Confidence: 0.826827033636364

00:26:08.416 --> 00:26:10.404 critical role in maintaining the

NOTE Confidence: 0.826827033636364

00:26:10.404 --> 00:26:12.809 integrity of the extracellular matrix

NOTE Confidence: 0.826827033636364

00:26:12.809 --> 00:26:14.672 around the lymphatic vasculature

NOTE Confidence: 0.826827033636364

00:26:14.672 --> 00:26:16.790 in the lymph node as well.

NOTE Confidence: 0.826827033636364

00:26:16.790 --> 00:26:18.482 And when it happened,

NOTE Confidence: 0.826827033636364

00:26:18.482 --> 00:26:20.597 1 broke down during aging

NOTE Confidence: 0.826827033636364

00:26:20.600 --> 00:26:22.532 to primary tumor cells,

NOTE Confidence: 0.826827033636364

00:26:22.532 --> 00:26:24.464 leaving the primary tumor.

NOTE Confidence: 0.826827033636364

00:26:24.470 --> 00:26:26.732 Site could escape both through the

NOTE Confidence: 0.826827033636364

00:26:26.732 --> 00:26:28.587 lymphatic vasculature and not spend

NOTE Confidence: 0.826827033636364

00:26:28.587 --> 00:26:30.547 too much time in the lymph node.

NOTE Confidence: 0.826827033636364

00:26:30.550 --> 00:26:32.258 But go on to.

NOTE Confidence: 0.826827033636364

00:26:32.258 --> 00:26:33.966 Very quickly formed visceral

NOTE Confidence: 0.826827033636364

00:26:33.966 --> 00:26:36.362 metastases so that was one of the

NOTE Confidence: 0.826827033636364

00:26:36.362 --> 00:26:38.066 studies that first showed us that

NOTE Confidence: 0.826827033636364

00:26:38.066 --> 00:26:40.362 this loss of integrity of the ECM

NOTE Confidence: 0.826827033636364

00:26:40.362 --> 00:26:42.074 during aging might actually help

NOTE Confidence: 0.826827033636364

00:26:42.074 --> 00:26:44.198 to direct the route of metastatic

NOTE Confidence: 0.826827033636364

00:26:44.198 --> 00:26:46.136 dissemination from the primary tumor.

NOTE Confidence: 0.826827033636364

00:26:46.136 --> 00:26:48.764 So taking all of those data,

NOTE Confidence: 0.826827033636364

00:26:48.770 --> 00:26:50.725 the angiogenesis data and the

NOTE Confidence: 0.826827033636364

00:26:50.725 --> 00:26:51.898 matrix data together.

NOTE Confidence: 0.826827033636364

00:26:51.900 --> 00:26:52.408 Gloria Moreno,

NOTE Confidence: 0.826827033636364

00:26:52.408 --> 00:26:54.186 who's a grad student in the lab,

NOTE Confidence: 0.826827033636364

00:26:54.190 --> 00:26:56.806 currently decided to explore this further,

NOTE Confidence: 0.826827033636364

00:26:56.810 --> 00:26:59.114 and which she saw was that if she

NOTE Confidence: 0.826827033636364

00:26:59.114 --> 00:27:01.064 stained for blood vessels, the.

NOTE Confidence: 0.826827033636364

00:27:01.064 --> 00:27:03.548 They were sitting in very different

NOTE Confidence: 0.826827033636364

00:27:03.548 --> 00:27:06.178 matrices in aged versus young skin,

NOTE Confidence: 0.826827033636364

00:27:06.180 --> 00:27:08.580 and again to remind you this is what

NOTE Confidence: 0.826827033636364

00:27:08.580 --> 00:27:11.237 the age versus young skin looks like.

NOTE Confidence: 0.826827033636364

00:27:11.240 --> 00:27:13.736 So she wanted to know whether

NOTE Confidence: 0.826827033636364

00:27:13.736 --> 00:27:16.021 that difference in these matrices

NOTE Confidence: 0.826827033636364

00:27:16.021 --> 00:27:18.177 could impact angiogenesis and

NOTE Confidence: 0.826827033636364

00:27:18.177 --> 00:27:20.872 so she embedded her endothelial

NOTE Confidence: 0.826827033636364

00:27:20.957 --> 00:27:24.101 cells in a matrix that had aged or

NOTE Confidence: 0.826827033636364

00:27:24.101 --> 00:27:26.039 young fiberglass or H fiberglass

NOTE Confidence: 0.826827033636364

00:27:26.039 --> 00:27:27.571 treated with recombinant happen

NOTE Confidence: 0.826827033636364

00:27:27.571 --> 00:27:29.962 one or young fiberglass in which

NOTE Confidence: 0.826827033636364

00:27:29.962 --> 00:27:32.302 happened one had been knocked down.

NOTE Confidence: 0.826827033636364

00:27:32.310 --> 00:27:34.764 What Gloria saw was that the

NOTE Confidence: 0.826827033636364

00:27:34.764 --> 00:27:37.321 endothelial cells in the H matrices

NOTE Confidence: 0.826827033636364

00:27:37.321 --> 00:27:39.416 had all of these sprouting.

NOTE Confidence: 0.826827033636364

00:27:39.420 --> 00:27:40.338 You know these?

NOTE Confidence: 0.826827033636364

00:27:40.338 --> 00:27:42.480 These are basically what we think of

NOTE Confidence: 0.826827033636364

00:27:42.541 --> 00:27:44.336 as little artificial blood vessels

NOTE Confidence: 0.826827033636364

00:27:44.336 --> 00:27:46.538 that are sprouting off the endothelial

NOTE Confidence: 0.826827033636364

00:27:46.538 --> 00:27:48.960 cells as compared to the young and,

NOTE Confidence: 0.826827033636364

00:27:48.960 --> 00:27:52.050 and if she treats the aged.

NOTE Confidence: 0.826827033636364

00:27:52.050 --> 00:27:54.066 And to tell your cells with

NOTE Confidence: 0.826827033636364

00:27:54.066 --> 00:27:55.410 the endothelial cells in

NOTE Confidence: 0.739018084375

00:27:55.476 --> 00:27:57.480 the age matrix with happen one,

NOTE Confidence: 0.739018084375

00:27:57.480 --> 00:28:01.050 they decrease their ability to sprout.

NOTE Confidence: 0.739018084375

00:28:01.050 --> 00:28:03.122 And if she knocks down happen one in

NOTE Confidence: 0.739018084375

00:28:03.122 --> 00:28:05.431 the young fibroblasts and then embeds

NOTE Confidence: 0.739018084375

00:28:05.431 --> 00:28:07.239 endothelial cells, are they increased?

NOTE Confidence: 0.739018084375

00:28:07.239 --> 00:28:09.852 Her ability to spot so happen one was

NOTE Confidence: 0.739018084375

00:28:09.852 --> 00:28:12.024 having a direct impact on angiogenesis,

NOTE Confidence: 0.739018084375

00:28:12.030 --> 00:28:14.246 and so when she looked at mouse tumor,

NOTE Confidence: 0.739018084375

00:28:14.250 --> 00:28:15.828 she saw the same thing again.

NOTE Confidence: 0.739018084375

00:28:15.830 --> 00:28:16.862 There's more angiogenesis

NOTE Confidence: 0.739018084375

00:28:16.862 --> 00:28:18.926 and the age versus a young,

NOTE Confidence: 0.739018084375

00:28:18.930 --> 00:28:20.730 but if she treats the age

NOTE Confidence: 0.739018084375

00:28:20.730 --> 00:28:22.840 tumors with happen one, she can.

NOTE Confidence: 0.739018084375

00:28:22.840 --> 00:28:25.570 Directly, she can reduce quite dramatically

NOTE Confidence: 0.739018084375

00:28:25.570 --> 00:28:28.289 the amount of angiogenesis ongoing,

NOTE Confidence: 0.739018084375

00:28:28.290 --> 00:28:29.061 but was interesting,

NOTE Confidence: 0.739018084375

00:28:29.061 --> 00:28:31.230 though is that when we stayed for vCard

NOTE Confidence: 0.739018084375

00:28:31.230 --> 00:28:33.144 hearing we saw something quite different.

NOTE Confidence: 0.739018084375

00:28:33.150 --> 00:28:34.932 Again, there are far more blood

NOTE Confidence: 0.739018084375

00:28:34.932 --> 00:28:37.129 vessels in the tumors in the age mikes,

NOTE Confidence: 0.739018084375

00:28:37.130 --> 00:28:38.920 however they don't stain very

NOTE Confidence: 0.739018084375

00:28:38.920 --> 00:28:40.710 well for V could hear,

NOTE Confidence: 0.739018084375

00:28:40.710 --> 00:28:43.385 and they stay beautifully for CD31,

NOTE Confidence: 0.739018084375

00:28:43.385 --> 00:28:44.210 CD 105, etc.

NOTE Confidence: 0.739018084375

00:28:44.210 --> 00:28:46.279 But the V card here in standing

NOTE Confidence: 0.739018084375

00:28:46.279 --> 00:28:48.337 is super weak compared to the

NOTE Confidence: 0.739018084375

00:28:48.337 --> 00:28:50.778 young or the age plus happen one.

NOTE Confidence: 0.739018084375

00:28:50.780 --> 00:28:52.600 So Gloria wanted to understand

NOTE Confidence: 0.739018084375

00:28:52.600 --> 00:28:54.859 that better and our hypothesis was

NOTE Confidence: 0.739018084375

00:28:54.859 --> 00:28:56.739 that young fibroblasts lay down

NOTE Confidence: 0.739018084375

00:28:56.739 --> 00:28:58.588 and matrix that endothelial cells

NOTE Confidence: 0.739018084375

00:28:58.588 --> 00:29:00.276 can anchor to really beautifully,

NOTE Confidence: 0.739018084375

00:29:00.276 --> 00:29:02.366 and that sustains the interactions

NOTE Confidence: 0.739018084375

00:29:02.366 --> 00:29:04.130 between their cells as well.

NOTE Confidence: 0.739018084375

00:29:04.130 --> 00:29:05.480 However, age fibroblasts,

NOTE Confidence: 0.739018084375

00:29:05.480 --> 00:29:07.280 that matrix is disrupted,

NOTE Confidence: 0.739018084375

00:29:07.280 --> 00:29:09.215 disrupting the integrin connections between

NOTE Confidence: 0.739018084375

00:29:09.215 --> 00:29:12.269 the age matrix and the endothelial cells.

NOTE Confidence: 0.739018084375

00:29:12.270 --> 00:29:13.658 And we hypothesize that

NOTE Confidence: 0.739018084375

00:29:13.658 --> 00:29:15.046 the cell cell interactions,

NOTE Confidence: 0.739018084375

00:29:15.050 --> 00:29:16.940 specifically V could hear it

NOTE Confidence: 0.739018084375

00:29:16.940 --> 00:29:18.452 would also be disrupted.

NOTE Confidence: 0.739018084375

00:29:18.460 --> 00:29:21.510 And so that's exactly what.

NOTE Confidence: 0.739018084375

00:29:21.510 --> 00:29:23.622 Gloria C So she laid down in dathyl

NOTE Confidence: 0.739018084375

00:29:23.622 --> 00:29:25.578 cells on matrices that she had

NOTE Confidence: 0.739018084375

00:29:25.578 --> 00:29:27.630 made from young or each fiberglass.

NOTE Confidence: 0.739018084375

00:29:27.630 --> 00:29:29.232 You can see that the endothelial

NOTE Confidence: 0.739018084375

00:29:29.232 --> 00:29:30.945 cells on the young matrices have

NOTE Confidence: 0.739018084375

00:29:30.945 --> 00:29:32.405 beautiful V card here in,

NOTE Confidence: 0.739018084375

00:29:32.410 --> 00:29:34.895 but on the age they lose these

NOTE Confidence: 0.739018084375

00:29:34.895 --> 00:29:36.470 connections and now she wanted

NOTE Confidence: 0.739018084375

00:29:36.470 --> 00:29:38.300 to manipulate happen one to sort

NOTE Confidence: 0.739018084375

00:29:38.360 --> 00:29:40.411 of not up these matrices and see

NOTE Confidence: 0.739018084375

00:29:40.411 --> 00:29:42.346 what happened if she knocks happen

NOTE Confidence: 0.739018084375

00:29:42.346 --> 00:29:44.338 one out of the young fibroblast,

NOTE Confidence: 0.739018084375

00:29:44.340 --> 00:29:45.750 they now lose their ability to

NOTE Confidence: 0.739018084375

00:29:45.750 --> 00:29:46.690 make these nice feet.

NOTE Confidence: 0.739018084375

00:29:46.690 --> 00:29:48.760 Could hearing connections and if she

NOTE Confidence: 0.739018084375

00:29:48.760 --> 00:29:51.349 adds happen one into the age fiberglass,

NOTE Confidence: 0.739018084375

00:29:51.350 --> 00:29:53.054 now the endothelial cells?

NOTE Confidence: 0.739018084375

00:29:53.054 --> 00:29:55.184 Have beautiful vegan hearing connections

NOTE Confidence: 0.739018084375

00:29:55.190 --> 00:29:57.570 so that was super exciting but she

NOTE Confidence: 0.739018084375

00:29:57.570 --> 00:29:59.968 also wanted to know did that mean

NOTE Confidence: 0.739018084375

00:29:59.968 --> 00:30:02.499 that if they have these nice tight

NOTE Confidence: 0.739018084375

00:30:02.499 --> 00:30:04.499 end vCard hearing connections,

NOTE Confidence: 0.739018084375

00:30:04.500 --> 00:30:07.062 was there barrier integrity of these

NOTE Confidence: 0.739018084375

00:30:07.062 --> 00:30:09.750 endothelial cells and to measure that?

NOTE Confidence: 0.739018084375

00:30:09.750 --> 00:30:12.902 But Gloria did was to use an electrode

NOTE Confidence: 0.739018084375

00:30:12.902 --> 00:30:16.796 assay where she ceded the CDM so the

NOTE Confidence: 0.739018084375

00:30:16.796 --> 00:30:18.308 fibroblast derived extracellular

NOTE Confidence: 0.739018084375

00:30:18.308 --> 00:30:20.920 matrix and then she played at the

NOTE Confidence: 0.739018084375

00:30:20.920 --> 00:30:23.430 endothelial cells on top of that matrix.

NOTE Confidence: 0.739018084375

00:30:23.430 --> 00:30:25.386 And then she measured the current.

NOTE Confidence: 0.739018084375

00:30:25.390 --> 00:30:27.946 So the more resistance there is,

NOTE Confidence: 0.739018084375

00:30:27.950 --> 00:30:29.870 that better the barriers are and

NOTE Confidence: 0.739018084375

00:30:29.870 --> 00:30:31.410 the tighter these interactions are.

NOTE Confidence: 0.739018084375

00:30:31.410 --> 00:30:34.280 So in in in in endothelial cells,

NOTE Confidence: 0.739018084375

00:30:34.280 --> 00:30:36.190 seated on an HTC M,

NOTE Confidence: 0.739018084375

00:30:36.190 --> 00:30:38.255 there's very little barrier integrity

NOTE Confidence: 0.739018084375

00:30:38.255 --> 00:30:41.109 on those seated on a young CDM,

NOTE Confidence: 0.739018084375

00:30:41.110 --> 00:30:42.970 there's a lot of better integrity,

NOTE Confidence: 0.739018084375

00:30:42.970 --> 00:30:45.066 and if we take our cells that are

NOTE Confidence: 0.739018084375

00:30:45.066 --> 00:30:46.270 on an aged man,

NOTE Confidence: 0.739018084375

00:30:46.270 --> 00:30:48.118 we give them half and one to not

NOTE Confidence: 0.739018084375

00:30:48.118 --> 00:30:49.040 up there matrix.

NOTE Confidence: 0.739018084375

00:30:49.040 --> 00:30:50.587 We can now see that there is

NOTE Confidence: 0.739018084375

00:30:50.587 --> 00:30:51.250 an increase in

NOTE Confidence: 0.8986207525

00:30:51.304 --> 00:30:52.230 barrier integrity.

NOTE Confidence: 0.8986207525

00:30:52.230 --> 00:30:54.078 So basically all of these data.

NOTE Confidence: 0.8986207525

00:30:54.080 --> 00:30:56.614 From Gloria so far are telling us

NOTE Confidence: 0.8986207525

00:30:56.614 --> 00:30:59.319 that the more happen one there is,

NOTE Confidence: 0.8986207525

00:30:59.320 --> 00:31:01.760 the tighter these matrices are,

NOTE Confidence: 0.8986207525

00:31:01.760 --> 00:31:03.884 the more intact these

NOTE Confidence: 0.8986207525

00:31:03.884 --> 00:31:06.539 blood vessels are as well,

NOTE Confidence: 0.8986207525

00:31:06.540 --> 00:31:08.428 which can have significant

NOTE Confidence: 0.8986207525

00:31:08.428 --> 00:31:10.316 impact for tumor cells.

NOTE Confidence: 0.8986207525

00:31:10.320 --> 00:31:12.300 Being able to invade in and out of that,

NOTE Confidence: 0.8986207525

00:31:12.300 --> 00:31:14.442 and so now what or is doing is some

NOTE Confidence: 0.8986207525

00:31:14.442 --> 00:31:16.328 very beautiful in vivo imaging of

NOTE Confidence: 0.8986207525

00:31:16.328 --> 00:31:18.533 these vessels and of the flux of

NOTE Confidence: 0.8986207525

00:31:18.533 --> 00:31:20.493 tumor cells in and out of these

NOTE Confidence: 0.8986207525

00:31:20.493 --> 00:31:23.868 vessels in these different conditions.

NOTE Confidence: 0.8986207525

00:31:23.870 --> 00:31:26.656 So I'll move on to the next

NOTE Confidence: 0.8986207525

00:31:26.656 --> 00:31:29.799 story that we recently published.

NOTE Confidence: 0.8986207525

00:31:29.800 --> 00:31:32.160 So this was work conducted by Gretchen Ellis,

NOTE Confidence: 0.8986207525

00:31:32.160 --> 00:31:33.624 CEO, who's a grad student in

NOTE Confidence: 0.8986207525

00:31:33.624 --> 00:31:34.950 my lab at the time,

NOTE Confidence: 0.8986207525

00:31:34.950 --> 00:31:38.298 and what she did was to notice that each

NOTE Confidence: 0.8986207525

00:31:38.298 --> 00:31:40.756 fiberglass made a ton of lipids and

NOTE Confidence: 0.8986207525

00:31:40.756 --> 00:31:43.490 they've created a lot of these leopards,

NOTE Confidence: 0.8986207525

00:31:43.490 --> 00:31:44.855 and when they see created

NOTE Confidence: 0.8986207525

00:31:44.855 --> 00:31:46.220 a lot of those lipids,

NOTE Confidence: 0.8986207525

00:31:46.220 --> 00:31:48.845 Melanoma cells would take those lipids up.

NOTE Confidence: 0.8986207525

00:31:48.850 --> 00:31:50.880 And so these are Melanoma cells grown

NOTE Confidence: 0.8986207525

00:31:50.880 --> 00:31:53.060 in young or each condition media,

NOTE Confidence: 0.8986207525

00:31:53.060 --> 00:31:54.596 and then simply staying.

NOTE Confidence: 0.8986207525

00:31:54.596 --> 00:31:55.748 Or for Debbie,

NOTE Confidence: 0.8986207525

00:31:55.750 --> 00:31:59.565 and if Gretchen looks at the lipidomics

NOTE Confidence: 0.8986207525

00:31:59.565 --> 00:32:02.155 of the the what is being secreted

NOTE Confidence: 0.8986207525

00:32:02.155 --> 00:32:04.420 by the young or each fiberglass,

NOTE Confidence: 0.8986207525

00:32:04.420 --> 00:32:05.640 she can see that it,

NOTE Confidence: 0.8986207525

00:32:05.640 --> 00:32:07.640 whatever age fibroblasts are secreting

NOTE Confidence: 0.8986207525

00:32:07.640 --> 00:32:09.640 Melanoma cells are taking up.

NOTE Confidence: 0.8986207525

00:32:09.640 --> 00:32:11.740 So that was super interesting and the

NOTE Confidence: 0.8986207525

00:32:11.740 --> 00:32:13.439 question there were two questions.

NOTE Confidence: 0.8986207525

00:32:13.440 --> 00:32:15.609 One what are how are they taking it up?

NOTE Confidence: 0.8986207525

00:32:15.610 --> 00:32:18.010 And two what are they doing with it?

NOTE Confidence: 0.8986207525

00:32:18.010 --> 00:32:20.481 So Gretchen looked at a bunch of

NOTE Confidence: 0.8986207525

00:32:20.481 --> 00:32:22.531 different fatty acid transporters and

NOTE Confidence: 0.8986207525

00:32:22.531 --> 00:32:25.744 identified this particular one called fat P2.

NOTE Confidence: 0.8986207525

00:32:25.750 --> 00:32:26.494 In fact,

NOTE Confidence: 0.8986207525

00:32:26.494 --> 00:32:28.726 P2 is increased in Melanoma cells

NOTE Confidence: 0.8986207525

00:32:28.726 --> 00:32:30.949 exposed to age condition media.

NOTE Confidence: 0.8986207525

00:32:30.950 --> 00:32:33.560 It's increased in Melanoma cells prone

NOTE Confidence: 0.8986207525

00:32:33.560 --> 00:32:36.380 and skin reconstructs with age fiberglass.

NOTE Confidence: 0.8986207525

00:32:36.380 --> 00:32:38.290 It's increased in Melanoma cells

NOTE Confidence: 0.8986207525

00:32:38.290 --> 00:32:41.409 that we put an age tumors in mice.

NOTE Confidence: 0.8986207525

00:32:41.410 --> 00:32:43.888 If we look at patient tumors,

NOTE Confidence: 0.8986207525

00:32:43.890 --> 00:32:45.530 this is just TSJ data.

NOTE Confidence: 0.8986207525

00:32:45.530 --> 00:32:47.582 We can see that patients over

NOTE Confidence: 0.8986207525

00:32:47.582 --> 00:32:50.587 the age of 50 are the ones who

NOTE Confidence: 0.8986207525

00:32:50.587 --> 00:32:52.921 have the most fat P2 expression.

NOTE Confidence: 0.8986207525

00:32:52.930 --> 00:32:54.760 So the other thing that we

NOTE Confidence: 0.8986207525

00:32:54.760 --> 00:32:55.980 noticed is when we.

NOTE Confidence: 0.8986207525

00:32:55.980 --> 00:32:58.647 We're standing patient tumors for Fabry 2.

NOTE Confidence: 0.8986207525

00:32:58.650 --> 00:33:01.191 We noticed that the patients who survived

NOTE Confidence: 0.8986207525

00:33:01.191 --> 00:33:03.995 UM the the shortest time after being

NOTE Confidence: 0.8986207525

00:33:03.995 --> 00:33:06.946 treated with B RAF MEK inhibitors were

NOTE Confidence: 0.8986207525

00:33:06.946 --> 00:33:10.278 patients who had very high fat P2,

NOTE Confidence: 0.8986207525

00:33:10.280 --> 00:33:12.198 so that may Gretchen asked the question,

NOTE Confidence: 0.8986207525

00:33:12.200 --> 00:33:15.352 could fat be two and lipid metabolism be

NOTE Confidence: 0.8986207525

00:33:15.352 --> 00:33:17.656 playing a role in therapy resistance?

NOTE Confidence: 0.8986207525

00:33:17.656 --> 00:33:19.871 So something we've seen before

NOTE Confidence: 0.8986207525

00:33:19.871 --> 00:33:22.260 is that patients over the age of

NOTE Confidence: 0.8986207525

00:33:22.260 --> 00:33:26.010 65 have a lower response this.

NOTE Confidence: 0.8986207525

00:33:26.010 --> 00:33:28.170 These data on this slide are single agent.

NOTE Confidence: 0.8986207525

00:33:28.170 --> 00:33:30.942 I'll show you double agent in just a second.

NOTE Confidence: 0.8986207525

00:33:30.950 --> 00:33:32.774 So this is just very rough and ebb

NOTE Confidence: 0.8986207525

00:33:32.774 --> 00:33:34.778 and these are data from the very early

NOTE Confidence: 0.8986207525

00:33:34.778 --> 00:33:36.326 trials and we found that patients

NOTE Confidence: 0.8986207525

00:33:36.326 --> 00:33:38.530 over the age of 65 in those trials

NOTE Confidence: 0.8986207525

00:33:38.530 --> 00:33:40.806 were less likely to mount a complete

NOTE Confidence: 0.8986207525

00:33:40.806 --> 00:33:43.236 response to be rough inhibitors in

NOTE Confidence: 0.8986207525

00:33:43.236 --> 00:33:45.492 patients under the age of 65 and

NOTE Confidence: 0.8986207525

00:33:45.492 --> 00:33:47.529 in our mouse studies we showed that

NOTE Confidence: 0.8986207525

00:33:47.529 --> 00:33:49.411 the exact same tumors implanted

NOTE Confidence: 0.8986207525

00:33:49.411 --> 00:33:51.691 into young mice would respond to

NOTE Confidence: 0.8986207525

00:33:51.760 --> 00:33:53.790 the venue rafanan tool compound,

NOTE Confidence: 0.808251298333333

00:33:53.790 --> 00:33:56.436 whereas those planted into age monks.

NOTE Confidence: 0.808251298333333

00:33:56.440 --> 00:33:58.462 Would not so Gretchen wanted to

NOTE Confidence: 0.808251298333333

00:33:58.462 --> 00:34:00.940 know how fat P2 could affect this

NOTE Confidence: 0.808251298333333

00:34:00.940 --> 00:34:03.397 and she wanted to do this using

NOTE Confidence: 0.808251298333333

00:34:03.477 --> 00:34:05.559 the B RAF and MEK inhibitors.

NOTE Confidence: 0.808251298333333

00:34:05.560 --> 00:34:08.862 So she created a cell line in which

NOTE Confidence: 0.808251298333333

00:34:08.862 --> 00:34:12.315 she had knocked down fat P2 and a docs

NOTE Confidence: 0.808251298333333

00:34:12.315 --> 00:34:14.979 inducible manner and what she found is

NOTE Confidence: 0.808251298333333

00:34:14.979 --> 00:34:17.746 that when she knocks down so she has

NOTE Confidence: 0.808251298333333

00:34:17.746 --> 00:34:19.790 an empty vector control and then she

NOTE Confidence: 0.808251298333333

00:34:19.853 --> 00:34:22.285 has the empty vector plus to be RAF

NOTE Confidence: 0.808251298333333

00:34:22.285 --> 00:34:24.700 MEK inhibitor and in tumors in young mice.

NOTE Confidence: 0.808251298333333

00:34:24.700 --> 00:34:26.470 Of course they respond to

NOTE Confidence: 0.808251298333333

00:34:26.470 --> 00:34:27.886 the beer afmic inhibitor.

NOTE Confidence: 0.808251298333333

00:34:27.890 --> 00:34:29.584 And after some time they grow back.

NOTE Confidence: 0.808251298333333

00:34:29.590 --> 00:34:32.254 So we've all seen this a million times.

NOTE Confidence: 0.808251298333333

00:34:32.260 --> 00:34:35.900 UM, if she now knocks down fat P2 using docs

NOTE Confidence: 0.808251298333333

00:34:35.992 --> 00:34:39.304 and treats with the B RAF MEK inhibitor,

NOTE Confidence: 0.808251298333333

00:34:39.310 --> 00:34:40.518 it's exactly the same.

NOTE Confidence: 0.808251298333333

00:34:40.518 --> 00:34:42.330 And the young Lisa tumors respond.

NOTE Confidence: 0.808251298333333

00:34:42.330 --> 00:34:44.218 They eventually grow back.

NOTE Confidence: 0.808251298333333

00:34:44.218 --> 00:34:45.974 However, in the age mice,

NOTE Confidence: 0.808251298333333

00:34:45.974 --> 00:34:47.579 it's a completely different story.

NOTE Confidence: 0.808251298333333

00:34:47.580 --> 00:34:49.764 What we see is that the tumors,

NOTE Confidence: 0.808251298333333

00:34:49.770 --> 00:34:51.634 first of all treated with B RAF MEK

NOTE Confidence: 0.808251298333333

00:34:51.634 --> 00:34:53.296 inhibitor in the age wise kind of

NOTE Confidence: 0.808251298333333

00:34:53.296 --> 00:34:54.732 just stopped growing for a little

NOTE Confidence: 0.808251298333333

00:34:54.732 --> 00:34:56.398 bit but then continue to grow so

NOTE Confidence: 0.808251298333333

00:34:56.398 --> 00:34:59.072 they they rarely respond at all.

NOTE Confidence: 0.808251298333333

00:34:59.072 --> 00:34:59.620 Uhm,

NOTE Confidence: 0.808251298333333

00:34:59.620 --> 00:35:01.804 but now she first treats them

NOTE Confidence: 0.808251298333333

00:35:01.804 --> 00:35:03.849 by knocking down the fat P2.

NOTE Confidence: 0.808251298333333

00:35:03.850 --> 00:35:06.559 You can see that those tumors basically

NOTE Confidence: 0.808251298333333

00:35:06.559 --> 00:35:08.703 go into remission and stay grimmest

NOTE Confidence: 0.808251298333333

00:35:08.703 --> 00:35:11.250 if you will for a very long time.

NOTE Confidence: 0.808251298333333

00:35:11.250 --> 00:35:13.112 So this was super exciting data to

NOTE Confidence: 0.808251298333333

00:35:13.112 --> 00:35:15.385 us 'cause it was one of the first

NOTE Confidence: 0.808251298333333

00:35:15.385 --> 00:35:17.216 incidences we really had of targeting

NOTE Confidence: 0.808251298333333

00:35:17.216 --> 00:35:19.652 this very age specific change in a

NOTE Confidence: 0.808251298333333

00:35:19.652 --> 00:35:22.342 Melanoma cell and showing that it we

NOTE Confidence: 0.808251298333333

00:35:22.342 --> 00:35:23.858 could overcome therapy resistance

NOTE Confidence: 0.808251298333333

00:35:23.928 --> 00:35:25.918 quite dramatically in this case.

NOTE Confidence: 0.808251298333333

00:35:25.920 --> 00:35:30.070 So you know, a lot of times I think that.

NOTE Confidence: 0.808251298333333

00:35:30.070 --> 00:35:30.341 We,

NOTE Confidence: 0.808251298333333

00:35:30.341 --> 00:35:30.612 UM,

NOTE Confidence: 0.808251298333333

00:35:30.612 --> 00:35:32.509 the questions are my favorite part of

NOTE Confidence: 0.808251298333333

00:35:32.509 --> 00:35:34.780 a talk because they make me think and

NOTE Confidence: 0.808251298333333

00:35:34.780 --> 00:35:36.940 they make me think about what we want

NOTE Confidence: 0.808251298333333

00:35:36.940 --> 00:35:39.642 to do in the future and out of the

NOTE Confidence: 0.808251298333333

00:35:39.642 --> 00:35:41.790 questions have come some questions about,

NOTE Confidence: 0.808251298333333

00:35:41.790 --> 00:35:42.107 well,

NOTE Confidence: 0.808251298333333

00:35:42.107 --> 00:35:44.960 you see a lot of changes in with age

NOTE Confidence: 0.808251298333333

00:35:45.044 --> 00:35:48.188 does gender or I guess tag to be

NOTE Confidence: 0.808251298333333

00:35:48.188 --> 00:35:50.189 technically correct biological sex,

NOTE Confidence: 0.808251298333333

00:35:50.190 --> 00:35:52.486 player role and so this is something

NOTE Confidence: 0.808251298333333

00:35:52.486 --> 00:35:54.787 we've just started exploring in the lab.

NOTE Confidence: 0.808251298333333

00:35:54.790 --> 00:35:56.940 We see that there are.

NOTE Confidence: 0.808251298333333

00:35:56.940 --> 00:35:58.770 We see that in Melanoma,

NOTE Confidence: 0.808251298333333

00:35:58.770 --> 00:36:00.490 there's a big difference.

NOTE Confidence: 0.808251298333333

00:36:00.490 --> 00:36:02.640 In mortality estimates in males

NOTE Confidence: 0.808251298333333

00:36:02.640 --> 00:36:03.680 versus females,

NOTE Confidence: 0.808251298333333

00:36:03.680 --> 00:36:07.032 as well as incidences in as well

NOTE Confidence: 0.808251298333333

00:36:07.032 --> 00:36:08.636 as differences in incidence,

NOTE Confidence: 0.808251298333333

00:36:08.640 --> 00:36:10.008 and so yes, chabra,

NOTE Confidence: 0.808251298333333

00:36:10.008 --> 00:36:12.659 who is a junior faculty in my lab,

NOTE Confidence: 0.808251298333333

00:36:12.660 --> 00:36:14.784 started to explore this and what

NOTE Confidence: 0.808251298333333

00:36:14.784 --> 00:36:17.245 he found was that while there

NOTE Confidence: 0.808251298333333

00:36:17.245 --> 00:36:19.193 are certainly differences between

NOTE Confidence: 0.808251298333333

00:36:19.193 --> 00:36:20.654 male and female,

NOTE Confidence: 0.808251298333333

00:36:20.660 --> 00:36:23.552 they tend to be less qualitative

NOTE Confidence: 0.808251298333333

00:36:23.552 --> 00:36:24.998 and more quantitative.

NOTE Confidence: 0.808251298333333

00:36:25.000 --> 00:36:26.209 So, for example,

NOTE Confidence: 0.808251298333333

00:36:26.209 --> 00:36:29.030 if we look at something like senescence,

NOTE Confidence: 0.808251298333333

00:36:29.030 --> 00:36:29.836 senescence increases.

NOTE Confidence: 0.808251298333333

00:36:29.836 --> 00:36:32.254 With age and both female and

NOTE Confidence: 0.808251298333333

00:36:32.254 --> 00:36:33.910 male dermal fibroblasts,

NOTE Confidence: 0.808251298333333

00:36:33.910 --> 00:36:36.304 but they it increases to a higher

NOTE Confidence: 0.808251298333333

00:36:36.304 --> 00:36:39.561 extent from the start point in the male

NOTE Confidence: 0.808251298333333

00:36:39.561 --> 00:36:41.721 fiberglass versus a female fiberglass.

NOTE Confidence: 0.808251298333333

00:36:41.730 --> 00:36:43.858 If we look at changes in lipid

NOTE Confidence: 0.808251298333333

00:36:43.858 --> 00:36:45.671 oxidation we see the same thing

NOTE Confidence: 0.808251298333333

00:36:45.671 --> 00:36:47.617 and if we look at changes in

NOTE Confidence: 0.808251298333333

00:36:47.684 --> 00:36:49.028 things like exosomal content

NOTE Confidence: 0.808251298333333

00:36:49.028 --> 00:36:51.044 so this is work done by

NOTE Confidence: 0.745573157

00:36:51.050 --> 00:36:52.210 Laura who's are who's

NOTE Confidence: 0.745573157

00:36:52.210 --> 00:36:53.950 also a postdoc in the lab,

NOTE Confidence: 0.745573157

00:36:53.950 --> 00:36:57.387 we see that again between males and

NOTE Confidence: 0.745573157

00:36:57.387 --> 00:37:00.900 females there are distinct differences.

NOTE Confidence: 0.745573157

00:37:00.900 --> 00:37:03.604 In the changes that we see in CD9,

NOTE Confidence: 0.745573157

00:37:03.610 --> 00:37:06.208 so CD9 is decreased in both

NOTE Confidence: 0.745573157

00:37:06.208 --> 00:37:08.719 males and females during aging as

NOTE Confidence: 0.745573157

00:37:08.719 --> 00:37:10.734 compared to the young exosomes.

NOTE Confidence: 0.745573157

00:37:10.740 --> 00:37:12.750 This is an EXO view chip,

NOTE Confidence: 0.745573157

00:37:12.750 --> 00:37:14.998 but we see that in the males it's

NOTE Confidence: 0.745573157

00:37:14.998 --> 00:37:16.449 far more dramatically decreased

NOTE Confidence: 0.745573157

00:37:16.449 --> 00:37:18.909 than it is in the females.

NOTE Confidence: 0.745573157

00:37:18.910 --> 00:37:22.030 If we look at the impact of these

NOTE Confidence: 0.745573157

00:37:22.030 --> 00:37:24.150 fiberglass on Melanoma cells,

NOTE Confidence: 0.745573157

00:37:24.150 --> 00:37:25.400 we see the same thing.

NOTE Confidence: 0.745573157

00:37:25.400 --> 00:37:27.312 So we see that if we treat Melanoma

NOTE Confidence: 0.745573157

00:37:27.312 --> 00:37:29.099 cells with the B RAF MEK inhibitor,

NOTE Confidence: 0.745573157

00:37:29.100 --> 00:37:30.910 this is a spheroid assay.

NOTE Confidence: 0.745573157

00:37:30.910 --> 00:37:32.870 We're just looking at survival.

NOTE Confidence: 0.745573157

00:37:32.870 --> 00:37:34.414 We see that, UM,

NOTE Confidence: 0.745573157

00:37:34.414 --> 00:37:37.263 Melanoma cells treated with B RAF MEK

NOTE Confidence: 0.745573157

00:37:37.263 --> 00:37:39.951 inhibitor and the presence of age

NOTE Confidence: 0.745573157

00:37:39.951 --> 00:37:42.895 male condition media do not die as

NOTE Confidence: 0.745573157

00:37:42.895 --> 00:37:45.169 effectively as they do when they're

NOTE Confidence: 0.745573157

00:37:45.170 --> 00:37:47.588 treated with young male condition media.

NOTE Confidence: 0.745573157

00:37:47.590 --> 00:37:48.808 So the more red you see,

NOTE Confidence: 0.745573157

00:37:48.810 --> 00:37:50.970 the more dead cells there are and the

NOTE Confidence: 0.745573157

00:37:50.970 --> 00:37:53.503 same is true for Melanoma cells treated

NOTE Confidence: 0.745573157

00:37:53.503 --> 00:37:55.428 with age female condition media.

NOTE Confidence: 0.745573157

00:37:55.430 --> 00:38:00.300 But again, the impact is not as great, so.

NOTE Confidence: 0.745573157

00:38:00.300 --> 00:38:02.659 You can see that quantified here age,

NOTE Confidence: 0.745573157

00:38:02.660 --> 00:38:04.140 Melanoma cells treated with age,

NOTE Confidence: 0.745573157

00:38:04.140 --> 00:38:06.558 male conditioned media have far less

NOTE Confidence: 0.745573157

00:38:06.558 --> 00:38:09.115 relative cell death than those treated

NOTE Confidence: 0.745573157

00:38:09.115 --> 00:38:11.290 with age female condition media.

NOTE Confidence: 0.745573157

00:38:11.290 --> 00:38:13.600 The same is also true for invasion,

NOTE Confidence: 0.745573157

00:38:13.600 --> 00:38:14.341 so in vitro,

NOTE Confidence: 0.745573157

00:38:14.341 --> 00:38:16.492 at least we see that there is an

NOTE Confidence: 0.745573157

00:38:16.492 --> 00:38:18.262 increase in invasion and Melanoma

NOTE Confidence: 0.745573157

00:38:18.262 --> 00:38:19.678 cells created with age.

NOTE Confidence: 0.745573157

00:38:19.680 --> 00:38:22.500 Males conditioned media versus

NOTE Confidence: 0.745573157

00:38:22.500 --> 00:38:25.320 age female condition media.

NOTE Confidence: 0.745573157

00:38:25.320 --> 00:38:26.900 What's been fascinating is that

NOTE Confidence: 0.745573157

00:38:26.900 --> 00:38:28.824 recently we've been able to get

NOTE Confidence: 0.745573157

00:38:28.824 --> 00:38:30.564 fiber blasts from the same people.

NOTE Confidence: 0.745573157

00:38:30.570 --> 00:38:32.310 So they're genetically identical,

NOTE Confidence: 0.745573157

00:38:32.310 --> 00:38:34.050 and they've been collected

NOTE Confidence: 0.745573157

00:38:34.050 --> 00:38:35.759 20 plus years apart,

NOTE Confidence: 0.745573157

00:38:35.760 --> 00:38:37.976 and where what we're seeing is that even

NOTE Confidence: 0.745573157

00:38:37.976 --> 00:38:39.895 within the same individual that's now

NOTE Confidence: 0.745573157

00:38:39.895 --> 00:38:42.130 reflecting some of the changes we see,

NOTE Confidence: 0.745573157

00:38:42.130 --> 00:38:43.530 so that's been super exciting.

NOTE Confidence: 0.745573157

00:38:43.530 --> 00:38:45.644 So here within the males you can

NOTE Confidence: 0.745573157

00:38:45.644 --> 00:38:48.018 see that there is a distinct impact

NOTE Confidence: 0.745573157

00:38:48.018 --> 00:38:49.768 in the increase in invasion.

NOTE Confidence: 0.745573157

00:38:49.770 --> 00:38:53.310 This is two different men.

NOTE Confidence: 0.745573157

00:38:53.310 --> 00:38:55.105 Their fibroblast taken over 20

NOTE Confidence: 0.745573157

00:38:55.105 --> 00:38:57.627 years apart in each case in the

NOTE Confidence: 0.745573157

00:38:57.627 --> 00:38:59.589 females again the trend is there,

NOTE Confidence: 0.745573157

00:38:59.590 --> 00:39:00.990 but it's not as dramatic as it

NOTE Confidence: 0.745573157

00:39:00.990 --> 00:39:01.900 is in the mail,

NOTE Confidence: 0.745573157

00:39:01.900 --> 00:39:04.246 and that's sort of a constant

NOTE Confidence: 0.745573157

00:39:04.246 --> 00:39:06.310 theme that we see here.

NOTE Confidence: 0.745573157

00:39:06.310 --> 00:39:06.775 Uhm,

NOTE Confidence: 0.745573157

00:39:06.775 --> 00:39:09.565 Yash also did the in vivo

NOTE Confidence: 0.745573157

00:39:09.565 --> 00:39:12.192 experiment where he took a young.

NOTE Confidence: 0.745573157

00:39:12.192 --> 00:39:14.859 He took both the Yum cells which

NOTE Confidence: 0.745573157

00:39:14.859 --> 00:39:17.327 are male and these PST 9AJ2 cells

NOTE Confidence: 0.745573157

00:39:17.327 --> 00:39:19.600 which are female and he sort of did

NOTE Confidence: 0.745573157

00:39:19.600 --> 00:39:21.210 the crisscross experiment where he

NOTE Confidence: 0.745573157

00:39:21.210 --> 00:39:23.326 put them both in male and female

NOTE Confidence: 0.745573157

00:39:23.326 --> 00:39:25.940 or both in and these both male and

NOTE Confidence: 0.745573157

00:39:25.940 --> 00:39:28.602 female and what he sees again over

NOTE Confidence: 0.745573157

00:39:28.602 --> 00:39:31.258 and over again is that when he puts

NOTE Confidence: 0.745573157

00:39:31.258 --> 00:39:34.754 the Yum cells in young versus age male again,

NOTE Confidence: 0.745573157

00:39:34.760 --> 00:39:37.180 they grow far more slowly.

NOTE Confidence: 0.745573157

00:39:37.180 --> 00:39:40.920 But if he does this in females in the yums,

NOTE Confidence: 0.745573157

00:39:40.920 --> 00:39:42.348 there's a little bit of a difference.

NOTE Confidence: 0.745573157

00:39:42.350 --> 00:39:44.558 But in the female to female

NOTE Confidence: 0.745573157

00:39:44.558 --> 00:39:46.030 there's very little difference,

NOTE Confidence: 0.745573157

00:39:46.030 --> 00:39:48.788 although again there is a big difference

NOTE Confidence: 0.745573157

00:39:48.788 --> 00:39:51.307 between the way the age males bro.

NOTE Confidence: 0.745573157

00:39:51.310 --> 00:39:53.566 If he looks at Ki 67,

NOTE Confidence: 0.745573157

00:39:53.570 --> 00:39:55.538 he sees that the tumors are

NOTE Confidence: 0.745573157

00:39:55.538 --> 00:39:56.850 proliferating far less in

NOTE Confidence: 0.851640780454546

00:39:56.919 --> 00:39:58.479 the age male mice than they

NOTE Confidence: 0.851640780454546

00:39:58.479 --> 00:40:00.330 are in the age female mice,

NOTE Confidence: 0.851640780454546

00:40:00.330 --> 00:40:02.430 so telling us again that there are

NOTE Confidence: 0.851640780454546

00:40:02.430 --> 00:40:04.047 distinct differences in the micro

NOTE Confidence: 0.851640780454546

00:40:04.047 --> 00:40:06.027 environments between the male and female,

NOTE Confidence: 0.851640780454546

00:40:06.030 --> 00:40:07.549 and we're still trying to figure out.

NOTE Confidence: 0.851640780454546

00:40:07.550 --> 00:40:09.833 Actually, what those differences are, we

NOTE Confidence: 0.851640780454546

00:40:09.833 --> 00:40:11.884 see that there are changes in angiogenesis.

NOTE Confidence: 0.851640780454546

00:40:11.890 --> 00:40:13.550 Again, the same story.

NOTE Confidence: 0.851640780454546

00:40:13.550 --> 00:40:15.625 There's more angiogenesis with aging,

NOTE Confidence: 0.851640780454546

00:40:15.630 --> 00:40:17.688 but again, it's more dramatic in the

NOTE Confidence: 0.851640780454546

00:40:17.688 --> 00:40:19.698 males than it is in the females.

NOTE Confidence: 0.851640780454546

00:40:19.700 --> 00:40:21.540 If we look at metastasis,

NOTE Confidence: 0.851640780454546

00:40:21.540 --> 00:40:24.970 we see the same thing where we

NOTE Confidence: 0.851640780454546

00:40:24.970 --> 00:40:27.788 have more metastasis in the males.

NOTE Confidence: 0.851640780454546

00:40:27.790 --> 00:40:29.980 Actually, I take that back.

NOTE Confidence: 0.851640780454546

00:40:29.980 --> 00:40:32.346 The one thing that's not as different,

NOTE Confidence: 0.851640780454546

00:40:32.350 --> 00:40:34.576 and so these were earlier data,

NOTE Confidence: 0.851640780454546

00:40:34.580 --> 00:40:37.712 we have more data now from about 20 miles.

NOTE Confidence: 0.851640780454546

00:40:37.720 --> 00:40:39.883 And we're now seeing that there is

NOTE Confidence: 0.851640780454546

00:40:39.883 --> 00:40:42.137 actually not much of a difference in

NOTE Confidence: 0.851640780454546

00:40:42.137 --> 00:40:44.570 invasion between age males and age females.

NOTE Confidence: 0.851640780454546

00:40:44.570 --> 00:40:46.488 So that's going to be really interesting

NOTE Confidence: 0.851640780454546

00:40:46.488 --> 00:40:48.908 to sort of tease out because we're seeing

NOTE Confidence: 0.851640780454546

00:40:48.908 --> 00:40:51.199 so many differences in the growth rates.

NOTE Confidence: 0.851640780454546

00:40:51.200 --> 00:40:52.484 So just to summarize,

NOTE Confidence: 0.851640780454546

00:40:52.484 --> 00:40:54.993 some of the key changes we've seen

NOTE Confidence: 0.851640780454546

00:40:54.993 --> 00:40:57.069 female dermal fiberglass undergo

NOTE Confidence: 0.851640780454546

00:40:57.069 --> 00:40:58.626 early replicative senescent,

NOTE Confidence: 0.851640780454546

00:40:58.630 --> 00:41:01.336 so there's elevated Ross in the

NOTE Confidence: 0.851640780454546

00:41:01.336 --> 00:41:03.140 age male dermal fibroblasts,

NOTE Confidence: 0.851640780454546

00:41:03.140 --> 00:41:05.876 but female dermal fiberglass are better

NOTE Confidence: 0.851640780454546

00:41:05.876 --> 00:41:08.561 equipped with repairing the Ross and.

NOTE Confidence: 0.851640780454546

00:41:08.561 --> 00:41:10.094 Age male fibroblast.

NOTE Confidence: 0.851640780454546

00:41:10.094 --> 00:41:12.138 Promote invasion and therapy

NOTE Confidence: 0.851640780454546

00:41:12.138 --> 00:41:15.048 resistance in Melanoma cells in vitro.

NOTE Confidence: 0.851640780454546

00:41:15.050 --> 00:41:17.396 However, both age male and aged.

NOTE Confidence: 0.851640780454546

00:41:17.400 --> 00:41:19.808 Female drive invasion and

NOTE Confidence: 0.851640780454546

00:41:19.808 --> 00:41:22.216 therapy resistance in vivo.

NOTE Confidence: 0.851640780454546

00:41:22.220 --> 00:41:25.136 And finally, we're moving beyond Melanoma.

NOTE Confidence: 0.851640780454546

00:41:25.140 --> 00:41:26.996 I know this is a Melanoma sport talk,

NOTE Confidence: 0.851640780454546

00:41:27.000 --> 00:41:28.236 so I'll be very quick here,

NOTE Confidence: 0.851640780454546

00:41:28.240 --> 00:41:29.896 but we're super excited to be

NOTE Confidence: 0.851640780454546

00:41:29.896 --> 00:41:31.719 working with my dear friend list.

NOTE Confidence: 0.851640780454546

00:41:31.720 --> 00:41:33.344 Jaffe, Huerco, mentoring guns.

NOTE Confidence: 0.851640780454546

00:41:33.344 --> 00:41:36.868 Bronski is a very talented he monk fellow UM,

NOTE Confidence: 0.851640780454546

00:41:36.870 --> 00:41:40.334 and what we've done is to obtain human,

NOTE Confidence: 0.851640780454546

00:41:40.340 --> 00:41:41.795 young age pancreatic fibroblasts and

NOTE Confidence: 0.851640780454546

00:41:41.795 --> 00:41:44.545 do a lot of the same assets we're doing

NOTE Confidence: 0.851640780454546

00:41:44.545 --> 00:41:46.790 and have done with the Melanoma cells.

NOTE Confidence: 0.851640780454546

00:41:46.790 --> 00:41:50.614 And we're also using mouse models of cancer,

NOTE Confidence: 0.851640780454546

00:41:50.620 --> 00:41:52.024 both having taken.

NOTE Confidence: 0.851640780454546

00:41:52.024 --> 00:41:54.364 Young age pancreatic fibroblasts from

NOTE Confidence: 0.851640780454546

00:41:54.364 --> 00:41:56.777 these knives and using the transgenic

NOTE Confidence: 0.851640780454546

00:41:56.777 --> 00:41:59.323 APC models and what Dan has seen

NOTE Confidence: 0.851640780454546

00:41:59.323 --> 00:42:01.836 is he's already started to see some

NOTE Confidence: 0.851640780454546

00:42:01.836 --> 00:42:03.314 really super interesting stuff,

NOTE Confidence: 0.851640780454546

00:42:03.314 --> 00:42:05.953 so if he takes pancreatic cancer cells,

NOTE Confidence: 0.851640780454546

00:42:05.960 --> 00:42:07.076 human pancreatic cancer cells

NOTE Confidence: 0.851640780454546

00:42:07.076 --> 00:42:08.750 and treats them with young age,

NOTE Confidence: 0.851640780454546

00:42:08.750 --> 00:42:10.112 fiberglass conditioned media,

NOTE Confidence: 0.851640780454546

00:42:10.112 --> 00:42:12.836 he sees that actually they increased

NOTE Confidence: 0.851640780454546

00:42:12.836 --> 00:42:15.118 their proliferation quite rapidly.

NOTE Confidence: 0.851640780454546

00:42:15.120 --> 00:42:17.586 They have an increased and invasion.

NOTE Confidence: 0.851640780454546

00:42:17.590 --> 00:42:19.906 It's not very dramatic in vitro,

NOTE Confidence: 0.851640780454546

00:42:19.910 --> 00:42:21.290 but when we look in vivo,

NOTE Confidence: 0.851640780454546

00:42:21.290 --> 00:42:22.879 what we see is in the KPC.

NOTE Confidence: 0.851640780454546

00:42:22.880 --> 00:42:25.504 Model that we put into 18 month old

NOTE Confidence: 0.851640780454546

00:42:25.504 --> 00:42:27.498 mice compared to 8 week old mice.

NOTE Confidence: 0.851640780454546

00:42:27.500 --> 00:42:29.985 The tumors grow very grow up very

NOTE Confidence: 0.851640780454546

00:42:29.985 --> 00:42:32.565 rapidly in the age mice as compared

NOTE Confidence: 0.851640780454546

00:42:32.565 --> 00:42:34.005 to the young mice.

NOTE Confidence: 0.851640780454546

00:42:34.010 --> 00:42:36.522 If he looks at angiogenesis as far more

NOTE Confidence: 0.851640780454546

00:42:36.522 --> 00:42:38.285 angiogenesis and the tumors of the

NOTE Confidence: 0.851640780454546

00:42:38.285 --> 00:42:40.240 age mice compared to the young mice.

NOTE Confidence: 0.851640780454546

00:42:40.240 --> 00:42:43.216 And now if he looks at the metastases,

NOTE Confidence: 0.851640780454546

00:42:43.220 --> 00:42:45.038 he sees that there's far more

NOTE Confidence: 0.851640780454546

00:42:45.038 --> 00:42:46.881 metastases in general to the different

NOTE Confidence: 0.851640780454546

00:42:46.881 --> 00:42:48.883 sites and the age mice than there

NOTE Confidence: 0.851640780454546

00:42:48.883 --> 00:42:50.237 are in the young life.

NOTE Confidence: 0.851640780454546

00:42:50.240 --> 00:42:53.039 So that has been super exciting to see these.

NOTE Confidence: 0.851640780454546

00:42:53.040 --> 00:42:54.768 Kind of data holding up in

NOTE Confidence: 0.851640780454546

00:42:54.768 --> 00:42:55.920 a whole different cancer

NOTE Confidence: 0.888865881666666

00:42:55.978 --> 00:42:57.990 as well, and I'm excited to explore

NOTE Confidence: 0.888865881666666

00:42:57.990 --> 00:43:00.569 this and tell you more about it later,

NOTE Confidence: 0.888865881666666

00:43:00.570 --> 00:43:03.126 so I hope at this point I haven't run

NOTE Confidence: 0.888865881666666

00:43:03.126 --> 00:43:05.012 overtime and I hope I've convinced

NOTE Confidence: 0.888865881666666

00:43:05.012 --> 00:43:07.300 you that the aging micro environment

NOTE Confidence: 0.888865881666666

00:43:07.300 --> 00:43:09.952 is critical to consider when you're

NOTE Confidence: 0.888865881666666

00:43:09.952 --> 00:43:11.720 designing your preclinical studies.

NOTE Confidence: 0.888865881666666

00:43:11.720 --> 00:43:13.570 And when you're treating patients,

NOTE Confidence: 0.888865881666666

00:43:13.570 --> 00:43:15.299 I've told you a little bit about

NOTE Confidence: 0.888865881666666

00:43:15.299 --> 00:43:17.020 how things like the matrix change.

NOTE Confidence: 0.888865881666666

00:43:17.020 --> 00:43:19.350 Andrew Genesis changes in metabolism

NOTE Confidence: 0.888865881666666

00:43:19.350 --> 00:43:22.135 as well as metastasis and all

NOTE Confidence: 0.888865881666666

00:43:22.135 --> 00:43:24.642 of these are impacted by.

NOTE Confidence: 0.888865881666666

00:43:24.642 --> 00:43:28.650 Fiberglass, specifically aging fiberglass.

NOTE Confidence: 0.888865881666666

00:43:28.650 --> 00:43:29.840 These did the wonderful people

NOTE Confidence: 0.888865881666666

00:43:29.840 --> 00:43:31.030 who do all the work.

NOTE Confidence: 0.888865881666666

00:43:31.030 --> 00:43:32.848 I've tried to call them out as I go,

NOTE Confidence: 0.888865881666666

00:43:32.850 --> 00:43:35.274 but really the lab is a team and

NOTE Confidence: 0.888865881666666

00:43:35.274 --> 00:43:37.159 works very closely together.

NOTE Confidence: 0.888865881666666

00:43:37.160 --> 00:43:39.792 I've been so happy or at Hopkins the

NOTE Confidence: 0.888865881666666

00:43:39.792 --> 00:43:41.925 last couple of years that I've been

NOTE Confidence: 0.888865881666666

00:43:41.925 --> 00:43:44.859 here and I have a whole cadre of

NOTE Confidence: 0.888865881666666

00:43:44.859 --> 00:43:47.289 amazing collaborators from engineers to

NOTE Confidence: 0.888865881666666

00:43:47.289 --> 00:43:49.398 immunologists to buy informatics experts.

NOTE Confidence: 0.888865881666666

00:43:49.398 --> 00:43:52.030 It's really been a lot of fun.

NOTE Confidence: 0.888865881666666

00:43:52.030 --> 00:43:53.866 Uhm, I'm also very lucky 'cause

NOTE Confidence: 0.888865881666666

00:43:53.866 --> 00:43:56.009 Melanoma is such a global effort.

NOTE Confidence: 0.888865881666666

00:43:56.010 --> 00:43:58.560 We have collaborators all around,

NOTE Confidence: 0.888865881666666

00:43:58.560 --> 00:44:00.150 like I say across the street,

NOTE Confidence: 0.888865881666666

00:44:00.150 --> 00:44:02.530 across the country and across the world.

NOTE Confidence: 0.888865881666666

00:44:02.530 --> 00:44:04.342 I usually end with the picture

NOTE Confidence: 0.888865881666666

00:44:04.342 --> 00:44:05.970 of my favorite agent study,

NOTE Confidence: 0.888865881666666

00:44:05.970 --> 00:44:08.790 which is my daughter who is now 16 and a

NOTE Confidence: 0.888865881666666

00:44:08.860 --> 00:44:11.604 half almost 17 and looking at colleges,

NOTE Confidence: 0.888865881666666

00:44:11.610 --> 00:44:14.053 which is just about breaking my heart

NOTE Confidence: 0.888865881666666

00:44:14.053 --> 00:44:17.199 to think of her leaving and I will

NOTE Confidence: 0.888865881666666

00:44:17.199 --> 00:44:20.730 end as I always do as Marcus said,

NOTE Confidence: 0.888865881666666

00:44:20.730 --> 00:44:24.210 promoting diversity. And women in science.

NOTE Confidence: 0.888865881666666

00:44:24.210 --> 00:44:27.157 You know women, especially women of color,

NOTE Confidence: 0.888865881666666

00:44:27.160 --> 00:44:29.080 really earn a tiny percentage

NOTE Confidence: 0.888865881666666

00:44:29.080 --> 00:44:30.616 of even bachelors degree.

NOTE Confidence: 0.888865881666666

00:44:30.620 --> 00:44:32.425 And when you think about PHD's,

NOTE Confidence: 0.888865881666666

00:44:32.425 --> 00:44:34.495 this is an even smaller percentage.

NOTE Confidence: 0.888865881666666

00:44:34.500 --> 00:44:36.940 If any of you are interested in my

NOTE Confidence: 0.888865881666666

00:44:36.940 --> 00:44:39.406 dear friend Danita Brady and I have

NOTE Confidence: 0.888865881666666

00:44:39.406 --> 00:44:41.860 written a commentary in cancer discovery

NOTE Confidence: 0.888865881666666

00:44:41.860 --> 00:44:44.190 with some actually actionable items

NOTE Confidence: 0.888865881666666

00:44:44.190 --> 00:44:46.520 and interesting websites and reading

NOTE Confidence: 0.888865881666666

00:44:46.591 --> 00:44:48.726 material if you're interested in

NOTE Confidence: 0.888865881666666

00:44:48.726 --> 00:44:50.746 promoting diversity in your local

NOTE Confidence: 0.888865881666666

00:44:50.746 --> 00:44:53.168 community as well. So I'll stop there.

NOTE Confidence: 0.888865881666666

00:44:53.168 --> 00:44:54.636 Really take any questions.

NOTE Confidence: 0.888865881666666

00:44:54.640 --> 00:44:55.700 Thank you so much.

NOTE Confidence: 0.885921965

00:44:59.160 --> 00:45:01.566 Thanks Ashley, that was really great

NOTE Confidence: 0.885921965

00:45:01.570 --> 00:45:05.881 and what I'd like to do is invite folks

NOTE Confidence: 0.885921965

00:45:05.881 --> 00:45:10.466 to come to post questions in the chat.

NOTE Confidence: 0.885921965

00:45:10.470 --> 00:45:12.390 I don't think we have a Q&A area,

NOTE Confidence: 0.885921965

00:45:12.390 --> 00:45:16.431 so I see one already from Harriet Cougar and

NOTE Confidence: 0.885921965

00:45:16.431 --> 00:45:20.988 I will read that and so it is welcome here.

NOTE Confidence: 0.885921965

00:45:20.990 --> 00:45:22.466 Thank you for a terrific talk.

NOTE Confidence: 0.885921965

00:45:22.470 --> 00:45:25.006 Do you think we should be looking at

NOTE Confidence: 0.885921965

00:45:25.006 --> 00:45:27.593 old versus young in a binarized fashion

NOTE Confidence: 0.885921965

00:45:27.593 --> 00:45:30.159 and young versus old humans and mice?

NOTE Confidence: 0.885921965

00:45:30.160 --> 00:45:32.260 Do you think there is a difference

NOTE Confidence: 0.885921965

00:45:32.260 --> 00:45:33.760 between old and very old?

NOTE Confidence: 0.885921965

00:45:33.760 --> 00:45:37.430 And that's real question, harrietta.

NOTE Confidence: 0.885921965

00:45:37.430 --> 00:45:38.466 You know, from my point of view,

NOTE Confidence: 0.885921965

00:45:38.470 --> 00:45:39.700 that changes as I get older.

NOTE Confidence: 0.885921965

00:45:39.700 --> 00:45:42.064 But what does that mean?

NOTE Confidence: 0.885921965

00:45:42.064 --> 00:45:44.882 But anyway, I think I was going to

NOTE Confidence: 0.885921965

00:45:44.882 --> 00:45:47.375 ask a similar question about you

NOTE Confidence: 0.885921965

00:45:47.375 --> 00:45:49.785 had shown that bevacizumab study

NOTE Confidence: 0.885921965

00:45:49.790 --> 00:45:51.420 re looking at clinical data.

NOTE Confidence: 0.885921965

00:45:51.420 --> 00:45:53.982 Should we be looking at all clinical

NOTE Confidence: 0.885921965

00:45:53.982 --> 00:45:56.567 data and trials in a similar manner?

NOTE Confidence: 0.905031192727273

00:45:57.290 --> 00:45:59.120 So my bias to that last

NOTE Confidence: 0.905031192727273

00:45:59.120 --> 00:46:00.680 question of course is yes.

NOTE Confidence: 0.905031192727273

00:46:00.680 --> 00:46:02.717 I do think we should be looking

NOTE Confidence: 0.905031192727273

00:46:02.717 --> 00:46:04.863 at all clinical data according

NOTE Confidence: 0.905031192727273

00:46:04.863 --> 00:46:07.468 you know according to age.

NOTE Confidence: 0.905031192727273

00:46:07.470 --> 00:46:10.650 To answer Harriet's question specifically,

NOTE Confidence: 0.905031192727273

00:46:10.650 --> 00:46:12.960 you know what we, although I often

NOTE Confidence: 0.905031192727273

00:46:12.960 --> 00:46:14.809 present the results as binarized.

NOTE Confidence: 0.905031192727273

00:46:14.810 --> 00:46:17.170 What we really do is to look at

NOTE Confidence: 0.905031192727273

00:46:17.170 --> 00:46:20.186 it in bins so we have our under 50

NOTE Confidence: 0.905031192727273

00:46:20.186 --> 00:46:23.130 age group are 50 to 65 or over 65.

NOTE Confidence: 0.905031192727273

00:46:23.130 --> 00:46:25.754 To answer your question about old and

NOTE Confidence: 0.905031192727273

00:46:25.754 --> 00:46:28.904 very old we call them aged and super aged.

NOTE Confidence: 0.905031192727273

00:46:28.910 --> 00:46:29.993 In the lab.

NOTE Confidence: 0.905031192727273

00:46:29.993 --> 00:46:31.437 There are definitely differences

NOTE Confidence: 0.905031192727273

00:46:31.437 --> 00:46:33.468 and the reason we even started

NOTE Confidence: 0.905031192727273

00:46:33.468 --> 00:46:35.526 looking at that is 'cause if you

NOTE Confidence: 0.905031192727273

00:46:35.587 --> 00:46:37.669 look at the incidence of Melanoma.

NOTE Confidence: 0.905031192727273

00:46:37.670 --> 00:46:39.987 Right, there's this bell curve where

NOTE Confidence: 0.905031192727273

00:46:39.987 --> 00:46:41.490 it kind of goes up and up and up,

NOTE Confidence: 0.905031192727273

00:46:41.490 --> 00:46:42.618 and then suddenly,

NOTE Confidence: 0.905031192727273

00:46:42.618 --> 00:46:45.210 after like 8085 the incidence drops off,

NOTE Confidence: 0.905031192727273

00:46:45.210 --> 00:46:47.010 the mortality rates drop off

NOTE Confidence: 0.905031192727273

00:46:47.010 --> 00:46:48.450 and the question is,

NOTE Confidence: 0.905031192727273

00:46:48.450 --> 00:46:50.122 you know if you if you get that

NOTE Confidence: 0.905031192727273

00:46:50.122 --> 00:46:52.028 old or you just a super survivor.

NOTE Confidence: 0.905031192727273

00:46:52.030 --> 00:46:54.100 There's a lot more going on.

NOTE Confidence: 0.905031192727273

00:46:54.100 --> 00:46:56.788 Or is there something actually physical?

NOTE Confidence: 0.905031192727273

00:46:56.790 --> 00:46:57.903 So for example,

NOTE Confidence: 0.905031192727273

00:46:57.903 --> 00:47:00.129 one of the physical changes we've

NOTE Confidence: 0.905031192727273

00:47:00.129 --> 00:47:02.364 seen are that you know if you

NOTE Confidence: 0.905031192727273

00:47:02.364 --> 00:47:03.924 look at the biophysical matrix,

NOTE Confidence: 0.905031192727273

00:47:03.930 --> 00:47:07.780 for example, there is a bell curve.

NOTE Confidence: 0.905031192727273

00:47:07.780 --> 00:47:11.070 Of how a cell can make its way through that.

NOTE Confidence: 0.905031192727273

00:47:11.070 --> 00:47:13.030 So if you have a super stiff matrix,

NOTE Confidence: 0.905031192727273

00:47:13.030 --> 00:47:15.198 the cell can only go so far 'cause

NOTE Confidence: 0.905031192727273

00:47:15.198 --> 00:47:17.240 then nucleus gets stuck and as you

NOTE Confidence: 0.905031192727273

00:47:17.240 --> 00:47:19.307 decrease the density of that matrix the

NOTE Confidence: 0.905031192727273

00:47:19.307 --> 00:47:21.813 cell starts to be able to move through it.

NOTE Confidence: 0.905031192727273

00:47:21.813 --> 00:47:23.757 But if you decrease it too far then

NOTE Confidence: 0.905031192727273

00:47:23.757 --> 00:47:25.961 it's got nothing to hold onto and it

NOTE Confidence: 0.905031192727273

00:47:25.961 --> 00:47:28.000 kind of flounders as if it's in a soup.

NOTE Confidence: 0.905031192727273

00:47:28.000 --> 00:47:30.758 So that's sort of one of the

NOTE Confidence: 0.905031192727273

00:47:30.758 --> 00:47:33.371 things that we're looking at in

NOTE Confidence: 0.905031192727273

00:47:33.371 --> 00:47:36.053 context of age versus super aged.

NOTE Confidence: 0.905031192727273

00:47:36.060 --> 00:47:38.380 And there are definitely.

NOTE Confidence: 0.905031192727273

00:47:38.380 --> 00:47:38.960 Differences,

NOTE Confidence: 0.905031192727273

00:47:38.960 --> 00:47:39.408 so yes,

NOTE Confidence: 0.905031192727273

00:47:39.408 --> 00:47:40.976 we do think there is a difference

NOTE Confidence: 0.905031192727273

00:47:40.976 --> 00:47:42.850 and we are looking at some of those.

NOTE Confidence: 0.68738651

00:47:45.110 --> 00:47:48.053 And and I'll, I'll follow up on that now

NOTE Confidence: 0.68738651

00:47:48.053 --> 00:47:51.540 she you know with regard to you know,

NOTE Confidence: 0.68738651

00:47:51.540 --> 00:47:53.276 there should be a lot of data

NOTE Confidence: 0.68738651

00:47:53.276 --> 00:47:54.330 in this particular area.

NOTE Confidence: 0.68738651

00:47:54.330 --> 00:47:56.205 So AJC staging for Melanoma

NOTE Confidence: 0.68738651

00:47:56.205 --> 00:47:58.080 has been in existence for,

NOTE Confidence: 0.68738651

00:47:58.080 --> 00:48:00.144 you know for decades.

NOTE Confidence: 0.68738651

00:48:00.144 --> 00:48:03.372 And there are some very well characterized

NOTE Confidence: 0.68738651

00:48:03.372 --> 00:48:05.668 parameters that predict prognosis that

NOTE Confidence: 0.68738651

00:48:05.668 --> 00:48:08.194 are very closely correlated to metastasis.

NOTE Confidence: 0.68738651

00:48:08.200 --> 00:48:10.562 So one of the predictions with some

NOTE Confidence: 0.68738651

00:48:10.562 --> 00:48:12.674 of the discoveries that you've made

NOTE Confidence: 0.68738651

00:48:12.674 --> 00:48:14.930 is that with depending on like.

NOTE Confidence: 0.68738651

00:48:14.930 --> 00:48:16.530 Breslow thickness or thickness

NOTE Confidence: 0.68738651

00:48:16.530 --> 00:48:17.730 of the Melanoma.

NOTE Confidence: 0.68738651

00:48:17.730 --> 00:48:19.630 You might have different prognosis

NOTE Confidence: 0.68738651

00:48:19.630 --> 00:48:21.964 and old versus young because they're

NOTE Confidence: 0.68738651

00:48:21.964 --> 00:48:24.184 more likely to metastasize and old.

NOTE Confidence: 0.68738651

00:48:24.190 --> 00:48:26.010 I don't know if you've tried to

NOTE Confidence: 0.68738651

00:48:26.010 --> 00:48:27.539 do something like that already,

NOTE Confidence: 0.68738651

00:48:27.540 --> 00:48:30.116 or what your thoughts are about about that.

NOTE Confidence: 0.892848648

00:48:30.630 --> 00:48:32.076 Yeah, that's a great point, Marcus,

NOTE Confidence: 0.892848648

00:48:32.076 --> 00:48:34.470 so we have not yet tried to do that,

NOTE Confidence: 0.892848648

00:48:34.470 --> 00:48:39.266 only because I think we haven't really had.

NOTE Confidence: 0.892848648

00:48:39.270 --> 00:48:41.111 You know, one of the things we

NOTE Confidence: 0.892848648

00:48:41.111 --> 00:48:42.921 haven't done since we moved here

NOTE Confidence: 0.892848648

00:48:42.921 --> 00:48:44.209 is really fully established.

NOTE Confidence: 0.892848648

00:48:44.210 --> 00:48:45.554 All of the clinical.

NOTE Confidence: 0.892848648

00:48:45.554 --> 00:48:50.286 A collaboration, so we need a man and.

NOTE Confidence: 0.892848648

00:48:50.290 --> 00:48:51.990 Yeah, I mean I I,

NOTE Confidence: 0.892848648

00:48:51.990 --> 00:48:54.638 I would imagine that I mean I think

NOTE Confidence: 0.892848648

00:48:54.638 --> 00:48:57.504 even with the AJC staging age is

NOTE Confidence: 0.892848648

00:48:57.504 --> 00:48:59.881 really the overriding factor, right?

NOTE Confidence: 0.892848648

00:48:59.881 --> 00:49:04.578 So Breslow thickness is a close second,

NOTE Confidence: 0.892848648

00:49:04.580 --> 00:49:06.631 but it would be really interesting to

NOTE Confidence: 0.892848648

00:49:06.631 --> 00:49:09.180 go back and look at thin lesions and

NOTE Confidence: 0.892848648

00:49:09.180 --> 00:49:11.485 old versus young patients and see if

NOTE Confidence: 0.892848648

00:49:11.485 --> 00:49:13.363 there is an increase in metastasis.

NOTE Confidence: 0.892848648

00:49:13.370 --> 00:49:15.945 Things like certainly things like lymph

NOTE Confidence: 0.892848648

00:49:15.945 --> 00:49:18.050 node metastases are dramatically different.

NOTE Confidence: 0.892848648

00:49:18.050 --> 00:49:20.246 Were actually younger patients have more

NOTE Confidence: 0.892848648

00:49:20.246 --> 00:49:22.590 lymph node metastases than older patients,

NOTE Confidence: 0.892848648

00:49:22.590 --> 00:49:24.210 but the older patients have more

NOTE Confidence: 0.892848648

00:49:24.210 --> 00:49:25.810 visceral Mets and we you know,

NOTE Confidence: 0.892848648

00:49:25.810 --> 00:49:28.148 we think some of these disruptive changes

NOTE Confidence: 0.892848648

00:49:28.148 --> 00:49:31.180 to the matrix etc are part of that.

NOTE Confidence: 0.881891515

00:49:32.360 --> 00:49:34.114 It would be interesting to ask, you know.

NOTE Confidence: 0.881891515

00:49:34.114 --> 00:49:35.386 So like Jefferson or someone else,

NOTE Confidence: 0.881891515

00:49:35.390 --> 00:49:37.340 you know who does The Who has access to that

NOTE Confidence: 0.881891515

00:49:37.340 --> 00:49:39.888 data and have had them do it, you know?

NOTE Confidence: 0.866404185714286

00:49:41.300 --> 00:49:43.090 Great point, I'll reach out to him. That's

NOTE Confidence: 0.9305195752

00:49:43.100 --> 00:49:45.242 OK and I guess another question

NOTE Confidence: 0.9305195752

00:49:45.242 --> 00:49:48.354 I would have to is that and you

NOTE Confidence: 0.9305195752

00:49:48.354 --> 00:49:50.766 probably guess this might be question

NOTE Confidence: 0.9305195752

00:49:50.847 --> 00:49:53.664 I might ask is that it's been kind

NOTE Confidence: 0.9305195752

00:49:53.664 --> 00:49:56.164 of surprising that responses for

NOTE Confidence: 0.9305195752

00:49:56.164 --> 00:49:58.974 older versus younger patients and

NOTE Confidence: 0.9305195752

00:49:58.974 --> 00:50:01.612 Melanoma with immune checkpoint

NOTE Confidence: 0.9305195752

00:50:01.612 --> 00:50:04.935 inhibitors have been better in older

NOTE Confidence: 0.9305195752

00:50:04.935 --> 00:50:07.980 patients and and sort of that.

NOTE Confidence: 0.9305195752

00:50:07.980 --> 00:50:09.880 That also introduces a complication

NOTE Confidence: 0.9305195752

00:50:09.880 --> 00:50:11.400 in terms of survival.

NOTE Confidence: 0.9305195752

00:50:11.400 --> 00:50:13.320 Because there could be immune editing

NOTE Confidence: 0.9305195752

00:50:13.320 --> 00:50:14.980 in some older Melanoma patients

NOTE Confidence: 0.9305195752

00:50:14.980 --> 00:50:16.580 because their immune system might

NOTE Confidence: 0.9305195752

00:50:16.580 --> 00:50:18.399 be more primed to fight it,

NOTE Confidence: 0.9305195752

00:50:18.400 --> 00:50:22.056 but any thoughts about you know how the

NOTE Confidence: 0.9305195752

00:50:22.056 --> 00:50:24.619 micro environment might be affecting

NOTE Confidence: 0.9305195752

00:50:24.619 --> 00:50:27.224 those enhanced rates of response,

NOTE Confidence: 0.929814838

00:50:27.480 --> 00:50:28.840 right? It's a great question,

NOTE Confidence: 0.929814838

00:50:28.840 --> 00:50:32.518 so we think it's several full,

NOTE Confidence: 0.929814838

00:50:32.520 --> 00:50:35.306 so we published, I think back in

NOTE Confidence: 0.929814838

00:50:35.306 --> 00:50:37.356 2018 that observation right that

NOTE Confidence: 0.929814838

00:50:37.356 --> 00:50:39.696 older patients getting anti PD one

NOTE Confidence: 0.929814838

00:50:39.696 --> 00:50:42.020 do much better than younger patients.

NOTE Confidence: 0.929814838

00:50:42.020 --> 00:50:44.185 And you know, part of it is that

NOTE Confidence: 0.929814838

00:50:44.185 --> 00:50:45.330 the immune microenvironment is very

NOTE Confidence: 0.929814838

00:50:45.379 --> 00:50:46.739 different between young and age.

NOTE Confidence: 0.929814838

00:50:46.740 --> 00:50:48.994 Actually young younger patients have more T.

NOTE Confidence: 0.929814838

00:50:49.000 --> 00:50:52.780 Rex, so that CD8T rec ratio is

NOTE Confidence: 0.929814838

00:50:52.780 --> 00:50:55.065 off in the younger patients as

NOTE Confidence: 0.929814838

00:50:55.065 --> 00:50:56.810 compared to the older patients.

NOTE Confidence: 0.929814838

00:50:56.810 --> 00:50:59.169 However, our recent data and data I

NOTE Confidence: 0.929814838

00:50:59.169 --> 00:51:01.930 didn't really talk about today is how much

NOTE Confidence: 0.929814838

00:51:01.930 --> 00:51:04.180 angiogenesis is playing a role in this.

NOTE Confidence: 0.929814838

00:51:04.180 --> 00:51:06.600 And so, as you know,

NOTE Confidence: 0.929814838

00:51:06.600 --> 00:51:08.935 angiogenesis can have a quote

NOTE Confidence: 0.929814838

00:51:08.935 --> 00:51:10.803 unquote beneficial effect by

NOTE Confidence: 0.929814838

00:51:10.803 --> 00:51:13.250 being a good venue for delivery.

NOTE Confidence: 0.929814838

00:51:13.250 --> 00:51:14.801 Of immunotherapeutic agents,

NOTE Confidence: 0.929814838

00:51:14.801 --> 00:51:19.297 and so although Veg F can be a

NOTE Confidence: 0.929814838

00:51:19.297 --> 00:51:22.409 negative prognostic factor for

NOTE Confidence: 0.929814838

00:51:22.409 --> 00:51:23.965 immunotherapeutic delivery,

NOTE Confidence: 0.929814838

00:51:23.970 --> 00:51:26.329 having angiogenesis in the absence of veg.

NOTE Confidence: 0.929814838

00:51:26.330 --> 00:51:29.273 F, which is what we're seeing in the aged,

NOTE Confidence: 0.929814838

00:51:29.280 --> 00:51:31.696 seems to be sort of the sweet spot

NOTE Confidence: 0.929814838

00:51:31.696 --> 00:51:34.249 for the delivery of immunotherapy,

NOTE Confidence: 0.929814838

00:51:34.250 --> 00:51:35.671 which might just might be a part

NOTE Confidence: 0.929814838

00:51:35.671 --> 00:51:36.580 of it as well.

NOTE Confidence: 0.878398268421053

00:51:37.870 --> 00:51:39.585 Super and it's funny, 'cause I think

NOTE Confidence: 0.878398268421053

00:51:39.585 --> 00:51:42.142 a lot of people had assumed that this

NOTE Confidence: 0.878398268421053

00:51:42.142 --> 00:51:44.090 concept of immune senescence, you know,

NOTE Confidence: 0.878398268421053

00:51:44.090 --> 00:51:45.710 in older individuals might be happening,

NOTE Confidence: 0.878398268421053

00:51:45.710 --> 00:51:47.648 but it might be in specific

NOTE Confidence: 0.878398268421053

00:51:47.648 --> 00:51:49.629 subsets like T regs as you're

NOTE Confidence: 0.878398268421053

00:51:49.630 --> 00:51:52.902 mentioning the observation there.

NOTE Confidence: 0.878398268421053

00:51:52.902 --> 00:51:56.656 So I am I could go on all day,

NOTE Confidence: 0.878398268421053

00:51:56.660 --> 00:51:57.724 but here we got.

NOTE Confidence: 0.878398268421053

00:51:57.724 --> 00:51:59.320 We got a question just when

NOTE Confidence: 0.878398268421053

00:51:59.387 --> 00:52:00.791 I was getting desperate here.

NOTE Confidence: 0.878398268421053

00:52:00.791 --> 00:52:03.360 So Brenda IMO has a question in

NOTE Confidence: 0.878398268421053

00:52:03.428 --> 00:52:05.628 terms of fatty acid transporters.

NOTE Confidence: 0.878398268421053

00:52:05.630 --> 00:52:07.034 Was fat P2.

NOTE Confidence: 0.878398268421053

00:52:07.034 --> 00:52:08.906 Uniquely upregulated in tumors

NOTE Confidence: 0.878398268421053

00:52:08.906 --> 00:52:11.370 from older than individuals,

NOTE Confidence: 0.878398268421053

00:52:11.370 --> 00:52:13.610 or is this true for other fatty

NOTE Confidence: 0.878398268421053

00:52:13.610 --> 00:52:14.940 acid transporters as well,

NOTE Confidence: 0.878398268421053

00:52:14.940 --> 00:52:16.047 including like CD36,

NOTE Confidence: 0.878398268421053

00:52:16.047 --> 00:52:17.892 which there has been interest

NOTE Confidence: 0.878398268421053

00:52:17.892 --> 00:52:19.458 at Yale and as well,

NOTE Confidence: 0.878398268421053

00:52:19.460 --> 00:52:20.729 and in particular,

NOTE Confidence: 0.878398268421053

00:52:20.729 --> 00:52:22.844 are there particular lipid species

NOTE Confidence: 0.878398268421053

00:52:22.844 --> 00:52:25.089 that agent fibroblasts secrete?

NOTE Confidence: 0.943126935555556

00:52:26.420 --> 00:52:28.355 That's a great question, so we did look at.

NOTE Confidence: 0.943126935555556

00:52:28.360 --> 00:52:30.240 We looked at CD 36.

NOTE Confidence: 0.943126935555556

00:52:30.240 --> 00:52:33.168 We looked at fat P1 through six and

NOTE Confidence: 0.943126935555556

00:52:33.168 --> 00:52:36.068 the only one that was up regulated

NOTE Confidence: 0.943126935555556

00:52:36.070 --> 00:52:39.136 according to age was fat P2.

NOTE Confidence: 0.943126935555556

00:52:39.140 --> 00:52:41.002 Now that's not to say these others

NOTE Confidence: 0.943126935555556

00:52:41.002 --> 00:52:42.364 aren't upregulated simply by virtue

NOTE Confidence: 0.943126935555556

00:52:42.364 --> 00:52:43.894 of these cells being Melanoma cells.

NOTE Confidence: 0.943126935555556

00:52:43.900 --> 00:52:45.744 They are, however, fat.

NOTE Confidence: 0.943126935555556

00:52:45.744 --> 00:52:49.051 P2 is uniquely upregulated with age in

NOTE Confidence: 0.943126935555556

00:52:49.051 --> 00:52:51.799 terms of the particular lipid species,

NOTE Confidence: 0.943126935555556

00:52:51.800 --> 00:52:54.152 yes, so our lipidomics analysis showed

NOTE Confidence: 0.943126935555556

00:52:54.152 --> 00:52:57.050 us that probably the lipid species that.

NOTE Confidence: 0.943126935555556

00:52:57.050 --> 00:52:59.506 We were most interested in were Sarah mind,

NOTE Confidence: 0.943126935555556

00:52:59.510 --> 00:53:02.282 so Sir, mine seemed to be the

NOTE Confidence: 0.943126935555556

00:53:02.282 --> 00:53:03.925 most differentially expressed or

NOTE Confidence: 0.943126935555556

00:53:03.925 --> 00:53:05.830 secreted by the age fiberglass,

NOTE Confidence: 0.943126935555556

00:53:05.830 --> 00:53:08.455 the most efficiently taken up by the

NOTE Confidence: 0.943126935555556

00:53:08.455 --> 00:53:10.839 Melanoma cells in that environment,

NOTE Confidence: 0.943126935555556

00:53:10.840 --> 00:53:14.188 and the ones that have the most impact on.

NOTE Confidence: 0.943126935555556

00:53:14.190 --> 00:53:14.838 You know,

NOTE Confidence: 0.943126935555556

00:53:14.838 --> 00:53:17.106 that wasn't in the cancer Discovery paper,

NOTE Confidence: 0.943126935555556

00:53:17.110 --> 00:53:19.475 but we've shown that Ceramides

NOTE Confidence: 0.943126935555556

00:53:19.475 --> 00:53:21.840 can drive invasion and metastasis

NOTE Confidence: 0.943126935555556

00:53:21.917 --> 00:53:23.837 in Melanoma cells as well.

NOTE Confidence: 0.870101398666667

00:53:25.180 --> 00:53:26.539 Interesting question, interesting,

NOTE Confidence: 0.870101398666667

00:53:26.539 --> 00:53:28.804 it's really interesting results from

NOTE Confidence: 0.870101398666667

00:53:28.804 --> 00:53:31.236 last chance for folks to ask questions,

NOTE Confidence: 0.870101398666667

00:53:31.240 --> 00:53:34.040 as is really been a wonderful summary,

NOTE Confidence: 0.870101398666667

00:53:34.040 --> 00:53:35.117 especially for you.

NOTE Confidence: 0.870101398666667

00:53:35.117 --> 00:53:37.271 Know us at Yeles were interested

NOTE Confidence: 0.870101398666667

00:53:37.271 --> 00:53:41.200 in getting in aging center set up.

NOTE Confidence: 0.870101398666667

00:53:41.200 --> 00:53:43.208 I was I had emailed a mutual friend

NOTE Confidence: 0.870101398666667

00:53:43.208 --> 00:53:45.071 of ashes in mind so deep I don't

NOTE Confidence: 0.870101398666667

00:53:45.071 --> 00:53:46.908 know if he was able to make it.

NOTE Confidence: 0.838598025714286

00:53:49.800 --> 00:53:52.250 Don't kick them in the shins too hard,

NOTE Confidence: 0.838598025714286

00:53:52.250 --> 00:53:54.770 but anyway, I'm obviously a really

NOTE Confidence: 0.838598025714286

00:53:54.770 --> 00:53:57.428 great interest for us here. Jeff.

NOTE Confidence: 0.838598025714286

00:53:57.428 --> 00:54:00.933 Jeff Townsend also has a question I

NOTE Confidence: 0.838598025714286

00:54:00.933 --> 00:54:02.931 think I saw three fibroblast lines

NOTE Confidence: 0.838598025714286

00:54:02.931 --> 00:54:05.470 used for at least one comparison,

NOTE Confidence: 0.838598025714286

00:54:05.470 --> 00:54:07.525 and in that comparison results

NOTE Confidence: 0.838598025714286

00:54:07.525 --> 00:54:08.758 were very consistent.

NOTE Confidence: 0.838598025714286

00:54:08.760 --> 00:54:10.488 Are there any inconsistencies

NOTE Confidence: 0.838598025714286

00:54:10.488 --> 00:54:12.648 among different samples or lines?

NOTE Confidence: 0.804387368

00:54:12.680 --> 00:54:15.300 Sure, so Jeff, of course.

NOTE Confidence: 0.804387368

00:54:15.300 --> 00:54:17.156 So we, you know, for most of the

NOTE Confidence: 0.804387368

00:54:17.156 --> 00:54:18.559 experiments we've done at this point,

NOTE Confidence: 0.804387368

00:54:18.560 --> 00:54:22.186 we've used up to. Get 12 or even 15

NOTE Confidence: 0.804387368

00:54:22.186 --> 00:54:25.174 in one case different cell lines.

NOTE Confidence: 0.804387368

00:54:25.180 --> 00:54:27.850 There are definitely some inconsistencies.

NOTE Confidence: 0.804387368

00:54:27.850 --> 00:54:29.905 The most consistent inconsistency that

NOTE Confidence: 0.804387368

00:54:29.905 --> 00:54:33.503 we see is that we have some young lines

NOTE Confidence: 0.804387368

00:54:33.503 --> 00:54:36.439 that behave as if they're an old line,

NOTE Confidence: 0.804387368

00:54:36.440 --> 00:54:38.375 and when we go back and sort of dig

NOTE Confidence: 0.804387368

00:54:38.375 --> 00:54:39.990 through the history of those lines,

NOTE Confidence: 0.804387368

00:54:39.990 --> 00:54:41.808 they tend to be from young

NOTE Confidence: 0.804387368

00:54:41.808 --> 00:54:43.610 women with a tanning history.

NOTE Confidence: 0.804387368

00:54:43.610 --> 00:54:45.666 So that's another ongoing project in the lab.

NOTE Confidence: 0.804387368

00:54:45.670 --> 00:54:46.810 I didn't talk about is you?

NOTE Confidence: 0.804387368

00:54:46.810 --> 00:54:48.655 Keep looking at the effect

NOTE Confidence: 0.804387368

00:54:48.655 --> 00:54:51.050 of UV as a premature aging.

NOTE Confidence: 0.804387368

00:54:51.050 --> 00:54:53.150 Agent, so wear your sunblock,

NOTE Confidence: 0.804387368

00:54:53.150 --> 00:54:54.800 everybody, but you already know that.

NOTE Confidence: 0.96123333

00:54:56.950 --> 00:54:59.967 One question related to that is that

NOTE Confidence: 0.96123333

00:54:59.967 --> 00:55:02.985 there's including some work from Yale

NOTE Confidence: 0.96123333

00:55:02.985 --> 00:55:06.770 interest in looking at DNA methylation.

NOTE Confidence: 0.96123333

00:55:06.770 --> 00:55:10.010 Epigenetic changes as an aging clock,

NOTE Confidence: 0.96123333

00:55:10.010 --> 00:55:12.061 and have you done any looking into

NOTE Confidence: 0.96123333

00:55:12.061 --> 00:55:15.301 as to in those cases where there's a

NOTE Confidence: 0.96123333

00:55:15.301 --> 00:55:17.586 disconnect between biological between a

NOTE Confidence: 0.96123333

00:55:17.662 --> 00:55:20.187 chronological age and biological age?

NOTE Confidence: 0.96123333

00:55:20.190 --> 00:55:22.409 You know if if there's a component

NOTE Confidence: 0.96123333

00:55:22.409 --> 00:55:24.229 related to DNA methylation that

NOTE Confidence: 0.96123333

00:55:24.229 --> 00:55:26.080 might be UV induced, right,

NOTE Confidence: 0.920532395714286

00:55:26.310 --> 00:55:29.775 right so? So in terms of Melanoma,

NOTE Confidence: 0.920532395714286

00:55:29.780 --> 00:55:32.608 where just beginning to delve into that,

NOTE Confidence: 0.920532395714286

00:55:32.610 --> 00:55:34.302 however, we are collaborating

NOTE Confidence: 0.920532395714286

00:55:34.302 --> 00:55:35.994 very closely with Harris.

NOTE Confidence: 0.920532395714286

00:55:36.000 --> 00:55:38.401 Warren, who is a associate professor here

NOTE Confidence: 0.920532395714286

00:55:38.401 --> 00:55:40.840 at Hopkins who works on colon cancer,

NOTE Confidence: 0.920532395714286

00:55:40.840 --> 00:55:42.464 and we've got a lot of interesting

NOTE Confidence: 0.920532395714286

00:55:42.464 --> 00:55:43.999 data coming out of those studies,

NOTE Confidence: 0.920532395714286

00:55:44.000 --> 00:55:45.560 so I'm super excited about that.

NOTE Confidence: 0.920532395714286

00:55:45.560 --> 00:55:46.820 And of course, people like John,

NOTE Confidence: 0.920532395714286

00:55:46.820 --> 00:55:48.752 Pierre Issa and Shelly Berger have

NOTE Confidence: 0.920532395714286

00:55:48.752 --> 00:55:51.312 done a ton of work in, you know,

NOTE Confidence: 0.920532395714286

00:55:51.312 --> 00:55:52.305 understanding this epigenetic

NOTE Confidence: 0.920532395714286

00:55:52.305 --> 00:55:54.330 drift that we see during aging.

NOTE Confidence: 0.770020742833333

00:55:56.180 --> 00:55:58.721 Well, super well, I and less we

NOTE Confidence: 0.770020742833333

00:55:58.721 --> 00:56:01.069 have another last minute question.

NOTE Confidence: 0.770020742833333

00:56:01.070 --> 00:56:03.110 I would really like to thank you Ashley

NOTE Confidence: 0.770020742833333

00:56:03.110 --> 00:56:05.047 for giving us such a stimulating talk.

NOTE Confidence: 0.770020742833333

00:56:05.050 --> 00:56:06.886 Obviously generated a lot of interest.

NOTE Confidence: 0.770020742833333

00:56:06.890 --> 00:56:08.384 We're looking forward to actually having

NOTE Confidence: 0.770020742833333

00:56:08.384 --> 00:56:10.399 you here in person sometime in the future,

NOTE Confidence: 0.770020742833333

00:56:10.400 --> 00:56:12.984 but thanks so much for sharing all of

NOTE Confidence: 0.770020742833333

00:56:12.984 --> 00:56:15.498 your work and I would encourage folks

NOTE Confidence: 0.770020742833333

00:56:15.498 --> 00:56:18.050 to also read that cancer discovery.

NOTE Confidence: 0.770020742833333

00:56:18.050 --> 00:56:21.690 Yeah, article about increasing

NOTE Confidence: 0.770020742833333

00:56:21.690 --> 00:56:23.510 opportunities for.

NOTE Confidence: 0.770020742833333

00:56:23.510 --> 00:56:25.520 Scientists of color and of

NOTE Confidence: 0.770020742833333

00:56:25.520 --> 00:56:27.530 other backgrounds that are less

NOTE Confidence: 0.770020742833333

00:56:27.606 --> 00:56:29.618 advantageous to move forward.

NOTE Confidence: 0.770020742833333

00:56:29.620 --> 00:56:30.690 So thanks so much. Ashley

NOTE Confidence: 0.91174241375

00:56:30.750 --> 00:56:32.654 Marcus. Thank you so much for having

NOTE Confidence: 0.91174241375

00:56:32.654 --> 00:56:38.000 me absolutely take care. Take care.