WEBVTT

NOTE duration:"00:47:45"

NOTE recognizability:0.882

NOTE language:en-us

NOTE Confidence: 0.83336418875

00:00:00.000 --> 00:00:04.600 2 Long term colleagues and friends from Yale.

NOTE Confidence: 0.83336418875

00:00:04.600 --> 00:00:07.526 Today one is there actually speaking on

NOTE Confidence: 0.83336418875

00:00:07.526 --> 00:00:11.054 the same topic which is by which he said

NOTE Confidence: 0.83336418875

00:00:11.054 --> 00:00:13.090 degradable nanoparticles for skin cancer.

NOTE Confidence: 0.83336418875

00:00:13.090 --> 00:00:16.514 So it's great to have them here today.

NOTE Confidence: 0.83336418875

00:00:16.520 --> 00:00:20.219 And one second left to find some notes right?

NOTE Confidence: 0.83336418875

00:00:20.220 --> 00:00:22.956 OK, so our first speaker is Mark Salzman.

NOTE Confidence: 0.83336418875

00:00:22.960 --> 00:00:25.320 He's with Cela foundation professor,

NOTE Confidence: 0.83336418875

00:00:25.320 --> 00:00:27.376 biomedical engineering and professor

NOTE Confidence: 0.83336418875

00:00:27.376 --> 00:00:28.918 cellular molecular Physiology.

NOTE Confidence: 0.83336418875

00:00:28.920 --> 00:00:31.212 He focuses on trying to develop

NOTE Confidence: 0.83336418875

00:00:31.212 --> 00:00:33.540 methods for disease prevention and to

NOTE Confidence: 0.83336418875

00:00:33.540 --> 00:00:35.385 effectively deliver drugs to cells,

NOTE Confidence: 0.83336418875

00:00:35.390 --> 00:00:36.413 particularly to deliver

NOTE Confidence: 0.83336418875

00:00:36.413 --> 00:00:38.240 chemotherapy to brain tumors.

NOTE Confidence: 0.83336418875

00:00:38.240 --> 00:00:40.480 He's interested in controlled drug

NOTE Confidence: 0.83336418875

00:00:40.480 --> 00:00:42.280 delivery to brain bow polymers,

NOTE Confidence: 0.83336418875

00:00:42.280 --> 00:00:44.740 to supplement or stimulate immune function.

NOTE Confidence: 0.83336418875

00:00:44.740 --> 00:00:46.652 Still, interactions with polymers.

NOTE Confidence: 0.83336418875

00:00:46.652 --> 00:00:49.102 In tissue engineering and in fact he's

NOTE Confidence: 0.83336418875

00:00:49.102 --> 00:00:51.254 developed what is now the standard care for

NOTE Confidence: 0.83336418875

00:00:51.254 --> 00:00:53.298 treating some brain tumors is very exciting.

NOTE Confidence: 0.83336418875

00:00:53.300 --> 00:00:55.334 He will be joined today by

NOTE Confidence: 0.83336418875

00:00:55.334 --> 00:00:56.690 another colleague and friend,

NOTE Confidence: 0.83336418875

00:00:56.690 --> 00:00:57.821 Mark Mike Gerardi,

NOTE Confidence: 0.83336418875

00:00:57.821 --> 00:00:59.706 who's a professor of dermatology.

NOTE Confidence: 0.83336418875

00:00:59.710 --> 00:01:00.730 He received his MD degree

NOTE Confidence: 0.83336418875

00:01:00.730 --> 00:01:02.030 here as many of you know,

NOTE Confidence: 0.83336418875

00:01:02.030 --> 00:01:04.940 and also his clinical training here.

NOTE Confidence: 0.83336418875

00:01:04.940 --> 00:01:06.866 His principal focus of research has

NOTE Confidence: 0.83336418875

00:01:06.866 --> 00:01:08.551 been on the relationship between

NOTE Confidence: 0.83336418875

00:01:08.551 --> 00:01:10.241 the immune system and cancer

NOTE Confidence: 0.83336418875

00:01:10.241 --> 00:01:12.022 with clinical expertise in areas

NOTE Confidence: 0.83336418875

00:01:12.022 --> 00:01:13.897 including cutaneous T cell lymphoma,

NOTE Confidence: 0.83336418875

00:01:13.900 --> 00:01:18.388 squamous cell carcinoma in the and

NOTE Confidence: 0.83336418875

00:01:18.388 --> 00:01:19.884 extracorporeal photochemotherapy.

NOTE Confidence: 0.83336418875

00:01:19.890 --> 00:01:21.900 He's credited with major contributions

NOTE Confidence: 0.83336418875

00:01:21.900 --> 00:01:23.508 to understanding skin biology,

NOTE Confidence: 0.83336418875

00:01:23.510 --> 00:01:27.090 immunology and skin cancer development,

NOTE Confidence: 0.83336418875

00:01:27.090 --> 00:01:28.840 and has actually foot co-founder

NOTE Confidence: 0.83336418875

00:01:28.840 --> 00:01:31.005 of two Yale startup companies to

NOTE Confidence: 0.83336418875

00:01:31.005 --> 00:01:32.750 exploit some of these discoveries.

NOTE Confidence: 0.83336418875

00:01:32.750 --> 00:01:35.702 So today they're going to talk on a

NOTE Confidence: 0.83336418875

00:01:35.702 --> 00:01:37.985 collaboration looking at Bio case of

NOTE Confidence: 0.83336418875

00:01:37.985 --> 00:01:39.830 nanoparticles with long interest of

NOTE Confidence: 0.83336418875

00:01:39.830 --> 00:01:42.307 Doctor Salzman to treat skin cancer

NOTE Confidence: 0.83336418875

00:01:42.307 --> 00:01:44.347 along interests of Doctor Gerardi.

NOTE Confidence: 0.83336418875

00:01:44.350 --> 00:01:47.239 And so I think it will be very exciting.

NOTE Confidence: 0.83336418875

00:01:47.240 --> 00:01:48.818 Talk about a new approach that's

NOTE Confidence: 0.83336418875

00:01:48.818 --> 00:01:50.120 an alternative to fit too.

NOTE Confidence: 0.83336418875

00:01:50.120 --> 00:01:52.269 Surgery so will start out with Mark.

NOTE Confidence: 0.894057096666667

00:01:54.650 --> 00:01:56.048 Great thank you. Thank you Dan.

NOTE Confidence: 0.894057096666667

00:01:56.050 --> 00:01:59.147 It's a pleasure for me to to to be

NOTE Confidence: 0.894057096666667

00:01:59.147 --> 00:02:02.640 here and to speak in this forum again.

NOTE Confidence: 0.894057096666667

00:02:02.640 --> 00:02:05.133 I I was. I was hopeful that that this

NOTE Confidence: 0.894057096666667

00:02:05.133 --> 00:02:07.481 month we'd be back to meeting in the

NOTE Confidence: 0.894057096666667

00:02:07.481 --> 00:02:09.400 usual way where I actually have to

NOTE Confidence: 0.894057096666667

00:02:09.400 --> 00:02:11.790 stand up to give a talk but but we

NOTE Confidence: 0.894057096666667

00:02:11.790 --> 00:02:14.232 will do it this way and I look forward

NOTE Confidence: 0.894057096666667

00:02:14.232 --> 00:02:16.500 to talking to you today about this

NOTE Confidence: 0.894057096666667

00:02:16.500 --> 00:02:18.908 work that that Michael Gerardi and I

NOTE Confidence: 0.894057096666667

00:02:18.975 --> 00:02:21.160 have been collaborating on over the

NOTE Confidence: 0.894057096666667

00:02:21.160 --> 00:02:23.560 past over the past several years.

NOTE Confidence: 0.894057096666667

00:02:23.560 --> 00:02:24.796 First some.

NOTE Confidence: 0.894057096666667

00:02:24.796 --> 00:02:27.268 Financial disclosures the most

NOTE Confidence: 0.894057096666667

00:02:27.268 --> 00:02:30.999 important one here is the top one.

NOTE Confidence: 0.894057096666667

00:02:31.000 --> 00:02:33.637 Mike and I have our Co founders of a

NOTE Confidence: 0.894057096666667

00:02:33.637 --> 00:02:35.725 company called Stratified Biosciences

NOTE Confidence: 0.894057096666667

00:02:35.725 --> 00:02:38.600 which is licensed intellectual property

NOTE Confidence: 0.894057096666667

00:02:38.600 --> 00:02:40.412 to the technologies that we'll be

NOTE Confidence: 0.894057096666667

00:02:40.412 --> 00:02:42.330 talking about today and we receive

NOTE Confidence: 0.894057096666667

00:02:42.330 --> 00:02:43.960 some research funding from them.

NOTE Confidence: 0.894057096666667

00:02:43.960 --> 00:02:48.910 Next so I'll start with just a

NOTE Confidence: 0.894057096666667

00:02:48.910 --> 00:02:51.090 general introduction to both.

NOTE Confidence: 0.894057096666667

00:02:51.090 --> 00:02:53.225 Health care products that are

NOTE Confidence: 0.894057096666667

00:02:53.225 --> 00:02:54.933 collaborations of physicians and

NOTE Confidence: 0.894057096666667

00:02:54.933 --> 00:02:57.079 engineers and then to some biomaterials

NOTE Confidence: 0.894057096666667

00:02:57.079 --> 00:02:59.164 and then to the particular technology

NOTE Confidence: 0.894057096666667

00:02:59.164 --> 00:03:01.348 that we've used in this project.

NOTE Confidence: 0.894057096666667

00:03:01.350 --> 00:03:02.534 And so you know,

NOTE Confidence: 0.894057096666667

00:03:02.534 --> 00:03:04.014 general statement that you probably

NOTE Confidence: 0.894057096666667

00:03:04.014 --> 00:03:06.364 all know many of the products that

NOTE Confidence: 0.894057096666667

00:03:06.364 --> 00:03:07.696 make modern healthcare effective

NOTE Confidence: 0.894057096666667

00:03:07.753 --> 00:03:09.813 are innovations that came from

NOTE Confidence: 0.894057096666667

00:03:09.813 --> 00:03:11.049 collaborations between physicians

NOTE Confidence: 0.894057096666667

00:03:11.049 --> 00:03:13.800 and engineers and the first one I

NOTE Confidence: 0.894057096666667

00:03:13.800 --> 00:03:16.313 show here is is hemodialysis for

NOTE Confidence: 0.894057096666667

00:03:16.313 --> 00:03:18.848 treating end stage kidney disease.

NOTE Confidence: 0.894057096666667

00:03:18.850 --> 00:03:20.488 This is a medical device with

NOTE Confidence: 0.894057096666667

00:03:20.488 --> 00:03:21.580 a specially designed material.

NOTE Confidence: 0.894057096666667

00:03:21.580 --> 00:03:22.144 This is.

NOTE Confidence: 0.894057096666667

00:03:22.144 --> 00:03:23.836 Responsible for his most important function.

NOTE Confidence: 0.894057096666667

00:03:23.840 --> 00:03:25.280 In this case, it's a.

NOTE Confidence: 0.894057096666667

00:03:25.280 --> 00:03:28.150 It's a polymer hollow fiber that allows

NOTE Confidence: 0.894057096666667

00:03:28.150 --> 00:03:31.329 for separation of waste products from blood.

NOTE Confidence: 0.894057096666667

00:03:31.330 --> 00:03:33.650 The second is shown here on the on

NOTE Confidence: 0.894057096666667

00:03:33.650 --> 00:03:35.757 the right is drug eluting stent.

NOTE Confidence: 0.894057096666667

00:03:35.760 --> 00:03:37.864 This is one that's made all of polymers.

NOTE Confidence: 0.894057096666667

00:03:37.870 --> 00:03:41.890 Stents have made remarkable progress

NOTE Confidence: 0.894057096666667

00:03:41.890 --> 00:03:44.690 for treating. A vascular disease.

NOTE Confidence: 0.894057096666667

00:03:44.690 --> 00:03:46.610 This is again a medical device

NOTE Confidence: 0.894057096666667

00:03:46.610 --> 00:03:48.100 with a special function.

NOTE Confidence: 0.894057096666667

00:03:48.100 --> 00:03:49.063 In this case.

NOTE Confidence: 0.894057096666667

00:03:49.063 --> 00:03:50.989 Here there's a coating on this

NOTE Confidence: 0.894057096666667

00:03:50.989 --> 00:03:53.301 stent that slowly releases drug to

NOTE Confidence: 0.894057096666667

00:03:53.301 --> 00:03:55.226 prevent re stenosis of vessels.

NOTE Confidence: 0.894057096666667

00:03:55.230 --> 00:03:58.597 And last is a an orthopedic product.

NOTE Confidence: 0.894057096666667

00:03:58.600 --> 00:03:59.422 Another medical device.

NOTE Confidence: 0.894057096666667

00:03:59.422 --> 00:04:01.066 This one formed of two different

NOTE Confidence: 0.894057096666667

00:04:01.066 --> 00:04:01.959 kinds of materials.

NOTE Confidence: 0.894057096666667

00:04:01.960 --> 00:04:03.790 It's an artificial hip affirmative

NOTE Confidence: 0.894057096666667

00:04:03.790 --> 00:04:05.254 metal strong material so

NOTE Confidence: 0.894057096666667

00:04:05.254 --> 00:04:07.098 it can support your weight.

NOTE Confidence: 0.894057096666667

00:04:07.100 --> 00:04:08.725 But there's a polymer involved

NOTE Confidence: 0.894057096666667

00:04:08.725 --> 00:04:11.564 and you can see that as the white

NOTE Confidence: 0.894057096666667

00:04:11.564 --> 00:04:13.474 replacement for the acetabular cup,

NOTE Confidence: 0.894057096666667

00:04:13.480 --> 00:04:15.568 which provides lubrication between

NOTE Confidence: 0.894057096666667

00:04:15.568 --> 00:04:18.225 the two components of the artificial

NOTE Confidence: 0.894057096666667

00:04:18.225 --> 00:04:20.710 hip and other medical device with

NOTE Confidence: 0.894057096666667

00:04:20.710 --> 00:04:24.370 who that uses a material that's

NOTE Confidence: 0.894057096666667

00:04:24.370 --> 00:04:25.406 specially designed.

NOTE Confidence: 0.894057096666667

00:04:25.410 --> 00:04:28.368 And responsible for its most important

NOTE Confidence: 0.894057096666667

00:04:28.368 --> 00:04:30.340 function which is replacement

NOTE Confidence: 0.894057096666667

00:04:30.412 --> 00:04:32.077 of mobility in the hip.

NOTE Confidence: 0.894057096666667

00:04:32.080 --> 00:04:34.250 Now the and these products that were

NOTE Confidence: 0.894057096666667

00:04:34.250 --> 00:04:35.776 the collaborative works of teams

NOTE Confidence: 0.894057096666667

00:04:35.776 --> 00:04:37.121 of physicians and engineers have

NOTE Confidence: 0.894057096666667

00:04:37.121 --> 00:04:39.117 had a huge impact on health care,

NOTE Confidence: 0.894057096666667

00:04:39.120 --> 00:04:41.262 and you can see some evidence for that here.

NOTE Confidence: 0.844175834814815

00:04:43.910 --> 00:04:46.451 We're going to talk about using degradable

NOTE Confidence: 0.844175834814815

00:04:46.451 --> 00:04:49.241 polymers as a basis of drug delivery

NOTE Confidence: 0.844175834814815

00:04:49.241 --> 00:04:51.281 systems and the degradable polymers

NOTE Confidence: 0.844175834814815

00:04:51.281 --> 00:04:53.968 have a long history of use in medicine.

NOTE Confidence: 0.844175834814815

00:04:53.970 --> 00:04:55.328 This is an example of one that's

NOTE Confidence: 0.844175834814815

00:04:55.328 --> 00:04:56.458 been used for a long time.

NOTE Confidence: 0.844175834814815

00:04:56.460 --> 00:04:59.253 A product of ethicon's called vicryl sutures

NOTE Confidence: 0.844175834814815

00:04:59.253 --> 00:05:03.109 made of a copolymer of lactide and glycolide,

NOTE Confidence: 0.844175834814815

00:05:03.110 --> 00:05:06.225 and it's a material that has mechanical

NOTE Confidence: 0.844175834814815

00:05:06.225 --> 00:05:07.916 strength, so you can use it as a

NOTE Confidence: 0.844175834814815

00:05:07.916 --> 00:05:09.648 suture as you see on the bottom here.

NOTE Confidence: 0.844175834814815

00:05:09.650 --> 00:05:12.177 You can also use it in orthopedic

NOTE Confidence: 0.844175834814815

00:05:12.177 --> 00:05:13.653 applications by forming this

NOTE Confidence: 0.844175834814815

00:05:13.653 --> 00:05:15.288 polymer into a bone screw.

NOTE Confidence: 0.844175834814815

00:05:15.290 --> 00:05:17.062 And it remains mechanically

NOTE Confidence: 0.844175834814815

00:05:17.062 --> 00:05:18.834 strong for some period,

NOTE Confidence: 0.844175834814815

00:05:18.840 --> 00:05:20.832 typically weeks or months,

NOTE Confidence: 0.844175834814815

00:05:20.832 --> 00:05:23.322 and then it slowly degrades

NOTE Confidence: 0.844175834814815

00:05:23.322 --> 00:05:25.068 down to safe components.

NOTE Confidence: 0.844175834814815

00:05:25.068 --> 00:05:27.908 Lactic acid and glycolic acid.

NOTE Confidence: 0.844175834814815

00:05:27.910 --> 00:05:31.189 Next So what we've done?

NOTE Confidence: 0.844175834814815

00:05:31.189 --> 00:05:33.142 We and others have done over the

NOTE Confidence: 0.844175834814815

00:05:33.142 --> 00:05:34.928 last twenty years or so is is is.

NOTE Confidence: 0.844175834814815

00:05:34.930 --> 00:05:37.718 Figure out how to make these degradable

NOTE Confidence: 0.844175834814815

00:05:37.718 --> 00:05:41.030 polymers into tiny particles,

NOTE Confidence: 0.844175834814815

00:05:41.030 --> 00:05:42.890 and that's shown in this scanning

NOTE Confidence: 0.844175834814815

00:05:42.890 --> 00:05:43.820 electron micrograph here.

NOTE Confidence: 0.844175834814815

00:05:43.820 --> 00:05:45.550 These are spherical particles that

NOTE Confidence: 0.844175834814815

00:05:45.550 --> 00:05:47.840 are about 100 nanometers in diameter,

NOTE Confidence: 0.844175834814815

00:05:47.840 --> 00:05:51.800 so that's about the same diameter as a virus,

NOTE Confidence: 0.844175834814815

00:05:51.800 --> 00:05:54.080 but they're made of all synthetic

NOTE Confidence: 0.844175834814815

00:05:54.080 --> 00:05:55.600 components in this case.

NOTE Confidence: 0.844175834814815

00:05:55.600 --> 00:05:58.852 This picture is of pure plga.

NOTE Confidence: 0.844175834814815

00:05:58.852 --> 00:05:59.284 Nanoparticles,

NOTE Confidence: 0.844175834814815

00:05:59.284 --> 00:06:02.740 but you can load them with agents like

NOTE Confidence: 0.844175834814815

00:06:02.814 --> 00:06:05.229 chemotherapy agents or or others,

NOTE Confidence: 0.844175834814815

00:06:05.230 --> 00:06:08.470 and make them into pharmacologically

NOTE Confidence: 0.844175834814815

00:06:08.470 --> 00:06:09.766 active particles.

NOTE Confidence: 0.844175834814815

00:06:09.770 --> 00:06:13.340 Next, and they have some features

NOTE Confidence: 0.844175834814815

00:06:13.340 --> 00:06:14.692 which make them interesting.

NOTE Confidence: 0.844175834814815

00:06:14.692 --> 00:06:16.610 One is that if made of the

NOTE Confidence: 0.844175834814815

00:06:16.666 --> 00:06:18.118 right materials like Plga,

NOTE Confidence: 0.844175834814815

00:06:18.120 --> 00:06:20.278 which I just showed you, they're non toxic.

NOTE Confidence: 0.844175834814815

00:06:20.278 --> 00:06:22.828 If you add them to into cell cultures

NOTE Confidence: 0.844175834814815

00:06:22.828 --> 00:06:25.201 or you inject them into animals and

NOTE Confidence: 0.844175834814815

00:06:25.201 --> 00:06:27.670 in fact you can deliver very high

NOTE Confidence: 0.844175834814815

00:06:27.670 --> 00:06:30.554 doses of these into animals and people

NOTE Confidence: 0.844175834814815

00:06:30.554 --> 00:06:33.439 without any significant side effects.

NOTE Confidence: 0.844175834814815

00:06:33.440 --> 00:06:35.694 If the particles are loaded with drugs,

NOTE Confidence: 0.844175834814815

00:06:35.700 --> 00:06:37.476 then if they're engineered in the right way,

NOTE Confidence: 0.844175834814815

00:06:37.480 --> 00:06:38.980 the drugs are slowly released

NOTE Confidence: 0.844175834814815

00:06:38.980 --> 00:06:39.880 from the particles.

NOTE Confidence: 0.844175834814815

00:06:39.880 --> 00:06:42.696 Into in this case, into an aqueous medium,

NOTE Confidence: 0.844175834814815

00:06:42.700 --> 00:06:45.316 but also released into the body

NOTE Confidence: 0.844175834814815

00:06:45.316 --> 00:06:47.450 if they're deployed that way.

NOTE Confidence: 0.844175834814815

00:06:47.450 --> 00:06:47.954 Sometimes,

NOTE Confidence: 0.844175834814815

00:06:47.954 --> 00:06:51.482 and when it's shown in the bottom

NOTE Confidence: 0.844175834814815

00:06:51.482 --> 00:06:53.050 left panel here,

NOTE Confidence: 0.844175834814815

00:06:53.050 --> 00:06:55.240 this is when we added different

NOTE Confidence: 0.844175834814815

00:06:55.240 --> 00:06:57.184 concentrations of camp to Thiessen

NOTE Confidence: 0.844175834814815

00:06:57.184 --> 00:06:59.264 loaded nanoparticles to cells in

NOTE Confidence: 0.844175834814815

00:06:59.264 --> 00:07:01.845 culture that the loaded particles are

NOTE Confidence: 0.844175834814815

00:07:01.845 --> 00:07:03.960 actually more effective at killing

NOTE Confidence: 0.844175834814815

00:07:03.960 --> 00:07:06.206 these tumor cells than the drug is

NOTE Confidence: 0.844175834814815

00:07:06.206 --> 00:07:07.670 when it's delivered on its own.

NOTE Confidence: 0.844175834814815

00:07:07.670 --> 00:07:09.042 And so there's some.

NOTE Confidence: 0.844175834814815

00:07:09.042 --> 00:07:10.757 There's some property of the

NOTE Confidence: 0.844175834814815

00:07:10.757 --> 00:07:12.305 particles which makes the drugs

NOTE Confidence: 0.844175834814815

00:07:12.305 --> 00:07:14.397 more active and as a result you

NOTE Confidence: 0.844175834814815

00:07:14.397 --> 00:07:15.997 can inject these particles into

NOTE Confidence: 0.844175834814815

00:07:15.997 --> 00:07:19.233 tumors and is shown in the bottom.

NOTE Confidence: 0.844175834814815

00:07:19.233 --> 00:07:21.186 Right diagram here,

NOTE Confidence: 0.844175834814815

00:07:21.190 --> 00:07:22.447 in this case,

NOTE Confidence: 0.844175834814815

00:07:22.447 --> 00:07:26.259 injected into a tumor in the flank of a rat.

NOTE Confidence: 0.844175834814815

00:07:26.260 --> 00:07:27.860 You can arrest the growth of the tumor

NOTE Confidence: 0.844175834814815

00:07:27.860 --> 00:07:29.829 with a single injection of nanoparticles,

NOTE Confidence: 0.844175834814815

00:07:29.830 --> 00:07:31.575 and these features of nanoparticles

NOTE Confidence: 0.844175834814815

00:07:31.575 --> 00:07:34.184 seem to be related to the fact

NOTE Confidence: 0.844175834814815

00:07:34.184 --> 00:07:35.776 that the particles themselves.

NOTE Confidence: 0.844175834814815

00:07:35.780 --> 00:07:37.622 Can be highly loaded with drugs

NOTE Confidence: 0.844175834814815

00:07:37.622 --> 00:07:39.187 and they're much smaller than

NOTE Confidence: 0.844175834814815

00:07:39.187 --> 00:07:40.831 tumor cells that we're using to

NOTE Confidence: 0.844175834814815

00:07:40.831 --> 00:07:42.540 treat them in these examples,

NOTE Confidence: 0.844175834814815

00:07:42.540 --> 00:07:44.095 and so the particles get

NOTE Confidence: 0.844175834814815

00:07:44.095 --> 00:07:45.650 internalized into tumor cells as

NOTE Confidence: 0.844175834814815

00:07:45.713 --> 00:07:47.298 shown in this confocal image.

NOTE Confidence: 0.844175834814815

00:07:47.300 --> 00:07:50.462 Here you can see the green

NOTE Confidence: 0.844175834814815

00:07:50.462 --> 00:07:53.160 nanoparticles are inside of these

NOTE Confidence: 0.8979493904

00:07:53.160 --> 00:07:54.564 tumor cells in culture,

NOTE Confidence: 0.8979493904

00:07:54.564 --> 00:07:56.670 and they surround the nucleus and

NOTE Confidence: 0.8979493904

00:07:56.736 --> 00:07:58.766 they're releasing their their active

NOTE Confidence: 0.8979493904

00:07:58.766 --> 00:08:01.187 ingredients very close to the target

NOTE Confidence: 0.8979493904

00:08:01.187 --> 00:08:03.769 of action from many anti cancer drugs.

NOTE Confidence: 0.97003435

00:08:05.840 --> 00:08:07.891 The technology that we've developed

NOTE Confidence: 0.97003435

00:08:07.891 --> 00:08:09.719 for this collaborative project

NOTE Confidence: 0.97003435

00:08:09.719 --> 00:08:11.470 is shown schematically here.

NOTE Confidence: 0.97003435

00:08:11.470 --> 00:08:13.780 It involves a block copolymer,

NOTE Confidence: 0.97003435

00:08:13.780 --> 00:08:16.048 so there's so there's two polymers

NOTE Confidence: 0.97003435

00:08:16.048 --> 00:08:18.180 that are covalently coupled together.

NOTE Confidence: 0.97003435

00:08:18.180 --> 00:08:20.896 One is lactic acid and that's shown

NOTE Confidence: 0.97003435

00:08:20.896 --> 00:08:23.960 as as the blue in this diagram,

NOTE Confidence: 0.97003435

00:08:23.960 --> 00:08:27.320 and the second is hyperbranched polyglycerol,

NOTE Confidence: 0.97003435

00:08:27.320 --> 00:08:30.001 which is shown as the green with

NOTE Confidence: 0.97003435

00:08:30.001 --> 00:08:32.478 red pendant branches coming off of

NOTE Confidence: 0.97003435

00:08:32.478 --> 00:08:34.558 the surface of the nanoparticle,

NOTE Confidence: 0.97003435

00:08:34.560 --> 00:08:36.276 so the core is this degradable.

NOTE Confidence: 0.97003435

00:08:36.280 --> 00:08:38.541 Poly lactic acid polymer that can be

NOTE Confidence: 0.97003435

00:08:38.541 --> 00:08:40.580 loaded with drugs or active ingredients

NOTE Confidence: 0.97003435

00:08:40.580 --> 00:08:43.290 and that's shown by the white dots here.

NOTE Confidence: 0.97003435

00:08:43.290 --> 00:08:45.264 And because it's a block copolymer

NOTE Confidence: 0.97003435

00:08:45.264 --> 00:08:47.519 that's assembled in a particular way,

NOTE Confidence: 0.97003435

00:08:47.520 --> 00:08:49.455 you have this degradable core

NOTE Confidence: 0.97003435

00:08:49.455 --> 00:08:52.569 surrounded by a green sort of corona

NOTE Confidence: 0.97003435

00:08:52.569 --> 00:08:54.228 of Hyperbranched polyglycerol.

NOTE Confidence: 0.97003435

00:08:54.230 --> 00:08:56.460 And it's that hyperbranched polyglycerol,

NOTE Confidence: 0.97003435

00:08:56.460 --> 00:08:58.636 which gives the nanoparticles

NOTE Confidence: 0.97003435

00:08:58.636 --> 00:09:00.812 certain surface properties which

NOTE Confidence: 0.97003435

00:09:00.812 --> 00:09:02.770 we've wanted to exploit.

NOTE Confidence: 0.97148824

00:09:05.320 --> 00:09:07.715 And one of the interesting things

NOTE Confidence: 0.97148824

00:09:07.715 --> 00:09:09.471 about Hyperbranched polyglycerol is

NOTE Confidence: 0.97148824

00:09:09.471 --> 00:09:11.956 that in its native state it has a

NOTE Confidence: 0.97148824

00:09:11.956 --> 00:09:14.282 lot of hydroxyls at the end of the

NOTE Confidence: 0.97148824

00:09:14.282 --> 00:09:16.010 end of the branched polymer chain,

NOTE Confidence: 0.97148824

00:09:16.010 --> 00:09:18.490 so this would be a a particle is

NOTE Confidence: 0.97148824

00:09:18.490 --> 00:09:20.687 shown on the left here that we

NOTE Confidence: 0.97148824

00:09:20.687 --> 00:09:22.474 call a non adhesive nanoparticle

NOTE Confidence: 0.97148824

00:09:22.474 --> 00:09:24.999 that has hydroxyl rich surface,

NOTE Confidence: 0.97148824

00:09:25.000 --> 00:09:27.574 and so it doesn't adhere very

NOTE Confidence: 0.97148824

00:09:27.574 --> 00:09:30.340 well to to proteins or to cells

NOTE Confidence: 0.97148824

00:09:30.340 --> 00:09:31.750 has a property of stealth.

NOTE Confidence: 0.97148824

00:09:31.750 --> 00:09:34.153 But I'll show you in just a few moments,

NOTE Confidence: 0.97148824

00:09:34.160 --> 00:09:35.072 but you can.

NOTE Confidence: 0.97148824

00:09:35.072 --> 00:09:36.288 Convert this particle into

NOTE Confidence: 0.97148824

00:09:36.288 --> 00:09:38.088 a different form by a brief

NOTE Confidence: 0.97148824

00:09:38.088 --> 00:09:39.478 exposure to sodium per iodate,

NOTE Confidence: 0.97148824

00:09:39.480 --> 00:09:41.385 which convert which converts the

NOTE Confidence: 0.97148824

00:09:41.385 --> 00:09:43.798 vicinal dials on the surface of

NOTE Confidence: 0.97148824

00:09:43.798 --> 00:09:45.550 the nanoparticle into aldehydes,

NOTE Confidence: 0.97148824

00:09:45.550 --> 00:09:49.449 and it then becomes a very adhesive

NOTE Confidence: 0.97148824

00:09:49.449 --> 00:09:50.563 particle adhesive.

NOTE Confidence: 0.97148824

00:09:50.570 --> 00:09:52.285 Because the aldehydes that are

NOTE Confidence: 0.97148824

00:09:52.285 --> 00:09:54.416 now covering the surface of the

NOTE Confidence: 0.97148824

00:09:54.416 --> 00:09:56.161 nanoparticle can react with amines

NOTE Confidence: 0.97148824

00:09:56.161 --> 00:09:58.662 in proteins or means on a a cell

NOTE Confidence: 0.97148824

00:09:58.662 --> 00:10:00.744 surface and they'll form a shift base

NOTE Confidence: 0.97148824

00:10:00.744 --> 00:10:03.314 covalent attachment which allows the

NOTE Confidence: 0.97148824

00:10:03.314 --> 00:10:06.139 nanoparticle to adhere to the cell.

NOTE Confidence: 0.97148824

00:10:06.140 --> 00:10:08.570 Or a matrix of very strongly.

NOTE Confidence: 0.894694784615385

00:10:10.610 --> 00:10:13.970 So this shows two of the typical properties

NOTE Confidence: 0.894694784615385

00:10:13.970 --> 00:10:17.170 of our non adhesive nanoparticles,

NOTE Confidence: 0.894694784615385

00:10:17.170 --> 00:10:20.986 NPS or bio hesive nanoparticles BMPS.

NOTE Confidence: 0.894694784615385

00:10:20.990 --> 00:10:23.130 The non adhesive particles because

NOTE Confidence: 0.894694784615385

00:10:23.130 --> 00:10:25.270 they have very little interaction

NOTE Confidence: 0.894694784615385

00:10:25.338 --> 00:10:27.478 with biological cells and tissues,

NOTE Confidence: 0.894694784615385

00:10:27.480 --> 00:10:29.811 will circulate for a long time if

NOTE Confidence: 0.894694784615385

00:10:29.811 --> 00:10:31.830 you inject them intravenously.

NOTE Confidence: 0.894694784615385

00:10:31.830 --> 00:10:34.455 They avoid uptake in most organs and

NOTE Confidence: 0.894694784615385

00:10:34.455 --> 00:10:36.889 that results in long circulation.

NOTE Confidence: 0.894694784615385

00:10:36.890 --> 00:10:39.662 You can see here the blue dots

NOTE Confidence: 0.894694784615385

00:10:39.662 --> 00:10:41.632 show a circulation half type.

NOTE Confidence: 0.894694784615385

00:10:41.632 --> 00:10:43.990 Time of about 10 hours compared

NOTE Confidence: 0.894694784615385

00:10:44.063 --> 00:10:46.239 to a conventional nanoparticle,

NOTE Confidence: 0.894694784615385

00:10:46.240 --> 00:10:48.340 which has a half life of of

NOTE Confidence: 0.894694784615385

00:10:48.340 --> 00:10:49.889 much less than an hour.

NOTE Confidence: 0.894694784615385

00:10:49.890 --> 00:10:52.501 And so that gives you the opportunity

NOTE Confidence: 0.894694784615385

00:10:52.501 --> 00:10:55.184 to to deliver nanoparticles to

NOTE Confidence: 0.894694784615385

00:10:55.184 --> 00:10:58.388 highly dispersed regions of the body.

NOTE Confidence: 0.894694784615385

00:10:58.390 --> 00:10:59.998 On the other hand,

NOTE Confidence: 0.894694784615385

00:10:59.998 --> 00:11:02.410 the bio adhesive nanoparticles are BMPS

NOTE Confidence: 0.894694784615385

00:11:02.488 --> 00:11:05.810 because they'll adhere to a tissue surface,

NOTE Confidence: 0.894694784615385

00:11:05.810 --> 00:11:08.072 can be made into very local

NOTE Confidence: 0.894694784615385

00:11:08.072 --> 00:11:09.203 drug delivery systems,

NOTE Confidence: 0.894694784615385

00:11:09.210 --> 00:11:12.202 and we show you this here in the

NOTE Confidence: 0.894694784615385

00:11:12.202 --> 00:11:15.522 diagram on the right which shows BNP

NOTE Confidence: 0.894694784615385

00:11:15.522 --> 00:11:18.789 adhesion to the outside surface of skin.

NOTE Confidence: 0.894694784615385

00:11:18.790 --> 00:11:20.442 So in this example,

NOTE Confidence: 0.894694784615385

00:11:20.442 --> 00:11:22.507 the red fluorescent nanoparticles were

NOTE Confidence: 0.894694784615385

00:11:22.507 --> 00:11:25.060 just added in solution on top of the

NOTE Confidence: 0.894694784615385

00:11:25.060 --> 00:11:27.180 skin on the side of the stratum cornea,

NOTE Confidence: 0.894694784615385

00:11:27.180 --> 00:11:29.004 and you can see that even after extensive.

NOTE Confidence: 0.894694784615385

00:11:29.010 --> 00:11:31.986 Washing those particles not only for

NOTE Confidence: 0.894694784615385

00:11:31.986 --> 00:11:34.619 mcconn formal coating on the on,

NOTE Confidence: 0.894694784615385

00:11:34.620 --> 00:11:35.868 the stratum corny AM,

NOTE Confidence: 0.894694784615385

00:11:35.868 --> 00:11:38.435 but they they are abundant on the surface

NOTE Confidence: 0.894694784615385

00:11:38.435 --> 00:11:40.931 as well and very difficult to wash off.

NOTE Confidence: 0.941754650588235

00:11:43.320 --> 00:11:45.084 So we want to talk about using

NOTE Confidence: 0.941754650588235

00:11:45.084 --> 00:11:47.150 these kinds of materials in two

NOTE Confidence: 0.941754650588235

00:11:47.150 --> 00:11:48.814 different but related applications.

NOTE Confidence: 0.941754650588235

00:11:48.820 --> 00:11:51.676 One for prevention of skin cancer,

NOTE Confidence: 0.941754650588235

00:11:51.680 --> 00:11:55.656 and in this case we'd like to convert

NOTE Confidence: 0.941754650588235

00:11:55.656 --> 00:11:58.536 the nanoparticles into a sunscreen

NOTE Confidence: 0.941754650588235

00:11:58.536 --> 00:12:01.629 by incorporating FDA approved UV

NOTE Confidence: 0.941754650588235

00:12:01.629 --> 00:12:04.794 absorbing agents into the nanoparticles.

NOTE Confidence: 0.941754650588235

00:12:04.800 --> 00:12:06.085 And we think that will

NOTE Confidence: 0.941754650588235

00:12:06.085 --> 00:12:06.856 have several advantages.

NOTE Confidence: 0.941754650588235

00:12:06.860 --> 00:12:08.332 Safety, because the adhesive

NOTE Confidence: 0.941754650588235

00:12:08.332 --> 00:12:10.172 nanoparticles don't enter the skin,

NOTE Confidence: 0.941754650588235

00:12:10.180 --> 00:12:11.605 and so they'll keep these

NOTE Confidence: 0.941754650588235

00:12:11.605 --> 00:12:13.030 chemicals outside of your body.

NOTE Confidence: 0.941754650588235

00:12:13.030 --> 00:12:14.992 But they'll still provide long lasting

NOTE Confidence: 0.941754650588235

00:12:14.992 --> 00:12:16.791 protection because of the adhesion

NOTE Confidence: 0.941754650588235

00:12:16.791 --> 00:12:18.547 and presumably increased efficacy.

NOTE Confidence: 0.941754650588235

00:12:18.550 --> 00:12:21.014 And then secondly want to talk about using

NOTE Confidence: 0.941754650588235

00:12:21.014 --> 00:12:23.208 these same materials to treat tumors,

NOTE Confidence: 0.941754650588235

00:12:23.210 --> 00:12:25.716 and we're going to give some examples

NOTE Confidence: 0.941754650588235

00:12:25.716 --> 00:12:27.928 of different tumors in animal models,

NOTE Confidence: 0.941754650588235

00:12:27.930 --> 00:12:29.820 but our focus here is on treating

NOTE Confidence: 0.941754650588235

00:12:29.820 --> 00:12:31.813 skin cancer and the advantages of the

NOTE Confidence: 0.941754650588235

00:12:31.813 --> 00:12:33.955 approach here is that you can load

NOTE Confidence: 0.941754650588235

00:12:33.955 --> 00:12:35.940 chemotherapy agents that are slowly

NOTE Confidence: 0.941754650588235

00:12:35.940 --> 00:12:37.870 released from the nanoparticles because

NOTE Confidence: 0.941754650588235

00:12:37.870 --> 00:12:39.230 of their bioadhesive properties,

NOTE Confidence: 0.941754650588235

00:12:39.230 --> 00:12:41.309 they are get retained in the tumor

NOTE Confidence: 0.941754650588235

00:12:41.309 --> 00:12:43.150 microenvironment, and they said that.

NOTE Confidence: 0.941754650588235

00:12:43.150 --> 00:12:45.075 That bio adhesion also facilitates

NOTE Confidence: 0.941754650588235

00:12:45.075 --> 00:12:46.600 uptake into tumor cells,

NOTE Confidence: 0.941754650588235

00:12:46.600 --> 00:12:49.302 and you can create a localized treatment

NOTE Confidence: 0.941754650588235

00:12:49.302 --> 00:12:51.729 that that reduces systemic toxicity.

NOTE Confidence: 0.88004255

00:12:54.420 --> 00:12:55.875 I think my friend and colleague

NOTE Confidence: 0.88004255

00:12:55.875 --> 00:12:57.730 is going to take over from here.

NOTE Confidence: 0.9095454748

00:12:58.380 --> 00:12:59.868 Yes, thank you Mark.

NOTE Confidence: 0.9095454748

00:12:59.868 --> 00:13:02.478 So sunscreens are something we use all

NOTE Confidence: 0.9095454748

00:13:02.478 --> 00:13:04.910 the time and may take it for granted

NOTE Confidence: 0.9095454748

00:13:04.910 --> 00:13:07.116 what we're putting on our skins.

NOTE Confidence: 0.9095454748

00:13:07.120 --> 00:13:09.650 In particular, these multi benzene

NOTE Confidence: 0.9095454748

00:13:09.650 --> 00:13:12.743 ring structures that form what are

NOTE Confidence: 0.9095454748

00:13:12.743 --> 00:13:15.635 called the chemical types of actives

NOTE Confidence: 0.9095454748

00:13:15.635 --> 00:13:18.912 within sunscreens and and as such being

NOTE Confidence: 0.9095454748

00:13:18.912 --> 00:13:21.092 so hydrophobic they penetrate into

NOTE Confidence: 0.9095454748

00:13:21.092 --> 00:13:23.504 and through the skin right into the

NOTE Confidence: 0.9095454748

00:13:23.504 --> 00:13:25.389 bloodstream and deposit in your fat.

NOTE Confidence: 0.9095454748

00:13:25.390 --> 00:13:27.420 There are concerns about off target effects,

NOTE Confidence: 0.9095454748

00:13:27.420 --> 00:13:30.160 in particular estrogen and

NOTE Confidence: 0.9095454748

00:13:30.160 --> 00:13:31.530 progesterone receptors,

NOTE Confidence: 0.9095454748

00:13:31.530 --> 00:13:34.182 and another major effect is as

NOTE Confidence: 0.9095454748

00:13:34.182 --> 00:13:37.593 they absorb this UV energy and and

NOTE Confidence: 0.9095454748

00:13:37.593 --> 00:13:40.908 help protect against UV exposure,

NOTE Confidence: 0.9095454748

00:13:40.910 --> 00:13:43.528 they are prone to give off reactive

NOTE Confidence: 0.9095454748

00:13:43.528 --> 00:13:46.107 oxygen species and that is a major

NOTE Confidence: 0.9095454748

00:13:46.107 --> 00:13:47.837 focus of something we're trying

NOTE Confidence: 0.9095454748

00:13:47.837 --> 00:13:50.267 to prevent with this technology.

NOTE Confidence: 0.9095454748

00:13:50.270 --> 00:13:50.890 On the other hand,

NOTE Confidence: 0.9095454748

00:13:50.890 --> 00:13:52.620 we can use some of the physical sunscreens,

NOTE Confidence: 0.9095454748

00:13:52.620 --> 00:13:54.930 in particular zinc oxide and

NOTE Confidence: 0.9095454748

00:13:54.930 --> 00:13:55.854 titanium dioxide.

NOTE Confidence: 0.9095454748

00:13:55.860 --> 00:13:57.252 They have limited penetration

NOTE Confidence: 0.9095454748

00:13:57.252 --> 00:13:58.644 really through the skin.

NOTE Confidence: 0.9095454748

00:13:58.650 --> 00:14:01.593 They will kind of work their way through hair

NOTE Confidence: 0.9095454748

00:14:01.593 --> 00:14:03.947 follicles and through broken areas of skin.

NOTE Confidence: 0.9095454748

00:14:03.950 --> 00:14:06.068 Even micro breaks a major concern

NOTE Confidence: 0.9095454748

00:14:06.068 --> 00:14:08.100 about their use in general,

NOTE Confidence: 0.9095454748

00:14:08.100 --> 00:14:09.536 as their aesthetic appearance,

NOTE Confidence: 0.9095454748

00:14:09.536 --> 00:14:12.040 but they are major producers of Ross.

NOTE Confidence: 0.9095454748

00:14:12.040 --> 00:14:14.290 If they do get into cells,

NOTE Confidence: 0.9095454748

00:14:14.290 --> 00:14:16.186 even though they're less likely to.

NOTE Confidence: 0.9095454748

00:14:16.190 --> 00:14:17.990 They're not just physical blockers,

NOTE Confidence: 0.9095454748

00:14:17.990 --> 00:14:19.978 they clearly will generate Ross as well.

NOTE Confidence: 0.9095454748

00:14:19.980 --> 00:14:22.844 And here you can see why they don't have

NOTE Confidence: 0.9095454748

00:14:22.844 --> 00:14:26.499 some of the appeal of a views otherwise.

NOTE Confidence: 0.9095454748

00:14:26.500 --> 00:14:30.180 So this is a confocal we made of the skin.

NOTE Confidence: 0.9095454748

00:14:30.180 --> 00:14:30.684 You know,

NOTE Confidence: 0.9095454748

00:14:30.684 --> 00:14:31.944 we're studying some of the

NOTE Confidence: 0.9095454748

00:14:31.944 --> 00:14:32.970 relationship of cells here,

NOTE Confidence: 0.9095454748

00:14:32.970 --> 00:14:34.586 but I want to point to one thing

NOTE Confidence: 0.9095454748

00:14:34.586 --> 00:14:36.213 this is towards the top of the

NOTE Confidence: 0.9095454748

00:14:36.213 --> 00:14:37.771 skin and you see longer hansel's.

NOTE Confidence: 0.9095454748

00:14:37.771 --> 00:14:39.335 These dendritic cells are

NOTE Confidence: 0.9095454748

00:14:39.335 --> 00:14:40.508 populate the epidermis,

NOTE Confidence: 0.9095454748

00:14:40.510 --> 00:14:43.720 extend their dendrites really right up

NOTE Confidence: 0.9095454748

00:14:43.720 --> 00:14:46.978 through these claudin tight junctions to

NOTE Confidence: 0.9095454748

00:14:46.978 --> 00:14:50.080 really be samplers of the environment.

NOTE Confidence: 0.9095454748

00:14:50.080 --> 00:14:50.640 And people.

NOTE Confidence: 0.9095454748

00:14:50.640 --> 00:14:51.760 Think of, you know,

NOTE Confidence: 0.9095454748

00:14:51.760 --> 00:14:54.720 skin as an impenetrable barrier

NOTE Confidence: 0.9095454748

00:14:54.720 --> 00:14:56.240 with its stratum, cornea, minutes,

NOTE Confidence: 0.9095454748

00:14:56.240 --> 00:14:56.676 lipid.

NOTE Confidence: 0.9095454748

00:14:56.676 --> 00:14:58.856 A protective components but in

NOTE Confidence: 0.9095454748

00:14:58.856 --> 00:15:02.342 point of fact it is very interactive

NOTE Confidence: 0.9095454748

00:15:02.342 --> 00:15:03.998 with the environment.

NOTE Confidence: 0.9095454748

00:15:04.000 --> 00:15:07.017 In many ways oops circulate that for

NOTE Confidence: 0.9095454748

00:15:07.017 --> 00:15:10.519 you a little bit and you can see how

NOTE Confidence: 0.9095454748

00:15:10.519 --> 00:15:13.153 they can bring potential agents down

NOTE Confidence: 0.9095454748

00:15:13.153 --> 00:15:16.429 into the deeper layers of the epidermis,

NOTE Confidence: 0.9095454748

00:15:16.430 --> 00:15:18.270 and they will actually navigate

NOTE Confidence: 0.9095454748

00:15:18.270 --> 00:15:20.110 from there through the dermis,

NOTE Confidence: 0.9095454748

00:15:20.110 --> 00:15:23.560 into lymphatics and lymph nodes too.

NOTE Confidence: 0.9095454748

00:15:23.560 --> 00:15:26.276 So another kind of spark on the

NOTE Confidence: 0.9095454748

00:15:26.276 --> 00:15:28.286 controversy of of sunscreen usage

NOTE Confidence: 0.9095454748

00:15:28.286 --> 00:15:31.326 came about a year and a half ago

NOTE Confidence: 0.9095454748

00:15:31.413 --> 00:15:34.625 when FDA was studying the plasma

NOTE Confidence: 0.9095454748

00:15:34.625 --> 00:15:36.941 concentrations within folks that

NOTE Confidence: 0.9095454748

00:15:36.941 --> 00:15:39.216 frequently applied these sunscreens

NOTE Confidence: 0.9095454748

00:15:39.216 --> 00:15:42.444 and noted that they achieved these

NOTE Confidence: 0.9095454748

00:15:42.444 --> 00:15:45.377 levels of concentration that are known

NOTE Confidence: 0.9095454748

00:15:45.377 --> 00:15:49.512 to have a special designation by the

NOTE Confidence: 0.9095454748

00:15:49.512 --> 00:15:52.242 FDA as requiring toxicology studies,

NOTE Confidence: 0.9095454748

00:15:52.242 --> 00:15:52.688 which.

NOTE Confidence: 0.9095454748

00:15:52.688 --> 00:15:53.580 Of course,

NOTE Confidence: 0.9095454748

00:15:53.580 --> 00:15:54.945 have never really been done

NOTE Confidence: 0.9095454748

00:15:54.945 --> 00:15:56.037 by the sunscreen industry,

NOTE Confidence: 0.9095454748

00:15:56.040 --> 00:16:02.160 but are taking place now after that study.

NOTE Confidence: 0.9095454748

00:16:02.160 --> 00:16:04.388 So the bioadhesive nanoparticle

NOTE Confidence: 0.9095454748

00:16:04.388 --> 00:16:07.730 technology really allows for us to

NOTE Confidence: 0.9095454748

00:16:07.821 --> 00:16:09.948 develop nonpenetrating sunscreen

NOTE Confidence: 0.9095454748

00:16:09.948 --> 00:16:12.626 and avoid some of these concerns

NOTE Confidence: 0.9095454748

00:16:12.626 --> 00:16:14.196 about these agents getting in.

NOTE Confidence: 0.9095454748

00:16:14.200 --> 00:16:15.460 In particular,

NOTE Confidence: 0.9095454748

00:16:15.460 --> 00:16:17.980 these hydrophobic chemical agents.

NOTE Confidence: 0.9095454748

00:16:17.980 --> 00:16:19.926 If you apply just on the surface,

NOTE Confidence: 0.9095454748

00:16:19.930 --> 00:16:21.150 it doesn't just sit there.

NOTE Confidence: 0.9095454748

00:16:21.150 --> 00:16:22.991 There are a lot of film formers

NOTE Confidence: 0.9095454748

00:16:22.991 --> 00:16:23.780 and technologies that

NOTE Confidence: 0.920084252666667

00:16:23.830 --> 00:16:25.120 the industry tries to use,

NOTE Confidence: 0.920084252666667

00:16:25.120 --> 00:16:26.849 but they work only to some degree,

NOTE Confidence: 0.920084252666667

00:16:26.850 --> 00:16:29.298 as the FDA showed.

NOTE Confidence: 0.920084252666667

00:16:29.300 --> 00:16:31.760 But if we're able to

NOTE Confidence: 0.920084252666667

00:16:31.760 --> 00:16:33.582 encapsulate those within BMP's,

NOTE Confidence: 0.920084252666667

00:16:33.582 --> 00:16:35.976 we can keep these agents on the

NOTE Confidence: 0.920084252666667

00:16:35.976 --> 00:16:38.310 surface bound to the stratum corny AM.

NOTE Confidence: 0.920084252666667

00:16:38.310 --> 00:16:40.322 Otherwise, if they penetrate

NOTE Confidence: 0.920084252666667

00:16:40.322 --> 00:16:42.334 within after photo exposure,

NOTE Confidence: 0.920084252666667

00:16:42.340 --> 00:16:45.476 you'll see very high levels of Ros

NOTE Confidence: 0.920084252666667

00:16:45.476 --> 00:16:46.820 generation directly attributable

NOTE Confidence: 0.920084252666667

00:16:46.894 --> 00:16:48.934 to those sunscreen agents that

NOTE Confidence: 0.920084252666667

00:16:48.934 --> 00:16:50.974 are supposed to be protecting.

NOTE Confidence: 0.920084252666667

00:16:50.980 --> 00:16:54.260 Here's what it looks like when we use

NOTE Confidence: 0.920084252666667

00:16:54.260 --> 00:16:56.012 fluorescent loaded BMP nanoparticles

NOTE Confidence: 0.920084252666667

00:16:56.012 --> 00:16:58.808 on the on the skin surface,

NOTE Confidence: 0.920084252666667

00:16:58.810 --> 00:17:02.994 and you can almost form a a confluent.

NOTE Confidence: 0.920084252666667

00:17:03.000 --> 00:17:05.790 Blanket as a as the sun might see it.

NOTE Confidence: 0.920186898333333

00:17:09.620 --> 00:17:13.760 So this affords several major advantages.

NOTE Confidence: 0.920186898333333

00:17:13.760 --> 00:17:15.995 One of them is this

NOTE Confidence: 0.920186898333333

00:17:15.995 --> 00:17:17.336 durability after application.

NOTE Confidence: 0.920186898333333

00:17:17.340 --> 00:17:18.880 This is a covalent bond.

NOTE Confidence: 0.920186898333333

00:17:18.880 --> 00:17:21.120 It's a shift based bonding that takes

NOTE Confidence: 0.920186898333333

00:17:21.120 --> 00:17:23.379 place with the aldehydes on the on,

NOTE Confidence: 0.920186898333333

00:17:23.380 --> 00:17:24.736 the bioadhesive nanoparticles

NOTE Confidence: 0.920186898333333

00:17:24.736 --> 00:17:26.996 and in particular affords it

NOTE Confidence: 0.920186898333333

00:17:26.996 --> 00:17:29.800 a a waterproofing protection,

NOTE Confidence: 0.920186898333333

00:17:29.800 --> 00:17:31.762 water resistance and so that can

NOTE Confidence: 0.920186898333333

00:17:31.762 --> 00:17:33.862 be tested in these animals that

NOTE Confidence: 0.920186898333333

00:17:33.862 --> 00:17:36.028 can be tested on other surfaces.

NOTE Confidence: 0.920186898333333

00:17:36.030 --> 00:17:40.118 And it can be applied to industry standards.

NOTE Confidence: 0.920186898333333

00:17:40.120 --> 00:17:42.328 Like to wash off these agents

NOTE Confidence: 0.920186898333333

00:17:42.328 --> 00:17:44.509 and see how protective they are.

NOTE Confidence: 0.920186898333333

00:17:44.510 --> 00:17:46.256 Current sunscreen formulations

NOTE Confidence: 0.920186898333333

00:17:46.256 --> 00:17:49.166 require reapplication every two hours.

NOTE Confidence: 0.920186898333333

00:17:49.170 --> 00:17:50.405 You don't see anything that

NOTE Confidence: 0.920186898333333

00:17:50.405 --> 00:17:51.393 lasts longer than that,

NOTE Confidence: 0.920186898333333

00:17:51.400 --> 00:17:53.955 but we can see these sticking around

NOTE Confidence: 0.920186898333333

00:17:53.955 --> 00:17:56.529 for much longer than a couple hours.

NOTE Confidence: 0.889953155555556

00:17:59.370 --> 00:18:03.276 The other thing that clearly helpful by

NOTE Confidence: 0.889953155555556

00:18:03.276 --> 00:18:06.000 using BMP to incorporate these agents

NOTE Confidence: 0.889953155555556

00:18:06.000 --> 00:18:08.913 within is that we don't see penetration

NOTE Confidence: 0.889953155555556

00:18:08.913 --> 00:18:11.965 of the active sunscreen agents to the

NOTE Confidence: 0.889953155555556

00:18:11.965 --> 00:18:15.283 point that with free sunscreen we might

NOTE Confidence: 0.889953155555556

00:18:15.283 --> 00:18:17.648 generate endproducts of Ross damage.

NOTE Confidence: 0.889953155555556

00:18:17.650 --> 00:18:20.863 For example gamma H2X or recruited proteins

NOTE Confidence: 0.889953155555556

00:18:20.863 --> 00:18:24.248 to sites of DNA damage due to Ross,

NOTE Confidence: 0.889953155555556

00:18:24.250 --> 00:18:27.239 but if the agent is incorporated within

NOTE Confidence: 0.889953155555556

00:18:27.239 --> 00:18:28.990 the BMP's, we don't see that damage.

NOTE Confidence: 0.889953155555556

00:18:28.990 --> 00:18:30.304 After UV exposure,

NOTE Confidence: 0.889953155555556

00:18:30.304 --> 00:18:33.370 we've already applied these to human skin.

NOTE Confidence: 0.889953155555556

00:18:33.370 --> 00:18:34.610 We don't see we.

NOTE Confidence: 0.889953155555556

00:18:34.610 --> 00:18:37.578 We see a nice physical appearance to him.

NOTE Confidence: 0.889953155555556

00:18:37.578 --> 00:18:41.244 We see the capacity for them to protect

NOTE Confidence: 0.889953155555556

00:18:41.244 --> 00:18:44.278 against what's called minimal or THEMA doses,

NOTE Confidence: 0.889953155555556

00:18:44.278 --> 00:18:47.579 and we can do SPF testing for example

NOTE Confidence: 0.889953155555556

00:18:47.579 --> 00:18:50.279 with them and see their performance

NOTE Confidence: 0.889953155555556

00:18:50.279 --> 00:18:53.910 and their aesthetic advantages.

NOTE Confidence: 0.889953155555556

00:18:53.910 --> 00:18:56.829 But if we really want to kind

NOTE Confidence: 0.889953155555556

00:18:56.829 --> 00:18:59.620 of vigorously studies and.

NOTE Confidence: 0.889953155555556

00:18:59.620 --> 00:19:01.700 And according to industry standards,

NOTE Confidence: 0.889953155555556

00:19:01.700 --> 00:19:04.339 we use materials such as vitro skin.

NOTE Confidence: 0.889953155555556

00:19:04.340 --> 00:19:06.475 This is a proprietary material

NOTE Confidence: 0.889953155555556

00:19:06.475 --> 00:19:08.920 that has the means within it,

NOTE Confidence: 0.889953155555556

00:19:08.920 --> 00:19:11.456 which is actually quite good for us to

NOTE Confidence: 0.889953155555556

00:19:11.456 --> 00:19:14.096 look at and study this bio adhesion.

NOTE Confidence: 0.889953155555556

00:19:14.100 --> 00:19:15.500 This is evil Ben Zona,

NOTE Confidence: 0.889953155555556

00:19:15.500 --> 00:19:18.590 very active in the UV spectrum.

NOTE Confidence: 0.889953155555556

00:19:18.590 --> 00:19:20.430 Agent incorporated into NMPS.

NOTE Confidence: 0.889953155555556

00:19:20.430 --> 00:19:24.381 So you see how that looks on a pre

NOTE Confidence: 0.889953155555556

00:19:24.381 --> 00:19:27.210 wash and you see after it's exposed to

NOTE Confidence: 0.889953155555556

00:19:27.210 --> 00:19:29.530 washing for three hours in a water bath.

NOTE Confidence: 0.889953155555556

00:19:29.530 --> 00:19:32.485 What happens to the the

NOTE Confidence: 0.889953155555556

00:19:32.485 --> 00:19:33.667 PHOTOPROTECTIVE Spectra?

NOTE Confidence: 0.889953155555556

00:19:33.670 --> 00:19:36.428 And you can see that just deteriorates

NOTE Confidence: 0.889953155555556

00:19:36.428 --> 00:19:39.136 immediately and in contrast to Eva

NOTE Confidence: 0.889953155555556

00:19:39.136 --> 00:19:41.166 Benzon incorporated within BMP's,

NOTE Confidence: 0.889953155555556

00:19:41.166 --> 00:19:44.046 which maintain quite nicely there.

NOTE Confidence: 0.889953155555556

00:19:44.050 --> 00:19:45.463 The photoprotective capacity

NOTE Confidence: 0.889953155555556

00:19:45.463 --> 00:19:48.289 across the full spectrum of the

NOTE Confidence: 0.889953155555556

00:19:48.289 --> 00:19:49.809 performance of evil Benzon.

NOTE Confidence: 0.889953155555556

00:19:49.810 --> 00:19:51.286 We've done it with other agents,

NOTE Confidence: 0.889953155555556

00:19:51.290 --> 00:19:56.379 including Juvenil A to see that continued

NOTE Confidence: 0.889953155555556

00:19:56.380 --> 00:20:00.616 protection even clearly after three hours.

NOTE Confidence: 0.889953155555556

00:20:00.620 --> 00:20:01.310 And longer.

NOTE Confidence: 0.933467077777778

00:20:04.100 --> 00:20:06.809 We've taken this to the next level

NOTE Confidence: 0.933467077777778

00:20:06.809 --> 00:20:11.370 of using poor sign skin and really

NOTE Confidence: 0.933467077777778

00:20:11.370 --> 00:20:14.838 trying to vigorously wash that off,

NOTE Confidence: 0.933467077777778

00:20:14.840 --> 00:20:17.312 wrapping up the revolution per minute

NOTE Confidence: 0.933467077777778

00:20:17.312 --> 00:20:19.681 and the time constraints and then

NOTE Confidence: 0.933467077777778

00:20:19.681 --> 00:20:21.956 using HPLC in a very quantitative way

NOTE Confidence: 0.933467077777778

00:20:21.956 --> 00:20:24.450 to see how much evil benzon we were

NOTE Confidence: 0.933467077777778

00:20:24.450 --> 00:20:27.440 able to keep it here to the skin.

NOTE Confidence: 0.933467077777778

00:20:27.440 --> 00:20:31.358 Here it is at 150 RPM for 20 minutes.

NOTE Confidence: 0.933467077777778

00:20:31.358 --> 00:20:33.318 This is the industry standard

NOTE Confidence: 0.933467077777778

00:20:33.318 --> 00:20:35.021 for waterproof measurements and

NOTE Confidence: 0.933467077777778

00:20:35.021 --> 00:20:38.314 MPs will come off at a 60% lost.

NOTE Confidence: 0.933467077777778

00:20:38.314 --> 00:20:40.786 The BMP's will adhere quite nicely.

NOTE Confidence: 0.933467077777778

00:20:40.790 --> 00:20:42.878 Stayed here through all of that

NOTE Confidence: 0.933467077777778

00:20:42.878 --> 00:20:45.205 at greater than 95% retained and

NOTE Confidence: 0.933467077777778

00:20:45.205 --> 00:20:48.680 then we start to Rev it up too.

NOTE Confidence: 0.933467077777778

00:20:48.680 --> 00:20:51.728 Way past industry standards 450 RPM's

NOTE Confidence: 0.933467077777778

00:20:51.728 --> 00:20:55.302 three hours and see that you know we

NOTE Confidence: 0.933467077777778

00:20:55.302 --> 00:20:57.850 get the same relationship and the the

NOTE Confidence: 0.933467077777778

00:20:57.934 --> 00:21:01.140 full adherence of BMP's upwards of about 80%.

NOTE Confidence: 0.933467077777778

00:21:01.140 --> 00:21:02.910 After three hours at that level.

NOTE Confidence: 0.90180464125

00:21:05.930 --> 00:21:08.779 We were quite surprised to actually see

NOTE Confidence: 0.90180464125

00:21:08.779 --> 00:21:11.146 that BMP's that gave us another advantage,

NOTE Confidence: 0.90180464125

00:21:11.150 --> 00:21:12.890 and that is the capacity to

NOTE Confidence: 0.90180464125

00:21:12.890 --> 00:21:15.482 prevent photodegradation of a

NOTE Confidence: 0.90180464125

00:21:15.482 --> 00:21:17.426 quality called photostability.

NOTE Confidence: 0.90180464125

00:21:17.430 --> 00:21:20.220 This is very important in sunscreen

NOTE Confidence: 0.90180464125

00:21:20.220 --> 00:21:22.770 formulation, able benzon in particular

NOTE Confidence: 0.90180464125

00:21:22.770 --> 00:21:25.890 as being really the main UV,

NOTE Confidence: 0.90180464125

00:21:25.890 --> 00:21:27.394 a protector active agent.

NOTE Confidence: 0.90180464125

00:21:27.394 --> 00:21:29.650 It's a major concern 'cause it's

NOTE Confidence: 0.90180464125

00:21:29.719 --> 00:21:31.987 so susceptible to photodegradation.

NOTE Confidence: 0.90180464125

00:21:31.990 --> 00:21:34.600 You could see that here after.

NOTE Confidence: 0.90180464125

00:21:34.600 --> 00:21:37.240 An industry standard dose of UV.

NOTE Confidence: 0.90180464125

00:21:37.240 --> 00:21:39.345 What happens to the performance

NOTE Confidence: 0.90180464125

00:21:39.345 --> 00:21:40.608 of evil Benzon?

NOTE Confidence: 0.90180464125

00:21:40.610 --> 00:21:42.647 So you imagine you put it on.

NOTE Confidence: 0.90180464125

00:21:42.650 --> 00:21:44.555 You get exposed to ultraviolet

NOTE Confidence: 0.90180464125

00:21:44.555 --> 00:21:46.460 light and it just degrades.

NOTE Confidence: 0.90180464125

00:21:46.460 --> 00:21:52.130 So if you incorporate it within BMP's.

NOTE Confidence: 0.90180464125

00:21:52.130 --> 00:21:53.654 And we're not completely sure of

NOTE Confidence: 0.90180464125

00:21:53.654 --> 00:21:55.210 exactly how this is happening,

NOTE Confidence: 0.90180464125

00:21:55.210 --> 00:21:58.834 but obviously within the PLA there's

NOTE Confidence: 0.90180464125

00:21:58.834 --> 00:22:01.354 a protective millou that help

NOTE Confidence: 0.90180464125

00:22:01.354 --> 00:22:03.114 prevent some of that degradation

NOTE Confidence: 0.90180464125

00:22:03.114 --> 00:22:05.519 from the Eva benzon quite nicely.

NOTE Confidence: 0.82204423

00:22:08.230 --> 00:22:11.296 So Octocrylene is a nice partner for

NOTE Confidence: 0.82204423

00:22:11.296 --> 00:22:14.800 able benzon because it's a UV absorber,

NOTE Confidence: 0.82204423

00:22:14.800 --> 00:22:16.165 so it complements it in that way,

NOTE Confidence: 0.82204423

00:22:16.170 --> 00:22:20.298 but also because it itself is a photo

NOTE Confidence: 0.82204423

00:22:20.298 --> 00:22:22.799 degradation stabilizer for able benzon.

NOTE Confidence: 0.82204423

00:22:22.800 --> 00:22:24.921 So we were very interested if we

NOTE Confidence: 0.82204423

00:22:24.921 --> 00:22:26.280 just incorporated able benzon.

NOTE Confidence: 0.82204423

00:22:26.280 --> 00:22:28.890 We can see a rate of

NOTE Confidence: 0.82204423

00:22:28.890 --> 00:22:29.760 degradation photodegradation,

NOTE Confidence: 0.82204423

00:22:29.760 --> 00:22:32.742 but if we come incorporated with

NOTE Confidence: 0.82204423

00:22:32.742 --> 00:22:35.682 octocrylene we were hoping to maintain a

NOTE Confidence: 0.82204423

00:22:35.682 --> 00:22:38.330 photostability at very high levels of UV.

NOTE Confidence: 0.82204423

00:22:38.330 --> 00:22:41.230 Exposure upwards of three hours

NOTE Confidence: 0.82204423

00:22:41.230 --> 00:22:43.489 and we were able to do that by Co,

NOTE Confidence: 0.82204423

00:22:43.490 --> 00:22:45.945 incorporating those agents and and

NOTE Confidence: 0.82204423

00:22:45.945 --> 00:22:49.370 found an optimal ratio for those also,

NOTE Confidence: 0.82204423

00:22:49.370 --> 00:22:51.491 but we were very surprised to see

NOTE Confidence: 0.82204423

00:22:51.491 --> 00:22:53.186 if we incorporated them separately

NOTE Confidence: 0.82204423

00:22:53.186 --> 00:22:55.713 that we still had that capacity for

NOTE Confidence: 0.82204423

00:22:55.713 --> 00:22:57.599 protection against photodegradation.

NOTE Confidence: 0.82204423

00:22:57.600 --> 00:22:59.845 Again, not something we completely

NOTE Confidence: 0.82204423

00:22:59.845 --> 00:23:01.192 understand as relationship

NOTE Confidence: 0.82204423

00:23:01.192 --> 00:23:03.131 between particles where agents

NOTE Confidence: 0.82204423

00:23:03.131 --> 00:23:04.598 are individually incorporated.

NOTE Confidence: 0.956106594285714

00:23:06.680 --> 00:23:10.516 And then one more surprise from incorporation

NOTE Confidence: 0.956106594285714

00:23:10.520 --> 00:23:13.010 came about when we measured reflectance.

NOTE Confidence: 0.956106594285714

00:23:13.010 --> 00:23:14.760 So if you look at zinc oxide,

NOTE Confidence: 0.956106594285714

00:23:14.760 --> 00:23:16.700 so-called physical blocker as we

NOTE Confidence: 0.956106594285714

00:23:16.700 --> 00:23:19.990 described before, you're going to see a

NOTE Confidence: 0.956106594285714

00:23:19.990 --> 00:23:23.280 lot of of reflectance that helps in its

NOTE Confidence: 0.956106594285714

00:23:23.280 --> 00:23:24.880 performance and protection against UV.

NOTE Confidence: 0.956106594285714

00:23:24.880 --> 00:23:28.732 But it also gives it some of this shiny,

NOTE Confidence: 0.956106594285714

00:23:28.740 --> 00:23:30.684 sometimes even purplish

NOTE Confidence: 0.956106594285714

00:23:30.684 --> 00:23:33.924 whitish hue to people skin.

NOTE Confidence: 0.956106594285714

00:23:33.930 --> 00:23:36.630 Whereas if you just use 3.

NOTE Confidence: 0.956106594285714

00:23:36.630 --> 00:23:38.082 Able benzon and octocrylene.

NOTE Confidence: 0.956106594285714

00:23:38.082 --> 00:23:41.159 You don't really get much of any reflectance

NOTE Confidence: 0.956106594285714

00:23:41.159 --> 00:23:44.483 from those chemical sunscreen agents,

NOTE Confidence: 0.956106594285714

00:23:44.483 --> 00:23:48.010 but within bpce for whatever

NOTE Confidence: 0.956106594285714

00:23:48.010 --> 00:23:51.100 reason able benzo not crawling do

NOTE Confidence: 0.956106594285714

00:23:51.100 --> 00:23:53.874 provide provide some reflective or

NOTE Confidence: 0.956106594285714

00:23:53.874 --> 00:23:56.629 extra protection from UV exposure,

NOTE Confidence: 0.956106594285714

00:23:56.630 --> 00:23:59.945 probably because of the state

NOTE Confidence: 0.956106594285714

00:23:59.945 --> 00:24:01.934 that they're in.

NOTE Confidence: 0.956106594285714

00:24:01.940 --> 00:24:05.276 Something that we might refer to as kind

NOTE Confidence: 0.956106594285714

00:24:05.276 --> 00:24:09.041 of a hydrophobic crystal if you will.

NOTE Confidence: 0.956106594285714

00:24:09.041 --> 00:24:12.830 If you can imagine as opposed to being in

NOTE Confidence: 0.956106594285714

00:24:12.920 --> 00:24:17.314 a a more of an oily millou or emulsion.

NOTE Confidence: 0.956106594285714

00:24:17.320 --> 00:24:19.130 Empty BMP's don't do that,

NOTE Confidence: 0.956106594285714

00:24:19.130 --> 00:24:20.918 so this is really about the

NOTE Confidence: 0.956106594285714

00:24:20.918 --> 00:24:22.110 actives within the PLA.

NOTE Confidence: 0.838786426363636

00:24:25.210 --> 00:24:29.125 And then we can do some in vitro SPF

NOTE Confidence: 0.838786426363636

00:24:29.125 --> 00:24:31.326 measurements using some industry

NOTE Confidence: 0.838786426363636

00:24:31.326 --> 00:24:33.778 standard spectrophotometry and and

NOTE Confidence: 0.838786426363636

00:24:33.778 --> 00:24:36.978 see that we can gain a level of

NOTE Confidence: 0.838786426363636

00:24:36.978 --> 00:24:38.801 performance that would be predicted

NOTE Confidence: 0.838786426363636

00:24:38.801 --> 00:24:41.435 to be above the active ingredients.

NOTE Confidence: 0.838786426363636

00:24:41.440 --> 00:24:43.744 In addition, we can see that we can sprinkle

NOTE Confidence: 0.838786426363636

00:24:43.744 --> 00:24:45.968 in some of the physical blockers here,

NOTE Confidence: 0.838786426363636

00:24:45.970 --> 00:24:47.956 in this case titanium dioxide at

NOTE Confidence: 0.838786426363636

00:24:47.956 --> 00:24:51.615 1% or 5% and get levels of SPF

NOTE Confidence: 0.838786426363636

00:24:51.615 --> 00:24:54.642 protection with that combination that.

NOTE Confidence: 0.838786426363636

00:24:54.642 --> 00:24:57.114 Kind of speaks to where we're

NOTE Confidence: 0.838786426363636

00:24:57.114 --> 00:25:00.000 heading with a prototype for this,

NOTE Confidence: 0.838786426363636

00:25:00.000 --> 00:25:02.704 use as a as a novel sunscreen formulation.

NOTE Confidence: 0.900935326

00:25:05.720 --> 00:25:09.825 I want to just come use this slide to talk

NOTE Confidence: 0.900935326

00:25:09.825 --> 00:25:11.940 about our other major collaborator here.

NOTE Confidence: 0.900935326

00:25:11.940 --> 00:25:15.853 Douglas Brash, who is a really a

NOTE Confidence: 0.900935326

00:25:15.853 --> 00:25:20.290 pioneer in understanding triplet state.

NOTE Confidence: 0.900935326

00:25:20.290 --> 00:25:22.996 Species that get generated after UV

NOTE Confidence: 0.900935326

00:25:22.996 --> 00:25:25.910 exposure and how they do damage DNA

NOTE Confidence: 0.900935326

00:25:25.910 --> 00:25:30.229 even well after the lights are out.

NOTE Confidence: 0.900935326

00:25:30.230 --> 00:25:32.566 We are also working with a with the

NOTE Confidence: 0.900935326

00:25:32.566 --> 00:25:34.567 Center for molecular discovery here at

NOTE Confidence: 0.900935326

00:25:34.567 --> 00:25:37.290 Yale to screen a bunch of compounds.

NOTE Confidence: 0.900935326

00:25:37.290 --> 00:25:40.522 In this case a about 1000 natural found

NOTE Confidence: 0.900935326

00:25:40.522 --> 00:25:43.468 in nature compounds and and looking

NOTE Confidence: 0.900935326

00:25:43.468 --> 00:25:47.120 for their capacity to be photostable UV

NOTE Confidence: 0.900935326

00:25:47.120 --> 00:25:50.585 absorbers and then looking at their capacity.

NOTE Confidence: 0.900935326

00:25:50.590 --> 00:25:54.940 To not be so toxic to the skin and then

NOTE Confidence: 0.900935326

00:25:54.940 --> 00:25:58.060 not generate Ros after UV exposure

NOTE Confidence: 0.900935326

00:25:58.060 --> 00:26:01.070 and using this series of steps,

NOTE Confidence: 0.900935326

00:26:01.070 --> 00:26:03.835 we've really come down to a handful

NOTE Confidence: 0.900935326

00:26:03.835 --> 00:26:06.539 of major candidates that we're really

NOTE Confidence: 0.900935326

00:26:06.539 --> 00:26:08.467 excited about moving forward.

NOTE Confidence: 0.900935326

00:26:08.470 --> 00:26:10.600 With that we might use.

NOTE Confidence: 0.900935326

00:26:10.600 --> 00:26:11.666 For example,

NOTE Confidence: 0.900935326

00:26:11.666 --> 00:26:15.397 if we deem them safer than current

NOTE Confidence: 0.900935326

00:26:15.397 --> 00:26:17.186 agents outside of the particles.

NOTE Confidence: 0.900935326

00:26:17.186 --> 00:26:19.070 If there needs to be protection,

NOTE Confidence: 0.900935326

00:26:19.070 --> 00:26:21.016 we can put them inside the particles.

NOTE Confidence: 0.900935326

00:26:21.020 --> 00:26:23.498 So this is something that we think

NOTE Confidence: 0.900935326

00:26:23.498 --> 00:26:26.432 that we can will be very complementary

NOTE Confidence: 0.900935326

00:26:26.432 --> 00:26:28.070 to to what we're working on.

NOTE Confidence: 0.9587778

00:26:30.380 --> 00:26:30.830 Mark

NOTE Confidence: 0.77446055

00:26:35.420 --> 00:26:36.712 going to change gears for

NOTE Confidence: 0.77446055

00:26:36.712 --> 00:26:38.380 the for the rest of the

NOTE Confidence: 0.897164958636364

00:26:38.445 --> 00:26:41.203 talk slightly and talk about using these

NOTE Confidence: 0.897164958636364

00:26:41.203 --> 00:26:43.359 bpce for therapeutic drug delivery.

NOTE Confidence: 0.897164958636364

00:26:43.360 --> 00:26:46.080 So this slide just sort of reminds you

NOTE Confidence: 0.897164958636364

00:26:46.080 --> 00:26:49.371 of the potential for the particles that

NOTE Confidence: 0.897164958636364

00:26:49.371 --> 00:26:52.440 are converted into the bioadhesive state.

NOTE Confidence: 0.897164958636364

00:26:52.440 --> 00:26:54.472 BMP's to interact with

NOTE Confidence: 0.897164958636364

00:26:54.472 --> 00:26:58.250 the proteins or any any.

NOTE Confidence: 0.897164958636364

00:26:58.250 --> 00:27:00.575 Amine containing group by because

NOTE Confidence: 0.897164958636364

00:27:00.575 --> 00:27:03.709 the aldehyde that's on the surface of

NOTE Confidence: 0.897164958636364

00:27:03.709 --> 00:27:06.621 the BMP will form a shift base which

NOTE Confidence: 0.897164958636364

00:27:06.703 --> 00:27:09.338 leads to this covalent attachment,

NOTE Confidence: 0.897164958636364

00:27:09.340 --> 00:27:11.788 and so we think there's potential

NOTE Confidence: 0.897164958636364

00:27:11.788 --> 00:27:13.420 advantages for particles that

NOTE Confidence: 0.897164958636364

00:27:13.487 --> 00:27:16.157 work by this mechanism to deliver

NOTE Confidence: 0.897164958636364

00:27:16.157 --> 00:27:17.047 therapeutics locally.

NOTE Confidence: 0.897164958636364

00:27:17.050 --> 00:27:18.934 And in addition,

NOTE Confidence: 0.897164958636364

00:27:18.934 --> 00:27:21.768 because the core of the particle is Poly,

NOTE Confidence: 0.897164958636364

00:27:21.770 --> 00:27:24.265 lactic acid and pretty hydrophobic

NOTE Confidence: 0.897164958636364

00:27:24.265 --> 00:27:26.760 polymer that's really compatible with

NOTE Confidence: 0.897164958636364

00:27:26.832 --> 00:27:28.521 drugs that have low solubility's.

NOTE Confidence: 0.897164958636364

00:27:28.521 --> 00:27:30.376 In in in aqueous media,

NOTE Confidence: 0.897164958636364

00:27:30.380 --> 00:27:33.080 so you can so you can use drugs that are

NOTE Confidence: 0.897164958636364

00:27:33.154 --> 00:27:36.130 difficult to formulate in conventional ways,

NOTE Confidence: 0.897164958636364

00:27:36.130 --> 00:27:38.251 but you can load them highly inside

NOTE Confidence: 0.897164958636364

00:27:38.251 --> 00:27:40.554 the particles and that allows you to

NOTE Confidence: 0.897164958636364

00:27:40.554 --> 00:27:42.214 have controlled release overtime at

NOTE Confidence: 0.897164958636364

00:27:42.214 --> 00:27:44.636 the site of action and hopefully limit

NOTE Confidence: 0.897164958636364

00:27:44.636 --> 00:27:47.070 systemic exposure to the toxic compounds.

NOTE Confidence: 0.9834833

00:27:50.120 --> 00:27:55.378 So here's one example of using these.

NOTE Confidence: 0.9834833

00:27:55.380 --> 00:27:56.796 Biodiesel nanoparticles to

NOTE Confidence: 0.9834833

00:27:56.796 --> 00:27:58.684 treat tumors in animals,

NOTE Confidence: 0.9834833

00:27:58.690 --> 00:28:01.156 and this is a collaboration with

NOTE Confidence: 0.9834833

00:28:01.156 --> 00:28:03.170 Alessandro Santin in OB GYN.

NOTE Confidence: 0.9834833

00:28:03.170 --> 00:28:06.593 And here, what we did was deliver

NOTE Confidence: 0.9834833

00:28:06.593 --> 00:28:08.060 the particles intraperitoneally.

NOTE Confidence: 0.9834833

00:28:08.060 --> 00:28:11.354 So these in the in the panel be shown

NOTE Confidence: 0.9834833

00:28:11.354 --> 00:28:14.476 here shows you the retention of either

NOTE Confidence: 0.9834833

00:28:14.476 --> 00:28:18.010 NNPS which are on the left or bppe

NOTE Confidence: 0.9834833

00:28:18.010 --> 00:28:19.850 Switcher on the right you see if you

NOTE Confidence: 0.9834833

00:28:19.903 --> 00:28:22.098 inject them intraperitoneally and animals.

NOTE Confidence: 0.9834833

00:28:22.100 --> 00:28:24.488 After five minutes they distributed widely

NOTE Confidence: 0.9834833

00:28:24.488 --> 00:28:26.080 throughout the intraperitoneal space.

NOTE Confidence: 0.9834833

00:28:26.080 --> 00:28:27.106 After four hours,

NOTE Confidence: 0.9834833

00:28:27.106 --> 00:28:29.500 the concentration of of NPS and not

NOTE Confidence: 0.9834833

00:28:29.569 --> 00:28:31.957 easy particles dropped substantially,

NOTE Confidence: 0.9834833

00:28:31.960 --> 00:28:33.780 while the BMP concentration and

NOTE Confidence: 0.9834833

00:28:33.780 --> 00:28:35.236 distribution remains pretty much

NOTE Confidence: 0.9834833

00:28:35.236 --> 00:28:36.677 the same after one day.

NOTE Confidence: 0.9834833

00:28:36.680 --> 00:28:38.736 Still a lot of BMP's in the IP

NOTE Confidence: 0.9834833

00:28:38.736 --> 00:28:40.532 space where most of the NPS are

NOTE Confidence: 0.9834833

00:28:40.532 --> 00:28:42.408 gone and we even see persistence in

NOTE Confidence: 0.9834833

00:28:42.408 --> 00:28:44.752 the IP space for up to five days.

NOTE Confidence: 0.9834833

00:28:44.760 --> 00:28:46.713 So this this kind of data convinced

NOTE Confidence: 0.9834833

00:28:46.713 --> 00:28:48.528 us that maybe you could treat.

NOTE Confidence: 0.64508884

00:28:50.870 --> 00:28:52.586 My peritoneal carcinomatosis with

NOTE Confidence: 0.64508884

00:28:52.586 --> 00:28:55.001 these kinds of nanoparticles by

NOTE Confidence: 0.64508884

00:28:55.001 --> 00:28:58.074 injecting them IP and and exploiting

NOTE Confidence: 0.64508884

00:28:58.074 --> 00:29:00.664 the mechanism where the bioadhesive

NOTE Confidence: 0.64508884

00:29:00.664 --> 00:29:02.946 nanoparticles would associate with the

NOTE Confidence: 0.64508884

00:29:02.946 --> 00:29:05.690 tumor cells or tumor nodules that are

NOTE Confidence: 0.64508884

00:29:05.690 --> 00:29:07.162 distributed throughout the peritoneum.

NOTE Confidence: 0.64508884

00:29:07.162 --> 00:29:09.370 We tested this with a drug

NOTE Confidence: 0.64508884

00:29:09.432 --> 00:29:10.677 called a path alone B.

NOTE Confidence: 0.64508884

00:29:10.680 --> 00:29:12.480 You can see that when it's loaded in

NOTE Confidence: 0.64508884

00:29:12.480 --> 00:29:13.769 the nanoparticles and panel see here,

NOTE Confidence: 0.64508884

00:29:13.770 --> 00:29:16.350 it comes out.

NOTE Confidence: 0.64508884

00:29:16.350 --> 00:29:17.244 Relatively slowly overtime,

NOTE Confidence: 0.64508884

00:29:17.244 --> 00:29:19.032 although most of it comes out

NOTE Confidence: 0.64508884

00:29:19.032 --> 00:29:20.648 over the first 12 hours and then

NOTE Confidence: 0.64508884

00:29:20.648 --> 00:29:22.268 it sort of leaks out after that.

NOTE Confidence: 0.64508884

00:29:22.270 --> 00:29:24.178 This is an in vitro release,

NOTE Confidence: 0.64508884

00:29:24.180 --> 00:29:25.628 very difficult to measure.

NOTE Confidence: 0.64508884

00:29:25.628 --> 00:29:27.076 The corresponding release once

NOTE Confidence: 0.64508884

00:29:27.076 --> 00:29:28.569 it's deployed in the animal,

NOTE Confidence: 0.64508884

00:29:28.570 --> 00:29:30.622 but you see the the most

NOTE Confidence: 0.64508884

00:29:30.622 --> 00:29:32.639 impressive result up in panel a.

NOTE Confidence: 0.64508884

00:29:32.640 --> 00:29:36.468 These are animals that that got

NOTE Confidence: 0.64508884

00:29:36.470 --> 00:29:39.884 intraperitoneal injections of a of a

NOTE Confidence: 0.64508884

00:29:39.884 --> 00:29:43.200 uterine serous carcinoma cell line that

NOTE Confidence: 0.64508884

00:29:43.200 --> 00:29:45.382 doctor Ellis Dr Stanton had developed.

NOTE Confidence: 0.64508884

00:29:45.382 --> 00:29:46.922 If you don't treat them,

NOTE Confidence: 0.64508884

00:29:46.930 --> 00:29:48.730 they die within about 60 days.

NOTE Confidence: 0.64508884

00:29:48.730 --> 00:29:50.466 If you treat them with EB alone,

NOTE Confidence: 0.64508884

00:29:50.470 --> 00:29:51.090 it's it's.

NOTE Confidence: 0.64508884

00:29:51.090 --> 00:29:53.260 It's difficult to find a dose that

NOTE Confidence: 0.64508884

00:29:53.260 --> 00:29:55.528 doesn't cause early toxicity and still

NOTE Confidence: 0.64508884

00:29:55.528 --> 00:29:57.428 provide some increase in survival.

NOTE Confidence: 0.64508884

00:29:57.430 --> 00:29:58.960 You can see that by the black line here,

NOTE Confidence: 0.64508884

00:29:58.960 --> 00:30:00.899 but if you put the EB inside

NOTE Confidence: 0.64508884

00:30:00.899 --> 00:30:01.730 the biodiesel nanoparticles,

NOTE Confidence: 0.64508884

00:30:01.730 --> 00:30:05.391 we see no toxicity and a dramatic

NOTE Confidence: 0.64508884

00:30:05.391 --> 00:30:06.960 improvement in survival.

NOTE Confidence: 0.921098228181818

00:30:09.360 --> 00:30:11.208 A similar example, but now we're

NOTE Confidence: 0.921098228181818

00:30:11.208 --> 00:30:12.830 treating locally in the brain.

NOTE Confidence: 0.921098228181818

00:30:12.830 --> 00:30:15.175 Here we're infusing the nanoparticles

NOTE Confidence: 0.921098228181818

00:30:15.175 --> 00:30:17.051 by convection enhanced delivery

NOTE Confidence: 0.921098228181818

00:30:17.051 --> 00:30:19.606 into the brain of animals that

NOTE Confidence: 0.921098228181818

00:30:19.606 --> 00:30:20.818 have intracranial tumors.

NOTE Confidence: 0.921098228181818

00:30:20.820 --> 00:30:23.754 This is work by Yazi Wang in my laboratory

NOTE Confidence: 0.921098228181818

00:30:23.754 --> 00:30:26.121 in collaboration with Raymond Hall

NOTE Confidence: 0.921098228181818

00:30:26.121 --> 00:30:29.073 at at the University of Connecticut.

NOTE Confidence: 0.921098228181818

00:30:29.080 --> 00:30:32.592 And here we put into the into the

NOTE Confidence: 0.921098228181818

00:30:32.592 --> 00:30:34.599 nanoparticles and anti mirror.

NOTE Confidence: 0.921098228181818

00:30:34.600 --> 00:30:36.388 Actually two anti mirrors,

NOTE Confidence: 0.921098228181818

00:30:36.388 --> 00:30:39.480 anti mirror 21 and anti mere 10B.

NOTE Confidence: 0.921098228181818

00:30:39.480 --> 00:30:42.350 These are two micro RNA's that have

NOTE Confidence: 0.921098228181818

00:30:42.350 --> 00:30:44.569 been highly associated with gliomas,

NOTE Confidence: 0.921098228181818

00:30:44.570 --> 00:30:46.136 so we do in the animals.

NOTE Confidence: 0.921098228181818

00:30:46.140 --> 00:30:48.030 One infusion we introduce the tumor as

NOTE Confidence: 0.921098228181818

00:30:48.030 --> 00:30:50.357 you can see on the timeline at the top,

NOTE Confidence: 0.921098228181818

00:30:50.360 --> 00:30:52.718 at day zero, at day six.

NOTE Confidence: 0.921098228181818

00:30:52.720 --> 00:30:54.040 At the tumor is growing,

NOTE Confidence: 0.921098228181818

00:30:54.040 --> 00:30:56.788 we infuse the nano particles that

NOTE Confidence: 0.921098228181818

00:30:56.788 --> 00:30:59.339 contain these anti mirrors and then

NOTE Confidence: 0.921098228181818

00:30:59.339 --> 00:31:01.899 one day later we given IP dose of

NOTE Confidence: 0.921098228181818

00:31:01.983 --> 00:31:04.727 Tim's Olamide and so the the hope is

NOTE Confidence: 0.921098228181818

00:31:04.727 --> 00:31:06.556 that the anti mirror activity will

NOTE Confidence: 0.921098228181818

00:31:06.556 --> 00:31:08.260 sensitize the tumor cells to Tim's

NOTE Confidence: 0.921098228181818

00:31:08.314 --> 00:31:09.875 Olamide and so it will be active.

NOTE Confidence: 0.921098228181818

00:31:09.880 --> 00:31:11.602 At low doses and you can see

NOTE Confidence: 0.921098228181818

00:31:11.602 --> 00:31:12.680 the result down here,

NOTE Confidence: 0.921098228181818

00:31:12.680 --> 00:31:14.695 which is pretty dramatic animals

NOTE Confidence: 0.921098228181818

00:31:14.695 --> 00:31:17.299 without any treatment dead by 50 days.

NOTE Confidence: 0.921098228181818

00:31:17.300 --> 00:31:19.036 If you just treat them with the bio

NOTE Confidence: 0.921098228181818

00:31:19.036 --> 00:31:20.338 adhesive nanoparticles with the anti mirrors,

NOTE Confidence: 0.921098228181818

00:31:20.340 --> 00:31:22.170 you see some prolongation in survival.

NOTE Confidence: 0.921098228181818

00:31:22.170 --> 00:31:23.532 That's the green line if you

NOTE Confidence: 0.921098228181818

00:31:23.532 --> 00:31:24.680 just treat them with TMZ,

NOTE Confidence: 0.921098228181818

00:31:24.680 --> 00:31:26.420 you see some prolongation and survival.

NOTE Confidence: 0.921098228181818

00:31:26.420 --> 00:31:27.668 That's the red line.

NOTE Confidence: 0.921098228181818

00:31:27.668 --> 00:31:30.081 If you treat them with both we see

NOTE Confidence: 0.921098228181818

00:31:30.081 --> 00:31:32.420 100% survival out to 120 days here,

NOTE Confidence: 0.921098228181818

00:31:32.420 --> 00:31:34.940 which is pretty remarkable.

NOTE Confidence: 0.921098228181818

00:31:34.940 --> 00:31:37.166 Next and you can deliver other

NOTE Confidence: 0.921098228181818

00:31:37.166 --> 00:31:39.270 agents to other tissues as well,

NOTE Confidence: 0.921098228181818

00:31:39.270 --> 00:31:40.902 so this is an example of

NOTE Confidence: 0.921098228181818

00:31:40.902 --> 00:31:41.990 delivering to mucosal surface.

NOTE Confidence: 0.921098228181818

00:31:41.990 --> 00:31:44.290 These were nanoparticles that were

NOTE Confidence: 0.921098228181818

00:31:44.290 --> 00:31:46.130 delivered intravaginally in mice,

NOTE Confidence: 0.921098228181818

00:31:46.130 --> 00:31:47.514 either NPS or BMP'S.

NOTE Confidence: 0.921098228181818

00:31:47.514 --> 00:31:50.137 You see the same sort of effect

NOTE Confidence: 0.921098228181818

00:31:50.137 --> 00:31:52.447 on sustained retention of the

NOTE Confidence: 0.921098228181818

00:31:52.450 --> 00:31:55.586 BMP's in the up to 24 hours,

NOTE Confidence: 0.921098228181818

00:31:55.590 --> 00:32:00.390 and these these particles were delivering.

NOTE Confidence: 0.921098228181818

00:32:00.390 --> 00:32:02.694 Antiretroviral drugs to

NOTE Confidence: 0.921098228181818

00:32:02.694 --> 00:32:04.998 the reproductive tract.

NOTE Confidence: 0.921098228181818

00:32:05.000 --> 00:32:07.176 And you can see if you take that

NOTE Confidence: 0.921098228181818

00:32:07.176 --> 00:32:09.136 issue and you dissociate it and

NOTE Confidence: 0.921098228181818

00:32:09.136 --> 00:32:11.593 look for cells that express CD 45

NOTE Confidence: 0.921098228181818

00:32:11.593 --> 00:32:13.438 or cells that express epithelial

NOTE Confidence: 0.921098228181818

00:32:13.438 --> 00:32:15.483 markers that with the bioadhesive

NOTE Confidence: 0.921098228181818

00:32:15.483 --> 00:32:18.298 nanoparticles the majority of the

NOTE Confidence: 0.921098228181818

00:32:18.298 --> 00:32:20.852 cells are are have nanoparticles

NOTE Confidence: 0.921098228181818

00:32:20.852 --> 00:32:22.576 within them and nanoparticles

NOTE Confidence: 0.921098228181818

00:32:22.576 --> 00:32:24.660 that contain the active drug.

NOTE Confidence: 0.9652903

00:32:30.000 --> 00:32:34.961 So. You know the the burden of human

NOTE Confidence: 0.9652903

00:32:34.961 --> 00:32:38.678 skin cancer is most striking when we

NOTE Confidence: 0.9652903

00:32:38.678 --> 00:32:41.444 consider volumes, numbers of cases per

NOTE Confidence: 0.9652903

00:32:41.444 --> 00:32:45.010 year at 5.5 million in EU. S. Uhm?

NOTE Confidence: 0.9652903

00:32:45.010 --> 00:32:48.370 You know more more cases of skin cancer

NOTE Confidence: 0.9652903

00:32:48.370 --> 00:32:51.988 than all other cancers combined and this.

NOTE Confidence: 0.9652903

00:32:51.988 --> 00:32:55.500 Though most of them in particular basil cell

NOTE Confidence: 0.9652903

00:32:55.588 --> 00:32:59.164 not and squamous cell a little bit Melanoma.

NOTE Confidence: 0.9652903

00:32:59.170 --> 00:33:02.796 Much more can result in death Accumulatively

NOTE Confidence: 0.9652903

00:33:02.796 --> 00:33:06.390 it's about 15,000 per year in EU.

NOTE Confidence: 0.9652903

00:33:06.390 --> 00:33:08.352 S and it's just a burden

NOTE Confidence: 0.9652903

00:33:08.352 --> 00:33:10.270 on the health care system.

NOTE Confidence: 0.9652903

00:33:10.270 --> 00:33:11.910 Tremendous burden on treating all

NOTE Confidence: 0.9652903

00:33:11.910 --> 00:33:13.971 of these cases of skin cancer

NOTE Confidence: 0.9652903

00:33:13.971 --> 00:33:16.470 multiple on a lot of patients in

NOTE Confidence: 0.9652903

00:33:16.470 --> 00:33:17.780 particular transplant patients.

NOTE Confidence: 0.9652903

00:33:17.780 --> 00:33:19.391 Fair skinned individuals,

NOTE Confidence: 0.9652903

00:33:19.391 --> 00:33:22.613 multiple scars that can run into.

NOTE Confidence: 0.9652903

00:33:22.620 --> 00:33:27.474 Each other and cause other complications

NOTE Confidence: 0.9652903

00:33:27.474 --> 00:33:31.329 from destructive and surgical procedures.

NOTE Confidence: 0.9652903

00:33:31.330 --> 00:33:34.914 So there's really an unmet need for

NOTE Confidence: 0.9652903

00:33:34.914 --> 00:33:36.656 non-surgical options for patients.

NOTE Confidence: 0.9652903

00:33:36.656 --> 00:33:38.446 Those that may not be

NOTE Confidence: 0.9652903

00:33:38.446 --> 00:33:39.520 great surgical candidates,

NOTE Confidence: 0.9652903

00:33:39.520 --> 00:33:42.232 or those who would like something a little

NOTE Confidence: 0.9652903

00:33:42.232 --> 00:33:46.678 more simpler and less cost dependent.

NOTE Confidence: 0.9652903

00:33:46.680 --> 00:33:49.200 So a minimally invasive local alternative

NOTE Confidence: 0.9652903

00:33:49.200 --> 00:33:52.630 would be ideal for patients who might have.

NOTE Confidence: 0.9652903

00:33:52.630 --> 00:33:54.940 Superficial or minimally invasive lesions,

NOTE Confidence: 0.9652903

00:33:54.940 --> 00:33:57.782 so numerous simple ones they may have

NOTE Confidence: 0.9652903

00:33:57.782 --> 00:34:00.050 locally advanced cancers where you want

NOTE Confidence: 0.9652903

00:34:00.050 --> 00:34:02.618 to come in with something local and

NOTE Confidence: 0.9652903

00:34:02.618 --> 00:34:05.866 that could be used in in conjunction.

NOTE Confidence: 0.9652903

00:34:05.870 --> 00:34:09.643 For example with a with a systemic

NOTE Confidence: 0.9652903

00:34:09.643 --> 00:34:11.260 agent or combination,

NOTE Confidence: 0.9652903

00:34:11.260 --> 00:34:13.170 that could be an immunotherapeutic.

NOTE Confidence: 0.9652903

00:34:13.170 --> 00:34:15.620 Agents such as checkpoint inhibitors

NOTE Confidence: 0.9652903

00:34:15.620 --> 00:34:16.600 for example.

NOTE Confidence: 0.9652903

00:34:16.600 --> 00:34:18.824 Or there may be some that you really

NOTE Confidence: 0.9652903

00:34:18.824 --> 00:34:20.622 have really deep ones and you

NOTE Confidence: 0.9652903

00:34:20.622 --> 00:34:22.392 want to minimize the side effects

NOTE Confidence: 0.9652903

00:34:22.458 --> 00:34:23.850 of providing a systemic.

NOTE Confidence: 0.9652903

00:34:23.850 --> 00:34:25.465 Chemotherapeutic agent and how you

NOTE Confidence: 0.9652903

00:34:25.465 --> 00:34:27.655 might deliver it locally and in those

NOTE Confidence: 0.9652903

00:34:27.655 --> 00:34:29.489 cases it could be a targeted therapy.

NOTE Confidence: 0.9652903

00:34:29.490 --> 00:34:31.038 It could be a chemotherapeutic agent.

NOTE Confidence: 0.9652903

00:34:31.040 --> 00:34:32.936 The point is you're going to

NOTE Confidence: 0.9652903

00:34:32.936 --> 00:34:34.554 maintain high concentrations of the

NOTE Confidence: 0.9652903

00:34:34.554 --> 00:34:36.360 actives where you put the particles.

NOTE Confidence: 0.90793277875

00:34:39.440 --> 00:34:41.208 So here's a model that I've worked with.

NOTE Confidence: 0.90793277875

00:34:41.210 --> 00:34:45.818 Uhm. For many years of keratinocyte

NOTE Confidence: 0.90793277875

00:34:45.820 --> 00:34:48.940 tumor squamous cell carcinoma,

NOTE Confidence: 0.90793277875

00:34:48.940 --> 00:34:52.685 it's a set up quite simply by

NOTE Confidence: 0.90793277875

00:34:52.685 --> 00:34:54.433 transplantable injection and it

NOTE Confidence: 0.90793277875

00:34:54.433 --> 00:34:56.591 grows over a course of about

NOTE Confidence: 0.90793277875

00:34:56.591 --> 00:34:59.074 four weeks and forms a nice big

NOTE Confidence: 0.90793277875

00:34:59.074 --> 00:35:01.769 nodular blue ball of cells.

NOTE Confidence: 0.90793277875

00:35:01.769 --> 00:35:03.698 It's very aggressive.

NOTE Confidence: 0.90793277875

00:35:03.700 --> 00:35:06.196 But if we treat it with BMPS with

NOTE Confidence: 0.90793277875

00:35:06.196 --> 00:35:08.786 camp to thicken incorporated as

NOTE Confidence: 0.90793277875

00:35:08.786 --> 00:35:11.306 the chemotherapeutic active agent,

NOTE Confidence: 0.90793277875

00:35:11.310 --> 00:35:14.046 we can get complete clinical and

NOTE Confidence: 0.90793277875

00:35:14.046 --> 00:35:15.870 histologic resolution and those

NOTE Confidence: 0.90793277875

00:35:15.870 --> 00:35:18.185 pathologists in the audience can

NOTE Confidence: 0.90793277875

00:35:18.185 --> 00:35:20.037 appreciate the tumor destruction

NOTE Confidence: 0.90793277875

00:35:20.037 --> 00:35:23.178 and amorphis changes that that we

NOTE Confidence: 0.90793277875

00:35:23.178 --> 00:35:25.763 see here after after resolution.

NOTE Confidence: 0.914908908

00:35:29.760 --> 00:35:33.140 So I'm trying to understand.

NOTE Confidence: 0.914908908

00:35:33.140 --> 00:35:37.284 Process here and so that we can maybe

NOTE Confidence: 0.914908908

00:35:37.284 --> 00:35:39.570 potentially leverage some of that.

NOTE Confidence: 0.914908908

00:35:39.570 --> 00:35:41.768 We can look at how the particles,

NOTE Confidence: 0.914908908

00:35:41.770 --> 00:35:46.590 for example, die Incorporated BMPS.

NOTE Confidence: 0.914908908

00:35:46.590 --> 00:35:48.078 Might interact with the tumor cells

NOTE Confidence: 0.914908908

00:35:48.078 --> 00:35:49.934 and Mark alluded to some of the

NOTE Confidence: 0.914908908

00:35:49.934 --> 00:35:51.289 interactions with other tumor cells,

NOTE Confidence: 0.914908908

00:35:51.290 --> 00:35:53.922 but we were studying here in in

NOTE Confidence: 0.914908908

00:35:53.922 --> 00:35:55.833 skin cancer squamous cell carcinoma

NOTE Confidence: 0.914908908

00:35:55.833 --> 00:35:58.311 PDB cells and you can see that

NOTE Confidence: 0.914908908

00:35:58.311 --> 00:36:00.645 the NPS barely will stick to the

NOTE Confidence: 0.914908908

00:36:00.645 --> 00:36:02.330 cells and barely getting side.

NOTE Confidence: 0.914908908

00:36:02.330 --> 00:36:04.286 But you can just see this

NOTE Confidence: 0.914908908

00:36:04.286 --> 00:36:06.150 tremendous adhesion to cell surface,

NOTE Confidence: 0.914908908

00:36:06.150 --> 00:36:09.230 which of course that is a protein

NOTE Confidence: 0.914908908

00:36:09.230 --> 00:36:11.871 rich environment and that further

NOTE Confidence: 0.914908908

00:36:11.871 --> 00:36:13.728 facilitates and triggers.

NOTE Confidence: 0.914908908

00:36:13.730 --> 00:36:15.818 And we've broken down the mechanism

NOTE Confidence: 0.914908908

00:36:15.818 --> 00:36:19.323 a little bit of micro Pinot cytosis a

NOTE Confidence: 0.914908908

00:36:19.323 --> 00:36:21.340 passive internalization that occurs

NOTE Confidence: 0.914908908

00:36:21.340 --> 00:36:24.310 to bring these particles and their

NOTE Confidence: 0.914908908

00:36:24.310 --> 00:36:27.258 payloads right within the tumor cells.

NOTE Confidence: 0.935385716

00:36:30.330 --> 00:36:32.598 And we can really get very

NOTE Confidence: 0.935385716

00:36:32.598 --> 00:36:34.110 quantitative with this interaction,

NOTE Confidence: 0.935385716

00:36:34.110 --> 00:36:36.630 and we can use dyes that are

NOTE Confidence: 0.935385716

00:36:36.630 --> 00:36:38.389 bound covalently to the PLA.

NOTE Confidence: 0.935385716

00:36:38.390 --> 00:36:40.937 Or we can do in ones that are loosely

NOTE Confidence: 0.935385716

00:36:40.937 --> 00:36:42.969 within the appeal doesn't matter,

NOTE Confidence: 0.935385716

00:36:42.970 --> 00:36:46.216 they they will readily get incorporated

NOTE Confidence: 0.935385716

00:36:46.216 --> 00:36:49.848 with into the tumor cells taken up.

NOTE Confidence: 0.935385716

00:36:49.850 --> 00:36:53.594 Very readily over the course of three days.

NOTE Confidence: 0.851390034

00:36:55.990 --> 00:36:59.266 Relative to BMP's that don't have that

NOTE Confidence: 0.851390034

00:36:59.266 --> 00:37:03.520 bio adherent surface component to him.

NOTE Confidence: 0.851390034

00:37:03.520 --> 00:37:06.620 We can also create kind of a an in vitro

NOTE Confidence: 0.851390034

00:37:06.704 --> 00:37:09.560 tumor matrix where we put use Poly L

NOTE Confidence: 0.851390034

00:37:09.560 --> 00:37:12.678 lysine as a tumor rich environment and

NOTE Confidence: 0.851390034

00:37:12.678 --> 00:37:17.312 adhered adjacent to cells and show that

NOTE Confidence: 0.851390034

00:37:17.312 --> 00:37:20.003 our BMP's are the ones that are going

NOTE Confidence: 0.851390034

00:37:20.003 --> 00:37:22.396 to provide a kill because they will bind

NOTE Confidence: 0.851390034

00:37:22.396 --> 00:37:24.809 not just to cell surface but just to

NOTE Confidence: 0.851390034

00:37:24.809 --> 00:37:27.021 this tumor matrix and MP's don't do that.

NOTE Confidence: 0.851390034

00:37:27.021 --> 00:37:28.988 So we don't see that tumor kill

NOTE Confidence: 0.851390034

00:37:28.988 --> 00:37:31.020 and we don't see it with CPT.

NOTE Confidence: 0.851390034

00:37:31.020 --> 00:37:33.258 These were our with a washout.

NOTE Confidence: 0.851390034

00:37:33.260 --> 00:37:34.580 From the tumor matrix.

NOTE Confidence: 0.851390034

00:37:34.580 --> 00:37:36.329 But the BMP's in here,

NOTE Confidence: 0.851390034

00:37:36.329 --> 00:37:38.233 there and then are readily available

NOTE Confidence: 0.851390034

00:37:38.233 --> 00:37:39.859 to the tumor cells to kill,

NOTE Confidence: 0.851390034

00:37:39.860 --> 00:37:42.630 so we think there's two.

NOTE Confidence: 0.851390034

00:37:42.630 --> 00:37:45.265 Mechanisms that work together there

NOTE Confidence: 0.851390034

00:37:45.265 --> 00:37:48.454 one where the BMP's with their payloads

NOTE Confidence: 0.851390034

00:37:48.454 --> 00:37:51.363 or binding to the tumor rich matrix

NOTE Confidence: 0.851390034

00:37:51.363 --> 00:37:54.324 of tumors as well as readily being

NOTE Confidence: 0.851390034

00:37:54.324 --> 00:37:57.260 internalized by the tumor cells themselves.

NOTE Confidence: 0.851390034

00:37:57.260 --> 00:38:00.364 We can move to in vivo established tumors,

NOTE Confidence: 0.851390034

00:38:00.370 --> 00:38:04.318 inject our bpce with with Die

NOTE Confidence: 0.851390034

00:38:04.318 --> 00:38:06.950 or MPs for comparison,

NOTE Confidence: 0.851390034

00:38:06.950 --> 00:38:09.374 and see what kind of distribution

NOTE Confidence: 0.851390034

00:38:09.374 --> 00:38:11.798 we get through the tumor cells

NOTE Confidence: 0.851390034

00:38:11.798 --> 00:38:14.036 and what kind of staying.

NOTE Confidence: 0.851390034

00:38:14.036 --> 00:38:17.180 Power we might get.

NOTE Confidence: 0.851390034

00:38:17.180 --> 00:38:20.141 Uhm, in fact, we can measure that over days

NOTE Confidence: 0.851390034

00:38:20.141 --> 00:38:23.340 and we can do that by harvesting the tumors,

NOTE Confidence: 0.851390034

00:38:23.340 --> 00:38:26.034 pulverising them and extracting and doing

NOTE Confidence: 0.851390034

00:38:26.034 --> 00:38:28.689 HPLC quantification on the drug levels.

NOTE Confidence: 0.851390034

00:38:28.690 --> 00:38:30.769 And you can see here this is intralipid with

NOTE Confidence: 0.851390034

00:38:30.769 --> 00:38:32.940 the capital seeking chemotherapeutic agent.

NOTE Confidence: 0.851390034

00:38:32.940 --> 00:38:34.698 We just don't detect it after

NOTE Confidence: 0.851390034

00:38:34.698 --> 00:38:36.768 day zero if it's in any piece,

NOTE Confidence: 0.851390034

00:38:36.770 --> 00:38:38.876 there is a little bit of detection today too,

NOTE Confidence: 0.851390034

00:38:38.880 --> 00:38:42.576 but that pales in comparison to what

NOTE Confidence: 0.851390034

00:38:42.580 --> 00:38:44.686 BMP's due to keeping drug present.

NOTE Confidence: 0.851390034

00:38:44.690 --> 00:38:47.560 Again, there may be released.

NOTE Confidence: 0.851390034

00:38:47.560 --> 00:38:50.596 From the particles, but it's there.

NOTE Confidence: 0.851390034

00:38:50.600 --> 00:38:52.452 Maybe particles that contain

NOTE Confidence: 0.851390034

00:38:52.452 --> 00:38:54.304 depost more slowly release.

NOTE Confidence: 0.851390034

00:38:54.310 --> 00:38:55.745 They may do that in the Peri

NOTE Confidence: 0.851390034

00:38:55.745 --> 00:38:57.200 tumoral area of the tumor matrix.

NOTE Confidence: 0.851390034

00:38:57.200 --> 00:38:59.130 They may do that within

NOTE Confidence: 0.851390034

00:38:59.130 --> 00:39:00.288 tumor cells themselves.

NOTE Confidence: 0.940593850769231

00:39:03.540 --> 00:39:06.044 And then we can look at the therapeutic

NOTE Confidence: 0.940593850769231

00:39:06.044 --> 00:39:07.838 efficacy of using for example,

NOTE Confidence: 0.940593850769231

00:39:07.840 --> 00:39:10.460 camp to thicken incorporated within

NOTE Confidence: 0.940593850769231

00:39:10.460 --> 00:39:13.796 BMP'S to treat establish screen or

NOTE Confidence: 0.940593850769231

00:39:13.796 --> 00:39:17.152 cell carcinomas injected here at day

NOTE Confidence: 0.940593850769231

00:39:17.152 --> 00:39:20.588 four we can measure tumor size and and

NOTE Confidence: 0.940593850769231

00:39:20.588 --> 00:39:23.520 and see what we do to tomb of growth.

NOTE Confidence: 0.940593850769231

00:39:23.520 --> 00:39:26.192 We can also harvest at the end and

NOTE Confidence: 0.940593850769231

00:39:26.192 --> 00:39:28.154 do histological analysis for the

NOTE Confidence: 0.940593850769231

00:39:28.154 --> 00:39:30.199 presence of any residual tumors.

NOTE Confidence: 0.940593850769231

00:39:30.200 --> 00:39:33.548 We do get an inflammation with the BNP CPT.

NOTE Confidence: 0.940593850769231

00:39:33.550 --> 00:39:34.970 As you might expect,

NOTE Confidence: 0.940593850769231

00:39:34.970 --> 00:39:38.319 we do with both arms of the CPT alone.

NOTE Confidence: 0.97936355

00:39:41.030 --> 00:39:43.664 So that. You know,

NOTE Confidence: 0.97936355

00:39:43.664 --> 00:39:45.896 clinical tumor measurements are are not

NOTE Confidence: 0.97936355

00:39:45.896 --> 00:39:48.057 as definitive as the histologic ones,

NOTE Confidence: 0.97936355

00:39:48.060 --> 00:39:51.848 but both the clinical tumor growth

NOTE Confidence: 0.97936355

00:39:51.848 --> 00:39:54.768 curves were showed protection with

NOTE Confidence: 0.97936355

00:39:54.768 --> 00:39:58.485 btes relative to CPT alone at the same

NOTE Confidence: 0.97936355

00:39:58.485 --> 00:40:01.500 dose of drug and in histologically we

NOTE Confidence: 0.97936355

00:40:01.500 --> 00:40:06.351 saw a 62% tumor free rate with the BNP

NOTE Confidence: 0.97936355

00:40:06.351 --> 00:40:09.690 skeds that was impressive in a parallel

NOTE Confidence: 0.97936355

00:40:09.690 --> 00:40:12.350 experiment at at four weeks out.

NOTE Confidence: 0.927088468333333

00:40:15.270 --> 00:40:18.434 So we were really interested in whether

NOTE Confidence: 0.927088468333333

00:40:18.434 --> 00:40:21.698 this localized treatment could be combined

NOTE Confidence: 0.927088468333333

00:40:21.698 --> 00:40:24.170 with with immunotherapeutic strategies,

NOTE Confidence: 0.927088468333333

00:40:24.170 --> 00:40:26.840 and the first thing we did was to go local.

NOTE Confidence: 0.927088468333333

00:40:26.840 --> 00:40:29.010 We are designing experiments for

NOTE Confidence: 0.927088468333333

00:40:29.010 --> 00:40:30.746 checkpoint inhibitors which might

NOTE Confidence: 0.927088468333333

00:40:30.746 --> 00:40:33.198 be on the minds of several people.

NOTE Confidence: 0.927088468333333

00:40:33.200 --> 00:40:34.975 We're working with Marcus Bosenberg

NOTE Confidence: 0.927088468333333

00:40:34.975 --> 00:40:37.120 on what that might look like,

NOTE Confidence: 0.927088468333333

00:40:37.120 --> 00:40:41.710 for example with a localized.

NOTE Confidence: 0.927088468333333

00:40:41.710 --> 00:40:44.194 Invasive Melanoma or metastatic

NOTE Confidence: 0.927088468333333

00:40:44.194 --> 00:40:46.057 nodule of Melanoma,

NOTE Confidence: 0.927088468333333

00:40:46.060 --> 00:40:49.075 but in this case this is our our BMP

NOTE Confidence: 0.927088468333333

00:40:49.075 --> 00:40:50.970 screen PDV squamous cell carcinoma

NOTE Confidence: 0.927088468333333

00:40:50.970 --> 00:40:55.054 again and we looked at again the

NOTE Confidence: 0.927088468333333

00:40:55.054 --> 00:40:58.495 capacity for BMP's to incorporate

NOTE Confidence: 0.927088468333333

00:40:58.495 --> 00:41:01.540 CPT but be combined with a local

NOTE Confidence: 0.927088468333333

00:41:01.629 --> 00:41:04.669 immunotherapeutic agent in this case.

NOTE Confidence: 0.927088468333333

00:41:04.670 --> 00:41:05.998 Kcse people familiar with

NOTE Confidence: 0.927088468333333

00:41:05.998 --> 00:41:08.330 that know this this is a TLR.

NOTE Confidence: 0.927088468333333

00:41:08.330 --> 00:41:12.306 Nine login, so we're kind of creating a.

NOTE Confidence: 0.927088468333333

00:41:12.310 --> 00:41:15.182 Kill and thrill strategy,

NOTE Confidence: 0.927088468333333

00:41:15.182 --> 00:41:18.580 where we're not just killing tumor cells,

NOTE Confidence: 0.927088468333333

00:41:18.580 --> 00:41:21.268 but help trying to harness local

NOTE Confidence: 0.927088468333333

00:41:21.268 --> 00:41:24.530 immunity to help clean up residual ones.

NOTE Confidence: 0.927088468333333

00:41:24.530 --> 00:41:26.540 Maybe some of that tumor debris,

NOTE Confidence: 0.927088468333333

00:41:26.540 --> 00:41:28.900 tumor antigen rich material,

NOTE Confidence: 0.927088468333333

00:41:28.900 --> 00:41:30.670 and immunostimulation might

NOTE Confidence: 0.927088468333333

00:41:30.670 --> 00:41:32.960 create an in vivo.

NOTE Confidence: 0.927088468333333

00:41:32.960 --> 00:41:34.860 Vaccination effect when we compare

NOTE Confidence: 0.927088468333333

00:41:34.860 --> 00:41:37.572 it to just intralipid CPT with that

NOTE Confidence: 0.927088468333333

00:41:37.572 --> 00:41:39.064 with that same immunostimulatory

NOTE Confidence: 0.927088468333333

00:41:39.064 --> 00:41:41.768 agent we just do not get the level

NOTE Confidence: 0.927088468333333

00:41:41.768 --> 00:41:43.858 of protection we can get by pushing

NOTE Confidence: 0.927088468333333

00:41:43.858 --> 00:41:46.504 the system hard on the tumor side.

NOTE Confidence: 0.830675177

00:41:49.470 --> 00:41:52.830 This might be a little bit more easy to see,

NOTE Confidence: 0.830675177

00:41:52.830 --> 00:41:55.154 and when we look at individual tumor

NOTE Confidence: 0.830675177

00:41:55.154 --> 00:41:57.258 growths and you see the the the

NOTE Confidence: 0.830675177

00:41:57.258 --> 00:41:59.769 shutting down of a lot of those tumors

NOTE Confidence: 0.830675177

00:41:59.769 --> 00:42:01.954 that were treated with combination.

NOTE Confidence: 0.93733746

00:42:06.670 --> 00:42:07.080 Mark

NOTE Confidence: 0.770743134

00:42:10.200 --> 00:42:11.492 just to finish up.

NOTE Confidence: 0.770743134

00:42:11.492 --> 00:42:13.997 Just remind you of the of the

NOTE Confidence: 0.770743134

00:42:13.997 --> 00:42:15.937 two classes of nanoparticles.

NOTE Confidence: 0.770743134

00:42:15.940 --> 00:42:17.770 We've worked here really the

NOTE Confidence: 0.770743134

00:42:17.770 --> 00:42:19.600 same when they're synthesized and

NOTE Confidence: 0.770743134

00:42:19.661 --> 00:42:21.407 converted from NPS into BMP's.

NOTE Confidence: 0.770743134

00:42:21.407 --> 00:42:24.265 We can load agents into the into

NOTE Confidence: 0.770743134

00:42:24.265 --> 00:42:26.940 the PLA polylactic acid shell,

NOTE Confidence: 0.770743134

00:42:26.940 --> 00:42:28.938 and then we manipulate the hyperbranched

NOTE Confidence: 0.770743134

00:42:28.938 --> 00:42:30.925 polyglycerol in the order to either

NOTE Confidence: 0.770743134

00:42:30.925 --> 00:42:32.435 make stealthy particles and NPS,

NOTE Confidence: 0.770743134

00:42:32.440 --> 00:42:36.440 or adhesive particles BMPS.

NOTE Confidence: 0.770743134

00:42:36.440 --> 00:42:40.160 So Polly PLA is made from L.

NOTE Confidence: 0.770743134

00:42:40.160 --> 00:42:42.284 Lactide is a monomer that costs

NOTE Confidence: 0.770743134

00:42:42.284 --> 00:42:43.848 about $5000 per 10 kilograms.

NOTE Confidence: 0.770743134

00:42:43.848 --> 00:42:45.660 It's been going up over time

NOTE Confidence: 0.770743134

00:42:45.722 --> 00:42:47.350 because of worldwide demand,

NOTE Confidence: 0.770743134

00:42:47.350 --> 00:42:50.800 for for for lactide based polymers.

NOTE Confidence: 0.770743134

00:42:50.800 --> 00:42:52.258 There are some alternates that have

NOTE Confidence: 0.770743134

00:42:52.258 --> 00:42:54.342 been used quite a lot in medicine like

NOTE Confidence: 0.770743134

00:42:54.342 --> 00:42:56.260 caprolactone or or Penta deco lactone loser,

NOTE Confidence: 0.770743134

00:42:56.260 --> 00:42:56.844 shown here.

NOTE Confidence: 0.770743134

00:42:56.844 --> 00:42:58.392 They're they're cheaper, but not.

NOTE Confidence: 0.770743134

00:42:58.392 --> 00:43:01.500 But but but maybe by a factor of two,

NOTE Confidence: 0.770743134

00:43:01.500 --> 00:43:03.460 but we focused on ethylene brassil 8,

NOTE Confidence: 0.770743134

00:43:03.460 --> 00:43:06.208 which is also a a lactone.

NOTE Confidence: 0.770743134

00:43:06.210 --> 00:43:07.293 But it it,

NOTE Confidence: 0.770743134

00:43:07.293 --> 00:43:09.098 but it's much cheaper 10

NOTE Confidence: 0.770743134

00:43:09.098 --> 00:43:11.009 times cheaper than L lactide,

NOTE Confidence: 0.770743134

00:43:11.010 --> 00:43:13.686 which makes a big difference in

NOTE Confidence: 0.770743134

00:43:13.686 --> 00:43:15.470 terms of manufacturing costs.

NOTE Confidence: 0.770743134

00:43:15.470 --> 00:43:17.108 Another advantage of ethylene brassil 8

NOTE Confidence: 0.770743134

00:43:17.108 --> 00:43:19.149 is that it's produced in large quantities.

NOTE Confidence: 0.770743134

00:43:19.150 --> 00:43:20.928 It's been used it a lot in

NOTE Confidence: 0.770743134

00:43:20.928 --> 00:43:21.690 the fragrance industry,

NOTE Confidence: 0.770743134

00:43:21.690 --> 00:43:23.594 so it's been put on lots of people

NOTE Confidence: 0.770743134

00:43:23.594 --> 00:43:25.510 skin and its properties are known.

NOTE Confidence: 0.770743134

00:43:25.510 --> 00:43:27.256 It's a sustainable product 'cause it's

NOTE Confidence: 0.770743134

00:43:27.256 --> 00:43:28.969 'cause it's produced from Castor oil.

NOTE Confidence: 0.770743134

00:43:28.970 --> 00:43:31.100 It's not made from petroleum like

NOTE Confidence: 0.770743134

00:43:31.100 --> 00:43:33.138 those other like those other polymers

NOTE Confidence: 0.770743134

00:43:33.138 --> 00:43:35.932 are an it we knew going into this

NOTE Confidence: 0.770743134

00:43:35.932 --> 00:43:38.128 that that others had made these

NOTE Confidence: 0.770743134

00:43:38.128 --> 00:43:41.064 polymers and you could make them with

NOTE Confidence: 0.770743134

00:43:41.064 --> 00:43:43.199 similar mechanical properties to play.

NOTE Confidence: 0.770743134

00:43:43.200 --> 00:43:45.768 So can you make them into bio adhesive?

NOTE Confidence: 0.770743134

00:43:45.770 --> 00:43:46.240 Nanoparticles,

NOTE Confidence: 0.770743134

00:43:46.240 --> 00:43:48.120 the answer is yes,

NOTE Confidence: 0.770743134

00:43:48.120 --> 00:43:51.568 and post auction all put up Pythia

NOTE Confidence: 0.770743134

00:43:51.568 --> 00:43:53.410 and graduate student Alex Johnson,

NOTE Confidence: 0.770743134

00:43:53.410 --> 00:43:56.344 which have shown that in the

NOTE Confidence: 0.770743134

00:43:56.344 --> 00:43:58.794 next slide that there's these are

NOTE Confidence: 0.770743134

00:43:58.794 --> 00:44:00.029 particles that were made variety,

NOTE Confidence: 0.770743134

00:44:00.030 --> 00:44:00.542 different conditions,

NOTE Confidence: 0.770743134

00:44:00.542 --> 00:44:02.078 which shown in the graph here,

NOTE Confidence: 0.770743134

00:44:02.080 --> 00:44:03.728 but you can see some of the particles,

NOTE Confidence: 0.770743134

00:44:03.730 --> 00:44:06.720 but by scandal around micrographs.

NOTE Confidence: 0.770743134

00:44:06.720 --> 00:44:08.190 In this scanning electron micrograph,

NOTE Confidence: 0.770743134

00:44:08.190 --> 00:44:09.576 so we're encouraged that there this

NOTE Confidence: 0.770743134

00:44:09.576 --> 00:44:11.159 is something that we can accomplish,

NOTE Confidence: 0.770743134

00:44:11.160 --> 00:44:13.504 not just with the material we've shown here.

NOTE Confidence: 0.770743134

00:44:13.510 --> 00:44:15.302 We certainly have proof of principle that

NOTE Confidence: 0.770743134

00:44:15.302 --> 00:44:17.168 that material works in a variety of settings,

NOTE Confidence: 0.770743134

00:44:17.170 --> 00:44:18.400 but one can innovate on

NOTE Confidence: 0.770743134

00:44:18.400 --> 00:44:19.630 the material side as well,

NOTE Confidence: 0.770743134

00:44:19.630 --> 00:44:20.850 and potentially make things

NOTE Confidence: 0.770743134

00:44:20.850 --> 00:44:22.375 that are that are better.

NOTE Confidence: 0.792018294

00:44:26.630 --> 00:44:30.020 Alright, I'll I'll summarize our.

NOTE Confidence: 0.792018294

00:44:30.020 --> 00:44:32.975 Joint efforts and skin cancer

NOTE Confidence: 0.792018294

00:44:32.975 --> 00:44:34.748 prevention and treatment.

NOTE Confidence: 0.792018294

00:44:34.750 --> 00:44:37.621 So we've worked on in formulating

NOTE Confidence: 0.792018294

00:44:37.621 --> 00:44:39.727 a prototype for our sunscreen that

NOTE Confidence: 0.792018294

00:44:39.727 --> 00:44:41.939 shows this bio adhesion advantage,

NOTE Confidence: 0.792018294

00:44:41.940 --> 00:44:45.304 photostability advantage anti permeation

NOTE Confidence: 0.792018294

00:44:45.304 --> 00:44:49.509 advantage and SPF optimization advantages.

NOTE Confidence: 0.792018294

00:44:49.510 --> 00:44:52.096 We're working now on preclinical modeling.

NOTE Confidence: 0.792018294

00:44:52.100 --> 00:44:55.472 For that, this is the MC1RE mouse,

NOTE Confidence: 0.792018294

00:44:55.472 --> 00:44:59.708 so it has the same defect as fair skin red

NOTE Confidence: 0.792018294

00:44:59.708 --> 00:45:03.130 haired people with freckles to look at

NOTE Confidence: 0.792018294

00:45:03.130 --> 00:45:06.350 both acute and chronic kind of modeling.

NOTE Confidence: 0.792018294

00:45:06.350 --> 00:45:08.786 With that to really try to optimize

NOTE Confidence: 0.792018294

00:45:08.786 --> 00:45:10.604 our performance prior to moving

NOTE Confidence: 0.792018294

00:45:10.604 --> 00:45:12.028 to the clinical spectrum.

NOTE Confidence: 0.792018294

00:45:12.030 --> 00:45:13.527 All in addition,

NOTE Confidence: 0.792018294

00:45:13.527 --> 00:45:16.022 we're also looking at protecting

NOTE Confidence: 0.792018294

00:45:16.022 --> 00:45:18.150 specifically against both squamous

NOTE Confidence: 0.792018294

00:45:18.150 --> 00:45:20.795 cell carcinoma and Melanoma mutations.

NOTE Confidence: 0.792018294

00:45:20.800 --> 00:45:23.424 Over chronic exposure protocols.

NOTE Confidence: 0.792018294

00:45:23.424 --> 00:45:26.668 With that as part of the sport and

NOTE Confidence: 0.792018294

00:45:26.668 --> 00:45:29.104 and then you heard about some further

NOTE Confidence: 0.792018294

00:45:29.104 --> 00:45:30.984 BMP bio engineering improvements

NOTE Confidence: 0.792018294

00:45:30.984 --> 00:45:33.208 that we're working on.

NOTE Confidence: 0.792018294

00:45:33.210 --> 00:45:34.188 In addition,

NOTE Confidence: 0.792018294

00:45:34.188 --> 00:45:37.122 you heard about our efforts on

NOTE Confidence: 0.792018294

00:45:37.122 --> 00:45:39.727 localized therapy for skin cancer

NOTE Confidence: 0.792018294

00:45:39.727 --> 00:45:41.787 as a nonsurgical alternative,

NOTE Confidence: 0.792018294

00:45:41.790 --> 00:45:43.878 the advantage of matrix bio adhesion,

NOTE Confidence: 0.792018294

00:45:43.880 --> 00:45:46.940 tumor cell binding and uptake advantages,

NOTE Confidence: 0.792018294

00:45:46.940 --> 00:45:49.365 and how this translates into

NOTE Confidence: 0.792018294

00:45:49.365 --> 00:45:51.305 a drug retention advantages,

NOTE Confidence: 0.792018294

00:45:51.310 --> 00:45:53.885 efficient drug delivery and tumor

NOTE Confidence: 0.792018294

00:45:53.885 --> 00:45:55.945 elimination when delivered locally

NOTE Confidence: 0.792018294

00:45:55.945 --> 00:45:57.737 decrease systemic toxicity levels

NOTE Confidence: 0.792018294

00:45:57.737 --> 00:46:00.143 which we had didn't show here

NOTE Confidence: 0.792018294

00:46:00.150 --> 00:46:01.380 compatibility with immunotherapy.

NOTE Confidence: 0.792018294

00:46:01.380 --> 00:46:03.840 Which I to me is very,

NOTE Confidence: 0.792018294

00:46:03.840 --> 00:46:07.142 very exciting for the potential to

NOTE Confidence: 0.792018294

00:46:07.142 --> 00:46:09.290 use a localized therapy in combination

NOTE Confidence: 0.792018294

00:46:09.356 --> 00:46:11.332 with a systemic immunotherapy

NOTE Confidence: 0.792018294

00:46:11.332 --> 00:46:12.814 or localized immunotherapy.

NOTE Confidence: 0.819461146666667

00:46:15.410 --> 00:46:19.020 And that is. Are ping pong

NOTE Confidence: 0.819461146666667

00:46:19.020 --> 00:46:21.000 tag team talk for the day?

NOTE Confidence: 0.819461146666667

00:46:21.000 --> 00:46:23.412 UM, obviously a lot of people

NOTE Confidence: 0.819461146666667

00:46:23.412 --> 00:46:25.860 working in in both our labs,

NOTE Confidence: 0.819461146666667

00:46:25.860 --> 00:46:28.412 in particular, Julie Lewis,

NOTE Confidence: 0.819461146666667

00:46:28.412 --> 00:46:31.064 Sholud Komar, and Amanda Zoo

NOTE Confidence: 0.819461146666667

00:46:31.064 --> 00:46:33.354 contributed extensively to to data

NOTE Confidence: 0.819461146666667

00:46:33.354 --> 00:46:36.963 you saw on the skin cancer side and

NOTE Confidence: 0.819461146666667

00:46:36.963 --> 00:46:39.430 mark highlighted people in his lab,

NOTE Confidence: 0.819461146666667

00:46:39.430 --> 00:46:43.000 but in particular he wants to has

NOTE Confidence: 0.819461146666667

00:46:43.000 --> 00:46:45.594 been the tremendous link between

NOTE Confidence: 0.819461146666667

00:46:45.594 --> 00:46:48.816 our two labs to bring up the.

NOTE Confidence: 0.819461146666667

00:46:48.816 --> 00:46:51.480 By many engineering component to skin

NOTE Confidence: 0.819461146666667

00:46:51.565 --> 00:46:54.440 cancer and skin cancer prevention

NOTE Confidence: 0.819461146666667

00:46:54.440 --> 00:46:58.182 modeling and Doug crashes are also

NOTE Confidence: 0.819461146666667

00:46:58.182 --> 00:47:00.642 our partner and developing other

NOTE Confidence: 0.819461146666667

00:47:00.642 --> 00:47:03.550 strategies on skin cancer prevention.

NOTE Confidence: 0.819461146666667

00:47:03.550 --> 00:47:05.272 Who's also been very much involved

NOTE Confidence: 0.819461146666667

00:47:05.272 --> 00:47:08.696 in in in in how we try to make these

NOTE Confidence: 0.819461146666667

00:47:08.696 --> 00:47:10.168 formulations that might ultimately

NOTE Confidence: 0.819461146666667

00:47:10.239 --> 00:47:12.339 also prevent some of the oxidative

NOTE Confidence: 0.819461146666667

00:47:12.339 --> 00:47:14.152 damage that we talked about.

NOTE Confidence: 0.819461146666667

00:47:14.152 --> 00:47:16.212 Marcus Bosenberg and Harriet Kluger

NOTE Confidence: 0.819461146666667

00:47:16.212 --> 00:47:18.379 in particular as part of the.

NOTE Confidence: 0.819461146666667

00:47:18.380 --> 00:47:21.030 Or have been tremendously supportive

NOTE Confidence: 0.819461146666667

00:47:21.030 --> 00:47:24.654 of our work and Ruth Taliban runs

NOTE Confidence: 0.819461146666667

00:47:24.654 --> 00:47:28.052 a core here that has provided us

NOTE Confidence: 0.819461146666667

00:47:28.052 --> 00:47:30.773 with numerous human skin samples

NOTE Confidence: 0.819461146666667

00:47:30.773 --> 00:47:32.338 and they were very appreciative,

NOTE Confidence: 0.819461146666667

00:47:32.340 --> 00:47:35.358 especially Antonella as part of that.

NOTE Confidence: 0.819461146666667

00:47:35.360 --> 00:47:36.851 And of course,

NOTE Confidence: 0.819461146666667

00:47:36.851 --> 00:47:39.833 funding sources include the cancer spore,

NOTE Confidence: 0.819461146666667

00:47:39.840 --> 00:47:45.000 but other grants from NCI, NIAMS, and IEHS.