WEBVTT

NOTE duration:"00:47:51.8080000"

NOTE language:en-us

NOTE Confidence: 0.795572

00:00:00.000 --> 00:00:02.506 Today too, are y'all catch Santa grand

NOTE Confidence: 0.795572

00:00:02.510 --> 00:00:05.690 rounds? Today is a special day. It's one of

NOTE Confidence: 0.795572

00:00:05.690 --> 00:00:06.785 our endowed lectureships.

NOTE Confidence: 0.795572

00:00:06.785 --> 00:00:09.340 This is the blanched Omen lecture series

NOTE Confidence: 0.795572

00:00:09.404 --> 00:00:11.686 was established in 2012 by Marvin Sears,

NOTE Confidence: 0.795572

00:00:11.686 --> 00:00:14.509 who many of you might remember was a

NOTE Confidence: 0.795572

00:00:14.509 --> 00:00:16.274 longtime chairman of our Department

NOTE Confidence: 0.795572

00:00:16.274 --> 00:00:18.135 of Optomology and Visual Sciences.

NOTE Confidence: 0.795572

00:00:18.135 --> 00:00:20.805 He established his series in honor

NOTE Confidence: 0.795572

00:00:20.805 --> 00:00:22.757 of his mother Blanched Holman,

NOTE Confidence: 0.795572

00:00:22.757 --> 00:00:24.265 who eventually succumbed to

NOTE Confidence: 0.795572

00:00:24.265 --> 00:00:25.396 acute myelogenous leukemia,

NOTE Confidence: 0.795572

00:00:25.400 --> 00:00:27.656 and this is the first and

NOTE Confidence: 0.795572

00:00:27.656 --> 00:00:29.536 I'll lecture series at Yale.

NOTE Confidence: 0.795572

00:00:29.540 --> 00:00:31.202 Devoted to hematology, malignancy's.

NOTE Confidence: 0.795572

00:00:31.202 --> 00:00:33.330 It's intended to bring

NOTE Confidence: 0.8043628

00:00:33.330 --> 00:00:34.389 into Yale pioneers

NOTE Confidence: 0.8043628

00:00:34.390 --> 00:00:36.110 that have made major contributions

NOTE Confidence: 0.8043628

00:00:36.110 --> 00:00:38.280 to our understanding of the current

NOTE Confidence: 0.8043628

00:00:38.280 --> 00:00:39.700 trends in hematologic oncology

NOTE Confidence: 0.8043628

00:00:39.700 --> 00:00:42.176 to a very exciting today to have

NOTE Confidence: 0.8043628

00:00:42.176 --> 00:00:43.946 Marcel Vandenbrink as our speaker

NOTE Confidence: 0.8043628

00:00:43.946 --> 00:00:45.714 and to introduce myself today.

NOTE Confidence: 0.8043628

00:00:45.714 --> 00:00:47.840 I'm going to turn the podium

NOTE Confidence: 0.8043628

00:00:47.840 --> 00:00:49.260 over to Stephanie Helene,

NOTE Confidence: 0.8043628

00:00:49.260 --> 00:00:51.378 the director of our Division of

NOTE Confidence: 0.8043628

00:00:51.380 --> 00:00:53.150 Hematology. So Stephanie, the floor

NOTE Confidence: 0.8043628

00:00:53.150 --> 00:00:54.920 is yours. Thank you, Dan.

NOTE Confidence: 0.8043628

00:00:54.920 --> 00:00:56.690 So it's my absolute pleasure

NOTE Confidence: 0.8043628

00:00:56.690 --> 00:00:58.106 to introduce Doctor myself,

NOTE Confidence: 0.8043628

00:00:58.110 --> 00:01:00.371 wondering who is the head of division

NOTE Confidence: 0.8043628

00:01:00.371 --> 00:01:01.816 of hematologic malignancy Malignancy's

NOTE Confidence: 0.8043628

00:01:01.816 --> 00:01:03.500 at Memorial Sloan Kettering.

NOTE Confidence: 0.8043628

00:01:03.500 --> 00:01:05.474 Cancer Center so Doctor Funding Bank

NOTE Confidence: 0.8043628

00:01:05.474 --> 00:01:08.107 is an expert in hematopoietic stem cell

NOTE Confidence: 0.8043628

00:01:08.107 --> 00:01:10.609 transplantation and he obtained his MD

NOTE Confidence: 0.8043628

00:01:10.609 --> 00:01:13.245 and PhD from the University of Leiden,

NOTE Confidence: 0.8043628

00:01:13.250 --> 00:01:15.165 completed a postdoctoral fellowship at

NOTE Confidence: 0.8043628

00:01:15.165 --> 00:01:17.495 the Pittsburgh Cancer Institute and his

NOTE Confidence: 0.8043628

00:01:17.495 --> 00:01:19.625 residency at Duke University Medical Center.

NOTE Confidence: 0.8043628

00:01:19.630 --> 00:01:22.182 He has been the head of the Division

NOTE Confidence: 0.8043628

00:01:22.182 --> 00:01:24.022 of Hematology Malignancies since 2008

NOTE Confidence: 0.8043628

00:01:24.022 --> 00:01:26.661 is also a professor of medicine and

NOTE Confidence: 0.8043628

00:01:26.727 --> 00:01:28.822 immunology at Weill Cornell Medical

NOTE Confidence: 0.8043628

00:01:28.822 --> 00:01:30.906 College as a physician, scientist,

NOTE Confidence: 0.8043628

00:01:30.906 --> 00:01:32.124 Doctor, Vandenbrink studies,

NOTE Confidence: 0.8043628

00:01:32.124 --> 00:01:33.748 allogeneic stem cell transplantation.

NOTE Confidence: 0.8043628

00:01:33.750 --> 00:01:36.130 Both in the clinic and the laboratory,

NOTE Confidence: 0.8043628

00:01:36.130 --> 00:01:37.830 and his research is currently

NOTE Confidence: 0.8043628

00:01:37.830 --> 00:01:39.190 focused on two areas.

NOTE Confidence: 0.8043628

00:01:39.190 --> 00:01:41.234 One is to study the role that

NOTE Confidence: 0.8043628

00:01:41.234 --> 00:01:42.944 microorganisms living in the testing

NOTE Confidence: 0.8043628

00:01:42.944 --> 00:01:44.889 playing in patients undergoing stem

NOTE Confidence: 0.8043628

00:01:44.889 --> 00:01:46.980 cell transplantation and in those

NOTE Confidence: 0.8043628

00:01:46.980 --> 00:01:48.276 receiving cancer immunotherapy.

NOTE Confidence: 0.8043628

00:01:48.280 --> 00:01:49.810 He's developing strategies to help

NOTE Confidence: 0.8043628

00:01:49.810 --> 00:01:51.799 the body rebuild the immune system

NOTE Confidence: 0.8043628

00:01:51.799 --> 00:01:53.419 after bone marrow transplantation.

NOTE Confidence: 0.8043628

00:01:53.420 --> 00:01:55.765 His research in both of these areas

NOTE Confidence: 0.8043628

00:01:55.765 --> 00:01:57.643 is being translated into clinical

NOTE Confidence: 0.8043628

00:01:57.643 --> 00:01:59.653 trials that are currently ongoing

NOTE Confidence: 0.8043628

00:01:59.653 --> 00:02:01.599 at Sloan Kettering and beyond.

NOTE Confidence: 0.8043628

00:02:01.600 --> 00:02:02.214 In 2010,

NOTE Confidence: 0.8043628

00:02:02.214 --> 00:02:04.363 Doctor Finder bring started the Susan and

NOTE Confidence: 0.8043628

00:02:04.363 --> 00:02:06.698 Peter Solomon Divisional Genomics program,

NOTE Confidence: 0.8043628

00:02:06.700 --> 00:02:08.740 which focuses on targeted therapeutic

NOTE Confidence: 0.8043628

00:02:08.740 --> 00:02:10.372 therapy approaches for patients

NOTE Confidence: 0.8043628

00:02:10.372 --> 00:02:12.720 with less with blood cancers such as

NOTE Confidence: 0.8043628

00:02:12.720 --> 00:02:14.751 leukemia and this program was actually

NOTE Confidence: 0.8043628

00:02:14.751 --> 00:02:16.541 instrumental in the development of

NOTE Confidence: 0.8043628

00:02:16.541 --> 00:02:18.474 the first genomic profiling test.

NOTE Confidence: 0.8043628

00:02:18.474 --> 00:02:20.182 Pro Haematological malignancy is

NOTE Confidence: 0.8043628

00:02:20.182 --> 00:02:22.203 called Foundation One Heme which

NOTE Confidence: 0.8043628

00:02:22.203 --> 00:02:23.438 we are happy to use,

NOTE Confidence: 0.8043628

00:02:23.440 --> 00:02:25.722 so I'm turning over the podium to

NOTE Confidence: 0.8043628

00:02:25.722 --> 00:02:27.569 Doctor Vandenbrink who will tell

NOTE Confidence: 0.8043628

00:02:27.569 --> 00:02:29.579 us incredibly exciting stories on

NOTE Confidence: 0.8043628

00:02:29.579 --> 00:02:31.694 the intestinal microbiome in stem

NOTE Confidence: 0.8043628

00:02:31.694 --> 00:02:33.332 cell transplantation. So welcome.

NOTE Confidence: 0.8043628

00:02:33.332 --> 00:02:36.104 And we look forward to your presentation.

NOTE Confidence: 0.8666846

00:02:37.240 --> 00:02:38.500 Thank you so much.

NOTE Confidence: 0.8666846

00:02:38.500 --> 00:02:41.336 Thank you so much for these kind kind words.

NOTE Confidence: 0.8666846

00:02:41.336 --> 00:02:44.354 Of course this is again going to be a

NOTE Confidence: 0.8666846

00:02:44.354 --> 00:02:47.587 lecture by zoom and we were just saying how?

NOTE Confidence: 0.8666846

00:02:47.590 --> 00:02:49.578 Slowly but steadily we're getting a little

NOTE Confidence: 0.8666846

00:02:49.578 --> 00:02:52.194 bit tired of that and would like to have

NOTE Confidence: 0.8666846

00:02:52.194 --> 00:02:54.260 some real physical lectures again and see

NOTE Confidence: 0.8666846

00:02:54.260 --> 00:02:56.290 your audience and work with your audience.

NOTE Confidence: 0.8666846

00:02:56.290 --> 00:02:58.918 But no matter what, it is a fantastic honor

NOTE Confidence: 0.8666846

00:02:58.918 --> 00:03:01.506 to be your guest and to speak for you.

NOTE Confidence: 0.8666846

00:03:01.510 --> 00:03:03.832 So the first thing that I have to tell

NOTE Confidence: 0.8666846

00:03:03.832 --> 00:03:06.560 you honestly is that I do have a conflict

NOTE Confidence: 0.8666846

00:03:06.560 --> 00:03:08.759 of interest because some of the data,

NOTE Confidence: 0.8666846

00:03:08.760 --> 00:03:10.566 some of the studies that I

NOTE Confidence: 0.8666846

00:03:10.566 --> 00:03:12.285 will be showing were actually

NOTE Confidence: 0.8666846

00:03:12.285 --> 00:03:14.525 sponsored by the company serious.

NOTE Confidence: 0.8666846

00:03:14.530 --> 00:03:17.190 I'm not sure if I still need

NOTE Confidence: 0.8666846

00:03:17.190 --> 00:03:19.778 to show these kind of slides.

NOTE Confidence: 0.8666846

00:03:19.780 --> 00:03:23.065 I think that most of us will have

NOTE Confidence: 0.8666846

00:03:23.065 --> 00:03:25.795 a concept now that the microbiome

NOTE Confidence: 0.8666846

00:03:25.795 --> 00:03:29.389 that lives inside of us and on us is

NOTE Confidence: 0.8666846

00:03:29.389 --> 00:03:32.053 definitely relevant for a lot of the

NOTE Confidence: 0.8666846

00:03:32.053 --> 00:03:34.345 Physiology and one way of looking

NOTE Confidence: 0.8666846

00:03:34.345 --> 00:03:37.148 at that is what is summarized here.

NOTE Confidence: 0.8666846

00:03:37.150 --> 00:03:39.424 That one should start thinking about

NOTE Confidence: 0.8666846

00:03:39.424 --> 00:03:41.441 a human multi species symbiotic

NOTE Confidence: 0.8666846

00:03:41.441 --> 00:03:43.616 supra Organism with a constant

NOTE Confidence: 0.8666846

00:03:43.620 --> 00:03:44.940 interaction between microbes.

NOTE Confidence: 0.8666846

00:03:44.940 --> 00:03:48.648 And human human cells.

NOTE Confidence: 0.8666846

00:03:48.650 --> 00:03:51.037 So we've been doing that basically since

NOTE Confidence: 0.8666846

00:03:51.037 --> 00:03:54.441 2009 and our focus was very much when we

NOTE Confidence: 0.8666846

00:03:54.441 --> 00:03:56.630 started on allogeneic transplant patients,

NOTE Confidence: 0.8666846

00:03:56.630 --> 00:03:58.910 but since then we have broadened

NOTE Confidence: 0.8666846

00:03:58.910 --> 00:04:00.050 our whole scope.

NOTE Confidence: 0.8666846

00:04:00.050 --> 00:04:02.360 These are the current leaders of our

NOTE Confidence: 0.8666846

00:04:02.360 --> 00:04:04.610 group and the original gangster,

NOTE Confidence: 0.8666846

00:04:04.610 --> 00:04:05.302 Eric Pamer.

NOTE Confidence: 0.8666846

00:04:05.302 --> 00:04:08.070 As since then left us and has bolted

NOTE Confidence: 0.8666846

00:04:08.145 --> 00:04:10.310 for the University of Chicago,

NOTE Confidence: 0.8666846

00:04:10.310 --> 00:04:12.816 so these are the folks within my

NOTE Confidence: 0.8666846

00:04:12.816 --> 00:04:15.250 lap that are working on this,

NOTE Confidence: 0.8666846

00:04:15.250 --> 00:04:18.354 and I will mention some of their names.

NOTE Confidence: 0.8666846

00:04:18.360 --> 00:04:21.948 When we get to their studies.

NOTE Confidence: 0.8666846

00:04:21.950 --> 00:04:24.654 So an easy way to summarize about 10

NOTE Confidence: 0.8666846

00:04:24.654 --> 00:04:27.870 years of work by our group and by others

NOTE Confidence: 0.8666846

00:04:27.870 --> 00:04:30.240 within the context of allogeneic bone

NOTE Confidence: 0.8666846

00:04:30.240 --> 00:04:31.976 marrow transplantation and trying to

NOTE Confidence: 0.8666846

00:04:31.976 --> 00:04:34.260 see if there's a clinical relevance to it.

NOTE Confidence: 0.8666846

00:04:34.260 --> 00:04:35.844 Changes within the gut flora is

NOTE Confidence: 0.8666846

00:04:35.844 --> 00:04:37.971 to take as a starting point the

NOTE Confidence: 0.8666846

00:04:37.971 --> 00:04:39.987 causes of death within the first

NOTE Confidence: 0.8666846

00:04:39.987 --> 00:04:42.128 year after allogeneic transplants.

NOTE Confidence: 0.8666846

00:04:42.130 --> 00:04:43.840 And if you do that,

NOTE Confidence: 0.8666846

00:04:43.840 --> 00:04:46.094 then you can paint a cladogram an

NOTE Confidence: 0.8666846

00:04:46.094 --> 00:04:48.548 indicate with a blue color text said

NOTE Confidence: 0.8666846

00:04:48.548 --> 00:04:50.678 that are linked to good outcomes,

NOTE Confidence: 0.8666846

00:04:50.680 --> 00:04:52.804 and with red color text editor

NOTE Confidence: 0.8666846

00:04:52.804 --> 00:04:54.220 linked with bad outcomes.

NOTE Confidence: 0.8666846

00:04:54.220 --> 00:04:56.285 And you can differentiate the

NOTE Confidence: 0.8666846

00:04:56.285 --> 00:04:57.937 various clinically relevant outcomes

NOTE Confidence: 0.8666846

00:04:57.937 --> 00:04:59.359 1st and most of all,

NOTE Confidence: 0.8666846

00:04:59.360 --> 00:05:00.092 of course,

NOTE Confidence: 0.8666846

00:05:00.092 --> 00:05:02.288 the overall the overall survival rate,

NOTE Confidence: 0.8666846

00:05:02.290 --> 00:05:05.226 where you can see that certain texts are

NOTE Confidence: 0.8666846

00:05:05.226 --> 00:05:08.169 linked in a positive or a negative way.

NOTE Confidence: 0.8666846

00:05:08.170 --> 00:05:11.146 Then of course the second one that we

NOTE Confidence: 0.8666846

00:05:11.146 --> 00:05:14.031 have focused on very much is if certain

NOTE Confidence: 0.8666846

00:05:14.031 --> 00:05:16.970 texts are linked to a graft versus host,

NOTE Confidence: 0.8666846

00:05:16.970 --> 00:05:19.690 and I'm giving you one study here from

NOTE Confidence: 0.8666846

00:05:19.690 --> 00:05:22.324 2015 where we demonstrated in a patients

NOTE Confidence: 0.8666846

00:05:22.324 --> 00:05:25.109 that during the time the time period.

NOTE Confidence: 0.8666846

00:05:25.110 --> 00:05:26.950 Of neutrophil engraftment which is

NOTE Confidence: 0.8666846

00:05:26.950 --> 00:05:29.323 about 14 days out from allogeneic

NOTE Confidence: 0.8666846

00:05:29.323 --> 00:05:31.618 transplant that the abundance of

NOTE Confidence: 0.8666846

00:05:31.618 --> 00:05:33.978 a commensal enercell called sub

NOTE Confidence: 0.8666846

00:05:33.978 --> 00:05:35.790 laudia was clinically relevant.

NOTE Confidence: 0.8666846

00:05:35.790 --> 00:05:38.316 It seemed because patients who at

NOTE Confidence: 0.8666846

00:05:38.316 --> 00:05:41.835 that point had low levels of that of

NOTE Confidence: 0.8666846

00:05:41.835 --> 00:05:44.457 that texture had a greater incidence

NOTE Confidence: 0.7821491

00:05:44.546 --> 00:05:47.381 of little a graph versus host which

NOTE Confidence: 0.7821491

00:05:47.381 --> 00:05:50.995 is marked here with these red bars and

NOTE Confidence: 0.7821491

00:05:50.995 --> 00:05:54.330 that leads to overall worse outcomes.

NOTE Confidence: 0.7821491

00:05:54.330 --> 00:05:55.810 Many other clinically relevant

NOTE Confidence: 0.7821491

00:05:55.810 --> 00:05:58.472 outcomes can also be linked to changes

NOTE Confidence: 0.7821491

00:05:58.472 --> 00:06:00.738 within the flora, such as infections,

NOTE Confidence: 0.7821491

00:06:00.738 --> 00:06:02.561 organ toxicity, and even relapse.

NOTE Confidence: 0.7821491

00:06:02.561 --> 00:06:05.536 So now you can start to paint a

NOTE Confidence: 0.7821491

00:06:05.536 --> 00:06:07.906 picture really of what the different

NOTE Confidence: 0.7821491

00:06:07.906 --> 00:06:10.158 taxa could be linked to an.

NOTE Confidence: 0.7821491

00:06:10.160 --> 00:06:13.176 In some cases we have some mechanism also,

NOTE Confidence: 0.7821491

00:06:13.180 --> 00:06:17.580 and I will show you some of that.

NOTE Confidence: 0.7821491

00:06:17.580 --> 00:06:19.482 Now, many of these studies that

NOTE Confidence: 0.7821491

00:06:19.482 --> 00:06:21.930 we did and that others who did

NOTE Confidence: 0.7821491

00:06:21.930 --> 00:06:24.138 were limited by small group sizes.

NOTE Confidence: 0.7821491

00:06:24.140 --> 00:06:24.728 For instance,

NOTE Confidence: 0.7821491

00:06:24.728 --> 00:06:27.080 here I am showing a study early on

NOTE Confidence: 0.7821491

00:06:27.141 --> 00:06:29.013 where we demonstrated that if you

NOTE Confidence: 0.7821491

00:06:29.013 --> 00:06:31.574 look again at the time of neutrophil

NOTE Confidence: 0.7821491

00:06:31.574 --> 00:06:33.238 engraftment after an allogeneic

NOTE Confidence: 0.7821491

00:06:33.238 --> 00:06:35.144 transplant at the diversity within

NOTE Confidence: 0.7821491

00:06:35.144 --> 00:06:37.106 the gut flora that patients who

NOTE Confidence: 0.7821491

00:06:37.106 --> 00:06:39.250 had that point had higher diversity

NOTE Confidence: 0.7821491

00:06:39.250 --> 00:06:41.035 had a better overall outcome,

NOTE Confidence: 0.7821491

00:06:41.040 --> 00:06:42.990 and that seemed to be linked

NOTE Confidence: 0.7821491

00:06:42.990 --> 00:06:44.840 to the incidence of lethal.

NOTE Confidence: 0.7821491

00:06:44.840 --> 00:06:46.220 A graft versus host.

NOTE Confidence: 0.7821491

00:06:46.220 --> 00:06:46.910 But again,

NOTE Confidence: 0.7821491

00:06:46.910 --> 00:06:49.598 this was a single center small study.

NOTE Confidence: 0.7821491

00:06:49.600 --> 00:06:51.664 So we felt very fortunate when

NOTE Confidence: 0.7821491

00:06:51.664 --> 00:06:53.987 some of our dear friends and

NOTE Confidence: 0.7821491

00:06:53.987 --> 00:06:56.579 colleagues from all over the world

NOTE Confidence: 0.7821491

00:06:56.579 --> 00:06:58.698 were willing to work with us,

NOTE Confidence: 0.7821491

00:06:58.700 --> 00:07:01.670 so that now we could do a much larger

NOTE Confidence: 0.7821491

00:07:01.670 --> 00:07:04.377 study looking at 1300 plus patients.

NOTE Confidence: 0.7821491

00:07:04.380 --> 00:07:06.765 These patients were getting allogeneic

NOTE Confidence: 0.7821491

00:07:06.765 --> 00:07:09.520 transplants for AML and DS NHL.

NOTE Confidence: 0.7821491

00:07:09.520 --> 00:07:11.782 And the first thing that really

NOTE Confidence: 0.7821491

00:07:11.782 --> 00:07:14.462 struck us that if we looked at

NOTE Confidence: 0.7821491

00:07:14.462 --> 00:07:16.996 the at the at the baseline sample,

NOTE Confidence: 0.7821491

00:07:17.000 --> 00:07:19.034 so the samples when patients come

NOTE Confidence: 0.7821491

00:07:19.034 --> 00:07:21.110 in for their allogeneic transplant,

NOTE Confidence: 0.7821491

00:07:21.110 --> 00:07:23.525 that the composition of the flora was

NOTE Confidence: 0.7821491

00:07:23.525 --> 00:07:25.980 not that different between those centers.

NOTE Confidence: 0.7821491

00:07:25.980 --> 00:07:28.218 And I'll give you some reasons

NOTE Confidence: 0.7821491

00:07:28.218 --> 00:07:29.337 for that later,

NOTE Confidence: 0.7821491

00:07:29.340 --> 00:07:33.080 an SEC that in all four in all four centers.

NOTE Confidence: 0.7821491

00:07:33.080 --> 00:07:35.656 What we notice is that the moment that

NOTE Confidence: 0.7821491

00:07:35.656 --> 00:07:38.320 they come in for allogeneic transplant,

NOTE Confidence: 0.7821491

00:07:38.320 --> 00:07:39.904 there is a.

NOTE Confidence: 0.7821491

00:07:39.904 --> 00:07:42.544 A dramatic drop within the

NOTE Confidence: 0.7821491

00:07:42.544 --> 00:07:45.158 diversity of the gut flora.

NOTE Confidence: 0.7821491

00:07:45.160 --> 00:07:47.708 And thus that matter a clinically yes

NOTE Confidence: 0.7821491

00:07:47.708 --> 00:07:50.260 it does, as I'm showing here again,

NOTE Confidence: 0.7821491

00:07:50.260 --> 00:07:52.438 taking as a time point around

NOTE Confidence: 0.7821491

00:07:52.438 --> 00:07:53.164 neutrophil engraftment,

NOTE Confidence: 0.7821491

00:07:53.170 --> 00:07:53.534 which,

NOTE Confidence: 0.7821491

00:07:53.534 --> 00:07:54.990 as I said already,

NOTE Confidence: 0.7821491

00:07:54.990 --> 00:07:57.566 is about 14 days out from allergen

NOTE Confidence: 0.7821491

00:07:57.566 --> 00:07:59.438 echo transplant patients who at

NOTE Confidence: 0.7821491

00:07:59.438 --> 00:08:01.178 that point had higher diversity,

NOTE Confidence: 0.7821491

00:08:01.180 --> 00:08:02.660 that better overall outcomes.

NOTE Confidence: 0.7821491

00:08:02.660 --> 00:08:04.880 And this was holding up for

NOTE Confidence: 0.7821491

00:08:04.950 --> 00:08:06.640 the New York and patients,

NOTE Confidence: 0.7821491

00:08:06.640 --> 00:08:09.502 but also for the combined cohort

NOTE Confidence: 0.7821491

00:08:09.502 --> 00:08:12.260 of the other three centers.

NOTE Confidence: 0.7821491

00:08:12.260 --> 00:08:14.408 When we took a deeper dive,

NOTE Confidence: 0.7821491

00:08:14.410 --> 00:08:16.564 So what makes or what leads

NOTE Confidence: 0.7821491

00:08:16.564 --> 00:08:18.000 to that a difference?

NOTE Confidence: 0.7821491

00:08:18.000 --> 00:08:20.310 Then it seemed to be mostly linked

NOTE Confidence: 0.7821491

00:08:20.310 --> 00:08:21.950 to transplant related mortality,

NOTE Confidence: 0.7821491

00:08:21.950 --> 00:08:24.560 not so much relapse and within

NOTE Confidence: 0.7821491

00:08:24.560 --> 00:08:26.805 that category it actually seems

NOTE Confidence: 0.7821491

00:08:26.805 --> 00:08:29.325 to be mostly a difference in

NOTE Confidence: 0.7821491

00:08:29.325 --> 00:08:31.520 lethal graft versus host again.

NOTE Confidence: 0.7821491

00:08:31.520 --> 00:08:33.494 You can go one step further and

NOTE Confidence: 0.7821491

00:08:33.494 --> 00:08:35.409 you can start to think about

NOTE Confidence: 0.7821491

00:08:35.409 --> 00:08:37.074 certain attacks are that are

NOTE Confidence: 0.7821491

00:08:37.074 --> 00:08:39.283 linked to more favorable or worse

NOTE Confidence: 0.7821491

00:08:39.283 --> 00:08:41.503 outcomes and that you can validate.

NOTE Confidence: 0.7821491

00:08:41.510 --> 00:08:43.603 Then again by taking all of the

NOTE Confidence: 0.7821491

00:08:43.603 --> 00:08:45.838 patients of the other three cohorts,

NOTE Confidence: 0.7821491

00:08:45.840 --> 00:08:47.796 and indeed see that certain a

NOTE Confidence: 0.7821491

00:08:47.796 --> 00:08:49.499 consortia would be linked to

NOTE Confidence: 0.7821491

00:08:49.499 --> 00:08:50.827 better or worse outcomes.

NOTE Confidence: 0.7821491

00:08:50.830 --> 00:08:52.951 As you can tell we're not so

NOTE Confidence: 0.7821491

00:08:52.951 --> 00:08:54.663 focused on really zooming in

NOTE Confidence: 0.7821491

00:08:54.663 --> 00:08:56.498 too much on certain attacks,

NOTE Confidence: 0.8554378

00:08:56.500 --> 00:08:58.990 a except for one and I'll

NOTE Confidence: 0.8554378

00:08:58.990 --> 00:09:01.739 get back to that one later.

NOTE Confidence: 0.8554378

00:09:01.740 --> 00:09:04.204 I told you already that these patients

NOTE Confidence: 0.8554378

00:09:04.204 --> 00:09:06.721 came in with fairly similar diversity

NOTE Confidence: 0.8554378

00:09:06.721 --> 00:09:09.487 and the composition of their flora,

NOTE Confidence: 0.8554378

00:09:09.490 --> 00:09:11.938 and when we analyze that actually

NOTE Confidence: 0.8554378

00:09:11.938 --> 00:09:13.570 against normal healthy folks,

NOTE Confidence: 0.8554378

00:09:13.570 --> 00:09:16.261 what we saw is that all at all of

NOTE Confidence: 0.8554378

00:09:16.261 --> 00:09:18.719 these centers patients come into

NOTE Confidence: 0.8554378

00:09:18.719 --> 00:09:21.319 a transplant with lower diversity,

NOTE Confidence: 0.8554378

00:09:21.320 --> 00:09:23.696 and we speculate that that is

NOTE Confidence: 0.8554378

00:09:23.696 --> 00:09:26.596 because most of them will have gone

NOTE Confidence: 0.8554378

00:09:26.596 --> 00:09:29.480 through a year or so of chemotherapy.

NOTE Confidence: 0.8554378

00:09:29.480 --> 00:09:30.734 Neutropenic fevers treated

NOTE Confidence: 0.8554378

00:09:30.734 --> 00:09:32.824 with all kinds of antibiotics.

NOTE Confidence: 0.8554378

00:09:32.830 --> 00:09:34.015 And so on.

NOTE Confidence: 0.8554378

00:09:34.015 --> 00:09:36.385 But what was interesting is that

NOTE Confidence: 0.8554378

00:09:36.385 --> 00:09:39.074 coming in with an even lower

NOTE Confidence: 0.8554378

00:09:39.074 --> 00:09:41.284 diversity coming into a transplant

NOTE Confidence: 0.8554378

00:09:41.372 --> 00:09:44.138 was again linked to worse outcomes.

NOTE Confidence: 0.8554378

00:09:44.140 --> 00:09:46.654 Similar findings we have now also

NOTE Confidence: 0.8554378

00:09:46.654 --> 00:09:49.157 for Ottawa transplant where we see

NOTE Confidence: 0.8554378

00:09:49.157 --> 00:09:51.425 a similar drop within the diversity

NOTE Confidence: 0.8554378

00:09:51.425 --> 00:09:53.865 which starts at the moment that these

NOTE Confidence: 0.8554378

00:09:53.865 --> 00:09:55.843 patients come in for a transplant.

NOTE Confidence: 0.8554378

00:09:55.843 --> 00:09:58.021 And again if we take asmark

NOTE Confidence: 0.8554378

00:09:58.021 --> 00:10:00.119 the time point of neutrophil.

NOTE Confidence: 0.8554378

00:10:00.120 --> 00:10:00.854 So engraftment,

NOTE Confidence: 0.8554378

00:10:00.854 --> 00:10:03.790 which is about 9 days out from Ottawa

NOTE Confidence: 0.8554378

00:10:03.864 --> 00:10:06.150 transplants we see again that having

NOTE Confidence: 0.8554378

00:10:06.150 --> 00:10:08.682 at that time point higher diversity

NOTE Confidence: 0.8554378

00:10:08.682 --> 00:10:11.490 is linked to better overall outcomes.

NOTE Confidence: 0.86777544

00:10:13.630 --> 00:10:16.228 Now, Meanwhile, a number of studies,

NOTE Confidence: 0.86777544

00:10:16.230 --> 00:10:18.605 specifically within checkpoints and blockades

NOTE Confidence: 0.86777544

00:10:18.605 --> 00:10:20.980 have also demonstrated that diversity

NOTE Confidence: 0.86777544

00:10:21.041 --> 00:10:23.159 seems to matter for certain outcomes.

NOTE Confidence: 0.86777544

00:10:23.160 --> 00:10:26.304 In this case, responses to checkpoint

NOTE Confidence: 0.86777544

00:10:26.304 --> 00:10:29.883 blockade and we have some early data

NOTE Confidence: 0.86777544

00:10:29.883 --> 00:10:32.649 also that this might matter for

NOTE Confidence: 0.86777544

00:10:32.649 --> 00:10:35.826 the efficacy of car cell therapy.

NOTE Confidence: 0.86777544

00:10:35.830 --> 00:10:37.846 Some studies that were still finishing

NOTE Confidence: 0.86777544

00:10:37.846 --> 00:10:40.301 at the moment seem to indicate also

NOTE Confidence: 0.86777544

00:10:40.301 --> 00:10:42.389 that changes within the gut flora

NOTE Confidence: 0.86777544

00:10:42.389 --> 00:10:44.188 specific texture could be linked with

NOTE Confidence: 0.86777544

00:10:44.188 --> 00:10:46.555 the pace of the CD four and regeneration

NOTE Confidence: 0.86777544

00:10:46.555 --> 00:10:47.855 after an allogeneic transplants.

NOTE Confidence: 0.86777544

00:10:47.860 --> 00:10:50.272 I don't want to make too much of a

NOTE Confidence: 0.86777544

00:10:50.272 --> 00:10:52.513 deal here of these various attacks

NOTE Confidence: 0.86777544

00:10:52.513 --> 00:10:55.098 are because we still want to take

NOTE Confidence: 0.86777544

00:10:55.098 --> 00:10:56.958 that into a germ free mouse.

NOTE Confidence: 0.86777544

00:10:56.960 --> 00:10:58.580 Models and study data further,

NOTE Confidence: 0.86777544

00:10:58.580 --> 00:11:01.205 but this gives us hints of which

NOTE Confidence: 0.86777544

00:11:01.205 --> 00:11:03.516 assault apps might be or which

NOTE Confidence: 0.86777544

00:11:03.516 --> 00:11:05.356 text that might be relevant.

NOTE Confidence: 0.86777544

00:11:05.360 --> 00:11:06.900 Another critical feature is

NOTE Confidence: 0.86777544

00:11:06.900 --> 00:11:09.210 that with the loss of diversity,

NOTE Confidence: 0.86777544

00:11:09.210 --> 00:11:11.429 what happens also is that in some

NOTE Confidence: 0.86777544

00:11:11.429 --> 00:11:12.933 of these patients specifically

NOTE Confidence: 0.86777544

00:11:12.933 --> 00:11:15.368 within the post transplant period,

NOTE Confidence: 0.86777544

00:11:15.370 --> 00:11:18.274 there is a moment that their whole flora

NOTE Confidence: 0.86777544

00:11:18.274 --> 00:11:21.150 is being dominated by a single taxer.

NOTE Confidence: 0.86777544

00:11:21.150 --> 00:11:24.142 If you use as a definition that domination

NOTE Confidence: 0.86777544

00:11:24.142 --> 00:11:26.995 is when more than 1/3 of your flora

NOTE Confidence: 0.86777544

00:11:26.995 --> 00:11:29.619 is dominated by a certain attacks,

NOTE Confidence: 0.86777544

00:11:29.620 --> 00:11:32.644 and then we actually notice that in all

NOTE Confidence: 0.86777544

00:11:32.644 --> 00:11:35.477 patients at all centres they will have.

NOTE Confidence: 0.86777544

00:11:35.480 --> 00:11:37.880 At a certain at time points,

NOTE Confidence: 0.86777544

00:11:37.880 --> 00:11:39.880 a dominance or almost all,

NOTE Confidence: 0.86777544

00:11:39.880 --> 00:11:42.784 and what was very striking is that all

NOTE Confidence: 0.86777544

00:11:42.784 --> 00:11:45.292 four centers had all former centers

NOTE Confidence: 0.86777544

00:11:45.292 --> 00:11:47.854 that the most prominent bacteria that

NOTE Confidence: 0.86777544

00:11:47.929 --> 00:11:50.275 would do that is Enterococcus an.

NOTE Confidence: 0.86777544

00:11:50.280 --> 00:11:52.650 We knew already from studies at

NOTE Confidence: 0.86777544

00:11:52.650 --> 00:11:55.729 our center that having a state of

NOTE Confidence: 0.86777544

00:11:55.729 --> 00:11:57.629 dominance with Enterococcus within

NOTE Confidence: 0.86777544

00:11:57.629 --> 00:12:00.076 the post transplant period was linked

NOTE Confidence: 0.86777544

00:12:00.076 --> 00:12:02.938 to a 9 faults of risk for bacteremia,

NOTE Confidence: 0.86777544

00:12:02.938 --> 00:12:05.570 with VRE for instance.

NOTE Confidence: 0.86777544

00:12:05.570 --> 00:12:06.886 Bob was very striking.

NOTE Confidence: 0.86777544

00:12:06.886 --> 00:12:08.860 Is that at all four centers?

NOTE Confidence: 0.86777544

00:12:08.860 --> 00:12:10.738 It was one specific species that

NOTE Confidence: 0.86777544

00:12:10.738 --> 00:12:12.614 would do that that would lead

NOTE Confidence: 0.86777544

00:12:12.614 --> 00:12:14.553 to a state of a dominance and

NOTE Confidence: 0.86777544

00:12:14.553 --> 00:12:16.430 that was Enterococcus aficion.

NOTE Confidence: 0.86777544

00:12:16.430 --> 00:12:18.070 As I'm showing you here.

NOTE Confidence: 0.8248834

00:12:20.100 --> 00:12:22.236 And that seemed to matter clinically.

NOTE Confidence: 0.8248834

00:12:22.240 --> 00:12:24.166 Also because what we know Tist

NOTE Confidence: 0.8248834

00:12:24.166 --> 00:12:26.158 is having during the period or

NOTE Confidence: 0.8248834

00:12:26.158 --> 00:12:28.084 the post transplant period at one

NOTE Confidence: 0.8248834

00:12:28.084 --> 00:12:30.452 point a state of dominance with

NOTE Confidence: 0.8248834

00:12:30.452 --> 00:12:32.527 Enterococcus aficion was linked to

NOTE Confidence: 0.8248834

00:12:32.527 --> 00:12:34.740 greater risk of graft versus host,

NOTE Confidence: 0.8248834

00:12:34.740 --> 00:12:36.159 worse overall outcomes,

NOTE Confidence: 0.8248834

00:12:36.159 --> 00:12:38.051 and specifically an increased

NOTE Confidence: 0.8248834

00:12:38.051 --> 00:12:40.398 incidence of lethal a graft versus

NOTE Confidence: 0.8248834

00:12:40.398 --> 00:12:42.762 host that was true for all of the

NOTE Confidence: 0.8248834

00:12:42.762 --> 00:12:44.848 New York of patients and also held

NOTE Confidence: 0.8248834

00:12:44.848 --> 00:12:48.090 up when we took the three cohorts

NOTE Confidence: 0.8248834

00:12:48.090 --> 00:12:50.730 from the other centers together.

NOTE Confidence: 0.8248834

00:12:50.730 --> 00:12:52.949 So we took that into mouse models

NOTE Confidence: 0.8248834

00:12:52.949 --> 00:12:55.246 and what I'm showing you here is

NOTE Confidence: 0.8248834

00:12:55.246 --> 00:12:57.930 every box is 1 mouse where we did

NOTE Confidence: 0.8248834

00:12:57.930 --> 00:13:00.042 sequential a sequencing an in this

NOTE Confidence: 0.8248834

00:13:00.042 --> 00:13:02.710 case here if we add some of T cells

NOTE Confidence: 0.8248834

00:13:02.710 --> 00:13:04.782 to the allograft with which these

NOTE Confidence: 0.8248834

00:13:04.782 --> 00:13:07.104 mice were being a transplanted which

NOTE Confidence: 0.8248834

00:13:07.104 --> 00:13:09.426 will lead to a graft versus host.

NOTE Confidence: 0.8248834

00:13:09.430 --> 00:13:11.100 As you can see here,

NOTE Confidence: 0.8248834

00:13:11.100 --> 00:13:12.770 lethal a graft versus host.

NOTE Confidence: 0.8248834

00:13:12.770 --> 00:13:15.450 Then you must notice that there are these.

NOTE Confidence: 0.8248834

00:13:15.450 --> 00:13:17.120 These these red diamonds here,

NOTE Confidence: 0.8248834

00:13:17.120 --> 00:13:19.292 which means that there's a blooming

NOTE Confidence: 0.8248834

00:13:19.292 --> 00:13:21.097 of Enterococcus happening during the

NOTE Confidence: 0.8248834

00:13:21.097 --> 00:13:22.879 development of a graft versus host.

NOTE Confidence: 0.8248834

00:13:22.880 --> 00:13:23.840 In these mice,

NOTE Confidence: 0.8248834

00:13:23.840 --> 00:13:26.080 these mice are not getting any type

NOTE Confidence: 0.8248834

00:13:26.145 --> 00:13:28.130 of antibiotic or anything else.

NOTE Confidence: 0.8248834

00:13:28.130 --> 00:13:29.150 We thought first.

NOTE Confidence: 0.8248834

00:13:29.150 --> 00:13:29.490 Well,

NOTE Confidence: 0.8248834

00:13:29.490 --> 00:13:31.961 maybe that is just for one strain

NOTE Confidence: 0.8248834

00:13:31.961 --> 00:13:33.377 or for one setting,

NOTE Confidence: 0.8248834

00:13:33.380 --> 00:13:35.130 so we did different strains

NOTE Confidence: 0.8248834

00:13:35.130 --> 00:13:36.530 in three different settings.

NOTE Confidence: 0.8248834

00:13:36.530 --> 00:13:38.696 For for monitoring a graft versus

NOTE Confidence: 0.8248834

00:13:38.696 --> 00:13:40.531 host causing a graft versus

NOTE Confidence: 0.8248834

00:13:40.531 --> 00:13:42.475 host in all of these cases,

NOTE Confidence: 0.8248834

00:13:42.480 --> 00:13:45.032 we kept on finding about seven days out

NOTE Confidence: 0.8248834

00:13:45.032 --> 00:13:46.861 from Allergan Aker transplant during

NOTE Confidence: 0.8248834

00:13:46.861 --> 00:13:49.479 the development of a graft versus host.

NOTE Confidence: 0.8248834

00:13:49.480 --> 00:13:52.910 There's a blooming of Enterococcus.

NOTE Confidence: 0.8248834

00:13:52.910 --> 00:13:55.570 Those that matter in these mouse models.

NOTE Confidence: 0.8248834

00:13:55.570 --> 00:13:55.937 Well,

NOTE Confidence: 0.8248834

00:13:55.937 --> 00:13:59.750 we test the debt by taking a germ free mice,

NOTE Confidence: 0.8248834

00:13:59.750 --> 00:14:01.650 giving them a minimal flora

NOTE Confidence: 0.8248834

00:14:01.650 --> 00:14:03.170 plus or minus Enterococcus.

NOTE Confidence: 0.8248834

00:14:03.170 --> 00:14:04.490 In these mouse models.

NOTE Confidence: 0.8248834

00:14:04.490 --> 00:14:07.398 By the way we saw blooming with different

NOTE Confidence: 0.8248834

00:14:07.398 --> 00:14:10.387 with a different species was not physiome,

NOTE Confidence: 0.8248834

00:14:10.390 --> 00:14:11.910 but Enterococcus faecalis an.

NOTE Confidence: 0.8248834

00:14:11.910 --> 00:14:13.430 If we did that.

NOTE Confidence: 0.8248834

00:14:13.430 --> 00:14:14.950 If these mice had

NOTE Confidence: 0.8248834

00:14:14.950 --> 00:14:16.470 Enterococcus in their flora,

NOTE Confidence: 0.8248834

00:14:16.470 --> 00:14:18.370 then indeed they had worse

NOTE Confidence: 0.8248834

00:14:18.370 --> 00:14:19.890 a graft versus host,

NOTE Confidence: 0.8248834

00:14:19.890 --> 00:14:23.698 and again had a blooming of Enterococcus.

NOTE Confidence: 0.8248834

00:14:23.700 --> 00:14:25.926 So we took that further into these

NOTE Confidence: 0.8248834

00:14:25.926 --> 00:14:28.189 mouse models and analyzed mechanisms,

NOTE Confidence: 0.8248834

00:14:28.190 --> 00:14:30.060 and since this is published,

NOTE Confidence: 0.8248834

00:14:30.060 --> 00:14:31.930 I'm only going to summarize

NOTE Confidence: 0.8248834

00:14:31.930 --> 00:14:33.800 it here with Soma schematics.

NOTE Confidence: 0.8248834

00:14:33.800 --> 00:14:36.236 So what we think is happening and

NOTE Confidence: 0.8248834

00:14:36.236 --> 00:14:39.068 what kind of data we have so far

NOTE Confidence: 0.8248834

00:14:39.068 --> 00:14:41.684 is that the damage caused by chemo

NOTE Confidence: 0.8248834

00:14:41.684 --> 00:14:43.769 and by the conditioning regiments

NOTE Confidence: 0.8248834

00:14:43.769 --> 00:14:46.355 plus the Elo activated T cells

NOTE Confidence: 0.8248834

00:14:46.355 --> 00:14:48.135 which specifically targets the

NOTE Confidence: 0.8248834

00:14:48.135 --> 00:14:50.612 crypt stem cells and causing a

NOTE Confidence: 0.8248834

00:14:50.612 --> 00:14:52.754 graft versus host within the gut.

NOTE Confidence: 0.8248834

00:14:52.760 --> 00:14:55.568 That will lead to enterocyte damage.

NOTE Confidence: 0.8248834

00:14:55.570 --> 00:14:57.630 The enter sites therefore start

NOTE Confidence: 0.8248834

00:14:57.630 --> 00:15:00.717 to make less of an anti microbial

NOTE Confidence: 0.8248834

00:15:00.717 --> 00:15:03.067 approaching called REC 3 which

NOTE Confidence: 0.8248834

00:15:03.067 --> 00:15:06.242 is known as we and others have

NOTE Confidence: 0.8248834

00:15:06.242 --> 00:15:08.762 actually demonstrated to be a an

NOTE Confidence: 0.8248834

00:15:08.770 --> 00:15:10.970 anti and anti microbial approaching

NOTE Confidence: 0.8248834

00:15:10.970 --> 00:15:12.730 that can contain Enterococcus.

NOTE Confidence: 0.8248834

00:15:12.730 --> 00:15:15.580 Another thing that also happens is

NOTE Confidence: 0.8248834

00:15:15.580 --> 00:15:17.480 that he enterocytes specifically

NOTE Confidence: 0.8248834

00:15:17.556 --> 00:15:19.326 within the ilium or less,

NOTE Confidence: 0.8248834

00:15:19.330 --> 00:15:21.355 are capable of making electees

NOTE Confidence: 0.8248834

00:15:21.355 --> 00:15:23.962 that will lead them to increase

NOTE Confidence: 0.8248834

00:15:23.962 --> 00:15:25.978 levels within the lumen.

NOTE Confidence: 0.8248834

00:15:25.980 --> 00:15:30.378 Of lactose and that plus the fact that

NOTE Confidence: 0.8248834

00:15:30.378 --> 00:15:32.825 there's less of rec rec three will

NOTE Confidence: 0.8248834

00:15:32.825 --> 00:15:35.033 then lead to an Enterococcus blue.

NOTE Confidence: 0.7907168

00:15:35.040 --> 00:15:36.078 The Enterococcus Bloom

NOTE Confidence: 0.7907168

00:15:36.078 --> 00:15:38.154 pushes away some of the year.

NOTE Confidence: 0.7907168

00:15:38.160 --> 00:15:39.228 Commensal flora well.

NOTE Confidence: 0.7907168

00:15:39.228 --> 00:15:41.720 One of the beneficial things that the

NOTE Confidence: 0.7907168

00:15:41.789 --> 00:15:44.389 commensal flora does is we and others have.

NOTE Confidence: 0.7907168

00:15:44.390 --> 00:15:46.644 A demonstrated is that it makes a

NOTE Confidence: 0.7907168

00:15:46.644 --> 00:15:48.774 butyrate and butyrate is an intraluminal

NOTE Confidence: 0.7907168

00:15:48.774 --> 00:15:50.604 nutrient for these intro sites.

NOTE Confidence: 0.7907168

00:15:50.610 --> 00:15:52.602 So if there's less a butyrates

NOTE Confidence: 0.7907168

00:15:52.602 --> 00:15:55.062 then that will lead to even more

NOTE Confidence: 0.7907168

00:15:55.062 --> 00:15:56.822 damage to the enterocytes and

NOTE Confidence: 0.7907168

00:15:56.822 --> 00:15:58.998 now you're in a downward spiral.

NOTE Confidence: 0.7907168

00:15:59.000 --> 00:16:01.826 And things get worse and worse.

NOTE Confidence: 0.7907168

00:16:01.830 --> 00:16:04.168 So we're trying to figure out are

NOTE Confidence: 0.7907168

00:16:04.168 --> 00:16:06.717 there ways that we can maybe blocked

NOTE Confidence: 0.7907168

00:16:06.717 --> 00:16:08.925 AT and we thought initially about

NOTE Confidence: 0.7907168

00:16:09.003 --> 00:16:11.528 some bacteriophages and other things.

NOTE Confidence: 0.7907168

00:16:11.530 --> 00:16:13.917 But then the post Doc who was

NOTE Confidence: 0.7907168

00:16:13.917 --> 00:16:15.885 working on this Christof Stein

NOTE Confidence: 0.7907168

00:16:15.885 --> 00:16:18.895 touring are did a very simple thing.

NOTE Confidence: 0.7907168

00:16:18.900 --> 00:16:21.228 He analyzed simply what are the

NOTE Confidence: 0.7907168

00:16:21.228 --> 00:16:22.780 pathways with already nutrients.

NOTE Confidence: 0.7907168

00:16:22.780 --> 00:16:24.332 As I mentioned already,

NOTE Confidence: 0.7907168

00:16:24.332 --> 00:16:25.884 that Enterococcus favors well.

NOTE Confidence: 0.7907168

00:16:25.890 --> 00:16:28.599 As I said already, it likes Electo,

NOTE Confidence: 0.7907168

00:16:28.600 --> 00:16:31.218 so in his culture system for intro

NOTE Confidence: 0.7907168

00:16:31.218 --> 00:16:33.729 Enterococcus he simply poured some lactaid.

NOTE Confidence: 0.7907168

00:16:33.730 --> 00:16:35.650 From the local pharmacy and

NOTE Confidence: 0.7907168

00:16:35.650 --> 00:16:37.186 demonstrated that with that.

NOTE Confidence: 0.7907168

00:16:37.190 --> 00:16:39.890 Of course he could block the

NOTE Confidence: 0.7907168

00:16:39.890 --> 00:16:41.690 growth of these bacteria.

NOTE Confidence: 0.7907168

00:16:41.690 --> 00:16:44.133 He then went back to these mouse

NOTE Confidence: 0.7907168

00:16:44.133 --> 00:16:46.199 models and what he did there,

NOTE Confidence: 0.7907168

00:16:46.200 --> 00:16:47.940 he's bought Chow without electrons,

NOTE Confidence: 0.7907168

00:16:47.940 --> 00:16:49.824 which is actually difficult because lactose

NOTE Confidence: 0.7907168

00:16:49.824 --> 00:16:52.099 is everywhere in many different nutrients.

NOTE Confidence: 0.7907168

00:16:52.100 --> 00:16:54.564 But he was able to get that mate

NOTE Confidence: 0.7907168

00:16:54.564 --> 00:16:57.416 and when he put these mice in two

NOTE Confidence: 0.7907168

00:16:57.416 --> 00:16:59.390 different models on the child,

NOTE Confidence: 0.7907168

00:16:59.390 --> 00:17:00.738 it was lactose free.

NOTE Confidence: 0.7907168

00:17:00.738 --> 00:17:02.760 Who could get somewhat less a

NOTE Confidence: 0.7907168

00:17:02.832 --> 00:17:04.248 graft versus host me.

NOTE Confidence: 0.7907168

00:17:04.250 --> 00:17:05.980 You're not curing a graft

NOTE Confidence: 0.7907168

00:17:05.980 --> 00:17:07.364 versus host with this,

NOTE Confidence: 0.7907168

00:17:07.370 --> 00:17:09.575 and he could block the

NOTE Confidence: 0.7907168

00:17:09.575 --> 00:17:10.898 blooming of Enterococcus.

NOTE Confidence: 0.7907168

00:17:10.900 --> 00:17:15.103 So then he took that finding back to humans.

NOTE Confidence: 0.7907168

00:17:15.110 --> 00:17:17.318 And we looked in our patients.

NOTE Confidence: 0.7907168

00:17:17.320 --> 00:17:18.058 A cohort.

NOTE Confidence: 0.7907168

00:17:18.058 --> 00:17:19.903 Are there maybe patients who

NOTE Confidence: 0.7907168

00:17:19.903 --> 00:17:21.010 have lactose intolerance?

NOTE Confidence: 0.7907168

00:17:21.010 --> 00:17:23.600 When we looked at that we hoped,

NOTE Confidence: 0.7907168

00:17:23.600 --> 00:17:24.310 of course,

NOTE Confidence: 0.7907168

00:17:24.310 --> 00:17:26.795 is that that would be linked to

NOTE Confidence: 0.7907168

00:17:26.795 --> 00:17:29.128 increased levels of graft versus host.

NOTE Confidence: 0.7907168

00:17:29.130 --> 00:17:32.442 We didn't really find that there was a trend,

NOTE Confidence: 0.7907168

00:17:32.450 --> 00:17:35.026 but what we did notice is the

NOTE Confidence: 0.7907168

00:17:35.026 --> 00:17:36.933 moment that patients come off

NOTE Confidence: 0.7907168

00:17:36.933 --> 00:17:39.453 antibiotics and that is the 0 here.

NOTE Confidence: 0.7907168

00:17:39.460 --> 00:17:41.195 Then those patients who are

NOTE Confidence: 0.7907168

00:17:41.195 --> 00:17:42.583 lactose intolerant will have

NOTE Confidence: 0.7907168

00:17:42.583 --> 00:17:44.260 higher levels of Enterococcus.

NOTE Confidence: 0.8346875

00:17:46.540 --> 00:17:48.997 So as I've been trying to show you here

NOTE Confidence: 0.8346875

00:17:48.997 --> 00:17:51.445 in this part so the Enterococcus can

NOTE Confidence: 0.8346875

00:17:51.445 --> 00:17:54.090 dominate in the post transplant period,

NOTE Confidence: 0.8346875

00:17:54.090 --> 00:17:56.826 it is linked to a graft versus host,

NOTE Confidence: 0.8346875

00:17:56.830 --> 00:17:59.702 and lactose is one of the basic nutrients

NOTE Confidence: 0.8346875

00:17:59.702 --> 00:18:01.976 for Enterococcus and using lactate or or.

NOTE Confidence: 0.8346875

00:18:01.980 --> 00:18:03.830 Basically strategies like that could

NOTE Confidence: 0.8346875

00:18:03.830 --> 00:18:06.051 potentially block the bloom of Enterococcus

NOTE Confidence: 0.8346875

00:18:06.051 --> 00:18:08.832 an in that way limit the graft versus host.

NOTE Confidence: 0.8346875

00:18:08.840 --> 00:18:11.115 This of course begs for a clinical

NOTE Confidence: 0.8346875

00:18:11.115 --> 00:18:13.289 study which we haven't done yet,

NOTE Confidence: 0.8346875

00:18:13.290 --> 00:18:16.930 so I can't tell you anything about that.

NOTE Confidence: 0.8346875

00:18:16.930 --> 00:18:18.890 Meanwhile, other centers have also

NOTE Confidence: 0.8346875

00:18:18.890 --> 00:18:20.850 demonstrated that the levels of

NOTE Confidence: 0.8346875

00:18:20.914 --> 00:18:22.784 Enterococcus within the post transplant

NOTE Confidence: 0.8346875

00:18:22.784 --> 00:18:25.788 periods are linked to a graft versus host.

NOTE Confidence: 0.8346875

00:18:25.790 --> 00:18:29.246 I'm just showing you one out of several here.

NOTE Confidence: 0.85659957

00:18:31.310 --> 00:18:32.930 Another disease that we were interested

NOTE Confidence: 0.85659957

00:18:32.930 --> 00:18:35.707 in is the a complication of chronic graft

NOTE Confidence: 0.85659957

00:18:35.707 --> 00:18:37.762 versus host after allogeneic transplant,

NOTE Confidence: 0.85659957

00:18:37.770 --> 00:18:40.686 so we try to figure out if changes within

NOTE Confidence: 0.85659957

00:18:40.686 --> 00:18:43.890 the four I could be relevant for that also.

NOTE Confidence: 0.85659957

00:18:43.890 --> 00:18:45.822 Now, the onset of chronic graft

NOTE Confidence: 0.85659957

00:18:45.822 --> 00:18:47.970 versus host is of course much,

NOTE Confidence: 0.85659957

00:18:47.970 --> 00:18:50.350 much later is about 200 days out,

NOTE Confidence: 0.85659957

00:18:50.350 --> 00:18:53.077 and what we did in this case is we

NOTE Confidence: 0.85659957

00:18:53.077 --> 00:18:55.729 looked at the samples about 100 days out

NOTE Confidence: 0.85659957

00:18:55.729 --> 00:18:58.665 and try to see if there were certain

NOTE Confidence: 0.85659957

00:18:58.665 --> 00:19:01.292 texts on maybe that could be linked.

NOTE Confidence: 0.85659957

00:19:01.292 --> 00:19:03.518 In a favorable or an unfavorable

NOTE Confidence: 0.85659957

00:19:03.518 --> 00:19:06.291 way with the onset of chronic graft

NOTE Confidence: 0.85659957

00:19:06.291 --> 00:19:08.126 versus host much, much later,

NOTE Confidence: 0.85659957

00:19:08.126 --> 00:19:10.750 and indeed we have some hints now such

NOTE Confidence: 0.85659957

00:19:10.815 --> 00:19:12.980 as Streptococcus in Accra Mencia.

NOTE Confidence: 0.85659957

00:19:12.980 --> 00:19:15.152 That seems to favor the onset

NOTE Confidence: 0.85659957

00:19:15.152 --> 00:19:17.010 of chronic graft versus host.

NOTE Confidence: 0.85659957

00:19:17.010 --> 00:19:19.579 So of course that this needs much

NOTE Confidence: 0.85659957

00:19:19.579 --> 00:19:20.680 much more work.

NOTE Confidence: 0.85659957

00:19:20.680 --> 00:19:23.014 Another feature in this article that

NOTE Confidence: 0.85659957

00:19:23.014 --> 00:19:25.605 I'm not summarizing is that there might

NOTE Confidence: 0.85659957

00:19:25.605 --> 00:19:28.307 be also a role for certain short chain

NOTE Confidence: 0.85659957

00:19:28.307 --> 00:19:30.932 fatty fatty acids that might limit the

NOTE Confidence: 0.85659957

00:19:30.932 --> 00:19:34.590 incidence of chronic graft versus host.

NOTE Confidence: 0.85659957

00:19:34.590 --> 00:19:37.012 Now I mentioned already a few times

NOTE Confidence: 0.85659957

00:19:37.012 --> 00:19:39.670 that this drop in the diversity within

NOTE Confidence: 0.85659957

00:19:39.670 --> 00:19:42.534 the gut flora is pretty dramatic in

NOTE Confidence: 0.85659957

00:19:42.534 --> 00:19:45.318 all patients who have an allogeneic

NOTE Confidence: 0.85659957

00:19:45.318 --> 00:19:46.710 bone marrow transplantation.

NOTE Confidence: 0.85659957

00:19:46.710 --> 00:19:49.286 So we went back and we try to

NOTE Confidence: 0.85659957

00:19:49.286 --> 00:19:51.470 analyze what are possible factors

NOTE Confidence: 0.85659957

00:19:51.470 --> 00:19:54.386 that might cause that dramatic loss,

NOTE Confidence: 0.85659957

00:19:54.390 --> 00:19:56.808 and the first one of course,

NOTE Confidence: 0.85659957

00:19:56.810 --> 00:20:00.536 that we looked at was antibiotics.

NOTE Confidence: 0.85659957

00:20:00.540 --> 00:20:01.144 And indeed,

NOTE Confidence: 0.85659957

00:20:01.144 --> 00:20:03.258 if you look at the use of

NOTE Confidence: 0.85659957

00:20:03.258 --> 00:20:05.110 broad spectrum antibiotics,

NOTE Confidence: 0.85659957

00:20:05.110 --> 00:20:07.312 so those type of antibiotics that

NOTE Confidence: 0.85659957

00:20:07.312 --> 00:20:09.635 we typically give when a patient

NOTE Confidence: 0.85659957

00:20:09.635 --> 00:20:11.207 has fever and neutropenia,

NOTE Confidence: 0.85659957

00:20:11.210 --> 00:20:13.454 and specifically will do damage to

NOTE Confidence: 0.85659957

00:20:13.454 --> 00:20:15.400 their commensal enter up flora,

NOTE Confidence: 0.85659957

00:20:15.400 --> 00:20:18.472 then indeed the exposure to those

NOTE Confidence: 0.85659957

00:20:18.472 --> 00:20:21.476 types of antibiotics will lead to

NOTE Confidence: 0.85659957

00:20:21.476 --> 00:20:24.080 a greater drop in the diversity.

NOTE Confidence: 0.85659957

00:20:24.080 --> 00:20:26.418 We analyzed over a period about 10

NOTE Confidence: 0.85659957

00:20:26.418 --> 00:20:28.825 years the use of antibiotics in

NOTE Confidence: 0.85659957

00:20:28.825 --> 00:20:30.605 our allogeneic transplants patients

NOTE Confidence: 0.85659957

00:20:30.605 --> 00:20:34.029 and try to see if certain types of

NOTE Confidence: 0.85659957

00:20:34.029 --> 00:20:36.044 antibiotics were linked to greater

NOTE Confidence: 0.85659957

00:20:36.050 --> 00:20:37.988 incidence of lethal graft versus host

NOTE Confidence: 0.85659957

00:20:37.988 --> 00:20:40.747 an we came up with two piperacillin

NOTE Confidence: 0.85659957

00:20:40.747 --> 00:20:42.619 tazobactam and imipenem also

NOTE Confidence: 0.85659957

00:20:42.619 --> 00:20:44.023 mirror mirror Panama's.

NOTE Confidence: 0.85659957

00:20:44.030 --> 00:20:45.542 We're using it now,

NOTE Confidence: 0.85659957

00:20:45.542 --> 00:20:49.051 but for this study we could only look at

NOTE Confidence: 0.85659957

00:20:49.051 --> 00:20:52.266 me Pennant and those are indeed two types

NOTE Confidence: 0.85659957

00:20:52.266 --> 00:20:55.698 of antibiotics that do more damage to the.

NOTE Confidence: 0.85659957

00:20:55.700 --> 00:20:56.780 Commensal anaerobic flora,

NOTE Confidence: 0.85659957

00:20:56.780 --> 00:20:58.580 then many other types of

NOTE Confidence: 0.85659957

00:20:58.580 --> 00:21:00.020 broad spectrum antibiotics,

NOTE Confidence: 0.85659957

00:21:00.020 --> 00:21:01.990 such as it's ever been.

NOTE Confidence: 0.85659957

00:21:01.990 --> 00:21:05.527 As I'm showing you here that was LinkedIn D2,

NOTE Confidence: 0.85659957

00:21:05.530 --> 00:21:08.274 higher incidence of lethal graft versus host.

NOTE Confidence: 0.85659957

00:21:08.280 --> 00:21:10.478 We took that again into a mouse

NOTE Confidence: 0.85659957

00:21:10.478 --> 00:21:13.295 model and we could see indeed that

NOTE Confidence: 0.85659957

00:21:13.295 --> 00:21:15.545 these two broad spectrum antibiotics

NOTE Confidence: 0.85659957

00:21:15.545 --> 00:21:18.069 that damage the analog flora would

NOTE Confidence: 0.85659957

00:21:18.069 --> 00:21:20.548 lead to worse graft versus host.

NOTE Confidence: 0.85659957

00:21:20.548 --> 00:21:23.894 And to make a Long story short,

NOTE Confidence: 0.85659957

00:21:23.900 --> 00:21:26.276 because this is all published when

NOTE Confidence: 0.85659957

00:21:26.276 --> 00:21:28.541 we studied this further in this

NOTE Confidence: 0.85659957

00:21:28.541 --> 00:21:30.662 mouse model we saw a few things.

NOTE Confidence: 0.85659957

00:21:30.670 --> 00:21:31.648 First of all,

NOTE Confidence: 0.85659957

00:21:31.648 --> 00:21:34.392 we saw a change within the gut flora

NOTE Confidence: 0.85659957

00:21:34.392 --> 00:21:37.424 that there was a blooming of a bacteria.

NOTE Confidence: 0.85659957

00:21:37.430 --> 00:21:38.142 Ecker, Ecker,

NOTE Confidence: 0.85659957

00:21:38.142 --> 00:21:39.210 Mencia and Accra.

NOTE Confidence: 0.85659957

00:21:39.210 --> 00:21:41.352 Mencia lives very close to the mucus

NOTE Confidence: 0.85659957

00:21:41.352 --> 00:21:43.537 layer and has mucolytic enzymes and

NOTE Confidence: 0.85659957

00:21:43.537 --> 00:21:46.330 therefore will lead to a greater breakdown.

NOTE Confidence: 0.80423427

00:21:46.330 --> 00:21:48.418 We actually speculate of the mucus

NOTE Confidence: 0.80423427

00:21:48.418 --> 00:21:50.725 layer and we could to demonstrate

NOTE Confidence: 0.80423427

00:21:50.725 --> 00:21:52.835 that the gut barrier function.

NOTE Confidence: 0.80423427

00:21:52.840 --> 00:21:55.521 More impaired in these mice treated with

NOTE Confidence: 0.80423427

00:21:55.521 --> 00:21:58.008 this broad spectrum antibiotic than not,

NOTE Confidence: 0.80423427

00:21:58.010 --> 00:22:00.565 and that again, might set up a

NOTE Confidence: 0.80423427

00:22:00.565 --> 00:22:03.189 cascade of a number of things,

NOTE Confidence: 0.80423427

00:22:03.190 --> 00:22:05.740 more stimulation of potentially of certain

NOTE Confidence: 0.80423427

00:22:05.740 --> 00:22:08.759 dendritic cells that I won't get into now.

NOTE Confidence: 0.80423427

00:22:08.760 --> 00:22:11.262 They will make higher levels of

NOTE Confidence: 0.80423427

00:22:11.262 --> 00:22:13.746 aside account that we know is

NOTE Confidence: 0.80423427

00:22:13.746 --> 00:22:16.315 linked to gut a graft versus host,

NOTE Confidence: 0.80423427

00:22:16.320 --> 00:22:18.546 which is all 2020 three that

NOTE Confidence: 0.80423427

00:22:18.546 --> 00:22:20.547 will lead to greater activation

NOTE Confidence: 0.80423427

00:22:20.547 --> 00:22:23.145 of Elo activated CD 4T cells.

NOTE Confidence: 0.80423427

00:22:23.150 --> 00:22:25.467 In this model that we are using,

NOTE Confidence: 0.80423427

00:22:25.470 --> 00:22:27.780 those are the driving donor T cells

NOTE Confidence: 0.80423427

00:22:27.780 --> 00:22:30.428 that will give you a graph versus host,

NOTE Confidence: 0.80423427

00:22:30.430 --> 00:22:32.747 leading to worse overall graph versus host.

NOTE Confidence: 0.80423427

00:22:32.750 --> 00:22:34.070 Specifically within the column.

NOTE Confidence: 0.8688149

00:22:36.340 --> 00:22:39.189 So a number of studies have looked

NOTE Confidence: 0.8688149

00:22:39.189 --> 00:22:42.150 now over the last decades or so.

NOTE Confidence: 0.8688149

00:22:42.150 --> 00:22:44.286 If the use of broad spectrum

NOTE Confidence: 0.8688149

00:22:44.286 --> 00:22:46.303 antibiotics has any impact on

NOTE Confidence: 0.8688149

00:22:46.303 --> 00:22:48.379 outcomes after allogeneic transplant,

NOTE Confidence: 0.8688149

00:22:48.380 --> 00:22:50.630 and as we were chatting earlier

NOTE Confidence: 0.8688149

00:22:50.630 --> 00:22:53.130 the the the first studies looking

NOTE Confidence: 0.8688149

00:22:53.130 --> 00:22:55.425 at the use of antibiotics,

NOTE Confidence: 0.8688149

00:22:55.430 --> 00:22:57.445 broad spectrum antibiotics in humans

NOTE Confidence: 0.8688149

00:22:57.445 --> 00:23:00.371 in the 1970s and 80s actually seemed

NOTE Confidence: 0.8688149

00:23:00.371 --> 00:23:03.290 to indicate that wiping out the whole

NOTE Confidence: 0.8688149

00:23:03.290 --> 00:23:05.906 flora would lead to better outcomes.

NOTE Confidence: 0.8688149

00:23:05.910 --> 00:23:07.870 Specifically, less graft versus host,

NOTE Confidence: 0.8688149

00:23:07.870 --> 00:23:10.084 and there are some pediatric studies

NOTE Confidence: 0.8688149

00:23:10.084 --> 00:23:12.570 that still seem to indicate that,

NOTE Confidence: 0.8688149

00:23:12.570 --> 00:23:14.928 but the bulk of the stories,

NOTE Confidence: 0.8688149

00:23:14.930 --> 00:23:17.282 the bulk of the studies over

NOTE Confidence: 0.8688149

00:23:17.282 --> 00:23:18.850 the last two years,

NOTE Confidence: 0.8688149

00:23:18.850 --> 00:23:21.258 do seem to indicate that the use

NOTE Confidence: 0.8688149

00:23:21.258 --> 00:23:22.823 of broad spectrum antibiotics

NOTE Confidence: 0.8688149

00:23:22.823 --> 00:23:25.118 is linked to worse outcomes,

NOTE Confidence: 0.8688149

00:23:25.120 --> 00:23:25.507 specifically,

NOTE Confidence: 0.8688149

00:23:25.507 --> 00:23:27.829 increased levels of lethal graft versus

NOTE Confidence: 0.8688149

00:23:27.829 --> 00:23:30.208 host or graft versus host overall.

NOTE Confidence: 0.8515854

00:23:32.790 --> 00:23:35.296 So what can we do about that?

NOTE Confidence: 0.8515854

00:23:35.300 --> 00:23:38.172 Well, one of the things that we have

NOTE Confidence: 0.8515854

00:23:38.172 --> 00:23:40.758 been looking at is a beta lactamase

NOTE Confidence: 0.8515854

00:23:40.758 --> 00:23:43.315 that you would give orally so that

NOTE Confidence: 0.8515854

00:23:43.315 --> 00:23:45.379 within the lumen you can block

NOTE Confidence: 0.8515854

00:23:45.379 --> 00:23:47.506 any kind of effects of whatever

NOTE Confidence: 0.8515854

00:23:47.506 --> 00:23:49.660 type of antibiotic you are using.

NOTE Confidence: 0.8515854

00:23:49.660 --> 00:23:51.814 So these are some early studies

NOTE Confidence: 0.8515854

00:23:51.814 --> 00:23:53.250 with such a compound,

NOTE Confidence: 0.8515854

00:23:53.250 --> 00:23:55.650 so if we get gift that then indeed

NOTE Confidence: 0.8515854

00:23:55.650 --> 00:23:58.377 we can block in a normal mouse

NOTE Confidence: 0.8515854

00:23:58.377 --> 00:24:00.427 the change within the diversity.

NOTE Confidence: 0.8515854

00:24:00.430 --> 00:24:01.866 The blooming of Enterococcus.

NOTE Confidence: 0.8515854

00:24:01.866 --> 00:24:04.841 When you treat a mouse with both an

NOTE Confidence: 0.8515854

00:24:04.841 --> 00:24:07.109 antibiotic and this beta beta lactamase,

NOTE Confidence: 0.8515854

00:24:07.110 --> 00:24:09.702 and if you take it to a mouse

NOTE Confidence: 0.8515854

00:24:09.702 --> 00:24:11.938 model for graft versus host,

NOTE Confidence: 0.8515854

00:24:11.940 --> 00:24:14.298 similarly you can somewhat block the

NOTE Confidence: 0.8515854

00:24:14.298 --> 00:24:16.961 worsening of graft versus host that you

NOTE Confidence: 0.8515854

00:24:16.961 --> 00:24:19.355 would get with the with the antibiotics.

NOTE Confidence: 0.8515854

00:24:19.360 --> 00:24:21.825 Of course, we're looking forward

NOTE Confidence: 0.8515854

00:24:21.825 --> 00:24:24.710 to taking this into trials now.

NOTE Confidence: 0.8515854

00:24:24.710 --> 00:24:26.150 A second major factor,

NOTE Confidence: 0.8515854

00:24:26.150 --> 00:24:29.227 we think that can impact on the dramatic

NOTE Confidence: 0.8515854

00:24:29.227 --> 00:24:32.153 loss of diversity are are the different

NOTE Confidence: 0.8515854

00:24:32.153 --> 00:24:34.669 types of a conditioning regiments.

NOTE Confidence: 0.8515854

00:24:34.670 --> 00:24:37.099 So we took a deep dive here.

NOTE Confidence: 0.8515854

00:24:37.100 --> 00:24:39.557 As all of the different types of

NOTE Confidence: 0.8515854

00:24:39.557 --> 00:24:40.951 air conditioning regiments that

NOTE Confidence: 0.8515854

00:24:40.951 --> 00:24:42.925 we have been using at our center,

NOTE Confidence: 0.8515854

00:24:42.930 --> 00:24:44.550 and as you can see,

NOTE Confidence: 0.8515854

00:24:44.550 --> 00:24:45.456 there are many.

NOTE Confidence: 0.8515854

00:24:45.456 --> 00:24:47.268 You can put them into three

NOTE Confidence: 0.8515854

00:24:47.268 --> 00:24:49.089 categories based upon their strength.

NOTE Confidence: 0.8515854

00:24:49.090 --> 00:24:52.842 Going from my lower blade of two reduced

NOTE Confidence: 0.8515854

00:24:52.842 --> 00:24:55.397 intensity tune on my lower blade.

NOTE Confidence: 0.8515854

00:24:55.400 --> 00:24:58.550 And if you do that as you would expect,

NOTE Confidence: 0.8515854

00:24:58.550 --> 00:25:01.136 the ones with lower strength indeed

NOTE Confidence: 0.8515854

00:25:01.136 --> 00:25:04.777 curfew less of a drop in the diversity.

NOTE Confidence: 0.8515854

00:25:04.780 --> 00:25:06.484 And even if you were control

NOTE Confidence: 0.8515854

00:25:06.484 --> 00:25:08.490 for the use of antibiotics,

NOTE Confidence: 0.8515854

00:25:08.490 --> 00:25:12.570 you still keep on finding that same thing.

NOTE Confidence: 0.8515854

00:25:12.570 --> 00:25:14.640 Another thing that was very interesting

NOTE Confidence: 0.8515854

00:25:14.640 --> 00:25:17.653 when we looked at it in some more detail

NOTE Confidence: 0.8515854

00:25:17.653 --> 00:25:19.873 is that certain regiments and we don't

NOTE Confidence: 0.8515854

00:25:19.873 --> 00:25:22.193 know why we need to study that further,

NOTE Confidence: 0.8515854

00:25:22.200 --> 00:25:24.126 such as this one with fludarabine,

NOTE Confidence: 0.8515854

00:25:24.130 --> 00:25:26.050 cyclophosphamide and low dose at TV.

NOTE Confidence: 0.8515854

00:25:26.050 --> 00:25:28.080 I seem to be linked to the

NOTE Confidence: 0.8515854

00:25:28.080 --> 00:25:29.580 blooming of certain bacteria,

NOTE Confidence: 0.8515854

00:25:29.580 --> 00:25:31.218 and here I'm pointing out again

NOTE Confidence: 0.8515854

00:25:31.218 --> 00:25:33.439 the one that I mentioned earlier,

NOTE Confidence: 0.8515854

00:25:33.440 --> 00:25:34.080 Accra Mencia.

NOTE Confidence: 0.88154554

00:25:36.790 --> 00:25:38.700 Another factor that hasn't been

NOTE Confidence: 0.88154554

00:25:38.700 --> 00:25:40.930 studied with that much detail yet,

NOTE Confidence: 0.88154554

00:25:40.930 --> 00:25:44.562 but we know is a major factor for

NOTE Confidence: 0.88154554

00:25:44.562 --> 00:25:47.267 changes within the flora is diet.

NOTE Confidence: 0.88154554

00:25:47.270 --> 00:25:51.500 So to be able to get accurate dietze data,

NOTE Confidence: 0.88154554

00:25:51.500 --> 00:25:54.790 we hired a nutritionist who very carefully

NOTE Confidence: 0.88154554

00:25:54.790 --> 00:25:58.559 day by day and almost 100 patients

NOTE Confidence: 0.88154554

00:25:58.559 --> 00:26:01.961 monitored exactly what these patients 8.

NOTE Confidence: 0.88154554

00:26:01.970 --> 00:26:04.112 The first thing that he notices

NOTE Confidence: 0.88154554

00:26:04.112 --> 00:26:07.100 if he looked at the onset when

NOTE Confidence: 0.88154554

00:26:07.100 --> 00:26:09.570 patients come into transplant that

NOTE Confidence: 0.88154554

00:26:09.570 --> 00:26:12.230 calculating the Nutrition risk index.

NOTE Confidence: 0.88154554

00:26:12.230 --> 00:26:15.170 Patients coming in with lower levels

NOTE Confidence: 0.88154554

00:26:15.170 --> 00:26:18.906 for that index have already a lower

NOTE Confidence: 0.88154554

00:26:18.906 --> 00:26:21.154 diversity within their flora.

NOTE Confidence: 0.88154554

00:26:21.160 --> 00:26:23.344 Another thing that he notices that

NOTE Confidence: 0.88154554

00:26:23.344 --> 00:26:25.677 the calorie intake the moment that

NOTE Confidence: 0.88154554

00:26:25.677 --> 00:26:28.095 these patients are comin goes down

NOTE Confidence: 0.88154554

00:26:28.095 --> 00:26:30.597 dramatically and follow sort of the same

NOTE Confidence: 0.88154554

00:26:30.597 --> 00:26:33.760 pattern as that drop within diversity.

NOTE Confidence: 0.88154554

00:26:33.760 --> 00:26:36.274 And he first would have analyzed

NOTE Confidence: 0.88154554

00:26:36.274 --> 00:26:38.871 the usual aspects that people look

NOTE Confidence: 0.88154554

00:26:38.871 --> 00:26:41.385 at when they're studying a diet.

NOTE Confidence: 0.88154554

00:26:41.390 --> 00:26:44.358 So calories, protein, fats, fiber and swim.

NOTE Confidence: 0.88154554

00:26:44.360 --> 00:26:46.940 And he found indeed that calorie

NOTE Confidence: 0.88154554

00:26:46.940 --> 00:26:48.660 intake was positively correlated

NOTE Confidence: 0.88154554

00:26:48.733 --> 00:26:50.783 with the diversity fiber also

NOTE Confidence: 0.88154554

00:26:50.783 --> 00:26:52.833 and also positively with blodia.

NOTE Confidence: 0.88154554

00:26:52.840 --> 00:26:56.368 And that is a true for both calories and

NOTE Confidence: 0.88154554

00:26:56.368 --> 00:26:59.837 fiber and negatively for Enterococcus so.

NOTE Confidence: 0.88154554

00:26:59.840 --> 00:27:01.064 That was interesting,

NOTE Confidence: 0.88154554

00:27:01.064 --> 00:27:03.512 but what I actually found even

NOTE Confidence: 0.88154554

00:27:03.512 --> 00:27:05.392 more interesting is a different

NOTE Confidence: 0.88154554

00:27:05.392 --> 00:27:07.492 way to look at a diet,

NOTE Confidence: 0.88154554

00:27:07.500 --> 00:27:11.330 and that is to look at it as a taxonomy.

NOTE Confidence: 0.88154554

00:27:11.330 --> 00:27:13.610 So now you look at all of the

NOTE Confidence: 0.88154554

00:27:13.610 --> 00:27:16.304 fruits of products more than these

NOTE Confidence: 0.88154554

00:27:16.304 --> 00:27:19.312 categories like protein, fat and so on.

NOTE Confidence: 0.88154554

00:27:19.312 --> 00:27:22.440 And when we analyzed our data like that,

NOTE Confidence: 0.88154554

00:27:22.440 --> 00:27:25.135 what we saw was that the footer

NOTE Confidence: 0.88154554

00:27:25.135 --> 00:27:26.726 diversity immediately dropped when

NOTE Confidence: 0.88154554

00:27:26.726 --> 00:27:28.566 patients come into a hospital,

NOTE Confidence: 0.88154554

00:27:28.570 --> 00:27:30.234 and that that diversity.

NOTE Confidence: 0.88154554

00:27:30.234 --> 00:27:30.650 Again,

NOTE Confidence: 0.88154554

00:27:30.650 --> 00:27:34.202 drops more for those patients who get a

NOTE Confidence: 0.88154554

00:27:34.202 --> 00:27:37.447 stronger type of a conditioning regiment.

NOTE Confidence: 0.8777928

00:27:39.620 --> 00:27:42.266 You can then start to look at

NOTE Confidence: 0.8777928

00:27:42.266 --> 00:27:44.237 certain food groups and how

NOTE Confidence: 0.8777928

00:27:44.237 --> 00:27:46.493 they are linked to a diversity,

NOTE Confidence: 0.8777928

00:27:46.500 --> 00:27:48.996 and that was very interesting because

NOTE Confidence: 0.8777928

00:27:48.996 --> 00:27:51.731 then you find something that we didn't

NOTE Confidence: 0.8777928

00:27:51.731 --> 00:27:54.522 really thought of and that is that the

NOTE Confidence: 0.8777928

00:27:54.522 --> 00:27:57.196 intake of fruits and sugars and sweets

NOTE Confidence: 0.8777928

00:27:57.196 --> 00:27:59.484 and beverages that that is actually

NOTE Confidence: 0.8777928

00:27:59.484 --> 00:28:01.389 linked negatively to the diversity.

NOTE Confidence: 0.8777928

00:28:01.390 --> 00:28:04.334 So we're still trying to figure out why

NOTE Confidence: 0.8777928

00:28:04.334 --> 00:28:07.227 that is and one of the theories that

NOTE Confidence: 0.8777928

00:28:07.227 --> 00:28:10.180 we have is that these these sugars.

NOTE Confidence: 0.8777928

00:28:10.180 --> 00:28:11.904 These very simple sugars.

NOTE Confidence: 0.8777928

00:28:11.904 --> 00:28:14.948 That they actually might feed some of

NOTE Confidence: 0.8777928

00:28:14.948 --> 00:28:17.615 the pathogens or the bacteria that are

NOTE Confidence: 0.8777928

00:28:17.615 --> 00:28:20.320 taking over in times of low diversity.

NOTE Confidence: 0.8777928

00:28:20.320 --> 00:28:23.560 And in that case might make matters worse,

NOTE Confidence: 0.8777928

00:28:23.560 --> 00:28:25.180 as has been shown.

NOTE Confidence: 0.8777928

00:28:25.180 --> 00:28:27.205 For instance, for an enteritis,

NOTE Confidence: 0.8777928

00:28:27.205 --> 00:28:28.420 ferrea colitis model.

NOTE Confidence: 0.8777928

00:28:28.420 --> 00:28:31.276 And again you see there if you feed

NOTE Confidence: 0.8777928

00:28:31.276 --> 00:28:34.087 these mice while they're getting DSS.

NOTE Confidence: 0.8777928

00:28:34.090 --> 00:28:36.125 Also, simple sugars and you

NOTE Confidence: 0.8777928

00:28:36.125 --> 00:28:38.620 see him blossoming of again and

NOTE Confidence: 0.8777928

00:28:38.620 --> 00:28:40.160 bug like Accra Mencia.

NOTE Confidence: 0.8706345

00:28:42.570 --> 00:28:45.585 So now we can start to make these kind

NOTE Confidence: 0.8706345

00:28:45.585 --> 00:28:48.914 of tables where we can see what food

NOTE Confidence: 0.8706345

00:28:48.914 --> 00:28:52.048 groups might have impact on certain tax.

NOTE Confidence: 0.8706345

00:28:52.050 --> 00:28:54.030 And of course this can.

NOTE Confidence: 0.8706345

00:28:54.030 --> 00:28:57.576 This can help us to start to a compose,

NOTE Confidence: 0.8706345

00:28:57.580 --> 00:29:00.628 maybe a diet that would be a beneficial

NOTE Confidence: 0.8706345

00:29:00.628 --> 00:29:02.677 for specific patients in specific

NOTE Confidence: 0.8706345

00:29:02.677 --> 00:29:05.498 settings and that is of course our

NOTE Confidence: 0.8706345

00:29:05.576 --> 00:29:07.850 ultimate goal with all of this.

NOTE Confidence: 0.89225054

00:29:09.930 --> 00:29:14.260 Another category is drugs and.

NOTE Confidence: 0.89225054

00:29:14.260 --> 00:29:16.852 Patients who are getting an allogeneic

NOTE Confidence: 0.89225054

00:29:16.852 --> 00:29:18.580 bone marrow transplantation at

NOTE Confidence: 0.89225054

00:29:18.648 --> 00:29:20.790 any given moment are probably on

NOTE Confidence: 0.89225054

00:29:20.790 --> 00:29:22.660 seven or eight different drugs.

NOTE Confidence: 0.89225054

00:29:22.660 --> 00:29:25.324 And it was a very nice study a couple

NOTE Confidence: 0.89225054

00:29:25.324 --> 00:29:28.219 of years back where it was demonstrated

NOTE Confidence: 0.89225054

00:29:28.219 --> 00:29:30.931 that many drugs that weren't antibiotics

NOTE Confidence: 0.89225054

00:29:30.931 --> 00:29:33.769 that they actually could also impact

NOTE Confidence: 0.89225054

00:29:33.769 --> 00:29:36.700 on many of the bacteria that are

NOTE Confidence: 0.89225054

00:29:36.700 --> 00:29:39.559 part of the commensal flora and just

NOTE Confidence: 0.89225054

00:29:39.559 --> 00:29:41.959 to highlight some of these drugs.

NOTE Confidence: 0.89225054

00:29:41.960 --> 00:29:44.168 These are all drugs that we

NOTE Confidence: 0.89225054

00:29:44.168 --> 00:29:46.380 frequently give to our patients,

NOTE Confidence: 0.89225054

00:29:46.380 --> 00:29:50.350 including things like slight cyclosporin.

NOTE Confidence: 0.89225054

00:29:50.350 --> 00:29:51.702 So a very talented,

NOTE Confidence: 0.89225054

00:29:51.702 --> 00:29:52.712 say, graduate student.

NOTE Confidence: 0.89225054

00:29:52.712 --> 00:29:54.056 It's the following thing.

NOTE Confidence: 0.89225054

00:29:54.060 --> 00:29:57.039 She took all of the data that we have

NOTE Confidence: 0.89225054

00:29:57.039 --> 00:30:00.286 from all of the samples on 1100 patients.

NOTE Confidence: 0.89225054

00:30:00.290 --> 00:30:03.242 And she put them in a you map and

NOTE Confidence: 0.89225054

00:30:03.242 --> 00:30:05.868 therefore could see all these clusters.

NOTE Confidence: 0.89225054

00:30:05.870 --> 00:30:07.730 Then she analyzed these clusters

NOTE Confidence: 0.89225054

00:30:07.730 --> 00:30:09.218 a little bit better.

NOTE Confidence: 0.89225054

00:30:09.220 --> 00:30:11.761 She came up with 10 different clusters

NOTE Confidence: 0.89225054

00:30:11.761 --> 00:30:14.050 and labeled them and then analyze.

NOTE Confidence: 0.89225054

00:30:14.050 --> 00:30:16.416 Since we had to kinetic data if

NOTE Confidence: 0.89225054

00:30:16.416 --> 00:30:18.608 the starting or stopping of a

NOTE Confidence: 0.89225054

00:30:18.608 --> 00:30:20.443 certain drug would have impact

NOTE Confidence: 0.89225054

00:30:20.443 --> 00:30:22.980 on the flora in these patients,

NOTE Confidence: 0.89225054

00:30:22.980 --> 00:30:26.039 moving from one cluster to another cluster

NOTE Confidence: 0.89225054

00:30:26.039 --> 00:30:29.187 or staying put in that same a cluster.

NOTE Confidence: 0.89225054

00:30:29.190 --> 00:30:32.205 And when she did that kind of an analysis,

NOTE Confidence: 0.89225054

00:30:32.210 --> 00:30:34.226 what was very striking is that,

NOTE Confidence: 0.89225054

00:30:34.230 --> 00:30:36.270 of course the antibiotics will have

NOTE Confidence: 0.89225054

00:30:36.270 --> 00:30:38.779 impact if you a transition to another

NOTE Confidence: 0.89225054

00:30:38.779 --> 00:30:41.657 cluster or if you stay where you are

NOTE Confidence: 0.89225054

00:30:41.657 --> 00:30:43.969 so you can see here from this data.

NOTE Confidence: 0.89225054

00:30:43.970 --> 00:30:46.112 But all of these other drugs and

NOTE Confidence: 0.89225054

00:30:46.112 --> 00:30:48.865 she looked at a grand total of 6063

NOTE Confidence: 0.89225054

00:30:48.865 --> 00:30:51.030 different drugs can have impact also.

NOTE Confidence: 0.89225054

00:30:51.030 --> 00:30:53.347 So it's a little bit early to

NOTE Confidence: 0.89225054

00:30:53.347 --> 00:30:54.730 show you data yet,

NOTE Confidence: 0.89225054

00:30:54.730 --> 00:30:57.218 but we have we have some data now

NOTE Confidence: 0.89225054

00:30:57.218 --> 00:30:59.509 that seem to indicate a certain.

NOTE Confidence: 0.89225054

00:30:59.510 --> 00:31:01.095 Pain medicines might have impact

NOTE Confidence: 0.89225054

00:31:01.095 --> 00:31:03.070 on changes within the gut flora,

NOTE Confidence: 0.89225054

00:31:03.070 --> 00:31:06.290 so there's a lot of work still

NOTE Confidence: 0.89225054

00:31:06.290 --> 00:31:09.248 there that we can expand on.

NOTE Confidence: 0.89225054

00:31:09.250 --> 00:31:10.243 Now of course,

NOTE Confidence: 0.89225054

00:31:10.243 --> 00:31:12.560 the ultimate goal for many people is

NOTE Confidence: 0.89225054

00:31:12.630 --> 00:31:14.835 to take this back into the clinic,

NOTE Confidence: 0.89225054

00:31:14.840 --> 00:31:16.820 and we've been thinking, of course,

NOTE Confidence: 0.89225054

00:31:16.820 --> 00:31:17.496 about that.

NOTE Confidence: 0.89225054

00:31:17.496 --> 00:31:17.834 Also,

NOTE Confidence: 0.89225054

00:31:17.834 --> 00:31:19.862 I'm still very cautious because I

NOTE Confidence: 0.89225054

00:31:19.862 --> 00:31:22.078 feel that we're in the early going,

NOTE Confidence: 0.89225054

00:31:22.080 --> 00:31:25.066 so we still need to know much, much more.

NOTE Confidence: 0.89225054

00:31:25.066 --> 00:31:27.124 But if you categorize the difference

NOTE Confidence: 0.89225054

00:31:27.124 --> 00:31:28.330 in therapies in four,

NOTE Confidence: 0.89225054

00:31:28.330 --> 00:31:30.298 then you can think about the

NOTE Confidence: 0.89225054

00:31:30.298 --> 00:31:31.282 use of antibiotics,

NOTE Confidence: 0.89225054

00:31:31.290 --> 00:31:33.733 and that is probably the lowest hanging

NOTE Confidence: 0.89225054

00:31:33.733 --> 00:31:35.753 fruit because those are drugs that

NOTE Confidence: 0.89225054

00:31:35.753 --> 00:31:37.867 we given that we can easily monitor.

NOTE Confidence: 0.89225054

00:31:37.870 --> 00:31:39.570 The second category would be.

NOTE Confidence: 0.89225054

00:31:39.570 --> 00:31:41.454 Pre biotics were thinking of there

NOTE Confidence: 0.89225054

00:31:41.454 --> 00:31:43.523 is to maybe give specific nutrients

NOTE Confidence: 0.89225054

00:31:43.523 --> 00:31:45.773 that would help that would feed

NOTE Confidence: 0.89225054

00:31:45.773 --> 00:31:47.577 that would favor texture that

NOTE Confidence: 0.89225054

00:31:47.577 --> 00:31:49.545 we think could be of benefit.

NOTE Confidence: 0.89225054

00:31:49.550 --> 00:31:51.482 The one that most people are

NOTE Confidence: 0.89225054

00:31:51.482 --> 00:31:53.330 focused on is Pro Biotic.

NOTE Confidence: 0.89225054

00:31:53.330 --> 00:31:55.790 So now we're talking bout fecal

NOTE Confidence: 0.89225054

00:31:55.790 --> 00:31:57.430 transplant engineered microbes and

NOTE Confidence: 0.89225054

00:31:57.495 --> 00:31:59.631 so on and so on and there certainly

NOTE Confidence: 0.89225054

00:31:59.631 --> 00:32:01.254 with an allergen Aker transplant

NOTE Confidence: 0.89225054

00:32:01.254 --> 00:32:03.641 there's a lot of work going on

NOTE Confidence: 0.89225054

00:32:03.650 --> 00:32:05.932 within that field and then a fourth

NOTE Confidence: 0.89225054

00:32:05.932 --> 00:32:08.070 category would be post biotics so

NOTE Confidence: 0.89225054

00:32:08.070 --> 00:32:10.248 those could be certain products made.

NOTE Confidence: 0.89225054

00:32:10.250 --> 00:32:12.590 By bacteria I mentioned already short

NOTE Confidence: 0.89225054

00:32:12.590 --> 00:32:15.128 chain fatty acids such as a butyrate,

NOTE Confidence: 0.8246579

00:32:15.130 --> 00:32:18.130 and there are trials going on with that.

NOTE Confidence: 0.8246579

00:32:18.130 --> 00:32:20.748 What are we doing at the moment?

NOTE Confidence: 0.8246579

00:32:20.750 --> 00:32:22.630 Well, as I said already,

NOTE Confidence: 0.8246579

00:32:22.630 --> 00:32:25.395 for us the lowest hanging fruit is

NOTE Confidence: 0.8246579

00:32:25.395 --> 00:32:27.274 antibiotic stewardship avoids the use

NOTE Confidence: 0.8246579

00:32:27.274 --> 00:32:29.479 as much as possible of these broad

NOTE Confidence: 0.8246579

00:32:29.479 --> 00:32:31.472 spectrum antibiotics that do damage

NOTE Confidence: 0.8246579

00:32:31.472 --> 00:32:33.492 to the commensal enrolled flora.

NOTE Confidence: 0.8246579

00:32:33.500 --> 00:32:35.908 So we have a a trial open at

NOTE Confidence: 0.8246579

00:32:35.908 --> 00:32:38.011 the moment where patients who

NOTE Confidence: 0.8246579

00:32:38.011 --> 00:32:40.376 get fever neutropenia will be.

NOTE Confidence: 0.8246579

00:32:40.380 --> 00:32:43.236 A randomized to either getting our

NOTE Confidence: 0.8246579

00:32:43.236 --> 00:32:46.277 standard of care which is piperacillin

NOTE Confidence: 0.8246579

00:32:46.277 --> 00:32:48.907 tazobactam versus cefepime and try

NOTE Confidence: 0.8246579

00:32:48.907 --> 00:32:52.287 to win these patients as quickly

NOTE Confidence: 0.8246579

00:32:52.287 --> 00:32:54.575 as possible off antibiotics.

NOTE Confidence: 0.8246579

00:32:54.580 --> 00:32:57.058 A second study that we have finished

NOTE Confidence: 0.8246579

00:32:57.058 --> 00:32:59.749 already as an auto fecal transplant.

NOTE Confidence: 0.8246579

00:32:59.750 --> 00:33:02.599 So the thinking there was when patients

NOTE Confidence: 0.8246579

00:33:02.599 --> 00:33:05.228 come off antibiotics which is about 14

NOTE Confidence: 0.8246579

00:33:05.228 --> 00:33:08.110 days out from the allergen acre transplants,

NOTE Confidence: 0.8246579

00:33:08.110 --> 00:33:10.679 why don't we give them back their

NOTE Confidence: 0.8246579

00:33:10.679 --> 00:33:12.889 original flora from pre transplant?

NOTE Confidence: 0.8246579

00:33:12.890 --> 00:33:15.683 And since this was led by Eric

NOTE Confidence: 0.8246579

00:33:15.683 --> 00:33:18.354 Pamer Ann Young Tower our primary

NOTE Confidence: 0.8246579

00:33:18.354 --> 00:33:21.574 focus was the prevention of C diff.

NOTE Confidence: 0.8246579

00:33:21.580 --> 00:33:23.950 So we looked at that mostly,

NOTE Confidence: 0.8246579

00:33:23.950 --> 00:33:27.110 and as these things go in this series,

NOTE Confidence: 0.8246579

00:33:27.110 --> 00:33:29.480 the incidence of a C diff

NOTE Confidence: 0.8246579

00:33:29.480 --> 00:33:31.060 was actually relatively low,

NOTE Confidence: 0.8246579

00:33:31.060 --> 00:33:33.430 so we didn't see much there.

NOTE Confidence: 0.8246579

00:33:33.430 --> 00:33:35.915 But what we did notice is first

NOTE Confidence: 0.8246579

00:33:35.915 --> 00:33:38.568 of all that's the concept worked.

NOTE Confidence: 0.8246579

00:33:38.570 --> 00:33:41.762 You could indeed this is the pre transplant

NOTE Confidence: 0.8246579

00:33:41.762 --> 00:33:44.098 and diversity pattern of a patient,

NOTE Confidence: 0.8246579

00:33:44.100 --> 00:33:46.075 who then was transplant again

NOTE Confidence: 0.8246579

00:33:46.075 --> 00:33:48.050 with an auto fecal transplant,

NOTE Confidence: 0.8246579

00:33:48.050 --> 00:33:50.070 and indeed would get pretty

NOTE Confidence: 0.8246579

00:33:50.070 --> 00:33:51.686 much their own flora.

NOTE Confidence: 0.8246579

00:33:51.690 --> 00:33:54.714 Back so the concept seemed to be working,

NOTE Confidence: 0.8246579

00:33:54.720 --> 00:33:57.380 but in terms of clinically relevant outcomes,

NOTE Confidence: 0.8246579

00:33:57.380 --> 00:33:59.868 the only thing that we saw in this

NOTE Confidence: 0.8246579

00:33:59.868 --> 00:34:01.903 very small series was actually

NOTE Confidence: 0.8246579

00:34:01.903 --> 00:34:04.579 something that we weren't counting on,

NOTE Confidence: 0.8246579

00:34:04.580 --> 00:34:06.841 and that is that the activation of

NOTE Confidence: 0.8246579

00:34:06.841 --> 00:34:08.754 certain viruses which commonly happens

NOTE Confidence: 0.8246579

00:34:08.754 --> 00:34:11.394 within the context of allogeneic transplant,

NOTE Confidence: 0.8246579

00:34:11.400 --> 00:34:13.990 such as CMV and EBV was somewhat

NOTE Confidence: 0.8246579

00:34:13.990 --> 00:34:17.111 lower in those patients who have been

NOTE Confidence: 0.8246579

00:34:17.111 --> 00:34:19.997 treated with an auto fecal transplant.

NOTE Confidence: 0.8246579

00:34:20.000 --> 00:34:23.290 Another thing that we notice is that

NOTE Confidence: 0.8246579

00:34:23.290 --> 00:34:26.667 auto fecal transplant seemed to favor

NOTE Confidence: 0.8246579

00:34:26.667 --> 00:34:29.179 the engraftment reconstitution of

NOTE Confidence: 0.8246579

00:34:29.179 --> 00:34:31.448 neutrophils, lymphocytes and monocytes.

NOTE Confidence: 0.83641374

00:34:33.810 --> 00:34:35.748 A study that we're working on

NOTE Confidence: 0.83641374

00:34:35.748 --> 00:34:38.654 that is not open yet is to really

NOTE Confidence: 0.83641374

00:34:38.654 --> 00:34:40.970 rationally design A consortia of these

NOTE Confidence: 0.83641374

00:34:41.042 --> 00:34:43.640 bacteria pretty much based upon that,

NOTE Confidence: 0.83641374

00:34:43.640 --> 00:34:46.237 we'll that I started out with that

NOTE Confidence: 0.83641374

00:34:46.237 --> 00:34:48.659 whole a cladograms where I indicated

NOTE Confidence: 0.83641374

00:34:48.659 --> 00:34:50.724 how certain flora elements were

NOTE Confidence: 0.83641374

00:34:50.724 --> 00:34:53.300 linked to good or bad outcomes and

NOTE Confidence: 0.83641374

00:34:53.300 --> 00:34:55.684 based upon that we have created a

NOTE Confidence: 0.83641374

00:34:55.684 --> 00:34:58.148 consortium and we want to give these

NOTE Confidence: 0.83641374

00:34:58.148 --> 00:35:00.560 bacteria back again at that time

NOTE Confidence: 0.83641374

00:35:00.560 --> 00:35:02.152 point of neutrophil engraftment,

NOTE Confidence: 0.83641374

00:35:02.160 --> 00:35:04.422 which is about 14 days out

NOTE Confidence: 0.83641374

00:35:04.422 --> 00:35:05.553 from allogeneic transplant.

NOTE Confidence: 0.83641374

00:35:05.560 --> 00:35:10.096 As I've said many times by now.

NOTE Confidence: 0.83641374

00:35:10.100 --> 00:35:13.196 So with that I would like to stop.

NOTE Confidence: 0.83641374

00:35:13.200 --> 00:35:15.516 I would like to summarize basically

NOTE Confidence: 0.83641374

00:35:15.516 --> 00:35:18.172 that what I've been trying to show

NOTE Confidence: 0.83641374

00:35:18.172 --> 00:35:20.580 you is that changes within the gut

NOTE Confidence: 0.83641374

00:35:20.657 --> 00:35:23.255 flora are linked to overall survival.

NOTE Confidence: 0.83641374

00:35:23.260 --> 00:35:25.190 Lethal graft versus host bacteremia,

NOTE Confidence: 0.83641374

00:35:25.190 --> 00:35:27.518 sepsis, engraftment and even a relapse.

NOTE Confidence: 0.83641374

00:35:27.520 --> 00:35:30.061 I gave you a specific story about

NOTE Confidence: 0.83641374

00:35:30.061 --> 00:35:32.163 how the dominance with Enterococcus

NOTE Confidence: 0.83641374

00:35:32.163 --> 00:35:34.513 within the post transplant period

NOTE Confidence: 0.83641374

00:35:34.513 --> 00:35:37.419 is linked both in mouse and men

NOTE Confidence: 0.83641374

00:35:37.419 --> 00:35:39.199 to lethal graft versus host.

NOTE Confidence: 0.83641374

00:35:39.200 --> 00:35:41.783 And I told you about the various

NOTE Confidence: 0.83641374

00:35:41.783 --> 00:35:44.095 factors that we think can have

NOTE Confidence: 0.83641374

00:35:44.095 --> 00:35:45.970 impact on the gut flora,

NOTE Confidence: 0.83641374

00:35:45.970 --> 00:35:48.220 such as the use of antibiotics,

NOTE Confidence: 0.83641374

00:35:48.220 --> 00:35:50.476 but also other types of drugs,

NOTE Confidence: 0.83641374

00:35:50.480 --> 00:35:52.104 diet and conditioning regiments.

NOTE Confidence: 0.83641374

00:35:52.104 --> 00:35:55.626 So with that I would like to of course

NOTE Confidence: 0.83641374

00:35:55.626 --> 00:35:58.383 thank all of my funding agencies in my

NOTE Confidence: 0.83641374

00:35:58.383 --> 00:36:00.686 fantastic lap and the many folks who

NOTE Confidence: 0.83641374

00:36:00.686 --> 00:36:03.010 we have worked with at other centers.

NOTE Confidence: 0.83641374

00:36:03.010 --> 00:36:05.971 So with that I would like to stop and

NOTE Confidence: 0.83641374

00:36:05.971 --> 00:36:09.258 I should probably stop sharing also.

NOTE Confidence: 0.83641374

00:36:09.260 --> 00:36:14.390 If I can do that? It seems to be.

NOTE Confidence: 0.83641374

00:36:14.390 --> 00:36:14.790 But

NOTE Confidence: 0.83835495

00:36:14.790 --> 00:36:17.196 thank you myself for this really,

NOTE Confidence: 0.83835495

00:36:17.200 --> 00:36:18.295 really fascinating talk.

NOTE Confidence: 0.83835495

00:36:18.295 --> 00:36:21.325 I have to say I coming up with

NOTE Confidence: 0.83835495

00:36:21.325 --> 00:36:23.695 questions and was every next step

NOTE Confidence: 0.83835495

00:36:23.695 --> 00:36:26.049 you answered my first question,

NOTE Confidence: 0.83835495

00:36:26.050 --> 00:36:31.178 so maybe I can start with one so.

NOTE Confidence: 0.83835495

00:36:31.180 --> 00:36:34.127 Right, so you are receiving these patients

NOTE Confidence: 0.83835495

00:36:34.127 --> 00:36:36.662 for transplant after they have gone

NOTE Confidence: 0.83835495

00:36:36.662 --> 00:36:39.068 through months and months of treatment.

NOTE Confidence: 0.83835495

00:36:39.070 --> 00:36:42.390 And have you looked at how you know?

NOTE Confidence: 0.83835495

00:36:42.390 --> 00:36:43.218 For example,

NOTE Confidence: 0.83835495

00:36:43.218 --> 00:36:46.068 you know whether patients receive, you know,

NOTE Confidence: 0.83835495

00:36:46.068 --> 00:36:48.791 is decided in or targeted therapy or

NOTE Confidence: 0.83835495

00:36:48.791 --> 00:36:51.099 chemotherapy before coming to transplant,

NOTE Confidence: 0.83835495

00:36:51.100 --> 00:36:52.819 does that effect?

NOTE Confidence: 0.83835495

00:36:52.819 --> 00:36:54.946 What you see, then,

NOTE Confidence: 0.83835495

00:36:54.946 --> 00:36:56.976 in terms of transplant outcomes,

NOTE Confidence: 0.8748975

00:36:56.980 --> 00:36:58.608 yes. So this is

NOTE Confidence: 0.8748975

00:36:58.610 --> 00:37:00.645 of course, where we still

NOTE Confidence: 0.8748975

00:37:00.645 --> 00:37:02.680 don't have very good data.

NOTE Confidence: 0.8748975

00:37:02.680 --> 00:37:05.235 We do have some collection also of

NOTE Confidence: 0.8748975

00:37:05.235 --> 00:37:07.570 samples from patients before transplant,

NOTE Confidence: 0.8748975

00:37:07.570 --> 00:37:08.749 specifically with AML.

NOTE Confidence: 0.8748975

00:37:08.749 --> 00:37:12.340 We see a bit of the same patterns,

NOTE Confidence: 0.8748975

00:37:12.340 --> 00:37:14.482 but it hasn't been analyzed that well

NOTE Confidence: 0.8748975

00:37:14.482 --> 00:37:17.143 yet that we see with allogeneic bone

NOTE Confidence: 0.8748975

00:37:17.143 --> 00:37:19.238 marrow transplantation that an AML

NOTE Confidence: 0.8748975

00:37:19.238 --> 00:37:21.196 patient getting in induction regiment

NOTE Confidence: 0.8748975

00:37:21.196 --> 00:37:24.074 will have the same pattern of the loss

NOTE Confidence: 0.8748975

00:37:24.074 --> 00:37:26.066 of a diversity dominance with certain

NOTE Confidence: 0.8748975

00:37:26.066 --> 00:37:28.579 tax are specifically with with again,

NOTE Confidence: 0.8748975

00:37:28.580 --> 00:37:28.949 Enterococcus,

NOTE Confidence: 0.8748975

00:37:28.949 --> 00:37:32.270 but we need much more work to analyze that,

NOTE Confidence: 0.8748975

00:37:32.270 --> 00:37:34.108 and as I hinted at,

NOTE Confidence: 0.8748975

00:37:34.110 --> 00:37:36.595 almost every drug that they might have

NOTE Confidence: 0.8748975

00:37:36.595 --> 00:37:39.647 seen in the year prior to a transplant,

NOTE Confidence: 0.8748975

00:37:39.650 --> 00:37:40.050 potentially.

NOTE Confidence: 0.8748975

00:37:40.050 --> 00:37:42.450 Could have impacted on their floor,

NOTE Confidence: 0.8748975

00:37:42.450 --> 00:37:45.410 so it's very worthwhile to look at that.

NOTE Confidence: 0.81575745

00:37:46.260 --> 00:37:48.732 OK, awesome. So we have questions

NOTE Confidence: 0.81575745

00:37:48.732 --> 00:37:51.339 from the audience from Lucas Cauda,

NOTE Confidence: 0.81575745

00:37:51.340 --> 00:37:53.860 who says great talk in his first

NOTE Confidence: 0.81575745

00:37:53.860 --> 00:37:56.949 question is how well does this correlate

NOTE Confidence: 0.81575745

00:37:56.949 --> 00:37:59.364 with amino acid magic biomarkers?

NOTE Confidence: 0.81575745

00:37:59.370 --> 00:38:01.490 Rank 3 S, T2, etc.

NOTE Confidence: 0.8281397

00:38:04.640 --> 00:38:07.028 So as you know, since you

NOTE Confidence: 0.8281397

00:38:07.028 --> 00:38:08.620 know about these markets,

NOTE Confidence: 0.8281397

00:38:08.620 --> 00:38:11.329 then you know of course those are

NOTE Confidence: 0.8281397

00:38:11.329 --> 00:38:13.759 the markets that have been developed

NOTE Confidence: 0.8281397

00:38:13.759 --> 00:38:16.524 by Jamie by Jamie Ferrara an he

NOTE Confidence: 0.8281397

00:38:16.606 --> 00:38:18.976 is doing these kind of studies

NOTE Confidence: 0.8281397

00:38:18.976 --> 00:38:21.356 with Ernst Holler at the moment,

NOTE Confidence: 0.8281397

00:38:21.356 --> 00:38:24.140 within the context of the Magic Consortium,

NOTE Confidence: 0.8281397

00:38:24.140 --> 00:38:26.528 and I haven't seen direct connections

NOTE Confidence: 0.8281397

00:38:26.528 --> 00:38:28.124 yet between, for instance,

NOTE Confidence: 0.8281397

00:38:28.124 --> 00:38:30.506 which would be really interested rectally,

NOTE Confidence: 0.8281397

00:38:30.510 --> 00:38:31.728 gamma and form.

NOTE Confidence: 0.8281397

00:38:31.728 --> 00:38:34.164 So those are the studies that.

NOTE Confidence: 0.8281397

00:38:34.170 --> 00:38:35.181 They are doing,

NOTE Confidence: 0.8281397

00:38:35.181 --> 00:38:38.249 but I haven't seen any data from them yet.

NOTE Confidence: 0.8281397

00:38:38.250 --> 00:38:40.356 We have only very limited data

NOTE Confidence: 0.8281397

00:38:40.356 --> 00:38:42.148 because we haven't used that

NOTE Confidence: 0.8281397

00:38:42.148 --> 00:38:44.367 panel that they are using so much.

NOTE Confidence: 0.8043221

00:38:45.080 --> 00:38:46.739 OK, awesome and I'm gonna read you.

NOTE Confidence: 0.8043221

00:38:46.740 --> 00:38:48.615 The second question from Lewis

NOTE Confidence: 0.8043221

00:38:48.615 --> 00:38:50.490 is one of our transplanters.

NOTE Confidence: 0.8043221

00:38:50.490 --> 00:38:52.356 Is the New York poupan commercialized

NOTE Confidence: 0.8043221

00:38:52.356 --> 00:38:53.990 for other sites to study?

NOTE Confidence: 0.8375062

00:38:55.590 --> 00:38:58.990 The New York School bank. Well,

NOTE Confidence: 0.8375062

00:38:58.990 --> 00:39:02.118 we we don't have a New York school bank.

NOTE Confidence: 0.8375062

00:39:02.118 --> 00:39:04.639 I wish actually that we have one

NOTE Confidence: 0.8375062

00:39:04.639 --> 00:39:06.810 and the one that most people have

NOTE Confidence: 0.8375062

00:39:06.810 --> 00:39:09.446 used is open open Biome and I was

NOTE Confidence: 0.8375062

00:39:09.446 --> 00:39:11.542 just reading that they might have

NOTE Confidence: 0.8375062

00:39:11.542 --> 00:39:13.702 some trouble and that they are

NOTE Confidence: 0.8375062

00:39:13.702 --> 00:39:16.089 closing and that is a company and

NOTE Confidence: 0.8375062

00:39:16.089 --> 00:39:18.003 not for profit company in Boston.

NOTE Confidence: 0.8375062

00:39:18.003 --> 00:39:20.194 So that's where a lot of people

NOTE Confidence: 0.8375062

00:39:20.194 --> 00:39:22.108 have been getting flora from.

NOTE Confidence: 0.8375062

00:39:22.110 --> 00:39:24.784 We at the moment are working with

NOTE Confidence: 0.8375062

00:39:24.784 --> 00:39:26.917 some companies also and I put

NOTE Confidence: 0.8375062

00:39:26.917 --> 00:39:29.038 didn't put that into my slide 2.

NOTE Confidence: 0.8375062

00:39:29.040 --> 00:39:31.280 Potentially do a sequel transplant

NOTE Confidence: 0.8375062

00:39:31.280 --> 00:39:34.330 for Graft versus host and you might

NOTE Confidence: 0.8375062

00:39:34.330 --> 00:39:36.892 have seen very small as series from

NOTE Confidence: 0.8375062

00:39:36.892 --> 00:39:39.192 all over the world where people

NOTE Confidence: 0.8375062

00:39:39.192 --> 00:39:41.625 have tried that for steroids or

NOTE Confidence: 0.8375062

00:39:41.625 --> 00:39:43.245 refractory graft versus host.

NOTE Confidence: 0.8375062

00:39:43.250 --> 00:39:45.686 They would do a fecal transplant.

NOTE Confidence: 0.8375062

00:39:45.690 --> 00:39:47.494 Different concepts sometimes that

NOTE Confidence: 0.8375062

00:39:47.494 --> 00:39:51.058 you just do a normal donor or even

NOTE Confidence: 0.8375062

00:39:51.058 --> 00:39:53.404 one company is sponsoring a trial

NOTE Confidence: 0.8375062

00:39:53.404 --> 00:39:55.836 where they take a whole bunch of

NOTE Confidence: 0.8375062

00:39:55.840 --> 00:39:57.864 healthy healthy folks and literally

NOTE Confidence: 0.8375062

00:39:57.864 --> 00:39:59.958 mix all of the feces.

NOTE Confidence: 0.8375062

00:39:59.960 --> 00:40:01.745 And give One Giants and

NOTE Confidence: 0.8375062

00:40:01.745 --> 00:40:02.816 transplants with that,

NOTE Confidence: 0.8375062

00:40:02.820 --> 00:40:05.654 and they seem to have some benefit,

NOTE Confidence: 0.8375062

00:40:05.654 --> 00:40:09.269 so there is a lot of focus at the moment

NOTE Confidence: 0.8375062

00:40:09.269 --> 00:40:12.407 on doing fecal transplant for steroids.

NOTE Confidence: 0.8375062

00:40:12.410 --> 00:40:14.798 Refractory graft versus host and with

NOTE Confidence: 0.8375062

00:40:14.798 --> 00:40:17.000 small series showing showing benefits,

NOTE Confidence: 0.8375062

00:40:17.000 --> 00:40:19.745 but we need much more work and I want

NOTE Confidence: 0.8375062

00:40:19.745 --> 00:40:22.338 to emphasize that there are also

NOTE Confidence: 0.8375062

00:40:22.338 --> 00:40:25.116 risks because we all realize you're

NOTE Confidence: 0.8375062

00:40:25.116 --> 00:40:27.556 dealing with patients where the

NOTE Confidence: 0.8375062

00:40:27.556 --> 00:40:30.022 gut barrier is negatively impacted

NOTE Confidence: 0.8375062

00:40:30.022 --> 00:40:32.070 by the conditioning regiment.

NOTE Confidence: 0.8375062

00:40:32.070 --> 00:40:34.942 I'm so any kind of bacteria that you

NOTE Confidence: 0.8375062

00:40:34.942 --> 00:40:37.387 give there have a higher likelihood

NOTE Confidence: 0.8375062

00:40:37.387 --> 00:40:40.355 to pass the gut Scott Barrier and

NOTE Confidence: 0.8375062

00:40:40.355 --> 00:40:42.827 you might know of the negative

NOTE Confidence: 0.8375062

00:40:42.827 --> 00:40:44.784 outcomes that we're seeing with

NOTE Confidence: 0.8375062

00:40:44.784 --> 00:40:46.569 some of these fecal transplants

NOTE Confidence: 0.8375062

00:40:46.569 --> 00:40:48.608 where the product wasn't carefully

NOTE Confidence: 0.8375062

00:40:48.608 --> 00:40:50.868 screened enough for certain bacteria,

NOTE Confidence: 0.8375062

00:40:50.870 --> 00:40:53.732 which led to two patients getting

NOTE Confidence: 0.8375062

00:40:53.732 --> 00:40:56.949 seriously ill and one of them dying.

NOTE Confidence: 0.8375062

00:40:56.950 --> 00:40:58.455 So there there are a lot of

NOTE Confidence: 0.8375062

00:40:58.455 --> 00:41:00.120 a lot of risks there, so.

NOTE Confidence: 0.8816916

00:41:01.690 --> 00:41:02.790 Then you have a question.

NOTE Confidence: 0.8816916

00:41:02.790 --> 00:41:04.316 Do you want to ask it directly?

NOTE Confidence: 0.73999095

00:41:06.880 --> 00:41:10.660 Hi, fantastic talk thank you.

NOTE Confidence: 0.73999095

00:41:10.660 --> 00:41:13.124 Do you see similar effects of the

NOTE Confidence: 0.8718298

00:41:13.130 --> 00:41:15.660 microbiome in auto transplants?

NOTE Confidence: 0.8167996

00:41:15.660 --> 00:41:18.593 Yeah, so I showed some of the data.

NOTE Confidence: 0.8167996

00:41:18.593 --> 00:41:20.308 So for autotransplant we see

NOTE Confidence: 0.8167996

00:41:20.308 --> 00:41:22.690 the same drop in the diversity,

NOTE Confidence: 0.8167996

00:41:22.690 --> 00:41:24.170 again starting immediately and

NOTE Confidence: 0.8167996

00:41:24.170 --> 00:41:26.390 we see also links to outcomes.

NOTE Confidence: 0.8167996

00:41:26.390 --> 00:41:27.542 So for instance,

NOTE Confidence: 0.8167996

00:41:27.542 --> 00:41:29.846 for myeloma we could very nicely

NOTE Confidence: 0.8167996

00:41:29.846 --> 00:41:31.857 see that patients with a with

NOTE Confidence: 0.8167996

00:41:31.857 --> 00:41:34.304 less of a loss in their diversity

NOTE Confidence: 0.8167996

00:41:34.304 --> 00:41:36.746 would have better PFS and OS,

NOTE Confidence: 0.8167996

00:41:36.750 --> 00:41:40.080 so that that seems to be a real benefit.

NOTE Confidence: 0.8167996

00:41:40.080 --> 00:41:42.670 All of this needs to be studied

NOTE Confidence: 0.8167996

00:41:42.670 --> 00:41:45.293 in much more detail because now of

NOTE Confidence: 0.8167996

00:41:45.293 --> 00:41:47.198 course you're talking about it.

NOTE Confidence: 0.8167996

00:41:47.200 --> 00:41:49.558 Order whatever transplants are not talking

NOTE Confidence: 0.8167996

00:41:49.558 --> 00:41:52.318 about a graft versus host or something.

NOTE Confidence: 0.8167996

00:41:52.320 --> 00:41:53.313 Things like that,

NOTE Confidence: 0.8167996

00:41:53.313 --> 00:41:55.630 but there are signals there that are

NOTE Confidence: 0.8167996

00:41:55.693 --> 00:41:57.837 absolutely worthwhile studying for.

NOTE Confidence: 0.8480624

00:42:00.300 --> 00:42:02.520 Now, so I think it's it's

NOTE Confidence: 0.8480624

00:42:02.520 --> 00:42:04.390 fascinating where that in this

NOTE Confidence: 0.8480624

00:42:04.468 --> 00:42:06.853 population you are studying the

NOTE Confidence: 0.8480624

00:42:06.853 --> 00:42:09.238 immune system so intricately and.

NOTE Confidence: 0.8480624

00:42:09.240 --> 00:42:10.860 And can some of this work

NOTE Confidence: 0.8480624

00:42:10.860 --> 00:42:11.940 trying to be transplanted?

NOTE Confidence: 0.8480624

00:42:11.940 --> 00:42:13.675 You know their translator to

NOTE Confidence: 0.8480624

00:42:13.675 --> 00:42:15.750 patients who are not in the.

NOTE Confidence: 0.8480624

00:42:15.750 --> 00:42:17.755 Transplant setting in terms of

NOTE Confidence: 0.8480624

00:42:17.755 --> 00:42:19.359 you know immune interaction.

NOTE Confidence: 0.8480624

00:42:19.360 --> 00:42:21.766 I think you were mentioning the

NOTE Confidence: 0.8480624

00:42:21.766 --> 00:42:23.370 the effects on immunotherapy.

NOTE Confidence: 0.8356063

00:42:25.150 --> 00:42:27.446 So I think that is of course

NOTE Confidence: 0.8356063

00:42:27.446 --> 00:42:29.867 where a number of companies and

NOTE Confidence: 0.8356063

00:42:29.867 --> 00:42:32.573 number of centers and number of

NOTE Confidence: 0.8356063

00:42:32.573 --> 00:42:34.629 scientists are going with this.

NOTE Confidence: 0.8356063

00:42:34.630 --> 00:42:36.850 The general concept being that the

NOTE Confidence: 0.8356063

00:42:36.850 --> 00:42:38.980 gut flora can modulate immunity,

NOTE Confidence: 0.8356063

00:42:38.980 --> 00:42:41.080 which it almost has to write

NOTE Confidence: 0.8356063

00:42:41.080 --> 00:42:43.002 because you're in a constant

NOTE Confidence: 0.8356063

00:42:43.002 --> 00:42:45.690 interaction there with God for us.

NOTE Confidence: 0.8356063

00:42:45.690 --> 00:42:48.826 So it's very clear that T cell repertoire

NOTE Confidence: 0.8356063

00:42:48.826 --> 00:42:51.645 and activation of innate cells is very

NOTE Confidence: 0.8356063

00:42:51.645 --> 00:42:54.379 much modulated by changes within the floor.

NOTE Confidence: 0.8356063

00:42:54.380 --> 00:42:55.619 That is obvious.

NOTE Confidence: 0.8356063

00:42:55.619 --> 00:42:57.684 So people have taken this,

NOTE Confidence: 0.8356063

00:42:57.690 --> 00:43:00.154 of course within the field of a

NOTE Confidence: 0.8356063

00:43:00.154 --> 00:43:02.089 checkpoint blockade much much further.

NOTE Confidence: 0.8356063

00:43:02.090 --> 00:43:03.826 You might know there was a back

NOTE Confidence: 0.8356063

00:43:03.826 --> 00:43:05.941 to back to back science articles

NOTE Confidence: 0.8356063

00:43:05.941 --> 00:43:07.689 demonstrating that certain compositions

NOTE Confidence: 0.8356063

00:43:07.689 --> 00:43:10.713 of the flora were linked to better

NOTE Confidence: 0.8356063

00:43:10.713 --> 00:43:12.365 outcomes with checkpoint blockade,

NOTE Confidence: 0.8356063

00:43:12.370 --> 00:43:14.200 foreign Melanoma and so on,

NOTE Confidence: 0.8356063

00:43:14.200 --> 00:43:17.395 and that has led to a series of trials

NOTE Confidence: 0.8356063

00:43:17.395 --> 00:43:20.070 that are going on at the moment.

NOTE Confidence: 0.8356063

00:43:20.070 --> 00:43:23.060 It has also and I always tell that

NOTE Confidence: 0.8356063

00:43:23.060 --> 00:43:26.000 story because I want to warn people.

NOTE Confidence: 0.8356063

00:43:26.000 --> 00:43:28.289 It has led to negative outcomes and

NOTE Confidence: 0.8356063

00:43:28.289 --> 00:43:31.515 what I mean by that is that because so

NOTE Confidence: 0.8356063

00:43:31.515 --> 00:43:34.009 many patients heard about these stories?

NOTE Confidence: 0.8356063

00:43:34.010 --> 00:43:36.558 Oh, you can do something with microbiome,

NOTE Confidence: 0.8356063

00:43:36.560 --> 00:43:38.735 and my checkpoint therapy is

NOTE Confidence: 0.8356063

00:43:38.735 --> 00:43:40.475 going to go better.

NOTE Confidence: 0.8356063

00:43:40.480 --> 00:43:43.078 They went to their own pharmacy.

NOTE Confidence: 0.8356063

00:43:43.080 --> 00:43:45.690 They started to buy local Pro,

NOTE Confidence: 0.8356063

00:43:45.690 --> 00:43:46.083 Pro,

NOTE Confidence: 0.8356063

00:43:46.083 --> 00:43:48.834 Biotic and Drugs etc and A and

NOTE Confidence: 0.8356063

00:43:48.834 --> 00:43:51.398 a scientist at Anderson had

NOTE Confidence: 0.8356063

00:43:51.398 --> 00:43:53.646 actually carefully analyzed it.

NOTE Confidence: 0.8356063

00:43:53.650 --> 00:43:55.620 And found that those people

NOTE Confidence: 0.8356063

00:43:55.620 --> 00:44:00.345 who did do it do it yourself.

NOTE Confidence: 0.8356063

00:44:00.350 --> 00:44:01.710 Probiotics had worse outcomes

NOTE Confidence: 0.8356063

00:44:01.710 --> 00:44:02.730 from their check.

NOTE Confidence: 0.8356063

00:44:02.730 --> 00:44:04.090 One blockades then patients

NOTE Confidence: 0.8356063

00:44:04.090 --> 00:44:05.450 who didn't do that.

NOTE Confidence: 0.8356063

00:44:05.450 --> 00:44:08.242 So there are certain dangers and I think

NOTE Confidence: 0.8356063

00:44:08.242 --> 00:44:10.847 we have to warn people also about this.

NOTE Confidence: 0.8356063

00:44:10.847 --> 00:44:13.973 This is not sort of a free for all and

NOTE Confidence: 0.8356063

00:44:13.973 --> 00:44:17.005 and we still need to understand much more.

NOTE Confidence: 0.8356063

00:44:17.010 --> 00:44:18.710 What are the dietary elements?

NOTE Confidence: 0.8356063

00:44:18.710 --> 00:44:20.750 What are the bacteria that really

NOTE Confidence: 0.8356063

00:44:20.750 --> 00:44:22.110 matter for certain outcomes?

NOTE Confidence: 0.8356063

00:44:22.110 --> 00:44:23.915 As I illustrated also simply

NOTE Confidence: 0.8356063

00:44:23.915 --> 00:44:26.460 telling people to eat a lot of

NOTE Confidence: 0.8356063

00:44:26.460 --> 00:44:28.458 fruit well in certain context it

NOTE Confidence: 0.8356063

00:44:28.458 --> 00:44:30.660 might be a bad thing actually.

NOTE Confidence: 0.8356063

00:44:30.660 --> 00:44:31.770 Who would have thought that?

NOTE Confidence: 0.7930988

00:44:33.360 --> 00:44:35.650 Dance, it's understand the questions.

NOTE Confidence: 0.7930988

00:44:35.650 --> 00:44:38.494 I think it's fascinating that cross

NOTE Confidence: 0.7930988

00:44:38.494 --> 00:44:41.598 centers you know in in the world,

NOTE Confidence: 0.7930988

00:44:41.600 --> 00:44:43.545 whereas diet is probably quite

NOTE Confidence: 0.7930988

00:44:43.545 --> 00:44:46.144 different that you have such homogeneous

NOTE Confidence: 0.7930988

00:44:46.144 --> 00:44:48.468 or similar starting populations.

NOTE Confidence: 0.7930988

00:44:48.470 --> 00:44:51.676 Yeah, yeah, that we found very fascinating,

NOTE Confidence: 0.7930988

00:44:51.680 --> 00:44:54.416 right? I mean, you're talking with

NOTE Confidence: 0.7930988

00:44:54.416 --> 00:44:57.628 patients from by iron versus the North

NOTE Confidence: 0.7930988

00:44:57.630 --> 00:45:00.836 of and of Japan, and you would

NOTE Confidence: 0.7930988

00:45:00.840 --> 00:45:02.832 really think the diets

NOTE Confidence: 0.7930988

00:45:02.832 --> 00:45:04.326 are completely different.

NOTE Confidence: 0.7930988

00:45:04.330 --> 00:45:06.766 And they will go into these transplant

NOTE Confidence: 0.7930988

00:45:06.766 --> 00:45:08.200 with completely different flora.

NOTE Confidence: 0.7930988

00:45:08.200 --> 00:45:10.600 But as I mentioned during my talk,

NOTE Confidence: 0.7930988

00:45:10.600 --> 00:45:12.840 also, we really think that that is

NOTE Confidence: 0.7930988

00:45:12.840 --> 00:45:15.114 because most of these people have

NOTE Confidence: 0.7930988

00:45:15.114 --> 00:45:16.999 injured microbiomes to start with.

NOTE Confidence: 0.7930988

00:45:17.000 --> 00:45:19.406 They come, they come into transplant

NOTE Confidence: 0.7930988

00:45:19.406 --> 00:45:21.927 already having steam for a year or so.

NOTE Confidence: 0.7930988

00:45:21.930 --> 00:45:23.690 So many drugs and antibiotics.

NOTE Confidence: 0.7930988

00:45:23.690 --> 00:45:26.147 That is probably why it's so simple.

NOTE Confidence: 0.783098002857143

00:45:28.180 --> 00:45:29.650 Something something so.

NOTE Confidence: 0.783098002857143

00:45:29.650 --> 00:45:32.994 Do you have a? Do you have a

NOTE Confidence: 0.783098002857143

00:45:32.994 --> 00:45:34.724 suggestion of a simple measure?

NOTE Confidence: 0.783098002857143

00:45:34.730 --> 00:45:39.707 So we ask our hospital to change the diet.

NOTE Confidence: 0.783098002857143

00:45:39.710 --> 00:45:42.398 What food is served in the cafeteria?

NOTE Confidence: 0.783098002857143

00:45:42.400 --> 00:45:43.549 Well, I think

NOTE Confidence: 0.8297896

00:45:43.550 --> 00:45:45.405 first of all, when we

NOTE Confidence: 0.8297896

00:45:45.405 --> 00:45:47.770 started to look at the diet,

NOTE Confidence: 0.8297896

00:45:47.770 --> 00:45:51.226 I don't know how it is at your center.

NOTE Confidence: 0.8297896

00:45:51.230 --> 00:45:53.920 But on our transplants floor we it's

NOTE Confidence: 0.8297896

00:45:53.920 --> 00:45:56.599 almost like an like an ICU, right?

NOTE Confidence: 0.8297896

00:45:56.599 --> 00:45:58.873 We have such detailed data about

NOTE Confidence: 0.8297896

00:45:58.873 --> 00:46:00.423 everything finals every eight

NOTE Confidence: 0.8297896

00:46:00.423 --> 00:46:02.168 hours and and daily chemistries

NOTE Confidence: 0.8297896

00:46:02.168 --> 00:46:04.290 and blood counts and everything.

NOTE Confidence: 0.8297896

00:46:04.290 --> 00:46:06.594 But when it comes to what

NOTE Confidence: 0.8297896

00:46:06.594 --> 00:46:08.130 do patients actually eat?

NOTE Confidence: 0.8297896

00:46:08.130 --> 00:46:10.506 Most of what we saw is?

NOTE Confidence: 0.8297896

00:46:10.510 --> 00:46:12.694 Eight half sandwich or something like that,

NOTE Confidence: 0.8297896

00:46:12.700 --> 00:46:14.578 so we have no detail about

NOTE Confidence: 0.8297896

00:46:14.578 --> 00:46:15.830 what we're actually eating,

NOTE Confidence: 0.8297896

00:46:15.830 --> 00:46:17.860 so I think that is a moment

NOTE Confidence: 0.8297896

00:46:17.860 --> 00:46:19.590 where we need to operate.

NOTE Confidence: 0.8297896

00:46:19.590 --> 00:46:21.790 We need to take that a little bit

NOTE Confidence: 0.8297896

00:46:21.790 --> 00:46:23.778 more serious now that we know that

NOTE Confidence: 0.8297896

00:46:23.778 --> 00:46:26.054 it's a major factor that can have

NOTE Confidence: 0.8297896

00:46:26.054 --> 00:46:27.730 impacts on microbiome microbiome.

NOTE Confidence: 0.8297896

00:46:27.730 --> 00:46:30.860 I hope that you got that out of this lecture.

NOTE Confidence: 0.8297896

00:46:30.860 --> 00:46:32.420 Really seems to impact on

NOTE Confidence: 0.8297896

00:46:32.420 --> 00:46:33.356 clinically relevant outcomes,

NOTE Confidence: 0.8297896

00:46:33.360 --> 00:46:35.397 so that's one of the things that

NOTE Confidence: 0.8297896

00:46:35.397 --> 00:46:37.339 I'm trying to fight for within

NOTE Confidence: 0.8297896

00:46:37.339 --> 00:46:39.304 our hospital so that we take

NOTE Confidence: 0.8297896

00:46:39.304 --> 00:46:41.254 that a little bit more serious.

NOTE Confidence: 0.8297896

00:46:41.254 --> 00:46:44.390 We really need to know what our patients eat,

NOTE Confidence: 0.8297896

00:46:44.390 --> 00:46:46.826 not just nurses scribbling down like well,

NOTE Confidence: 0.8297896

00:46:46.830 --> 00:46:47.524 ate something,

NOTE Confidence: 0.8297896

00:46:47.524 --> 00:46:50.540 and then we can learn a lot from it.

NOTE Confidence: 0.8297896

00:46:50.540 --> 00:46:52.400 And then we need to understand

NOTE Confidence: 0.8297896

00:46:52.400 --> 00:46:54.308 in much more detail which

NOTE Confidence: 0.8297896

00:46:54.308 --> 00:46:56.218 of dietary elements do what.

NOTE Confidence: 0.842861

00:46:57.500 --> 00:46:58.604 OK, that's that's fascinating,

NOTE Confidence: 0.842861

00:46:58.604 --> 00:47:01.079 so I'm not going to get more questions,

NOTE Confidence: 0.842861

00:47:01.080 --> 00:47:03.340 so I get to have all the questions in the

NOTE Confidence: 0.842861

00:47:03.398 --> 00:47:05.548 entire conversation here for everybody.

NOTE Confidence: 0.842861

00:47:05.550 --> 00:47:07.671 But you know that that seems like

NOTE Confidence: 0.842861

00:47:07.671 --> 00:47:09.791 a fantastic project where you could

NOTE Confidence: 0.842861

00:47:09.791 --> 00:47:11.706 potentially engage the patient right

NOTE Confidence: 0.842861

00:47:11.706 --> 00:47:14.093 in documenting using Epic using. Well,

NOTE Confidence: 0.842861

00:47:14.093 --> 00:47:19.340 I maybe maybe we close on the House and.

NOTE Confidence: 0.842861

00:47:19.340 --> 00:47:20.452 Maybe a fantastic collaboration

NOTE Confidence: 0.842861

00:47:20.452 --> 00:47:22.410 that we would could then do with.

NOTE Confidence: 0.842861

00:47:22.410 --> 00:47:23.801 You have to do that.

NOTE Confidence: 0.842861

00:47:23.801 --> 00:47:25.172 Take that epic interface and

NOTE Confidence: 0.842861

00:47:25.172 --> 00:47:27.150 put it to use for patient care.

NOTE Confidence: 0.842861

00:47:27.150 --> 00:47:28.207 That'd be wonderful.

NOTE Confidence: 0.842861

00:47:28.207 --> 00:47:29.698 Thank you awesome.

NOTE Confidence: 0.842861

00:47:29.700 --> 00:47:31.686 So we're not getting more questions

NOTE Confidence: 0.842861

00:47:31.686 --> 00:47:32.679 you have answered.

NOTE Confidence: 0.842861

00:47:32.680 --> 00:47:34.550 Everybody's questions so thank you

NOTE Confidence: 0.842861

00:47:34.550 --> 00:47:37.196 so much again for giving a fantastic

NOTE Confidence: 0.842861

00:47:37.196 --> 00:47:39.326 talk and you certainly have my

NOTE Confidence: 0.842861

00:47:39.326 --> 00:47:41.620 mind spinning and I don't know if I

NOTE Confidence: 0.842861

00:47:41.620 --> 00:47:44.191 should drink on my ginger tea now.

NOTE Confidence: 0.842861

00:47:44.191 --> 00:47:46.776 Let's see how that goes.

NOTE Confidence: 0.842861

00:47:46.780 --> 00:47:48.840 OK, thank you very much.

NOTE Confidence: 0.842861

00:47:48.840 --> 00:47:50.070 Much is great.

NOTE Confidence: 0.842861

00:47:50.070 --> 00:47:51.808 Thank you.