

WEBVTT

NOTE duration:"01:05:51"

NOTE recognizability:0.870

NOTE language:en-us

NOTE Confidence: 0.717054400909091

00:00:04.030 --> 00:00:06.249 First, the uh, you know, do you

NOTE Confidence: 0.717054400909091

00:00:06.249 --> 00:00:07.740 know the introduction perfect?

NOTE Confidence: 0.86109732

00:00:11.030 --> 00:00:15.314 OK, we'll start a good afternoon everyone.

NOTE Confidence: 0.86109732

00:00:15.320 --> 00:00:18.940 Welcome to pathology grand rounds,

NOTE Confidence: 0.86109732

00:00:18.940 --> 00:00:21.476 so it is really my great pleasure and

NOTE Confidence: 0.86109732

00:00:21.476 --> 00:00:23.668 a privilege to introduce you today.

NOTE Confidence: 0.86109732

00:00:23.670 --> 00:00:25.886 Speaker Doctor Mark Atkinson

NOTE Confidence: 0.86109732

00:00:25.886 --> 00:00:28.656 from the University of Florida.

NOTE Confidence: 0.86109732

00:00:28.660 --> 00:00:30.562 So doctor I concern is a

NOTE Confidence: 0.86109732

00:00:30.562 --> 00:00:32.230 really a world renowned type.

NOTE Confidence: 0.86109732

00:00:32.230 --> 00:00:34.686 One diabetic diabetic investigator,

NOTE Confidence: 0.86109732

00:00:34.686 --> 00:00:38.370 an outstanding teacher and a mentor,

NOTE Confidence: 0.86109732

00:00:38.370 --> 00:00:40.582 an end a prominent.

NOTE Confidence: 0.86109732

00:00:40.582 --> 00:00:43.347 Leader in the scientific community.  
NOTE Confidence: 0.86109732

00:00:43.350 --> 00:00:45.414 So he has a really long  
NOTE Confidence: 0.86109732

00:00:45.414 --> 00:00:46.790 and very impressive CV,  
NOTE Confidence: 0.86109732

00:00:46.790 --> 00:00:49.046 and it will take the whole hour to  
NOTE Confidence: 0.86109732

00:00:49.046 --> 00:00:50.770 talk about the marks achievement  
NOTE Confidence: 0.86109732

00:00:50.770 --> 00:00:52.782 over the past 30 decades.  
NOTE Confidence: 0.86109732

00:00:52.782 --> 00:00:55.974 So I decided just to you know,  
NOTE Confidence: 0.86109732

00:00:55.980 --> 00:00:58.010 to do a brief introduction,  
NOTE Confidence: 0.86109732

00:00:58.010 --> 00:00:59.471 introduction to mark.  
NOTE Confidence: 0.86109732

00:00:59.471 --> 00:01:01.906 So I had the privilege,  
NOTE Confidence: 0.86109732

00:01:01.910 --> 00:01:05.345 privilege and opportunity to work with  
NOTE Confidence: 0.86109732

00:01:05.345 --> 00:01:08.153 Mark in the Department of Pathology  
NOTE Confidence: 0.86109732

00:01:08.153 --> 00:01:10.680 at the US will almost 16 years.  
NOTE Confidence: 0.86109732

00:01:10.680 --> 00:01:13.880 So I think I really know a lot about him.  
NOTE Confidence: 0.86109732

00:01:13.880 --> 00:01:19.352 Mark so Mark is currently the American  
NOTE Confidence: 0.86109732

00:01:19.352 --> 00:01:22.413 Diabetes Association eminent scholar for

NOTE Confidence: 0.86109732

00:01:22.413 --> 00:01:25.328 diabetic Research and Jeffrey Kinney,

NOTE Confidence: 0.86109732

00:01:25.330 --> 00:01:27.570 family professor at the

NOTE Confidence: 0.86109732

00:01:27.570 --> 00:01:29.250 Department of Pathology,

NOTE Confidence: 0.86109732

00:01:29.250 --> 00:01:31.926 Immunology and Laboratory Medicine at EU.

NOTE Confidence: 0.86109732

00:01:31.930 --> 00:01:32.447 F.

NOTE Confidence: 0.86109732

00:01:32.447 --> 00:01:35.549 He he is the founding director

NOTE Confidence: 0.86109732

00:01:35.549 --> 00:01:38.899 of the Diabetes Institute at UF.

NOTE Confidence: 0.86109732

00:01:38.900 --> 00:01:41.340 Market received his bachelor's degree

NOTE Confidence: 0.86109732

00:01:41.340 --> 00:01:43.752 from University of Michigan and

NOTE Confidence: 0.86109732

00:01:43.752 --> 00:01:46.916 his PhD Tigre at the University of

NOTE Confidence: 0.86109732

00:01:46.916 --> 00:01:50.980 Florida and then stated there things.

NOTE Confidence: 0.86109732

00:01:50.980 --> 00:01:54.160 A Marca has been working on

NOTE Confidence: 0.86109732

00:01:54.160 --> 00:01:55.668 diabetic type one diabetes.

NOTE Confidence: 0.86109732

00:01:55.668 --> 00:01:58.259 For most, I believe is almost 40 years right?

NOTE Confidence: 0.86109732

00:01:58.260 --> 00:02:00.960 Correct me if I'm wrong, if I'm wrong.

NOTE Confidence: 0.86109732

00:02:00.960 --> 00:02:03.217 So he has published nearly 600  
NOTE Confidence: 0.86109732

00:02:03.217 --> 00:02:06.073 papers and I I know several of his  
NOTE Confidence: 0.86109732

00:02:06.073 --> 00:02:08.383 papers are among the most quoted  
NOTE Confidence: 0.86109732

00:02:08.383 --> 00:02:11.050 paper in the field of diabetes.  
NOTE Confidence: 0.86109732

00:02:11.050 --> 00:02:12.838 So he hasn't received the most  
NOTE Confidence: 0.86109732

00:02:12.838 --> 00:02:14.286 and 75 million grants,  
NOTE Confidence: 0.86109732

00:02:14.286 --> 00:02:16.358 and he's always well, Ralph,  
NOTE Confidence: 0.86109732

00:02:16.358 --> 00:02:19.048 well funded from multiple sources.  
NOTE Confidence: 0.86109732

00:02:19.050 --> 00:02:21.018 That certainly is the, you know,  
NOTE Confidence: 0.86109732

00:02:21.020 --> 00:02:23.258 an age and he has holding  
NOTE Confidence: 0.86109732

00:02:23.258 --> 00:02:25.220 this type one diabetes pill,  
NOTE Confidence: 0.86109732

00:02:25.220 --> 00:02:27.668 one for long period of time.  
NOTE Confidence: 0.86109732

00:02:27.670 --> 00:02:30.595 Mark has been the recipient  
NOTE Confidence: 0.86109732

00:02:30.595 --> 00:02:32.935 recipients of multiple scientific  
NOTE Confidence: 0.86109732

00:02:32.935 --> 00:02:35.770 and humanitarian based wars.  
NOTE Confidence: 0.86109732

00:02:35.770 --> 00:02:38.619 I will just mention a few here.

NOTE Confidence: 0.86109732

00:02:38.620 --> 00:02:42.150 He received a Gerald Gala,

NOTE Confidence: 0.86109732

00:02:42.150 --> 00:02:43.274 Grosky award,

NOTE Confidence: 0.86109732

00:02:43.274 --> 00:02:46.646 Mary Tyler Moore and Robert Levin

NOTE Confidence: 0.86109732

00:02:46.646 --> 00:02:50.020 Award from juvenile Diabetes Research

NOTE Confidence: 0.86109732

00:02:50.020 --> 00:02:53.595 Foundation the he's also called.

NOTE Confidence: 0.86109732

00:02:53.600 --> 00:02:56.695 He received a prestigious Eli

NOTE Confidence: 0.86109732

00:02:56.695 --> 00:02:59.171 Lilly Award for Understanding

NOTE Confidence: 0.86109732

00:02:59.171 --> 00:03:01.353 scientific achievement from

NOTE Confidence: 0.86109732

00:03:01.353 --> 00:03:03.582 American Diabetes Association,

NOTE Confidence: 0.86109732

00:03:03.582 --> 00:03:05.820 also called JDA.

NOTE Confidence: 0.86109732

00:03:05.820 --> 00:03:08.640 He received that they hire strong

NOTE Confidence: 0.86109732

00:03:08.640 --> 00:03:11.150 award from Sweden and recently

NOTE Confidence: 0.86109732

00:03:11.150 --> 00:03:14.921 he received the UF College of

NOTE Confidence: 0.86109732

00:03:14.921 --> 00:03:17.749 Medicine Lifetime Achievement Award.

NOTE Confidence: 0.86109732

00:03:17.750 --> 00:03:21.012 And he also received the Jacob Jacobo

NOTE Confidence: 0.86109732

00:03:21.012 --> 00:03:24.650 Award from the Nova Nordisk Foundation,  
NOTE Confidence: 0.86109732

00:03:24.650 --> 00:03:28.215 really the most prestigious international  
NOTE Confidence: 0.86109732

00:03:28.215 --> 00:03:31.780 award in endocrinology and Metabolism.  
NOTE Confidence: 0.86109732

00:03:31.780 --> 00:03:34.204 Besides his scientific achievement,  
NOTE Confidence: 0.86109732

00:03:34.204 --> 00:03:37.840 mark has also actively engaged in  
NOTE Confidence: 0.86109732

00:03:37.934 --> 00:03:41.314 leadership services to type one  
NOTE Confidence: 0.86109732

00:03:41.314 --> 00:03:44.018 diabetes community with active  
NOTE Confidence: 0.86109732

00:03:44.018 --> 00:03:47.336 administrative or advisory services to JD RF,  
NOTE Confidence: 0.86109732

00:03:47.340 --> 00:03:49.580 the American Diabetic Association,  
NOTE Confidence: 0.86109732

00:03:49.580 --> 00:03:52.380 the National Institute of Health,  
NOTE Confidence: 0.86109732

00:03:52.380 --> 00:03:54.700 at the Immunology of Diabetes,  
NOTE Confidence: 0.86109732

00:03:54.700 --> 00:03:55.291 Society,  
NOTE Confidence: 0.86109732

00:03:55.291 --> 00:03:58.837 and various variety of companies from  
NOTE Confidence: 0.86109732

00:03:58.837 --> 00:04:01.450 pharmaceutical and about industry.  
NOTE Confidence: 0.86109732

00:04:01.450 --> 00:04:04.186 And I would particularly like to  
NOTE Confidence: 0.86109732

00:04:04.186 --> 00:04:06.622 highlight the two great programs

NOTE Confidence: 0.86109732  
00:04:06.622 --> 00:04:09.267 that Mark funded from scratch,  
NOTE Confidence: 0.86109732  
00:04:09.270 --> 00:04:12.420 and I had the opportunity to  
NOTE Confidence: 0.86109732  
00:04:12.420 --> 00:04:13.995 actually witness myself.  
NOTE Confidence: 0.86109732  
00:04:14.000 --> 00:04:18.116 One is the JDRF network for pancreatic  
NOTE Confidence: 0.86109732  
00:04:18.116 --> 00:04:21.409 organ donate donors with diabetes.  
NOTE Confidence: 0.86109732  
00:04:21.410 --> 00:04:23.234 The acronym is Empire,  
NOTE Confidence: 0.86109732  
00:04:23.234 --> 00:04:25.970 which you will hear from Mark  
NOTE Confidence: 0.586016895454545  
00:04:26.063 --> 00:04:29.635 today. I would say it is epic example  
NOTE Confidence: 0.586016895454545  
00:04:29.635 --> 00:04:33.028 of how tissue repository can make.  
NOTE Confidence: 0.586016895454545  
00:04:33.030 --> 00:04:34.742 Impact on scientific discovery.  
NOTE Confidence: 0.586016895454545  
00:04:34.742 --> 00:04:37.310 The end part is now supporting  
NOTE Confidence: 0.586016895454545  
00:04:37.380 --> 00:04:39.590 more than 300 research projects.  
NOTE Confidence: 0.586016895454545  
00:04:39.590 --> 00:04:42.040 Over 200 / 24 countries.  
NOTE Confidence: 0.586016895454545  
00:04:42.040 --> 00:04:45.232 The other program is that he founded the  
NOTE Confidence: 0.586016895454545  
00:04:45.232 --> 00:04:49.058 university level Diabetic Institute at USC.  
NOTE Confidence: 0.586016895454545

00:04:49.060 --> 00:04:52.116 So Mark are all also serves in many  
NOTE Confidence: 0.586016895454545

00:04:52.120 --> 00:04:53.740 scientific organization editorial,  
NOTE Confidence: 0.586016895454545

00:04:53.740 --> 00:04:55.360 board of journals,  
NOTE Confidence: 0.586016895454545

00:04:55.360 --> 00:04:56.952 and the charitable foundations.  
NOTE Confidence: 0.586016895454545

00:04:56.952 --> 00:04:59.340 I just highlighted one particular one.  
NOTE Confidence: 0.586016895454545

00:04:59.340 --> 00:05:01.000 I think it's really remarkable.  
NOTE Confidence: 0.586016895454545

00:05:01.000 --> 00:05:03.016 So Mark is now the president  
NOTE Confidence: 0.586016895454545

00:05:03.016 --> 00:05:04.360 of insulin for life.  
NOTE Confidence: 0.586016895454545

00:05:04.360 --> 00:05:08.116 USA, the world's second largest charity,  
NOTE Confidence: 0.586016895454545

00:05:08.120 --> 00:05:10.874 dedicated to providing insulin to people  
NOTE Confidence: 0.586016895454545

00:05:10.874 --> 00:05:14.289 living with diabetes in the developing world.  
NOTE Confidence: 0.586016895454545

00:05:14.290 --> 00:05:16.468 I will say without further ado,  
NOTE Confidence: 0.586016895454545

00:05:16.470 --> 00:05:19.629 I now turn it to mark for his lecture  
NOTE Confidence: 0.586016895454545

00:05:19.630 --> 00:05:23.386 titled license from the Human Pancreas,  
NOTE Confidence: 0.586016895454545

00:05:23.390 --> 00:05:25.098 rewriting the textbooks and  
NOTE Confidence: 0.586016895454545

00:05:25.098 --> 00:05:27.233 how type one diabetes develop.



NOTE Confidence: 0.586016895454545

00:05:27.240 --> 00:05:28.302 Mark is yours.

NOTE Confidence: 0.586016895454545

00:05:28.302 --> 00:05:29.010 Thank you.

NOTE Confidence: 0.586016895454545

00:05:29.010 --> 00:05:29.631 Again,

NOTE Confidence: 0.586016895454545

00:05:29.631 --> 00:05:32.736 thank you for visiting Yale

NOTE Confidence: 0.853657078

00:05:33.230 --> 00:05:35.822 chanting. Thank you very much for

NOTE Confidence: 0.853657078

00:05:35.822 --> 00:05:38.254 that warm introduction and you can

NOTE Confidence: 0.853657078

00:05:38.254 --> 00:05:40.782 write my eulogy one day if you want.

NOTE Confidence: 0.853657078

00:05:40.790 --> 00:05:42.904 Won't be for awhile, but anyway,

NOTE Confidence: 0.853657078

00:05:42.904 --> 00:05:45.460 that was very kind of you and I to

NOTE Confidence: 0.853657078

00:05:45.532 --> 00:05:47.964 everybody at Yale like I wish I were

NOTE Confidence: 0.853657078

00:05:47.970 --> 00:05:50.007 up there in person to present this,

NOTE Confidence: 0.853657078

00:05:50.010 --> 00:05:52.789 but we will try and make it

NOTE Confidence: 0.853657078

00:05:52.789 --> 00:05:55.290 through as good as we can today.

NOTE Confidence: 0.853657078

00:05:55.290 --> 00:05:57.558 So thank you again and what I

NOTE Confidence: 0.853657078

00:05:57.558 --> 00:06:00.119 wanted to do is kind of build on

NOTE Confidence: 0.853657078

00:06:00.119 --> 00:06:02.796 what Ken said is to try and show  
NOTE Confidence: 0.853657078

00:06:02.796 --> 00:06:05.337 some lessons on how studies of the  
NOTE Confidence: 0.853657078

00:06:05.340 --> 00:06:08.406 tissues can really contribute to an  
NOTE Confidence: 0.853657078

00:06:08.406 --> 00:06:10.450 improved understanding of disease.  
NOTE Confidence: 0.853657078

00:06:10.450 --> 00:06:11.758 And I think in the case.  
NOTE Confidence: 0.853657078

00:06:11.760 --> 00:06:13.131 So then pod,  
NOTE Confidence: 0.853657078

00:06:13.131 --> 00:06:15.873 the effort that Chen introduced below.  
NOTE Confidence: 0.853657078

00:06:15.880 --> 00:06:19.345 That's a we we really are doing that in  
NOTE Confidence: 0.853657078

00:06:19.345 --> 00:06:24.190 terms of updating our understanding so.  
NOTE Confidence: 0.853657078

00:06:24.190 --> 00:06:26.555 Yeah, again, just keeping with CMA,  
NOTE Confidence: 0.853657078

00:06:26.555 --> 00:06:29.155 he notions these are some of the companies  
NOTE Confidence: 0.853657078

00:06:29.155 --> 00:06:31.988 that I worked with over the past five years,  
NOTE Confidence: 0.853657078

00:06:31.990 --> 00:06:35.483 but nothing today will discuss will relate  
NOTE Confidence: 0.853657078

00:06:35.483 --> 00:06:39.868 to any of their activities or drugs so.  
NOTE Confidence: 0.853657078

00:06:39.870 --> 00:06:42.960 Wanna add like like one of the  
NOTE Confidence: 0.853657078

00:06:42.960 --> 00:06:45.854 things that in that goes with type

NOTE Confidence: 0.853657078

00:06:45.854 --> 00:06:48.382 one diabetes research is when you,

NOTE Confidence: 0.853657078

00:06:48.382 --> 00:06:49.737 especially when you speak to

NOTE Confidence: 0.853657078

00:06:49.737 --> 00:06:51.230 groups of lay individuals.

NOTE Confidence: 0.853657078

00:06:51.230 --> 00:06:52.193 People say well,

NOTE Confidence: 0.853657078

00:06:52.193 --> 00:06:53.798 when is type one diabetes

NOTE Confidence: 0.853657078

00:06:53.798 --> 00:06:55.260 is going to be cured.

NOTE Confidence: 0.853657078

00:06:55.260 --> 00:06:58.984 And part of this is driven because in them.

NOTE Confidence: 0.853657078

00:06:58.984 --> 00:07:01.219 So either social media or

NOTE Confidence: 0.853657078

00:07:01.219 --> 00:07:02.113 old-fashioned newspapers.

NOTE Confidence: 0.853657078

00:07:02.120 --> 00:07:04.160 There's just constantly been essentially

NOTE Confidence: 0.853657078

00:07:04.160 --> 00:07:06.887 almost in my whole career news reports

NOTE Confidence: 0.853657078

00:07:06.887 --> 00:07:09.050 that the cure of type one diabetes

NOTE Confidence: 0.853657078

00:07:09.050 --> 00:07:11.209 is around the corner or three to

NOTE Confidence: 0.853657078

00:07:11.209 --> 00:07:14.380 five years away is a common thing,

NOTE Confidence: 0.853657078

00:07:14.380 --> 00:07:18.484 and it's been one of the biggest challenges

NOTE Confidence: 0.853657078

00:07:18.484 --> 00:07:21.835 is to try and convince people that  
NOTE Confidence: 0.853657078

00:07:21.835 --> 00:07:25.770 you know we're trying to do this and.  
NOTE Confidence: 0.853657078

00:07:25.770 --> 00:07:27.978 Try and take on this challenge  
NOTE Confidence: 0.853657078

00:07:27.978 --> 00:07:30.548 of what they see in the media,  
NOTE Confidence: 0.853657078

00:07:30.550 --> 00:07:33.174 but this is not a new event and  
NOTE Confidence: 0.853657078

00:07:33.174 --> 00:07:35.503 that actually this year marks the  
NOTE Confidence: 0.853657078

00:07:35.503 --> 00:07:37.503 100th anniversary of the ability  
NOTE Confidence: 0.853657078

00:07:37.503 --> 00:07:39.150 to isolate insulin,  
NOTE Confidence: 0.853657078

00:07:39.150 --> 00:07:41.928 which back again 100 years ago,  
NOTE Confidence: 0.853657078

00:07:41.930 --> 00:07:43.970 was a Nobel Prize winning event.  
NOTE Confidence: 0.853657078

00:07:43.970 --> 00:07:46.390 But this newspaper headline from  
NOTE Confidence: 0.853657078

00:07:46.390 --> 00:07:49.300 the Toronto Daily Star back then.  
NOTE Confidence: 0.853657078

00:07:49.300 --> 00:07:52.936 It even says the doctors on track of the  
NOTE Confidence: 0.853657078

00:07:52.936 --> 00:07:55.830 cure for diabetes didn't quite turn out that.  
NOTE Confidence: 0.853657078

00:07:55.830 --> 00:07:57.294 Wait, but uhm,  
NOTE Confidence: 0.853657078

00:07:57.294 --> 00:08:00.222 it's it's been 100 years of

NOTE Confidence: 0.853657078

00:08:00.230 --> 00:08:02.786 trials to try and do that.

NOTE Confidence: 0.853657078

00:08:02.790 --> 00:08:04.974 And then the reason I put this slide

NOTE Confidence: 0.853657078

00:08:04.974 --> 00:08:07.270 in here and it's a couple of years.

NOTE Confidence: 0.853657078

00:08:07.270 --> 00:08:10.432 Old now is certainly not been

NOTE Confidence: 0.853657078

00:08:10.432 --> 00:08:12.540 for lack of trying.

NOTE Confidence: 0.853657078

00:08:12.540 --> 00:08:13.866 At this time on this Lancet

NOTE Confidence: 0.853657078

00:08:13.866 --> 00:08:15.220 article that we put together,

NOTE Confidence: 0.853657078

00:08:15.220 --> 00:08:17.635 we just looked back in the previous

NOTE Confidence: 0.853657078

00:08:17.635 --> 00:08:20.020 decade of attempts to try and intervene

NOTE Confidence: 0.853657078

00:08:20.020 --> 00:08:22.696 in terms of type one diabetes.

NOTE Confidence: 0.853657078

00:08:22.700 --> 00:08:25.082 This just being on the immune

NOTE Confidence: 0.853657078

00:08:25.082 --> 00:08:25.876 mediated trials.

NOTE Confidence: 0.853657078

00:08:25.880 --> 00:08:30.056 This did not include things like.

NOTE Confidence: 0.853657078

00:08:30.060 --> 00:08:30.822 The antigen,

NOTE Confidence: 0.853657078

00:08:30.822 --> 00:08:32.727 specific therapies and the like,

NOTE Confidence: 0.853657078

00:08:32.730 --> 00:08:35.190 but just targeting the immune system

NOTE Confidence: 0.853657078

00:08:35.190 --> 00:08:37.822 and in many different ways and so

NOTE Confidence: 0.853657078

00:08:37.822 --> 00:08:39.950 at that time they were about 52

NOTE Confidence: 0.853657078

00:08:40.028 --> 00:08:42.680 completed trials and 25 that we

NOTE Confidence: 0.853657078

00:08:42.680 --> 00:08:44.410 recruit recruiting and we're still

NOTE Confidence: 0.853657078

00:08:44.410 --> 00:08:46.090 in that situation today in many

NOTE Confidence: 0.853657078

00:08:46.090 --> 00:08:47.672 ways and that there are trials

NOTE Confidence: 0.853657078

00:08:47.672 --> 00:08:48.912 going on both in the

NOTE Confidence: 0.932194666666667

00:08:48.970 --> 00:08:50.318 United States and Europe.

NOTE Confidence: 0.932194666666667

00:08:50.320 --> 00:08:52.198 All that they're attempting to do.

NOTE Confidence: 0.932194666666667

00:08:52.200 --> 00:08:54.190 Usually one of two things,

NOTE Confidence: 0.932194666666667

00:08:54.190 --> 00:08:57.470 either delay the prevention

NOTE Confidence: 0.932194666666667

00:08:57.470 --> 00:09:00.310 of onset of the disease so.

NOTE Confidence: 0.932194666666667

00:09:00.310 --> 00:09:02.790 If you have individuals that are high risk,

NOTE Confidence: 0.932194666666667

00:09:02.790 --> 00:09:06.228 try and keep them from developing.

NOTE Confidence: 0.932194666666667

00:09:06.230 --> 00:09:08.708 The need for exogenous insulin therapy,

NOTE Confidence: 0.932194666666667  
00:09:08.710 --> 00:09:10.628 but then or the other thing is,  
NOTE Confidence: 0.932194666666667  
00:09:10.630 --> 00:09:13.255 is if you're diagnosed with the disease  
NOTE Confidence: 0.932194666666667  
00:09:13.255 --> 00:09:16.113 to try and again continue to have  
NOTE Confidence: 0.932194666666667  
00:09:16.113 --> 00:09:18.232 the person produce insulin in the  
NOTE Confidence: 0.932194666666667  
00:09:18.232 --> 00:09:20.930 OR we what we measure in C peptide.  
NOTE Confidence: 0.932194666666667  
00:09:20.930 --> 00:09:23.130 So a lot of attempts to try and do this.  
NOTE Confidence: 0.932194666666667  
00:09:23.130 --> 00:09:25.286 But as of today we we don't  
NOTE Confidence: 0.932194666666667  
00:09:25.286 --> 00:09:28.052 have such a therapy that's been  
NOTE Confidence: 0.932194666666667  
00:09:28.052 --> 00:09:30.400 approved by regulatory agencies,  
NOTE Confidence: 0.932194666666667  
00:09:30.400 --> 00:09:32.992 although thanks to one of your own doctor  
NOTE Confidence: 0.932194666666667  
00:09:32.992 --> 00:09:35.207 Harold and others in the Community,  
NOTE Confidence: 0.932194666666667  
00:09:35.210 --> 00:09:36.654 we we feel like.  
NOTE Confidence: 0.932194666666667  
00:09:36.654 --> 00:09:38.098 We're closer than ever,  
NOTE Confidence: 0.932194666666667  
00:09:38.100 --> 00:09:41.212 but one of the reasons so I wanted to  
NOTE Confidence: 0.932194666666667  
00:09:41.212 --> 00:09:42.990 set this up in this first five minutes.  
NOTE Confidence: 0.932194666666667

00:09:42.990 --> 00:09:45.789 Why haven't we been able to cure the disease?

NOTE Confidence: 0.932194666666667

00:09:45.790 --> 00:09:48.198 And I think there's a number of

NOTE Confidence: 0.932194666666667

00:09:48.198 --> 00:09:50.329 reasons to that underlie this,

NOTE Confidence: 0.932194666666667

00:09:50.330 --> 00:09:51.386 and one is,

NOTE Confidence: 0.932194666666667

00:09:51.386 --> 00:09:54.337 is that we still have knowledge voids in

NOTE Confidence: 0.932194666666667

00:09:54.337 --> 00:09:57.228 terms of how exactly the disease developed,

NOTE Confidence: 0.932194666666667

00:09:57.230 --> 00:09:59.048 and this is not meant to

NOTE Confidence: 0.932194666666667

00:09:59.048 --> 00:10:00.260 be a sarcastic slide.

NOTE Confidence: 0.932194666666667

00:10:00.260 --> 00:10:02.276 But what I did was I went back

NOTE Confidence: 0.932194666666667

00:10:02.276 --> 00:10:03.956 and found like major articles

NOTE Confidence: 0.932194666666667

00:10:03.956 --> 00:10:06.328 that were published back in 1992.

NOTE Confidence: 0.932194666666667

00:10:06.328 --> 00:10:08.400 Number of years later,

NOTE Confidence: 0.932194666666667

00:10:08.400 --> 00:10:08.728 2007,

NOTE Confidence: 0.932194666666667

00:10:08.728 --> 00:10:11.680 and then even last year and you can see

NOTE Confidence: 0.932194666666667

00:10:11.754 --> 00:10:15.860 that actually all the way back to 1992.

NOTE Confidence: 0.932194666666667

00:10:15.860 --> 00:10:18.044 That they said that you know there's



NOTE Confidence: 0.932194666666667  
00:10:18.044 --> 00:10:20.260 these B cells that make antibody.  
NOTE Confidence: 0.932194666666667  
00:10:20.260 --> 00:10:22.276 There's the beta cells,  
NOTE Confidence: 0.932194666666667  
00:10:22.276 --> 00:10:25.936 the cells that are destroyed there's an  
NOTE Confidence: 0.932194666666667  
00:10:25.936 --> 00:10:28.666 antigen presenting cell involved in.  
NOTE Confidence: 0.932194666666667  
00:10:28.670 --> 00:10:30.454 What I I guess the point I'm trying  
NOTE Confidence: 0.932194666666667  
00:10:30.454 --> 00:10:32.333 to make here is that the key  
NOTE Confidence: 0.932194666666667  
00:10:32.333 --> 00:10:33.708 and core elements really haven't  
NOTE Confidence: 0.932194666666667  
00:10:33.766 --> 00:10:35.170 changed that much overtime.  
NOTE Confidence: 0.932194666666667  
00:10:35.170 --> 00:10:36.826 I I'm not mocking the field,  
NOTE Confidence: 0.932194666666667  
00:10:36.830 --> 00:10:38.630 there are where we certainly have  
NOTE Confidence: 0.932194666666667  
00:10:38.630 --> 00:10:40.439 a lot more complexity than this,  
NOTE Confidence: 0.932194666666667  
00:10:40.440 --> 00:10:43.056 but we still are faced with a situation  
NOTE Confidence: 0.932194666666667  
00:10:43.056 --> 00:10:45.518 where we really don't know how Type  
NOTE Confidence: 0.932194666666667  
00:10:45.518 --> 00:10:48.168 1 develops and when that occurs it  
NOTE Confidence: 0.932194666666667  
00:10:48.168 --> 00:10:50.308 you're forced into situations like  
NOTE Confidence: 0.932194666666667

00:10:50.308 --> 00:10:52.740 the previous slide where you have  
NOTE Confidence: 0.932194666666667

00:10:52.740 --> 00:10:54.994 to try a lot of different things.  
NOTE Confidence: 0.932194666666667

00:10:55.000 --> 00:10:56.158 In order to try and see,  
NOTE Confidence: 0.932194666666667

00:10:56.160 --> 00:10:59.436 find something that perhaps made success.  
NOTE Confidence: 0.932194666666667

00:10:59.440 --> 00:11:00.420 That's just one thing,  
NOTE Confidence: 0.932194666666667

00:11:00.420 --> 00:11:02.210 and that if you were to pull.  
NOTE Confidence: 0.92283092375

00:11:04.340 --> 00:11:06.150 100 different type one diabetes  
NOTE Confidence: 0.92283092375

00:11:06.150 --> 00:11:07.236 investigators and say,  
NOTE Confidence: 0.92283092375

00:11:07.240 --> 00:11:09.296 why do you think we haven't cured it?  
NOTE Confidence: 0.92283092375

00:11:09.300 --> 00:11:11.142 Everybody would have their own list  
NOTE Confidence: 0.92283092375

00:11:11.142 --> 00:11:13.158 and I'm not going to go through  
NOTE Confidence: 0.92283092375

00:11:13.158 --> 00:11:15.210 all of these for the sake of time,  
NOTE Confidence: 0.92283092375

00:11:15.210 --> 00:11:17.739 but I'm going to just highlight the last two.  
NOTE Confidence: 0.92283092375

00:11:17.740 --> 00:11:20.506 This would be my list and I think  
NOTE Confidence: 0.92283092375

00:11:20.506 --> 00:11:22.831 one of them has been the influence of  
NOTE Confidence: 0.92283092375

00:11:22.831 --> 00:11:24.819 dogma in the field over the years.

NOTE Confidence: 0.92283092375

00:11:24.820 --> 00:11:27.368 Meaning there there were a number of

NOTE Confidence: 0.92283092375

00:11:27.368 --> 00:11:29.499 assumptions or that people thought.

NOTE Confidence: 0.92283092375

00:11:29.500 --> 00:11:31.756 Well, this is true about type one diabetes

NOTE Confidence: 0.92283092375

00:11:31.756 --> 00:11:34.229 and there weren't a whole lot of challenges.

NOTE Confidence: 0.92283092375

00:11:34.230 --> 00:11:37.227 To them, in all cases and the other thing,

NOTE Confidence: 0.92283092375

00:11:37.230 --> 00:11:39.686 and this is maybe good for this audience.

NOTE Confidence: 0.92283092375

00:11:39.690 --> 00:11:42.426 In particular, I think we had a lack

NOTE Confidence: 0.92283092375

00:11:42.426 --> 00:11:44.540 of understanding pancreatic pathology,

NOTE Confidence: 0.92283092375

00:11:44.540 --> 00:11:47.876 or there there has been up until date.

NOTE Confidence: 0.92283092375

00:11:47.880 --> 00:11:50.520 And so let's start out there talking about

NOTE Confidence: 0.92283092375

00:11:50.520 --> 00:11:53.365 some of those dogmas that are out there.

NOTE Confidence: 0.92283092375

00:11:53.370 --> 00:11:56.202 And I think if you were to actually

NOTE Confidence: 0.92283092375

00:11:56.202 --> 00:11:58.990 take the literature on type one

NOTE Confidence: 0.92283092375

00:11:58.990 --> 00:12:01.658 diabetes almost in its pathogenesis,

NOTE Confidence: 0.92283092375

00:12:01.658 --> 00:12:03.284 it's Natural History.

NOTE Confidence: 0.92283092375

00:12:03.290 --> 00:12:04.620 Almost every.  
NOTE Confidence: 0.92283092375

00:12:04.620 --> 00:12:07.280 Article the first sentence,  
NOTE Confidence: 0.92283092375

00:12:07.280 --> 00:12:08.480 if not the first sentence,  
NOTE Confidence: 0.92283092375

00:12:08.480 --> 00:12:10.864 the second sentence is this up at the  
NOTE Confidence: 0.92283092375

00:12:10.864 --> 00:12:13.083 top that type one diabetes results  
NOTE Confidence: 0.92283092375

00:12:13.083 --> 00:12:15.417 from an autoimmune T cell mediated  
NOTE Confidence: 0.92283092375

00:12:15.482 --> 00:12:18.140 destruction of the pancreatic beta cells.  
NOTE Confidence: 0.92283092375

00:12:18.140 --> 00:12:20.620 This this is a central document for disease  
NOTE Confidence: 0.92283092375

00:12:20.620 --> 00:12:22.820 and everybody puts it out there and there.  
NOTE Confidence: 0.92283092375

00:12:22.820 --> 00:12:24.720 There's good reason for it,  
NOTE Confidence: 0.92283092375

00:12:24.720 --> 00:12:26.820 if that we've known for well over  
NOTE Confidence: 0.92283092375

00:12:26.820 --> 00:12:29.257 100 years that the pancreas of type  
NOTE Confidence: 0.92283092375

00:12:29.257 --> 00:12:31.097 one diabetes has this insulinitis.  
NOTE Confidence: 0.92283092375

00:12:31.100 --> 00:12:33.235 So if you remember that in the  
NOTE Confidence: 0.92283092375

00:12:33.235 --> 00:12:35.740 pancreas about 1 to 2% of that organ.  
NOTE Confidence: 0.92283092375

00:12:35.740 --> 00:12:38.238 Is made up of these insulin,

NOTE Confidence: 0.92283092375

00:12:38.238 --> 00:12:39.732 producing another hormone,

NOTE Confidence: 0.92283092375

00:12:39.732 --> 00:12:41.226 producing islet cells,

NOTE Confidence: 0.92283092375

00:12:41.230 --> 00:12:44.758 and they do have a a limp acidic

NOTE Confidence: 0.92283092375

00:12:44.758 --> 00:12:46.350 infiltration associated with it.

NOTE Confidence: 0.92283092375

00:12:46.350 --> 00:12:49.430 We know that in terms of genetic

NOTE Confidence: 0.92283092375

00:12:49.430 --> 00:12:51.675 susceptibility and the the major genes

NOTE Confidence: 0.92283092375

00:12:51.675 --> 00:12:54.094 forming type one diabetes are associated

NOTE Confidence: 0.92283092375

00:12:54.094 --> 00:12:56.819 with the major compatibility complex.

NOTE Confidence: 0.92283092375

00:12:56.820 --> 00:12:59.946 So right central to immune responsiveness

NOTE Confidence: 0.92283092375

00:12:59.950 --> 00:13:01.228 and then the third thing is,

NOTE Confidence: 0.92283092375

00:13:01.230 --> 00:13:04.026 is the presence of autoantibodies that

NOTE Confidence: 0.92283092375

00:13:04.026 --> 00:13:06.868 we've known again since the mid 70s?

NOTE Confidence: 0.92283092375

00:13:06.870 --> 00:13:09.105 Their patients with the disease

NOTE Confidence: 0.92283092375

00:13:09.105 --> 00:13:11.340 develop antibodies that react with

NOTE Confidence: 0.92283092375

00:13:11.410 --> 00:13:14.116 different constituents of of the island,

NOTE Confidence: 0.92283092375

00:13:14.120 --> 00:13:17.024 and you could if you do immuno indirect  
NOTE Confidence: 0.92283092375

00:13:17.024 --> 00:13:18.778 immunofluorescence tests you can see them.  
NOTE Confidence: 0.92283092375

00:13:18.780 --> 00:13:21.228 The other, the second probably most  
NOTE Confidence: 0.92283092375

00:13:21.228 --> 00:13:23.879 touted dogma of type one diabetes,  
NOTE Confidence: 0.92283092375

00:13:23.880 --> 00:13:25.520 is this Natural History model,  
NOTE Confidence: 0.92283092375

00:13:25.520 --> 00:13:27.390 and it was put together.  
NOTE Confidence: 0.92283092375

00:13:27.390 --> 00:13:30.624 By one of my best friends and  
NOTE Confidence: 0.92283092375

00:13:30.630 --> 00:13:32.118 mentors in life,  
NOTE Confidence: 0.92283092375

00:13:32.118 --> 00:13:33.110 George Eisenbarth,  
NOTE Confidence: 0.92283092375

00:13:33.110 --> 00:13:36.410 he published this back in the mid 80s.  
NOTE Confidence: 0.92283092375

00:13:36.410 --> 00:13:38.996 This model for the disease and  
NOTE Confidence: 0.92283092375

00:13:38.996 --> 00:13:40.289 unfortunately George passed  
NOTE Confidence: 0.92283092375

00:13:40.289 --> 00:13:42.472 in 2012 of pancreatic cancer.  
NOTE Confidence: 0.92283092375

00:13:42.472 --> 00:13:46.014 But this this has been the central road  
NOTE Confidence: 0.92283092375

00:13:46.014 --> 00:13:49.098 map since the mid 1980s for almost all  
NOTE Confidence: 0.92283092375

00:13:49.098 --> 00:13:51.240 of human type one diabetes research.

NOTE Confidence: 0.92283092375

00:13:51.240 --> 00:13:53.550 When you talk about the Natural

NOTE Confidence: 0.92283092375

00:13:53.550 --> 00:13:55.674 History of the disease and the

NOTE Confidence: 0.92283092375

00:13:55.674 --> 00:13:57.426 challenge we have and will will.

NOTE Confidence: 0.92283092375

00:13:57.430 --> 00:13:59.846 Re address this at the end is is

NOTE Confidence: 0.92283092375

00:13:59.846 --> 00:14:01.334 that I'm unfortunately and George

NOTE Confidence: 0.92283092375

00:14:01.334 --> 00:14:03.490 would have if he were still alive.

NOTE Confidence: 0.92283092375

00:14:03.490 --> 00:14:05.954 He would admit this to the day

NOTE Confidence: 0.92283092375

00:14:05.954 --> 00:14:08.314 this is served as an exceptional

NOTE Confidence: 0.92283092375

00:14:08.314 --> 00:14:10.420 road map for the disease,

NOTE Confidence: 0.92283092375

00:14:10.420 --> 00:14:13.000 but so many components of it

NOTE Confidence: 0.850860981666667

00:14:13.000 --> 00:14:14.716 are not quite right.

NOTE Confidence: 0.850860981666667

00:14:14.716 --> 00:14:18.279 But and they they needed to update it.

NOTE Confidence: 0.850860981666667

00:14:18.280 --> 00:14:19.171 But it's again.

NOTE Confidence: 0.850860981666667

00:14:19.171 --> 00:14:21.250 It's been a dogma so few few

NOTE Confidence: 0.850860981666667

00:14:21.322 --> 00:14:23.078 people have questioned it.

NOTE Confidence: 0.850860981666667

00:14:23.080 --> 00:14:25.546 And so I thought again, just in the  
NOTE Confidence: 0.850860981666667

00:14:25.546 --> 00:14:27.106 closing down the introduction here,  
NOTE Confidence: 0.850860981666667

00:14:27.110 --> 00:14:27.866 I'm going to give you some.  
NOTE Confidence: 0.850860981666667

00:14:27.870 --> 00:14:29.766 Examples of the dogma that have  
NOTE Confidence: 0.850860981666667

00:14:29.766 --> 00:14:32.090 existed in terms of type 1 diabetes.  
NOTE Confidence: 0.850860981666667

00:14:32.090 --> 00:14:33.930 But now thanks to pathology,  
NOTE Confidence: 0.850860981666667

00:14:33.930 --> 00:14:35.238 I'll show later.  
NOTE Confidence: 0.850860981666667

00:14:35.238 --> 00:14:38.760 You'll see that they're not all exactly true.  
NOTE Confidence: 0.850860981666667

00:14:38.760 --> 00:14:42.464 So one of the realities is that as  
NOTE Confidence: 0.850860981666667

00:14:42.464 --> 00:14:44.690 the individuals throughout the United  
NOTE Confidence: 0.850860981666667

00:14:44.690 --> 00:14:46.890 States and actually globally today,  
NOTE Confidence: 0.850860981666667

00:14:46.890 --> 00:14:48.600 if they're diagnosed with type  
NOTE Confidence: 0.850860981666667

00:14:48.600 --> 00:14:50.310 one diabetes on most occasions,  
NOTE Confidence: 0.850860981666667

00:14:50.310 --> 00:14:53.439 they're going to be told that the  
NOTE Confidence: 0.850860981666667

00:14:53.439 --> 00:14:55.824 reason that you're here today is  
NOTE Confidence: 0.850860981666667

00:14:55.824 --> 00:14:57.679 because of this autoimmune destruction



NOTE Confidence: 0.850860981666667  
00:14:57.679 --> 00:15:00.007 and somewhere around 85 to 90% of  
NOTE Confidence: 0.850860981666667  
00:15:00.007 --> 00:15:02.149 your beta cells have been destroyed.  
NOTE Confidence: 0.850860981666667  
00:15:02.150 --> 00:15:04.026 Well, now through studies of the pancreas,  
NOTE Confidence: 0.850860981666667  
00:15:04.030 --> 00:15:05.836 we now know that actually you  
NOTE Confidence: 0.850860981666667  
00:15:05.836 --> 00:15:07.609 can have as little as a 50%  
NOTE Confidence: 0.850860981666667  
00:15:07.610 --> 00:15:09.780 loss of functional beta cells.  
NOTE Confidence: 0.850860981666667  
00:15:09.780 --> 00:15:10.755 And about disease,  
NOTE Confidence: 0.850860981666667  
00:15:10.755 --> 00:15:13.030 and in some cases it is quite  
NOTE Confidence: 0.850860981666667  
00:15:13.102 --> 00:15:14.997 high in terms of percentage,  
NOTE Confidence: 0.850860981666667  
00:15:15.000 --> 00:15:17.583 but it actually varies from person to  
NOTE Confidence: 0.850860981666667  
00:15:17.583 --> 00:15:20.640 person and will explain some of that later.  
NOTE Confidence: 0.850860981666667  
00:15:20.640 --> 00:15:22.662 But this is a dogma that  
NOTE Confidence: 0.850860981666667  
00:15:22.662 --> 00:15:24.430 people just keep getting told.  
NOTE Confidence: 0.850860981666667  
00:15:24.430 --> 00:15:27.780 Another thing is, is that and I,  
NOTE Confidence: 0.850860981666667  
00:15:27.780 --> 00:15:30.510 I think pathology is bearing this out.  
NOTE Confidence: 0.850860981666667

00:15:30.510 --> 00:15:31.878 This is that we pretty much  
NOTE Confidence: 0.850860981666667

00:15:31.878 --> 00:15:33.254 worked as type one, diabetes,  
NOTE Confidence: 0.850860981666667

00:15:33.254 --> 00:15:35.110 being a singular disease,  
NOTE Confidence: 0.850860981666667

00:15:35.110 --> 00:15:37.926 and it's true that in type one diabetes  
NOTE Confidence: 0.850860981666667

00:15:37.926 --> 00:15:39.900 people become insulin requiring.  
NOTE Confidence: 0.850860981666667

00:15:39.900 --> 00:15:41.956 But in the reality is is you can  
NOTE Confidence: 0.850860981666667

00:15:41.956 --> 00:15:44.020 develop this disease as a one year old,  
NOTE Confidence: 0.850860981666667

00:15:44.020 --> 00:15:45.168 a 10 year old,  
NOTE Confidence: 0.850860981666667

00:15:45.168 --> 00:15:46.316 a 30 year old,  
NOTE Confidence: 0.850860981666667

00:15:46.320 --> 00:15:48.288 a 60 year old individual and  
NOTE Confidence: 0.850860981666667

00:15:48.288 --> 00:15:50.220 we now know through studies.  
NOTE Confidence: 0.850860981666667

00:15:50.220 --> 00:15:52.278 Like I said a pathology genetics,  
NOTE Confidence: 0.850860981666667

00:15:52.280 --> 00:15:54.300 the immune response that there's  
NOTE Confidence: 0.850860981666667

00:15:54.300 --> 00:15:57.084 differences that seem to be aligning here  
NOTE Confidence: 0.850860981666667

00:15:57.084 --> 00:15:59.836 that it may be that type one diabetes  
NOTE Confidence: 0.850860981666667

00:15:59.906 --> 00:16:02.195 is more of a syndrome of disorders

NOTE Confidence: 0.850860981666667  
00:16:02.200 --> 00:16:04.924 with different pathogenic processes  
NOTE Confidence: 0.850860981666667  
00:16:04.924 --> 00:16:08.329 leading to this insulin requirement.  
NOTE Confidence: 0.850860981666667  
00:16:08.330 --> 00:16:11.522 Another thing is is that for almost my  
NOTE Confidence: 0.850860981666667  
00:16:11.522 --> 00:16:14.668 total career here is is that it was there.  
NOTE Confidence: 0.850860981666667  
00:16:14.670 --> 00:16:17.330 Was this clear separation between  
NOTE Confidence: 0.850860981666667  
00:16:17.330 --> 00:16:20.482 what's type one diabetes versus type  
NOTE Confidence: 0.850860981666667  
00:16:20.482 --> 00:16:23.690 2 diabetes and that type one type 2  
NOTE Confidence: 0.850860981666667  
00:16:23.690 --> 00:16:26.230 diabetes was a disease of obesity.  
NOTE Confidence: 0.850860981666667  
00:16:26.230 --> 00:16:28.799 And had different genetics and and the  
NOTE Confidence: 0.850860981666667  
00:16:28.799 --> 00:16:30.859 pathogenic mechanisms were quite different.  
NOTE Confidence: 0.850860981666667  
00:16:30.860 --> 00:16:32.084 The reality is is now that  
NOTE Confidence: 0.850860981666667  
00:16:32.084 --> 00:16:33.430 we go to the pancreas,  
NOTE Confidence: 0.850860981666667  
00:16:33.430 --> 00:16:35.650 although they're still limited.  
NOTE Confidence: 0.850860981666667  
00:16:35.650 --> 00:16:38.425 There are some commonalities that  
NOTE Confidence: 0.850860981666667  
00:16:38.425 --> 00:16:40.752 we're beginning to see between  
NOTE Confidence: 0.850860981666667

00:16:40.752 --> 00:16:43.284 type one and type 2 diabetes,  
NOTE Confidence: 0.850860981666667

00:16:43.290 --> 00:16:45.010 and another thing that's partially  
NOTE Confidence: 0.850860981666667

00:16:45.010 --> 00:16:47.519 supportive of this is is that we're  
NOTE Confidence: 0.850860981666667

00:16:47.519 --> 00:16:49.329 actually now seeing a situation  
NOTE Confidence: 0.850860981666667

00:16:49.329 --> 00:16:51.401 where drugs created for type 2  
NOTE Confidence: 0.850860981666667

00:16:51.401 --> 00:16:52.946 diabetes are being utilized in  
NOTE Confidence: 0.850860981666667

00:16:52.946 --> 00:16:56.380 settings of type one diabetes and so.  
NOTE Confidence: 0.850860981666667

00:16:56.380 --> 00:16:58.360 I think there's a little bit more Gray here,  
NOTE Confidence: 0.850860981666667

00:16:58.360 --> 00:16:59.968 but historically these have  
NOTE Confidence: 0.850860981666667

00:16:59.968 --> 00:17:01.576 been siloed as disorders,  
NOTE Confidence: 0.850860981666667

00:17:01.580 --> 00:17:03.000 but these are documents,  
NOTE Confidence: 0.850860981666667

00:17:03.000 --> 00:17:05.846 So what what's led to some of the  
NOTE Confidence: 0.850860981666667

00:17:05.846 --> 00:17:07.778 changes in the dogmas and why?  
NOTE Confidence: 0.850860981666667

00:17:07.780 --> 00:17:10.517 Why am I here today promoting pathology?  
NOTE Confidence: 0.850860981666667

00:17:10.520 --> 00:17:10.919 Actually,  
NOTE Confidence: 0.850860981666667

00:17:10.919 --> 00:17:13.313 it's some of the greatest discoveries

NOTE Confidence: 0.850860981666667  
00:17:13.313 --> 00:17:16.048 we've had in the field of diabetes.  
NOTE Confidence: 0.850860981666667  
00:17:16.050 --> 00:17:18.374 Have come through studies  
NOTE Confidence: 0.850860981666667  
00:17:18.374 --> 00:17:20.698 of pathology by pathologists  
NOTE Confidence: 0.934121565714286  
00:17:20.700 --> 00:17:22.576 and I just put some examples here.  
NOTE Confidence: 0.934121565714286  
00:17:22.580 --> 00:17:24.960 On the left. We call them islet  
NOTE Confidence: 0.934121565714286  
00:17:24.960 --> 00:17:26.852 of langerhan's because of that,  
NOTE Confidence: 0.934121565714286  
00:17:26.852 --> 00:17:29.604 that Discovery Schmidt on the right and  
NOTE Confidence: 0.934121565714286  
00:17:29.604 --> 00:17:31.782 German pathologist was the one that  
NOTE Confidence: 0.934121565714286  
00:17:31.782 --> 00:17:34.086 first discovered the infiltrate and then  
NOTE Confidence: 0.934121565714286  
00:17:34.086 --> 00:17:36.378 we've had individuals that notice that  
NOTE Confidence: 0.934121565714286  
00:17:36.378 --> 00:17:38.560 some people with diabetes had this.  
NOTE Confidence: 0.934121565714286  
00:17:38.560 --> 00:17:41.072 Infiltrate other ones didn't.  
NOTE Confidence: 0.934121565714286  
00:17:41.072 --> 00:17:43.640 But with the decline of autopsies  
NOTE Confidence: 0.934121565714286  
00:17:43.640 --> 00:17:46.700 in the 1960s and over the years,  
NOTE Confidence: 0.934121565714286  
00:17:46.700 --> 00:17:50.756 improvements in diabetes management at onset.  
NOTE Confidence: 0.934121565714286

00:17:50.760 --> 00:17:52.476 The studies of the human pancreas  
NOTE Confidence: 0.934121565714286

00:17:52.476 --> 00:17:54.770 kind of fell out of favor and another  
NOTE Confidence: 0.934121565714286

00:17:54.770 --> 00:17:56.660 reason is because of the availability  
NOTE Confidence: 0.934121565714286

00:17:56.660 --> 00:17:58.537 of mouse models of the disease.  
NOTE Confidence: 0.934121565714286

00:17:58.540 --> 00:18:02.823 So back in the early to the mid 2000s,  
NOTE Confidence: 0.934121565714286

00:18:02.823 --> 00:18:05.434 George had an idea and met with  
NOTE Confidence: 0.934121565714286

00:18:05.434 --> 00:18:07.590 me and we talked about.  
NOTE Confidence: 0.934121565714286

00:18:07.590 --> 00:18:09.822 Could we use organ donors to try and  
NOTE Confidence: 0.934121565714286

00:18:09.822 --> 00:18:12.386 study the pathology of the human pancreas?  
NOTE Confidence: 0.934121565714286

00:18:12.390 --> 00:18:13.986 Not going into all the details  
NOTE Confidence: 0.934121565714286

00:18:13.986 --> 00:18:15.050 on how that happened,  
NOTE Confidence: 0.934121565714286

00:18:15.050 --> 00:18:17.668 but we ended up as Ken said,  
NOTE Confidence: 0.934121565714286

00:18:17.670 --> 00:18:20.112 forming this network called N Pod  
NOTE Confidence: 0.934121565714286

00:18:20.112 --> 00:18:22.410 for the network for pancreatic  
NOTE Confidence: 0.934121565714286

00:18:22.410 --> 00:18:24.746 organ donors with diabetes.  
NOTE Confidence: 0.934121565714286

00:18:24.750 --> 00:18:27.358 And the goal here was pretty simple was

NOTE Confidence: 0.934121565714286

00:18:27.358 --> 00:18:30.790 to try and obtain pancreas and other tissues.

NOTE Confidence: 0.934121565714286

00:18:30.790 --> 00:18:32.629 Transplant quality tissues,

NOTE Confidence: 0.934121565714286

00:18:32.629 --> 00:18:34.468 not autopsy tissues,

NOTE Confidence: 0.934121565714286

00:18:34.470 --> 00:18:37.236 from individuals with the goal of

NOTE Confidence: 0.934121565714286

00:18:37.236 --> 00:18:40.002 trying to better understand how and

NOTE Confidence: 0.934121565714286

00:18:40.002 --> 00:18:42.107 why type one diabetes develops.

NOTE Confidence: 0.934121565714286

00:18:42.110 --> 00:18:44.670 And so this is an example of a

NOTE Confidence: 0.934121565714286

00:18:44.670 --> 00:18:46.668 screenshot I took a couple days

NOTE Confidence: 0.934121565714286

00:18:46.668 --> 00:18:48.762 ago in that in just referred to.

NOTE Confidence: 0.934121565714286

00:18:48.762 --> 00:18:51.439 So what we do is collect transplant grade

NOTE Confidence: 0.934121565714286

00:18:51.439 --> 00:18:54.175 tissues and they're they're listed there.

NOTE Confidence: 0.934121565714286

00:18:54.180 --> 00:18:58.140 We operate 24/7 365 UM we we've

NOTE Confidence: 0.934121565714286

00:18:58.140 --> 00:19:00.500 collected actually almost 1000 organ

NOTE Confidence: 0.934121565714286

00:19:00.589 --> 00:19:03.157 donors with all of our program,

NOTE Confidence: 0.934121565714286

00:19:03.160 --> 00:19:05.525 but those related to impound

NOTE Confidence: 0.934121565714286

00:19:05.525 --> 00:19:08.330 or some almost 600 number now.  
NOTE Confidence: 0.934121565714286

00:19:08.330 --> 00:19:08.866 And again,  
NOTE Confidence: 0.934121565714286

00:19:08.866 --> 00:19:11.010 you can see we collect them from controls,  
NOTE Confidence: 0.934121565714286

00:19:11.010 --> 00:19:13.229 which is very important to us to  
NOTE Confidence: 0.934121565714286

00:19:13.229 --> 00:19:14.855 understand what controls are and  
NOTE Confidence: 0.934121565714286

00:19:14.855 --> 00:19:16.385 then individuals with type one  
NOTE Confidence: 0.934121565714286

00:19:16.385 --> 00:19:18.209 diabetes or this very informative  
NOTE Confidence: 0.934121565714286

00:19:18.209 --> 00:19:20.319 group called auto antibody positive.  
NOTE Confidence: 0.934121565714286

00:19:20.320 --> 00:19:22.165 So these are individuals that  
NOTE Confidence: 0.934121565714286

00:19:22.165 --> 00:19:24.010 are increased risk for diabetes  
NOTE Confidence: 0.934121565714286

00:19:24.076 --> 00:19:25.891 but actually have not developed  
NOTE Confidence: 0.934121565714286

00:19:25.891 --> 00:19:27.706 the symptoms of the disease.  
NOTE Confidence: 0.934121565714286

00:19:27.710 --> 00:19:30.279 And then we collect diabetes and a  
NOTE Confidence: 0.934121565714286

00:19:30.279 --> 00:19:33.464 number of other forms to to kind  
NOTE Confidence: 0.934121565714286

00:19:33.464 --> 00:19:36.909 of round out the the analysis.  
NOTE Confidence: 0.934121565714286

00:19:36.910 --> 00:19:38.935 So what what I want to talk today and



NOTE Confidence: 0.934121565714286  
00:19:38.935 --> 00:19:40.938 over the next few minutes is what did  
NOTE Confidence: 0.934121565714286  
00:19:40.938 --> 00:19:42.969 we learn from studies of the tissues.  
NOTE Confidence: 0.934121565714286  
00:19:42.970 --> 00:19:45.189 So the first lesson we've learned is,  
NOTE Confidence: 0.934121565714286  
00:19:45.190 --> 00:19:45.970 and I I would say,  
NOTE Confidence: 0.934121565714286  
00:19:45.970 --> 00:19:46.556 we've affirmed.  
NOTE Confidence: 0.934121565714286  
00:19:46.556 --> 00:19:48.900 It is that type one diabetes is an  
NOTE Confidence: 0.934121565714286  
00:19:48.967 --> 00:19:50.795 autoimmune disorder with immune  
NOTE Confidence: 0.934121565714286  
00:19:50.795 --> 00:19:53.080 infiltration of the pancreatic islets,  
NOTE Confidence: 0.934121565714286  
00:19:53.080 --> 00:19:55.890 as shown here or again, red.  
NOTE Confidence: 0.934121565714286  
00:19:55.890 --> 00:19:58.590 The red stain represents insulin,  
NOTE Confidence: 0.934121565714286  
00:19:58.590 --> 00:20:00.574 and then the brown,  
NOTE Confidence: 0.934121565714286  
00:20:00.574 --> 00:20:02.172 the lymphocytic infiltration.  
NOTE Confidence: 0.934121565714286  
00:20:02.172 --> 00:20:02.723 Well,  
NOTE Confidence: 0.934121565714286  
00:20:02.723 --> 00:20:06.950 one of the first things that we re  
NOTE Confidence: 0.934121565714286  
00:20:06.950 --> 00:20:09.540 noticed if you would was is that  
NOTE Confidence: 0.934121565714286

00:20:09.540 --> 00:20:12.387 the type of insulitis you see in  
NOTE Confidence: 0.934121565714286

00:20:12.387 --> 00:20:15.024 our mouse models is very very  
NOTE Confidence: 0.934121565714286

00:20:15.024 --> 00:20:17.248 different from as a whole.  
NOTE Confidence: 0.934121565714286

00:20:17.248 --> 00:20:19.564 With that in the human disease  
NOTE Confidence: 0.934121565714286

00:20:19.564 --> 00:20:22.587 and we've even noticed overtime  
NOTE Confidence: 0.934121565714286

00:20:22.587 --> 00:20:24.495 that it's quantitatively.  
NOTE Confidence: 0.934121565714286

00:20:24.500 --> 00:20:25.964 Qualitatively and quantitatively different.  
NOTE Confidence: 0.934121565714286

00:20:25.964 --> 00:20:29.038 So if you look at the mouse model on  
NOTE Confidence: 0.934121565714286

00:20:29.038 --> 00:20:32.290 the left, often we it's in stages.  
NOTE Confidence: 0.934121565714286

00:20:32.290 --> 00:20:34.990 It's almost like staging cancer,  
NOTE Confidence: 0.934121565714286

00:20:34.990 --> 00:20:38.875 or that where you have the grades,  
NOTE Confidence: 0.944945992

00:20:38.880 --> 00:20:41.407 whereas in the humans it's more just  
NOTE Confidence: 0.944945992

00:20:41.407 --> 00:20:44.370 what we say is it present or absent.  
NOTE Confidence: 0.910612616470588

00:20:46.530 --> 00:20:49.522 And we actually a few years ago now  
NOTE Confidence: 0.910612616470588

00:20:49.522 --> 00:20:51.676 brought together pathologists from around  
NOTE Confidence: 0.910612616470588

00:20:51.676 --> 00:20:54.995 the world that had and we met in in

NOTE Confidence: 0.910612616470588

00:20:54.995 --> 00:20:57.837 Cambridge and tried to come up with a

NOTE Confidence: 0.910612616470588

00:20:57.837 --> 00:21:00.273 universal definition of what insulinitis is.

NOTE Confidence: 0.910612616470588

00:21:00.280 --> 00:21:03.437 And what we the we are consensus

NOTE Confidence: 0.910612616470588

00:21:03.437 --> 00:21:05.884 definition of INSULITIS was is that

NOTE Confidence: 0.910612616470588

00:21:05.884 --> 00:21:09.031 you had to have within a given case 3

NOTE Confidence: 0.910612616470588

00:21:09.031 --> 00:21:12.800 islets with 15 white blood cells present.

NOTE Confidence: 0.910612616470588

00:21:12.800 --> 00:21:14.851 And then we would say that that

NOTE Confidence: 0.910612616470588

00:21:14.851 --> 00:21:15.730 case had insulinitis.

NOTE Confidence: 0.910612616470588

00:21:15.730 --> 00:21:19.234 If we went very much off of that,

NOTE Confidence: 0.910612616470588

00:21:19.240 --> 00:21:22.284 we would be, we would have a lot of cases of

NOTE Confidence: 0.910612616470588

00:21:22.284 --> 00:21:24.675 type one diabetes that didn't have insulinitis.

NOTE Confidence: 0.910612616470588

00:21:24.675 --> 00:21:26.865 Another thing that and I'll show

NOTE Confidence: 0.910612616470588

00:21:26.865 --> 00:21:28.820 example of this is we said there

NOTE Confidence: 0.910612616470588

00:21:28.820 --> 00:21:30.420 needed to be pseudo atrophic.

NOTE Confidence: 0.910612616470588

00:21:30.420 --> 00:21:32.994 Pilots within this section, meaning islets

NOTE Confidence: 0.910612616470588

00:21:32.994 --> 00:21:35.859 devoid of the insulin producing cells.  
NOTE Confidence: 0.910612616470588

00:21:35.860 --> 00:21:37.530 But this is very different  
NOTE Confidence: 0.910612616470588

00:21:37.530 --> 00:21:39.804 from the NOD's as a whole,  
NOTE Confidence: 0.910612616470588

00:21:39.804 --> 00:21:41.408 although exceptions do exist,  
NOTE Confidence: 0.910612616470588

00:21:41.410 --> 00:21:44.700 it's just much more common in NOD.  
NOTE Confidence: 0.910612616470588

00:21:44.700 --> 00:21:47.070 Now, in terms of the type  
NOTE Confidence: 0.910612616470588

00:21:47.070 --> 00:21:49.780 of of cells that infiltrate,  
NOTE Confidence: 0.910612616470588

00:21:49.780 --> 00:21:51.340 it's pretty much a catch catch.  
NOTE Confidence: 0.910612616470588

00:21:51.340 --> 00:21:54.976 Can there's B cells, T cells,  
NOTE Confidence: 0.910612616470588

00:21:54.980 --> 00:21:57.809 CD4 CD, 8 macrophages,  
NOTE Confidence: 0.910612616470588

00:21:57.809 --> 00:21:59.007 dendritic cells,  
NOTE Confidence: 0.910612616470588

00:21:59.007 --> 00:22:02.601 but in humans the most predominant  
NOTE Confidence: 0.910612616470588

00:22:02.601 --> 00:22:04.822 one is the CD8T cell.  
NOTE Confidence: 0.910612616470588

00:22:04.822 --> 00:22:07.327 But another dogma that we  
NOTE Confidence: 0.910612616470588

00:22:07.327 --> 00:22:09.859 were able to bust was.  
NOTE Confidence: 0.910612616470588

00:22:09.860 --> 00:22:12.422 There there were thoughts that actually

NOTE Confidence: 0.910612616470588  
00:22:12.422 --> 00:22:14.809 mostly insulinitis would occur at or  
NOTE Confidence: 0.910612616470588  
00:22:14.809 --> 00:22:16.958 around the onset of type one diabetes,  
NOTE Confidence: 0.910612616470588  
00:22:16.960 --> 00:22:20.215 and that within a few months to  
NOTE Confidence: 0.910612616470588  
00:22:20.215 --> 00:22:22.130 a couple years of disease onset,  
NOTE Confidence: 0.910612616470588  
00:22:22.130 --> 00:22:23.726 that with the losses of beta  
NOTE Confidence: 0.910612616470588  
00:22:23.726 --> 00:22:25.299 cells that it would go away.  
NOTE Confidence: 0.910612616470588  
00:22:25.300 --> 00:22:27.240 And actually through studies of  
NOTE Confidence: 0.910612616470588  
00:22:27.240 --> 00:22:29.520 long term patients we can act.  
NOTE Confidence: 0.910612616470588  
00:22:29.520 --> 00:22:31.660 We've actually shown that it  
NOTE Confidence: 0.910612616470588  
00:22:31.660 --> 00:22:33.800 insulinitis can exist for many,  
NOTE Confidence: 0.910612616470588  
00:22:33.800 --> 00:22:34.203 many,  
NOTE Confidence: 0.910612616470588  
00:22:34.203 --> 00:22:36.621 many years after the onset of  
NOTE Confidence: 0.910612616470588  
00:22:36.621 --> 00:22:38.480 symptomatic onset of disease,  
NOTE Confidence: 0.910612616470588  
00:22:38.480 --> 00:22:40.110 as can the presence of.  
NOTE Confidence: 0.910612616470588  
00:22:40.110 --> 00:22:43.908 Insulin positive cells.  
NOTE Confidence: 0.910612616470588

00:22:43.910 --> 00:22:45.870 And this is an example of this is  
NOTE Confidence: 0.910612616470588

00:22:45.870 --> 00:22:47.607 actually the first time I've ever  
NOTE Confidence: 0.910612616470588

00:22:47.607 --> 00:22:49.395 shown this publicly to an audience.  
NOTE Confidence: 0.910612616470588

00:22:49.400 --> 00:22:50.795 We've developed a new technique  
NOTE Confidence: 0.910612616470588

00:22:50.795 --> 00:22:52.970 where we can take live tissue slices.  
NOTE Confidence: 0.910612616470588

00:22:52.970 --> 00:22:56.270 These are about 125 Micron thick  
NOTE Confidence: 0.910612616470588

00:22:56.270 --> 00:22:57.920 sections stained them,  
NOTE Confidence: 0.910612616470588

00:22:57.920 --> 00:22:59.310 so this is within hours.  
NOTE Confidence: 0.910612616470588

00:22:59.310 --> 00:23:03.240 They have actually case recovery and we do.  
NOTE Confidence: 0.910612616470588

00:23:03.240 --> 00:23:06.285 This is like a 30 minute video  
NOTE Confidence: 0.910612616470588

00:23:06.285 --> 00:23:08.482 collapse down to 88 seconds,  
NOTE Confidence: 0.910612616470588

00:23:08.482 --> 00:23:11.488 but those magenta colored cells are  
NOTE Confidence: 0.910612616470588

00:23:11.488 --> 00:23:14.598 stained T cells that are stained.  
NOTE Confidence: 0.910612616470588

00:23:14.600 --> 00:23:15.512 And the.  
NOTE Confidence: 0.910612616470588

00:23:15.512 --> 00:23:17.336 Autofluorescence in white and  
NOTE Confidence: 0.910612616470588

00:23:17.336 --> 00:23:20.429 the yellow is a viability dye,

NOTE Confidence: 0.910612616470588  
00:23:20.430 --> 00:23:22.120 but this just again shows  
NOTE Confidence: 0.910612616470588  
00:23:22.120 --> 00:23:23.134 the autoreactivity here.  
NOTE Confidence: 0.910612616470588  
00:23:23.140 --> 00:23:25.072 In this patient I should have said  
NOTE Confidence: 0.910612616470588  
00:23:25.072 --> 00:23:27.241 that this is from a patient that  
NOTE Confidence: 0.910612616470588  
00:23:27.241 --> 00:23:29.947 about two weeks ago that unfortunately  
NOTE Confidence: 0.910612616470588  
00:23:29.947 --> 00:23:32.886 expired right at the onset of type  
NOTE Confidence: 0.910612616470588  
00:23:32.886 --> 00:23:34.712 one diabetes or at the diagnosis  
NOTE Confidence: 0.910612616470588  
00:23:34.712 --> 00:23:36.610 they were about 20 years of age,  
NOTE Confidence: 0.910612616470588  
00:23:36.610 --> 00:23:40.048 had autoantibodies but died in onset.  
NOTE Confidence: 0.910612616470588  
00:23:40.050 --> 00:23:43.536 So we are that again.  
NOTE Confidence: 0.910612616470588  
00:23:43.536 --> 00:23:46.940 We believe shows proof of the auto.  
NOTE Confidence: 0.910612616470588  
00:23:46.940 --> 00:23:49.710 Community being important than disease.  
NOTE Confidence: 0.910612616470588  
00:23:49.710 --> 00:23:52.998 Another facet that we know supports  
NOTE Confidence: 0.910612616470588  
00:23:52.998 --> 00:23:55.268 the autoimmune nature of the  
NOTE Confidence: 0.910612616470588  
00:23:55.268 --> 00:23:57.431 disease has to do with an article  
NOTE Confidence: 0.910612616470588

00:23:57.431 --> 00:23:59.148 we and Sally can't publish,  
NOTE Confidence: 0.910612616470588

00:23:59.148 --> 00:24:01.260 and a number of others published  
NOTE Confidence: 0.910612616470588

00:24:01.327 --> 00:24:03.357 in Nature Medicine a few years ago  
NOTE Confidence: 0.910612616470588

00:24:03.357 --> 00:24:05.437 now where we actually took tissue  
NOTE Confidence: 0.910612616470588

00:24:05.437 --> 00:24:07.459 samples like those I just showed  
NOTE Confidence: 0.910612616470588

00:24:07.459 --> 00:24:09.935 you grew out the T cells or from  
NOTE Confidence: 0.910612616470588

00:24:09.935 --> 00:24:11.330 him and then asked what  
NOTE Confidence: 0.889186961666666

00:24:11.395 --> 00:24:12.691 they were responding to  
NOTE Confidence: 0.889186961666666

00:24:12.691 --> 00:24:14.635 and the good news here is,  
NOTE Confidence: 0.889186961666666

00:24:14.640 --> 00:24:17.106 is that a number of the.  
NOTE Confidence: 0.889186961666666

00:24:17.110 --> 00:24:18.450 Targets that are listed there,  
NOTE Confidence: 0.889186961666666

00:24:18.450 --> 00:24:20.750 like Gadai 2 and insulin.  
NOTE Confidence: 0.889186961666666

00:24:20.750 --> 00:24:22.920 These are targets of autoantibodies  
NOTE Confidence: 0.889186961666666

00:24:22.920 --> 00:24:26.057 that for years we've been measuring in  
NOTE Confidence: 0.889186961666666

00:24:26.057 --> 00:24:28.727 peripheral blood in serum and plasma,  
NOTE Confidence: 0.889186961666666

00:24:28.730 --> 00:24:30.018 so this was very.



NOTE Confidence: 0.889186961666666

00:24:30.018 --> 00:24:31.628 Informative to us because it

NOTE Confidence: 0.889186961666666

00:24:31.628 --> 00:24:33.610 told us that we were kind of

NOTE Confidence: 0.889186961666666

00:24:33.610 --> 00:24:36.010 on the right trail in terms of

NOTE Confidence: 0.889186961666666

00:24:36.010 --> 00:24:37.279 understanding the autoantigens

NOTE Confidence: 0.889186961666666

00:24:37.279 --> 00:24:41.020 responsible for type one diabetes.

NOTE Confidence: 0.889186961666666

00:24:41.020 --> 00:24:43.400 Now another thing that will that touts

NOTE Confidence: 0.889186961666666

00:24:43.400 --> 00:24:45.330 this notion of disease heterogeneity

NOTE Confidence: 0.889186961666666

00:24:45.330 --> 00:24:47.838 or subgroups of type one diabetes

NOTE Confidence: 0.889186961666666

00:24:47.838 --> 00:24:49.993 came from more pathology based

NOTE Confidence: 0.889186961666666

00:24:49.993 --> 00:24:52.501 studies that first started with a

NOTE Confidence: 0.889186961666666

00:24:52.501 --> 00:24:56.242 historical collection in Europe and

NOTE Confidence: 0.889186961666666

00:24:56.242 --> 00:24:58.898 then now have moved on to end pot.

NOTE Confidence: 0.889186961666666

00:24:58.900 --> 00:25:00.475 So I'll just break it up here

NOTE Confidence: 0.889186961666666

00:25:00.475 --> 00:25:01.760 on the left hand side.

NOTE Confidence: 0.889186961666666

00:25:01.760 --> 00:25:04.019 I'm only going to focus on it is if

NOTE Confidence: 0.889186961666666

00:25:04.019 --> 00:25:06.191 you look at the B cell population  
NOTE Confidence: 0.889186961666666

00:25:06.191 --> 00:25:08.904 that are high expresser's of CD 20.  
NOTE Confidence: 0.889186961666666

00:25:08.904 --> 00:25:11.580 If you're diagnosed with the disease.  
NOTE Confidence: 0.889186961666666

00:25:11.580 --> 00:25:13.710 Less than 15 years of age,  
NOTE Confidence: 0.889186961666666

00:25:13.710 --> 00:25:16.014 you tend to have a high percentage of  
NOTE Confidence: 0.889186961666666

00:25:16.014 --> 00:25:18.008 B lymphocytes in that infiltrate that.  
NOTE Confidence: 0.889186961666666

00:25:18.010 --> 00:25:20.470 I showed you the insulitis lesion,  
NOTE Confidence: 0.889186961666666

00:25:20.470 --> 00:25:22.606 but if you're diagnosed with type  
NOTE Confidence: 0.889186961666666

00:25:22.606 --> 00:25:24.938 one diabetes above 15 years of age,  
NOTE Confidence: 0.889186961666666

00:25:24.940 --> 00:25:29.100 the frequency of those CD 20 cells and  
NOTE Confidence: 0.889186961666666

00:25:29.100 --> 00:25:32.076 their intensity is much, much less.  
NOTE Confidence: 0.889186961666666

00:25:32.076 --> 00:25:34.862 Switch again starts to tell us that  
NOTE Confidence: 0.889186961666666

00:25:34.862 --> 00:25:37.116 there may be different pathogenic  
NOTE Confidence: 0.889186961666666

00:25:37.116 --> 00:25:40.320 mechanisms based on the age of onset.  
NOTE Confidence: 0.889186961666666

00:25:40.320 --> 00:25:41.136 Another thing,  
NOTE Confidence: 0.889186961666666

00:25:41.136 --> 00:25:43.584 and it's kind of interesting that

NOTE Confidence: 0.889186961666666

00:25:43.584 --> 00:25:45.976 early on we started noticing this

NOTE Confidence: 0.889186961666666

00:25:45.976 --> 00:25:48.334 phenomenon in in the tissue samples

NOTE Confidence: 0.889186961666666

00:25:48.334 --> 00:25:51.057 from in pot in George views that in

NOTE Confidence: 0.889186961666666

00:25:51.057 --> 00:25:54.182 a a major lecture that was given at

NOTE Confidence: 0.889186961666666

00:25:54.182 --> 00:25:55.990 the American Diabetes Association

NOTE Confidence: 0.889186961666666

00:25:55.990 --> 00:25:58.816 meeting was is that the loss of insulin

NOTE Confidence: 0.889186961666666

00:25:58.816 --> 00:26:01.490 secreting cells was quite lobular in nature,

NOTE Confidence: 0.889186961666666

00:26:01.490 --> 00:26:03.863 and if you look and he called

NOTE Confidence: 0.889186961666666

00:26:03.863 --> 00:26:06.168 it the vitiligo of the pancreas,

NOTE Confidence: 0.889186961666666

00:26:06.170 --> 00:26:07.724 meaning if you if you everybody

NOTE Confidence: 0.889186961666666

00:26:07.724 --> 00:26:09.790 here on this call will know about

NOTE Confidence: 0.889186961666666

00:26:09.790 --> 00:26:11.090 the deep pigmentation that.

NOTE Confidence: 0.889186961666666

00:26:11.090 --> 00:26:12.810 Occurs in bilago as shown

NOTE Confidence: 0.889186961666666

00:26:12.810 --> 00:26:14.530 on the right hand side.

NOTE Confidence: 0.889186961666666

00:26:14.530 --> 00:26:17.365 What we have is you'll have lobules

NOTE Confidence: 0.889186961666666

00:26:17.365 --> 00:26:20.608 where the pink is the insulin staining,  
NOTE Confidence: 0.889186961666666

00:26:20.610 --> 00:26:22.686 and but then they'll be right  
NOTE Confidence: 0.889186961666666

00:26:22.686 --> 00:26:24.518 adjacent to lobules where there  
NOTE Confidence: 0.889186961666666

00:26:24.518 --> 00:26:26.408 won't be any insulin staining.  
NOTE Confidence: 0.889186961666666

00:26:26.410 --> 00:26:28.106 Now if we were to do other counter  
NOTE Confidence: 0.889186961666666

00:26:28.106 --> 00:26:29.408 stains for other island hormones  
NOTE Confidence: 0.889186961666666

00:26:29.408 --> 00:26:31.326 you would see there I'll it's there,  
NOTE Confidence: 0.889186961666666

00:26:31.330 --> 00:26:35.785 but the the loss of islets is quite patchy,  
NOTE Confidence: 0.889186961666666

00:26:35.790 --> 00:26:38.430 hence why we this called little I go.  
NOTE Confidence: 0.889186961666666

00:26:38.430 --> 00:26:41.286 Now we're not sure exactly why some I  
NOTE Confidence: 0.889186961666666

00:26:41.286 --> 00:26:44.130 let's get destroyed and others don't,  
NOTE Confidence: 0.889186961666666

00:26:44.130 --> 00:26:46.280 but we have some clues,  
NOTE Confidence: 0.889186961666666

00:26:46.280 --> 00:26:48.863 and one of them is what we call the  
NOTE Confidence: 0.889186961666666

00:26:48.863 --> 00:26:51.186 hyper expression of class one MHC,  
NOTE Confidence: 0.889186961666666

00:26:51.190 --> 00:26:53.234 and I give some examples across the  
NOTE Confidence: 0.889186961666666

00:26:53.234 --> 00:26:55.974 top of what a normal in an island of

NOTE Confidence: 0.889186961666666

00:26:55.974 --> 00:26:58.229 what a normal classroom would look like,

NOTE Confidence: 0.889186961666666

00:26:58.230 --> 00:26:58.684 elevated,

NOTE Confidence: 0.889186961666666

00:26:58.684 --> 00:27:01.408 or what we call hyper expression.

NOTE Confidence: 0.889186961666666

00:27:01.410 --> 00:27:05.130 And then there's a A on the right hand side,

NOTE Confidence: 0.889186961666666

00:27:05.130 --> 00:27:06.882 shows three different groups.

NOTE Confidence: 0.889186961666666

00:27:06.882 --> 00:27:08.634 One is the controls.

NOTE Confidence: 0.889186961666666

00:27:08.640 --> 00:27:11.167 And what there the MFA for the

NOTE Confidence: 0.889186961666666

00:27:11.167 --> 00:27:13.198 expression of class one is like?

NOTE Confidence: 0.889186961666666

00:27:13.200 --> 00:27:14.887 And then the other one is type

NOTE Confidence: 0.889186961666666

00:27:14.887 --> 00:27:16.865 one diabetes and I see I means

NOTE Confidence: 0.889186961666666

00:27:16.865 --> 00:27:17.765 insulin containing islands.

NOTE Confidence: 0.917909204545455

00:27:17.770 --> 00:27:19.882 So if you have insulin and you have

NOTE Confidence: 0.917909204545455

00:27:19.882 --> 00:27:21.839 type one diabetes, those islands seem

NOTE Confidence: 0.917909204545455

00:27:21.839 --> 00:27:24.462 to have a lot of Class 1, whereas if

NOTE Confidence: 0.917909204545455

00:27:24.462 --> 00:27:26.598 you go in insulin deficient islets,

NOTE Confidence: 0.917909204545455

00:27:26.600 --> 00:27:30.260 which is the far right column, no insulin.  
NOTE Confidence: 0.917909204545455

00:27:30.260 --> 00:27:32.716 Their their level of class one is is  
NOTE Confidence: 0.917909204545455

00:27:32.716 --> 00:27:35.138 more much more like control tissues.  
NOTE Confidence: 0.917909204545455

00:27:35.140 --> 00:27:37.121 So one of the things we feel  
NOTE Confidence: 0.917909204545455

00:27:37.121 --> 00:27:38.550 like May distinguish in islet.  
NOTE Confidence: 0.917909204545455

00:27:38.550 --> 00:27:40.746 That's going to be destroyed versus  
NOTE Confidence: 0.917909204545455

00:27:40.746 --> 00:27:43.368 one that isn't has to do with this.  
NOTE Confidence: 0.917909204545455

00:27:43.370 --> 00:27:44.444 Class one MHC,  
NOTE Confidence: 0.917909204545455

00:27:44.444 --> 00:27:47.730 which may be more like a danger response.  
NOTE Confidence: 0.917909204545455

00:27:47.730 --> 00:27:50.547 So we have a clear view that type one  
NOTE Confidence: 0.917909204545455

00:27:50.547 --> 00:27:52.629 diabetes is an autoimmune disease.  
NOTE Confidence: 0.917909204545455

00:27:52.630 --> 00:27:56.026 But now with the the each next  
NOTE Confidence: 0.917909204545455

00:27:56.026 --> 00:27:57.622 lesson that I'm going to give him,  
NOTE Confidence: 0.917909204545455

00:27:57.630 --> 00:27:58.830 there's four in total.  
NOTE Confidence: 0.917909204545455

00:27:58.830 --> 00:28:01.414 Is is that we also now believe that  
NOTE Confidence: 0.917909204545455

00:28:01.414 --> 00:28:03.538 type one diabetes is a disease

NOTE Confidence: 0.917909204545455  
00:28:03.538 --> 00:28:05.319 of islets and beta cells.  
NOTE Confidence: 0.917909204545455  
00:28:05.320 --> 00:28:06.460 And that let me go.  
NOTE Confidence: 0.917909204545455  
00:28:06.460 --> 00:28:07.816 Why say that?  
NOTE Confidence: 0.917909204545455  
00:28:07.816 --> 00:28:09.128 So again, if you,  
NOTE Confidence: 0.917909204545455  
00:28:09.128 --> 00:28:11.520 if you take a look at the type one pancreas,  
NOTE Confidence: 0.917909204545455  
00:28:11.520 --> 00:28:13.196 what you'll see the?  
NOTE Confidence: 0.917909204545455  
00:28:13.196 --> 00:28:15.710 Depending on the degree of duration,  
NOTE Confidence: 0.917909204545455  
00:28:15.710 --> 00:28:16.532 disease, duration,  
NOTE Confidence: 0.917909204545455  
00:28:16.532 --> 00:28:18.998 you'll see varying amounts of these.  
NOTE Confidence: 0.917909204545455  
00:28:19.000 --> 00:28:21.590 What we again called pseudo atrophic islets.  
NOTE Confidence: 0.917909204545455  
00:28:21.590 --> 00:28:22.380 These ones in the middle,  
NOTE Confidence: 0.917909204545455  
00:28:22.380 --> 00:28:25.452 where they'll be hormone island hormone  
NOTE Confidence: 0.917909204545455  
00:28:25.452 --> 00:28:28.920 positive but deficient of insulin staining.  
NOTE Confidence: 0.917909204545455  
00:28:28.920 --> 00:28:30.654 And then there will be other  
NOTE Confidence: 0.917909204545455  
00:28:30.654 --> 00:28:32.741 types of violence like the one on  
NOTE Confidence: 0.917909204545455

00:28:32.741 --> 00:28:34.475 the right which will be insulin  
NOTE Confidence: 0.917909204545455

00:28:34.475 --> 00:28:36.018 positive islet with insulinitis.  
NOTE Confidence: 0.917909204545455

00:28:36.020 --> 00:28:37.392 And then they're all even be one  
NOTE Confidence: 0.917909204545455

00:28:37.392 --> 00:28:38.961 like on the left where you have  
NOTE Confidence: 0.917909204545455

00:28:38.961 --> 00:28:40.353 it in an insulin positive islet,  
NOTE Confidence: 0.917909204545455

00:28:40.360 --> 00:28:41.518 but without insulinitis.  
NOTE Confidence: 0.917909204545455

00:28:41.518 --> 00:28:45.039 So you end up with this mosaic of  
NOTE Confidence: 0.917909204545455

00:28:45.039 --> 00:28:47.277 different types of islets in there.  
NOTE Confidence: 0.917909204545455

00:28:47.280 --> 00:28:50.060 But why is one destroyed?  
NOTE Confidence: 0.917909204545455

00:28:50.060 --> 00:28:51.124 And why is not?  
NOTE Confidence: 0.917909204545455

00:28:51.124 --> 00:28:53.078 And are they really like on the  
NOTE Confidence: 0.917909204545455

00:28:53.078 --> 00:28:53.960 left hand side?  
NOTE Confidence: 0.917909204545455

00:28:53.960 --> 00:28:57.128 Are they really normal and so?  
NOTE Confidence: 0.917909204545455

00:28:57.130 --> 00:28:58.250 The answer is no.  
NOTE Confidence: 0.917909204545455

00:28:58.250 --> 00:29:00.646 And I'm going to go through these next  
NOTE Confidence: 0.917909204545455

00:29:00.646 --> 00:29:03.238 slides very quickly for the sake of time,



NOTE Confidence: 0.917909204545455

00:29:03.240 --> 00:29:05.361 but one of the things that impot

NOTE Confidence: 0.917909204545455

00:29:05.361 --> 00:29:06.699 investigators have found out is,

NOTE Confidence: 0.917909204545455

00:29:06.700 --> 00:29:09.870 is that if you look at expression

NOTE Confidence: 0.917909204545455

00:29:09.870 --> 00:29:13.366 markers of stress responses that there

NOTE Confidence: 0.917909204545455

00:29:13.366 --> 00:29:15.206 are footprints of stress responses.

NOTE Confidence: 0.917909204545455

00:29:15.210 --> 00:29:18.060 They're very much elevated in

NOTE Confidence: 0.917909204545455

00:29:18.060 --> 00:29:20.910 the type one diabetes pancreas.

NOTE Confidence: 0.917909204545455

00:29:20.910 --> 00:29:22.686 Another thing is that if you

NOTE Confidence: 0.917909204545455

00:29:22.686 --> 00:29:25.156 start to take a look at certain

NOTE Confidence: 0.917909204545455

00:29:25.156 --> 00:29:27.176 processes within the islets of

NOTE Confidence: 0.917909204545455

00:29:27.176 --> 00:29:29.268 somebody with type one diabetes,

NOTE Confidence: 0.917909204545455

00:29:29.270 --> 00:29:31.418 things like this is a science

NOTE Confidence: 0.917909204545455

00:29:31.418 --> 00:29:32.492 translational medicine paper.

NOTE Confidence: 0.917909204545455

00:29:32.500 --> 00:29:35.194 The unfolded protein response is abnormal

NOTE Confidence: 0.917909204545455

00:29:35.194 --> 00:29:38.419 in the type one diabetic eye lid,

NOTE Confidence: 0.917909204545455

00:29:38.420 --> 00:29:42.116 so it doesn't process normal as normal.

NOTE Confidence: 0.917909204545455

00:29:42.120 --> 00:29:42.632 Another thing,

NOTE Confidence: 0.917909204545455

00:29:42.632 --> 00:29:44.168 and this is big in the

NOTE Confidence: 0.917909204545455

00:29:44.168 --> 00:29:45.450 cancer field that you know,

NOTE Confidence: 0.917909204545455

00:29:45.450 --> 00:29:48.122 Senate markers of senescence

NOTE Confidence: 0.917909204545455

00:29:48.122 --> 00:29:49.458 essentially aging.

NOTE Confidence: 0.917909204545455

00:29:49.460 --> 00:29:52.380 If you take a look at aging markers

NOTE Confidence: 0.917909204545455

00:29:52.380 --> 00:29:55.132 in the in the island of a non

NOTE Confidence: 0.917909204545455

00:29:55.132 --> 00:29:57.029 diabetic shown on the left hand side.

NOTE Confidence: 0.917909204545455

00:29:57.030 --> 00:29:59.508 So P21P16 if you look at the

NOTE Confidence: 0.917909204545455

00:29:59.508 --> 00:30:01.270 auto antibody positive pancreas.

NOTE Confidence: 0.917909204545455

00:30:01.270 --> 00:30:04.336 So again these are don't have

NOTE Confidence: 0.917909204545455

00:30:04.336 --> 00:30:06.755 diabetes yet but are at risk for

NOTE Confidence: 0.917909204545455

00:30:06.755 --> 00:30:08.591 disease or the type one diabetic

NOTE Confidence: 0.917909204545455

00:30:08.591 --> 00:30:10.817 on the right and quantitate it.

NOTE Confidence: 0.917909204545455

00:30:10.820 --> 00:30:14.180 Type one and at risk people have far

NOTE Confidence: 0.917909204545455

00:30:14.180 --> 00:30:16.710 higher levels of senescent cells,

NOTE Confidence: 0.917909204545455

00:30:16.710 --> 00:30:19.010 senescent beta cells than

NOTE Confidence: 0.917909204545455

00:30:19.010 --> 00:30:20.160 control individuals,

NOTE Confidence: 0.917909204545455

00:30:20.160 --> 00:30:22.656 suggesting almost like a premature aging.

NOTE Confidence: 0.903235253333333

00:30:22.660 --> 00:30:25.086 If you would again another

NOTE Confidence: 0.903235253333333

00:30:25.086 --> 00:30:26.538 marker of ER stress.

NOTE Confidence: 0.903235253333333

00:30:26.540 --> 00:30:29.854 If you look at some of the molecules

NOTE Confidence: 0.903235253333333

00:30:29.854 --> 00:30:32.360 that we know are expressed in islets.

NOTE Confidence: 0.903235253333333

00:30:32.360 --> 00:30:33.816 Hormones such as GAD.

NOTE Confidence: 0.903235253333333

00:30:33.816 --> 00:30:36.579 They they don't end up with the

NOTE Confidence: 0.903235253333333

00:30:36.579 --> 00:30:38.599 right spaces within processes.

NOTE Confidence: 0.903235253333333

00:30:38.600 --> 00:30:41.120 They get either hung up in

NOTE Confidence: 0.903235253333333

00:30:41.120 --> 00:30:44.200 places like the Golgi or the ER

NOTE Confidence: 0.903235253333333

00:30:44.200 --> 00:30:46.385 and and they accumulate there.

NOTE Confidence: 0.903235253333333

00:30:46.390 --> 00:30:48.427 We've had a couple papers with my

NOTE Confidence: 0.903235253333333

00:30:48.427 --> 00:30:50.128 colleague at Phelps on this that  
NOTE Confidence: 0.9032352533333333

00:30:50.128 --> 00:30:51.664 are either out or coming out,  
NOTE Confidence: 0.9032352533333333

00:30:51.670 --> 00:30:54.640 but it looks like there's processing  
NOTE Confidence: 0.9032352533333333

00:30:54.640 --> 00:30:56.472 deficiencies in both individuals  
NOTE Confidence: 0.9032352533333333

00:30:56.472 --> 00:30:58.998 at risk for type one diabetes  
NOTE Confidence: 0.9032352533333333

00:30:58.998 --> 00:31:01.198 and those with the disease.  
NOTE Confidence: 0.9032352533333333

00:31:01.200 --> 00:31:03.558 If you look at sensing mechanisms,  
NOTE Confidence: 0.9032352533333333

00:31:03.560 --> 00:31:04.078 glucose is,  
NOTE Confidence: 0.9032352533333333

00:31:04.078 --> 00:31:06.150 you know if you think of islet cells  
NOTE Confidence: 0.9032352533333333

00:31:06.211 --> 00:31:08.413 and beta cells as being essentially  
NOTE Confidence: 0.9032352533333333

00:31:08.413 --> 00:31:09.881 factories for producing insulin.  
NOTE Confidence: 0.9032352533333333

00:31:09.890 --> 00:31:12.224 I mean, they're just insulin factories  
NOTE Confidence: 0.9032352533333333

00:31:12.224 --> 00:31:15.218 they have in order to work efficiently.  
NOTE Confidence: 0.9032352533333333

00:31:15.220 --> 00:31:16.486 You know they have to sense.  
NOTE Confidence: 0.9032352533333333

00:31:16.490 --> 00:31:18.062 Glucose, and so.  
NOTE Confidence: 0.9032352533333333

00:31:18.062 --> 00:31:19.110 A colleague.

NOTE Confidence: 0.9032352533333333

00:31:19.110 --> 00:31:21.618 Another colleague of mine next door.

NOTE Confidence: 0.9032352533333333

00:31:21.620 --> 00:31:23.834 Actually he started taking a look

NOTE Confidence: 0.9032352533333333

00:31:23.834 --> 00:31:26.194 at the expression of the molecules

NOTE Confidence: 0.9032352533333333

00:31:26.194 --> 00:31:28.618 that are both associated with sensing

NOTE Confidence: 0.9032352533333333

00:31:28.618 --> 00:31:31.328 as well as responses to insulin and

NOTE Confidence: 0.9032352533333333

00:31:31.328 --> 00:31:33.650 what you can see is things like ATP ace,

NOTE Confidence: 0.9032352533333333

00:31:33.650 --> 00:31:35.156 gluco kinase.

NOTE Confidence: 0.9032352533333333

00:31:35.156 --> 00:31:38.610 They're reduced both in individuals

NOTE Confidence: 0.9032352533333333

00:31:38.610 --> 00:31:40.370 with type one diabetes,

NOTE Confidence: 0.9032352533333333

00:31:40.370 --> 00:31:41.940 which are the middle column,

NOTE Confidence: 0.9032352533333333

00:31:41.940 --> 00:31:43.770 but they're also reduced in again.

NOTE Confidence: 0.9032352533333333

00:31:43.770 --> 00:31:45.243 Individuals with Autoantibody

NOTE Confidence: 0.9032352533333333

00:31:45.243 --> 00:31:46.716 positive no diabetes.

NOTE Confidence: 0.9032352533333333

00:31:46.720 --> 00:31:47.035 Yeah,

NOTE Confidence: 0.9032352533333333

00:31:47.035 --> 00:31:48.925 but at risk for the disease.

NOTE Confidence: 0.89788117625

00:31:51.060 --> 00:31:54.676 So we're starting to stack up here again,  
NOTE Confidence: 0.89788117625

00:31:54.680 --> 00:31:56.612 evidence that it's not just the  
NOTE Confidence: 0.89788117625

00:31:56.612 --> 00:31:58.230 autoimmunity that's in play here,  
NOTE Confidence: 0.89788117625

00:31:58.230 --> 00:32:00.380 but beta cells are abnormal.  
NOTE Confidence: 0.89788117625

00:32:00.380 --> 00:32:01.670 Now. Here's here's some other  
NOTE Confidence: 0.89788117625

00:32:01.670 --> 00:32:02.960 ways that we've shown that,  
NOTE Confidence: 0.89788117625

00:32:02.960 --> 00:32:05.768 and this is a paper we've published in cell.  
NOTE Confidence: 0.89788117625

00:32:05.770 --> 00:32:06.690 I'm just going to highlight  
NOTE Confidence: 0.89788117625

00:32:06.690 --> 00:32:07.610 one thing in the middle.  
NOTE Confidence: 0.89788117625

00:32:07.610 --> 00:32:11.530 Here again, these are.  
NOTE Confidence: 0.89788117625

00:32:11.530 --> 00:32:13.598 Tissue site top results.  
NOTE Confidence: 0.89788117625

00:32:13.598 --> 00:32:15.149 Looking at insulin,  
NOTE Confidence: 0.89788117625

00:32:15.150 --> 00:32:17.180 Glucagon and Samantha Staten staining  
NOTE Confidence: 0.89788117625

00:32:17.180 --> 00:32:19.210 so they're the three predominant  
NOTE Confidence: 0.89788117625

00:32:19.268 --> 00:32:21.524 hormones that you look at in the island  
NOTE Confidence: 0.89788117625

00:32:21.530 --> 00:32:23.826 and with the insulin being in red,

NOTE Confidence: 0.89788117625

00:32:23.830 --> 00:32:24.430 these are.

NOTE Confidence: 0.89788117625

00:32:24.430 --> 00:32:26.530 I know there's only four individuals here,

NOTE Confidence: 0.89788117625

00:32:26.530 --> 00:32:29.407 but this is looking at the insulin

NOTE Confidence: 0.89788117625

00:32:29.407 --> 00:32:31.906 staining and individuals that died within

NOTE Confidence: 0.89788117625

00:32:31.906 --> 00:32:34.685 one week of type one diabetes diagnosis,

NOTE Confidence: 0.89788117625

00:32:34.690 --> 00:32:36.174 and you can see like in the

NOTE Confidence: 0.89788117625

00:32:36.174 --> 00:32:37.410 first column in the middle.

NOTE Confidence: 0.89788117625

00:32:37.410 --> 00:32:40.110 Some people do have a marked

NOTE Confidence: 0.89788117625

00:32:40.110 --> 00:32:41.460 reduction in the.

NOTE Confidence: 0.89788117625

00:32:41.460 --> 00:32:43.950 Degree of insulin positive itself,

NOTE Confidence: 0.89788117625

00:32:43.950 --> 00:32:45.810 but in other cases don't.

NOTE Confidence: 0.89788117625

00:32:45.810 --> 00:32:46.494 So again,

NOTE Confidence: 0.89788117625

00:32:46.494 --> 00:32:48.546 the amount of insulin that you

NOTE Confidence: 0.89788117625

00:32:48.546 --> 00:32:50.940 can find in the pancreas at

NOTE Confidence: 0.89788117625

00:32:50.940 --> 00:32:52.580 onset can vary dramatically,

NOTE Confidence: 0.89788117625

00:32:52.580 --> 00:32:55.380 and it's not everybody is not the 90%,  
NOTE Confidence: 0.89788117625

00:32:55.380 --> 00:32:58.828 as I mentioned earlier on as a dogma.  
NOTE Confidence: 0.89788117625

00:32:58.830 --> 00:33:00.355 Another thing that we've been  
NOTE Confidence: 0.89788117625

00:33:00.355 --> 00:33:02.190 able to do with side top,  
NOTE Confidence: 0.89788117625

00:33:02.190 --> 00:33:04.647 and I know Yale has this technology  
NOTE Confidence: 0.89788117625

00:33:04.647 --> 00:33:07.790 is we've been able to make panels of  
NOTE Confidence: 0.89788117625

00:33:07.790 --> 00:33:09.800 different antibodies and then do.  
NOTE Confidence: 0.89788117625

00:33:09.800 --> 00:33:12.860 Look at by pseudo time analysis.  
NOTE Confidence: 0.89788117625

00:33:12.860 --> 00:33:16.310 And and by doing pairings,  
NOTE Confidence: 0.89788117625

00:33:16.310 --> 00:33:19.270 what we've been able to identify is is  
NOTE Confidence: 0.89788117625

00:33:19.270 --> 00:33:22.424 that that at the onset of type one diabetes,  
NOTE Confidence: 0.89788117625

00:33:22.430 --> 00:33:24.550 which is that middle column on the right,  
NOTE Confidence: 0.89788117625

00:33:24.550 --> 00:33:28.100 I'd like you to just focus on the D panel.  
NOTE Confidence: 0.89788117625

00:33:28.100 --> 00:33:30.070 This is islets from individuals  
NOTE Confidence: 0.89788117625

00:33:30.070 --> 00:33:32.040 at the onset of disease,  
NOTE Confidence: 0.89788117625

00:33:32.040 --> 00:33:35.220 the red.



NOTE Confidence: 0.89788117625

00:33:35.220 --> 00:33:37.290 Column is individuals who had type

NOTE Confidence: 0.89788117625

00:33:37.290 --> 00:33:39.578 one diabetes for seven years or more,

NOTE Confidence: 0.89788117625

00:33:39.580 --> 00:33:41.631 and then the yellow panel on the

NOTE Confidence: 0.89788117625

00:33:41.631 --> 00:33:43.477 left is islets from individuals

NOTE Confidence: 0.89788117625

00:33:43.477 --> 00:33:45.269 without type one diabetes.

NOTE Confidence: 0.89788117625

00:33:45.270 --> 00:33:47.062 And what you can see is that

NOTE Confidence: 0.89788117625

00:33:47.062 --> 00:33:49.000 the answer to type one diabetes.

NOTE Confidence: 0.89788117625

00:33:49.000 --> 00:33:50.404 They're not exactly normal,

NOTE Confidence: 0.89788117625

00:33:50.404 --> 00:33:53.000 and we all based on you again.

NOTE Confidence: 0.89788117625

00:33:53.000 --> 00:33:56.018 Just using 7 antibodies in combination.

NOTE Confidence: 0.89788117625

00:33:56.020 --> 00:33:58.687 So why this is and what percentage

NOTE Confidence: 0.89788117625

00:33:58.687 --> 00:34:00.260 I can tell you?

NOTE Confidence: 0.89788117625

00:34:00.260 --> 00:34:01.676 By different cases,

NOTE Confidence: 0.89788117625

00:34:01.676 --> 00:34:04.036 the percentage that that fit

NOTE Confidence: 0.89788117625

00:34:04.036 --> 00:34:05.620 into these stages?

NOTE Confidence: 0.89788117625

00:34:05.620 --> 00:34:07.476 Can vary quite dramatically,  
NOTE Confidence: 0.89788117625

00:34:07.476 --> 00:34:10.260 but we've found this site off  
NOTE Confidence: 0.89788117625

00:34:10.340 --> 00:34:12.580 very useful for phenotyping.  
NOTE Confidence: 0.89788117625

00:34:12.580 --> 00:34:14.295 Another thing that we've been  
NOTE Confidence: 0.89788117625

00:34:14.295 --> 00:34:16.644 doing with site talk is to start  
NOTE Confidence: 0.89788117625

00:34:16.644 --> 00:34:19.264 taking a look at expression panels  
NOTE Confidence: 0.89788117625

00:34:19.264 --> 00:34:22.204 and identifying early on what.  
NOTE Confidence: 0.89788117625

00:34:22.210 --> 00:34:24.034 When do things changes occur in  
NOTE Confidence: 0.89788117625

00:34:24.034 --> 00:34:25.760 the Natural History of disease?  
NOTE Confidence: 0.89788117625

00:34:25.760 --> 00:34:26.936 So for example,  
NOTE Confidence: 0.89788117625

00:34:26.936 --> 00:34:30.280 like on the bottom left of the class,  
NOTE Confidence: 0.89788117625

00:34:30.280 --> 00:34:33.256 one HLA that I spoke about.  
NOTE Confidence: 0.89788117625

00:34:33.260 --> 00:34:35.924 When does this occur and we're  
NOTE Confidence: 0.89788117625

00:34:35.924 --> 00:34:38.198 identifying a whole series of  
NOTE Confidence: 0.89788117625

00:34:38.198 --> 00:34:40.146 molecules and just randomly going  
NOTE Confidence: 0.89788117625

00:34:40.146 --> 00:34:42.378 through here from beta 2 microglobulin

NOTE Confidence: 0.732862927142857  
00:34:45.120 --> 00:34:49.929 IPPP? C SK1 is a prohormone processing.  
NOTE Confidence: 0.732862927142857  
00:34:49.930 --> 00:34:51.688 These are all molecules that we've  
NOTE Confidence: 0.732862927142857  
00:34:51.688 --> 00:34:53.783 been able to identify in the Natural  
NOTE Confidence: 0.732862927142857  
00:34:53.783 --> 00:34:56.348 History of disease in beta cells.  
NOTE Confidence: 0.732862927142857  
00:34:56.348 --> 00:34:59.744 Or in islands that that show  
NOTE Confidence: 0.732862927142857  
00:34:59.744 --> 00:35:02.999 abnormalities long before disease onset.  
NOTE Confidence: 0.732862927142857  
00:35:03.000 --> 00:35:05.178 Another thing that we've been able  
NOTE Confidence: 0.732862927142857  
00:35:05.178 --> 00:35:08.624 to use site top is to try and to  
NOTE Confidence: 0.732862927142857  
00:35:08.624 --> 00:35:11.025 densitometric standing up the number of  
NOTE Confidence: 0.732862927142857  
00:35:11.025 --> 00:35:13.818 blood vessels per eyelid and the the  
NOTE Confidence: 0.732862927142857  
00:35:13.818 --> 00:35:16.260 actual diameter of those blood vessels,  
NOTE Confidence: 0.732862927142857  
00:35:16.260 --> 00:35:20.278 and one of the things that we can say and it.  
NOTE Confidence: 0.732862927142857  
00:35:20.280 --> 00:35:22.260 I'm apologize if it's not cleared,  
NOTE Confidence: 0.732862927142857  
00:35:22.260 --> 00:35:25.292 but the the green would be normal cases.  
NOTE Confidence: 0.732862927142857  
00:35:25.292 --> 00:35:27.714 The green line in the green dots,  
NOTE Confidence: 0.732862927142857

00:35:27.720 --> 00:35:29.868 and then the pink ones magenta  
NOTE Confidence: 0.732862927142857

00:35:29.868 --> 00:35:32.500 ones are the long term diabetics.  
NOTE Confidence: 0.732862927142857

00:35:32.500 --> 00:35:35.404 And then the blue are people at onset.  
NOTE Confidence: 0.732862927142857

00:35:35.410 --> 00:35:37.629 What we can see through this study  
NOTE Confidence: 0.732862927142857

00:35:37.629 --> 00:35:40.014 is is that islets in individuals  
NOTE Confidence: 0.732862927142857

00:35:40.014 --> 00:35:41.826 with type one diabetes,  
NOTE Confidence: 0.732862927142857

00:35:41.830 --> 00:35:44.190 their their blood vessels are  
NOTE Confidence: 0.732862927142857

00:35:44.190 --> 00:35:46.999 actually shorter and have a thinner  
NOTE Confidence: 0.732862927142857

00:35:46.999 --> 00:35:49.314 diameter to them versus normals.  
NOTE Confidence: 0.732862927142857

00:35:49.320 --> 00:35:51.210 So it's almost as if the type  
NOTE Confidence: 0.732862927142857

00:35:51.210 --> 00:35:52.800 one diabetic eyelid is strangled.  
NOTE Confidence: 0.732862927142857

00:35:52.800 --> 00:35:53.910 In a way,  
NOTE Confidence: 0.732862927142857

00:35:53.910 --> 00:35:56.130 it's a very highly vascularized organ,  
NOTE Confidence: 0.732862927142857

00:35:56.130 --> 00:35:58.866 but in the type one diabetic  
NOTE Confidence: 0.732862927142857

00:35:58.866 --> 00:36:00.690 case it's not normal.  
NOTE Confidence: 0.732862927142857

00:36:00.690 --> 00:36:02.685 We've also published this article

NOTE Confidence: 0.732862927142857  
00:36:02.685 --> 00:36:05.600 in Cell and we have another one  
NOTE Confidence: 0.732862927142857  
00:36:05.600 --> 00:36:08.049 coming out soon there where that.  
NOTE Confidence: 0.732862927142857  
00:36:08.049 --> 00:36:10.492 The eyelets and type one diabetics they  
NOTE Confidence: 0.732862927142857  
00:36:10.492 --> 00:36:12.305 they don't process hormones naturally  
NOTE Confidence: 0.732862927142857  
00:36:12.305 --> 00:36:15.142 and to go through all this in great  
NOTE Confidence: 0.732862927142857  
00:36:15.142 --> 00:36:17.750 detail would would take up too much time,  
NOTE Confidence: 0.732862927142857  
00:36:17.750 --> 00:36:20.334 but one of the things we've been able  
NOTE Confidence: 0.732862927142857  
00:36:20.334 --> 00:36:22.768 to identify is is that in individuals,  
NOTE Confidence: 0.732862927142857  
00:36:22.770 --> 00:36:24.618 both with type one diabetes as  
NOTE Confidence: 0.732862927142857  
00:36:24.618 --> 00:36:27.000 well as at risk for the disease,  
NOTE Confidence: 0.732862927142857  
00:36:27.000 --> 00:36:29.891 they are deficient in some of the  
NOTE Confidence: 0.732862927142857  
00:36:29.891 --> 00:36:31.130 prohormones processing enzymes.  
NOTE Confidence: 0.732862927142857  
00:36:31.130 --> 00:36:33.855 That allow for conversion of  
NOTE Confidence: 0.732862927142857  
00:36:33.855 --> 00:36:35.490 proinsulin to insulin,  
NOTE Confidence: 0.732862927142857  
00:36:35.490 --> 00:36:38.747 and this has been validated in living humans.  
NOTE Confidence: 0.732862927142857

00:36:38.747 --> 00:36:41.470 This was again through studies of tissue.  
NOTE Confidence: 0.732862927142857

00:36:41.470 --> 00:36:44.098 In looking at the degree of  
NOTE Confidence: 0.732862927142857

00:36:44.098 --> 00:36:45.850 of insulin and proinsulin.  
NOTE Confidence: 0.732862927142857

00:36:45.850 --> 00:36:48.384 C peptide that you could extract from  
NOTE Confidence: 0.732862927142857

00:36:48.384 --> 00:36:50.854 these tissues and then doing quantitative  
NOTE Confidence: 0.732862927142857

00:36:50.854 --> 00:36:53.470 PCR and looking for the quantitate,  
NOTE Confidence: 0.732862927142857

00:36:53.470 --> 00:36:56.398 the amount of the processing enzymes.  
NOTE Confidence: 0.732862927142857

00:36:56.400 --> 00:36:58.242 But we've again seen this in  
NOTE Confidence: 0.732862927142857

00:36:58.242 --> 00:36:59.834 human living samples that they  
NOTE Confidence: 0.732862927142857

00:36:59.834 --> 00:37:01.640 seemed also in the pre diabetic.  
NOTE Confidence: 0.732862927142857

00:37:01.640 --> 00:37:05.364 Stage have alterations in the C peptide  
NOTE Confidence: 0.732862927142857

00:37:05.364 --> 00:37:08.369 that amplified by disease onset.  
NOTE Confidence: 0.732862927142857

00:37:08.370 --> 00:37:09.670 Couple more things occur in  
NOTE Confidence: 0.732862927142857

00:37:09.670 --> 00:37:10.970 the type of the type.  
NOTE Confidence: 0.732862927142857

00:37:10.970 --> 00:37:11.646 One pancreas,  
NOTE Confidence: 0.732862927142857

00:37:11.646 --> 00:37:13.674 one of them is is the

NOTE Confidence: 0.732862927142857  
00:37:13.674 --> 00:37:15.150 accumulation of hyaluronan,  
NOTE Confidence: 0.732862927142857  
00:37:15.150 --> 00:37:18.498 hyaluron and binding proteins.  
NOTE Confidence: 0.732862927142857  
00:37:18.500 --> 00:37:21.412 They form almost a capsule around the  
NOTE Confidence: 0.732862927142857  
00:37:21.412 --> 00:37:23.879 type one diabetes diabetic islet.  
NOTE Confidence: 0.732862927142857  
00:37:23.880 --> 00:37:26.848 We also have some evidence that suggests  
NOTE Confidence: 0.732862927142857  
00:37:26.848 --> 00:37:30.609 that it too is as a potential marker of  
NOTE Confidence: 0.732862927142857  
00:37:30.609 --> 00:37:33.598 islets that are going to be destroyed.  
NOTE Confidence: 0.732862927142857  
00:37:33.600 --> 00:37:36.318 Or essentially a hallmark for signaling.  
NOTE Confidence: 0.732862927142857  
00:37:36.320 --> 00:37:38.448 I'll just close the beta cell part  
NOTE Confidence: 0.732862927142857  
00:37:38.450 --> 00:37:40.895 by saying there's actually now  
NOTE Confidence: 0.732862927142857  
00:37:40.895 --> 00:37:43.340 about 17 different features that  
NOTE Confidence: 0.732862927142857  
00:37:43.418 --> 00:37:45.833 we've identified that are present  
NOTE Confidence: 0.732862927142857  
00:37:45.833 --> 00:37:47.397 in the auto antibody,  
NOTE Confidence: 0.732862927142857  
00:37:47.400 --> 00:37:50.010 positive pancreas or new onset pancreas  
NOTE Confidence: 0.732862927142857  
00:37:50.010 --> 00:37:53.667 that tell us that beta cells are involved.  
NOTE Confidence: 0.732862927142857

00:37:53.670 --> 00:37:55.530 It's it's not just the disease  
NOTE Confidence: 0.732862927142857

00:37:55.530 --> 00:37:56.770 of the immune system.  
NOTE Confidence: 0.958452

00:38:00.230 --> 00:38:02.756 The last two lessons will go relatively  
NOTE Confidence: 0.958452

00:38:02.756 --> 00:38:05.229 quickly, but the third thing that I think  
NOTE Confidence: 0.958452

00:38:05.229 --> 00:38:07.281 we've learned that again wasn't in the  
NOTE Confidence: 0.958452

00:38:07.281 --> 00:38:09.570 textbooks or is not in most textbooks.  
NOTE Confidence: 0.958452

00:38:09.570 --> 00:38:12.818 It's that beta cell replication in number is  
NOTE Confidence: 0.958452

00:38:12.818 --> 00:38:15.838 important in type one diabetes development.  
NOTE Confidence: 0.958452

00:38:15.840 --> 00:38:18.520 And that actually until  
NOTE Confidence: 0.958452

00:38:18.520 --> 00:38:20.048 recently it was widely.  
NOTE Confidence: 0.958452

00:38:20.048 --> 00:38:22.484 If you were to go just particularly like  
NOTE Confidence: 0.958452

00:38:22.484 --> 00:38:24.746 a transplant audience where people would  
NOTE Confidence: 0.958452

00:38:24.746 --> 00:38:26.740 do islet transplants and you'd say,  
NOTE Confidence: 0.958452

00:38:26.740 --> 00:38:28.924 well, how many islands are in  
NOTE Confidence: 0.958452

00:38:28.924 --> 00:38:31.090 the normal adult human pancreas?  
NOTE Confidence: 0.958452

00:38:31.090 --> 00:38:32.635 And most people would say, oh,



NOTE Confidence: 0.958452

00:38:32.635 --> 00:38:35.005 you know, a million or so?

NOTE Confidence: 0.958452

00:38:35.010 --> 00:38:38.814 Well, a collaborator of mine, Peter Butler,

NOTE Confidence: 0.958452

00:38:38.814 --> 00:38:41.278 did this study from Mayo Clinic cases

NOTE Confidence: 0.958452

00:38:41.278 --> 00:38:44.066 and some in pod cases of a few years ago,

NOTE Confidence: 0.958452

00:38:44.070 --> 00:38:44.708 and actually.

NOTE Confidence: 0.958452

00:38:44.708 --> 00:38:46.941 Depending on how you find it this

NOTE Confidence: 0.958452

00:38:46.941 --> 00:38:49.390 way in this paper was beta cell mass.

NOTE Confidence: 0.958452

00:38:49.390 --> 00:38:51.800 Actually, in normal individuals this

NOTE Confidence: 0.958452

00:38:51.800 --> 00:38:53.728 is normal individuals nondiabetic.

NOTE Confidence: 0.958452

00:38:53.730 --> 00:38:57.393 The amount of beta cell mass in the human

NOTE Confidence: 0.958452

00:38:57.393 --> 00:39:00.250 pancreas is varies quite dramatically.

NOTE Confidence: 0.958452

00:39:00.250 --> 00:39:02.878 It's not just a standard like

NOTE Confidence: 0.958452

00:39:02.878 --> 00:39:04.192 that everybody has.

NOTE Confidence: 0.958452

00:39:04.200 --> 00:39:05.820 And here's some very innovative

NOTE Confidence: 0.958452

00:39:05.820 --> 00:39:08.060 work that we did from studying.

NOTE Confidence: 0.958452

00:39:08.060 --> 00:39:13.116 The pancreas is to take a look at when is  
NOTE Confidence: 0.958452

00:39:13.116 --> 00:39:17.260 that mass set in life and what we did is,  
NOTE Confidence: 0.958452

00:39:17.260 --> 00:39:18.504 and we've probably are.  
NOTE Confidence: 0.958452

00:39:18.504 --> 00:39:20.059 We haven't published an update,  
NOTE Confidence: 0.958452

00:39:20.060 --> 00:39:22.251 but we probably have six times the  
NOTE Confidence: 0.958452

00:39:22.251 --> 00:39:24.508 number of cases that are shown here.  
NOTE Confidence: 0.958452

00:39:24.510 --> 00:39:26.666 But just to cut to the chase,  
NOTE Confidence: 0.958452

00:39:26.670 --> 00:39:30.270 you really are by about the age of four,  
NOTE Confidence: 0.958452

00:39:30.270 --> 00:39:31.380 if not earlier.  
NOTE Confidence: 0.958452

00:39:31.380 --> 00:39:34.550 You pretty much are locked into the number.  
NOTE Confidence: 0.958452

00:39:34.550 --> 00:39:37.511 Of of islet cells or beta cells  
NOTE Confidence: 0.958452

00:39:37.511 --> 00:39:40.260 that you're going to have in life.  
NOTE Confidence: 0.958452

00:39:40.260 --> 00:39:42.384 And unlike some of the mouse  
NOTE Confidence: 0.958452

00:39:42.384 --> 00:39:44.840 models where if you have a mouse,  
NOTE Confidence: 0.958452

00:39:44.840 --> 00:39:47.590 if they become pregnant or  
NOTE Confidence: 0.958452

00:39:47.590 --> 00:39:49.240 have pancreatic injury,

NOTE Confidence: 0.958452  
00:39:49.240 --> 00:39:51.970 the mice have a tremendous  
NOTE Confidence: 0.958452  
00:39:51.970 --> 00:39:53.608 ability to recover.  
NOTE Confidence: 0.958452  
00:39:53.610 --> 00:39:56.859 It's not so quite that way in in humans,  
NOTE Confidence: 0.958452  
00:39:56.860 --> 00:39:59.002 and so I think we tend to think of  
NOTE Confidence: 0.958452  
00:39:59.002 --> 00:40:01.392 this as almost a growth curve like  
NOTE Confidence: 0.958452  
00:40:01.392 --> 00:40:03.520 situation where sometime in early life,  
NOTE Confidence: 0.958452  
00:40:03.520 --> 00:40:06.248 and we're not sure why is it microbiome  
NOTE Confidence: 0.958452  
00:40:06.248 --> 00:40:08.310 driven? Is it nutrition driven?  
NOTE Confidence: 0.958452  
00:40:08.310 --> 00:40:10.030 Is to genetic driven?  
NOTE Confidence: 0.958452  
00:40:10.030 --> 00:40:12.620 But you end up with some number  
NOTE Confidence: 0.958452  
00:40:12.620 --> 00:40:14.957 of islet cells and that will  
NOTE Confidence: 0.958452  
00:40:14.957 --> 00:40:17.610 largely be what you have in life.  
NOTE Confidence: 0.958452  
00:40:17.610 --> 00:40:18.858 And we that's important.  
NOTE Confidence: 0.958452  
00:40:18.858 --> 00:40:19.170 Oh,  
NOTE Confidence: 0.958452  
00:40:19.170 --> 00:40:21.326 and here's an example of some unpublished  
NOTE Confidence: 0.958452

00:40:21.326 --> 00:40:23.308 data from a person down the road from you,  
NOTE Confidence: 0.958452

00:40:23.310 --> 00:40:25.822 Susan Bonner, where where?  
NOTE Confidence: 0.958452

00:40:25.822 --> 00:40:26.450 Again,  
NOTE Confidence: 0.958452

00:40:26.450 --> 00:40:27.656 that's what she did was take  
NOTE Confidence: 0.958452

00:40:27.656 --> 00:40:28.850 a look at two things.  
NOTE Confidence: 0.958452

00:40:28.850 --> 00:40:31.521 One, she looked at pancreas weight,  
NOTE Confidence: 0.958452

00:40:31.521 --> 00:40:33.627 which is in the blue lines  
NOTE Confidence: 0.958452

00:40:33.630 --> 00:40:36.730 versus the beta cell.  
NOTE Confidence: 0.958452

00:40:36.730 --> 00:40:40.030 Number in that particular pancreas.  
NOTE Confidence: 0.958452

00:40:40.030 --> 00:40:42.026 And for normal individuals,  
NOTE Confidence: 0.958452

00:40:42.026 --> 00:40:44.521 your pancreas continues to grow  
NOTE Confidence: 0.958452

00:40:44.521 --> 00:40:47.355 on until about 25 years of age.  
NOTE Confidence: 0.958452

00:40:47.360 --> 00:40:50.040 I've not shown the whole lifetime data here,  
NOTE Confidence: 0.958452

00:40:50.040 --> 00:40:52.007 but at about 25 years of age,  
NOTE Confidence: 0.958452

00:40:52.010 --> 00:40:53.430 your pancreas stops growing.  
NOTE Confidence: 0.958452

00:40:53.430 --> 00:40:56.729 But in terms of the actual beta cell number,

NOTE Confidence: 0.958452  
00:40:56.730 --> 00:41:00.010 that again stops at around  
NOTE Confidence: 0.958452  
00:41:00.010 --> 00:41:01.966 4-4 years of age or so,  
NOTE Confidence: 0.958452  
00:41:01.970 --> 00:41:04.980 and the mechanisms that control  
NOTE Confidence: 0.958452  
00:41:04.980 --> 00:41:07.388 that are undergoing investigation.  
NOTE Confidence: 0.958452  
00:41:07.390 --> 00:41:09.206 So one of the things that we believe,  
NOTE Confidence: 0.958452  
00:41:09.210 --> 00:41:12.451 and it published now on is is  
NOTE Confidence: 0.958452  
00:41:12.451 --> 00:41:14.515 that when why we think islet  
NOTE Confidence: 0.958452  
00:41:14.515 --> 00:41:16.110 cell numbers are important is  
NOTE Confidence: 0.866103092  
00:41:16.177 --> 00:41:18.284 is that perhaps early in life you're  
NOTE Confidence: 0.866103092  
00:41:18.284 --> 00:41:20.698 the amount of beta cell mass you have.  
NOTE Confidence: 0.866103092  
00:41:20.700 --> 00:41:23.535 It is fixed and whether or not you have  
NOTE Confidence: 0.866103092  
00:41:23.535 --> 00:41:26.789 a high beta cell mass and intermediate or  
NOTE Confidence: 0.866103092  
00:41:26.789 --> 00:41:30.396 low will form a degree will be important  
NOTE Confidence: 0.866103092  
00:41:30.396 --> 00:41:32.701 in terms of diabetes development.  
NOTE Confidence: 0.866103092  
00:41:32.710 --> 00:41:35.206 Both type one and Type 2.  
NOTE Confidence: 0.866103092

00:41:35.210 --> 00:41:37.090 In that if you have a high beta cell mass,  
NOTE Confidence: 0.866103092

00:41:37.090 --> 00:41:39.015 maybe be more resistant disease  
NOTE Confidence: 0.866103092

00:41:39.015 --> 00:41:41.750 in the low lower beta cell mass,  
NOTE Confidence: 0.866103092

00:41:41.750 --> 00:41:44.578 more susceptible to disease.  
NOTE Confidence: 0.866103092

00:41:44.580 --> 00:41:46.236 So in the last five minutes of the  
NOTE Confidence: 0.866103092

00:41:46.236 --> 00:41:47.915 talk here I wanna just leave it out.  
NOTE Confidence: 0.866103092

00:41:47.920 --> 00:41:49.736 We started small and now we're going big.  
NOTE Confidence: 0.866103092

00:41:49.740 --> 00:41:51.160 Is that type one?  
NOTE Confidence: 0.866103092

00:41:51.160 --> 00:41:54.350 Diabetes is also a disease of the pancreas.  
NOTE Confidence: 0.866103092

00:41:54.350 --> 00:41:56.762 And as I was sharing with one of you  
NOTE Confidence: 0.866103092

00:41:56.762 --> 00:41:59.690 this morning, we are one of the lab.  
NOTE Confidence: 0.866103092

00:41:59.690 --> 00:42:01.316 This was actually known back in  
NOTE Confidence: 0.866103092

00:42:01.316 --> 00:42:03.778 the 1960s from autopsy material,  
NOTE Confidence: 0.866103092

00:42:03.778 --> 00:42:05.966 where but it was.  
NOTE Confidence: 0.866103092

00:42:05.970 --> 00:42:09.146 It was reports that said well in people.  
NOTE Confidence: 0.866103092

00:42:09.150 --> 00:42:12.228 With some cake cases of diabetes,

NOTE Confidence: 0.866103092

00:42:12.230 --> 00:42:15.350 more often insulin requiring diabetes,

NOTE Confidence: 0.866103092

00:42:15.350 --> 00:42:17.708 their pancreas appeared to be smaller.

NOTE Confidence: 0.866103092

00:42:17.710 --> 00:42:20.654 But what we published this a few years

NOTE Confidence: 0.866103092

00:42:20.654 --> 00:42:23.686 ago in JAMA was because one of the

NOTE Confidence: 0.866103092

00:42:23.690 --> 00:42:26.696 mythology techs came to me one day and said,

NOTE Confidence: 0.866103092

00:42:26.700 --> 00:42:27.101 hey.

NOTE Confidence: 0.866103092

00:42:27.101 --> 00:42:30.309 Do you ever notice that the pancreas from

NOTE Confidence: 0.866103092

00:42:30.309 --> 00:42:33.926 the type ones there's so much smaller than?

NOTE Confidence: 0.866103092

00:42:33.930 --> 00:42:35.960 The normal set we get.

NOTE Confidence: 0.866103092

00:42:35.960 --> 00:42:38.214 And so we started going back and

NOTE Confidence: 0.866103092

00:42:38.214 --> 00:42:40.353 analyzed it and found in published

NOTE Confidence: 0.866103092

00:42:40.353 --> 00:42:42.549 this paper because it was true

NOTE Confidence: 0.866103092

00:42:42.550 --> 00:42:44.698 at the type ones were smaller.

NOTE Confidence: 0.866103092

00:42:44.700 --> 00:42:46.668 But the reason this ended up in jam

NOTE Confidence: 0.866103092

00:42:46.668 --> 00:42:48.996 is that middle middle group that even

NOTE Confidence: 0.866103092

00:42:48.996 --> 00:42:51.425 people without type one diabetes but at  
NOTE Confidence: 0.866103092

00:42:51.425 --> 00:42:53.801 risk for disease they had a smaller pancreas.  
NOTE Confidence: 0.866103092

00:42:53.810 --> 00:42:56.987 And if the picture is worth 1000 words here,  
NOTE Confidence: 0.866103092

00:42:56.990 --> 00:42:59.528 I'll just show these two pancreata,  
NOTE Confidence: 0.866103092

00:42:59.530 --> 00:43:00.330 one front.  
NOTE Confidence: 0.866103092

00:43:00.330 --> 00:43:02.805 They're both from their age matched  
NOTE Confidence: 0.866103092

00:43:02.805 --> 00:43:05.655 our age similar 1413 year old,  
NOTE Confidence: 0.866103092

00:43:05.660 --> 00:43:06.662 similar BMI's,  
NOTE Confidence: 0.866103092

00:43:06.662 --> 00:43:10.169 but if you see the top pancreas,  
NOTE Confidence: 0.866103092

00:43:10.170 --> 00:43:12.767 its weight is about half of that.  
NOTE Confidence: 0.866103092

00:43:12.770 --> 00:43:14.666 Of the normal pancreas down at  
NOTE Confidence: 0.866103092

00:43:14.666 --> 00:43:16.657 the bottom and what you'll see  
NOTE Confidence: 0.866103092

00:43:16.657 --> 00:43:18.643 is most of the losses actually,  
NOTE Confidence: 0.866103092

00:43:18.650 --> 00:43:19.868 at the tail of the pancreas.  
NOTE Confidence: 0.866103092

00:43:19.870 --> 00:43:22.426 So to the far right and far less at  
NOTE Confidence: 0.866103092

00:43:22.426 --> 00:43:24.494 the head of the pancreas and the



NOTE Confidence: 0.866103092

00:43:24.494 --> 00:43:26.762 tail of the pancreas is the region

NOTE Confidence: 0.866103092

00:43:26.762 --> 00:43:28.855 that usually has the most highest

NOTE Confidence: 0.866103092

00:43:28.855 --> 00:43:30.530 number of insulin producing cells,

NOTE Confidence: 0.866103092

00:43:30.530 --> 00:43:32.770 and then we publish this as a

NOTE Confidence: 0.866103092

00:43:32.770 --> 00:43:34.787 follow up with far bigger numbers.

NOTE Confidence: 0.866103092

00:43:34.790 --> 00:43:37.742 But if you look at what we call relative

NOTE Confidence: 0.866103092

00:43:37.742 --> 00:43:40.547 pancreas weight or TPW on the left hand side,

NOTE Confidence: 0.866103092

00:43:40.550 --> 00:43:42.426 what you can see is is that

NOTE Confidence: 0.866103092

00:43:42.426 --> 00:43:43.910 the type one pancreas.

NOTE Confidence: 0.866103092

00:43:43.910 --> 00:43:47.810 And is about 1/3 to half the size on average.

NOTE Confidence: 0.866103092

00:43:47.810 --> 00:43:51.552 At at onset it's about 25 to 35%

NOTE Confidence: 0.866103092

00:43:51.552 --> 00:43:53.806 and within two years it'll be about

NOTE Confidence: 0.866103092

00:43:53.810 --> 00:43:57.667 35% to 50% reduced type 2 diabetes.

NOTE Confidence: 0.866103092

00:43:57.670 --> 00:43:59.441 It seems to more of a type

NOTE Confidence: 0.866103092

00:43:59.441 --> 00:44:00.990 one effect type 2 diabetics,

NOTE Confidence: 0.866103092

00:44:00.990 --> 00:44:02.600 maybe a tad bit reduced,  
NOTE Confidence: 0.866103092

00:44:02.600 --> 00:44:04.556 but nothing like the type one  
NOTE Confidence: 0.866103092

00:44:04.556 --> 00:44:06.440 and has noticed noted earlier.  
NOTE Confidence: 0.866103092

00:44:06.440 --> 00:44:09.488 The greatest loss if we take the organ  
NOTE Confidence: 0.866103092

00:44:09.488 --> 00:44:12.351 in segmented into head body tail its  
NOTE Confidence: 0.866103092

00:44:12.351 --> 00:44:15.119 smallest in grace reduction in the tail.  
NOTE Confidence: 0.866103092

00:44:15.120 --> 00:44:15.480 Uhm,  
NOTE Confidence: 0.866103092

00:44:15.480 --> 00:44:16.920 we were all always,  
NOTE Confidence: 0.882367645

00:44:16.920 --> 00:44:19.521 as I'm sure you all are in terms of  
NOTE Confidence: 0.882367645

00:44:19.521 --> 00:44:21.478 pathology and working with tissues.  
NOTE Confidence: 0.882367645

00:44:21.480 --> 00:44:22.092 People said, well,  
NOTE Confidence: 0.882367645

00:44:22.092 --> 00:44:23.840 how do you know that that's real or not?  
NOTE Confidence: 0.882367645

00:44:23.840 --> 00:44:26.495 An artifact of of your  
NOTE Confidence: 0.882367645

00:44:26.495 --> 00:44:28.619 processing or or something?  
NOTE Confidence: 0.882367645

00:44:28.620 --> 00:44:30.876 So we published with Mike Halloran,  
NOTE Confidence: 0.882367645

00:44:30.880 --> 00:44:32.353 Martha, another colleague,

NOTE Confidence: 0.882367645

00:44:32.353 --> 00:44:35.790 I a study of about 300 patients

NOTE Confidence: 0.882367645

00:44:35.790 --> 00:44:38.674 where we did Mrs of the individual.

NOTE Confidence: 0.882367645

00:44:38.680 --> 00:44:40.162 And again, I'm just going to

NOTE Confidence: 0.882367645

00:44:40.162 --> 00:44:41.830 highlight this sort of sake of time.

NOTE Confidence: 0.882367645

00:44:41.830 --> 00:44:45.346 If you blind analysis by radiologists.

NOTE Confidence: 0.882367645

00:44:45.350 --> 00:44:47.079 But if you look at the pancreas

NOTE Confidence: 0.882367645

00:44:47.079 --> 00:44:48.955 in blue here of individuals with

NOTE Confidence: 0.882367645

00:44:48.955 --> 00:44:50.745 recent onset type one diabetes,

NOTE Confidence: 0.882367645

00:44:50.750 --> 00:44:52.845 you see they're quite reduced

NOTE Confidence: 0.882367645

00:44:52.845 --> 00:44:54.940 relative to the control population,

NOTE Confidence: 0.882367645

00:44:54.940 --> 00:44:57.060 which is the green bar.

NOTE Confidence: 0.882367645

00:44:57.060 --> 00:44:58.986 And the auto antibody positive were

NOTE Confidence: 0.882367645

00:44:58.986 --> 00:45:01.767 also reduced as we assume from the other

NOTE Confidence: 0.882367645

00:45:01.767 --> 00:45:03.909 studies about what was interesting and

NOTE Confidence: 0.882367645

00:45:03.975 --> 00:45:06.357 we still don't have exactly explanation.

NOTE Confidence: 0.882367645

00:45:06.360 --> 00:45:09.450 But even from first degree relatives,  
NOTE Confidence: 0.882367645

00:45:09.450 --> 00:45:10.560 that's FDR.  
NOTE Confidence: 0.882367645

00:45:10.560 --> 00:45:12.780 With autoantibodies no autoantibodies,  
NOTE Confidence: 0.882367645

00:45:12.780 --> 00:45:16.028 even their pancreas was a little smaller  
NOTE Confidence: 0.882367645

00:45:16.028 --> 00:45:18.919 relative to age matched controls.  
NOTE Confidence: 0.882367645

00:45:18.920 --> 00:45:21.535 Suggesting that there might even  
NOTE Confidence: 0.882367645

00:45:21.535 --> 00:45:24.710 be some genetics in play here.  
NOTE Confidence: 0.882367645

00:45:24.710 --> 00:45:27.506 Uhm, we know that the exocrine  
NOTE Confidence: 0.882367645

00:45:27.506 --> 00:45:29.370 function is also decrease.  
NOTE Confidence: 0.882367645

00:45:29.370 --> 00:45:30.510 We've looked at amylase,  
NOTE Confidence: 0.882367645

00:45:30.510 --> 00:45:32.625 life pace and then in this case  
NOTE Confidence: 0.882367645

00:45:32.625 --> 00:45:34.350 I'm showing data on trypsinogen.  
NOTE Confidence: 0.882367645

00:45:34.350 --> 00:45:37.689 They're all reduced in both the pre  
NOTE Confidence: 0.882367645

00:45:37.689 --> 00:45:40.926 diabetic state as well as at the time  
NOTE Confidence: 0.882367645

00:45:40.926 --> 00:45:42.736 of disease onset or established.  
NOTE Confidence: 0.882367645

00:45:42.740 --> 00:45:45.255 So exocrine functions declines and

NOTE Confidence: 0.882367645

00:45:45.255 --> 00:45:48.308 the other thing that we've noticed

NOTE Confidence: 0.882367645

00:45:48.308 --> 00:45:50.998 as have others that if you just

NOTE Confidence: 0.882367645

00:45:50.998 --> 00:45:52.658 look at exocrine infiltrates now

NOTE Confidence: 0.882367645

00:45:52.658 --> 00:45:54.780 this is not pancreatitis chronic.

NOTE Confidence: 0.882367645

00:45:54.780 --> 00:45:57.990 Pancreatitis but just exocrine infiltrates.

NOTE Confidence: 0.882367645

00:45:57.990 --> 00:46:01.616 They seem to be higher in type

NOTE Confidence: 0.882367645

00:46:01.616 --> 00:46:03.170 one diabetes patients.

NOTE Confidence: 0.882367645

00:46:03.170 --> 00:46:06.930 Rather your new onset or.

NOTE Confidence: 0.882367645

00:46:06.930 --> 00:46:08.590 Long established Type one diabetes,

NOTE Confidence: 0.882367645

00:46:08.590 --> 00:46:11.382 then control individuals suggesting

NOTE Confidence: 0.882367645

00:46:11.382 --> 00:46:13.728 that again, it's an interplay,

NOTE Confidence: 0.882367645

00:46:13.728 --> 00:46:15.376 but something is abnormal

NOTE Confidence: 0.882367645

00:46:15.376 --> 00:46:17.559 in the exocrine pancreas.

NOTE Confidence: 0.882367645

00:46:17.560 --> 00:46:19.784 So just in the last couple of slides

NOTE Confidence: 0.882367645

00:46:19.784 --> 00:46:21.350 here I want to leave you with a kind

NOTE Confidence: 0.882367645

00:46:21.350 --> 00:46:23.136 of a situation that we're working on.

NOTE Confidence: 0.882367645

00:46:23.140 --> 00:46:25.306 Moving forward is is we're faced

NOTE Confidence: 0.882367645

00:46:25.306 --> 00:46:27.779 with a major burning question here,

NOTE Confidence: 0.882367645

00:46:27.780 --> 00:46:29.922 and this is something that one

NOTE Confidence: 0.882367645

00:46:29.922 --> 00:46:31.966 of your own Kevin Harold and I.

NOTE Confidence: 0.882367645

00:46:31.970 --> 00:46:34.440 We published an article together

NOTE Confidence: 0.882367645

00:46:34.440 --> 00:46:38.298 almost a decade ago now where?

NOTE Confidence: 0.882367645

00:46:38.300 --> 00:46:40.316 We we asked this question and I

NOTE Confidence: 0.882367645

00:46:40.316 --> 00:46:42.422 should say that this question was

NOTE Confidence: 0.882367645

00:46:42.422 --> 00:46:45.034 actually asked about 30 years prior,

NOTE Confidence: 0.882367645

00:46:45.034 --> 00:46:47.970 but we asked it again is type

NOTE Confidence: 0.882367645

00:46:47.970 --> 00:46:49.920 one diabetes as a result from

NOTE Confidence: 0.882367645

00:46:49.920 --> 00:46:51.080 an autoimmune attack,

NOTE Confidence: 0.882367645

00:46:51.080 --> 00:46:53.030 meaning where the immune response

NOTE Confidence: 0.882367645

00:46:53.030 --> 00:46:54.980 is doing what it's supposed,

NOTE Confidence: 0.882367645

00:46:54.980 --> 00:46:56.438 not what it's supposed to do,

NOTE Confidence: 0.882367645

00:46:56.440 --> 00:46:58.180 meaning it has a loss of

NOTE Confidence: 0.882367645

00:46:58.180 --> 00:46:59.770 tolerance to these beta cells,

NOTE Confidence: 0.882367645

00:46:59.770 --> 00:47:03.010 both central and peripheral, and that.

NOTE Confidence: 0.882367645

00:47:03.010 --> 00:47:06.418 It's destroying the beta cells or.

NOTE Confidence: 0.882367645

00:47:06.420 --> 00:47:08.219 Is it with through the evidence that

NOTE Confidence: 0.882367645

00:47:08.219 --> 00:47:09.609 I've shown you the contributions

NOTE Confidence: 0.882367645

00:47:09.609 --> 00:47:11.583 of the beta cells in the pancreas

NOTE Confidence: 0.882367645

00:47:11.583 --> 00:47:13.071 that actually the immune system

NOTE Confidence: 0.882367645

00:47:13.071 --> 00:47:15.170 is doing what it's supposed to do?

NOTE Confidence: 0.882367645

00:47:15.170 --> 00:47:17.390 That when you have beta cell

NOTE Confidence: 0.882367645

00:47:17.390 --> 00:47:19.537 dysfunction and things like metabolic

NOTE Confidence: 0.882367645

00:47:19.537 --> 00:47:21.465 stress or that inflammation.

NOTE Confidence: 0.882367645

00:47:21.470 --> 00:47:23.494 That it's actually destroying

NOTE Confidence: 0.882367645

00:47:23.494 --> 00:47:26.024 these and which occurs first.

NOTE Confidence: 0.882367645

00:47:26.030 --> 00:47:28.242 So this is a burning question that

NOTE Confidence: 0.882367645

00:47:28.242 --> 00:47:30.146 we're spending a lot of time on  
NOTE Confidence: 0.882367645

00:47:30.146 --> 00:47:32.248 now and think that it could really  
NOTE Confidence: 0.882367645

00:47:32.248 --> 00:47:33.500 help on intervention and  
NOTE Confidence: 0.920172645

00:47:33.566 --> 00:47:35.703 biomarker analysis, but without it's  
NOTE Confidence: 0.920172645

00:47:35.703 --> 00:47:38.160 a little difficult to study in the  
NOTE Confidence: 0.920172645

00:47:38.237 --> 00:47:40.925 humans 'cause we only have cross  
NOTE Confidence: 0.920172645

00:47:40.925 --> 00:47:42.717 sectional sections are announced  
NOTE Confidence: 0.920172645

00:47:42.790 --> 00:47:44.880 system not longitudinal like you can  
NOTE Confidence: 0.920172645

00:47:44.880 --> 00:47:47.490 do in fortunately do in mouse models.  
NOTE Confidence: 0.920172645

00:47:47.490 --> 00:47:49.464 So I think we're on time here,  
NOTE Confidence: 0.920172645

00:47:49.470 --> 00:47:51.750 but again, there's so many people.  
NOTE Confidence: 0.920172645

00:47:51.750 --> 00:47:54.850 To thank UM that are part of the team here.  
NOTE Confidence: 0.920172645

00:47:54.850 --> 00:47:57.910 It takes a huge operation to like I say,  
NOTE Confidence: 0.920172645

00:47:57.910 --> 00:48:00.518 collect all of these.  
NOTE Confidence: 0.920172645

00:48:00.520 --> 00:48:02.290 Organs and tissues for the studies.  
NOTE Confidence: 0.920172645

00:48:02.290 --> 00:48:04.789 So I want to give them appropriate



NOTE Confidence: 0.920172645  
00:48:04.789 --> 00:48:05.860 knowledgement and again,  
NOTE Confidence: 0.920172645  
00:48:05.860 --> 00:48:07.492 thank you for listening and I'll  
NOTE Confidence: 0.920172645  
00:48:07.492 --> 00:48:09.389 be happy to answer any questions.  
NOTE Confidence: 0.904463242  
00:48:11.210 --> 00:48:12.660 Thank you very much, Mark,  
NOTE Confidence: 0.904463242  
00:48:12.660 --> 00:48:13.976 and that this is a you know,  
NOTE Confidence: 0.904463242  
00:48:13.980 --> 00:48:14.952 fantastic seminar.  
NOTE Confidence: 0.904463242  
00:48:14.952 --> 00:48:17.868 So now is open for question,  
NOTE Confidence: 0.904463242  
00:48:17.870 --> 00:48:20.950 and while other you know you can just  
NOTE Confidence: 0.904463242  
00:48:20.950 --> 00:48:23.769 because we cannot steal so you can  
NOTE Confidence: 0.904463242  
00:48:23.769 --> 00:48:26.667 either just type you know into the  
NOTE Confidence: 0.904463242  
00:48:26.667 --> 00:48:29.600 you know question and answer you know  
NOTE Confidence: 0.904463242  
00:48:29.600 --> 00:48:32.840 chat box or you can just speak up.  
NOTE Confidence: 0.904463242  
00:48:32.840 --> 00:48:35.304 So before other people ask maybe I  
NOTE Confidence: 0.904463242  
00:48:35.304 --> 00:48:38.232 will ask one question Mark and this  
NOTE Confidence: 0.904463242  
00:48:38.232 --> 00:48:40.926 is related to beta cell regeneration.  
NOTE Confidence: 0.904463242

00:48:40.930 --> 00:48:42.136 The overall concept,  
NOTE Confidence: 0.904463242

00:48:42.136 --> 00:48:44.146 for example through all these,  
NOTE Confidence: 0.904463242

00:48:44.150 --> 00:48:47.158 you know the the donor tissue from pancreas,  
NOTE Confidence: 0.904463242

00:48:47.160 --> 00:48:47.940 have you?  
NOTE Confidence: 0.904463242

00:48:47.940 --> 00:48:50.280 You know your team have gained  
NOTE Confidence: 0.904463242

00:48:50.280 --> 00:48:51.843 additional insight into the  
NOTE Confidence: 0.904463242

00:48:51.843 --> 00:48:53.973 potential for beta cell and dodge,  
NOTE Confidence: 0.904463242

00:48:53.980 --> 00:48:56.927 and I mean endogenous beta cell regeneration.  
NOTE Confidence: 0.904463242

00:48:56.930 --> 00:48:58.250 All the precursor.  
NOTE Confidence: 0.904463242

00:48:58.250 --> 00:48:59.570 In other words,  
NOTE Confidence: 0.904463242

00:48:59.570 --> 00:49:02.506 the stem cell of the potential bid cells.  
NOTE Confidence: 0.904463242

00:49:02.510 --> 00:49:04.980 Have you gain additional insight?  
NOTE Confidence: 0.904463242

00:49:04.980 --> 00:49:05.400 Yeah,  
NOTE Confidence: 0.85531676777778

00:49:05.430 --> 00:49:08.904 so let me give one little insight about this.  
NOTE Confidence: 0.85531676777778

00:49:08.910 --> 00:49:10.860 Again, the the world grew  
NOTE Confidence: 0.85531676777778

00:49:10.860 --> 00:49:12.420 a lot of encouragement.

NOTE Confidence: 0.85531676777778

00:49:12.420 --> 00:49:15.157 Comment on the announcement about two weeks

NOTE Confidence: 0.85531676777778

00:49:15.157 --> 00:49:18.319 ago on Monday of a study by Vertex Pharma,

NOTE Confidence: 0.85531676777778

00:49:18.320 --> 00:49:20.000 where they've been studying,

NOTE Confidence: 0.85531676777778

00:49:20.000 --> 00:49:23.699 it grew out of Doug Melton's lab at Harvard,

NOTE Confidence: 0.85531676777778

00:49:23.700 --> 00:49:26.480 and they have a now a stem cell line that

NOTE Confidence: 0.85531676777778

00:49:26.551 --> 00:49:28.980 they've that's been put into. Patients.

NOTE Confidence: 0.85531676777778

00:49:28.980 --> 00:49:32.200 It you transfuse it into the they,

NOTE Confidence: 0.85531676777778

00:49:32.200 --> 00:49:35.148 transfuse it into the liver, and the

NOTE Confidence: 0.85531676777778

00:49:35.148 --> 00:49:36.918 patients have to take immunosuppression,

NOTE Confidence: 0.85531676777778

00:49:36.920 --> 00:49:40.016 but at least the after 90 days these

NOTE Confidence: 0.85531676777778

00:49:40.016 --> 00:49:42.950 individuals are starting to produce insulin.

NOTE Confidence: 0.85531676777778

00:49:42.950 --> 00:49:45.446 Or or as measured by C peptide and

NOTE Confidence: 0.85531676777778

00:49:45.446 --> 00:49:47.890 the need for taking less insulin.

NOTE Confidence: 0.85531676777778

00:49:47.890 --> 00:49:51.138 So regenerative medicine stem cell is alive

NOTE Confidence: 0.85531676777778

00:49:51.138 --> 00:49:54.599 and well in type one still has challenges,

NOTE Confidence: 0.85531676777778

00:49:54.599 --> 00:49:56.764 but now to your question  
NOTE Confidence: 0.855316767777778

00:49:56.764 --> 00:49:57.782 about endogenous replication.  
NOTE Confidence: 0.855316767777778

00:49:57.782 --> 00:50:00.690 That's have been a bit more of a challenge.  
NOTE Confidence: 0.855316767777778

00:50:00.690 --> 00:50:03.298 We do understand a lot of this works  
NOTE Confidence: 0.855316767777778

00:50:03.298 --> 00:50:06.148 been done by individuals at Mount Sinai,  
NOTE Confidence: 0.855316767777778

00:50:06.150 --> 00:50:07.940 but there's these molecules that  
NOTE Confidence: 0.855316767777778

00:50:07.940 --> 00:50:09.990 called Dirk 1A and Dirk 1B.  
NOTE Confidence: 0.855316767777778

00:50:09.990 --> 00:50:11.358 They're like breaks.  
NOTE Confidence: 0.855316767777778

00:50:11.358 --> 00:50:13.166 If you would that.  
NOTE Confidence: 0.855316767777778

00:50:13.166 --> 00:50:16.654 Go on in and inhibit the beta cells  
NOTE Confidence: 0.855316767777778

00:50:16.654 --> 00:50:19.560 from replication and an adult,  
NOTE Confidence: 0.855316767777778

00:50:19.560 --> 00:50:20.919 uh, islet cell.  
NOTE Confidence: 0.855316767777778

00:50:20.919 --> 00:50:25.156 Now there's a lot of efforts to try and  
NOTE Confidence: 0.855316767777778

00:50:25.156 --> 00:50:29.340 develop ways that you could deliver.  
NOTE Confidence: 0.855316767777778

00:50:29.340 --> 00:50:31.380 Molecules that are that are capable  
NOTE Confidence: 0.855316767777778

00:50:31.380 --> 00:50:33.160 of essentially removing those breaks,

NOTE Confidence: 0.85531676777778  
00:50:33.160 --> 00:50:34.889 and there's I know of at least  
NOTE Confidence: 0.85531676777778  
00:50:34.889 --> 00:50:35.880 four compounds than one.  
NOTE Confidence: 0.85531676777778  
00:50:35.880 --> 00:50:38.915 Most common is called harmine that do that,  
NOTE Confidence: 0.85531676777778  
00:50:38.915 --> 00:50:41.394 but the challenges is how do you X vivo  
NOTE Confidence: 0.85531676777778  
00:50:41.394 --> 00:50:43.599 deliver them and get beta cells specificity?  
NOTE Confidence: 0.85531676777778  
00:50:43.600 --> 00:50:45.584 A lot of these.  
NOTE Confidence: 0.85531676777778  
00:50:45.584 --> 00:50:48.064 Molecules that are lindwood induced  
NOTE Confidence: 0.85531676777778  
00:50:48.064 --> 00:50:50.738 replication of beta cells in the body.  
NOTE Confidence: 0.85531676777778  
00:50:50.738 --> 00:50:52.874 They they have off target effects.  
NOTE Confidence: 0.85531676777778  
00:50:52.880 --> 00:50:55.370 So like you know you,  
NOTE Confidence: 0.85531676777778  
00:50:55.370 --> 00:50:57.880 you don't necessarily want you  
NOTE Confidence: 0.85531676777778  
00:50:57.880 --> 00:50:59.888 know your cardiac replication,  
NOTE Confidence: 0.85531676777778  
00:50:59.890 --> 00:51:00.664 hepatic replications,  
NOTE Confidence: 0.85531676777778  
00:51:00.664 --> 00:51:03.373 stuff like that so that that field  
NOTE Confidence: 0.85531676777778  
00:51:03.373 --> 00:51:05.479 still is a little too long an  
NOTE Confidence: 0.85531676777778

00:51:05.479 --> 00:51:07.330 answer to say people are trying,  
NOTE Confidence: 0.855316767777778

00:51:07.330 --> 00:51:10.160 but it's a little bit of a challenge to get  
NOTE Confidence: 0.855316767777778

00:51:10.226 --> 00:51:12.660 specificity and targeting to the pancreas.  
NOTE Confidence: 0.806944202307692

00:51:13.510 --> 00:51:15.589 Saints Mark now I have a question  
NOTE Confidence: 0.806944202307692

00:51:15.589 --> 00:51:18.042 from a Kevin and you know he say.  
NOTE Confidence: 0.806944202307692

00:51:18.042 --> 00:51:20.208 Can you say anything about the  
NOTE Confidence: 0.806944202307692

00:51:20.208 --> 00:51:22.488 features of the beta cells in  
NOTE Confidence: 0.806944202307692

00:51:22.488 --> 00:51:24.702 long term surviving beta cells in  
NOTE Confidence: 0.806944202307692

00:51:24.776 --> 00:51:27.016 someone with type one diabetes?  
NOTE Confidence: 0.846460643571429

00:51:27.390 --> 00:51:29.736 Yeah, so that yeah, that's that's  
NOTE Confidence: 0.846460643571429

00:51:29.736 --> 00:51:32.388 a great question and we we are now.  
NOTE Confidence: 0.846460643571429

00:51:32.390 --> 00:51:34.892 I have 12 different cases that  
NOTE Confidence: 0.846460643571429

00:51:34.892 --> 00:51:37.480 are just what Kevin asked for.  
NOTE Confidence: 0.846460643571429

00:51:37.480 --> 00:51:38.872 They are longstanding.  
NOTE Confidence: 0.846460643571429

00:51:38.872 --> 00:51:42.547 They've had type one diabetes at least 20  
NOTE Confidence: 0.846460643571429

00:51:42.547 --> 00:51:44.490 years, and we're running those source.

NOTE Confidence: 0.846460643571429

00:51:44.490 --> 00:51:46.930 I talk panel. Right now,

NOTE Confidence: 0.846460643571429

00:51:46.930 --> 00:51:48.876 and I hope you know, maybe by the

NOTE Confidence: 0.846460643571429

00:51:48.876 --> 00:51:50.430 end pod meeting that will stand it.

NOTE Confidence: 0.846460643571429

00:51:50.430 --> 00:51:53.581 So just serve virus stands that

NOTE Confidence: 0.846460643571429

00:51:53.581 --> 00:51:55.927 same Susan monitor weird that I

NOTE Confidence: 0.846460643571429

00:51:55.927 --> 00:51:58.170 mentioned with the growth charts,

NOTE Confidence: 0.846460643571429

00:51:58.170 --> 00:51:59.544 they've been stunning.

NOTE Confidence: 0.846460643571429

00:51:59.544 --> 00:52:02.750 Dozens and dozens of patients that had

NOTE Confidence: 0.846460643571429

00:52:02.832 --> 00:52:06.505 type one diabetes for at least 50 years, 50.

NOTE Confidence: 0.846460643571429

00:52:06.505 --> 00:52:10.495 They're called medalists and what she

NOTE Confidence: 0.846460643571429

00:52:10.495 --> 00:52:13.018 published was essentially, you know.

NOTE Confidence: 0.846460643571429

00:52:13.018 --> 00:52:14.602 Again, it's central dogma is is

NOTE Confidence: 0.846460643571429

00:52:14.602 --> 00:52:16.505 that within a few years all the

NOTE Confidence: 0.846460643571429

00:52:16.505 --> 00:52:17.825 insulin producing cells are gone,

NOTE Confidence: 0.846460643571429

00:52:17.830 --> 00:52:19.306 wiped out the like.

NOTE Confidence: 0.846460643571429

00:52:19.306 --> 00:52:22.462 She's found that if you have a whole  
NOTE Confidence: 0.846460643571429

00:52:22.462 --> 00:52:25.458 pancreas and look hard enough you'll find.  
NOTE Confidence: 0.846460643571429

00:52:25.460 --> 00:52:27.680 Insulin positive beta cells.  
NOTE Confidence: 0.846460643571429

00:52:27.680 --> 00:52:29.900 Decades after disease onset.  
NOTE Confidence: 0.846460643571429

00:52:29.900 --> 00:52:32.448 So they may autoimmune response for some.  
NOTE Confidence: 0.846460643571429

00:52:32.450 --> 00:52:33.272 Whatever reason.  
NOTE Confidence: 0.846460643571429

00:52:33.272 --> 00:52:35.327 It never goes quite completion.  
NOTE Confidence: 0.846460643571429

00:52:35.330 --> 00:52:38.356 It never wipes out all of the beta cells.  
NOTE Confidence: 0.846460643571429

00:52:38.356 --> 00:52:41.177 So Kevin's question is a great one.  
NOTE Confidence: 0.846460643571429

00:52:41.180 --> 00:52:44.000 So what makes though? Is it?  
NOTE Confidence: 0.846460643571429

00:52:44.000 --> 00:52:46.295 It almost is a chicken and egg thing there.  
NOTE Confidence: 0.846460643571429

00:52:46.300 --> 00:52:49.250 What makes those cells resistant  
NOTE Confidence: 0.846460643571429

00:52:49.250 --> 00:52:51.020 to final destruction?  
NOTE Confidence: 0.846460643571429

00:52:51.020 --> 00:52:51.370 What?  
NOTE Confidence: 0.846460643571429

00:52:51.370 --> 00:52:53.120 What property do they have?  
NOTE Confidence: 0.846460643571429

00:52:53.120 --> 00:52:55.010 And if we knew that that that



NOTE Confidence: 0.846460643571429  
00:52:55.010 --> 00:52:56.640 might be very informative.  
NOTE Confidence: 0.846460643571429  
00:52:56.640 --> 00:52:59.062 To you know, a clinical trial or  
NOTE Confidence: 0.846460643571429  
00:52:59.062 --> 00:53:01.770 something to do to make a like a bait.  
NOTE Confidence: 0.846460643571429  
00:53:01.770 --> 00:53:04.100 People, sometimes called beta guard.  
NOTE Confidence: 0.846460643571429  
00:53:04.100 --> 00:53:05.320 Or is it the immune?  
NOTE Confidence: 0.846460643571429  
00:53:05.320 --> 00:53:07.504 What is it some problem with the immune  
NOTE Confidence: 0.846460643571429  
00:53:07.504 --> 00:53:09.055 response where the immune response  
NOTE Confidence: 0.846460643571429  
00:53:09.055 --> 00:53:10.945 just doesn't bring it to completion?  
NOTE Confidence: 0.846460643571429  
00:53:10.950 --> 00:53:13.690 So it's a great question.  
NOTE Confidence: 0.846460643571429  
00:53:13.690 --> 00:53:15.208 And we're working on but don't  
NOTE Confidence: 0.846460643571429  
00:53:15.208 --> 00:53:16.220 have an answer yet.  
NOTE Confidence: 0.803819335217391  
00:53:17.070 --> 00:53:17.878 Thanks, Margaret.  
NOTE Confidence: 0.803819335217391  
00:53:17.878 --> 00:53:20.302 Now we have question from Johnson  
NOTE Confidence: 0.803819335217391  
00:53:20.302 --> 00:53:22.993 Art and it's a current belief  
NOTE Confidence: 0.803819335217391  
00:53:22.993 --> 00:53:24.801 that autoantibodies to eyelids  
NOTE Confidence: 0.803819335217391

00:53:24.801 --> 00:53:26.810 are secondary to the disease,  
NOTE Confidence: 0.803819335217391

00:53:26.810 --> 00:53:29.960 rather than having a causative role.  
NOTE Confidence: 0.877898436

00:53:30.610 --> 00:53:34.750 Yeah, another great question so.  
NOTE Confidence: 0.877898436

00:53:34.750 --> 00:53:37.732 It I one thing people agree on  
NOTE Confidence: 0.877898436

00:53:37.732 --> 00:53:40.066 is that autoantibodies are the  
NOTE Confidence: 0.877898436

00:53:40.066 --> 00:53:41.998 smoke representing the fire,  
NOTE Confidence: 0.877898436

00:53:42.000 --> 00:53:44.989 and that they they're used as tremendous  
NOTE Confidence: 0.877898436

00:53:44.989 --> 00:53:47.140 markers of disease prediction,  
NOTE Confidence: 0.877898436

00:53:47.140 --> 00:53:49.508 identifying people at risk.  
NOTE Confidence: 0.877898436

00:53:49.508 --> 00:53:53.540 The assays have gotten really good now.  
NOTE Confidence: 0.877898436

00:53:53.540 --> 00:53:55.675 And so they're used as a uh,  
NOTE Confidence: 0.877898436

00:53:55.680 --> 00:53:58.150 as a biomarker is unquestioned  
NOTE Confidence: 0.877898436

00:53:58.150 --> 00:54:01.060 now in terms of pathogenic Lee.  
NOTE Confidence: 0.877898436

00:54:01.060 --> 00:54:02.398 What they do?  
NOTE Confidence: 0.877898436

00:54:02.398 --> 00:54:05.074 There's few people that believe the  
NOTE Confidence: 0.877898436

00:54:05.074 --> 00:54:07.138 antibodies in and of themselves

NOTE Confidence: 0.877898436

00:54:07.138 --> 00:54:09.454 play a functional role in terms

NOTE Confidence: 0.877898436

00:54:09.534 --> 00:54:11.689 of destruction of beta cells,

NOTE Confidence: 0.877898436

00:54:11.690 --> 00:54:14.562 save through cytolytic mechanisms,

NOTE Confidence: 0.877898436

00:54:14.562 --> 00:54:15.998 for example.

NOTE Confidence: 0.877898436

00:54:16.000 --> 00:54:18.160 But what has there is evidence

NOTE Confidence: 0.877898436

00:54:18.160 --> 00:54:21.365 to show is is that these are

NOTE Confidence: 0.877898436

00:54:21.365 --> 00:54:23.609 very effective antigen producing.

NOTE Confidence: 0.877898436

00:54:23.610 --> 00:54:26.710 Uh, presenting cells excuse me

NOTE Confidence: 0.877898436

00:54:26.710 --> 00:54:28.880 Apcs and so that's right now

NOTE Confidence: 0.877898436

00:54:28.880 --> 00:54:31.165 pretty much the state of the art

NOTE Confidence: 0.877898436

00:54:31.165 --> 00:54:32.825 in terms of functional role.

NOTE Confidence: 0.877898436

00:54:32.830 --> 00:54:33.878 And I should say,

NOTE Confidence: 0.877898436

00:54:33.878 --> 00:54:34.926 and Kevin knows this,

NOTE Confidence: 0.877898436

00:54:34.930 --> 00:54:36.778 he was part of the study.

NOTE Confidence: 0.877898436

00:54:36.780 --> 00:54:38.688 There has been one of those

NOTE Confidence: 0.877898436

00:54:38.688 --> 00:54:40.403 clinical trials I mentioned the  
NOTE Confidence: 0.877898436

00:54:40.403 --> 00:54:42.472 beginning and people probably are  
NOTE Confidence: 0.877898436

00:54:42.472 --> 00:54:45.204 familiar with Rituxan mab you can.  
NOTE Confidence: 0.877898436

00:54:45.204 --> 00:54:45.721 Uhm,  
NOTE Confidence: 0.877898436

00:54:45.721 --> 00:54:48.306 delay the progression of type  
NOTE Confidence: 0.877898436

00:54:48.306 --> 00:54:50.550 one diabetes after onset.  
NOTE Confidence: 0.877898436

00:54:50.550 --> 00:54:53.130 The loss of the beta cells  
NOTE Confidence: 0.877898436

00:54:53.130 --> 00:54:54.850 by using that agent.  
NOTE Confidence: 0.877898436

00:54:54.850 --> 00:54:57.370 Rotax map and kind of consistent  
NOTE Confidence: 0.877898436

00:54:57.370 --> 00:54:58.210 with pathology.  
NOTE Confidence: 0.877898436

00:54:58.210 --> 00:55:00.110 It seems to work better  
NOTE Confidence: 0.877898436

00:55:00.110 --> 00:55:01.250 in younger individuals.  
NOTE Confidence: 0.877898436

00:55:01.250 --> 00:55:03.140 Sort of consistent with that B  
NOTE Confidence: 0.877898436

00:55:03.140 --> 00:55:05.110 lymphocyte being may be pathogenic.  
NOTE Confidence: 0.877898436

00:55:05.110 --> 00:55:07.969 Lee involved so.  
NOTE Confidence: 0.877898436

00:55:07.970 --> 00:55:10.896 There there are hints that B cells

NOTE Confidence: 0.877898436

00:55:10.896 --> 00:55:14.530 are are involved in the disease pathogenesis,

NOTE Confidence: 0.877898436

00:55:14.530 --> 00:55:15.366 but antibodies,

NOTE Confidence: 0.877898436

00:55:15.366 --> 00:55:16.620 not so much.

NOTE Confidence: 0.721823852

00:55:17.900 --> 00:55:20.342 Thanks, now I have Caesar Laura

NOTE Confidence: 0.721823852

00:55:20.342 --> 00:55:23.594 Manuelidis that her hands up Laura.

NOTE Confidence: 0.721823852

00:55:23.600 --> 00:55:25.539 Please go ahead to ask their questions.

NOTE Confidence: 0.721823852

00:55:25.540 --> 00:55:27.706 Great, I was just thank you for your talk.

NOTE Confidence: 0.721823852

00:55:27.706 --> 00:55:29.409 I thought it was wonderful and very

NOTE Confidence: 0.888809284166667

00:55:29.420 --> 00:55:31.821 clear. So my first question is sort

NOTE Confidence: 0.888809284166667

00:55:31.821 --> 00:55:34.565 of broad question because what really

NOTE Confidence: 0.888809284166667

00:55:34.565 --> 00:55:37.752 insights or what ignites these sort of

NOTE Confidence: 0.888809284166667

00:55:37.752 --> 00:55:39.738 stress of of the diabetic response,

NOTE Confidence: 0.888809284166667

00:55:39.740 --> 00:55:41.052 especially over the age groups.

NOTE Confidence: 0.888809284166667

00:55:41.052 --> 00:55:42.610 So one of my questions was

NOTE Confidence: 0.800246492727273

00:55:42.930 --> 00:55:44.754 do you think that there's a role for

NOTE Confidence: 0.800246492727273

00:55:44.754 --> 00:55:48.272 any viruses or COVID viruses in sort of?

NOTE Confidence: 0.800246492727273

00:55:48.272 --> 00:55:51.490 Inciting some cases of diabetes.

NOTE Confidence: 0.800246492727273

00:55:51.490 --> 00:55:53.560 Early diabetes. Insulin was

NOTE Confidence: 0.800246492727273

00:55:53.560 --> 00:55:54.670 the second question, is this

NOTE Confidence: 0.884446582

00:55:54.680 --> 00:55:56.230 sort of more detailed question

NOTE Confidence: 0.78950165

00:55:56.700 --> 00:55:58.950 that I let cells are extremely

NOTE Confidence: 0.8403899875

00:55:58.960 --> 00:56:00.388 high in pryon protein?

NOTE Confidence: 0.879863501666667

00:56:01.130 --> 00:56:03.056 And in fact, prime protein is

NOTE Confidence: 0.833736915

00:56:03.070 --> 00:56:04.036 involved in neurogenesis

NOTE Confidence: 0.833736915

00:56:04.036 --> 00:56:05.646 in the very early stage.

NOTE Confidence: 0.833736915

00:56:05.650 --> 00:56:06.490 That's where it's critical

NOTE Confidence: 0.833736915

00:56:06.490 --> 00:56:08.890 stages and synopsis in Genesis,

NOTE Confidence: 0.833736915

00:56:08.890 --> 00:56:10.195 and I was wondering if you

NOTE Confidence: 0.833736915

00:56:10.195 --> 00:56:11.491 studied any prime protein in

NOTE Confidence: 0.833736915

00:56:11.491 --> 00:56:13.213 some of the early cases before

NOTE Confidence: 0.804943438

00:56:13.230 --> 00:56:14.766 the age of four versus later

NOTE Confidence: 0.804943438  
00:56:14.766 --> 00:56:16.796 to see if the expression really  
NOTE Confidence: 0.804943438  
00:56:16.796 --> 00:56:18.420 varies or is some indication  
NOTE Confidence: 0.965161538571429  
00:56:18.430 --> 00:56:20.775 of what's happening in terms of development  
NOTE Confidence: 0.7495057325  
00:56:20.790 --> 00:56:22.818 of islet cells. Thank  
NOTE Confidence: 0.861308632857143  
00:56:22.830 --> 00:56:24.526 you, oh thank you.  
NOTE Confidence: 0.861308632857143  
00:56:24.526 --> 00:56:25.798 Here's the challenge.  
NOTE Confidence: 0.861308632857143  
00:56:25.800 --> 00:56:27.180 I gotta remember both questions.  
NOTE Confidence: 0.861308632857143  
00:56:27.180 --> 00:56:28.530 Let me send the first one.  
NOTE Confidence: 0.861308632857143  
00:56:28.530 --> 00:56:31.120 So invite role of environment  
NOTE Confidence: 0.861308632857143  
00:56:31.120 --> 00:56:33.192 and type for decades.  
NOTE Confidence: 0.861308632857143  
00:56:33.200 --> 00:56:34.770 50 years people have looked,  
NOTE Confidence: 0.861308632857143  
00:56:34.770 --> 00:56:36.798 tried to look for the environment,  
NOTE Confidence: 0.861308632857143  
00:56:36.800 --> 00:56:38.492 contribution to diabetes.  
NOTE Confidence: 0.861308632857143  
00:56:38.492 --> 00:56:41.876 There's a lot of evidence were  
NOTE Confidence: 0.861308632857143  
00:56:41.876 --> 00:56:44.518 environment is playing a factor one.  
NOTE Confidence: 0.861308632857143

00:56:44.520 --> 00:56:46.956 If you look at incidence rates,  
NOTE Confidence: 0.861308632857143

00:56:46.960 --> 00:56:47.920 they're going up.  
NOTE Confidence: 0.861308632857143

00:56:47.920 --> 00:56:49.840 Can't be explained by genetics in  
NOTE Confidence: 0.861308632857143

00:56:49.840 --> 00:56:52.089 the like button and the the NIH for  
NOTE Confidence: 0.861308632857143

00:56:52.089 --> 00:56:54.671 about 18 years now has had a huge  
NOTE Confidence: 0.861308632857143

00:56:54.671 --> 00:56:56.043 environmental study where they've  
NOTE Confidence: 0.861308632857143

00:56:56.043 --> 00:56:59.370 looked at like 160 different things  
NOTE Confidence: 0.861308632857143

00:56:59.370 --> 00:57:02.350 in the environment from dietary.  
NOTE Confidence: 0.861308632857143

00:57:02.350 --> 00:57:06.616 Lifestyle practices yeah no smoking guns.  
NOTE Confidence: 0.77026268625

00:57:08.090 --> 00:57:09.570 Voice speaking about viruses  
NOTE Confidence: 0.77026268625

00:57:09.570 --> 00:57:11.050 covert virus is unknown.  
NOTE Confidence: 0.77026268625

00:57:11.050 --> 00:57:13.000 Viruses viruses at the security  
NOTE Confidence: 0.822603754

00:57:13.010 --> 00:57:15.329 bug they've been. They've taken samples  
NOTE Confidence: 0.822603754

00:57:15.329 --> 00:57:18.472 and unjust blast sequencing to try and  
NOTE Confidence: 0.822603754

00:57:18.472 --> 00:57:21.056 identify viral sequences, saying it,  
NOTE Confidence: 0.822603754

00:57:21.056 --> 00:57:24.150 it's it's murky at best. No smoking gun.



NOTE Confidence: 0.822603754

00:57:24.150 --> 00:57:25.950 Now to the quote kovid question.

NOTE Confidence: 0.822603754

00:57:25.950 --> 00:57:29.064 We've been involved and I've had a paper in

NOTE Confidence: 0.822603754

00:57:29.064 --> 00:57:32.259 cell and then Lance it within the last year

NOTE Confidence: 0.822603754

00:57:32.259 --> 00:57:35.197 and their evidence there is again murky.

NOTE Confidence: 0.822603754

00:57:35.200 --> 00:57:38.654 There's clearly an association.

NOTE Confidence: 0.822603754

00:57:38.654 --> 00:57:41.039 Between diet, diabetes and COVID,

NOTE Confidence: 0.822603754

00:57:41.040 --> 00:57:42.690 and in fact I'm working with,

NOTE Confidence: 0.822603754

00:57:42.690 --> 00:57:46.710 uh, Ruth, Montgomery and.

NOTE Confidence: 0.822603754

00:57:46.710 --> 00:57:49.830 David Hafler at your institution.

NOTE Confidence: 0.822603754

00:57:49.830 --> 00:57:51.594 We're part of a big consortium and

NOTE Confidence: 0.822603754

00:57:51.594 --> 00:57:53.682 this is one of the questions that

NOTE Confidence: 0.822603754

00:57:53.682 --> 00:57:55.590 we're looking at is the relationship

NOTE Confidence: 0.822603754

00:57:55.648 --> 00:57:57.128 between diabetes and COVID?

NOTE Confidence: 0.822603754

00:57:57.130 --> 00:57:59.715 Clearly you're susceptible for poor

NOTE Confidence: 0.822603754

00:57:59.715 --> 00:58:02.300 outcomes if you have diabetes?

NOTE Confidence: 0.822603754

00:58:02.300 --> 00:58:05.990 We've looked at like 54 pancreases.  
NOTE Confidence: 0.822603754

00:58:05.990 --> 00:58:08.468 From people who died from cold that  
NOTE Confidence: 0.822603754

00:58:08.468 --> 00:58:11.411 and tried to show that the there's  
NOTE Confidence: 0.822603754

00:58:11.411 --> 00:58:13.211 a relationship between positive  
NOTE Confidence: 0.822603754

00:58:13.211 --> 00:58:16.148 ITI for COVID in the pancreas and  
NOTE Confidence: 0.822603754

00:58:16.148 --> 00:58:18.103 diabetes and can't find it.  
NOTE Confidence: 0.822603754

00:58:18.110 --> 00:58:20.518 We've set up in vitro culture systems,  
NOTE Confidence: 0.822603754

00:58:20.520 --> 00:58:23.976 infected beta cells and islet cells,  
NOTE Confidence: 0.822603754

00:58:23.980 --> 00:58:26.884 and those you the number percentage of beta  
NOTE Confidence: 0.822603754

00:58:26.884 --> 00:58:30.080 cells you can affect is like 2% or less.  
NOTE Confidence: 0.822603754

00:58:30.080 --> 00:58:31.520 Very inefficient process.  
NOTE Confidence: 0.822603754

00:58:31.520 --> 00:58:33.236 We don't believe that.  
NOTE Confidence: 0.822603754

00:58:33.236 --> 00:58:35.381 There's people that believe that  
NOTE Confidence: 0.822603754

00:58:35.381 --> 00:58:37.577 COVID induces diabetes so far.  
NOTE Confidence: 0.822603754

00:58:37.580 --> 00:58:40.616 I don't that's unproven at best,  
NOTE Confidence: 0.822603754

00:58:40.620 --> 00:58:43.988 but it would take longer to answer that

NOTE Confidence: 0.822603754

00:58:43.988 --> 00:58:47.290 it would now to your Brian question,

NOTE Confidence: 0.822603754

00:58:47.290 --> 00:58:49.026 we published a paper about two months

NOTE Confidence: 0.822603754

00:58:49.026 --> 00:58:51.238 ago in this journal called Diabetologia,

NOTE Confidence: 0.822603754

00:58:51.240 --> 00:58:53.040 where we've looked at that and

NOTE Confidence: 0.822603754

00:58:53.040 --> 00:58:53.940 just nailed it.

NOTE Confidence: 0.822603754

00:58:53.940 --> 00:58:56.313 Just like what you said is that

NOTE Confidence: 0.822603754

00:58:56.313 --> 00:58:58.443 its expression is much higher in

NOTE Confidence: 0.822603754

00:58:58.443 --> 00:58:59.827 the Type 1 pancreas.

NOTE Confidence: 0.822603754

00:58:59.830 --> 00:59:01.732 And even in the Autoantibody positive

NOTE Confidence: 0.822603754

00:59:01.732 --> 00:59:03.550 pancreas than in the controls.

NOTE Confidence: 0.822603754

00:59:03.550 --> 00:59:04.918 We have not, however,

NOTE Confidence: 0.822603754

00:59:04.918 --> 00:59:07.539 looked at it as a function of age,

NOTE Confidence: 0.822603754

00:59:07.540 --> 00:59:09.860 and I'm going to write that down and

NOTE Confidence: 0.822603754

00:59:09.860 --> 00:59:12.999 then try and look and look at that

NOTE Confidence: 0.822603754

00:59:12.999 --> 00:59:15.515 after to see you know if we if we parse

NOTE Confidence: 0.822603754

00:59:15.515 --> 00:59:17.200 that out or at least like I can't,  
NOTE Confidence: 0.822603754

00:59:17.200 --> 00:59:18.130 I don't recall.  
NOTE Confidence: 0.822603754

00:59:18.130 --> 00:59:21.490 That we did it, but yes, you're right.  
NOTE Confidence: 0.822603754

00:59:21.490 --> 00:59:23.080 That is a.  
NOTE Confidence: 0.822603754

00:59:23.080 --> 00:59:25.186 Another factor that seems to be associated,  
NOTE Confidence: 0.827371251666667

00:59:25.440 --> 00:59:29.730 thanks another question from Doctor Merati.  
NOTE Confidence: 0.827371251666667

00:59:29.730 --> 00:59:32.621 So she's asking actually say how the  
NOTE Confidence: 0.827371251666667

00:59:32.621 --> 00:59:35.620 collection of the pancreas is organized?  
NOTE Confidence: 0.827371251666667

00:59:35.620 --> 00:59:38.660 Rapid autopsies? Specific pancreas  
NOTE Confidence: 0.827371251666667

00:59:38.660 --> 00:59:40.206 collection, biopsy, bulbank.  
NOTE Confidence: 0.827371251666667

00:59:40.206 --> 00:59:42.564 This is more relatable to empire.  
NOTE Confidence: 0.888864271666667

00:59:43.120 --> 00:59:44.836 Yeah, so that's a great question.  
NOTE Confidence: 0.888864271666667

00:59:44.840 --> 00:59:46.898 So no, although none of these  
NOTE Confidence: 0.888864271666667

00:59:46.900 --> 00:59:49.028 samples that I showed you or none  
NOTE Confidence: 0.888864271666667

00:59:49.028 --> 00:59:51.080 of our studies are with autopsy,  
NOTE Confidence: 0.888864271666667

00:59:51.080 --> 00:59:53.580 they are all with transplant.

NOTE Confidence: 0.888864271666667  
00:59:53.580 --> 00:59:54.286 Organ transplants,  
NOTE Confidence: 0.888864271666667  
00:59:54.286 --> 00:59:56.757 So what happens is we worked out  
NOTE Confidence: 0.888864271666667  
00:59:56.757 --> 00:59:58.960 with all of these doppio's in the  
NOTE Confidence: 0.888864271666667  
00:59:58.960 --> 01:00:01.000 United States that the same surgical  
NOTE Confidence: 0.888864271666667  
01:00:01.000 --> 01:00:03.016 recovery team that's taking the heart,  
NOTE Confidence: 0.888864271666667  
01:00:03.020 --> 01:00:05.222 lung, liver, kidney.  
NOTE Confidence: 0.888864271666667  
01:00:05.222 --> 01:00:06.690 Uhm, four.  
NOTE Confidence: 0.888864271666667  
01:00:06.690 --> 01:00:09.189 Then the next thing they do is  
NOTE Confidence: 0.888864271666667  
01:00:09.189 --> 01:00:11.649 take the pancreas for us so it's  
NOTE Confidence: 0.888864271666667  
01:00:11.649 --> 01:00:13.180 flushed and it's shipped here  
NOTE Confidence: 0.888864271666667  
01:00:13.180 --> 01:00:14.980 as if it's going for transplant.  
NOTE Confidence: 0.888864271666667  
01:00:14.980 --> 01:00:17.976 So although the processing is is done,  
NOTE Confidence: 0.888864271666667  
01:00:17.980 --> 01:00:20.578 just as if that the average  
NOTE Confidence: 0.888864271666667  
01:00:20.578 --> 01:00:22.827 time between cross clamp and  
NOTE Confidence: 0.888864271666667  
01:00:22.827 --> 01:00:25.395 delivery here is about 13 hours.  
NOTE Confidence: 0.888864271666667

01:00:25.400 --> 01:00:29.356 And so they're all the pancreatic biopsies  
NOTE Confidence: 0.888864271666667

01:00:29.356 --> 01:00:32.730 of living subjects are not thought ethical,  
NOTE Confidence: 0.888864271666667

01:00:32.730 --> 01:00:34.270 and for good reason.  
NOTE Confidence: 0.888864271666667

01:00:34.270 --> 01:00:35.040 I mean,  
NOTE Confidence: 0.888864271666667

01:00:35.040 --> 01:00:36.804 it was tried again about 10  
NOTE Confidence: 0.888864271666667

01:00:36.804 --> 01:00:38.899 years ago and had bad outcomes.  
NOTE Confidence: 0.888864271666667

01:00:38.900 --> 01:00:40.280 You don't biopsy the pancreas  
NOTE Confidence: 0.888864271666667

01:00:40.280 --> 01:00:41.660 unless you have two in.  
NOTE Confidence: 0.888864271666667

01:00:41.660 --> 01:00:43.858 I'm sure I'm all I'm doing is  
NOTE Confidence: 0.888864271666667

01:00:43.858 --> 01:00:45.490 telling you what you know.  
NOTE Confidence: 0.888864271666667

01:00:45.490 --> 01:00:47.320 In the autopsy tissues you  
NOTE Confidence: 0.888864271666667

01:00:47.320 --> 01:00:50.034 know on the few times those we  
NOTE Confidence: 0.888864271666667

01:00:50.034 --> 01:00:52.049 are getting using park obit.  
NOTE Confidence: 0.888864271666667

01:00:52.050 --> 01:00:54.822 For those cases we were bound to  
NOTE Confidence: 0.888864271666667

01:00:54.822 --> 01:00:57.838 use for COVID for the most part,  
NOTE Confidence: 0.888864271666667

01:00:57.838 --> 01:00:59.666 but we are recovering.

NOTE Confidence: 0.888864271666667  
01:00:59.670 --> 01:01:01.908 On pancreas for for transplant from  
NOTE Confidence: 0.888864271666667  
01:01:01.908 --> 01:01:03.763 transplant cases where they once  
NOTE Confidence: 0.888864271666667  
01:01:03.763 --> 01:01:05.835 had COVID but are now PCR negative.  
NOTE Confidence: 0.742804702857143  
01:01:07.910 --> 01:01:11.144 Thanks, we have a question from a.  
NOTE Confidence: 0.742804702857143  
01:01:11.150 --> 01:01:13.766 I think wins hands down wins.  
NOTE Confidence: 0.742804702857143  
01:01:13.770 --> 01:01:15.866 You know you can ask your question please.  
NOTE Confidence: 0.742804702857143  
01:01:15.870 --> 01:01:18.294 Yes, you mentioned that the blood  
NOTE Confidence: 0.742804702857143  
01:01:18.294 --> 01:01:20.442 Kappel Aries in blood vessels  
NOTE Confidence: 0.742804702857143  
01:01:20.442 --> 01:01:22.707 in like the pilots breakdown.  
NOTE Confidence: 0.742804702857143  
01:01:22.710 --> 01:01:24.210 How does that work?  
NOTE Confidence: 0.742804702857143  
01:01:24.210 --> 01:01:27.190 What do you think is happening? So  
NOTE Confidence: 0.788389783333333  
01:01:28.140 --> 01:01:30.300 yeah, that we don't know yet.  
NOTE Confidence: 0.788389783333333  
01:01:30.300 --> 01:01:31.416 And again I was my second  
NOTE Confidence: 0.788389783333333  
01:01:31.416 --> 01:01:32.579 time we're going to use this.  
NOTE Confidence: 0.788389783333333  
01:01:32.580 --> 01:01:35.900 We don't know exactly the there's a lot  
NOTE Confidence: 0.788389783333333

01:01:35.900 --> 01:01:38.720 of there's a lot of speculation about  
NOTE Confidence: 0.7883897833333333

01:01:38.720 --> 01:01:42.162 the the impact of having a loss of  
NOTE Confidence: 0.7883897833333333

01:01:42.162 --> 01:01:44.796 insulin at the self communication level,  
NOTE Confidence: 0.7883897833333333

01:01:44.800 --> 01:01:47.240 and that again you start out in life.  
NOTE Confidence: 0.7883897833333333

01:01:47.240 --> 01:01:49.205 You have these essentially factories  
NOTE Confidence: 0.7883897833333333

01:01:49.205 --> 01:01:52.229 that just produce a lot of insulin and.  
NOTE Confidence: 0.7883897833333333

01:01:52.230 --> 01:01:54.612 It's both a trophic factor and  
NOTE Confidence: 0.7883897833333333

01:01:54.612 --> 01:01:56.200 has so many other.  
NOTE Confidence: 0.7883897833333333

01:01:56.200 --> 01:01:58.660 Properties that there's the speculation is,  
NOTE Confidence: 0.7883897833333333

01:01:58.660 --> 01:02:00.301 although it's unproven  
NOTE Confidence: 0.7883897833333333

01:02:00.301 --> 01:02:03.036 that as you lose insulin,  
NOTE Confidence: 0.7883897833333333

01:02:03.040 --> 01:02:06.550 the insulin producing cells that that'll  
NOTE Confidence: 0.7883897833333333

01:02:06.550 --> 01:02:10.035 have downstream effects and one will  
NOTE Confidence: 0.7883897833333333

01:02:10.035 --> 01:02:12.675 be again vasculature or capillary.  
NOTE Confidence: 0.7883897833333333

01:02:12.680 --> 01:02:14.564 Shared with one of your colleagues  
NOTE Confidence: 0.7883897833333333

01:02:14.564 --> 01:02:16.424 this morning I turned into grant



NOTE Confidence: 0.7883897833333333  
01:02:16.424 --> 01:02:18.068 two weeks ago where we're going  
NOTE Confidence: 0.7883897833333333  
01:02:18.068 --> 01:02:20.396 to try and take a look at this  
NOTE Confidence: 0.7883897833333333  
01:02:20.396 --> 01:02:22.668 functionally and figure out why it is.  
NOTE Confidence: 0.7883897833333333  
01:02:22.668 --> 01:02:25.190 But yeah, I.  
NOTE Confidence: 0.7883897833333333  
01:02:25.190 --> 01:02:27.134 I should say, and I didn't put in here.  
NOTE Confidence: 0.7883897833333333  
01:02:27.140 --> 01:02:28.100 The other thing is,  
NOTE Confidence: 0.7883897833333333  
01:02:28.100 --> 01:02:29.540 is that people have been looking  
NOTE Confidence: 0.7883897833333333  
01:02:29.593 --> 01:02:30.745 at a lot of the neuronal.  
NOTE Confidence: 0.8330083193333333  
01:02:32.910 --> 01:02:35.220 Yeah, impacts and that are  
NOTE Confidence: 0.8330083193333333  
01:02:35.220 --> 01:02:37.530 occurring there and those networks  
NOTE Confidence: 0.8330083193333333  
01:02:37.615 --> 01:02:39.740 also appear to be disrupted.  
NOTE Confidence: 0.9427557  
01:02:41.220 --> 01:02:44.728 OK, alright so then another  
NOTE Confidence: 0.9427557  
01:02:44.728 --> 01:02:46.636 question from David Rain.  
NOTE Confidence: 0.9427557  
01:02:46.640 --> 01:02:49.209 So what does it cost to get  
NOTE Confidence: 0.9427557  
01:02:49.209 --> 01:02:50.310 this transplant pancreas?  
NOTE Confidence: 0.763199199090909

01:02:50.860 --> 01:02:54.101 Yeah, so if you're going or pancreas  
NOTE Confidence: 0.763199199090909

01:02:54.101 --> 01:02:56.500 goals for clinical transplant,  
NOTE Confidence: 0.763199199090909

01:02:56.500 --> 01:02:59.675 the price can vary dramatically  
NOTE Confidence: 0.763199199090909

01:02:59.675 --> 01:03:03.434 from 28 thousand, \$35,000, or more,  
NOTE Confidence: 0.763199199090909

01:03:03.434 --> 01:03:07.176 but we've negotiated with with all the  
NOTE Confidence: 0.763199199090909

01:03:07.176 --> 01:03:09.286 opos either individual contracts or  
NOTE Confidence: 0.763199199090909

01:03:09.286 --> 01:03:11.440 through research and intermediaries.  
NOTE Confidence: 0.763199199090909

01:03:11.440 --> 01:03:14.010 We obtain the pancreas, spleen,  
NOTE Confidence: 0.763199199090909

01:03:14.010 --> 01:03:15.858 peripheral blood and started  
NOTE Confidence: 0.763199199090909

01:03:15.858 --> 01:03:19.680 tissues for about \$8000 a case.  
NOTE Confidence: 0.763199199090909

01:03:19.680 --> 01:03:23.117 8 So we get a research discount.  
NOTE Confidence: 0.763199199090909

01:03:23.120 --> 01:03:24.020 If you would say.  
NOTE Confidence: 0.763199199090909

01:03:24.020 --> 01:03:26.130 But we we are processing we collect about.  
NOTE Confidence: 0.845507102

01:03:28.150 --> 01:03:34.660 125 pancreas is a year, so it's a it's a lot.  
NOTE Confidence: 0.824249336190476

01:03:35.400 --> 01:03:38.096 OK thanks Mark, I know the time is  
NOTE Confidence: 0.824249336190476

01:03:38.096 --> 01:03:40.489 we have last question from Paul

NOTE Confidence: 0.824249336190476  
01:03:40.489 --> 01:03:43.270 and so I think his question is,  
NOTE Confidence: 0.824249336190476  
01:03:43.270 --> 01:03:46.085 given the microvascular pathology that  
NOTE Confidence: 0.824249336190476  
01:03:46.085 --> 01:03:48.337 characterized the clinical course,  
NOTE Confidence: 0.824249336190476  
01:03:48.340 --> 01:03:50.930 is there damage to the other blood  
NOTE Confidence: 0.824249336190476  
01:03:50.930 --> 01:03:53.010 vessels in other organs? Yeah,  
NOTE Confidence: 0.884090671923077  
01:03:53.230 --> 01:03:55.624 so the answer is yes and that this again  
NOTE Confidence: 0.884090671923077  
01:03:55.624 --> 01:03:58.181 goes back to that grant I just put in two  
NOTE Confidence: 0.884090671923077  
01:03:58.181 --> 01:04:00.500 weeks ago where what are moving forward,  
NOTE Confidence: 0.884090671923077  
01:04:00.500 --> 01:04:02.555 what we're proposing to do  
NOTE Confidence: 0.884090671923077  
01:04:02.555 --> 01:04:05.660 is collect hearts and.  
NOTE Confidence: 0.884090671923077  
01:04:05.660 --> 01:04:08.270 Uh, different vascular peripheral  
NOTE Confidence: 0.884090671923077  
01:04:08.270 --> 01:04:10.230 vascular tissues from individuals  
NOTE Confidence: 0.884090671923077  
01:04:10.230 --> 01:04:13.714 with type one diabetes, type 2 diabetes,  
NOTE Confidence: 0.884090671923077  
01:04:13.714 --> 01:04:16.004 and then people with cardiovascular  
NOTE Confidence: 0.884090671923077  
01:04:16.004 --> 01:04:18.215 disease that that don't have either  
NOTE Confidence: 0.884090671923077

01:04:18.215 --> 01:04:20.447 form of diabetes and we're hoping  
NOTE Confidence: 0.884090671923077

01:04:20.447 --> 01:04:22.547 to answer that question because,  
NOTE Confidence: 0.884090671923077

01:04:22.550 --> 01:04:25.006 again, this kind of goes back to my  
NOTE Confidence: 0.884090671923077

01:04:25.006 --> 01:04:26.850 earlier answer about insulin loss.  
NOTE Confidence: 0.884090671923077

01:04:26.850 --> 01:04:29.238 Is is that?  
NOTE Confidence: 0.884090671923077

01:04:29.240 --> 01:04:32.480 We we hope to identify differences  
NOTE Confidence: 0.884090671923077

01:04:32.480 --> 01:04:34.658 between type one and type 2 diabetes,  
NOTE Confidence: 0.884090671923077

01:04:34.660 --> 01:04:36.376 where again on the type one.  
NOTE Confidence: 0.884090671923077

01:04:36.380 --> 01:04:38.504 You don't have your endogenous insulin  
NOTE Confidence: 0.884090671923077

01:04:38.504 --> 01:04:40.336 production, where is in the Type 2.  
NOTE Confidence: 0.884090671923077

01:04:40.340 --> 01:04:43.398 It's going to be more on insulin action, etc.  
NOTE Confidence: 0.884090671923077

01:04:43.398 --> 01:04:44.754 So again,  
NOTE Confidence: 0.884090671923077

01:04:44.754 --> 01:04:47.502 a great question and I hope to  
NOTE Confidence: 0.884090671923077

01:04:47.502 --> 01:04:48.882 you know within a couple of years  
NOTE Confidence: 0.884090671923077

01:04:48.882 --> 01:04:50.187 we'll have some answers there.  
NOTE Confidence: 0.740390535

01:04:51.130 --> 01:04:54.049 OK with that and I was just

NOTE Confidence: 0.740390535

01:04:54.049 --> 01:04:55.310 really fantastic lecture.

NOTE Confidence: 0.740390535

01:04:55.310 --> 01:04:57.560 You know mark? I mean I, I just said,

NOTE Confidence: 0.740390535

01:04:57.560 --> 01:04:59.808 you know this is a really sad example.

NOTE Confidence: 0.740390535

01:04:59.808 --> 01:05:02.090 Say how to you know really using

NOTE Confidence: 0.740390535

01:05:02.158 --> 01:05:04.192 human tissue to discover all this

NOTE Confidence: 0.740390535

01:05:04.192 --> 01:05:06.490 new knowledge is and this is great.

NOTE Confidence: 0.740390535

01:05:06.490 --> 01:05:08.604 You know we wish you well and

NOTE Confidence: 0.740390535

01:05:08.604 --> 01:05:10.389 by selecting impact and study.

NOTE Confidence: 0.740390535

01:05:10.389 --> 01:05:13.140 And once again thank you very much

NOTE Confidence: 0.740390535

01:05:13.217 --> 01:05:16.089 for giving us the lecture and we will.

NOTE Confidence: 0.740390535

01:05:16.090 --> 01:05:18.619 I will you know when this all open up

NOTE Confidence: 0.740390535

01:05:18.619 --> 01:05:21.355 we want you to come here to visit us.

NOTE Confidence: 0.740390535

01:05:21.360 --> 01:05:22.865 Thank you, have a lot of connection

NOTE Confidence: 0.740390535

01:05:22.865 --> 01:05:23.510 at a year.

NOTE Confidence: 0.740390535

01:05:23.510 --> 01:05:25.843 You know, as you know you might feel OK.

NOTE Confidence: 0.740390535

01:05:25.843 --> 01:05:27.544 Once again, thank you very much Mark.

NOTE Confidence: 0.740390535

01:05:27.550 --> 01:05:29.516 And then we'll we'll be in contact.

NOTE Confidence: 0.740390535

01:05:29.516 --> 01:05:30.168 So Manjula,

NOTE Confidence: 0.740390535

01:05:30.168 --> 01:05:32.750 who is the director of our grandma man?

NOTE Confidence: 0.740390535

01:05:32.750 --> 01:05:36.020 Do you have any last word?

NOTE Confidence: 0.740390535

01:05:36.020 --> 01:05:38.648 No, really very exciting talk and

NOTE Confidence: 0.740390535

01:05:38.648 --> 01:05:41.310 there are many more questions,

NOTE Confidence: 0.740390535

01:05:41.310 --> 01:05:43.566 but we are out of time.

NOTE Confidence: 0.740390535

01:05:43.570 --> 01:05:46.488 OK, thank you again, Mark, thank you.

NOTE Confidence: 0.740390535

01:05:46.488 --> 01:05:49.550 Thank you. Have a nice day markets you too.

NOTE Confidence: 0.740390535

01:05:49.550 --> 01:05:50.240 OK, goodnight,

NOTE Confidence: 0.76274809

01:05:50.250 --> 01:05:51.000 see it's always.