

WEBVTT

NOTE duration:"00:58:09"

NOTE recognizability:0.873

NOTE language:en-us

NOTE Confidence: 0.852777176

00:00:00.000 --> 00:00:02.312 So good afternoon, afternoon

NOTE Confidence: 0.852777176

00:00:02.312 --> 00:00:05.780 again and welcome to grand Rounds.

NOTE Confidence: 0.852777176

00:00:05.780 --> 00:00:07.764 It's great to see so many of you

NOTE Confidence: 0.852777176

00:00:07.764 --> 00:00:09.310 joining us on zoom remotely.

NOTE Confidence: 0.852777176

00:00:09.310 --> 00:00:11.900 I hope that there's at least one or two of

NOTE Confidence: 0.852777176

00:00:11.968 --> 00:00:14.749 you in sunnier climes than here in New Haven.

NOTE Confidence: 0.852777176

00:00:14.750 --> 00:00:16.640 The only way that I can describe the weather

NOTE Confidence: 0.852777176

00:00:16.640 --> 00:00:18.393 here in New Haven is a little bit Irish,

NOTE Confidence: 0.852777176

00:00:18.400 --> 00:00:20.980 so I'm feeling very at home.

NOTE Confidence: 0.852777176

00:00:20.980 --> 00:00:23.038 And now when we launched this

NOTE Confidence: 0.852777176

00:00:23.038 --> 00:00:24.970 new series of grand rounds,

NOTE Confidence: 0.852777176

00:00:24.970 --> 00:00:26.850 we talked about the importance

NOTE Confidence: 0.852777176

00:00:26.850 --> 00:00:27.978 of building bridges,

NOTE Confidence: 0.852777176

00:00:27.980 --> 00:00:29.788 building bridges across research.

NOTE Confidence: 0.852777176

00:00:29.788 --> 00:00:31.596 Programs and clinical programs

NOTE Confidence: 0.852777176

00:00:31.596 --> 00:00:33.230 within our department,

NOTE Confidence: 0.852777176

00:00:33.230 --> 00:00:35.830 but also building bridges across

NOTE Confidence: 0.852777176

00:00:35.830 --> 00:00:36.870 different departments.

NOTE Confidence: 0.852777176

00:00:36.870 --> 00:00:37.986 Here at Yale,

NOTE Confidence: 0.852777176

00:00:37.986 --> 00:00:40.218 and I think that's really exemplified

NOTE Confidence: 0.852777176

00:00:40.218 --> 00:00:43.010 by our next to grand rounds speakers.

NOTE Confidence: 0.852777176

00:00:43.010 --> 00:00:45.747 So next week we'll hear from Doctor

NOTE Confidence: 0.852777176

00:00:45.747 --> 00:00:47.932 Marietta Vasquez who will talk to

NOTE Confidence: 0.852777176

00:00:47.932 --> 00:00:50.130 us about her work to address and

NOTE Confidence: 0.852777176

00:00:50.202 --> 00:00:52.837 combat structural racism in academic

NOTE Confidence: 0.852777176

00:00:52.837 --> 00:00:54.945 medicine and medical education.

NOTE Confidence: 0.852777176

00:00:54.950 --> 00:00:57.372 And today it is our great privilege

NOTE Confidence: 0.852777176

00:00:57.372 --> 00:00:59.373 to welcome another speaker from

NOTE Confidence: 0.852777176

00:00:59.373 --> 00:01:01.165 the Department of Pediatrics.

NOTE Confidence: 0.852777176

00:01:01.170 --> 00:01:03.135 Doctor most difficult who will

NOTE Confidence: 0.852777176

00:01:03.135 --> 00:01:06.092 speak to us today and Doctor Copas

NOTE Confidence: 0.852777176

00:01:06.092 --> 00:01:08.414 work really merges his fantastic

NOTE Confidence: 0.852777176

00:01:08.414 --> 00:01:11.150 and important work in the pediatric

NOTE Confidence: 0.852777176

00:01:11.223 --> 00:01:13.573 intensive care unit with critically

NOTE Confidence: 0.852777176

00:01:13.573 --> 00:01:15.923 ill children with some really

NOTE Confidence: 0.852777176

00:01:16.000 --> 00:01:18.280 elegant molecular biology and that

NOTE Confidence: 0.852777176

00:01:18.280 --> 00:01:20.815 molecular biology is done in the

NOTE Confidence: 0.852777176

00:01:20.815 --> 00:01:22.924 service of his patience and his

NOTE Confidence: 0.852777176

00:01:22.924 --> 00:01:24.709 families who are seeking answers

NOTE Confidence: 0.852777176

00:01:24.709 --> 00:01:27.865 at a time of a lot of stress and

NOTE Confidence: 0.852777176

00:01:27.865 --> 00:01:29.793 where their children are being

NOTE Confidence: 0.852777176

00:01:29.793 --> 00:01:32.328 born and suffering with congenital

NOTE Confidence: 0.852777176

00:01:32.328 --> 00:01:34.356 malformations and doctor Coco.

NOTE Confidence: 0.852777176

00:01:34.360 --> 00:01:36.458 Elegant molecular work really tries to

NOTE Confidence: 0.852777176

00:01:36.460 --> 00:01:38.791 find an answer to why these children

NOTE Confidence: 0.852777176

00:01:38.791 --> 00:01:40.756 are born with these congenital

NOTE Confidence: 0.852777176

00:01:40.756 --> 00:01:43.438 malformations and really to try and

NOTE Confidence: 0.852777176

00:01:43.438 --> 00:01:45.599 determine have medicine can help.

NOTE Confidence: 0.852777176

00:01:45.600 --> 00:01:47.704 So with that I would ask you to

NOTE Confidence: 0.852777176

00:01:47.704 --> 00:01:49.460 please join me in welcoming Dr.

NOTE Confidence: 0.852777176

00:01:49.460 --> 00:01:51.385 Moustapha Coca to grand rounds

NOTE Confidence: 0.852777176

00:01:51.385 --> 00:01:52.925 into job study center.

NOTE Confidence: 0.87350893

00:01:56.210 --> 00:02:00.520 Alright. Mask off.

NOTE Confidence: 0.87350893

00:02:00.520 --> 00:02:02.818 Thanks Karen for that very nice

NOTE Confidence: 0.87350893

00:02:02.818 --> 00:02:04.763 introduction and and the invitation

NOTE Confidence: 0.87350893

00:02:04.763 --> 00:02:07.499 to come here to talk to you today.

NOTE Confidence: 0.87350893

00:02:07.500 --> 00:02:10.882 You hear me OK, Yep, alright,

NOTE Confidence: 0.87350893

00:02:10.882 --> 00:02:12.570 so let's get started.

NOTE Confidence: 0.72118907

00:02:15.610 --> 00:02:17.759 OK, uh, no I don't have any.

NOTE Confidence: 0.72118907

00:02:17.760 --> 00:02:19.020 Well, I have one conflict.

NOTE Confidence: 0.72118907

00:02:19.020 --> 00:02:21.348 It's not at all relevant to the talk

NOTE Confidence: 0.72118907

00:02:21.348 --> 00:02:24.018 that I'm going to give today. See here.

NOTE Confidence: 0.72118907

00:02:24.018 --> 00:02:27.450 OK, so this is the outline of my talk.

NOTE Confidence: 0.72118907

00:02:27.450 --> 00:02:29.998 I I'd like to introduce the child

NOTE Confidence: 0.72118907

00:02:29.998 --> 00:02:31.822 with critical illness and our

NOTE Confidence: 0.72118907

00:02:31.822 --> 00:02:33.808 our efforts to sort of identify.

NOTE Confidence: 0.90536140875

00:02:35.850 --> 00:02:37.776 Genetic changes gene changes in the

NOTE Confidence: 0.90536140875

00:02:37.776 --> 00:02:39.839 genome that might address why these

NOTE Confidence: 0.90536140875

00:02:39.839 --> 00:02:41.279 children have critical illness,

NOTE Confidence: 0.90536140875

00:02:41.280 --> 00:02:42.870 so we'll talk about genomic testing

NOTE Confidence: 0.90536140875

00:02:42.870 --> 00:02:44.420 and the different kinds of genomic

NOTE Confidence: 0.90536140875

00:02:44.420 --> 00:02:45.960 testing that we could do at Yale,

NOTE Confidence: 0.90536140875

00:02:45.960 --> 00:02:47.752 both clinically and in the research realm

NOTE Confidence: 0.90536140875

00:02:47.752 --> 00:02:49.637 and and we'll talk about our program,

NOTE Confidence: 0.90536140875

00:02:49.640 --> 00:02:51.830 called the Pediatric Genomics Discovery

NOTE Confidence: 0.90536140875

00:02:51.830 --> 00:02:54.642 Program, really a translational research,
NOTE Confidence: 0.90536140875

00:02:54.642 --> 00:02:57.607 basic science and clinical translational
NOTE Confidence: 0.90536140875

00:02:57.607 --> 00:03:01.045 program in order to understand the
NOTE Confidence: 0.90536140875

00:03:01.045 --> 00:03:03.890 causes of children critical illness.
NOTE Confidence: 0.90536140875

00:03:03.890 --> 00:03:05.204 Uh, then it then that that's
NOTE Confidence: 0.90536140875

00:03:05.204 --> 00:03:06.559 the first part of the talk,
NOTE Confidence: 0.90536140875

00:03:06.560 --> 00:03:09.144 and then I'll talk about 3 short stories,
NOTE Confidence: 0.90536140875

00:03:09.150 --> 00:03:11.106 which include basic science,
NOTE Confidence: 0.90536140875

00:03:11.106 --> 00:03:13.551 and I've chosen these three
NOTE Confidence: 0.90536140875

00:03:13.551 --> 00:03:15.465 stories more for their.
NOTE Confidence: 0.90536140875

00:03:15.465 --> 00:03:17.365 I think clinical relevance,
NOTE Confidence: 0.90536140875

00:03:17.370 --> 00:03:19.715 and in the way they informed our
NOTE Confidence: 0.90536140875

00:03:19.715 --> 00:03:21.673 work with patients as opposed
NOTE Confidence: 0.90536140875

00:03:21.673 --> 00:03:23.429 to basic science discoveries.
NOTE Confidence: 0.90536140875

00:03:23.430 --> 00:03:25.674 So I hope that you'll find
NOTE Confidence: 0.90536140875

00:03:25.674 --> 00:03:27.530 them very interesting and and.

NOTE Confidence: 0.90536140875

00:03:27.530 --> 00:03:29.742 And for us it's been really powerful

NOTE Confidence: 0.90536140875

00:03:29.742 --> 00:03:31.625 because they've been so after the

NOTE Confidence: 0.90536140875

00:03:31.625 --> 00:03:33.676 results that we've gotten from them have

NOTE Confidence: 0.90536140875

00:03:33.740 --> 00:03:35.678 been so applicable to patient care.

NOTE Confidence: 0.90536140875

00:03:35.680 --> 00:03:35.920 OK,

NOTE Confidence: 0.90536140875

00:03:35.920 --> 00:03:37.840 so you know this is this is the

NOTE Confidence: 0.90536140875

00:03:37.840 --> 00:03:40.424 kind of care that we provide in in

NOTE Confidence: 0.90536140875

00:03:40.424 --> 00:03:41.399 pediatric critical care.

NOTE Confidence: 0.90536140875

00:03:41.400 --> 00:03:44.011 You can see there's this tiny baby

NOTE Confidence: 0.90536140875

00:03:44.011 --> 00:03:46.508 surrounded by enormous amount of machinery.

NOTE Confidence: 0.90536140875

00:03:46.510 --> 00:03:48.654 And what we find now is that you

NOTE Confidence: 0.90536140875

00:03:48.654 --> 00:03:51.412 know a huge cause of the reasons why

NOTE Confidence: 0.90536140875

00:03:51.412 --> 00:03:53.669 children are coming to the pediatric

NOTE Confidence: 0.90536140875

00:03:53.669 --> 00:03:56.315 ICU into my clinical care is because

NOTE Confidence: 0.90536140875

00:03:56.315 --> 00:03:58.614 they have variations in their DNA that

NOTE Confidence: 0.90536140875

00:03:58.614 --> 00:04:00.939 can lead to errors and development.
NOTE Confidence: 0.90536140875

00:04:00.940 --> 00:04:02.818 So certainly that includes birth defects
NOTE Confidence: 0.90536140875

00:04:02.818 --> 00:04:04.510 such as congenital heart disease,
NOTE Confidence: 0.90536140875

00:04:04.510 --> 00:04:06.463 but there are so many different kinds
NOTE Confidence: 0.90536140875

00:04:06.463 --> 00:04:08.586 of birth defects that are out there and
NOTE Confidence: 0.90536140875

00:04:08.586 --> 00:04:10.954 and and as well as seizures or shock.
NOTE Confidence: 0.90536140875

00:04:10.960 --> 00:04:13.208 I mean there's just a host of different
NOTE Confidence: 0.90536140875

00:04:13.208 --> 00:04:15.119 reasons why they may present to the
NOTE Confidence: 0.90536140875

00:04:15.119 --> 00:04:16.817 ICU and present with such illness.
NOTE Confidence: 0.90536140875

00:04:16.820 --> 00:04:20.900 If they require really lifesaving measures.
NOTE Confidence: 0.90536140875

00:04:20.900 --> 00:04:22.204 So what I'd like to say to you,
NOTE Confidence: 0.90536140875

00:04:22.210 --> 00:04:25.242 maybe one of the key take home message
NOTE Confidence: 0.90536140875

00:04:25.242 --> 00:04:28.013 messages today is that the huge impact of
NOTE Confidence: 0.90536140875

00:04:28.013 --> 00:04:31.169 of these rare life threatening disorders so.
NOTE Confidence: 0.90536140875

00:04:31.170 --> 00:04:33.588 If you really combine rare disorders,
NOTE Confidence: 0.90536140875

00:04:33.590 --> 00:04:34.616 rare genetic disorders,

NOTE Confidence: 0.90536140875

00:04:34.616 --> 00:04:36.668 it's really a huge percentage of

NOTE Confidence: 0.90536140875

00:04:36.668 --> 00:04:38.719 the population that are affected.

NOTE Confidence: 0.90536140875

00:04:38.720 --> 00:04:41.536 In fact, if you just consider birth defects,

NOTE Confidence: 0.90536140875

00:04:41.540 --> 00:04:43.493 this now is the number one cause

NOTE Confidence: 0.90536140875

00:04:43.493 --> 00:04:44.929 of infant mortality in the US,

NOTE Confidence: 0.90536140875

00:04:44.930 --> 00:04:45.731 and so it's.

NOTE Confidence: 0.90536140875

00:04:45.731 --> 00:04:47.066 It's really a huge effort.

NOTE Confidence: 0.90536140875

00:04:47.070 --> 00:04:47.674 And really,

NOTE Confidence: 0.90536140875

00:04:47.674 --> 00:04:51.022 what what these all are is a is a huge

NOTE Confidence: 0.90536140875

00:04:51.022 --> 00:04:53.709 constellation of many rare disorders and

NOTE Confidence: 0.90536140875

00:04:53.709 --> 00:04:56.354 rare disorders are challenging because

NOTE Confidence: 0.90536140875

00:04:56.354 --> 00:04:59.260 one they're difficult to diagnose.

NOTE Confidence: 0.90536140875

00:04:59.260 --> 00:05:00.700 And they're difficult to diagnosis.

NOTE Confidence: 0.90536140875

00:05:00.700 --> 00:05:02.464 So oftentimes what we do is

NOTE Confidence: 0.90536140875

00:05:02.464 --> 00:05:03.640 give them very uninformative,

NOTE Confidence: 0.90536140875

00:05:03.640 --> 00:05:04.726 descriptive diagnosis, right?
NOTE Confidence: 0.90536140875

00:05:04.726 --> 00:05:06.174 So in the context,
NOTE Confidence: 0.90536140875

00:05:06.180 --> 00:05:06.981 congenital heart disease,
NOTE Confidence: 0.90536140875

00:05:06.981 --> 00:05:08.583 we might say that the child
NOTE Confidence: 0.90536140875

00:05:08.583 --> 00:05:09.740 has tetralogy of flow,
NOTE Confidence: 0.90536140875

00:05:09.740 --> 00:05:11.198 which is sort of an explanation
NOTE Confidence: 0.90536140875

00:05:11.198 --> 00:05:11.927 of the Phoenix,
NOTE Confidence: 0.90536140875

00:05:11.930 --> 00:05:13.694 or is a description of the
NOTE Confidence: 0.90536140875

00:05:13.694 --> 00:05:14.870 phenotype that you see,
NOTE Confidence: 0.90536140875

00:05:14.870 --> 00:05:16.240 but really doesn't tell us
NOTE Confidence: 0.90536140875

00:05:16.240 --> 00:05:17.336 molecularly what's going on.
NOTE Confidence: 0.90536140875

00:05:17.340 --> 00:05:19.146 Same thing with the term seizures, right?
NOTE Confidence: 0.90536140875

00:05:19.146 --> 00:05:21.218 I mean the child is having convulsions,
NOTE Confidence: 0.90536140875

00:05:21.220 --> 00:05:23.205 but we don't understand molecularly
NOTE Confidence: 0.90536140875

00:05:23.205 --> 00:05:24.396 why that's occurring.
NOTE Confidence: 0.90536140875

00:05:24.400 --> 00:05:25.690 And So what we really want

NOTE Confidence: 0.90536140875
00:05:25.690 --> 00:05:26.550 to understand is what's
NOTE Confidence: 0.948554268333333
00:05:26.599 --> 00:05:28.384 really wrong, and that's important
NOTE Confidence: 0.948554268333333
00:05:28.384 --> 00:05:29.934 for prognosis, right? Because?
NOTE Confidence: 0.948554268333333
00:05:29.934 --> 00:05:31.769 Oftentimes we take all children
NOTE Confidence: 0.948554268333333
00:05:31.769 --> 00:05:33.827 with tetralogy of flow and lump
NOTE Confidence: 0.948554268333333
00:05:33.827 --> 00:05:35.322 them together when in fact
NOTE Confidence: 0.948554268333333
00:05:35.322 --> 00:05:36.999 they present quite differently.
NOTE Confidence: 0.948554268333333
00:05:37.000 --> 00:05:39.338 Uh, or they can have a outcome
NOTE Confidence: 0.948554268333333
00:05:39.338 --> 00:05:41.775 that's quite different and so really
NOTE Confidence: 0.948554268333333
00:05:41.775 --> 00:05:44.060 understanding that molecularly is important.
NOTE Confidence: 0.948554268333333
00:05:44.060 --> 00:05:44.744 And then finally,
NOTE Confidence: 0.948554268333333
00:05:44.744 --> 00:05:46.340 one of the challenges that we have
NOTE Confidence: 0.948554268333333
00:05:46.385 --> 00:05:47.987 with rare disorders is that families
NOTE Confidence: 0.948554268333333
00:05:47.987 --> 00:05:49.569 often feel very isolated and desperate
NOTE Confidence: 0.948554268333333
00:05:49.569 --> 00:05:51.193 for answers and and they can't get
NOTE Confidence: 0.948554268333333

00:05:51.193 --> 00:05:52.954 them as critical care physicians.
NOTE Confidence: 0.948554268333333

00:05:52.954 --> 00:05:55.240 These these patients present with unexpected.
NOTE Confidence: 0.93317857368421

00:05:57.480 --> 00:05:59.526 Clinical courses and and and and
NOTE Confidence: 0.93317857368421

00:05:59.526 --> 00:06:01.984 so we don't know how to manage
NOTE Confidence: 0.93317857368421

00:06:01.984 --> 00:06:04.024 them in the best way possible,
NOTE Confidence: 0.93317857368421

00:06:04.030 --> 00:06:06.207 which is very frustrating to the clinician.
NOTE Confidence: 0.93317857368421

00:06:06.210 --> 00:06:08.457 But you can imagine the terror that
NOTE Confidence: 0.93317857368421

00:06:08.457 --> 00:06:11.044 leads to the family so many of them are
NOTE Confidence: 0.93317857368421

00:06:11.044 --> 00:06:12.739 asking why did this happen and will
NOTE Confidence: 0.93317857368421

00:06:12.739 --> 00:06:14.523 my next child be affected in in in?
NOTE Confidence: 0.93317857368421

00:06:14.530 --> 00:06:16.036 These can be really challenging questions
NOTE Confidence: 0.93317857368421

00:06:16.036 --> 00:06:17.869 to answer if you don't know what's
NOTE Confidence: 0.93317857368421

00:06:17.869 --> 00:06:19.985 going on molecular and so one of our
NOTE Confidence: 0.93317857368421

00:06:19.985 --> 00:06:21.320 exciting things that have happened
NOTE Confidence: 0.93317857368421

00:06:21.373 --> 00:06:23.381 in the last ten years is that next
NOTE Confidence: 0.93317857368421

00:06:23.381 --> 00:06:24.981 generation DNA sequencing has come

NOTE Confidence: 0.93317857368421

00:06:24.981 --> 00:06:27.997 through and we have now the opportunity to.

NOTE Confidence: 0.93317857368421

00:06:28.000 --> 00:06:29.431 Potentially asked the

NOTE Confidence: 0.93317857368421

00:06:29.431 --> 00:06:31.339 question what's going on?

NOTE Confidence: 0.93317857368421

00:06:31.340 --> 00:06:34.740 OK, so to that end we have created a hill.

NOTE Confidence: 0.93317857368421

00:06:34.740 --> 00:06:36.740 The pediatric Genomics Discovery program,

NOTE Confidence: 0.93317857368421

00:06:36.740 --> 00:06:38.780 which is a translational research program.

NOTE Confidence: 0.93317857368421

00:06:38.780 --> 00:06:41.395 We're particularly interested in rare

NOTE Confidence: 0.93317857368421

00:06:41.395 --> 00:06:43.048 disorders that lead to unexplained

NOTE Confidence: 0.93317857368421

00:06:43.048 --> 00:06:45.115 critical illness and and a lot of

NOTE Confidence: 0.93317857368421

00:06:45.115 --> 00:06:46.700 those patients have birth defects,

NOTE Confidence: 0.93317857368421

00:06:46.700 --> 00:06:47.822 but we've actually branched out to

NOTE Confidence: 0.93317857368421

00:06:47.822 --> 00:06:49.259 a number of other disorders as well,

NOTE Confidence: 0.93317857368421

00:06:49.260 --> 00:06:52.166 such as seizures or shock, for example,

NOTE Confidence: 0.93317857368421

00:06:52.166 --> 00:06:54.344 that presents that we can't explain

NOTE Confidence: 0.93317857368421

00:06:54.344 --> 00:06:55.820 by an infection,

NOTE Confidence: 0.93317857368421

00:06:55.820 --> 00:06:57.430 and then we leverage next
NOTE Confidence: 0.93317857368421

00:06:57.430 --> 00:06:58.074 generation technologies,
NOTE Confidence: 0.93317857368421

00:06:58.080 --> 00:07:00.128 particularly whole exome sequencing.
NOTE Confidence: 0.93317857368421

00:07:00.128 --> 00:07:02.176 To identify candidate genes
NOTE Confidence: 0.93317857368421

00:07:02.176 --> 00:07:04.709 that might explain the disorder.
NOTE Confidence: 0.93317857368421

00:07:04.710 --> 00:07:06.714 And often then we also launched
NOTE Confidence: 0.93317857368421

00:07:06.714 --> 00:07:09.043 right into the lab to do basic
NOTE Confidence: 0.93317857368421

00:07:09.043 --> 00:07:10.885 science research and see if we
NOTE Confidence: 0.93317857368421

00:07:10.885 --> 00:07:13.105 can understand the path,
NOTE Confidence: 0.93317857368421

00:07:13.105 --> 00:07:17.146 the pathology or the the the the
NOTE Confidence: 0.93317857368421

00:07:17.146 --> 00:07:18.878 the molecular biology that's
NOTE Confidence: 0.93317857368421

00:07:18.878 --> 00:07:21.290 that's leading to the illness.
NOTE Confidence: 0.93317857368421

00:07:21.290 --> 00:07:22.781 So we have a couple of different
NOTE Confidence: 0.93317857368421

00:07:22.781 --> 00:07:23.830 aspects of the program.
NOTE Confidence: 0.93317857368421

00:07:23.830 --> 00:07:25.606 First, we have patient oriented care,
NOTE Confidence: 0.93317857368421

00:07:25.610 --> 00:07:28.010 so we have a collaborative outpatient

NOTE Confidence: 0.93317857368421

00:07:28.010 --> 00:07:30.429 clinic with the Department of Genetics.

NOTE Confidence: 0.93317857368421

00:07:30.430 --> 00:07:32.038 They're here right now.

NOTE Confidence: 0.93317857368421

00:07:32.038 --> 00:07:33.646 Consultations from the outside.

NOTE Confidence: 0.882631994

00:07:37.120 --> 00:07:38.350 We also have a basic

NOTE Confidence: 0.882631994

00:07:38.350 --> 00:07:39.580 science research that we do,

NOTE Confidence: 0.882631994

00:07:39.580 --> 00:07:42.282 so we certainly do a research oriented

NOTE Confidence: 0.882631994

00:07:42.282 --> 00:07:44.174 bioinformatic analysis and then we

NOTE Confidence: 0.882631994

00:07:44.174 --> 00:07:46.172 ourselves actually do a number of

NOTE Confidence: 0.882631994

00:07:46.172 --> 00:07:48.775 experiments in my lab as well as

NOTE Confidence: 0.882631994

00:07:48.775 --> 00:07:50.275 collaborative efforts with Yale

NOTE Confidence: 0.882631994

00:07:50.275 --> 00:07:51.865 investigators and outside researchers

NOTE Confidence: 0.882631994

00:07:51.865 --> 00:07:54.295 in order to investigate the molecular

NOTE Confidence: 0.882631994

00:07:54.295 --> 00:07:55.938 mechanisms that lead to disease.

NOTE Confidence: 0.882631994

00:07:55.940 --> 00:07:57.866 And ideally, then we return these

NOTE Confidence: 0.882631994

00:07:57.866 --> 00:07:59.797 results to families and and referring

NOTE Confidence: 0.882631994

00:07:59.797 --> 00:08:01.555 providers and all of this work
NOTE Confidence: 0.882631994

00:08:01.555 --> 00:08:03.740 is sort of coordinated through an
NOTE Confidence: 0.882631994

00:08:03.740 --> 00:08:05.615 exciting meeting that we have.
NOTE Confidence: 0.882631994

00:08:05.620 --> 00:08:06.900 Which we called Genomics board.
NOTE Confidence: 0.882631994

00:08:06.900 --> 00:08:09.405 So this is a multidisciplinary
NOTE Confidence: 0.882631994

00:08:09.405 --> 00:08:11.910 meeting where we invite clinicians.
NOTE Confidence: 0.882631994

00:08:11.910 --> 00:08:14.158 And the by informatics team as well as
NOTE Confidence: 0.882631994

00:08:14.158 --> 00:08:16.708 the basic science scientist to all present.
NOTE Confidence: 0.882631994

00:08:16.710 --> 00:08:19.860 It is at one meeting.
NOTE Confidence: 0.882631994

00:08:19.860 --> 00:08:22.248 Which requires a lot of coordination.
NOTE Confidence: 0.882631994

00:08:22.250 --> 00:08:24.287 But then at that meeting we all
NOTE Confidence: 0.882631994

00:08:24.287 --> 00:08:26.452 discussed the results as well as the
NOTE Confidence: 0.882631994

00:08:26.452 --> 00:08:27.992 clinical presentation that we've found
NOTE Confidence: 0.882631994

00:08:27.992 --> 00:08:30.389 to be extremely powerful for all groups.
NOTE Confidence: 0.882631994

00:08:30.390 --> 00:08:31.754 The clinicians are excited
NOTE Confidence: 0.882631994

00:08:31.754 --> 00:08:33.459 to see basic research done.

NOTE Confidence: 0.882631994

00:08:33.460 --> 00:08:35.580 The basic scientists are excited

NOTE Confidence: 0.882631994

00:08:35.580 --> 00:08:37.700 about seeing a clinical opportunity

NOTE Confidence: 0.882631994

00:08:37.764 --> 00:08:40.064 to connect with and so this is

NOTE Confidence: 0.882631994

00:08:40.064 --> 00:08:41.769 actually been a really powerful

NOTE Confidence: 0.882631994

00:08:41.769 --> 00:08:43.274 force for continuing our research.

NOTE Confidence: 0.882631994

00:08:43.274 --> 00:08:45.818 And so this is that's been an important

NOTE Confidence: 0.882631994

00:08:45.818 --> 00:08:48.188 lesson to connect these people together.

NOTE Confidence: 0.882631994

00:08:48.190 --> 00:08:48.994 And then importantly,

NOTE Confidence: 0.882631994

00:08:48.994 --> 00:08:50.334 we return results to families

NOTE Confidence: 0.882631994

00:08:50.334 --> 00:08:51.340 in referring providers,

NOTE Confidence: 0.882631994

00:08:51.340 --> 00:08:53.835 even if their research results and

NOTE Confidence: 0.882631994

00:08:53.835 --> 00:08:55.425 and that that has been exciting.

NOTE Confidence: 0.882631994

00:08:55.430 --> 00:08:57.516 And we've been surprised that it's been,

NOTE Confidence: 0.882631994

00:08:57.520 --> 00:09:00.228 it's been met with some concerns

NOTE Confidence: 0.882631994

00:09:00.228 --> 00:09:02.518 which we've pushed through there.

NOTE Confidence: 0.882631994

00:09:02.520 --> 00:09:04.788 We think it's really important to
NOTE Confidence: 0.882631994

00:09:04.788 --> 00:09:06.722 consider families and patients is
NOTE Confidence: 0.882631994

00:09:06.722 --> 00:09:08.662 as participants in the research.
NOTE Confidence: 0.882631994

00:09:08.670 --> 00:09:10.058 And so we, we,
NOTE Confidence: 0.882631994

00:09:10.058 --> 00:09:12.890 we work hard to engage them as well.
NOTE Confidence: 0.882631994

00:09:12.890 --> 00:09:13.130 OK,
NOTE Confidence: 0.882631994

00:09:13.130 --> 00:09:14.294 so I just want to take one or
NOTE Confidence: 0.882631994

00:09:14.294 --> 00:09:15.672 two minutes to talk about next
NOTE Confidence: 0.882631994

00:09:15.672 --> 00:09:16.228 generation sequencing.
NOTE Confidence: 0.882631994

00:09:16.230 --> 00:09:17.054 The kind of sequencing
NOTE Confidence: 0.882631994

00:09:17.054 --> 00:09:18.290 that we can do at Yale.
NOTE Confidence: 0.882631994

00:09:18.290 --> 00:09:19.697 So one of the things that really
NOTE Confidence: 0.882631994

00:09:19.697 --> 00:09:21.055 a sequencer today is no different
NOTE Confidence: 0.882631994

00:09:21.055 --> 00:09:21.999 than any other sequencer,
NOTE Confidence: 0.882631994

00:09:22.000 --> 00:09:24.180 except that it's massively parallel.
NOTE Confidence: 0.882631994

00:09:24.180 --> 00:09:26.610 So instead of having one sequencer

NOTE Confidence: 0.882631994
00:09:26.610 --> 00:09:28.230 running and generating sequence,
NOTE Confidence: 0.882631994
00:09:28.230 --> 00:09:30.771 you have a machine that produces millions
NOTE Confidence: 0.882631994
00:09:30.771 --> 00:09:32.989 of sequences all at the same time,
NOTE Confidence: 0.882631994
00:09:32.990 --> 00:09:34.982 and that has made it possible to do
NOTE Confidence: 0.882631994
00:09:34.982 --> 00:09:36.708 sequencing at really remarkable cost,
NOTE Confidence: 0.882631994
00:09:36.710 --> 00:09:39.926 so you know we now at Yale have
NOTE Confidence: 0.882631994
00:09:39.926 --> 00:09:43.149 a number of clinical sequencing.
NOTE Confidence: 0.882631994
00:09:43.150 --> 00:09:43.990 Efforts that we have.
NOTE Confidence: 0.882631994
00:09:43.990 --> 00:09:46.490 So for example, in the PICU and NICU.
NOTE Confidence: 0.882631994
00:09:46.490 --> 00:09:49.192 We are doing a rapid whole genome
NOTE Confidence: 0.882631994
00:09:49.192 --> 00:09:51.410 sequencing where we can identify
NOTE Confidence: 0.882631994
00:09:51.410 --> 00:09:53.855 patient and produce genome sequence
NOTE Confidence: 0.882631994
00:09:53.855 --> 00:09:56.707 and results within five days in that
NOTE Confidence: 0.882631994
00:09:56.707 --> 00:09:59.167 can often we usually have a clinical
NOTE Confidence: 0.882631994
00:09:59.167 --> 00:10:01.115 requirement that's that's necessary
NOTE Confidence: 0.882631994

00:10:01.115 --> 00:10:03.390 that includes Courier servicing, alerting,
NOTE Confidence: 0.882631994

00:10:03.390 --> 00:10:04.990 Yale Center for Genomic Analysis,
NOTE Confidence: 0.882631994

00:10:04.990 --> 00:10:06.390 and rush sequencing to really
NOTE Confidence: 0.882631994

00:10:06.390 --> 00:10:08.506 push this as fast as possible so
NOTE Confidence: 0.882631994

00:10:08.506 --> 00:10:10.146 that it could be immediately.
NOTE Confidence: 0.951830714

00:10:12.250 --> 00:10:15.030 Return back to the clinic.
NOTE Confidence: 0.951830714

00:10:15.030 --> 00:10:17.039 We also have clinical whole exome sequencing
NOTE Confidence: 0.951830714

00:10:17.039 --> 00:10:19.195 where we just sequence the exons right
NOTE Confidence: 0.951830714

00:10:19.195 --> 00:10:21.061 as opposed to whole genome sequencing.
NOTE Confidence: 0.951830714

00:10:21.070 --> 00:10:22.690 Here, sequencing just the exons and
NOTE Confidence: 0.951830714

00:10:22.690 --> 00:10:24.360 there were trying to stab establish
NOTE Confidence: 0.951830714

00:10:24.360 --> 00:10:26.222 causes of genetic disease and one of
NOTE Confidence: 0.951830714

00:10:26.222 --> 00:10:28.132 the challenges whenever you do clinical
NOTE Confidence: 0.951830714

00:10:28.132 --> 00:10:30.059 Hawks and sequencing is you're often
NOTE Confidence: 0.951830714

00:10:30.059 --> 00:10:31.704 finding variants of unknown significance
NOTE Confidence: 0.951830714

00:10:31.704 --> 00:10:34.321 and this is a big challenge and one of

NOTE Confidence: 0.951830714

00:10:34.321 --> 00:10:35.918 the things that we do on a research

NOTE Confidence: 0.951830714

00:10:35.918 --> 00:10:38.060 side is try to convert variants of

NOTE Confidence: 0.951830714

00:10:38.060 --> 00:10:39.285 unknown significance to significance

NOTE Confidence: 0.951830714

00:10:39.285 --> 00:10:40.953 right to do scientific studies in

NOTE Confidence: 0.951830714

00:10:40.953 --> 00:10:42.814 order to investigate them and and

NOTE Confidence: 0.951830714

00:10:42.814 --> 00:10:44.444 that again is another basis.

NOTE Confidence: 0.951830714

00:10:44.450 --> 00:10:46.208 For the pediatric generalists very program,

NOTE Confidence: 0.951830714

00:10:46.210 --> 00:10:49.540 it's something we'll talk about today.

NOTE Confidence: 0.951830714

00:10:49.540 --> 00:10:52.645 OK, so you know we have exciting way forward.

NOTE Confidence: 0.951830714

00:10:52.650 --> 00:10:54.794 This is sort of the path that we've

NOTE Confidence: 0.951830714

00:10:54.794 --> 00:10:56.526 created for the pediatric Genomic

NOTE Confidence: 0.951830714

00:10:56.526 --> 00:10:58.416 Discovery program where we have

NOTE Confidence: 0.951830714

00:10:58.420 --> 00:11:00.445 my colleagues Tsakani and Lauren

NOTE Confidence: 0.951830714

00:11:00.445 --> 00:11:02.470 Jeffries who are reviewing children's

NOTE Confidence: 0.951830714

00:11:02.528 --> 00:11:04.380 diseases and Monica Constantino,

NOTE Confidence: 0.951830714

00:11:04.380 --> 00:11:08.646 who collects DNA and consents families.
NOTE Confidence: 0.951830714

00:11:08.650 --> 00:11:10.972 DNA is then sent to Yale Center for Genome
NOTE Confidence: 0.951830714

00:11:10.972 --> 00:11:12.654 Analysis and Wage in who is our bar.
NOTE Confidence: 0.951830714

00:11:12.660 --> 00:11:15.300 Informatician wizard analyzes that DNA
NOTE Confidence: 0.951830714

00:11:15.300 --> 00:11:18.830 and then returns results to all of us.
NOTE Confidence: 0.951830714

00:11:18.830 --> 00:11:20.310 And then my team.
NOTE Confidence: 0.951830714

00:11:20.310 --> 00:11:23.190 He also works to do basic science
NOTE Confidence: 0.951830714

00:11:23.190 --> 00:11:26.586 research to try to identify molecular.
NOTE Confidence: 0.951830714

00:11:26.590 --> 00:11:28.330 So sort of bring those molecular
NOTE Confidence: 0.951830714

00:11:28.330 --> 00:11:30.807 changes to the lab to try to understand
NOTE Confidence: 0.951830714

00:11:30.807 --> 00:11:32.382 the impact of those variants,
NOTE Confidence: 0.951830714

00:11:32.390 --> 00:11:34.950 and then you know soccer in his team.
NOTE Confidence: 0.951830714

00:11:34.950 --> 00:11:36.476 Go back to return any of those
NOTE Confidence: 0.951830714

00:11:36.476 --> 00:11:37.700 results back to the family,
NOTE Confidence: 0.951830714

00:11:37.700 --> 00:11:39.289 and so it's actually become a very
NOTE Confidence: 0.951830714

00:11:39.289 --> 00:11:40.893 exciting team and and we'd love for

NOTE Confidence: 0.951830714

00:11:40.893 --> 00:11:42.201 you guys to participate as well.

NOTE Confidence: 0.951830714

00:11:42.210 --> 00:11:43.484 So if you have patients that you

NOTE Confidence: 0.951830714

00:11:43.484 --> 00:11:44.670 think could benefit from our program,

NOTE Confidence: 0.951830714

00:11:44.670 --> 00:11:47.145 we'd love to hear from you and I'll give

NOTE Confidence: 0.951830714

00:11:47.145 --> 00:11:49.865 you those contact information in a minute.

NOTE Confidence: 0.951830714

00:11:49.870 --> 00:11:50.297 OK,

NOTE Confidence: 0.951830714

00:11:50.297 --> 00:11:53.713 so let me now start with three different

NOTE Confidence: 0.951830714

00:11:53.713 --> 00:11:56.860 stories that I'd like to tell you about.

NOTE Confidence: 0.951830714

00:11:56.860 --> 00:11:57.498 In in,

NOTE Confidence: 0.951830714

00:11:57.498 --> 00:11:59.731 in each of these stories are they

NOTE Confidence: 0.951830714

00:11:59.731 --> 00:12:02.077 clearly have clinical impact and and in

NOTE Confidence: 0.951830714

00:12:02.077 --> 00:12:05.179 each case I'd I'd like to point out the

NOTE Confidence: 0.951830714

00:12:05.179 --> 00:12:07.372 reasons for why I'm presenting them today,

NOTE Confidence: 0.951830714

00:12:07.372 --> 00:12:08.758 so one of them is about

NOTE Confidence: 0.951830714

00:12:08.758 --> 00:12:10.110 a gene called Dell G5.

NOTE Confidence: 0.951830714

00:12:10.110 --> 00:12:10.911 In that case,
NOTE Confidence: 0.951830714

00:12:10.911 --> 00:12:13.235 we had a clear need for the bench
NOTE Confidence: 0.951830714

00:12:13.235 --> 00:12:15.185 in in studying those variants,
NOTE Confidence: 0.951830714

00:12:15.190 --> 00:12:18.043 but we then have another gene called a RS2,
NOTE Confidence: 0.951830714

00:12:18.050 --> 00:12:19.940 where we actually could lead to
NOTE Confidence: 0.951830714

00:12:19.940 --> 00:12:20.570 an intervention.
NOTE Confidence: 0.951830714

00:12:20.570 --> 00:12:23.010 Actually, that the family initiated,
NOTE Confidence: 0.951830714

00:12:23.010 --> 00:12:24.218 which was extremely exciting,
NOTE Confidence: 0.951830714

00:12:24.218 --> 00:12:26.619 and then our full I'll tell you about.
NOTE Confidence: 0.951830714

00:12:26.620 --> 00:12:29.284 A story where I actually have one of
NOTE Confidence: 0.951830714

00:12:29.284 --> 00:12:32.096 the rare times where we actually have
NOTE Confidence: 0.951830714

00:12:32.100 --> 00:12:34.506 the story as it comes particularly
NOTE Confidence: 0.951830714

00:12:34.506 --> 00:12:36.906 straight from the mom and her
NOTE Confidence: 0.951830714

00:12:36.906 --> 00:12:39.054 how it's been impactful for her?
NOTE Confidence: 0.951830714

00:12:39.060 --> 00:12:41.364 So those are the three stories
NOTE Confidence: 0.951830714

00:12:41.364 --> 00:12:42.900 we'll talk about today.

NOTE Confidence: 0.951830714
00:12:42.900 --> 00:12:43.170 OK,
NOTE Confidence: 0.951830714
00:12:43.170 --> 00:12:44.790 so this is how often are
NOTE Confidence: 0.951830714
00:12:44.790 --> 00:12:46.060 our genomics board starts?
NOTE Confidence: 0.951830714
00:12:46.060 --> 00:12:47.936 We start with the case so there's
NOTE Confidence: 0.951830714
00:12:47.936 --> 00:12:49.506 a fetus with multiple anomalies
NOTE Confidence: 0.951830714
00:12:49.506 --> 00:12:51.606 that have been presented to us
NOTE Confidence: 0.951830714
00:12:51.606 --> 00:12:53.880 from the maternal fetal medicine
NOTE Confidence: 0.951830714
00:12:53.880 --> 00:12:55.920 group that there's a 21 week.
NOTE Confidence: 0.951830714
00:12:55.920 --> 00:12:57.395 I just just just stationary
NOTE Confidence: 0.951830714
00:12:57.395 --> 00:12:58.870 age fetus that has extra
NOTE Confidence: 0.741103625714286
00:12:58.933 --> 00:13:00.149 dakhli and club feed.
NOTE Confidence: 0.741103625714286
00:13:00.150 --> 00:13:02.110 You could see the X rays here that
NOTE Confidence: 0.741103625714286
00:13:02.110 --> 00:13:03.939 show that there's missing digits.
NOTE Confidence: 0.741103625714286
00:13:03.940 --> 00:13:05.998 The child also has a VSD and
NOTE Confidence: 0.741103625714286
00:13:05.998 --> 00:13:06.880 extremely cystic kidney,
NOTE Confidence: 0.741103625714286

00:13:06.880 --> 00:13:08.637 so these are the kidneys here and
NOTE Confidence: 0.741103625714286

00:13:08.637 --> 00:13:10.681 you can see this one is extremely
NOTE Confidence: 0.741103625714286

00:13:10.681 --> 00:13:12.523 cystic with all these cysts here.
NOTE Confidence: 0.741103625714286

00:13:12.530 --> 00:13:14.246 And so when sequencing this child,
NOTE Confidence: 0.741103625714286

00:13:14.250 --> 00:13:17.043 we actually found a de Novo mutation
NOTE Confidence: 0.741103625714286

00:13:17.043 --> 00:13:20.406 in DL G5 and so DL G5 has never
NOTE Confidence: 0.741103625714286

00:13:20.406 --> 00:13:22.243 been associated with disease before
NOTE Confidence: 0.741103625714286

00:13:22.243 --> 00:13:24.787 and so we were curious as to what
NOTE Confidence: 0.741103625714286

00:13:24.787 --> 00:13:27.309 that de Novo mutation really meant.
NOTE Confidence: 0.741103625714286

00:13:27.310 --> 00:13:29.416 And and and one of the things that has
NOTE Confidence: 0.741103625714286

00:13:29.416 --> 00:13:31.272 been shown in the literature is that
NOTE Confidence: 0.741103625714286

00:13:31.272 --> 00:13:33.410 Dell G5 may have a role in in Syria,
NOTE Confidence: 0.741103625714286

00:13:33.410 --> 00:13:34.964 although that's not been well worked out,
NOTE Confidence: 0.741103625714286

00:13:34.970 --> 00:13:36.410 and so, you know,
NOTE Confidence: 0.741103625714286

00:13:36.410 --> 00:13:37.850 looking at these phenotypes,
NOTE Confidence: 0.741103625714286

00:13:37.850 --> 00:13:40.550 polycystic kidney disease, limb defects,

NOTE Confidence: 0.741103625714286
00:13:40.550 --> 00:13:42.800 we certainly were thinking that there
NOTE Confidence: 0.741103625714286
00:13:42.800 --> 00:13:45.669 might be a defect in cilia signaling.
NOTE Confidence: 0.741103625714286
00:13:45.670 --> 00:13:48.134 And so we promptly went to frogs.
NOTE Confidence: 0.741103625714286
00:13:48.140 --> 00:13:51.730 So in my lab we use frogs as a model system.
NOTE Confidence: 0.741103625714286
00:13:51.730 --> 00:13:54.050 So frogs are extremely efficient
NOTE Confidence: 0.741103625714286
00:13:54.050 --> 00:13:55.800 for studying a gene function,
NOTE Confidence: 0.741103625714286
00:13:55.800 --> 00:13:58.677 and that's mainly because we can generate
NOTE Confidence: 0.741103625714286
00:13:58.680 --> 00:14:01.749 frog embryos in the 10s of thousands a day.
NOTE Confidence: 0.741103625714286
00:14:01.750 --> 00:14:04.310 So we can just basically,
NOTE Confidence: 0.741103625714286
00:14:04.310 --> 00:14:05.942 frogs were, oddly enough,
NOTE Confidence: 0.741103625714286
00:14:05.942 --> 00:14:07.574 the first pregnancy test.
NOTE Confidence: 0.741103625714286
00:14:07.580 --> 00:14:09.410 So if you take HCG and
NOTE Confidence: 0.741103625714286
00:14:09.410 --> 00:14:10.630 inject them into frogs,
NOTE Confidence: 0.741103625714286
00:14:10.630 --> 00:14:12.958 you get eggs the next the next day,
NOTE Confidence: 0.741103625714286
00:14:12.960 --> 00:14:15.080 and so we can produce eggs in the
NOTE Confidence: 0.741103625714286

00:14:15.080 --> 00:14:16.329 thousands whenever we need them.
NOTE Confidence: 0.741103625714286

00:14:16.330 --> 00:14:18.024 And then by doing in vitro fertilization,
NOTE Confidence: 0.741103625714286

00:14:18.030 --> 00:14:21.010 get hundreds of synchronized embryos.
NOTE Confidence: 0.741103625714286

00:14:21.010 --> 00:14:23.314 And so in this case will inject a
NOTE Confidence: 0.741103625714286

00:14:23.314 --> 00:14:25.647 DLG 5 morpholino antisense oligo
NOTE Confidence: 0.741103625714286

00:14:25.647 --> 00:14:27.594 that blocks protein translation
NOTE Confidence: 0.741103625714286

00:14:27.594 --> 00:14:30.066 and ask the question what happens.
NOTE Confidence: 0.741103625714286

00:14:30.070 --> 00:14:32.410 So it's also exciting about frogs,
NOTE Confidence: 0.741103625714286

00:14:32.410 --> 00:14:33.750 is that they're extremely fast,
NOTE Confidence: 0.741103625714286

00:14:33.750 --> 00:14:35.734 so you can go from a cleavage stage
NOTE Confidence: 0.741103625714286

00:14:35.734 --> 00:14:37.325 embryo that's just been fertilized and
NOTE Confidence: 0.741103625714286

00:14:37.325 --> 00:14:39.721 then two or three days you can have a
NOTE Confidence: 0.741103625714286

00:14:39.721 --> 00:14:41.305 tadpole that has a functioning kidney
NOTE Confidence: 0.741103625714286

00:14:41.305 --> 00:14:43.070 and ask the question in this case,
NOTE Confidence: 0.741103625714286

00:14:43.070 --> 00:14:44.978 what has happened to the kidney?
NOTE Confidence: 0.741103625714286

00:14:44.980 --> 00:14:46.510 Here's the kidney tubule here.

NOTE Confidence: 0.741103625714286
00:14:46.510 --> 00:14:48.750 In purple is is the Floyd in standing
NOTE Confidence: 0.741103625714286
00:14:48.750 --> 00:14:50.826 that shows the tubule of the kidney.
NOTE Confidence: 0.741103625714286
00:14:50.830 --> 00:14:53.168 This is right where the glomerulus is,
NOTE Confidence: 0.741103625714286
00:14:53.170 --> 00:14:55.318 and acetylated tubulin marks the silliest.
NOTE Confidence: 0.741103625714286
00:14:55.320 --> 00:14:58.064 So all this this this screen inside the
NOTE Confidence: 0.741103625714286
00:14:58.064 --> 00:15:00.169 tubular actually cilia that are in the.
NOTE Confidence: 0.741103625714286
00:15:00.170 --> 00:15:01.856 In the lumen of this tubule,
NOTE Confidence: 0.741103625714286
00:15:01.860 --> 00:15:03.764 and when we knocked down DLG five,
NOTE Confidence: 0.741103625714286
00:15:03.770 --> 00:15:05.541 you could see that indeed we can
NOTE Confidence: 0.741103625714286
00:15:05.541 --> 00:15:06.810 start forming cysts just like
NOTE Confidence: 0.741103625714286
00:15:06.810 --> 00:15:07.955 we did for the patient,
NOTE Confidence: 0.741103625714286
00:15:07.960 --> 00:15:10.004 and the effect you also see a
NOTE Confidence: 0.741103625714286
00:15:10.004 --> 00:15:11.470 rather dramatic loss of cilia,
NOTE Confidence: 0.741103625714286
00:15:11.470 --> 00:15:13.640 suggesting that you know indeed
NOTE Confidence: 0.741103625714286
00:15:13.640 --> 00:15:15.642 this could be a silly opathy that
NOTE Confidence: 0.741103625714286

00:15:15.642 --> 00:15:17.269 is happening in the patient,
NOTE Confidence: 0.741103625714286

00:15:17.270 --> 00:15:20.174 and that the cystic part of the kidney
NOTE Confidence: 0.741103625714286

00:15:20.174 --> 00:15:23.007 is something that we can very readily
NOTE Confidence: 0.741103625714286

00:15:23.007 --> 00:15:25.037 recapitulate in the frog embryo.
NOTE Confidence: 0.741103625714286

00:15:25.040 --> 00:15:26.354 Now one of the exciting things
NOTE Confidence: 0.741103625714286

00:15:26.354 --> 00:15:27.958 about this kind of research is
NOTE Confidence: 0.741103625714286

00:15:27.958 --> 00:15:29.326 the opportunity for collaboration.
NOTE Confidence: 0.741103625714286

00:15:29.330 --> 00:15:29.611 Now,
NOTE Confidence: 0.741103625714286

00:15:29.611 --> 00:15:31.297 what we've identified is a single
NOTE Confidence: 0.741103625714286

00:15:31.297 --> 00:15:33.369 patient with a denovo mutation in DL,
NOTE Confidence: 0.741103625714286

00:15:33.370 --> 00:15:33.976 G5, and,
NOTE Confidence: 0.741103625714286

00:15:33.976 --> 00:15:36.400 and while it's exciting to see that in
NOTE Confidence: 0.741103625714286

00:15:36.469 --> 00:15:39.025 this frog model we can recapitulate
NOTE Confidence: 0.741103625714286

00:15:39.025 --> 00:15:40.729 the polycystic kidney disease.
NOTE Confidence: 0.741103625714286

00:15:40.730 --> 00:15:42.014 One of the challenges is always
NOTE Confidence: 0.741103625714286

00:15:42.014 --> 00:15:42.870 is what it you

NOTE Confidence: 0.854650091818182
00:15:42.917 --> 00:15:44.578 know. Is this also potentially
NOTE Confidence: 0.854650091818182
00:15:44.578 --> 00:15:45.649 just irrelevant right?
NOTE Confidence: 0.854650091818182
00:15:45.650 --> 00:15:47.108 Is it just something finding and?
NOTE Confidence: 0.854650091818182
00:15:47.110 --> 00:15:48.622 And maybe this doesn't really matter
NOTE Confidence: 0.854650091818182
00:15:48.622 --> 00:15:50.395 to the patient and so one of the
NOTE Confidence: 0.854650091818182
00:15:50.395 --> 00:15:52.037 things we can use is this tool called
NOTE Confidence: 0.854650091818182
00:15:52.037 --> 00:15:53.603 gene matcher which is a website
NOTE Confidence: 0.854650091818182
00:15:53.603 --> 00:15:55.054 that connects researchers that and
NOTE Confidence: 0.854650091818182
00:15:55.054 --> 00:15:57.210 what they do is they basically enter
NOTE Confidence: 0.854650091818182
00:15:57.268 --> 00:15:59.050 the gene that they're interested in
NOTE Confidence: 0.854650091818182
00:15:59.050 --> 00:16:01.181 because they have a patient and then
NOTE Confidence: 0.854650091818182
00:16:01.181 --> 00:16:02.945 once you everyone enters a gene,
NOTE Confidence: 0.854650091818182
00:16:02.950 --> 00:16:04.306 that sort of sends emails to
NOTE Confidence: 0.854650091818182
00:16:04.306 --> 00:16:04.984 everyone saying hey,
NOTE Confidence: 0.854650091818182
00:16:04.990 --> 00:16:07.050 would you guys like to connect and
NOTE Confidence: 0.854650091818182

00:16:07.050 --> 00:16:09.010 so we did that and we identified
NOTE Confidence: 0.854650091818182

00:16:09.010 --> 00:16:11.068 a number of additional patients.
NOTE Confidence: 0.854650091818182

00:16:11.070 --> 00:16:14.390 Uh, including one patient that has a huge,
NOTE Confidence: 0.854650091818182

00:16:14.390 --> 00:16:16.750 so your ureter probable junction,
NOTE Confidence: 0.854650091818182

00:16:16.750 --> 00:16:20.190 obstruction hydronephrosis so kidney defects.
NOTE Confidence: 0.854650091818182

00:16:20.190 --> 00:16:24.936 Also us maybe a particularly abnormal foot.
NOTE Confidence: 0.854650091818182

00:16:24.940 --> 00:16:26.980 We also found patients that has
NOTE Confidence: 0.854650091818182

00:16:26.980 --> 00:16:28.696 steroid resistant product syndrome and
NOTE Confidence: 0.854650091818182

00:16:28.696 --> 00:16:30.520 increased ventricles on ahead and and
NOTE Confidence: 0.854650091818182

00:16:30.520 --> 00:16:32.360 then two patients at hydrocephalus,
NOTE Confidence: 0.854650091818182

00:16:32.360 --> 00:16:34.481 which is this disease where you have
NOTE Confidence: 0.854650091818182

00:16:34.481 --> 00:16:36.484 swelling in the brain because the
NOTE Confidence: 0.854650091818182

00:16:36.484 --> 00:16:38.480 CSF circulation is not normal and
NOTE Confidence: 0.854650091818182

00:16:38.480 --> 00:16:40.440 all of them had mutations in DL,
NOTE Confidence: 0.854650091818182

00:16:40.440 --> 00:16:42.192 G5 in fact and of course when we
NOTE Confidence: 0.854650091818182

00:16:42.192 --> 00:16:43.748 first saw this we're thought what

NOTE Confidence: 0.854650091818182

00:16:43.748 --> 00:16:45.710 in the world does this mean right?

NOTE Confidence: 0.854650091818182

00:16:45.710 --> 00:16:47.930 I mean clearly there's kidney abnormalities

NOTE Confidence: 0.854650091818182

00:16:47.930 --> 00:16:50.560 but then also hydrocephalus and in

NOTE Confidence: 0.854650091818182

00:16:50.560 --> 00:16:53.771 fact the researchers before us were

NOTE Confidence: 0.854650091818182

00:16:53.771 --> 00:16:56.088 the paint had patients with this huge.

NOTE Confidence: 0.854650091818182

00:16:56.090 --> 00:16:56.630 Construction hydrocephalus.

NOTE Confidence: 0.854650091818182

00:16:56.630 --> 00:16:58.250 In it they actually thought they

NOTE Confidence: 0.854650091818182

00:16:58.250 --> 00:16:59.688 had nothing to do with one another,

NOTE Confidence: 0.854650091818182

00:16:59.690 --> 00:17:01.082 and that maybe there is something

NOTE Confidence: 0.854650091818182

00:17:01.082 --> 00:17:01.778 else going on.

NOTE Confidence: 0.854650091818182

00:17:01.780 --> 00:17:03.824 But when we also had the hydrocephalus.

NOTE Confidence: 0.854650091818182

00:17:03.830 --> 00:17:06.620 Sorry, the polycystic kidney disease.

NOTE Confidence: 0.854650091818182

00:17:06.620 --> 00:17:08.524 Then it became more clear that maybe

NOTE Confidence: 0.854650091818182

00:17:08.524 --> 00:17:10.331 all of these phenotypes might be

NOTE Confidence: 0.854650091818182

00:17:10.331 --> 00:17:12.197 reflective in the fact that you

NOTE Confidence: 0.854650091818182

00:17:12.197 --> 00:17:13.750 have a silly a defect.
NOTE Confidence: 0.854650091818182

00:17:13.750 --> 00:17:16.360 Because in all cases have been shown to
NOTE Confidence: 0.854650091818182

00:17:16.360 --> 00:17:19.096 be important for all of these freedom types,
NOTE Confidence: 0.854650091818182

00:17:19.100 --> 00:17:21.683 so so we actually thought that maybe
NOTE Confidence: 0.854650091818182

00:17:21.683 --> 00:17:24.105 this was connecting and and and it
NOTE Confidence: 0.854650091818182

00:17:24.105 --> 00:17:25.965 led to some some questions next,
NOTE Confidence: 0.854650091818182

00:17:25.970 --> 00:17:27.390 which was, you know what?
NOTE Confidence: 0.854650091818182

00:17:27.390 --> 00:17:29.245 What's going on with all these different
NOTE Confidence: 0.854650091818182

00:17:29.245 --> 00:17:30.830 variants that we were identified?
NOTE Confidence: 0.854650091818182

00:17:30.830 --> 00:17:33.558 So the variant that we found in our
NOTE Confidence: 0.854650091818182

00:17:33.558 --> 00:17:36.132 patient was this Arch 249 missense mutation.
NOTE Confidence: 0.854650091818182

00:17:36.132 --> 00:17:38.748 There was also a termination codon
NOTE Confidence: 0.854650091818182

00:17:38.750 --> 00:17:40.478 and and the other thing is that you
NOTE Confidence: 0.854650091818182

00:17:40.478 --> 00:17:42.058 could see is that our our patients
NOTE Confidence: 0.854650091818182

00:17:42.058 --> 00:17:44.030 seem to have the most of European type.
NOTE Confidence: 0.854650091818182

00:17:44.030 --> 00:17:44.831 Really, you know.

NOTE Confidence: 0.854650091818182

00:17:44.831 --> 00:17:46.433 Is a fetus was presenting while

NOTE Confidence: 0.854650091818182

00:17:46.433 --> 00:17:48.085 many of these other patients were

NOTE Confidence: 0.854650091818182

00:17:48.085 --> 00:17:49.420 were not quite so severe.

NOTE Confidence: 0.854650091818182

00:17:49.420 --> 00:17:51.010 So what's going on there?

NOTE Confidence: 0.854650091818182

00:17:51.010 --> 00:17:53.313 And so we had some key questions

NOTE Confidence: 0.854650091818182

00:17:53.313 --> 00:17:55.997 there with we thought that the we

NOTE Confidence: 0.854650091818182

00:17:55.997 --> 00:17:58.022 could answer in the laboratory.

NOTE Confidence: 0.854650091818182

00:17:58.030 --> 00:17:59.718 One of which is that we could clearly

NOTE Confidence: 0.854650091818182

00:17:59.718 --> 00:18:01.569 see a kidney phenotype in *Xenopus*.

NOTE Confidence: 0.854650091818182

00:18:01.570 --> 00:18:02.575 The question is,

NOTE Confidence: 0.854650091818182

00:18:02.575 --> 00:18:04.585 could we see a hydrocephalus phenotype

NOTE Confidence: 0.854650091818182

00:18:04.585 --> 00:18:06.927 'cause this was something else that we saw?

NOTE Confidence: 0.854650091818182

00:18:06.930 --> 00:18:08.806 And then you know the severity of

NOTE Confidence: 0.854650091818182

00:18:08.806 --> 00:18:10.479 the symptoms seemed quite different.

NOTE Confidence: 0.854650091818182

00:18:10.480 --> 00:18:14.358 Ours had cystic kidneys and severely malformations.

NOTE Confidence: 0.854650091818182

00:18:14.360 --> 00:18:16.170 Others had hydrocephalus and others,
NOTE Confidence: 0.854650091818182

00:18:16.170 --> 00:18:17.982 yet had nephrotic syndrome or or
NOTE Confidence: 0.854650091818182

00:18:17.982 --> 00:18:19.839 UPJ obstruction which is really sort
NOTE Confidence: 0.854650091818182

00:18:19.839 --> 00:18:20.730 of a difference.
NOTE Confidence: 0.854650091818182

00:18:20.730 --> 00:18:23.768 And so we wondered if what we
NOTE Confidence: 0.854650091818182

00:18:23.768 --> 00:18:25.840 really need to do is see if these
NOTE Confidence: 0.889698658333333

00:18:25.904 --> 00:18:27.859 variants of unknown significance right
NOTE Confidence: 0.889698658333333

00:18:27.859 --> 00:18:30.310 which all of these were characterized
NOTE Confidence: 0.889698658333333

00:18:30.310 --> 00:18:32.920 at this point might also give us some
NOTE Confidence: 0.889698658333333

00:18:32.920 --> 00:18:34.994 insight as to the severity of the phenotype
NOTE Confidence: 0.889698658333333

00:18:34.994 --> 00:18:37.130 and so this is sort of the genotype.
NOTE Confidence: 0.889698658333333

00:18:37.130 --> 00:18:38.243 Phenotype correlation that
NOTE Confidence: 0.889698658333333

00:18:38.243 --> 00:18:39.727 people are looking for,
NOTE Confidence: 0.889698658333333

00:18:39.730 --> 00:18:42.138 and we thought we would do some some
NOTE Confidence: 0.889698658333333

00:18:42.138 --> 00:18:44.000 investigation into what's going on there.
NOTE Confidence: 0.889698658333333

00:18:44.000 --> 00:18:45.785 But first, let's look at this hydrocephalus.

NOTE Confidence: 0.889698658333333
00:18:45.790 --> 00:18:47.734 You know, could we actually see
NOTE Confidence: 0.889698658333333
00:18:47.734 --> 00:18:49.430 hydrocephalus in our frog model?
NOTE Confidence: 0.889698658333333
00:18:49.430 --> 00:18:51.418 And to do that we took advantage
NOTE Confidence: 0.889698658333333
00:18:51.418 --> 00:18:53.949 to some of the tools that my
NOTE Confidence: 0.889698658333333
00:18:53.949 --> 00:18:55.964 colleague ending in Denise developed.
NOTE Confidence: 0.889698658333333
00:18:55.970 --> 00:18:57.010 Which is this this tool,
NOTE Confidence: 0.889698658333333
00:18:57.010 --> 00:18:58.902 called optical coherence tomography.
NOTE Confidence: 0.889698658333333
00:18:58.902 --> 00:19:01.740 So hydrocephalus is is an abnormal
NOTE Confidence: 0.889698658333333
00:19:01.810 --> 00:19:04.006 collection of fluid in the brain.
NOTE Confidence: 0.889698658333333
00:19:04.010 --> 00:19:04.886 There's a,
NOTE Confidence: 0.889698658333333
00:19:04.886 --> 00:19:07.076 there's a ventricular system that
NOTE Confidence: 0.889698658333333
00:19:07.076 --> 00:19:09.110 circulates CSF through the brain,
NOTE Confidence: 0.889698658333333
00:19:09.110 --> 00:19:10.540 and when that gets clogged,
NOTE Confidence: 0.889698658333333
00:19:10.540 --> 00:19:13.690 the CSF can accumulate and can lead to brain
NOTE Confidence: 0.889698658333333
00:19:13.690 --> 00:19:15.858 compression actually can lead to severe.
NOTE Confidence: 0.889698658333333

00:19:15.860 --> 00:19:17.990 It can be life threatening.
NOTE Confidence: 0.8896986583333333

00:19:17.990 --> 00:19:19.026 And so one of the questions is,
NOTE Confidence: 0.8896986583333333

00:19:19.030 --> 00:19:20.830 could we visualize ventricles in the
NOTE Confidence: 0.8896986583333333

00:19:20.830 --> 00:19:23.089 brain of the frog and we use this
NOTE Confidence: 0.8896986583333333

00:19:23.089 --> 00:19:26.182 tool called Oct which is is like CT
NOTE Confidence: 0.8896986583333333

00:19:26.182 --> 00:19:28.486 scans except rather than using X rays,
NOTE Confidence: 0.8896986583333333

00:19:28.490 --> 00:19:31.266 it uses light. And so here's a tadpole.
NOTE Confidence: 0.8896986583333333

00:19:31.270 --> 00:19:32.866 You can see the eyes here.
NOTE Confidence: 0.8896986583333333

00:19:32.870 --> 00:19:34.050 This is the brain here.
NOTE Confidence: 0.8896986583333333

00:19:34.050 --> 00:19:34.731 Here's the gut.
NOTE Confidence: 0.8896986583333333

00:19:34.731 --> 00:19:36.950 And then the tail as it extends posteriorly.
NOTE Confidence: 0.8896986583333333

00:19:36.950 --> 00:19:38.502 So this is sort of a dorsal view
NOTE Confidence: 0.8896986583333333

00:19:38.502 --> 00:19:40.497 and you can see when we do OC T you
NOTE Confidence: 0.8896986583333333

00:19:40.497 --> 00:19:41.683 can actually make sections through
NOTE Confidence: 0.8896986583333333

00:19:41.683 --> 00:19:43.978 the brain and you can see the entire
NOTE Confidence: 0.8896986583333333

00:19:43.978 --> 00:19:46.768 ventricular system as this space

NOTE Confidence: 0.889698658333333
00:19:46.768 --> 00:19:50.399 here where CSF fluid is accumulated
NOTE Confidence: 0.889698658333333
00:19:50.400 --> 00:19:52.720 and if you now take a section you
NOTE Confidence: 0.889698658333333
00:19:52.720 --> 00:19:54.488 know along the midline here.
NOTE Confidence: 0.889698658333333
00:19:54.490 --> 00:19:55.580 That's what this section is.
NOTE Confidence: 0.889698658333333
00:19:55.580 --> 00:19:57.140 So here's the forebrain.
NOTE Confidence: 0.889698658333333
00:19:57.140 --> 00:19:58.310 Here's the hindbrain.
NOTE Confidence: 0.889698658333333
00:19:58.310 --> 00:19:59.670 This is the brain itself,
NOTE Confidence: 0.889698658333333
00:19:59.670 --> 00:20:00.300 and you could see this.
NOTE Confidence: 0.889698658333333
00:20:00.300 --> 00:20:02.090 Ventricular system and it's very
NOTE Confidence: 0.889698658333333
00:20:02.090 --> 00:20:04.518 cool about this is that while it
NOTE Confidence: 0.889698658333333
00:20:04.518 --> 00:20:06.814 can give us sections like a CT scan,
NOTE Confidence: 0.889698658333333
00:20:06.820 --> 00:20:09.060 the embryo is like in a CT scan,
NOTE Confidence: 0.889698658333333
00:20:09.060 --> 00:20:12.174 completely alive and so we can
NOTE Confidence: 0.889698658333333
00:20:12.174 --> 00:20:14.250 actually visualize CSF circulation.
NOTE Confidence: 0.889698658333333
00:20:14.250 --> 00:20:15.300 So here's a movie again,
NOTE Confidence: 0.889698658333333

00:20:15.300 --> 00:20:17.106 here's the forebrain at the tadpole.
NOTE Confidence: 0.8896986583333333

00:20:17.110 --> 00:20:17.532 I'm sorry.
NOTE Confidence: 0.8896986583333333

00:20:17.532 --> 00:20:18.798 Here's the forebrain of the tadpole.
NOTE Confidence: 0.8896986583333333

00:20:18.800 --> 00:20:19.961 Here's the hindbrain.
NOTE Confidence: 0.8896986583333333

00:20:19.961 --> 00:20:22.605 You can see the whole CSF ventricle
NOTE Confidence: 0.8896986583333333

00:20:22.605 --> 00:20:24.810 system here at certain room or a
NOTE Confidence: 0.8896986583333333

00:20:24.810 --> 00:20:26.807 section sort of going right through
NOTE Confidence: 0.8896986583333333

00:20:26.807 --> 00:20:28.504 that middle and you can actually
NOTE Confidence: 0.8896986583333333

00:20:28.504 --> 00:20:30.070 see that there's fluid flow that's
NOTE Confidence: 0.8896986583333333

00:20:30.125 --> 00:20:31.600 occurring because of the cilia.
NOTE Confidence: 0.8896986583333333

00:20:31.600 --> 00:20:34.318 That are driving these these small
NOTE Confidence: 0.8896986583333333

00:20:34.318 --> 00:20:37.360 particles and moving through the circulation.
NOTE Confidence: 0.8896986583333333

00:20:37.360 --> 00:20:39.472 So really we can really see not only
NOTE Confidence: 0.8896986583333333

00:20:39.472 --> 00:20:41.423 the size of the ventricles with
NOTE Confidence: 0.8896986583333333

00:20:41.423 --> 00:20:43.123 CSF circulation and actually we
NOTE Confidence: 0.8896986583333333

00:20:43.123 --> 00:20:45.568 can even do particle tracking and

NOTE Confidence: 0.889698658333333
00:20:45.568 --> 00:20:48.976 calculate velocities of that as well.
NOTE Confidence: 0.889698658333333
00:20:48.980 --> 00:20:50.709 And so then the question of course
NOTE Confidence: 0.889698658333333
00:20:50.709 --> 00:20:52.423 is do we get hydrocephalus and
NOTE Confidence: 0.889698658333333
00:20:52.423 --> 00:20:54.551 so when we knock down DLG five?
NOTE Confidence: 0.889698658333333
00:20:54.560 --> 00:20:56.816 You can see that in our control embryos,
NOTE Confidence: 0.889698658333333
00:20:56.820 --> 00:20:58.236 the ventricles or a one size,
NOTE Confidence: 0.889698658333333
00:20:58.240 --> 00:20:59.852 and they're considerably larger.
NOTE Confidence: 0.889698658333333
00:20:59.852 --> 00:21:02.674 And we quantitative this and you can
NOTE Confidence: 0.889698658333333
00:21:02.674 --> 00:21:04.720 clearly see that our frog embryos
NOTE Confidence: 0.889698658333333
00:21:04.720 --> 00:21:07.570 that are depleted of DLG 5 do indeed
NOTE Confidence: 0.889698658333333
00:21:07.570 --> 00:21:08.982 have enlarged ventricles suggestive
NOTE Confidence: 0.889698658333333
00:21:08.982 --> 00:21:11.068 of the hydrocephalus that we see in.
NOTE Confidence: 0.851587736666667
00:21:11.070 --> 00:21:14.886 In the patients that we enrolled.
NOTE Confidence: 0.851587736666667
00:21:14.890 --> 00:21:16.228 OK, so then the second question
NOTE Confidence: 0.851587736666667
00:21:16.228 --> 00:21:17.802 is what about these variants of
NOTE Confidence: 0.851587736666667

00:21:17.802 --> 00:21:19.062 unknown significance and the
NOTE Confidence: 0.851587736666667

00:21:19.062 --> 00:21:20.550 differential phenotypes that we saw.
NOTE Confidence: 0.851587736666667

00:21:20.550 --> 00:21:23.115 You know, can we make some sense of that?
NOTE Confidence: 0.851587736666667

00:21:23.120 --> 00:21:24.180 So remember, these are all
NOTE Confidence: 0.851587736666667

00:21:24.180 --> 00:21:24.816 the different variants.
NOTE Confidence: 0.851587736666667

00:21:24.820 --> 00:21:26.100 This is the one that we saw in.
NOTE Confidence: 0.851587736666667

00:21:26.100 --> 00:21:27.180 These are the different
NOTE Confidence: 0.851587736666667

00:21:27.180 --> 00:21:28.800 ones that are are seen I.
NOTE Confidence: 0.851587736666667

00:21:28.800 --> 00:21:32.932 I think these two are more seem to have a
NOTE Confidence: 0.851587736666667

00:21:32.932 --> 00:21:34.397 more striking phenotype like hydrocephalus,
NOTE Confidence: 0.851587736666667

00:21:34.400 --> 00:21:37.576 while this one was the most mild phenotype.
NOTE Confidence: 0.851587736666667

00:21:37.580 --> 00:21:39.396 And what we wanted to do is test
NOTE Confidence: 0.851587736666667

00:21:39.396 --> 00:21:40.771 these variants and see if they
NOTE Confidence: 0.851587736666667

00:21:40.771 --> 00:21:42.328 had also impact in our system and
NOTE Confidence: 0.851587736666667

00:21:42.328 --> 00:21:43.920 one of the things that we can do.
NOTE Confidence: 0.851587736666667

00:21:43.920 --> 00:21:45.480 That's pretty cool in frogs is

NOTE Confidence: 0.851587736666667
00:21:45.480 --> 00:21:47.102 that we can fertilize embryos and
NOTE Confidence: 0.851587736666667
00:21:47.102 --> 00:21:48.964 inject things at the one cell stage.
NOTE Confidence: 0.851587736666667
00:21:48.970 --> 00:21:50.998 If we do that,
NOTE Confidence: 0.851587736666667
00:21:50.998 --> 00:21:55.118 the whole embryo has a depletion of dog 5.
NOTE Confidence: 0.851587736666667
00:21:55.120 --> 00:21:57.540 Then what we can do is wait at the two
NOTE Confidence: 0.851587736666667
00:21:57.608 --> 00:21:59.701 cell stage because of the two cell
NOTE Confidence: 0.851587736666667
00:21:59.701 --> 00:22:02.010 stage we can inject drug five RNA.
NOTE Confidence: 0.851587736666667
00:22:02.010 --> 00:22:03.855 So the human morning expecting
NOTE Confidence: 0.851587736666667
00:22:03.855 --> 00:22:06.587 that one side of the embryo will
NOTE Confidence: 0.851587736666667
00:22:06.587 --> 00:22:09.017 rescue while the other side will
NOTE Confidence: 0.851587736666667
00:22:09.017 --> 00:22:11.905 be depleted of the LG five and then
NOTE Confidence: 0.851587736666667
00:22:11.905 --> 00:22:13.968 use that depleted side that rescued
NOTE Confidence: 0.851587736666667
00:22:13.968 --> 00:22:16.152 side compared to the depleted side
NOTE Confidence: 0.851587736666667
00:22:16.152 --> 00:22:17.730 and actually make a ratio.
NOTE Confidence: 0.851587736666667
00:22:17.730 --> 00:22:21.122 So here you can see that what we're
NOTE Confidence: 0.851587736666667

00:22:21.122 --> 00:22:24.447 measuring is the kidney tubule diameter.

NOTE Confidence: 0.851587736666667

00:22:24.450 --> 00:22:25.790 And we're measuring one side

NOTE Confidence: 0.851587736666667

00:22:25.790 --> 00:22:26.594 versus the other.

NOTE Confidence: 0.851587736666667

00:22:26.600 --> 00:22:29.147 So here you can see that normally if we

NOTE Confidence: 0.851587736666667

00:22:29.147 --> 00:22:32.016 just inject DLG 5 morpholino and a mock RNA.

NOTE Confidence: 0.851587736666667

00:22:32.020 --> 00:22:33.648 So GFP for example,

NOTE Confidence: 0.851587736666667

00:22:33.648 --> 00:22:36.090 the the ratio is about 1,

NOTE Confidence: 0.851587736666667

00:22:36.090 --> 00:22:36.441 right?

NOTE Confidence: 0.851587736666667

00:22:36.441 --> 00:22:38.547 So that the depleted sides basically

NOTE Confidence: 0.851587736666667

00:22:38.547 --> 00:22:40.648 on both sides are not rescued.

NOTE Confidence: 0.851587736666667

00:22:40.650 --> 00:22:42.883 But if we inject DLG frog morpholino

NOTE Confidence: 0.851587736666667

00:22:42.883 --> 00:22:44.754 and then on one side injected

NOTE Confidence: 0.851587736666667

00:22:44.754 --> 00:22:46.440 DLG 5 M human M RNA,

NOTE Confidence: 0.851587736666667

00:22:46.440 --> 00:22:48.320 you can see that we get a rescue

NOTE Confidence: 0.851587736666667

00:22:48.320 --> 00:22:50.156 right the the size of that tubulin

NOTE Confidence: 0.851587736666667

00:22:50.156 --> 00:22:52.111 on the rescued side on the side

NOTE Confidence: 0.851587736666667

00:22:52.111 --> 00:22:53.561 with where we've injected human

NOTE Confidence: 0.851587736666667

00:22:53.561 --> 00:22:55.664 DLG five is actually quite smaller,

NOTE Confidence: 0.851587736666667

00:22:55.664 --> 00:22:58.880 and so the ratio becomes less than one.

NOTE Confidence: 0.851587736666667

00:22:58.880 --> 00:22:59.948 On the other hand,

NOTE Confidence: 0.851587736666667

00:22:59.948 --> 00:23:02.145 if we take this Arch 166 histidine marker,

NOTE Confidence: 0.851587736666667

00:23:02.145 --> 00:23:04.140 you see that there is no rescue

NOTE Confidence: 0.851587736666667

00:23:04.202 --> 00:23:06.112 that's occurred suggesting that this

NOTE Confidence: 0.851587736666667

00:23:06.112 --> 00:23:08.570 variant actually is detrimental to function,

NOTE Confidence: 0.851587736666667

00:23:08.570 --> 00:23:11.202 and so maybe that would suggest that This

NOTE Confidence: 0.851587736666667

00:23:11.202 --> 00:23:14.407 is why this this patient has hydrocephalus,

NOTE Confidence: 0.851587736666667

00:23:14.410 --> 00:23:15.032 for example.

NOTE Confidence: 0.851587736666667

00:23:15.032 --> 00:23:16.898 In fact, it was very striking.

NOTE Confidence: 0.851587736666667

00:23:16.900 --> 00:23:18.734 Is is these patients were homozygous for

NOTE Confidence: 0.851587736666667

00:23:18.734 --> 00:23:20.551 the variant and so that made sense that

NOTE Confidence: 0.851587736666667

00:23:20.551 --> 00:23:22.566 they had a loss of function of the LG 5.

NOTE Confidence: 0.851587736666667

00:23:22.570 --> 00:23:24.418 But we're more our patient was de Novo,
NOTE Confidence: 0.851587736666667

00:23:24.420 --> 00:23:26.396 so it had one copy that was abnormal.
NOTE Confidence: 0.851587736666667

00:23:26.400 --> 00:23:27.762 One copy that was normal and
NOTE Confidence: 0.851587736666667

00:23:27.762 --> 00:23:29.169 in fact you could see that.
NOTE Confidence: 0.851587736666667

00:23:29.170 --> 00:23:30.097 When we deplete,
NOTE Confidence: 0.851587736666667

00:23:30.097 --> 00:23:32.720 when we use this variant in our assay,
NOTE Confidence: 0.851587736666667

00:23:32.720 --> 00:23:35.728 it actually harms the size of the tubule,
NOTE Confidence: 0.851587736666667

00:23:35.730 --> 00:23:36.189 right?
NOTE Confidence: 0.851587736666667

00:23:36.189 --> 00:23:38.943 The tubule actually gets more dilated
NOTE Confidence: 0.851587736666667

00:23:38.943 --> 00:23:40.870 by overexpressing this variant
NOTE Confidence: 0.851587736666667

00:23:40.870 --> 00:23:43.265 completely opposite of the rescue.
NOTE Confidence: 0.851587736666667

00:23:43.270 --> 00:23:45.870 Really suggesting that it could
NOTE Confidence: 0.851587736666667

00:23:45.870 --> 00:23:48.988 have a dominant effect in the sense
NOTE Confidence: 0.851587736666667

00:23:48.988 --> 00:23:51.064 that this this this this sorry,
NOTE Confidence: 0.851587736666667

00:23:51.070 --> 00:23:51.682 this variant,
NOTE Confidence: 0.851587736666667

00:23:51.682 --> 00:23:54.130 even if it's in a in a region

NOTE Confidence: 0.829579325294118
00:23:54.209 --> 00:23:56.344 that is is not a known domain.
NOTE Confidence: 0.829579325294118
00:23:56.350 --> 00:23:57.522 It actually really harms
NOTE Confidence: 0.829579325294118
00:23:57.522 --> 00:23:58.987 the function of the protein.
NOTE Confidence: 0.829579325294118
00:23:58.990 --> 00:24:01.545 Literally giving it a what we call
NOTE Confidence: 0.829579325294118
00:24:01.545 --> 00:24:03.390 a dominant negative phenotype.
NOTE Confidence: 0.829579325294118
00:24:03.390 --> 00:24:05.010 And then interesting, this last variant,
NOTE Confidence: 0.829579325294118
00:24:05.010 --> 00:24:06.906 which sorry, this is a typo.
NOTE Confidence: 0.829579325294118
00:24:06.910 --> 00:24:09.423 It should really be this glycine 1509.
NOTE Confidence: 0.829579325294118
00:24:09.423 --> 00:24:11.075 Leucine actually has relatively
NOTE Confidence: 0.829579325294118
00:24:11.075 --> 00:24:12.727 mild loss of function.
NOTE Confidence: 0.829579325294118
00:24:12.730 --> 00:24:14.683 You could almost see that it kind of rescues,
NOTE Confidence: 0.829579325294118
00:24:14.690 --> 00:24:17.020 really suggesting that maybe this
NOTE Confidence: 0.829579325294118
00:24:17.020 --> 00:24:21.029 variant is not so a strikingly harmed,
NOTE Confidence: 0.829579325294118
00:24:21.030 --> 00:24:22.188 and in fact that makes sense,
NOTE Confidence: 0.829579325294118
00:24:22.190 --> 00:24:23.560 because that these this variant
NOTE Confidence: 0.829579325294118

00:24:23.560 --> 00:24:24.930 was identified in those patients

NOTE Confidence: 0.829579325294118

00:24:24.980 --> 00:24:26.310 that had the mildest phenotype.

NOTE Confidence: 0.829579325294118

00:24:26.310 --> 00:24:26.800 So again,

NOTE Confidence: 0.829579325294118

00:24:26.800 --> 00:24:28.515 this is the kind of assay that

NOTE Confidence: 0.829579325294118

00:24:28.515 --> 00:24:30.455 you can do that can really help

NOTE Confidence: 0.829579325294118

00:24:30.455 --> 00:24:32.072 you connect the Geno types that

NOTE Confidence: 0.829579325294118

00:24:32.072 --> 00:24:33.412 we're seeing with the phenotypes.

NOTE Confidence: 0.829579325294118

00:24:33.420 --> 00:24:35.149 And so that was that was exciting

NOTE Confidence: 0.829579325294118

00:24:35.149 --> 00:24:37.350 to us and really sort of highlighted

NOTE Confidence: 0.829579325294118

00:24:37.350 --> 00:24:39.100 the importance of of bringing

NOTE Confidence: 0.829579325294118

00:24:39.100 --> 00:24:40.547 this work into the lab.

NOTE Confidence: 0.932984798333333

00:24:42.680 --> 00:24:45.371 OK, so one of the things I'd like to

NOTE Confidence: 0.932984798333333

00:24:45.371 --> 00:24:47.564 summarize at this point is that we do

NOTE Confidence: 0.932984798333333

00:24:47.564 --> 00:24:49.375 have clinical genetic testing at Yale

NOTE Confidence: 0.932984798333333

00:24:49.375 --> 00:24:52.167 and like it is in many places and that

NOTE Confidence: 0.932984798333333

00:24:52.167 --> 00:24:54.630 could be used to a clinical diagnosis.

NOTE Confidence: 0.932984798333333
00:24:54.630 --> 00:24:55.758 And there's a lot of types
NOTE Confidence: 0.932984798333333
00:24:55.758 --> 00:24:56.879 of genomics that we can use.
NOTE Confidence: 0.932984798333333
00:24:56.880 --> 00:24:58.693 So if there's a patient with real
NOTE Confidence: 0.932984798333333
00:24:58.693 --> 00:25:00.006 critical illness that we need
NOTE Confidence: 0.932984798333333
00:25:00.006 --> 00:25:01.216 to make a diagnosis quickly,
NOTE Confidence: 0.932984798333333
00:25:01.220 --> 00:25:03.506 there is the option for rapid
NOTE Confidence: 0.932984798333333
00:25:03.506 --> 00:25:04.649 whole genome sequencing,
NOTE Confidence: 0.932984798333333
00:25:04.650 --> 00:25:07.458 which you know it's more expensive for sure,
NOTE Confidence: 0.932984798333333
00:25:07.460 --> 00:25:09.371 but we can then also do clinical
NOTE Confidence: 0.932984798333333
00:25:09.371 --> 00:25:10.813 exome sequencing and and and
NOTE Confidence: 0.932984798333333
00:25:10.813 --> 00:25:11.945 this kind of information.
NOTE Confidence: 0.932984798333333
00:25:11.950 --> 00:25:14.624 Can get right into the medical record.
NOTE Confidence: 0.932984798333333
00:25:14.630 --> 00:25:15.820 Then one of the things we can
NOTE Confidence: 0.932984798333333
00:25:15.820 --> 00:25:17.405 do is that if in these sorts
NOTE Confidence: 0.932984798333333
00:25:17.405 --> 00:25:18.429 of strategies were identified,
NOTE Confidence: 0.932984798333333

00:25:18.430 --> 00:25:19.502 variants of unknown significance,
NOTE Confidence: 0.932984798333333

00:25:19.502 --> 00:25:21.110 we can try to discover that
NOTE Confidence: 0.932984798333333

00:25:21.158 --> 00:25:22.610 significance by going into the lab
NOTE Confidence: 0.932984798333333

00:25:22.610 --> 00:25:24.274 and and that's where our pediatric
NOTE Confidence: 0.932984798333333

00:25:24.274 --> 00:25:25.904 genomics Discovery program is working.
NOTE Confidence: 0.932984798333333

00:25:25.910 --> 00:25:28.090 Very hard to do.
NOTE Confidence: 0.932984798333333

00:25:28.090 --> 00:25:30.298 This is the power of animal model testing.
NOTE Confidence: 0.932984798333333

00:25:30.300 --> 00:25:32.589 It allows us to understand the biology
NOTE Confidence: 0.932984798333333

00:25:32.589 --> 00:25:34.987 and tested the US is for a phenotype,
NOTE Confidence: 0.932984798333333

00:25:34.990 --> 00:25:37.228 genotype correlation and just to see
NOTE Confidence: 0.932984798333333

00:25:37.228 --> 00:25:39.710 if they are actually dysfunctional.
NOTE Confidence: 0.932984798333333

00:25:39.710 --> 00:25:42.126 Now one of the other things that was
NOTE Confidence: 0.932984798333333

00:25:42.126 --> 00:25:44.394 interesting to do is because we then
NOTE Confidence: 0.932984798333333

00:25:44.394 --> 00:25:46.649 identified as cilia phenotype in our fetus,
NOTE Confidence: 0.932984798333333

00:25:46.650 --> 00:25:49.236 the family decided to terminate that
NOTE Confidence: 0.932984798333333

00:25:49.236 --> 00:25:52.310 based on the severity of the phenotype.

NOTE Confidence: 0.932984798333333
00:25:52.310 --> 00:25:54.750 But we took some of those tissues and
NOTE Confidence: 0.932984798333333
00:25:54.750 --> 00:25:57.113 asked the question can we see defects
NOTE Confidence: 0.932984798333333
00:25:57.113 --> 00:25:59.390 in cilia and those fetal tissues,
NOTE Confidence: 0.932984798333333
00:25:59.390 --> 00:26:00.470 and in fact we did.
NOTE Confidence: 0.932984798333333
00:26:00.470 --> 00:26:02.006 We definitely saw lots of silly and the
NOTE Confidence: 0.932984798333333
00:26:02.006 --> 00:26:04.065 key I don't have time to show you that data,
NOTE Confidence: 0.932984798333333
00:26:04.070 --> 00:26:05.252 but we did.
NOTE Confidence: 0.932984798333333
00:26:05.252 --> 00:26:07.222 But interestingly we saw totally
NOTE Confidence: 0.932984798333333
00:26:07.222 --> 00:26:09.120 normal silly in the trachea.
NOTE Confidence: 0.932984798333333
00:26:09.120 --> 00:26:11.688 Suggesting that this gene clearly has
NOTE Confidence: 0.932984798333333
00:26:11.688 --> 00:26:14.857 effects on certain cilia and not other cilia,
NOTE Confidence: 0.932984798333333
00:26:14.860 --> 00:26:16.844 and so again this is an Ave that
NOTE Confidence: 0.932984798333333
00:26:16.844 --> 00:26:18.820 we're now starting to investigate.
NOTE Confidence: 0.932984798333333
00:26:18.820 --> 00:26:19.145 What?
NOTE Confidence: 0.932984798333333
00:26:19.145 --> 00:26:21.095 What is this silly a predilection
NOTE Confidence: 0.932984798333333

00:26:21.095 --> 00:26:23.599 for DLG 5 and and and that then,
NOTE Confidence: 0.932984798333333

00:26:23.600 --> 00:26:26.316 is really the launch of a basic
NOTE Confidence: 0.932984798333333

00:26:26.316 --> 00:26:27.092 science study.
NOTE Confidence: 0.932984798333333

00:26:27.100 --> 00:26:27.630 And importantly,
NOTE Confidence: 0.932984798333333

00:26:27.630 --> 00:26:28.955 we can return these research
NOTE Confidence: 0.932984798333333

00:26:28.955 --> 00:26:30.200 results to the patients.
NOTE Confidence: 0.932984798333333

00:26:30.200 --> 00:26:31.604 You can imagine for this family
NOTE Confidence: 0.932984798333333

00:26:31.604 --> 00:26:33.445 that we saw here at de Novo
NOTE Confidence: 0.932984798333333

00:26:33.445 --> 00:26:34.860 mutations really would suggest that
NOTE Confidence: 0.932984798333333

00:26:34.860 --> 00:26:36.466 it's pretty unlikely that they'd
NOTE Confidence: 0.932984798333333

00:26:36.466 --> 00:26:37.778 have this phenotype again.
NOTE Confidence: 0.932984798333333

00:26:37.780 --> 00:26:39.684 Of course, you never say never in genetics,
NOTE Confidence: 0.932984798333333

00:26:39.690 --> 00:26:44.166 but it's really powerful to know.
NOTE Confidence: 0.932984798333333

00:26:44.170 --> 00:26:49.538 OK time yeah. OK, good so uh next talk.
NOTE Confidence: 0.932984798333333

00:26:49.540 --> 00:26:51.900 I'd like to talk about a RST which
NOTE Confidence: 0.932984798333333

00:26:51.900 --> 00:26:54.257 actually led to an exciting intervention

NOTE Confidence: 0.932984798333333
00:26:54.260 --> 00:26:56.045 that was really driven by the family.
NOTE Confidence: 0.932984798333333
00:26:56.050 --> 00:26:57.995 So there's a young couple
NOTE Confidence: 0.932984798333333
00:26:57.995 --> 00:26:59.940 that plans to have children.
NOTE Confidence: 0.932984798333333
00:26:59.940 --> 00:27:01.700 Mom has some fertility issues,
NOTE Confidence: 0.932984798333333
00:27:01.700 --> 00:27:05.590 so you can see that she lost two pregnancies.
NOTE Confidence: 0.932984798333333
00:27:05.590 --> 00:27:09.270 Then the child that we first met had
NOTE Confidence: 0.932984798333333
00:27:09.270 --> 00:27:12.462 some polyhydramnios at 35 weeks and
NOTE Confidence: 0.932984798333333
00:27:12.462 --> 00:27:15.613 some fluid around her pregnancy and
NOTE Confidence: 0.932984798333333
00:27:15.613 --> 00:27:18.949 then was born at term after a C-section.
NOTE Confidence: 0.932984798333333
00:27:18.950 --> 00:27:20.490 In the delivery room,
NOTE Confidence: 0.932984798333333
00:27:20.490 --> 00:27:22.800 the baby immediately had severe hypoxia
NOTE Confidence: 0.932984798333333
00:27:22.873 --> 00:27:25.525 and was promptly intubated and ventilated.
NOTE Confidence: 0.932984798333333
00:27:25.530 --> 00:27:27.310 But despite all of their
NOTE Confidence: 0.932984798333333
00:27:27.310 --> 00:27:28.378 efforts at resuscitation,
NOTE Confidence: 0.932984798333333
00:27:28.380 --> 00:27:30.450 the baby died within an hour.
NOTE Confidence: 0.932984798333333

00:27:30.450 --> 00:27:32.568 Really sort of a severe effect,
NOTE Confidence: 0.853886118

00:27:32.570 --> 00:27:34.350 and in fact, on autopsy.
NOTE Confidence: 0.853886118

00:27:34.350 --> 00:27:36.380 It was really unremarkable except
NOTE Confidence: 0.853886118

00:27:36.380 --> 00:27:38.410 for the striking finding that
NOTE Confidence: 0.853886118

00:27:38.477 --> 00:27:40.667 there were very hypoplastic lungs.
NOTE Confidence: 0.853886118

00:27:40.670 --> 00:27:42.889 Normally the weight of the lung should
NOTE Confidence: 0.853886118

00:27:42.889 --> 00:27:45.372 be about 53 grams at birth and these
NOTE Confidence: 0.853886118

00:27:45.372 --> 00:27:47.979 were only 14 grams or very hypoplastic.
NOTE Confidence: 0.853886118

00:27:47.980 --> 00:27:49.798 They had a second pregnancy and
NOTE Confidence: 0.853886118

00:27:49.798 --> 00:27:52.139 had a healthy girl and then hoping
NOTE Confidence: 0.853886118

00:27:52.139 --> 00:27:53.919 to expand their family further.
NOTE Confidence: 0.853886118

00:27:53.920 --> 00:27:56.086 They had another baby that unfortunately
NOTE Confidence: 0.853886118

00:27:56.086 --> 00:27:58.354 passed away so that third pregnancy
NOTE Confidence: 0.853886118

00:27:58.354 --> 00:28:00.204 was smooth until birth again.
NOTE Confidence: 0.853886118

00:28:00.204 --> 00:28:02.472 You can see that the baby boy
NOTE Confidence: 0.853886118

00:28:02.472 --> 00:28:03.740 had severe hypoxia,

NOTE Confidence: 0.853886118

00:28:03.740 --> 00:28:05.125 was then intubated and ventilated

NOTE Confidence: 0.853886118

00:28:05.125 --> 00:28:06.897 again was unable to be resuscitated

NOTE Confidence: 0.853886118

00:28:06.897 --> 00:28:08.913 and again they could see pulmonary

NOTE Confidence: 0.853886118

00:28:08.913 --> 00:28:10.617 hyperplasia and this is the X ray.

NOTE Confidence: 0.853886118

00:28:10.620 --> 00:28:13.007 You can see that there's just literally

NOTE Confidence: 0.853886118

00:28:13.007 --> 00:28:15.371 no lung tissue there, and an autopsy.

NOTE Confidence: 0.853886118

00:28:15.371 --> 00:28:17.153 You can see the heart normally,

NOTE Confidence: 0.853886118

00:28:17.160 --> 00:28:18.330 but where you should see.

NOTE Confidence: 0.853886118

00:28:18.330 --> 00:28:20.644 His lungs, it's just empty, right?

NOTE Confidence: 0.853886118

00:28:20.644 --> 00:28:21.580 There's no lungs there.

NOTE Confidence: 0.751329613846154

00:28:23.690 --> 00:28:27.554 And so we did exon sequencing and

NOTE Confidence: 0.751329613846154

00:28:27.554 --> 00:28:30.440 identified a variant in error 2.

NOTE Confidence: 0.751329613846154

00:28:30.440 --> 00:28:32.100 These are quite rare.

NOTE Confidence: 0.751329613846154

00:28:32.100 --> 00:28:33.760 Not not entirely missing

NOTE Confidence: 0.751329613846154

00:28:33.760 --> 00:28:35.580 from the populations.

NOTE Confidence: 0.751329613846154

00:28:35.580 --> 00:28:37.547 But you could see that father was
NOTE Confidence: 0.751329613846154

00:28:37.547 --> 00:28:38.850 heterozygous for this variant.
NOTE Confidence: 0.751329613846154

00:28:38.850 --> 00:28:40.922 Mom was Heterozygous and his and the
NOTE Confidence: 0.751329613846154

00:28:40.922 --> 00:28:42.546 affected brother of the program that
NOTE Confidence: 0.751329613846154

00:28:42.546 --> 00:28:44.130 we studied was also carrying both.
NOTE Confidence: 0.751329613846154

00:28:44.130 --> 00:28:45.945 So his compound heterozygotes for
NOTE Confidence: 0.751329613846154

00:28:45.945 --> 00:28:48.757 this error is too and I think to
NOTE Confidence: 0.751329613846154

00:28:48.757 --> 00:28:50.896 look at the pedigree and importantly the
NOTE Confidence: 0.751329613846154

00:28:50.896 --> 00:28:52.898 affected brother was also hit but his
NOTE Confidence: 0.751329613846154

00:28:52.898 --> 00:28:54.818 his healthy sister was heterozygous.
NOTE Confidence: 0.751329613846154

00:28:54.820 --> 00:28:56.578 So really the genetics make sense.
NOTE Confidence: 0.751329613846154

00:28:56.580 --> 00:28:57.948 It looks like this.
NOTE Confidence: 0.751329613846154

00:28:57.948 --> 00:29:00.440 So the mother and father are
NOTE Confidence: 0.751329613846154

00:29:00.440 --> 00:29:02.590 heterozygous for these two variants.
NOTE Confidence: 0.751329613846154

00:29:02.590 --> 00:29:06.280 Both affected children are compound.
NOTE Confidence: 0.751329613846154

00:29:06.280 --> 00:29:08.148 Compound heterozygous while the

NOTE Confidence: 0.751329613846154

00:29:08.148 --> 00:29:11.351 healthy child healthy girl is is is

NOTE Confidence: 0.751329613846154

00:29:11.351 --> 00:29:13.584 is has the same genotype as mom.

NOTE Confidence: 0.8126070875

00:29:15.780 --> 00:29:17.472 So, uh, you know the family

NOTE Confidence: 0.8126070875

00:29:17.472 --> 00:29:19.555 very much wanted to have a, uh,

NOTE Confidence: 0.8126070875

00:29:19.555 --> 00:29:21.930 expand and have more children.

NOTE Confidence: 0.8126070875

00:29:21.930 --> 00:29:25.430 And so, uh, we started wondering how

NOTE Confidence: 0.8126070875

00:29:25.430 --> 00:29:28.139 relevant this arrasta mutation was.

NOTE Confidence: 0.8126070875

00:29:28.140 --> 00:29:30.891 So RS2 is a protein that's involved

NOTE Confidence: 0.8126070875

00:29:30.891 --> 00:29:32.800 in mitochondrial protein synthesis.

NOTE Confidence: 0.8126070875

00:29:32.800 --> 00:29:34.930 It's a T RNA synthesis.

NOTE Confidence: 0.8126070875

00:29:34.930 --> 00:29:36.982 And we know mitochondrial diseases can

NOTE Confidence: 0.8126070875

00:29:36.982 --> 00:29:38.742 certainly cause brain, skeletal muscle,

NOTE Confidence: 0.8126070875

00:29:38.742 --> 00:29:40.206 heart and kidney defects,

NOTE Confidence: 0.8126070875

00:29:40.210 --> 00:29:42.298 but no one had really identified

NOTE Confidence: 0.8126070875

00:29:42.298 --> 00:29:43.690 them in pulmonary hypoplasia.

NOTE Confidence: 0.8126070875

00:29:43.690 --> 00:29:44.178 And remember,
NOTE Confidence: 0.8126070875

00:29:44.178 --> 00:29:45.886 all of the other organs were normal,
NOTE Confidence: 0.8126070875

00:29:45.890 --> 00:29:47.976 and so we weren't sure what to
NOTE Confidence: 0.8126070875

00:29:47.976 --> 00:29:51.498 make of that for this family.
NOTE Confidence: 0.8126070875

00:29:51.500 --> 00:29:54.560 And in fact, uh, uh,
NOTE Confidence: 0.8126070875

00:29:54.560 --> 00:29:56.248 most of the there was a few reports
NOTE Confidence: 0.8126070875

00:29:56.248 --> 00:29:57.876 on areas to the suggested that
NOTE Confidence: 0.8126070875

00:29:57.876 --> 00:29:59.316 the maybe the pulmonary hypoplasia
NOTE Confidence: 0.8126070875

00:29:59.316 --> 00:30:00.618 was due to cardiomegaly.
NOTE Confidence: 0.8126070875

00:30:00.620 --> 00:30:01.024 But again,
NOTE Confidence: 0.8126070875

00:30:01.024 --> 00:30:02.880 in in this in the patient that we saw,
NOTE Confidence: 0.8126070875

00:30:02.880 --> 00:30:05.586 there wasn't any evidence of cardiomegaly.
NOTE Confidence: 0.8126070875

00:30:05.590 --> 00:30:06.418 And in fact,
NOTE Confidence: 0.8126070875

00:30:06.418 --> 00:30:07.798 the variants that we've seen
NOTE Confidence: 0.8126070875

00:30:07.798 --> 00:30:09.349 are present in the population.
NOTE Confidence: 0.8126070875

00:30:09.350 --> 00:30:10.925 There was another report with

NOTE Confidence: 0.8126070875

00:30:10.925 --> 00:30:12.185 exactly the same variance.

NOTE Confidence: 0.8126070875

00:30:12.190 --> 00:30:13.110 This R.

NOTE Confidence: 0.8126070875

00:30:13.110 --> 00:30:15.870 592 W in in this frameshift,

NOTE Confidence: 0.8126070875

00:30:15.870 --> 00:30:18.523 in an infant that died but from

NOTE Confidence: 0.8126070875

00:30:18.523 --> 00:30:20.430 cardiomyopathy without pulmonary hyperplasia,

NOTE Confidence: 0.8126070875

00:30:20.430 --> 00:30:22.138 and so trying to get at the

NOTE Confidence: 0.8126070875

00:30:22.138 --> 00:30:23.463 relevance of these variants for

NOTE Confidence: 0.8126070875

00:30:23.463 --> 00:30:25.059 the family was a bit tough.

NOTE Confidence: 0.8126070875

00:30:25.060 --> 00:30:27.097 But then two siblings with Arrows 2

NOTE Confidence: 0.8126070875

00:30:27.097 --> 00:30:29.294 variants were also published that did

NOTE Confidence: 0.8126070875

00:30:29.294 --> 00:30:30.986 have primary pulmonary hypertension,

NOTE Confidence: 0.8126070875

00:30:30.990 --> 00:30:33.110 and so this was very reassuring to us.

NOTE Confidence: 0.8126070875

00:30:33.110 --> 00:30:35.620 Then maybe these errors 2

NOTE Confidence: 0.8126070875

00:30:35.620 --> 00:30:37.126 variants are relevant.

NOTE Confidence: 0.8126070875

00:30:37.130 --> 00:30:38.086 And so we wanted.

NOTE Confidence: 0.8126070875

00:30:38.086 --> 00:30:40.007 So we communicated all these results to the
NOTE Confidence: 0.8126070875

00:30:40.007 --> 00:30:41.743 family and wondered where to go from here.
NOTE Confidence: 0.8126070875

00:30:41.750 --> 00:30:41.898 Well,
NOTE Confidence: 0.8126070875

00:30:41.898 --> 00:30:42.490 one of the things.
NOTE Confidence: 0.8126070875

00:30:42.490 --> 00:30:44.610 Of course we can do is we recognize
NOTE Confidence: 0.8126070875

00:30:44.610 --> 00:30:46.319 that mitochondrial genes have very
NOTE Confidence: 0.8126070875

00:30:46.319 --> 00:30:47.447 highly pleiotropic phenotypes,
NOTE Confidence: 0.8126070875

00:30:47.450 --> 00:30:49.850 partly because of the inheritance.
NOTE Confidence: 0.8126070875

00:30:49.850 --> 00:30:51.188 And this is always the challenge
NOTE Confidence: 0.8126070875

00:30:51.188 --> 00:30:52.730 of rare diseases in small numbers.
NOTE Confidence: 0.8126070875

00:30:52.730 --> 00:30:54.390 So we discussed these research
NOTE Confidence: 0.8126070875

00:30:54.390 --> 00:30:56.050 with jobs with the family.
NOTE Confidence: 0.8126070875

00:30:56.050 --> 00:30:58.830 And they were extremely grateful.
NOTE Confidence: 0.8126070875

00:30:58.830 --> 00:31:00.874 I also had a strong desire to
NOTE Confidence: 0.8126070875

00:31:00.874 --> 00:31:02.491 expand their family and they
NOTE Confidence: 0.8126070875

00:31:02.491 --> 00:31:04.181 were planning to have another

NOTE Confidence: 0.8126070875

00:31:04.181 --> 00:31:06.540 child anyway because they have us

NOTE Confidence: 0.8126070875

00:31:06.540 --> 00:31:08.220 incredible health care system.

NOTE Confidence: 0.8126070875

00:31:08.220 --> 00:31:09.440 They actually convinced their

NOTE Confidence: 0.8126070875

00:31:09.440 --> 00:31:11.270 health care system to do pre

NOTE Confidence: 0.8126070875

00:31:11.326 --> 00:31:12.870 implantation genomics so they

NOTE Confidence: 0.8126070875

00:31:12.870 --> 00:31:14.800 actually did in vitro fertilization,

NOTE Confidence: 0.8126070875

00:31:14.800 --> 00:31:16.688 identified those embryos that

NOTE Confidence: 0.8126070875

00:31:16.688 --> 00:31:19.048 were wild type ferreras too,

NOTE Confidence: 0.8126070875

00:31:19.050 --> 00:31:21.550 and just implanted those embryos.

NOTE Confidence: 0.8126070875

00:31:21.550 --> 00:31:22.960 And have to admit that was

NOTE Confidence: 0.8126070875

00:31:22.960 --> 00:31:24.110 a bit terrifying for us.

NOTE Confidence: 0.8126070875

00:31:24.110 --> 00:31:25.289 'cause you know,

NOTE Confidence: 0.8126070875

00:31:25.289 --> 00:31:28.040 there's just so few patients with this,

NOTE Confidence: 0.8126070875

00:31:28.040 --> 00:31:32.040 we weren't sure if there S2 was really.

NOTE Confidence: 0.8126070875

00:31:32.040 --> 00:31:33.015 Causative gene here.

NOTE Confidence: 0.8126070875

00:31:33.015 --> 00:31:35.660 And so we counseled them and said look,
NOTE Confidence: 0.8126070875

00:31:35.660 --> 00:31:38.068 you know we could be wrong you
NOTE Confidence: 0.8126070875

00:31:38.068 --> 00:31:40.573 could have wild type for us too
NOTE Confidence: 0.8126070875

00:31:40.573 --> 00:31:42.880 but still have the disease and they
NOTE Confidence: 0.8126070875

00:31:42.880 --> 00:31:44.560 understood that and and said look,
NOTE Confidence: 0.8126070875

00:31:44.560 --> 00:31:45.952 we're going to have another child
NOTE Confidence: 0.8126070875

00:31:45.952 --> 00:31:47.690 anyway and we feel this is important
NOTE Confidence: 0.8126070875

00:31:47.690 --> 00:31:48.706 information we're not willing
NOTE Confidence: 0.8126070875

00:31:48.706 --> 00:31:50.280 to take a chance otherwise.
NOTE Confidence: 0.8126070875

00:31:50.280 --> 00:31:52.555 Our chance is one in four anyway.
NOTE Confidence: 0.8126070875

00:31:52.560 --> 00:31:54.880 And so we hope that this would improve
NOTE Confidence: 0.8126070875

00:31:54.880 --> 00:31:57.062 our chances and so knowing that we
NOTE Confidence: 0.8126070875

00:31:57.062 --> 00:31:59.018 were reassured and then happily.
NOTE Confidence: 0.8126070875

00:31:59.018 --> 00:32:03.310 Uh, this is my hip, a sort of OK picture.
NOTE Confidence: 0.8126070875

00:32:03.310 --> 00:32:04.798 You can see that there's a
NOTE Confidence: 0.8126070875

00:32:04.798 --> 00:32:05.790 beautiful baby girl there,

NOTE Confidence: 0.8126070875

00:32:05.790 --> 00:32:07.110 and so it was really

NOTE Confidence: 0.8126070875

00:32:07.110 --> 00:32:08.430 exciting to see the family

NOTE Confidence: 0.917383092

00:32:08.491 --> 00:32:10.493 be able to take advantage of of

NOTE Confidence: 0.917383092

00:32:10.493 --> 00:32:12.541 some knowledge that we gave and and

NOTE Confidence: 0.917383092

00:32:12.541 --> 00:32:14.531 hopefully that led to this healthy baby.

NOTE Confidence: 0.917383092

00:32:14.531 --> 00:32:16.638 And instead of the sort of the

NOTE Confidence: 0.917383092

00:32:16.638 --> 00:32:18.459 challenges that they had previously.

NOTE Confidence: 0.889253558

00:32:20.770 --> 00:32:23.470 OK, so the summary of Part 2 is that genetic

NOTE Confidence: 0.889253558

00:32:23.533 --> 00:32:26.006 testing can be extremely powerful, right?

NOTE Confidence: 0.889253558

00:32:26.006 --> 00:32:29.094 And the ability to make a molecular diagnosis

NOTE Confidence: 0.889253558

00:32:29.094 --> 00:32:31.456 immediately opens up the things that you

NOTE Confidence: 0.889253558

00:32:31.456 --> 00:32:33.921 can do and opportunities for management and

NOTE Confidence: 0.889253558

00:32:33.921 --> 00:32:36.539 and I think that's that's really important.

NOTE Confidence: 0.889253558

00:32:36.540 --> 00:32:38.549 It also is important to return research

NOTE Confidence: 0.889253558

00:32:38.549 --> 00:32:40.640 results, and we really view patients

NOTE Confidence: 0.889253558

00:32:40.640 --> 00:32:42.440 as participants in the research,
NOTE Confidence: 0.889253558

00:32:42.440 --> 00:32:46.256 not subjects, and so that's challenging.
NOTE Confidence: 0.889253558

00:32:46.260 --> 00:32:48.396 In fact, we've faced some criticism from some
NOTE Confidence: 0.889253558

00:32:48.396 --> 00:32:50.778 of our colleagues that returning research.
NOTE Confidence: 0.889253558

00:32:50.780 --> 00:32:53.315 Results is challenging and and
NOTE Confidence: 0.889253558

00:32:53.315 --> 00:32:56.316 can be confusing to patients and
NOTE Confidence: 0.889253558

00:32:56.316 --> 00:32:58.596 so many people don't do it.
NOTE Confidence: 0.889253558

00:32:58.600 --> 00:33:00.329 Or we felt that it's really critical
NOTE Confidence: 0.889253558

00:33:00.329 --> 00:33:01.922 to return those results, because,
NOTE Confidence: 0.889253558

00:33:01.922 --> 00:33:04.454 again, we sort of view these
NOTE Confidence: 0.889253558

00:33:04.454 --> 00:33:06.088 patients as partners in research.
NOTE Confidence: 0.889253558

00:33:06.088 --> 00:33:09.048 And so we work hard to make sure that
NOTE Confidence: 0.889253558

00:33:09.048 --> 00:33:11.568 their information is is returned to them.
NOTE Confidence: 0.889253558

00:33:11.570 --> 00:33:12.914 It's particularly important because
NOTE Confidence: 0.889253558

00:33:12.914 --> 00:33:14.556 these are rare disorders, right?
NOTE Confidence: 0.889253558

00:33:14.556 --> 00:33:15.740 And so you know,

NOTE Confidence: 0.889253558

00:33:15.740 --> 00:33:17.258 it's not like there's a large

NOTE Confidence: 0.889253558

00:33:17.258 --> 00:33:18.826 cohort of these patients that they

NOTE Confidence: 0.889253558

00:33:18.826 --> 00:33:20.338 can use that kind of information,

NOTE Confidence: 0.889253558

00:33:20.340 --> 00:33:21.380 and so returning results.

NOTE Confidence: 0.889253558

00:33:21.380 --> 00:33:22.420 In these rare cases,

NOTE Confidence: 0.889253558

00:33:22.420 --> 00:33:23.248 is really powerful.

NOTE Confidence: 0.953955021875

00:33:25.360 --> 00:33:27.646 OK, so in the last story here in the

NOTE Confidence: 0.953955021875

00:33:27.646 --> 00:33:29.816 last 1015 minutes I hope to finish.

NOTE Confidence: 0.953955021875

00:33:29.820 --> 00:33:31.796 I'll tell you about a last gene and

NOTE Confidence: 0.953955021875

00:33:31.796 --> 00:33:33.882 this is exciting for me to share

NOTE Confidence: 0.953955021875

00:33:33.882 --> 00:33:36.012 with you because we actually have an

NOTE Confidence: 0.953955021875

00:33:36.012 --> 00:33:37.909 opportunity to talk to or hear from

NOTE Confidence: 0.953955021875

00:33:37.909 --> 00:33:41.200 the mother of the patient involved.

NOTE Confidence: 0.953955021875

00:33:41.200 --> 00:33:43.622 OK, so case three is lung disease

NOTE Confidence: 0.953955021875

00:33:43.622 --> 00:33:45.056 in a toddler, right?

NOTE Confidence: 0.953955021875

00:33:45.056 --> 00:33:47.036 So there's a young boy,
NOTE Confidence: 0.953955021875

00:33:47.040 --> 00:33:48.937 so this is the patient that was
NOTE Confidence: 0.953955021875

00:33:48.937 --> 00:33:50.985 referred to us who died in 18
NOTE Confidence: 0.953955021875

00:33:50.985 --> 00:33:52.749 months from severe lung disease and
NOTE Confidence: 0.953955021875

00:33:52.814 --> 00:33:54.697 and and without any cause was on
NOTE Confidence: 0.953955021875

00:33:54.700 --> 00:33:57.348 actually on his way to get his lung
NOTE Confidence: 0.953955021875

00:33:57.348 --> 00:33:58.956 transplanted and then passed away.
NOTE Confidence: 0.953955021875

00:33:58.956 --> 00:34:01.691 He had an older sister who died from
NOTE Confidence: 0.953955021875

00:34:01.691 --> 00:34:03.929 a similar mysterious lung disease at
NOTE Confidence: 0.953955021875

00:34:03.929 --> 00:34:06.536 26 months and and and had an older
NOTE Confidence: 0.953955021875

00:34:06.536 --> 00:34:09.680 brother who was nine year old and perfect.
NOTE Confidence: 0.953955021875

00:34:09.680 --> 00:34:10.650 Perfectly well.
NOTE Confidence: 0.953955021875

00:34:10.650 --> 00:34:12.300 What's striking about this story?
NOTE Confidence: 0.953955021875

00:34:12.300 --> 00:34:13.052 Story is.
NOTE Confidence: 0.953955021875

00:34:13.052 --> 00:34:14.556 When our patient died,
NOTE Confidence: 0.953955021875

00:34:14.560 --> 00:34:16.520 mom was pregnant with another baby and

NOTE Confidence: 0.953955021875

00:34:16.520 --> 00:34:19.355 so you can imagine what she must be thinking.

NOTE Confidence: 0.953955021875

00:34:19.360 --> 00:34:21.385 I've just lost two children

NOTE Confidence: 0.953955021875

00:34:21.385 --> 00:34:24.099 at 18 and 26 months of age.

NOTE Confidence: 0.953955021875

00:34:24.100 --> 00:34:26.460 What's going to happen to this baby right?

NOTE Confidence: 0.953955021875

00:34:26.460 --> 00:34:28.728 And so it's it's really a striking

NOTE Confidence: 0.953955021875

00:34:28.728 --> 00:34:31.119 story and and what's also powerful

NOTE Confidence: 0.953955021875

00:34:31.120 --> 00:34:34.046 is that when this child Sister died,

NOTE Confidence: 0.953955021875

00:34:34.050 --> 00:34:35.436 the parents were told they would

NOTE Confidence: 0.953955021875

00:34:35.436 --> 00:34:36.678 never have another child with

NOTE Confidence: 0.953955021875

00:34:36.678 --> 00:34:37.500 this terrible disease.

NOTE Confidence: 0.953955021875

00:34:37.500 --> 00:34:38.643 And of course,

NOTE Confidence: 0.953955021875

00:34:38.643 --> 00:34:40.872 whenever you say that you're always wrong

NOTE Confidence: 0.953955021875

00:34:40.872 --> 00:34:42.510 and so one should always be careful.

NOTE Confidence: 0.953955021875

00:34:42.510 --> 00:34:43.786 And so, of course.

NOTE Confidence: 0.953955021875

00:34:43.786 --> 00:34:46.060 They had another child that passed away

NOTE Confidence: 0.953955021875

00:34:46.060 --> 00:34:48.420 and now you can imagine her terror on
NOTE Confidence: 0.953955021875

00:34:48.420 --> 00:34:51.006 what's going to happen to her 4th pregnancy.
NOTE Confidence: 0.953955021875

00:34:51.010 --> 00:34:53.570 So we did xom sequencing.
NOTE Confidence: 0.953955021875

00:34:53.570 --> 00:34:56.102 We identified a variance
NOTE Confidence: 0.953955021875

00:34:56.102 --> 00:34:57.368 compound heterozygosity,
NOTE Confidence: 0.953955021875

00:34:57.370 --> 00:34:58.696 again for norful.
NOTE Confidence: 0.953955021875

00:34:58.696 --> 00:35:00.464 It's a nuclear preliminary
NOTE Confidence: 0.953955021875

00:35:00.464 --> 00:35:01.348 recognition factor,
NOTE Confidence: 0.953955021875

00:35:01.350 --> 00:35:04.038 like I have no idea how this could
NOTE Confidence: 0.953955021875

00:35:04.038 --> 00:35:05.789 possibly affect a lung disease,
NOTE Confidence: 0.953955021875

00:35:05.790 --> 00:35:07.375 and this is something that
NOTE Confidence: 0.953955021875

00:35:07.375 --> 00:35:08.326 we're now investigating,
NOTE Confidence: 0.953955021875

00:35:08.330 --> 00:35:12.026 but you could see that again.
NOTE Confidence: 0.953955021875

00:35:12.030 --> 00:35:13.614 He became a very strong candidate
NOTE Confidence: 0.953955021875

00:35:13.614 --> 00:35:15.388 because if we look at the family
NOTE Confidence: 0.953955021875

00:35:15.390 --> 00:35:16.706 you can see that mom is heteros.

NOTE Confidence: 0.953955021875

00:35:16.710 --> 00:35:19.486 I guess Dad is heterozygous for this gene.

NOTE Confidence: 0.953955021875

00:35:19.490 --> 00:35:21.200 The brother has the same genotype,

NOTE Confidence: 0.953955021875

00:35:21.200 --> 00:35:22.946 his mom and his hetero zigas.

NOTE Confidence: 0.953955021875

00:35:22.950 --> 00:35:25.398 But both children that passed away

NOTE Confidence: 0.953955021875

00:35:25.398 --> 00:35:27.414 are compound heterozygotes for this

NOTE Confidence: 0.953955021875

00:35:27.414 --> 00:35:29.926 and so I have what we think are

NOTE Confidence: 0.953955021875

00:35:29.926 --> 00:35:31.434 dysfunctional proteins and so of

NOTE Confidence: 0.953955021875

00:35:31.434 --> 00:35:32.890 course the question now is is what's

NOTE Confidence: 0.953955021875

00:35:32.945 --> 00:35:34.331 happening with this unborn child and

NOTE Confidence: 0.953955021875

00:35:34.331 --> 00:35:36.326 and one of the things that I want to

NOTE Confidence: 0.953955021875

00:35:36.326 --> 00:35:38.268 make clear here is that this is one

NOTE Confidence: 0.953955021875

00:35:38.268 --> 00:35:40.104 of those unique situations we can

NOTE Confidence: 0.953955021875

00:35:40.104 --> 00:35:42.335 actually put names to these pedigrees and.

NOTE Confidence: 0.953955021875

00:35:42.340 --> 00:35:43.740 I think it's really important

NOTE Confidence: 0.953955021875

00:35:43.740 --> 00:35:45.140 to understand that these aren't

NOTE Confidence: 0.953955021875

00:35:45.191 --> 00:35:46.339 just squares and circles,
NOTE Confidence: 0.953955021875

00:35:46.340 --> 00:35:47.579 but they're people.
NOTE Confidence: 0.953955021875

00:35:47.579 --> 00:35:51.264 And so the unborn child was named Stone and
NOTE Confidence: 0.953955021875

00:35:51.264 --> 00:35:54.600 I'm happy to report that he was wild type,
NOTE Confidence: 0.953955021875

00:35:54.600 --> 00:35:56.118 and so that was really exciting
NOTE Confidence: 0.953955021875

00:35:56.118 --> 00:35:57.840 for the family and and actually,
NOTE Confidence: 0.953955021875

00:35:57.840 --> 00:36:02.550 he's now few years old and big is a bull.
NOTE Confidence: 0.86791754125

00:36:06.730 --> 00:36:09.930 So, so I'm going to play a video,
NOTE Confidence: 0.86791754125

00:36:09.930 --> 00:36:11.911 so one of the things that happened
NOTE Confidence: 0.86791754125

00:36:11.911 --> 00:36:13.949 is after this case was presented.
NOTE Confidence: 0.86791754125

00:36:13.950 --> 00:36:17.686 I was invited by Diana Bianchi who's the
NOTE Confidence: 0.86791754125

00:36:17.690 --> 00:36:22.370 division head of the NICHD at the NIH
NOTE Confidence: 0.86791754125

00:36:22.370 --> 00:36:24.666 to present at the voice of a patient
NOTE Confidence: 0.86791754125

00:36:24.666 --> 00:36:26.907 which is at their Council meeting.
NOTE Confidence: 0.86791754125

00:36:26.910 --> 00:36:29.118 They present the case and then
NOTE Confidence: 0.86791754125

00:36:29.118 --> 00:36:31.250 bring the patient family there as

NOTE Confidence: 0.86791754125

00:36:31.250 --> 00:36:33.602 well to sort of talk about sort of.

NOTE Confidence: 0.86791754125

00:36:33.610 --> 00:36:35.898 Give them a perspective of what the goals

NOTE Confidence: 0.86791754125

00:36:35.898 --> 00:36:39.620 of the NICHD it's really to help patients,

NOTE Confidence: 0.86791754125

00:36:39.620 --> 00:36:40.500 and so this is.

NOTE Confidence: 0.86791754125

00:36:40.500 --> 00:36:42.090 This is exciting because you know this.

NOTE Confidence: 0.86791754125

00:36:42.090 --> 00:36:44.160 This is actually available to anyone.

NOTE Confidence: 0.86791754125

00:36:44.160 --> 00:36:46.850 On video, and I think,

NOTE Confidence: 0.86791754125

00:36:46.850 --> 00:36:49.034 well I think and and Kendra haifley the

NOTE Confidence: 0.86791754125

00:36:49.034 --> 00:36:51.319 mother of these children will will will,

NOTE Confidence: 0.86791754125

00:36:51.320 --> 00:36:54.120 will talked about her experience.

NOTE Confidence: 0.86791754125

00:36:54.120 --> 00:36:55.618 I think you'll find it extremely powerful.

NOTE Confidence: 0.86791754125

00:36:55.620 --> 00:36:56.478 I'm going to play for it,

NOTE Confidence: 0.86791754125

00:36:56.480 --> 00:36:58.496 play it for you in just a minute

NOTE Confidence: 0.86791754125

00:36:58.500 --> 00:37:00.348 and I think it's rare because

NOTE Confidence: 0.86791754125

00:37:00.348 --> 00:37:02.040 we actually have a video,

NOTE Confidence: 0.86791754125

00:37:02.040 --> 00:37:03.620 but it's not really rare.
NOTE Confidence: 0.86791754125

00:37:03.620 --> 00:37:05.060 And what Kendra is going to
NOTE Confidence: 0.86791754125

00:37:05.060 --> 00:37:06.714 describe to you is something that
NOTE Confidence: 0.86791754125

00:37:06.714 --> 00:37:08.314 many of these families feel.
NOTE Confidence: 0.86791754125

00:37:08.320 --> 00:37:10.138 And there's some points that are
NOTE Confidence: 0.86791754125

00:37:10.138 --> 00:37:12.443 worth pointing out here is that the
NOTE Confidence: 0.86791754125

00:37:12.443 --> 00:37:14.168 diagnostic odyssey that multiple tests.
NOTE Confidence: 0.86791754125

00:37:14.170 --> 00:37:16.410 No answers, referrals, multiple hospitals.
NOTE Confidence: 0.86791754125

00:37:16.410 --> 00:37:18.360 She's gone everywhere to try
NOTE Confidence: 0.86791754125

00:37:18.360 --> 00:37:19.920 to diagnose her children.
NOTE Confidence: 0.86791754125

00:37:19.920 --> 00:37:22.321 The severity of the illness has led
NOTE Confidence: 0.86791754125

00:37:22.321 --> 00:37:23.932 to severe desperation, isolation,
NOTE Confidence: 0.86791754125

00:37:23.932 --> 00:37:26.260 feeling of completely alone.
NOTE Confidence: 0.86791754125

00:37:26.260 --> 00:37:27.220 In fact, you know,
NOTE Confidence: 0.86791754125

00:37:27.220 --> 00:37:28.660 I think you'll find that mom
NOTE Confidence: 0.86791754125

00:37:28.711 --> 00:37:29.629 becomes an expert.

NOTE Confidence: 0.86791754125

00:37:29.630 --> 00:37:31.205 She'll tell you how she

NOTE Confidence: 0.86791754125

00:37:31.205 --> 00:37:32.780 managed her is the oscillator.

NOTE Confidence: 0.86791754125

00:37:32.780 --> 00:37:33.382 I mean,

NOTE Confidence: 0.86791754125

00:37:33.382 --> 00:37:34.887 you know there's many critical

NOTE Confidence: 0.86791754125

00:37:34.887 --> 00:37:36.481 care fellows that joined critical

NOTE Confidence: 0.86791754125

00:37:36.481 --> 00:37:38.383 care that know less about a

NOTE Confidence: 0.86791754125

00:37:38.383 --> 00:37:39.720 ventilator than this mother.

NOTE Confidence: 0.86791754125

00:37:39.720 --> 00:37:41.025 And then there's this incredible

NOTE Confidence: 0.86791754125

00:37:41.025 --> 00:37:42.812 guilt that she feels right, I think.

NOTE Confidence: 0.86791754125

00:37:42.812 --> 00:37:44.258 And that's the part that breaks.

NOTE Confidence: 0.86791754125

00:37:44.260 --> 00:37:46.430 My heart is it somehow she feels

NOTE Confidence: 0.86791754125

00:37:46.430 --> 00:37:48.043 that she's supposed to protect

NOTE Confidence: 0.86791754125

00:37:48.043 --> 00:37:49.903 her child and she's failed and

NOTE Confidence: 0.86791754125

00:37:49.903 --> 00:37:51.839 that's why her child's got sick.

NOTE Confidence: 0.86791754125

00:37:51.840 --> 00:37:54.384 And so I think by providing a genetic

NOTE Confidence: 0.86791754125

00:37:54.384 --> 00:37:57.258 reason we can really kind of address that.
NOTE Confidence: 0.86791754125

00:37:57.260 --> 00:38:00.404 And that's so knowledge of self
NOTE Confidence: 0.86791754125

00:38:00.404 --> 00:38:02.500 is extremely powerful there.
NOTE Confidence: 0.86791754125

00:38:02.500 --> 00:38:02.696 And,
NOTE Confidence: 0.86791754125

00:38:02.696 --> 00:38:03.088 you know,
NOTE Confidence: 0.86791754125

00:38:03.088 --> 00:38:04.460 as being one of these critical care
NOTE Confidence: 0.86791754125

00:38:04.508 --> 00:38:06.278 physicians who sometimes face these children,
NOTE Confidence: 0.86791754125

00:38:06.280 --> 00:38:07.988 I'm not going to deny that it
NOTE Confidence: 0.86791754125

00:38:07.988 --> 00:38:09.379 is powerful for us as well,
NOTE Confidence: 0.86791754125

00:38:09.380 --> 00:38:10.802 because we'd lots of time see
NOTE Confidence: 0.86791754125

00:38:10.802 --> 00:38:12.735 these kids and try to take care of
NOTE Confidence: 0.86791754125

00:38:12.735 --> 00:38:14.127 them and are just completely at
NOTE Confidence: 0.86791754125

00:38:14.185 --> 00:38:15.769 the loss as to what is going on.
NOTE Confidence: 0.86791754125

00:38:15.770 --> 00:38:18.374 And so to provide a a genetic
NOTE Confidence: 0.86791754125

00:38:18.374 --> 00:38:19.945 molecular diagnosis that might
NOTE Confidence: 0.86791754125

00:38:19.945 --> 00:38:22.249 help us is it's really important.

NOTE Confidence: 0.86791754125

00:38:22.250 --> 00:38:25.610 OK, so let me end this.

NOTE Confidence: 0.86791754125

00:38:25.610 --> 00:38:28.290 Here's the video started off.

NOTE Confidence: 0.6953798075

00:38:30.410 --> 00:38:31.398 Please let my name

NOTE Confidence: 0.854973207

00:38:31.430 --> 00:38:34.286 is Kendra Haifley and I'm just one

NOTE Confidence: 0.854973207

00:38:34.286 --> 00:38:37.340 of many faces of rare diseases.

NOTE Confidence: 0.854973207

00:38:37.340 --> 00:38:39.958 I always dreamt of being a mother.

NOTE Confidence: 0.854973207

00:38:39.960 --> 00:38:41.550 I am the mother to Rome.

NOTE Confidence: 0.912818329

00:38:44.300 --> 00:38:46.428 I would call the doctors and beg them

NOTE Confidence: 0.912818329

00:38:46.428 --> 00:38:49.216 to listen, begged them to get her in.

NOTE Confidence: 0.912818329

00:38:49.220 --> 00:38:50.599 We added lay 6 and had a

NOTE Confidence: 0.912818329

00:38:50.599 --> 00:38:51.919 heart Cath on the calendar,

NOTE Confidence: 0.912818329

00:38:51.920 --> 00:38:55.256 but I knew something wasn't right.

NOTE Confidence: 0.912818329

00:38:55.260 --> 00:38:56.391 Isabel's concentrator malfunctioned

NOTE Confidence: 0.912818329

00:38:56.391 --> 00:38:59.429 while I was packing to head to children

NOTE Confidence: 0.912818329

00:38:59.429 --> 00:39:01.439 one morning and she turned blue.

NOTE Confidence: 0.912818329

00:39:01.440 --> 00:39:03.368 I made sure I had enough oxygen to
NOTE Confidence: 0.912818329

00:39:03.368 --> 00:39:05.527 get her through the 45 minute drive.
NOTE Confidence: 0.912818329

00:39:05.530 --> 00:39:06.898 In the ER, as Isabel was
NOTE Confidence: 0.912818329

00:39:06.898 --> 00:39:07.810 switched to Wall air,
NOTE Confidence: 0.912818329

00:39:07.810 --> 00:39:10.382 her stats dropped to 58 and
NOTE Confidence: 0.912818329

00:39:10.382 --> 00:39:12.110 again she turned blue.
NOTE Confidence: 0.912818329

00:39:12.110 --> 00:39:15.486 I kept begging for anyone to do something.
NOTE Confidence: 0.912818329

00:39:15.490 --> 00:39:18.450 Find out what is wrong with my daughter.
NOTE Confidence: 0.912818329

00:39:18.450 --> 00:39:20.158 The next morning I had no idea.
NOTE Confidence: 0.930948781818182

00:39:22.460 --> 00:39:24.248 As I was kissing her and
NOTE Confidence: 0.930948781818182

00:39:24.248 --> 00:39:25.780 telling her I loved her,
NOTE Confidence: 0.930948781818182

00:39:25.780 --> 00:39:27.418 I meant she was going to be OK that
NOTE Confidence: 0.930948781818182

00:39:27.418 --> 00:39:29.057 it was going to be the last time
NOTE Confidence: 0.930948781818182

00:39:29.057 --> 00:39:30.906 that I would hold my daughter at life.
NOTE Confidence: 0.930948781818182

00:39:30.910 --> 00:39:32.240 I never want to let her go.
NOTE Confidence: 0.730603912

00:39:34.740 --> 00:39:36.830 Isabel did have pulmonary hypertension,

NOTE Confidence: 0.730603912

00:39:36.830 --> 00:39:39.006 but it was due to her incredibly sick

NOTE Confidence: 0.730603912

00:39:39.006 --> 00:39:41.200 lungs lungs, so sick that they were

NOTE Confidence: 0.730603912

00:39:41.200 --> 00:39:42.850 struggling to inflate and oxygenate.

NOTE Confidence: 0.730603912

00:39:42.850 --> 00:39:44.626 He told me he believed Isabel

NOTE Confidence: 0.730603912

00:39:44.626 --> 00:39:46.115 would require lung transplant and

NOTE Confidence: 0.730603912

00:39:46.115 --> 00:39:47.591 that we needed to consider getting

NOTE Confidence: 0.730603912

00:39:47.591 --> 00:39:49.290 her into a transplant center.

NOTE Confidence: 0.730603912

00:39:49.290 --> 00:39:51.939 Ourworld immediately shifted.

NOTE Confidence: 0.730603912

00:39:51.940 --> 00:39:53.935 Isabel was placed on the

NOTE Confidence: 0.730603912

00:39:53.935 --> 00:39:55.531 oscillating ventilator and had

NOTE Confidence: 0.730603912

00:39:55.531 --> 00:39:56.958 incredibly high CO2 levels.

NOTE Confidence: 0.730603912

00:39:56.960 --> 00:39:59.640 I immediately went into shock.

NOTE Confidence: 0.730603912

00:39:59.640 --> 00:40:01.014 After a trip to the hospital

NOTE Confidence: 0.730603912

00:40:01.014 --> 00:40:02.563 across the street to get my

NOTE Confidence: 0.730603912

00:40:02.563 --> 00:40:03.719 stress vomiting under control,

NOTE Confidence: 0.730603912

00:40:03.720 --> 00:40:05.760 I started researching everything I could.
NOTE Confidence: 0.730603912

00:40:05.760 --> 00:40:08.500 Everyone was perplexed. Day 12.
NOTE Confidence: 0.730603912

00:40:08.500 --> 00:40:10.558 We took a turn for the worse.
NOTE Confidence: 0.730603912

00:40:10.560 --> 00:40:14.710 Is the most P, CO2 and her blood was 212.
NOTE Confidence: 0.730603912

00:40:14.710 --> 00:40:15.602 ECMO became our life.
NOTE Confidence: 0.730603912

00:40:15.602 --> 00:40:17.245 Our doctors work to get us accepted
NOTE Confidence: 0.730603912

00:40:17.245 --> 00:40:18.775 into a transplant facility and we
NOTE Confidence: 0.730603912

00:40:18.775 --> 00:40:20.571 waited on as well to tell us when
NOTE Confidence: 0.730603912

00:40:20.571 --> 00:40:22.160 she was ready to come off ECMO.
NOTE Confidence: 0.730603912

00:40:22.160 --> 00:40:24.600 After 21 days she was ready and she
NOTE Confidence: 0.730603912

00:40:24.668 --> 00:40:27.038 did great on the conventional vent.
NOTE Confidence: 0.730603912

00:40:27.040 --> 00:40:29.428 We got accepted to Texas children.
NOTE Confidence: 0.730603912

00:40:29.430 --> 00:40:30.840 We felt optimistic and hopeful.
NOTE Confidence: 0.730603912

00:40:30.840 --> 00:40:33.352 New lungs were just weeks away and Isabel
NOTE Confidence: 0.730603912

00:40:33.352 --> 00:40:36.180 would be able to breathe freely once again.
NOTE Confidence: 0.730603912

00:40:36.180 --> 00:40:37.359 Transport with Smith.

NOTE Confidence: 0.730603912

00:40:37.359 --> 00:40:39.324 Isabel was showing beautiful blood

NOTE Confidence: 0.730603912

00:40:39.324 --> 00:40:41.787 gases and we were able to grab Damon.

NOTE Confidence: 0.730603912

00:40:41.790 --> 00:40:43.280 My husband had traveled commercial

NOTE Confidence: 0.730603912

00:40:43.280 --> 00:40:45.209 from the hospital lobby to join us.

NOTE Confidence: 0.730603912

00:40:45.210 --> 00:40:47.310 As we entered the hospital.

NOTE Confidence: 0.730603912

00:40:47.310 --> 00:40:47.966 Within minutes,

NOTE Confidence: 0.730603912

00:40:47.966 --> 00:40:49.934 Texas children was working to transfer

NOTE Confidence: 0.730603912

00:40:49.934 --> 00:40:52.327 as well to their machines and for some

NOTE Confidence: 0.730603912

00:40:52.327 --> 00:40:54.089 reason they decided to handbag her

NOTE Confidence: 0.730603912

00:40:54.090 --> 00:40:55.700 instead of transferring her directly

NOTE Confidence: 0.730603912

00:40:55.700 --> 00:40:57.990 to the same vent settings as in Omaha.

NOTE Confidence: 0.730603912

00:40:57.990 --> 00:41:00.090 The 275 pound male nurse not

NOTE Confidence: 0.730603912

00:41:00.090 --> 00:41:01.895 knowing Isabelle saw her Brady

NOTE Confidence: 0.730603912

00:41:01.895 --> 00:41:03.550 due to a vagal response,

NOTE Confidence: 0.730603912

00:41:03.550 --> 00:41:07.070 and he jumped on her to perform CPR.

NOTE Confidence: 0.730603912

00:41:07.070 --> 00:41:08.018 Isabelle's aorta was torn.

NOTE Confidence: 0.905825049

00:41:11.360 --> 00:41:13.404 I immediately went out of body and

NOTE Confidence: 0.905825049

00:41:13.404 --> 00:41:15.090 after 30 minutes our nurse Angel

NOTE Confidence: 0.905825049

00:41:15.090 --> 00:41:17.171 touched my arm and told me I could

NOTE Confidence: 0.905825049

00:41:17.171 --> 00:41:19.227 still hold her while she was warm and

NOTE Confidence: 0.905825049

00:41:19.227 --> 00:41:22.090 I could ask them to stop at any time.

NOTE Confidence: 0.905825049

00:41:22.090 --> 00:41:23.596 I asked the doctor in charge

NOTE Confidence: 0.905825049

00:41:23.596 --> 00:41:24.950 how long it had been.

NOTE Confidence: 0.905825049

00:41:24.950 --> 00:41:27.596 And then I asked them to stop.

NOTE Confidence: 0.905825049

00:41:27.600 --> 00:41:28.699 And then I asked them to leave

NOTE Confidence: 0.905825049

00:41:28.699 --> 00:41:29.962 the room so that my nurses could

NOTE Confidence: 0.905825049

00:41:29.962 --> 00:41:31.084 help me clean up my daughter.

NOTE Confidence: 0.948050935

00:41:33.170 --> 00:41:34.705 That night my daughter became

NOTE Confidence: 0.948050935

00:41:34.705 --> 00:41:36.240 a star amongst the heavens.

NOTE Confidence: 0.9340343233333333

00:41:39.050 --> 00:41:43.550 She was two years, two months, two days.

NOTE Confidence: 0.9340343233333333

00:41:43.550 --> 00:41:45.542 We held on hope knowing Isabel was our

NOTE Confidence: 0.9340343233333333

00:41:45.542 --> 00:41:47.403 guiding light and knowing we didn't want

NOTE Confidence: 0.9340343233333333

00:41:47.403 --> 00:41:49.199 other families to go through our pain.

NOTE Confidence: 0.9340343233333333

00:41:49.200 --> 00:41:50.765 We started the Warrior Princess

NOTE Confidence: 0.9340343233333333

00:41:50.765 --> 00:41:52.330 Foundation in honor of her.

NOTE Confidence: 0.9340343233333333

00:41:52.330 --> 00:41:54.073 Our goal was to advocate for rare

NOTE Confidence: 0.9340343233333333

00:41:54.073 --> 00:41:55.754 disease research and also to help

NOTE Confidence: 0.9340343233333333

00:41:55.754 --> 00:41:57.224 families struggling with rare disease.

NOTE Confidence: 0.9340343233333333

00:41:57.230 --> 00:41:59.600 That February raised over \$8000,

NOTE Confidence: 0.9340343233333333

00:41:59.600 --> 00:42:00.794 which we gifted to for families

NOTE Confidence: 0.9340343233333333

00:42:00.794 --> 00:42:01.860 to use as they wish.

NOTE Confidence: 0.9340343233333333

00:42:01.860 --> 00:42:03.324 Knowing the financial struggles

NOTE Confidence: 0.9340343233333333

00:42:03.324 --> 00:42:05.154 of rare disease having almost

NOTE Confidence: 0.9340343233333333

00:42:05.154 --> 00:42:06.749 lost everything ourselves.

NOTE Confidence: 0.9340343233333333

00:42:06.750 --> 00:42:08.962 Just days before I found out I

NOTE Confidence: 0.9340343233333333

00:42:08.962 --> 00:42:10.790 was carrying our sweet Silas.

NOTE Confidence: 0.9340343233333333

00:42:10.790 --> 00:42:12.834 The struggles of family faces after losing
NOTE Confidence: 0.9340343233333333

00:42:12.834 --> 00:42:15.229 a child are unnatural and immeasurable.
NOTE Confidence: 0.9340343233333333

00:42:15.230 --> 00:42:16.214 We grieved differently,
NOTE Confidence: 0.9340343233333333

00:42:16.214 --> 00:42:17.854 and we grew apart and
NOTE Confidence: 0.9340343233333333

00:42:17.854 --> 00:42:19.380 together at the same time.
NOTE Confidence: 0.9340343233333333

00:42:19.380 --> 00:42:20.864 I knew throwing in the towel was
NOTE Confidence: 0.9340343233333333

00:42:20.864 --> 00:42:22.431 not an option and I would fight
NOTE Confidence: 0.9340343233333333

00:42:22.431 --> 00:42:23.757 for my marriage to my husband.
NOTE Confidence: 0.9340343233333333

00:42:23.760 --> 00:42:25.428 There were days that my husband
NOTE Confidence: 0.9340343233333333

00:42:25.428 --> 00:42:27.364 struggled so deeply that I believe the
NOTE Confidence: 0.9340343233333333

00:42:27.364 --> 00:42:29.170 only reason he survived was because he
NOTE Confidence: 0.9340343233333333

00:42:29.222 --> 00:42:30.958 didn't want to hurt our oldest son.
NOTE Confidence: 0.9340343233333333

00:42:30.960 --> 00:42:33.718 We wondered why he hadn't gotten sick.
NOTE Confidence: 0.9340343233333333

00:42:33.720 --> 00:42:34.880 Through meeting with our doctors,
NOTE Confidence: 0.9340343233333333

00:42:34.880 --> 00:42:36.710 we were assured we could have
NOTE Confidence: 0.9340343233333333

00:42:36.710 --> 00:42:38.562 100,000 more kids and I would

NOTE Confidence: 0.9340343233333333
00:42:38.562 --> 00:42:40.266 never have a sick child again.
NOTE Confidence: 0.9340343233333333
00:42:40.270 --> 00:42:41.923 This wasn't genetic.
NOTE Confidence: 0.9340343233333333
00:42:41.923 --> 00:42:45.780 This was just a fluke in nature.
NOTE Confidence: 0.9340343233333333
00:42:45.780 --> 00:42:48.300 Sweet Silas arrived and loved Cuddles,
NOTE Confidence: 0.9340343233333333
00:42:48.300 --> 00:42:50.310 which were therapeutic and welcomed.
NOTE Confidence: 0.9340343233333333
00:42:50.310 --> 00:42:53.073 He reminded us of his sweet sister at times.
NOTE Confidence: 0.9340343233333333
00:42:53.080 --> 00:42:56.482 He was also silly and love Dragons and books.
NOTE Confidence: 0.9340343233333333
00:42:56.490 --> 00:42:58.008 The days were filled with hope
NOTE Confidence: 0.9340343233333333
00:42:58.008 --> 00:42:59.939 and it felt like we were healing.
NOTE Confidence: 0.9340343233333333
00:42:59.940 --> 00:43:01.515 After his first bout with
NOTE Confidence: 0.9340343233333333
00:43:01.515 --> 00:43:02.775 hypoxemia during an illness,
NOTE Confidence: 0.9340343233333333
00:43:02.780 --> 00:43:04.178 I requested a console at Colorado
NOTE Confidence: 0.9340343233333333
00:43:04.178 --> 00:43:06.041 children to meet with one of the
NOTE Confidence: 0.9340343233333333
00:43:06.041 --> 00:43:07.225 world's leading specialists in
NOTE Confidence: 0.9340343233333333
00:43:07.225 --> 00:43:08.500 children's interstitial lung disease.
NOTE Confidence: 0.9340343233333333

00:43:08.500 --> 00:43:09.850 We had an appointment scheduled
NOTE Confidence: 0.9340343233333333

00:43:09.850 --> 00:43:11.200 less than a month away.
NOTE Confidence: 0.9340343233333333

00:43:11.200 --> 00:43:12.988 Silas caught RSV and we drove
NOTE Confidence: 0.9340343233333333

00:43:12.988 --> 00:43:14.502 immediately to children where he
NOTE Confidence: 0.9340343233333333

00:43:14.502 --> 00:43:16.343 was stayed for the next 14 days
NOTE Confidence: 0.9340343233333333

00:43:16.343 --> 00:43:17.751 before convincing them to let us
NOTE Confidence: 0.9340343233333333

00:43:17.751 --> 00:43:19.496 leave on oxygen to head to Colorado.
NOTE Confidence: 0.9340343233333333

00:43:19.496 --> 00:43:21.976 It couldn't be a coincidence.
NOTE Confidence: 0.9340343233333333

00:43:21.980 --> 00:43:23.972 This was too similar to Isabel
NOTE Confidence: 0.9340343233333333

00:43:23.972 --> 00:43:25.711 and happening just months apart
NOTE Confidence: 0.9340343233333333

00:43:25.711 --> 00:43:27.087 from her first illness.
NOTE Confidence: 0.9340343233333333

00:43:27.090 --> 00:43:28.968 Stylus had a CT bronk with
NOTE Confidence: 0.9340343233333333

00:43:28.968 --> 00:43:30.220 lavage and echo done.
NOTE Confidence: 0.9340343233333333

00:43:30.220 --> 00:43:32.740 He did not have interstitial lung disease.
NOTE Confidence: 0.9340343233333333

00:43:32.740 --> 00:43:34.144 We were so relieved.
NOTE Confidence: 0.9340343233333333

00:43:34.144 --> 00:43:36.250 We plan to keep silence on

NOTE Confidence: 0.9340343233333333

00:43:36.327 --> 00:43:38.117 oxygen to help him grow.

NOTE Confidence: 0.9340343233333333

00:43:38.120 --> 00:43:40.213 We came home and almost immediately Silas

NOTE Confidence: 0.9340343233333333

00:43:40.213 --> 00:43:42.807 is need for oxygen continued to increase.

NOTE Confidence: 0.9340343233333333

00:43:42.810 --> 00:43:44.280 I was confident in my ability to

NOTE Confidence: 0.9340343233333333

00:43:44.280 --> 00:43:45.936 care for Silas on oxygen with a cold,

NOTE Confidence: 0.9340343233333333

00:43:45.940 --> 00:43:47.750 but this didn't feel right.

NOTE Confidence: 0.9340343233333333

00:43:47.750 --> 00:43:49.276 I was told Silas's Echo had been

NOTE Confidence: 0.9340343233333333

00:43:49.276 --> 00:43:50.590 slightly off when we were there,

NOTE Confidence: 0.9340343233333333

00:43:50.590 --> 00:43:52.669 so maybe we should have that checked.

NOTE Confidence: 0.9340343233333333

00:43:52.670 --> 00:43:54.420 I took Silas to children's and once

NOTE Confidence: 0.9340343233333333

00:43:54.420 --> 00:43:56.778 we were admitted, Silas had an echo.

NOTE Confidence: 0.9340343233333333

00:43:56.778 --> 00:43:59.520 The pressures in his heart were 90.

NOTE Confidence: 0.9340343233333333

00:43:59.520 --> 00:44:01.580 Normal is 25 and under.

NOTE Confidence: 0.9340343233333333

00:44:01.580 --> 00:44:03.068 Silas had pulmonary hypertension.

NOTE Confidence: 0.9340343233333333

00:44:03.068 --> 00:44:05.300 We decided to attempt attempt at

NOTE Confidence: 0.9340343233333333

00:44:05.360 --> 00:44:07.165 different way of ventilating and
NOTE Confidence: 0.9340343233333333

00:44:07.165 --> 00:44:08.970 the moment Bipap was attempted,
NOTE Confidence: 0.9340343233333333

00:44:08.970 --> 00:44:10.704 stylist turned Gray and his eyes
NOTE Confidence: 0.9340343233333333

00:44:10.704 --> 00:44:12.569 rolled into the back of his head.
NOTE Confidence: 0.9340343233333333

00:44:12.570 --> 00:44:14.910 My sister was with me when Silas coded soon.
NOTE Confidence: 0.9340343233333333

00:44:14.910 --> 00:44:16.490 My whole family was there.
NOTE Confidence: 0.907869652307692

00:44:16.490 --> 00:44:18.114 Damon was immediately on a flight home
NOTE Confidence: 0.907869652307692

00:44:18.114 --> 00:44:19.730 and once again the nightmare began.
NOTE Confidence: 0.907869652307692

00:44:19.730 --> 00:44:23.146 Only this time I was eight months pregnant.
NOTE Confidence: 0.907869652307692

00:44:23.150 --> 00:44:25.446 Silas ended up on the oscillating ventilator,
NOTE Confidence: 0.907869652307692

00:44:25.450 --> 00:44:26.890 one of the most nauseating
NOTE Confidence: 0.907869652307692

00:44:26.890 --> 00:44:28.042 sounds triggering past trauma.
NOTE Confidence: 0.907869652307692

00:44:28.050 --> 00:44:30.732 From Isabel stay, I worked daily on PT with
NOTE Confidence: 0.907869652307692

00:44:30.732 --> 00:44:33.108 Silas while we searched and researched,
NOTE Confidence: 0.907869652307692

00:44:33.110 --> 00:44:34.526 and although we had an incredible
NOTE Confidence: 0.907869652307692

00:44:34.526 --> 00:44:35.850 team of doctors working with us,

NOTE Confidence: 0.907869652307692
00:44:35.850 --> 00:44:38.325 no one had ever seen anything like our kids.
NOTE Confidence: 0.907869652307692
00:44:38.330 --> 00:44:40.665 We were once again alone
NOTE Confidence: 0.907869652307692
00:44:40.665 --> 00:44:42.533 on this unknown island.
NOTE Confidence: 0.907869652307692
00:44:42.540 --> 00:44:44.668 Some doctors gave up hope you could
NOTE Confidence: 0.907869652307692
00:44:44.668 --> 00:44:47.098 see the pity on some of their faces.
NOTE Confidence: 0.907869652307692
00:44:47.100 --> 00:44:48.370 After weeks on the ventilator,
NOTE Confidence: 0.907869652307692
00:44:48.370 --> 00:44:50.617 I requested a trach and GJ tube
NOTE Confidence: 0.907869652307692
00:44:50.620 --> 00:44:52.020 stylist deserved quality of life,
NOTE Confidence: 0.907869652307692
00:44:52.020 --> 00:44:53.220 and if we ever had a chance of
NOTE Confidence: 0.907869652307692
00:44:53.220 --> 00:44:54.883 bringing him home, this was it.
NOTE Confidence: 0.907869652307692
00:44:54.883 --> 00:44:58.090 Our desire for full healing was still there.
NOTE Confidence: 0.907869652307692
00:44:58.090 --> 00:44:59.320 We always held on to hope,
NOTE Confidence: 0.907869652307692
00:44:59.320 --> 00:45:02.496 but I always stood by quality over quantity.
NOTE Confidence: 0.907869652307692
00:45:02.500 --> 00:45:05.755 Silas had surgery and was so brave.
NOTE Confidence: 0.907869652307692
00:45:05.760 --> 00:45:07.250 I took over his care.
NOTE Confidence: 0.907869652307692

00:45:07.250 --> 00:45:10.482 I looked at every blood gas and every
NOTE Confidence: 0.907869652307692

00:45:10.482 --> 00:45:13.654 blood panel. I watched the trends.
NOTE Confidence: 0.907869652307692

00:45:13.654 --> 00:45:17.990 I was the expert. I was also in labor.
NOTE Confidence: 0.907869652307692

00:45:17.990 --> 00:45:19.202 4th Baby first time.
NOTE Confidence: 0.907869652307692

00:45:19.202 --> 00:45:21.720 The night before had been a rough one.
NOTE Confidence: 0.907869652307692

00:45:21.720 --> 00:45:23.308 Little to no sleep.
NOTE Confidence: 0.907869652307692

00:45:23.308 --> 00:45:24.896 CO2 creeping up sometimes
NOTE Confidence: 0.907869652307692

00:45:24.896 --> 00:45:26.610 incredibly high that changes.
NOTE Confidence: 0.907869652307692

00:45:26.610 --> 00:45:29.186 He woke around four and we read and
NOTE Confidence: 0.907869652307692

00:45:29.186 --> 00:45:31.650 he grabbed my face and laughed and
NOTE Confidence: 0.907869652307692

00:45:31.650 --> 00:45:33.820 we had the most incredible hour.
NOTE Confidence: 0.907869652307692

00:45:33.820 --> 00:45:35.934 And I knew what this meeting was.
NOTE Confidence: 0.907869652307692

00:45:35.940 --> 00:45:37.298 I told our team that even if
NOTE Confidence: 0.907869652307692

00:45:37.298 --> 00:45:38.822 Silas were to get better and we
NOTE Confidence: 0.907869652307692

00:45:38.822 --> 00:45:40.154 were able to transfer to shop,
NOTE Confidence: 0.907869652307692

00:45:40.160 --> 00:45:42.672 I would have to decide at that time

NOTE Confidence: 0.907869652307692
00:45:42.672 --> 00:45:45.826 if it was for him or if it was for me.
NOTE Confidence: 0.907869652307692
00:45:45.830 --> 00:45:47.860 I would not put him through trauma
NOTE Confidence: 0.907869652307692
00:45:47.860 --> 00:45:50.110 to extend his life if it didn't
NOTE Confidence: 0.907869652307692
00:45:50.110 --> 00:45:51.094 improve his quality.
NOTE Confidence: 0.907869652307692
00:45:51.100 --> 00:45:52.628 I told the doctors I was going to
NOTE Confidence: 0.907869652307692
00:45:52.628 --> 00:45:54.264 be headed to Lincoln to have a baby
NOTE Confidence: 0.907869652307692
00:45:54.264 --> 00:45:56.029 and it was arranged so that I could
NOTE Confidence: 0.907869652307692
00:45:56.029 --> 00:45:57.169 watch through a video monitor.
NOTE Confidence: 0.907869652307692
00:45:57.170 --> 00:45:59.368 My sweet baby boy while I brought
NOTE Confidence: 0.907869652307692
00:45:59.368 --> 00:46:01.010 his brother into the world,
NOTE Confidence: 0.907869652307692
00:46:01.010 --> 00:46:03.103 I arrived at the hospital at five
NOTE Confidence: 0.907869652307692
00:46:03.103 --> 00:46:04.568 and delivered stone at 9 via.
NOTE Confidence: 0.907869652307692
00:46:04.570 --> 00:46:06.280 C-section.
NOTE Confidence: 0.907869652307692
00:46:06.280 --> 00:46:07.452 Roman, our oldest son,
NOTE Confidence: 0.907869652307692
00:46:07.452 --> 00:46:08.917 came and met his brother,
NOTE Confidence: 0.907869652307692

00:46:08.920 --> 00:46:10.369 and he told me how Silas would
NOTE Confidence: 0.907869652307692

00:46:10.369 --> 00:46:11.989 love him so much and he couldn't
NOTE Confidence: 0.907869652307692

00:46:11.989 --> 00:46:13.169 wait for them to meet.
NOTE Confidence: 0.907869652307692

00:46:13.170 --> 00:46:16.610 I was devastated and elated.
NOTE Confidence: 0.907869652307692

00:46:16.610 --> 00:46:17.942 I remember this scream Roman let
NOTE Confidence: 0.907869652307692

00:46:17.942 --> 00:46:19.827 out when we sat on the couch the
NOTE Confidence: 0.907869652307692

00:46:19.827 --> 00:46:21.243 night we arrived home from Houston
NOTE Confidence: 0.907869652307692

00:46:21.295 --> 00:46:22.639 and he asked where is Isabel?
NOTE Confidence: 0.907869652307692

00:46:22.640 --> 00:46:25.132 Did she get her new lungs fully expecting
NOTE Confidence: 0.907869652307692

00:46:25.132 --> 00:46:26.878 her to be running around upstairs?
NOTE Confidence: 0.932490488333333

00:46:29.390 --> 00:46:32.180 We told them she had died.
NOTE Confidence: 0.932490488333333

00:46:32.180 --> 00:46:34.235 And the screen was unworldly
NOTE Confidence: 0.932490488333333

00:46:34.235 --> 00:46:35.468 followed by sobbing.
NOTE Confidence: 0.932490488333333

00:46:35.470 --> 00:46:37.437 He had lost his best friend and
NOTE Confidence: 0.932490488333333

00:46:37.437 --> 00:46:39.104 his baby sister, and here I was,
NOTE Confidence: 0.932490488333333

00:46:39.104 --> 00:46:39.928 holding his little brother,

NOTE Confidence: 0.932490488333333
00:46:39.930 --> 00:46:43.178 knowing his little brother might not make it.
NOTE Confidence: 0.932490488333333
00:46:43.180 --> 00:46:45.609 The next morning I received a call
NOTE Confidence: 0.932490488333333
00:46:45.609 --> 00:46:47.580 that Silas Hemoglobin was down to 5.
NOTE Confidence: 0.932490488333333
00:46:47.580 --> 00:46:49.040 I knew what that meant.
NOTE Confidence: 0.932490488333333
00:46:49.040 --> 00:46:51.090 He needed a blood transfusion.
NOTE Confidence: 0.932490488333333
00:46:51.090 --> 00:46:53.225 The last one had resulted in tralia
NOTE Confidence: 0.932490488333333
00:46:53.225 --> 00:46:54.800 transfusion related acute lung injury,
NOTE Confidence: 0.932490488333333
00:46:54.800 --> 00:46:57.392 which sets us back and LED to him coding.
NOTE Confidence: 0.932490488333333
00:46:57.400 --> 00:46:59.976 But I knew he would die without it.
NOTE Confidence: 0.932490488333333
00:46:59.980 --> 00:47:02.718 By friends more like my brother, the man
NOTE Confidence: 0.932490488333333
00:47:02.718 --> 00:47:04.920 who cared for Isabel for 21 days on ECMO.
NOTE Confidence: 0.932490488333333
00:47:04.920 --> 00:47:06.792 Justin started the transfusion.
NOTE Confidence: 0.932490488333333
00:47:06.792 --> 00:47:09.460 A couple hours, then I got the call.
NOTE Confidence: 0.932490488333333
00:47:09.460 --> 00:47:10.536 Things weren't going well.
NOTE Confidence: 0.932490488333333
00:47:10.536 --> 00:47:12.470 I called my pede and my midwife
NOTE Confidence: 0.932490488333333

00:47:12.470 --> 00:47:14.304 and both told me I could leave.
NOTE Confidence: 0.932490488333333
00:47:14.310 --> 00:47:15.744 They would give me meds and
NOTE Confidence: 0.932490488333333
00:47:15.744 --> 00:47:17.110 Get Me Out of there.
NOTE Confidence: 0.932490488333333
00:47:17.110 --> 00:47:20.230 By 5:00 PM that evening I was back in Omaha
NOTE Confidence: 0.932490488333333
00:47:20.230 --> 00:47:22.645 less than 19 hours from having surgery.
NOTE Confidence: 0.932490488333333
00:47:22.650 --> 00:47:24.900 I was bringing my son to meet his brother.
NOTE Confidence: 0.932490488333333
00:47:24.900 --> 00:47:27.190 The first and last time.
NOTE Confidence: 0.932490488333333
00:47:27.190 --> 00:47:29.030 I was exhausted and destroyed
NOTE Confidence: 0.932490488333333
00:47:29.030 --> 00:47:31.064 and so tired and so happy.
NOTE Confidence: 0.932490488333333
00:47:31.064 --> 00:47:31.988 It's so sad.
NOTE Confidence: 0.793254252727273
00:47:38.090 --> 00:47:39.645 Roman and Silas made hand
NOTE Confidence: 0.793254252727273
00:47:39.645 --> 00:47:41.670 molds and we all read books.
NOTE Confidence: 0.793254252727273
00:47:41.670 --> 00:47:43.308 When we were ready to let him
NOTE Confidence: 0.793254252727273
00:47:43.308 --> 00:47:44.270 gracefully and peacefully pass,
NOTE Confidence: 0.793254252727273
00:47:44.270 --> 00:47:45.630 Roman held him first.
NOTE Confidence: 0.793254252727273
00:47:45.630 --> 00:47:47.330 They laid together for hours

NOTE Confidence: 0.793254252727273

00:47:47.330 --> 00:47:49.380 and Roman slept one last time,

NOTE Confidence: 0.793254252727273

00:47:49.380 --> 00:47:52.789 holding his baby brother his best friend.

NOTE Confidence: 0.793254252727273

00:47:52.790 --> 00:47:54.638 Then it was time for Dad.

NOTE Confidence: 0.793254252727273

00:47:54.640 --> 00:47:56.299 They laid and snuggled and I knew

NOTE Confidence: 0.793254252727273

00:47:56.299 --> 00:47:58.200 he needed to hold him as he passed.

NOTE Confidence: 0.793254252727273

00:47:58.200 --> 00:48:00.150 So I just loved onsite listened

NOTE Confidence: 0.793254252727273

00:48:00.150 --> 00:48:02.334 stone and Roman in demon as we

NOTE Confidence: 0.793254252727273

00:48:02.334 --> 00:48:04.028 waited until he took his final breath

NOTE Confidence: 0.793254252727273

00:48:04.028 --> 00:48:05.825 and his heart had its final beat.

NOTE Confidence: 0.793254252727273

00:48:05.830 --> 00:48:08.040 He was 19 months old.

NOTE Confidence: 0.793254252727273

00:48:08.040 --> 00:48:09.750 One of our intensivists with a

NOTE Confidence: 0.793254252727273

00:48:09.750 --> 00:48:11.155 passion for research stopped us

NOTE Confidence: 0.793254252727273

00:48:11.155 --> 00:48:12.639 and asked if we would sign papers

NOTE Confidence: 0.793254252727273

00:48:12.639 --> 00:48:14.037 to send or genetics to you.

NOTE Confidence: 0.793254252727273

00:48:14.040 --> 00:48:17.120 I said absolutely and we all signed.

NOTE Confidence: 0.793254252727273

00:48:17.120 --> 00:48:18.590 He promised no matter what
NOTE Confidence: 0.793254252727273

00:48:18.590 --> 00:48:20.060 we would hear the results.
NOTE Confidence: 0.793254252727273

00:48:20.060 --> 00:48:23.644 Yale would share any results with us.
NOTE Confidence: 0.793254252727273

00:48:23.650 --> 00:48:25.090 The next year was a blur.
NOTE Confidence: 0.793254252727273

00:48:25.090 --> 00:48:26.750 It was painful and joyous.
NOTE Confidence: 0.793254252727273

00:48:26.750 --> 00:48:27.992 Wondering how long we had with
NOTE Confidence: 0.793254252727273

00:48:27.992 --> 00:48:29.395 our new baby and worried our
NOTE Confidence: 0.793254252727273

00:48:29.395 --> 00:48:30.715 oldest would someday fall ill.
NOTE Confidence: 0.793254252727273

00:48:30.720 --> 00:48:33.438 And then we got a call.
NOTE Confidence: 0.793254252727273

00:48:33.440 --> 00:48:34.736 Yale had found something.
NOTE Confidence: 0.793254252727273

00:48:34.736 --> 00:48:39.150 Did I want to know? Yes now?
NOTE Confidence: 0.793254252727273

00:48:39.150 --> 00:48:40.980 My husband and I both carry
NOTE Confidence: 0.793254252727273

00:48:40.980 --> 00:48:42.830 different mutations in the same gene.
NOTE Confidence: 0.793254252727273

00:48:42.830 --> 00:48:45.170 Isabelle and Silas received both.
NOTE Confidence: 0.793254252727273

00:48:45.170 --> 00:48:46.649 Roman carries mine.
NOTE Confidence: 0.793254252727273

00:48:46.649 --> 00:48:48.128 Stone carries neither.

NOTE Confidence: 0.906266402142857
00:48:50.400 --> 00:48:52.339 Did we wanna video conference and hear
NOTE Confidence: 0.906266402142857
00:48:52.339 --> 00:48:54.369 from the research team that was possible?
NOTE Confidence: 0.906266402142857
00:48:54.370 --> 00:48:58.186 Yes, please answers tell me everything.
NOTE Confidence: 0.906266402142857
00:48:58.190 --> 00:48:59.495 A video conference was scheduled
NOTE Confidence: 0.906266402142857
00:48:59.495 --> 00:49:01.323 and all at once. I wasn't alone.
NOTE Confidence: 0.906266402142857
00:49:01.323 --> 00:49:03.655 I found someone who cared as much as I
NOTE Confidence: 0.906266402142857
00:49:03.655 --> 00:49:05.447 did about finding an answer as to why
NOTE Confidence: 0.906266402142857
00:49:05.500 --> 00:49:07.505 my children got sick, why they died,
NOTE Confidence: 0.906266402142857
00:49:07.505 --> 00:49:09.570 but what's more is they want to
NOTE Confidence: 0.906266402142857
00:49:09.634 --> 00:49:11.750 understand their disease process.
NOTE Confidence: 0.906266402142857
00:49:11.750 --> 00:49:13.570 They want to know more.
NOTE Confidence: 0.906266402142857
00:49:13.570 --> 00:49:15.829 They want to know if there is a treatment.
NOTE Confidence: 0.906266402142857
00:49:15.830 --> 00:49:19.510 So do I. They want to know and they will,
NOTE Confidence: 0.906266402142857
00:49:19.510 --> 00:49:22.016 and they became our beacon of hope.
NOTE Confidence: 0.906266402142857
00:49:22.020 --> 00:49:24.780 This news was life changing.
NOTE Confidence: 0.906266402142857

00:49:24.780 --> 00:49:26.916 After so many years of trauma and tragedy,
NOTE Confidence: 0.906266402142857

00:49:26.920 --> 00:49:29.560 we could finally actually breathe.
NOTE Confidence: 0.906266402142857

00:49:29.560 --> 00:49:31.385 The thing we so desperately
NOTE Confidence: 0.906266402142857

00:49:31.385 --> 00:49:32.845 wanted for our babies.
NOTE Confidence: 0.906266402142857

00:49:32.850 --> 00:49:34.350 The joy and excitement Roman expressed
NOTE Confidence: 0.906266402142857

00:49:34.350 --> 00:49:36.120 when he found out his littlest brother
NOTE Confidence: 0.906266402142857

00:49:36.120 --> 00:49:37.807 wasn't going to get sick and die,
NOTE Confidence: 0.906266402142857

00:49:37.810 --> 00:49:40.043 and neither was he inspired him to
NOTE Confidence: 0.906266402142857

00:49:40.043 --> 00:49:42.216 donate his 10th birthday to raising
NOTE Confidence: 0.906266402142857

00:49:42.216 --> 00:49:44.830 over \$1000 for Yale's research team.
NOTE Confidence: 0.906266402142857

00:49:44.830 --> 00:49:47.290 We are dealing with real
NOTE Confidence: 0.906266402142857

00:49:47.290 --> 00:49:48.766 and intimate information.
NOTE Confidence: 0.906266402142857

00:49:48.770 --> 00:49:51.493 We had two of four children known
NOTE Confidence: 0.906266402142857

00:49:51.493 --> 00:49:54.278 in the world with this disease.
NOTE Confidence: 0.906266402142857

00:49:54.280 --> 00:49:56.737 But I am just one of millions of people
NOTE Confidence: 0.906266402142857

00:49:56.737 --> 00:49:59.147 around the world affected by rare disease.

NOTE Confidence: 0.906266402142857
00:49:59.150 --> 00:50:01.110 Just because the disease is rare doesn't
NOTE Confidence: 0.906266402142857
00:50:01.110 --> 00:50:02.999 mean it's not common to have one.
NOTE Confidence: 0.906266402142857
00:50:03.000 --> 00:50:05.238 We need a clinical research infrastructure
NOTE Confidence: 0.906266402142857
00:50:05.238 --> 00:50:07.310 that allows these rare diseases to
NOTE Confidence: 0.906266402142857
00:50:07.310 --> 00:50:09.374 be found so that we can treat and
NOTE Confidence: 0.906266402142857
00:50:09.438 --> 00:50:11.218 understand the disease process.
NOTE Confidence: 0.906266402142857
00:50:11.220 --> 00:50:13.140 It is vital the scientists share
NOTE Confidence: 0.906266402142857
00:50:13.140 --> 00:50:14.837 this information with the affected
NOTE Confidence: 0.906266402142857
00:50:14.837 --> 00:50:16.967 families because we deserve to know.
NOTE Confidence: 0.906266402142857
00:50:16.970 --> 00:50:18.830 We deserve some Peace of Mind
NOTE Confidence: 0.906266402142857
00:50:18.830 --> 00:50:20.650 and we deserve some answers.
NOTE Confidence: 0.906266402142857
00:50:20.650 --> 00:50:22.936 That is what Yale's program does.
NOTE Confidence: 0.906266402142857
00:50:22.940 --> 00:50:24.905 What are family experience was
NOTE Confidence: 0.906266402142857
00:50:24.905 --> 00:50:27.368 painful and traumatic five years ago
NOTE Confidence: 0.906266402142857
00:50:27.368 --> 00:50:29.072 yields pediatric genomics Discovery
NOTE Confidence: 0.906266402142857

00:50:29.072 --> 00:50:31.040 program wasn't in existence.
NOTE Confidence: 0.906266402142857

00:50:31.040 --> 00:50:32.275 Had this program been around
NOTE Confidence: 0.906266402142857

00:50:32.275 --> 00:50:33.510 when we lost our daughter,
NOTE Confidence: 0.906266402142857

00:50:33.510 --> 00:50:35.456 we would have had the opportunity to
NOTE Confidence: 0.906266402142857

00:50:35.456 --> 00:50:37.347 find what caused Israel to get sick.
NOTE Confidence: 0.906266402142857

00:50:37.350 --> 00:50:38.970 It could have helped us understand
NOTE Confidence: 0.906266402142857

00:50:38.970 --> 00:50:39.780 what was happening,
NOTE Confidence: 0.906266402142857

00:50:39.780 --> 00:50:42.756 how to move forward for family planning and
NOTE Confidence: 0.906266402142857

00:50:42.756 --> 00:50:44.859 additional research and treatment options.
NOTE Confidence: 0.906266402142857

00:50:44.860 --> 00:50:48.020 PDP is the pinnacle of research and medicine.
NOTE Confidence: 0.906266402142857

00:50:48.020 --> 00:50:50.052 They not only search for a diagnosis but
NOTE Confidence: 0.906266402142857

00:50:50.052 --> 00:50:52.588 also a way to treat the disease the way
NOTE Confidence: 0.906266402142857

00:50:52.588 --> 00:50:54.926 they have changed our lives is immeasurable.
NOTE Confidence: 0.906266402142857

00:50:54.930 --> 00:50:56.970 They gave us back in innocence and freedom.
NOTE Confidence: 0.906266402142857

00:50:56.970 --> 00:50:58.820 We had taken from us.
NOTE Confidence: 0.906266402142857

00:50:58.820 --> 00:51:01.256 They are the hope for the future.

NOTE Confidence: 0.906266402142857
00:51:01.260 --> 00:51:01.904 My children.
NOTE Confidence: 0.906266402142857
00:51:01.904 --> 00:51:04.480 Are lucky and that my husband and I
NOTE Confidence: 0.906266402142857
00:51:04.554 --> 00:51:06.839 are educated and live comfortably.
NOTE Confidence: 0.906266402142857
00:51:06.840 --> 00:51:08.472 We had a community that surrounded
NOTE Confidence: 0.906266402142857
00:51:08.472 --> 00:51:10.360 and supported us so we didn't lose
NOTE Confidence: 0.906266402142857
00:51:10.360 --> 00:51:12.089 our home and could pay to properly
NOTE Confidence: 0.906266402142857
00:51:12.146 --> 00:51:13.506 place our children to rest.
NOTE Confidence: 0.906266402142857
00:51:13.510 --> 00:51:15.364 We had resources and the ability
NOTE Confidence: 0.906266402142857
00:51:15.364 --> 00:51:17.338 to advocate for our children and
NOTE Confidence: 0.906266402142857
00:51:17.338 --> 00:51:19.348 to understand what was going on.
NOTE Confidence: 0.906266402142857
00:51:19.350 --> 00:51:22.110 This is not true for many Americans or
NOTE Confidence: 0.906266402142857
00:51:22.110 --> 00:51:25.060 any family with a medically fragile child.
NOTE Confidence: 0.906266402142857
00:51:25.060 --> 00:51:26.719 Yale's mission to find answers and to
NOTE Confidence: 0.906266402142857
00:51:26.719 --> 00:51:28.712 be a resource to the families needs to
NOTE Confidence: 0.906266402142857
00:51:28.712 --> 00:51:30.394 be marketed so that families can have
NOTE Confidence: 0.906266402142857

00:51:30.394 --> 00:51:32.250 the help they are so desperately seeking.

NOTE Confidence: 0.862823888

00:51:48.320 --> 00:51:51.434 OK, so it's very hard to

NOTE Confidence: 0.862823888

00:51:51.434 --> 00:51:53.510 follow anything after that,

NOTE Confidence: 0.862823888

00:51:53.510 --> 00:51:55.680 so I think I think the points

NOTE Confidence: 0.862823888

00:51:55.680 --> 00:51:57.630 there are are pretty clear.

NOTE Confidence: 0.862823888

00:51:57.630 --> 00:52:00.101 Is it is to the desperation these

NOTE Confidence: 0.862823888

00:52:00.101 --> 00:52:03.162 families have and the impact that we can

NOTE Confidence: 0.862823888

00:52:03.162 --> 00:52:06.020 have by studying these rare disorders.

NOTE Confidence: 0.862823888

00:52:06.020 --> 00:52:08.588 So I'd like to finish at that point.

NOTE Confidence: 0.862823888

00:52:08.590 --> 00:52:11.443 And and really ask you guys to to join

NOTE Confidence: 0.862823888

00:52:11.443 --> 00:52:14.550 us that you know if if any of you have

NOTE Confidence: 0.862823888

00:52:14.550 --> 00:52:16.854 patients that you could benefit from

NOTE Confidence: 0.862823888

00:52:16.854 --> 00:52:19.490 genome sequencing or or exon sequencing.

NOTE Confidence: 0.862823888

00:52:19.490 --> 00:52:21.346 All you have to do is email peeds

NOTE Confidence: 0.862823888

00:52:21.346 --> 00:52:22.590 discovery at yale.edu and we'll

NOTE Confidence: 0.862823888

00:52:22.590 --> 00:52:24.410 be happy to get back to you.

NOTE Confidence: 0.862823888

00:52:24.410 --> 00:52:26.786 We see we see a wide variety of phenotypes,

NOTE Confidence: 0.862823888

00:52:26.790 --> 00:52:27.663 structural birth defects,

NOTE Confidence: 0.862823888

00:52:27.663 --> 00:52:29.632 we've been doing, metabolic diseases,

NOTE Confidence: 0.862823888

00:52:29.632 --> 00:52:31.270 unexplained critical illness,

NOTE Confidence: 0.862823888

00:52:31.270 --> 00:52:32.414 seizures and developmental delay.

NOTE Confidence: 0.862823888

00:52:32.414 --> 00:52:35.046 So I I think there's a lot of possibilities

NOTE Confidence: 0.862823888

00:52:35.046 --> 00:52:37.362 and I think we haven't yet explored all

NOTE Confidence: 0.862823888

00:52:37.362 --> 00:52:39.410 of the possibilities and I have no doubt.

NOTE Confidence: 0.862823888

00:52:39.410 --> 00:52:41.280 That you guys have collections

NOTE Confidence: 0.862823888

00:52:41.280 --> 00:52:43.923 of patients or even one or two

NOTE Confidence: 0.862823888

00:52:43.923 --> 00:52:45.870 patients that if we could help,

NOTE Confidence: 0.862823888

00:52:45.870 --> 00:52:46.814 we'd be.

NOTE Confidence: 0.862823888

00:52:46.814 --> 00:52:49.646 We'd be happy to participate and

NOTE Confidence: 0.862823888

00:52:49.646 --> 00:52:51.728 collaborate with you to do so.

NOTE Confidence: 0.862823888

00:52:51.730 --> 00:52:53.518 I'm very thankful to the patients

NOTE Confidence: 0.862823888

00:52:53.518 --> 00:52:55.054 and families who are the
NOTE Confidence: 0.862823888

00:52:55.054 --> 00:52:56.758 inspiration for all of our work.
NOTE Confidence: 0.862823888

00:52:56.760 --> 00:52:57.895 We've gotten support from a
NOTE Confidence: 0.862823888

00:52:57.895 --> 00:52:58.803 number of different groups,
NOTE Confidence: 0.862823888

00:52:58.810 --> 00:52:59.884 including the hospital,
NOTE Confidence: 0.862823888

00:52:59.884 --> 00:53:02.028 the Yale Medicine, and School of Medicine.
NOTE Confidence: 0.862823888

00:53:02.028 --> 00:53:03.630 In order to create this program,
NOTE Confidence: 0.862823888

00:53:03.630 --> 00:53:05.480 we're always grateful for our
NOTE Confidence: 0.862823888

00:53:05.480 --> 00:53:07.252 funding sources and the people
NOTE Confidence: 0.862823888

00:53:07.252 --> 00:53:09.316 who have done all the work.
NOTE Confidence: 0.862823888

00:53:09.320 --> 00:53:10.520 I think I'll stop there and
NOTE Confidence: 0.862823888

00:53:10.520 --> 00:53:11.810 I'll happy to take questions.
NOTE Confidence: 0.706460078333333

00:53:19.170 --> 00:53:21.700 Let's see, how do you do? Is it in the chat?
NOTE Confidence: 0.773336528333333

00:53:22.800 --> 00:53:23.800 Thanks so much Mr.
NOTE Confidence: 0.773336528333333

00:53:23.800 --> 00:53:25.636 Uhm there's already a couple of comments
NOTE Confidence: 0.773336528333333

00:53:25.636 --> 00:53:27.603 that have come in from Carla Stover.

NOTE Confidence: 0.773336528333333
00:53:27.610 --> 00:53:28.528 He says thank you so much.
NOTE Confidence: 0.773336528333333
00:53:28.530 --> 00:53:30.270 That was a powerful story.
NOTE Confidence: 0.773336528333333
00:53:30.270 --> 00:53:32.214 She told thank you and her for sharing
NOTE Confidence: 0.773336528333333
00:53:32.214 --> 00:53:34.545 with us and and the office and saying yes,
NOTE Confidence: 0.773336528333333
00:53:34.550 --> 00:53:36.510 thank you so powerful.
NOTE Confidence: 0.773336528333333
00:53:36.510 --> 00:53:39.066 And indeed that is an incredibly
NOTE Confidence: 0.773336528333333
00:53:39.066 --> 00:53:40.770 moving and powerful video.
NOTE Confidence: 0.773336528333333
00:53:40.770 --> 00:53:42.666 And I think some of the points that
NOTE Confidence: 0.773336528333333
00:53:42.666 --> 00:53:44.110 you've raised about the you know,
NOTE Confidence: 0.773336528333333
00:53:44.110 --> 00:53:45.430 the the the Odyssey that these
NOTE Confidence: 0.773336528333333
00:53:45.430 --> 00:53:46.789 families go on is really something
NOTE Confidence: 0.773336528333333
00:53:46.789 --> 00:53:48.509 that I think is is shared by a
NOTE Confidence: 0.773336528333333
00:53:48.563 --> 00:53:49.991 number of the patients and families
NOTE Confidence: 0.773336528333333
00:53:49.991 --> 00:53:51.550 that are seen by our clinical
NOTE Confidence: 0.773336528333333
00:53:51.550 --> 00:53:53.288 colleagues absolutely center.
NOTE Confidence: 0.773336528333333

00:53:53.288 --> 00:53:55.316 And do you have any questions
NOTE Confidence: 0.773336528333333
00:53:55.316 --> 00:53:57.160 in the room or on zoom?
NOTE Confidence: 0.773336528333333
00:53:57.160 --> 00:53:58.475 Please raise your hands or
NOTE Confidence: 0.773336528333333
00:53:58.475 --> 00:53:59.790 pop them into the chat.
NOTE Confidence: 0.619503178333333
00:54:08.980 --> 00:54:11.140 So while people are collecting there,
NOTE Confidence: 0.619503178333333
00:54:11.140 --> 00:54:13.270 Oh yeah, go ahead, go ahead.
NOTE Confidence: 0.619503178333333
00:54:13.270 --> 00:54:14.520 Just wait for the microphone.
NOTE Confidence: 0.96526399
00:54:17.120 --> 00:54:19.220 Thank you so much. That was a very
NOTE Confidence: 0.96526399
00:54:19.220 --> 00:54:22.420 powerful thank you for the presentation.
NOTE Confidence: 0.864470192
00:54:22.640 --> 00:54:24.280 I just have a question.
NOTE Confidence: 0.864470192
00:54:24.280 --> 00:54:26.512 Do you know what is the state of
NOTE Confidence: 0.864470192
00:54:26.512 --> 00:54:29.330 the the diagnosis odysseys for this
NOTE Confidence: 0.864470192
00:54:29.330 --> 00:54:31.804 disease is and I know that these
NOTE Confidence: 0.864470192
00:54:31.804 --> 00:54:34.450 diseases are very heterogeneous, right?
NOTE Confidence: 0.864470192
00:54:34.450 --> 00:54:38.164 But what can be done to at least like
NOTE Confidence: 0.864470192
00:54:38.164 --> 00:54:41.838 shorten or alleviate the diagnostics?

NOTE Confidence: 0.864470192

00:54:41.840 --> 00:54:44.698 Odysseys, yeah, so that's a good question.

NOTE Confidence: 0.864470192

00:54:44.700 --> 00:54:45.876 I don't. I don't know if everyone

NOTE Confidence: 0.864470192

00:54:45.876 --> 00:54:47.138 could hear that one of the questions.

NOTE Confidence: 0.864470192

00:54:47.140 --> 00:54:49.130 This is that you know,

NOTE Confidence: 0.864470192

00:54:49.130 --> 00:54:50.455 perhaps part of the challenge

NOTE Confidence: 0.864470192

00:54:50.455 --> 00:54:52.191 for some of these rare diseases

NOTE Confidence: 0.864470192

00:54:52.191 --> 00:54:53.619 is the diagnostic odyssey,

NOTE Confidence: 0.864470192

00:54:53.620 --> 00:54:55.797 which can be very desperate for families.

NOTE Confidence: 0.864470192

00:54:55.800 --> 00:54:58.344 And is there a way to shorten them?

NOTE Confidence: 0.864470192

00:54:58.350 --> 00:55:00.138 You know, to me to me,

NOTE Confidence: 0.864470192

00:55:00.140 --> 00:55:02.924 I think one of the ways to shorten

NOTE Confidence: 0.864470192

00:55:02.924 --> 00:55:05.208 the diagnostic odyssey is certainly

NOTE Confidence: 0.864470192

00:55:05.208 --> 00:55:07.728 to implement exome sequencing or

NOTE Confidence: 0.864470192

00:55:07.728 --> 00:55:09.740 genome sequencing much earlier,

NOTE Confidence: 0.864470192

00:55:09.740 --> 00:55:12.650 and I think you know.

NOTE Confidence: 0.864470192

00:55:12.650 --> 00:55:13.482 Genome sequencing,
NOTE Confidence: 0.864470192

00:55:13.482 --> 00:55:16.394 like any other test is is it
NOTE Confidence: 0.864470192

00:55:16.394 --> 00:55:18.968 requires some expertise to interpret.
NOTE Confidence: 0.864470192

00:55:18.970 --> 00:55:21.091 But the one challenge with it is
NOTE Confidence: 0.864470192

00:55:21.091 --> 00:55:22.824 that it's always evolving, right?
NOTE Confidence: 0.864470192

00:55:22.824 --> 00:55:23.640 So, like you know,
NOTE Confidence: 0.864470192

00:55:23.640 --> 00:55:25.614 we've had we've had cases where it
NOTE Confidence: 0.864470192

00:55:25.614 --> 00:55:27.626 was very hard to make a diagnosis
NOTE Confidence: 0.864470192

00:55:27.626 --> 00:55:29.675 and then a year later there was
NOTE Confidence: 0.864470192

00:55:29.675 --> 00:55:31.649 a whole cohort of patients that
NOTE Confidence: 0.864470192

00:55:31.649 --> 00:55:33.184 were identified that allows us
NOTE Confidence: 0.864470192

00:55:33.184 --> 00:55:34.544 to make a diagnosis right,
NOTE Confidence: 0.864470192

00:55:34.550 --> 00:55:37.130 and so that the evolution of it is is very
NOTE Confidence: 0.864470192

00:55:37.194 --> 00:55:39.960 fast and really requires continuous updating.
NOTE Confidence: 0.864470192

00:55:39.960 --> 00:55:40.809 So to me,
NOTE Confidence: 0.864470192

00:55:40.809 --> 00:55:42.507 there's no question that this is

NOTE Confidence: 0.864470192

00:55:42.507 --> 00:55:44.800 a very powerful diagnostic tool.

NOTE Confidence: 0.864470192

00:55:44.800 --> 00:55:46.536 EXO more genome sequencing.

NOTE Confidence: 0.864470192

00:55:46.536 --> 00:55:49.140 The question is implementing it is.

NOTE Confidence: 0.864470192

00:55:49.140 --> 00:55:50.540 Is as quickly as possible,

NOTE Confidence: 0.864470192

00:55:50.540 --> 00:55:52.400 and to recognize that it's not.

NOTE Confidence: 0.864470192

00:55:52.400 --> 00:55:55.160 It's far from perfect right now,

NOTE Confidence: 0.864470192

00:55:55.160 --> 00:55:55.832 but you know,

NOTE Confidence: 0.864470192

00:55:55.832 --> 00:55:56.280 for example,

NOTE Confidence: 0.864470192

00:55:56.280 --> 00:55:58.779 we sometimes say that we can get

NOTE Confidence: 0.864470192

00:55:58.779 --> 00:56:00.820 diagnosis in about 30 to 40% of

NOTE Confidence: 0.864470192

00:56:00.820 --> 00:56:02.380 the patients that we see through

NOTE Confidence: 0.864470192

00:56:02.380 --> 00:56:04.080 extreme seeking or genome sequencing,

NOTE Confidence: 0.864470192

00:56:04.080 --> 00:56:06.216 even after they've had a huge

NOTE Confidence: 0.864470192

00:56:06.216 --> 00:56:08.080 battery of other diagnostic tests.

NOTE Confidence: 0.864470192

00:56:08.080 --> 00:56:10.082 And to me some people say, well,

NOTE Confidence: 0.864470192

00:56:10.082 --> 00:56:11.774 that's 70% that you didn't diagnose,
NOTE Confidence: 0.864470192

00:56:11.780 --> 00:56:14.294 but I would say that's 30% that we
NOTE Confidence: 0.864470192

00:56:14.294 --> 00:56:16.079 can diagnose that we're undiagnosable.
NOTE Confidence: 0.864470192

00:56:16.080 --> 00:56:18.110 So to me, that's already infinitely better.
NOTE Confidence: 0.6336148

00:56:21.110 --> 00:56:23.062 And Mr. Could you talk a
NOTE Confidence: 0.6336148

00:56:23.062 --> 00:56:24.630 little bit about the. The
NOTE Confidence: 0.75550197

00:56:24.630 --> 00:56:25.850 role of genetic counseling
NOTE Confidence: 0.75550197

00:56:25.850 --> 00:56:27.070 in the pediatric genomic
NOTE Confidence: 0.887291086363636

00:56:27.270 --> 00:56:29.550 Discovery program right so so genetic
NOTE Confidence: 0.887291086363636

00:56:29.550 --> 00:56:31.700 counseling is is really critical.
NOTE Confidence: 0.887291086363636

00:56:31.700 --> 00:56:33.900 I think you know one of the things we had.
NOTE Confidence: 0.887291086363636

00:56:33.900 --> 00:56:37.143 One of the challenges is that what
NOTE Confidence: 0.887291086363636

00:56:37.143 --> 00:56:39.381 what we're often doing is returning
NOTE Confidence: 0.887291086363636

00:56:39.381 --> 00:56:41.688 research results to patients you know.
NOTE Confidence: 0.887291086363636

00:56:41.690 --> 00:56:44.147 So I think genetic counseling is tough
NOTE Confidence: 0.887291086363636

00:56:44.150 --> 00:56:46.094 when you have a clinical diagnosis

NOTE Confidence: 0.887291086363636

00:56:46.094 --> 00:56:48.230 right when you have enormous amounts

NOTE Confidence: 0.887291086363636

00:56:48.230 --> 00:56:50.570 of evidence defining a diseases as

NOTE Confidence: 0.887291086363636

00:56:50.570 --> 00:56:52.790 causative for the patients phenotype.

NOTE Confidence: 0.887291086363636

00:56:52.790 --> 00:56:55.135 But when you have a research result?

NOTE Confidence: 0.887291086363636

00:56:55.140 --> 00:56:58.092 Uh, you need to very carefully

NOTE Confidence: 0.887291086363636

00:56:58.092 --> 00:56:59.076 temper expectations.

NOTE Confidence: 0.887291086363636

00:56:59.080 --> 00:57:02.096 Saying that you know research can be wrong.

NOTE Confidence: 0.887291086363636

00:57:02.100 --> 00:57:04.680 It is not definitive, right?

NOTE Confidence: 0.887291086363636

00:57:04.680 --> 00:57:07.080 I mean, you know, we might, you know,

NOTE Confidence: 0.887291086363636

00:57:07.080 --> 00:57:08.760 we, it may not be reproducible.

NOTE Confidence: 0.887291086363636

00:57:08.760 --> 00:57:10.482 'cause this is the first patient that

NOTE Confidence: 0.887291086363636

00:57:10.482 --> 00:57:11.940 we're seeing with this diagnosis,

NOTE Confidence: 0.887291086363636

00:57:11.940 --> 00:57:13.256 and so we have.

NOTE Confidence: 0.887291086363636

00:57:13.256 --> 00:57:14.901 We're always very careful to

NOTE Confidence: 0.887291086363636

00:57:14.901 --> 00:57:16.884 explain to families that research

NOTE Confidence: 0.887291086363636

00:57:16.884 --> 00:57:18.468 results are not perfect,
NOTE Confidence: 0.887291086363636

00:57:18.470 --> 00:57:20.644 but that recognize that this, of course,
NOTE Confidence: 0.887291086363636

00:57:20.644 --> 00:57:21.856 if you don't start with research,
NOTE Confidence: 0.887291086363636

00:57:21.860 --> 00:57:23.080 you won't actually make it
NOTE Confidence: 0.887291086363636

00:57:23.080 --> 00:57:24.056 to a clinical diagnosis,
NOTE Confidence: 0.887291086363636

00:57:24.060 --> 00:57:26.508 and so this is an important first step.
NOTE Confidence: 0.887291086363636

00:57:26.510 --> 00:57:26.800 Uhm,
NOTE Confidence: 0.887291086363636

00:57:26.800 --> 00:57:28.830 and so I think the genetic counseling
NOTE Confidence: 0.887291086363636

00:57:28.830 --> 00:57:31.389 part is is really critical and and it
NOTE Confidence: 0.887291086363636

00:57:31.389 --> 00:57:33.357 requires a different kind of genetic
NOTE Confidence: 0.887291086363636

00:57:33.357 --> 00:57:35.548 counseling 'cause we need to make sure
NOTE Confidence: 0.887291086363636

00:57:35.548 --> 00:57:37.700 that the people who are doing this
NOTE Confidence: 0.887291086363636

00:57:37.700 --> 00:57:39.269 kind of counseling recognized that
NOTE Confidence: 0.887291086363636

00:57:39.269 --> 00:57:41.033 it's it's a research result which
NOTE Confidence: 0.887291086363636

00:57:41.033 --> 00:57:42.700 adds another layer of complexity.
NOTE Confidence: 0.767673924285714

00:57:46.190 --> 00:57:47.926 My supper weird just at time now,

NOTE Confidence: 0.767673924285714
00:57:47.930 --> 00:57:49.622 but as you can see the comments rolling in,
NOTE Confidence: 0.767673924285714
00:57:49.630 --> 00:57:51.364 everyone is just commenting on more
NOTE Confidence: 0.767673924285714
00:57:51.364 --> 00:57:53.170 powerful and important work you're doing.
NOTE Confidence: 0.767673924285714
00:57:53.170 --> 00:57:54.345 So please join me once
NOTE Confidence: 0.767673924285714
00:57:54.345 --> 00:57:55.340 again attacking Dr. Coker
NOTE Confidence: 0.782350775
00:57:55.350 --> 00:57:59.770 for a fantastic dog. It's.
NOTE Confidence: 0.782350775
00:57:59.770 --> 00:58:02.600 Thanks again for the invitation.
NOTE Confidence: 0.782350775
00:58:02.600 --> 00:58:04.245 If people would like to email me,
NOTE Confidence: 0.782350775
00:58:04.250 --> 00:58:07.100 I'd be happy to continue this
NOTE Confidence: 0.782350775
00:58:07.100 --> 00:58:09.000 conversation in the future.