WEBVTT

NOTE duration: ”00:03:41.525”

NOTE Confidence: 0.983831

00:00:05.440 --> 00:00:07.040 If you look at us

NOTE Confidence: 0.983831

00:00:07.040 --> 00:00:08.639 on the outside, we're pretty

NOTE Confidence: 0.983831

00:00:08.639 --> 00:00:09.139 symmetrical.

NOTE Confidence: 0.97985667

00:00:09.440 --> 00:00:10.400 But if you look on

NOTE Confidence: 0.97985667

00:00:10.400 --> 00:00:12.820 the inside, we're incredibly asymmetric.

NOTE Confidence: 0.9988111

00:00:13.280 --> 00:00:15.040 And the most asymmetric thing

NOTE Confidence: 0.9988111

00:00:15.040 --> 00:00:15.975 is our heart.

NOTE Confidence: 0.96401054

00:00:16.855 --> 00:00:18.295 Early in development, you have

NOTE Confidence: 0.96401054

00:00:18.295 --> 00:00:19.335 a head and a tail

NOTE Confidence: 0.96401054

00:00:19.335 --> 00:00:20.135 and a front and a

NOTE Confidence: 0.96401054

00:00:20.135 --> 00:00:21.095 back, but you don't have

NOTE Confidence: 0.96401054

00:00:21.095 --> 00:00:22.135 a left and a right

NOTE Confidence: 0.96401054

00:00:22.135 --> 00:00:23.415 and you need the embryo

NOTE Confidence: 0.96401054

00:00:23.415 --> 00:00:25.675 to have this internal reference.

NOTE Confidence: 0.9878995

00:00:26.375 --> 00:00:28.475 Cilia are these little structures

NOTE Confidence: 0.9878995

00:00:28.535 --> 00:00:29.494 that are stuck on the

NOTE Confidence: 0.9878995

00:00:29.494 --> 00:00:31.110 top of every cell. So

NOTE Confidence: 0.9878995

00:00:31.110 --> 00:00:32.710 what the embryo does is

NOTE Confidence: 0.9878995

00:00:32.710 --> 00:00:34.570 it takes these very asymmetric

NOTE Confidence: 0.9954274

00:00:34.870 --> 00:00:35.370 cilia

NOTE Confidence: 0.98701847

00:00:35.750 --> 00:00:37.270 and positions them on a

NOTE Confidence: 0.98701847

00:00:37.270 --> 00:00:38.630 group of about two hundred

NOTE Confidence: 0.98701847

00:00:38.630 --> 00:00:39.690 and fifty cells

NOTE Confidence: 0.993495

00:00:40.150 --> 00:00:41.690 that come up at about

NOTE Confidence: 0.99871767

00:00:42.070 --> 00:00:43.530 eighteen days of human

NOTE Confidence: 0.8748896

00:00:43.995 --> 00:00:44.495 gestation.

NOTE Confidence: 0.9474201

00:00:44.955 --> 00:00:46.255 And now those cells

NOTE Confidence: 0.97549826

00:00:46.635 --> 00:00:48.155 have their own internal reference.

NOTE Confidence: 0.97549826

00:00:48.155 --> 00:00:49.435 Oh, I am asymmetric. This

NOTE Confidence: 0.97549826

00:00:49.435 --> 00:00:50.635 is my left side. This

NOTE Confidence: 0.97549826

00:00:50.635 --> 00:00:52.155 is my right side because

NOTE Confidence: 0.97549826

00:00:52.155 --> 00:00:53.435 the cilium on top of

NOTE Confidence: 0.97549826

00:00:53.435 --> 00:00:55.035 me points the way. And

NOTE Confidence: 0.97549826

00:00:55.035 --> 00:00:56.795 that mechanical signal is then

NOTE Confidence: 0.97549826

00:00:56.795 --> 00:00:58.390 transmitted to the whole rest

NOTE Confidence: 0.97549826

00:00:58.390 --> 00:01:00.070 of the embryo, including your

NOTE Confidence: 0.97549826

00:01:00.070 --> 00:01:01.050 heart, your lungs,

NOTE Confidence: 0.9737855

00:01:01.590 --> 00:01:03.450 your liver, your gut, etcetera,

NOTE Confidence: 0.9737855

00:01:03.510 --> 00:01:04.790 etcetera, to tell them, oh,

NOTE Confidence: 0.9737855

00:01:04.790 --> 00:01:06.230 this is left and this

NOTE Confidence: 0.9737855

00:01:06.230 --> 00:01:06.890 is right.

NOTE Confidence: 0.9930422

00:01:10.675 --> 00:01:12.035 So we're part of a

NOTE Confidence: 0.9930422

00:01:12.035 --> 00:01:13.175 national consortium

NOTE Confidence: 0.99745244

00:01:13.635 --> 00:01:15.395 that is essentially trying to

NOTE Confidence: 0.99745244

00:01:15.395 --> 00:01:15.895 build

NOTE Confidence: 0.96038014

00:01:16.435 --> 00:01:18.595 the largest congenital heart disease

NOTE Confidence: 0.96038014

00:01:18.595 --> 00:01:19.095 database,

NOTE Confidence: 0.99768645

00:01:19.475 --> 00:01:20.755 and we have recruited a

NOTE Confidence: 0.99768645

00:01:20.755 --> 00:01:22.435 total of about seventeen thousand

NOTE Confidence: 0.99768645

00:01:22.435 --> 00:01:23.690 patients. And what we're trying

NOTE Confidence: 0.99768645

00:01:23.690 --> 00:01:24.970 to do now is link

NOTE Confidence: 0.99768645

00:01:24.970 --> 00:01:27.690 that genetic cause to a

NOTE Confidence: 0.99768645

00:01:27.690 --> 00:01:29.610 developmental mechanism that makes the

NOTE Confidence: 0.99768645

00:01:29.610 --> 00:01:30.909 heart develop improperly.

NOTE Confidence: 0.9929232

00:01:31.369 --> 00:01:32.650 So my lab is focusing

NOTE Confidence: 0.9929232

00:01:32.650 --> 00:01:34.090 on cilia, which we've turned

NOTE Confidence: 0.9929232

00:01:34.090 --> 00:01:35.550 up in the genetic analysis

NOTE Confidence: 0.9929232

00:01:35.690 --> 00:01:36.190 also

NOTE Confidence: 0.99875283

00:01:36.735 --> 00:01:38.414 as a significant cause of

NOTE Confidence: 0.99875283

00:01:38.414 --> 00:01:40.194 human congenital heart disease.

NOTE Confidence: 0.98440135

00:01:40.575 --> 00:01:41.615 We're trying to see how

NOTE Confidence: 0.98440135

00:01:41.615 --> 00:01:43.375 they impact not just whether

NOTE Confidence: 0.98440135

00:01:43.375 --> 00:01:44.334 your heart's on the left

NOTE Confidence: 0.98440135

00:01:44.334 --> 00:01:46.034 or the right, but also

NOTE Confidence: 0.9684467

00:01:46.575 --> 00:01:48.195 they might impact heart function.

NOTE Confidence: 0.9684467

00:01:48.494 --> 00:01:50.354 We know that they impact

NOTE Confidence: 0.9684467

00:01:50.414 --> 00:01:51.715 early valve development,

NOTE Confidence: 0.9985286

00:01:52.040 --> 00:01:53.820 And those are places where

NOTE Confidence: 0.999387

00:01:54.200 --> 00:01:55.100 you could imagine

NOTE Confidence: 0.9994884

00:01:55.400 --> 00:01:56.840 that you could have some

NOTE Confidence: 0.9994884

00:01:56.840 --> 00:01:58.680 potential to intervene and make

NOTE Confidence: 0.9994884

00:01:58.680 --> 00:01:59.420 things better.

NOTE Confidence: 0.9772672

00:02:03.000 --> 00:02:04.520 We go from two angles.

NOTE Confidence: 0.9772672

00:02:04.520 --> 00:02:05.560 The first angle is the

NOTE Confidence: 0.9772672

00:02:05.560 --> 00:02:07.454 large scale genomic studies. So

NOTE Confidence: 0.9772672

00:02:07.454 --> 00:02:08.415 a lot of our work

NOTE Confidence: 0.9772672

00:02:08.415 --> 00:02:10.415 was supported by Yale Center

NOTE Confidence: 0.9772672

00:02:10.415 --> 00:02:11.474 for Genome Analysis.

NOTE Confidence: 0.9797894

00:02:11.775 --> 00:02:13.535 And so one aspect works

NOTE Confidence: 0.9797894

00:02:13.535 --> 00:02:14.514 through the geneticists

NOTE Confidence: 0.99021935

00:02:14.815 --> 00:02:17.715 and the more statistical genetics

NOTE Confidence: 0.99021935

00:02:17.935 --> 00:02:20.035 approach to defining what the

NOTE Confidence: 0.99021935

00:02:20.310 --> 00:02:21.850 contributing causes are.

NOTE Confidence: 0.98529696

00:02:22.390 --> 00:02:23.830 And the other aspect, we

NOTE Confidence: 0.98529696

00:02:23.830 --> 00:02:25.670 work with models to try

NOTE Confidence: 0.98529696

00:02:25.670 --> 00:02:28.310 to better understand how the

NOTE Confidence: 0.98529696

00:02:28.310 --> 00:02:30.170 genes we identify in humans

NOTE Confidence: 0.98529696

00:02:30.470 --> 00:02:32.745 actually function in heart development.

NOTE Confidence: 0.9942916

00:02:33.125 --> 00:02:34.665 And we're trying to determine

NOTE Confidence: 0.9942916

00:02:34.725 --> 00:02:36.105 at what point in development

NOTE Confidence: 0.97742206

00:02:36.645 --> 00:02:38.565 the heart has its very

NOTE Confidence: 0.97742206

00:02:38.565 --> 00:02:39.065 earliest

NOTE Confidence: 0.9729076

00:02:40.165 --> 00:02:40.665 structural

NOTE Confidence: 0.972204

00:02:41.045 --> 00:02:42.105 left right asymmetry

NOTE Confidence: 0.9229359

00:02:43.205 --> 00:02:45.065 and how those early signals

NOTE Confidence: 0.9229359

00:02:45.205 --> 00:02:47.210 from the ciliated cells cells

NOTE Confidence: 0.9229359

00:02:47.210 --> 00:02:48.430 in the left right organizer

NOTE Confidence: 0.99423

00:02:49.050 --> 00:02:50.889 communicate to the developing heart

NOTE Confidence: 0.99423

00:02:50.889 --> 00:02:52.110 tube to make it go

NOTE Confidence: 0.99423

00:02:52.169 --> 00:02:53.389 left or right.

NOTE Confidence: 0.9777144

00:02:57.130 --> 00:02:58.730 Our hope is that we

NOTE Confidence: 0.9777144

00:02:58.730 --> 00:02:59.415 can first

NOTE Confidence: 0.97475696

00:03:00.375 --> 00:03:02.855 really understand the genetic architecture

NOTE Confidence: 0.97475696

00:03:02.855 --> 00:03:04.614 of congenital heart disease on

NOTE Confidence: 0.97475696

00:03:04.614 --> 00:03:05.355 one hand,

NOTE Confidence: 0.9913954

00:03:05.655 --> 00:03:06.794 and then understand

NOTE Confidence: 0.9451885

00:03:07.254 --> 00:03:09.334 how the heart develops, especially

NOTE Confidence: 0.9451885

00:03:09.334 --> 00:03:10.954 in its most early steps,

NOTE Confidence: 0.9451885

00:03:11.174 --> 00:03:13.800 to understand the molecular mechanism

NOTE Confidence: 0.9451885

00:03:13.860 --> 00:03:15.459 that drives heart development. And

NOTE Confidence: 0.9451885

00:03:15.459 --> 00:03:15.959 understanding

NOTE Confidence: 0.9951633

00:03:16.260 --> 00:03:18.280 that will give us some

NOTE Confidence: 0.9529134

00:03:18.660 --> 00:03:19.160 cues

NOTE Confidence: 0.9979352

00:03:20.180 --> 00:03:20.840 as to

NOTE Confidence: 0.99171346

00:03:21.860 --> 00:03:23.780 which patients might respond to

NOTE Confidence: 0.99171346

00:03:23.780 --> 00:03:25.300 what therapy. I mean, we

NOTE Confidence: 0.99171346

00:03:25.300 --> 00:03:26.525 can't make the heart loop

NOTE Confidence: 0.99171346

00:03:26.525 --> 00:03:27.745 in the other direction

NOTE Confidence: 0.97067124

00:03:28.525 --> 00:03:30.764 because that happens at twenty

NOTE Confidence: 0.97067124

00:03:30.764 --> 00:03:32.065 days of human gestation,

NOTE Confidence: 0.99938667

00:03:32.525 --> 00:03:33.885 but we can help deal

NOTE Confidence: 0.99938667

00:03:33.885 --> 00:03:35.265 with the outcome

NOTE Confidence: 0.9904024

00:03:35.805 --> 00:03:36.305 postnatally.