WEBVTT

NOTE duration:"00:12:25.6320000"

NOTE language:en-us

NOTE Confidence: 0.801072

00:00:03.590 --> 00:00:05.274 Hello I'm Florida carino,

NOTE Confidence: 0.801072

00:00:05.274 --> 00:00:08.320 I'm a professor at their child study

NOTE Confidence: 0.801072

00:00:08.320 --> 00:00:10.500 center and Department of Neuroscience

NOTE Confidence: 0.801072

00:00:10.500 --> 00:00:14.316 and today I am sharing with you latest

NOTE Confidence: 0.801072

00:00:14.316 --> 00:00:17.298 highlights of research from my laboratory.

NOTE Confidence: 0.801072

00:00:17.300 --> 00:00:20.036 We are focusing on two projects.

NOTE Confidence: 0.801072

00:00:20.040 --> 00:00:22.854 One is an induced pluripotent stem

NOTE Confidence: 0.801072

00:00:22.854 --> 00:00:25.421 cells as models of developmental

NOTE Confidence: 0.801072

00:00:25.421 --> 00:00:29.579 disorders and the 2nd is on somatic

NOTE Confidence: 0.801072

00:00:29.579 --> 00:00:32.540 genomic mosaicism in the human brain.

NOTE Confidence: 0.801072

00:00:32.540 --> 00:00:36.488 So the first part.

NOTE Confidence: 0.801072

00:00:36.490 --> 00:00:38.830 Is about induced proponents themselves.

NOTE Confidence: 0.801072

00:00:38.830 --> 00:00:40.698 You can see here.

NOTE Confidence: 0.801072

00:00:40.698 --> 00:00:43.510 You probably know this, says R.

NOTE Confidence: 0.80069906

00:00:45.920 --> 00:00:48.632 Clearly Button says mean means immortal

NOTE Confidence: 0.80069906

00:00:48.632 --> 00:00:51.859 cell lines that are derived from a

NOTE Confidence: 0.80069906

00:00:51.859 --> 00:00:54.115 living person, typically from his

NOTE Confidence: 0.80069906

00:00:54.115 --> 00:00:56.390 small biopsy of fibroblast cells.

NOTE Confidence: 0.80069906

00:00:56.390 --> 00:00:59.694 But it could be also other cells obtained

NOTE Confidence: 0.80069906

00:00:59.694 --> 00:01:03.135 from the adult human body and they are

NOTE Confidence: 0.80069906

00:01:03.135 --> 00:01:05.965 expanded in vitro and we differentiate

NOTE Confidence: 0.80069906

00:01:05.965 --> 00:01:09.127 them in different type of neurons.

NOTE Confidence: 0.80069906

00:01:09.130 --> 00:01:11.662 So they undergo recapitulation

NOTE Confidence: 0.80069906

00:01:11.662 --> 00:01:14.194 of the neuronal development.

NOTE Confidence: 0.80069906

00:01:14.200 --> 00:01:16.310 Over several days and they

NOTE Confidence: 0.80069906

00:01:16.310 --> 00:01:18.940 can be used in various ways.

NOTE Confidence: 0.80069906

00:01:18.940 --> 00:01:21.100 We develop them into organoids.

NOTE Confidence: 0.80069906

00:01:21.100 --> 00:01:23.000 I'll show you later,

NOTE Confidence: 0.80069906

00:01:23.000 --> 00:01:25.850 but typically they can be used

NOTE Confidence: 0.80069906

00:01:25.945 --> 00:01:28.457 in screening and discovery.

NOTE Confidence: 0.80069906

00:01:28.460 --> 00:01:29.744 Of, for example,

NOTE Confidence: 0.80069906

00:01:29.744 --> 00:01:32.312 genes that are important in development

NOTE Confidence: 0.80069906

00:01:32.312 --> 00:01:35.000 or disease or for drug screening,

NOTE Confidence: 0.80069906

00:01:35.000 --> 00:01:38.608 or they can be used as models of

NOTE Confidence: 0.80069906

00:01:38.608 --> 00:01:41.223 human development in both normal

NOTE Confidence: 0.80069906

00:01:41.223 --> 00:01:43.928 development and and these orders.

NOTE Confidence: 0.80069906

00:01:43.930 --> 00:01:47.434 And various sizes have been applied to them,

NOTE Confidence: 0.80069906

00:01:47.440 --> 00:01:51.016 so we started this project about 10 years

NOTE Confidence: 0.80069906

00:01:51.016 --> 00:01:54.264 ago when we started recruiting first

NOTE Confidence: 0.80069906

00:01:54.264 --> 00:01:57.648 patients of the Child Study Center.

NOTE Confidence: 0.80069906

00:01:57.650 --> 00:02:00.520 With various new psychiatric diseases,

NOTE Confidence: 0.80069906

00:02:00.520 --> 00:02:03.390 and since then, we've acquired,

NOTE Confidence: 0.80069906

00:02:03.390 --> 00:02:05.626 we've developed about 600.

NOTE Confidence: 0.80069906

00:02:05.626 --> 00:02:10.280 I PS lines from more than 100 people,

NOTE Confidence: 0.80069906

00:02:10.280 --> 00:02:13.150 including both patients with autism,

NOTE Confidence: 0.80069906

00:02:13.150 --> 00:02:14.452 Tourette syndrome,

NOTE Confidence: 0.80069906

00:02:14.452 --> 00:02:17.056 and other developmental disorders

NOTE Confidence: 0.80069906

00:02:17.056 --> 00:02:18.358 and controls.

NOTE Confidence: 0.80069906

00:02:18.360 --> 00:02:21.426 And so we can grow these organoids

NOTE Confidence: 0.80069906

00:02:21.426 --> 00:02:24.019 in vitro over several days,

NOTE Confidence: 0.80069906

00:02:24.020 --> 00:02:27.100 and you can see the increase in

NOTE Confidence: 0.80069906

00:02:27.100 --> 00:02:30.627 size we grow them by the hundreds.

NOTE Confidence: 0.80069906

00:02:30.630 --> 00:02:33.682 We have a highly efficient protocol for

NOTE Confidence: 0.80069906

00:02:33.682 --> 00:02:36.300 developing them into these structures.

NOTE Confidence: 0.80069906

00:02:36.300 --> 00:02:39.492 You can see here if you cross section

NOTE Confidence: 0.80069906

00:02:39.492 --> 00:02:42.898 them and stained with various markers,

NOTE Confidence: 0.80069906

00:02:42.900 --> 00:02:45.260 you identify substructure within them.

NOTE Confidence: 0.80069906

00:02:45.260 --> 00:02:47.930 These are new epithelial progenitor

NOTE Confidence: 0.80069906

00:02:47.930 --> 00:02:51.389 cells that are staying in red for.

NOTE Confidence: 0.80069906

00:02:51.390 --> 00:02:53.885 Assess undergoing cell division and

NOTE Confidence: 0.80069906

00:02:53.885 --> 00:02:57.123 in green for a neuronal progenitor

NOTE Confidence: 0.80069906

00:02:57.123 --> 00:03:00.368 marker which is expressing expressing

NOTE Confidence: 0.80069906

00:03:00.368 --> 00:03:02.315 the cerebral cortex.

NOTE Confidence: 0.80069906

00:03:02.320 --> 00:03:05.148 And if you going more higher magnification

NOTE Confidence: 0.80069906

00:03:05.148 --> 00:03:08.269 in in in one of these organized,

NOTE Confidence: 0.80069906

00:03:08.270 --> 00:03:10.574 you can see that they express

NOTE Confidence: 0.80069906

00:03:10.574 --> 00:03:12.678 various cell types that are

NOTE Confidence: 0.80069906

00:03:12.678 --> 00:03:14.650 proper for normal development.

NOTE Confidence: 0.80069906

00:03:14.650 --> 00:03:18.038 Normal human development in red you see

NOTE Confidence: 0.80069906

00:03:18.038 --> 00:03:19.974 ventricular zone progenitors thankful

NOTE Confidence: 0.80069906

00:03:19.974 --> 00:03:22.816 pack six and cortical layer one neuron

NOTE Confidence: 0.80069906

00:03:22.816 --> 00:03:25.267 stain for a gene called TVR one.

NOTE Confidence: 0.80069906

00:03:25.270 --> 00:03:27.400 They are positive for Foxy,

NOTE Confidence: 0.80069906

00:03:27.400 --> 00:03:31.927 One which is expressed in the hole for brain.

NOTE Confidence: 0.80069906

00:03:31.930 --> 00:03:34.996 Here you see a marker City 2,

NOTE Confidence: 0.80069906

00:03:35.000 --> 00:03:38.600 Four layer 5 and here down here in red

NOTE Confidence: 0.80069906

00:03:38.600 --> 00:03:42.434 and marker for layer 23 neurons in red.

NOTE Confidence: 0.80069906

00:03:42.440 --> 00:03:45.068 So they like capitulate fairly faithfully.

NOTE Confidence: 0.80069906

00:03:45.070 --> 00:03:48.136 Early stages of human in this case.

NOTE Confidence: 0.80069906

00:03:48.140 --> 00:03:49.448 Human cortical development.

NOTE Confidence: 0.7614749

00:03:52.310 --> 00:03:55.565 And they can be stained with viruses.

NOTE Confidence: 0.7614749

00:03:55.570 --> 00:03:59.298 And then in this way you can visualize

NOTE Confidence: 0.7614749

00:03:59.298 --> 00:04:02.179 their morphology in finer detail and

NOTE Confidence: 0.7614749

00:04:02.179 --> 00:04:04.975 even down to showing early synaptic

NOTE Confidence: 0.7614749

00:04:05.059 --> 00:04:08.202 spines and we we can do electrical

NOTE Confidence: 0.7614749

00:04:08.202 --> 00:04:11.137 recording on these cells by Patch

NOTE Confidence: 0.7614749

00:04:11.137 --> 00:04:14.311 clamp and they actually have synaptic

NOTE Confidence: 0.7614749

00:04:14.311 --> 00:04:17.189 currents develop synaptic currents.

NOTE Confidence: 0.7614749

00:04:17.190 --> 00:04:19.525 Overtime we've used them for

NOTE Confidence: 0.7614749

00:04:19.525 --> 00:04:20.926 studying various disorders.

NOTE Confidence: 0.7614749

00:04:20.930 --> 00:04:23.722 This is a paper we published in 2015

NOTE Confidence: 0.7614749

00:04:23.722 --> 00:04:26.164 on Autism Spectrum Disorder where

NOTE Confidence: 0.7614749

00:04:26.164 --> 00:04:28.934 we identified an imbalance between

NOTE Confidence: 0.7614749

00:04:28.934 --> 00:04:31.298 excitatory and inhibitory early

NOTE Confidence: 0.7614749

00:04:31.298 --> 00:04:34.228 developing neurons in these patients.

NOTE Confidence: 0.7614749

00:04:34.230 --> 00:04:37.242 And now we're in the middle

NOTE Confidence: 0.7614749

00:04:37.242 --> 00:04:39.250 of an ongoing study.

NOTE Confidence: 0.7614749

00:04:39.250 --> 00:04:41.760 Larger study of ASD families,

NOTE Confidence: 0.7614749

00:04:41.760 --> 00:04:44.844 which comprises eleven families in which

NOTE Confidence: 0.7614749

00:04:44.844 --> 00:04:48.790 we have one problem and one control pair,

NOTE Confidence: 0.7614749

00:04:48.790 --> 00:04:50.850 typically an effective father,

NOTE Confidence: 0.7614749

00:04:50.850 --> 00:04:54.310 and they are grouped into microcephalic ASD,

NOTE Confidence: 0.7614749

00:04:54.310 --> 00:04:57.316 meaning people that have large brains.

NOTE Confidence: 0.7614749

00:04:57.320 --> 00:04:59.830 An normal cephalic ASD individuals,

NOTE Confidence: 0.7614749

00:04:59.830 --> 00:05:03.344 an excitingly we find differences among them.

NOTE Confidence: 0.7614749

00:05:03.350 --> 00:05:04.637 Here, you see.

NOTE Confidence: 0.7614749

00:05:04.637 --> 00:05:07.211 Then see in mapping of single

NOTE Confidence: 0.7614749

00:05:07.211 --> 00:05:09.478 cell phenotypes by irony,

NOTE Confidence: 0.7614749

00:05:09.480 --> 00:05:11.930 single cell RNA sequencing in

NOTE Confidence: 0.7614749

00:05:11.930 --> 00:05:14.865 these families in the whole data

NOTE Confidence: 0.7614749

00:05:14.865 --> 00:05:17.644 set we can see that for example,

NOTE Confidence: 0.7614749

00:05:17.650 --> 00:05:20.590 in patients with microcephaly we have an

NOTE Confidence: 0.7614749

00:05:20.590 --> 00:05:23.548 imbalance in the distribution of sales.

NOTE Confidence: 0.7614749

00:05:23.550 --> 00:05:26.358 So this is up here in in Blue Excel

NOTE Confidence: 0.7614749

00:05:26.358 --> 00:05:29.582 Group that we identify as deep cortical

NOTE Confidence: 0.7614749

00:05:29.582 --> 00:05:32.236 plate excitatory neurons and in

NOTE Confidence: 0.7614749

00:05:32.236 --> 00:05:34.976 macrocephalic individuals patients versus.

NOTE Confidence: 0.7614749

00:05:34.980 --> 00:05:38.085 Others you see the day there is an increase

NOTE Confidence: 0.7614749

00:05:38.085 --> 00:05:40.908 in a subgroup of excitatory neuron,

NOTE Confidence: 0.7614749

00:05:40.910 --> 00:05:42.382 shown here in red,

NOTE Confidence: 0.7614749

00:05:42.382 --> 00:05:44.590 and a decrease in another subtype

NOTE Confidence: 0.7614749

00:05:44.670 --> 00:05:47.596 of excitatory neuron here and also a

NOTE Confidence: 0.7614749

00:05:47.596 --> 00:05:49.988 decrease of inhibitory neuron as well.

NOTE Confidence: 0.7614749

00:05:49.990 --> 00:05:52.608 So so at higher and higher the

NOTE Confidence: 0.7614749

00:05:52.608 --> 00:05:54.682 different type of resolution when

NOTE Confidence: 0.7614749

00:05:54.682 --> 00:05:57.298 we look at gene expression with

NOTE Confidence: 0.7614749

00:05:57.298 --> 00:06:00.044 this sub within each of these sub

NOTE Confidence: 0.7614749

00:06:00.044 --> 00:06:02.702 group of cells we can also identify

NOTE Confidence: 0.7614749

00:06:02.702 --> 00:06:05.288 certain imbalances you see here they.

NOTE Confidence: 0.7614749

00:06:05.290 --> 00:06:06.646 Differential gene expression

NOTE Confidence: 0.7614749

00:06:06.646 --> 00:06:08.454 in two cellular subproof,

NOTE Confidence: 0.7614749

00:06:08.460 --> 00:06:10.675 this the deep cortical plate

NOTE Confidence: 0.7614749

00:06:10.675 --> 00:06:12.890 excitatory neuron have an increase

NOTE Confidence: 0.7614749

00:06:12.968 --> 00:06:15.824 in markers for jeans that are typical

NOTE Confidence: 0.7614749

00:06:15.824 --> 00:06:17.970 of excitatory neuron development,

NOTE Confidence: 0.7614749

00:06:17.970 --> 00:06:19.329 such as emx.

NOTE Confidence: 0.7614749

00:06:19.329 --> 00:06:21.594 One an in the other,

NOTE Confidence: 0.7614749

00:06:21.600 --> 00:06:24.141 in another sub group of cells you

NOTE Confidence: 0.7614749

00:06:24.141 --> 00:06:26.943 have a decrease in jeans that

NOTE Confidence: 0.7614749

00:06:26.943 --> 00:06:29.119 are characteristic of inhibitory

NOTE Confidence: 0.7614749

00:06:29.119 --> 00:06:30.207 neuron development,

NOTE Confidence: 0.7614749

00:06:30.210 --> 00:06:32.814 suggesting again that there is an

NOTE Confidence: 0.7614749

00:06:32.814 --> 00:06:35.320 imbalance between excited or inhibited.

NOTE Confidence: 0.7614749

00:06:35.320 --> 00:06:37.894 Keep inhibitory neurons in in ASD

NOTE Confidence: 0.7614749

00:06:37.894 --> 00:06:41.214 and even more exciting we find that

NOTE Confidence: 0.7614749

00:06:41.214 --> 00:06:43.238 normal cephalic and microcephalic

NOTE Confidence: 0.7614749

00:06:43.238 --> 00:06:45.529 individuals are not the same,

NOTE Confidence: 0.7614749

00:06:45.530 --> 00:06:48.308 suggesting that using IP's season organoid.

NOTE Confidence: 0.7614749

00:06:48.310 --> 00:06:51.292 Perhaps we can identify finer differences

NOTE Confidence: 0.7614749

00:06:51.292 --> 00:06:54.250 between group of patients that can

NOTE Confidence: 0.7614749

00:06:54.250 --> 00:06:56.920 be useful for clinical phenotype and

NOTE Confidence: 0.7614749

00:06:56.920 --> 00:06:59.450 drug screening and things like that.

NOTE Confidence: 0.7614749

00:06:59.450 --> 00:07:02.698 We've also done studies in Tourette syndrome.

NOTE Confidence: 0.7614749

00:07:02.700 --> 00:07:05.430 This is my graduate student.

NOTE Confidence: 0.7614749

00:07:05.430 --> 00:07:06.258 Johnny Brady.

NOTE Confidence: 0.7614749

00:07:06.258 --> 00:07:08.328 She's spearheaded a project where

NOTE Confidence: 0.7614749

00:07:08.328 --> 00:07:10.621 she developed basal ganglia organoid

NOTE Confidence: 0.7614749

00:07:10.621 --> 00:07:12.597 rather than cortical organoids.

NOTE Confidence: 0.7614749

00:07:12.600 --> 00:07:15.192 There they develop many neurons that

NOTE Confidence: 0.7614749

00:07:15.192 --> 00:07:17.970 are characteristic of the basal ganglia,

NOTE Confidence: 0.7614749

00:07:17.970 --> 00:07:20.840 and she asked the question of whether

NOTE Confidence: 0.7614749

00:07:20.840 --> 00:07:23.067 this development was affected in

NOTE Confidence: 0.7614749

00:07:23.067 --> 00:07:25.367 Tourette syndrome because in another

NOTE Confidence: 0.7614749

00:07:25.367 --> 00:07:28.727 earlier study on adult brain with Tourettes,

NOTE Confidence: 0.7614749

00:07:28.730 --> 00:07:32.174 we found a decrease in certain types

NOTE Confidence: 0.7614749

00:07:32.174 --> 00:07:35.348 of interneurons in the basal ganglia.

NOTE Confidence: 0.7614749

00:07:35.350 --> 00:07:37.639 In so she asked the question whether

NOTE Confidence: 0.7614749

00:07:37.639 --> 00:07:39.544 this degrees was a developmental

NOTE Confidence: 0.7614749

00:07:39.544 --> 00:07:41.699 type decrease by growing organized

NOTE Confidence: 0.7614749

00:07:41.699 --> 00:07:42.992 from these patients

NOTE Confidence: 0.8114302

00:07:43.062 --> 00:07:45.526 and basically making a Long story short,

NOTE Confidence: 0.8114302

00:07:45.530 --> 00:07:47.275 she developed basal ganglia organoid

NOTE Confidence: 0.8114302

00:07:47.275 --> 00:07:49.725 down here and found that indeed there

NOTE Confidence: 0.8114302

00:07:49.725 --> 00:07:51.651 is an early imbalance in certain

NOTE Confidence: 0.8114302

00:07:51.651 --> 00:07:53.838 genes that are characteristic of

NOTE Confidence: 0.8114302

00:07:53.838 --> 00:07:55.326 inhibitory neuron development.

NOTE Confidence: 0.8114302

00:07:55.330 --> 00:07:58.260 You can see here NCX 2.1 is one of the

NOTE Confidence: 0.8114302

00:07:58.339 --> 00:08:01.171 earliest jeans that develop in the

NOTE Confidence: 0.8114302

00:08:01.171 --> 00:08:04.000 basal ganglia, and as you can see,

NOTE Confidence: 0.8114302

00:08:04.000 --> 00:08:05.970 while is very prevalent in.

NOTE Confidence: 0.8114302

00:08:05.970 --> 00:08:08.430 Basal ganglia from control is much

NOTE Confidence: 0.8114302

00:08:08.430 --> 00:08:10.530 decrease in basal ganglia organoid

NOTE Confidence: 0.8114302

00:08:10.530 --> 00:08:12.828 from patients with threats and you

NOTE Confidence: 0.8114302

00:08:12.828 --> 00:08:15.474 can see this quantified here on the

NOTE Confidence: 0.8114302

00:08:15.474 --> 00:08:18.280 right where you see a summary of five

NOTE Confidence: 0.8114302

00:08:18.280 --> 00:08:20.290 patient with red and tank controls

NOTE Confidence: 0.8114302

00:08:20.290 --> 00:08:22.269 with highly significant degrees.

NOTE Confidence: 0.8114302

00:08:22.270 --> 00:08:24.825 Foreign players 2.1 which is in the

NOTE Confidence: 0.8114302

00:08:24.825 --> 00:08:27.309 middle and Lonnie Kalmenson also DLX.

NOTE Confidence: 0.8114302

00:08:27.310 --> 00:08:29.445 Another change which is expressed

NOTE Confidence: 0.8114302

00:08:29.445 --> 00:08:31.580 throughout the basal ganglia and

NOTE Confidence: 0.8114302

00:08:31.650 --> 00:08:33.744 this is also imbalance is also

NOTE Confidence: 0.8114302

00:08:33.744 --> 00:08:35.967 evident in the preoptic area where

NOTE Confidence: 0.8114302

00:08:35.967 --> 00:08:37.475 again you see decreases.

NOTE Confidence: 0.8114302

00:08:37.480 --> 00:08:39.400 In inhibitory interneurons,

NOTE Confidence: 0.8114302

00:08:39.400 --> 00:08:41.320 an cholinergic interneuron,

NOTE Confidence: 0.8114302

00:08:41.320 --> 00:08:43.330 impatience versus control.

NOTE Confidence: 0.8114302

00:08:43.330 --> 00:08:48.020 But this is not evident in the

NOTE Confidence: 0.8114302

00:08:48.142 --> 00:08:50.728 in cortical organoids.

NOTE Confidence: 0.8114302

00:08:50.730 --> 00:08:53.634 So moving on a second project I was

NOTE Confidence: 0.8114302

00:08:53.634 --> 00:08:57.229 going to talk to you about is about

NOTE Confidence: 0.8114302

00:08:57.229 --> 00:09:00.528 semantic mosaicism and this is a

NOTE Confidence: 0.8114302

00:09:00.528 --> 00:09:03.488 phenomenon that is attracted recently.

NOTE Confidence: 0.8114302

00:09:03.490 --> 00:09:06.450 A lot of attention because.

NOTE Confidence: 0.7337406

00:09:08.700 --> 00:09:11.855 Deals with mutations that are

NOTE Confidence: 0.7337406

00:09:11.855 --> 00:09:15.720 developed in the body in each.

NOTE Confidence: 0.7337406

00:09:15.720 --> 00:09:17.905 Organism basically from the time

NOTE Confidence: 0.7337406

00:09:17.905 --> 00:09:19.653 of fertilization on throughout

NOTE Confidence: 0.7337406

00:09:19.653 --> 00:09:21.467 the life of that person.

NOTE Confidence: 0.7337406

00:09:21.470 --> 00:09:24.144 And here you see that mutations can

NOTE Confidence: 0.7337406

00:09:24.144 --> 00:09:26.728 occur at anytime and the earlier

NOTE Confidence: 0.7337406

00:09:26.728 --> 00:09:28.939 they developed, the more sales.

NOTE Confidence: 0.7337406

00:09:28.939 --> 00:09:31.104 Of course they involve typically

NOTE Confidence: 0.7337406

00:09:31.104 --> 00:09:33.389 however they occur at any stage.

NOTE Confidence: 0.7337406

00:09:33.390 --> 00:09:35.856 In the later they do develop.

NOTE Confidence: 0.7337406

00:09:35.860 --> 00:09:37.915 The smaller the part of

NOTE Confidence: 0.7337406

00:09:37.915 --> 00:09:39.970 the body that harbors them,

NOTE Confidence: 0.7337406

00:09:39.970 --> 00:09:42.436 and they're very difficult to detect.

NOTE Confidence: 0.7337406

00:09:42.440 --> 00:09:44.180 As you can imagine.

NOTE Confidence: 0.7337406

00:09:44.180 --> 00:09:46.790 So you have to develop particular

NOTE Confidence: 0.7337406

00:09:46.880 --> 00:09:49.834 protocols in order to Geno type the.

NOTE Confidence: 0.7337406

00:09:49.840 --> 00:09:52.458 This is of high resolution in order

NOTE Confidence: 0.7337406

00:09:52.458 --> 00:09:54.406 to identify and characterize them

NOTE Confidence: 0.7337406

00:09:54.406 --> 00:09:57.398 an in the past three years ago we

NOTE Confidence: 0.7337406

00:09:57.477 --> 00:10:00.117 developed we developed a method for.

NOTE Confidence: 0.7337406

00:10:00.120 --> 00:10:02.704 Assessing this mutation and

NOTE Confidence: 0.7337406

00:10:02.704 --> 00:10:05.934 we use them to reconstruct.

NOTE Confidence: 0.7337406

00:10:05.940 --> 00:10:07.748 Reconstruct the cellular mutation

NOTE Confidence: 0.7337406

00:10:07.748 --> 00:10:10.460 and history of three individuals in

NOTE Confidence: 0.7337406

00:10:10.526 --> 00:10:13.302 the reason you can do that is because

NOTE Confidence: 0.7337406

00:10:13.302 --> 00:10:15.438 these mutations are actually markers,

NOTE Confidence: 0.7337406

00:10:15.440 --> 00:10:17.500 indelible marker of every cell,

NOTE Confidence: 0.7337406

00:10:17.500 --> 00:10:19.570 division in the human body,

NOTE Confidence: 0.7337406

00:10:19.570 --> 00:10:20.704 and more recently,

NOTE Confidence: 0.7337406

00:10:20.704 --> 00:10:23.350 in an unpublished study we found a

NOTE Confidence: 0.7337406

00:10:23.424 --> 00:10:26.088 way to actually map this mutation

NOTE Confidence: 0.7337406

00:10:26.088 --> 00:10:27.420 in living individuals.

NOTE Confidence: 0.7337406

00:10:27.420 --> 00:10:30.327 The way we do that is we take six

NOTE Confidence: 0.7337406

00:10:30.327 --> 00:10:32.942 small skin biopsy biopsies from a

NOTE Confidence: 0.7337406

00:10:32.942 --> 00:10:36.140 person an we develop this fibroblast.

NOTE Confidence: 0.7337406

00:10:36.140 --> 00:10:37.950 Into I PS lines an.

NOTE Confidence: 0.7337406

00:10:37.950 --> 00:10:40.122 We genotyped each line and compare

NOTE Confidence: 0.7337406

00:10:40.122 --> 00:10:41.570 the genomes of these.

NOTE Confidence: 0.7337406

00:10:41.570 --> 00:10:43.874 I PS lines each of them is a

NOTE Confidence: 0.7337406

00:10:43.874 --> 00:10:45.954 descendant of a single cell and

NOTE Confidence: 0.7337406

00:10:45.954 --> 00:10:47.739 so any difference between them

NOTE Confidence: 0.7337406

00:10:47.739 --> 00:10:50.298 are clearly due to mutations that

NOTE Confidence: 0.7337406

00:10:50.298 --> 00:10:52.428 developed during the lifetime of

NOTE Confidence: 0.7337406

00:10:52.430 --> 00:10:54.656 that person and then we genotyped

NOTE Confidence: 0.7337406

00:10:54.656 --> 00:10:57.138 this mutation found in Ipas in blood,

NOTE Confidence: 0.7337406

00:10:57.140 --> 00:10:57.471 saliva,

NOTE Confidence: 0.7337406

00:10:57.471 --> 00:10:59.788 and urine and that is enough to

NOTE Confidence: 0.7337406

00:10:59.788 --> 00:11:01.322 reconstruct the ancestry tree

NOTE Confidence: 0.7337406

00:11:01.322 --> 00:11:02.930 of that particular person.

NOTE Confidence: 0.7337406

00:11:02.930 --> 00:11:05.730 And you can see an example here in

NOTE Confidence: 0.7337406

00:11:05.730 --> 00:11:08.350 a patient with Tourette syndrome.

NOTE Confidence: 0.7337406

00:11:08.350 --> 00:11:11.062 Where we could map the early

NOTE Confidence: 0.7337406

00:11:11.062 --> 00:11:12.870 lineages of that person,

NOTE Confidence: 0.7337406

00:11:12.870 --> 00:11:16.272 starting from the very first cell division

NOTE Confidence: 0.7337406

00:11:16.272 --> 00:11:19.800 up to about the 5th cell division.

NOTE Confidence: 0.7337406

00:11:19.800 --> 00:11:21.585 And one remarkable finding of

NOTE Confidence: 0.7337406

00:11:21.585 --> 00:11:23.882 this mapping is that you often

NOTE Confidence: 0.7337406

00:11:23.882 --> 00:11:26.504 find that there is a dominant

NOTE Confidence: 0.7337406

00:11:26.504 --> 00:11:27.815 l'imaginaire recessive leaner,

NOTE Confidence: 0.7337406

00:11:27.820 --> 00:11:30.476 and by that I mean one lineages that

NOTE Confidence: 0.7337406

00:11:30.476 --> 00:11:32.821 is over represented in the tissue

NOTE Confidence: 0.7337406

00:11:32.821 --> 00:11:35.793 in the body of that persons versus

NOTE Confidence: 0.7337406

00:11:35.793 --> 00:11:38.248 one that is less representative.

NOTE Confidence: 0.7337406

00:11:38.250 --> 00:11:40.777 So this is very short but just

NOTE Confidence: 0.7337406

00:11:40.777 --> 00:11:43.550 wanted you to give a brief overview

NOTE Confidence: 0.7337406

00:11:43.550 --> 00:11:46.481 and in closing I would like to

NOTE Confidence: 0.7337406

00:11:46.481 --> 00:11:48.666 acknowledge people in my lab,

NOTE Confidence: 0.7337406

00:11:48.670 --> 00:11:50.790 particularly Jessica Mariani, who developed.

NOTE Confidence: 0.7337406

00:11:50.790 --> 00:11:53.844 Organized protocol and Alex to down

NOTE Confidence: 0.7337406

00:11:53.844 --> 00:11:56.961 and finance who were involved very

NOTE Confidence: 0.7337406

00:11:56.961 --> 00:11:59.907 much so in their recent project

NOTE Confidence: 0.7337406

00:11:59.907 --> 00:12:03.078 with ASD and also our knowledge,

NOTE Confidence: 0.7337406

00:12:03.080 --> 00:12:06.146 our collaborator at the Trustor Dissenter,

NOTE Confidence: 0.7337406

00:12:06.150 --> 00:12:08.074 including various clinicians that

NOTE Confidence: 0.7337406

00:12:08.074 --> 00:12:10.479 have been instrumental in patients

NOTE Confidence: 0.7337406

00:12:10.479 --> 00:12:12.290 recruitment and characterization,

NOTE Confidence: 0.7337406

00:12:12.290 --> 00:12:15.362 which is of course essential to

NOTE Confidence: 0.7337406

00:12:15.362 --> 00:12:17.410 finally put everything together.

NOTE Confidence: 0.7337406

00:12:17.410 --> 00:12:21.506 And thank you very much for your attention.