WEBVTT

NOTE duration: ”00:12:17.960”

NOTE Confidence: 0.99750054

00:00:01.040 --> 00:00:02.820 Great. So I'm excited to

NOTE Confidence: 0.93343914

00:00:03.360 --> 00:00:05.120 kick off with, talk about

NOTE Confidence: 0.93343914

00:00:05.120 --> 00:00:06.420 the work in my laboratory.

NOTE Confidence: 0.9851041

00:00:07.040 --> 00:00:09.059 And and, with the ambitious

NOTE Confidence: 0.9851041

00:00:09.200 --> 00:00:10.660 goal to decode

NOTE Confidence: 0.93246746

00:00:11.200 --> 00:00:11.860 and simulate

NOTE Confidence: 0.9840764

00:00:12.535 --> 00:00:14.395 the genetic software of Parkinson's

NOTE Confidence: 0.9840764

00:00:14.455 --> 00:00:16.375 disease. We are very grateful

NOTE Confidence: 0.9840764

00:00:16.375 --> 00:00:17.735 to our sponsors. This is

NOTE Confidence: 0.9840764

00:00:17.735 --> 00:00:19.755 really a team effort. Parkinson's

NOTE Confidence: 0.9840764

00:00:19.975 --> 00:00:20.475 disease

NOTE Confidence: 0.9890219

00:00:20.855 --> 00:00:22.395 is a very important,

NOTE Confidence: 0.97626925

00:00:23.095 --> 00:00:25.095 problem. There it's actually now

NOTE Confidence: 0.97626925

00:00:25.095 --> 00:00:26.314 the fastest growing

NOTE Confidence: 0.9517886

00:00:26.810 --> 00:00:28.270 brain disease in the world,

NOTE Confidence: 0.9947702

00:00:28.730 --> 00:00:29.230 outpacing,

NOTE Confidence: 0.9965573

00:00:29.930 --> 00:00:31.710 the growth rates of Alzheimer's

NOTE Confidence: 0.9965573

00:00:31.770 --> 00:00:32.270 disease.

NOTE Confidence: 0.9367724

00:00:32.650 --> 00:00:33.770 There are ten million people

NOTE Confidence: 0.9367724

00:00:33.770 --> 00:00:35.370 with Parkinson's disease in the

NOTE Confidence: 0.9367724

00:00:35.370 --> 00:00:37.210 world today, and this in

NOTE Confidence: 0.9367724

00:00:37.370 --> 00:00:38.970 by some estimates, this number

NOTE Confidence: 0.9367724

00:00:38.970 --> 00:00:40.409 may increase to twenty five

NOTE Confidence: 0.9367724

00:00:40.409 --> 00:00:42.515 millions in in twenty fifty.

NOTE Confidence: 0.90301794

00:00:42.975 --> 00:00:44.755 And the burden for patients

NOTE Confidence: 0.90301794

00:00:44.815 --> 00:00:46.335 and their families and the

NOTE Confidence: 0.90301794

00:00:46.335 --> 00:00:47.615 health care costs are an

NOTE Confidence: 0.90301794

00:00:47.854 --> 00:00:48.354 enormous.

NOTE Confidence: 0.77912855

00:00:49.055 --> 00:00:49.795 And today's

NOTE Confidence: 0.99567443

00:00:50.255 --> 00:00:50.755 medicine

NOTE Confidence: 0.99758565

00:00:51.534 --> 00:00:52.995 does not stop the disease.

NOTE Confidence: 0.9686017

00:00:53.810 --> 00:00:54.710 It is reactive,

NOTE Confidence: 0.99928504

00:00:55.170 --> 00:00:56.550 and it treats patients

NOTE Confidence: 0.9986016

00:00:57.010 --> 00:00:58.290 as if they were all

NOTE Confidence: 0.9986016

00:00:58.290 --> 00:00:58.870 the same.

NOTE Confidence: 0.9747322

00:01:00.530 --> 00:01:02.450 So we want to change

NOTE Confidence: 0.9747322

00:01:02.450 --> 00:01:03.270 this paradigm.

NOTE Confidence: 0.98705465

00:01:03.890 --> 00:01:05.430 And and the big question

NOTE Confidence: 0.98705465

00:01:05.650 --> 00:01:07.250 that we're trying to tackle

NOTE Confidence: 0.98705465

00:01:07.250 --> 00:01:08.550 is, can we develop

NOTE Confidence: 0.9836012

00:01:09.090 --> 00:01:10.365 a predictive,

NOTE Confidence: 0.9801163

00:01:11.545 --> 00:01:12.045 precise,

NOTE Confidence: 0.99730265

00:01:12.905 --> 00:01:13.725 and preventive

NOTE Confidence: 0.96687794

00:01:14.185 --> 00:01:16.125 medicine for Parkinson's disease?

NOTE Confidence: 0.9985766

00:01:16.825 --> 00:01:18.505 And to to make this

NOTE Confidence: 0.9985766

00:01:18.505 --> 00:01:19.005 possible,

NOTE Confidence: 0.98572

00:01:19.545 --> 00:01:20.584 we are we have set

NOTE Confidence: 0.98572

00:01:20.584 --> 00:01:22.345 ourselves a very ambitious goal,

NOTE Confidence: 0.98572

00:01:22.345 --> 00:01:23.545 and that is to make,

NOTE Confidence: 0.98572

00:01:23.785 --> 00:01:26.110 digital twins of Parkinson's brain

NOTE Confidence: 0.98572

00:01:26.110 --> 00:01:27.729 cells and and Parkinson's,

NOTE Confidence: 0.9794282

00:01:29.549 --> 00:01:30.049 patients.

NOTE Confidence: 0.97649306

00:01:30.430 --> 00:01:31.310 And so how are we

NOTE Confidence: 0.97649306

00:01:31.310 --> 00:01:32.290 going about this?

NOTE Confidence: 0.8378207

00:01:35.869 --> 00:01:37.005 And under the hood

NOTE Confidence: 0.95557374

00:01:37.564 --> 00:01:39.185 are, ten multimodal,

NOTE Confidence: 0.8350957

00:01:39.564 --> 00:01:40.064 multiomics,

NOTE Confidence: 0.9626843

00:01:41.244 --> 00:01:41.744 technologies.

NOTE Confidence: 0.98209286

00:01:42.844 --> 00:01:44.524 We're doing short and and

NOTE Confidence: 0.98209286

00:01:44.524 --> 00:01:45.645 long single,

NOTE Confidence: 0.97503424

00:01:46.125 --> 00:01:48.064 read sequencing of single cells.

NOTE Confidence: 0.97503424

00:01:48.284 --> 00:01:49.905 We've done about a million.

NOTE Confidence: 0.96183544

00:01:50.210 --> 00:01:52.130 We're we're going moving towards

NOTE Confidence: 0.96183544

00:01:52.130 --> 00:01:52.869 ten million.

NOTE Confidence: 0.9740092

00:01:53.329 --> 00:01:54.789 We do spatial transcriptomics,

NOTE Confidence: 0.95487565

00:01:56.289 --> 00:01:57.649 on the spot level and

NOTE Confidence: 0.95487565

00:01:57.649 --> 00:01:59.350 on the cellular and subcellular

NOTE Confidence: 0.95487565

00:01:59.570 --> 00:02:01.189 level, with the xenon,

NOTE Confidence: 0.96637976

00:02:02.049 --> 00:02:04.005 looking at ATAC seq for

NOTE Confidence: 0.96637976

00:02:04.005 --> 00:02:06.085 open chromatin and whole genome

NOTE Confidence: 0.96637976

00:02:06.085 --> 00:02:06.585 sequences.

NOTE Confidence: 0.9639659

00:02:07.685 --> 00:02:09.125 And we're integrating all of

NOTE Confidence: 0.9639659

00:02:09.125 --> 00:02:10.105 that. And

NOTE Confidence: 0.9689323

00:02:10.805 --> 00:02:12.585 so what are the components

NOTE Confidence: 0.9852073

00:02:12.965 --> 00:02:13.625 to develop,

NOTE Confidence: 0.9890885

00:02:14.085 --> 00:02:15.845 digital twins of of brain

NOTE Confidence: 0.9890885

00:02:15.845 --> 00:02:17.044 cells? Well, number one, we

NOTE Confidence: 0.9890885

00:02:17.044 --> 00:02:17.764 need to know all the

NOTE Confidence: 0.9890885

00:02:17.764 --> 00:02:19.710 brain cells. So far, we

NOTE Confidence: 0.9890885

00:02:19.710 --> 00:02:20.530 have cataloged

NOTE Confidence: 0.9961831

00:02:20.830 --> 00:02:21.330 ninety

NOTE Confidence: 0.9542935

00:02:21.790 --> 00:02:22.110 two,

NOTE Confidence: 0.9991541

00:02:22.830 --> 00:02:23.730 cell types

NOTE Confidence: 0.9629688

00:02:24.030 --> 00:02:25.470 based on the sequencing of

NOTE Confidence: 0.9629688

00:02:25.470 --> 00:02:26.850 a million brain cells.

NOTE Confidence: 0.9542314

00:02:32.035 --> 00:02:33.715 And and we have started

NOTE Confidence: 0.9542314

00:02:33.715 --> 00:02:34.035 to map,

NOTE Confidence: 0.9089155

00:02:35.475 --> 00:02:36.775 the the

NOTE Confidence: 0.93634856

00:02:37.075 --> 00:02:38.835 the brain space, the layers,

NOTE Confidence: 0.93634856

00:02:38.835 --> 00:02:40.535 and and the spatial niches,

NOTE Confidence: 0.93733585

00:02:41.315 --> 00:02:42.915 to which the cell types,

NOTE Confidence: 0.93733585

00:02:43.235 --> 00:02:44.215 can be localized.

NOTE Confidence: 0.8107358

00:02:44.915 --> 00:02:45.235 And,

NOTE Confidence: 0.9013198

00:02:46.330 --> 00:02:48.490 doctor Junjun Dong will delve

NOTE Confidence: 0.9013198

00:02:48.490 --> 00:02:49.230 into this,

NOTE Confidence: 0.95288926

00:02:50.090 --> 00:02:51.450 in much more detail in

NOTE Confidence: 0.95288926

00:02:51.450 --> 00:02:52.250 in in a in a

NOTE Confidence: 0.95288926

00:02:52.250 --> 00:02:52.750 second.

NOTE Confidence: 0.9924328

00:02:53.290 --> 00:02:55.130 But here here is sort

NOTE Confidence: 0.9924328

00:02:55.130 --> 00:02:56.569 of an initial version of

NOTE Confidence: 0.9924328

00:02:56.569 --> 00:02:58.665 the integration of cells and

NOTE Confidence: 0.9924328

00:02:58.665 --> 00:02:59.165 space,

NOTE Confidence: 0.9755908

00:02:59.785 --> 00:03:01.965 done by Jacob Parker, who

NOTE Confidence: 0.9259412

00:03:02.264 --> 00:03:03.224 is somewhere here.

NOTE Confidence: 0.6158551

00:03:03.544 --> 00:03:04.285 They are,

NOTE Confidence: 0.99967134

00:03:05.305 --> 00:03:05.805 showing

NOTE Confidence: 0.9417204

00:03:06.185 --> 00:03:07.325 how these different

NOTE Confidence: 0.99969935

00:03:08.185 --> 00:03:09.005 cell types

NOTE Confidence: 0.9709679

00:03:09.465 --> 00:03:09.965 localize

NOTE Confidence: 0.9895477

00:03:10.720 --> 00:03:12.560 to specific layers in the

NOTE Confidence: 0.9895477

00:03:12.560 --> 00:03:14.580 temporal cortex or to specific

NOTE Confidence: 0.9895477

00:03:14.720 --> 00:03:15.220 niches,

NOTE Confidence: 0.9837132

00:03:16.080 --> 00:03:17.440 in in in the human

NOTE Confidence: 0.9837132

00:03:17.440 --> 00:03:17.940 midbrain.

NOTE Confidence: 0.9691836

00:03:19.760 --> 00:03:20.959 So what can we do

NOTE Confidence: 0.9691836

00:03:20.959 --> 00:03:22.605 with this Atlas? Well,

NOTE Confidence: 0.9829967

00:03:23.245 --> 00:03:24.685 number one, we can,

NOTE Confidence: 0.85142386

00:03:25.245 --> 00:03:26.864 lay out all this multi,

NOTE Confidence: 0.75400066

00:03:28.364 --> 00:03:28.864 omic

NOTE Confidence: 0.9224175

00:03:29.325 --> 00:03:31.885 datasets and integrate them, and

NOTE Confidence: 0.9224175

00:03:31.885 --> 00:03:32.525 we can,

NOTE Confidence: 0.965478

00:03:33.084 --> 00:03:35.265 see how disease progresses,

NOTE Confidence: 0.96727616

00:03:36.129 --> 00:03:37.430 in this dynamic,

NOTE Confidence: 0.9979405

00:03:38.129 --> 00:03:39.430 view of transcriptional

NOTE Confidence: 0.9338324

00:03:39.810 --> 00:03:40.310 changes.

NOTE Confidence: 0.98976624

00:03:41.489 --> 00:03:41.970 And,

NOTE Confidence: 0.9112124

00:03:42.370 --> 00:03:43.810 again, the next talk will

NOTE Confidence: 0.9112124

00:03:43.810 --> 00:03:44.870 look at the dynamic

NOTE Confidence: 0.99804586

00:03:45.250 --> 00:03:47.430 evolution of the disease across

NOTE Confidence: 0.99804586

00:03:47.569 --> 00:03:49.110 space and time.

NOTE Confidence: 0.9992113

00:03:49.855 --> 00:03:51.395 We can also link this

NOTE Confidence: 0.9992113

00:03:51.535 --> 00:03:52.275 to pathology

NOTE Confidence: 0.9968339

00:03:53.535 --> 00:03:55.075 and to clinical phenotypes

NOTE Confidence: 0.97911114

00:03:55.535 --> 00:03:57.375 with the ultimate goal to

NOTE Confidence: 0.97911114

00:03:57.375 --> 00:03:57.875 use

NOTE Confidence: 0.81064

00:03:58.335 --> 00:03:58.835 this,

NOTE Confidence: 0.92358494

00:03:59.855 --> 00:04:00.355 molecular

NOTE Confidence: 0.9985324

00:04:00.655 --> 00:04:01.155 signatures

NOTE Confidence: 0.93412423

00:04:01.695 --> 00:04:03.315 to predict and prevent,

NOTE Confidence: 0.94944847

00:04:04.400 --> 00:04:06.400 disease in in patients and

NOTE Confidence: 0.94944847

00:04:06.400 --> 00:04:07.700 prevent this progression.

NOTE Confidence: 0.9906093

00:04:08.560 --> 00:04:10.580 So but one of the

NOTE Confidence: 0.9981804

00:04:11.280 --> 00:04:13.140 very cool applications

NOTE Confidence: 0.9819177

00:04:14.080 --> 00:04:15.860 of this prototype

NOTE Confidence: 0.9611335

00:04:16.160 --> 00:04:18.020 digital twins is

NOTE Confidence: 0.99589777

00:04:18.400 --> 00:04:19.300 that it

NOTE Confidence: 0.97993547

00:04:19.815 --> 00:04:20.315 allows

NOTE Confidence: 0.9944011

00:04:20.775 --> 00:04:23.195 to infer genome function,

NOTE Confidence: 0.943906

00:04:24.455 --> 00:04:26.154 in particular brain cells.

NOTE Confidence: 0.9790042

00:04:27.015 --> 00:04:29.255 And and and so this

NOTE Confidence: 0.9790042

00:04:29.255 --> 00:04:29.755 allows

NOTE Confidence: 0.8782221

00:04:30.135 --> 00:04:30.635 to

NOTE Confidence: 0.942743

00:04:31.175 --> 00:04:32.795 look at the genome sequence,

NOTE Confidence: 0.942743

00:04:33.095 --> 00:04:34.635 input the genome sequence,

NOTE Confidence: 0.8987461

00:04:35.029 --> 00:04:36.570 and have as a readout

NOTE Confidence: 0.8987461

00:04:36.790 --> 00:04:37.450 a prediction

NOTE Confidence: 0.99958265

00:04:38.150 --> 00:04:40.650 of RNA changes in specific

NOTE Confidence: 0.99252677

00:04:41.110 --> 00:04:41.930 brain cells.

NOTE Confidence: 0.89766574

00:04:42.950 --> 00:04:43.430 And,

NOTE Confidence: 0.9983224

00:04:45.029 --> 00:04:45.910 to do this, what are

NOTE Confidence: 0.9983224

00:04:45.910 --> 00:04:47.510 the components that we need?

NOTE Confidence: 0.9983224

00:04:47.510 --> 00:04:49.029 Well, we need to we

NOTE Confidence: 0.9983224

00:04:49.029 --> 00:04:49.850 need to

NOTE Confidence: 0.9656334

00:04:50.845 --> 00:04:51.345 have,

NOTE Confidence: 0.9703225

00:04:52.125 --> 00:04:53.505 all the DNA variants.

NOTE Confidence: 0.9987904

00:04:54.525 --> 00:04:55.964 We want we need to

NOTE Confidence: 0.9987904

00:04:55.964 --> 00:04:57.505 wire them to the RNA

NOTE Confidence: 0.9987904

00:04:57.565 --> 00:04:58.065 changes

NOTE Confidence: 0.91507465

00:04:59.805 --> 00:05:01.425 in specific brain cells,

NOTE Confidence: 0.97518706

00:05:03.089 --> 00:05:04.230 combine convergent,

NOTE Confidence: 0.9500965

00:05:05.170 --> 00:05:07.730 pathways to identify processes, and

NOTE Confidence: 0.9500965

00:05:07.730 --> 00:05:08.870 thereby, delineate

NOTE Confidence: 0.92656237

00:05:09.330 --> 00:05:11.890 the gene regulatory networks from

NOTE Confidence: 0.92656237

00:05:11.890 --> 00:05:12.950 DNA variants

NOTE Confidence: 0.96614796

00:05:13.490 --> 00:05:15.190 to, cellular processes.

NOTE Confidence: 0.9906643

00:05:16.375 --> 00:05:17.915 And if we are successful

NOTE Confidence: 0.9906643

00:05:18.055 --> 00:05:19.835 with this, it will give

NOTE Confidence: 0.9974948

00:05:20.214 --> 00:05:20.794 us targets

NOTE Confidence: 0.9637033

00:05:21.654 --> 00:05:22.135 to,

NOTE Confidence: 0.804815

00:05:23.014 --> 00:05:24.395 prevent that patient's

NOTE Confidence: 0.9934526

00:05:25.255 --> 00:05:26.235 disease progresses,

NOTE Confidence: 0.99438065

00:05:28.294 --> 00:05:29.435 to slow movements,

NOTE Confidence: 0.9556078

00:05:30.089 --> 00:05:31.710 motor Parkinson's, and cognitive

NOTE Confidence: 0.9546657

00:05:32.010 --> 00:05:33.310 decline, and instead

NOTE Confidence: 0.8716204

00:05:34.170 --> 00:05:35.070 turn patients,

NOTE Confidence: 0.8886967

00:05:36.650 --> 00:05:38.029 into slow progressors

NOTE Confidence: 0.9939653

00:05:38.330 --> 00:05:39.310 that are able

NOTE Confidence: 0.979638

00:05:39.610 --> 00:05:41.770 to enjoy an awesome quality

NOTE Confidence: 0.979638

00:05:41.770 --> 00:05:43.390 of life and play golf,

NOTE Confidence: 0.9729293

00:05:43.854 --> 00:05:46.175 for fifteen years and, enjoy

NOTE Confidence: 0.9729293

00:05:46.175 --> 00:05:47.555 time with the grandchildren.

NOTE Confidence: 0.9989875

00:05:48.574 --> 00:05:49.074 So

NOTE Confidence: 0.9622766

00:05:49.935 --> 00:05:51.375 what do we know about

NOTE Confidence: 0.9622766

00:05:51.375 --> 00:05:52.354 the noncode

NOTE Confidence: 0.9329948

00:05:52.654 --> 00:05:54.814 about the, DNA variants? What

NOTE Confidence: 0.9329948

00:05:54.814 --> 00:05:56.414 can we input in into

NOTE Confidence: 0.9329948

00:05:56.414 --> 00:05:57.235 our prototype?

NOTE Confidence: 0.8208291

00:06:00.130 --> 00:06:01.190 They're in principle

NOTE Confidence: 0.7284587

00:06:01.650 --> 00:06:02.150 two

NOTE Confidence: 0.97040206

00:06:02.690 --> 00:06:04.130 two types of,

NOTE Confidence: 0.8623307

00:06:05.650 --> 00:06:07.510 two two ways the genome

NOTE Confidence: 0.8623307

00:06:07.810 --> 00:06:10.150 of functions functions. One is

NOTE Confidence: 0.8623307

00:06:10.290 --> 00:06:11.270 sequence modulation,

NOTE Confidence: 0.99823594

00:06:13.089 --> 00:06:13.589 where

NOTE Confidence: 0.9992422

00:06:14.395 --> 00:06:14.895 mutations

NOTE Confidence: 0.9841586

00:06:15.675 --> 00:06:17.695 change the protein coding sequence.

NOTE Confidence: 0.9841586

00:06:17.915 --> 00:06:19.375 And that's the case in

NOTE Confidence: 0.9841586

00:06:19.675 --> 00:06:20.175 Mendelian

NOTE Confidence: 0.9663924

00:06:20.475 --> 00:06:22.475 forms of the disease that

NOTE Confidence: 0.9663924

00:06:22.475 --> 00:06:24.315 comprise about three percent of

NOTE Confidence: 0.9663924

00:06:24.315 --> 00:06:25.695 all Parkinson's patients.

NOTE Confidence: 0.98859954

00:06:26.074 --> 00:06:26.315 And,

NOTE Confidence: 0.7071365

00:06:26.875 --> 00:06:27.695 Shri Ganachandra

NOTE Confidence: 0.94810146

00:06:28.430 --> 00:06:30.029 and Pietro de Camille will

NOTE Confidence: 0.94810146

00:06:30.029 --> 00:06:31.710 take a deep dive on

NOTE Confidence: 0.94810146

00:06:31.710 --> 00:06:32.690 some of these,

NOTE Confidence: 0.952004

00:06:33.150 --> 00:06:33.650 familial

NOTE Confidence: 0.9991671

00:06:34.110 --> 00:06:34.610 genes.

NOTE Confidence: 0.99946463

00:06:35.710 --> 00:06:36.210 However,

NOTE Confidence: 0.99802804

00:06:37.310 --> 00:06:38.850 most Parkinson's patients

NOTE Confidence: 0.98987895

00:06:39.630 --> 00:06:41.630 don't have a mutation that

NOTE Confidence: 0.98987895

00:06:41.630 --> 00:06:43.010 changes protein sequence.

NOTE Confidence: 0.9914043

00:06:43.365 --> 00:06:43.865 Instead,

NOTE Confidence: 0.99370193

00:06:44.165 --> 00:06:46.085 there are seven thousand fifty

NOTE Confidence: 0.99370193

00:06:46.085 --> 00:06:46.585 seven

NOTE Confidence: 0.8588473

00:06:46.885 --> 00:06:48.665 non coding DNA variants,

NOTE Confidence: 0.993061

00:06:49.365 --> 00:06:51.305 linked to Parkinson's disease.

NOTE Confidence: 0.99615294

00:06:52.805 --> 00:06:54.005 They account for up to

NOTE Confidence: 0.99615294

00:06:54.005 --> 00:06:55.445 thirty six percent of the

NOTE Confidence: 0.99615294

00:06:55.445 --> 00:06:56.505 genetic heritability

NOTE Confidence: 0.88836336

00:06:57.205 --> 00:06:57.945 of the disease.

NOTE Confidence: 0.99767923

00:06:58.819 --> 00:06:59.960 But the key question

NOTE Confidence: 0.90549386

00:07:00.500 --> 00:07:01.800 is, how do these function?

NOTE Confidence: 0.99494743

00:07:03.060 --> 00:07:04.680 And, what we have previously

NOTE Confidence: 0.99494743

00:07:04.819 --> 00:07:05.319 seen

NOTE Confidence: 0.9116438

00:07:05.860 --> 00:07:07.460 is that these non coding

NOTE Confidence: 0.9116438

00:07:07.460 --> 00:07:09.780 variants are highly enriched in,

NOTE Confidence: 0.9116438

00:07:10.259 --> 00:07:11.080 cis regulatory

NOTE Confidence: 0.9238937

00:07:11.380 --> 00:07:11.880 regions,

NOTE Confidence: 0.78574264

00:07:12.340 --> 00:07:13.720 of the genome and enhances

NOTE Confidence: 0.9073528

00:07:14.315 --> 00:07:15.835 and promoters. And so we

NOTE Confidence: 0.9073528

00:07:15.835 --> 00:07:16.975 therefore hypothesize

NOTE Confidence: 0.99444336

00:07:17.995 --> 00:07:18.495 that

NOTE Confidence: 0.8182818

00:07:19.115 --> 00:07:20.095 really the key,

NOTE Confidence: 0.99793386

00:07:21.755 --> 00:07:22.255 function

NOTE Confidence: 0.9833769

00:07:22.715 --> 00:07:24.815 genome function perturbed in Parkinson's

NOTE Confidence: 0.9833769

00:07:24.955 --> 00:07:25.455 disease

NOTE Confidence: 0.97966194

00:07:25.755 --> 00:07:27.135 might be modulation

NOTE Confidence: 0.9985623

00:07:27.675 --> 00:07:29.135 of RNA quantity

NOTE Confidence: 0.8836714

00:07:29.789 --> 00:07:31.169 based on cis regulatory,

NOTE Confidence: 0.92953265

00:07:31.949 --> 00:07:33.970 effects of this noncoding variant.

NOTE Confidence: 0.98278606

00:07:34.830 --> 00:07:36.110 How how can we treat

NOTE Confidence: 0.98278606

00:07:36.110 --> 00:07:38.210 this with precision drugs? Obviously,

NOTE Confidence: 0.98278606

00:07:38.349 --> 00:07:39.629 a lot more to do,

NOTE Confidence: 0.98278606

00:07:39.629 --> 00:07:40.830 but we do have some

NOTE Confidence: 0.98278606

00:07:40.830 --> 00:07:41.330 exciting,

NOTE Confidence: 0.9720496

00:07:41.870 --> 00:07:42.930 initial results.

NOTE Confidence: 0.95850426

00:07:43.445 --> 00:07:44.805 And most of all, we

NOTE Confidence: 0.95850426

00:07:44.805 --> 00:07:45.925 have what I think is

NOTE Confidence: 0.95850426

00:07:45.925 --> 00:07:47.545 really a cool way

NOTE Confidence: 0.97005695

00:07:47.925 --> 00:07:49.925 to try our best to,

NOTE Confidence: 0.97005695

00:07:50.165 --> 00:07:51.945 bring new drugs to patients

NOTE Confidence: 0.97005695

00:07:52.005 --> 00:07:53.225 as fast as possible,

NOTE Confidence: 0.9489603

00:07:53.605 --> 00:07:54.325 and that is,

NOTE Confidence: 0.93891793

00:07:55.205 --> 00:07:57.465 machine learning, big data powered,

NOTE Confidence: 0.94216347

00:07:57.970 --> 00:08:00.130 drug repurposing to teach new

NOTE Confidence: 0.94216347

00:08:00.130 --> 00:08:01.590 tricks to old drugs.

NOTE Confidence: 0.96217537

00:08:01.970 --> 00:08:03.190 This work is,

NOTE Confidence: 0.96520627

00:08:03.810 --> 00:08:05.490 performed in collaboration with the

NOTE Confidence: 0.96520627

00:08:05.490 --> 00:08:06.710 University of Burdon.

NOTE Confidence: 0.88931155

00:08:07.250 --> 00:08:09.010 The TronTrees has been a

NOTE Confidence: 0.88931155

00:08:09.010 --> 00:08:10.610 partner with us, first at

NOTE Confidence: 0.88931155

00:08:10.610 --> 00:08:12.375 Harvard and now here at

NOTE Confidence: 0.88931155

00:08:12.375 --> 00:08:13.895 the Stephen and Denise Adams

NOTE Confidence: 0.88931155

00:08:13.895 --> 00:08:14.395 Center.

NOTE Confidence: 0.9767645

00:08:14.775 --> 00:08:16.075 The way this works is,

NOTE Confidence: 0.9687419

00:08:17.895 --> 00:08:19.975 in Norway, we have,

NOTE Confidence: 0.9480904

00:08:20.775 --> 00:08:23.355 access on well curated databases

NOTE Confidence: 0.9533901

00:08:23.895 --> 00:08:25.350 for four point five million

NOTE Confidence: 0.9533901

00:08:25.350 --> 00:08:27.509 Norwegians over fifteen years with

NOTE Confidence: 0.9533901

00:08:27.509 --> 00:08:28.810 fifteen years of follow-up.

NOTE Confidence: 0.9783257

00:08:30.310 --> 00:08:32.230 There's, about seven hundred fifty

NOTE Confidence: 0.9783257

00:08:32.230 --> 00:08:33.290 million prescriptions

NOTE Confidence: 0.97539085

00:08:33.670 --> 00:08:35.589 given to these patients, and

NOTE Confidence: 0.97539085

00:08:35.589 --> 00:08:36.890 so we can now

NOTE Confidence: 0.99847347

00:08:38.405 --> 00:08:38.905 algorithmically

NOTE Confidence: 0.9927163

00:08:39.845 --> 00:08:41.145 test for associations

NOTE Confidence: 0.99638987

00:08:41.605 --> 00:08:43.365 between any drug approved in

NOTE Confidence: 0.99638987

00:08:43.365 --> 00:08:43.865 Norway

NOTE Confidence: 0.92613447

00:08:44.325 --> 00:08:44.985 and the

NOTE Confidence: 0.98529685

00:08:45.365 --> 00:08:47.385 future risk of healthy Norwegians

NOTE Confidence: 0.98529685

00:08:47.684 --> 00:08:49.845 of developing Parkinson's disease. And

NOTE Confidence: 0.98529685

00:08:49.845 --> 00:08:50.885 so you do this over

NOTE Confidence: 0.98529685

00:08:50.885 --> 00:08:52.345 and over for each drug,

NOTE Confidence: 0.97647136

00:08:52.780 --> 00:08:55.260 to identify drugs linked to

NOTE Confidence: 0.97647136

00:08:55.260 --> 00:08:56.480 reduce risk.

NOTE Confidence: 0.90591705

00:08:57.100 --> 00:08:58.720 Then we're taking these drugs

NOTE Confidence: 0.90591705

00:08:58.860 --> 00:09:01.260 into into clinical trials in

NOTE Confidence: 0.90591705

00:09:01.260 --> 00:09:02.720 a dish animal models

NOTE Confidence: 0.9727237

00:09:03.260 --> 00:09:05.179 and to medicinal chemistry. And

NOTE Confidence: 0.9727237

00:09:05.179 --> 00:09:05.679 one

NOTE Confidence: 0.9261749

00:09:06.165 --> 00:09:06.665 one,

NOTE Confidence: 0.99964553

00:09:07.125 --> 00:09:08.345 class of drugs

NOTE Confidence: 0.9972093

00:09:08.725 --> 00:09:10.084 that was very strong

NOTE Confidence: 0.9018985

00:09:10.644 --> 00:09:12.985 strongly associated with reduced risk

NOTE Confidence: 0.9683267

00:09:13.365 --> 00:09:13.845 are,

NOTE Confidence: 0.9764599

00:09:14.325 --> 00:09:15.705 asthma drugs, surprisingly.

NOTE Confidence: 0.97474897

00:09:16.165 --> 00:09:17.625 Those are beta two,

NOTE Confidence: 0.9808907

00:09:18.485 --> 00:09:18.985 adrenoreceptor

NOTE Confidence: 0.9158632

00:09:19.605 --> 00:09:20.105 agonists.

NOTE Confidence: 0.90832424

00:09:20.644 --> 00:09:22.300 And we have since shown

NOTE Confidence: 0.90832424

00:09:22.300 --> 00:09:22.959 that, actually,

NOTE Confidence: 0.9898079

00:09:23.260 --> 00:09:24.860 the longer acting they are,

NOTE Confidence: 0.9898079

00:09:24.860 --> 00:09:26.620 the more lipophilic and brain

NOTE Confidence: 0.9898079

00:09:26.620 --> 00:09:28.220 penetrant they are, the stronger

NOTE Confidence: 0.9898079

00:09:28.220 --> 00:09:29.820 the effect is. This has

NOTE Confidence: 0.9898079

00:09:29.820 --> 00:09:31.980 now been, replicated in more

NOTE Confidence: 0.9898079

00:09:31.980 --> 00:09:33.040 than eight countries

NOTE Confidence: 0.7827774

00:09:33.420 --> 00:09:34.059 and in,

NOTE Confidence: 0.99886936

00:09:35.019 --> 00:09:35.519 ten

NOTE Confidence: 0.991586

00:09:36.275 --> 00:09:38.434 toxic and genetic models of

NOTE Confidence: 0.991586

00:09:38.434 --> 00:09:39.955 Parkinson's disease. So there is

NOTE Confidence: 0.991586

00:09:39.955 --> 00:09:40.695 an association

NOTE Confidence: 0.9477188

00:09:41.395 --> 00:09:43.235 between these asthma drugs and

NOTE Confidence: 0.9477188

00:09:43.235 --> 00:09:45.735 reduced risk of Parkinson's disease.

NOTE Confidence: 0.9477188

00:09:46.035 --> 00:09:46.855 And excitingly,

NOTE Confidence: 0.8697876

00:09:47.395 --> 00:09:49.635 what Monica Sharmer in,

NOTE Confidence: 0.8726409

00:09:50.420 --> 00:09:52.040 the Adam Center and instructor

NOTE Confidence: 0.8726409

00:09:52.100 --> 00:09:53.300 in the Adam Center has

NOTE Confidence: 0.8726409

00:09:53.300 --> 00:09:54.120 found is

NOTE Confidence: 0.966682

00:09:54.500 --> 00:09:55.640 that if you use,

NOTE Confidence: 0.98039526

00:09:56.500 --> 00:09:58.500 stem cells of Parkinson's patients

NOTE Confidence: 0.98039526

00:09:58.500 --> 00:09:59.940 as as avatars in a

NOTE Confidence: 0.98039526

00:09:59.940 --> 00:10:01.460 test tube and look at

NOTE Confidence: 0.98039526

00:10:01.460 --> 00:10:02.280 the mitochondrial

NOTE Confidence: 0.78399765

00:10:02.660 --> 00:10:03.160 networks.

NOTE Confidence: 0.9375482

00:10:03.545 --> 00:10:04.605 So this is a healthy

NOTE Confidence: 0.9375482

00:10:04.665 --> 00:10:06.905 nit mitochondrial network with this

NOTE Confidence: 0.9375482

00:10:06.905 --> 00:10:08.684 nice tubular structure.

NOTE Confidence: 0.97086555

00:10:09.385 --> 00:10:11.165 In patients carrying the synuclein

NOTE Confidence: 0.97086555

00:10:11.305 --> 00:10:11.805 triplications,

NOTE Confidence: 0.96775967

00:10:12.505 --> 00:10:14.605 the mitochondrial network is busted

NOTE Confidence: 0.96775967

00:10:14.905 --> 00:10:15.785 into this,

NOTE Confidence: 0.9988659

00:10:16.985 --> 00:10:17.485 disjointed

NOTE Confidence: 0.9603322

00:10:21.429 --> 00:10:24.329 spherical forms. But treatment with

NOTE Confidence: 0.9545195

00:10:24.790 --> 00:10:25.850 beta two agonists

NOTE Confidence: 0.98561925

00:10:26.390 --> 00:10:29.130 partially restores the mitochondrial network.

NOTE Confidence: 0.98561925

00:10:29.429 --> 00:10:30.630 And in, you know, an

NOTE Confidence: 0.98561925

00:10:30.630 --> 00:10:32.250 immense body of work,

NOTE Confidence: 0.89911485

00:10:34.035 --> 00:10:36.195 Monica has shown that the

NOTE Confidence: 0.89911485

00:10:36.195 --> 00:10:37.175 beta two agonist

NOTE Confidence: 0.9837711

00:10:37.554 --> 00:10:38.054 actually

NOTE Confidence: 0.5663272

00:10:38.434 --> 00:10:38.934 affect,

NOTE Confidence: 0.9048933

00:10:39.554 --> 00:10:40.054 modulate

NOTE Confidence: 0.7819332

00:10:40.595 --> 00:10:41.654 mitochondrial respiration,

NOTE Confidence: 0.9648015

00:10:42.195 --> 00:10:42.695 remodel

NOTE Confidence: 0.98838115

00:10:43.075 --> 00:10:43.575 mitochondria

NOTE Confidence: 0.9708603

00:10:44.115 --> 00:10:45.654 to exactly counter,

NOTE Confidence: 0.9941883

00:10:46.595 --> 00:10:47.255 the effects

NOTE Confidence: 0.86076206

00:10:48.050 --> 00:10:49.990 conferred by uncoupled uncoupled,

NOTE Confidence: 0.9046357

00:10:50.370 --> 00:10:51.649 such as PM twenty d

NOTE Confidence: 0.9046357

00:10:51.649 --> 00:10:53.809 one. So so we think

NOTE Confidence: 0.9046357

00:10:53.809 --> 00:10:55.970 that these drugs actually meant

NOTE Confidence: 0.9046357

00:10:55.970 --> 00:10:56.790 to be excellent

NOTE Confidence: 0.7866179

00:10:57.570 --> 00:10:58.870 candidates for,

NOTE Confidence: 0.9928222

00:10:59.985 --> 00:11:01.445 as precision therapeutics

NOTE Confidence: 0.92644995

00:11:02.065 --> 00:11:03.985 for patients with the PM

NOTE Confidence: 0.92644995

00:11:03.985 --> 00:11:04.804 twenty one,

NOTE Confidence: 0.8969584

00:11:05.985 --> 00:11:07.825 risk variant. Here is the

NOTE Confidence: 0.8969584

00:11:07.825 --> 00:11:09.045 sea, seahorse,

NOTE Confidence: 0.8610678

00:11:10.065 --> 00:11:10.565 respirometry

NOTE Confidence: 0.8093271

00:11:10.945 --> 00:11:12.165 data where,

NOTE Confidence: 0.9959391

00:11:13.000 --> 00:11:15.340 respiration is reduced in Parkinson's

NOTE Confidence: 0.71962273

00:11:16.520 --> 00:11:17.020 neurons,

NOTE Confidence: 0.7628923

00:11:17.559 --> 00:11:19.260 be the two agonists, partially

NOTE Confidence: 0.7628923

00:11:19.400 --> 00:11:20.600 restore it here to help

NOTE Confidence: 0.7628923

00:11:20.600 --> 00:11:21.580 healthy neurons.

NOTE Confidence: 0.9755306

00:11:22.440 --> 00:11:22.920 And,

NOTE Confidence: 0.9965886

00:11:23.559 --> 00:11:24.380 with that,

NOTE Confidence: 0.9246049

00:11:25.025 --> 00:11:26.145 here's what we are ho

NOTE Confidence: 0.9246049

00:11:26.385 --> 00:11:27.505 where we are hoping to

NOTE Confidence: 0.9246049

00:11:27.505 --> 00:11:28.945 be in the future in

NOTE Confidence: 0.9246049

00:11:28.945 --> 00:11:30.705 twenty thirty four. When a

NOTE Confidence: 0.9246049

00:11:30.705 --> 00:11:32.325 patient comes to the clinic,

NOTE Confidence: 0.83666706

00:11:32.865 --> 00:11:34.645 ask the discovery engine, says

NOTE Confidence: 0.97535586

00:11:35.105 --> 00:11:36.465 the patient says, hi, discovery

NOTE Confidence: 0.97535586

00:11:36.465 --> 00:11:37.605 engine. What medication

NOTE Confidence: 0.9992911

00:11:38.385 --> 00:11:39.445 works for me?

NOTE Confidence: 0.9864311

00:11:40.050 --> 00:11:41.650 Patient inputs three drops of

NOTE Confidence: 0.9864311

00:11:41.650 --> 00:11:43.809 blood. The engine scans the

NOTE Confidence: 0.9864311

00:11:43.809 --> 00:11:45.410 genome and sucks in the

NOTE Confidence: 0.9864311

00:11:45.410 --> 00:11:46.230 health data

NOTE Confidence: 0.8658407

00:11:49.490 --> 00:11:50.450 and and spits out the

NOTE Confidence: 0.8658407

00:11:50.450 --> 00:11:53.110 result. Hi. Your bioscan suggests

NOTE Confidence: 0.8658407

00:11:53.250 --> 00:11:54.610 that gene x drives your

NOTE Confidence: 0.8658407

00:11:54.610 --> 00:11:55.510 disease progression.

NOTE Confidence: 0.9969252

00:11:55.944 --> 00:11:57.625 May I recommend the following

NOTE Confidence: 0.9969252

00:11:57.625 --> 00:11:58.125 precision,

NOTE Confidence: 0.97135997

00:11:59.065 --> 00:12:01.464 drug and precision biomarker to

NOTE Confidence: 0.97135997

00:12:01.464 --> 00:12:03.245 correct this? And don't forget

NOTE Confidence: 0.97135997

00:12:03.464 --> 00:12:04.985 to discuss this with your

NOTE Confidence: 0.97135997

00:12:04.985 --> 00:12:06.824 physician. So thank you for

NOTE Confidence: 0.97135997

00:12:06.824 --> 00:12:07.865 listening to me, and thank

NOTE Confidence: 0.97135997

00:12:07.865 --> 00:12:09.464 you, everybody in the lab

NOTE Confidence: 0.97135997

00:12:09.464 --> 00:12:10.665 and the Adam Center for

NOTE Confidence: 0.97135997

00:12:10.665 --> 00:12:12.154 this awesome work and to

NOTE Confidence: 0.97135997

00:12:12.154 --> 00:12:13.294 the ASAP team,

NOTE Confidence: 0.93165433

00:12:14.234 --> 00:12:15.274 who is working with us

NOTE Confidence: 0.93165433

00:12:15.274 --> 00:12:15.934 on that.