WEBVTT

NOTE duration: ”00:17:31.392”

NOTE Confidence: 0.9994935

00:00:00.320 --> 00:00:02.500 It's my pleasure to introduce

NOTE Confidence: 0.9173651

00:00:02.879 --> 00:00:04.559 doctor Sanjun Dong. He's an

NOTE Confidence: 0.9173651

00:00:04.559 --> 00:00:06.259 associate professor in neurology

NOTE Confidence: 0.96212476

00:00:06.960 --> 00:00:07.680 and in,

NOTE Confidence: 0.9563089

00:00:08.480 --> 00:00:08.980 biomedical

NOTE Confidence: 0.9985797

00:00:09.280 --> 00:00:11.059 informatics and data science.

NOTE Confidence: 0.9928361

00:00:11.519 --> 00:00:13.219 He he I was fortunate

NOTE Confidence: 0.9928361

00:00:13.280 --> 00:00:13.940 to recruit

NOTE Confidence: 0.96765953

00:00:14.264 --> 00:00:15.545 him from Harvard where he

NOTE Confidence: 0.96765953

00:00:15.545 --> 00:00:16.364 was directing,

NOTE Confidence: 0.9622466

00:00:16.985 --> 00:00:18.925 the genomics and bioinformatics

NOTE Confidence: 0.75030655

00:00:19.384 --> 00:00:19.884 hub,

NOTE Confidence: 0.99633884

00:00:20.265 --> 00:00:22.744 and, I'm thrilled that you're

NOTE Confidence: 0.99633884

00:00:22.744 --> 00:00:25.244 here. Actually, your lab is

NOTE Confidence: 0.98470277

00:00:25.625 --> 00:00:27.145 now fifteen people already or

NOTE Confidence: 0.98470277

00:00:27.145 --> 00:00:29.305 something. It's really, amazing, and

NOTE Confidence: 0.98470277

00:00:29.305 --> 00:00:30.590 I can't can't wait

NOTE Confidence: 0.994915

00:00:31.210 --> 00:00:32.409 to to hear more about

NOTE Confidence: 0.994915

00:00:32.409 --> 00:00:34.190 your work. Thank you, Clemens.

NOTE Confidence: 0.933192

00:00:34.729 --> 00:00:36.010 So honored to be here.

NOTE Confidence: 0.933192

00:00:36.010 --> 00:00:37.130 Last time I was so

NOTE Confidence: 0.933192

00:00:37.130 --> 00:00:38.570 excited and nervous was when

NOTE Confidence: 0.933192

00:00:38.570 --> 00:00:39.450 I was giving a speech

NOTE Confidence: 0.933192

00:00:39.450 --> 00:00:40.670 on my wedding, actually.

NOTE Confidence: 0.8442879

00:00:41.130 --> 00:00:42.989 But, let's see. So,

NOTE Confidence: 0.9189413

00:00:44.945 --> 00:00:46.005 good afternoon, everybody

NOTE Confidence: 0.9110973

00:00:46.385 --> 00:00:48.065 everybody. And, at first, I'd

NOTE Confidence: 0.9110973

00:00:48.065 --> 00:00:50.465 like to, welcome and, of

NOTE Confidence: 0.9110973

00:00:50.465 --> 00:00:52.225 course, congratulations to Clemens for

NOTE Confidence: 0.9110973

00:00:52.225 --> 00:00:54.085 the Adam Center. Welcome here.

NOTE Confidence: 0.9110973

00:00:54.225 --> 00:00:56.145 Ladies and gentlemen, and, today,

NOTE Confidence: 0.9110973

00:00:56.145 --> 00:00:57.845 I'm going to report you

NOTE Confidence: 0.9110973

00:00:58.100 --> 00:00:59.220 what one of the project

NOTE Confidence: 0.9110973

00:00:59.220 --> 00:01:00.980 that, we are working here

NOTE Confidence: 0.9110973

00:01:00.980 --> 00:01:02.420 with Clemens about the spatial

NOTE Confidence: 0.9110973

00:01:02.420 --> 00:01:03.960 transformers of human brain.

NOTE Confidence: 0.99340296

00:01:06.020 --> 00:01:06.900 As we know,

NOTE Confidence: 0.9213113

00:01:07.220 --> 00:01:09.160 Clemens already give good enough,

NOTE Confidence: 0.9213113

00:01:09.459 --> 00:01:11.300 enough intro introduction about the

NOTE Confidence: 0.9213113

00:01:11.300 --> 00:01:13.065 the disease of progression when

NOTE Confidence: 0.86217993

00:01:13.525 --> 00:01:14.745 the Parkinson progress

NOTE Confidence: 0.5296419

00:01:15.125 --> 00:01:15.944 and basically

NOTE Confidence: 0.8230003

00:01:16.245 --> 00:01:17.925 moving start with, like, a

NOTE Confidence: 0.8230003

00:01:17.925 --> 00:01:19.205 a non motor symptom and

NOTE Confidence: 0.8230003

00:01:19.205 --> 00:01:20.165 then motor symptom and then

NOTE Confidence: 0.8230003

00:01:20.165 --> 00:01:22.265 later dimensional, like, cognitive impairment.

NOTE Confidence: 0.9338873

00:01:22.885 --> 00:01:24.965 But, that's clinically happened. But

NOTE Confidence: 0.9338873

00:01:24.965 --> 00:01:25.465 pathologically,

NOTE Confidence: 0.8184503

00:01:25.765 --> 00:01:26.805 when you look into the

NOTE Confidence: 0.8184503

00:01:26.805 --> 00:01:27.305 brain,

NOTE Confidence: 0.8902854

00:01:27.740 --> 00:01:28.860 the Lewy body, which is

NOTE Confidence: 0.8902854

00:01:28.860 --> 00:01:30.060 a whole marker for,

NOTE Confidence: 0.8604155

00:01:30.460 --> 00:01:32.060 pathologic whole marker of Parkinson's

NOTE Confidence: 0.8604155

00:01:32.060 --> 00:01:33.760 is aggregate of alpha synuclein

NOTE Confidence: 0.8604155

00:01:33.820 --> 00:01:35.740 protein, also spread across the

NOTE Confidence: 0.8604155

00:01:35.740 --> 00:01:37.020 brain from the,

NOTE Confidence: 0.95831406

00:01:37.740 --> 00:01:39.580 olfactory bulb to the stem

NOTE Confidence: 0.95831406

00:01:39.820 --> 00:01:41.900 brain stem to, limbic system

NOTE Confidence: 0.95831406

00:01:41.900 --> 00:01:43.395 and then eventually go to

NOTE Confidence: 0.95831406

00:01:43.395 --> 00:01:44.575 the cortex areas.

NOTE Confidence: 0.97107804

00:01:45.395 --> 00:01:45.895 So,

NOTE Confidence: 0.9471744

00:01:47.675 --> 00:01:49.135 how this has happened,

NOTE Confidence: 0.9374885

00:01:50.075 --> 00:01:51.215 how this happening,

NOTE Confidence: 0.7964069

00:01:51.835 --> 00:01:52.975 this kind of transition,

NOTE Confidence: 0.9454667

00:01:53.755 --> 00:01:55.375 clinically and, pathologically

NOTE Confidence: 0.87886065

00:01:56.369 --> 00:01:57.570 are whether they are driven

NOTE Confidence: 0.87886065

00:01:57.570 --> 00:01:59.009 by any marker or or

NOTE Confidence: 0.87886065

00:01:59.009 --> 00:02:00.149 driver molecularly.

NOTE Confidence: 0.9223436

00:02:00.689 --> 00:02:01.649 So that's a question we

NOTE Confidence: 0.9223436

00:02:01.649 --> 00:02:03.250 want to understand. So few

NOTE Confidence: 0.9223436

00:02:03.250 --> 00:02:04.130 years back when I was

NOTE Confidence: 0.9223436

00:02:04.130 --> 00:02:06.229 working with Clemens, in Harvard,

NOTE Confidence: 0.941743

00:02:06.610 --> 00:02:08.050 we look at this human

NOTE Confidence: 0.941743

00:02:08.050 --> 00:02:09.110 postmortem brain,

NOTE Confidence: 0.9175518

00:02:09.415 --> 00:02:10.615 a one hundred nineteen brain,

NOTE Confidence: 0.9175518

00:02:10.615 --> 00:02:11.975 and we dive into the

NOTE Confidence: 0.9175518

00:02:11.975 --> 00:02:13.615 specific brain regions and use

NOTE Confidence: 0.9175518

00:02:13.615 --> 00:02:15.115 a laser capture microdissection,

NOTE Confidence: 0.88042533

00:02:15.735 --> 00:02:17.514 which is, this this technology

NOTE Confidence: 0.88042533

00:02:17.575 --> 00:02:19.255 become available before the single

NOTE Confidence: 0.88042533

00:02:19.255 --> 00:02:20.955 cell is available there. So

NOTE Confidence: 0.88042533

00:02:21.014 --> 00:02:22.375 we manually do this capture

NOTE Confidence: 0.88042533

00:02:22.375 --> 00:02:24.135 single cell and specific brain

NOTE Confidence: 0.88042533

00:02:24.135 --> 00:02:24.635 region

NOTE Confidence: 0.89101124

00:02:25.110 --> 00:02:27.030 and, target to three brain

NOTE Confidence: 0.89101124

00:02:27.030 --> 00:02:28.470 regions like a middle brain

NOTE Confidence: 0.89101124

00:02:28.470 --> 00:02:29.209 for dopant

NOTE Confidence: 0.85523355

00:02:29.510 --> 00:02:31.510 dopant neuron and the corticoster

NOTE Confidence: 0.85523355

00:02:31.510 --> 00:02:33.290 regions for upper middle neurons.

NOTE Confidence: 0.93306386

00:02:33.750 --> 00:02:35.430 And, then we pull the

NOTE Confidence: 0.93306386

00:02:35.430 --> 00:02:36.549 neuron together, each type of

NOTE Confidence: 0.93306386

00:02:36.549 --> 00:02:37.510 neuron together and do the

NOTE Confidence: 0.93306386

00:02:37.510 --> 00:02:38.950 total RNA and deep RNA

NOTE Confidence: 0.93306386

00:02:38.950 --> 00:02:39.450 sequencing.

NOTE Confidence: 0.9486824

00:02:40.525 --> 00:02:42.044 And there are several interesting

NOTE Confidence: 0.9486824

00:02:42.044 --> 00:02:43.485 messages from the work. One

NOTE Confidence: 0.9486824

00:02:43.485 --> 00:02:44.865 of the main message is,

NOTE Confidence: 0.96025133

00:02:45.245 --> 00:02:46.445 we found many,

NOTE Confidence: 0.972206

00:02:46.925 --> 00:02:47.425 known,

NOTE Confidence: 0.8563504

00:02:48.044 --> 00:02:49.645 polycholine gene and link RNA

NOTE Confidence: 0.8563504

00:02:49.645 --> 00:02:51.005 or non coding RNA expressed

NOTE Confidence: 0.8563504

00:02:51.005 --> 00:02:51.885 in the in the brain,

NOTE Confidence: 0.8563504

00:02:51.885 --> 00:02:53.325 of course. For example, seventeen

NOTE Confidence: 0.8563504

00:02:53.325 --> 00:02:54.990 thousand of polygonal gene and

NOTE Confidence: 0.8563504

00:02:54.990 --> 00:02:56.510 seven thousand known non coding

NOTE Confidence: 0.8563504

00:02:56.510 --> 00:02:57.950 RNA expressed. But we also

NOTE Confidence: 0.8563504

00:02:57.950 --> 00:02:59.410 identified many novel

NOTE Confidence: 0.92628115

00:02:59.870 --> 00:03:01.310 non coding RNA that nobody

NOTE Confidence: 0.92628115

00:03:01.310 --> 00:03:02.830 had found them before also

NOTE Confidence: 0.92628115

00:03:02.830 --> 00:03:04.510 highly expressed in document neuron.

NOTE Confidence: 0.92628115

00:03:04.510 --> 00:03:05.889 For example, we found, like,

NOTE Confidence: 0.92628115

00:03:05.950 --> 00:03:07.470 around twenty six thousand of

NOTE Confidence: 0.92628115

00:03:07.470 --> 00:03:09.775 enhanced RNA and around ten,

NOTE Confidence: 0.92628115

00:03:09.775 --> 00:03:10.595 eleven thousand

NOTE Confidence: 0.9797824

00:03:11.055 --> 00:03:12.655 of circular RNA in the

NOTE Confidence: 0.9797824

00:03:12.655 --> 00:03:13.395 in the brain.

NOTE Confidence: 0.95843947

00:03:13.775 --> 00:03:15.055 So I want to spend

NOTE Confidence: 0.95843947

00:03:15.055 --> 00:03:16.255 a minute here to talk

NOTE Confidence: 0.95843947

00:03:16.255 --> 00:03:17.455 about one of the RNA,

NOTE Confidence: 0.95843947

00:03:17.455 --> 00:03:18.755 which is circular RNA.

NOTE Confidence: 0.95799

00:03:19.294 --> 00:03:20.655 Usually, the DNA can be

NOTE Confidence: 0.95799

00:03:20.655 --> 00:03:22.755 transcribed linearly to linear RNA

NOTE Confidence: 0.84705085

00:03:23.180 --> 00:03:24.460 like this happened. But they

NOTE Confidence: 0.84705085

00:03:24.460 --> 00:03:24.940 also,

NOTE Confidence: 0.95024514

00:03:25.419 --> 00:03:26.240 show that,

NOTE Confidence: 0.87243146

00:03:26.860 --> 00:03:28.620 since, around two thousand fourteen,

NOTE Confidence: 0.87243146

00:03:28.620 --> 00:03:30.300 two found there's the RNA

NOTE Confidence: 0.87243146

00:03:30.300 --> 00:03:30.860 can also,

NOTE Confidence: 0.9054024

00:03:31.260 --> 00:03:33.260 form circular RNA through back

NOTE Confidence: 0.9054024

00:03:33.260 --> 00:03:34.780 splicing as you can see

NOTE Confidence: 0.9054024

00:03:34.780 --> 00:03:36.435 here. And this circular RNA,

NOTE Confidence: 0.9054024

00:03:36.435 --> 00:03:37.715 because their shape is circular,

NOTE Confidence: 0.9054024

00:03:37.715 --> 00:03:38.915 there's no free end. They

NOTE Confidence: 0.9054024

00:03:38.915 --> 00:03:40.035 are more stable. The half

NOTE Confidence: 0.9054024

00:03:40.035 --> 00:03:41.235 life is ten times longer

NOTE Confidence: 0.9054024

00:03:41.235 --> 00:03:42.515 than the linear RNA. So

NOTE Confidence: 0.9054024

00:03:42.515 --> 00:03:44.295 they're perfect candidate for biomarker.

NOTE Confidence: 0.9054024

00:03:44.515 --> 00:03:45.635 And this circular RNA, very

NOTE Confidence: 0.9054024

00:03:45.635 --> 00:03:47.655 interesting to show they're dominant

NOTE Confidence: 0.9054024

00:03:47.795 --> 00:03:49.815 in brain versus the other,

NOTE Confidence: 0.9611535

00:03:50.370 --> 00:03:52.530 tissues. And more interestingly, as

NOTE Confidence: 0.9611535

00:03:52.530 --> 00:03:53.570 you can see in the

NOTE Confidence: 0.9611535

00:03:53.570 --> 00:03:55.190 bottom right corner here,

NOTE Confidence: 0.76627845

00:03:55.490 --> 00:03:57.970 comparing the synapsosome versus neuron

NOTE Confidence: 0.76627845

00:03:57.970 --> 00:03:59.410 soma, this sarcoid RNA is

NOTE Confidence: 0.76627845

00:03:59.410 --> 00:04:00.950 more enriched in the synapses

NOTE Confidence: 0.91815805

00:04:01.970 --> 00:04:03.670 which is, kind of puzzling

NOTE Confidence: 0.91815805

00:04:03.810 --> 00:04:04.310 too.

NOTE Confidence: 0.8818846

00:04:05.325 --> 00:04:06.605 And in our data, we

NOTE Confidence: 0.8818846

00:04:06.605 --> 00:04:08.605 look at this, eleven southern

NOTE Confidence: 0.8818846

00:04:08.605 --> 00:04:09.725 circle RNA. We found many

NOTE Confidence: 0.8818846

00:04:09.725 --> 00:04:11.405 of them actually transcribed from,

NOTE Confidence: 0.8818846

00:04:11.725 --> 00:04:13.485 Parkinson risk gene. For example,

NOTE Confidence: 0.8818846

00:04:13.485 --> 00:04:16.045 snoopling GBA log two and

NOTE Confidence: 0.8818846

00:04:16.045 --> 00:04:17.645 the rims two, rims one,

NOTE Confidence: 0.8818846

00:04:17.805 --> 00:04:19.565 and, VPS thirteen c, for

NOTE Confidence: 0.8818846

00:04:19.565 --> 00:04:20.065 example.

NOTE Confidence: 0.8293469

00:04:20.750 --> 00:04:21.870 And, also, many of them

NOTE Confidence: 0.8293469

00:04:21.870 --> 00:04:23.470 also transcribe from a synaptic

NOTE Confidence: 0.8293469

00:04:23.470 --> 00:04:25.650 genes. Like, out of, eleven

NOTE Confidence: 0.8293469

00:04:25.790 --> 00:04:27.410 hundred synaptic gene,

NOTE Confidence: 0.9420097

00:04:27.950 --> 00:04:29.150 nine hundred of them transcribed

NOTE Confidence: 0.9420097

00:04:29.150 --> 00:04:30.770 in, circular RNA.

NOTE Confidence: 0.9432253

00:04:31.310 --> 00:04:32.750 And many circular RNA actually

NOTE Confidence: 0.9432253

00:04:32.910 --> 00:04:33.710 when we look at this,

NOTE Confidence: 0.9432253

00:04:34.029 --> 00:04:35.955 brain sample between different stage

NOTE Confidence: 0.9432253

00:04:35.955 --> 00:04:38.115 of Parkinson's, like, control versus

NOTE Confidence: 0.9432253

00:04:38.115 --> 00:04:39.714 late stage and early stage,

NOTE Confidence: 0.9432253

00:04:39.714 --> 00:04:41.154 some sarcoRNA even start to

NOTE Confidence: 0.9432253

00:04:41.154 --> 00:04:41.654 show

NOTE Confidence: 0.5316887

00:04:42.115 --> 00:04:42.615 changes

NOTE Confidence: 0.86814684

00:04:42.915 --> 00:04:44.035 even in early stage of

NOTE Confidence: 0.86814684

00:04:44.035 --> 00:04:45.415 prodromal stage of PD.

NOTE Confidence: 0.9830609

00:04:46.115 --> 00:04:47.330 And one of the targets

NOTE Confidence: 0.9830609

00:04:47.490 --> 00:04:49.010 one of the candidates from,

NOTE Confidence: 0.9830609

00:04:49.330 --> 00:04:50.370 this study is,

NOTE Confidence: 0.9075786

00:04:51.570 --> 00:04:53.089 is DNA j c six.

NOTE Confidence: 0.9075786

00:04:53.089 --> 00:04:54.690 We are quite interested in.

NOTE Confidence: 0.9075786

00:04:54.690 --> 00:04:55.650 As you can see here,

NOTE Confidence: 0.9075786

00:04:55.650 --> 00:04:57.190 the DNA j c six,

NOTE Confidence: 0.9075786

00:04:57.410 --> 00:04:59.330 the messenger RNA does not

NOTE Confidence: 0.9075786

00:04:59.330 --> 00:05:00.850 change between PD control, but

NOTE Confidence: 0.9075786

00:05:00.850 --> 00:05:02.130 the circular RNA as the

NOTE Confidence: 0.9075786

00:05:02.130 --> 00:05:02.415 the

NOTE Confidence: 0.8717497

00:05:03.375 --> 00:05:04.595 form, it it changes significantly

NOTE Confidence: 0.8717497

00:05:04.654 --> 00:05:05.695 and drop a lot in

NOTE Confidence: 0.8717497

00:05:05.695 --> 00:05:07.455 PD. And DNA j c

NOTE Confidence: 0.8717497

00:05:07.455 --> 00:05:09.455 six, I mean, there's the

NOTE Confidence: 0.8717497

00:05:09.455 --> 00:05:11.295 following talk talking about this

NOTE Confidence: 0.8717497

00:05:11.295 --> 00:05:12.815 two but, DNA j c

NOTE Confidence: 0.8717497

00:05:12.815 --> 00:05:14.095 six is a known, a

NOTE Confidence: 0.8717497

00:05:14.095 --> 00:05:15.714 protein also known as auxilin.

NOTE Confidence: 0.929433

00:05:16.110 --> 00:05:17.169 It's a very important,

NOTE Confidence: 0.99351496

00:05:17.710 --> 00:05:18.909 player in the,

NOTE Confidence: 0.9531602

00:05:19.389 --> 00:05:21.550 encoding of the cholesterol mediate

NOTE Confidence: 0.9531602

00:05:21.550 --> 00:05:22.050 endocytosis.

NOTE Confidence: 0.9114605

00:05:22.909 --> 00:05:24.669 So this, Vasco in the

NOTE Confidence: 0.9114605

00:05:24.669 --> 00:05:26.370 snatches need to be encoded

NOTE Confidence: 0.9421408

00:05:26.750 --> 00:05:28.270 and then be reused, recycled.

NOTE Confidence: 0.9421408

00:05:28.270 --> 00:05:29.629 If this encoding is not

NOTE Confidence: 0.9421408

00:05:29.629 --> 00:05:30.129 working,

NOTE Confidence: 0.9017973

00:05:30.485 --> 00:05:31.445 then there's a lot of

NOTE Confidence: 0.9017973

00:05:31.445 --> 00:05:33.545 buildup or accumulation of coated

NOTE Confidence: 0.9017973

00:05:33.605 --> 00:05:34.885 vesicle and then then a

NOTE Confidence: 0.9017973

00:05:34.885 --> 00:05:36.645 neurotransmitter like dopamine cannot be

NOTE Confidence: 0.9017973

00:05:36.645 --> 00:05:38.325 released timely. So that's a

NOTE Confidence: 0.9017973

00:05:38.325 --> 00:05:39.845 very important player there. Of

NOTE Confidence: 0.9017973

00:05:39.845 --> 00:05:41.285 course, the protein itself. But

NOTE Confidence: 0.9017973

00:05:41.285 --> 00:05:42.645 whether circular RNA play a

NOTE Confidence: 0.9017973

00:05:42.645 --> 00:05:44.370 function in that step of,

NOTE Confidence: 0.9017973

00:05:44.449 --> 00:05:45.810 for example, synaptic loss in

NOTE Confidence: 0.9017973

00:05:45.810 --> 00:05:47.250 early stage of PD that's

NOTE Confidence: 0.9017973

00:05:47.250 --> 00:05:48.850 still a question mark. So

NOTE Confidence: 0.9017973

00:05:48.850 --> 00:05:50.210 in my lab we follow-up

NOTE Confidence: 0.9017973

00:05:50.210 --> 00:05:50.610 this

NOTE Confidence: 0.9008614

00:05:51.089 --> 00:05:52.370 discovery. Now we go to

NOTE Confidence: 0.9008614

00:05:52.370 --> 00:05:53.169 the white lab. I mean

NOTE Confidence: 0.9008614

00:05:53.169 --> 00:05:54.370 this is something really I

NOTE Confidence: 0.9008614

00:05:54.370 --> 00:05:55.810 start to learn from after

NOTE Confidence: 0.9008614

00:05:55.810 --> 00:05:57.810 moving here with using a

NOTE Confidence: 0.9008614

00:05:57.810 --> 00:05:59.190 build organoid model.

NOTE Confidence: 0.9538601

00:05:59.505 --> 00:06:00.245 We want to,

NOTE Confidence: 0.8844004

00:06:01.185 --> 00:06:02.865 inject or or treat this

NOTE Confidence: 0.8844004

00:06:02.865 --> 00:06:04.305 organoid p d organoid model

NOTE Confidence: 0.8844004

00:06:04.305 --> 00:06:05.425 with DNA j c c

NOTE Confidence: 0.8844004

00:06:05.425 --> 00:06:07.105 circular RNA to see whether

NOTE Confidence: 0.8844004

00:06:07.105 --> 00:06:08.305 they can rescue the p

NOTE Confidence: 0.8844004

00:06:08.305 --> 00:06:09.665 d symptom. This is really

NOTE Confidence: 0.8844004

00:06:09.665 --> 00:06:11.310 pioneered by, one of the

NOTE Confidence: 0.8844004

00:06:11.630 --> 00:06:13.230 Thailand poster in, Maria in

NOTE Confidence: 0.8844004

00:06:13.230 --> 00:06:14.430 my lab, and, we are

NOTE Confidence: 0.8844004

00:06:14.430 --> 00:06:16.589 testing different way of deliver

NOTE Confidence: 0.8844004

00:06:16.589 --> 00:06:18.430 circular RNA. For example, using

NOTE Confidence: 0.8844004

00:06:18.430 --> 00:06:19.630 EV to wrap into the

NOTE Confidence: 0.8844004

00:06:19.630 --> 00:06:22.270 axon extracellular vesicle and, put

NOTE Confidence: 0.8844004

00:06:22.270 --> 00:06:23.550 a surface marker to make

NOTE Confidence: 0.8844004

00:06:23.550 --> 00:06:25.305 the brain target specific and

NOTE Confidence: 0.8844004

00:06:25.305 --> 00:06:26.345 also try another way, the

NOTE Confidence: 0.8844004

00:06:26.345 --> 00:06:28.265 lipid nanoparticle there is too.

NOTE Confidence: 0.8844004

00:06:28.265 --> 00:06:29.625 So please stay in tune

NOTE Confidence: 0.8844004

00:06:29.625 --> 00:06:31.305 on this, research and there's

NOTE Confidence: 0.8844004

00:06:31.305 --> 00:06:32.505 really a lot of risk

NOTE Confidence: 0.8844004

00:06:32.505 --> 00:06:33.625 on the on the way

NOTE Confidence: 0.8844004

00:06:33.625 --> 00:06:35.225 I can see. Okay. Back

NOTE Confidence: 0.8844004

00:06:35.225 --> 00:06:36.445 to today's focus.

NOTE Confidence: 0.864016

00:06:37.610 --> 00:06:39.210 We more previously, we focused

NOTE Confidence: 0.864016

00:06:39.210 --> 00:06:40.890 on specific brain regions and

NOTE Confidence: 0.864016

00:06:40.890 --> 00:06:42.589 like middle brain or cortex,

NOTE Confidence: 0.9742704

00:06:42.890 --> 00:06:44.089 but the brain region is

NOTE Confidence: 0.9742704

00:06:44.089 --> 00:06:45.210 not just one piece of

NOTE Confidence: 0.9742704

00:06:45.210 --> 00:06:46.330 block. Right? If you look

NOTE Confidence: 0.9742704

00:06:46.330 --> 00:06:48.650 at this, very famous, figure

NOTE Confidence: 0.9742704

00:06:48.650 --> 00:06:49.870 from Santiago,

NOTE Confidence: 0.6018355

00:06:51.485 --> 00:06:51.985 Ramani

NOTE Confidence: 0.61804044

00:06:52.525 --> 00:06:54.145 Haaha's figure is drawing.

NOTE Confidence: 0.92632097

00:06:54.604 --> 00:06:55.884 And you see the the

NOTE Confidence: 0.92632097

00:06:55.884 --> 00:06:57.245 the cortex region is actually

NOTE Confidence: 0.92632097

00:06:57.245 --> 00:06:58.525 formed by different layers or

NOTE Confidence: 0.92632097

00:06:58.525 --> 00:07:00.125 sub layers. They are not

NOTE Confidence: 0.92632097

00:07:00.125 --> 00:07:01.985 exactly the same uniform. Right?

NOTE Confidence: 0.92632097

00:07:02.205 --> 00:07:03.805 And, so that's why we

NOTE Confidence: 0.92632097

00:07:03.805 --> 00:07:05.104 studied spatial transformics.

NOTE Confidence: 0.8419884

00:07:05.669 --> 00:07:07.029 And spatial transform is we

NOTE Confidence: 0.8419884

00:07:07.029 --> 00:07:08.229 use technology called ten x

NOTE Confidence: 0.8419884

00:07:08.229 --> 00:07:09.669 vision and cut the brain

NOTE Confidence: 0.8419884

00:07:09.669 --> 00:07:11.270 slice and put barcode on

NOTE Confidence: 0.8419884

00:07:11.270 --> 00:07:12.550 each spot of the x

NOTE Confidence: 0.8419884

00:07:12.550 --> 00:07:13.990 y coordinate of the of

NOTE Confidence: 0.8419884

00:07:13.990 --> 00:07:15.430 the slice and it measures

NOTE Confidence: 0.8419884

00:07:15.430 --> 00:07:17.270 RNA each coordinate. And then

NOTE Confidence: 0.8419884

00:07:17.270 --> 00:07:18.229 and then meanwhile, we do

NOTE Confidence: 0.8419884

00:07:18.229 --> 00:07:19.485 single cell RNA seek

NOTE Confidence: 0.94646835

00:07:19.965 --> 00:07:21.085 to to match up the

NOTE Confidence: 0.94646835

00:07:21.085 --> 00:07:22.365 same data to see whether

NOTE Confidence: 0.94646835

00:07:22.365 --> 00:07:24.145 the cell type deconvolution there's.

NOTE Confidence: 0.94646835

00:07:24.284 --> 00:07:25.004 So for those that are

NOTE Confidence: 0.94646835

00:07:25.004 --> 00:07:26.444 less familiar with single cell

NOTE Confidence: 0.94646835

00:07:26.444 --> 00:07:27.425 and and spatial,

NOTE Confidence: 0.8524079

00:07:27.805 --> 00:07:29.245 I borrowed this analog for

NOTE Confidence: 0.8524079

00:07:29.245 --> 00:07:30.844 you to understand. Basically, if

NOTE Confidence: 0.8524079

00:07:30.844 --> 00:07:31.884 you do the bulk is

NOTE Confidence: 0.8524079

00:07:31.884 --> 00:07:32.925 you make it a smoothie

NOTE Confidence: 0.8524079

00:07:32.925 --> 00:07:35.039 for everything together. A single

NOTE Confidence: 0.8524079

00:07:35.039 --> 00:07:36.159 cell, you mix the different

NOTE Confidence: 0.8524079

00:07:36.159 --> 00:07:37.360 things together, but they are

NOTE Confidence: 0.8524079

00:07:37.360 --> 00:07:38.400 still like a mix but

NOTE Confidence: 0.8524079

00:07:38.400 --> 00:07:38.900 individually.

NOTE Confidence: 0.9318436

00:07:39.280 --> 00:07:40.400 And spatial, you form a

NOTE Confidence: 0.9318436

00:07:40.400 --> 00:07:41.680 pattern there based on the

NOTE Confidence: 0.9318436

00:07:41.680 --> 00:07:43.280 the location of of the,

NOTE Confidence: 0.9318436

00:07:43.520 --> 00:07:44.719 of the cells and the

NOTE Confidence: 0.9318436

00:07:44.719 --> 00:07:46.020 expression levels there.

NOTE Confidence: 0.93958205

00:07:48.025 --> 00:07:49.465 So we start with around

NOTE Confidence: 0.93958205

00:07:49.465 --> 00:07:51.324 hundred brains, and this brain

NOTE Confidence: 0.93958205

00:07:51.544 --> 00:07:53.724 are very well characterized clinically

NOTE Confidence: 0.93958205

00:07:53.785 --> 00:07:54.525 and pathologically.

NOTE Confidence: 0.85687983

00:07:54.905 --> 00:07:56.664 And they can span the

NOTE Confidence: 0.85687983

00:07:56.664 --> 00:07:57.724 whole ten post,

NOTE Confidence: 0.9055924

00:07:58.345 --> 00:08:00.444 trajectory of Parkinson's, development

NOTE Confidence: 0.8698306

00:08:00.905 --> 00:08:02.284 from healthy control

NOTE Confidence: 0.882896

00:08:02.700 --> 00:08:03.660 to the late stage PD

NOTE Confidence: 0.882896

00:08:03.660 --> 00:08:05.580 and also some, one third

NOTE Confidence: 0.882896

00:08:05.580 --> 00:08:07.280 of sample, we have also

NOTE Confidence: 0.882896

00:08:07.340 --> 00:08:08.780 called instant Lewy body, which

NOTE Confidence: 0.882896

00:08:08.780 --> 00:08:10.400 means they are clinically healthy.

NOTE Confidence: 0.882896

00:08:10.460 --> 00:08:12.780 No tremor, no, dementia. But

NOTE Confidence: 0.882896

00:08:12.780 --> 00:08:14.380 pathologically, there's brain already had

NOTE Confidence: 0.882896

00:08:14.380 --> 00:08:15.180 Lewy body found in the

NOTE Confidence: 0.882896

00:08:15.180 --> 00:08:16.060 brain. So this is very

NOTE Confidence: 0.882896

00:08:16.060 --> 00:08:17.385 unique sample to help us

NOTE Confidence: 0.882896

00:08:17.545 --> 00:08:19.225 identify those markers on early

NOTE Confidence: 0.882896

00:08:19.225 --> 00:08:19.725 PD.

NOTE Confidence: 0.70675766

00:08:21.945 --> 00:08:22.745 So j a is a

NOTE Confidence: 0.70675766

00:08:22.745 --> 00:08:24.045 very talented post scientist

NOTE Confidence: 0.9395268

00:08:24.985 --> 00:08:26.185 in my lab. He developed

NOTE Confidence: 0.9395268

00:08:26.185 --> 00:08:27.885 this computational advanced computational,

NOTE Confidence: 0.9923523

00:08:28.425 --> 00:08:29.725 algorithm or pipelines

NOTE Confidence: 0.929735

00:08:30.105 --> 00:08:31.385 to look into those spatial

NOTE Confidence: 0.929735

00:08:31.385 --> 00:08:33.600 data, and we identify seven

NOTE Confidence: 0.929735

00:08:33.600 --> 00:08:35.600 clusters in the space, based

NOTE Confidence: 0.929735

00:08:35.600 --> 00:08:36.800 on the spot data. And

NOTE Confidence: 0.929735

00:08:36.800 --> 00:08:38.320 these seven cluster align pretty

NOTE Confidence: 0.929735

00:08:38.320 --> 00:08:39.679 well to the seven layers

NOTE Confidence: 0.929735

00:08:39.679 --> 00:08:41.280 of cortical like layer one

NOTE Confidence: 0.929735

00:08:41.280 --> 00:08:42.660 to six and why matters.

NOTE Confidence: 0.929735

00:08:42.800 --> 00:08:44.160 And we also benchmark with

NOTE Confidence: 0.929735

00:08:44.160 --> 00:08:45.360 another data set which is

NOTE Confidence: 0.929735

00:08:45.360 --> 00:08:47.460 manually annotated by a pathologist

NOTE Confidence: 0.94560546

00:08:47.985 --> 00:08:49.585 and our layer marker gene

NOTE Confidence: 0.94560546

00:08:49.585 --> 00:08:51.025 highly correlated with what they

NOTE Confidence: 0.94560546

00:08:51.025 --> 00:08:52.725 found in their manual annotations.

NOTE Confidence: 0.92120945

00:08:53.904 --> 00:08:54.145 And,

NOTE Confidence: 0.9297667

00:08:54.865 --> 00:08:56.865 we also, he also developed

NOTE Confidence: 0.9297667

00:08:56.865 --> 00:08:58.145 a a machine learning based

NOTE Confidence: 0.9297667

00:08:58.145 --> 00:08:59.825 tool called layer smoother. As

NOTE Confidence: 0.9297667

00:08:59.825 --> 00:09:01.025 you can see, the original

NOTE Confidence: 0.9297667

00:09:01.025 --> 00:09:01.710 data looks

NOTE Confidence: 0.82283115

00:09:02.190 --> 00:09:03.790 sparse and and very,

NOTE Confidence: 0.93279254

00:09:04.270 --> 00:09:05.870 kind of noisy noisy in

NOTE Confidence: 0.93279254

00:09:05.870 --> 00:09:06.929 some layer boundary.

NOTE Confidence: 0.98983586

00:09:07.309 --> 00:09:08.770 And with this layer smoother,

NOTE Confidence: 0.93164057

00:09:09.150 --> 00:09:10.429 the border is much cleaner

NOTE Confidence: 0.93164057

00:09:10.429 --> 00:09:12.110 and, data is cleaner too.

NOTE Confidence: 0.93164057

00:09:12.110 --> 00:09:13.230 So we enhance the data

NOTE Confidence: 0.93164057

00:09:13.230 --> 00:09:14.190 a lot based on this,

NOTE Confidence: 0.93164057

00:09:14.429 --> 00:09:15.730 machine learning algorithm.

NOTE Confidence: 0.91954815

00:09:16.654 --> 00:09:18.014 And it also show this

NOTE Confidence: 0.91954815

00:09:18.014 --> 00:09:19.535 algorithm works pretty well when

NOTE Confidence: 0.91954815

00:09:19.535 --> 00:09:21.375 we compare their benchmark or

NOTE Confidence: 0.91954815

00:09:21.375 --> 00:09:22.434 ground truth tools

NOTE Confidence: 0.84382886

00:09:22.894 --> 00:09:24.894 ground truth annotation based on

NOTE Confidence: 0.84382886

00:09:24.894 --> 00:09:26.334 the based on the from

NOTE Confidence: 0.84382886

00:09:26.334 --> 00:09:27.074 the pathologist

NOTE Confidence: 0.8403458

00:09:27.774 --> 00:09:30.589 our layer smoother actually improved

NOTE Confidence: 0.8403458

00:09:30.649 --> 00:09:32.570 the original clustering a lot.

NOTE Confidence: 0.8403458

00:09:32.570 --> 00:09:34.510 And also, we also identify

NOTE Confidence: 0.8403458

00:09:34.730 --> 00:09:35.450 some of the,

NOTE Confidence: 0.8783572

00:09:36.410 --> 00:09:37.929 regions. For example, here is

NOTE Confidence: 0.8783572

00:09:37.929 --> 00:09:39.250 not really annotated by the

NOTE Confidence: 0.8783572

00:09:39.290 --> 00:09:40.490 even by the pathologist, but

NOTE Confidence: 0.8783572

00:09:40.490 --> 00:09:42.570 we identified those substructure stairs

NOTE Confidence: 0.8783572

00:09:42.570 --> 00:09:44.029 based on our laser smoother.

NOTE Confidence: 0.9617683

00:09:45.735 --> 00:09:47.095 So next question we ask

NOTE Confidence: 0.9617683

00:09:47.095 --> 00:09:48.955 is what kind of cells

NOTE Confidence: 0.9197504

00:09:49.335 --> 00:09:51.495 presented in each layers. Right?

NOTE Confidence: 0.9197504

00:09:51.495 --> 00:09:53.895 And whether, they're uniform distributed

NOTE Confidence: 0.9197504

00:09:53.895 --> 00:09:55.575 or some cells are more,

NOTE Confidence: 0.8778606

00:09:56.615 --> 00:09:59.380 presented in, certain layers. So

NOTE Confidence: 0.8778606

00:09:59.380 --> 00:10:00.920 this joint work between

NOTE Confidence: 0.8662975

00:10:01.459 --> 00:10:02.820 my lab and Clem's lab

NOTE Confidence: 0.8662975

00:10:02.820 --> 00:10:04.100 and Jacob and Jay, a

NOTE Confidence: 0.8662975

00:10:04.100 --> 00:10:05.700 team of very beautifully to

NOTE Confidence: 0.8662975

00:10:05.700 --> 00:10:06.440 get this

NOTE Confidence: 0.93719596

00:10:06.820 --> 00:10:08.440 cell type convolution

NOTE Confidence: 0.90596586

00:10:08.820 --> 00:10:10.100 in a spatial wise and

NOTE Confidence: 0.90596586

00:10:10.100 --> 00:10:11.459 we see each major cell

NOTE Confidence: 0.90596586

00:10:11.459 --> 00:10:11.959 types

NOTE Confidence: 0.8726334

00:10:12.295 --> 00:10:14.535 they, their relative location in

NOTE Confidence: 0.8726334

00:10:14.535 --> 00:10:16.054 each layers. And one of

NOTE Confidence: 0.8726334

00:10:16.054 --> 00:10:17.255 the take home message here

NOTE Confidence: 0.8726334

00:10:17.255 --> 00:10:18.015 is when you look at

NOTE Confidence: 0.8726334

00:10:18.015 --> 00:10:18.875 the glu glutamatergic

NOTE Confidence: 0.8770498

00:10:20.215 --> 00:10:22.535 neurons and the glutamatergic neuron

NOTE Confidence: 0.8770498

00:10:22.535 --> 00:10:24.075 have show very strong

NOTE Confidence: 0.7053416

00:10:24.615 --> 00:10:25.515 layer specificity.

NOTE Confidence: 0.78098005

00:10:25.895 --> 00:10:26.395 Meaning,

NOTE Confidence: 0.8975233

00:10:26.990 --> 00:10:29.009 the subtype of glutaminergic neurons,

NOTE Confidence: 0.999418

00:10:29.550 --> 00:10:30.990 they can present in certain

NOTE Confidence: 0.999418

00:10:30.990 --> 00:10:31.490 layers.

NOTE Confidence: 0.9564703

00:10:32.429 --> 00:10:33.309 On the other hand, if

NOTE Confidence: 0.9564703

00:10:33.309 --> 00:10:34.370 you look at the GABAergic

NOTE Confidence: 0.9564703

00:10:34.429 --> 00:10:35.790 neuron, they don't have so

NOTE Confidence: 0.9564703

00:10:35.790 --> 00:10:38.129 strong layer specificity as glutaminergic

NOTE Confidence: 0.9985228

00:10:38.429 --> 00:10:38.929 neurons.

NOTE Confidence: 0.9810164

00:10:39.535 --> 00:10:40.815 Maybe this figure is not

NOTE Confidence: 0.9810164

00:10:40.815 --> 00:10:42.655 so, intuitive. Let's look at

NOTE Confidence: 0.9810164

00:10:42.655 --> 00:10:43.635 the movie here.

NOTE Confidence: 0.94106954

00:10:44.655 --> 00:10:45.535 This is one of the

NOTE Confidence: 0.94106954

00:10:45.535 --> 00:10:47.375 sample we found and you

NOTE Confidence: 0.94106954

00:10:47.375 --> 00:10:49.295 can still see the layer

NOTE Confidence: 0.94106954

00:10:49.295 --> 00:10:50.915 marker gene for certain,

NOTE Confidence: 0.8891155

00:10:51.455 --> 00:10:52.975 sub cell types. They are

NOTE Confidence: 0.8891155

00:10:52.975 --> 00:10:53.475 highly

NOTE Confidence: 0.85946935

00:10:54.000 --> 00:10:55.679 presented. I wanna show this

NOTE Confidence: 0.85946935

00:10:55.679 --> 00:10:56.880 again but it's kind of

NOTE Confidence: 0.85946935

00:10:56.880 --> 00:10:57.860 positive and

NOTE Confidence: 0.8589131

00:10:58.320 --> 00:10:59.679 you can imagine the the

NOTE Confidence: 0.8589131

00:10:59.679 --> 00:11:00.179 different

NOTE Confidence: 0.8676795

00:11:00.800 --> 00:11:02.400 subtype of marker gene. They're

NOTE Confidence: 0.8676795

00:11:02.400 --> 00:11:04.480 highly correlated or highly specific

NOTE Confidence: 0.8676795

00:11:04.480 --> 00:11:05.540 in certain layers.

NOTE Confidence: 0.8082668

00:11:06.795 --> 00:11:08.315 And there are more samples

NOTE Confidence: 0.8082668

00:11:08.315 --> 00:11:09.755 there and we have a

NOTE Confidence: 0.8082668

00:11:09.755 --> 00:11:11.355 hundred samples but there's a

NOTE Confidence: 0.8082668

00:11:11.355 --> 00:11:12.715 few other samples we show

NOTE Confidence: 0.8082668

00:11:12.715 --> 00:11:14.395 the glucanergic neuron show very

NOTE Confidence: 0.8082668

00:11:14.395 --> 00:11:16.335 strong layer specific copper neuron

NOTE Confidence: 0.8082668

00:11:16.554 --> 00:11:17.054 more

NOTE Confidence: 0.8599092

00:11:17.434 --> 00:11:19.995 uniform relatively and other glial

NOTE Confidence: 0.8599092

00:11:19.995 --> 00:11:21.610 cells also show there's their

NOTE Confidence: 0.8599092

00:11:21.610 --> 00:11:23.790 own, cell layer specificity there.

NOTE Confidence: 0.92607063

00:11:24.570 --> 00:11:25.850 Now next question is, of

NOTE Confidence: 0.92607063

00:11:25.850 --> 00:11:27.230 course, we wanna study Parkinson.

NOTE Confidence: 0.92607063

00:11:27.290 --> 00:11:28.570 Right? We may want to

NOTE Confidence: 0.92607063

00:11:28.570 --> 00:11:30.970 understand how this location or

NOTE Confidence: 0.92607063

00:11:30.970 --> 00:11:33.690 this, marker molecular signal change

NOTE Confidence: 0.92607063

00:11:33.690 --> 00:11:35.470 along the Parkinson progressions.

NOTE Confidence: 0.92107564

00:11:36.065 --> 00:11:38.225 So we viewed a, using

NOTE Confidence: 0.92107564

00:11:38.225 --> 00:11:39.825 the a metric binomial model

NOTE Confidence: 0.92107564

00:11:39.825 --> 00:11:40.865 to test each gene and

NOTE Confidence: 0.92107564

00:11:40.865 --> 00:11:42.625 each layers and see whether

NOTE Confidence: 0.92107564

00:11:42.625 --> 00:11:43.845 any gene show

NOTE Confidence: 0.92245644

00:11:44.705 --> 00:11:45.845 a link to the Parkinson

NOTE Confidence: 0.92245644

00:11:45.904 --> 00:11:47.904 progression by regress with the

NOTE Confidence: 0.92245644

00:11:47.904 --> 00:11:49.800 Lewy body scores and also

NOTE Confidence: 0.92245644

00:11:49.800 --> 00:11:51.080 with just other covariance here

NOTE Confidence: 0.92245644

00:11:51.080 --> 00:11:52.059 as you can see.

NOTE Confidence: 0.93357474

00:11:53.080 --> 00:11:54.080 So what we found very

NOTE Confidence: 0.93357474

00:11:54.200 --> 00:11:54.920 we found a lot of

NOTE Confidence: 0.93357474

00:11:54.920 --> 00:11:55.960 gene, but this gene formed

NOTE Confidence: 0.93357474

00:11:55.960 --> 00:11:57.640 very interesting pathway. So this

NOTE Confidence: 0.93357474

00:11:57.640 --> 00:11:58.760 figure I'm sorry. I apologize

NOTE Confidence: 0.93357474

00:11:58.760 --> 00:12:00.120 for the busy figure, but,

NOTE Confidence: 0.9637148

00:12:01.385 --> 00:12:03.065 the the the figure is

NOTE Confidence: 0.9637148

00:12:03.065 --> 00:12:04.605 a circle plot. Each layer

NOTE Confidence: 0.9637148

00:12:04.904 --> 00:12:05.865 is a,

NOTE Confidence: 0.95240086

00:12:06.745 --> 00:12:07.865 each circle is a layer.

NOTE Confidence: 0.95240086

00:12:07.865 --> 00:12:09.145 So layer one to to

NOTE Confidence: 0.95240086

00:12:09.145 --> 00:12:10.445 six and then y matters.

NOTE Confidence: 0.95240086

00:12:10.665 --> 00:12:12.345 And the pathway if the

NOTE Confidence: 0.95240086

00:12:12.345 --> 00:12:12.845 pathway

NOTE Confidence: 0.8539631

00:12:13.145 --> 00:12:14.365 is operate regulated

NOTE Confidence: 0.95102423

00:12:15.179 --> 00:12:16.940 in, that layer along the

NOTE Confidence: 0.95102423

00:12:16.940 --> 00:12:18.940 Parkinson's progression, it will show

NOTE Confidence: 0.95102423

00:12:18.940 --> 00:12:20.300 a purple color. If it's

NOTE Confidence: 0.95102423

00:12:20.300 --> 00:12:21.040 down regulated

NOTE Confidence: 0.92591876

00:12:21.420 --> 00:12:22.940 along the progression, it show

NOTE Confidence: 0.92591876

00:12:22.940 --> 00:12:24.460 the the yellow color. As

NOTE Confidence: 0.92591876

00:12:24.460 --> 00:12:26.380 you can see, this pathway

NOTE Confidence: 0.92591876

00:12:26.380 --> 00:12:27.580 are clustered based on their

NOTE Confidence: 0.92591876

00:12:27.580 --> 00:12:29.115 similarity of the leading adenines

NOTE Confidence: 0.92591876

00:12:29.274 --> 00:12:30.554 and we show some group

NOTE Confidence: 0.92591876

00:12:30.554 --> 00:12:32.714 are are highly significant across

NOTE Confidence: 0.92591876

00:12:32.714 --> 00:12:35.035 multiple multiple region. For example,

NOTE Confidence: 0.92591876

00:12:35.035 --> 00:12:37.375 this is octave, oxidative phosphorylation

NOTE Confidence: 0.90379715

00:12:37.915 --> 00:12:39.595 is a critical role for

NOTE Confidence: 0.90379715

00:12:39.595 --> 00:12:40.735 mitochondrial energy,

NOTE Confidence: 0.99904794

00:12:41.115 --> 00:12:41.615 generation

NOTE Confidence: 0.917809

00:12:41.980 --> 00:12:43.040 and for ATP

NOTE Confidence: 0.7835087

00:12:43.420 --> 00:12:45.360 metabolic. And see this pathway

NOTE Confidence: 0.7835087

00:12:45.420 --> 00:12:45.920 kind

NOTE Confidence: 0.9135186

00:12:46.940 --> 00:12:47.580 of, getting,

NOTE Confidence: 0.8393722

00:12:48.860 --> 00:12:49.360 downregulated

NOTE Confidence: 0.77103823

00:12:49.740 --> 00:12:51.520 in along Parkinson reg regression.

NOTE Confidence: 0.971011

00:12:53.020 --> 00:12:54.860 There's other pathway linked to

NOTE Confidence: 0.971011

00:12:54.860 --> 00:12:55.920 this, energy

NOTE Confidence: 0.85528624

00:12:56.300 --> 00:12:56.800 generation.

NOTE Confidence: 0.7873676

00:12:57.105 --> 00:12:58.385 For example, the the protein

NOTE Confidence: 0.7873676

00:12:58.385 --> 00:12:59.605 synthesis is a ribosome,

NOTE Confidence: 0.7530655

00:13:00.065 --> 00:13:00.565 biogenesis.

NOTE Confidence: 0.9198688

00:13:00.945 --> 00:13:02.644 They also get down spatially

NOTE Confidence: 0.9117443

00:13:02.945 --> 00:13:05.125 in Parkinson across multiple layers.

NOTE Confidence: 0.9866985

00:13:06.385 --> 00:13:06.885 And

NOTE Confidence: 0.8565147

00:13:07.264 --> 00:13:09.125 meanwhile, we see other pathway

NOTE Confidence: 0.8565147

00:13:09.184 --> 00:13:10.625 which is for example, immune

NOTE Confidence: 0.8565147

00:13:10.625 --> 00:13:12.120 related pathway like t t

NOTE Confidence: 0.8565147

00:13:12.120 --> 00:13:13.179 seventeen activation

NOTE Confidence: 0.89004874

00:13:13.720 --> 00:13:15.879 and immune response and and

NOTE Confidence: 0.89004874

00:13:15.879 --> 00:13:17.480 t cell regulation and and

NOTE Confidence: 0.89004874

00:13:17.480 --> 00:13:19.240 also b cell top six

NOTE Confidence: 0.89004874

00:13:19.240 --> 00:13:19.980 path response

NOTE Confidence: 0.683766

00:13:20.360 --> 00:13:21.660 they also get upregulated

NOTE Confidence: 0.8384453

00:13:22.199 --> 00:13:23.319 in the along the pro

NOTE Confidence: 0.8384453

00:13:23.399 --> 00:13:24.300 three d progression.

NOTE Confidence: 0.996869

00:13:25.134 --> 00:13:26.595 But we also see some

NOTE Confidence: 0.996869

00:13:26.815 --> 00:13:27.454 kind of,

NOTE Confidence: 0.87145716

00:13:27.934 --> 00:13:28.735 hard to explain,

NOTE Confidence: 0.80774516

00:13:29.295 --> 00:13:30.975 since, like, a neutrophil mediated

NOTE Confidence: 0.80774516

00:13:30.975 --> 00:13:31.475 immunity

NOTE Confidence: 0.8866506

00:13:32.334 --> 00:13:33.694 pathway that actually get down

NOTE Confidence: 0.8866506

00:13:33.694 --> 00:13:34.574 here. So this is kind

NOTE Confidence: 0.8866506

00:13:34.574 --> 00:13:35.454 of a little bit puzzling

NOTE Confidence: 0.8866506

00:13:35.454 --> 00:13:36.355 for us too.

NOTE Confidence: 0.86923176

00:13:38.320 --> 00:13:39.840 Another thing we see many

NOTE Confidence: 0.86923176

00:13:39.840 --> 00:13:40.960 parts that relate to cell

NOTE Confidence: 0.86923176

00:13:40.960 --> 00:13:42.800 response to the environment to

NOTE Confidence: 0.86923176

00:13:42.800 --> 00:13:44.580 the, external stimuli

NOTE Confidence: 0.8614743

00:13:44.960 --> 00:13:47.360 or environment of surveillance, they

NOTE Confidence: 0.8614743

00:13:47.360 --> 00:13:48.740 also get go up,

NOTE Confidence: 0.95460737

00:13:49.760 --> 00:13:51.945 including a drug response to

NOTE Confidence: 0.95460737

00:13:51.945 --> 00:13:52.925 virus infection

NOTE Confidence: 0.6427169

00:13:55.465 --> 00:13:56.205 to a biotic

NOTE Confidence: 0.84868395

00:13:56.825 --> 00:13:58.985 infection there's this this pathway

NOTE Confidence: 0.84868395

00:13:58.985 --> 00:14:00.265 the purple color show they

NOTE Confidence: 0.84868395

00:14:00.265 --> 00:14:01.165 go up too.

NOTE Confidence: 0.89380324

00:14:01.785 --> 00:14:03.385 And lastly, we see the

NOTE Confidence: 0.89380324

00:14:03.385 --> 00:14:05.485 cell cell communication, synaptic activity,

NOTE Confidence: 0.89380324

00:14:05.545 --> 00:14:07.350 those pathway go up along

NOTE Confidence: 0.89380324

00:14:07.350 --> 00:14:09.270 progression, especially in the white

NOTE Confidence: 0.89380324

00:14:09.270 --> 00:14:11.050 matter. This is likely to

NOTE Confidence: 0.89380324

00:14:11.270 --> 00:14:12.730 do a, compensatory

NOTE Confidence: 0.8890235

00:14:13.110 --> 00:14:15.270 response of neural degeneration that

NOTE Confidence: 0.8890235

00:14:15.270 --> 00:14:16.710 the neural neural connection need

NOTE Confidence: 0.8890235

00:14:16.710 --> 00:14:18.309 to go up at, along

NOTE Confidence: 0.8890235

00:14:18.309 --> 00:14:18.970 the progression.

NOTE Confidence: 0.9453815

00:14:20.945 --> 00:14:22.385 So last question we'll try

NOTE Confidence: 0.9453815

00:14:22.385 --> 00:14:24.145 to address here is, do

NOTE Confidence: 0.9453815

00:14:24.145 --> 00:14:26.705 those pathway change already early

NOTE Confidence: 0.9453815

00:14:26.705 --> 00:14:28.225 of the PD or they

NOTE Confidence: 0.9453815

00:14:28.225 --> 00:14:29.045 happen later?

NOTE Confidence: 0.930734

00:14:29.425 --> 00:14:30.945 So because we have well

NOTE Confidence: 0.930734

00:14:30.945 --> 00:14:32.305 characterized a sample in different

NOTE Confidence: 0.930734

00:14:32.305 --> 00:14:33.285 stage of Parkinson's,

NOTE Confidence: 0.96420383

00:14:33.590 --> 00:14:34.950 we specifically look at the

NOTE Confidence: 0.96420383

00:14:34.950 --> 00:14:36.330 early PD versus control.

NOTE Confidence: 0.98511916

00:14:36.710 --> 00:14:37.750 And this group, as you

NOTE Confidence: 0.98511916

00:14:37.750 --> 00:14:38.490 can see,

NOTE Confidence: 0.9668284

00:14:38.950 --> 00:14:39.830 we when we,

NOTE Confidence: 0.9579716

00:14:41.750 --> 00:14:42.710 when we look at late

NOTE Confidence: 0.9579716

00:14:42.710 --> 00:14:45.050 PD and, versus control,

NOTE Confidence: 0.9409459

00:14:45.350 --> 00:14:47.965 the the pathway looks pretty

NOTE Confidence: 0.9409459

00:14:47.965 --> 00:14:49.885 mimic well with the Lewy

NOTE Confidence: 0.9409459

00:14:49.885 --> 00:14:50.625 body progression.

NOTE Confidence: 0.947905

00:14:51.085 --> 00:14:52.045 But if you look at

NOTE Confidence: 0.947905

00:14:52.045 --> 00:14:53.025 the early PD

NOTE Confidence: 0.9098319

00:14:53.405 --> 00:14:54.705 and some of the pathway

NOTE Confidence: 0.9098319

00:14:54.765 --> 00:14:56.225 actually flipped the direction

NOTE Confidence: 0.8452287

00:14:56.525 --> 00:14:58.125 as for example, in this

NOTE Confidence: 0.8452287

00:14:58.125 --> 00:14:59.805 category highlight here, these are

NOTE Confidence: 0.8452287

00:14:59.805 --> 00:15:01.585 energy generation like mitochondrial,

NOTE Confidence: 0.9017614

00:15:01.965 --> 00:15:02.465 like,

NOTE Confidence: 0.63888836

00:15:02.860 --> 00:15:03.680 oxygen phosphorylation.

NOTE Confidence: 0.96234125

00:15:04.460 --> 00:15:06.400 They they speed up first

NOTE Confidence: 0.96234125

00:15:06.700 --> 00:15:08.220 and pump up energy, but

NOTE Confidence: 0.96234125

00:15:08.220 --> 00:15:09.660 later they get exhausted and

NOTE Confidence: 0.96234125

00:15:09.660 --> 00:15:11.180 then they get, power off

NOTE Confidence: 0.96234125

00:15:11.180 --> 00:15:12.620 globally. That's what we see

NOTE Confidence: 0.96234125

00:15:12.620 --> 00:15:13.340 from this,

NOTE Confidence: 0.8599633

00:15:15.180 --> 00:15:15.680 example.

NOTE Confidence: 0.9300215

00:15:17.435 --> 00:15:18.714 And we also give live

NOTE Confidence: 0.9300215

00:15:18.714 --> 00:15:20.555 a, this is ongoing work,

NOTE Confidence: 0.9300215

00:15:20.555 --> 00:15:21.774 actually. This is a prototype.

NOTE Confidence: 0.9300215

00:15:21.915 --> 00:15:23.195 We've had to build a

NOTE Confidence: 0.9300215

00:15:23.195 --> 00:15:25.135 online open source web portal

NOTE Confidence: 0.9300215

00:15:25.195 --> 00:15:26.714 to integrate all this data

NOTE Confidence: 0.9300215

00:15:26.714 --> 00:15:28.415 to so biologists and neurologists

NOTE Confidence: 0.9300215

00:15:28.475 --> 00:15:28.975 can

NOTE Confidence: 0.95637375

00:15:29.450 --> 00:15:30.810 look into this system and

NOTE Confidence: 0.95637375

00:15:30.810 --> 00:15:32.010 type their favorite gene and

NOTE Confidence: 0.95637375

00:15:32.010 --> 00:15:33.050 check our sample and and

NOTE Confidence: 0.95637375

00:15:33.050 --> 00:15:34.670 their how the gene change.

NOTE Confidence: 0.95637375

00:15:34.890 --> 00:15:36.089 And this work is really

NOTE Confidence: 0.95637375

00:15:36.089 --> 00:15:37.210 ongoing. I think this is

NOTE Confidence: 0.95637375

00:15:37.210 --> 00:15:38.430 going to build a foundation

NOTE Confidence: 0.95637375

00:15:38.490 --> 00:15:40.010 for for the AI model

NOTE Confidence: 0.95637375

00:15:40.010 --> 00:15:41.230 in the future too.

NOTE Confidence: 0.94143105

00:15:42.644 --> 00:15:43.485 So by that, I want

NOTE Confidence: 0.94143105

00:15:43.485 --> 00:15:45.065 to wrap up my, presentation

NOTE Confidence: 0.94143105

00:15:45.125 --> 00:15:47.045 today. PD five d provide

NOTE Confidence: 0.94143105

00:15:47.045 --> 00:15:48.584 a unique, resources

NOTE Confidence: 0.9002997

00:15:48.964 --> 00:15:50.404 and also hopefully build a

NOTE Confidence: 0.9002997

00:15:50.404 --> 00:15:50.904 foundation

NOTE Confidence: 0.9203727

00:15:51.205 --> 00:15:52.644 for precision medicine in the

NOTE Confidence: 0.9203727

00:15:52.644 --> 00:15:54.245 future. And we look at

NOTE Confidence: 0.9203727

00:15:54.245 --> 00:15:55.685 this Parkinson brain in multi

NOTE Confidence: 0.9203727

00:15:55.685 --> 00:15:57.700 omics view and, glucanergic

NOTE Confidence: 0.9245658

00:15:58.080 --> 00:15:59.840 neuron show very strong layer

NOTE Confidence: 0.9245658

00:15:59.840 --> 00:16:01.920 specificity where GABAergic neuron is

NOTE Confidence: 0.9245658

00:16:01.920 --> 00:16:04.820 more, relatively uniform, spatially distributed.

NOTE Confidence: 0.9245658

00:16:05.120 --> 00:16:06.560 And as PD progress, we

NOTE Confidence: 0.9245658

00:16:06.560 --> 00:16:08.020 see many interesting pathway

NOTE Confidence: 0.87355626

00:16:08.400 --> 00:16:09.700 either go up down,

NOTE Confidence: 0.7838528

00:16:10.195 --> 00:16:11.075 some will go up or

NOTE Confidence: 0.7838528

00:16:11.075 --> 00:16:12.755 go up like synapses or

NOTE Confidence: 0.7838528

00:16:12.755 --> 00:16:13.255 neurotransmission

NOTE Confidence: 0.8101644

00:16:13.635 --> 00:16:15.714 communication or vesicle trafficking and

NOTE Confidence: 0.8101644

00:16:15.714 --> 00:16:16.214 neuroinflammation

NOTE Confidence: 0.9178707

00:16:16.915 --> 00:16:18.035 and the cell response to

NOTE Confidence: 0.9178707

00:16:18.035 --> 00:16:20.115 external stimuli. Some go down

NOTE Confidence: 0.9178707

00:16:20.115 --> 00:16:21.635 for some energy generations and

NOTE Confidence: 0.9178707

00:16:21.635 --> 00:16:23.334 protein synthesis and metabolisms

NOTE Confidence: 0.9160336

00:16:23.635 --> 00:16:25.415 and neutral field pathway too.

NOTE Confidence: 0.9160336

00:16:25.660 --> 00:16:27.020 And we only see very

NOTE Confidence: 0.9160336

00:16:27.020 --> 00:16:29.420 marginal cell composition change along

NOTE Confidence: 0.9160336

00:16:29.420 --> 00:16:30.780 PD progression. This data is

NOTE Confidence: 0.9160336

00:16:30.780 --> 00:16:32.160 not included in this slide.

NOTE Confidence: 0.97213995

00:16:32.460 --> 00:16:34.880 And, energy related pathway appear,

NOTE Confidence: 0.9295556

00:16:35.900 --> 00:16:37.500 activating in early stage of

NOTE Confidence: 0.9295556

00:16:37.500 --> 00:16:39.280 PD but later become depleted

NOTE Confidence: 0.9295556

00:16:39.420 --> 00:16:40.785 in, in the PD.

NOTE Confidence: 0.9989546

00:16:41.105 --> 00:16:42.304 So this hopefully,

NOTE Confidence: 0.96813977

00:16:42.785 --> 00:16:43.524 I can,

NOTE Confidence: 0.915926

00:16:44.065 --> 00:16:46.384 just show this, data as,

NOTE Confidence: 0.915926

00:16:46.704 --> 00:16:48.384 convince you really build up

NOTE Confidence: 0.915926

00:16:48.384 --> 00:16:50.305 data and get knowledge there

NOTE Confidence: 0.915926

00:16:50.305 --> 00:16:51.425 as a training center for

NOTE Confidence: 0.915926

00:16:51.425 --> 00:16:53.105 next phase of AI based

NOTE Confidence: 0.915926

00:16:53.105 --> 00:16:54.004 modeling there.

NOTE Confidence: 0.9037438

00:16:54.450 --> 00:16:55.330 So lastly, I want to

NOTE Confidence: 0.9037438

00:16:55.330 --> 00:16:57.170 thank everybody here to hear

NOTE Confidence: 0.9037438

00:16:57.170 --> 00:16:58.850 my talk and, also like

NOTE Confidence: 0.9037438

00:16:58.850 --> 00:17:00.230 to thank all the members

NOTE Confidence: 0.9037438

00:17:00.370 --> 00:17:01.650 in my lab. This work

NOTE Confidence: 0.9037438

00:17:01.650 --> 00:17:03.570 largely driven by, done by

NOTE Confidence: 0.9037438

00:17:03.570 --> 00:17:04.790 by j in my lab

NOTE Confidence: 0.9037438

00:17:04.930 --> 00:17:06.050 and a few other member

NOTE Confidence: 0.9037438

00:17:06.050 --> 00:17:07.570 working on different aspect ASO

NOTE Confidence: 0.9037438

00:17:07.570 --> 00:17:09.090 project. I also like especially

NOTE Confidence: 0.9037438

00:17:09.090 --> 00:17:10.275 like to thank Clemens to

NOTE Confidence: 0.9037438

00:17:10.275 --> 00:17:11.315 bring me to the stage

NOTE Confidence: 0.9037438

00:17:11.315 --> 00:17:12.675 and to the field. This

NOTE Confidence: 0.9037438

00:17:12.675 --> 00:17:13.955 is really great to follow

NOTE Confidence: 0.9037438

00:17:13.955 --> 00:17:15.155 the whole scenes that you

NOTE Confidence: 0.9037438

00:17:15.155 --> 00:17:16.435 lead in the years and

NOTE Confidence: 0.9037438

00:17:16.435 --> 00:17:18.135 the many collaborator in ASOP,

NOTE Confidence: 0.7204647

00:17:18.435 --> 00:17:20.135 also Brainco project.

NOTE Confidence: 0.9434438

00:17:20.595 --> 00:17:22.435 And, and thank all the

NOTE Confidence: 0.9434438

00:17:22.435 --> 00:17:24.535 sponsors here too including APDA.

NOTE Confidence: 0.9123907

00:17:24.907 --> 00:17:26.586 I see Rebecca here at

NOTE Confidence: 0.9123907

00:17:26.667 --> 00:17:27.867 is, where I gave my

NOTE Confidence: 0.9123907

00:17:27.867 --> 00:17:29.307 first grant to start my

NOTE Confidence: 0.9123907

00:17:29.307 --> 00:17:30.686 lab. Thank you so much.