WEBVTT

NOTE duration: ”00:08:07.720”

NOTE Confidence: 0.78591967

00:00:00.880 --> 00:00:01.360 Hello.

NOTE Confidence: 0.92925215

00:00:02.480 --> 00:00:03.840 So when you knock out,

NOTE Confidence: 0.86139745

00:00:04.559 --> 00:00:06.259 the DNA j c six,

NOTE Confidence: 0.96317893

00:00:07.040 --> 00:00:07.520 do you,

NOTE Confidence: 0.8452301

00:00:08.400 --> 00:00:10.240 do you see with, I'm

NOTE Confidence: 0.8452301

00:00:10.240 --> 00:00:11.360 not sure you ever performed

NOTE Confidence: 0.8452301

00:00:11.360 --> 00:00:12.880 a spatial transformers or any

NOTE Confidence: 0.8452301

00:00:12.880 --> 00:00:14.099 spatial photonics

NOTE Confidence: 0.959893

00:00:14.974 --> 00:00:17.135 technology to the knockout mouse,

NOTE Confidence: 0.959893

00:00:17.135 --> 00:00:19.055 see where where this knockout

NOTE Confidence: 0.959893

00:00:19.055 --> 00:00:19.555 effect,

NOTE Confidence: 0.9239218

00:00:20.095 --> 00:00:21.295 happened in which part of

NOTE Confidence: 0.9239218

00:00:21.295 --> 00:00:22.414 the body or with part

NOTE Confidence: 0.9239218

00:00:22.414 --> 00:00:23.715 of the brain middle brain?

NOTE Confidence: 0.9239218

00:00:23.935 --> 00:00:25.875 So it's a conventional knockout.

NOTE Confidence: 0.9239218

00:00:25.935 --> 00:00:27.375 So it's in knocked out

NOTE Confidence: 0.9239218

00:00:27.375 --> 00:00:28.035 in all

NOTE Confidence: 0.99644303

00:00:28.370 --> 00:00:29.430 parts of the body.

NOTE Confidence: 0.99694896

00:00:29.730 --> 00:00:31.110 We have done proteomics

NOTE Confidence: 0.997987

00:00:31.650 --> 00:00:32.790 on the brain.

NOTE Confidence: 0.93901724

00:00:33.890 --> 00:00:35.510 We also have done proteomics

NOTE Confidence: 0.93901724

00:00:35.729 --> 00:00:37.729 on synaptic turtles and in

NOTE Confidence: 0.93901724

00:00:37.729 --> 00:00:38.550 this vesicle

NOTE Confidence: 0.93469095

00:00:39.170 --> 00:00:39.670 fraction.

NOTE Confidence: 0.96576685

00:00:40.130 --> 00:00:41.250 What we see even in

NOTE Confidence: 0.96576685

00:00:41.250 --> 00:00:42.450 the brain, even though it's

NOTE Confidence: 0.96576685

00:00:42.450 --> 00:00:43.750 a whole body knockout,

NOTE Confidence: 0.68371016

00:00:44.135 --> 00:00:45.835 is there dopenergic selective,

NOTE Confidence: 0.9625324

00:00:47.415 --> 00:00:48.935 effects. So the pathways are

NOTE Confidence: 0.9625324

00:00:48.935 --> 00:00:50.935 all dopenergic even though it's

NOTE Confidence: 0.9625324

00:00:50.935 --> 00:00:52.854 a whole brain knockout. And

NOTE Confidence: 0.9625324

00:00:52.854 --> 00:00:54.135 I think we think in

NOTE Confidence: 0.9625324

00:00:54.135 --> 00:00:55.675 part because of the biology

NOTE Confidence: 0.9625324

00:00:55.815 --> 00:00:57.835 of dopamine and dopamine transporter

NOTE Confidence: 0.84759307

00:00:58.535 --> 00:00:59.035 that

NOTE Confidence: 0.9536848

00:00:59.400 --> 00:01:00.680 that even though this is

NOTE Confidence: 0.9536848

00:01:00.680 --> 00:01:02.440 occurring in all synapses, they

NOTE Confidence: 0.9536848

00:01:02.440 --> 00:01:03.180 are preferentially

NOTE Confidence: 0.733304

00:01:04.120 --> 00:01:04.620 one.

NOTE Confidence: 0.8876299

00:01:06.680 --> 00:01:09.000 But maybe those, latest technology

NOTE Confidence: 0.8876299

00:01:09.000 --> 00:01:10.520 and spatial transforms can also

NOTE Confidence: 0.8876299

00:01:10.520 --> 00:01:12.220 measure be used to see

NOTE Confidence: 0.8876299

00:01:12.360 --> 00:01:14.135 other genes, not just DNA

NOTE Confidence: 0.8876299

00:01:14.135 --> 00:01:15.415 t six itself, but other

NOTE Confidence: 0.8876299

00:01:15.415 --> 00:01:16.694 genes That's great. That's great.

NOTE Confidence: 0.8876299

00:01:16.694 --> 00:01:18.055 That is correct. You couldn't

NOTE Confidence: 0.8876299

00:01:18.135 --> 00:01:19.834 we've just done mainly proteomic.

NOTE Confidence: 0.8876299

00:01:19.975 --> 00:01:21.115 We have not done.

NOTE Confidence: 0.9865625

00:01:24.615 --> 00:01:26.375 Other questions? I know it's

NOTE Confidence: 0.9865625

00:01:26.375 --> 00:01:27.515 been a long day.

NOTE Confidence: 0.66264737

00:01:29.280 --> 00:01:29.780 Steve.

NOTE Confidence: 0.8805461

00:01:30.720 --> 00:01:32.260 As a question of Pietro,

NOTE Confidence: 0.8803243

00:01:35.840 --> 00:01:37.220 with regard to lysosomal

NOTE Confidence: 0.9997767

00:01:37.680 --> 00:01:38.180 fragility

NOTE Confidence: 0.98182434

00:01:38.640 --> 00:01:39.459 and Parkinson's,

NOTE Confidence: 0.95993924

00:01:40.604 --> 00:01:41.645 is there any reason to

NOTE Confidence: 0.95993924

00:01:41.645 --> 00:01:42.784 think the nigrostriatal

NOTE Confidence: 0.9991192

00:01:43.244 --> 00:01:44.545 system would be particularly

NOTE Confidence: 0.9681789

00:01:44.845 --> 00:01:45.345 sensitive?

NOTE Confidence: 0.99079514

00:01:45.805 --> 00:01:47.485 For mitochondrial genes, there's been

NOTE Confidence: 0.99079514

00:01:47.485 --> 00:01:48.524 a lot of, you know,

NOTE Confidence: 0.99079514

00:01:48.524 --> 00:01:50.604 thought that dopamine makes them

NOTE Confidence: 0.99079514

00:01:50.604 --> 00:01:51.985 more sensitive to

NOTE Confidence: 0.9835223

00:01:52.730 --> 00:01:54.650 oxidation. But for lysosomes, is

NOTE Confidence: 0.9835223

00:01:54.650 --> 00:01:55.770 there some reason to think

NOTE Confidence: 0.9835223

00:01:55.770 --> 00:01:56.830 that this pathway

NOTE Confidence: 0.9993217

00:01:57.930 --> 00:01:59.150 would be more sensitive?

NOTE Confidence: 0.97310656

00:02:00.410 --> 00:02:01.550 It's a good question.

NOTE Confidence: 0.84503174

00:02:01.850 --> 00:02:02.750 There is

NOTE Confidence: 0.8502954

00:02:03.130 --> 00:02:04.990 cannot imagine why the dopaminergic

NOTE Confidence: 0.9723067

00:02:05.370 --> 00:02:06.410 system, they should be more

NOTE Confidence: 0.9723067

00:02:06.410 --> 00:02:06.910 fragile.

NOTE Confidence: 0.98512596

00:02:07.875 --> 00:02:09.415 I tend to believe, however,

NOTE Confidence: 0.98512596

00:02:09.475 --> 00:02:11.335 that this fragility is particularly

NOTE Confidence: 0.98512596

00:02:11.555 --> 00:02:13.415 important in microglia cells

NOTE Confidence: 0.82155

00:02:13.875 --> 00:02:15.655 because some of these Parkinson's

NOTE Confidence: 0.82155

00:02:15.794 --> 00:02:17.715 disease protein are highest pressing

NOTE Confidence: 0.82155

00:02:17.715 --> 00:02:19.575 microglia cells. We find VB13

NOTE Confidence: 0.9251463

00:02:20.195 --> 00:02:21.335 c is higher in microglia

NOTE Confidence: 0.97688746

00:02:21.635 --> 00:02:22.135 cell.

NOTE Confidence: 0.8674298

00:02:22.680 --> 00:02:23.960 Sean is working on our

NOTE Confidence: 0.8674298

00:02:23.960 --> 00:02:24.919 two. We find this go

NOTE Confidence: 0.8674298

00:02:24.919 --> 00:02:25.980 up in microglia.

NOTE Confidence: 0.95814395

00:02:26.680 --> 00:02:28.200 And so there might be

NOTE Confidence: 0.95814395

00:02:28.200 --> 00:02:30.200 something in microglial cell, which

NOTE Confidence: 0.95814395

00:02:30.200 --> 00:02:30.700 then

NOTE Confidence: 0.72534245

00:02:31.240 --> 00:02:32.460 transform a neuroinflammation,

NOTE Confidence: 0.9380821

00:02:33.000 --> 00:02:34.520 etcetera, if you don't if

NOTE Confidence: 0.9380821

00:02:34.520 --> 00:02:35.580 you have, dysplagility.

NOTE Confidence: 0.9346456

00:02:41.255 --> 00:02:42.135 I also have a question

NOTE Confidence: 0.9346456

00:02:42.135 --> 00:02:43.895 for Pietro. Yeah. So you

NOTE Confidence: 0.9346456

00:02:43.895 --> 00:02:46.235 referred to the sequential recruitment

NOTE Confidence: 0.9346456

00:02:46.294 --> 00:02:48.215 of BPS thirteen c and

NOTE Confidence: 0.9346456

00:02:48.215 --> 00:02:49.115 LURK two.

NOTE Confidence: 0.95965666

00:02:49.990 --> 00:02:50.870 Do you have any data

NOTE Confidence: 0.95965666

00:02:50.870 --> 00:02:51.370 that

NOTE Confidence: 0.90320235

00:02:51.750 --> 00:02:53.270 the LURK two recruitment depends

NOTE Confidence: 0.90320235

00:02:53.270 --> 00:02:54.790 on BPS thirty c thirteen

NOTE Confidence: 0.90320235

00:02:54.790 --> 00:02:57.190 c? And is there in

NOTE Confidence: 0.90320235

00:02:57.190 --> 00:02:58.810 any data from human genetics

NOTE Confidence: 0.90320235

00:02:59.030 --> 00:03:00.950 that show that, mutations in

NOTE Confidence: 0.90320235

00:03:00.950 --> 00:03:03.370 BPS thirteen c alters susceptibility

NOTE Confidence: 0.98942995

00:03:03.830 --> 00:03:05.050 to LURK two mutations?

NOTE Confidence: 0.99408287

00:03:07.135 --> 00:03:08.735 I cannot comment on the

NOTE Confidence: 0.99408287

00:03:08.735 --> 00:03:10.255 genetic data. As far as

NOTE Confidence: 0.99408287

00:03:10.255 --> 00:03:11.055 I know, there is no

NOTE Confidence: 0.99408287

00:03:11.055 --> 00:03:11.555 evidence.

NOTE Confidence: 0.88076466

00:03:13.135 --> 00:03:14.575 Yeah. The so we know

NOTE Confidence: 0.88076466

00:03:14.575 --> 00:03:15.775 for sure the VP of

NOTE Confidence: 0.88076466

00:03:15.775 --> 00:03:17.075 thirteen c is recruited

NOTE Confidence: 0.8757915

00:03:17.940 --> 00:03:19.379 really in thirty second is

NOTE Confidence: 0.8757915

00:03:19.379 --> 00:03:20.500 already there, and then it

NOTE Confidence: 0.8757915

00:03:20.500 --> 00:03:21.940 goes up and goes up

NOTE Confidence: 0.8757915

00:03:21.940 --> 00:03:22.680 very rapidly.

NOTE Confidence: 0.8223688

00:03:23.060 --> 00:03:24.919 LRR two is much delayed,

NOTE Confidence: 0.88076544

00:03:25.700 --> 00:03:27.220 and, Sean has shown very

NOTE Confidence: 0.88076544

00:03:27.220 --> 00:03:28.660 nicely that is dependent on

NOTE Confidence: 0.88076544

00:03:28.660 --> 00:03:30.500 CASM, and CASM seems to

NOTE Confidence: 0.88076544

00:03:30.500 --> 00:03:31.160 be delayed.

NOTE Confidence: 0.84231794

00:03:32.224 --> 00:03:33.525 We are trying to investigate

NOTE Confidence: 0.84231794

00:03:33.665 --> 00:03:35.045 whether there is a potential

NOTE Confidence: 0.84231794

00:03:35.105 --> 00:03:36.965 relationship. I told you that

NOTE Confidence: 0.84231794

00:03:37.105 --> 00:03:37.905 if you don't have a

NOTE Confidence: 0.84231794

00:03:37.905 --> 00:03:39.525 V13 in in in inactivation

NOTE Confidence: 0.89696044

00:03:40.305 --> 00:03:41.284 of innate immunity,

NOTE Confidence: 0.8629194

00:03:41.745 --> 00:03:43.424 shown that innate immunity is

NOTE Confidence: 0.8629194

00:03:43.424 --> 00:03:45.105 upstream of CASM. So there

NOTE Confidence: 0.8629194

00:03:45.105 --> 00:03:45.844 are potential

NOTE Confidence: 0.85316515

00:03:46.305 --> 00:03:46.805 interrelationship,

NOTE Confidence: 0.9680027

00:03:47.530 --> 00:03:48.830 which are very interesting.

NOTE Confidence: 0.9753927

00:03:51.690 --> 00:03:53.230 Yeah. I have a question,

NOTE Confidence: 0.98283887

00:03:53.690 --> 00:03:54.190 regarding,

NOTE Confidence: 0.8247552

00:03:54.810 --> 00:03:56.190 alpha synuclein pathology

NOTE Confidence: 0.9007676

00:03:56.650 --> 00:03:57.950 in patients. Sometimes,

NOTE Confidence: 0.9394322

00:03:58.890 --> 00:04:00.409 the disease is localized in

NOTE Confidence: 0.9394322

00:04:00.409 --> 00:04:02.534 certain areas in other types

NOTE Confidence: 0.9394322

00:04:02.534 --> 00:04:04.295 of PD such as, the

NOTE Confidence: 0.9394322

00:04:04.295 --> 00:04:05.894 case of VPS thirteen c

NOTE Confidence: 0.9394322

00:04:05.894 --> 00:04:06.795 is very diffusely

NOTE Confidence: 0.9942536

00:04:07.575 --> 00:04:09.015 accumulated in the brain. Is

NOTE Confidence: 0.9942536

00:04:09.015 --> 00:04:09.754 there any,

NOTE Confidence: 0.9981639

00:04:10.295 --> 00:04:11.834 insights of why

NOTE Confidence: 0.9513765

00:04:12.135 --> 00:04:13.515 a disease can be widespread

NOTE Confidence: 0.9513765

00:04:13.575 --> 00:04:14.314 or localized?

NOTE Confidence: 0.91599095

00:04:17.870 --> 00:04:19.070 I wish I had answers

NOTE Confidence: 0.91599095

00:04:19.070 --> 00:04:19.729 to this.

NOTE Confidence: 0.96455026

00:04:20.270 --> 00:04:21.389 I wish I had answers

NOTE Confidence: 0.96455026

00:04:21.389 --> 00:04:22.449 to these questions.

NOTE Confidence: 0.91289955

00:04:23.150 --> 00:04:24.750 The protein is sort of

NOTE Confidence: 0.91289955

00:04:24.750 --> 00:04:25.250 ubiquitously

NOTE Confidence: 0.9008019

00:04:25.790 --> 00:04:27.310 expressed in the brain, so

NOTE Confidence: 0.9008019

00:04:27.310 --> 00:04:28.750 there is not something that

NOTE Confidence: 0.9008019

00:04:28.750 --> 00:04:29.490 will explain.

NOTE Confidence: 0.9252918

00:04:29.854 --> 00:04:31.134 The idea is that maybe

NOTE Confidence: 0.9252918

00:04:31.134 --> 00:04:32.975 it's templated like Steve said

NOTE Confidence: 0.9252918

00:04:32.975 --> 00:04:34.514 in certain regions,

NOTE Confidence: 0.8895006

00:04:36.415 --> 00:04:38.255 sort of corresponding to Brock's

NOTE Confidence: 0.8895006

00:04:38.255 --> 00:04:40.755 staging. But, overall, that's a

NOTE Confidence: 0.8895006

00:04:40.895 --> 00:04:42.335 sort of this question of

NOTE Confidence: 0.8895006

00:04:42.335 --> 00:04:43.475 regional vulnerability

NOTE Confidence: 0.8286499

00:04:43.854 --> 00:04:44.514 is a

NOTE Confidence: 0.8315101

00:04:45.240 --> 00:04:46.920 question that's complex with us

NOTE Confidence: 0.8315101

00:04:46.920 --> 00:04:48.940 all, not just in Parkinson's,

NOTE Confidence: 0.8315101

00:04:49.160 --> 00:04:50.220 but in all neurodegenerative.

NOTE Confidence: 0.9655769

00:04:55.240 --> 00:04:56.600 Can I ask Pietro a

NOTE Confidence: 0.9655769

00:04:56.600 --> 00:04:58.220 question? Okay. Sure.

NOTE Confidence: 0.92765343

00:04:59.480 --> 00:05:01.125 So the the you said

NOTE Confidence: 0.92765343

00:05:01.125 --> 00:05:02.565 this is sort of an

NOTE Confidence: 0.92765343

00:05:02.565 --> 00:05:04.264 interplay between lysophagy

NOTE Confidence: 0.96098363

00:05:05.205 --> 00:05:06.104 and repair.

NOTE Confidence: 0.9846245

00:05:06.724 --> 00:05:07.625 And so

NOTE Confidence: 0.9887108

00:05:08.324 --> 00:05:09.384 how is that

NOTE Confidence: 0.9643571

00:05:09.685 --> 00:05:10.345 sort of

NOTE Confidence: 0.81923884

00:05:10.805 --> 00:05:12.745 balance or point that point,

NOTE Confidence: 0.9378563

00:05:13.205 --> 00:05:13.705 regulate?

NOTE Confidence: 0.8906175

00:05:15.279 --> 00:05:16.160 Yeah. First of all, I'm

NOTE Confidence: 0.8906175

00:05:16.160 --> 00:05:17.440 not sure whether it's correct

NOTE Confidence: 0.8906175

00:05:17.440 --> 00:05:18.800 to say balance. It is

NOTE Confidence: 0.8906175

00:05:18.800 --> 00:05:19.839 either or. You know? It's

NOTE Confidence: 0.8906175

00:05:19.839 --> 00:05:20.960 just too much damage to

NOTE Confidence: 0.8906175

00:05:20.960 --> 00:05:21.699 go to isophagy.

NOTE Confidence: 0.98940367

00:05:22.479 --> 00:05:22.979 And,

NOTE Confidence: 0.9341479

00:05:24.639 --> 00:05:25.680 yeah, I don't I don't

NOTE Confidence: 0.9341479

00:05:25.680 --> 00:05:26.720 have a good answer. I

NOTE Confidence: 0.9341479

00:05:26.720 --> 00:05:28.320 guess if it's eventually, it

NOTE Confidence: 0.9341479

00:05:28.320 --> 00:05:29.220 doesn't repair,

NOTE Confidence: 0.88233453

00:05:30.665 --> 00:05:31.625 it goes into the Do

NOTE Confidence: 0.88233453

00:05:31.625 --> 00:05:32.365 you see that?

NOTE Confidence: 0.90265477

00:05:32.745 --> 00:05:34.105 Do you see that? If

NOTE Confidence: 0.90265477

00:05:34.105 --> 00:05:35.005 you don't repair,

NOTE Confidence: 0.8359304

00:05:35.705 --> 00:05:36.585 I see Yes. For sure.

NOTE Confidence: 0.8359304

00:05:36.585 --> 00:05:37.325 There is.

NOTE Confidence: 0.9228845

00:05:37.945 --> 00:05:39.085 No. No. No. There is.

NOTE Confidence: 0.9228845

00:05:39.225 --> 00:05:40.345 But if you don't repair,

NOTE Confidence: 0.9228845

00:05:40.345 --> 00:05:42.045 are you moving the balance?

NOTE Confidence: 0.9224616

00:05:43.900 --> 00:05:45.660 I I I I let's

NOTE Confidence: 0.9224616

00:05:45.660 --> 00:05:47.039 say, I don't have experiment

NOTE Confidence: 0.9224616

00:05:47.099 --> 00:05:48.000 to show that

NOTE Confidence: 0.91661555

00:05:48.380 --> 00:05:49.900 since there is lysophagy and

NOTE Confidence: 0.91661555

00:05:49.900 --> 00:05:50.720 there is repair,

NOTE Confidence: 0.88689077

00:05:51.900 --> 00:05:53.339 I assume that it's either

NOTE Confidence: 0.88689077

00:05:53.339 --> 00:05:54.460 or. But we we never

NOTE Confidence: 0.88689077

00:05:54.460 --> 00:05:55.759 really look into that

NOTE Confidence: 0.9507353

00:05:56.300 --> 00:05:57.839 direct. Good point.

NOTE Confidence: 0.9424284

00:05:59.065 --> 00:06:00.105 I guess that raises the

NOTE Confidence: 0.9424284

00:06:00.105 --> 00:06:01.245 question. Is

NOTE Confidence: 0.9783933

00:06:02.185 --> 00:06:02.685 lysosomal

NOTE Confidence: 0.9997701

00:06:03.145 --> 00:06:03.645 repair

NOTE Confidence: 0.9470625

00:06:04.985 --> 00:06:05.485 a

NOTE Confidence: 0.87726295

00:06:06.505 --> 00:06:08.605 an an interesting therapeutic target

NOTE Confidence: 0.9799148

00:06:09.305 --> 00:06:10.605 in your mind for Parkinson's

NOTE Confidence: 0.9799148

00:06:10.745 --> 00:06:12.345 disease? Yeah. I thought a

NOTE Confidence: 0.9799148

00:06:12.345 --> 00:06:13.885 lot about this, and

NOTE Confidence: 0.9846315

00:06:16.480 --> 00:06:17.780 I cannot imagine

NOTE Confidence: 0.9758633

00:06:18.400 --> 00:06:19.600 I mean, I find I

NOTE Confidence: 0.9758633

00:06:19.600 --> 00:06:21.200 would find very difficult to

NOTE Confidence: 0.9758633

00:06:21.200 --> 00:06:22.400 think that we could find

NOTE Confidence: 0.9758633

00:06:22.400 --> 00:06:22.980 a way

NOTE Confidence: 0.911277

00:06:23.280 --> 00:06:24.960 to repair lysosome with the

NOTE Confidence: 0.911277

00:06:24.960 --> 00:06:27.645 magic bullet. I think, however,

NOTE Confidence: 0.911277

00:06:27.645 --> 00:06:29.325 these data suggest that anything

NOTE Confidence: 0.911277

00:06:29.325 --> 00:06:30.845 you can do to avoid

NOTE Confidence: 0.911277

00:06:30.845 --> 00:06:31.904 lysosomal damage

NOTE Confidence: 0.9831946

00:06:32.445 --> 00:06:33.345 can be beneficial.

NOTE Confidence: 0.9392017

00:06:33.964 --> 00:06:35.725 And so you can imagine

NOTE Confidence: 0.9392017

00:06:35.725 --> 00:06:36.464 that environmental

NOTE Confidence: 0.9738569

00:06:36.925 --> 00:06:37.425 factor

NOTE Confidence: 0.95001566

00:06:38.205 --> 00:06:39.985 that affect lysosome biology,

NOTE Confidence: 0.9255365

00:06:40.365 --> 00:06:42.705 including defection diseases, etcetera,

NOTE Confidence: 0.99910575

00:06:43.540 --> 00:06:44.040 may

NOTE Confidence: 0.8667013

00:06:44.340 --> 00:06:46.120 result in damage of lysosome.

NOTE Confidence: 0.8667013

00:06:46.260 --> 00:06:47.080 So I think

NOTE Confidence: 0.87252927

00:06:47.460 --> 00:06:48.500 with the the kind of

NOTE Confidence: 0.87252927

00:06:48.500 --> 00:06:49.400 data I showed

NOTE Confidence: 0.9537273

00:06:50.340 --> 00:06:51.540 suggest more than what we

NOTE Confidence: 0.9537273

00:06:51.540 --> 00:06:52.660 have to think about is

NOTE Confidence: 0.9537273

00:06:52.660 --> 00:06:54.280 how can we avoid lysosomal

NOTE Confidence: 0.9537273

00:06:54.420 --> 00:06:54.920 damage

NOTE Confidence: 0.98085475

00:06:55.345 --> 00:06:56.464 rather than think that we

NOTE Confidence: 0.98085475

00:06:56.464 --> 00:06:58.464 have a a a pill

NOTE Confidence: 0.98085475

00:06:58.464 --> 00:06:59.205 that you

NOTE Confidence: 0.8494878

00:06:59.505 --> 00:07:00.945 that you could take and

NOTE Confidence: 0.8494878

00:07:00.945 --> 00:07:02.065 then you'll you'll rescue your

NOTE Confidence: 0.8494878

00:07:02.065 --> 00:07:03.285 lysosome. Yeah.

NOTE Confidence: 0.70801073

00:07:05.985 --> 00:07:07.585 Sean? Floor, is there go

NOTE Confidence: 0.70801073

00:07:07.585 --> 00:07:08.085 ahead.

NOTE Confidence: 0.9902517

00:07:09.180 --> 00:07:10.300 I should be thinking a

NOTE Confidence: 0.9902517

00:07:10.300 --> 00:07:11.660 lot about this question. So

NOTE Confidence: 0.9902517

00:07:11.980 --> 00:07:13.740 Mhmm. Yeah. So my my

NOTE Confidence: 0.9902517

00:07:13.740 --> 00:07:15.600 comment on that question was

NOTE Confidence: 0.38462263

00:07:16.940 --> 00:07:17.180 the

NOTE Confidence: 0.9919265

00:07:18.140 --> 00:07:20.060 I'm very curious about what's

NOTE Confidence: 0.9919265

00:07:20.060 --> 00:07:20.960 gonna happen,

NOTE Confidence: 0.94768345

00:07:21.895 --> 00:07:24.255 with ongoing clinical trials related

NOTE Confidence: 0.94768345

00:07:24.255 --> 00:07:25.855 to LRRK two inhibitors or

NOTE Confidence: 0.94768345

00:07:25.855 --> 00:07:27.535 just further development of that

NOTE Confidence: 0.94768345

00:07:27.535 --> 00:07:29.475 pathway because in looking at,

NOTE Confidence: 0.93218434

00:07:30.415 --> 00:07:32.035 first, how LRRK two,

NOTE Confidence: 0.9997814

00:07:32.815 --> 00:07:33.315 mutations

NOTE Confidence: 0.93076116

00:07:34.170 --> 00:07:35.470 what they're doing to lysosomes

NOTE Confidence: 0.93076116

00:07:35.610 --> 00:07:37.610 as Pietro showed there with

NOTE Confidence: 0.93076116

00:07:37.610 --> 00:07:39.930 the VBS thirteen c. More

NOTE Confidence: 0.93076116

00:07:39.930 --> 00:07:41.770 LRRK two kinase activity makes

NOTE Confidence: 0.93076116

00:07:41.770 --> 00:07:42.270 lysosomes

NOTE Confidence: 0.9187134

00:07:42.810 --> 00:07:44.010 apparent seems to be more

NOTE Confidence: 0.9187134

00:07:44.010 --> 00:07:44.510 fragile.

NOTE Confidence: 0.9932276

00:07:45.050 --> 00:07:46.810 And when we genetically deplete

NOTE Confidence: 0.9932276

00:07:46.810 --> 00:07:47.630 it or pharmacologically

NOTE Confidence: 0.99971

00:07:48.090 --> 00:07:48.590 inhibit

NOTE Confidence: 0.9979951

00:07:49.055 --> 00:07:50.415 by various measures in a

NOTE Confidence: 0.9979951

00:07:50.415 --> 00:07:51.395 dish, the lysosomes

NOTE Confidence: 0.98962474

00:07:51.935 --> 00:07:52.595 look better.

NOTE Confidence: 0.9608541

00:07:53.215 --> 00:07:54.495 And so there may be

NOTE Confidence: 0.9608541

00:07:54.495 --> 00:07:56.335 opportunities there for LRRK two

NOTE Confidence: 0.9608541

00:07:56.335 --> 00:07:58.175 inhibition to make lysosomes, if

NOTE Confidence: 0.9608541

00:07:58.175 --> 00:08:00.095 not, more repairable, but more

NOTE Confidence: 0.9608541

00:08:00.095 --> 00:08:01.555 durable in the first place.

NOTE Confidence: 0.9009593

00:08:03.884 --> 00:08:04.925 Thank you. And I guess

NOTE Confidence: 0.9009593

00:08:04.925 --> 00:08:05.985 on that note,

NOTE Confidence: 0.9962729

00:08:06.525 --> 00:08:07.720 our time is up.