

WEBVTT

NOTE duration:"00:07:15.6800000"

NOTE language:en-us

NOTE Confidence: 0.8662191

00:00:02.480 --> 00:00:04.355 Hello, thank you for coming

NOTE Confidence: 0.8662191

00:00:04.355 --> 00:00:05.855 to my virtual poster.

NOTE Confidence: 0.8662191

00:00:05.860 --> 00:00:07.760 It's great to have the

NOTE Confidence: 0.8662191

00:00:07.760 --> 00:00:09.660 opportunity to tell you about

NOTE Confidence: 0.8662191

00:00:09.741 --> 00:00:12.226 the research that my lab is doing.

NOTE Confidence: 0.8662191

00:00:12.230 --> 00:00:14.186 We use zebrafish as a model

NOTE Confidence: 0.8662191

00:00:14.186 --> 00:00:16.421 system to help us to understand

NOTE Confidence: 0.8662191

00:00:16.421 --> 00:00:18.977 more about the biology of autism.

NOTE Confidence: 0.8662191

00:00:18.980 --> 00:00:22.058 So just walk you through my poster to so

NOTE Confidence: 0.8662191

00:00:22.058 --> 00:00:25.359 to give you a little bit of background.

NOTE Confidence: 0.8662191

00:00:25.360 --> 00:00:26.539 In recent years,

NOTE Confidence: 0.8662191

00:00:26.539 --> 00:00:28.504 we've identified over 100 genes

NOTE Confidence: 0.8662191

00:00:28.504 --> 00:00:30.250 that are strongly associated

NOTE Confidence: 0.8662191

00:00:30.250 --> 00:00:32.465 with the risk for autism.

NOTE Confidence: 0.8662191

00:00:32.470 --> 00:00:34.846 But we really don't have an

NOTE Confidence: 0.8662191

00:00:34.846 --> 00:00:36.430 understanding of what these

NOTE Confidence: 0.8662191

00:00:36.510 --> 00:00:38.886 genes do in the developing brain,

NOTE Confidence: 0.8662191

00:00:38.890 --> 00:00:41.869 and so our goal is to to use a

NOTE Confidence: 0.8662191

00:00:41.869 --> 00:00:43.538 relatively simple nervous system

NOTE Confidence: 0.8662191

00:00:43.538 --> 00:00:46.996 model system to try to help us to

NOTE Confidence: 0.8662191

00:00:46.996 --> 00:00:49.176 understand more about what these

NOTE Confidence: 0.8662191

00:00:49.176 --> 00:00:51.540 jeans are doing in the developing

NOTE Confidence: 0.8662191

00:00:51.540 --> 00:00:54.020 vertebrate brain as a path to gain a

NOTE Confidence: 0.8662191

00:00:54.086 --> 00:00:55.941 better understanding of the biology

NOTE Confidence: 0.8662191

00:00:55.941 --> 00:00:58.530 of autism and to possibly develop

NOTE Confidence: 0.8662191

00:00:58.530 --> 00:01:00.537 improved pharmacological treatments.

NOTE Confidence: 0.8662191

00:01:00.540 --> 00:01:02.946 So why do we study zebrafish?

NOTE Confidence: 0.8662191

00:01:02.950 --> 00:01:05.350 There are really three key advantages.

NOTE Confidence: 0.8662191

00:01:05.350 --> 00:01:05.808 One.

NOTE Confidence: 0.8662191

00:01:05.808 --> 00:01:07.640 They have external development
NOTE Confidence: 0.8662191

00:01:07.640 --> 00:01:09.930 of transparent embryos so they're
NOTE Confidence: 0.8662191

00:01:10.003 --> 00:01:11.199 fully transparent,
NOTE Confidence: 0.8662191

00:01:11.200 --> 00:01:15.960 so we can visualize in real time what it is.
NOTE Confidence: 0.8662191

00:01:15.960 --> 00:01:17.780 A developing vertebrate brain.
NOTE Confidence: 0.8662191

00:01:17.780 --> 00:01:20.055 We can visualize basic neural
NOTE Confidence: 0.8662191

00:01:20.055 --> 00:01:21.190 developmental processes.
NOTE Confidence: 0.8662191

00:01:21.190 --> 00:01:23.570 Second, zebrafish are highly tractable,
NOTE Confidence: 0.8662191

00:01:23.570 --> 00:01:26.545 so they're easy for to use for
NOTE Confidence: 0.8662191

00:01:26.545 --> 00:01:28.997 performing large scale drug screens
NOTE Confidence: 0.8662191

00:01:28.997 --> 00:01:31.189 to identify novel compounds.
NOTE Confidence: 0.8662191

00:01:31.190 --> 00:01:32.070 And finally,
NOTE Confidence: 0.8662191

00:01:32.070 --> 00:01:34.270 with the introduction of crisper
NOTE Confidence: 0.8662191

00:01:34.270 --> 00:01:37.030 as a gene targeting method.
NOTE Confidence: 0.8662191

00:01:37.030 --> 00:01:39.580 It's possible to to easily genetically
NOTE Confidence: 0.8662191

00:01:39.580 --> 00:01:41.692 manipulate the zebrafish so that

NOTE Confidence: 0.8662191
00:01:41.692 --> 00:01:43.738 we can disrupt the function of
NOTE Confidence: 0.8662191
00:01:43.738 --> 00:01:45.220 these autism risk genes.
NOTE Confidence: 0.8662191
00:01:45.220 --> 00:01:46.504 And to date,
NOTE Confidence: 0.8662191
00:01:46.504 --> 00:01:48.644 my lab has already generated
NOTE Confidence: 0.8662191
00:01:48.644 --> 00:01:51.264 zebrafish mutants in at least 10
NOTE Confidence: 0.8662191
00:01:51.264 --> 00:01:52.948 different high confidence autism
NOTE Confidence: 0.8662191
00:01:52.948 --> 00:01:55.698 risk genes and so to give you an
NOTE Confidence: 0.8662191
00:01:55.698 --> 00:01:57.282 over overview of the workflow,
NOTE Confidence: 0.8662191
00:01:57.282 --> 00:02:00.178 if you look at the central panel and
NOTE Confidence: 0.8662191
00:02:00.178 --> 00:02:03.132 the idea is that we generate these
NOTE Confidence: 0.8662191
00:02:03.132 --> 00:02:05.297 zebrafish mutants that lack the
NOTE Confidence: 0.8662191
00:02:05.297 --> 00:02:07.775 function of these autism risk genes.
NOTE Confidence: 0.8662191
00:02:07.780 --> 00:02:10.288 And then we take advantage of
NOTE Confidence: 0.8662191
00:02:10.288 --> 00:02:11.542 their transparent embryos.
NOTE Confidence: 0.8662191
00:02:11.550 --> 00:02:14.268 The ability to visualize the entire
NOTE Confidence: 0.8662191

00:02:14.268 --> 00:02:16.531 brain during development so that
NOTE Confidence: 0.8662191

00:02:16.531 --> 00:02:19.149 we can see how the disruption of
NOTE Confidence: 0.8662191

00:02:19.149 --> 00:02:21.408 these specific genes affects the
NOTE Confidence: 0.8662191

00:02:21.408 --> 00:02:24.282 development of specific neural cell types.
NOTE Confidence: 0.8662191

00:02:24.290 --> 00:02:26.648 And then we can also perform
NOTE Confidence: 0.8662191

00:02:26.648 --> 00:02:28.719 these large scale behavior based
NOTE Confidence: 0.8662191

00:02:28.719 --> 00:02:31.287 drug screens where we can pipette
NOTE Confidence: 0.8662191

00:02:31.287 --> 00:02:33.679 individual fish into the wells of
NOTE Confidence: 0.8662191

00:02:33.679 --> 00:02:36.080 a 96 well plate and track different
NOTE Confidence: 0.8662191

00:02:36.080 --> 00:02:38.005 aspects of their locomotor activity
NOTE Confidence: 0.8662191

00:02:38.005 --> 00:02:40.787 and ask how that changes when these
NOTE Confidence: 0.8662191

00:02:40.787 --> 00:02:43.145 autism risk genes are not functioning.
NOTE Confidence: 0.8662191

00:02:43.150 --> 00:02:45.508 So how does this affect as
NOTE Confidence: 0.8662191

00:02:45.508 --> 00:02:46.687 simple behavioral circuits?
NOTE Confidence: 0.8662191

00:02:46.690 --> 00:02:48.986 And then we can use this as the
NOTE Confidence: 0.8662191

00:02:48.986 --> 00:02:50.685 basis for screening different

NOTE Confidence: 0.8662191
00:02:50.685 --> 00:02:52.785 compounds to identify potential
NOTE Confidence: 0.8662191
00:02:52.785 --> 00:02:55.788 drug candidates that we could then
NOTE Confidence: 0.8662191
00:02:55.788 --> 00:02:58.260 test further in the million systems.
NOTE Confidence: 0.8662191
00:02:58.260 --> 00:03:00.340 And so here's an overview.
NOTE Confidence: 0.8662191
00:03:00.340 --> 00:03:03.000 What we're doing in terms of the
NOTE Confidence: 0.8662191
00:03:03.000 --> 00:03:04.920 aims of our project.
NOTE Confidence: 0.8662191
00:03:04.920 --> 00:03:07.209 We were going to use all these
NOTE Confidence: 0.8662191
00:03:07.209 --> 00:03:09.186 autism risk gene mutants identified
NOTE Confidence: 0.8662191
00:03:09.186 --> 00:03:11.486 differences in their brain structures
NOTE Confidence: 0.8662191
00:03:11.486 --> 00:03:14.295 so we can understand more about
NOTE Confidence: 0.8662191
00:03:14.295 --> 00:03:16.560 how these genes affect effect.
NOTE Confidence: 0.8662191
00:03:16.560 --> 00:03:17.724 Overall, brain development,
NOTE Confidence: 0.8662191
00:03:17.724 --> 00:03:20.898 brain structure and to see if we can
NOTE Confidence: 0.8662191
00:03:20.898 --> 00:03:22.868 identify commonality's in terms of
NOTE Confidence: 0.8662191
00:03:22.868 --> 00:03:25.591 how these genes affect affect brain
NOTE Confidence: 0.8662191

00:03:25.591 --> 00:03:28.018 development. Second, we're going to.
NOTE Confidence: 0.8662191

00:03:28.018 --> 00:03:29.434 As I said,
NOTE Confidence: 0.8269625

00:03:29.440 --> 00:03:32.198 do large scale drug screens to identify
NOTE Confidence: 0.8269625

00:03:32.198 --> 00:03:34.711 compounds that might that might reverse
NOTE Confidence: 0.8269625

00:03:34.711 --> 00:03:37.651 abnormalities in the behaviors of these fish.
NOTE Confidence: 0.8269625

00:03:37.660 --> 00:03:40.537 So we look at very simple behaviors
NOTE Confidence: 0.8269625

00:03:40.537 --> 00:03:42.596 like rest, wake behavior, rest,
NOTE Confidence: 0.8269625

00:03:42.596 --> 00:03:44.455 wake circuitry, and visual startle
NOTE Confidence: 0.8269625

00:03:44.455 --> 00:03:46.525 circuitry as a readout of looking
NOTE Confidence: 0.8269625

00:03:46.525 --> 00:03:48.759 at sensory processing behaviors.
NOTE Confidence: 0.8269625

00:03:48.760 --> 00:03:50.755 And finally, because zebrafish are
NOTE Confidence: 0.8269625

00:03:50.755 --> 00:03:53.236 fully transparent and they have a
NOTE Confidence: 0.8269625

00:03:53.236 --> 00:03:54.928 relatively simple nervous system,
NOTE Confidence: 0.8269625

00:03:54.930 --> 00:03:57.898 we can visualize changes in brain activity.
NOTE Confidence: 0.8269625

00:03:57.900 --> 00:04:00.875 In real time in awake behaving zebrafish,
NOTE Confidence: 0.8269625

00:04:00.880 --> 00:04:03.814 I'm using a new microscope technology

NOTE Confidence: 0.8269625

00:04:03.814 --> 00:04:06.910 that my lab is developing.

NOTE Confidence: 0.8269625

00:04:06.910 --> 00:04:09.118 And so I'll take you over

NOTE Confidence: 0.8269625

00:04:09.118 --> 00:04:11.200 to the right hand panel,

NOTE Confidence: 0.8269625

00:04:11.200 --> 00:04:13.510 take you through some of our our

NOTE Confidence: 0.8269625

00:04:13.510 --> 00:04:16.000 results so some of our published data

NOTE Confidence: 0.8269625

00:04:16.000 --> 00:04:18.688 has shown that when we disrupt one

NOTE Confidence: 0.8269625

00:04:18.688 --> 00:04:20.560 particular gene that's associated

NOTE Confidence: 0.8269625

00:04:20.560 --> 00:04:22.900 with both autism and epilepsy,

NOTE Confidence: 0.8269625

00:04:22.900 --> 00:04:24.300 contacta associated protein two,

NOTE Confidence: 0.8269625

00:04:24.300 --> 00:04:25.700 that this this disruption

NOTE Confidence: 0.8269625

00:04:25.700 --> 00:04:27.190 leads to abnormalities,

NOTE Confidence: 0.8269625

00:04:27.190 --> 00:04:28.360 particularly in inhibitory

NOTE Confidence: 0.8269625

00:04:28.360 --> 00:04:29.920 neurons in the forebrain.

NOTE Confidence: 0.8269625

00:04:29.920 --> 00:04:32.461 So what you're looking at here are

NOTE Confidence: 0.8269625

00:04:32.461 --> 00:04:34.910 transgenic lines that allow us to

NOTE Confidence: 0.8269625

00:04:34.910 --> 00:04:37.060 visualize these different populations of.

NOTE Confidence: 0.8269625

00:04:37.060 --> 00:04:39.028 Nerve cells and what we can see is

NOTE Confidence: 0.8269625

00:04:39.028 --> 00:04:41.252 that in the forebrain when we disrupt

NOTE Confidence: 0.8269625

00:04:41.252 --> 00:04:43.570 the function of this autism risk gene,

NOTE Confidence: 0.8269625

00:04:43.570 --> 00:04:46.265 it leads to a loss of these

NOTE Confidence: 0.8269625

00:04:46.265 --> 00:04:47.035 inhibitory neurons.

NOTE Confidence: 0.8269625

00:04:47.040 --> 00:04:49.248 I'm second in the same fish.

NOTE Confidence: 0.8269625

00:04:49.250 --> 00:04:51.296 We performed a large scale behavior

NOTE Confidence: 0.8269625

00:04:51.296 --> 00:04:53.680 based drug screen and interesting Lee.

NOTE Confidence: 0.8269625

00:04:53.680 --> 00:04:55.702 What we found was that drugs

NOTE Confidence: 0.8269625

00:04:55.702 --> 00:04:57.503 that had estrogenic activity were

NOTE Confidence: 0.8269625

00:04:57.503 --> 00:04:59.453 able to suppress the behavioral

NOTE Confidence: 0.8269625

00:04:59.453 --> 00:05:01.447 abnormalities in these mutant fish

NOTE Confidence: 0.8269625

00:05:01.447 --> 00:05:03.649 and so specifically we finally found

NOTE Confidence: 0.8269625

00:05:03.649 --> 00:05:06.222 that disrupting this gene led to a

NOTE Confidence: 0.8269625

00:05:06.222 --> 00:05:07.694 phenotype of nighttime hyperactivity.

NOTE Confidence: 0.8269625

00:05:07.700 --> 00:05:09.674 So these fish were two active

NOTE Confidence: 0.8269625

00:05:09.674 --> 00:05:12.083 during the night and what we found

NOTE Confidence: 0.8269625

00:05:12.083 --> 00:05:14.135 through our screen was that drugs

NOTE Confidence: 0.8269625

00:05:14.135 --> 00:05:16.486 that had estrogenic activity were

NOTE Confidence: 0.8269625

00:05:16.486 --> 00:05:18.426 able to specifically suppress.

NOTE Confidence: 0.8269625

00:05:18.430 --> 00:05:20.686 That phenotype and so now through

NOTE Confidence: 0.8269625

00:05:20.686 --> 00:05:22.190 collaborations we are testing

NOTE Confidence: 0.8269625

00:05:22.250 --> 00:05:24.504 these drugs in a mouse model of

NOTE Confidence: 0.8269625

00:05:24.504 --> 00:05:26.010 contact and associated protein.

NOTE Confidence: 0.8269625

00:05:26.010 --> 00:05:28.327 Two to see if this candidate molecule

NOTE Confidence: 0.8269625

00:05:28.327 --> 00:05:30.175 that we identify Nurse screen

NOTE Confidence: 0.8269625

00:05:30.175 --> 00:05:32.145 can translate 2 million systems.

NOTE Confidence: 0.8269625

00:05:32.150 --> 00:05:34.436 And finally we're now looking across

NOTE Confidence: 0.8269625

00:05:34.436 --> 00:05:36.621 all of our different autism risk

NOTE Confidence: 0.8269625

00:05:36.621 --> 00:05:39.447 gene mutants to try to see if we can

NOTE Confidence: 0.8269625

00:05:39.447 --> 00:05:42.254 identify what we call points of convergence.

NOTE Confidence: 0.8269625

00:05:42.260 --> 00:05:44.325 Can we see similarities in the way

NOTE Confidence: 0.8269625

00:05:44.325 --> 00:05:46.216 that these genes affect simple

NOTE Confidence: 0.8269625

00:05:46.216 --> 00:05:48.566 behavioral circuits at the behavioral

NOTE Confidence: 0.8269625

00:05:48.566 --> 00:05:49.506 circuits controlling?

NOTE Confidence: 0.8269625

00:05:49.510 --> 00:05:50.142 The processing,

NOTE Confidence: 0.8269625

00:05:50.142 --> 00:05:53.156 and So what we're able to do is identify

NOTE Confidence: 0.8269625

00:05:53.156 --> 00:05:55.658 what we call a behavioral fingerprint

NOTE Confidence: 0.8269625

00:05:55.658 --> 00:05:58.066 for each mutant associated with the

NOTE Confidence: 0.8269625

00:05:58.066 --> 00:06:00.607 loss of function of each risk gene

NOTE Confidence: 0.8269625

00:06:00.610 --> 00:06:02.460 using very simple behavioral assays.

NOTE Confidence: 0.8269625

00:06:02.460 --> 00:06:03.591 Looking at rest,

NOTE Confidence: 0.8269625

00:06:03.591 --> 00:06:05.476 wake activity or visual startle

NOTE Confidence: 0.8269625

00:06:05.476 --> 00:06:07.654 activity to begin to identify ways

NOTE Confidence: 0.8269625

00:06:07.654 --> 00:06:09.688 in which these genes affect the

NOTE Confidence: 0.8269625

00:06:09.759 --> 00:06:11.709 nervous system in similar ways,

NOTE Confidence: 0.8269625

00:06:11.710 --> 00:06:13.985 and we're going to use these points

NOTE Confidence: 0.8269625

00:06:13.985 --> 00:06:15.830 of conversions and these behavioral

NOTE Confidence: 0.8269625

00:06:15.830 --> 00:06:18.248 fingerprints as a way of identifying

NOTE Confidence: 0.8269625

00:06:18.248 --> 00:06:20.018 potential new pharmacological candidates

NOTE Confidence: 0.8269625

00:06:20.018 --> 00:06:23.154 that we're currently testing in the lab.

NOTE Confidence: 0.8269625

00:06:23.160 --> 00:06:25.440 And in terms of the future

NOTE Confidence: 0.8269625

00:06:25.440 --> 00:06:26.960 directions of the work,

NOTE Confidence: 0.8269625

00:06:26.960 --> 00:06:29.048 we're now testing compounds that we

NOTE Confidence: 0.8269625

00:06:29.048 --> 00:06:31.243 think could be potential drug candidates

NOTE Confidence: 0.8269625

00:06:31.243 --> 00:06:33.098 that target these neural circuit

NOTE Confidence: 0.8269625

00:06:33.098 --> 00:06:35.319 deficits in the zebrafish mutants.

NOTE Confidence: 0.8269625

00:06:35.320 --> 00:06:37.498 And we're developing an in collaboration

NOTE Confidence: 0.8269625

00:06:37.498 --> 00:06:40.258 with the Yale Center for Neuro Technology,

NOTE Confidence: 0.8269625

00:06:40.260 --> 00:06:42.612 and you two photon light sheet

NOTE Confidence: 0.8269625

00:06:42.612 --> 00:06:44.180 microscope that will allow

NOTE Confidence: 0.850215

00:06:44.253 --> 00:06:47.286 us to image the entire brain of an awake
NOTE Confidence: 0.850215

00:06:47.286 --> 00:06:49.760 behaving zebrafish in under one second.
NOTE Confidence: 0.850215

00:06:49.760 --> 00:06:53.280 With the idea that it can help us to identify
NOTE Confidence: 0.850215

00:06:53.363 --> 00:06:56.338 circuit mechanisms that are disrupted.
NOTE Confidence: 0.850215

00:06:56.340 --> 00:06:58.250 When these autism risk genes
NOTE Confidence: 0.850215

00:06:58.250 --> 00:06:59.778 are not functioning properly,
NOTE Confidence: 0.850215

00:06:59.780 --> 00:07:02.500 so I want to 1st thank funding sources
NOTE Confidence: 0.850215

00:07:02.500 --> 00:07:05.217 of which the support and the Child
NOTE Confidence: 0.850215

00:07:05.217 --> 00:07:07.649 Study Center for the support for
NOTE Confidence: 0.850215

00:07:07.649 --> 00:07:10.435 this research and thank you very much
NOTE Confidence: 0.850215

00:07:10.435 --> 00:07:12.768 for listening to my virtual poster.