

WEBVTT

NOTE duration:"01:19:55.6160000"

NOTE language:en-us

NOTE Confidence: 0.8092062

00:00:00.000 --> 00:00:04.928 I first was introduced to Doctor Bale.

NOTE Confidence: 0.8092062

00:00:04.930 --> 00:00:08.120 Uh, maybe 5 six years ago at SFN I heard

NOTE Confidence: 0.8092062

00:00:08.203 --> 00:00:11.011 her give a talk at a women's symposium

NOTE Confidence: 0.8092062

00:00:11.011 --> 00:00:14.105 and I have to say I was mesmerized.

NOTE Confidence: 0.8092062

00:00:14.110 --> 00:00:16.926 There were a lot of strong women speakers,

NOTE Confidence: 0.8092062

00:00:16.930 --> 00:00:20.575 but I had an impression on me and so

NOTE Confidence: 0.8092062

00:00:20.575 --> 00:00:23.869 followed work for a few years and asked.

NOTE Confidence: 0.8092062

00:00:23.870 --> 00:00:25.868 To actually be able to come and give a

NOTE Confidence: 0.8092062

00:00:25.868 --> 00:00:27.896 grand rounds talk at Yale and between

NOTE Confidence: 0.8092062

00:00:27.896 --> 00:00:30.010 our schedules, this was over a year ago,

NOTE Confidence: 0.8092062

00:00:30.010 --> 00:00:34.830 so now she's finally. Here, Sortof.

NOTE Confidence: 0.8092062

00:00:34.830 --> 00:00:37.273 Seattle is a professor pharmacology and drug

NOTE Confidence: 0.8092062

00:00:37.273 --> 00:00:40.074 tour of the center of epigenetic research

NOTE Confidence: 0.8092062

00:00:40.074 --> 00:00:42.612 in child health and brain development.

NOTE Confidence: 0.8092062

00:00:42.620 --> 00:00:45.532 In the School of Medicine and yelling

NOTE Confidence: 0.8092062

00:00:45.532 --> 00:00:48.558 at University of Maryland in Baltimore.

NOTE Confidence: 0.8092062

00:00:48.560 --> 00:00:51.464 She completed her PhD University of

NOTE Confidence: 0.8092062

00:00:51.464 --> 00:00:53.400 Washington Department of pharmacology

NOTE Confidence: 0.8092062

00:00:53.471 --> 00:00:55.491 and her postdoctoral work at

NOTE Confidence: 0.8092062

00:00:55.491 --> 00:00:57.511 Salk Institute with doctor Vail.

NOTE Confidence: 0.8092062

00:00:57.520 --> 00:00:59.760 Doctor bail was Professor Neuroscience,

NOTE Confidence: 0.8092062

00:00:59.760 --> 00:01:01.281 an onion soup,

NOTE Confidence: 0.8092062

00:01:01.281 --> 00:01:04.830 and city in 15 years before moving.

NOTE Confidence: 0.8092062

00:01:04.830 --> 00:01:06.980 Her research focuses on understanding

NOTE Confidence: 0.8092062

00:01:06.980 --> 00:01:10.089 the role of stress dysregulation in your

NOTE Confidence: 0.8092062

00:01:10.089 --> 00:01:12.324 developmental and your psychiatric disease.

NOTE Confidence: 0.8092062

00:01:12.330 --> 00:01:15.306 And the sex differences in underlying

NOTE Confidence: 0.8092062

00:01:15.306 --> 00:01:18.053 disease vulnerability in humans in using

NOTE Confidence: 0.8092062

00:01:18.053 --> 00:01:20.813 the mouse model as it the Monster Model

NOTE Confidence: 0.8092062

00:01:20.886 --> 00:01:23.688 she's interested in developing models of
NOTE Confidence: 0.8092062

00:01:23.688 --> 00:01:26.883 Parenteau stress and the germ cell movement.
NOTE Confidence: 0.8092062

00:01:26.883 --> 00:01:28.206 An intergenerational programming
NOTE Confidence: 0.8092062

00:01:28.206 --> 00:01:29.529 of newer development,
NOTE Confidence: 0.8092062

00:01:29.530 --> 00:01:32.176 she serves on many internal and
NOTE Confidence: 0.8092062

00:01:32.176 --> 00:01:33.499 external advisory committees,
NOTE Confidence: 0.8092062

00:01:33.500 --> 00:01:34.544 panels and boards.
NOTE Confidence: 0.8092062

00:01:34.544 --> 00:01:36.980 She's been the recipient of many many
NOTE Confidence: 0.8092062

00:01:37.043 --> 00:01:39.403 awards including early career award
NOTE Confidence: 0.8092062

00:01:39.403 --> 00:01:41.763 achievements by Society for neuroscience
NOTE Confidence: 0.8092062

00:01:41.829 --> 00:01:44.001 and exceptionally promising an
NOTE Confidence: 0.8092062

00:01:44.001 --> 00:01:46.173 investigator through Endocrine Society.
NOTE Confidence: 0.8092062

00:01:46.180 --> 00:01:47.010 And others,
NOTE Confidence: 0.8092062

00:01:47.010 --> 00:01:49.085 and especially Metro Matronic Award
NOTE Confidence: 0.8092062

00:01:49.085 --> 00:01:51.570 from Society of Women's Health for
NOTE Confidence: 0.8092062

00:01:51.570 --> 00:01:53.515 Outstanding Research that has led

NOTE Confidence: 0.8092062

00:01:53.515 --> 00:01:56.210 to the improvement of women's help.

NOTE Confidence: 0.8092062

00:01:56.210 --> 00:01:58.790 She was recently elected president

NOTE Confidence: 0.8092062

00:01:58.790 --> 00:02:01.370 of the international brain research

NOTE Confidence: 0.8092062

00:02:01.443 --> 00:02:04.327 organization and it's my honor to welcome

NOTE Confidence: 0.8092062

00:02:04.327 --> 00:02:07.337 doctor bill to give grand rounds here.

NOTE Confidence: 0.8092062

00:02:07.340 --> 00:02:08.540 Thanks so much,

NOTE Confidence: 0.8092062

00:02:08.540 --> 00:02:08.940 Irina,

NOTE Confidence: 0.8092062

00:02:08.940 --> 00:02:11.832 and thank you again for the invitation

NOTE Confidence: 0.8092062

00:02:11.832 --> 00:02:15.504 and I guess one of the benefits of Kovid

NOTE Confidence: 0.8092062

00:02:15.587 --> 00:02:18.611 if there can be any is that we're all

NOTE Confidence: 0.8092062

00:02:18.611 --> 00:02:21.659 sort of trapped at home with no travel,

NOTE Confidence: 0.8092062

00:02:21.660 --> 00:02:23.204 which makes availability of

NOTE Confidence: 0.8092062

00:02:23.204 --> 00:02:25.134 scheduling a little bit easier.

NOTE Confidence: 0.8092062

00:02:25.140 --> 00:02:27.360 I think I really excited to

NOTE Confidence: 0.8092062

00:02:27.360 --> 00:02:29.400 talk about our data today,

NOTE Confidence: 0.8092062

00:02:29.400 --> 00:02:32.018 and I think the Yale Psychiatry audience

NOTE Confidence: 0.8092062

00:02:32.018 --> 00:02:35.200 is just such a tremendous group of broad,

NOTE Confidence: 0.8092062

00:02:35.200 --> 00:02:36.436 basic clinical translation.

NOTE Confidence: 0.8092062

00:02:36.436 --> 00:02:38.496 Are researchers that makes this.

NOTE Confidence: 0.8092062

00:02:38.500 --> 00:02:41.116 Even more exciting for me to be able

NOTE Confidence: 0.8092062

00:02:41.116 --> 00:02:44.389 to talk science and the translation of

NOTE Confidence: 0.8092062

00:02:44.389 --> 00:02:47.700 potential, I think of the of the science,

NOTE Confidence: 0.8092062

00:02:47.700 --> 00:02:50.500 and I'd love to hear your feedback.

NOTE Confidence: 0.8092062

00:02:50.500 --> 00:02:51.562 So with that,

NOTE Confidence: 0.8092062

00:02:51.562 --> 00:02:54.507 I also know that because there is such

NOTE Confidence: 0.8092062

00:02:54.507 --> 00:02:57.195 a broad background of people on the

NOTE Confidence: 0.8092062

00:02:57.195 --> 00:02:59.827 zoom today that rather than waiting

NOTE Confidence: 0.8092062

00:02:59.827 --> 00:03:02.497 until the very end with questions.

NOTE Confidence: 0.8092062

00:03:02.500 --> 00:03:04.320 If there's something that really

NOTE Confidence: 0.8092062

00:03:04.320 --> 00:03:06.140 clarification would make my talk

NOTE Confidence: 0.8092062

00:03:06.196 --> 00:03:08.100 more digestible or understandable,

NOTE Confidence: 0.8092062

00:03:08.100 --> 00:03:09.195 please don't hesitate.

NOTE Confidence: 0.8092062

00:03:09.195 --> 00:03:11.020 To interrupt just for clarification,

NOTE Confidence: 0.8092062

00:03:11.020 --> 00:03:13.666 points 'cause I'm happy I'm happy to do that,

NOTE Confidence: 0.8092062

00:03:13.670 --> 00:03:16.376 especially for a grand wrong talk.

NOTE Confidence: 0.8092062

00:03:16.380 --> 00:03:19.691 The topic I decided to put together

NOTE Confidence: 0.8092062

00:03:19.691 --> 00:03:22.948 today encompass is a kind of a wide

NOTE Confidence: 0.8092062

00:03:22.948 --> 00:03:25.894 area of the research in my lab and

NOTE Confidence: 0.8092062

00:03:25.894 --> 00:03:28.470 the common theme is going to be

NOTE Confidence: 0.8719525

00:03:28.470 --> 00:03:30.485 about extracellular vesicles and it's

NOTE Confidence: 0.8719525

00:03:30.485 --> 00:03:32.784 actually a timely topic, I think.

NOTE Confidence: 0.8719525

00:03:32.784 --> 00:03:34.836 But it's also to me personally

NOTE Confidence: 0.8719525

00:03:34.836 --> 00:03:36.781 relevant to meaningful to Yale

NOTE Confidence: 0.8719525

00:03:36.781 --> 00:03:39.157 because the first time I started

NOTE Confidence: 0.8719525

00:03:39.157 --> 00:03:40.991 talking about these extracellular

NOTE Confidence: 0.8719525

00:03:40.991 --> 00:03:43.271 vesicles was actually about five

NOTE Confidence: 0.8719525

00:03:43.271 --> 00:03:46.896 years ago at the ACM P the American
NOTE Confidence: 0.8719525

00:03:46.896 --> 00:03:48.249 College of Neuropsychopharmacology.
NOTE Confidence: 0.8719525

00:03:48.250 --> 00:03:50.155 Meeting and in that session
NOTE Confidence: 0.8719525

00:03:50.155 --> 00:03:52.475 actually was was organized by one
NOTE Confidence: 0.8719525

00:03:52.475 --> 00:03:54.539 of the organizers was Ron Duman,
NOTE Confidence: 0.8719525

00:03:54.540 --> 00:03:56.610 and we had a great discussion
NOTE Confidence: 0.8719525

00:03:56.610 --> 00:03:58.444 afterwards and he was really
NOTE Confidence: 0.8719525

00:03:58.444 --> 00:04:01.097 intrigued and excited by this idea of
NOTE Confidence: 0.8719525

00:04:01.097 --> 00:04:03.417 these extra set of their vesicles,
NOTE Confidence: 0.8719525

00:04:03.420 --> 00:04:06.220 and so to me it's very meaningful to
NOTE Confidence: 0.8719525

00:04:06.220 --> 00:04:08.598 be discussing this with the audience.
NOTE Confidence: 0.8719525

00:04:08.600 --> 00:04:10.430 Again thinking of Ron missing
NOTE Confidence: 0.8719525

00:04:10.430 --> 00:04:13.433 him so much so many I know it's
NOTE Confidence: 0.8719525

00:04:13.433 --> 00:04:14.885 a Yale and psychiatry,
NOTE Confidence: 0.8719525

00:04:14.890 --> 00:04:16.804 especially their interested in stress as
NOTE Confidence: 0.8719525

00:04:16.804 --> 00:04:19.329 it relates to nuro psychiatric disorders,

NOTE Confidence: 0.8719525

00:04:19.330 --> 00:04:22.258 so I hope that you find.

NOTE Confidence: 0.8719525

00:04:22.260 --> 00:04:22.890 This talk,

NOTE Confidence: 0.8719525

00:04:22.890 --> 00:04:24.780 even though sometimes it might get

NOTE Confidence: 0.8719525

00:04:24.780 --> 00:04:27.327 down in the weeds a little bit for

NOTE Confidence: 0.8719525

00:04:27.327 --> 00:04:29.429 clinicians to think about the translation

NOTE Confidence: 0.8719525

00:04:29.429 --> 00:04:31.835 of value of thinking about Biomarkers,

NOTE Confidence: 0.8719525

00:04:31.840 --> 00:04:33.375 and I think great conversation

NOTE Confidence: 0.8719525

00:04:33.375 --> 00:04:35.939 to have is is the word biomarker.

NOTE Confidence: 0.8719525

00:04:35.940 --> 00:04:38.327 What does biomarker mean in some cases?

NOTE Confidence: 0.8719525

00:04:38.330 --> 00:04:39.665 Biomarker means indicative

NOTE Confidence: 0.8719525

00:04:39.665 --> 00:04:41.000 or associated with.

NOTE Confidence: 0.8719525

00:04:41.000 --> 00:04:42.722 But a lot of times biomarkers can

NOTE Confidence: 0.8719525

00:04:42.722 --> 00:04:44.937 be pushed a little bit further to

NOTE Confidence: 0.8719525

00:04:44.937 --> 00:04:46.712 talk about mechanisms that those

NOTE Confidence: 0.8719525

00:04:46.712 --> 00:04:48.278 biomarkers that are identified

NOTE Confidence: 0.8719525

00:04:48.278 --> 00:04:50.193 in many clinical studies actually
NOTE Confidence: 0.8719525

00:04:50.193 --> 00:04:51.704 have mechanistic or causal value.
NOTE Confidence: 0.8719525

00:04:51.704 --> 00:04:51.952 2,
NOTE Confidence: 0.8719525

00:04:51.952 --> 00:04:53.902 and I think that there's an incredible
NOTE Confidence: 0.8719525

00:04:53.902 --> 00:04:55.932 value in partnerships between clinical
NOTE Confidence: 0.8719525

00:04:55.932 --> 00:04:57.948 research and basic research that
NOTE Confidence: 0.8719525

00:04:57.948 --> 00:05:00.258 those biomarkers can cross cross that divide.
NOTE Confidence: 0.8719525

00:05:00.260 --> 00:05:00.591 Alright,
NOTE Confidence: 0.8719525

00:05:00.591 --> 00:05:01.584 here we go.
NOTE Confidence: 0.8719525

00:05:01.584 --> 00:05:02.577 Let's do this.
NOTE Confidence: 0.8719525

00:05:02.580 --> 00:05:02.890 OK,
NOTE Confidence: 0.8719525

00:05:02.890 --> 00:05:04.750 so before I get started then
NOTE Confidence: 0.8719525

00:05:04.750 --> 00:05:06.634 because I want to make sure
NOTE Confidence: 0.8719525

00:05:06.634 --> 00:05:08.706 everybody is on the same page of
NOTE Confidence: 0.8719525

00:05:08.780 --> 00:05:11.412 what in the world is she talking
NOTE Confidence: 0.8719525

00:05:11.412 --> 00:05:12.933 about with extracellular vesicles?

NOTE Confidence: 0.8719525
00:05:12.933 --> 00:05:14.898 I'm going to sprinkle this
NOTE Confidence: 0.8719525
00:05:14.898 --> 00:05:16.940 in throughout the talk today,
NOTE Confidence: 0.8719525
00:05:16.940 --> 00:05:19.061 but I wanted to just make sure
NOTE Confidence: 0.8719525
00:05:19.061 --> 00:05:21.282 everyone's on the same page as to
NOTE Confidence: 0.8719525
00:05:21.282 --> 00:05:23.142 what exercise or vesicles are and
NOTE Confidence: 0.8719525
00:05:23.208 --> 00:05:25.296 that they really do hold great
NOTE Confidence: 0.8719525
00:05:25.296 --> 00:05:27.079 translation of value but also
NOTE Confidence: 0.8719525
00:05:27.079 --> 00:05:28.635 reverse translation with potential
NOTE Confidence: 0.8719525
00:05:28.635 --> 00:05:29.802 toward understanding mechanisms
NOTE Confidence: 0.8719525
00:05:29.802 --> 00:05:31.528 and causal aspects of disease.
NOTE Confidence: 0.8719525
00:05:31.530 --> 00:05:33.235 So an extracellular vesicle is
NOTE Confidence: 0.8719525
00:05:33.235 --> 00:05:35.365 broadly termed as a small lipid
NOTE Confidence: 0.8719525
00:05:35.365 --> 00:05:37.507 and contain draft that is released.
NOTE Confidence: 0.8719525
00:05:37.510 --> 00:05:39.628 It is not a cell itself,
NOTE Confidence: 0.8719525
00:05:39.630 --> 00:05:42.130 but it is lipid contained.
NOTE Confidence: 0.8719525

00:05:42.130 --> 00:05:44.625 That contains many proteins in
NOTE Confidence: 0.8719525

00:05:44.625 --> 00:05:47.120 its membrane's structure and many
NOTE Confidence: 0.8719525

00:05:47.202 --> 00:05:49.502 small noncoding RNA's and other
NOTE Confidence: 0.8719525

00:05:49.502 --> 00:05:52.430 proteins that are its cargo inside.
NOTE Confidence: 0.8719525

00:05:52.430 --> 00:05:54.160 These exercise are vesicles you
NOTE Confidence: 0.8719525

00:05:54.160 --> 00:05:56.370 may have heard them called exomes.
NOTE Confidence: 0.8719525

00:05:56.370 --> 00:05:58.512 Exosomes are a small version of
NOTE Confidence: 0.8719525

00:05:58.512 --> 00:05:59.583 an extracellular vesicle,
NOTE Confidence: 0.8719525

00:05:59.590 --> 00:06:02.358 so exercise vesicle is a broad term that
NOTE Confidence: 0.8719525

00:06:02.358 --> 00:06:04.600 encompasses all types of these vesicles.
NOTE Confidence: 0.8719525

00:06:04.600 --> 00:06:06.580 Whereas eggs om is only one
NOTE Confidence: 0.8719525

00:06:06.580 --> 00:06:08.540 type of exercise or vesicle,
NOTE Confidence: 0.8719525

00:06:08.540 --> 00:06:10.688 I will abbreviate exercise in vesicles,
NOTE Confidence: 0.8719525

00:06:10.690 --> 00:06:12.838 often in the slides as Yves.
NOTE Confidence: 0.8719525

00:06:12.840 --> 00:06:15.588 Just you know what that is.
NOTE Confidence: 0.8719525

00:06:15.590 --> 00:06:17.552 And so in order for anybody

NOTE Confidence: 0.8719525

00:06:17.552 --> 00:06:19.650 to really say that something,

NOTE Confidence: 0.8719525

00:06:19.650 --> 00:06:22.674 for instance is an eggs ome versus just

NOTE Confidence: 0.8719525

00:06:22.674 --> 00:06:25.180 classifying it more generally as an EV,

NOTE Confidence: 0.8719525

00:06:25.180 --> 00:06:28.140 you have to actually go to great lengths.

NOTE Confidence: 0.8719525

00:06:28.140 --> 00:06:30.015 And there are actually societies

NOTE Confidence: 0.8719525

00:06:30.015 --> 00:06:31.890 and rules that determine the

NOTE Confidence: 0.8719525

00:06:31.952 --> 00:06:33.352 clarification and the rigor

NOTE Confidence: 0.8719525

00:06:33.352 --> 00:06:35.452 by which you have to validate

NOTE Confidence: 0.81225276

00:06:35.518 --> 00:06:38.094 that you're calling something and eggs om.

NOTE Confidence: 0.81225276

00:06:38.100 --> 00:06:40.660 So my lab we stay away from really

NOTE Confidence: 0.81225276

00:06:40.660 --> 00:06:42.764 defining these small types of

NOTE Confidence: 0.81225276

00:06:42.764 --> 00:06:45.084 vesicles versus just more grandly

NOTE Confidence: 0.81225276

00:06:45.084 --> 00:06:47.130 extracellular vesicles for that reason.

NOTE Confidence: 0.81225276

00:06:47.130 --> 00:06:49.210 The proteins have been characterized

NOTE Confidence: 0.81225276

00:06:49.210 --> 00:06:52.370 greatly in the content of these vesicles.

NOTE Confidence: 0.81225276

00:06:52.370 --> 00:06:54.668 All tissues in all mammals secrete
NOTE Confidence: 0.81225276

00:06:54.668 --> 00:06:56.710 exercise their vesicles into circulation
NOTE Confidence: 0.81225276

00:06:56.710 --> 00:06:59.404 and these vesicles travel in high
NOTE Confidence: 0.81225276

00:06:59.404 --> 00:07:01.550 concentration throughout the circulation.
NOTE Confidence: 0.81225276

00:07:01.550 --> 00:07:04.609 They travel in a somewhat specific manner.
NOTE Confidence: 0.81225276

00:07:04.610 --> 00:07:07.930 I like to use the analogy to the
NOTE Confidence: 0.81225276

00:07:07.930 --> 00:07:10.289 endocrine system whereby you have,
NOTE Confidence: 0.81225276

00:07:10.290 --> 00:07:12.755 for instance, gonadal release of
NOTE Confidence: 0.81225276

00:07:12.755 --> 00:07:15.220 steroid hormones that travel in
NOTE Confidence: 0.81225276

00:07:15.305 --> 00:07:18.155 circulation and act at distant sites.
NOTE Confidence: 0.81225276

00:07:18.160 --> 00:07:20.624 EV's are similar to that only in that
NOTE Confidence: 0.81225276

00:07:20.624 --> 00:07:22.685 they travel in circulation to distant
NOTE Confidence: 0.81225276

00:07:22.685 --> 00:07:25.329 sites or they can act locally as well.
NOTE Confidence: 0.81225276

00:07:25.330 --> 00:07:27.605 And I'll give you examples of both.
NOTE Confidence: 0.81225276

00:07:27.610 --> 00:07:29.590 But TV's also have an incredible
NOTE Confidence: 0.81225276

00:07:29.590 --> 00:07:31.200 specificity of where they act.

NOTE Confidence: 0.81225276

00:07:31.200 --> 00:07:33.258 Unlike things in the endocrine system

NOTE Confidence: 0.81225276

00:07:33.258 --> 00:07:36.128 that can act in many different issues.

NOTE Confidence: 0.81225276

00:07:36.130 --> 00:07:38.223 The way that that specificity happens is

NOTE Confidence: 0.81225276

00:07:38.223 --> 00:07:41.191 that if you actually look at the membranous

NOTE Confidence: 0.81225276

00:07:41.191 --> 00:07:43.201 structure of an extracellular vesicle,

NOTE Confidence: 0.81225276

00:07:43.210 --> 00:07:45.155 there are very specific protein

NOTE Confidence: 0.81225276

00:07:45.155 --> 00:07:47.100 combinations that determine both the

NOTE Confidence: 0.81225276

00:07:47.166 --> 00:07:49.224 tissue that the EV is released from,

NOTE Confidence: 0.81225276

00:07:49.230 --> 00:07:51.603 and the tissue in circulation that they

NOTE Confidence: 0.81225276

00:07:51.603 --> 00:07:54.540 will act upon that cargo that they deliver,

NOTE Confidence: 0.81225276

00:07:54.540 --> 00:07:56.658 both in interacting at the membrane

NOTE Confidence: 0.81225276

00:07:56.658 --> 00:07:58.812 at local cells, in a tissue.

NOTE Confidence: 0.81225276

00:07:58.812 --> 00:08:00.632 Oftentimes, the immune system will

NOTE Confidence: 0.81225276

00:08:00.632 --> 00:08:02.677 deliver cargo internally to a cell,

NOTE Confidence: 0.81225276

00:08:02.680 --> 00:08:04.450 and as you can imagine,

NOTE Confidence: 0.81225276

00:08:04.450 --> 00:08:05.862 if that cargo contains,
NOTE Confidence: 0.81225276

00:08:05.862 --> 00:08:06.568 for instance,
NOTE Confidence: 0.81225276

00:08:06.570 --> 00:08:07.581 small noncoding RNA.
NOTE Confidence: 0.81225276

00:08:07.581 --> 00:08:09.940 Lot of Micro RNA's is an example
NOTE Confidence: 0.81225276

00:08:10.005 --> 00:08:12.448 that those micro RNA can have an
NOTE Confidence: 0.81225276

00:08:12.448 --> 00:08:14.959 immediate and profound effect on the
NOTE Confidence: 0.81225276

00:08:14.959 --> 00:08:17.279 translation of Gene and transcription
NOTE Confidence: 0.81225276

00:08:17.279 --> 00:08:18.958 translation machinery such that
NOTE Confidence: 0.81225276

00:08:18.958 --> 00:08:21.576 the more of a given micro RNA
NOTE Confidence: 0.81225276

00:08:21.576 --> 00:08:23.858 delivered rapidly to a given cell,
NOTE Confidence: 0.81225276

00:08:23.860 --> 00:08:26.588 the more rapidly it can degrade a given
NOTE Confidence: 0.81225276

00:08:26.588 --> 00:08:29.518 targeted M RNA and prevent its translation.
NOTE Confidence: 0.81225276

00:08:29.520 --> 00:08:31.400 So it's really important I
NOTE Confidence: 0.81225276

00:08:31.400 --> 00:08:32.904 think is a biomarker,
NOTE Confidence: 0.81225276

00:08:32.910 --> 00:08:35.166 both Association with many disease states.
NOTE Confidence: 0.81225276

00:08:35.170 --> 00:08:37.746 Some of the greatest examples are that

NOTE Confidence: 0.81225276

00:08:37.746 --> 00:08:39.716 extracellular vesicles are being discovered

NOTE Confidence: 0.81225276

00:08:39.716 --> 00:08:42.134 as being communication within the brain.

NOTE Confidence: 0.81225276

00:08:42.140 --> 00:08:44.184 As well as released from the brain,

NOTE Confidence: 0.81225276

00:08:44.190 --> 00:08:45.948 but they also travel in circulation

NOTE Confidence: 0.81225276

00:08:45.948 --> 00:08:47.120 from many other tissues.

NOTE Confidence: 0.81225276

00:08:47.120 --> 00:08:48.933 The cancer field has really done the

NOTE Confidence: 0.81225276

00:08:48.933 --> 00:08:50.930 most work on exercise are vesicles,

NOTE Confidence: 0.81225276

00:08:50.930 --> 00:08:53.657 and they've done a lot of that work in

NOTE Confidence: 0.81225276

00:08:53.657 --> 00:08:55.428 relationship to signals to the immune

NOTE Confidence: 0.81225276

00:08:55.428 --> 00:08:57.960 system so will kind of come back to that.

NOTE Confidence: 0.81225276

00:08:57.960 --> 00:09:00.606 So that's what an exercise or vesicle is just

NOTE Confidence: 0.81225276

00:09:00.606 --> 00:09:03.240 to make sure we're all on the same page.

NOTE Confidence: 0.81225276

00:09:03.240 --> 00:09:03.866 There is,

NOTE Confidence: 0.81225276

00:09:03.866 --> 00:09:04.179 unfortunately,

NOTE Confidence: 0.81225276

00:09:04.179 --> 00:09:06.057 at this time alack of really

NOTE Confidence: 0.81225276

00:09:06.057 --> 00:09:07.758 rigorous tools and that is something
NOTE Confidence: 0.81225276

00:09:07.758 --> 00:09:09.093 that labs are working on.
NOTE Confidence: 0.81225276

00:09:09.100 --> 00:09:11.221 My lab is in the process now
NOTE Confidence: 0.81225276

00:09:11.221 --> 00:09:12.660 of making a mouse.
NOTE Confidence: 0.81225276

00:09:12.660 --> 00:09:14.410 That allows us to conditionally
NOTE Confidence: 0.81225276

00:09:14.410 --> 00:09:16.579 target and look at release of
NOTE Confidence: 0.81225276

00:09:16.579 --> 00:09:18.003 vesicles from specified tissues
NOTE Confidence: 0.81225276

00:09:18.003 --> 00:09:20.330 and follow them to other tissues,
NOTE Confidence: 0.81225276

00:09:20.330 --> 00:09:22.514 but those are tools that don't
NOTE Confidence: 0.81225276

00:09:22.514 --> 00:09:23.606 currently exist unfortunately,
NOTE Confidence: 0.81225276

00:09:23.610 --> 00:09:26.130 and that limits a lot of our
NOTE Confidence: 0.81225276

00:09:26.130 --> 00:09:27.630 interpretation of these Eves.
NOTE Confidence: 0.81225276

00:09:27.630 --> 00:09:30.066 These eaves have also been associated
NOTE Confidence: 0.81225276

00:09:30.066 --> 00:09:32.065 with many different disease States
NOTE Confidence: 0.81225276

00:09:32.065 --> 00:09:34.200 and will will come back to that.
NOTE Confidence: 0.81225276

00:09:34.200 --> 00:09:35.790 So as Irina introduced my

NOTE Confidence: 0.81225276

00:09:35.790 --> 00:09:37.380 lab covers a different areas

NOTE Confidence: 0.839502

00:09:37.444 --> 00:09:40.036 around stress and neuro psychiatric disease.

NOTE Confidence: 0.839502

00:09:40.040 --> 00:09:42.728 We focus a lot in my lab and

NOTE Confidence: 0.839502

00:09:42.728 --> 00:09:44.850 understanding stress across the lifespan.

NOTE Confidence: 0.839502

00:09:44.850 --> 00:09:45.885 And its impacts,

NOTE Confidence: 0.839502

00:09:45.885 --> 00:09:47.265 especially in neuro development.

NOTE Confidence: 0.839502

00:09:47.270 --> 00:09:49.830 I'm going to tell you a couple different

NOTE Confidence: 0.839502

00:09:49.830 --> 00:09:52.108 stories from the lab today that focus

NOTE Confidence: 0.839502

00:09:52.108 --> 00:09:54.133 a lot on understanding both male

NOTE Confidence: 0.839502

00:09:54.133 --> 00:09:56.068 and female experiences with stress

NOTE Confidence: 0.839502

00:09:56.068 --> 00:09:57.964 in their environment and adversity.

NOTE Confidence: 0.839502

00:09:57.964 --> 00:10:00.112 One of the aspects, a spec.

NOTE Confidence: 0.839502

00:10:00.112 --> 00:10:02.428 And now that I'm in Baltimore,

NOTE Confidence: 0.839502

00:10:02.430 --> 00:10:04.733 which is a majority black city and

NOTE Confidence: 0.839502

00:10:04.733 --> 00:10:06.877 engagement with the community that we're

NOTE Confidence: 0.839502

00:10:06.877 --> 00:10:09.067 very interested in in doing service
NOTE Confidence: 0.839502

00:10:09.067 --> 00:10:11.304 and understanding and appreciating the
NOTE Confidence: 0.839502

00:10:11.304 --> 00:10:14.010 health disparities to this community is
NOTE Confidence: 0.839502

00:10:14.010 --> 00:10:15.940 understanding the mental health aspects,
NOTE Confidence: 0.839502

00:10:15.940 --> 00:10:16.301 especially.
NOTE Confidence: 0.839502

00:10:16.301 --> 00:10:18.467 As you can imagine nowadays and
NOTE Confidence: 0.839502

00:10:18.467 --> 00:10:20.436 understanding how it contributes to
NOTE Confidence: 0.839502

00:10:20.436 --> 00:10:22.084 intergenerational changes in Nuro
NOTE Confidence: 0.839502

00:10:22.084 --> 00:10:24.810 Development and risk for things like neuro,
NOTE Confidence: 0.839502

00:10:24.810 --> 00:10:26.022 psychiatric neurodevelopmental disorders.
NOTE Confidence: 0.839502

00:10:26.022 --> 00:10:28.446 So we know that there's disparities
NOTE Confidence: 0.839502

00:10:28.446 --> 00:10:30.299 across mental health especially for.
NOTE Confidence: 0.839502

00:10:30.300 --> 00:10:33.310 African Americans that now more than ever,
NOTE Confidence: 0.839502

00:10:33.310 --> 00:10:35.038 that racism and discrimination
NOTE Confidence: 0.839502

00:10:35.038 --> 00:10:36.766 produced profound effects and
NOTE Confidence: 0.839502

00:10:36.766 --> 00:10:38.469 exacerbate mental health issues.

NOTE Confidence: 0.839502
00:10:38.470 --> 00:10:40.790 But what I want to show you is
NOTE Confidence: 0.839502
00:10:40.790 --> 00:10:42.990 models and translation of potential
NOTE Confidence: 0.839502
00:10:42.990 --> 00:10:45.570 for understanding the long term
NOTE Confidence: 0.839502
00:10:45.570 --> 00:10:47.338 consequences and intergenerational
NOTE Confidence: 0.839502
00:10:47.338 --> 00:10:50.638 impacts of that discrimination stress.
NOTE Confidence: 0.839502
00:10:50.640 --> 00:10:52.632 One of the key aspects that my lab
NOTE Confidence: 0.839502
00:10:52.632 --> 00:10:54.516 is interested in is really modeling
NOTE Confidence: 0.839502
00:10:54.516 --> 00:10:56.176 and understanding impacts on both
NOTE Confidence: 0.839502
00:10:56.176 --> 00:10:57.660 maternal and infant mortality.
NOTE Confidence: 0.839502
00:10:57.660 --> 00:10:58.664 In the long term,
NOTE Confidence: 0.839502
00:10:58.664 --> 00:10:59.919 risks of even the survivors
NOTE Confidence: 0.839502
00:10:59.919 --> 00:11:01.010 of discrimination,
NOTE Confidence: 0.839502
00:11:01.010 --> 00:11:02.840 distress and how it's passed on.
NOTE Confidence: 0.839502
00:11:02.840 --> 00:11:05.351 So as you can see from this graph here
NOTE Confidence: 0.839502
00:11:05.351 --> 00:11:08.026 that that only currently goes up to 2013.
NOTE Confidence: 0.839502

00:11:08.030 --> 00:11:10.142 If you compare a white mom versus a
NOTE Confidence: 0.839502

00:11:10.142 --> 00:11:12.144 black mom in the United States that
NOTE Confidence: 0.839502

00:11:12.144 --> 00:11:13.992 they have a four times increased
NOTE Confidence: 0.839502

00:11:13.992 --> 00:11:16.254 risk for maternal and infant death,
NOTE Confidence: 0.839502

00:11:16.260 --> 00:11:18.006 the bottom panel had just shows
NOTE Confidence: 0.839502

00:11:18.006 --> 00:11:19.859 you within the state of Maryland
NOTE Confidence: 0.839502

00:11:19.859 --> 00:11:21.749 that even though this green line,
NOTE Confidence: 0.839502

00:11:21.750 --> 00:11:24.305 which is black babies has been decreasing.
NOTE Confidence: 0.839502

00:11:24.310 --> 00:11:25.646 That infant mortality rates
NOTE Confidence: 0.839502

00:11:25.646 --> 00:11:27.316 remain still four times higher,
NOTE Confidence: 0.839502

00:11:27.320 --> 00:11:29.245 so a black mom with an advanced
NOTE Confidence: 0.839502

00:11:29.245 --> 00:11:30.888 degree so it advanced education
NOTE Confidence: 0.839502

00:11:30.888 --> 00:11:33.138 still has a four times increased
NOTE Confidence: 0.839502

00:11:33.138 --> 00:11:35.310 risk for maternal and infant death
NOTE Confidence: 0.839502

00:11:35.310 --> 00:11:37.672 within the first year than a white
NOTE Confidence: 0.839502

00:11:37.672 --> 00:11:39.664 mom with a high school education.

NOTE Confidence: 0.839502
00:11:39.670 --> 00:11:42.070 So it is not just related to social
NOTE Confidence: 0.839502
00:11:42.070 --> 00:11:43.679 economic that there are many
NOTE Confidence: 0.839502
00:11:43.679 --> 00:11:45.870 factors we need to understand in the
NOTE Confidence: 0.839502
00:11:45.933 --> 00:11:48.018 environment and related to stress.
NOTE Confidence: 0.839502
00:11:48.020 --> 00:11:49.742 We're very interested in trying to
NOTE Confidence: 0.839502
00:11:49.742 --> 00:11:51.383 understand the long term influences
NOTE Confidence: 0.839502
00:11:51.383 --> 00:11:52.697 of discrimination stress.
NOTE Confidence: 0.839502
00:11:52.700 --> 00:11:54.698 So this term has been defined,
NOTE Confidence: 0.839502
00:11:54.700 --> 00:11:56.450 brought more broadly in the.
NOTE Confidence: 0.839502
00:11:56.450 --> 00:11:57.870 The social sphere is weathering
NOTE Confidence: 0.839502
00:11:57.870 --> 00:11:59.670 and the toll that racism places
NOTE Confidence: 0.839502
00:11:59.670 --> 00:12:01.280 as a social psychological tale,
NOTE Confidence: 0.839502
00:12:01.280 --> 00:12:03.282 but also a physiological toll on the
NOTE Confidence: 0.839502
00:12:03.282 --> 00:12:05.600 body and the germ cells as well that
NOTE Confidence: 0.839502
00:12:05.600 --> 00:12:08.229 give rise to effects for the next generation.
NOTE Confidence: 0.839502

00:12:08.230 --> 00:12:09.133 So Arlene Jeronimus,
NOTE Confidence: 0.839502

00:12:09.133 --> 00:12:10.036 who's in Michigan,
NOTE Confidence: 0.839502

00:12:10.040 --> 00:12:12.252 has studied this for many years and
NOTE Confidence: 0.839502

00:12:12.252 --> 00:12:14.950 I give her credit for all of her
NOTE Confidence: 0.839502

00:12:14.950 --> 00:12:17.050 are incredible work in this area.
NOTE Confidence: 0.839502

00:12:17.050 --> 00:12:18.928 And an coining the term weather,
NOTE Confidence: 0.839502

00:12:18.930 --> 00:12:19.265 rain,
NOTE Confidence: 0.839502

00:12:19.265 --> 00:12:21.275 and the stresses that impact black
NOTE Confidence: 0.839502

00:12:21.275 --> 00:12:23.053 individuals are chronic and repeated
NOTE Confidence: 0.839502

00:12:23.053 --> 00:12:24.848 throughout their whole life course.
NOTE Confidence: 0.839502

00:12:24.850 --> 00:12:27.125 And one of the aspects that we're
NOTE Confidence: 0.839502

00:12:27.125 --> 00:12:28.944 particularly interested in trying to
NOTE Confidence: 0.839502

00:12:28.944 --> 00:12:30.914 understand those influences in pregnancy.
NOTE Confidence: 0.839502

00:12:30.920 --> 00:12:32.789 So many of you have heard the
NOTE Confidence: 0.839502

00:12:32.789 --> 00:12:33.590 term aces or
NOTE Confidence: 0.83556825

00:12:33.653 --> 00:12:35.558 adverse childhood experiences,

NOTE Confidence: 0.83556825

00:12:35.560 --> 00:12:37.165 you know that Kaiser Permanente

NOTE Confidence: 0.83556825

00:12:37.165 --> 00:12:38.770 developed this ace protocol for

NOTE Confidence: 0.83556825

00:12:38.823 --> 00:12:40.383 understanding the effects throughout

NOTE Confidence: 0.83556825

00:12:40.383 --> 00:12:42.333 the lifespan on health outcomes.

NOTE Confidence: 0.83556825

00:12:42.340 --> 00:12:44.252 The original aces were

NOTE Confidence: 0.83556825

00:12:44.252 --> 00:12:46.164 really being the California.

NOTE Confidence: 0.83556825

00:12:46.170 --> 00:12:48.706 So can I ask that everybody try and

NOTE Confidence: 0.83556825

00:12:48.706 --> 00:12:50.455 mute themselves and getting lots

NOTE Confidence: 0.83556825

00:12:50.455 --> 00:12:52.543 of feedback for people in their

NOTE Confidence: 0.83556825

00:12:52.543 --> 00:12:54.769 offices were coming up on lunch time?

NOTE Confidence: 0.83556825

00:12:54.770 --> 00:12:56.335 Thank you so adverse childhood

NOTE Confidence: 0.83556825

00:12:56.335 --> 00:12:57.900 experiences as they relate to

NOTE Confidence: 0.83556825

00:12:57.957 --> 00:12:59.417 the Kaiser Permanente study,

NOTE Confidence: 0.83556825

00:12:59.420 --> 00:13:01.800 which was done in the state of

NOTE Confidence: 0.83556825

00:13:01.800 --> 00:13:03.689 California which many of you I'm

NOTE Confidence: 0.83556825

00:13:03.689 --> 00:13:06.034 sure are very aware of his was done
NOTE Confidence: 0.83556825

00:13:06.034 --> 00:13:08.049 in the largely white population.
NOTE Confidence: 0.83556825

00:13:08.050 --> 00:13:10.178 Many of those aces are now being
NOTE Confidence: 0.83556825

00:13:10.178 --> 00:13:12.232 redone and evaluated in inner city
NOTE Confidence: 0.83556825

00:13:12.232 --> 00:13:14.027 and especially in black populations,
NOTE Confidence: 0.83556825

00:13:14.030 --> 00:13:15.685 but there originally done to
NOTE Confidence: 0.83556825

00:13:15.685 --> 00:13:17.009 determine if adversity experienced,
NOTE Confidence: 0.83556825

00:13:17.010 --> 00:13:18.294 especially prior to adulthood,
NOTE Confidence: 0.83556825

00:13:18.294 --> 00:13:20.615 could predict risks for all kinds of
NOTE Confidence: 0.83556825

00:13:20.615 --> 00:13:22.330 health disparities in health outcomes.
NOTE Confidence: 0.83556825

00:13:22.330 --> 00:13:25.098 And so they were really qualified as 10.
NOTE Confidence: 0.83556825

00:13:25.100 --> 00:13:27.140 Adverse childhood experiences and those
NOTE Confidence: 0.83556825

00:13:27.140 --> 00:13:29.180 childhood experiences give rise to
NOTE Confidence: 0.83556825

00:13:29.242 --> 00:13:31.162 risk for many things that behavioral
NOTE Confidence: 0.83556825

00:13:31.162 --> 00:13:33.658 outcomes such as drug abuse and addictions,
NOTE Confidence: 0.83556825

00:13:33.660 --> 00:13:36.859 as well as physiological and mental risk.

NOTE Confidence: 0.83556825

00:13:36.860 --> 00:13:38.906 But there are also determined that

NOTE Confidence: 0.83556825

00:13:38.906 --> 00:13:41.374 the number of these aces prior to the

NOTE Confidence: 0.83556825

00:13:41.374 --> 00:13:43.690 age of 18 was also very productive,

NOTE Confidence: 0.83556825

00:13:43.690 --> 00:13:45.622 and in their study they determined

NOTE Confidence: 0.83556825

00:13:45.622 --> 00:13:47.933 that the accumulation of four or more

NOTE Confidence: 0.83556825

00:13:47.933 --> 00:13:49.538 of these adverse childhood events,

NOTE Confidence: 0.83556825

00:13:49.540 --> 00:13:51.165 which include things like divorce

NOTE Confidence: 0.83556825

00:13:51.165 --> 00:13:52.140 of your parents,

NOTE Confidence: 0.83556825

00:13:52.140 --> 00:13:53.440 incarceration of apparent drug

NOTE Confidence: 0.83556825

00:13:53.440 --> 00:13:54.740 addiction in the household,

NOTE Confidence: 0.83556825

00:13:54.740 --> 00:13:55.394 and violence,

NOTE Confidence: 0.83556825

00:13:55.394 --> 00:13:55.721 neglect,

NOTE Confidence: 0.83556825

00:13:55.721 --> 00:13:57.356 accumulation of four more of

NOTE Confidence: 0.83556825

00:13:57.356 --> 00:13:58.960 these aces in an individual,

NOTE Confidence: 0.83556825

00:13:58.960 --> 00:14:00.910 was a strong predictor of a

NOTE Confidence: 0.83556825

00:14:00.910 --> 00:14:02.210 lifetime of health consequences.
NOTE Confidence: 0.83556825

00:14:02.210 --> 00:14:05.218 So that's the number of the cloud software
NOTE Confidence: 0.83556825

00:14:05.218 --> 00:14:07.398 they determined was the highest risk.
NOTE Confidence: 0.83556825

00:14:07.400 --> 00:14:09.122 So going back to the interests of
NOTE Confidence: 0.83556825

00:14:09.122 --> 00:14:10.840 my lab and trying to understand
NOTE Confidence: 0.83556825

00:14:10.840 --> 00:14:12.682 so we can develop better models
NOTE Confidence: 0.83556825

00:14:12.682 --> 00:14:14.337 to look at the mechanisms.
NOTE Confidence: 0.83556825

00:14:14.340 --> 00:14:16.524 If you just look at the term of
NOTE Confidence: 0.83556825

00:14:16.524 --> 00:14:17.954 pregnancy itself and you were
NOTE Confidence: 0.83556825

00:14:17.954 --> 00:14:19.592 to look across the United States
NOTE Confidence: 0.83556825

00:14:19.592 --> 00:14:21.470 of America and ask all pregnant
NOTE Confidence: 0.83556825

00:14:21.470 --> 00:14:23.326 women the number of their adverse
NOTE Confidence: 0.83556825

00:14:23.326 --> 00:14:24.906 childhood events so those exposed
NOTE Confidence: 0.83556825

00:14:24.906 --> 00:14:26.760 to them before the age of 18,
NOTE Confidence: 0.83556825

00:14:26.760 --> 00:14:28.560 now that they're much older and
NOTE Confidence: 0.83556825

00:14:28.560 --> 00:14:30.350 pregnant themselves and you can look

NOTE Confidence: 0.83556825

00:14:30.350 --> 00:14:32.205 at the distribution across the US for

NOTE Confidence: 0.83556825

00:14:32.205 --> 00:14:33.973 those experiencing zero all the way

NOTE Confidence: 0.83556825

00:14:33.973 --> 00:14:36.038 up to four more highlighted in yellow,

NOTE Confidence: 0.83556825

00:14:36.038 --> 00:14:38.166 is that point of increased health risk?

NOTE Confidence: 0.83556825

00:14:38.170 --> 00:14:40.890 So across the US is about 12 1/2%

NOTE Confidence: 0.83556825

00:14:40.890 --> 00:14:42.930 of women who are currently pregnant

NOTE Confidence: 0.83556825

00:14:42.930 --> 00:14:44.630 that have experienced for more.

NOTE Confidence: 0.83556825

00:14:44.630 --> 00:14:46.034 But understanding the population

NOTE Confidence: 0.83556825

00:14:46.034 --> 00:14:48.492 that we are trying to serve and

NOTE Confidence: 0.83556825

00:14:48.492 --> 00:14:49.952 understand the risk factors for

NOTE Confidence: 0.83556825

00:14:49.952 --> 00:14:51.770 in the city of Baltimore.

NOTE Confidence: 0.83556825

00:14:51.770 --> 00:14:53.735 A recent Baltimore mom study found

NOTE Confidence: 0.83556825

00:14:53.735 --> 00:14:56.091 an actual evaluation of inner city

NOTE Confidence: 0.83556825

00:14:56.091 --> 00:14:58.359 women here that that number is much

NOTE Confidence: 0.83556825

00:14:58.359 --> 00:15:00.412 greater and in fact that six more

NOTE Confidence: 0.83556825

00:15:00.412 --> 00:15:03.050 than 61% of pregnant women in inner

NOTE Confidence: 0.83556825

00:15:03.050 --> 00:15:05.150 city Baltimore have experienced four

NOTE Confidence: 0.83556825

00:15:05.217 --> 00:15:07.494 more aces and I think I want to take

NOTE Confidence: 0.83556825

00:15:07.494 --> 00:15:10.148 a second just to reflect on what that

NOTE Confidence: 0.83556825

00:15:10.148 --> 00:15:12.434 means in terms of trying to understand.

NOTE Confidence: 0.83556825

00:15:12.434 --> 00:15:14.360 The experiences and the risk factors

NOTE Confidence: 0.83556825

00:15:14.413 --> 00:15:16.369 for these women during their pregnancy

NOTE Confidence: 0.83556825

00:15:16.369 --> 00:15:18.455 for both themselves and as well as

NOTE Confidence: 0.83556825

00:15:18.455 --> 00:15:20.149 that of the health and the outcomes

NOTE Confidence: 0.8854406

00:15:20.150 --> 00:15:21.598 for their their baby,

NOTE Confidence: 0.8854406

00:15:21.598 --> 00:15:23.408 and I think that's incredibly

NOTE Confidence: 0.8854406

00:15:23.408 --> 00:15:25.263 important for us to think about

NOTE Confidence: 0.8854406

00:15:25.263 --> 00:15:27.110 in terms of the developing brain.

NOTE Confidence: 0.8854406

00:15:27.110 --> 00:15:29.020 So back to the translation

NOTE Confidence: 0.8854406

00:15:29.020 --> 00:15:30.548 of potential and biological

NOTE Confidence: 0.8854406

00:15:30.548 --> 00:15:32.356 signals that we want to study.

NOTE Confidence: 0.8854406

00:15:32.360 --> 00:15:34.240 So on the left is is a schematic

NOTE Confidence: 0.8854406

00:15:34.240 --> 00:15:36.318 from a recent review from Rachel

NOTE Confidence: 0.8854406

00:15:36.318 --> 00:15:38.634 Yehuda's group that I think highlights

NOTE Confidence: 0.8854406

00:15:38.696 --> 00:15:41.192 on the human side reflects the

NOTE Confidence: 0.8854406

00:15:41.192 --> 00:15:42.856 differences across adverse experiences

NOTE Confidence: 0.8854406

00:15:42.860 --> 00:15:44.960 that gives rise and influences on

NOTE Confidence: 0.8854406

00:15:44.960 --> 00:15:47.060 things like the gametes, the cell,

NOTE Confidence: 0.8854406

00:15:47.060 --> 00:15:49.160 the cells that come together at

NOTE Confidence: 0.8854406

00:15:49.160 --> 00:15:50.521 fertilization, egg and sperm.

NOTE Confidence: 0.8854406

00:15:50.521 --> 00:15:52.880 The Neo Nate itself in the developing

NOTE Confidence: 0.8854406

00:15:52.950 --> 00:15:54.936 infant and all of the experiences

NOTE Confidence: 0.8854406

00:15:54.936 --> 00:15:57.077 of mom during her pregnancy prior

NOTE Confidence: 0.8854406

00:15:57.077 --> 00:15:59.709 to her pregnancy and giving rise to

NOTE Confidence: 0.8854406

00:15:59.709 --> 00:16:01.700 health risks and resiliency as well

NOTE Confidence: 0.8854406

00:16:01.700 --> 00:16:03.823 for the 1st and next generations

NOTE Confidence: 0.8854406

00:16:03.823 --> 00:16:06.018 is important to think about.
NOTE Confidence: 0.8854406

00:16:06.020 --> 00:16:08.324 It is very difficult in a human and
NOTE Confidence: 0.8854406

00:16:08.324 --> 00:16:10.130 there really is relatively little
NOTE Confidence: 0.8854406

00:16:10.130 --> 00:16:12.860 evidence at the mechanistic or causal level.
NOTE Confidence: 0.8854406

00:16:12.860 --> 00:16:13.205 Especially,
NOTE Confidence: 0.8854406

00:16:13.205 --> 00:16:14.930 we're thinking about germ cells
NOTE Confidence: 0.8854406

00:16:14.930 --> 00:16:17.015 of what really contributes to the
NOTE Confidence: 0.8854406

00:16:17.015 --> 00:16:18.327 differences in brain development.
NOTE Confidence: 0.8854406

00:16:18.330 --> 00:16:20.654 We really have to look at models
NOTE Confidence: 0.8854406

00:16:20.654 --> 00:16:23.054 and largely we have to use again
NOTE Confidence: 0.8854406

00:16:23.054 --> 00:16:25.046 mice and rats and other other
NOTE Confidence: 0.8854406

00:16:25.123 --> 00:16:27.545 models to think about how we can
NOTE Confidence: 0.8854406

00:16:27.545 --> 00:16:28.899 mimic stress and adversity.
NOTE Confidence: 0.8854406

00:16:28.899 --> 00:16:31.062 While of course never being able to
NOTE Confidence: 0.8854406

00:16:31.062 --> 00:16:33.215 fully model that adverse environment that
NOTE Confidence: 0.8854406

00:16:33.215 --> 00:16:35.423 that someone of color might experience,

NOTE Confidence: 0.8854406

00:16:35.430 --> 00:16:36.220 especially in.

NOTE Confidence: 0.8854406

00:16:36.220 --> 00:16:38.590 In inner cities such as Baltimore,

NOTE Confidence: 0.8854406

00:16:38.590 --> 00:16:40.942 but in order for us to really

NOTE Confidence: 0.8854406

00:16:40.942 --> 00:16:42.910 get at these mechanisms,

NOTE Confidence: 0.8854406

00:16:42.910 --> 00:16:44.875 even going back to thinking

NOTE Confidence: 0.8854406

00:16:44.875 --> 00:16:46.447 about the extracellular vesicles,

NOTE Confidence: 0.8854406

00:16:46.450 --> 00:16:49.180 we really have to begin to understand

NOTE Confidence: 0.8854406

00:16:49.180 --> 00:16:52.457 both the risks and the changes in germ

NOTE Confidence: 0.8854406

00:16:52.457 --> 00:16:55.090 cells related to Dadan related to mom,

NOTE Confidence: 0.8854406

00:16:55.090 --> 00:16:56.086 mom's preconception,

NOTE Confidence: 0.8854406

00:16:56.086 --> 00:16:56.584 environment,

NOTE Confidence: 0.8854406

00:16:56.584 --> 00:16:58.576 pregnancy environment itself and

NOTE Confidence: 0.8854406

00:16:58.576 --> 00:17:00.476 postpartum environment are all

NOTE Confidence: 0.8854406

00:17:00.476 --> 00:17:01.888 encompassing in disease risk.

NOTE Confidence: 0.8854406

00:17:01.890 --> 00:17:04.417 So this is a very sensitive subject

NOTE Confidence: 0.8854406

00:17:04.417 --> 00:17:05.500 in getting into.
NOTE Confidence: 0.8854406

00:17:05.500 --> 00:17:07.460 How do we develop models in a
NOTE Confidence: 0.8854406

00:17:07.460 --> 00:17:09.730 mouse to begin to understand those
NOTE Confidence: 0.8854406

00:17:09.730 --> 00:17:12.000 mechanisms of something so important,
NOTE Confidence: 0.8854406

00:17:12.000 --> 00:17:13.083 such as discrimination,
NOTE Confidence: 0.8854406

00:17:13.083 --> 00:17:15.249 stress or high aces and adversity.
NOTE Confidence: 0.8854406

00:17:15.250 --> 00:17:16.654 So obviously we can't.
NOTE Confidence: 0.8854406

00:17:16.654 --> 00:17:19.212 Mice are not humans and they do
NOTE Confidence: 0.8854406

00:17:19.212 --> 00:17:21.456 not live in those same experiences,
NOTE Confidence: 0.8854406

00:17:21.460 --> 00:17:23.860 but what we can do is we can begin to
NOTE Confidence: 0.8854406

00:17:23.930 --> 00:17:26.140 appreciate the stress axis itself.
NOTE Confidence: 0.8854406

00:17:26.140 --> 00:17:28.317 The responses to stress in the environment,
NOTE Confidence: 0.8854406

00:17:28.320 --> 00:17:30.497 whether it be acute or chronic effects,
NOTE Confidence: 0.8854406

00:17:30.500 --> 00:17:32.060 and begin to understand things
NOTE Confidence: 0.8854406

00:17:32.060 --> 00:17:33.620 at the very cellular level,
NOTE Confidence: 0.8854406

00:17:33.620 --> 00:17:35.804 and I think that's an important topic,

NOTE Confidence: 0.8854406
00:17:35.810 --> 00:17:37.370 especially for a grand rounds.
NOTE Confidence: 0.8854406
00:17:37.370 --> 00:17:38.930 Is that what is stress?
NOTE Confidence: 0.8854406
00:17:38.930 --> 00:17:40.490 So it is psychiatric level
NOTE Confidence: 0.8854406
00:17:40.490 --> 00:17:42.050 are relative to the brain.
NOTE Confidence: 0.8854406
00:17:42.050 --> 00:17:43.610 The perception of stress can
NOTE Confidence: 0.8854406
00:17:43.610 --> 00:17:44.858 be psychological in nature,
NOTE Confidence: 0.8854406
00:17:44.860 --> 00:17:46.420 can be physical in nature,
NOTE Confidence: 0.8854406
00:17:46.420 --> 00:17:47.864 you're hungry, you're cold,
NOTE Confidence: 0.8854406
00:17:47.864 --> 00:17:48.947 those are stresses.
NOTE Confidence: 0.8854406
00:17:48.950 --> 00:17:50.475 But you're you're feeling chronic
NOTE Confidence: 0.8854406
00:17:50.475 --> 00:17:52.340 stress at work or at home,
NOTE Confidence: 0.8854406
00:17:52.340 --> 00:17:53.875 covid within the black lives
NOTE Confidence: 0.8854406
00:17:53.875 --> 00:17:54.489 matter community.
NOTE Confidence: 0.8854406
00:17:54.490 --> 00:17:56.250 Those are all stresses and
NOTE Confidence: 0.8854406
00:17:56.250 --> 00:17:58.590 they can be chronic in nature.
NOTE Confidence: 0.8854406

00:17:58.590 --> 00:18:00.720 But we also have to remember
NOTE Confidence: 0.8854406

00:18:00.720 --> 00:18:02.140 that the cell itself,
NOTE Confidence: 0.8854406

00:18:02.140 --> 00:18:05.335 whether it be in neuron or a germ cell,
NOTE Confidence: 0.8854406

00:18:05.340 --> 00:18:06.756 as somatic cell lining
NOTE Confidence: 0.8854406

00:18:06.756 --> 00:18:07.818 the reproductive track,
NOTE Confidence: 0.8854406

00:18:07.820 --> 00:18:08.678 is an example.
NOTE Confidence: 0.8854406

00:18:08.678 --> 00:18:10.394 We'll come back to that the
NOTE Confidence: 0.8854406

00:18:10.394 --> 00:18:12.061 cell itself doesn't understand
NOTE Confidence: 0.8854406

00:18:12.061 --> 00:18:14.251 it's not connected directly to
NOTE Confidence: 0.8854406

00:18:14.251 --> 00:18:15.989 the perceptions of the brain.
NOTE Confidence: 0.8434784

00:18:15.990 --> 00:18:17.850 So how do we model biologically
NOTE Confidence: 0.8434784

00:18:17.850 --> 00:18:19.890 the stresses in the environment?
NOTE Confidence: 0.8434784

00:18:19.890 --> 00:18:21.787 The minimal aspect of this and Jane
NOTE Confidence: 0.8434784

00:18:21.787 --> 00:18:23.590 Taylor's work has contributed tremendously
NOTE Confidence: 0.8434784

00:18:23.590 --> 00:18:25.930 to thinking just about glucocorticoids.
NOTE Confidence: 0.8434784

00:18:25.930 --> 00:18:27.930 You can't have stress without

NOTE Confidence: 0.8434784
00:18:27.930 --> 00:18:28.730 elevating glucocorticoids.
NOTE Confidence: 0.8434784
00:18:28.730 --> 00:18:30.686 But there are many other aspects.
NOTE Confidence: 0.8434784
00:18:30.690 --> 00:18:32.315 Of course with stress that
NOTE Confidence: 0.8434784
00:18:32.315 --> 00:18:33.290 are beyond glucocorticoids.
NOTE Confidence: 0.8434784
00:18:33.290 --> 00:18:35.246 But at the very cellular level,
NOTE Confidence: 0.8434784
00:18:35.250 --> 00:18:36.880 the perception of a cell,
NOTE Confidence: 0.8434784
00:18:36.880 --> 00:18:38.836 whether it be a liver cell,
NOTE Confidence: 0.8434784
00:18:38.840 --> 00:18:40.465 whether it be a reproductive
NOTE Confidence: 0.8434784
00:18:40.465 --> 00:18:41.765 cell along reproductive tract,
NOTE Confidence: 0.8434784
00:18:41.770 --> 00:18:43.726 or whether it be in neuron,
NOTE Confidence: 0.8434784
00:18:43.730 --> 00:18:45.608 the perception of stress in the
NOTE Confidence: 0.8434784
00:18:45.608 --> 00:18:47.207 environment minimally has to be
NOTE Confidence: 0.8434784
00:18:47.207 --> 00:18:48.355 an elevation in glucocorticoids
NOTE Confidence: 0.8434784
00:18:48.355 --> 00:18:50.215 that can be acute or chronic
NOTE Confidence: 0.8434784
00:18:50.215 --> 00:18:52.411 in nature and those will change
NOTE Confidence: 0.8434784

00:18:52.411 --> 00:18:53.509 your intracellular structures.
NOTE Confidence: 0.8434784

00:18:53.510 --> 00:18:55.652 And I'm going to give credit to
NOTE Confidence: 0.8434784

00:18:55.652 --> 00:18:57.681 Bruce McEwen as well for his
NOTE Confidence: 0.8434784

00:18:57.681 --> 00:18:59.763 incredible career work on the term.
NOTE Confidence: 0.8434784

00:18:59.770 --> 00:19:02.656 Allostasis, which will come back to.
NOTE Confidence: 0.8434784

00:19:02.660 --> 00:19:04.562 But the perception of the cell
NOTE Confidence: 0.8434784

00:19:04.562 --> 00:19:07.592 of stress of what stress is is a
NOTE Confidence: 0.8434784

00:19:07.592 --> 00:19:09.280 change in glucocorticoids minimally.
NOTE Confidence: 0.8434784

00:19:09.280 --> 00:19:11.422 And I'm also going to highlight that
NOTE Confidence: 0.8434784

00:19:11.422 --> 00:19:13.199 that change in glucocorticoids is
NOTE Confidence: 0.8434784

00:19:13.199 --> 00:19:15.575 really important for the cell when
NOTE Confidence: 0.8434784

00:19:15.575 --> 00:19:18.120 it's outside the normal circadian rhythm.
NOTE Confidence: 0.8434784

00:19:18.120 --> 00:19:20.388 So the Google Corticoids in all
NOTE Confidence: 0.8434784

00:19:20.388 --> 00:19:23.379 mammals rise and fall in a 24 hour
NOTE Confidence: 0.8434784

00:19:23.379 --> 00:19:25.479 cycle that happens every single day.
NOTE Confidence: 0.8434784

00:19:25.480 --> 00:19:27.688 The cells are aligned in their

NOTE Confidence: 0.8434784

00:19:27.688 --> 00:19:29.160 rhythm by those glucocorticoids.

NOTE Confidence: 0.8434784

00:19:29.160 --> 00:19:31.778 So really to model stress is really

NOTE Confidence: 0.8434784

00:19:31.778 --> 00:19:32.900 just elevating glucocorticoids.

NOTE Confidence: 0.8434784

00:19:32.900 --> 00:19:34.580 Outside that normal rhythm, right?

NOTE Confidence: 0.8434784

00:19:34.580 --> 00:19:36.512 That's where about so at the

NOTE Confidence: 0.8434784

00:19:36.512 --> 00:19:38.260 at the most cellular level,

NOTE Confidence: 0.8434784

00:19:38.260 --> 00:19:41.149 so I'm going to give you an example of

NOTE Confidence: 0.8434784

00:19:41.149 --> 00:19:44.000 some of our work of how we think about

NOTE Confidence: 0.8434784

00:19:44.000 --> 00:19:46.640 this at the in terms of pregnancy.

NOTE Confidence: 0.8434784

00:19:46.640 --> 00:19:47.678 So moms experiences,

NOTE Confidence: 0.8434784

00:19:47.678 --> 00:19:49.408 whether it be preconception or

NOTE Confidence: 0.8434784

00:19:49.408 --> 00:19:50.832 during pregnancy are manifested

NOTE Confidence: 0.8434784

00:19:50.832 --> 00:19:52.512 in intersections at very important

NOTE Confidence: 0.8434784

00:19:52.512 --> 00:19:54.511 issue that gives rise to signals

NOTE Confidence: 0.8434784

00:19:54.511 --> 00:19:56.066 to the developing embryo and

NOTE Confidence: 0.8434784

00:19:56.066 --> 00:19:57.024 fetus throughout gestation,
NOTE Confidence: 0.8434784

00:19:57.024 --> 00:19:59.028 and that tissue is the placenta,
NOTE Confidence: 0.8434784

00:19:59.030 --> 00:20:00.074 so the Internet.
NOTE Confidence: 0.8434784

00:20:00.074 --> 00:20:02.510 Action of maternal stress and that again
NOTE Confidence: 0.8434784

00:20:02.579 --> 00:20:05.204 that stress can be psychological in nature.
NOTE Confidence: 0.8434784

00:20:05.210 --> 00:20:07.000 That stress can be changes
NOTE Confidence: 0.8434784

00:20:07.000 --> 00:20:08.432 in her diabetic status.
NOTE Confidence: 0.8434784

00:20:08.440 --> 00:20:10.570 That stress can be many different
NOTE Confidence: 0.8434784

00:20:10.570 --> 00:20:12.422 factors that influence her perception
NOTE Confidence: 0.8434784

00:20:12.422 --> 00:20:14.654 and maintenance of homeostasis so we
NOTE Confidence: 0.8434784

00:20:14.654 --> 00:20:17.185 know I'm giving you example here of
NOTE Confidence: 0.8434784

00:20:17.185 --> 00:20:18.870 showing you that that intersection
NOTE Confidence: 0.8434784

00:20:18.870 --> 00:20:21.010 of the maternal endometrium and moms
NOTE Confidence: 0.8434784

00:20:21.010 --> 00:20:22.810 cells that have been experiencing
NOTE Confidence: 0.8434784

00:20:22.872 --> 00:20:25.032 moms life adversity at that first
NOTE Confidence: 0.8434784

00:20:25.032 --> 00:20:26.472 intersection where the blastocyst

NOTE Confidence: 0.8434784

00:20:26.534 --> 00:20:28.598 these purple cells outlined here are

NOTE Confidence: 0.8434784

00:20:28.598 --> 00:20:30.796 the trophectoderm that will give rise

NOTE Confidence: 0.8434784

00:20:30.796 --> 00:20:33.244 to trophoblast cells of the Placenta.

NOTE Confidence: 0.8434784

00:20:33.250 --> 00:20:35.620 And the inner cell mass here,

NOTE Confidence: 0.8434784

00:20:35.620 --> 00:20:38.189 which will give rise to the Amber

NOTE Confidence: 0.8434784

00:20:38.189 --> 00:20:40.359 developing embryo and eventual fetus.

NOTE Confidence: 0.8434784

00:20:40.360 --> 00:20:42.260 These cells are feeding information

NOTE Confidence: 0.8434784

00:20:42.260 --> 00:20:44.160 from moms environment and our

NOTE Confidence: 0.8434784

00:20:44.225 --> 00:20:46.157 programming themselves that will

NOTE Confidence: 0.8434784

00:20:46.157 --> 00:20:48.089 be remained throughout pregnancy.

NOTE Confidence: 0.8434784

00:20:48.090 --> 00:20:49.780 These this trophectoderm Here that

NOTE Confidence: 0.8434784

00:20:49.780 --> 00:20:51.470 gives rise to the trophoblast,

NOTE Confidence: 0.8434784

00:20:51.470 --> 00:20:53.190 will differentiate into all necessary

NOTE Confidence: 0.8434784

00:20:53.190 --> 00:20:55.859 cells of the Placenta as it invades moms,

NOTE Confidence: 0.8434784

00:20:55.860 --> 00:20:58.170 and Dmitri 'em and develop developing

NOTE Confidence: 0.8434784

00:20:58.170 --> 00:21:00.812 the decidua that gives rise to all
NOTE Confidence: 0.8434784

00:21:00.812 --> 00:21:02.870 the different cells of the Placenta.
NOTE Confidence: 0.8434784

00:21:02.870 --> 00:21:03.530 So why,
NOTE Confidence: 0.8434784

00:21:03.530 --> 00:21:05.510 in a psychiatric psychiatry grand rounds
NOTE Confidence: 0.8434784

00:21:05.510 --> 00:21:07.850 are we talking about the placenta?
NOTE Confidence: 0.8434784

00:21:07.850 --> 00:21:10.698 Well then to is an ender can tissue.
NOTE Confidence: 0.8434784

00:21:10.700 --> 00:21:11.753 It is critical,
NOTE Confidence: 0.8434784

00:21:11.753 --> 00:21:13.157 obviously for survival and
NOTE Confidence: 0.8434784

00:21:13.157 --> 00:21:14.210 development of the
NOTE Confidence: 0.84614635

00:21:14.274 --> 00:21:16.036 fetus, the trans placental signals
NOTE Confidence: 0.84614635

00:21:16.036 --> 00:21:17.806 coming from the placenta are
NOTE Confidence: 0.84614635

00:21:17.806 --> 00:21:19.598 intersecting with that developing fetus,
NOTE Confidence: 0.84614635

00:21:19.600 --> 00:21:21.104 including the developing brain.
NOTE Confidence: 0.84614635

00:21:21.104 --> 00:21:23.360 It's going to feed that developing
NOTE Confidence: 0.84614635

00:21:23.427 --> 00:21:25.515 fetus all the information about the
NOTE Confidence: 0.84614635

00:21:25.515 --> 00:21:28.291 environment it's about to be born into and

NOTE Confidence: 0.84614635

00:21:28.291 --> 00:21:30.277 throughout the course of pregnancy first,

NOTE Confidence: 0.84614635

00:21:30.280 --> 00:21:31.393 second trimesters especially.

NOTE Confidence: 0.84614635

00:21:31.393 --> 00:21:33.619 But even into the 3rd trimester.

NOTE Confidence: 0.84614635

00:21:33.620 --> 00:21:35.012 The Placenta provides all

NOTE Confidence: 0.84614635

00:21:35.012 --> 00:21:36.404 the necessary growth factors,

NOTE Confidence: 0.84614635

00:21:36.410 --> 00:21:37.802 oxygen support and information

NOTE Confidence: 0.84614635

00:21:37.802 --> 00:21:39.542 that the developing brain needs,

NOTE Confidence: 0.84614635

00:21:39.550 --> 00:21:42.000 but it also shapes the developing brain.

NOTE Confidence: 0.84614635

00:21:42.000 --> 00:21:44.436 So if there's changes in moms stress

NOTE Confidence: 0.84614635

00:21:44.436 --> 00:21:45.486 environment, her glucocorticoid

NOTE Confidence: 0.84614635

00:21:45.486 --> 00:21:47.226 levels are going to change.

NOTE Confidence: 0.84614635

00:21:47.230 --> 00:21:49.360 That's going to intersect at the

NOTE Confidence: 0.84614635

00:21:49.360 --> 00:21:51.770 level of the Placenta as an example,

NOTE Confidence: 0.84614635

00:21:51.770 --> 00:21:54.206 but also of her energy availability changes

NOTE Confidence: 0.84614635

00:21:54.206 --> 00:21:56.309 because of diabetes because of famine,

NOTE Confidence: 0.84614635

00:21:56.310 --> 00:21:57.110 those those.
NOTE Confidence: 0.84614635

00:21:57.110 --> 00:21:59.510 Those clues are also really important
NOTE Confidence: 0.84614635

00:21:59.510 --> 00:22:01.770 for the developing placenta.
NOTE Confidence: 0.84614635

00:22:01.770 --> 00:22:03.562 OK, so the way that we have
NOTE Confidence: 0.84614635

00:22:03.562 --> 00:22:04.933 thought about this in modeling
NOTE Confidence: 0.84614635

00:22:04.933 --> 00:22:06.837 over the last decade in the lab,
NOTE Confidence: 0.84614635

00:22:06.840 --> 00:22:08.370 this is just giving you an
NOTE Confidence: 0.84614635

00:22:08.370 --> 00:22:09.780 example of a rodent model.
NOTE Confidence: 0.84614635

00:22:09.780 --> 00:22:11.649 Here you have F0, which is mom.
NOTE Confidence: 0.84614635

00:22:11.650 --> 00:22:12.980 You can model this in
NOTE Confidence: 0.84614635

00:22:12.980 --> 00:22:14.044 terms of maternal stress,
NOTE Confidence: 0.84614635

00:22:14.050 --> 00:22:15.550 which we've studied in the lab
NOTE Confidence: 0.84614635

00:22:15.550 --> 00:22:17.518 and I'm going to talk about today.
NOTE Confidence: 0.84614635

00:22:17.520 --> 00:22:18.860 We've also manipulated mom's diet,
NOTE Confidence: 0.84614635

00:22:18.860 --> 00:22:20.390 which I'm not going to have
NOTE Confidence: 0.84614635

00:22:20.390 --> 00:22:21.800 time to talk about today,

NOTE Confidence: 0.84614635

00:22:21.800 --> 00:22:23.396 so that's the F zero generation.

NOTE Confidence: 0.84614635

00:22:23.400 --> 00:22:25.528 Just stating in mom is the F1 generation,

NOTE Confidence: 0.84614635

00:22:25.530 --> 00:22:26.805 so these are largely somatic

NOTE Confidence: 0.84614635

00:22:26.805 --> 00:22:28.690 cells as well as germ cells which

NOTE Confidence: 0.84614635

00:22:28.690 --> 00:22:30.340 give rise to the F2 generation.

NOTE Confidence: 0.84614635

00:22:30.340 --> 00:22:32.279 So those are the primordial germ cells.

NOTE Confidence: 0.84614635

00:22:32.280 --> 00:22:34.398 Those are also programmed during gestation,

NOTE Confidence: 0.84614635

00:22:34.400 --> 00:22:36.605 so you can imagine a scenario where

NOTE Confidence: 0.84614635

00:22:36.605 --> 00:22:38.630 moms stress in her environment,

NOTE Confidence: 0.84614635

00:22:38.630 --> 00:22:40.748 be it preconception or during pregnancy,

NOTE Confidence: 0.84614635

00:22:40.750 --> 00:22:41.898 changes in her diet,

NOTE Confidence: 0.84614635

00:22:41.898 --> 00:22:44.098 give rise to changes in a developing

NOTE Confidence: 0.84614635

00:22:44.098 --> 00:22:46.158 placenta that will guide and

NOTE Confidence: 0.84614635

00:22:46.158 --> 00:22:47.806 shape these somatic cells,

NOTE Confidence: 0.84614635

00:22:47.810 --> 00:22:49.575 putting within a range of

NOTE Confidence: 0.84614635

00:22:49.575 --> 00:22:50.634 risk and resiliency.
NOTE Confidence: 0.84614635

00:22:50.640 --> 00:22:52.400 Because of course you're on
NOTE Confidence: 0.84614635

00:22:52.400 --> 00:22:53.808 a genetic background here,
NOTE Confidence: 0.84614635

00:22:53.810 --> 00:22:55.784 so this is again goes back to
NOTE Confidence: 0.84614635

00:22:55.784 --> 00:22:58.049 RGB Y your genetic background.
NOTE Confidence: 0.84614635

00:22:58.050 --> 00:22:59.952 That's mom and dad contributes to
NOTE Confidence: 0.84614635

00:22:59.952 --> 00:23:02.409 as well as the environment this.
NOTE Confidence: 0.84614635

00:23:02.410 --> 00:23:04.774 Is a very specific timing window
NOTE Confidence: 0.84614635

00:23:04.774 --> 00:23:06.350 of a shaping environment,
NOTE Confidence: 0.84614635

00:23:06.350 --> 00:23:09.462 but it also shapes a lot about these
NOTE Confidence: 0.84614635

00:23:09.462 --> 00:23:11.493 primordial germ cells that will
NOTE Confidence: 0.84614635

00:23:11.493 --> 00:23:13.839 give rise to a next generation.
NOTE Confidence: 0.84614635

00:23:13.840 --> 00:23:15.964 This is intergenerational future
NOTE Confidence: 0.84614635

00:23:15.964 --> 00:23:18.619 generations make it trans generational.
NOTE Confidence: 0.84614635

00:23:18.620 --> 00:23:21.044 So I don't have time to go into
NOTE Confidence: 0.84614635

00:23:21.044 --> 00:23:23.211 how this model has developed over

NOTE Confidence: 0.84614635

00:23:23.211 --> 00:23:25.437 the last 10 to 15 years.

NOTE Confidence: 0.84614635

00:23:25.440 --> 00:23:27.827 All of this work has been published,

NOTE Confidence: 0.84614635

00:23:27.830 --> 00:23:29.870 but let me just quickly summarize,

NOTE Confidence: 0.84614635

00:23:29.870 --> 00:23:31.580 we developed a mouse model.

NOTE Confidence: 0.84614635

00:23:31.580 --> 00:23:33.285 We're really wanted to understand

NOTE Confidence: 0.84614635

00:23:33.285 --> 00:23:34.990 chronic stress in moms environment.

NOTE Confidence: 0.84614635

00:23:34.990 --> 00:23:35.648 During pregnancy,

NOTE Confidence: 0.84614635

00:23:35.648 --> 00:23:37.293 we identified a particular window

NOTE Confidence: 0.84614635

00:23:37.293 --> 00:23:39.080 which is basically early pregnancy,

NOTE Confidence: 0.84614635

00:23:39.080 --> 00:23:41.257 the equivalent in the human of the

NOTE Confidence: 0.84614635

00:23:41.257 --> 00:23:42.877 1st trimester where moms experience

NOTE Confidence: 0.84614635

00:23:42.877 --> 00:23:45.054 with stress in a chronic manner out

NOTE Confidence: 0.84614635

00:23:45.054 --> 00:23:47.485 of sync with her normal circadian

NOTE Confidence: 0.84614635

00:23:47.485 --> 00:23:48.718 rhythm produced offspring.

NOTE Confidence: 0.84614635

00:23:48.720 --> 00:23:50.610 Where the male offspring because

NOTE Confidence: 0.84614635

00:23:50.610 --> 00:23:52.910 they were doing this in mice,
NOTE Confidence: 0.84614635

00:23:52.910 --> 00:23:54.820 so they have a litter,
NOTE Confidence: 0.84614635

00:23:54.820 --> 00:23:57.480 were able to study sex differences here.
NOTE Confidence: 0.84614635

00:23:57.480 --> 00:23:59.145 This in Utoro stress provided
NOTE Confidence: 0.84614635

00:23:59.145 --> 00:24:01.301 male offspring but not her female
NOTE Confidence: 0.84614635

00:24:01.301 --> 00:24:03.441 offspring with changes in their
NOTE Confidence: 0.84614635

00:24:03.441 --> 00:24:05.153 adult behavioral stress responses
NOTE Confidence: 0.84614635

00:24:05.219 --> 00:24:07.433 as they grow and develop changes
NOTE Confidence: 0.84614635

00:24:07.433 --> 00:24:08.909 in their physiological stress
NOTE Confidence: 0.83360183

00:24:08.910 --> 00:24:10.815 axis. Changes in their stress
NOTE Confidence: 0.83360183

00:24:10.815 --> 00:24:12.720 regulatory genes in their brain,
NOTE Confidence: 0.83360183

00:24:12.720 --> 00:24:14.630 cognitive learning and memory deficits,
NOTE Confidence: 0.83360183

00:24:14.630 --> 00:24:17.012 as well as some really interesting
NOTE Confidence: 0.83360183

00:24:17.012 --> 00:24:18.203 neuroendocrine phenotypes of
NOTE Confidence: 0.83360183

00:24:18.203 --> 00:24:20.050 their weight gain and changes.
NOTE Confidence: 0.83360183

00:24:20.050 --> 00:24:22.156 Post puberty, so again to summarize,

NOTE Confidence: 0.83360183

00:24:22.160 --> 00:24:23.920 this is all published work.

NOTE Confidence: 0.83360183

00:24:23.920 --> 00:24:26.448 It is in male offspring of the moms

NOTE Confidence: 0.83360183

00:24:26.448 --> 00:24:28.822 that were stressed, not female.

NOTE Confidence: 0.83360183

00:24:28.822 --> 00:24:30.886 Why is this relevant?

NOTE Confidence: 0.83360183

00:24:30.890 --> 00:24:33.728 Because we know that most neurodevelopmental

NOTE Confidence: 0.83360183

00:24:33.728 --> 00:24:36.857 disorders in humans also show a male bias.

NOTE Confidence: 0.83360183

00:24:36.860 --> 00:24:38.564 So autism, early onset,

NOTE Confidence: 0.83360183

00:24:38.564 --> 00:24:40.678 schizophrenia, oh oh, CD, etc.

NOTE Confidence: 0.83360183

00:24:40.678 --> 00:24:42.366 Most nuro psychiatric disorders

NOTE Confidence: 0.83360183

00:24:42.366 --> 00:24:44.132 related to neuro developmental

NOTE Confidence: 0.83360183

00:24:44.132 --> 00:24:47.079 timing tend to show a male bias.

NOTE Confidence: 0.83360183

00:24:47.080 --> 00:24:49.796 There seems to be something in utero

NOTE Confidence: 0.83360183

00:24:49.796 --> 00:24:52.556 that is either extra at risk for

NOTE Confidence: 0.83360183

00:24:52.556 --> 00:24:54.836 males that are in development or

NOTE Confidence: 0.83360183

00:24:54.915 --> 00:24:57.730 resilient or preventative in females,

NOTE Confidence: 0.83360183

00:24:57.730 --> 00:24:58.350 or both.
NOTE Confidence: 0.83360183

00:24:58.350 --> 00:25:01.304 We know that if you go into a Nick
NOTE Confidence: 0.83360183

00:25:01.304 --> 00:25:04.020 you any necu nurse will tell you.
NOTE Confidence: 0.83360183

00:25:04.020 --> 00:25:05.500 They often see more males
NOTE Confidence: 0.83360183

00:25:05.500 --> 00:25:06.980 in the neque than females.
NOTE Confidence: 0.83360183

00:25:06.980 --> 00:25:08.792 Females tend to be more resilient
NOTE Confidence: 0.83360183

00:25:08.792 --> 00:25:10.529 going home earlier than males do,
NOTE Confidence: 0.83360183

00:25:10.530 --> 00:25:12.721 and that there's again seems to be
NOTE Confidence: 0.83360183

00:25:12.721 --> 00:25:14.380 this protective effect of in utero.
NOTE Confidence: 0.83360183

00:25:14.380 --> 00:25:16.310 Insults or females are protected
NOTE Confidence: 0.83360183

00:25:16.310 --> 00:25:18.240 in males are at risk.
NOTE Confidence: 0.83360183

00:25:18.240 --> 00:25:20.248 So in modeling that one of the genes
NOTE Confidence: 0.83360183

00:25:20.248 --> 00:25:22.324 that we have identified looking in
NOTE Confidence: 0.83360183

00:25:22.324 --> 00:25:24.209 the placenta is potentially this
NOTE Confidence: 0.83360183

00:25:24.209 --> 00:25:26.367 tissue that is protected for females,
NOTE Confidence: 0.83360183

00:25:26.370 --> 00:25:28.164 we identified 1 gene through many

NOTE Confidence: 0.83360183
00:25:28.164 --> 00:25:29.061 different transcriptomic approaches
NOTE Confidence: 0.83360183
00:25:29.061 --> 00:25:30.589 called OG tierro glycosyltransferase.
NOTE Confidence: 0.83360183
00:25:30.590 --> 00:25:31.890 This is an enzyme,
NOTE Confidence: 0.83360183
00:25:31.890 --> 00:25:33.515 it's an X linked gene.
NOTE Confidence: 0.83360183
00:25:33.520 --> 00:25:35.864 I'm not going to go into all the
NOTE Confidence: 0.83360183
00:25:35.864 --> 00:25:38.069 work of how we identified it,
NOTE Confidence: 0.83360183
00:25:38.070 --> 00:25:40.318 but it turned out to be what I
NOTE Confidence: 0.83360183
00:25:40.318 --> 00:25:42.429 defined as sort of a Canary in
NOTE Confidence: 0.83360183
00:25:42.429 --> 00:25:44.743 the coal mine gene that in the
NOTE Confidence: 0.83360183
00:25:44.743 --> 00:25:46.663 placenta in the trophoblast cells
NOTE Confidence: 0.83360183
00:25:46.663 --> 00:25:48.225 coming from the developing.
NOTE Confidence: 0.83360183
00:25:48.225 --> 00:25:50.250 Embryo that this X linked
NOTE Confidence: 0.83360183
00:25:50.250 --> 00:25:51.870 Gene Escapes X inactivation,
NOTE Confidence: 0.83360183
00:25:51.870 --> 00:25:53.770 meaning in female placental tissue.
NOTE Confidence: 0.83360183
00:25:53.770 --> 00:25:56.056 So if it's a female fetus,
NOTE Confidence: 0.83360183

00:25:56.060 --> 00:25:59.276 that placenta that is developed out of that
NOTE Confidence: 0.83360183

00:25:59.276 --> 00:26:02.537 embryo has more oh GT than a male placenta.
NOTE Confidence: 0.83360183

00:26:02.540 --> 00:26:04.440 So in the rodent world,
NOTE Confidence: 0.83360183

00:26:04.440 --> 00:26:05.656 because we have litters,
NOTE Confidence: 0.83360183

00:26:05.656 --> 00:26:07.480 we can look at the same
NOTE Confidence: 0.83360183

00:26:07.552 --> 00:26:08.956 intrauterine environment and
NOTE Confidence: 0.83360183

00:26:08.956 --> 00:26:11.296 look at sex specific outcomes.
NOTE Confidence: 0.83360183

00:26:11.300 --> 00:26:13.586 Why is this gene so interesting?
NOTE Confidence: 0.83360183

00:26:13.590 --> 00:26:13.980 Well,
NOTE Confidence: 0.83360183

00:26:13.980 --> 00:26:15.150 for many reasons,
NOTE Confidence: 0.83360183

00:26:15.150 --> 00:26:18.259 one of which is if you were to.
NOTE Confidence: 0.83360183

00:26:18.260 --> 00:26:20.366 Postulate what gene could produce hosts
NOTE Confidence: 0.83360183

00:26:20.366 --> 00:26:22.496 of effects very quickly that would
NOTE Confidence: 0.83360183

00:26:22.496 --> 00:26:24.166 be relevant evolutionarily to develop
NOTE Confidence: 0.83360183

00:26:24.166 --> 00:26:26.399 in terms of the developing brain.
NOTE Confidence: 0.83360183

00:26:26.400 --> 00:26:27.780 You would say, Well,

NOTE Confidence: 0.83360183

00:26:27.780 --> 00:26:29.850 something related to energy availability in

NOTE Confidence: 0.83360183

00:26:29.910 --> 00:26:32.070 the environment would be very important.

NOTE Confidence: 0.83360183

00:26:32.070 --> 00:26:32.949 Turns out oh,

NOTE Confidence: 0.83360183

00:26:32.949 --> 00:26:35.000 GT is an enzyme is regulated by

NOTE Confidence: 0.83360183

00:26:35.066 --> 00:26:37.018 glucose and mom's environment.

NOTE Confidence: 0.83360183

00:26:37.020 --> 00:26:39.012 It's also associated with hosts of

NOTE Confidence: 0.83360183

00:26:39.012 --> 00:26:40.779 effects that are really important

NOTE Confidence: 0.83360183

00:26:40.779 --> 00:26:43.035 for the developing embryo and fetus.

NOTE Confidence: 0.83360183

00:26:43.040 --> 00:26:44.810 It is strong epigenetic regulator,

NOTE Confidence: 0.83360183

00:26:44.810 --> 00:26:47.226 so it allows it to regulate at the

NOTE Confidence: 0.83360183

00:26:47.226 --> 00:26:49.241 level of the trophoblast cells

NOTE Confidence: 0.83360183

00:26:49.241 --> 00:26:50.576 in the Placenta.

NOTE Confidence: 0.83360183

00:26:50.580 --> 00:26:52.445 Very dynamically responses to moms

NOTE Confidence: 0.83360183

00:26:52.445 --> 00:26:54.310 environment and for those interested

NOTE Confidence: 0.83360183

00:26:54.365 --> 00:26:55.675 in sex differences in outcomes

NOTE Confidence: 0.83360183

00:26:55.675 --> 00:26:57.729 this gene is on the X chromosome,
NOTE Confidence: 0.83360183

00:26:57.730 --> 00:26:59.386 and in fact it's located very
NOTE Confidence: 0.83360183

00:26:59.386 --> 00:27:01.785 close to the long non coding RNA
NOTE Confidence: 0.83360183

00:27:01.785 --> 00:27:02.607 exist biochemically.
NOTE Confidence: 0.83360183

00:27:02.610 --> 00:27:04.590 There are interactions of these two
NOTE Confidence: 0.83360183

00:27:04.590 --> 00:27:06.590 genes that may provide again this
NOTE Confidence: 0.83360183

00:27:06.590 --> 00:27:09.054 extra resilience that will come back to for
NOTE Confidence: 0.8337124

00:27:09.111 --> 00:27:10.080 females in Utoro.
NOTE Confidence: 0.8337124

00:27:10.080 --> 00:27:12.336 This is all the boring biochemistry
NOTE Confidence: 0.8337124

00:27:12.336 --> 00:27:14.699 than required by law to show you
NOTE Confidence: 0.8337124

00:27:14.699 --> 00:27:17.246 that oh GT not only its RNA but its
NOTE Confidence: 0.8337124

00:27:17.246 --> 00:27:19.500 protein levels twice as high in a
NOTE Confidence: 0.8337124

00:27:19.500 --> 00:27:21.720 female placenta in a male placenta.
NOTE Confidence: 0.8337124

00:27:21.720 --> 00:27:23.722 The data I'm showing you here is
NOTE Confidence: 0.8337124

00:27:23.722 --> 00:27:25.438 all from mouse, but we've replicated
NOTE Confidence: 0.8337124

00:27:25.438 --> 00:27:27.440 this all in human placenta as well,

NOTE Confidence: 0.8337124

00:27:27.440 --> 00:27:29.784 so it escapes X inactivation twice as high

NOTE Confidence: 0.8337124

00:27:29.784 --> 00:27:32.620 in a female placenta compared to a male.

NOTE Confidence: 0.8337124

00:27:32.620 --> 00:27:33.980 And as an enzyme,

NOTE Confidence: 0.8337124

00:27:33.980 --> 00:27:36.506 what one of the things that Ogede

NOTE Confidence: 0.8337124

00:27:36.506 --> 00:27:38.912 Duzer by its effects on regulation

NOTE Confidence: 0.8337124

00:27:38.912 --> 00:27:41.179 is it places a sugar mark,

NOTE Confidence: 0.8337124

00:27:41.180 --> 00:27:42.664 an oblique inoculation mark

NOTE Confidence: 0.8337124

00:27:42.664 --> 00:27:44.148 on Syrian threonine residues.

NOTE Confidence: 0.8337124

00:27:44.150 --> 00:27:46.566 So you can think of any of your

NOTE Confidence: 0.8337124

00:27:46.566 --> 00:27:48.463 favorite enzymes or other proteins

NOTE Confidence: 0.8337124

00:27:48.463 --> 00:27:50.508 that are regulated by phosphorylation

NOTE Confidence: 0.8337124

00:27:50.508 --> 00:27:51.960 on Syrian training,

NOTE Confidence: 0.8337124

00:27:51.960 --> 00:27:54.578 and chances are it competes with old

NOTE Confidence: 0.8337124

00:27:54.578 --> 00:27:57.168 Lincoln alkylation and the take home message.

NOTE Confidence: 0.8337124

00:27:57.170 --> 00:27:59.252 Here is that typically Algonac olation

NOTE Confidence: 0.8337124

00:27:59.252 --> 00:28:02.378 is a break or phosphorylation is a gas,
NOTE Confidence: 0.8337124

00:28:02.380 --> 00:28:04.977 so the regulation of hundreds of proteins.
NOTE Confidence: 0.8337124

00:28:04.980 --> 00:28:06.054 Bio Glick Inoculation.
NOTE Confidence: 0.8337124

00:28:06.054 --> 00:28:08.202 Is what I'm showing you here.
NOTE Confidence: 0.8337124

00:28:08.210 --> 00:28:10.220 If you take out the placenta,
NOTE Confidence: 0.8337124

00:28:10.220 --> 00:28:11.564 either this is mouse,
NOTE Confidence: 0.8337124

00:28:11.564 --> 00:28:13.580 same results in a human placenta.
NOTE Confidence: 0.8337124

00:28:13.580 --> 00:28:15.260 There is way more protein,
NOTE Confidence: 0.8337124

00:28:15.260 --> 00:28:16.940 oblique inoculation in a female
NOTE Confidence: 0.8337124

00:28:16.940 --> 00:28:18.620 placenta compared to a male,
NOTE Confidence: 0.8337124

00:28:18.620 --> 00:28:20.378 and that's important because it says
NOTE Confidence: 0.8337124

00:28:20.378 --> 00:28:22.990 not only are its protein levels important,
NOTE Confidence: 0.8337124

00:28:22.990 --> 00:28:25.482 but it's what it's doing is similarly
NOTE Confidence: 0.8337124

00:28:25.482 --> 00:28:27.787 regulated and what that says is that
NOTE Confidence: 0.8337124

00:28:27.787 --> 00:28:30.303 the ability to break is much higher in
NOTE Confidence: 0.8337124

00:28:30.303 --> 00:28:32.725 a female placenta than a male placenta.

NOTE Confidence: 0.8337124

00:28:32.730 --> 00:28:34.002 By this biochemical mark.

NOTE Confidence: 0.8337124

00:28:34.002 --> 00:28:35.910 So our current model is is

NOTE Confidence: 0.8337124

00:28:35.978 --> 00:28:37.510 that there's a threshold.

NOTE Confidence: 0.8337124

00:28:37.510 --> 00:28:39.967 A vulnerability here where if you compare

NOTE Confidence: 0.8337124

00:28:39.967 --> 00:28:41.856 a control versus early prenatally

NOTE Confidence: 0.8337124

00:28:41.856 --> 00:28:43.791 stressed within females and males

NOTE Confidence: 0.8337124

00:28:43.791 --> 00:28:46.258 coming out of the same uterus so we

NOTE Confidence: 0.8337124

00:28:46.258 --> 00:28:48.499 can take out a male placenta in a

NOTE Confidence: 0.8337124

00:28:48.499 --> 00:28:50.497 female presenter from the same uterus,

NOTE Confidence: 0.8337124

00:28:50.500 --> 00:28:52.929 the same experience and show you that

NOTE Confidence: 0.8337124

00:28:52.929 --> 00:28:55.349 the levels protein and M RNA levels

NOTE Confidence: 0.8337124

00:28:55.349 --> 00:28:57.317 and Oakley can alkylation itself are

NOTE Confidence: 0.8337124

00:28:57.388 --> 00:28:59.558 much higher in the female and even

NOTE Confidence: 0.8337124

00:28:59.558 --> 00:29:01.834 though they are all affected by this

NOTE Confidence: 0.8337124

00:29:01.834 --> 00:29:03.850 stress that the male presented drops

NOTE Confidence: 0.8337124

00:29:03.913 --> 00:29:05.738 below some threshold of vulnerability
NOTE Confidence: 0.8337124

00:29:05.738 --> 00:29:08.232 where by its actions the break being
NOTE Confidence: 0.8337124

00:29:08.232 --> 00:29:10.640 placed on it is now released such that.
NOTE Confidence: 0.8337124

00:29:10.640 --> 00:29:12.488 The male placenta is going to
NOTE Confidence: 0.8337124

00:29:12.488 --> 00:29:14.072 dynamically respond to changes in
NOTE Confidence: 0.8337124

00:29:14.072 --> 00:29:15.562 moms environment where the female
NOTE Confidence: 0.8337124

00:29:15.562 --> 00:29:17.320 placenta is much more resilient,
NOTE Confidence: 0.8337124

00:29:17.320 --> 00:29:18.910 and that's important for functionality.
NOTE Confidence: 0.8337124

00:29:18.910 --> 00:29:21.142 One of the things locally if we dig
NOTE Confidence: 0.8337124

00:29:21.142 --> 00:29:23.445 way down in the weeds for those who
NOTE Confidence: 0.8337124

00:29:23.445 --> 00:29:26.218 don't spend a lot of time thinking
NOTE Confidence: 0.8337124

00:29:26.218 --> 00:29:27.805 about transcriptional regulation.
NOTE Confidence: 0.8337124

00:29:27.810 --> 00:29:30.442 One of the things that this important
NOTE Confidence: 0.8337124

00:29:30.442 --> 00:29:33.041 enzyme does broadly is it regulates
NOTE Confidence: 0.8337124

00:29:33.041 --> 00:29:34.445 dynamically the transcriptional
NOTE Confidence: 0.8337124

00:29:34.445 --> 00:29:36.850 and epigenetic state of a cell.

NOTE Confidence: 0.8337124

00:29:36.850 --> 00:29:40.287 So GT is a stabilizer of a

NOTE Confidence: 0.8337124

00:29:40.287 --> 00:29:42.120 methyltransferase called Easy H2.

NOTE Confidence: 0.8337124

00:29:42.120 --> 00:29:44.773 All you need to take home message

NOTE Confidence: 0.8337124

00:29:44.773 --> 00:29:46.819 from this is that easy.

NOTE Confidence: 0.8337124

00:29:46.820 --> 00:29:49.160 H2 is a predominant methyltransferase

NOTE Confidence: 0.8337124

00:29:49.160 --> 00:29:52.231 for histone three at Leising 27 so

NOTE Confidence: 0.8337124

00:29:52.231 --> 00:29:54.187 that take home messages if there

NOTE Confidence: 0.8337124

00:29:54.187 --> 00:29:55.838 is more oh GT around,

NOTE Confidence: 0.8337124

00:29:55.840 --> 00:29:57.795 it will stabilize more of

NOTE Confidence: 0.8337124

00:29:57.795 --> 00:29:58.577 this methyltransferase,

NOTE Confidence: 0.8337124

00:29:58.580 --> 00:30:00.164 resulting ultimately within the.

NOTE Confidence: 0.8337124

00:30:00.164 --> 00:30:02.790 Now of more histone three lysine 27,

NOTE Confidence: 0.8337124

00:30:02.790 --> 00:30:04.155 what's called Trimethylation,

NOTE Confidence: 0.8337124

00:30:04.155 --> 00:30:07.340 and that mark can be shown here

NOTE Confidence: 0.8017147

00:30:07.421 --> 00:30:09.833 by where if there is more oh GT in

NOTE Confidence: 0.8017147

00:30:09.833 --> 00:30:12.242 a female cell compared to a males
NOTE Confidence: 0.8017147

00:30:12.242 --> 00:30:14.368 male cell of a placenta, right?
NOTE Confidence: 0.8017147

00:30:14.368 --> 00:30:15.116 Female placenta?
NOTE Confidence: 0.8017147

00:30:15.116 --> 00:30:16.986 Male placenta comparison that you
NOTE Confidence: 0.8017147

00:30:16.986 --> 00:30:19.027 should see more of this trimethylation,
NOTE Confidence: 0.8017147

00:30:19.030 --> 00:30:21.557 and in fact we do again both.
NOTE Confidence: 0.8017147

00:30:21.560 --> 00:30:23.360 This is actually from mouse.
NOTE Confidence: 0.8017147

00:30:23.360 --> 00:30:25.614 We see the same effect within human
NOTE Confidence: 0.8017147

00:30:25.614 --> 00:30:27.700 placenta in a female placenta,
NOTE Confidence: 0.8017147

00:30:27.700 --> 00:30:30.668 you see way more of the H3K27
NOTE Confidence: 0.8017147

00:30:30.668 --> 00:30:33.228 trimethylation than you do of the Mail.
NOTE Confidence: 0.8017147

00:30:33.230 --> 00:30:36.126 And I'm going to go back to that
NOTE Confidence: 0.8017147

00:30:36.126 --> 00:30:38.499 that same take home message,
NOTE Confidence: 0.8017147

00:30:38.500 --> 00:30:40.380 which is more oblique,
NOTE Confidence: 0.8017147

00:30:40.380 --> 00:30:41.790 inoculation more trimethylation
NOTE Confidence: 0.8017147

00:30:41.790 --> 00:30:43.200 is more break.

NOTE Confidence: 0.8017147

00:30:43.200 --> 00:30:45.720 What that break allows is it allows

NOTE Confidence: 0.8017147

00:30:45.720 --> 00:30:47.659 the female placenta to really

NOTE Confidence: 0.8017147

00:30:47.659 --> 00:30:50.017 titrate its responses to an ever

NOTE Confidence: 0.8017147

00:30:50.017 --> 00:30:51.660 changing maternal environment.

NOTE Confidence: 0.8017147

00:30:51.660 --> 00:30:54.174 Mails missing that break are more

NOTE Confidence: 0.8017147

00:30:54.174 --> 00:30:56.303 vulnerable because they're going to

NOTE Confidence: 0.8017147

00:30:56.303 --> 00:30:58.625 respond there percent is going to

NOTE Confidence: 0.8017147

00:30:58.625 --> 00:31:00.615 constantly be responding to moms

NOTE Confidence: 0.8017147

00:31:00.615 --> 00:31:02.543 stress or dietary challenge, etc.

NOTE Confidence: 0.8017147

00:31:02.543 --> 00:31:04.155 Producing hosts of differences

NOTE Confidence: 0.8017147

00:31:04.155 --> 00:31:05.767 in the transplacental signals,

NOTE Confidence: 0.8017147

00:31:05.770 --> 00:31:08.188 making it to the developing brains,

NOTE Confidence: 0.8017147

00:31:08.190 --> 00:31:11.270 developing fetal and fetal brain.

NOTE Confidence: 0.8017147

00:31:11.270 --> 00:31:12.926 So I'm just going to show you a

NOTE Confidence: 0.8017147

00:31:12.926 --> 00:31:14.513 couple of quick pieces of evidence

NOTE Confidence: 0.8017147

00:31:14.513 --> 00:31:15.913 of why this is important.
NOTE Confidence: 0.8017147

00:31:15.920 --> 00:31:16.271 OK,
NOTE Confidence: 0.8017147

00:31:16.271 --> 00:31:18.728 so this is showing you if we
NOTE Confidence: 0.8017147

00:31:18.728 --> 00:31:21.270 just look at just broadly at
NOTE Confidence: 0.8017147

00:31:21.270 --> 00:31:23.455 mid gestation of a placenta.
NOTE Confidence: 0.8017147

00:31:23.460 --> 00:31:25.434 And we look at sex differences
NOTE Confidence: 0.8017147

00:31:25.434 --> 00:31:26.750 just broadly in transcription
NOTE Confidence: 0.8017147

00:31:26.811 --> 00:31:28.126 that are related to OGT.
NOTE Confidence: 0.8017147

00:31:28.130 --> 00:31:29.985 So what I'm showing you here for
NOTE Confidence: 0.8017147

00:31:29.985 --> 00:31:32.639 those again that don't do a lot of
NOTE Confidence: 0.8017147

00:31:32.639 --> 00:31:33.716 transcriptional regulation studies.
NOTE Confidence: 0.8017147

00:31:33.720 --> 00:31:35.897 This is from an RNA sequencing experiment.
NOTE Confidence: 0.8017147

00:31:35.900 --> 00:31:37.742 This is just asking all genes
NOTE Confidence: 0.8017147

00:31:37.742 --> 00:31:39.933 expressed in a female placenta at the
NOTE Confidence: 0.8017147

00:31:39.933 --> 00:31:42.040 same time point as a male placenta
NOTE Confidence: 0.8017147

00:31:42.100 --> 00:31:44.291 from the same uterus and looking at

NOTE Confidence: 0.8017147
00:31:44.291 --> 00:31:45.934 all genes widely being expressed.
NOTE Confidence: 0.8017147
00:31:45.934 --> 00:31:48.750 So this is plotted here on the Y
NOTE Confidence: 0.8017147
00:31:48.822 --> 00:31:51.062 axis is showing you at least in a
NOTE Confidence: 0.8017147
00:31:51.062 --> 00:31:53.775 log 2 fold change on the Y axis so.
NOTE Confidence: 0.8017147
00:31:53.780 --> 00:31:54.893 Increased gene expression
NOTE Confidence: 0.8017147
00:31:54.893 --> 00:31:56.006 decreased gene expression.
NOTE Confidence: 0.8017147
00:31:56.010 --> 00:31:58.236 The X axis is showing you
NOTE Confidence: 0.8017147
00:31:58.236 --> 00:31:59.720 the level of expression,
NOTE Confidence: 0.8017147
00:31:59.720 --> 00:32:01.200 so really highly expressed
NOTE Confidence: 0.8017147
00:32:01.200 --> 00:32:02.680 genes are out here.
NOTE Confidence: 0.8017147
00:32:02.680 --> 00:32:05.590 Lowly expressed genes are in here.
NOTE Confidence: 0.8017147
00:32:05.590 --> 00:32:09.286 A red dot is showing you a robust,
NOTE Confidence: 0.8017147
00:32:09.290 --> 00:32:10.218 significant difference
NOTE Confidence: 0.8017147
00:32:10.218 --> 00:32:12.538 between a male and female,
NOTE Confidence: 0.8017147
00:32:12.540 --> 00:32:14.820 both increased and decreased gene
NOTE Confidence: 0.8017147

00:32:14.820 --> 00:32:17.630 expression at this one time point.
NOTE Confidence: 0.8017147

00:32:17.630 --> 00:32:18.048 OK,
NOTE Confidence: 0.8017147

00:32:18.048 --> 00:32:20.974 if oh GT is important for titrating
NOTE Confidence: 0.8017147

00:32:20.974 --> 00:32:23.179 responses to the environment.
NOTE Confidence: 0.8017147

00:32:23.180 --> 00:32:26.012 If we are able to transcriptionally
NOTE Confidence: 0.8017147

00:32:26.012 --> 00:32:29.667 genetically alter oh GT in a female placenta,
NOTE Confidence: 0.8017147

00:32:29.670 --> 00:32:31.518 making her hemizygous meaning
NOTE Confidence: 0.8017147

00:32:31.518 --> 00:32:33.828 her level of oh GT,
NOTE Confidence: 0.8017147

00:32:33.830 --> 00:32:36.220 because now we're eliminating 1X.
NOTE Confidence: 0.8017147

00:32:36.220 --> 00:32:37.452 Of Oh GT expression,
NOTE Confidence: 0.8017147

00:32:37.452 --> 00:32:39.765 so her levels in a heavy zigzag
NOTE Confidence: 0.8017147

00:32:39.765 --> 00:32:42.105 environment should be very similar to
NOTE Confidence: 0.8017147

00:32:42.105 --> 00:32:44.925 the levels of oh GT in a normal male.
NOTE Confidence: 0.8017147

00:32:44.930 --> 00:32:47.462 Now what happens to those differences
NOTE Confidence: 0.8017147

00:32:47.462 --> 00:32:49.150 between males and females?
NOTE Confidence: 0.8017147

00:32:49.150 --> 00:32:50.840 They are almost completely eliminated,

NOTE Confidence: 0.8017147

00:32:50.840 --> 00:32:53.101 and in fact the jeans that remain

NOTE Confidence: 0.8017147

00:32:53.101 --> 00:32:54.910 here that are significantly different

NOTE Confidence: 0.8017147

00:32:54.910 --> 00:32:58.540 between the two or either X or Y linked.

NOTE Confidence: 0.8017147

00:32:58.540 --> 00:32:59.194 Suggesting again,

NOTE Confidence: 0.8017147

00:32:59.194 --> 00:33:01.156 those are not going to be

NOTE Confidence: 0.8017147

00:33:01.156 --> 00:33:03.129 affected by the OG transcription.

NOTE Confidence: 0.8017147

00:33:03.130 --> 00:33:03.818 This evidence,

NOTE Confidence: 0.8017147

00:33:03.818 --> 00:33:05.882 the take home message here being

NOTE Confidence: 0.8017147

00:33:05.882 --> 00:33:08.043 this one gene that we identified

NOTE Confidence: 0.8017147

00:33:08.043 --> 00:33:10.149 shows you as a candidate approach

NOTE Confidence: 0.8017147

00:33:10.211 --> 00:33:11.961 that is widely important for

NOTE Confidence: 0.8017147

00:33:11.961 --> 00:33:13.711 what happens in the Placenta

NOTE Confidence: 0.8017147

00:33:13.720 --> 00:33:16.072 and then altering all of those

NOTE Confidence: 0.8017147

00:33:16.072 --> 00:33:17.640 differences in the transplacental

NOTE Confidence: 0.8349228

00:33:17.707 --> 00:33:19.982 signals that are going to happen being

NOTE Confidence: 0.8349228

00:33:19.982 --> 00:33:22.429 relayed to the developing fetal brain.

NOTE Confidence: 0.8349228

00:33:22.430 --> 00:33:24.740 Where's our evidence of that?

NOTE Confidence: 0.8349228

00:33:24.740 --> 00:33:26.798 What I'm showing you here is now

NOTE Confidence: 0.8349228

00:33:26.798 --> 00:33:28.390 an RNA sequencing experiment.

NOTE Confidence: 0.8349228

00:33:28.390 --> 00:33:30.050 This is these are heatmaps.

NOTE Confidence: 0.8349228

00:33:30.050 --> 00:33:31.710 These are the identical brains.

NOTE Confidence: 0.8349228

00:33:31.710 --> 00:33:33.066 From those placentas whoops,

NOTE Confidence: 0.8349228

00:33:33.066 --> 00:33:34.422 sorry from these placentas

NOTE Confidence: 0.8349228

00:33:34.422 --> 00:33:36.028 that I just showed you.

NOTE Confidence: 0.8349228

00:33:36.030 --> 00:33:38.254 So if we take out the fetal brain

NOTE Confidence: 0.8349228

00:33:38.254 --> 00:33:40.265 from the same midpoint of gestation

NOTE Confidence: 0.8349228

00:33:40.265 --> 00:33:42.789 and we now examine it for gene

NOTE Confidence: 0.8349228

00:33:42.789 --> 00:33:44.661 expression in the brain, OK,

NOTE Confidence: 0.8349228

00:33:44.661 --> 00:33:46.647 we already know in all mammals,

NOTE Confidence: 0.8349228

00:33:46.650 --> 00:33:48.519 mice, and humans that at any given

NOTE Confidence: 0.8349228

00:33:48.519 --> 00:33:50.121 time point in brain development

NOTE Confidence: 0.8349228

00:33:50.121 --> 00:33:51.981 or fetal development in general

NOTE Confidence: 0.8349228

00:33:51.981 --> 00:33:53.977 because males and females develop

NOTE Confidence: 0.8349228

00:33:53.977 --> 00:33:55.609 it slightly different rates.

NOTE Confidence: 0.8349228

00:33:55.610 --> 00:33:57.085 Likely accounting for differences that

NOTE Confidence: 0.8349228

00:33:57.085 --> 00:33:59.260 we're seeing here in gene transcription.

NOTE Confidence: 0.8349228

00:33:59.260 --> 00:34:01.290 OK, so this is the The Geno

NOTE Confidence: 0.8349228

00:34:01.290 --> 00:34:02.910 type of the placenta.

NOTE Confidence: 0.8349228

00:34:02.910 --> 00:34:04.238 That transcription I'm showing

NOTE Confidence: 0.8349228

00:34:04.238 --> 00:34:06.230 you here is of the brain,

NOTE Confidence: 0.8349228

00:34:06.230 --> 00:34:08.568 so a normal female brain had mid

NOTE Confidence: 0.8349228

00:34:08.568 --> 00:34:10.880 gestation compared to a normal male brain.

NOTE Confidence: 0.8349228

00:34:10.880 --> 00:34:12.540 Same pot, same time point.

NOTE Confidence: 0.8349228

00:34:12.540 --> 00:34:15.033 You can see that a lot of the jeans

NOTE Confidence: 0.8349228

00:34:15.033 --> 00:34:17.190 that are really elevated right?

NOTE Confidence: 0.8349228

00:34:17.190 --> 00:34:19.846 So each column here is a different brain.

NOTE Confidence: 0.8349228

00:34:19.850 --> 00:34:21.836 Each row is a different gene.

NOTE Confidence: 0.8349228

00:34:21.840 --> 00:34:24.488 OK so this is this is RNA sequencing.

NOTE Confidence: 0.8349228

00:34:24.490 --> 00:34:26.770 What this is showing you?

NOTE Confidence: 0.8349228

00:34:26.770 --> 00:34:27.010 Again,

NOTE Confidence: 0.8349228

00:34:27.010 --> 00:34:28.930 is that if we examine this by looking

NOTE Confidence: 0.8349228

00:34:28.930 --> 00:34:30.781 at the effects in a normal female

NOTE Confidence: 0.8349228

00:34:30.781 --> 00:34:32.498 versus a normal male jeans that

NOTE Confidence: 0.8349228

00:34:32.498 --> 00:34:34.053 are ultimately highly expressed at

NOTE Confidence: 0.8349228

00:34:34.053 --> 00:34:35.962 this time point in a female are

NOTE Confidence: 0.8349228

00:34:35.962 --> 00:34:37.772 not so highly expressed in a male

NOTE Confidence: 0.8349228

00:34:37.772 --> 00:34:39.530 and jeans that are lowly expressed

NOTE Confidence: 0.8349228

00:34:39.530 --> 00:34:41.019 in the female brain are.

NOTE Confidence: 0.8349228

00:34:41.020 --> 00:34:41.288 Again,

NOTE Confidence: 0.8349228

00:34:41.288 --> 00:34:43.164 this is the hypothalamus of the brain

NOTE Confidence: 0.8349228

00:34:43.164 --> 00:34:45.130 are more highly expressed in a male.

NOTE Confidence: 0.8349228

00:34:45.130 --> 00:34:46.738 The take home message here is

NOTE Confidence: 0.8349228

00:34:46.738 --> 00:34:48.140 that we already know this.

NOTE Confidence: 0.8349228

00:34:48.140 --> 00:34:49.556 We know that even before birth

NOTE Confidence: 0.8349228

00:34:49.556 --> 00:34:51.229 the male and female brain are

NOTE Confidence: 0.8349228

00:34:51.229 --> 00:34:52.249 in different trajectories.

NOTE Confidence: 0.8349228

00:34:52.250 --> 00:34:53.972 But if we now alter the level

NOTE Confidence: 0.8349228

00:34:53.972 --> 00:34:55.809 of oh GT in the placenta,

NOTE Confidence: 0.8349228

00:34:55.810 --> 00:34:57.260 leaving the brain totally normal.

NOTE Confidence: 0.8349228

00:34:57.260 --> 00:35:00.125 Trance. Altering transplacental signals?

NOTE Confidence: 0.8349228

00:35:00.125 --> 00:35:02.135 What does her brain look like?

NOTE Confidence: 0.8349228

00:35:02.140 --> 00:35:04.956 And I think you can see here that

NOTE Confidence: 0.8349228

00:35:04.956 --> 00:35:06.723 ultimately you're seeing is that

NOTE Confidence: 0.8349228

00:35:06.723 --> 00:35:09.040 this female brain were not her OG

NOTE Confidence: 0.8349228

00:35:09.113 --> 00:35:10.973 T levels in Placenta are similar

NOTE Confidence: 0.8349228

00:35:10.973 --> 00:35:13.616 to that of a male, not a female.

NOTE Confidence: 0.8349228

00:35:13.616 --> 00:35:15.710 Her brain becomes more male like

NOTE Confidence: 0.8349228

00:35:15.787 --> 00:35:17.936 and that tells us is that these,
NOTE Confidence: 0.8349228

00:35:17.940 --> 00:35:18.640 oh GTO,
NOTE Confidence: 0.8349228

00:35:18.640 --> 00:35:20.390 Glick inoculated proteins are really
NOTE Confidence: 0.8349228

00:35:20.390 --> 00:35:21.799 important for transplacental signals
NOTE Confidence: 0.8349228

00:35:21.799 --> 00:35:23.647 guiding the development of the fetus,
NOTE Confidence: 0.8349228

00:35:23.650 --> 00:35:26.330 and no doubt the rate of the fetal
NOTE Confidence: 0.8349228

00:35:26.330 --> 00:35:28.266 development, and that no doubt,
NOTE Confidence: 0.8349228

00:35:28.266 --> 00:35:30.261 is important for risk for
NOTE Confidence: 0.8349228

00:35:30.261 --> 00:35:31.360 neurodevelopmental disorders.
NOTE Confidence: 0.8349228

00:35:31.360 --> 00:35:33.165 Ultimate thing we've been working
NOTE Confidence: 0.8349228

00:35:33.165 --> 00:35:35.662 on for the past decade that we
NOTE Confidence: 0.8349228

00:35:35.662 --> 00:35:36.910 keep sort of running,
NOTE Confidence: 0.8349228

00:35:36.910 --> 00:35:38.986 beating our heads against the wall,
NOTE Confidence: 0.8349228

00:35:38.990 --> 00:35:41.078 trying to figure out is OK.
NOTE Confidence: 0.8349228

00:35:41.080 --> 00:35:42.810 What are these transplacental signals?
NOTE Confidence: 0.8349228

00:35:42.810 --> 00:35:44.748 We've identified many host of effects

NOTE Confidence: 0.8349228

00:35:44.748 --> 00:35:47.319 at the level of the placenta itself.

NOTE Confidence: 0.8349228

00:35:47.320 --> 00:35:49.408 We've identified even many of the

NOTE Confidence: 0.8349228

00:35:49.408 --> 00:35:50.452 transplacental potential signals

NOTE Confidence: 0.8349228

00:35:50.452 --> 00:35:51.490 from the placenta,

NOTE Confidence: 0.8349228

00:35:51.490 --> 00:35:53.919 but it's really difficult to get at.

NOTE Confidence: 0.8349228

00:35:53.920 --> 00:35:55.685 Are there steroid hormone differences

NOTE Confidence: 0.8349228

00:35:55.685 --> 00:35:57.450 that guide the developing fetal

NOTE Confidence: 0.8349228

00:35:57.507 --> 00:35:58.428 tissues and brain?

NOTE Confidence: 0.8349228

00:35:58.430 --> 00:36:00.572 Are there other proteins that are

NOTE Confidence: 0.8349228

00:36:00.572 --> 00:36:02.000 important information for relaying?

NOTE Confidence: 0.8349228

00:36:02.000 --> 00:36:03.975 Both the rate of development

NOTE Confidence: 0.8349228

00:36:03.975 --> 00:36:05.555 and fetal brain development.

NOTE Confidence: 0.84944886

00:36:05.560 --> 00:36:08.073 One of the signals that we found

NOTE Confidence: 0.84944886

00:36:08.073 --> 00:36:11.358 that I'm going to talk to you about

NOTE Confidence: 0.84944886

00:36:11.358 --> 00:36:13.058 is the extracellular vesicle.

NOTE Confidence: 0.84944886

00:36:13.060 --> 00:36:15.580 There is no time in million lifespan
NOTE Confidence: 0.84944886

00:36:15.580 --> 00:36:19.172 where if you were to take out through the
NOTE Confidence: 0.84944886

00:36:19.172 --> 00:36:21.750 blood and isolate exercise or vesicles,
NOTE Confidence: 0.84944886

00:36:21.750 --> 00:36:23.840 the highest concentration of extracellular
NOTE Confidence: 0.84944886

00:36:23.840 --> 00:36:25.930 vesicles in circulation is pregnancy
NOTE Confidence: 0.84944886

00:36:25.992 --> 00:36:27.817 because the placenta itself produces
NOTE Confidence: 0.84944886

00:36:27.817 --> 00:36:29.642 a ton of extracellular vesicles.
NOTE Confidence: 0.84944886

00:36:29.650 --> 00:36:32.331 Those both come from the trophoblast cells
NOTE Confidence: 0.84944886

00:36:32.331 --> 00:36:34.869 that interact with the developing fetus.
NOTE Confidence: 0.84944886

00:36:34.870 --> 00:36:36.610 But also the decidua side that
NOTE Confidence: 0.84944886

00:36:36.610 --> 00:36:38.450 interacts again with moms circulation.
NOTE Confidence: 0.84944886

00:36:38.450 --> 00:36:40.550 So trying to understand these extracellular
NOTE Confidence: 0.84944886

00:36:40.550 --> 00:36:42.566 vesicles and what signal that they
NOTE Confidence: 0.84944886

00:36:42.566 --> 00:36:44.512 might pose and how stress affects them
NOTE Confidence: 0.84944886

00:36:44.512 --> 00:36:46.857 could be a really a potential important
NOTE Confidence: 0.84944886

00:36:46.857 --> 00:36:48.524 biomarker that we're interested in.

NOTE Confidence: 0.84944886

00:36:48.524 --> 00:36:50.468 So just to remind you again,

NOTE Confidence: 0.84944886

00:36:50.470 --> 00:36:52.214 what are extracellular vesicles?

NOTE Confidence: 0.84944886

00:36:52.214 --> 00:36:55.564 There are many different types says from a

NOTE Confidence: 0.84944886

00:36:55.564 --> 00:36:57.902 review for you from your Sadowski's lab.

NOTE Confidence: 0.84944886

00:36:57.910 --> 00:37:00.940 He also said ASCII is at Pitt and he runs

NOTE Confidence: 0.84944886

00:37:01.021 --> 00:37:04.277 the Magee Women's center and is really done.

NOTE Confidence: 0.84944886

00:37:04.280 --> 00:37:07.000 The most work in this field and understanding

NOTE Confidence: 0.84944886

00:37:07.000 --> 00:37:08.180 placental extracellular vesicles.

NOTE Confidence: 0.84944886

00:37:08.180 --> 00:37:10.370 There important signals for fetal development

NOTE Confidence: 0.84944886

00:37:10.370 --> 00:37:12.070 and maintaining homeostasis for mom.

NOTE Confidence: 0.84944886

00:37:12.070 --> 00:37:14.266 So those exercise the vesicles produced

NOTE Confidence: 0.84944886

00:37:14.266 --> 00:37:17.183 by the Placenta Act both locally on all

NOTE Confidence: 0.84944886

00:37:17.183 --> 00:37:19.265 different cell types of the Placenta

NOTE Confidence: 0.84944886

00:37:19.333 --> 00:37:21.629 and also can be found in circulation.

NOTE Confidence: 0.84944886

00:37:21.630 --> 00:37:23.375 Larger exerciser vesicles are termed

NOTE Confidence: 0.84944886

00:37:23.375 --> 00:37:26.300 Micro Vesicles and as I told you small
NOTE Confidence: 0.84944886

00:37:26.300 --> 00:37:28.155 exercise vesicles are termed exomes.
NOTE Confidence: 0.84944886

00:37:28.160 --> 00:37:28.469 Again,
NOTE Confidence: 0.84944886

00:37:28.469 --> 00:37:30.632 there are many different types that you
NOTE Confidence: 0.84944886

00:37:30.632 --> 00:37:32.879 can detect that contain different cargo,
NOTE Confidence: 0.84944886

00:37:32.880 --> 00:37:34.352 both intracellular cargo protein
NOTE Confidence: 0.84944886

00:37:34.352 --> 00:37:36.884 cargo weather going and a lot of
NOTE Confidence: 0.84944886

00:37:36.884 --> 00:37:37.928 work is being done.
NOTE Confidence: 0.84944886

00:37:37.930 --> 00:37:39.664 Now to develop these tools to
NOTE Confidence: 0.84944886

00:37:39.664 --> 00:37:41.697 try and understand how they are
NOTE Confidence: 0.84944886

00:37:41.697 --> 00:37:43.329 released from intracellular stores.
NOTE Confidence: 0.84944886

00:37:43.330 --> 00:37:45.010 So that's a really important
NOTE Confidence: 0.84944886

00:37:45.010 --> 00:37:46.018 and interesting point.
NOTE Confidence: 0.84944886

00:37:46.020 --> 00:37:48.302 That way in which these vesicles are
NOTE Confidence: 0.84944886

00:37:48.302 --> 00:37:50.651 loaded up and are secreted from the
NOTE Confidence: 0.84944886

00:37:50.651 --> 00:37:53.033 cell differ from the type of vesicle

NOTE Confidence: 0.84944886
00:37:53.033 --> 00:37:55.118 that they are, how they released,
NOTE Confidence: 0.84944886
00:37:55.118 --> 00:37:57.134 and how they travel in circulation.
NOTE Confidence: 0.84944886
00:37:57.140 --> 00:37:58.855 So they're super super interesting
NOTE Confidence: 0.84944886
00:37:58.855 --> 00:37:59.884 and really important.
NOTE Confidence: 0.84944886
00:37:59.890 --> 00:38:01.410 Cellular signaling mechanisms for
NOTE Confidence: 0.84944886
00:38:01.410 --> 00:38:02.550 these extracellular vesicles.
NOTE Confidence: 0.84944886
00:38:02.550 --> 00:38:03.594 As I've said,
NOTE Confidence: 0.84944886
00:38:03.594 --> 00:38:05.682 there are many components of the
NOTE Confidence: 0.84944886
00:38:05.682 --> 00:38:07.743 protein content related to coming
NOTE Confidence: 0.84944886
00:38:07.743 --> 00:38:09.387 from the placenta itself,
NOTE Confidence: 0.84944886
00:38:09.390 --> 00:38:11.290 although none that are truly
NOTE Confidence: 0.84944886
00:38:11.290 --> 00:38:12.810 exclusively from the placenta,
NOTE Confidence: 0.84944886
00:38:12.810 --> 00:38:15.029 so there's not really any way to
NOTE Confidence: 0.84944886
00:38:15.029 --> 00:38:17.033 say that they're absolutely from
NOTE Confidence: 0.84944886
00:38:17.033 --> 00:38:18.509 the trophoblast cells,
NOTE Confidence: 0.84944886

00:38:18.510 --> 00:38:21.142 but the cargo has also been well
NOTE Confidence: 0.84944886

00:38:21.142 --> 00:38:23.216 characterized of many of these
NOTE Confidence: 0.84944886

00:38:23.216 --> 00:38:25.406 vesicles and their contribution for
NOTE Confidence: 0.84944886

00:38:25.406 --> 00:38:28.049 maternal millu and fetal development.
NOTE Confidence: 0.84944886

00:38:28.050 --> 00:38:29.842 So I'm just going to show you touch
NOTE Confidence: 0.84944886

00:38:29.842 --> 00:38:32.003 on a little bit of work just to
NOTE Confidence: 0.84944886

00:38:32.003 --> 00:38:33.884 Pique your interest in why these
NOTE Confidence: 0.84944886

00:38:33.884 --> 00:38:35.689 things are so incredibly important.
NOTE Confidence: 0.84944886

00:38:35.690 --> 00:38:37.910 Is that thinking about exercising
NOTE Confidence: 0.84944886

00:38:37.910 --> 00:38:38.798 vesicles and?
NOTE Confidence: 0.84944886

00:38:38.800 --> 00:38:40.210 Understanding them as a biomarker
NOTE Confidence: 0.84944886

00:38:40.210 --> 00:38:41.958 you can both sequence the exercise
NOTE Confidence: 0.84944886

00:38:41.958 --> 00:38:43.680 of vesicles that you can isolate.
NOTE Confidence: 0.84944886

00:38:43.680 --> 00:38:45.689 This is showing you some of this
NOTE Confidence: 0.84944886

00:38:45.689 --> 00:38:46.550 small noncoding RNA.
NOTE Confidence: 0.84944886

00:38:46.550 --> 00:38:48.216 The thing I want to draw your

NOTE Confidence: 0.84944886

00:38:48.216 --> 00:38:49.909 attention to is that we've sequenced

NOTE Confidence: 0.84944886

00:38:49.909 --> 00:38:51.751 by small non coding RNA sequencing

NOTE Confidence: 0.84944886

00:38:51.751 --> 00:38:53.439 of the exercise in vesicles,

NOTE Confidence: 0.84944886

00:38:53.440 --> 00:38:54.524 in circulation in mice.

NOTE Confidence: 0.84944886

00:38:54.524 --> 00:38:56.744 You can see that if you look at

NOTE Confidence: 0.84944886

00:38:56.744 --> 00:38:58.599 this heat map that is showing you

NOTE Confidence: 0.84944886

00:38:58.599 --> 00:39:01.114 here on the far end is non pregnant

NOTE Confidence: 0.84944886

00:39:01.114 --> 00:39:02.050 females versus pregnant

NOTE Confidence: 0.8228827

00:39:02.050 --> 00:39:04.528 that have been control or stressed.

NOTE Confidence: 0.8228827

00:39:04.530 --> 00:39:06.605 Obviously the biggest difference in

NOTE Confidence: 0.8228827

00:39:06.605 --> 00:39:09.365 that the micro RNA content I'm not

NOTE Confidence: 0.8228827

00:39:09.365 --> 00:39:11.829 even showing you all of the data here,

NOTE Confidence: 0.8228827

00:39:11.830 --> 00:39:14.020 I just want to show you

NOTE Confidence: 0.8228827

00:39:14.020 --> 00:39:15.115 that pregnancy itself,

NOTE Confidence: 0.8228827

00:39:15.120 --> 00:39:17.424 just to highlight again the presence

NOTE Confidence: 0.8228827

00:39:17.424 --> 00:39:19.385 of placenta dramatically shift the
NOTE Confidence: 0.8228827

00:39:19.385 --> 00:39:21.220 content of circulation of extracellular
NOTE Confidence: 0.8228827

00:39:21.220 --> 00:39:23.741 vesicle in the micro RNA content and
NOTE Confidence: 0.8228827

00:39:23.741 --> 00:39:25.733 that there are some really important
NOTE Confidence: 0.8228827

00:39:25.733 --> 00:39:27.948 known micro RNA that can be very
NOTE Confidence: 0.8228827

00:39:27.948 --> 00:39:30.126 specific clues as to what effect
NOTE Confidence: 0.8228827

00:39:30.126 --> 00:39:32.266 they're having on distal tissues,
NOTE Confidence: 0.8228827

00:39:32.270 --> 00:39:33.130 especially intersecting
NOTE Confidence: 0.8228827

00:39:33.130 --> 00:39:34.850 with the immune system.
NOTE Confidence: 0.8228827

00:39:34.850 --> 00:39:37.610 And to that point in our proteomics studies,
NOTE Confidence: 0.8228827

00:39:37.610 --> 00:39:40.074 this is work done by Brigid Nugent
NOTE Confidence: 0.8228827

00:39:40.074 --> 00:39:42.788 when she was a postdoc in the lab.
NOTE Confidence: 0.8228827

00:39:42.790 --> 00:39:44.510 The protein content of these
NOTE Confidence: 0.8228827

00:39:44.510 --> 00:39:45.886 extracellular vesicles really important,
NOTE Confidence: 0.8228827

00:39:45.890 --> 00:39:47.840 also because it tells you both
NOTE Confidence: 0.8228827

00:39:47.840 --> 00:39:49.570 the tissues it's being released

NOTE Confidence: 0.8228827

00:39:49.570 --> 00:39:51.410 from and where it's acting,

NOTE Confidence: 0.8228827

00:39:51.410 --> 00:39:53.696 but what's really important here is

NOTE Confidence: 0.8228827

00:39:53.696 --> 00:39:55.570 thinking about the intersection of

NOTE Confidence: 0.8228827

00:39:55.570 --> 00:39:57.280 where we found that with stress,

NOTE Confidence: 0.8228827

00:39:57.280 --> 00:40:00.318 the protein content dramatically shifts in A.

NOTE Confidence: 0.8228827

00:40:00.320 --> 00:40:02.245 Ocean of immune related protein

NOTE Confidence: 0.8228827

00:40:02.245 --> 00:40:04.170 signaling molecules in these vesicles

NOTE Confidence: 0.8228827

00:40:04.232 --> 00:40:06.297 to a huge increase in metabolic anan,

NOTE Confidence: 0.8228827

00:40:06.300 --> 00:40:08.060 proteolysis and complement activation etc.

NOTE Confidence: 0.8228827

00:40:08.060 --> 00:40:10.748 Proteins in these vesicles so the take

NOTE Confidence: 0.8228827

00:40:10.748 --> 00:40:13.173 home message here is the cargo both

NOTE Confidence: 0.8228827

00:40:13.173 --> 00:40:15.766 in terms of its actions at the distal

NOTE Confidence: 0.8228827

00:40:15.766 --> 00:40:18.258 site for the small noncoding RNA but

NOTE Confidence: 0.8228827

00:40:18.258 --> 00:40:20.620 also the tissues it's traveling to

NOTE Confidence: 0.8228827

00:40:20.620 --> 00:40:22.620 seem to significantly change with

NOTE Confidence: 0.8228827

00:40:22.691 --> 00:40:24.406 stress and moms environment and
NOTE Confidence: 0.8228827

00:40:24.406 --> 00:40:26.788 just one last slide on these 'cause
NOTE Confidence: 0.8228827

00:40:26.788 --> 00:40:29.180 I want to move on to other topics.
NOTE Confidence: 0.8228827

00:40:29.180 --> 00:40:31.020 Here is that when we.
NOTE Confidence: 0.8228827

00:40:31.020 --> 00:40:33.078 Take out these exercise in vesicles
NOTE Confidence: 0.8228827

00:40:33.078 --> 00:40:35.090 from a mouse who's pregnant.
NOTE Confidence: 0.8228827

00:40:35.090 --> 00:40:36.620 From both stress and controls,
NOTE Confidence: 0.8228827

00:40:36.620 --> 00:40:38.200 we fluorescently labeled these vesicles
NOTE Confidence: 0.8228827

00:40:38.200 --> 00:40:40.579 and inject him back into a pregnant mom.
NOTE Confidence: 0.8228827

00:40:40.580 --> 00:40:42.750 To ask the question of is there
NOTE Confidence: 0.8228827

00:40:42.750 --> 00:40:44.318 transplacental signaling going from the
NOTE Confidence: 0.8228827

00:40:44.318 --> 00:40:46.376 maternal mil you into the fetal compartment.
NOTE Confidence: 0.8228827

00:40:46.380 --> 00:40:48.210 We have no evidence that it
NOTE Confidence: 0.8228827

00:40:48.210 --> 00:40:49.430 actually makes it through.
NOTE Confidence: 0.8228827

00:40:49.430 --> 00:40:50.012 In fact,
NOTE Confidence: 0.8228827

00:40:50.012 --> 00:40:52.723 if you take out the uterus you can see

NOTE Confidence: 0.8228827

00:40:52.723 --> 00:40:55.522 here by this way this is lighting up here.

NOTE Confidence: 0.8228827

00:40:55.530 --> 00:40:57.890 This is only in the Placenta And if

NOTE Confidence: 0.8228827

00:40:57.890 --> 00:40:59.802 you actually dissect out the Placenta

NOTE Confidence: 0.8228827

00:40:59.802 --> 00:41:02.240 and fetus you can see that in fact,

NOTE Confidence: 0.8228827

00:41:02.240 --> 00:41:04.292 no crossing of maternal produced exercise

NOTE Confidence: 0.8228827

00:41:04.292 --> 00:41:06.890 vesicles makes it into the fetal compartment.

NOTE Confidence: 0.8228827

00:41:06.890 --> 00:41:07.973 Why that's important?

NOTE Confidence: 0.8228827

00:41:07.973 --> 00:41:10.500 Because it tells us that the source

NOTE Confidence: 0.8228827

00:41:10.570 --> 00:41:12.586 of communication then from mom to

NOTE Confidence: 0.8228827

00:41:12.586 --> 00:41:14.755 the fetus is likely the vesicles

NOTE Confidence: 0.8228827

00:41:14.755 --> 00:41:16.655 acting again at the placenta,

NOTE Confidence: 0.8228827

00:41:16.660 --> 00:41:18.520 producing changes that then changed

NOTE Confidence: 0.8228827

00:41:18.520 --> 00:41:20.380 what is targeted and communicated

NOTE Confidence: 0.8228827

00:41:20.436 --> 00:41:21.728 to the developing fetus.

NOTE Confidence: 0.8228827

00:41:21.730 --> 00:41:24.210 But I want to return back to the

NOTE Confidence: 0.8228827

00:41:24.210 --> 00:41:25.963 weathering question and the adversity
NOTE Confidence: 0.8228827

00:41:25.963 --> 00:41:28.105 as detailed by the Aces questionnaires
NOTE Confidence: 0.8228827

00:41:28.105 --> 00:41:30.586 and thinking about the effect of
NOTE Confidence: 0.8228827

00:41:30.586 --> 00:41:32.230 racism and discrimination stress.
NOTE Confidence: 0.8228827

00:41:32.230 --> 00:41:34.185 We've recently developed a collaboration
NOTE Confidence: 0.8228827

00:41:34.185 --> 00:41:36.486 with Tonya Ivanovic as part of
NOTE Confidence: 0.8228827

00:41:36.486 --> 00:41:37.347 the Grady trauma.
NOTE Confidence: 0.8228827

00:41:37.350 --> 00:41:39.030 Project that Carrie wrestler first
NOTE Confidence: 0.8228827

00:41:39.030 --> 00:41:41.801 started at when he was at Emory and
NOTE Confidence: 0.8228827

00:41:41.801 --> 00:41:43.511 developing the Grady Trauma project
NOTE Confidence: 0.8228827

00:41:43.511 --> 00:41:45.439 that when he left for Harvard,
NOTE Confidence: 0.8228827

00:41:45.440 --> 00:41:47.827 Tonya took over and now Tonya has
NOTE Confidence: 0.8228827

00:41:47.827 --> 00:41:49.834 actually moved herself to wings state
NOTE Confidence: 0.8228827

00:41:49.834 --> 00:41:52.520 where she is now starting a similar project.
NOTE Confidence: 0.8228827

00:41:52.520 --> 00:41:55.208 I'm at Wayne State is the greatest trauma.
NOTE Confidence: 0.8228827

00:41:55.210 --> 00:41:57.296 I'm sure many of you are very

NOTE Confidence: 0.8228827

00:41:57.296 --> 00:41:58.190 familiar with the

NOTE Confidence: 0.8268261

00:41:58.257 --> 00:41:59.589 Grady Trauma Project.

NOTE Confidence: 0.8268261

00:41:59.590 --> 00:42:01.612 It's produced some of the best

NOTE Confidence: 0.8268261

00:42:01.612 --> 00:42:02.960 data looking at discrimination,

NOTE Confidence: 0.8268261

00:42:02.960 --> 00:42:04.976 stress and effects of the environment.

NOTE Confidence: 0.8268261

00:42:04.980 --> 00:42:06.328 Long-term health outcomes in

NOTE Confidence: 0.8268261

00:42:06.328 --> 00:42:07.339 neuro psychiatric disease,

NOTE Confidence: 0.8268261

00:42:07.340 --> 00:42:08.651 especially PTS di.

NOTE Confidence: 0.8268261

00:42:08.651 --> 00:42:11.480 So in this study, we had developed

NOTE Confidence: 0.8268261

00:42:11.480 --> 00:42:13.640 a mouse model of understanding the

NOTE Confidence: 0.8268261

00:42:13.640 --> 00:42:16.151 timing specificity of when trauma or

NOTE Confidence: 0.8268261

00:42:16.151 --> 00:42:18.231 stress happens in development itself.

NOTE Confidence: 0.8268261

00:42:18.240 --> 00:42:20.200 Does it produce those lasting

NOTE Confidence: 0.8268261

00:42:20.200 --> 00:42:22.160 effects and so just quickly,

NOTE Confidence: 0.8268261

00:42:22.160 --> 00:42:24.390 the current collaboration that we're

NOTE Confidence: 0.8268261

00:42:24.390 --> 00:42:27.034 working on took that mouse model
NOTE Confidence: 0.8268261

00:42:27.034 --> 00:42:29.414 and asked in a translation away if
NOTE Confidence: 0.8268261

00:42:29.414 --> 00:42:32.415 we look at a very specific type of
NOTE Confidence: 0.8268261

00:42:32.415 --> 00:42:34.312 trauma abbreviated here as IPV.
NOTE Confidence: 0.8268261

00:42:34.312 --> 00:42:35.880 This is actually interpersonal,
NOTE Confidence: 0.8268261

00:42:35.880 --> 00:42:38.226 not enter certain, not intimate partner.
NOTE Confidence: 0.8268261

00:42:38.230 --> 00:42:40.255 This is interpersonal a type
NOTE Confidence: 0.8268261

00:42:40.255 --> 00:42:41.470 of interpersonal trauma.
NOTE Confidence: 0.8268261

00:42:41.470 --> 00:42:44.263 Which is the greatest predictor of PTS
NOTE Confidence: 0.8268261

00:42:44.263 --> 00:42:46.650 di development and lasting effects?
NOTE Confidence: 0.8268261

00:42:46.650 --> 00:42:49.242 We wanted to know if we asked a
NOTE Confidence: 0.8268261

00:42:49.242 --> 00:42:51.387 specific type of interpersonal trauma
NOTE Confidence: 0.8268261

00:42:51.387 --> 00:42:54.237 that being sexual trauma because it's
NOTE Confidence: 0.8268261

00:42:54.237 --> 00:42:57.446 very easily identified when that happened.
NOTE Confidence: 0.8268261

00:42:57.450 --> 00:43:00.370 If that when that timing of that happened
NOTE Confidence: 0.8268261

00:43:00.370 --> 00:43:03.069 related to brain developmental timing.

NOTE Confidence: 0.8268261

00:43:03.070 --> 00:43:04.423 So under 14.

NOTE Confidence: 0.8268261

00:43:04.423 --> 00:43:06.678 So basically entering into the

NOTE Confidence: 0.8268261

00:43:06.678 --> 00:43:09.396 pubertal Timepoint and before or during

NOTE Confidence: 0.8268261

00:43:09.396 --> 00:43:11.576 adolescence or into adulthood or.

NOTE Confidence: 0.8268261

00:43:11.580 --> 00:43:12.864 After that adolescent window,

NOTE Confidence: 0.8268261

00:43:12.864 --> 00:43:15.090 so these three different time points here,

NOTE Confidence: 0.8268261

00:43:15.090 --> 00:43:16.980 could we look at physiological outcomes

NOTE Confidence: 0.8268261

00:43:16.980 --> 00:43:18.919 that were specific to that timing,

NOTE Confidence: 0.8268261

00:43:18.920 --> 00:43:20.828 whether it be adversity in PTS,

NOTE Confidence: 0.8268261

00:43:20.830 --> 00:43:21.440 D development,

NOTE Confidence: 0.8268261

00:43:21.440 --> 00:43:22.965 metabolic outcomes in other health

NOTE Confidence: 0.8268261

00:43:22.965 --> 00:43:24.340 issues related to diabetes,

NOTE Confidence: 0.8268261

00:43:24.340 --> 00:43:25.028 and hypertension?

NOTE Confidence: 0.8268261

00:43:25.028 --> 00:43:27.092 Could we then look at these

NOTE Confidence: 0.8268261

00:43:27.092 --> 00:43:29.290 exercise or vesicles or cell free

NOTE Confidence: 0.8268261

00:43:29.290 --> 00:43:31.100 mitochondrial DNA which will come
NOTE Confidence: 0.8268261

00:43:31.100 --> 00:43:33.426 back to as biomarkers related to
NOTE Confidence: 0.8268261

00:43:33.426 --> 00:43:34.946 these physiological outcomes and
NOTE Confidence: 0.8268261

00:43:34.946 --> 00:43:37.442 we can again take these exercise or
NOTE Confidence: 0.8268261

00:43:37.442 --> 00:43:39.260 vesicles from these human subjects
NOTE Confidence: 0.8268261

00:43:39.260 --> 00:43:41.300 with this specific timing and ask
NOTE Confidence: 0.8268261

00:43:41.300 --> 00:43:44.027 related to no trauma or no sexual trauma.
NOTE Confidence: 0.8268261

00:43:44.030 --> 00:43:45.322 In this particular case,
NOTE Confidence: 0.8268261

00:43:45.322 --> 00:43:47.260 and even doing proteomics by mass
NOTE Confidence: 0.8268261

00:43:47.316 --> 00:43:49.596 spectrometry and smaller in a sequencing,
NOTE Confidence: 0.8268261

00:43:49.600 --> 00:43:52.267 can we begin to identify what we
NOTE Confidence: 0.8268261

00:43:52.267 --> 00:43:54.617 would classify as a biomarker to
NOTE Confidence: 0.8268261

00:43:54.617 --> 00:43:57.235 then go in and ask about causality
NOTE Confidence: 0.8268261

00:43:57.313 --> 00:43:58.837 in our mouse models?
NOTE Confidence: 0.8268261

00:43:58.840 --> 00:44:00.628 So related to the timing sense
NOTE Confidence: 0.8268261

00:44:00.628 --> 00:44:01.224 of sensitivity,

NOTE Confidence: 0.8268261

00:44:01.230 --> 00:44:04.220 I'm not going to go into all of this data.

NOTE Confidence: 0.8268261

00:44:04.220 --> 00:44:05.720 We're working on with Tonya,

NOTE Confidence: 0.8268261

00:44:05.720 --> 00:44:07.709 but I want to show you that if you

NOTE Confidence: 0.8268261

00:44:07.709 --> 00:44:10.095 look at sort of the metabolic and

NOTE Confidence: 0.8268261

00:44:10.095 --> 00:44:11.148 physiological outcomes related

NOTE Confidence: 0.8268261

00:44:11.148 --> 00:44:12.299 to obesity risk,

NOTE Confidence: 0.8268261

00:44:12.300 --> 00:44:14.218 these are now women who were recruited

NOTE Confidence: 0.8268261

00:44:14.218 --> 00:44:16.180 in through the Grady Trauma Project,

NOTE Confidence: 0.8268261

00:44:16.180 --> 00:44:17.795 whose sexual trauma experiences were

NOTE Confidence: 0.8268261

00:44:17.795 --> 00:44:19.717 noted were then captured both for

NOTE Confidence: 0.8268261

00:44:19.717 --> 00:44:21.265 the readout of their body weight,

NOTE Confidence: 0.8268261

00:44:21.270 --> 00:44:22.956 which then Maps directly on with

NOTE Confidence: 0.8268261

00:44:22.956 --> 00:44:24.454 their hip circumference as well

NOTE Confidence: 0.8268261

00:44:24.454 --> 00:44:25.750 as their waist circumference,

NOTE Confidence: 0.8268261

00:44:25.750 --> 00:44:27.787 which I'm not showing you on here

NOTE Confidence: 0.8268261

00:44:27.787 --> 00:44:29.860 similar data as well as their
NOTE Confidence: 0.8268261

00:44:29.860 --> 00:44:30.620 hypertension risk.
NOTE Confidence: 0.8268261

00:44:30.620 --> 00:44:32.390 And what you'll see consistently
NOTE Confidence: 0.8268261

00:44:32.390 --> 00:44:34.860 is that there is effect of trauma
NOTE Confidence: 0.8268261

00:44:34.860 --> 00:44:36.756 of sexual trauma in this case.
NOTE Confidence: 0.8268261

00:44:36.760 --> 00:44:38.590 But if you actually parse it
NOTE Confidence: 0.8268261

00:44:38.590 --> 00:44:40.510 out for when it happened,
NOTE Confidence: 0.8268261

00:44:40.510 --> 00:44:42.210 you'll see again and again.
NOTE Confidence: 0.8268261

00:44:42.210 --> 00:44:44.244 In this case that women experienced
NOTE Confidence: 0.8268261

00:44:44.244 --> 00:44:45.993 it prior to adolescence and
NOTE Confidence: 0.8268261

00:44:45.993 --> 00:44:47.668 adulthood is driving this data,
NOTE Confidence: 0.8268261

00:44:47.670 --> 00:44:50.398 so both but there by increased body weight,
NOTE Confidence: 0.8268261

00:44:50.400 --> 00:44:52.100 increased hip and waist circumference,
NOTE Confidence: 0.8268261

00:44:52.100 --> 00:44:54.828 which I'm not showing you that these women,
NOTE Confidence: 0.8268261

00:44:54.830 --> 00:44:56.202 also with hypertension risk,
NOTE Confidence: 0.8268261

00:44:56.202 --> 00:44:58.260 which is known associations of these

NOTE Confidence: 0.8656061

00:44:58.319 --> 00:44:59.707 outcomes compared to no

NOTE Confidence: 0.8656061

00:44:59.707 --> 00:45:00.748 sexual trauma divided.

NOTE Confidence: 0.8656061

00:45:00.750 --> 00:45:02.238 Into elevated hypertension also

NOTE Confidence: 0.8656061

00:45:02.238 --> 00:45:03.726 there's got cutoff hypertension,

NOTE Confidence: 0.8656061

00:45:03.730 --> 00:45:05.968 stage one and two on here.

NOTE Confidence: 0.8656061

00:45:05.970 --> 00:45:07.314 What you see is,

NOTE Confidence: 0.8656061

00:45:07.314 --> 00:45:10.218 I think is fascinating is that if your

NOTE Confidence: 0.8656061

00:45:10.218 --> 00:45:13.053 sexual trauma experience and this is again,

NOTE Confidence: 0.8656061

00:45:13.060 --> 00:45:15.260 these women are all in there and mid

NOTE Confidence: 0.8656061

00:45:15.260 --> 00:45:18.128 to late 30s now that their earlier

NOTE Confidence: 0.8656061

00:45:18.128 --> 00:45:19.928 traumatic experience related to

NOTE Confidence: 0.8656061

00:45:19.928 --> 00:45:21.638 interpersonal violence or trauma.

NOTE Confidence: 0.8656061

00:45:21.640 --> 00:45:24.320 Under 14, they start to escalate or enter

NOTE Confidence: 0.8656061

00:45:24.320 --> 00:45:26.488 earlier into hypertension stage two,

NOTE Confidence: 0.8656061

00:45:26.490 --> 00:45:27.474 which is this?

NOTE Confidence: 0.8656061

00:45:27.474 --> 00:45:29.442 This this green aspect here versus
NOTE Confidence: 0.8656061

00:45:29.442 --> 00:45:31.800 if it happened during adolescence?
NOTE Confidence: 0.8656061

00:45:31.800 --> 00:45:34.698 Versus if it happened after the age of 17,
NOTE Confidence: 0.8656061

00:45:34.700 --> 00:45:36.744 I think he's very clearly shown here
NOTE Confidence: 0.8656061

00:45:36.744 --> 00:45:38.878 that this risk related likely again,
NOTE Confidence: 0.8656061

00:45:38.880 --> 00:45:40.776 are these women showing a phenotype
NOTE Confidence: 0.8656061

00:45:40.776 --> 00:45:42.430 unique or just earlier onset?
NOTE Confidence: 0.8656061

00:45:42.430 --> 00:45:44.677 I think is a really important question.
NOTE Confidence: 0.8656061

00:45:44.680 --> 00:45:46.723 OK, so now if you move that into the
NOTE Confidence: 0.8656061

00:45:46.723 --> 00:45:48.227 nuro psychiatric and neurophysiological
NOTE Confidence: 0.8656061

00:45:48.227 --> 00:45:50.657 outcomes at Tonya's group is worked
NOTE Confidence: 0.8656061

00:45:50.657 --> 00:45:52.730 on in the Greater China Project.
NOTE Confidence: 0.8656061

00:45:52.730 --> 00:45:55.130 If you start to look at startle related
NOTE Confidence: 0.8656061

00:45:55.130 --> 00:45:57.294 to PTS di outcomes, it's interesting.
NOTE Confidence: 0.8656061

00:45:57.294 --> 00:45:59.406 This is distinct from whether it's
NOTE Confidence: 0.8656061

00:45:59.406 --> 00:46:01.743 group here was 14 and under that this

NOTE Confidence: 0.8656061

00:46:01.743 --> 00:46:03.957 group between 14 and 17 is actually

NOTE Confidence: 0.8656061

00:46:03.957 --> 00:46:05.425 showing you unique differences.

NOTE Confidence: 0.8656061

00:46:05.430 --> 00:46:07.692 And baseline of fear potentiated startle

NOTE Confidence: 0.8656061

00:46:07.692 --> 00:46:11.220 as well as skin conductance outcomes as well.

NOTE Confidence: 0.8656061

00:46:11.220 --> 00:46:13.257 So the take home message here that

NOTE Confidence: 0.8656061

00:46:13.257 --> 00:46:15.147 we're starting to see in this

NOTE Confidence: 0.8656061

00:46:15.147 --> 00:46:16.423 collaboration with Tonya's group

NOTE Confidence: 0.8656061

00:46:16.423 --> 00:46:18.280 is that when trauma happens,

NOTE Confidence: 0.8656061

00:46:18.280 --> 00:46:20.296 can be a predictor or an Association

NOTE Confidence: 0.8656061

00:46:20.296 --> 00:46:22.459 for unique and distinct health risks,

NOTE Confidence: 0.8656061

00:46:22.460 --> 00:46:24.651 and I think that's interesting when you

NOTE Confidence: 0.8656061

00:46:24.651 --> 00:46:26.950 start to look at our biomarker data.

NOTE Confidence: 0.8656061

00:46:26.950 --> 00:46:29.078 So I'm just going to quickly show you

NOTE Confidence: 0.8656061

00:46:29.078 --> 00:46:31.652 some of this data just to just to be

NOTE Confidence: 0.8656061

00:46:31.652 --> 00:46:33.832 provocative here is that we isolated

NOTE Confidence: 0.8656061

00:46:33.832 --> 00:46:35.937 extracellular vesicles from these women.

NOTE Confidence: 0.8656061

00:46:35.940 --> 00:46:37.220 These are all black.

NOTE Confidence: 0.8656061

00:46:37.220 --> 00:46:39.150 95% of the cohort is black.

NOTE Confidence: 0.8656061

00:46:39.150 --> 00:46:40.962 They all have a high background

NOTE Confidence: 0.8656061

00:46:40.962 --> 00:46:42.990 of trauma in the environment.

NOTE Confidence: 0.8656061

00:46:42.990 --> 00:46:45.048 But this is again related specifically

NOTE Confidence: 0.8656061

00:46:45.048 --> 00:46:47.481 on a non sexual trauma versus

NOTE Confidence: 0.8656061

00:46:47.481 --> 00:46:48.969 sexual trauma experience.

NOTE Confidence: 0.8656061

00:46:48.970 --> 00:46:49.242 OK,

NOTE Confidence: 0.8656061

00:46:49.242 --> 00:46:51.146 so this is showing you a heat

NOTE Confidence: 0.8656061

00:46:51.146 --> 00:46:53.128 map of the proteomics data.

NOTE Confidence: 0.8656061

00:46:53.130 --> 00:46:55.244 All of the proteomics was isolated at

NOTE Confidence: 0.8656061

00:46:55.244 --> 00:46:57.841 the same time is all blinded when we

NOTE Confidence: 0.8656061

00:46:57.841 --> 00:46:59.850 do the proteomics assessment and I'm

NOTE Confidence: 0.8656061

00:46:59.850 --> 00:47:01.770 telling you that because for having

NOTE Confidence: 0.8656061

00:47:01.770 --> 00:47:04.330 worked in this field for a decade now,

NOTE Confidence: 0.8656061

00:47:04.330 --> 00:47:06.297 this is some of the most provocative

NOTE Confidence: 0.8656061

00:47:06.297 --> 00:47:08.628 data that I've seen in human subjects

NOTE Confidence: 0.8656061

00:47:08.628 --> 00:47:10.408 related to the proteomics outcomes.

NOTE Confidence: 0.8656061

00:47:10.410 --> 00:47:12.804 So you can see if we categorize

NOTE Confidence: 0.8656061

00:47:12.804 --> 00:47:14.249 all proteins here in H,

NOTE Confidence: 0.8656061

00:47:14.250 --> 00:47:15.850 showing you the non sexual

NOTE Confidence: 0.8656061

00:47:15.850 --> 00:47:16.810 versus sexual trauma.

NOTE Confidence: 0.8656061

00:47:16.810 --> 00:47:17.160 Overall,

NOTE Confidence: 0.8656061

00:47:17.160 --> 00:47:19.260 we're seeing thousands of differences in

NOTE Confidence: 0.8656061

00:47:19.260 --> 00:47:21.278 the protein content of these vesicles.

NOTE Confidence: 0.8656061

00:47:21.280 --> 00:47:23.653 If you parse it out by when

NOTE Confidence: 0.8656061

00:47:23.653 --> 00:47:24.670 the trauma happened,

NOTE Confidence: 0.8656061

00:47:24.670 --> 00:47:26.335 you'll see that there's this

NOTE Confidence: 0.8656061

00:47:26.335 --> 00:47:28.402 group of proteins down here in

NOTE Confidence: 0.8656061

00:47:28.402 --> 00:47:30.087 pink which are largely reduced,

NOTE Confidence: 0.8656061

00:47:30.090 --> 00:47:32.810 which will come back to in a second.

NOTE Confidence: 0.8656061

00:47:32.810 --> 00:47:34.655 And there's this really interesting

NOTE Confidence: 0.8656061

00:47:34.655 --> 00:47:36.865 group of proteins that are really

NOTE Confidence: 0.8656061

00:47:36.865 --> 00:47:39.249 increased only in this 14 to 17 group.

NOTE Confidence: 0.8656061

00:47:39.250 --> 00:47:41.194 Many of the proteins that we're

NOTE Confidence: 0.8656061

00:47:41.194 --> 00:47:42.980 seeing that are dramatically changed,

NOTE Confidence: 0.8656061

00:47:42.980 --> 00:47:44.670 I mean dramatically by either

NOTE Confidence: 0.8656061

00:47:44.670 --> 00:47:45.684 being only present,

NOTE Confidence: 0.8656061

00:47:45.690 --> 00:47:47.380 such as these protein cereal,

NOTE Confidence: 0.8656061

00:47:47.380 --> 00:47:48.995 come back two or hundred

NOTE Confidence: 0.8656061

00:47:48.995 --> 00:47:50.610 fold changed are related to

NOTE Confidence: 0.8610608

00:47:50.679 --> 00:47:52.734 skin proteins. Even if globulins and

NOTE Confidence: 0.8610608

00:47:52.734 --> 00:47:54.510 other things related to EV function,

NOTE Confidence: 0.8610608

00:47:54.510 --> 00:47:56.477 and if you actually look at the

NOTE Confidence: 0.8610608

00:47:56.477 --> 00:47:57.770 three sexual trauma groups,

NOTE Confidence: 0.8610608

00:47:57.770 --> 00:47:59.250 there was some overlap where

NOTE Confidence: 0.8610608

00:47:59.250 --> 00:48:00.730 they all show these differences.

NOTE Confidence: 0.8610608

00:48:00.730 --> 00:48:02.446 Some of these proteins in here

NOTE Confidence: 0.8610608

00:48:02.446 --> 00:48:03.980 and related I'll talk about,

NOTE Confidence: 0.8610608

00:48:03.980 --> 00:48:05.961 but there are very unique proteins that

NOTE Confidence: 0.8610608

00:48:05.961 --> 00:48:07.830 categorized by when the trauma happened.

NOTE Confidence: 0.8610608

00:48:07.830 --> 00:48:09.612 OK, which ones what I'm showing

NOTE Confidence: 0.8610608

00:48:09.612 --> 00:48:11.970 you here in KR again log 2 fold,

NOTE Confidence: 0.8610608

00:48:11.970 --> 00:48:13.450 change in these proteins and

NOTE Confidence: 0.8610608

00:48:13.450 --> 00:48:14.634 these are dramatic differences.

NOTE Confidence: 0.8610608

00:48:14.640 --> 00:48:16.900 These are not subtle.

NOTE Confidence: 0.8610608

00:48:16.900 --> 00:48:18.770 What stands out about these

NOTE Confidence: 0.8610608

00:48:18.770 --> 00:48:21.067 proteins and why I'm showing them

NOTE Confidence: 0.8610608

00:48:21.067 --> 00:48:23.185 to you across the sexual trauma,

NOTE Confidence: 0.8610608

00:48:23.190 --> 00:48:25.040 and these are these proteins

NOTE Confidence: 0.8610608

00:48:25.040 --> 00:48:26.520 down here in pink.

NOTE Confidence: 0.8610608

00:48:26.520 --> 00:48:28.688 There is a robust reduction in a number
NOTE Confidence: 0.8610608

00:48:28.688 --> 00:48:31.657 of key proteins and specific types of
NOTE Confidence: 0.8610608

00:48:31.657 --> 00:48:33.545 extracellular vesicles secretion broadly.
NOTE Confidence: 0.8610608

00:48:33.550 --> 00:48:36.134 So what these proteins in XNA one and
NOTE Confidence: 0.8610608

00:48:36.134 --> 00:48:38.727 two and collected three and seven.
NOTE Confidence: 0.8610608

00:48:38.730 --> 00:48:40.578 They point to specific.
NOTE Confidence: 0.8610608

00:48:40.578 --> 00:48:41.964 Types of exercise,
NOTE Confidence: 0.8610608

00:48:41.970 --> 00:48:42.736 their vesicles,
NOTE Confidence: 0.8610608

00:48:42.736 --> 00:48:45.417 but also how the vesicles are released.
NOTE Confidence: 0.8610608

00:48:45.420 --> 00:48:47.814 So that's super interesting and very
NOTE Confidence: 0.8610608

00:48:47.814 --> 00:48:50.399 important that we're finding in this cohort,
NOTE Confidence: 0.8610608

00:48:50.400 --> 00:48:52.848 but the piece I want to leave you
NOTE Confidence: 0.8610608

00:48:52.848 --> 00:48:54.837 with from this collaboration that
NOTE Confidence: 0.8610608

00:48:54.837 --> 00:48:57.007 we're currently working on is
NOTE Confidence: 0.8610608

00:48:57.007 --> 00:48:59.587 that we found we examined this.
NOTE Confidence: 0.8610608

00:48:59.590 --> 00:49:01.888 This blue group here of proteins,

NOTE Confidence: 0.8610608

00:49:01.890 --> 00:49:03.655 some really interesting outcomes we

NOTE Confidence: 0.8610608

00:49:03.655 --> 00:49:06.480 found about 24 carat and related proteins,

NOTE Confidence: 0.8610608

00:49:06.480 --> 00:49:09.161 so carrot and type one and two

NOTE Confidence: 0.8610608

00:49:09.161 --> 00:49:10.310 of cuticular origin.

NOTE Confidence: 0.8610608

00:49:10.310 --> 00:49:13.208 Meaning of the hair and skin.

NOTE Confidence: 0.8610608

00:49:13.210 --> 00:49:15.335 And keratin associated proteins again

NOTE Confidence: 0.8610608

00:49:15.335 --> 00:49:17.860 meaning related to hair and skin.

NOTE Confidence: 0.8610608

00:49:17.860 --> 00:49:19.768 Only in the sexual trauma experienced

NOTE Confidence: 0.8610608

00:49:19.768 --> 00:49:21.420 in adolescence in this group.

NOTE Confidence: 0.8610608

00:49:21.420 --> 00:49:22.066 Now remember,

NOTE Confidence: 0.8610608

00:49:22.066 --> 00:49:25.309 these women are now in their mid to late 30s,

NOTE Confidence: 0.8610608

00:49:25.310 --> 00:49:26.123 and this is.

NOTE Confidence: 0.8610608

00:49:26.123 --> 00:49:28.020 These are log 2 fold change meaning

NOTE Confidence: 0.8610608

00:49:28.086 --> 00:49:29.626 there are dramatically increased

NOTE Confidence: 0.8610608

00:49:29.626 --> 00:49:31.551 in expression and likely only

NOTE Confidence: 0.8610608

00:49:31.551 --> 00:49:33.409 found in this one unique group,
NOTE Confidence: 0.8610608

00:49:33.410 --> 00:49:34.702 and that's something we're
NOTE Confidence: 0.8610608

00:49:34.702 --> 00:49:35.994 currently following up on.
NOTE Confidence: 0.8610608

00:49:36.000 --> 00:49:38.382 But I just want to be
NOTE Confidence: 0.8610608

00:49:38.382 --> 00:49:40.380 provocative here and remind you.
NOTE Confidence: 0.8610608

00:49:40.380 --> 00:49:41.900 That the data we found,
NOTE Confidence: 0.8610608

00:49:41.900 --> 00:49:43.410 which is largely driven by
NOTE Confidence: 0.8610608

00:49:43.410 --> 00:49:44.618 this group in fear,
NOTE Confidence: 0.8610608

00:49:44.620 --> 00:49:46.140 potentiated startle and skin conductance,
NOTE Confidence: 0.8610608

00:49:46.140 --> 00:49:48.618 was was driven a lot by this
NOTE Confidence: 0.8610608

00:49:48.618 --> 00:49:50.150 specific group as well.
NOTE Confidence: 0.8610608

00:49:50.150 --> 00:49:52.496 Now this comes back to the
NOTE Confidence: 0.8610608

00:49:52.496 --> 00:49:53.669 provocative biomarker question.
NOTE Confidence: 0.8610608

00:49:53.670 --> 00:49:55.234 Some biomarkers are just
NOTE Confidence: 0.8610608

00:49:55.234 --> 00:49:57.580 biomarkers that can predict a risk.
NOTE Confidence: 0.8610608

00:49:57.580 --> 00:49:59.188 Some biomarkers are predicted

NOTE Confidence: 0.8610608

00:49:59.188 --> 00:50:00.394 actually of Amecon.

NOTE Confidence: 0.8610608

00:50:00.400 --> 00:50:01.432 Sticker causal outcome,

NOTE Confidence: 0.8610608

00:50:01.432 --> 00:50:03.840 and that's something we're following up on,

NOTE Confidence: 0.8610608

00:50:03.840 --> 00:50:05.527 and this is really gets to the

NOTE Confidence: 0.8610608

00:50:05.527 --> 00:50:07.384 point of the translation and

NOTE Confidence: 0.8610608

00:50:07.384 --> 00:50:08.998 reverse translational potential,

NOTE Confidence: 0.8610608

00:50:09.000 --> 00:50:10.918 because we can now model and are

NOTE Confidence: 0.8610608

00:50:10.918 --> 00:50:12.463 doing these in keratinocytes in

NOTE Confidence: 0.8610608

00:50:12.463 --> 00:50:14.787 culture where we can ask from eaves

NOTE Confidence: 0.8610608

00:50:14.787 --> 00:50:16.836 from human subjects applied in

NOTE Confidence: 0.8610608

00:50:16.836 --> 00:50:18.492 culture with keratinocyte because

NOTE Confidence: 0.8610608

00:50:18.492 --> 00:50:20.925 these turns out all of these proteins

NOTE Confidence: 0.8610608

00:50:20.925 --> 00:50:22.906 predict a dramatic change in something

NOTE Confidence: 0.8610608

00:50:22.906 --> 00:50:25.111 that happened at the level of the

NOTE Confidence: 0.8610608

00:50:25.111 --> 00:50:27.228 skin cell called the keratinocyte,

NOTE Confidence: 0.8610608

00:50:27.230 --> 00:50:30.670 and also fit with some of this data as well,

NOTE Confidence: 0.8610608

00:50:30.670 --> 00:50:31.690 so that suggests.

NOTE Confidence: 0.8610608

00:50:31.690 --> 00:50:33.390 That there may be something

NOTE Confidence: 0.8610608

00:50:33.390 --> 00:50:35.130 unique to the adolescent window

NOTE Confidence: 0.8610608

00:50:35.130 --> 00:50:37.461 related to the skin and the skin

NOTE Confidence: 0.8610608

00:50:37.531 --> 00:50:39.199 being your greatest tissue.

NOTE Confidence: 0.8610608

00:50:39.200 --> 00:50:41.150 The largest organ in the biggest

NOTE Confidence: 0.8610608

00:50:41.150 --> 00:50:42.879 barrier and involved highly and

NOTE Confidence: 0.8610608

00:50:42.879 --> 00:50:44.355 Autonomic Regulation is something

NOTE Confidence: 0.8610608

00:50:44.355 --> 00:50:46.200 very important to think about.

NOTE Confidence: 0.8610608

00:50:46.200 --> 00:50:47.184 For those biomarkers.

NOTE Confidence: 0.8610608

00:50:47.184 --> 00:50:47.512 OK,

NOTE Confidence: 0.8610608

00:50:47.512 --> 00:50:49.480 so I'm going to jump from

NOTE Confidence: 0.84522754

00:50:49.546 --> 00:50:52.157 that provocative statement to my last topic

NOTE Confidence: 0.84522754

00:50:52.157 --> 00:50:54.947 that I'm going to peak your interest in,

NOTE Confidence: 0.84522754

00:50:54.950 --> 00:50:57.400 which is which is jumping from females,

NOTE Confidence: 0.84522754

00:50:57.400 --> 00:50:59.416 whether it be in the studies

NOTE Confidence: 0.84522754

00:50:59.416 --> 00:51:01.250 were doing Tonya of women,

NOTE Confidence: 0.84522754

00:51:01.250 --> 00:51:04.178 specially in the black community at risk and.

NOTE Confidence: 0.84522754

00:51:04.180 --> 00:51:05.686 And during pregnancy.

NOTE Confidence: 0.84522754

00:51:05.686 --> 00:51:07.694 To thinking about dad,

NOTE Confidence: 0.84522754

00:51:07.700 --> 00:51:09.812 we oftentimes in neurodevelopmental

NOTE Confidence: 0.84522754

00:51:09.812 --> 00:51:12.452 disorders forget about dad's contribution

NOTE Confidence: 0.84522754

00:51:12.452 --> 00:51:15.195 and so it's really within the last five

NOTE Confidence: 0.84522754

00:51:15.195 --> 00:51:17.987 going on 10 years that this has become a

NOTE Confidence: 0.84522754

00:51:17.987 --> 00:51:20.468 very hot topic of discussion about dads.

NOTE Confidence: 0.84522754

00:51:20.468 --> 00:51:22.598 Germ cells and his adversity

NOTE Confidence: 0.84522754

00:51:22.598 --> 00:51:24.549 in experiences as he passes on.

NOTE Confidence: 0.84522754

00:51:24.550 --> 00:51:26.470 So what about the preconception,

NOTE Confidence: 0.84522754

00:51:26.470 --> 00:51:27.619 male stress effects,

NOTE Confidence: 0.84522754

00:51:27.619 --> 00:51:30.300 and how this may be passed on,

NOTE Confidence: 0.84522754

00:51:30.300 --> 00:51:31.377 so Rachel, Yehuda,
NOTE Confidence: 0.84522754

00:51:31.377 --> 00:51:33.172 and others have started doing
NOTE Confidence: 0.84522754

00:51:33.172 --> 00:51:34.900 these asking these questions,
NOTE Confidence: 0.84522754

00:51:34.900 --> 00:51:36.850 especially within the community of
NOTE Confidence: 0.84522754

00:51:36.850 --> 00:51:39.480 veterans as well as Holocaust survivors.
NOTE Confidence: 0.84522754

00:51:39.480 --> 00:51:41.140 Another traumatic life events.
NOTE Confidence: 0.84522754

00:51:41.140 --> 00:51:43.630 I think it's really important to
NOTE Confidence: 0.84522754

00:51:43.700 --> 00:51:45.863 think about the data that goes all
NOTE Confidence: 0.84522754

00:51:45.863 --> 00:51:48.417 the way back to aspects of the
NOTE Confidence: 0.84522754

00:51:48.417 --> 00:51:50.357 Swedish famine and Chinese famines.
NOTE Confidence: 0.84522754

00:51:50.360 --> 00:51:53.360 Data has been really well mind for dads.
NOTE Confidence: 0.84522754

00:51:53.360 --> 00:51:55.658 Effects related to the stress and
NOTE Confidence: 0.84522754

00:51:55.658 --> 00:51:57.634 traumatic intersection of a famine
NOTE Confidence: 0.84522754

00:51:57.634 --> 00:51:59.519 itself with incredible records that
NOTE Confidence: 0.84522754

00:51:59.519 --> 00:52:02.146 have been kept in this overkalix region
NOTE Confidence: 0.84522754

00:52:02.146 --> 00:52:04.610 of Sweden for looking at birth and

NOTE Confidence: 0.84522754

00:52:04.610 --> 00:52:06.860 death rates and growth and development,

NOTE Confidence: 0.84522754

00:52:06.860 --> 00:52:08.785 there's been some data mined

NOTE Confidence: 0.84522754

00:52:08.785 --> 00:52:10.710 here with schizophrenia risk and

NOTE Confidence: 0.84522754

00:52:10.778 --> 00:52:12.798 adds experiences and the timing.

NOTE Confidence: 0.84522754

00:52:12.800 --> 00:52:15.047 Of those experiences and the Dutch hunger,

NOTE Confidence: 0.84522754

00:52:15.050 --> 00:52:17.507 winter has also been really well mind

NOTE Confidence: 0.84522754

00:52:17.507 --> 00:52:19.355 again for autism and schizophrenia

NOTE Confidence: 0.84522754

00:52:19.355 --> 00:52:21.545 risk for some of that data.

NOTE Confidence: 0.84522754

00:52:21.550 --> 00:52:23.620 So how do we mechanistically or

NOTE Confidence: 0.84522754

00:52:23.620 --> 00:52:25.373 causally ask questions about a

NOTE Confidence: 0.84522754

00:52:25.373 --> 00:52:26.908 germ cell as neuro scientists?

NOTE Confidence: 0.84522754

00:52:26.910 --> 00:52:29.547 This was a topic that has piqued a lot

NOTE Confidence: 0.84522754

00:52:29.547 --> 00:52:32.270 of interest and a lot of skepticism.

NOTE Confidence: 0.84522754

00:52:32.270 --> 00:52:34.220 Shall I say it actually reached

NOTE Confidence: 0.84522754

00:52:34.220 --> 00:52:36.612 the level of the New York Times

NOTE Confidence: 0.84522754

00:52:36.612 --> 00:52:37.968 in December of 2018,
NOTE Confidence: 0.84522754
00:52:37.970 --> 00:52:40.354 where I had a New York Times Reporter
NOTE Confidence: 0.84522754
00:52:40.354 --> 00:52:42.988 who is very interested in this area?
NOTE Confidence: 0.84522754
00:52:42.990 --> 00:52:44.218 Contact me and say,
NOTE Confidence: 0.84522754
00:52:44.218 --> 00:52:46.478 not just that they wanted to talk
NOTE Confidence: 0.84522754
00:52:46.478 --> 00:52:48.590 about the data and the potential
NOTE Confidence: 0.84522754
00:52:48.590 --> 00:52:50.030 importance of the data,
NOTE Confidence: 0.84522754
00:52:50.030 --> 00:52:53.230 but you really wanted to talk about that.
NOTE Confidence: 0.84522754
00:52:53.230 --> 00:52:54.358 Controversy in this field,
NOTE Confidence: 0.84522754
00:52:54.358 --> 00:52:57.610 and so it is a It is a difficult aspect
NOTE Confidence: 0.84522754
00:52:57.610 --> 00:52:59.842 to get at mechanistically in humans,
NOTE Confidence: 0.84522754
00:52:59.850 --> 00:53:02.001 so we have to use a lot of our
NOTE Confidence: 0.84522754
00:53:02.001 --> 00:53:03.668 animal models to understand
NOTE Confidence: 0.84522754
00:53:03.668 --> 00:53:05.480 mechanisms about germ cells.
NOTE Confidence: 0.84522754
00:53:05.480 --> 00:53:06.416 And of course,
NOTE Confidence: 0.84522754
00:53:06.416 --> 00:53:09.019 it is very difficult to model many of

NOTE Confidence: 0.84522754

00:53:09.019 --> 00:53:11.095 these these experiences in a mouse.

NOTE Confidence: 0.84522754

00:53:11.100 --> 00:53:12.616 Mice are not humans.

NOTE Confidence: 0.84522754

00:53:12.616 --> 00:53:14.511 They cannot experience stress or

NOTE Confidence: 0.84522754

00:53:14.511 --> 00:53:16.730 trauma in the way that a human can,

NOTE Confidence: 0.84522754

00:53:16.730 --> 00:53:18.716 but we can begin to understand

NOTE Confidence: 0.84522754

00:53:18.716 --> 00:53:20.040 some of the mechanisms,

NOTE Confidence: 0.84522754

00:53:20.040 --> 00:53:23.256 and I'm just quickly touch on a couple.

NOTE Confidence: 0.84522754

00:53:23.260 --> 00:53:25.416 So in our mouse model that we've

NOTE Confidence: 0.84522754

00:53:25.416 --> 00:53:27.345 been working on for the better

NOTE Confidence: 0.84522754

00:53:27.345 --> 00:53:28.910 part of the last decade,

NOTE Confidence: 0.84522754

00:53:28.910 --> 00:53:30.480 we can expose male mice

NOTE Confidence: 0.84522754

00:53:30.480 --> 00:53:31.736 across many different windows.

NOTE Confidence: 0.84522754

00:53:31.740 --> 00:53:33.868 It turns out it doesn't matter the

NOTE Confidence: 0.84522754

00:53:33.868 --> 00:53:35.753 window of development because the germ

NOTE Confidence: 0.84522754

00:53:35.753 --> 00:53:37.577 cells that are affected with about

NOTE Confidence: 0.84522754

00:53:37.577 --> 00:53:39.898 four weeks it requires of chronic stress,
NOTE Confidence: 0.84522754

00:53:39.900 --> 00:53:41.156 again getting dad's stress
NOTE Confidence: 0.84522754

00:53:41.156 --> 00:53:42.098 levels elevated enough,
NOTE Confidence: 0.84522754

00:53:42.100 --> 00:53:44.686 requires about four weeks of stress.
NOTE Confidence: 0.84522754

00:53:44.690 --> 00:53:46.106 This is a model that his
NOTE Confidence: 0.84522754

00:53:46.106 --> 00:53:47.050 offspring show a very
NOTE Confidence: 0.8100047

00:53:47.102 --> 00:53:48.614 hyper responsive HPA strikes
NOTE Confidence: 0.8100047

00:53:48.614 --> 00:53:50.126 acid accesses their phenotype.
NOTE Confidence: 0.8100047

00:53:50.130 --> 00:53:51.936 There is no sex difference here.
NOTE Confidence: 0.8100047

00:53:51.940 --> 00:53:53.144 Males and females show
NOTE Confidence: 0.8100047

00:53:53.144 --> 00:53:54.348 the exact same phenotype.
NOTE Confidence: 0.8100047

00:53:54.350 --> 00:53:55.860 We've been able to mechanistically
NOTE Confidence: 0.8100047

00:53:55.860 --> 00:53:56.766 replicate this data.
NOTE Confidence: 0.8100047

00:53:56.770 --> 00:53:58.786 I don't have time to talk about
NOTE Confidence: 0.8100047

00:53:58.786 --> 00:54:00.022 by micro injecting specific
NOTE Confidence: 0.8100047

00:54:00.022 --> 00:54:01.894 micro RNA at the Zagat Level.

NOTE Confidence: 0.8100047

00:54:01.900 --> 00:54:03.616 I'll kind of come back to

NOTE Confidence: 0.8100047

00:54:03.616 --> 00:54:05.230 that a little bit later.

NOTE Confidence: 0.8100047

00:54:05.230 --> 00:54:07.633 Later on, I want to jump to in this

NOTE Confidence: 0.8100047

00:54:07.633 --> 00:54:10.157 model sort of showing you the phenotype

NOTE Confidence: 0.8100047

00:54:10.157 --> 00:54:12.529 and why this phenotype is important.

NOTE Confidence: 0.8100047

00:54:12.530 --> 00:54:13.802 So mice, like humans,

NOTE Confidence: 0.8100047

00:54:13.802 --> 00:54:14.756 like all mammals,

NOTE Confidence: 0.8100047

00:54:14.760 --> 00:54:17.144 one of the reasons I like studying the

NOTE Confidence: 0.8100047

00:54:17.144 --> 00:54:19.526 stress axis is that it's translate ribe.

NOTE Confidence: 0.8100047

00:54:19.530 --> 00:54:21.426 The jeans and involvement of the

NOTE Confidence: 0.8100047

00:54:21.426 --> 00:54:23.062 hypothalamus in the human brain

NOTE Confidence: 0.8100047

00:54:23.062 --> 00:54:24.607 are the exact same pathways.

NOTE Confidence: 0.8100047

00:54:24.610 --> 00:54:25.882 Circuitry in genes involved

NOTE Confidence: 0.8100047

00:54:25.882 --> 00:54:27.154 in the mouse brain.

NOTE Confidence: 0.8100047

00:54:27.160 --> 00:54:29.068 So it's the most translate Rible,

NOTE Confidence: 0.8100047

00:54:29.070 --> 00:54:31.212 and it's easy in a human error
NOTE Confidence: 0.8100047

00:54:31.212 --> 00:54:33.198 mouse to stimulate the stress axis.
NOTE Confidence: 0.8100047

00:54:33.200 --> 00:54:36.053 So this just shows you from our our paternal,
NOTE Confidence: 0.8100047

00:54:36.060 --> 00:54:37.968 so we stressed the male mice.
NOTE Confidence: 0.8100047

00:54:37.970 --> 00:54:40.506 We then gave them time off from stress,
NOTE Confidence: 0.8100047

00:54:40.510 --> 00:54:41.551 and that's important.
NOTE Confidence: 0.8100047

00:54:41.551 --> 00:54:42.939 We then bred them.
NOTE Confidence: 0.8100047

00:54:42.940 --> 00:54:44.782 This is the stress response of
NOTE Confidence: 0.8100047

00:54:44.782 --> 00:54:46.660 their male and female offspring,
NOTE Confidence: 0.8100047

00:54:46.660 --> 00:54:48.658 and this is just showing you
NOTE Confidence: 0.8100047

00:54:48.658 --> 00:54:50.380 the hypo responsive iti here.
NOTE Confidence: 0.8100047

00:54:50.380 --> 00:54:52.732 This is a normal in black when a
NOTE Confidence: 0.8100047

00:54:52.732 --> 00:54:55.270 mouse or a human will look like
NOTE Confidence: 0.8100047

00:54:55.270 --> 00:54:57.140 when you acutely stress them.
NOTE Confidence: 0.8100047

00:54:57.140 --> 00:54:58.193 Their glucocorticoids levels
NOTE Confidence: 0.8100047

00:54:58.193 --> 00:55:00.650 rise and fall in both males and

NOTE Confidence: 0.8100047

00:55:00.715 --> 00:55:03.256 females and if their dad had been

NOTE Confidence: 0.8100047

00:55:03.256 --> 00:55:04.982 previously stressed normally or if

NOTE Confidence: 0.8100047

00:55:04.982 --> 00:55:06.704 we really cranked up his stress

NOTE Confidence: 0.8100047

00:55:06.704 --> 00:55:08.628 during that same time window and

NOTE Confidence: 0.8100047

00:55:08.628 --> 00:55:10.313 then bread him doesn't matter.

NOTE Confidence: 0.8100047

00:55:10.320 --> 00:55:12.402 His male and female offspring show

NOTE Confidence: 0.8100047

00:55:12.402 --> 00:55:14.150 a hypo responsive stress axis.

NOTE Confidence: 0.8100047

00:55:14.150 --> 00:55:15.454 Why is that important?

NOTE Confidence: 0.8100047

00:55:15.454 --> 00:55:17.680 Because we know that in PTS di,

NOTE Confidence: 0.8100047

00:55:17.680 --> 00:55:18.000 oftentimes,

NOTE Confidence: 0.8100047

00:55:18.000 --> 00:55:19.600 in major depressive disorder that

NOTE Confidence: 0.8100047

00:55:19.600 --> 00:55:21.849 those individuals show a blunted stress axis.

NOTE Confidence: 0.8100047

00:55:21.850 --> 00:55:23.460 Blunted is not necessarily better,

NOTE Confidence: 0.8100047

00:55:23.460 --> 00:55:24.360 is just different,

NOTE Confidence: 0.8100047

00:55:24.360 --> 00:55:26.460 and I want to quickly highlight that

NOTE Confidence: 0.8100047

00:55:26.521 --> 00:55:28.266 this work from Jennifer Shannon,
NOTE Confidence: 0.8100047

00:55:28.270 --> 00:55:30.196 graduate student, which is all published.
NOTE Confidence: 0.8100047

00:55:30.200 --> 00:55:30.503 Now,
NOTE Confidence: 0.8100047

00:55:30.503 --> 00:55:32.321 that what's important here is that
NOTE Confidence: 0.8100047

00:55:32.321 --> 00:55:34.369 this is not an acute response,
NOTE Confidence: 0.8100047

00:55:34.370 --> 00:55:35.234 and in fact,
NOTE Confidence: 0.8100047

00:55:35.234 --> 00:55:36.962 if you breed the animals during
NOTE Confidence: 0.8100047

00:55:36.962 --> 00:55:38.610 the stress experience that they
NOTE Confidence: 0.8100047

00:55:38.610 --> 00:55:40.967 are exposed to or right at the
NOTE Confidence: 0.8100047

00:55:40.967 --> 00:55:42.717 end of their stress experience,
NOTE Confidence: 0.8100047

00:55:42.720 --> 00:55:44.700 you don't get this phenotype.
NOTE Confidence: 0.8100047

00:55:44.700 --> 00:55:46.343 In fact, if you breed, yeah,
NOTE Confidence: 0.8100047

00:55:46.343 --> 00:55:47.981 if you breed dad during or
NOTE Confidence: 0.8100047

00:55:47.981 --> 00:55:48.800 after immediately after.
NOTE Confidence: 0.8100047

00:55:48.800 --> 00:55:50.976 So one week after the stress is ended.
NOTE Confidence: 0.84546006

00:55:53.140 --> 00:55:55.282 Yet no phenotype, so it requires about

NOTE Confidence: 0.84546006

00:55:55.282 --> 00:55:58.169 four weeks to three months and it sorry it

NOTE Confidence: 0.84546006

00:55:58.169 --> 00:56:00.136 requires about four weeks of integration

NOTE Confidence: 0.84546006

00:56:00.136 --> 00:56:02.680 and lasts out to at least three months.

NOTE Confidence: 0.84546006

00:56:02.680 --> 00:56:04.270 As far as we've gone.

NOTE Confidence: 0.84546006

00:56:04.270 --> 00:56:07.132 So what that means is if we breed dad

NOTE Confidence: 0.84546006

00:56:07.132 --> 00:56:09.358 immediately, he doesn't pass on the effect.

NOTE Confidence: 0.84546006

00:56:09.360 --> 00:56:11.728 If we give him time for that post

NOTE Confidence: 0.84546006

00:56:11.728 --> 00:56:13.489 stress allostatic setpoint to happen,

NOTE Confidence: 0.84546006

00:56:13.490 --> 00:56:15.392 he passes on the effect and

NOTE Confidence: 0.84546006

00:56:15.392 --> 00:56:16.343 it's long lasting.

NOTE Confidence: 0.84546006

00:56:16.350 --> 00:56:17.622 It does not reverse,

NOTE Confidence: 0.84546006

00:56:17.622 --> 00:56:18.894 and that's really important,

NOTE Confidence: 0.84546006

00:56:18.900 --> 00:56:21.900 so we just quickly look at at at what we're

NOTE Confidence: 0.84546006

00:56:21.970 --> 00:56:25.034 currently thinking here as terms of how dad.

NOTE Confidence: 0.84546006

00:56:25.040 --> 00:56:26.140 Right, that's the mechanism

NOTE Confidence: 0.84546006

00:56:26.140 --> 00:56:27.790 we're looking for in the mice,
NOTE Confidence: 0.84546006

00:56:27.790 --> 00:56:29.742 so we can ask the question in humans
NOTE Confidence: 0.84546006

00:56:29.742 --> 00:56:31.890 if we compare at the end of stress
NOTE Confidence: 0.84546006

00:56:31.890 --> 00:56:33.925 here at this time point that the
NOTE Confidence: 0.84546006

00:56:33.925 --> 00:56:36.039 effect is not passed on to offspring.
NOTE Confidence: 0.84546006

00:56:36.040 --> 00:56:38.136 We see very few changes in the small
NOTE Confidence: 0.84546006

00:56:38.136 --> 00:56:40.169 non coding RNA content of dads sperm.
NOTE Confidence: 0.84546006

00:56:40.170 --> 00:56:43.818 If we wait three months and breed him.
NOTE Confidence: 0.84546006

00:56:43.820 --> 00:56:46.044 Where we see the effect passed on here
NOTE Confidence: 0.84546006

00:56:46.044 --> 00:56:48.667 that is required in three months of time.
NOTE Confidence: 0.84546006

00:56:48.670 --> 00:56:50.488 We in fact now see huge
NOTE Confidence: 0.84546006

00:56:50.488 --> 00:56:51.700 differences in these dads.
NOTE Confidence: 0.84546006

00:56:51.700 --> 00:56:53.566 So the control versus those that
NOTE Confidence: 0.84546006

00:56:53.566 --> 00:56:55.148 experience the stress but have
NOTE Confidence: 0.84546006

00:56:55.148 --> 00:56:56.846 now had three months to recover,
NOTE Confidence: 0.84546006

00:56:56.850 --> 00:56:58.542 which in the life of a

NOTE Confidence: 0.84546006

00:56:58.542 --> 00:57:00.489 mouse is a very long time.

NOTE Confidence: 0.84546006

00:57:00.490 --> 00:57:02.604 The take home message here is OK,

NOTE Confidence: 0.84546006

00:57:02.610 --> 00:57:03.862 so there's a signal.

NOTE Confidence: 0.84546006

00:57:03.862 --> 00:57:05.740 There's something in the sperm mice

NOTE Confidence: 0.84546006

00:57:05.801 --> 00:57:07.754 and I'll show you human data later.

NOTE Confidence: 0.84546006

00:57:07.760 --> 00:57:09.734 That is important for possibly transmitting

NOTE Confidence: 0.84546006

00:57:09.734 --> 00:57:12.080 the signal to the developing embryo.

NOTE Confidence: 0.84546006

00:57:12.080 --> 00:57:14.789 So I'm sure this is a little bit cloudy,

NOTE Confidence: 0.84546006

00:57:14.790 --> 00:57:17.030 but I just want to quickly say for

NOTE Confidence: 0.84546006

00:57:17.030 --> 00:57:18.930 those who think about the brain

NOTE Confidence: 0.84546006

00:57:18.930 --> 00:57:21.197 all the time and don't think about

NOTE Confidence: 0.84546006

00:57:21.197 --> 00:57:23.517 testes as much as my lab does that.

NOTE Confidence: 0.84546006

00:57:23.520 --> 00:57:24.524 Why is this important?

NOTE Confidence: 0.84546006

00:57:24.524 --> 00:57:26.030 The timing is important and the

NOTE Confidence: 0.84546006

00:57:26.080 --> 00:57:27.175 transcriptional inert activation

NOTE Confidence: 0.84546006

00:57:27.175 --> 00:57:28.635 of sperm is important,
NOTE Confidence: 0.84546006

00:57:28.640 --> 00:57:30.440 so sperm go through a course
NOTE Confidence: 0.84546006

00:57:30.440 --> 00:57:31.340 of spermatic Genesis.
NOTE Confidence: 0.84546006

00:57:31.340 --> 00:57:32.544 Everybody understands that that's
NOTE Confidence: 0.84546006

00:57:32.544 --> 00:57:34.350 about six weeks in most mammals.
NOTE Confidence: 0.84546006

00:57:34.350 --> 00:57:35.860 At the end of Schematic,
NOTE Confidence: 0.84546006

00:57:35.860 --> 00:57:37.360 Genesis sperm are not mature,
NOTE Confidence: 0.84546006

00:57:37.360 --> 00:57:39.467 they cannot swim, and they cannot fertilize.
NOTE Confidence: 0.84546006

00:57:39.470 --> 00:57:42.086 They are pushed by a fluid motion through.
NOTE Confidence: 0.84546006

00:57:42.090 --> 00:57:44.050 These DuckTales into the head
NOTE Confidence: 0.84546006

00:57:44.050 --> 00:57:45.226 of the epididymis.
NOTE Confidence: 0.84546006

00:57:45.230 --> 00:57:47.190 Epididymis is required portion of
NOTE Confidence: 0.84546006

00:57:47.190 --> 00:57:49.150 the reproductive track of dad.
NOTE Confidence: 0.84546006

00:57:49.150 --> 00:57:51.574 These tubules secrete all kinds of
NOTE Confidence: 0.84546006

00:57:51.574 --> 00:57:53.627 important factors to mature the
NOTE Confidence: 0.84546006

00:57:53.627 --> 00:57:55.805 sperm such that they can fertilize.

NOTE Confidence: 0.84546006
00:57:55.810 --> 00:57:56.950 They can swim,
NOTE Confidence: 0.84546006
00:57:56.950 --> 00:57:59.230 and they are fully mature into
NOTE Confidence: 0.84546006
00:57:59.230 --> 00:58:01.973 the lumen of many weeks that the
NOTE Confidence: 0.84546006
00:58:01.973 --> 00:58:04.430 sperm in all mammals go through.
NOTE Confidence: 0.84546006
00:58:04.430 --> 00:58:07.566 In this the capit region of the epididymis.
NOTE Confidence: 0.84546006
00:58:07.570 --> 00:58:10.307 There is another factor that is secreted,
NOTE Confidence: 0.84546006
00:58:10.310 --> 00:58:12.350 which is the extracellular vesicle.
NOTE Confidence: 0.84546006
00:58:12.350 --> 00:58:14.289 So in this tiny little piece of
NOTE Confidence: 0.84546006
00:58:14.289 --> 00:58:16.329 Anatomy of males is exercise are
NOTE Confidence: 0.84546006
00:58:16.329 --> 00:58:17.853 vesicles that are circulating
NOTE Confidence: 0.84546006
00:58:17.853 --> 00:58:19.410 interacting with the sperm.
NOTE Confidence: 0.84546006
00:58:19.410 --> 00:58:20.654 These extracellular vesicles we
NOTE Confidence: 0.84546006
00:58:20.654 --> 00:58:22.209 know are important for delivering
NOTE Confidence: 0.84546006
00:58:22.209 --> 00:58:23.929 the signals to the maturing sperm,
NOTE Confidence: 0.84546006
00:58:23.930 --> 00:58:25.430 so it's not transcription happening
NOTE Confidence: 0.84546006

00:58:25.430 --> 00:58:26.330 in this firm.
NOTE Confidence: 0.84546006

00:58:26.330 --> 00:58:28.346 It is a signal from cymatics cells
NOTE Confidence: 0.84546006

00:58:28.346 --> 00:58:30.846 and this is just quickly to show you.
NOTE Confidence: 0.84546006

00:58:30.850 --> 00:58:31.862 Why would this be?
NOTE Confidence: 0.84546006

00:58:31.862 --> 00:58:33.789 Because I know that as a neuro
NOTE Confidence: 0.84546006

00:58:33.789 --> 00:58:35.524 scientist I'm sure within psychiatry
NOTE Confidence: 0.84546006

00:58:35.524 --> 00:58:36.912 we often look at
NOTE Confidence: 0.8619336

00:58:36.977 --> 00:58:38.979 animal studies and say OK but why?
NOTE Confidence: 0.8619336

00:58:38.980 --> 00:58:41.438 I know you have an effect. Who cares?
NOTE Confidence: 0.8619336

00:58:41.438 --> 00:58:43.741 What does it matter and how does
NOTE Confidence: 0.8619336

00:58:43.741 --> 00:58:46.368 it happen and why would it happen?
NOTE Confidence: 0.8619336

00:58:46.370 --> 00:58:48.930 What I'm showing you here is the course
NOTE Confidence: 0.8619336

00:58:48.930 --> 00:58:50.929 of embryonic development in birth,
NOTE Confidence: 0.8619336

00:58:50.930 --> 00:58:52.970 and the germ cells that are
NOTE Confidence: 0.8619336

00:58:52.970 --> 00:58:55.149 important to what they go through.
NOTE Confidence: 0.8619336

00:58:55.150 --> 00:58:57.166 The take home message here is

NOTE Confidence: 0.8619336

00:58:57.166 --> 00:58:59.010 why would this mechanism happen?

NOTE Confidence: 0.8619336

00:58:59.010 --> 00:59:00.063 Well, because evolutionarily,

NOTE Confidence: 0.8619336

00:59:00.063 --> 00:59:02.169 you don't want Dad's germ cells.

NOTE Confidence: 0.8619336

00:59:02.170 --> 00:59:04.486 You don't want those primordial germ

NOTE Confidence: 0.8619336

00:59:04.486 --> 00:59:07.029 cells or those developing some additives.

NOTE Confidence: 0.8619336

00:59:07.030 --> 00:59:08.956 Where dad's DNA is vulnerable to

NOTE Confidence: 0.8619336

00:59:08.956 --> 00:59:11.060 be impacted by the environment.

NOTE Confidence: 0.8619336

00:59:11.060 --> 00:59:13.250 This is occurring in the testes,

NOTE Confidence: 0.8619336

00:59:13.250 --> 00:59:15.805 which is a privileged blood brain barrier.

NOTE Confidence: 0.8619336

00:59:15.810 --> 00:59:17.210 Sorry blood testis barrier,

NOTE Confidence: 0.8619336

00:59:17.210 --> 00:59:19.310 we can make some jokes about

NOTE Confidence: 0.8619336

00:59:19.376 --> 00:59:20.940 blood brain barrier here,

NOTE Confidence: 0.8619336

00:59:20.940 --> 00:59:23.004 but in the blood testis barrier

NOTE Confidence: 0.8619336

00:59:23.004 --> 00:59:25.108 that the environment itself it is

NOTE Confidence: 0.8619336

00:59:25.108 --> 00:59:27.100 privileged and these cells that are

NOTE Confidence: 0.8619336

00:59:27.100 --> 00:59:28.648 really required for preservation
NOTE Confidence: 0.8619336

00:59:28.648 --> 00:59:30.688 of the species evolutionarily are
NOTE Confidence: 0.8619336

00:59:30.688 --> 00:59:32.698 protected from dads environment right?
NOTE Confidence: 0.8619336

00:59:32.698 --> 00:59:35.032 This is protection happens through a
NOTE Confidence: 0.8619336

00:59:35.032 --> 00:59:37.488 course of proteins known as Pi RNA's.
NOTE Confidence: 0.8619336

00:59:37.490 --> 00:59:39.005 That are really highly expressed
NOTE Confidence: 0.8619336

00:59:39.005 --> 00:59:40.520 during these periods of time,
NOTE Confidence: 0.8619336

00:59:40.520 --> 00:59:42.688 but by the time the sperm leave the
NOTE Confidence: 0.8619336

00:59:42.688 --> 00:59:45.067 testes and enter into the Capital Region,
NOTE Confidence: 0.8619336

00:59:45.070 --> 00:59:47.184 there is still a slight protective barrier,
NOTE Confidence: 0.8619336

00:59:47.190 --> 00:59:49.300 but nothing like the testes.
NOTE Confidence: 0.8619336

00:59:49.300 --> 00:59:50.970 And the reason evolutionarily again,
NOTE Confidence: 0.8619336

00:59:50.970 --> 00:59:52.322 this is a hypothesis,
NOTE Confidence: 0.8619336

00:59:52.322 --> 00:59:54.350 is likely for those exercise vesicles
NOTE Confidence: 0.8619336

00:59:54.415 --> 00:59:56.305 to be interacting with the sperm.
NOTE Confidence: 0.8619336

00:59:56.310 --> 00:59:56.992 Here is,

NOTE Confidence: 0.8619336

00:59:56.992 --> 00:59:59.720 this is a way for dads germ cells

NOTE Confidence: 0.8619336

00:59:59.807 --> 01:00:02.663 to be impacted in a way that does

NOTE Confidence: 0.8619336

01:00:02.663 --> 01:00:04.279 not affect dad's DNA.

NOTE Confidence: 0.8619336

01:00:04.280 --> 01:00:06.428 OK, so sperm are transcriptionally inert,

NOTE Confidence: 0.8619336

01:00:06.430 --> 01:00:08.590 they are not responding to an

NOTE Confidence: 0.8619336

01:00:08.590 --> 01:00:09.310 active environment.

NOTE Confidence: 0.8619336

01:00:09.310 --> 01:00:10.950 Therefore they need to interact

NOTE Confidence: 0.8619336

01:00:10.950 --> 01:00:13.609 with in the lumen of the epididymis.

NOTE Confidence: 0.8619336

01:00:13.610 --> 01:00:15.210 These exercise are vesicles if

NOTE Confidence: 0.8619336

01:00:15.210 --> 01:00:17.655 they want to carry a message about

NOTE Confidence: 0.8619336

01:00:17.655 --> 01:00:19.989 dads environment and that is just

NOTE Confidence: 0.8619336

01:00:19.989 --> 01:00:21.150 simply modeled here,

NOTE Confidence: 0.8619336

01:00:21.150 --> 01:00:23.670 here is the lumen of the epididymis.

NOTE Confidence: 0.8619336

01:00:23.670 --> 01:00:25.824 Here are the sperm that are

NOTE Confidence: 0.8619336

01:00:25.824 --> 01:00:27.260 undergoing this maturation process.

NOTE Confidence: 0.8619336

01:00:27.260 --> 01:00:29.642 They are interacting with these somatic
NOTE Confidence: 0.8619336

01:00:29.642 --> 01:00:31.602 cell derived vesicles that contain
NOTE Confidence: 0.8619336

01:00:31.602 --> 01:00:33.786 all kinds of proteins and micro RNA
NOTE Confidence: 0.8619336

01:00:33.786 --> 01:00:35.345 that are transcriptionally actively
NOTE Confidence: 0.8619336

01:00:35.345 --> 01:00:38.809 changed by dad's environment in a lasting way.
NOTE Confidence: 0.8619336

01:00:38.810 --> 01:00:39.544 So quickly,
NOTE Confidence: 0.8619336

01:00:39.544 --> 01:00:42.480 how do we look at this in terms
NOTE Confidence: 0.8619336

01:00:42.569 --> 01:00:43.850 of a mechanism?
NOTE Confidence: 0.8619336

01:00:43.850 --> 01:00:47.146 Because we cannot ask about a pure population
NOTE Confidence: 0.8619336

01:00:47.146 --> 01:00:49.783 of vesicles to test our hypothesis in
NOTE Confidence: 0.8619336

01:00:49.783 --> 01:00:52.390 vivo because as I told you before,
NOTE Confidence: 0.8619336

01:00:52.390 --> 01:00:53.930 every tissue produces vesicles.
NOTE Confidence: 0.8619336

01:00:53.930 --> 01:00:55.855 So there's many different cell
NOTE Confidence: 0.8619336

01:00:55.855 --> 01:00:58.222 types in this lumen besides just
NOTE Confidence: 0.8619336

01:00:58.222 --> 01:00:59.758 these epididymal epithelial cells,
NOTE Confidence: 0.8619336

01:00:59.760 --> 01:01:02.088 but also, as you can imagine,

NOTE Confidence: 0.8619336
01:01:02.090 --> 01:01:04.400 the capit region of the epididymis
NOTE Confidence: 0.8619336
01:01:04.400 --> 01:01:07.254 and a mouse you cannot easily or
NOTE Confidence: 0.8619336
01:01:07.254 --> 01:01:09.720 really at all isolate a unique.
NOTE Confidence: 0.8619336
01:01:09.720 --> 01:01:10.947 Extracellular environment here.
NOTE Confidence: 0.8619336
01:01:10.947 --> 01:01:12.992 So this brilliant graduate student
NOTE Confidence: 0.8619336
01:01:12.992 --> 01:01:15.242 was able to model this in a dish
NOTE Confidence: 0.8619336
01:01:15.242 --> 01:01:17.163 where she was able to model these
NOTE Confidence: 0.8619336
01:01:17.163 --> 01:01:18.743 DC 2 mouse epididymal epithelial
NOTE Confidence: 0.8619336
01:01:18.743 --> 01:01:20.022 cells that secrete extracellular
NOTE Confidence: 0.8619336
01:01:20.022 --> 01:01:21.306 vesicles into the environment.
NOTE Confidence: 0.8619336
01:01:21.310 --> 01:01:23.662 She was able to develop a model
NOTE Confidence: 0.8619336
01:01:23.662 --> 01:01:26.156 which I'm not going to go into
NOTE Confidence: 0.8619336
01:01:26.156 --> 01:01:28.262 because it's way more down the
NOTE Confidence: 0.8619336
01:01:28.344 --> 01:01:30.288 weeds than you need to be.
NOTE Confidence: 0.8619336
01:01:30.290 --> 01:01:32.607 She was able to model exactly what
NOTE Confidence: 0.8619336

01:01:32.607 --> 01:01:35.277 we see in vivo on dad's sperm
NOTE Confidence: 0.8619336

01:01:35.277 --> 01:01:37.671 environment with what she sees in
NOTE Confidence: 0.8603789

01:01:37.751 --> 01:01:40.775 vitro with the micro RNA extracellular
NOTE Confidence: 0.8603789

01:01:40.775 --> 01:01:42.791 vesicle content from stress.
NOTE Confidence: 0.8603789

01:01:42.800 --> 01:01:45.047 This very complicated figure is a way
NOTE Confidence: 0.8603789

01:01:45.047 --> 01:01:47.043 of telling you she pharmacologically
NOTE Confidence: 0.8603789

01:01:47.043 --> 01:01:50.417 worked out the stress conditions with the
NOTE Confidence: 0.8603789

01:01:50.417 --> 01:01:52.389 glucocorticoid treatment and recovery.
NOTE Confidence: 0.8603789

01:01:52.390 --> 01:01:54.886 This is showing you 11 days
NOTE Confidence: 0.8603789

01:01:54.886 --> 01:01:56.134 after stress recovery.
NOTE Confidence: 0.8603789

01:01:56.140 --> 01:01:57.988 The concentration of stress,
NOTE Confidence: 0.8603789

01:01:57.988 --> 01:01:58.912 relevant glucocorticoids
NOTE Confidence: 0.8603789

01:01:58.912 --> 01:02:00.298 isolating those vesicles.
NOTE Confidence: 0.8603789

01:02:00.300 --> 01:02:02.508 And looking at them by proteomics,
NOTE Confidence: 0.8603789

01:02:02.510 --> 01:02:04.724 she was able to model this
NOTE Confidence: 0.8603789

01:02:04.724 --> 01:02:06.200 beautiful heat map here,

NOTE Confidence: 0.8603789

01:02:06.200 --> 01:02:08.288 where she looked at the vesicles

NOTE Confidence: 0.8603789

01:02:08.288 --> 01:02:09.680 in culture versus previously

NOTE Confidence: 0.8603789

01:02:09.739 --> 01:02:11.283 vehicle treated versus court

NOTE Confidence: 0.8603789

01:02:11.283 --> 01:02:13.213 treated but now recovered right.

NOTE Confidence: 0.8603789

01:02:13.220 --> 01:02:15.428 This is 11 days and three

NOTE Confidence: 0.8603789

01:02:15.428 --> 01:02:16.532 media changes later.

NOTE Confidence: 0.8603789

01:02:16.540 --> 01:02:18.385 The same vesicle protein changes

NOTE Confidence: 0.8603789

01:02:18.385 --> 01:02:20.960 we see in vivo and in vitro,

NOTE Confidence: 0.8603789

01:02:20.960 --> 01:02:23.592 and this is just showing you is

NOTE Confidence: 0.8603789

01:02:23.592 --> 01:02:25.813 orthogonal report here that they are

NOTE Confidence: 0.8603789

01:02:25.813 --> 01:02:28.200 very different and even the size of

NOTE Confidence: 0.8603789

01:02:28.273 --> 01:02:30.775 these vesicles is changed long term.

NOTE Confidence: 0.8603789

01:02:30.780 --> 01:02:31.868 By that court treatment,

NOTE Confidence: 0.8603789

01:02:31.868 --> 01:02:33.500 same thing we see in vivo.

NOTE Confidence: 0.8603789

01:02:33.500 --> 01:02:35.313 This just shows you that if we

NOTE Confidence: 0.8603789

01:02:35.313 --> 01:02:36.717 label those vesicles and injected
NOTE Confidence: 0.8603789

01:02:36.717 --> 01:02:38.427 into mouse they again have a
NOTE Confidence: 0.8603789

01:02:38.427 --> 01:02:39.758 specificity of where they go.
NOTE Confidence: 0.8603789

01:02:39.760 --> 01:02:41.368 This is showing you your meat
NOTE Confidence: 0.8603789

01:02:41.368 --> 01:02:42.750 market sort of approach here.
NOTE Confidence: 0.8603789

01:02:42.750 --> 01:02:44.955 If you go and look at where all your
NOTE Confidence: 0.8603789

01:02:44.955 --> 01:02:47.418 meat comes from and in your cow or pig
NOTE Confidence: 0.8603789

01:02:47.418 --> 01:02:49.817 or whatever this is showing you the mouse.
NOTE Confidence: 0.8603789

01:02:49.820 --> 01:02:51.772 If we take out all of these tissues
NOTE Confidence: 0.8603789

01:02:51.772 --> 01:02:54.082 lay them out and look at the DIII
NOTE Confidence: 0.8603789

01:02:54.082 --> 01:02:55.258 where it's been transferred.
NOTE Confidence: 0.8603789

01:02:55.260 --> 01:02:57.708 You can see everything shows up in the liver.
NOTE Confidence: 0.8603789

01:02:57.710 --> 01:02:59.070 Ignore that but it's going
NOTE Confidence: 0.8603789

01:02:59.070 --> 01:03:00.158 to be immune system.
NOTE Confidence: 0.8603789

01:03:00.160 --> 01:03:01.960 The spleen here and really amazingly.
NOTE Confidence: 0.8603789

01:03:01.960 --> 01:03:02.950 Dad's reproductive track.

NOTE Confidence: 0.8603789

01:03:02.950 --> 01:03:04.600 The testes and the capital,

NOTE Confidence: 0.8603789

01:03:04.600 --> 01:03:05.260 the epididymis.

NOTE Confidence: 0.8603789

01:03:05.260 --> 01:03:06.250 Amazing, profound specificity.

NOTE Confidence: 0.8603789

01:03:06.250 --> 01:03:08.560 But for everybody cares about the brain.

NOTE Confidence: 0.8603789

01:03:08.560 --> 01:03:10.478 It turns out it also gets into

NOTE Confidence: 0.8603789

01:03:10.478 --> 01:03:12.421 dad's brain that's a topic for

NOTE Confidence: 0.8603789

01:03:12.421 --> 01:03:14.191 another conversation of how these

NOTE Confidence: 0.8603789

01:03:14.191 --> 01:03:15.675 capit epididymal pacilio derived

NOTE Confidence: 0.8603789

01:03:15.675 --> 01:03:17.470 vesicles get into an effect.

NOTE Confidence: 0.8603789

01:03:17.470 --> 01:03:20.440 Adds brain, but we don't have time for that.

NOTE Confidence: 0.8603789

01:03:20.440 --> 01:03:22.624 What I do want to end with is

NOTE Confidence: 0.8603789

01:03:22.624 --> 01:03:24.787 the take home message of why

NOTE Confidence: 0.8603789

01:03:24.787 --> 01:03:26.707 these ev's are so important.

NOTE Confidence: 0.8603789

01:03:26.710 --> 01:03:28.702 'cause we're overtime if we actually

NOTE Confidence: 0.8603789

01:03:28.702 --> 01:03:31.144 take these eaves I was just telling

NOTE Confidence: 0.8603789

01:03:31.144 --> 01:03:33.244 you about and perform an experiment

NOTE Confidence: 0.8603789

01:03:33.244 --> 01:03:35.050 where we take out dads sperm.

NOTE Confidence: 0.8603789

01:03:35.050 --> 01:03:38.114 From a control mouse divided into 2 pools.

NOTE Confidence: 0.8603789

01:03:38.120 --> 01:03:39.281 Perform fertilization technique.

NOTE Confidence: 0.8603789

01:03:39.281 --> 01:03:41.990 Also used in humans where we can

NOTE Confidence: 0.8603789

01:03:42.053 --> 01:03:43.718 incubate the control vesicles with

NOTE Confidence: 0.8603789

01:03:43.718 --> 01:03:46.319 half of dad sperm and the formerly

NOTE Confidence: 0.8603789

01:03:46.319 --> 01:03:48.489 stress treated vesicles without sperm.

NOTE Confidence: 0.8603789

01:03:48.490 --> 01:03:51.010 Perform ixi where we're actually

NOTE Confidence: 0.8603789

01:03:51.010 --> 01:03:53.026 doing intracytoplasmic sperm injection

NOTE Confidence: 0.8603789

01:03:53.026 --> 01:03:55.702 so we can say in this pool versus

NOTE Confidence: 0.8603789

01:03:55.702 --> 01:03:57.672 this pool and transfer them into

NOTE Confidence: 0.8603789

01:03:57.672 --> 01:04:00.393 the left and right side of the same

NOTE Confidence: 0.8603789

01:04:00.393 --> 01:04:03.074 mom with eggs from a different mom.

NOTE Confidence: 0.8603789

01:04:03.080 --> 01:04:05.510 So all factors being controlled for.

NOTE Confidence: 0.8603789

01:04:05.510 --> 01:04:07.925 We can look at the outcome both

NOTE Confidence: 0.8603789

01:04:07.925 --> 01:04:09.756 during development at mid gestation

NOTE Confidence: 0.8603789

01:04:09.756 --> 01:04:11.940 for the developing brain and then

NOTE Confidence: 0.8603789

01:04:11.940 --> 01:04:14.626 the long term outcome and this is

NOTE Confidence: 0.8603789

01:04:14.626 --> 01:04:16.511 that capall amazing endpoint year

NOTE Confidence: 0.8603789

01:04:16.520 --> 01:04:19.427 to show you that if we look at the

NOTE Confidence: 0.8603789

01:04:19.427 --> 01:04:20.651 transcriptional mid gestational

NOTE Confidence: 0.8603789

01:04:20.651 --> 01:04:23.135 development of the brain we see

NOTE Confidence: 0.8603789

01:04:23.135 --> 01:04:25.080 huge differences only because and

NOTE Confidence: 0.8603789

01:04:25.080 --> 01:04:27.174 in partner to the vesicles that

NOTE Confidence: 0.8603789

01:04:27.174 --> 01:04:29.370 those the sperm are incubated with.

NOTE Confidence: 0.8603789

01:04:29.370 --> 01:04:31.435 So the developing brain around

NOTE Confidence: 0.8603789

01:04:31.435 --> 01:04:33.500 synaptic signaling etc likely changing

NOTE Confidence: 0.81403583

01:04:33.564 --> 01:04:35.159 again the rate of the

NOTE Confidence: 0.81403583

01:04:35.159 --> 01:04:36.435 brain but ultimately here.

NOTE Confidence: 0.81403583

01:04:36.440 --> 01:04:38.642 Those offspring showing you the same

NOTE Confidence: 0.81403583

01:04:38.642 --> 01:04:40.786 phenotype that stress signal coming from
NOTE Confidence: 0.81403583

01:04:40.786 --> 01:04:42.921 dad's epidemic up at the other cells
NOTE Confidence: 0.81403583

01:04:42.921 --> 01:04:45.437 shaped the developing brain of his offspring.
NOTE Confidence: 0.81403583

01:04:45.440 --> 01:04:48.200 They show the same hypo responsive HPA axis.
NOTE Confidence: 0.81403583

01:04:48.200 --> 01:04:51.323 I don't have time because we're way over to
NOTE Confidence: 0.81403583

01:04:51.323 --> 01:04:54.430 tell you all about the human side of this,
NOTE Confidence: 0.81403583

01:04:54.430 --> 01:04:56.125 but in a collaboration longstanding
NOTE Confidence: 0.81403583

01:04:56.125 --> 01:04:57.481 collaboration that we have
NOTE Confidence: 0.81403583

01:04:57.481 --> 01:04:58.579 with Neil Epperson,
NOTE Confidence: 0.81403583

01:04:58.580 --> 01:05:01.658 who is now chair of psychiatry.
NOTE Confidence: 0.81403583

01:05:01.660 --> 01:05:03.375 At Denver, we're doing the
NOTE Confidence: 0.81403583

01:05:03.375 --> 01:05:05.090 human side of this question,
NOTE Confidence: 0.81403583

01:05:05.090 --> 01:05:06.752 and so we've just published a
NOTE Confidence: 0.81403583

01:05:06.752 --> 01:05:08.384 study just came out actually
NOTE Confidence: 0.81403583

01:05:08.384 --> 01:05:10.240 yesterday in scientific reports,
NOTE Confidence: 0.81403583

01:05:10.240 --> 01:05:12.728 so you can look at all this amazing

NOTE Confidence: 0.81403583

01:05:12.728 --> 01:05:15.312 data where we are able to look at the

NOTE Confidence: 0.81403583

01:05:15.312 --> 01:05:17.929 micro RNA and looking at the small

NOTE Confidence: 0.81403583

01:05:17.929 --> 01:05:20.094 noncoding RNA content with perceived

NOTE Confidence: 0.81403583

01:05:20.094 --> 01:05:22.165 stress in human subjects and found

NOTE Confidence: 0.81403583

01:05:22.165 --> 01:05:24.978 amazing data here for the micro RNA content.

NOTE Confidence: 0.81403583

01:05:24.980 --> 01:05:27.038 the T RNA fragment content and

NOTE Confidence: 0.81403583

01:05:27.038 --> 01:05:28.410 the Pi RNA content.

NOTE Confidence: 0.81403583

01:05:28.410 --> 01:05:30.378 And I'm just going to point

NOTE Confidence: 0.81403583

01:05:30.378 --> 01:05:32.490 out to Q Your interest.

NOTE Confidence: 0.81403583

01:05:32.490 --> 01:05:34.320 If you look within subject here,

NOTE Confidence: 0.81403583

01:05:34.320 --> 01:05:36.252 so each of these is a different

NOTE Confidence: 0.81403583

01:05:36.252 --> 01:05:37.980 Mail over time of collection,

NOTE Confidence: 0.81403583

01:05:37.980 --> 01:05:39.810 so they came in each month.

NOTE Confidence: 0.81403583

01:05:39.810 --> 01:05:42.154 You start to see patterns in both the

NOTE Confidence: 0.81403583

01:05:42.154 --> 01:05:44.769 Pi RNA's and you can also see the same

NOTE Confidence: 0.81403583

01:05:44.769 --> 01:05:46.830 pattern in the micro RNA content.

NOTE Confidence: 0.81403583

01:05:46.830 --> 01:05:48.600 So cyclicity of pattern has never

NOTE Confidence: 0.81403583

01:05:48.600 --> 01:05:50.422 been shown before in male germ

NOTE Confidence: 0.81403583

01:05:50.422 --> 01:05:52.162 cells so I think super interesting

NOTE Confidence: 0.81403583

01:05:52.162 --> 01:05:53.840 and this just highlights it.

NOTE Confidence: 0.81403583

01:05:53.840 --> 01:05:56.280 Again the data is all in the paper.

NOTE Confidence: 0.81403583

01:05:56.280 --> 01:05:57.841 I'm not going to go through it

NOTE Confidence: 0.81403583

01:05:57.841 --> 01:05:59.944 that we were with really rigorous

NOTE Confidence: 0.81403583

01:05:59.944 --> 01:06:00.860 bioinformatic modeling,

NOTE Confidence: 0.81403583

01:06:00.860 --> 01:06:02.380 able to identify those specific

NOTE Confidence: 0.81403583

01:06:02.380 --> 01:06:03.596 within and between subjects.

NOTE Confidence: 0.81403583

01:06:03.600 --> 01:06:05.544 So we had 20 subjects with

NOTE Confidence: 0.81403583

01:06:05.544 --> 01:06:07.320 six donations a month apart.

NOTE Confidence: 0.81403583

01:06:07.320 --> 01:06:08.950 We could identify actually patterns

NOTE Confidence: 0.81403583

01:06:08.950 --> 01:06:11.274 of specific RNAs T RNA's in my

NOTE Confidence: 0.81403583

01:06:11.274 --> 01:06:13.194 garnas that fit with their perceived

NOTE Confidence: 0.81403583

01:06:13.194 --> 01:06:13.834 stress outcomes,

NOTE Confidence: 0.81403583

01:06:13.840 --> 01:06:16.765 and this is where you taking this back in,

NOTE Confidence: 0.81403583

01:06:16.770 --> 01:06:18.611 then to the mouse where we can

NOTE Confidence: 0.81403583

01:06:18.611 --> 01:06:20.784 now ask if we take those specific

NOTE Confidence: 0.81403583

01:06:20.784 --> 01:06:23.564 targets and ask what do they do to

NOTE Confidence: 0.81403583

01:06:23.564 --> 01:06:25.802 the developing brain is a really

NOTE Confidence: 0.81403583

01:06:25.802 --> 01:06:26.876 reverse translation approach.

NOTE Confidence: 0.81403583

01:06:26.876 --> 01:06:28.506 So just to summarize again,

NOTE Confidence: 0.81403583

01:06:28.510 --> 01:06:30.322 there are many different ways for

NOTE Confidence: 0.81403583

01:06:30.322 --> 01:06:32.286 these exercise or vesicles to be

NOTE Confidence: 0.81403583

01:06:32.286 --> 01:06:34.046 really important for different populations,

NOTE Confidence: 0.81403583

01:06:34.050 --> 01:06:35.838 whether it be related to maternal

NOTE Confidence: 0.81403583

01:06:35.838 --> 01:06:37.557 health within the black community

NOTE Confidence: 0.81403583

01:06:37.557 --> 01:06:38.970 and discrimination stress.

NOTE Confidence: 0.81403583

01:06:38.970 --> 01:06:41.364 Within moms and dads and how the

NOTE Confidence: 0.81403583

01:06:41.364 --> 01:06:43.010 environment influences their signaling.
NOTE Confidence: 0.81403583

01:06:43.010 --> 01:06:45.313 And I'm not going to go through
NOTE Confidence: 0.81403583

01:06:45.313 --> 01:06:47.202 all the conclusions because I
NOTE Confidence: 0.81403583

01:06:47.202 --> 01:06:48.878 already highlighted them all,
NOTE Confidence: 0.81403583

01:06:48.880 --> 01:06:51.365 but I think as as an example
NOTE Confidence: 0.81403583

01:06:51.365 --> 01:06:53.280 of how biomarkers this case,
NOTE Confidence: 0.81403583

01:06:53.280 --> 01:06:54.381 extracellular vesicles can
NOTE Confidence: 0.81403583

01:06:54.381 --> 01:06:56.216 both serve as a biomarker,
NOTE Confidence: 0.81403583

01:06:56.220 --> 01:06:58.434 but also likely reverse reverse translate
NOTE Confidence: 0.81403583

01:06:58.434 --> 01:07:00.620 Aghbal causal mechanism to be explored,
NOTE Confidence: 0.81403583

01:07:00.620 --> 01:07:03.110 I think is very important.
NOTE Confidence: 0.81403583

01:07:03.110 --> 01:07:05.207 I do need to take the time to thank
NOTE Confidence: 0.81403583

01:07:05.207 --> 01:07:07.515 all the amazing people in the lab that
NOTE Confidence: 0.81403583

01:07:07.515 --> 01:07:09.878 have done all of this incredible work.
NOTE Confidence: 0.81403583

01:07:09.880 --> 01:07:11.770 Bridget Nugent worked on all of the
NOTE Confidence: 0.81403583

01:07:11.770 --> 01:07:13.209 placental studies and started looking

NOTE Confidence: 0.81403583

01:07:13.209 --> 01:07:15.232 at those exercise or vesicles early on.

NOTE Confidence: 0.81403583

01:07:15.240 --> 01:07:16.969 Chris Morgan has been doing the mouse

NOTE Confidence: 0.81403583

01:07:16.969 --> 01:07:18.887 work as well as the human studies

NOTE Confidence: 0.81403583

01:07:18.887 --> 01:07:20.573 that we're currently working on with

NOTE Confidence: 0.8093921

01:07:20.632 --> 01:07:21.718 Neal Epperson's group.

NOTE Confidence: 0.8093921

01:07:21.720 --> 01:07:23.463 Katie Morrison who is now an assistant

NOTE Confidence: 0.8093921

01:07:23.463 --> 01:07:25.388 professor at the West Virginia University,

NOTE Confidence: 0.8093921

01:07:25.390 --> 01:07:27.436 West Virginia, started the studies in

NOTE Confidence: 0.8093921

01:07:27.436 --> 01:07:28.800 collaboration with Tonya Jovanovitch

NOTE Confidence: 0.8093921

01:07:28.847 --> 01:07:30.455 is group who is now at Wayne State.

NOTE Confidence: 0.8093921

01:07:30.460 --> 01:07:32.203 We're right in the midst of of

NOTE Confidence: 0.8093921

01:07:32.203 --> 01:07:34.377 submitting a grant right now taking those

NOTE Confidence: 0.8093921

01:07:34.377 --> 01:07:36.097 extracellular vesicles and doing some.

NOTE Confidence: 0.8093921

01:07:36.100 --> 01:07:37.620 Happy Genomic Studies and again,

NOTE Confidence: 0.8093921

01:07:37.620 --> 01:07:38.836 of course Neil Epperson,

NOTE Confidence: 0.8093921

01:07:38.836 --> 01:07:40.660 who I haven't changed the slide.
NOTE Confidence: 0.8093921

01:07:40.660 --> 01:07:43.084 It looks like who's on here as pen,
NOTE Confidence: 0.8093921

01:07:43.090 --> 01:07:44.230 but now is moved.
NOTE Confidence: 0.8093921

01:07:44.230 --> 01:07:46.230 His chair of psychiatry again or please
NOTE Confidence: 0.8093921

01:07:46.230 --> 01:07:48.327 follow us as we really do do a lot
NOTE Confidence: 0.8093921

01:07:48.391 --> 01:07:50.296 of community engagement around these
NOTE Confidence: 0.8093921

01:07:50.296 --> 01:07:52.978 topics in Baltimore and around the world,
NOTE Confidence: 0.8093921

01:07:52.978 --> 01:07:55.666 especially as I'm now president of Ebro.
NOTE Confidence: 0.8093921

01:07:55.670 --> 01:07:57.686 And all of our funding agencies,
NOTE Confidence: 0.8093921

01:07:57.690 --> 01:08:00.049 including any MH on ahs and NICHD,
NOTE Confidence: 0.8093921

01:08:00.050 --> 01:08:02.746 and I'm happy to take questions first time.
NOTE Confidence: 0.8093921

01:08:02.750 --> 01:08:05.369 And I apologize for for going off on too
NOTE Confidence: 0.8093921

01:08:05.369 --> 01:08:07.798 many tangents and take questions now.
NOTE Confidence: 0.8093921

01:08:07.800 --> 01:08:08.480 Thank you.
NOTE Confidence: 0.8859502

01:08:14.750 --> 01:08:20.748 Hi. I'm Rafael Perez hanging.
NOTE Confidence: 0.8859502

01:08:20.750 --> 01:08:22.670 It was an excellent talk.

NOTE Confidence: 0.8859502

01:08:22.670 --> 01:08:25.190 I have a question about.

NOTE Confidence: 0.8859502

01:08:25.190 --> 01:08:27.200 The sequencing that you had

NOTE Confidence: 0.8859502

01:08:27.200 --> 01:08:28.808 done when patients overnight

NOTE Confidence: 0.8859502

01:08:28.808 --> 01:08:30.639 patients against your subjects,

NOTE Confidence: 0.8859502

01:08:30.640 --> 01:08:33.250 so one of the things that we see in

NOTE Confidence: 0.8859502

01:08:33.250 --> 01:08:36.381 the Miz win stresses this segregation

NOTE Confidence: 0.8859502

01:08:36.381 --> 01:08:38.593 of resiliency and susceptibility,

NOTE Confidence: 0.8859502

01:08:38.600 --> 01:08:40.910 and I do see somebody ability

NOTE Confidence: 0.8859502

01:08:40.910 --> 01:08:43.630 to data that you showed today.

NOTE Confidence: 0.8859502

01:08:43.630 --> 01:08:46.072 Have you guys began stratifying the

NOTE Confidence: 0.8859502

01:08:46.072 --> 01:08:48.649 data looking at kind like Arnold,

NOTE Confidence: 0.8859502

01:08:48.650 --> 01:08:51.164 different outcomes in terms of startle

NOTE Confidence: 0.8859502

01:08:51.164 --> 01:08:52.840 or like psychiatric condition?

NOTE Confidence: 0.8859502

01:08:52.840 --> 01:08:55.210 Yeah, so several, great question.

NOTE Confidence: 0.8859502

01:08:55.210 --> 01:08:57.737 It is across a lot of our

NOTE Confidence: 0.8859502

01:08:57.737 --> 01:08:58.820 human subject studies,
NOTE Confidence: 0.8859502

01:08:58.820 --> 01:09:00.264 both the collaboration with
NOTE Confidence: 0.8859502

01:09:00.264 --> 01:09:02.430 Neil as well as with Tanya,
NOTE Confidence: 0.8859502

01:09:02.430 --> 01:09:04.596 that we started looking at looking
NOTE Confidence: 0.8859502

01:09:04.596 --> 01:09:06.040 at the different responses,
NOTE Confidence: 0.8859502

01:09:06.040 --> 01:09:08.371 both satisfying it as well as looking
NOTE Confidence: 0.8859502

01:09:08.371 --> 01:09:10.521 at trying to find associations within
NOTE Confidence: 0.8859502

01:09:10.521 --> 01:09:13.863 our data set so I didn't have time to
NOTE Confidence: 0.8859502

01:09:13.863 --> 01:09:16.502 talk about the cell free mitochondrial DNA,
NOTE Confidence: 0.8859502

01:09:16.510 --> 01:09:18.315 which also is an incredibly
NOTE Confidence: 0.8859502

01:09:18.315 --> 01:09:19.037 interesting biomarker,
NOTE Confidence: 0.8859502

01:09:19.040 --> 01:09:21.364 especially as has been recently shown by
NOTE Confidence: 0.8859502

01:09:21.364 --> 01:09:24.090 looking at many outcomes related to suicide.
NOTE Confidence: 0.8859502

01:09:24.090 --> 01:09:25.272 Alice, suicidality risk,
NOTE Confidence: 0.8859502

01:09:25.272 --> 01:09:26.848 and major depressive disorder.
NOTE Confidence: 0.8859502

01:09:26.850 --> 01:09:27.978 And responsiveness to

NOTE Confidence: 0.8859502

01:09:27.978 --> 01:09:28.730 antidepressant treatment.

NOTE Confidence: 0.8859502

01:09:28.730 --> 01:09:31.378 Also, something really is easy to look at

NOTE Confidence: 0.8859502

01:09:31.378 --> 01:09:33.987 if you're interested in new biomarkers,

NOTE Confidence: 0.8859502

01:09:33.990 --> 01:09:36.246 so trying to look at cell

NOTE Confidence: 0.8859502

01:09:36.246 --> 01:09:37.374 free mitochondrial DNA,

NOTE Confidence: 0.8859502

01:09:37.380 --> 01:09:39.630 which you can get from urine,

NOTE Confidence: 0.8859502

01:09:39.630 --> 01:09:40.758 plasma, saliva, hair.

NOTE Confidence: 0.8859502

01:09:40.758 --> 01:09:43.390 There's lots of ways to do this.

NOTE Confidence: 0.8859502

01:09:43.390 --> 01:09:46.774 Martin Picard is doing tons of work on this,

NOTE Confidence: 0.8859502

01:09:46.780 --> 01:09:48.284 so it's something really.

NOTE Confidence: 0.8859502

01:09:48.284 --> 01:09:50.540 And Raffield your question about both

NOTE Confidence: 0.8859502

01:09:50.602 --> 01:09:53.045 looking at the risk and resilience piece,

NOTE Confidence: 0.8859502

01:09:53.050 --> 01:09:55.318 but also the associations within the data.

NOTE Confidence: 0.8859502

01:09:55.320 --> 01:09:57.399 So those that have high levels of

NOTE Confidence: 0.8859502

01:09:57.399 --> 01:09:59.562 changes in protein in Eves or high

NOTE Confidence: 0.8859502

01:09:59.562 --> 01:10:01.077 levels of cell free mitochondrial
NOTE Confidence: 0.8859502

01:10:01.077 --> 01:10:03.238 DNA does that also associate with
NOTE Confidence: 0.8859502

01:10:03.238 --> 01:10:05.038 any of our physiological outcomes
NOTE Confidence: 0.8859502

01:10:05.040 --> 01:10:06.332 in those different groups.
NOTE Confidence: 0.8859502

01:10:06.332 --> 01:10:07.740 So yes, we are.
NOTE Confidence: 0.8859502

01:10:07.740 --> 01:10:10.400 We have begun looking at those outcomes
NOTE Confidence: 0.8859502

01:10:10.400 --> 01:10:12.449 related to risk and resilience.
NOTE Confidence: 0.8859502

01:10:12.450 --> 01:10:13.386 Doctor Bell,
NOTE Confidence: 0.8859502

01:10:13.386 --> 01:10:15.726 there's a question in chat.
NOTE Confidence: 0.8859502

01:10:15.730 --> 01:10:17.860 Are the stress related changes
NOTE Confidence: 0.8859502

01:10:17.860 --> 01:10:19.564 in sperm alleviated with
NOTE Confidence: 0.8859502

01:10:19.564 --> 01:10:20.890 pharmacological manipulations?
NOTE Confidence: 0.8859502

01:10:20.890 --> 01:10:23.240 SSR eyes, cortisol suppression, etc.
NOTE Confidence: 0.8859502

01:10:23.240 --> 01:10:24.668 Great great questions,
NOTE Confidence: 0.8859502

01:10:24.668 --> 01:10:27.524 so we're currently both looking at
NOTE Confidence: 0.8859502

01:10:27.524 --> 01:10:30.349 this question in the rodent model

NOTE Confidence: 0.8859502

01:10:30.349 --> 01:10:32.614 and inhuman studies with Neil,

NOTE Confidence: 0.8859502

01:10:32.620 --> 01:10:35.602 so I'll grant that we just submitted

NOTE Confidence: 0.8859502

01:10:35.602 --> 01:10:38.904 last cycle with Neil is doing another

NOTE Confidence: 0.8859502

01:10:38.904 --> 01:10:40.840 recruitment of human subjects

NOTE Confidence: 0.8859502

01:10:40.840 --> 01:10:43.859 to test our bioinformatic model.

NOTE Confidence: 0.8859502

01:10:43.860 --> 01:10:46.044 And so, in one of that Grant is

NOTE Confidence: 0.8859502

01:10:46.044 --> 01:10:47.860 dude really asked the question.

NOTE Confidence: 0.8859502

01:10:47.860 --> 01:10:49.300 We've developed this really complex

NOTE Confidence: 0.8859502

01:10:49.300 --> 01:10:51.560 model if we tested on another cohort,

NOTE Confidence: 0.8859502

01:10:51.560 --> 01:10:52.868 can we replicate it?

NOTE Confidence: 0.8859502

01:10:52.868 --> 01:10:55.173 But aim two is actually looking if

NOTE Confidence: 0.8859502

01:10:55.173 --> 01:10:57.405 we start to add factors to our model.

NOTE Confidence: 0.8859502

01:10:57.410 --> 01:11:00.173 So one of the things we're adding is aces,

NOTE Confidence: 0.8859502

01:11:00.180 --> 01:11:02.063 but we'd like to also go into

NOTE Confidence: 0.8859502

01:11:02.063 --> 01:11:03.570 different cohorts of individuals.

NOTE Confidence: 0.8859502

01:11:03.570 --> 01:11:04.560 So for instance,
NOTE Confidence: 0.8859502

01:11:04.560 --> 01:11:06.540 working with the VA and recruiting
NOTE Confidence: 0.8859502

01:11:06.540 --> 01:11:08.190 individuals with and without PTS di,
NOTE Confidence: 0.8859502

01:11:08.190 --> 01:11:10.346 or with and without PTS di treatment.
NOTE Confidence: 0.8859502

01:11:10.350 --> 01:11:12.974 So that answers the question of the human
NOTE Confidence: 0.8859502

01:11:12.974 --> 01:11:15.307 subject studies and looking at associations.
NOTE Confidence: 0.8859502

01:11:15.310 --> 01:11:17.236 We are just now because we
NOTE Confidence: 0.8859502

01:11:17.236 --> 01:11:19.139 have a culture model as well.
NOTE Confidence: 0.8859502

01:11:19.140 --> 01:11:21.054 So culture model as well as
NOTE Confidence: 0.8859502

01:11:21.054 --> 01:11:22.835 mouse model on this starting
NOTE Confidence: 0.8859502

01:11:22.835 --> 01:11:24.985 to ask about reverse ability.
NOTE Confidence: 0.8859502

01:11:24.990 --> 01:11:26.700 I want to be careful with
NOTE Confidence: 0.8859502

01:11:26.700 --> 01:11:27.840 that because I don't
NOTE Confidence: 0.858945

01:11:27.902 --> 01:11:30.541 want to suggest that the changes we're
NOTE Confidence: 0.858945

01:11:30.541 --> 01:11:32.300 seeing are necessarily diseased.
NOTE Confidence: 0.858945

01:11:32.300 --> 01:11:34.040 Predicting necessarily there just changes,

NOTE Confidence: 0.858945
01:11:34.040 --> 01:11:36.385 right? So we see differences in the
NOTE Confidence: 0.858945
01:11:36.385 --> 01:11:38.907 offspring and how they respond to stress.
NOTE Confidence: 0.858945
01:11:38.910 --> 01:11:41.339 That may be a predictor of other
NOTE Confidence: 0.858945
01:11:41.339 --> 01:11:42.740 nerve psychiatric disease risk,
NOTE Confidence: 0.858945
01:11:42.740 --> 01:11:45.516 but it could be, as Rafael pointed out,
NOTE Confidence: 0.858945
01:11:45.520 --> 01:11:47.260 a hallmark of resilience, right?
NOTE Confidence: 0.858945
01:11:47.260 --> 01:11:49.696 We don't know, because there are mice.
NOTE Confidence: 0.858945
01:11:49.700 --> 01:11:52.346 What we do know is that we can model
NOTE Confidence: 0.858945
01:11:52.346 --> 01:11:54.509 that stress in the environment
NOTE Confidence: 0.858945
01:11:54.509 --> 01:11:56.744 and resolution of that stress.
NOTE Confidence: 0.858945
01:11:56.750 --> 01:11:59.204 Returning the cells in their reproductive
NOTE Confidence: 0.858945
01:11:59.204 --> 01:12:02.184 track to a new allostatic setpoint alters
NOTE Confidence: 0.858945
01:12:02.184 --> 01:12:05.809 the content of the sperm that I can say.
NOTE Confidence: 0.858945
01:12:05.810 --> 01:12:08.428 But these questions of can we reverse
NOTE Confidence: 0.858945
01:12:08.428 --> 01:12:10.868 them with drug treatment, etc.
NOTE Confidence: 0.858945

01:12:10.868 --> 01:12:13.458 Something we're currently exploring we've.
NOTE Confidence: 0.858945

01:12:13.460 --> 01:12:15.962 Tossed around the idea in the mice of if
NOTE Confidence: 0.858945

01:12:15.962 --> 01:12:18.546 stress and resolution produces these changes.
NOTE Confidence: 0.858945

01:12:18.550 --> 01:12:20.240 What kind of effector would
NOTE Confidence: 0.858945

01:12:20.240 --> 01:12:21.592 reverse them at that.
NOTE Confidence: 0.858945

01:12:21.600 --> 01:12:23.728 We were looking at already at the
NOTE Confidence: 0.858945

01:12:23.728 --> 01:12:25.064 epigenetic the histone modifications
NOTE Confidence: 0.858945

01:12:25.064 --> 01:12:27.248 that produce these changes long lasting
NOTE Confidence: 0.858945

01:12:27.248 --> 01:12:29.409 So what would reverse that would
NOTE Confidence: 0.858945

01:12:29.409 --> 01:12:31.431 it be the perception of something
NOTE Confidence: 0.858945

01:12:31.431 --> 01:12:33.069 rewarding environment for example,
NOTE Confidence: 0.858945

01:12:33.069 --> 01:12:35.234 is something we're looking at.
NOTE Confidence: 0.858945

01:12:35.240 --> 01:12:37.064 It's a great question.
NOTE Confidence: 0.858945

01:12:37.064 --> 01:12:38.768 OK, there's another question.
NOTE Confidence: 0.858945

01:12:38.768 --> 01:12:40.848 There's evidence that in response
NOTE Confidence: 0.858945

01:12:40.848 --> 01:12:42.979 to a maternal infection,

NOTE Confidence: 0.858945

01:12:42.980 --> 01:12:44.884 placental inflammatory cytokines such

NOTE Confidence: 0.858945

01:12:44.884 --> 01:12:48.650 as one L-1B can be detrimental to fetal

NOTE Confidence: 0.858945

01:12:48.650 --> 01:12:51.170 brain development in your stress model.

NOTE Confidence: 0.858945

01:12:51.170 --> 01:12:53.440 Do you see evidence of

NOTE Confidence: 0.858945

01:12:53.440 --> 01:12:54.348 placental inflammation?

NOTE Confidence: 0.858945

01:12:54.350 --> 01:12:56.036 An if so,

NOTE Confidence: 0.858945

01:12:56.036 --> 01:12:59.408 are these responses also sex specific

NOTE Confidence: 0.858945

01:12:59.408 --> 01:13:02.069 correlating with placental oh GT?

NOTE Confidence: 0.858945

01:13:02.070 --> 01:13:03.320 'cause am I laughing because

NOTE Confidence: 0.858945

01:13:03.320 --> 01:13:04.570 it's such a great question.

NOTE Confidence: 0.858945

01:13:04.570 --> 01:13:06.453 It makes me wonder if someone like

NOTE Confidence: 0.858945

01:13:06.453 --> 01:13:08.320 actually already know our data to ask that.

NOTE Confidence: 0.858945

01:13:08.320 --> 01:13:09.036 But yes,

NOTE Confidence: 0.858945

01:13:09.036 --> 01:13:11.542 great question and we've done all of

NOTE Confidence: 0.858945

01:13:11.542 --> 01:13:14.019 those in the workers all published.

NOTE Confidence: 0.858945

01:13:14.020 --> 01:13:16.484 Uh Stephanie Bronson is first author in
NOTE Confidence: 0.858945

01:13:16.484 --> 01:13:19.758 a couple of those papers that we looked at.
NOTE Confidence: 0.858945

01:13:19.760 --> 01:13:22.112 We've done both looking at the
NOTE Confidence: 0.858945

01:13:22.112 --> 01:13:23.680 inflammasome and inflammatory responses
NOTE Confidence: 0.858945

01:13:23.740 --> 01:13:25.868 in the placenta with her stress model.
NOTE Confidence: 0.858945

01:13:25.870 --> 01:13:27.660 So the answer is yes,
NOTE Confidence: 0.858945

01:13:27.660 --> 01:13:29.704 we do see increases and we do
NOTE Confidence: 0.858945

01:13:29.704 --> 01:13:31.610 see it sex specifically.
NOTE Confidence: 0.858945

01:13:31.610 --> 01:13:36.331 So while I showed you data on Strat How
NOTE Confidence: 0.858945

01:13:36.331 --> 01:13:39.459 come we see this time and time again?
NOTE Confidence: 0.858945

01:13:39.460 --> 01:13:41.806 Whether it's giving mom an inflammatory
NOTE Confidence: 0.858945

01:13:41.806 --> 01:13:43.764 response, giving mom a stressor,
NOTE Confidence: 0.858945

01:13:43.764 --> 01:13:45.719 giving mom a dietary challenge,
NOTE Confidence: 0.858945

01:13:45.720 --> 01:13:46.578 that again,
NOTE Confidence: 0.858945

01:13:46.578 --> 01:13:49.581 the male placenta shows thousands of genes
NOTE Confidence: 0.858945

01:13:49.581 --> 01:13:52.570 that respond to that that challenge RE.

NOTE Confidence: 0.858945
01:13:52.570 --> 01:13:54.730 Little, very selectively that happens in
NOTE Confidence: 0.858945
01:13:54.730 --> 01:13:57.200 the female placenta in this same uterus,
NOTE Confidence: 0.858945
01:13:57.200 --> 01:13:59.566 so it fits the hypothesis that oh
NOTE Confidence: 0.858945
01:13:59.566 --> 01:14:01.828 GT is titrating that for females.
NOTE Confidence: 0.858945
01:14:01.830 --> 01:14:04.318 So again yes we see a lot of
NOTE Confidence: 0.858945
01:14:04.318 --> 01:14:05.740 those same outcomes.
NOTE Confidence: 0.858945
01:14:05.740 --> 01:14:07.520 Anna manuscript that just came
NOTE Confidence: 0.858945
01:14:07.520 --> 01:14:09.300 out in Placenta from Yasmine.
NOTE Confidence: 0.858945
01:14:09.300 --> 01:14:11.436 See say here she's doing again.
NOTE Confidence: 0.858945
01:14:11.440 --> 01:14:13.550 This is actually a picture
NOTE Confidence: 0.858945
01:14:13.550 --> 01:14:15.238 right here of Yasmine.
NOTE Confidence: 0.858945
01:14:15.240 --> 01:14:17.564 She's doing work in both the mouse
NOTE Confidence: 0.858945
01:14:17.564 --> 01:14:19.739 and the human studies as well.
NOTE Confidence: 0.858945
01:14:19.740 --> 01:14:21.076 In the black community,
NOTE Confidence: 0.858945
01:14:21.076 --> 01:14:23.080 where we see very similar outcomes
NOTE Confidence: 0.858945

01:14:23.142 --> 01:14:25.284 and that work just published in
NOTE Confidence: 0.858945

01:14:25.284 --> 01:14:26.712 Placenta shows really dramatic
NOTE Confidence: 0.858945

01:14:26.775 --> 01:14:29.113 changes in the Mail placenta as it
NOTE Confidence: 0.858945

01:14:29.113 --> 01:14:30.466 relates to inflammatory responses
NOTE Confidence: 0.858945

01:14:30.466 --> 01:14:32.196 and really very subtle differences
NOTE Confidence: 0.858945

01:14:32.196 --> 01:14:33.580 in the female placental.
NOTE Confidence: 0.8162925

01:14:37.770 --> 01:14:40.938 Tracy, I have a question Hygiene
NOTE Confidence: 0.8162925

01:14:40.938 --> 01:14:44.435 High that was just amazing talk on
NOTE Confidence: 0.8162925

01:14:44.435 --> 01:14:48.570 all fronts and I have a I guess sort
NOTE Confidence: 0.8162925

01:14:48.570 --> 01:14:51.738 of basic biology question and that
NOTE Confidence: 0.8162925

01:14:51.738 --> 01:14:55.392 is in terms of your placental oh GT
NOTE Confidence: 0.8162925

01:14:55.392 --> 01:14:58.810 data in this sex specific effects.
NOTE Confidence: 0.8162925

01:14:58.810 --> 01:15:02.602 When you did you manipulation in terms of
NOTE Confidence: 0.8162925

01:15:02.602 --> 01:15:06.375 the header zygoty of the effects, why?
NOTE Confidence: 0.8162925

01:15:06.375 --> 01:15:09.100 I guess I was thinking.
NOTE Confidence: 0.8162925

01:15:09.100 --> 01:15:14.660 Why wouldn't X? Inactivation.

NOTE Confidence: 0.8162925

01:15:14.660 --> 01:15:17.204 Mitigate some of the sex specific

NOTE Confidence: 0.8162925

01:15:17.204 --> 01:15:19.995 differences or do not have inactivation

NOTE Confidence: 0.8162925

01:15:19.995 --> 01:15:22.530 at that part of development.

NOTE Confidence: 0.8162925

01:15:22.530 --> 01:15:24.938 Yep, so this is a great question

NOTE Confidence: 0.8162925

01:15:24.938 --> 01:15:27.175 and something that we're looking at

NOTE Confidence: 0.8162925

01:15:27.175 --> 01:15:29.443 from a very genetic and molecular

NOTE Confidence: 0.8162925

01:15:29.443 --> 01:15:30.970 point we've looked at.

NOTE Confidence: 0.8162925

01:15:30.970 --> 01:15:33.994 Oh GT, we have an OG T conditional

NOTE Confidence: 0.8162925

01:15:33.994 --> 01:15:36.850 mouse that allows us to look at it,

NOTE Confidence: 0.8162925

01:15:36.850 --> 01:15:40.144 and in lots of places including the brain,

NOTE Confidence: 0.8162925

01:15:40.150 --> 01:15:42.621 the Placenta appears to be the only

NOTE Confidence: 0.8162925

01:15:42.621 --> 01:15:44.550 tissue that we've found where,

NOTE Confidence: 0.8162925

01:15:44.550 --> 01:15:46.920 oh GT escapes X inactivation.

NOTE Confidence: 0.8162925

01:15:46.920 --> 01:15:49.566 I don't have a justification or

NOTE Confidence: 0.8162925

01:15:49.566 --> 01:15:52.010 even a hypothesis as to why.

NOTE Confidence: 0.8162925

01:15:52.010 --> 01:15:54.453 So related to the point of why
NOTE Confidence: 0.8162925

01:15:54.453 --> 01:15:57.039 we see sex specific effects,
NOTE Confidence: 0.8162925

01:15:57.040 --> 01:16:00.352 or we know that oh GT and oblique
NOTE Confidence: 0.8162925

01:16:00.352 --> 01:16:02.070 inoculation intersects with exist.
NOTE Confidence: 0.8162925

01:16:02.070 --> 01:16:04.800 I don't know why oh GT escapes
NOTE Confidence: 0.8162925

01:16:04.800 --> 01:16:07.090 Axon activation of the placenta,
NOTE Confidence: 0.8162925

01:16:07.090 --> 01:16:10.114 but it clearly does in the
NOTE Confidence: 0.8162925

01:16:10.114 --> 01:16:11.626 trophoblast cells only.
NOTE Confidence: 0.8162925

01:16:11.630 --> 01:16:14.246 But oh GT and oblique inoculation
NOTE Confidence: 0.8162925

01:16:14.246 --> 01:16:17.690 as I showed you with the changes
NOTE Confidence: 0.8162925

01:16:17.690 --> 01:16:20.360 in H3K27 Trimethylation is a
NOTE Confidence: 0.8162925

01:16:20.360 --> 01:16:23.218 required event for X inactivation.
NOTE Confidence: 0.8162925

01:16:23.220 --> 01:16:26.199 So there is a lot of sex differences that
NOTE Confidence: 0.8162925

01:16:26.199 --> 01:16:29.114 end up resulting from the requirement
NOTE Confidence: 0.8162925

01:16:29.114 --> 01:16:31.619 of that increased repressive Mark.
NOTE Confidence: 0.8162925

01:16:31.620 --> 01:16:32.880 H3K27 Trimethylation necessity

NOTE Confidence: 0.8162925

01:16:32.880 --> 01:16:34.980 as part of X inactivation.

NOTE Confidence: 0.8162925

01:16:34.980 --> 01:16:37.920 So it's sort of a circular involvement.

NOTE Confidence: 0.8162925

01:16:37.920 --> 01:16:38.760 So Jane,

NOTE Confidence: 0.8162925

01:16:38.760 --> 01:16:41.280 I think that's a provocative question.

NOTE Confidence: 0.8162925

01:16:41.280 --> 01:16:42.988 Is there something evolutionarily

NOTE Confidence: 0.8162925

01:16:42.988 --> 01:16:46.017 as to why a female trophoblast cell

NOTE Confidence: 0.8162925

01:16:46.017 --> 01:16:48.417 escapes X inactivation for this gene?

NOTE Confidence: 0.8162925

01:16:48.420 --> 01:16:50.940 So if you look at our,

NOTE Confidence: 0.8162925

01:16:50.940 --> 01:16:55.000 there's a PNS paper from 2013, I think.

NOTE Confidence: 0.8162925

01:16:55.000 --> 01:16:57.310 From Chris Howerton.

NOTE Confidence: 0.8162925

01:16:57.310 --> 01:16:59.548 That that we did his initial

NOTE Confidence: 0.8162925

01:16:59.548 --> 01:17:01.480 screening looking for candidate genes.

NOTE Confidence: 0.8162925

01:17:01.480 --> 01:17:03.784 There was about seven or eight

NOTE Confidence: 0.8162925

01:17:03.784 --> 01:17:05.650 of them that came up,

NOTE Confidence: 0.8162925

01:17:05.650 --> 01:17:08.674 and they were all X or Y linked,

NOTE Confidence: 0.8162925

01:17:08.680 --> 01:17:10.570 so the placenta seems to
NOTE Confidence: 0.8162925

01:17:10.570 --> 01:17:12.082 be this interesting tissue.
NOTE Confidence: 0.8162925

01:17:12.090 --> 01:17:12.453 Evolutionarily,
NOTE Confidence: 0.8162925

01:17:12.453 --> 01:17:15.357 I don't know why that has very sex
NOTE Confidence: 0.8162925

01:17:15.357 --> 01:17:17.364 specific chromatin regulation that we
NOTE Confidence: 0.8162925

01:17:17.364 --> 01:17:19.728 have identified some of the players
NOTE Confidence: 0.8162925

01:17:19.793 --> 01:17:21.947 with no GT beans clearly important,
NOTE Confidence: 0.8162925

01:17:21.950 --> 01:17:23.840 but it's a great question.
NOTE Confidence: 0.8162925

01:17:23.840 --> 01:17:26.150 I wonder if the four core
NOTE Confidence: 0.8162925

01:17:26.150 --> 01:17:27.305 genotyped mice Mount.
NOTE Confidence: 0.8162925

01:17:27.310 --> 01:17:29.522 Might be a model where you could
NOTE Confidence: 0.8162925

01:17:29.522 --> 01:17:32.187 look at that right so S or Y for
NOTE Confidence: 0.8162925

01:17:32.187 --> 01:17:34.071 the four cores that James talking
NOTE Confidence: 0.8162925

01:17:34.071 --> 01:17:36.577 about this or why gene is what
NOTE Confidence: 0.8162925

01:17:36.577 --> 01:17:38.545 drives those four core that Jane
NOTE Confidence: 0.8162925

01:17:38.545 --> 01:17:39.829 your group is published.

NOTE Confidence: 0.8162925

01:17:39.830 --> 01:17:42.077 Some really intriguing brain data out of.

NOTE Confidence: 0.8162925

01:17:42.080 --> 01:17:44.920 For that those studies.

NOTE Confidence: 0.8162925

01:17:44.920 --> 01:17:46.968 The four core are based off of the

NOTE Confidence: 0.8162925

01:17:46.968 --> 01:17:48.650 SRY that's been placed AutoZone

NOTE Confidence: 0.8162925

01:17:48.650 --> 01:17:50.870 Moe so they can segregate testes

NOTE Confidence: 0.8162925

01:17:50.870 --> 01:17:52.362 development and testosterone production

NOTE Confidence: 0.8162925

01:17:52.362 --> 01:17:54.486 as part of those four cores.

NOTE Confidence: 0.8162925

01:17:54.490 --> 01:17:56.140 Yeah, it's an interesting question.

NOTE Confidence: 0.8162925

01:17:56.140 --> 01:17:58.642 If you if you made if you took oh

NOTE Confidence: 0.8162925

01:17:58.642 --> 01:18:01.487 GT out of its locus and made it

NOTE Confidence: 0.8162925

01:18:01.487 --> 01:18:03.997 over expressed in a way that it

NOTE Confidence: 0.8162925

01:18:03.997 --> 01:18:06.037 wasn't X inactivated or it's X

NOTE Confidence: 0.8162925

01:18:06.040 --> 01:18:07.292 levels increased his expression

NOTE Confidence: 0.8162925

01:18:07.292 --> 01:18:09.170 in the Mail trophoblast cell for

NOTE Confidence: 0.78433484

01:18:09.229 --> 01:18:11.405 instance, would you see the opposite

NOTE Confidence: 0.78433484

01:18:11.405 --> 01:18:13.140 sorts of effects and protective
NOTE Confidence: 0.78433484

01:18:13.202 --> 01:18:14.930 mechanism in males? Great question.
NOTE Confidence: 0.8999091

01:18:17.170 --> 01:18:18.822 There is another question.
NOTE Confidence: 0.8999091

01:18:18.822 --> 01:18:21.750 Will interventions at any specific age group,
NOTE Confidence: 0.8999091

01:18:21.750 --> 01:18:24.655 for example 13 to 18 year olds,
NOTE Confidence: 0.8999091

01:18:24.660 --> 01:18:27.295 reduce reverse stress related changes
NOTE Confidence: 0.8999091

01:18:27.295 --> 01:18:31.490 that could be passed on to the offspring?
NOTE Confidence: 0.8999091

01:18:31.490 --> 01:18:32.738 It's a great question.
NOTE Confidence: 0.8999091

01:18:32.738 --> 01:18:34.610 I assume that's in reference to
NOTE Confidence: 0.8999091

01:18:34.672 --> 01:18:36.348 the collaboration with Tonya,
NOTE Confidence: 0.8999091

01:18:36.350 --> 01:18:38.080 but there's lots of studies,
NOTE Confidence: 0.8999091

01:18:38.080 --> 01:18:39.468 certainly not just ours,
NOTE Confidence: 0.8999091

01:18:39.468 --> 01:18:41.550 like that field is pretty wide.
NOTE Confidence: 0.8999091

01:18:41.550 --> 01:18:43.590 That adolescence is a unique time
NOTE Confidence: 0.8999091

01:18:43.590 --> 01:18:45.370 window for specially for women,
NOTE Confidence: 0.8999091

01:18:45.370 --> 01:18:47.770 but not just women but a unique time

NOTE Confidence: 0.8999091
01:18:47.770 --> 01:18:50.227 window for vulnerability for the brain,
NOTE Confidence: 0.8999091
01:18:50.230 --> 01:18:51.960 for adversity in the environment.
NOTE Confidence: 0.8999091
01:18:51.960 --> 01:18:54.389 I I'm super excited about this data
NOTE Confidence: 0.8999091
01:18:54.389 --> 01:18:56.650 with Tonya, and this is really,
NOTE Confidence: 0.8999091
01:18:56.650 --> 01:18:58.990 really brand new data that Tony
NOTE Confidence: 0.8999091
01:18:59.068 --> 01:19:01.208 and I've been talking about.
NOTE Confidence: 0.8999091
01:19:01.210 --> 01:19:02.458 What does it mean?
NOTE Confidence: 0.8999091
01:19:02.458 --> 01:19:05.604 Why is this skin as part of your as part
NOTE Confidence: 0.8999091
01:19:05.604 --> 01:19:08.560 of your wide cast sort of stress network?
NOTE Confidence: 0.8999091
01:19:08.560 --> 01:19:10.898 This skin has really ultimately been ignored.
NOTE Confidence: 0.8999091
01:19:10.900 --> 01:19:12.232 How is that uniquely
NOTE Confidence: 0.8999091
01:19:12.232 --> 01:19:13.564 vulnerable during that window?
NOTE Confidence: 0.8999091
01:19:13.570 --> 01:19:14.902 I mean, it's there.
NOTE Confidence: 0.8999091
01:19:14.902 --> 01:19:15.568 Great questions,
NOTE Confidence: 0.8999091
01:19:15.570 --> 01:19:17.240 haven't really figured it out.
NOTE Confidence: 0.8999091

01:19:17.240 --> 01:19:18.830 I'm not sure that keratinocyte
NOTE Confidence: 0.8999091

01:19:18.830 --> 01:19:20.795 maturation or even the stem cells
NOTE Confidence: 0.8999091

01:19:20.795 --> 01:19:22.703 there have been that well documented
NOTE Confidence: 0.8999091

01:19:22.703 --> 01:19:24.919 changes in your skin over adolescence.
NOTE Confidence: 0.8999091

01:19:24.920 --> 01:19:27.258 I think we can all account for,
NOTE Confidence: 0.8999091

01:19:27.260 --> 01:19:29.924 but what it means for the stem cells?
NOTE Confidence: 0.8999091

01:19:29.930 --> 01:19:30.938 I don't know.
NOTE Confidence: 0.9157843

01:19:38.350 --> 01:19:41.635 That is it in chat. Unless
NOTE Confidence: 0.9157843

01:19:41.635 --> 01:19:43.610 anybody else has a question.
NOTE Confidence: 0.779569864

01:19:48.100 --> 01:19:51.470 Alright, thank. Q Doctor bail.
NOTE Confidence: 0.779569864

01:19:51.470 --> 01:19:53.340 Thank you so much, Tracy.
NOTE Confidence: 0.779569864

01:19:53.340 --> 01:19:55.614 Thank you. Nice to see everybody.