WEBVTT

NOTE Confidence: 0.6876348

00:00:00.000 --> 00:00:03.913 John, for having me see, I I I did it.

NOTE Confidence: 0.6876348

00:00:03.920 --> 00:00:05.915 I didn't call you Doctor Crystal and

NOTE Confidence: 0.6876348

00:00:05.915 --> 00:00:07.759 Arena Esterlis for also reaching out,

NOTE Confidence: 0.6876348

00:00:07.760 --> 00:00:10.000 which I really appreciate it.

NOTE Confidence: 0.6876348

00:00:10.000 --> 00:00:13.080 I'll just share my slides.

NOTE Confidence: 0.6876348

00:00:13.080 --> 00:00:16.056 And so, you know,

NOTE Confidence: 0.6876348

00:00:16.056 --> 00:00:18.879 I I've come a long way for my PhD as,

NOTE Confidence: 0.6876348

00:00:18.880 --> 00:00:19.680 as you were introducing me,

NOTE Confidence: 0.6876348

00:00:19.680 --> 00:00:20.838 I was reflecting on my path.

NOTE Confidence: 0.6876348

00:00:20.840 --> 00:00:21.560 And I think one of my,

NOTE Confidence: 0.6876348

00:00:21.560 --> 00:00:23.280 one of my absolutely favorite

NOTE Confidence: 0.6876348

00:00:23.280 --> 00:00:25.460 parts of being a scientist is just

NOTE Confidence: 0.6876348

00:00:25.460 --> 00:00:26.840 going where the science takes you.

NOTE Confidence: 0.6876348

00:00:26.840 --> 00:00:27.840 And I think that's really

00:00:27.840 --> 00:00:28.840 a gift that we have,

00:00:28.840 --> 00:00:30.810 those of us who do research and

00:00:30.810 --> 00:00:32.560 our physicians as well as we just

00:00:32.560 --> 00:00:34.454 get to go where the science and

00:00:34.454 --> 00:00:35.960 our lived experience take us.

00:00:35.960 --> 00:00:38.252 So I'm very passionate about the field

00:00:38.252 --> 00:00:40.122 of reproductive psychiatry and I'm

00:00:40.122 --> 00:00:42.000 very passionate about helping women.

00:00:42.000 --> 00:00:44.320 Has the best way to help help babies, right?

00:00:44.320 --> 00:00:46.320 I appreciate all child psychiatrists,

00:00:46.320 --> 00:00:47.532 child adolescent psychiatrists.

00:00:47.532 --> 00:00:49.956 I I just really admire it.

00:00:49.960 --> 00:00:51.556 I found myself during my rotations,

00:00:51.560 --> 00:00:53.600 during not being able to

00:00:53.600 --> 00:00:56.200 compartmentalize the trauma of children.

NOTE Confidence: 0.6876348

00:00:56.200 --> 00:00:57.667 And I thought to myself the best way to

NOTE Confidence: 0.6876348

00:00:57.667 --> 00:00:59.236 help children is by helping their mothers.

NOTE Confidence: 0.6876348

00:00:59.240 --> 00:01:01.436 So that's really was the nice for my work.

NOTE Confidence: 0.6876348

00:01:01.440 --> 00:01:03.568 And so I'm really delighted to be

NOTE Confidence: 0.6876348

00:01:03.568 --> 00:01:05.684 talking to you today about the progress

NOTE Confidence: 0.6876348

00:01:05.684 --> 00:01:07.238 that we've made and I'm very pleased

NOTE Confidence: 0.6876348

00:01:07.238 --> 00:01:08.999 in fact that we've made some progress.

NOTE Confidence: 0.6876348

00:01:09.000 --> 00:01:10.480 So I'd like to start,

NOTE Confidence: 0.6876348

00:01:10.480 --> 00:01:12.664 I had the pleasure and honor of guest

NOTE Confidence: 0.6876348

00:01:12.664 --> 00:01:15.037 editing an issue of biological psychiatry.

NOTE Confidence: 0.6876348

00:01:15.040 --> 00:01:16.318 Thanks to John with Elaine Sao,

NOTE Confidence: 0.6876348

00:01:16.320 --> 00:01:19.480 who's a nationally recognized expert,

NOTE Confidence: 0.6876348

00:01:19.480 --> 00:01:21.825 really put the microbiome on the map

NOTE Confidence: 0.6876348

00:01:21.825 --> 00:01:24.930 for us in psychiatry on the exposome,

NOTE Confidence: 0.6876348

00:01:24.930 --> 00:01:27.080 the microbiome and psychiatric disorder.

NOTE Confidence: 0.6876348

00:01:27.080 --> 00:01:29.640 So this is a figure from our commentary.

NOTE Confidence: 0.6876348

00:01:29.640 --> 00:01:33.420 And when I really think about the exposome,

NOTE Confidence: 0.6876348

00:01:33.420 --> 00:01:35.310 I really think about all the things

NOTE Confidence: 0.6876348

00:01:35.310 --> 00:01:37.424 that you encounter from the womb to the

NOTE Confidence: 0.6876348

00:01:37.424 --> 00:01:39.198 grave that could impact your health.

NOTE Confidence: 0.6876348

00:01:39.200 --> 00:01:40.544 And we really see the microbiome

NOTE Confidence: 0.6876348

00:01:40.544 --> 00:01:42.226 as being a real, a real,

NOTE Confidence: 0.6876348

00:01:42.226 --> 00:01:44.460 a really key transducer of that stimuli.

NOTE Confidence: 0.6876348

00:01:44.460 --> 00:01:45.798 So illustrated here, we have diet,

NOTE Confidence: 0.6876348

00:01:45.798 --> 00:01:47.299 we have medication, we have pollution.

NOTE Confidence: 0.6876348

00:01:47.299 --> 00:01:49.489 And what I'm going to be focusing on

NOTE Confidence: 0.6876348

00:01:49.489 --> 00:01:51.289 for you today is stress and how we

NOTE Confidence: 0.6876348

00:01:51.289 --> 00:01:53.359 think of stress as part of the exposome.

NOTE Confidence: 0.6876348

00:01:53.360 --> 00:01:54.740 We all encounter,

NOTE Confidence: 0.6876348

00:01:54.740 --> 00:01:55.200 stress,

NOTE Confidence: 0.6876348

00:01:55.200 --> 00:01:58.237 everything from daily hassles to major life

4

00:01:58.237 --> 00:02:01.720 events to wars and things of that nature.

00:02:01.720 --> 00:02:04.078 And how can that impact us?

00:02:04.080 --> 00:02:06.200 And then how does that impact our health?

00:02:06.200 --> 00:02:08.216 And so I'd love to call all of your

00:02:08.216 --> 00:02:09.680 attention to the special issue,

00:02:09.680 --> 00:02:12.641 which really just has a number of wonderful

00:02:12.641 --> 00:02:15.480 contributions Internet from across the world,

00:02:15.480 --> 00:02:16.344 across the lifespan.

00:02:16.344 --> 00:02:18.072 Thinking about how they expose them

00:02:18.072 --> 00:02:19.789 really shapes our risk for psychiatric

00:02:19.789 --> 00:02:21.440 disorders or shapes the path that,

00:02:21.440 --> 00:02:23.672 you know, the contributes to the

00:02:23.672 --> 00:02:25.160 pathogenesis of psychiatric disorders.

00:02:25.160 --> 00:02:27.560 And so I think it's worth a download,

00:02:27.560 --> 00:02:28.379 worth a read,

00:02:28.379 --> 00:02:30.017 and I really encourage you to

NOTE Confidence: 0.6876348

00:02:30.017 --> 00:02:30.959 think about that.

NOTE Confidence: 0.6876348

00:02:30.960 --> 00:02:32.304 So as I said,

NOTE Confidence: 0.6876348

00:02:32.304 --> 00:02:34.320 I'll be focusing today on stress.

NOTE Confidence: 0.6876348

00:02:34.320 --> 00:02:37.000 So and specifically in pregnancy.

NOTE Confidence: 0.6876348

00:02:37.000 --> 00:02:38.920 So when we think about stress,

NOTE Confidence: 0.976054468

00:02:38.920 --> 00:02:39.760 what do we think about?

NOTE Confidence: 0.976054468

00:02:39.760 --> 00:02:41.998 Well, there's several layers to type,

NOTE Confidence: 0.976054468

00:02:42.000 --> 00:02:42.812 different types of stress,

NOTE Confidence: 0.976054468

00:02:42.812 --> 00:02:44.299 and I think it's important to think

NOTE Confidence: 0.976054468

00:02:44.299 --> 00:02:45.439 about each of these individually

NOTE Confidence: 0.976054468

00:02:45.439 --> 00:02:46.351 as well as collectively.

NOTE Confidence: 0.976054468

00:02:46.360 --> 00:02:47.764 So there's interpersonal stress.

NOTE Confidence: 0.976054468

00:02:47.764 --> 00:02:49.870 This is things like the amount

NOTE Confidence: 0.976054468

00:02:49.928 --> 00:02:51.566 of sleep you're able to get or

NOTE Confidence: 0.976054468

00:02:51.566 --> 00:02:53.439 if you have difficulty sleeping,

00:02:53.440 --> 00:02:55.156 whether or not you are getting

00:02:55.156 --> 00:02:57.238 a diet that's rich in fruits and

00:02:57.238 --> 00:02:59.133 vegetables and minerals and important

00:02:59.133 --> 00:03:01.198 fibers and things of that nature.

00:03:01.200 --> 00:03:03.600 Or whether you have a more deprived diet,

00:03:03.600 --> 00:03:04.546 interpersonal stressors,

00:03:04.546 --> 00:03:06.438 so your social relationships,

00:03:06.440 --> 00:03:08.099 your financial state,

00:03:08.099 --> 00:03:11.329 your your workplace or work stressors.

00:03:11.329 --> 00:03:13.421 And then there's structural

00:03:13.421 --> 00:03:15.360 and institutional things like

00:03:15.360 --> 00:03:17.800 racism can impact an individual.

00:03:17.800 --> 00:03:19.368 Things like climate change,

00:03:19.368 --> 00:03:21.960 pollution in the neighbourhood you live in,

00:03:21.960 --> 00:03:22.648 the built,

00:03:22.648 --> 00:03:24.712 you're built environment can all impact

NOTE Confidence: 0.976054468

00:03:24.712 --> 00:03:26.489 a pregnant person during pregnancy

NOTE Confidence: 0.976054468

00:03:26.489 --> 00:03:28.553 as well as the next generation.

NOTE Confidence: 0.976054468

00:03:28.560 --> 00:03:30.100 And So what I really started to

NOTE Confidence: 0.976054468

00:03:30.100 --> 00:03:31.331 think about and thinking about

NOTE Confidence: 0.976054468

00:03:31.331 --> 00:03:32.879 the special issue and just in

NOTE Confidence: 0.976054468

00:03:32.879 --> 00:03:34.476 general in my career is we can't.

NOTE Confidence: 0.976054468

00:03:34.480 --> 00:03:36.400 I can't fix all those things.

NOTE Confidence: 0.976054468

00:03:36.400 --> 00:03:37.625 We were talking before everyone

NOTE Confidence: 0.976054468

00:03:37.625 --> 00:03:39.348 came on about how it's going to

NOTE Confidence: 0.976054468

00:03:39.348 --> 00:03:40.680 be 60° today here in Columbus,

NOTE Confidence: 0.976054468

00:03:40.680 --> 00:03:41.992 OH, and I wasn't sure if that I

NOTE Confidence: 0.976054468

00:03:41.992 --> 00:03:42.840 was going to enjoy it,

NOTE Confidence: 0.976054468

00:03:42.840 --> 00:03:44.352 but I didn't know if that was a sign,

NOTE Confidence: 0.976054468

00:03:44.360 --> 00:03:48.520 a portent of our climate changing too much.

NOTE Confidence: 0.976054468

00:03:48.520 --> 00:03:49.880 But I can't change that.

NOTE Confidence: 0.976054468

00:03:49.880 --> 00:03:51.240 I do have started composting.

NOTE Confidence: 0.976054468

00:03:51.240 --> 00:03:52.624 I can't change that.

NOTE Confidence: 0.976054468

00:03:52.624 --> 00:03:54.354 But can I change personally,

NOTE Confidence: 0.976054468

00:03:54.360 --> 00:03:55.980 how these adverse exposures

NOTE Confidence: 0.976054468

00:03:55.980 --> 00:03:57.195 and their contribution,

NOTE Confidence: 0.976054468

00:03:57.200 --> 00:03:58.361 contribution to pathophysiology,

NOTE Confidence: 0.976054468

00:03:58.361 --> 00:04:00.683 Can I do anything to positively

NOTE Confidence: 0.976054468

00:04:00.683 --> 00:04:02.160 impact that in that space?

NOTE Confidence: 0.976054468

00:04:02.160 --> 00:04:04.440 If we can, as researchers,

NOTE Confidence: 0.976054468

00:04:04.440 --> 00:04:07.128 as scientists, as psychiatrists,

NOTE Confidence: 0.976054468

00:04:07.128 --> 00:04:07.800 psychologists,

NOTE Confidence: 0.976054468

00:04:07.800 --> 00:04:10.004 help the individual deal

NOTE Confidence: 0.976054468

00:04:10.004 --> 00:04:12.759 with the sequela of stress,

NOTE Confidence: 0.976054468

00:04:12.760 --> 00:04:14.680 Is that the best way of helping them?

NOTE Confidence: 0.976054468

00:04:14.680 --> 00:04:15.877 And I I happen to think so.

NOTE Confidence: 0.976054468

00:04:15.880 --> 00:04:17.680 Spoiler.

NOTE Confidence: 0.976054468

00:04:17.680 --> 00:04:20.942 And so when we think mechanistically about

NOTE Confidence: 0.976054468

00:04:20.942 --> 00:04:24.440 pregnancy and how prenatal stress is shaping

NOTE Confidence: 0.976054468

00:04:24.440 --> 00:04:27.560 the pregnancy and the next generation,

NOTE Confidence: 0.976054468

00:04:27.560 --> 00:04:28.757 why do we even think about it?

NOTE Confidence: 0.976054468

00:04:28.760 --> 00:04:30.286 Well, it used to be, though.

NOTE Confidence: 0.976054468

00:04:30.286 --> 00:04:32.298 It used to be thought, you know,

NOTE Confidence: 0.976054468

00:04:32.298 --> 00:04:33.621 women used to be told that pregnancy

NOTE Confidence: 0.976054468

00:04:33.621 --> 00:04:34.839 was just this time of elation.

NOTE Confidence: 0.976054468

00:04:34.840 --> 00:04:36.289 I guess we were thought to float

NOTE Confidence: 0.976054468

00:04:36.289 --> 00:04:37.598 around on these clouds of pink,

NOTE Confidence: 0.976054468

00:04:37.600 --> 00:04:38.320 you know,

NOTE Confidence: 0.976054468

00:04:38.320 --> 00:04:40.120 pink pheromones the entire time,

NOTE Confidence: 0.976054468

00:04:40.120 --> 00:04:42.196 blissfully awaiting our bundle of joy.

NOTE Confidence: 0.976054468

00:04:42.200 --> 00:04:43.440 But the the the case,

NOTE Confidence: 0.976054468

00:04:43.440 --> 00:04:44.600 it's not actually the case.

NOTE Confidence: 0.976054468

00:04:44.600 --> 00:04:46.012 There's actually women experience

NOTE Confidence: 0.976054468

00:04:46.012 --> 00:04:47.777 depression and anxiety at the

NOTE Confidence: 0.976054468

00:04:47.777 --> 00:04:49.438 same rate during pregnancy as

NOTE Confidence: 0.976054468

00:04:49.438 --> 00:04:50.998 they do outside of pregnancy.

NOTE Confidence: 0.976054468

00:04:51.000 --> 00:04:53.825 So up to 1/4 of women do experience either

NOTE Confidence: 0.976054468

00:04:53.825 --> 00:04:55.800 depression or anxiety during pregnancy.

NOTE Confidence: 0.976054468

00:04:55.800 --> 00:04:57.400 And I have some statistics for you here.

NOTE Confidence: 0.976054468

00:04:57.400 --> 00:04:59.800 So the reason we think about

NOTE Confidence: 0.976054468

00:04:59.800 --> 00:05:01.360 stress and sequela of stress,

NOTE Confidence: 0.976054468

00:05:01.360 --> 00:05:02.998 which is how as I conceive of

NOTE Confidence: 0.976054468

00:05:03.000 --> 00:05:04.616 depression and anxiety amidst

NOTE Confidence: 0.976054468

00:05:04.616 --> 00:05:07.040 those stress is a known trigger

NOTE Confidence: 0.976054468

00:05:07.107 --> 00:05:09.159 for many psychiatric disorders.

NOTE Confidence: 0.976054468

00:05:09.160 --> 00:05:12.120 Beyond depression and anxiety,

NOTE Confidence: 0.976054468

00:05:12.120 --> 00:05:14.886 we we it's important because it's

NOTE Confidence: 0.976054468

00:05:14.886 --> 00:05:16.730 relevant because there's prevalent

NOTE Confidence: 0.976054468

00:05:16.806 --> 00:05:19.184 and so that's why this is worth worth

NOTE Confidence: 0.976054468

00:05:19.184 --> 00:05:21.600 your time today with me this morning.

NOTE Confidence: 0.976054468

00:05:21.600 --> 00:05:23.076 You're going to encounter this at

NOTE Confidence: 0.976054468

00:05:23.076 --> 00:05:24.674 some point either in your personal

NOTE Confidence: 0.976054468

00:05:24.674 --> 00:05:26.074 or in your professional life,

NOTE Confidence: 0.960455556

00:05:26.080 --> 00:05:29.320 depending on your patient population.

NOTE Confidence: 0.960455556

00:05:29.320 --> 00:05:31.728 And so most of the focus until about

NOTE Confidence: 0.960455556

00:05:31.728 --> 00:05:34.278 a decade ago was on these mechanisms.

NOTE Confidence: 0.960455556

00:05:34.280 --> 00:05:35.695 Really stellar work from Tracy

NOTE Confidence: 0.960455556

00:05:35.695 --> 00:05:37.569 Bale and Petit Guadwa have really

NOTE Confidence: 0.960455556

00:05:37.569 --> 00:05:39.197 focused on epigenetic programming.

NOTE Confidence: 0.960455556

00:05:39.200 --> 00:05:40.800 So it's not just the genes you inherit,

NOTE Confidence: 0.960455556

00:05:40.800 --> 00:05:42.492 it's how they're expressed that can

NOTE Confidence: 0.960455556

00:05:42.492 --> 00:05:44.199 contribute to your risk of disease.

NOTE Confidence: 0.960455556

00:05:44.200 --> 00:05:47.116 So epigenetic modifications can go a

NOTE Confidence: 0.960455556

00:05:47.116 --> 00:05:50.328 long way to increasing or reducing your

NOTE Confidence: 0.960455556

00:05:50.328 --> 00:05:52.560 risk of what's in your genetic code.

NOTE Confidence: 0.960455556

00:05:52.560 --> 00:05:53.760 There's been a lot of focus

NOTE Confidence: 0.960455556

00:05:53.760 --> 00:05:54.560 on the immune function.

NOTE Confidence: 0.960455556

00:05:54.560 --> 00:05:57.302 So there's a broad epidemiological and

NOTE Confidence: 0.960455556

00:05:57.302 --> 00:05:59.130 clinical research that demonstrates

NOTE Confidence: 0.960455556

00:05:59.192 --> 00:06:01.397 that infection with the influenza

NOTE Confidence: 0.960455556

00:06:01.397 --> 00:06:03.455 during pregnancy is is known as is

NOTE Confidence: 0.960455556

00:06:03.455 --> 00:06:05.124 known to be associated with increased

NOTE Confidence: 0.960455556

00:06:05.124 --> 00:06:06.880 risk of developing schizophrenia

NOTE Confidence: 0.960455556

00:06:06.880 --> 00:06:09.076 in the offspring exposed to that.

NOTE Confidence: 0.960455556

00:06:09.080 --> 00:06:09.839 And there's other

NOTE Confidence: 0.931758692

00:06:12.280 --> 00:06:13.785 lines of evidence that also

NOTE Confidence: 0.931758692

00:06:13.785 --> 00:06:15.290 suggests that the immune system

NOTE Confidence: 0.931758692

00:06:15.342 --> 00:06:17.052 during pregnancy plays a key role

NOTE Confidence: 0.931758692

13

00:06:17.052 --> 00:06:18.640 in the transmission of stress.

NOTE Confidence: 0.931758692

00:06:18.640 --> 00:06:19.960 HPA access regulation.

NOTE Confidence: 0.931758692

00:06:19.960 --> 00:06:21.674 That makes sense, right?

NOTE Confidence: 0.931758692

00:06:21.674 --> 00:06:24.038 That changes in your HPA access

NOTE Confidence: 0.931758692

00:06:24.040 --> 00:06:25.979 work from Tim Oberland up in Canada

NOTE Confidence: 0.931758692

00:06:25.979 --> 00:06:27.549 has shown that the offspring

NOTE Confidence: 0.931758692

00:06:27.549 --> 00:06:29.239 born to women with depression

NOTE Confidence: 0.931758692

00:06:29.239 --> 00:06:31.094 or anxiety during pregnancy have

NOTE Confidence: 0.931758692

00:06:31.094 --> 00:06:33.034 dysregulation in their HPA access.

NOTE Confidence: 0.931758692

00:06:33.040 --> 00:06:34.040 Then about a decade ago,

NOTE Confidence: 0.931758692

00:06:34.040 --> 00:06:36.360 right as I was coming on the scene,

NOTE Confidence: 0.931758692

00:06:36.360 --> 00:06:37.728 there was some work.

NOTE Confidence: 0.931758692

00:06:37.728 --> 00:06:40.150 The new contender in this field is

NOTE Confidence: 0.931758692

00:06:40.150 --> 00:06:42.518 now the the gut brain axis is also

NOTE Confidence: 0.931758692

00:06:42.518 --> 00:06:45.008 thought to play a role in how prenatal

NOTE Confidence: 0.931758692

00:06:45.008 --> 00:06:46.546 stress might be underlying some

NOTE Confidence: 0.931758692

00:06:46.546 --> 00:06:48.111 of the mechanisms in transmission

NOTE Confidence: 0.931758692

00:06:48.111 --> 00:06:50.119 of stress to the next generation,

NOTE Confidence: 0.931758692

00:06:50.120 --> 00:06:51.848 which will be really the focus

NOTE Confidence: 0.931758692

00:06:51.848 --> 00:06:53.000 of my talk today.

NOTE Confidence: 0.931758692

00:06:53.000 --> 00:06:55.060 So when I first started

NOTE Confidence: 0.931758692

00:06:55.060 --> 00:06:57.120 giving talks in this space,

NOTE Confidence: 0.931758692

00:06:57.120 --> 00:06:58.800 I remember I was at SOBP one year.

NOTE Confidence: 0.931758692

00:06:58.800 --> 00:07:00.680 Someone asked me, you know,

NOTE Confidence: 0.931758692

00:07:00.680 --> 00:07:02.960 the brains all the way up here and you know,

NOTE Confidence: 0.931758692

00:07:02.960 --> 00:07:05.116 the guts all the way down here.

NOTE Confidence: 0.931758692

00:07:05.120 --> 00:07:05.632 How?

NOTE Confidence: 0.931758692

00:07:05.632 --> 00:07:07.680 How, You know what,

NOTE Confidence: 0.931758692

00:07:07.680 --> 00:07:09.200 how are the two connected?

NOTE Confidence: 0.931758692

00:07:09.200 --> 00:07:11.324 And so I spent a lot of time thinking

NOTE Confidence: 0.931758692

00:07:11.324 --> 00:07:13.187 about that and writing about that

NOTE Confidence: 0.931758692

00:07:13.187 --> 00:07:14.752 and making slides about that.

NOTE Confidence: 0.931758692

00:07:14.760 --> 00:07:16.040 So I'm going to explain that to you.

NOTE Confidence: 0.931758692

00:07:16.040 --> 00:07:17.505 So hopefully today you'll leave

NOTE Confidence: 0.931758692

00:07:17.505 --> 00:07:18.970 with a better understanding of

NOTE Confidence: 0.931758692

00:07:19.021 --> 00:07:20.437 how how that might be working.

NOTE Confidence: 0.931758692

00:07:20.440 --> 00:07:23.142 And so really it's a it's $1,000,000

NOTE Confidence: 0.931758692

00:07:23.142 --> 00:07:25.144 question or multi $1,000,000 question.

NOTE Confidence: 0.931758692

00:07:25.144 --> 00:07:27.184 How are peripheral changes in

NOTE Confidence: 0.931758692

00:07:27.184 --> 00:07:29.232 the microbiome And when I say

NOTE Confidence: 0.931758692

00:07:29.232 --> 00:07:30.782 microbiome with something no more,

NOTE Confidence: 0.931758692

00:07:30.782 --> 00:07:32.648 no less than all the collective

NOTE Confidence: 0.931758692

00:07:32.648 --> 00:07:34.400 community of microbes that are

NOTE Confidence: 0.931758692

00:07:34.400 --> 00:07:35.900 present in different orifices in

NOTE Confidence: 0.931758692

00:07:35.900 --> 00:07:37.838 your body and the gut microbiome

NOTE Confidence: 0.931758692

00:07:37.840 --> 00:07:40.210 specifically is thought to have an

NOTE Confidence: 0.931758692

00:07:40.210 --> 00:07:42.522 important role in your overall health.

NOTE Confidence: 0.931758692

00:07:42.522 --> 00:07:45.140 So our how are changes in your

NOTE Confidence: 0.931758692

00:07:45.213 --> 00:07:46.834 gut microbiome being transduced.

NOTE Confidence: 0.931758692

00:07:46.834 --> 00:07:48.913 And so we really think about in

NOTE Confidence: 0.931758692

00:07:48.913 --> 00:07:50.598 pregnancy three major ways that this

NOTE Confidence: 0.931758692

00:07:50.598 --> 00:07:52.840 is being transduced to the developing brain.

NOTE Confidence: 0.931758692

00:07:52.840 --> 00:07:54.112 And so this is an illustration

NOTE Confidence: 0.931758692

00:07:54.112 --> 00:07:55.872 from a review I wrote a few years

NOTE Confidence: 0.931758692

00:07:55.872 --> 00:07:57.360 back now with a very talented MD,

NOTE Confidence: 0.931758692

00:07:57.360 --> 00:07:59.400 PhD student in my lab,

NOTE Confidence: 0.931758692

00:07:59.400 --> 00:08:01.200 which we'll be hearing more about.

NOTE Confidence: 0.931758692

00:08:01.200 --> 00:08:03.120 So the three major ways are

NOTE Confidence: 0.931758692

00:08:03.120 --> 00:08:04.468 through the first of all,

NOTE Confidence: 0.931758692

00:08:04.468 --> 00:08:05.884 it's thought that stress is shifting

NOTE Confidence: 0.931758692

00:08:05.884 --> 00:08:07.287 the microbes and I'll just like

NOTE Confidence: 0.931758692

00:08:07.287 --> 00:08:08.760 to illustrate this in a moment.

NOTE Confidence: 0.931758692

00:08:08.760 --> 00:08:11.106 The three major ways is that

NOTE Confidence: 0.931758692

00:08:11.106 --> 00:08:12.279 through vertical transmission.

NOTE Confidence: 0.931758692

00:08:12.280 --> 00:08:13.060 So at delivery,

NOTE Confidence: 0.931758692

00:08:13.060 --> 00:08:14.880 not to be too graphic before lunch,

NOTE Confidence: 0.931758692

00:08:14.880 --> 00:08:16.630 but during delivery the mother

NOTE Confidence: 0.931758692

00:08:16.630 --> 00:08:18.835 bequeaths her microbiome to the infant

NOTE Confidence: 0.931758692

00:08:18.835 --> 00:08:20.810 through a standard vaginal delivery

NOTE Confidence: 0.931758692

00:08:20.810 --> 00:08:22.636 or through C-section is one way

NOTE Confidence: 0.931758692

00:08:22.636 --> 00:08:24.120 that it's thought to shape the the

NOTE Confidence: 0.931758692

00:08:24.169 --> 00:08:25.957 governing axis of the next generation.

NOTE Confidence: 0.931758692

00:08:25.960 --> 00:08:27.840 The 2nd way is through

NOTE Confidence: 0.931758692

00:08:27.840 --> 00:08:29.720 modulation of the immune system,

NOTE Confidence: 0.931758692

00:08:29.720 --> 00:08:31.520 because microbes at the end of

NOTE Confidence: 0.931758692

00:08:31.520 --> 00:08:33.466 the day are microbes and they

NOTE Confidence: 0.931758692

00:08:33.466 --> 00:08:34.838 elicit an immune response.

NOTE Confidence: 0.931758692

00:08:34.840 --> 00:08:36.280 And then through the metabolites,

00:08:36.280 --> 00:08:37.655 they're not just sitting there

00:08:37.655 --> 00:08:38.755 quietly twiddling their thumbs,

00:08:38.760 --> 00:08:40.404 they're actually producing

00:08:40.404 --> 00:08:42.596 really bio active metabolites,

00:08:42.600 --> 00:08:45.552 and I'll be talking more about that as well.

00:08:45.560 --> 00:08:47.640 So to illustrate for you this even further,

00:08:47.640 --> 00:08:49.878 we have here a pregnant person

00:08:49.880 --> 00:08:51.704 and they're undergoing stress.

00:08:51.704 --> 00:08:54.440 What happens next is that there's

00:08:54.515 --> 00:08:57.718 activation of the HPA axis, release of ACTH,

00:08:57.718 --> 00:08:59.422 release of glucocorticoids from

00:08:59.422 --> 00:09:02.306 the adrenals as well as sympathetic

00:09:02.306 --> 00:09:03.839 nervous system activation.

00:09:03.840 --> 00:09:06.360 How this impacts the host,

00:09:06.360 --> 00:09:08.220 which is the pregnant person

00:09:08.220 --> 00:09:10.440 in this illustration is it can

NOTE Confidence: 0.838971793333333

00:09:10.440 --> 00:09:11.880 modulate their immune system.

NOTE Confidence: 0.838971793333333

00:09:11.880 --> 00:09:15.040 So lead to the recruitment of immune cells

NOTE Confidence: 0.838971793333333

00:09:15.040 --> 00:09:19.600 and the activation of immune cells to trans.

NOTE Confidence: 0.838971793333333

00:09:19.600 --> 00:09:20.940 You've raised something called cytokines

NOTE Confidence: 0.838971793333333

00:09:20.940 --> 00:09:22.280 which if there's any immunologists,

NOTE Confidence: 0.838971793333333

00:09:22.280 --> 00:09:24.000 I apologize in the audience,

NOTE Confidence: 0.838971793333333

00:09:24.000 --> 00:09:26.504 but I I sometimes think of cytokines as

NOTE Confidence: 0.838971793333333

00:09:26.504 --> 00:09:28.280 the neurotransmitter of the immune system.

NOTE Confidence: 0.838971793333333

00:09:28.280 --> 00:09:30.500 So these can travel and recruit

NOTE Confidence: 0.838971793333333

00:09:30.500 --> 00:09:32.469 additional immune cells and cytokines

NOTE Confidence: 0.838971793333333

00:09:32.469 --> 00:09:34.995 themselves can have impact on neurons

NOTE Confidence: 0.838971793333333

00:09:35.000 --> 00:09:39.080 and other and other cells in your brain.

NOTE Confidence: 0.838971793333333

00:09:39.080 --> 00:09:40.914 And then it also all these together,

NOTE Confidence: 0.838971793333333

00:09:40.920 --> 00:09:42.840 both the immune system activation

NOTE Confidence: 0.838971793333333

00:09:42.840 --> 00:09:44.760 as well the sympathetic nervous

00:09:44.828 --> 00:09:46.833 system activation has an effect

00:09:46.833 --> 00:09:48.437 on the intestinal epithelium.

00:09:48.440 --> 00:09:50.428 And so the impact on the intestinal

00:09:50.428 --> 00:09:52.627 epithelium can also give rise to and it

00:09:52.627 --> 00:09:54.440 can also separately impact the microbes.

00:09:54.440 --> 00:09:56.078 So the idea is that during stress,

00:09:56.080 --> 00:09:58.473 there's a shift from 1 homeostatic

00:09:58.473 --> 00:10:00.132 population of microbes.

00:10:00.132 --> 00:10:01.238 There's dysbiosis.

00:10:01.240 --> 00:10:03.980 So it gives rise to a shift in the community

00:10:04.045 --> 00:10:06.597 of microbes that are present in your gut.

00:10:06.600 --> 00:10:07.960 And why is this important?

00:10:07.960 --> 00:10:09.040 Well, for a few reasons.

00:10:09.040 --> 00:10:10.720 One, as I mentioned, they're not just

00:10:10.720 --> 00:10:11.999 sitting there twiddling their thumbs.

00:10:12.000 --> 00:10:12.723 They're making metabolites.

NOTE Confidence: 0.838971793333333

00:10:12.723 --> 00:10:14.169 If there's anyone in the audience

NOTE Confidence: 0.838971793333333

00:10:14.169 --> 00:10:15.000 that wants to guess.

NOTE Confidence: 0.838971793333333

00:10:15.000 --> 00:10:15.768 But these are.

NOTE Confidence: 0.838971793333333

00:10:15.768 --> 00:10:17.560 These are two of my favorite metabolites.

NOTE Confidence: 0.838971793333333

00:10:17.560 --> 00:10:19.420 This is I guess actually

NOTE Confidence: 0.838971793333333

00:10:19.420 --> 00:10:21.280 you you you can't unmute,

NOTE Confidence: 0.838971793333333

00:10:21.280 --> 00:10:23.155 it's actually serotonin and butyrate

NOTE Confidence: 0.838971793333333

00:10:23.155 --> 00:10:25.522 which butyrate for those of you

NOTE Confidence: 0.838971793333333

00:10:25.522 --> 00:10:28.000 interested in epigenetics is a very

NOTE Confidence: 0.838971793333333

00:10:28.000 --> 00:10:29.540 important epigenetic modifier and

NOTE Confidence: 0.838971793333333

00:10:29.540 --> 00:10:32.130 serotonin we all we all know and

NOTE Confidence: 0.838971793333333

00:10:32.130 --> 00:10:34.719 love and so they're actually major

NOTE Confidence: 0.838971793333333

00:10:34.720 --> 00:10:36.288 metabolizers of tryptophan and

NOTE Confidence: 0.838971793333333

00:10:36.288 --> 00:10:38.640 producers of short chain fatty acids.

NOTE Confidence: 0.838971793333333

00:10:38.640 --> 00:10:40.525 So it's incredibly important These

NOTE Confidence: 0.838971793333333

00:10:40.525 --> 00:10:43.194 together can have an immunomodulatory impact,

NOTE Confidence: 0.838971793333333

00:10:43.194 --> 00:10:47.233 these metabolites as well as well as

NOTE Confidence: 0.838971793333333

00:10:47.240 --> 00:10:50.802 at delivery the baby is going to be

NOTE Confidence: 0.838971793333333

00:10:50.802 --> 00:10:52.318 seated as I mentioned by the mother.

NOTE Confidence: 0.838971793333333

00:10:52.320 --> 00:10:54.278 So this sets up the next generation's

NOTE Confidence: 0.838971793333333

00:10:54.278 --> 00:10:56.784 got brain access in a way that

NOTE Confidence: 0.838971793333333

00:10:56.784 --> 00:10:58.400 could be maladaptive.

NOTE Confidence: 0.838971793333333

00:10:58.400 --> 00:10:59.960 And then why we worry about

NOTE Confidence: 0.838971793333333

00:10:59.960 --> 00:11:01.000 that is because Mycoglia,

NOTE Confidence: 0.838971793333333

00:11:01.000 --> 00:11:02.955 which are the innate immune

NOTE Confidence: 0.838971793333333

00:11:02.955 --> 00:11:04.519 cells of your brain,

NOTE Confidence: 0.838971793333333

00:11:04.520 --> 00:11:06.824 are increasingly understood to

NOTE Confidence: 0.838971793333333

00:11:06.824 --> 00:11:09.704 have an incredibly important role

NOTE Confidence: 0.838971793333333

00:11:09.704 --> 00:11:11.480 in psychiatric disorders like

NOTE Confidence: 0.838971793333333

00:11:11.480 --> 00:11:12.680 anxiety and depression.

NOTE Confidence: 0.838971793333333

00:11:12.680 --> 00:11:14.480 So a shift in microglia,

NOTE Confidence: 0.838971793333333

00:11:14.480 --> 00:11:16.280 both in terms of their population

NOTE Confidence: 0.838971793333333

00:11:16.280 --> 00:11:18.575 as well as their level of activity

NOTE Confidence: 0.838971793333333

00:11:18.575 --> 00:11:20.440 could understandably contribute to the

NOTE Confidence: 0.838971793333333

00:11:20.440 --> 00:11:21.960 emergence of psychiatric disorders.

NOTE Confidence: 0.838971793333333

00:11:21.960 --> 00:11:24.312 So this is sort of the 1000 foot

NOTE Confidence: 0.838971793333333

00:11:24.312 --> 00:11:26.542 view or 10,000 foot view of what

NOTE Confidence: 0.838971793333333

00:11:26.542 --> 00:11:27.879 I'll be speaking to you about today.

NOTE Confidence: 0.838971793333333

00:11:27.880 --> 00:11:29.544 And I really just wanted to give you

NOTE Confidence: 0.838971793333333

00:11:29.544 --> 00:11:31.074 a framework in which to put all the

NOTE Confidence: 0.838971793333333

00:11:31.074 --> 00:11:32.480 data I'm about to present to you.

NOTE Confidence: 0.838971793333333

00:11:32.480 --> 00:11:34.536 So this is sort of how I conceive

NOTE Confidence: 0.838971793333333

00:11:34.536 --> 00:11:36.486 of the gut brain access during

NOTE Confidence: 0.838971793333333

00:11:36.486 --> 00:11:38.532 pregnancy and how it might be

NOTE Confidence: 0.838971793333333

00:11:38.602 --> 00:11:40.598 impacting the developing brain.

NOTE Confidence: 0.838971793333333

00:11:40.600 --> 00:11:42.448 So one of the wonderful things

00:11:42.448 --> 00:11:43.680 about working with rodents,

00:11:43.680 --> 00:11:45.500 and this is an illustration

00:11:45.500 --> 00:11:47.626 from the special issue that I

00:11:47.626 --> 00:11:48.958 co-authored with Mary Kimmel,

00:11:48.960 --> 00:11:49.905 a close friend and colleague

00:11:49.905 --> 00:11:50.850 at the University of North

00:11:50.890 --> 00:11:51.710 Carolina, Chapel Hill,

00:11:51.710 --> 00:11:54.200 is that we can test some of these things.

00:11:54.200 --> 00:11:55.432 You know, human pregnancies

00:11:55.432 --> 00:11:57.095 take nine months, give or take.

00:11:57.095 --> 00:11:59.022 Mouse pregnancies or 21 days, give or take.

00:11:59.022 --> 00:12:00.660 And we can mechanistically get AT and

00:12:00.711 --> 00:12:02.314 over using a variety of tools that

00:12:02.314 --> 00:12:04.225 I'll be showing you today some of these

00:12:04.225 --> 00:12:05.787 bigger questions on a micro scale.

00:12:05.787 --> 00:12:08.109 And so this if you're interested

NOTE Confidence: 0.873995667272727

00:12:08.109 --> 00:12:10.119 in reading more about this,

NOTE Confidence: 0.873995667272727

00:12:10.120 --> 00:12:11.400 please go ahead and look at this review.

NOTE Confidence: 0.873995667272727

00:12:11.400 --> 00:12:12.849 But what I wanted to highlight for

NOTE Confidence: 0.873995667272727

00:12:12.849 --> 00:12:14.641 you now is that I'm really going to

NOTE Confidence: 0.873995667272727

00:12:14.641 --> 00:12:16.536 be focusing on this shift in maternal

NOTE Confidence: 0.873995667272727

00:12:16.536 --> 00:12:18.764 gut microbes as well as the upper

NOTE Confidence: 0.873995667272727

00:12:18.764 --> 00:12:20.798 left hand portion of this figure,

NOTE Confidence: 0.873995667272727

00:12:20.800 --> 00:12:23.800 which is the cytokine production.

NOTE Confidence: 0.873995667272727

00:12:23.800 --> 00:12:26.104 CCL 2 which is a chemokine that recruits

NOTE Confidence: 0.873995667272727

00:12:26.104 --> 00:12:27.769 immune cells to the site of injury

NOTE Confidence: 0.873995667272727

00:12:27.769 --> 00:12:30.033 like a cut or is also been shown by

NOTE Confidence: 0.873995667272727

00:12:30.033 --> 00:12:31.791 work from a colleague here Jonathan

NOTE Confidence: 0.873995667272727

00:12:31.800 --> 00:12:34.320 Godbout to be really important in

NOTE Confidence: 0.873995667272727

00:12:34.320 --> 00:12:37.840 increasing anxiety following a stressor.

NOTE Confidence: 0.873995667272727

00:12:37.840 --> 00:12:39.639 So within the absence of CCL 2,

00:12:39.640 --> 00:12:41.500 I work from Godbout's lab and

00:12:41.500 --> 00:12:43.419 Michael Bailey's labs and others have

00:12:43.419 --> 00:12:45.415 shown that you no longer see the

00:12:45.415 --> 00:12:46.790 emergence of anxiety like behaviour

00:12:46.840 --> 00:12:48.240 after a social defeat stress.

00:12:48.240 --> 00:12:50.005 So it's it's a critically

00:12:50.005 --> 00:12:50.631 important chemokine.

00:12:50.631 --> 00:12:52.799 So I just wanted to give you the,

00:12:52.800 --> 00:12:53.173 the,

00:12:53.173 --> 00:12:55.038 the basic framework and the

00:12:55.038 --> 00:12:56.954 clinical framework for what what

00:12:56.954 --> 00:12:58.719 we'll be talking about today.

00:12:58.720 --> 00:13:00.952 So how again we can model this in mice.

00:13:00.960 --> 00:13:03.144 And one of the reasons that I became

00:13:03.144 --> 00:13:04.901 so interested in this field is

00:13:04.901 --> 00:13:06.635 because I saw the high translational

NOTE Confidence: 0.873995667272727

00:13:06.640 --> 00:13:07.836 nature of the microbiome.

NOTE Confidence: 0.873995667272727

00:13:07.836 --> 00:13:10.406 I saw that it was both in in mouse

NOTE Confidence: 0.873995667272727

00:13:10.406 --> 00:13:12.280 and man or woman in this case.

NOTE Confidence: 0.873995667272727

00:13:12.280 --> 00:13:14.674 And so I really thought that we could really,

NOTE Confidence: 0.873995667272727

00:13:14.680 --> 00:13:16.486 I could really advance the advance

NOTE Confidence: 0.873995667272727

00:13:16.486 --> 00:13:18.920 the field in a way that was unique

NOTE Confidence: 0.873995667272727

00:13:18.920 --> 00:13:20.560 because there there are limits,

NOTE Confidence: 0.873995667272727

00:13:20.560 --> 00:13:20.883 translatability.

NOTE Confidence: 0.873995667272727

00:13:20.883 --> 00:13:23.467 And so I was really drawn to the

NOTE Confidence: 0.873995667272727

00:13:23.467 --> 00:13:25.196 microbiome for a variety of reasons,

NOTE Confidence: 0.873995667272727

00:13:25.200 --> 00:13:26.316 but that was one of them.

NOTE Confidence: 0.873995667272727

00:13:26.320 --> 00:13:28.720 So how do we model this in mice?

NOTE Confidence: 0.873995667272727

00:13:28.720 --> 00:13:30.680 And I'm just going to have to move

NOTE Confidence: 0.873995667272727

00:13:30.680 --> 00:13:32.372 my little zoom bar here so that

NOTE Confidence: 0.873995667272727

00:13:32.372 --> 00:13:33.512 I can see my slide.

NOTE Confidence: 0.873995667272727

00:13:33.520 --> 00:13:34.878 This is how we we model it.

NOTE Confidence: 0.873995667272727

00:13:34.880 --> 00:13:36.000 So in our lab,

NOTE Confidence: 0.873995667272727

00:13:36.000 --> 00:13:37.400 we do a restraint stress,

NOTE Confidence: 0.873995667272727

00:13:37.400 --> 00:13:39.871 which is not that mice are placed

NOTE Confidence: 0.873995667272727

00:13:39.871 --> 00:13:42.225 in conical tubes with air holes for

NOTE Confidence: 0.873995667272727

00:13:42.225 --> 00:13:43.575 two hours a day between gestational

NOTE Confidence: 0.873995667272727

00:13:43.575 --> 00:13:45.160 day 10 and gestational day 16,

NOTE Confidence: 0.873995667272727

00:13:45.160 --> 00:13:46.658 which you can see here is roughly

NOTE Confidence: 0.873995667272727

00:13:46.658 --> 00:13:48.477 correlated to the second trimester in humans,

NOTE Confidence: 0.873995667272727

00:13:48.480 --> 00:13:50.752 which has been shown in a variety of

NOTE Confidence: 0.873995667272727

00:13:50.752 --> 00:13:52.104 epidemiological and clinical studies

NOTE Confidence: 0.873995667272727

00:13:52.104 --> 00:13:53.991 to be critically important for

NOTE Confidence: 0.873995667272727

00:13:53.991 --> 00:13:55.715 neurodevelopment and increasing risk

NOTE Confidence: 0.873995667272727

00:13:55.715 --> 00:13:58.520 of psychiatric disorders in terms of stress.

NOTE Confidence: 0.873995667272727

00:13:58.520 --> 00:14:00.840 And then one cohort of mice is a

NOTE Confidence: 0.873995667272727

00:14:00.840 --> 00:14:02.719 sacrifice at gestational day 17.

NOTE Confidence: 0.873995667272727

00:14:02.720 --> 00:14:04.421 Another cohort is allowed to go through

NOTE Confidence: 0.873995667272727

00:14:04.421 --> 00:14:05.999 parturition and an age into adulthood.

NOTE Confidence: 0.873995667272727

00:14:06.000 --> 00:14:08.933 We don't have a second hit in this model.

NOTE Confidence: 0.873995667272727

00:14:08.933 --> 00:14:11.039 It's just the only stressor they

NOTE Confidence: 0.873995667272727

00:14:11.039 --> 00:14:12.990 experience is in utero and then we

NOTE Confidence: 0.873995667272727

00:14:12.990 --> 00:14:14.440 do behavioral testing in adulthood.

NOTE Confidence: 0.873995667272727

00:14:14.440 --> 00:14:16.256 You can see that a few things to

NOTE Confidence: 0.873995667272727

00:14:16.256 --> 00:14:18.044 point out is that mouse pregnancy

NOTE Confidence: 0.873995667272727

00:14:18.044 --> 00:14:19.316 is besides the duration

NOTE Confidence: 0.867559766

00:14:19.320 --> 00:14:22.320 of pregnancy has other differences.

NOTE Confidence: 0.867559766

00:14:22.320 --> 00:14:24.008 So in in mice and I'll be showing

NOTE Confidence: 0.867559766

00:14:24.008 --> 00:14:25.678 you a video in a little bit,

NOTE Confidence: 0.867559766

00:14:25.680 --> 00:14:27.174 there's it's like a Pearl necklace

NOTE Confidence: 0.867559766

00:14:27.174 --> 00:14:28.964 or like a necklace like the one

NOTE Confidence: 0.867559766

00:14:28.964 --> 00:14:30.199 I'm wearing where each mouse,

00:14:30.200 --> 00:14:32.582 each fetus is individually housed with

00:14:32.582 --> 00:14:35.360 a placenta and its own amniotic SAC

00:14:35.360 --> 00:14:37.250 and and there's litter sizes between

00:14:37.250 --> 00:14:39.320 8:00 and 10:00 are quite normal.

00:14:39.320 --> 00:14:40.508 Whereas obviously in humans

00:14:40.508 --> 00:14:41.993 Singleton pregnancies are the norm.

00:14:42.000 --> 00:14:44.440 Though of course there's you know

00:14:44.440 --> 00:14:46.400 twins and triplets out there and more.

00:14:46.400 --> 00:14:47.984 There's just several structural

00:14:47.984 --> 00:14:50.360 differences between the placenta as well

00:14:50.360 --> 00:14:53.120 and so there's absolutely differences.

00:14:53.120 --> 00:14:54.400 And another important difference to

00:14:54.400 --> 00:14:56.892 point out to you is that a lot of

00:14:56.892 --> 00:14:58.836 neurodevelopment occurs X utero in mice.

00:14:58.840 --> 00:15:00.968 So at post Natal day one that's roughly

00:15:00.968 --> 00:15:02.560 equivalent to the third trimester.

NOTE Confidence: 0.867559766

00:15:02.560 --> 00:15:05.040 So mice of course are not little people,

NOTE Confidence: 0.867559766

00:15:05.040 --> 00:15:08.142 but we can draw some mechanistic

NOTE Confidence: 0.867559766

00:15:08.142 --> 00:15:10.760 conclusions nevertheless from this model.

NOTE Confidence: 0.867559766

00:15:10.760 --> 00:15:12.308 So what we found,

NOTE Confidence: 0.867559766

00:15:12.308 --> 00:15:15.840 I'll tackle a few of the a few of the

NOTE Confidence: 0.867559766

00:15:15.840 --> 00:15:18.000 findings in rapid succession so that

NOTE Confidence: 0.867559766

00:15:18.000 --> 00:15:20.016 I can try to walk you through what

NOTE Confidence: 0.867559766

00:15:20.016 --> 00:15:21.840 I believe is the most exciting part,

NOTE Confidence: 0.867559766

00:15:21.840 --> 00:15:23.795 which is the translate translational

NOTE Confidence: 0.867559766

00:15:23.795 --> 00:15:25.359 nature of this research.

NOTE Confidence: 0.867559766

00:15:25.360 --> 00:15:27.412 But I'm happy to answer questions

NOTE Confidence: 0.867559766

00:15:27.412 --> 00:15:28.748 afterwards in the Q&amp;amp;A.

NOTE Confidence: 0.867559766

00:15:28.748 --> 00:15:30.904 So the first thing that was important

NOTE Confidence: 0.867559766

00:15:30.904 --> 00:15:32.664 to establish in this model was

NOTE Confidence: 0.867559766

00:15:32.664 --> 00:15:34.160 does this stress actually change?

NOTE Confidence: 0.867559766

00:15:34.160 --> 00:15:36.200 Does it actually lead to dysbiosis,

NOTE Confidence: 0.867559766

00:15:36.200 --> 00:15:37.600 a change in the microbes?

NOTE Confidence: 0.867559766

00:15:37.600 --> 00:15:39.080 And the answer, the short answer is yes.

NOTE Confidence: 0.867559766

00:15:39.080 --> 00:15:41.344 So what I see here on the left

NOTE Confidence: 0.867559766

00:15:41.344 --> 00:15:42.839 is the is the dam,

NOTE Confidence: 0.867559766

00:15:42.840 --> 00:15:45.395 which is what we call mouse moms.

NOTE Confidence: 0.867559766

00:15:45.400 --> 00:15:46.720 And this is PCOA plot.

NOTE Confidence: 0.867559766

00:15:46.720 --> 00:15:47.480 So this is no more,

NOTE Confidence: 0.867559766

00:15:47.480 --> 00:15:49.316 no less than the entire genome,

NOTE Confidence: 0.867559766

00:15:49.320 --> 00:15:51.876 microbiome genome of a specific mouse.

NOTE Confidence: 0.867559766

00:15:51.880 --> 00:15:53.794 So each dot represents the grand

NOTE Confidence: 0.867559766

00:15:53.794 --> 00:15:55.947 sum total of the genes expressed

NOTE Confidence: 0.867559766

00:15:55.947 --> 00:15:58.135 in the microbes of the mom.

NOTE Confidence: 0.867559766

00:15:58.135 --> 00:16:02.792 And this is taken on day 17 of gestation.

NOTE Confidence: 0.867559766

00:16:02.792 --> 00:16:04.808 So after the stressor is completed

NOTE Confidence: 0.867559766

00:16:04.808 --> 00:16:07.415 and what you can see here is that

NOTE Confidence: 0.867559766

00:16:07.415 --> 00:16:09.320 there's a significant effect of stress.

NOTE Confidence: 0.867559766

00:16:09.320 --> 00:16:11.154 So red is stress, blue is control,

NOTE Confidence: 0.867559766

00:16:11.160 --> 00:16:12.903 and there's a shift in the microbiome

NOTE Confidence: 0.867559766

00:16:12.903 --> 00:16:14.925 of the dams that were exposed to

NOTE Confidence: 0.867559766

00:16:14.925 --> 00:16:16.755 prenatal stress and those that weren't.

NOTE Confidence: 0.867559766

00:16:16.760 --> 00:16:17.140 Next,

NOTE Confidence: 0.867559766

00:16:17.140 --> 00:16:19.420 I'll turn your attention to male

NOTE Confidence: 0.867559766

00:16:19.420 --> 00:16:20.560 and female offspring.

NOTE Confidence: 0.867559766

00:16:20.560 --> 00:16:22.045 And what you can see is, again,

NOTE Confidence: 0.867559766

00:16:22.045 --> 00:16:24.235 blue is control, red is stress.

NOTE Confidence: 0.867559766

00:16:24.240 --> 00:16:27.078 There's a significant shift in adulthood.

NOTE Confidence: 0.867559766

00:16:27.080 --> 00:16:29.915 So these samples were taken in adulthood.

NOTE Confidence: 0.867559766

00:16:29.920 --> 00:16:31.360 So even though they were never

NOTE Confidence: 0.867559766

00:16:31.360 --> 00:16:31.840 stressed again,

NOTE Confidence: 0.867559766

00:16:31.840 --> 00:16:33.472 just the fact that they were

NOTE Confidence: 0.867559766

00:16:33.472 --> 00:16:35.460 exposed to stress in utero gave

NOTE Confidence: 0.867559766

00:16:35.460 --> 00:16:37.140 them a significantly different

NOTE Confidence: 0.867559766

00:16:37.140 --> 00:16:38.400 microbiome into adulthood.

NOTE Confidence: 0.867559766

00:16:38.400 --> 00:16:39.880 So it really does look like the gut.

NOTE Confidence: 0.867559766

00:16:39.880 --> 00:16:41.794 Brain access was shifted in these

NOTE Confidence: 0.867559766

00:16:41.794 --> 00:16:43.420 offspring who are exposed to

NOTE Confidence: 0.867559766

00:16:43.420 --> 00:16:44.880 prenatal stress and the citations

NOTE Confidence: 0.867559766

00:16:44.880 --> 00:16:47.078 are in the bottom right hand corner.

NOTE Confidence: 0.867559766

00:16:47.080 --> 00:16:48.935 In case you're interested in

NOTE Confidence: 0.867559766

00:16:48.935 --> 00:16:50.960 reading more next I'm turning my

NOTE Confidence: 0.867559766

00:16:50.960 --> 00:16:51.920 attention to adulthood.

NOTE Confidence: 0.867559766

00:16:51.920 --> 00:16:53.112 In the interest of time I'm just going

NOTE Confidence: 0.867559766

00:16:53.112 --> 00:16:54.320 to show you social behaviour today,

NOTE Confidence: 0.867559766

00:16:54.320 --> 00:16:56.570 but we have found increased in

NOTE Confidence: 0.867559766

00:16:56.570 --> 00:16:58.471 increased anxiety like behaviour in

NOTE Confidence: 0.867559766

00:16:58.471 --> 00:17:00.491 female and changes in cognitive tasks

NOTE Confidence: 0.867559766

00:17:00.491 --> 00:17:02.477 as well in the female offspring.

NOTE Confidence: 0.8129950245

00:17:02.480 --> 00:17:04.058 This changes in social behaviours were

NOTE Confidence: 0.8129950245

00:17:04.058 --> 00:17:06.358 found in both male and females and we've

NOTE Confidence: 0.8129950245

00:17:06.358 --> 00:17:08.158 now replicated and extended these findings.

NOTE Confidence: 0.8129950245

00:17:08.160 --> 00:17:09.918 But for the purpose of today,

NOTE Confidence: 0.8129950245

00:17:09.920 --> 00:17:11.032 for those of you that might not have

NOTE Confidence: 0.8129950245

00:17:11.032 --> 00:17:12.210 had the pleasure of doing mouse

NOTE Confidence: 0.8129950245

00:17:12.210 --> 00:17:13.078 behaviour during your training,

NOTE Confidence: 0.8129950245

00:17:13.080 --> 00:17:14.676 I thought I would share a video.

NOTE Confidence: 0.8129950245

00:17:14.680 --> 00:17:17.515 So this is a social approach paradigm.

NOTE Confidence: 0.8129950245

00:17:17.520 --> 00:17:19.235 It's the three chamber social behaviour test.

NOTE Confidence: 0.8129950245

00:17:19.240 --> 00:17:20.728 So in one of these little

NOTE Confidence: 0.8129950245

00:17:20.728 --> 00:17:22.120 chambers this is a mouse.

NOTE Confidence: 0.8129950245

00:17:22.120 --> 00:17:24.091 I'm blinded so I do not know if this

NOTE Confidence: 0.8129950245

00:17:24.091 --> 00:17:25.878 mouse was exposed to stress or not,

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NOTE Confidence: 0.8129950245

00:17:25.880 --> 00:17:27.840 but it can either choose to investigate.

NOTE Confidence: 0.8129950245

00:17:27.840 --> 00:17:31.197 In this little cage is either a mouse or,

NOTE Confidence: 0.8129950245

00:17:31.200 --> 00:17:33.000 and in this little cage is an object,

NOTE Confidence: 0.8129950245

00:17:33.000 --> 00:17:35.835 and we simply measure the amount of

NOTE Confidence: 0.8129950245

00:17:35.835 --> 00:17:37.685 time prefers to spend approaching a

NOTE Confidence: 0.8129950245

00:17:37.685 --> 00:17:40.238 it's a mouse from a very docile mouse.

NOTE Confidence: 0.8129950245

00:17:40.240 --> 00:17:43.892 Strain a DBA mouse and of the same

NOTE Confidence: 0.8129950245

00:17:43.892 --> 00:17:46.426 sex as the test mouse and it's able to

NOTE Confidence: 0.8129950245

00:17:46.426 --> 00:17:48.631 poke its little nose between the bars.

NOTE Confidence: 0.8129950245

00:17:48.640 --> 00:17:51.248 But it's not able to engage in aggressive

NOTE Confidence: 0.8129950245

00:17:51.248 --> 00:17:54.196 or sexual behavior with a mouse or an object.

NOTE Confidence: 0.8129950245

00:17:54.200 --> 00:17:56.152 And what you can see here is that

NOTE Confidence: 0.8129950245

00:17:56.152 --> 00:17:57.918 I'm showing this is a heat map of

NOTE Confidence: 0.8129950245

00:17:57.918 --> 00:17:59.399 where it chooses to spend time.

NOTE Confidence: 0.8129950245

00:17:59.400 --> 00:18:00.992 So what you can see is that there

NOTE Confidence: 0.8129950245

00:18:00.992 --> 00:18:02.758 was a significant reduction and

NOTE Confidence: 0.8129950245

00:18:02.758 --> 00:18:04.186 now we've extended this to other

NOTE Confidence: 0.8129950245

00:18:04.186 --> 00:18:05.160 social paradigms as well.

NOTE Confidence: 0.8129950245

00:18:05.160 --> 00:18:07.716 There's a significant reduction in the

NOTE Confidence: 0.8129950245

00:18:07.716 --> 00:18:09.885 social behaviour demonstrated by both

NOTE Confidence: 0.8129950245

00:18:09.885 --> 00:18:12.261 male and female offspring exposed to

NOTE Confidence: 0.8129950245

00:18:12.261 --> 00:18:14.717 prenatal stress compared to the control mice.

NOTE Confidence: 0.8129950245

00:18:14.720 --> 00:18:16.757 And so this showed us that yes,

NOTE Confidence: 0.8129950245

00:18:16.760 --> 00:18:19.875 so check there's changes in the microbiome,

NOTE Confidence: 0.8129950245

00:18:19.880 --> 00:18:21.640 check there's changes in

NOTE Confidence: 0.8129950245

00:18:21.640 --> 00:18:22.960 behaviours in adulthood.

NOTE Confidence: 0.8129950245

00:18:22.960 --> 00:18:24.402 And the next thing we wanted to

NOTE Confidence: 0.8129950245

00:18:24.402 --> 00:18:26.236 examine was that whether or not there

NOTE Confidence: 0.8129950245

00:18:26.236 --> 00:18:27.400 was changes in neuroinflammation.

NOTE Confidence: 0.8129950245

00:18:27.400 --> 00:18:29.479 So we did this in a number of ways.

NOTE Confidence: 0.8129950245

00:18:29.480 --> 00:18:30.600 So I'm showing two of them here.

NOTE Confidence: 0.8129950245

00:18:30.600 --> 00:18:32.560 We've done this now with full cytometry,

NOTE Confidence: 0.8129950245

00:18:32.560 --> 00:18:34.558 immunohistochemistry as well

NOTE Confidence: 0.8129950245

00:18:34.558 --> 00:18:36.556 as gene expression.

NOTE Confidence: 0.8129950245

00:18:36.560 --> 00:18:38.920 And I if you invite me back in a few years,

NOTE Confidence: 0.8129950245

00:18:38.920 --> 00:18:40.495 we currently are working on our single

NOTE Confidence: 0.8129950245

00:18:40.495 --> 00:18:42.476 cell RNA seek data and we're finding some

NOTE Confidence: 0.8129950245

00:18:42.476 --> 00:18:44.000 very exciting changes there as well.

NOTE Confidence: 0.8129950245

00:18:44.000 --> 00:18:45.555 So we've now interrogated this

NOTE Confidence: 0.8129950245

00:18:45.555 --> 00:18:46.799 in several different ways.

NOTE Confidence: 0.8129950245

00:18:46.800 --> 00:18:48.697 What I'm showing you here is that

NOTE Confidence: 0.8129950245

00:18:48.697 --> 00:18:50.060 there's a significant increase here

NOTE Confidence: 0.8129950245

00:18:50.060 --> 00:18:51.789 on the left side in fetal brain

NOTE Confidence: 0.8129950245

00:18:51.789 --> 00:18:53.317 gene expression of Illinois 6,

NOTE Confidence: 0.8129950245

00:18:53.320 --> 00:18:54.904 which is a key cytokine that's

NOTE Confidence: 0.8129950245

00:18:54.904 --> 00:18:56.866 been implicated in a variety of

NOTE Confidence: 0.8129950245

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00:18:56.866 --> 00:18:57.720 psychiatric disorders,

NOTE Confidence: 0.8129950245

00:18:57.720 --> 00:18:58.920 including anxiety and depression.

NOTE Confidence: 0.8129950245

00:18:58.920 --> 00:19:01.031 So this is in fetal brain and

NOTE Confidence: 0.8129950245

00:19:01.031 --> 00:19:02.555 embryonic day 17 and then half.

NOTE Confidence: 0.8129950245

00:19:02.560 --> 00:19:04.260 There's also a significant

NOTE Confidence: 0.8129950245

00:19:04.260 --> 00:19:05.960 increase in TNF alpha.

NOTE Confidence: 0.8129950245

00:19:05.960 --> 00:19:06.370 Next,

NOTE Confidence: 0.8129950245

00:19:06.370 --> 00:19:09.240 we did immuno labeling for IBA one,

NOTE Confidence: 0.8129950245

00:19:09.240 --> 00:19:11.958 which is a marker for microglia.

NOTE Confidence: 0.8129950245

00:19:11.960 --> 00:19:14.872 And what we found was a significant increase

NOTE Confidence: 0.8129950245

00:19:14.872 --> 00:19:18.316 in IBA one staining in the prefrontal cortex

NOTE Confidence: 0.8129950245

00:19:18.320 --> 00:19:21.596 in mice taken from stress pregnancies.

NOTE Confidence: 0.8129950245

00:19:21.600 --> 00:19:22.632 And compared to controls,

NOTE Confidence: 0.8129950245

00:19:22.632 --> 00:19:24.695 we also looked as a control region in

NOTE Confidence: 0.8129950245

00:19:24.695 --> 00:19:26.559 the motor cortex where we did not have

NOTE Confidence: 0.8129950245

00:19:26.614 --> 00:19:28.280 an A priori hypothesis that we would

00:19:28.280 --> 00:19:30.278 see a change in neuro inflammation

00:19:30.278 --> 00:19:31.976 or in microglia labeling there.

00:19:31.976 --> 00:19:32.600 And in fact,

00:19:32.600 --> 00:19:33.840 we did not see an

00:19:33.840 --> 00:19:34.716 an increase there.

00:19:34.716 --> 00:19:36.760 So this isn't just global neuro inflammation,

00:19:36.760 --> 00:19:38.640 it's specific to brain regions

00:19:38.640 --> 00:19:40.520 that are implicated in behavior.

00:19:40.520 --> 00:19:42.400 And we also saw an increase in loops,

00:19:42.400 --> 00:19:44.980 IL 1 beta in that in the prefrontal cortex as

00:19:45.037 --> 00:19:47.557 well as Illinois 6 and this is an adulthood.

00:19:47.560 --> 00:19:48.944 So on the left side of the slide

00:19:48.944 --> 00:19:50.200 we have embryonic offspring.

00:19:50.200 --> 00:19:51.874 And what I'm showing you here on the right

00:19:51.874 --> 00:19:53.558 is that this continues into adulthood.

00:19:53.560 --> 00:19:55.112 So the microbiome changes

NOTE Confidence: 0.839746436

00:19:55.112 --> 00:19:56.276 continue into adulthood,

NOTE Confidence: 0.839746436

00:19:56.280 --> 00:19:57.399 the behavioural changes

NOTE Confidence: 0.839746436

00:19:57.399 --> 00:19:58.518 continue into adulthood,

NOTE Confidence: 0.839746436

00:19:58.520 --> 00:20:00.680 and neuro inflammation continue

NOTE Confidence: 0.839746436

00:20:00.680 --> 00:20:02.840 into adulthood as well.

NOTE Confidence: 0.839746436

00:20:02.840 --> 00:20:04.572 So as I mentioned,

NOTE Confidence: 0.839746436

00:20:04.572 --> 00:20:06.980 CCL 2 is an important chemokine

NOTE Confidence: 0.839746436

00:20:06.980 --> 00:20:09.290 that recruits immune cells to a

NOTE Confidence: 0.839746436

00:20:09.366 --> 00:20:11.830 site of injury or to or and also

NOTE Confidence: 0.839746436

00:20:11.830 --> 00:20:13.680 increases in response to stress.

NOTE Confidence: 0.839746436

00:20:13.680 --> 00:20:15.759 And So what we hypothesized was that,

NOTE Confidence: 0.839746436

00:20:15.760 --> 00:20:17.580 and it has been shown to be

NOTE Confidence: 0.839746436

00:20:17.580 --> 00:20:18.768 required for behavioural changes

NOTE Confidence: 0.839746436

00:20:18.768 --> 00:20:20.558 following a social defeat stressor.

NOTE Confidence: 0.839746436

00:20:20.560 --> 00:20:22.000 So then we simply set to set up,

NOTE Confidence: 0.839746436

00:20:22.000 --> 00:20:24.107 we simply set out to test whether

NOTE Confidence: 0.839746436

00:20:24.107 --> 00:20:26.805 or not CCL 2 was required for

NOTE Confidence: 0.839746436

00:20:26.805 --> 00:20:28.960 the behavioural changes and the

NOTE Confidence: 0.839746436

00:20:28.960 --> 00:20:30.668 inflammatory changes that we

NOTE Confidence: 0.839746436

00:20:30.668 --> 00:20:32.678 saw following period of stress.

NOTE Confidence: 0.839746436

00:20:32.680 --> 00:20:34.680 So to do that we took CCL 2 knockout mice,

NOTE Confidence: 0.839746436

00:20:34.680 --> 00:20:36.845 which are commercially available and

NOTE Confidence: 0.839746436

00:20:36.845 --> 00:20:39.320 constitutively have CCL 2 knocked out.

NOTE Confidence: 0.839746436

00:20:39.320 --> 00:20:41.689 And we put them through the same stress

NOTE Confidence: 0.839746436

00:20:41.689 --> 00:20:43.903 paradigm that I showed you earlier

NOTE Confidence: 0.839746436

00:20:43.903 --> 00:20:46.040 with the regular wild type mice.

NOTE Confidence: 0.839746436

00:20:46.040 --> 00:20:47.461 And the first thing we found was

NOTE Confidence: 0.839746436

00:20:47.461 --> 00:20:48.834 that there was no longer that

NOTE Confidence: 0.839746436

00:20:48.834 --> 00:20:50.350 increase in Illinois six in the

NOTE Confidence: 0.839746436

00:20:50.350 --> 00:20:52.000 fetal brains or the increase in

NOTE Confidence: 0.839746436

00:20:52.000 --> 00:20:53.880 TNF alpha in those fetal brains.

NOTE Confidence: 0.839746436

00:20:53.880 --> 00:20:55.398 And when we looked at behaviour,

NOTE Confidence: 0.839746436

00:20:55.400 --> 00:20:58.179 we no longer saw a significant reduction

NOTE Confidence: 0.839746436

00:20:58.179 --> 00:21:00.826 in social behaviour in the adult

NOTE Confidence: 0.839746436

00:21:00.826 --> 00:21:02.678 offspring following prenatal stress,

NOTE Confidence: 0.839746436

00:21:02.680 --> 00:21:04.542 which was very different than what we

NOTE Confidence: 0.839746436

00:21:04.542 --> 00:21:06.655 had seen in the wild type medicine

NOTE Confidence: 0.839746436

00:21:06.655 --> 00:21:08.800 that came out during the pandemic

NOTE Confidence: 0.839746436

00:21:08.800 --> 00:21:11.758 and translational psychiatry.

NOTE Confidence: 0.839746436

00:21:11.760 --> 00:21:14.077 So then Helen, my very talented MD,

NOTE Confidence: 0.839746436

00:21:14.080 --> 00:21:15.680 PhD student that I've mentioned

NOTE Confidence: 0.839746436

00:21:15.680 --> 00:21:17.686 who's going to match in the

NOTE Confidence: 0.839746436

00:21:17.686 --> 00:21:19.038 next month in Pediatrics,

NOTE Confidence: 0.839746436

00:21:19.040 --> 00:21:20.204 didn't succeed in recruiting

NOTE Confidence: 0.839746436

00:21:20.204 --> 00:21:21.077 her into psychiatry.

NOTE Confidence: 0.839746436

00:21:21.080 --> 00:21:21.848 But that's OK.

NOTE Confidence: 0.839746436

00:21:21.848 --> 00:21:23.640 She'll be a phenomenal pediatrician and she's

NOTE Confidence: 0.839746436

00:21:23.687 --> 00:21:25.439 still interested in the developing brain.

NOTE Confidence: 0.839746436

00:21:25.440 --> 00:21:27.198 So I'll consider that a win.

NOTE Confidence: 0.839746436

00:21:27.200 --> 00:21:29.160 I wanted to ask a daring question,

NOTE Confidence: 0.839746436

00:21:29.160 --> 00:21:31.141 which is whether or not an increase

NOTE Confidence: 0.839746436

00:21:31.141 --> 00:21:33.359 in fetal CCL 2 would be sufficient.

NOTE Confidence: 0.839746436

00:21:33.360 --> 00:21:35.677 So it's required, but is it sufficient

NOTE Confidence: 0.839746436

00:21:35.680 --> 00:21:38.319 to induce the changes that we saw?

NOTE Confidence: 0.839746436

00:21:38.320 --> 00:21:41.200 So how was she going to do that?

NOTE Confidence: 0.839746436

00:21:41.200 --> 00:21:43.838 Well, she decided.

NOTE Confidence: 0.839746436

00:21:43.838 --> 00:21:46.833 We decided that she would

NOTE Confidence: 0.839746436

00:21:46.833 --> 00:21:48.920 inject intraemniotic CCL 2,

NOTE Confidence: 0.839746436

00:21:48.920 --> 00:21:50.198 recombinant CCL 2,

NOTE Confidence: 0.839746436

00:21:50.198 --> 00:21:51.476 mouse CCL 2,

NOTE Confidence: 0.839746436

00:21:51.480 --> 00:21:54.320 or saline on embryonic day 16 1/2.

NOTE Confidence: 0.839746436

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00:21:54.320 --> 00:21:55.760 She did a whole bunch of

NOTE Confidence: 0.839746436

00:21:55.760 --> 00:21:56.798 experiments leading up to this.

NOTE Confidence: 0.839746436

00:21:56.800 --> 00:21:59.040 Wish I'll spare you a time course.

NOTE Confidence: 0.839746436

00:21:59.040 --> 00:22:02.410 And we found that CCL 2 peaked on day 16.5,

NOTE Confidence: 0.839746436

00:22:02.410 --> 00:22:05.000 and so she wanted to emulate that

NOTE Confidence: 0.839746436

00:22:05.000 --> 00:22:07.236 with a injection of recombinant

NOTE Confidence: 0.839746436

00:22:07.236 --> 00:22:09.816 CCL 2 on embryonic day 16.5.

NOTE Confidence: 0.839746436

00:22:09.816 --> 00:22:11.760 And I'll show you a video in a moment

NOTE Confidence: 0.839746436

00:22:11.816 --> 00:22:13.680 to show you exactly how she did that.

NOTE Confidence: 0.839746436

00:22:13.680 --> 00:22:14.556 And then one cohort.

NOTE Confidence: 0.839746436

00:22:14.556 --> 00:22:16.559 And then she sewed the mice back up again.

NOTE Confidence: 0.839746436

00:22:16.560 --> 00:22:18.096 They recovered nicely from

NOTE Confidence: 0.839746436

00:22:18.096 --> 00:22:20.400 anaesthesia and from the surgery or.

NOTE Confidence: 0.880802032727273

00:22:20.400 --> 00:22:23.440 And then we one cohort we collected samples

NOTE Confidence: 0.880802032727273

00:22:23.440 --> 00:22:26.205 on embryonic day 17 1/2 and the other

NOTE Confidence: 0.880802032727273

00:22:26.205 --> 00:22:27.976 went through parturition, no problem.

00:22:27.976 --> 00:22:30.920 And then we looked at behaviour in adulthood.

00:22:30.920 --> 00:22:32.480 So for any of you who are squeamish,

00:22:32.480 --> 00:22:33.964 you might just want to look away

00:22:33.964 --> 00:22:35.800 for the next 1015 seconds or so,

00:22:35.800 --> 00:22:37.600 because what I'm going to show

00:22:37.660 --> 00:22:39.331 you is her surgery.

00:22:39.331 --> 00:22:42.313 So she would anesthetize the mice,

00:22:42.320 --> 00:22:43.392 do an incision remove.

00:22:43.392 --> 00:22:45.000 You can see this Pearl necklace,

00:22:45.000 --> 00:22:47.096 as I mentioned, of all the different fetus

00:22:47.096 --> 00:22:48.639 individually housed in their amniotic sacs.

00:22:48.640 --> 00:22:50.830 And this is her very gently

00:22:50.830 --> 00:22:52.145 and capably doing an injection.

00:22:52.145 --> 00:22:53.510 So you can see she holds it

00:22:53.556 --> 00:22:54.720 carefully with the tweezers.

00:22:54.720 --> 00:22:56.043 This has been labeled with dye so

NOTE Confidence: 0.880802032727273

00:22:56.043 --> 00:22:57.559 that you can see it and it's going.

NOTE Confidence: 0.880802032727273

00:22:57.560 --> 00:22:59.465 It's basically you could see

NOTE Confidence: 0.880802032727273

00:22:59.465 --> 00:23:01.720 the dye migrating from one side

NOTE Confidence: 0.97491049

00:23:04.120 --> 00:23:05.158 all the way through the other,

NOTE Confidence: 0.750873003636363

00:23:07.200 --> 00:23:08.502 so following and here it's coming

NOTE Confidence: 0.750873003636363

00:23:08.502 --> 00:23:12.536 all the way back through so and then

NOTE Confidence: 0.750873003636363

00:23:12.536 --> 00:23:15.131 after that she carefully taps it.

NOTE Confidence: 0.750873003636363

00:23:15.131 --> 00:23:17.320 There's no blood and we

NOTE Confidence: 0.750873003636363

00:23:17.320 --> 00:23:18.320 continue on with our day.

NOTE Confidence: 0.750873003636363

00:23:18.320 --> 00:23:19.316 So if you were looking away,

NOTE Confidence: 0.750873003636363

00:23:19.320 --> 00:23:21.400 you can look again.

NOTE Confidence: 0.750873003636363

00:23:21.400 --> 00:23:23.641 The exposed mouse fetuses are no

NOTE Confidence: 0.750873003636363

00:23:23.641 --> 00:23:25.230 no longer on screen and so we

NOTE Confidence: 0.750873003636363

00:23:25.286 --> 00:23:26.798 were very excited to have this

NOTE Confidence: 0.750873003636363

00:23:26.798 --> 00:23:29.096 work come out a couple months

NOTE Confidence: 0.750873003636363

00:23:29.096 --> 00:23:31.215 back in behavioural beta immunity,

NOTE Confidence: 0.750873003636363

00:23:31.215 --> 00:23:33.770 which is a leading journal in the

NOTE Confidence: 0.750873003636363

00:23:33.832 --> 00:23:35.837 field of psycho neuro immunology.

NOTE Confidence: 0.750873003636363

00:23:35.840 --> 00:23:37.527 And what we found is first all

NOTE Confidence: 0.750873003636363

00:23:37.527 --> 00:23:38.827 direct your attention here to

NOTE Confidence: 0.750873003636363

00:23:38.827 --> 00:23:39.879 the middle amniotic fluid.

NOTE Confidence: 0.750873003636363

00:23:39.880 --> 00:23:41.784 So we were thankful to see that

NOTE Confidence: 0.750873003636363

00:23:41.784 --> 00:23:43.397 there was a significant increase

NOTE Confidence: 0.750873003636363

00:23:43.397 --> 00:23:45.952 in CCL 2 in the amniotic fluid.

NOTE Confidence: 0.750873003636363

00:23:45.960 --> 00:23:48.360 So she successfully injected them.

NOTE Confidence: 0.750873003636363

00:23:48.360 --> 00:23:49.865 And then I think it's really interesting

NOTE Confidence: 0.750873003636363

00:23:49.865 --> 00:23:51.432 to note here on the left hand side

NOTE Confidence: 0.750873003636363

00:23:51.432 --> 00:23:53.080 that it stayed in the fetal compartment.

NOTE Confidence: 0.750873003636363

00:23:53.080 --> 00:23:54.796 There was no travelling of this

NOTE Confidence: 0.750873003636363

00:23:54.796 --> 00:23:56.600 protein into the maternal compartment.

NOTE Confidence: 0.750873003636363

00:23:56.600 --> 00:23:58.840 So we looked both at the plasma There,

NOTE Confidence: 0.750873003636363

00:23:58.840 --> 00:24:00.760 we looked at the maternal plasma.

NOTE Confidence: 0.750873003636363

00:24:00.760 --> 00:24:01.492 There was no,

NOTE Confidence: 0.750873003636363

00:24:01.492 --> 00:24:03.200 there was no change in CCL 2.

NOTE Confidence: 0.750873003636363

00:24:03.200 --> 00:24:04.957 And then we looked at the placenta.

NOTE Confidence: 0.750873003636363

00:24:04.960 --> 00:24:06.556 There was no increase in CCL 2.

NOTE Confidence: 0.750873003636363

00:24:06.560 --> 00:24:07.870 So this was really contained

NOTE Confidence: 0.750873003636363

00:24:07.870 --> 00:24:08.918 in the fetal compartment.

NOTE Confidence: 0.750873003636363

00:24:08.920 --> 00:24:10.236 When we looked at the fetal plasma,

NOTE Confidence: 0.750873003636363

00:24:10.240 --> 00:24:12.520 we saw a significant increase in CCL 2.

NOTE Confidence: 0.750873003636363

00:24:12.520 --> 00:24:14.278 We looked at the fetal liver,

NOTE Confidence: 0.750873003636363

00:24:14.280 --> 00:24:15.915 which we've identified as being

NOTE Confidence: 0.750873003636363

00:24:15.915 --> 00:24:17.720 an important source of CCL 2.

NOTE Confidence: 0.750873003636363

00:24:17.720 --> 00:24:18.992 I didn't have time to show you that

NOTE Confidence: 0.750873003636363

00:24:18.992 --> 00:24:20.193 data I originally thought and we

NOTE Confidence: 0.750873003636363

00:24:20.193 --> 00:24:21.640 spent about five years in the lab.

00:24:21.640 --> 00:24:23.440 So any new PIS out there don't feel bad.

00:24:23.440 --> 00:24:25.616 In my lab spent about five years worth

00:24:25.616 --> 00:24:27.680 of money trying to prove that those

00:24:27.680 --> 00:24:29.234 CCL 2 is coming from the placenta.

00:24:29.240 --> 00:24:29.960 But in fact it's not.

00:24:29.960 --> 00:24:31.437 It's actually coming from the fetal liver,

00:24:31.440 --> 00:24:32.313 which is fascinating.

00:24:32.313 --> 00:24:34.760 I don't have time to get into today,

00:24:34.760 --> 00:24:36.536 but it was up in the fetal liver

00:24:36.536 --> 00:24:38.476 when we looked at the fetal brain.

00:24:38.480 --> 00:24:40.772 It was also significantly increased and

00:24:40.772 --> 00:24:43.880 finally in so in terms of the behavior,

00:24:43.880 --> 00:24:45.914 so in what you see here on the left

00:24:45.914 --> 00:24:47.904 side side of the part of this graph

00:24:47.904 --> 00:24:50.640 in green circle of social squares

00:24:50.640 --> 00:24:52.888 object with a saline injection,

NOTE Confidence: 0.750873003636363

00:24:52.888 --> 00:24:54.934 there's a significant in the

NOTE Confidence: 0.750873003636363

00:24:54.934 --> 00:24:56.482 significant preference for engaging

NOTE Confidence: 0.750873003636363

00:24:56.482 --> 00:24:58.680 with a social con specific.

NOTE Confidence: 0.750873003636363

00:24:58.680 --> 00:25:00.672 Whereas with the CCL 2 mice they no

NOTE Confidence: 0.750873003636363

00:25:00.672 --> 00:25:03.077 longer had preference for social interaction.

NOTE Confidence: 0.750873003636363

00:25:03.080 --> 00:25:05.250 So there is a reduction in social

NOTE Confidence: 0.750873003636363

00:25:05.250 --> 00:25:06.889 behaviors with just this intra

NOTE Confidence: 0.750873003636363

00:25:06.889 --> 00:25:08.514 amniotic injection of CCL 2,

NOTE Confidence: 0.750873003636363

00:25:08.520 --> 00:25:12.330 which I really believe confirms our

NOTE Confidence: 0.750873003636363

00:25:12.330 --> 00:25:14.880 our belief or confirms our hypothesis

NOTE Confidence: 0.750873003636363

00:25:14.880 --> 00:25:18.025 that CCL 2 is integral to the it's an

NOTE Confidence: 0.750873003636363

00:25:18.025 --> 00:25:20.155 integral part of how prenatal stress

NOTE Confidence: 0.750873003636363

00:25:20.155 --> 00:25:22.179 is transmitting these behavioral

NOTE Confidence: 0.750873003636363

00:25:22.179 --> 00:25:24.834 changes to the next generation.

NOTE Confidence: 0.750873003636363

00:25:24.840 --> 00:25:27.480 So next I really struggled,

NOTE Confidence: 0.750873003636363

00:25:27.480 --> 00:25:28.058 or not.

NOTE Confidence: 0.750873003636363

00:25:28.058 --> 00:25:28.347 Next,

NOTE Confidence: 0.750873003636363

00:25:28.347 --> 00:25:30.370 this entire time I was really struggling

NOTE Confidence: 0.750873003636363

00:25:30.429 --> 00:25:32.515 with a question of does this translate.

NOTE Confidence: 0.750873003636363

00:25:32.520 --> 00:25:35.040 I'll never forget in medical school

NOTE Confidence: 0.750873003636363

00:25:35.040 --> 00:25:37.038 during my OBGYN rotation that the

NOTE Confidence: 0.750873003636363

00:25:37.038 --> 00:25:39.400 big paper came out suggesting that

NOTE Confidence: 0.750873003636363

00:25:39.400 --> 00:25:41.800 hormonal replacement therapy was

NOTE Confidence: 0.750873003636363

00:25:41.800 --> 00:25:44.800 potentially not advantageous for women.

NOTE Confidence: 0.750873003636363

00:25:44.800 --> 00:25:46.496 And so that a lot of the literature

NOTE Confidence: 0.750873003636363

00:25:46.496 --> 00:25:46.920 that had

NOTE Confidence: 0.882590803

00:25:46.977 --> 00:25:48.699 supported the use of and of course

NOTE Confidence: 0.882590803

00:25:48.699 --> 00:25:50.231 the pendulum has swung wildly back

NOTE Confidence: 0.882590803

00:25:50.231 --> 00:25:51.953 and forth a few times since then.

NOTE Confidence: 0.882590803

00:25:51.960 --> 00:25:53.936 But a lot of the literature at the

NOTE Confidence: 0.882590803

00:25:53.936 --> 00:25:55.796 time had been the world at work

NOTE Confidence: 0.882590803

00:25:55.796 --> 00:25:56.872 suggesting that hormone replacement

NOTE Confidence: 0.882590803

00:25:56.872 --> 00:25:58.080 therapy was very important.

NOTE Confidence: 0.882590803

00:25:58.080 --> 00:26:00.400 So I remember as a medical student thinking,

NOTE Confidence: 0.882590803

00:26:00.400 --> 00:26:01.292 I don't want that.

NOTE Confidence: 0.882590803

00:26:01.292 --> 00:26:03.124 I don't want to spend decades of my

NOTE Confidence: 0.882590803

00:26:03.124 --> 00:26:04.678 life doing something in mice and then

NOTE Confidence: 0.882590803

00:26:04.680 --> 00:26:07.176 bring it to clinic and find out that

NOTE Confidence: 0.882590803

00:26:07.176 --> 00:26:09.120 it's completely irrelevant in humans.

NOTE Confidence: 0.882590803

00:26:09.120 --> 00:26:11.328 And so we thought of a lot of

NOTE Confidence: 0.882590803

00:26:11.328 --> 00:26:13.096 different ways in lab to figure

NOTE Confidence: 0.882590803

00:26:13.096 --> 00:26:14.920 out whether or not it translated.

NOTE Confidence: 0.882590803

00:26:14.920 --> 00:26:17.968 And so we simultaneously collaborated with

NOTE Confidence: 0.882590803

00:26:17.968 --> 00:26:21.920 a group at UCLA who had an funded RO one.

NOTE Confidence: 0.882590803

00:26:21.920 --> 00:26:23.095 And we also launched our

NOTE Confidence: 0.882590803

00:26:23.095 --> 00:26:23.800 own clinical studies.

NOTE Confidence: 0.882590803

00:26:23.800 --> 00:26:25.920 So I'll be sharing, sharing data from both.

NOTE Confidence: 0.882590803

00:26:25.920 --> 00:26:26.916 So this is first of all,

NOTE Confidence: 0.882590803

00:26:26.920 --> 00:26:28.080 a graph of maternal health.

NOTE Confidence: 0.882590803

00:26:28.080 --> 00:26:29.680 So this is where I'm sitting right now,

NOTE Confidence: 0.882590803

00:26:29.680 --> 00:26:30.796 right in the middle of Ohio.

NOTE Confidence: 0.882590803

00:26:30.800 --> 00:26:32.697 So my kids like to say 4

NOTE Confidence: 0.882590803

00:26:32.697 --> 00:26:33.880 hours from anything good.

NOTE Confidence: 0.882590803

00:26:33.880 --> 00:26:35.686 No offense to Ohio, but right smack

NOTE Confidence: 0.882590803

00:26:35.686 --> 00:26:37.520 in the middle in Franklin County,

NOTE Confidence: 0.882590803

00:26:37.520 --> 00:26:39.880 Ohio and a priority here.

NOTE Confidence: 0.882590803

00:26:39.880 --> 00:26:40.345 Unfortunately,

NOTE Confidence: 0.882590803

00:26:40.345 --> 00:26:43.135 Ohio is right behind Mississippi in

NOTE Confidence: 0.882590803

00:26:43.135 --> 00:26:45.769 terms of morbidity and mortality during

NOTE Confidence: 0.882590803

00:26:45.769 --> 00:26:47.503 pregnancy and especially this is of

NOTE Confidence: 0.882590803

00:26:47.503 --> 00:26:49.799 concern in the African American community.

NOTE Confidence: 0.882590803

00:26:49.800 --> 00:26:51.816 So it's a major issue here in

NOTE Confidence: 0.882590803

00:26:51.816 --> 00:26:53.126 Franklin County and in fact,

NOTE Confidence: 0.882590803

00:26:53.126 --> 00:26:54.336 depression is a major issue

NOTE Confidence: 0.882590803

00:26:54.336 --> 00:26:56.078 here in Franklin County as well.

NOTE Confidence: 0.882590803

00:26:56.080 --> 00:26:57.879 And you can see that almost 20%

NOTE Confidence: 0.882590803

00:26:57.880 --> 00:27:00.491 of women here have a diagnosis of

NOTE Confidence: 0.882590803

00:27:00.491 --> 00:27:02.208 depression during pregnancy in 2022.

NOTE Confidence: 0.882590803

00:27:02.208 --> 00:27:03.840 So it's a met.

NOTE Confidence: 0.882590803

00:27:03.840 --> 00:27:05.360 Postpartum depression or prenatal

NOTE Confidence: 0.882590803

00:27:05.360 --> 00:27:07.988 depression is considered a many issue in

NOTE Confidence: 0.882590803

00:27:07.988 --> 00:27:10.076 many communities here in Franklin County.

NOTE Confidence: 0.882590803

00:27:10.080 --> 00:27:11.838 And also there's a major issue,

NOTE Confidence: 0.882590803

00:27:11.840 --> 00:27:12.704 as I mentioned,

NOTE Confidence: 0.882590803

00:27:12.704 --> 00:27:13.856 with morbidity and mortality

NOTE Confidence: 0.882590803

00:27:13.856 --> 00:27:14.432 during pregnancy.

NOTE Confidence: 0.882590803

00:27:14.440 --> 00:27:17.760 So preterm birth is a negative sequela

NOTE Confidence: 0.882590803

00:27:17.760 --> 00:27:19.813 of having depression or significant

NOTE Confidence: 0.882590803

00:27:19.813 --> 00:27:21.678 depression or anxiety during pregnancy.

NOTE Confidence: 0.882590803

00:27:21.680 --> 00:27:22.775 And there's other

NOTE Confidence: 0.882590803

00:27:22.775 --> 00:27:24.235 contributing factors to that.

NOTE Confidence: 0.882590803

00:27:24.240 --> 00:27:26.060 And the low birth weight or intriguing

NOTE Confidence: 0.882590803

00:27:26.060 --> 00:27:27.836 growth restriction is a major issue as well.

NOTE Confidence: 0.882590803

00:27:27.840 --> 00:27:29.802 So this is unfortunately a good

NOTE Confidence: 0.882590803

00:27:29.802 --> 00:27:31.760 place to study some of these,

NOTE Confidence: 0.882590803

00:27:31.760 --> 00:27:33.485 some of the issues that

NOTE Confidence: 0.882590803

00:27:33.485 --> 00:27:34.520 we're concerned about.

NOTE Confidence: 0.882590803

00:27:34.520 --> 00:27:36.500 And in addition,

NOTE Confidence: 0.882590803

00:27:36.500 --> 00:27:38.480 COVID-19 absolutely impacted

NOTE Confidence: 0.882590803

00:27:38.480 --> 00:27:39.914 the population here as it did

NOTE Confidence: 0.882590803

00:27:39.914 --> 00:27:41.200 I think throughout the world.

NOTE Confidence: 0.882590803

00:27:41.200 --> 00:27:43.288 And there was just a lot of restrictions

NOTE Confidence: 0.882590803

00:27:43.288 --> 00:27:45.556 here on who you could bring to delivery

NOTE Confidence: 0.882590803

00:27:45.560 --> 00:27:47.900 and a variety of other restrictions

NOTE Confidence: 0.882590803

00:27:47.900 --> 00:27:49.460 during pregnancies that really

NOTE Confidence: 0.882590803

00:27:49.528 --> 00:27:51.718 aggravated and stressed our patients.

NOTE Confidence: 0.882590803

00:27:51.720 --> 00:27:55.040 And so we conceived of much of the work

NOTE Confidence: 0.882590803

00:27:55.040 --> 00:27:57.850 to date in the field of the microbiome

NOTE Confidence: 0.882590803

00:27:57.850 --> 00:27:59.704 in pregnancy had one time point,

NOTE Confidence: 0.882590803

00:27:59.704 --> 00:28:02.199 so the second trimester or the 3rd trimester.

NOTE Confidence: 0.882590803

00:28:02.200 --> 00:28:04.684 And what I had grown to appreciate was that

NOTE Confidence: 0.882590803

00:28:04.684 --> 00:28:07.005 it was really the longitudinal changes

NOTE Confidence: 0.882590803

00:28:07.005 --> 00:28:09.180 in the microbiome that could be important.

NOTE Confidence: 0.882590803

00:28:09.180 --> 00:28:11.391 And so we set out to do a

NOTE Confidence: 0.882590803

00:28:11.391 --> 00:28:13.106 longitudinal study of the microbiome

NOTE Confidence: 0.882590803

00:28:13.106 --> 00:28:14.680 through pregnancy and delivery.

NOTE Confidence: 0.882590803

00:28:14.680 --> 00:28:16.568 You can see the inclusion criteria on the

NOTE Confidence: 0.882590803

00:28:16.568 --> 00:28:18.799 left and our exclusion criteria on the right.

NOTE Confidence: 0.882590803

00:28:18.800 --> 00:28:20.336 When we collected,

NOTE Confidence: 0.882590803

00:28:20.336 --> 00:28:21.360 we enrolled.

NOTE Confidence: 0.882590803

00:28:21.360 --> 00:28:25.270 So this started many years ago now I think in

NOTE Confidence: 0.842883530909091

00:28:25.365 --> 00:28:26.793 2019, so before the

NOTE Confidence: 0.842883530909091

00:28:26.793 --> 00:28:28.117 pandemic at two locations.

NOTE Confidence: 0.842883530909091

00:28:28.120 --> 00:28:28.840 So the Campbell Hall here

NOTE Confidence: 0.842883530909091

00:28:28.840 --> 00:28:29.760 on the left is the rest,

NOTE Confidence: 0.842883530909091

00:28:29.760 --> 00:28:32.060 the OBGYN resident clinic.

NOTE Confidence: 0.842883530909091

00:28:32.060 --> 00:28:34.805 So these are underinsured patients,

NOTE Confidence: 0.842883530909091

00:28:34.805 --> 00:28:36.140 insured but underinsured

NOTE Confidence: 0.842883530909091

00:28:36.140 --> 00:28:37.920 members of the community.

NOTE Confidence: 0.842883530909091

00:28:37.920 --> 00:28:39.348 And then the member of the picture

NOTE Confidence: 0.842883530909091

00:28:39.348 --> 00:28:40.917 on the right is on the Kenny Road.

NOTE Confidence: 0.842883530909091

00:28:40.920 --> 00:28:42.450 One of the faculty practices

NOTE Confidence: 0.842883530909091

00:28:42.450 --> 00:28:44.812 which tends to be OU insurance

NOTE Confidence: 0.842883530909091

00:28:44.812 --> 00:28:47.076 or well insured patients,

NOTE Confidence: 0.842883530909091

00:28:47.080 --> 00:28:47.904 was on the right.

NOTE Confidence: 0.842883530909091

00:28:47.904 --> 00:28:49.906 And I have to take the moment to

NOTE Confidence: 0.842883530909091

00:28:49.906 --> 00:28:51.318 thank Teresa Teresa Regisigura,

NOTE Confidence: 0.842883530909091

00:28:51.320 --> 00:28:53.032 who started in my lab as an undergraduate

NOTE Confidence: 0.842883530909091

00:28:53.032 --> 00:28:54.563 and is now completing a short postdoc

NOTE Confidence: 0.842883530909091

00:28:54.563 --> 00:28:56.599 in my lab as she applies for postdocs.

NOTE Confidence: 0.842883530909091

00:28:56.600 --> 00:28:59.435 If anyone on the call is interested in a

NOTE Confidence: 0.842883530909091

00:28:59.435 --> 00:29:01.224 really talented postdoctoral researcher,

NOTE Confidence: 0.842883530909091

00:29:01.224 --> 00:29:02.520 let me know.

NOTE Confidence: 0.842883530909091

00:29:02.520 --> 00:29:04.880 She's interested in going to the East Coast.

NOTE Confidence: 0.842883530909091

00:29:04.880 --> 00:29:06.175 And then the person on the right

NOTE Confidence: 0.842883530909091

00:29:06.175 --> 00:29:07.600 is my my wonderful husband,

NOTE Confidence: 0.842883530909091

00:29:07.600 --> 00:29:09.830 who is the world's tallest

NOTE Confidence: 0.842883530909091

00:29:09.830 --> 00:29:11.492 gynecologist at six foot 10,

NOTE Confidence: 0.842883530909091

00:29:11.492 --> 00:29:13.767 but also a really hard worker and

NOTE Confidence: 0.842883530909091

00:29:13.767 --> 00:29:16.136 collected all of these samples by hand,

NOTE Confidence: 0.842883530909091

00:29:16.136 --> 00:29:18.240 as it were that I'm about to show you.

NOTE Confidence: 0.842883530909091

00:29:18.240 --> 00:29:19.968 And so he was the faculty member at

NOTE Confidence: 0.842883530909091

00:29:19.968 --> 00:29:21.549 the practice that was collecting and

NOTE Confidence: 0.842883530909091

00:29:21.549 --> 00:29:23.199 he also overseas the resident clinic.

NOTE Confidence: 0.842883530909091

00:29:23.200 --> 00:29:25.480 So he was collecting samples at both places,

NOTE Confidence: 0.842883530909091

00:29:25.480 --> 00:29:28.460 which gave us a really cleanly

NOTE Confidence: 0.842883530909091

00:29:28.460 --> 00:29:32.345 gathered sample set to my my

NOTE Confidence: 0.842883530909091

00:29:32.345 --> 00:29:34.920 my deep gratitude for them.

NOTE Confidence: 0.842883530909091

00:29:34.920 --> 00:29:35.264 So what?

NOTE Confidence: 0.842883530909091

00:29:35.264 --> 00:29:36.468 I just want to shift your attention

NOTE Confidence: 0.842883530909091

00:29:36.468 --> 00:29:37.904 and give you some background about

NOTE Confidence: 0.842883530909091

00:29:37.904 --> 00:29:38.880 the human maternal microbiome.

NOTE Confidence: 0.842883530909091

00:29:38.880 --> 00:29:40.960 So I've shown you some data from mice.

NOTE Confidence: 0.842883530909091

00:29:40.960 --> 00:29:42.212 But just speaking in,

NOTE Confidence: 0.842883530909091

00:29:42.212 --> 00:29:44.320 in generalities, in terms of the gut,

NOTE Confidence: 0.842883530909091

00:29:44.320 --> 00:29:46.880 greater diversity is generally

NOTE Confidence: 0.842883530909091

00:29:46.880 --> 00:29:48.800 seen as beneficial.

NOTE Confidence: 0.842883530909091

00:29:48.800 --> 00:29:49.984 And a lot of this work, however,

NOTE Confidence: 0.842883530909091

00:29:49.984 --> 00:29:52.560 has come from C Clostridium difficile,

NOTE Confidence: 0.842883530909091

00:29:52.560 --> 00:29:54.500 which is a terrible, terrible once,

NOTE Confidence: 0.842883530909091

00:29:54.500 --> 00:29:56.000 if you ever encountered it clinically,

NOTE Confidence: 0.842883530909091

00:29:56.000 --> 00:29:57.248 you'll never forget it.

NOTE Confidence: 0.842883530909091

00:29:57.248 --> 00:29:59.612 Terrible, terrible form of diarrhoea.

NOTE Confidence: 0.842883530909091

00:29:59.612 --> 00:30:01.885 And so C diff happens when a

NOTE Confidence: 0.842883530909091

00:30:01.885 --> 00:30:03.130 patient has been treated with

NOTE Confidence: 0.842883530909091

00:30:03.188 --> 00:30:04.560 antibiotics in the hospital.

NOTE Confidence: 0.842883530909091

00:30:04.560 --> 00:30:06.730 So what we know about diversity in

NOTE Confidence: 0.842883530909091

00:30:06.730 --> 00:30:08.702 the gut is actually somewhat flawed

NOTE Confidence: 0.842883530909091

00:30:08.702 --> 00:30:10.390 in the sense that a lot of the

NOTE Confidence: 0.842883530909091

00:30:10.446 --> 00:30:11.916 literature comes from antibiotic use

NOTE Confidence: 0.842883530909091

00:30:11.916 --> 00:30:13.743 and that's not exactly what we're

NOTE Confidence: 0.842883530909091

00:30:13.743 --> 00:30:15.555 seeing necessarily out in the community.

NOTE Confidence: 0.842883530909091

00:30:15.560 --> 00:30:16.451 But in general,

NOTE Confidence: 0.842883530909091

00:30:16.451 --> 00:30:18.530 a greater diversity is seen as being

NOTE Confidence: 0.842883530909091

00:30:18.593 --> 00:30:20.338 beneficial and there's also known

NOTE Confidence: 0.842883530909091

00:30:20.338 --> 00:30:22.555 to be shifts in composition across

NOTE Confidence: 0.842883530909091

00:30:22.555 --> 00:30:24.280 pregnancy under normal conditions,

NOTE Confidence: 0.842883530909091

00:30:24.280 --> 00:30:26.200 under normal pregnancy conditions.

NOTE Confidence: 0.842883530909091

00:30:26.200 --> 00:30:27.418 And I have some citations for

NOTE Confidence: 0.842883530909091

00:30:27.418 --> 00:30:28.800 you in the bottom right there.

NOTE Confidence: 0.842883530909091

00:30:28.800 --> 00:30:30.620 When we turn our attention

NOTE Confidence: 0.842883530909091

00:30:30.620 --> 00:30:32.076 to the vaginal microbiome,

NOTE Confidence: 0.842883530909091

00:30:32.080 --> 00:30:33.764 diversity is actually decreased

NOTE Confidence: 0.842883530909091

00:30:33.764 --> 00:30:35.869 about across pregnancy and a

NOTE Confidence: 0.842883530909091

00:30:35.869 --> 00:30:37.798 more diverse vaginal microbiome

NOTE Confidence: 0.842883530909091

00:30:37.798 --> 00:30:39.714 community can actually increase

NOTE Confidence: 0.842883530909091

00:30:39.714 --> 00:30:42.040 risk of adverse OB outcomes.

NOTE Confidence: 0.842883530909091

00:30:42.040 --> 00:30:44.096 So less diversity in the

NOTE Confidence: 0.842883530909091

00:30:44.096 --> 00:30:45.200 vaginal microbiome community.

NOTE Confidence: 0.842883530909091

00:30:45.200 --> 00:30:47.461 So just there's a lot of Lactobacillus

NOTE Confidence: 0.842883530909091

00:30:47.461 --> 00:30:49.344 in the vaginal community and

NOTE Confidence: 0.842883530909091

00:30:49.344 --> 00:30:50.560 that's seen as beneficial.

NOTE Confidence: 0.842883530909091

00:30:50.560 --> 00:30:51.864 So there's a difference

NOTE Confidence: 0.842883530909091

00:30:51.864 --> 00:30:53.820 already between the gut and the

NOTE Confidence: 0.842883530909091

00:30:53.880 --> 00:30:55.599 vaginal microbiome community.

NOTE Confidence: 0.842883530909091

00:30:55.600 --> 00:30:57.600 But what we were trying to ask is

NOTE Confidence: 0.842883530909091

00:30:57.600 --> 00:30:59.420 how does stress impact this and

NOTE Confidence: 0.842883530909091

00:30:59.420 --> 00:31:01.310 really does it impact both the

NOTE Confidence: 0.842883530909091

00:31:01.374 --> 00:31:03.159 gut and the vaginal community?

NOTE Confidence: 0.842883530909091

00:31:03.160 --> 00:31:05.956 And how might this be impacting

NOTE Confidence: 0.842883530909091

00:31:05.960 --> 00:31:07.025 the community that the infant

NOTE Confidence: 0.842883530909091

00:31:07.025 --> 00:31:08.090 is exposed to at our

NOTE Confidence: 0.811799373666667

00:31:08.141 --> 00:31:09.629 tradition And unfortunately we did not

NOTE Confidence: 0.811799373666667

00:31:09.629 --> 00:31:11.291 have because of the pandemic coming in

NOTE Confidence: 0.811799373666667

00:31:11.291 --> 00:31:13.198 the midst of the study we did, we had.

NOTE Confidence: 0.811799373666667

00:31:13.198 --> 00:31:14.731 So I won't be able to answer

NOTE Confidence: 0.811799373666667

00:31:14.731 --> 00:31:16.437 for you today with this study.

NOTE Confidence: 0.811799373666667

00:31:16.440 --> 00:31:17.334 What's going on in the infant

NOTE Confidence: 0.811799373666667

00:31:17.334 --> 00:31:18.480 though we do have a collaboration,

NOTE Confidence: 0.811799373666667

00:31:18.480 --> 00:31:20.272 so I'll be able to give you some

NOTE Confidence: 0.811799373666667

00:31:20.272 --> 00:31:21.998 insight about the impact on the infant.

NOTE Confidence: 0.811799373666667

00:31:22.000 --> 00:31:23.477 So this is again our study design.

NOTE Confidence: 0.811799373666667

00:31:23.480 --> 00:31:25.920 We what we lacked for in sample size,

NOTE Confidence: 0.811799373666667

00:31:25.920 --> 00:31:27.918 we tried to make up for in again this

NOTE Confidence: 0.811799373666667

00:31:27.918 --> 00:31:30.160 is a pilot study we made-up for in the

NOTE Confidence: 0.811799373666667

00:31:30.160 --> 00:31:31.400 longitudinal nature of this study.

NOTE Confidence: 0.811799373666667

00:31:31.400 --> 00:31:32.860 So first, second, third,

NOTE Confidence: 0.811799373666667

00:31:32.860 --> 00:31:34.320 trimester delivery and nest,

NOTE Confidence: 0.811799373666667

00:31:34.320 --> 00:31:36.880 if when possible, postpartum visits.

NOTE Confidence: 0.811799373666667

00:31:36.880 --> 00:31:38.280 So the these are the study visits,

NOTE Confidence: 0.811799373666667

00:31:38.280 --> 00:31:39.655 these are the psychometric scales

NOTE Confidence: 0.811799373666667

00:31:39.655 --> 00:31:41.362 we obtained and these are the

NOTE Confidence: 0.811799373666667

00:31:41.362 --> 00:31:43.078 biospecimens that we obtained at these.

NOTE Confidence: 0.811799373666667

00:31:43.080 --> 00:31:44.598 And so we've got both rectal

NOTE Confidence: 0.811799373666667

00:31:44.598 --> 00:31:45.357 and vaginal swabs.

NOTE Confidence: 0.811799373666667

00:31:45.360 --> 00:31:46.816 Microbiome can be collected

NOTE Confidence: 0.811799373666667

00:31:46.816 --> 00:31:48.636 in all sorts of ways.

NOTE Confidence: 0.811799373666667

00:31:48.640 --> 00:31:50.956 Many studies use at home kits.

NOTE Confidence: 0.811799373666667

00:31:50.960 --> 00:31:53.036 I had some concerns about that

NOTE Confidence: 0.811799373666667

00:31:53.040 --> 00:31:54.120 for a variety of reasons I'm

NOTE Confidence: 0.811799373666667

00:31:54.120 --> 00:31:55.360 happy to get into in AQ and A.

NOTE Confidence: 0.811799373666667

00:31:55.360 --> 00:31:56.893 And so we just decided that my

NOTE Confidence: 0.811799373666667

00:31:56.893 --> 00:31:58.286 husband would have to collect all

NOTE Confidence: 0.811799373666667

00:31:58.286 --> 00:31:59.654 the samples and that worked out

NOTE Confidence: 0.811799373666667

00:31:59.654 --> 00:32:00.983 just fine for this pilot study

NOTE Confidence: 0.811799373666667

00:32:00.983 --> 00:32:02.790 and he did the rectal and vaginal

NOTE Confidence: 0.811799373666667

00:32:02.790 --> 00:32:05.040 swabs himself and then we obtained

NOTE Confidence: 0.811799373666667

00:32:05.040 --> 00:32:06.660 maternal blood and umbilical

NOTE Confidence: 0.811799373666667

00:32:06.660 --> 00:32:08.680 cord blood as demonstrated here.

NOTE Confidence: 0.811799373666667

00:32:08.680 --> 00:32:10.612 And so just for a moment about

NOTE Confidence: 0.811799373666667

00:32:10.612 --> 00:32:11.440 our sample demographics,

NOTE Confidence: 0.811799373666667

00:32:11.440 --> 00:32:13.673 we are very pleased There's been a

NOTE Confidence: 0.811799373666667

00:32:13.673 --> 00:32:15.322 historical exclusion of people of

NOTE Confidence: 0.811799373666667

00:32:15.322 --> 00:32:16.892 color from biomedical research and

NOTE Confidence: 0.811799373666667

00:32:16.892 --> 00:32:19.186 we were very pleased that we were

NOTE Confidence: 0.811799373666667

00:32:19.186 --> 00:32:22.190 able to recruit and study non weight

NOTE Confidence: 0.811799373666667

00:32:22.190 --> 00:32:24.200 individuals as well as reflected here.

NOTE Confidence: 0.811799373666667

00:32:24.200 --> 00:32:25.383 And you can see overall as I

NOTE Confidence: 0.811799373666667

00:32:25.383 --> 00:32:26.360 mentioned into the pilot study.

NOTE Confidence: 0.811799373666667

00:32:26.360 --> 00:32:28.120 So we have a small number of people,

NOTE Confidence: 0.811799373666667

00:32:28.120 --> 00:32:29.116 but the fact that we're able

NOTE Confidence: 0.811799373666667

00:32:29.116 --> 00:32:30.200 to get a signal from that,

NOTE Confidence: 0.811799373666667

00:32:30.200 --> 00:32:32.240 as I'll show you shortly,

NOTE Confidence: 0.811799373666667

00:32:32.240 --> 00:32:34.354 was we're still able to get a

NOTE Confidence: 0.811799373666667

00:32:34.354 --> 00:32:36.871 signal from even a small sample size

NOTE Confidence: 0.811799373666667

00:32:36.871 --> 00:32:39.400 suggesting that we are on to something.

NOTE Confidence: 0.811799373666667

00:32:39.400 --> 00:32:41.620 So we got stress scores and

NOTE Confidence: 0.811799373666667

00:32:41.620 --> 00:32:42.360 depression scores.

NOTE Confidence: 0.811799373666667

00:32:42.360 --> 00:32:44.480 And what you can see here is this

NOTE Confidence: 0.811799373666667

00:32:44.480 --> 00:32:46.480 is the scale of PSS and CSD.

NOTE Confidence: 0.811799373666667

00:32:46.480 --> 00:32:48.160 If you're not familiar with them,

NOTE Confidence: 0.811799373666667

00:32:48.160 --> 00:32:49.280 low is 0 to 13.

NOTE Confidence: 0.811799373666667

00:32:49.280 --> 00:32:50.160 So these were not,

NOTE Confidence: 0.90949403

00:32:52.200 --> 00:32:54.088 they were not clinically

NOTE Confidence: 0.90949403

00:32:54.088 --> 00:32:57.320 depressed individuals in general.

NOTE Confidence: 0.90949403

00:32:57.320 --> 00:32:58.500 So this is just all

NOTE Confidence: 0.90949403

00:32:58.500 --> 00:32:59.680 comers to an OBGYN clinic.

NOTE Confidence: 0.90949403

00:32:59.680 --> 00:33:01.268 These were not psychiatric

NOTE Confidence: 0.90949403

00:33:01.268 --> 00:33:03.253 patients coming to for psychiatric

NOTE Confidence: 0.90949403

00:33:03.253 --> 00:33:05.038 care or psychological care.

NOTE Confidence: 0.90949403

00:33:05.040 --> 00:33:06.744 So we really were setting out to ask

NOTE Confidence: 0.90949403

00:33:06.744 --> 00:33:08.365 if stress and depressive symptoms

NOTE Confidence: 0.90949403

00:33:08.365 --> 00:33:09.893 are associated with differential

NOTE Confidence: 0.90949403

00:33:09.893 --> 00:33:12.125 abundance of specific maternal

NOTE Confidence: 0.90949403

00:33:12.125 --> 00:33:15.200 microbial taxes or specific microbes.

NOTE Confidence: 0.90949403

00:33:15.200 --> 00:33:17.522 And So what we found is that there was

NOTE Confidence: 0.90949403

00:33:17.522 --> 00:33:20.040 in the third trimester Lactobacillus

NOTE Confidence: 0.90949403

00:33:20.040 --> 00:33:23.040 specifically Lactobacillus einers

NOTE Confidence: 0.90949403

00:33:23.040 --> 00:33:26.330 was significantly shifted with

NOTE Confidence: 0.90949403

00:33:26.330 --> 00:33:28.070 with stress and this was actually

NOTE Confidence: 0.90949403

00:33:28.070 --> 00:33:29.600 contrary to general expectation.

NOTE Confidence: 0.90949403

00:33:29.600 --> 00:33:31.800 They're generally thought to be beneficial.

NOTE Confidence: 0.90949403

00:33:31.800 --> 00:33:34.320 So this we were intrigued to see

NOTE Confidence: 0.90949403

00:33:34.320 --> 00:33:35.994 this and we also found that these

NOTE Confidence: 0.90949403

00:33:35.994 --> 00:33:37.784 are also known to be a dominant

NOTE Confidence: 0.90949403

00:33:37.784 --> 00:33:39.214 tax of the vaginal community

NOTE Confidence: 0.90949403

00:33:39.214 --> 00:33:40.320 especially during pregnancy.

NOTE Confidence: 0.90949403

00:33:40.320 --> 00:33:42.880 So as I mentioned Lactobacillus

NOTE Confidence: 0.90949403

00:33:42.880 --> 00:33:45.120 is a major vaginal microbe.

NOTE Confidence: 0.90949403

00:33:45.120 --> 00:33:47.488 And so one of the ways that preterm

NOTE Confidence: 0.90949403

00:33:47.488 --> 00:33:50.134 birth is thought of just in the

NOTE Confidence: 0.90949403

00:33:50.134 --> 00:33:51.722 obstetrical community is that

NOTE Confidence: 0.90949403

00:33:51.722 --> 00:33:53.544 others maturation is happens more

NOTE Confidence: 0.90949403

00:33:53.544 --> 00:33:55.680 rapidly both in the brain and

NOTE Confidence: 0.90949403

00:33:55.744 --> 00:33:57.489 the lungs and potentially what

NOTE Confidence: 0.90949403

00:33:57.489 --> 00:34:00.800 we're seeing here in the in the in

NOTE Confidence: 0.90949403

00:34:00.800 --> 00:34:03.026 the vaginal and gut microbiome.

NOTE Confidence: 0.90949403

00:34:03.026 --> 00:34:05.690 And so the idea is that preterm birth

NOTE Confidence: 0.90949403

00:34:05.759 --> 00:34:08.360 happens for for still unknown reasons,

NOTE Confidence: 0.90949403

00:34:08.360 --> 00:34:10.236 but part of what's seen in preterm

NOTE Confidence: 0.90949403

00:34:10.236 --> 00:34:13.725 birth is that the fetus and the the

NOTE Confidence: 0.90949403

00:34:13.725 --> 00:34:15.550 maternal pregnancy mature more rapidly.

NOTE Confidence: 0.90949403

00:34:15.550 --> 00:34:16.800 So is that in fact,

NOTE Confidence: 0.90949403

00:34:16.800 --> 00:34:18.879 maybe what we're seeing here is that

NOTE Confidence: 0.90949403

00:34:18.879 --> 00:34:20.600 there's an earlier migration of

NOTE Confidence: 0.90949403

00:34:20.600 --> 00:34:22.280 vaginal microbes to the gut microbiomes.

NOTE Confidence: 0.90949403

00:34:22.280 --> 00:34:23.860 That's that's something we're

NOTE Confidence: 0.90949403

00:34:23.860 --> 00:34:25.440 interested at in pursuing.

NOTE Confidence: 0.90949403

00:34:25.440 --> 00:34:26.120 At delivery,

NOTE Confidence: 0.90949403

00:34:26.120 --> 00:34:27.820 we saw a significant increase

NOTE Confidence: 0.90949403

00:34:27.820 --> 00:34:28.840 in these microbes,

NOTE Confidence: 0.90949403

00:34:28.840 --> 00:34:31.990 which are in fact pathogenic and

NOTE Confidence: 0.90949403

00:34:31.990 --> 00:34:34.080 associated with gestational complications

NOTE Confidence: 0.90949403

00:34:34.080 --> 00:34:36.440 as well as intrauterine inflammation.

NOTE Confidence: 0.90949403

00:34:36.440 --> 00:34:39.240 So we were interested to see a

NOTE Confidence: 0.90949403

00:34:39.240 --> 00:34:41.057 significant increase of those with

NOTE Confidence: 0.90949403

00:34:41.057 --> 00:34:44.066 stress at delivery and Gardinella is

NOTE Confidence: 0.90949403

00:34:44.066 --> 00:34:46.714 also associated with complications

NOTE Confidence: 0.90949403

00:34:46.720 --> 00:34:49.328 and we were also interested in to see

NOTE Confidence: 0.90949403

00:34:49.328 --> 00:34:51.416 an increase in Gardinella Gardinarella.

NOTE Confidence: 0.90949403

00:34:51.416 --> 00:34:51.912 Next,

NOTE Confidence: 0.90949403

00:34:51.912 --> 00:34:55.880 when we turn our attention to the plasma

NOTE Confidence: 0.90949403

00:34:55.972 --> 00:34:58.400 CCL 2 that the chemokine that I kept

NOTE Confidence: 0.90949403

00:34:58.400 --> 00:35:00.300 talking about in my mouse studies,

NOTE Confidence: 0.90949403

00:35:00.300 --> 00:35:02.400 we actually did a panel for a

NOTE Confidence: 0.90949403

00:35:02.400 --> 00:35:04.360 variety of inflammatory factors,

NOTE Confidence: 0.90949403

00:35:04.360 --> 00:35:05.480 some of which I'm showing you here.

NOTE Confidence: 0.90949403

00:35:05.480 --> 00:35:08.588 And yet CCL 2 emerged as being

NOTE Confidence: 0.90949403

00:35:08.588 --> 00:35:10.545 associated with stress and depressive

NOTE Confidence: 0.90949403

00:35:10.545 --> 00:35:12.320 symptoms in the third trimester.

NOTE Confidence: 0.90949403

00:35:12.320 --> 00:35:15.120 So I was very fascinated to see

NOTE Confidence: 0.90949403

00:35:15.120 --> 00:35:17.264 that this chemokine that plays such

NOTE Confidence: 0.90949403

00:35:17.264 --> 00:35:19.280 an important role in rodent models

NOTE Confidence: 0.90949403

00:35:19.336 --> 00:35:21.240 of stress was also here in humans.

NOTE Confidence: 0.90949403

00:35:21.240 --> 00:35:23.265 So it was associated with

NOTE Confidence: 0.90949403

00:35:23.265 --> 00:35:24.075 significant increases.

NOTE Confidence: 0.90949403

00:35:24.080 --> 00:35:26.610 So this is maternal plasma

NOTE Confidence: 0.90949403

00:35:26.610 --> 00:35:28.634 in the third trimester.

NOTE Confidence: 0.90949403

00:35:28.640 --> 00:35:29.628 So just to summarize,

NOTE Confidence: 0.90949403

00:35:29.628 --> 00:35:31.443 what I'm showing you so far is

NOTE Confidence: 0.90949403

00:35:31.443 --> 00:35:33.105 that an increase in stress and

NOTE Confidence: 0.90949403

00:35:33.105 --> 00:35:34.286 depressive scores was associated

NOTE Confidence: 0.90949403

00:35:34.286 --> 00:35:36.316 with an increase in maternal CCL 2.

NOTE Confidence: 0.90949403

00:35:36.320 --> 00:35:36.664 Next,

NOTE Confidence: 0.90949403

00:35:36.664 --> 00:35:39.416 when we looked at CCL 2 and its

NOTE Confidence: 0.90949403

00:35:39.416 --> 00:35:41.000 relationship to Lactobacillus,

NOTE Confidence: 0.90949403

00:35:41.000 --> 00:35:43.422 we were very heartened to see that

NOTE Confidence: 0.90949403

00:35:43.422 --> 00:35:46.280 there was a a relationship between these two.

NOTE Confidence: 0.90949403

00:35:46.280 --> 00:35:48.230 So in an extended previous findings

NOTE Confidence: 0.90949403

00:35:48.230 --> 00:35:49.911 that Lactobacilli are found in

NOTE Confidence: 0.90949403

00:35:49.911 --> 00:35:51.211 greater abundance and infants

NOTE Confidence: 0.90949403

00:35:51.211 --> 00:35:52.836 of mothers with lower prenatal

NOTE Confidence: 0.90949403

00:35:52.892 --> 00:35:54.080 anxiety and depression.

NOTE Confidence: 0.90949403

00:35:54.080 --> 00:35:57.476 So again if Lactobacillus is beneficial,

NOTE Confidence: 0.90949403

00:35:57.480 --> 00:35:59.525 it's very interesting that the

NOTE Confidence: 0.90949403

00:35:59.525 --> 00:36:01.570 more Lactobacillus there was the

NOTE Confidence: 0.884517043076923

00:36:01.644 --> 00:36:02.358 less CCL 2.

NOTE Confidence: 0.884517043076923

00:36:02.360 --> 00:36:05.558 So that extends our previous findings.

NOTE Confidence: 0.884517043076923

00:36:05.560 --> 00:36:07.385 So in summary, increased stress

NOTE Confidence: 0.884517043076923

00:36:07.385 --> 00:36:08.760 and depression. I'm sorry,

NOTE Confidence: 0.884517043076923

00:36:08.760 --> 00:36:11.215 I'm struggling to move this zoom bar.

NOTE Confidence: 0.884517043076923

00:36:11.215 --> 00:36:13.355 Increased stress and depressive

NOTE Confidence: 0.884517043076923

00:36:13.355 --> 00:36:16.030 scores were increased associated with

NOTE Confidence: 0.884517043076923

00:36:16.108 --> 00:36:18.274 increased maternal CCL 2 and umbilical

NOTE Confidence: 0.884517043076923

00:36:18.274 --> 00:36:21.679 CCL 2 and a reduction in lactobacilli.

NOTE Confidence: 0.884517043076923

00:36:21.680 --> 00:36:24.112 And again, this is exciting to me personally

NOTE Confidence: 0.884517043076923

00:36:24.112 --> 00:36:26.165 because this is mirroring what we were

NOTE Confidence: 0.884517043076923

00:36:26.165 --> 00:36:28.040 seeing in our rodent model as well,

NOTE Confidence: 0.884517043076923

00:36:28.040 --> 00:36:30.360 suggesting that we have found something

NOTE Confidence: 0.884517043076923

00:36:30.360 --> 00:36:32.160 that is translatable and important.

NOTE Confidence: 0.884517043076923

00:36:32.160 --> 00:36:33.800 It wasn't just in mice that we were

NOTE Confidence: 0.884517043076923

00:36:33.800 --> 00:36:35.207 starting to see signals that it

NOTE Confidence: 0.884517043076923

00:36:35.207 --> 00:36:38.760 could be important in humans as well.

NOTE Confidence: 0.884517043076923

00:36:38.760 --> 00:36:42.024 So this is what I've been showing you

NOTE Confidence: 0.884517043076923

00:36:42.024 --> 00:36:44.276 now in humans that there's an increase

NOTE Confidence: 0.884517043076923

00:36:44.276 --> 00:36:45.904 in natively vaginal taxon opportunistic

NOTE Confidence: 0.884517043076923

00:36:45.904 --> 00:36:48.319 pathogens just in the small pilot study,

NOTE Confidence: 0.884517043076923

00:36:48.320 --> 00:36:49.144 an increase.

NOTE Confidence: 0.884517043076923

00:36:49.144 --> 00:36:49.968 You know,

NOTE Confidence: 0.884517043076923

00:36:49.968 --> 00:36:51.616 there's a relationship between

NOTE Confidence: 0.884517043076923

00:36:51.616 --> 00:36:53.097 psychometric scores and maternal

NOTE Confidence: 0.884517043076923

00:36:53.097 --> 00:36:54.873 CCL 2 in the third trimester.

NOTE Confidence: 0.884517043076923

00:36:54.880 --> 00:36:57.440 And finally in AD delivery.

NOTE Confidence: 0.884517043076923

00:36:57.440 --> 00:36:59.128 There's also this relationship

NOTE Confidence: 0.884517043076923

00:36:59.128 --> 00:37:01.238 between CCL 2 and lactobacilli.

NOTE Confidence: 0.884517043076923

00:37:01.240 --> 00:37:03.392 So it really looks like we've hit upon

NOTE Confidence: 0.884517043076923

00:37:03.392 --> 00:37:05.355 something that we might be able to target,

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NOTE Confidence: 0.884517043076923

00:37:05.360 --> 00:37:06.512 which of course my,

NOTE Confidence: 0.884517043076923

00:37:06.512 --> 00:37:06.800 my,

NOTE Confidence: 0.884517043076923

00:37:06.800 --> 00:37:08.560 my hope and my dream and my goal

NOTE Confidence: 0.884517043076923

00:37:08.560 --> 00:37:10.499 as a psychiatrist is to actually

NOTE Confidence: 0.884517043076923

00:37:10.499 --> 00:37:12.647 be able to target something that

NOTE Confidence: 0.884517043076923

00:37:12.707 --> 00:37:14.930 will help my patients endure stress

NOTE Confidence: 0.884517043076923

00:37:14.930 --> 00:37:17.355 during pregnancy and overcome it.

NOTE Confidence: 0.884517043076923

00:37:17.360 --> 00:37:19.544 So I want to shift our attention a

NOTE Confidence: 0.884517043076923

00:37:19.544 --> 00:37:21.680 little bit to microbial metabolites,

NOTE Confidence: 0.884517043076923

00:37:21.680 --> 00:37:22.780 which as you'll remember from

NOTE Confidence: 0.884517043076923

00:37:22.780 --> 00:37:23.880 the beginning of my talk,

NOTE Confidence: 0.884517043076923

00:37:23.880 --> 00:37:25.917 we think is an important way that

NOTE Confidence: 0.884517043076923

00:37:25.917 --> 00:37:27.175 the microbiome is transmitted

NOTE Confidence: 0.884517043076923

00:37:27.175 --> 00:37:28.516 to the next generation.

NOTE Confidence: 0.884517043076923

00:37:28.516 --> 00:37:31.364 So I want to focus on a particular

NOTE Confidence: 0.884517043076923

00:37:31.364 --> 00:37:32.818 metabolite, which is tryptophan.

NOTE Confidence: 0.884517043076923

00:37:32.818 --> 00:37:35.014 And so tryptophan has a very

NOTE Confidence: 0.884517043076923

00:37:35.014 --> 00:37:36.920 mixed history in psychiatry.

NOTE Confidence: 0.884517043076923

00:37:36.920 --> 00:37:39.524 It's been tried over the years to

NOTE Confidence: 0.884517043076923

00:37:39.524 --> 00:37:41.684 cure a variety low tryptophan diets

NOTE Confidence: 0.884517043076923

00:37:41.684 --> 00:37:43.424 have been tried high tryptophan

NOTE Confidence: 0.884517043076923

00:37:43.424 --> 00:37:44.959 diets with mixed results.

NOTE Confidence: 0.884517043076923

00:37:44.960 --> 00:37:47.160 And So what we think is that in in my

NOTE Confidence: 0.884517043076923

00:37:47.223 --> 00:37:49.415 lab is that this one of the reasons

NOTE Confidence: 0.884517043076923

00:37:49.415 --> 00:37:51.210 that there might be mixed results

NOTE Confidence: 0.884517043076923

00:37:51.210 --> 00:37:53.484 is because there might be a lack of,

NOTE Confidence: 0.884517043076923

00:37:53.484 --> 00:37:55.420 there is a lack of consideration for the

NOTE Confidence: 0.884517043076923

00:37:55.472 --> 00:37:57.398 microbes that might be metabolizing it.

NOTE Confidence: 0.884517043076923

00:37:57.400 --> 00:37:59.115 So if you're giving a boatload of

NOTE Confidence: 0.884517043076923

00:37:59.115 --> 00:38:01.203 tryptophan to an individual who has a

NOTE Confidence: 0.884517043076923

00:38:01.203 --> 00:38:02.833 lower level of tryptophan metabolizers,

NOTE Confidence: 0.884517043076923

00:38:02.840 --> 00:38:04.478 they might not be using it and

NOTE Confidence: 0.884517043076923

00:38:04.478 --> 00:38:06.589 utilizing it in the same way that an

NOTE Confidence: 0.884517043076923

00:38:06.589 --> 00:38:08.314 individual with a healthy number of

NOTE Confidence: 0.884517043076923

00:38:08.314 --> 00:38:10.234 tryptophan metabolizers might be able to.

NOTE Confidence: 0.884517043076923

00:38:10.240 --> 00:38:11.842 So the hypothesis that we're going

NOTE Confidence: 0.884517043076923

00:38:11.842 --> 00:38:13.767 to be testing in the last portion

NOTE Confidence: 0.884517043076923

00:38:13.767 --> 00:38:15.636 of my talk is that maternal stress

NOTE Confidence: 0.884517043076923

00:38:15.692 --> 00:38:17.020 is reducing tryptophan metabolizers

NOTE Confidence: 0.884517043076923

00:38:17.020 --> 00:38:18.680 in a way that shifts,

NOTE Confidence: 0.884517043076923

00:38:18.680 --> 00:38:20.420 that disregulates the production

NOTE Confidence: 0.884517043076923

00:38:20.420 --> 00:38:22.160 of really key metabolites.

NOTE Confidence: 0.884517043076923

00:38:22.160 --> 00:38:24.651 Here in red are some metabolites that are

NOTE Confidence: 0.884517043076923

00:38:24.651 --> 00:38:27.216 known to be neurotoxic or Mal disadvantage,

NOTE Confidence: 0.884517043076923

00:38:27.216 --> 00:38:29.360 disadvantageous for your health.

NOTE Confidence: 0.884517043076923

00:38:29.360 --> 00:38:31.872 And in green on the right are some

NOTE Confidence: 0.884517043076923

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00:38:31.872 --> 00:38:33.240 beneficial tryptophan metabolites.

NOTE Confidence: 0.884517043076923

00:38:33.240 --> 00:38:34.437 And it gets a little bit confusing.

NOTE Confidence: 0.884517043076923

00:38:34.440 --> 00:38:35.232 So don't worry,

NOTE Confidence: 0.884517043076923

00:38:35.232 --> 00:38:37.251 I'll be helping you remember

NOTE Confidence: 0.884517043076923

00:38:37.251 --> 00:38:39.239 all your serotonin metabolism.

NOTE Confidence: 0.884517043076923

00:38:39.240 --> 00:38:41.754 So that's our hypothesis that prenatal

NOTE Confidence: 0.884517043076923

00:38:41.754 --> 00:38:44.092 stress might be influencing neurodevelopment

NOTE Confidence: 0.884517043076923

00:38:44.092 --> 00:38:46.480 through changes in metabolism.

NOTE Confidence: 0.884517043076923

00:38:46.480 --> 00:38:47.960 And so how do we go ahead and test that?

NOTE Confidence: 0.884517043076923

00:38:47.960 --> 00:38:48.980 So the tryptophan story

NOTE Confidence: 0.884517043076923

00:38:48.980 --> 00:38:50.510 again is complex and has a

NOTE Confidence: 0.768112198666666

00:38:50.569 --> 00:38:52.359 missed mixed history in psychiatry.

NOTE Confidence: 0.768112198666666

00:38:52.360 --> 00:38:54.238 But just to refresh your memory,

NOTE Confidence: 0.768112198666666

00:38:54.240 --> 00:38:56.160 the majority of the tryptophan,

NOTE Confidence: 0.768112198666666

00:38:56.160 --> 00:38:57.954 virtually all of it comes from

NOTE Confidence: 0.768112198666666

00:38:57.954 --> 00:38:59.870 your diet and it's either taken

00:38:59.870 --> 00:39:01.838 up by enterocytes in your gut,

00:39:01.840 --> 00:39:03.328 you as the host or it's

00:39:03.328 --> 00:39:04.320 metabolized by gut microbes.

00:39:04.320 --> 00:39:06.525 And it's thought that might the gut

00:39:06.525 --> 00:39:07.874 microbes are metabolizing tryptophan

00:39:07.874 --> 00:39:09.599 differently than the host is.

00:39:09.600 --> 00:39:12.388 So the metabolites of kind of tryptophan,

00:39:12.388 --> 00:39:15.196 Probably the most famous is serotonin,

00:39:15.200 --> 00:39:16.999 which of course is important in adulthood,

00:39:17.000 --> 00:39:19.184 but in the fetus is incredibly important

00:39:19.184 --> 00:39:21.240 for things like external migration,

00:39:21.240 --> 00:39:23.770 sceptogenesis just of a host

00:39:23.770 --> 00:39:25.794 of different mental processes.

00:39:25.800 --> 00:39:26.502 And then kinuranine,

00:39:26.502 --> 00:39:28.140 which is known to have a role

00:39:28.188 --> 00:39:29.638 in immune function and indulse,

NOTE Confidence: 0.768112198666666

00:39:29.640 --> 00:39:31.328 which is known to be anti-inflammatory

NOTE Confidence: 0.768112198666666

00:39:31.328 --> 00:39:32.960 and associated with health.

NOTE Confidence: 0.768112198666666

00:39:32.960 --> 00:39:33.878 And of note,

NOTE Confidence: 0.768112198666666

00:39:33.878 --> 00:39:35.408 microbes in terms of producing

NOTE Confidence: 0.768112198666666

00:39:35.408 --> 00:39:37.040 indulse is the major source,

NOTE Confidence: 0.768112198666666

00:39:37.040 --> 00:39:38.279 if not the only source of indulse.

NOTE Confidence: 0.768112198666666

00:39:38.280 --> 00:39:39.638 It's a little bit of a controversy.

NOTE Confidence: 0.768112198666666

00:39:39.640 --> 00:39:40.960 Every field has its controversy.

NOTE Confidence: 0.768112198666666

00:39:40.960 --> 00:39:43.360 This is one of the controversies

NOTE Confidence: 0.768112198666666

00:39:43.360 --> 00:39:44.560 in the field.

NOTE Confidence: 0.768112198666666

00:39:44.560 --> 00:39:46.093 So I'm going to be focusing now

NOTE Confidence: 0.768112198666666

00:39:46.093 --> 00:39:47.958 on some of these key metabolites.

NOTE Confidence: 0.768112198666666

00:39:47.960 --> 00:39:51.220 And so we were excited to see

NOTE Confidence: 0.768112198666666

00:39:51.220 --> 00:39:53.300 this is a few years ago now and

NOTE Confidence: 0.768112198666666

00:39:53.300 --> 00:39:54.400 pictured here is Jeff Galley,

NOTE Confidence: 0.768112198666666

00:39:54.400 --> 00:39:55.872 who's a really talented

NOTE Confidence: 0.768112198666666

00:39:55.872 --> 00:39:57.712 research scientist in my group.

NOTE Confidence: 0.768112198666666

00:39:57.720 --> 00:39:59.917 We were excited to see that on

NOTE Confidence: 0.768112198666666

00:39:59.917 --> 00:40:01.102 a collaboration we had with

NOTE Confidence: 0.768112198666666

00:40:01.102 --> 00:40:02.320 Chris Dunkel shedder at UCLA,

NOTE Confidence: 0.768112198666666

00:40:02.320 --> 00:40:04.372 which I mentioned earlier,

NOTE Confidence: 0.768112198666666

00:40:04.372 --> 00:40:05.398 Bifidobacteria dentium,

NOTE Confidence: 0.768112198666666

00:40:05.400 --> 00:40:08.196 which is a major triptophan metabolizer,

NOTE Confidence: 0.768112198666666

00:40:08.200 --> 00:40:09.340 this is AR1.

NOTE Confidence: 0.768112198666666

00:40:09.340 --> 00:40:11.240 They had funded to look

NOTE Confidence: 0.768112198666666

00:40:11.240 --> 00:40:13.120 at maternal infant dyads.

NOTE Confidence: 0.768112198666666

00:40:13.120 --> 00:40:15.500 They were very generous and sent us

NOTE Confidence: 0.768112198666666

00:40:15.500 --> 00:40:17.855 all their samples from the infant.

NOTE Confidence: 0.768112198666666

00:40:17.855 --> 00:40:20.028 So these are now infants.

NOTE Confidence: 0.768112198666666

00:40:20.028 --> 00:40:21.580 We're examining the infant's

NOTE Confidence: 0.768112198666666

00:40:21.580 --> 00:40:23.760 microbiome that were sent to us,

NOTE Confidence: 0.768112198666666

00:40:23.760 --> 00:40:26.168 and then looking back and looking at

NOTE Confidence: 0.768112198666666

00:40:26.168 --> 00:40:28.270 the relationship to maternal anxiety

NOTE Confidence: 0.768112198666666

00:40:28.270 --> 00:40:30.278 and depression during pregnancy.

NOTE Confidence: 0.768112198666666

00:40:30.280 --> 00:40:32.212 And what we found was that there

NOTE Confidence: 0.768112198666666

00:40:32.212 --> 00:40:34.060 was a significant reduction in

NOTE Confidence: 0.768112198666666

00:40:34.060 --> 00:40:35.900 bifidobacteria dentium in infants

NOTE Confidence: 0.768112198666666

00:40:35.900 --> 00:40:38.960 born to mothers with higher levels of

NOTE Confidence: 0.768112198666666

00:40:38.960 --> 00:40:40.897 depression and anxiety during pregnancy.

NOTE Confidence: 0.768112198666666

00:40:40.897 --> 00:40:42.439 And we were excited about that

NOTE Confidence: 0.768112198666666

00:40:42.439 --> 00:40:44.006 because we have been seeing for

NOTE Confidence: 0.768112198666666

00:40:44.006 --> 00:40:45.494 several years in our mouth studies

NOTE Confidence: 0.768112198666666

00:40:45.494 --> 00:40:47.237 that there's a significant reduction.

NOTE Confidence: 0.768112198666666

00:40:47.240 --> 00:40:48.980 And I'll point your attention

NOTE Confidence: 0.768112198666666

00:40:48.980 --> 00:40:50.720 here to the central figure,

NOTE Confidence: 0.768112198666666

00:40:50.720 --> 00:40:52.505 but we've now shown this over and

NOTE Confidence: 0.768112198666666

00:40:52.505 --> 00:40:54.601 over again that there's a significant

NOTE Confidence: 0.768112198666666

00:40:54.601 --> 00:40:55.876 reduction in Paracetarella,

NOTE Confidence: 0.768112198666666

00:40:55.880 --> 00:40:57.420 which is another major tryptophan

NOTE Confidence: 0.768112198666666

00:40:57.420 --> 00:40:58.960 metabolizer in our mouse model.

NOTE Confidence: 0.768112198666666

00:40:58.960 --> 00:41:00.208 So we now had two converging

NOTE Confidence: 0.768112198666666

00:41:00.208 --> 00:41:00.832 lines of evidence,

NOTE Confidence: 0.768112198666666

00:41:00.840 --> 00:41:02.490 one from humans collected across

NOTE Confidence: 0.768112198666666

00:41:02.490 --> 00:41:05.038 the country as well as our mice

NOTE Confidence: 0.768112198666666

00:41:05.038 --> 00:41:07.113 here in Ohio that tryptophan

NOTE Confidence: 0.768112198666666

00:41:07.113 --> 00:41:08.358 metabolizers were significantly

NOTE Confidence: 0.768112198666666

00:41:08.419 --> 00:41:10.280 reduced with stress during pregnancy.

NOTE Confidence: 0.768112198666666

00:41:10.280 --> 00:41:12.440 And so we also looked at,

NOTE Confidence: 0.781231298571428

00:41:14.640 --> 00:41:16.194 so if there's a reduction in metabolizers,

NOTE Confidence: 0.781231298571428

00:41:16.200 --> 00:41:18.120 is there an increase in tryptophan

NOTE Confidence: 0.781231298571428

00:41:18.120 --> 00:41:19.400 because it's not being,

NOTE Confidence: 0.781231298571428

00:41:19.400 --> 00:41:20.304 it's not being metabolized.

NOTE Confidence: 0.781231298571428

00:41:20.304 --> 00:41:21.434 The short answer is yes.

NOTE Confidence: 0.781231298571428

00:41:21.440 --> 00:41:23.760 This is now content from the maternal gut,

NOTE Confidence: 0.781231298571428

00:41:23.760 --> 00:41:24.639 the ileal content.

NOTE Confidence: 0.781231298571428

00:41:24.639 --> 00:41:25.811 There's a significant increase

NOTE Confidence: 0.781231298571428

00:41:25.811 --> 00:41:27.240 with stress of tryptophan,

NOTE Confidence: 0.781231298571428

00:41:27.240 --> 00:41:29.240 which dovetails nicely with that.

NOTE Confidence: 0.781231298571428

00:41:29.240 --> 00:41:31.522 And so we went ahead and looked

NOTE Confidence: 0.781231298571428

00:41:31.522 --> 00:41:33.191 at Bifidobacterium in our mice

NOTE Confidence: 0.781231298571428

00:41:33.191 --> 00:41:35.382 and what we found is there's a

NOTE Confidence: 0.781231298571428

00:41:35.382 --> 00:41:37.234 significant reduction into adulthood.

NOTE Confidence: 0.781231298571428

00:41:37.234 --> 00:41:39.765 So these are now offspring at

NOTE Confidence: 0.781231298571428

00:41:39.765 --> 00:41:41.235 week three-week four and week 5,

NOTE Confidence: 0.781231298571428

00:41:41.240 --> 00:41:42.605 which is adolescence and we

NOTE Confidence: 0.781231298571428

00:41:42.605 --> 00:41:44.399 continue to see a a significant

NOTE Confidence: 0.781231298571428

00:41:44.399 --> 00:41:46.239 reduction of this in mice.

NOTE Confidence: 0.781231298571428

00:41:46.240 --> 00:41:49.320 So again, we're seeing it in humans,

NOTE Confidence: 0.781231298571428

00:41:49.320 --> 00:41:51.633 in infants and we're also seeing it in in,

NOTE Confidence: 0.781231298571428

00:41:51.640 --> 00:41:53.848 in rodent offspring that there's a

NOTE Confidence: 0.781231298571428

00:41:53.848 --> 00:41:55.320 significant reduction in stress.

NOTE Confidence: 0.781231298571428

00:41:55.320 --> 00:41:57.760 And this is also true for the Parasiterella.

NOTE Confidence: 0.781231298571428

00:41:57.760 --> 00:42:00.028 So in two major electric treatment

NOTE Confidence: 0.781231298571428

00:42:00.028 --> 00:42:02.050 metabolizers we're seeing in the

NOTE Confidence: 0.781231298571428

00:42:02.050 --> 00:42:03.669 reduction during pregnancy as

NOTE Confidence: 0.781231298571428

00:42:03.669 --> 00:42:05.283 well as during the services here

NOTE Confidence: 0.781231298571428

00:42:05.283 --> 00:42:06.991 in the mothers and then we're

NOTE Confidence: 0.781231298571428

00:42:06.991 --> 00:42:08.677 also seeing it in the offspring.

NOTE Confidence: 0.781231298571428

00:42:08.680 --> 00:42:11.039 So we decided to focus on this.

NOTE Confidence: 0.781231298571428

00:42:11.040 --> 00:42:12.965 We looked at other aspects

NOTE Confidence: 0.781231298571428

00:42:12.965 --> 00:42:14.120 of tryptophan metabolism.

NOTE Confidence: 0.781231298571428

00:42:14.120 --> 00:42:15.836 So just to refresh everyone's memory,

NOTE Confidence: 0.781231298571428

00:42:15.840 --> 00:42:18.210 this is the the pathway so

NOTE Confidence: 0.781231298571428

00:42:18.210 --> 00:42:20.044 tryptophan can be metabolized to

NOTE Confidence: 0.781231298571428

00:42:20.044 --> 00:42:21.654 serotonin or kinurine and then

NOTE Confidence: 0.781231298571428

00:42:21.654 --> 00:42:23.639 go down the kinurine pathway.

NOTE Confidence: 0.781231298571428

00:42:23.640 --> 00:42:25.248 And what we're finding is I'm

NOTE Confidence: 0.781231298571428

00:42:25.248 --> 00:42:27.070 showing you here data that there's

NOTE Confidence: 0.781231298571428

00:42:27.070 --> 00:42:28.800 changes in the different enzymes.

NOTE Confidence: 0.781231298571428

00:42:28.800 --> 00:42:30.798 So these are increased with stress.

NOTE Confidence: 0.781231298571428

00:42:30.800 --> 00:42:32.767 You can see here in the maternal

NOTE Confidence: 0.781231298571428

00:42:32.767 --> 00:42:34.837 colon as well as in the placenta.

NOTE Confidence: 0.781231298571428

00:42:34.840 --> 00:42:37.265 There's also changes in the

NOTE Confidence: 0.781231298571428

00:42:37.265 --> 00:42:38.720 arrow hydrocarbon receptor,

NOTE Confidence: 0.781231298571428

00:42:38.720 --> 00:42:41.066 which is mediated by the change

NOTE Confidence: 0.781231298571428

00:42:41.066 --> 00:42:42.239 in tryptophan metabolite.

NOTE Confidence: 0.781231298571428

00:42:42.240 --> 00:42:44.347 So it really looks like we're on

NOTE Confidence: 0.781231298571428

00:42:44.347 --> 00:42:46.239 several key aspects of this pathway.

NOTE Confidence: 0.781231298571428

00:42:46.240 --> 00:42:47.180 We are seeing shifts.

NOTE Confidence: 0.781231298571428

00:42:47.180 --> 00:42:48.882 So I'm just trying to explain to

NOTE Confidence: 0.781231298571428

00:42:48.882 --> 00:42:50.346 you that there's shifts not just

NOTE Confidence: 0.781231298571428

00:42:50.346 --> 00:42:52.068 in tryptophan but as well as the

NOTE Confidence: 0.781231298571428

00:42:52.068 --> 00:42:53.008 enzymes that are metabolizing

NOTE Confidence: 0.781231298571428

00:42:53.008 --> 00:42:54.872 it and in several key locations,

NOTE Confidence: 0.781231298571428

00:42:54.872 --> 00:42:55.916 including the gut,

NOTE Confidence: 0.781231298571428

00:42:55.920 --> 00:43:00.276 the placenta and in the colon.

NOTE Confidence: 0.781231298571428

00:43:00.280 --> 00:43:01.659 We then looked in the fetal brain

NOTE Confidence: 0.781231298571428

00:43:01.659 --> 00:43:02.942 because we wanted to see if there

NOTE Confidence: 0.781231298571428

00:43:02.942 --> 00:43:03.914 was a shift there as well.

NOTE Confidence: 0.781231298571428

00:43:03.920 --> 00:43:05.276 And the short answer is yes.

NOTE Confidence: 0.781231298571428

00:43:05.280 --> 00:43:07.530 I'm not reminding you that tryptophan

NOTE Confidence: 0.781231298571428

00:43:07.530 --> 00:43:09.864 goes into the cells through transporters.

NOTE Confidence: 0.781231298571428

00:43:09.864 --> 00:43:11.844 And all along this pathway

NOTE Confidence: 0.781231298571428

00:43:11.844 --> 00:43:13.317 illustrated here on the right,

NOTE Confidence: 0.781231298571428

00:43:13.320 --> 00:43:16.050 we're seeing significant changes in

NOTE Confidence: 0.781231298571428

00:43:16.050 --> 00:43:18.234 tryptophan related gene expression.

NOTE Confidence: 0.781231298571428

00:43:18.240 --> 00:43:20.893 So this is all gene expression data

NOTE Confidence: 0.781231298571428

00:43:20.893 --> 00:43:24.037 from the fenial brain on embryonic day 17.

NOTE Confidence: 0.781231298571428

00:43:24.040 --> 00:43:25.108 So it's disrupted now.

NOTE Confidence: 0.781231298571428

00:43:25.108 --> 00:43:27.022 I'm now showing you it both on

NOTE Confidence: 0.781231298571428

00:43:27.022 --> 00:43:28.558 the maternal side and the placenta

NOTE Confidence: 0.781231298571428

00:43:28.558 --> 00:43:30.397 as well as in the fetal brain.

NOTE Confidence: 0.781231298571428

00:43:30.400 --> 00:43:32.748 So we decided to continue on this pathway.

NOTE Confidence: 0.781231298571428

00:43:32.748 --> 00:43:34.780 So what I've shown you so fire is

NOTE Confidence: 0.781231298571428

00:43:34.839 --> 00:43:36.679 that there's changes in tryptophan

NOTE Confidence: 0.781231298571428

00:43:36.680 --> 00:43:37.556 with maternal stress.

NOTE Confidence: 0.781231298571428

00:43:37.556 --> 00:43:39.308 And then we're looking at these

NOTE Confidence: 0.781231298571428

00:43:39.308 --> 00:43:41.017 metabolites and this is pilot data

NOTE Confidence: 0.781231298571428

00:43:41.017 --> 00:43:42.113 that we're actively replicating.

NOTE Confidence: 0.781231298571428

00:43:42.120 --> 00:43:43.537 But it does look like, yes,

NOTE Confidence: 0.781231298571428

00:43:43.537 --> 00:43:46.622 there's a significant increase in

NOTE Confidence: 0.781231298571428

00:43:46.622 --> 00:43:49.586 these more toxic metabolites in

NOTE Confidence: 0.781231298571428

00:43:49.586 --> 00:43:52.484 both the fetal plasma as well as

NOTE Confidence: 0.781231298571428

00:43:52.484 --> 00:43:54.080 in the ileal content of the fetus.

NOTE Confidence: 0.781231298571428

00:43:54.080 --> 00:43:57.234 And So what I think that the one

NOTE Confidence: 0.781231298571428

00:43:57.234 --> 00:43:58.656 of the exciting but also complex

NOTE Confidence: 0.781231298571428

00:43:58.656 --> 00:43:59.130 things that

NOTE Confidence: 0.88768057

00:43:59.183 --> 00:44:00.920 we face is that it's not just I can't,

NOTE Confidence: 0.88768057

00:44:00.920 --> 00:44:02.040 we can't just think of things as good,

NOTE Confidence: 0.88768057

00:44:02.040 --> 00:44:04.200 as bad it, but it's really the dysregulation.

NOTE Confidence: 0.88768057

00:44:04.200 --> 00:44:06.360 So even cytokines aren't just good or bad,

NOTE Confidence: 0.88768057

00:44:06.360 --> 00:44:08.194 but it's the dysregulation of the cytokine.

NOTE Confidence: 0.88768057

00:44:08.200 --> 00:44:09.304 And I don't think tryptophan is

NOTE Confidence: 0.88768057

00:44:09.304 --> 00:44:10.698 either good or bad, but it's,

NOTE Confidence: 0.88768057

00:44:10.698 --> 00:44:12.672 it's dysregulation and the shifting of

NOTE Confidence: 0.88768057

00:44:12.672 --> 00:44:14.884 the balance of its metabolites that we

NOTE Confidence: 0.88768057

00:44:14.884 --> 00:44:16.542 think might be shaping neurodevelopment.

NOTE Confidence: 0.88768057

00:44:16.542 --> 00:44:19.314 And so just to remind you,

NOTE Confidence: 0.88768057

00:44:19.320 --> 00:44:21.042 I showed you now it seems like

NOTE Confidence: 0.88768057

00:44:21.042 --> 00:44:23.017 lifetime ago there is a significant

NOTE Confidence: 0.88768057

00:44:23.017 --> 00:44:24.199 increase in neuroinflammation,

NOTE Confidence: 0.88768057

00:44:24.200 --> 00:44:25.885 which is the bottom part

NOTE Confidence: 0.88768057

00:44:25.885 --> 00:44:27.233 of this hypothesis here.

NOTE Confidence: 0.88768057

00:44:27.240 --> 00:44:29.358 So we are seeing key checks,

NOTE Confidence: 0.88768057

00:44:29.360 --> 00:44:31.600 checkpoints being met here

NOTE Confidence: 0.88768057

00:44:31.600 --> 00:44:33.280 along our hypothesis.

NOTE Confidence: 0.88768057

00:44:33.280 --> 00:44:34.936 So we really wanted to ask

NOTE Confidence: 0.88768057

00:44:34.936 --> 00:44:36.040 can we orchestrate this?

NOTE Confidence: 0.88768057

00:44:36.040 --> 00:44:39.080 Can we take advantage of what we're seeing

NOTE Confidence: 0.88768057

00:44:39.080 --> 00:44:41.104 and try to target this with the long

NOTE Confidence: 0.88768057

00:44:41.104 --> 00:44:43.156 term goal of bringing this to clinic.

NOTE Confidence: 0.88768057

00:44:43.160 --> 00:44:44.680 And so of course we have to start in mice,

NOTE Confidence: 0.88768057

00:44:44.680 --> 00:44:46.905 but if maternal stress is

NOTE Confidence: 0.88768057

00:44:46.905 --> 00:44:48.240 changing tryptophan metabolizers,

NOTE Confidence: 0.88768057

00:44:48.240 --> 00:44:51.520 can we then address this and shifting

NOTE Confidence: 0.88768057

00:44:51.520 --> 00:44:54.640 the balance towards more neurotoxic or

NOTE Confidence: 0.88768057

00:44:54.640 --> 00:44:56.708 less maladaptive tryptophan metabolites

NOTE Confidence: 0.88768057

00:44:56.708 --> 00:44:59.278 and this is impacting neuroinflammation.

NOTE Confidence: 0.88768057

00:44:59.280 --> 00:45:00.549 Can we hear,

NOTE Confidence: 0.88768057

00:45:00.549 --> 00:45:03.087 buffer the pregnancy in the developing

NOTE Confidence: 0.88768057

00:45:03.087 --> 00:45:06.119 fetus in a way that would be beneficial?

NOTE Confidence: 0.88768057

00:45:06.120 --> 00:45:08.200 And just to remind you that we do

NOTE Confidence: 0.88768057

00:45:08.200 --> 00:45:10.119 see changes in the HR which is the,

NOTE Confidence: 0.88768057

00:45:10.120 --> 00:45:11.662 among other things is a receptor

NOTE Confidence: 0.88768057

00:45:11.662 --> 00:45:12.433 for these metabolites.

NOTE Confidence: 0.88768057

00:45:12.440 --> 00:45:14.470 So This is why we're driven to

NOTE Confidence: 0.88768057

00:45:14.470 --> 00:45:16.080 do the following experiment.

NOTE Confidence: 0.88768057

00:45:16.080 --> 00:45:18.798 So what we did is we took our regular

NOTE Confidence: 0.88768057

00:45:18.798 --> 00:45:20.946 model of stress and we added a probiotic

NOTE Confidence: 0.88768057

00:45:20.946 --> 00:45:23.479 so that mice were administered A probiotic.

NOTE Confidence: 0.88768057

00:45:23.480 --> 00:45:24.855 I'll be showing you data

NOTE Confidence: 0.88768057

00:45:24.855 --> 00:45:25.680 both from parasitorella,

NOTE Confidence: 0.88768057

00:45:25.680 --> 00:45:27.240 which again we had seen reduced

NOTE Confidence: 0.88768057

00:45:27.240 --> 00:45:28.280 in the mouse pregnancies,

NOTE Confidence: 0.88768057

00:45:28.280 --> 00:45:29.472 and Bifido bacteria redemption,

NOTE Confidence: 0.88768057

00:45:29.472 --> 00:45:31.610 which we had seen reduced in human

NOTE Confidence: 0.88768057

00:45:31.610 --> 00:45:33.398 pregnancies and then we replaced it.

NOTE Confidence: 0.88768057

00:45:33.400 --> 00:45:35.440 So if it's reduced, simple question.

NOTE Confidence: 0.88768057

00:45:35.440 --> 00:45:36.478 If it goes down with stress,

NOTE Confidence: 0.88768057

00:45:36.480 --> 00:45:37.680 if we give it back,

NOTE Confidence: 0.88768057

00:45:37.680 --> 00:45:39.584 can we benefit some of the outcomes

NOTE Confidence: 0.88768057

00:45:39.584 --> 00:45:41.876 I've shown you in the course of my talk?

NOTE Confidence: 0.88768057

00:45:41.880 --> 00:45:43.608 And so the first thing that's

NOTE Confidence: 0.88768057

00:45:43.608 --> 00:45:45.053 important to me is whether or

NOTE Confidence: 0.88768057

00:45:45.053 --> 00:45:46.199 not it's going to stick around.

NOTE Confidence: 0.88768057

00:45:46.200 --> 00:45:46.791 So spoiler alert,

NOTE Confidence: 0.88768057

00:45:46.791 --> 00:45:48.170 if you go to Whole Foods and

NOTE Confidence: 0.88768057

00:45:48.220 --> 00:45:49.078 buy some probiotics,

NOTE Confidence: 0.88768057

00:45:49.080 --> 00:45:50.396 probably going to go right through you.

NOTE Confidence: 0.88768057

00:45:50.400 --> 00:45:52.542 If I were to do an experiment

NOTE Confidence: 0.88768057

00:45:52.542 --> 00:45:54.079 similar to this for you,

NOTE Confidence: 0.88768057

00:45:54.080 --> 00:45:56.264 you wouldn't see any change because it's

NOTE Confidence: 0.88768057

00:45:56.264 --> 00:45:58.200 actually they would just pass through.

NOTE Confidence: 0.88768057

00:45:58.200 --> 00:45:59.719 So that's part of why we were

NOTE Confidence: 0.88768057

00:45:59.719 --> 00:46:01.172 givaging and that's why we repeatedly

NOTE Confidence: 0.88768057

00:46:01.172 --> 00:46:02.684 administrated it as we really wanted

NOTE Confidence: 0.88768057

95

00:46:02.684 --> 00:46:04.990 it to stick around during this critical

NOTE Confidence: 0.88768057

00:46:04.990 --> 00:46:05.992 neurodevelopmental time points.

NOTE Confidence: 0.88768057

00:46:06.000 --> 00:46:06.686 So yes,

NOTE Confidence: 0.88768057

00:46:06.686 --> 00:46:08.744 you can see here that administration

NOTE Confidence: 0.88768057

00:46:08.744 --> 00:46:09.920 of Bifidobacterium dentium.

NOTE Confidence: 0.88768057

00:46:09.920 --> 00:46:11.516 We then looked at the colonic stool,

NOTE Confidence: 0.88768057

00:46:11.520 --> 00:46:12.372 it stuck around,

NOTE Confidence: 0.88768057

00:46:12.372 --> 00:46:13.508 which is critically important

NOTE Confidence: 0.88768057

00:46:13.508 --> 00:46:15.239 to us in this experiment.

NOTE Confidence: 0.88768057

00:46:15.240 --> 00:46:18.435 Next we wanted to see if it was beneficial.

NOTE Confidence: 0.88768057

00:46:18.440 --> 00:46:20.048 And you think four years into

NOTE Confidence: 0.88768057

00:46:20.048 --> 00:46:21.455 this pandemic I wouldn't be

NOTE Confidence: 0.88768057

00:46:21.455 --> 00:46:23.117 struggling with this silly zoom bar,

NOTE Confidence: 0.88768057

00:46:23.120 --> 00:46:24.584 but it's literally over my graph

NOTE Confidence: 0.88768057

00:46:24.584 --> 00:46:25.316 and I cannot

NOTE Confidence: 0.909713752

00:46:27.480 --> 00:46:30.160 move it, so I can't see what this graph says.

NOTE Confidence: 0.909713752

00:46:30.160 --> 00:46:33.589 Here we go. This is one of the important

NOTE Confidence: 0.909713752

00:46:33.589 --> 00:46:35.338 findings is that we have consistently

NOTE Confidence: 0.909713752

00:46:35.338 --> 00:46:37.649 seen and one of the ways we know that

NOTE Confidence: 0.909713752

00:46:37.649 --> 00:46:39.251 we're stressing the animals is that

NOTE Confidence: 0.909713752

00:46:39.251 --> 00:46:41.346 we see a change in weight even when

NOTE Confidence: 0.909713752

00:46:41.346 --> 00:46:43.110 we standardize it to litter size.

NOTE Confidence: 0.909713752

00:46:43.110 --> 00:46:45.470 So when we look at the weight gain

NOTE Confidence: 0.909713752

00:46:45.534 --> 00:46:47.480 of the dams of the rodent moms,

NOTE Confidence: 0.909713752

00:46:47.480 --> 00:46:49.100 significant weight loss or lack of

NOTE Confidence: 0.909713752

00:46:49.100 --> 00:46:51.237 weight gain is what we find with stress.

NOTE Confidence: 0.909713752

00:46:51.240 --> 00:46:52.605 And what we found is that when

NOTE Confidence: 0.909713752

00:46:52.605 --> 00:46:53.560 we administered Bifida bacteria,

NOTE Confidence: 0.909713752

00:46:53.560 --> 00:46:54.708 dentium, this was ameliorated.

NOTE Confidence: 0.909713752

00:46:54.708 --> 00:46:56.720 So we were very excited about that.

NOTE Confidence: 0.909713752

00:46:56.720 --> 00:46:58.406 Nothing we've ever done in the

NOTE Confidence: 0.909713752

97

00:46:58.406 --> 00:47:00.624 course of our lab work has ever

NOTE Confidence: 0.909713752

00:47:00.624 --> 00:47:01.996 prevented this weight loss.

NOTE Confidence: 0.909713752

00:47:02.000 --> 00:47:05.104 So this is really positive in our opinion.

NOTE Confidence: 0.909713752

00:47:05.104 --> 00:47:07.120 And then we also saw a significant

NOTE Confidence: 0.909713752

00:47:07.181 --> 00:47:09.533 reduction of levels of CCL 2 in the

NOTE Confidence: 0.909713752

00:47:09.533 --> 00:47:11.439 maternal plasma with the administration

NOTE Confidence: 0.909713752

00:47:11.439 --> 00:47:13.119 of Bifida bacteria dentium.

NOTE Confidence: 0.909713752

00:47:13.120 --> 00:47:14.938 Next we looked at the liver and we and

NOTE Confidence: 0.909713752

00:47:14.938 --> 00:47:16.796 this is now switching to parasitorella.

NOTE Confidence: 0.909713752

00:47:16.800 --> 00:47:18.774 We found a significant effect of

NOTE Confidence: 0.909713752

00:47:18.774 --> 00:47:20.620 parasitorella in both the fetal liver

NOTE Confidence: 0.909713752

00:47:20.620 --> 00:47:22.844 as well in the as well as the fetal

NOTE Confidence: 0.909713752

00:47:22.844 --> 00:47:25.162 grain in terms of reducing Illinois 6.

NOTE Confidence: 0.909713752

00:47:25.162 --> 00:47:27.568 And then finally and most importantly

NOTE Confidence: 0.909713752

00:47:27.568 --> 00:47:30.503 perhaps is that the reduction in social

NOTE Confidence: 0.909713752

00:47:30.503 --> 00:47:33.266 behavior that we see with stress was

NOTE Confidence: 0.909713752

00:47:33.266 --> 00:47:35.598 ameliorated as well in in females,

NOTE Confidence: 0.909713752

00:47:35.598 --> 00:47:36.756 not in males,

NOTE Confidence: 0.909713752

00:47:36.760 --> 00:47:38.960 which I'm happy to discuss during the Q&amp;amp;A.

NOTE Confidence: 0.909713752

00:47:38.960 --> 00:47:40.760 But we saw a significant,

NOTE Confidence: 0.909713752

00:47:40.760 --> 00:47:43.399 we saw a significant amelioration of that.

NOTE Confidence: 0.909713752

00:47:43.400 --> 00:47:44.261 So they won't,

NOTE Confidence: 0.909713752

00:47:44.261 --> 00:47:46.270 they went back to preferring to engage

NOTE Confidence: 0.909713752

00:47:46.333 --> 00:47:48.342 with a social with a con specific

NOTE Confidence: 0.909713752

00:47:48.342 --> 00:47:50.078 with another rodent over an object.

NOTE Confidence: 0.909713752

00:47:50.080 --> 00:47:51.540 Next we're turning our attention

NOTE Confidence: 0.909713752

00:47:51.540 --> 00:47:53.000 to some of these metabolites.

NOTE Confidence: 0.909713752

00:47:53.000 --> 00:47:55.008 So again to remind you here on the

NOTE Confidence: 0.909713752

00:47:55.008 --> 00:47:56.764 left kineric acid is thought to be

NOTE Confidence: 0.909713752

00:47:56.764 --> 00:47:58.362 beneficial and we saw a significant

NOTE Confidence: 0.909713752

00:47:58.362 --> 00:48:00.408 increase kryonic acid in the maternal

NOTE Confidence: 0.909713752

00:48:00.408 --> 00:48:03.190 plasma here on the left as and we

NOTE Confidence: 0.909713752

00:48:03.190 --> 00:48:04.940 saw a significant increase with

NOTE Confidence: 0.909713752

00:48:05.020 --> 00:48:07.430 Parasiterella in the fetal plasma

NOTE Confidence: 0.909713752

00:48:07.430 --> 00:48:09.137 of another beneficial metabolite

NOTE Confidence: 0.909713752

00:48:09.137 --> 00:48:10.679 which is Indo 3 acetic acid.

NOTE Confidence: 0.909713752

00:48:10.680 --> 00:48:12.630 So we were very excited about

NOTE Confidence: 0.909713752

00:48:12.630 --> 00:48:14.980 that and finally can urinate in

NOTE Confidence: 0.909713752

00:48:14.980 --> 00:48:16.596 the maternal ileal content.

NOTE Confidence: 0.909713752

00:48:16.600 --> 00:48:18.718 What we saw,

NOTE Confidence: 0.909713752

00:48:18.720 --> 00:48:20.970 we saw that Parasiterella reversed the

NOTE Confidence: 0.909713752

00:48:20.970 --> 00:48:23.200 significant increase of that with stress,

NOTE Confidence: 0.909713752

00:48:23.200 --> 00:48:25.100 which is very promising.

NOTE Confidence: 0.909713752

00:48:25.100 --> 00:48:27.716 And then finally Tryptophan school was

NOTE Confidence: 0.909713752

00:48:27.716 --> 00:48:29.864 normalized with the treatment of with

NOTE Confidence: 0.909713752

00:48:29.864 --> 00:48:31.997 paracettorella in the maternal gut content.

NOTE Confidence: 0.909713752

00:48:32.000 --> 00:48:34.752 So it really does appear that we have

00:48:34.752 --> 00:48:37.516 hit on a translatable target that we

00:48:37.516 --> 00:48:40.479 can then work to prevent the negative

00:48:40.479 --> 00:48:42.580 sequela of stress during pregnancy.

00:48:42.580 --> 00:48:44.800 So this is my main conclusion.

00:48:44.800 --> 00:48:46.360 I haven't wasted a decade of my life,

00:48:46.360 --> 00:48:48.280 which is quite the relief.

00:48:48.280 --> 00:48:50.638 But more seriously,

00:48:50.640 --> 00:48:52.720 there's both converging preclinical and

00:48:52.720 --> 00:48:54.800 clinical evidence that prenatal stress,

00:48:54.800 --> 00:48:56.540 it is associated with ultra microbiome

00:48:56.540 --> 00:48:58.483 in both human and rodent pregnancies on

00:48:58.483 --> 00:49:00.760 the mom as well as in the offspring.

00:49:00.760 --> 00:49:03.757 We have evidence that CCL 2 is a key

00:49:03.760 --> 00:49:05.872 factor in all of this and is both

00:49:05.872 --> 00:49:07.918 influenced by stress and the microbiome.

NOTE Confidence: 0.909713752

00:49:07.920 --> 00:49:09.691 And at least in in rodent we

NOTE Confidence: 0.909713752

00:49:09.691 --> 00:49:10.450 have shown that

NOTE Confidence: 0.73046562125

00:49:10.507 --> 00:49:12.517 it is sufficient to induce changes.

NOTE Confidence: 0.73046562125

00:49:12.520 --> 00:49:14.284 And in humans we are seeing an

NOTE Confidence: 0.73046562125

00:49:14.284 --> 00:49:16.297 emerging signal that it might also be

NOTE Confidence: 0.73046562125

00:49:16.297 --> 00:49:17.802 influenced by stress and potentially

NOTE Confidence: 0.73046562125

00:49:17.802 --> 00:49:19.196 playing a role there as well.

NOTE Confidence: 0.73046562125

00:49:19.200 --> 00:49:20.934 And that I hopefully have uncovered

NOTE Confidence: 0.73046562125

00:49:20.934 --> 00:49:22.627 something that could be a translational

NOTE Confidence: 0.73046562125

00:49:22.627 --> 00:49:24.307 target for me to focus on in

NOTE Confidence: 0.73046562125

00:49:24.307 --> 00:49:26.200 this next a decade of my career.

NOTE Confidence: 0.73046562125

00:49:26.200 --> 00:49:29.714 With that, I'll stop and I would

NOTE Confidence: 0.73046562125

00:49:29.720 --> 00:49:31.379 wouldn't be a good talk without thanking

NOTE Confidence: 0.73046562125

00:49:31.379 --> 00:49:32.520 the wonderful members of my lab.

NOTE Confidence: 0.73046562125

00:49:32.520 --> 00:49:33.920 I feel really lucky to work with

NOTE Confidence: 0.73046562125

00:49:33.920 --> 00:49:35.200 some really bright, dedicated

NOTE Confidence: 0.860485247

00:49:37.280 --> 00:49:39.184 scientists. I'd like to thank my husband

NOTE Confidence: 0.860485247

00:49:39.184 --> 00:49:40.818 again for manually collecting all the

NOTE Confidence: 0.860485247

00:49:40.818 --> 00:49:43.290 samples I showed you from our study, as well

NOTE Confidence: 0.860485247

00:49:43.290 --> 00:49:45.360 as and generally being very supportive.

NOTE Confidence: 0.860485247

00:49:45.360 --> 00:49:46.344 My mentor, Mike Bailey,

NOTE Confidence: 0.860485247

00:49:46.344 --> 00:49:47.574 who's at Nationwide Children's Hospital

NOTE Confidence: 0.860485247

00:49:47.574 --> 00:49:49.000 who taught me everything I Googled,

NOTE Confidence: 0.860485247

00:49:49.000 --> 00:49:51.330 I googled Ohio State stress

NOTE Confidence: 0.860485247

00:49:51.330 --> 00:49:53.453 microbiome back in 20, 14.

NOTE Confidence: 0.860485247

00:49:53.453 --> 00:49:55.477 And his name came up and I called,

NOTE Confidence: 0.860485247

00:49:55.480 --> 00:49:57.160 emailed him and he's been a

NOTE Confidence: 0.860485247

00:49:57.160 --> 00:49:58.120 wonderful mentor ever since.

NOTE Confidence: 0.860485247

00:49:58.120 --> 00:49:59.100 And then, of course,

NOTE Confidence: 0.860485247

00:49:59.100 --> 00:50:00.600 I'd love to thank my fund,

NOTE Confidence: 0.860485247

00:50:00.600 --> 00:50:01.431 my funding sources,

NOTE Confidence: 0.860485247

00:50:01.431 --> 00:50:03.720 and then all of you for your time,

NOTE Confidence: 0.860485247

00:50:03.720 --> 00:50:05.995 thank you for listening to me today.