

WEBVTT

NOTE duration:"00:55:47"

NOTE recognizability:0.833

NOTE language:en-us

NOTE Confidence: 0.554803523333333

00:00:02.160 --> 00:00:05.488 I'm going to. So Lisa is able

NOTE Confidence: 0.554803523333333

00:00:05.488 --> 00:00:07.432 to log in, but not as host.

NOTE Confidence: 0.554803523333333

00:00:07.432 --> 00:00:10.757 So what we need to do is open the webinar.

NOTE Confidence: 0.554803523333333

00:00:10.760 --> 00:00:12.600 Once the webinar is open,

NOTE Confidence: 0.554803523333333

00:00:12.600 --> 00:00:14.360 I will make her a host From there.

NOTE Confidence: 0.914959984

00:00:14.360 --> 00:00:17.250 It is open. It's open. Oh, OK.

NOTE Confidence: 0.914959984

00:00:17.250 --> 00:00:19.920 Sorry about that. It's OK Then

NOTE Confidence: 0.648386518571429

00:00:19.920 --> 00:00:21.958 let me share my. There she is. There she is.

NOTE Confidence: 0.746708826666667

00:00:25.200 --> 00:00:27.936 OK. Thank you. Lisa, you're on.

NOTE Confidence: 0.746708826666667

00:00:27.936 --> 00:00:29.559 You're perfect. Oh, my God. Just

NOTE Confidence: 0.770606646666667

00:00:31.840 --> 00:00:33.118 relax. Don't worry.

NOTE Confidence: 0.868533296666667

00:00:35.720 --> 00:00:37.840 Hi, everybody. We we're

NOTE Confidence: 0.868533296666667

00:00:37.840 --> 00:00:38.800 just getting struck. We'll

NOTE Confidence: 0.95863717

00:00:38.800 --> 00:00:40.000 get started in just a minute.
NOTE Confidence: 0.95863717

00:00:40.000 --> 00:00:43.280 Allow people to arrive.
NOTE Confidence: 0.95863717

00:00:43.280 --> 00:00:44.600 We're having some initial
NOTE Confidence: 0.9674326

00:00:46.640 --> 00:00:47.390 technical difficulties,
NOTE Confidence: 0.9674326

00:00:47.390 --> 00:00:49.319 but I think we've resolved them.
NOTE Confidence: 0.9674326

00:00:49.320 --> 00:00:51.488 And I'll start with announcements
NOTE Confidence: 0.9674326

00:00:51.488 --> 00:00:52.640 in about one minute,
NOTE Confidence: 0.7560082

00:01:14.010 --> 00:01:16.650 right. Looks like a lot
NOTE Confidence: 0.7560082

00:01:16.650 --> 00:01:17.490 of people have arrived.
NOTE Confidence: 0.7560082

00:01:17.490 --> 00:01:19.930 Welcome to Grand Rounds.
NOTE Confidence: 0.7560082

00:01:19.930 --> 00:01:21.990 And I have a few announcements
NOTE Confidence: 0.7560082

00:01:21.990 --> 00:01:24.130 before our speaker introduction.
NOTE Confidence: 0.9571313

00:01:26.330 --> 00:01:28.808 So our upcoming grand rounds next week for
NOTE Confidence: 0.6041774425

00:01:28.810 --> 00:01:31.720 Zana Pashankar who is in our own section
NOTE Confidence: 0.761827476

00:01:31.720 --> 00:01:35.160 of paediatric hematology and oncology,
NOTE Confidence: 0.761827476

00:01:35.160 --> 00:01:38.037 we'll be talking about germ cell tumors.

NOTE Confidence: 0.761827476

00:01:38.040 --> 00:01:40.760 And then on January 24th,

NOTE Confidence: 0.761827476

00:01:40.760 --> 00:01:43.440 we will have another installment

NOTE Confidence: 0.761827476

00:01:43.440 --> 00:01:45.786 of our Marjorie S Rosenthal

NOTE Confidence: 0.761827476

00:01:45.786 --> 00:01:49.200 stories in Pediatrics in 2024.

NOTE Confidence: 0.761827476

00:01:49.200 --> 00:01:52.440 So that's always a tremendous experience.

NOTE Confidence: 0.761827476

00:01:52.440 --> 00:01:53.640 I encourage you to join

NOTE Confidence: 0.6923368825

00:01:53.640 --> 00:01:56.600 us. There is no commercial

NOTE Confidence: 0.6923368825

00:01:56.600 --> 00:01:57.976 support for this Grand Rounds

NOTE Confidence: 0.6923368825

00:01:57.976 --> 00:01:59.280 and no conflicts of interest.

NOTE Confidence: 0.776824403

00:02:02.600 --> 00:02:04.560 And as usual, the Grand

NOTE Confidence: 0.776824403

00:02:04.560 --> 00:02:06.520 Rounds is accredited for CME.

NOTE Confidence: 0.776824403

00:02:06.520 --> 00:02:12.580 There's the number to text to the

NOTE Confidence: 0.776824403

00:02:12.580 --> 00:02:15.560 CME office on your mobile device

NOTE Confidence: 0.957811292

00:02:16.240 --> 00:02:18.328 and you'll get credit as long

NOTE Confidence: 0.957811292

00:02:18.328 --> 00:02:19.720 as you're registered with

NOTE Confidence: 0.9460353725

00:02:19.720 --> 00:02:20.960 that office for CME.

NOTE Confidence: 0.935449248

00:02:22.640 --> 00:02:26.404 And then please use the Q&A or chat or

NOTE Confidence: 0.935449248

00:02:26.404 --> 00:02:28.720 any questions you might have at the end.

NOTE Confidence: 0.935449248

00:02:28.720 --> 00:02:29.756 And with that, I'm going to turn

NOTE Confidence: 0.935449248

00:02:29.760 --> 00:02:31.800 it over to Mark Mercurio who's

NOTE Confidence: 0.935449248

00:02:31.800 --> 00:02:33.920 going to introduce today's speaker.

NOTE Confidence: 0.757781941666667

00:02:38.640 --> 00:02:39.652 Good afternoon.

NOTE Confidence: 0.757781941666667

00:02:39.652 --> 00:02:41.945 Our Chief, the neonatology. Chief,

NOTE Confidence: 0.757781941666667

00:02:41.945 --> 00:02:43.800 Senator Taylor is is off this meeting.

NOTE Confidence: 0.757781941666667

00:02:43.800 --> 00:02:46.128 And so I get the honor of introducing

NOTE Confidence: 0.757781941666667

00:02:46.128 --> 00:02:47.780 today's grand House Speaker who

NOTE Confidence: 0.757781941666667

00:02:47.780 --> 00:02:49.444 is Doctor Lisa Connaco. Dr.

NOTE Confidence: 0.757781941666667

00:02:49.444 --> 00:02:51.064 Connaco is an associate professor

NOTE Confidence: 0.757781941666667

00:02:51.064 --> 00:02:52.954 with a prime appointment, of course,

NOTE Confidence: 0.757781941666667

00:02:52.954 --> 00:02:54.439 in our department in Pediatrics,

NOTE Confidence: 0.757781941666667

00:02:54.440 --> 00:02:56.455 but also secondary appointments at
NOTE Confidence: 0.757781941666667

00:02:56.455 --> 00:02:59.600 OBGYN as well as in immunobiology.
NOTE Confidence: 0.757781941666667

00:02:59.600 --> 00:03:01.105 She also serves Yale through
NOTE Confidence: 0.757781941666667

00:03:01.105 --> 00:03:03.638 work as a member of the Human
NOTE Confidence: 0.757781941666667

00:03:03.638 --> 00:03:05.262 Translational Immunology Program,
NOTE Confidence: 0.757781941666667

00:03:05.262 --> 00:03:08.117 the Program in Translational Biomedicine,
NOTE Confidence: 0.757781941666667

00:03:08.120 --> 00:03:10.045 and the Center for Systems
NOTE Confidence: 0.757781941666667

00:03:10.045 --> 00:03:11.200 and Engineering Immunology.
NOTE Confidence: 0.757781941666667

00:03:11.200 --> 00:03:14.280 Lisa joined Yale in 2020 in the
NOTE Confidence: 0.757781941666667

00:03:14.280 --> 00:03:16.080 midst of the pandemic fund.
NOTE Confidence: 0.757781941666667

00:03:16.080 --> 00:03:17.795 She moved her lab and her family
NOTE Confidence: 0.757781941666667

00:03:17.795 --> 00:03:20.094 to New Haven and she came to Yale
NOTE Confidence: 0.757781941666667

00:03:20.094 --> 00:03:21.594 from the University of Pittsburgh.
NOTE Confidence: 0.757781941666667

00:03:21.600 --> 00:03:22.620 She was brought here because
NOTE Confidence: 0.757781941666667

00:03:22.620 --> 00:03:23.436 of a tremendous background,
NOTE Confidence: 0.757781941666667

00:03:23.440 --> 00:03:24.580 already wonderful accomplishments

NOTE Confidence: 0.757781941666667
00:03:24.580 --> 00:03:25.720 in the field.
NOTE Confidence: 0.757781941666667
00:03:25.720 --> 00:03:28.876 She went to college at Brandeis,
NOTE Confidence: 0.757781941666667
00:03:28.880 --> 00:03:30.630 got an MD and her PhD from
NOTE Confidence: 0.757781941666667
00:03:30.630 --> 00:03:32.000 Tufts School of Medicine,
NOTE Confidence: 0.757781941666667
00:03:32.000 --> 00:03:33.980 completed Pediatric and Neonatology
NOTE Confidence: 0.757781941666667
00:03:33.980 --> 00:03:36.328 fellowship at Boston Children's and
NOTE Confidence: 0.757781941666667
00:03:36.328 --> 00:03:39.056 a post doctoral fellowship in Mucosal
NOTE Confidence: 0.757781941666667
00:03:39.056 --> 00:03:42.196 immunity at Boston Children's Hospital.
NOTE Confidence: 0.757781941666667
00:03:42.200 --> 00:03:44.360 She was also a fantastic candidate
NOTE Confidence: 0.757781941666667
00:03:44.360 --> 00:03:46.348 to bring here because achievements
NOTE Confidence: 0.757781941666667
00:03:46.348 --> 00:03:49.636 elucidating in the immune system developed.
NOTE Confidence: 0.757781941666667
00:03:49.640 --> 00:03:51.446 Now her work has been integral to
NOTE Confidence: 0.757781941666667
00:03:51.446 --> 00:03:52.845 our realization that while the
NOTE Confidence: 0.757781941666667
00:03:52.845 --> 00:03:54.280 early immune system is maturing,
NOTE Confidence: 0.757781941666667
00:03:54.280 --> 00:03:56.140 it's already highly functional
NOTE Confidence: 0.757781941666667

00:03:56.140 --> 00:03:58.314 and this functional is critical
NOTE Confidence: 0.757781941666667

00:03:58.314 --> 00:04:00.198 to short and long term health.
NOTE Confidence: 0.757781941666667

00:04:00.200 --> 00:04:01.002 And Yale.
NOTE Confidence: 0.757781941666667

00:04:01.002 --> 00:04:03.408 She's developing A rigorous program in
NOTE Confidence: 0.757781941666667

00:04:03.408 --> 00:04:05.016 developmental immunology with federal
NOTE Confidence: 0.757781941666667

00:04:05.016 --> 00:04:08.428 and foundation funding and a wide
NOTE Confidence: 0.757781941666667

00:04:08.428 --> 00:04:10.012 range of innovative collaborations
NOTE Confidence: 0.757781941666667

00:04:10.012 --> 00:04:12.200 both local and international.
NOTE Confidence: 0.757781941666667

00:04:12.200 --> 00:04:13.392 If that's not enough,
NOTE Confidence: 0.757781941666667

00:04:13.392 --> 00:04:15.180 but Doctor Kanikova also is working
NOTE Confidence: 0.757781941666667

00:04:15.234 --> 00:04:16.774 in developing the next generation
NOTE Confidence: 0.757781941666667

00:04:16.774 --> 00:04:18.314 of scientists in her lab,
NOTE Confidence: 0.757781941666667

00:04:18.320 --> 00:04:19.838 in the classroom and of course,
NOTE Confidence: 0.757781941666667

00:04:19.840 --> 00:04:21.840 in the newborn intense security.
NOTE Confidence: 0.757781941666667

00:04:21.840 --> 00:04:24.150 We are delighted and honored to have
NOTE Confidence: 0.757781941666667

00:04:24.150 --> 00:04:26.799 Lisa as a member of our session.

NOTE Confidence: 0.757781941666667
00:04:26.800 --> 00:04:29.264 And she's got a long list of
NOTE Confidence: 0.757781941666667
00:04:29.264 --> 00:04:30.320 words and accomplishments.
NOTE Confidence: 0.757781941666667
00:04:30.320 --> 00:04:31.960 I'll just let you know of one award,
NOTE Confidence: 0.757781941666667
00:04:31.960 --> 00:04:33.048 which is in 2023,
NOTE Confidence: 0.757781941666667
00:04:33.048 --> 00:04:35.155 she she was given the New England
NOTE Confidence: 0.757781941666667
00:04:35.155 --> 00:04:37.597 Perinatal Society Mentor of the Year.
NOTE Confidence: 0.757781941666667
00:04:37.600 --> 00:04:39.200 That's one of just many.
NOTE Confidence: 0.757781941666667
00:04:39.200 --> 00:04:39.752 So today,
NOTE Confidence: 0.757781941666667
00:04:39.752 --> 00:04:41.132 Doctor Konnikov is gonna speak
NOTE Confidence: 0.757781941666667
00:04:41.132 --> 00:04:42.878 about the immune system of infants,
NOTE Confidence: 0.757781941666667
00:04:42.880 --> 00:04:44.616 not just miniature adults.
NOTE Confidence: 0.757781941666667
00:04:44.616 --> 00:04:45.918 And with that,
NOTE Confidence: 0.757781941666667
00:04:45.920 --> 00:04:48.116 I will turn it over to Doctor Lisa Konnikov.
NOTE Confidence: 0.757781941666667
00:04:48.120 --> 00:04:48.800 Welcome, Lisa.
NOTE Confidence: 0.865196539090909
00:04:50.440 --> 00:04:52.780 Thanks so much, Mark.
NOTE Confidence: 0.865196539090909

00:04:52.780 --> 00:04:56.960 It's really an honor to present here.
NOTE Confidence: 0.865196539090909

00:04:56.960 --> 00:04:58.958 And I guess the pandemic is
NOTE Confidence: 0.865196539090909

00:04:58.958 --> 00:05:00.417 continuing with some COVID,
NOTE Confidence: 0.865196539090909

00:05:00.417 --> 00:05:04.940 but I will do my best to make
NOTE Confidence: 0.865196539090909

00:05:04.940 --> 00:05:07.440 it through the grand rounds.
NOTE Confidence: 0.865196539090909

00:05:07.440 --> 00:05:09.996 Is it in this correct view?
NOTE Confidence: 0.865196539090909

00:05:10.000 --> 00:05:11.192 I can't really tell.
NOTE Confidence: 0.865196539090909

00:05:11.192 --> 00:05:14.120 You need to put it in presenter mode.
NOTE Confidence: 0.865196539090909

00:05:14.120 --> 00:05:15.168 That is that good?
NOTE Confidence: 0.865196539090909

00:05:15.168 --> 00:05:15.954 There you go.
NOTE Confidence: 0.865196539090909

00:05:15.960 --> 00:05:16.680 That's good.
NOTE Confidence: 0.865196539090909

00:05:16.680 --> 00:05:17.040 Perfect.
NOTE Confidence: 0.9215378625

00:05:19.080 --> 00:05:21.592 So I have no conflicts of interest to
NOTE Confidence: 0.9215378625

00:05:21.592 --> 00:05:23.200 disclose fortunately or unfortunately.
NOTE Confidence: 0.9215378625

00:05:23.200 --> 00:05:25.510 And I thought I would start with
NOTE Confidence: 0.9215378625

00:05:25.510 --> 00:05:28.054 some quotes to sort of see how far

NOTE Confidence: 0.9215378625

00:05:28.054 --> 00:05:30.240 we've gone in the past 20 years.

NOTE Confidence: 0.9215378625

00:05:30.240 --> 00:05:33.909 So the first one is from neonatal

NOTE Confidence: 0.9215378625

00:05:33.909 --> 00:05:37.203 immunology by Sri Lanka and Infante

NOTE Confidence: 0.9215378625

00:05:37.203 --> 00:05:40.080 from seminars with perinatology.

NOTE Confidence: 0.9215378625

00:05:40.080 --> 00:05:41.319 And the neonate,

NOTE Confidence: 0.9215378625

00:05:41.319 --> 00:05:43.797 whether premature or normal gestational age,

NOTE Confidence: 0.9215378625

00:05:43.800 --> 00:05:46.380 is a unique host from an

NOTE Confidence: 0.9215378625

00:05:46.380 --> 00:05:47.240 immunologic perspective.

NOTE Confidence: 0.9215378625

00:05:47.240 --> 00:05:48.865 Many components of the immune

NOTE Confidence: 0.9215378625

00:05:48.865 --> 00:05:50.490 system function less well in

NOTE Confidence: 0.9215378625

00:05:50.555 --> 00:05:52.239 neonates compared with adults,

NOTE Confidence: 0.9215378625

00:05:52.240 --> 00:05:54.606 giving rise to the concept of what

NOTE Confidence: 0.9215378625

00:05:54.606 --> 00:05:57.474 we sort of commonly referred to

NOTE Confidence: 0.9215378625

00:05:57.474 --> 00:05:59.838 as immunodeficiency of immaturity.

NOTE Confidence: 0.9215378625

00:05:59.840 --> 00:06:03.982 Now it's this beautiful issue about 2 1/2

NOTE Confidence: 0.9215378625

00:06:03.982 --> 00:06:06.579 three years ago in science that really
NOTE Confidence: 0.9215378625

00:06:06.579 --> 00:06:09.238 started to reshaping this conversation.
NOTE Confidence: 0.9215378625

00:06:09.240 --> 00:06:11.400 And so one of the quotes from this issue,
NOTE Confidence: 0.9215378625

00:06:11.400 --> 00:06:13.675 and that's sort of the illustration here,
NOTE Confidence: 0.9215378625

00:06:13.680 --> 00:06:15.648 is although the precise rules of
NOTE Confidence: 0.9215378625

00:06:15.648 --> 00:06:17.583 specific immune cells during development
NOTE Confidence: 0.9215378625

00:06:17.583 --> 00:06:19.278 require further investigation,
NOTE Confidence: 0.9215378625

00:06:19.280 --> 00:06:21.872 the system as a whole displays
NOTE Confidence: 0.9215378625

00:06:21.872 --> 00:06:23.600 malleable and responsive properties
NOTE Confidence: 0.9215378625

00:06:23.673 --> 00:06:25.833 according to the developmental
NOTE Confidence: 0.9215378625

00:06:25.833 --> 00:06:27.993 needs and environmental challenges.
NOTE Confidence: 0.9215378625

00:06:28.000 --> 00:06:29.866 And another quote from the same
NOTE Confidence: 0.9215378625

00:06:29.866 --> 00:06:31.518 issues suggests evidence is also
NOTE Confidence: 0.9215378625

00:06:31.518 --> 00:06:33.258 mounting that the immune system
NOTE Confidence: 0.9215378625

00:06:33.258 --> 00:06:35.027 programming that starts early in
NOTE Confidence: 0.9215378625

00:06:35.027 --> 00:06:36.929 life may influence the risk of

NOTE Confidence: 0.9215378625

00:06:36.929 --> 00:06:39.068 developing conditions such as allergic,

NOTE Confidence: 0.9215378625

00:06:39.068 --> 00:06:39.662 autoimmune,

NOTE Confidence: 0.9215378625

00:06:39.662 --> 00:06:41.444 reproductive and neuropsychiatric

NOTE Confidence: 0.9215378625

00:06:41.444 --> 00:06:43.066 disorders later in life.

NOTE Confidence: 0.9215378625

00:06:43.066 --> 00:06:45.894 Sort of all suggesting that maybe it's not

NOTE Confidence: 0.9215378625

00:06:45.894 --> 00:06:48.435 as immature as we had previously thought.

NOTE Confidence: 0.9215378625

00:06:48.440 --> 00:06:50.320 And maybe it's actually critically

NOTE Confidence: 0.9215378625

00:06:50.320 --> 00:06:52.546 important not only to the babies

NOTE Confidence: 0.9215378625

00:06:52.546 --> 00:06:54.520 that Mark and I take care of,

NOTE Confidence: 0.9215378625

00:06:54.520 --> 00:06:57.600 but also to adults.

NOTE Confidence: 0.9215378625

00:06:57.600 --> 00:06:59.856 And so I thought I would first start

NOTE Confidence: 0.9215378625

00:06:59.856 --> 00:07:01.952 out with some observations about

NOTE Confidence: 0.9215378625

00:07:01.952 --> 00:07:03.672 infants and their immune system,

NOTE Confidence: 0.9215378625

00:07:03.672 --> 00:07:06.678 then sort of focus on what we thought it was.

NOTE Confidence: 0.9215378625

00:07:06.680 --> 00:07:08.152 But it really isn't.

NOTE Confidence: 0.9215378625

00:07:08.152 --> 00:07:10.360 And then offer some novel insights
NOTE Confidence: 0.9215378625

00:07:10.428 --> 00:07:12.535 from our group and others on what
NOTE Confidence: 0.9215378625

00:07:12.535 --> 00:07:15.040 it might be and then finish up with
NOTE Confidence: 0.9215378625

00:07:15.040 --> 00:07:17.602 a couple of thoughts or ways to
NOTE Confidence: 0.9215378625

00:07:17.602 --> 00:07:19.837 optimize neonatal and lifelong health.
NOTE Confidence: 0.9215378625

00:07:19.840 --> 00:07:21.331 So the first thing that I thought
NOTE Confidence: 0.9215378625

00:07:21.331 --> 00:07:22.873 I would start with is that young
NOTE Confidence: 0.9215378625

00:07:22.873 --> 00:07:24.151 children are at high risk of
NOTE Confidence: 0.9215378625

00:07:24.201 --> 00:07:25.696 severe infection and that's sort
NOTE Confidence: 0.9215378625

00:07:25.696 --> 00:07:27.191 of the common prevailing thought.
NOTE Confidence: 0.9215378625

00:07:27.200 --> 00:07:29.918 And I think that's incredibly true.
NOTE Confidence: 0.9215378625

00:07:29.920 --> 00:07:32.744 This is a map of where sepsis and
NOTE Confidence: 0.9215378625

00:07:32.744 --> 00:07:35.118 neonatal deaths are incredibly common.
NOTE Confidence: 0.9215378625

00:07:35.120 --> 00:07:37.748 And you can see that sort of pretty much
NOTE Confidence: 0.9215378625

00:07:37.748 --> 00:07:40.159 covers almost the entirety of the world.
NOTE Confidence: 0.9215378625

00:07:40.160 --> 00:07:42.716 If you look at neonatal deaths,

NOTE Confidence: 0.9215378625

00:07:42.720 --> 00:07:44.200 almost a third of them,

NOTE Confidence: 0.9215378625

00:07:44.200 --> 00:07:46.992 if not a little bit more are actually

NOTE Confidence: 0.9215378625

00:07:46.992 --> 00:07:49.760 due to infection disease causes.

NOTE Confidence: 0.9215378625

00:07:49.760 --> 00:07:51.909 That's also true if you look at

NOTE Confidence: 0.9215378625

00:07:51.909 --> 00:07:53.482 children under 5 S infection.

NOTE Confidence: 0.9215378625

00:07:53.482 --> 00:07:56.092 Disease related deaths are incredibly

NOTE Confidence: 0.9215378625

00:07:56.092 --> 00:07:58.839 common even in children under 5.

NOTE Confidence: 0.9215378625

00:07:58.840 --> 00:08:01.198 If you look at particular hospitalizations,

NOTE Confidence: 0.9215378625

00:08:01.200 --> 00:08:04.640 this is focusing on the US You can

NOTE Confidence: 0.9215378625

00:08:04.640 --> 00:08:06.920 look at respiratory syncytial virus or

NOTE Confidence: 0.9215378625

00:08:06.920 --> 00:08:09.717 influenza and this is incredibly recent data.

NOTE Confidence: 0.9215378625

00:08:09.720 --> 00:08:12.312 You can see that the peaks are very high,

NOTE Confidence: 0.9215378625

00:08:12.320 --> 00:08:14.344 particularly in the young.

NOTE Confidence: 0.9215378625

00:08:14.344 --> 00:08:17.950 And so for sure for RSV that peak is

NOTE Confidence: 0.9215378625

00:08:17.950 --> 00:08:20.597 highest for zero to four age group.

NOTE Confidence: 0.9215378625

00:08:20.600 --> 00:08:22.240 But even for influenza though,
NOTE Confidence: 0.9215378625

00:08:22.240 --> 00:08:23.386 it's pretty high.
NOTE Confidence: 0.9215378625

00:08:23.386 --> 00:08:24.914 In the elderly population,
NOTE Confidence: 0.9215378625

00:08:24.920 --> 00:08:28.800 the second highest peak is in the young.
NOTE Confidence: 0.9215378625

00:08:28.800 --> 00:08:29.760 If you look at
NOTE Confidence: 0.793274768

00:08:32.200 --> 00:08:35.520 mortality rates in children overall,
NOTE Confidence: 0.793274768

00:08:35.520 --> 00:08:38.131 again both RSV and flu have a
NOTE Confidence: 0.793274768

00:08:38.131 --> 00:08:40.782 very high odds ratio in the those
NOTE Confidence: 0.793274768

00:08:40.782 --> 00:08:43.314 less than one years of age.
NOTE Confidence: 0.793274768

00:08:43.320 --> 00:08:45.868 But that's not true for all diseases and
NOTE Confidence: 0.793274768

00:08:45.868 --> 00:08:48.676 particularly for the COVID-19 one that
NOTE Confidence: 0.793274768

00:08:48.676 --> 00:08:51.119 we're ultimately familiar with recently.
NOTE Confidence: 0.793274768

00:08:51.120 --> 00:08:54.639 And I think I fall into this age group,
NOTE Confidence: 0.793274768

00:08:54.640 --> 00:08:56.775 but you can look and see that
NOTE Confidence: 0.793274768

00:08:56.775 --> 00:08:58.478 the in the zero to 4H group,
NOTE Confidence: 0.793274768

00:08:58.480 --> 00:09:00.700 it's actually by far not the

NOTE Confidence: 0.793274768

00:09:00.700 --> 00:09:02.520 highest and it's incredibly rare

NOTE Confidence: 0.793274768

00:09:02.520 --> 00:09:05.720 in children to be hospitalized.

NOTE Confidence: 0.793274768

00:09:05.720 --> 00:09:07.360 And even if you focus and you say

NOTE Confidence: 0.793274768

00:09:07.360 --> 00:09:08.639 well that's a pretty wide gap,

NOTE Confidence: 0.793274768

00:09:08.640 --> 00:09:09.492 right, zero to four,

NOTE Confidence: 0.793274768

00:09:09.492 --> 00:09:11.720 but even if you focus on zero to six months,

NOTE Confidence: 0.793274768

00:09:11.720 --> 00:09:14.640 so in the very young that again

NOTE Confidence: 0.793274768

00:09:14.640 --> 00:09:16.640 is still pretty low.

NOTE Confidence: 0.793274768

00:09:16.640 --> 00:09:19.592 So not all infections are common

NOTE Confidence: 0.793274768

00:09:19.592 --> 00:09:21.560 in in young children.

NOTE Confidence: 0.793274768

00:09:21.560 --> 00:09:23.245 The second sort of prevailing

NOTE Confidence: 0.793274768

00:09:23.245 --> 00:09:24.930 thought is that young children

NOTE Confidence: 0.793274768

00:09:24.991 --> 00:09:26.956 don't mount good vaccine responses,

NOTE Confidence: 0.793274768

00:09:26.960 --> 00:09:28.944 and that's certainly true.

NOTE Confidence: 0.793274768

00:09:28.944 --> 00:09:31.240 So this is a pretty old study,

NOTE Confidence: 0.793274768

00:09:31.240 --> 00:09:33.770 but it's a it's a review of a lot of
NOTE Confidence: 0.793274768

00:09:33.849 --> 00:09:36.597 studies looking at the measles vaccine.
NOTE Confidence: 0.793274768

00:09:36.600 --> 00:09:40.240 And you can see that overall if
NOTE Confidence: 0.793274768

00:09:40.240 --> 00:09:42.508 you divide kids into those younger
NOTE Confidence: 0.793274768

00:09:42.508 --> 00:09:44.350 than the nine months and those
NOTE Confidence: 0.793274768

00:09:44.416 --> 00:09:46.240 that are older than nine months,
NOTE Confidence: 0.793274768

00:09:46.240 --> 00:09:49.848 overall kids don't mount as good of a
NOTE Confidence: 0.793274768

00:09:49.848 --> 00:09:52.075 vaccine response than sort of older
NOTE Confidence: 0.793274768

00:09:52.075 --> 00:09:53.955 than one year old or nine months infants.
NOTE Confidence: 0.94083771

00:09:56.360 --> 00:09:57.634 But that's not true for all vaccines.
NOTE Confidence: 0.94083771

00:09:57.640 --> 00:09:58.990 There are some vaccines that
NOTE Confidence: 0.94083771

00:09:58.990 --> 00:09:59.800 actually work beautifully.
NOTE Confidence: 0.94083771

00:09:59.800 --> 00:10:02.160 So for example this is a pertussis vaccine
NOTE Confidence: 0.94083771

00:10:02.160 --> 00:10:03.858 where influence were immunized and then
NOTE Confidence: 0.94083771

00:10:03.858 --> 00:10:06.159 you re stimulate it with PTX or pertussis.
NOTE Confidence: 0.94083771

00:10:06.160 --> 00:10:08.272 You can see that they actually

NOTE Confidence: 0.94083771

00:10:08.272 --> 00:10:09.680 mound a beautiful response.

NOTE Confidence: 0.94083771

00:10:09.680 --> 00:10:12.104 The same is true for hepatitis

NOTE Confidence: 0.94083771

00:10:12.104 --> 00:10:13.720 B and actually surprisingly,

NOTE Confidence: 0.94083771

00:10:13.720 --> 00:10:15.340 infants mound a much better

NOTE Confidence: 0.94083771

00:10:15.340 --> 00:10:16.960 hepatitis B response than adults.

NOTE Confidence: 0.94083771

00:10:16.960 --> 00:10:19.533 And you can see sort of after three doses,

NOTE Confidence: 0.94083771

00:10:19.533 --> 00:10:21.879 the crossbars here are the infants,

NOTE Confidence: 0.94083771

00:10:21.880 --> 00:10:24.480 the clear bars are adults

NOTE Confidence: 0.94083771

00:10:24.480 --> 00:10:25.992 that although the you know,

NOTE Confidence: 0.94083771

00:10:25.992 --> 00:10:27.232 the range is pretty wide,

NOTE Confidence: 0.94083771

00:10:27.240 --> 00:10:30.194 infants mount a much better response to

NOTE Confidence: 0.94083771

00:10:30.194 --> 00:10:32.520 hepatitis B immunization than do adults.

NOTE Confidence: 0.94083771

00:10:32.520 --> 00:10:35.553 And that's true after a pose booster as well.

NOTE Confidence: 0.899879548

00:10:38.640 --> 00:10:41.298 Another interesting sort of observation is

NOTE Confidence: 0.899879548

00:10:41.298 --> 00:10:45.014 that not only do infants mount a better

NOTE Confidence: 0.899879548

00:10:45.014 --> 00:10:47.800 response to some vaccines than adults,
NOTE Confidence: 0.899879548

00:10:47.800 --> 00:10:49.390 infants in particular,
NOTE Confidence: 0.899879548

00:10:49.390 --> 00:10:52.040 when certain vaccines are given,
NOTE Confidence: 0.899879548

00:10:52.040 --> 00:10:55.596 have a reduction in the overall mortality.
NOTE Confidence: 0.899879548

00:10:55.600 --> 00:10:58.358 So one of these vaccines is BCG.
NOTE Confidence: 0.899879548

00:10:58.360 --> 00:11:00.929 So a number of studies have shown
NOTE Confidence: 0.899879548

00:11:00.929 --> 00:11:04.000 that if you give BCG early in life,
NOTE Confidence: 0.899879548

00:11:04.000 --> 00:11:06.072 there is a sort of a ranging
NOTE Confidence: 0.899879548

00:11:06.072 --> 00:11:09.560 from 6 to 72% but some degree of
NOTE Confidence: 0.899879548

00:11:09.560 --> 00:11:11.640 decreased mortality in infants.
NOTE Confidence: 0.899879548

00:11:11.640 --> 00:11:14.305 And this is also true
NOTE Confidence: 0.899879548

00:11:14.305 --> 00:11:15.785 for the measles vaccine,
NOTE Confidence: 0.899879548

00:11:15.785 --> 00:11:18.520 although not as strong as the BCG vaccine.
NOTE Confidence: 0.899879548

00:11:18.520 --> 00:11:20.050 You can look here that
NOTE Confidence: 0.899879548

00:11:20.050 --> 00:11:21.274 even in premature infants.
NOTE Confidence: 0.899879548

00:11:21.280 --> 00:11:23.952 So this is a study from Denmark that

NOTE Confidence: 0.899879548

00:11:23.952 --> 00:11:27.760 looked at infants less than 2 1/2 kilos,

NOTE Confidence: 0.899879548

00:11:27.760 --> 00:11:30.944 so premature but not severely

NOTE Confidence: 0.899879548

00:11:30.944 --> 00:11:31.636 premature infants.

NOTE Confidence: 0.899879548

00:11:31.640 --> 00:11:33.956 You can see that the overall,

NOTE Confidence: 0.899879548

00:11:33.960 --> 00:11:36.280 if you gave BCG early,

NOTE Confidence: 0.899879548

00:11:36.280 --> 00:11:38.368 this is the sort of the dashed

NOTE Confidence: 0.899879548

00:11:38.368 --> 00:11:41.608 line here both neonatal and

NOTE Confidence: 0.899879548

00:11:41.608 --> 00:11:43.552 infant mortality decreased.

NOTE Confidence: 0.899879548

00:11:43.560 --> 00:11:45.534 And this is a concept that we

NOTE Confidence: 0.899879548

00:11:45.534 --> 00:11:47.967 know now as trained immunity where

NOTE Confidence: 0.899879548

00:11:47.967 --> 00:11:49.979 there's some primary stimulation

NOTE Confidence: 0.899879548

00:11:49.979 --> 00:11:52.702 being BCG vaccine or some other

NOTE Confidence: 0.899879548

00:11:52.702 --> 00:11:54.976 vaccine that resets how the immune

NOTE Confidence: 0.899879548

00:11:54.976 --> 00:11:57.564 system responds and then responds

NOTE Confidence: 0.899879548

00:11:57.564 --> 00:12:00.319 much better to secondary stimuli.

NOTE Confidence: 0.899879548

00:12:00.320 --> 00:12:02.552 So something else that might have
NOTE Confidence: 0.899879548

00:12:02.552 --> 00:12:04.996 caused death in those kids because
NOTE Confidence: 0.899879548

00:12:04.996 --> 00:12:07.400 they had early stimulation with BCG
NOTE Confidence: 0.899879548

00:12:07.400 --> 00:12:09.640 vaccine no longer is fatal to those.
NOTE Confidence: 0.899363452631579

00:12:12.480 --> 00:12:14.923 So this sort of concept suggests that
NOTE Confidence: 0.899363452631579

00:12:14.923 --> 00:12:17.113 stimulation with the right adjuvant at
NOTE Confidence: 0.899363452631579

00:12:17.113 --> 00:12:19.279 the right time can improve immunity.
NOTE Confidence: 0.899363452631579

00:12:19.280 --> 00:12:21.310 And this is sort of the concept
NOTE Confidence: 0.899363452631579

00:12:21.310 --> 00:12:23.442 of window of opportunity that I
NOTE Confidence: 0.899363452631579

00:12:23.442 --> 00:12:25.660 think infants really belong in.
NOTE Confidence: 0.899363452631579

00:12:25.660 --> 00:12:27.480 And so of course,
NOTE Confidence: 0.899363452631579

00:12:27.480 --> 00:12:29.482 this together brings what I call sort
NOTE Confidence: 0.899363452631579

00:12:29.482 --> 00:12:32.006 of the paradox of neonatal immunity, right.
NOTE Confidence: 0.899363452631579

00:12:32.006 --> 00:12:34.784 I think it's much more complicated
NOTE Confidence: 0.899363452631579

00:12:34.784 --> 00:12:36.960 than just immature, right.
NOTE Confidence: 0.899363452631579

00:12:36.960 --> 00:12:39.312 Of course, I showed you data that there's

NOTE Confidence: 0.899363452631579
00:12:39.312 --> 00:12:41.877 sepsis and poor vaccine responses in infants,
NOTE Confidence: 0.899363452631579
00:12:41.880 --> 00:12:43.956 but by far vast majority of
NOTE Confidence: 0.899363452631579
00:12:43.956 --> 00:12:45.340 instruments actually quite healthy
NOTE Confidence: 0.899363452631579
00:12:45.400 --> 00:12:47.355 and there's some vaccine responses
NOTE Confidence: 0.899363452631579
00:12:47.355 --> 00:12:48.919 that they beautifully mound.
NOTE Confidence: 0.899363452631579
00:12:48.920 --> 00:12:52.160 And so that starts a lot of questions.
NOTE Confidence: 0.899363452631579
00:12:52.160 --> 00:12:54.240 Is neonatal immunity really mature?
NOTE Confidence: 0.899363452631579
00:12:54.240 --> 00:12:57.830 Is it just not adult immunity? If so,
NOTE Confidence: 0.899363452631579
00:12:57.830 --> 00:13:00.386 maybe it just serves a different role, right?
NOTE Confidence: 0.899363452631579
00:13:00.386 --> 00:13:02.475 And is it site specific, right?
NOTE Confidence: 0.899363452631579
00:13:02.475 --> 00:13:04.960 Is your immunity in sort of your
NOTE Confidence: 0.899363452631579
00:13:04.960 --> 00:13:06.978 circulation or your blood different
NOTE Confidence: 0.899363452631579
00:13:06.978 --> 00:13:09.033 from that that mucosal sites?
NOTE Confidence: 0.899363452631579
00:13:09.040 --> 00:13:10.552 And of course, if all of those are true,
NOTE Confidence: 0.899363452631579
00:13:10.560 --> 00:13:13.717 when does it first start to develop?
NOTE Confidence: 0.899363452631579

00:13:13.720 --> 00:13:16.393 And if you think about what do we ask
NOTE Confidence: 0.899363452631579

00:13:16.393 --> 00:13:19.436 of neonatal immunity or fetal immunity?
NOTE Confidence: 0.899363452631579

00:13:19.440 --> 00:13:20.930 The requirements are actually drastically
NOTE Confidence: 0.899363452631579

00:13:20.930 --> 00:13:23.078 different from what we ask for in adults,
NOTE Confidence: 0.899363452631579

00:13:23.080 --> 00:13:23.365 right?
NOTE Confidence: 0.899363452631579

00:13:23.365 --> 00:13:25.360 So in the fetus and the neonate,
NOTE Confidence: 0.899363452631579

00:13:25.360 --> 00:13:28.097 by far the most predominant function
NOTE Confidence: 0.899363452631579

00:13:28.097 --> 00:13:29.879 of the immune system is tolerance,
NOTE Confidence: 0.899363452631579

00:13:29.880 --> 00:13:30.154 right?
NOTE Confidence: 0.899363452631579

00:13:30.154 --> 00:13:31.798 We really don't want that fetus
NOTE Confidence: 0.899363452631579

00:13:31.798 --> 00:13:33.740 to reject the bomb because then
NOTE Confidence: 0.899363452631579

00:13:33.740 --> 00:13:35.156 the pregnancy won't continue.
NOTE Confidence: 0.899363452631579

00:13:35.160 --> 00:13:37.568 And even early of life it's still
NOTE Confidence: 0.899363452631579

00:13:37.568 --> 00:13:39.680 tolerance because the as the baby is born,
NOTE Confidence: 0.899363452631579

00:13:39.680 --> 00:13:41.840 it's exposed to myriads of bugs,
NOTE Confidence: 0.899363452631579

00:13:41.840 --> 00:13:42.105 right?

NOTE Confidence: 0.899363452631579
00:13:42.105 --> 00:13:43.960 And you really don't want the immune
NOTE Confidence: 0.899363452631579
00:13:43.960 --> 00:13:45.872 system to respond to all those bugs
NOTE Confidence: 0.899363452631579
00:13:45.872 --> 00:13:47.636 because then you would have caused
NOTE Confidence: 0.899363452631579
00:13:47.636 --> 00:13:49.160 an overwhelming cytokine storm.
NOTE Confidence: 0.899363452631579
00:13:49.160 --> 00:13:51.920 Whereas in adults by far what is really
NOTE Confidence: 0.899363452631579
00:13:51.920 --> 00:13:54.677 important is the protection from pathogens,
NOTE Confidence: 0.899363452631579
00:13:54.680 --> 00:13:55.040 right.
NOTE Confidence: 0.899363452631579
00:13:55.040 --> 00:13:57.920 And so they're the immune systems of the
NOTE Confidence: 0.899363452631579
00:13:57.920 --> 00:14:01.120 two are quite conflicting with one another.
NOTE Confidence: 0.899363452631579
00:14:01.120 --> 00:14:03.960 Just a brief primer on the immune system,
NOTE Confidence: 0.899363452631579
00:14:03.960 --> 00:14:05.766 the immune system in large is
NOTE Confidence: 0.899363452631579
00:14:05.766 --> 00:14:07.400 divided into two big farms.
NOTE Confidence: 0.899363452631579
00:14:07.400 --> 00:14:09.794 The innate immunity which is the fast
NOTE Confidence: 0.899363452631579
00:14:09.794 --> 00:14:11.855 acting immunity that's made-up of a
NOTE Confidence: 0.899363452631579
00:14:11.855 --> 00:14:13.793 lot of cells but includes neutrophils,
NOTE Confidence: 0.899363452631579

00:14:13.800 --> 00:14:15.124 monocytes, macrophages,
NOTE Confidence: 0.899363452631579

00:14:15.124 --> 00:14:18.920 dendritic cells and that is really
NOTE Confidence: 0.899363452631579

00:14:18.920 --> 00:14:21.800 the primary first response to any
NOTE Confidence: 0.899363452631579

00:14:21.800 --> 00:14:23.852 infection or any, any antigen.
NOTE Confidence: 0.899363452631579

00:14:23.852 --> 00:14:25.688 And then there's an adoptive immune
NOTE Confidence: 0.899363452631579

00:14:25.688 --> 00:14:27.243 response which is divided into both
NOTE Confidence: 0.899363452631579

00:14:27.243 --> 00:14:28.863 B cell which I won't talk that
NOTE Confidence: 0.899363452631579

00:14:28.863 --> 00:14:30.459 much about and T cell immunity that
NOTE Confidence: 0.899363452631579

00:14:30.459 --> 00:14:32.360 I will talk much more about.
NOTE Confidence: 0.899363452631579

00:14:32.360 --> 00:14:33.080 In general.
NOTE Confidence: 0.899363452631579

00:14:33.080 --> 00:14:34.790 It's thought to be slow
NOTE Confidence: 0.899363452631579

00:14:34.790 --> 00:14:36.158 and it's certainly slower,
NOTE Confidence: 0.899363452631579

00:14:36.160 --> 00:14:37.952 but there's some response that that T
NOTE Confidence: 0.899363452631579

00:14:37.952 --> 00:14:39.879 cells can mount actually quite quickly.
NOTE Confidence: 0.899363452631579

00:14:39.880 --> 00:14:42.050 And then there's a sort of this
NOTE Confidence: 0.899363452631579

00:14:42.050 --> 00:14:44.211 grey zone in between where they

NOTE Confidence: 0.899363452631579
00:14:44.211 --> 00:14:46.712 are more adaptive like cells,
NOTE Confidence: 0.899363452631579
00:14:46.712 --> 00:14:49.880 but there have innate like properties
NOTE Confidence: 0.899363452631579
00:14:49.880 --> 00:14:51.040 and particularly in the neonate,
NOTE Confidence: 0.899363452631579
00:14:51.040 --> 00:14:52.480 this is quite important.
NOTE Confidence: 0.960794748333333
00:14:54.840 --> 00:14:56.964 The T cells that I will talk a little
NOTE Confidence: 0.960794748333333
00:14:56.964 --> 00:14:58.825 bit more about have a lot of different
NOTE Confidence: 0.960794748333333
00:14:58.825 --> 00:15:00.252 subtypes and I don't think you need
NOTE Confidence: 0.960794748333333
00:15:00.252 --> 00:15:01.434 to really remember any of this.
NOTE Confidence: 0.960794748333333
00:15:01.440 --> 00:15:05.456 But the main ones that people think about
NOTE Confidence: 0.960794748333333
00:15:05.456 --> 00:15:09.194 are TH1TH2 and TH17 and regulatory T cells,
NOTE Confidence: 0.960794748333333
00:15:09.200 --> 00:15:10.555 they're all defined by their
NOTE Confidence: 0.960794748333333
00:15:10.555 --> 00:15:11.639 cytokines that they make.
NOTE Confidence: 0.960794748333333
00:15:11.640 --> 00:15:14.685 So TH ONE cells make a cytokine
NOTE Confidence: 0.960794748333333
00:15:14.685 --> 00:15:17.085 known as interfering gamma and
NOTE Confidence: 0.960794748333333
00:15:17.085 --> 00:15:19.595 those are really responsible for
NOTE Confidence: 0.960794748333333

00:15:19.600 --> 00:15:21.595 against intracellular pathogens.
NOTE Confidence: 0.9607947483333333

00:15:21.595 --> 00:15:24.920 TH2 once make an interferon,
NOTE Confidence: 0.9607947483333333

00:15:24.920 --> 00:15:27.776 Illinois four and Illinois 5 and
NOTE Confidence: 0.9607947483333333

00:15:27.776 --> 00:15:29.982 those are extracellular pathogens and
NOTE Confidence: 0.9607947483333333

00:15:29.982 --> 00:15:31.794 it's also very related to atrophy
NOTE Confidence: 0.9607947483333333

00:15:31.794 --> 00:15:33.839 like asthma and allergies etcetera.
NOTE Confidence: 0.9607947483333333

00:15:33.840 --> 00:15:36.904 And then TH 17 cells are really
NOTE Confidence: 0.9607947483333333

00:15:36.904 --> 00:15:38.440 associated with autoimmunity.
NOTE Confidence: 0.9607947483333333

00:15:38.440 --> 00:15:40.678 They make Illinois 17 and they're
NOTE Confidence: 0.9607947483333333

00:15:40.678 --> 00:15:42.560 responsible for extracellular and fungi.
NOTE Confidence: 0.9607947483333333

00:15:42.560 --> 00:15:45.716 And then finally regulatory T cells
NOTE Confidence: 0.9607947483333333

00:15:45.720 --> 00:15:48.492 are make Illinois 10 and they're
NOTE Confidence: 0.9607947483333333

00:15:48.492 --> 00:15:50.600 really there to dampen the immunity.
NOTE Confidence: 0.9607947483333333

00:15:50.600 --> 00:15:53.165 So that's really to put the brake on all
NOTE Confidence: 0.9607947483333333

00:15:53.165 --> 00:15:56.560 the other pro inflammatory immune cells.
NOTE Confidence: 0.9607947483333333

00:15:56.560 --> 00:15:57.240 Alright,

NOTE Confidence: 0.960794748333333
00:15:57.240 --> 00:16:01.144 So what do we really know about infant
NOTE Confidence: 0.960794748333333
00:16:01.144 --> 00:16:02.837 immunity and how do we really study this?
NOTE Confidence: 0.960794748333333
00:16:02.840 --> 00:16:04.387 So a lot of studies have been
NOTE Confidence: 0.960794748333333
00:16:04.387 --> 00:16:06.305 done in mice and we've learned a
NOTE Confidence: 0.960794748333333
00:16:06.305 --> 00:16:07.800 lot of very interesting things.
NOTE Confidence: 0.960794748333333
00:16:07.800 --> 00:16:10.243 But the problems with mice is that
NOTE Confidence: 0.960794748333333
00:16:10.243 --> 00:16:12.321 there's a really very limited
NOTE Confidence: 0.960794748333333
00:16:12.321 --> 00:16:14.716 adoptive immune cells in circulation
NOTE Confidence: 0.960794748333333
00:16:14.720 --> 00:16:16.988 and for sure almost none at mucosal
NOTE Confidence: 0.960794748333333
00:16:16.988 --> 00:16:18.600 sites when mice are born.
NOTE Confidence: 0.960794748333333
00:16:18.600 --> 00:16:20.316 But we did for mouse studies,
NOTE Confidence: 0.960794748333333
00:16:20.320 --> 00:16:22.931 they suggest that there's sort of Ath
NOTE Confidence: 0.960794748333333
00:16:22.931 --> 00:16:27.076 2 predominance in the in the T cells.
NOTE Confidence: 0.960794748333333
00:16:27.080 --> 00:16:29.078 There's also regulatory T cell skewing.
NOTE Confidence: 0.960794748333333
00:16:29.080 --> 00:16:31.760 So they have much more are T
NOTE Confidence: 0.960794748333333

00:16:31.760 --> 00:16:33.560 cells than a diet mice,
NOTE Confidence: 0.9607947483333333

00:16:33.560 --> 00:16:35.184 but of course mice are very inbred
NOTE Confidence: 0.9607947483333333

00:16:35.184 --> 00:16:36.999 and they have very limited exposure.
NOTE Confidence: 0.9607947483333333

00:16:37.000 --> 00:16:39.034 So how really reflective is this
NOTE Confidence: 0.9607947483333333

00:16:39.034 --> 00:16:40.920 of the human immune system?
NOTE Confidence: 0.9607947483333333

00:16:40.920 --> 00:16:42.336 Their gestation period is
NOTE Confidence: 0.9607947483333333

00:16:42.336 --> 00:16:43.398 also incredibly short,
NOTE Confidence: 0.9607947483333333

00:16:43.400 --> 00:16:43.766 right,
NOTE Confidence: 0.9607947483333333

00:16:43.766 --> 00:16:47.110 so about 20 days versus 280 days and a lot
NOTE Confidence: 0.9607947483333333

00:16:47.110 --> 00:16:49.724 of things can happen in that time frame.
NOTE Confidence: 0.9607947483333333

00:16:49.724 --> 00:16:51.942 The other sort of core substitute
NOTE Confidence: 0.9607947483333333

00:16:51.942 --> 00:16:54.714 that we've used is cord blood.
NOTE Confidence: 0.9607947483333333

00:16:54.720 --> 00:16:56.827 And what we've learned from cord blood
NOTE Confidence: 0.9607947483333333

00:16:56.827 --> 00:16:59.488 is that for sure the T&B cells that
NOTE Confidence: 0.9607947483333333

00:16:59.488 --> 00:17:01.600 are there are almost exclusively naive.
NOTE Confidence: 0.9607947483333333

00:17:01.600 --> 00:17:04.554 But this is studying term cord blood.

NOTE Confidence: 0.960794748333333
00:17:04.560 --> 00:17:06.600 When people actually looked
NOTE Confidence: 0.960794748333333
00:17:06.600 --> 00:17:08.640 at preterm cord blood,
NOTE Confidence: 0.960794748333333
00:17:08.640 --> 00:17:10.320 sort of a different picture started
NOTE Confidence: 0.960794748333333
00:17:10.320 --> 00:17:12.441 to appear and you can see this data
NOTE Confidence: 0.960794748333333
00:17:12.441 --> 00:17:14.360 from Tibi Mckenzie's group that
NOTE Confidence: 0.960794748333333
00:17:14.360 --> 00:17:17.336 suggests that CXCR 3 positive cells,
NOTE Confidence: 0.960794748333333
00:17:17.336 --> 00:17:21.120 these are TH one like cells in central
NOTE Confidence: 0.960794748333333
00:17:21.120 --> 00:17:23.400 memory. There's two types of memory.
NOTE Confidence: 0.960794748333333
00:17:23.400 --> 00:17:25.560 This is just one of them.
NOTE Confidence: 0.960794748333333
00:17:25.560 --> 00:17:27.940 If you look at the preterm cord
NOTE Confidence: 0.960794748333333
00:17:27.940 --> 00:17:29.799 blood versus term cord blood,
NOTE Confidence: 0.960794748333333
00:17:29.800 --> 00:17:32.120 there's actually a significant
NOTE Confidence: 0.960794748333333
00:17:32.120 --> 00:17:34.368 population of of the T cells.
NOTE Confidence: 0.960794748333333
00:17:34.368 --> 00:17:35.728 There's a significant population of
NOTE Confidence: 0.960794748333333
00:17:35.728 --> 00:17:37.839 memory T cells present in preterm cord blood,
NOTE Confidence: 0.960794748333333

00:17:37.840 --> 00:17:41.040 suggesting that fetuses can make
NOTE Confidence: 0.9607947483333333

00:17:41.040 --> 00:17:44.118 memory T cells.
NOTE Confidence: 0.9607947483333333

00:17:44.120 --> 00:17:44.488 Interestingly,
NOTE Confidence: 0.9607947483333333

00:17:44.488 --> 00:17:46.696 sort of more recent work has
NOTE Confidence: 0.9607947483333333

00:17:46.696 --> 00:17:48.775 suggested that cord blood is really
NOTE Confidence: 0.9607947483333333

00:17:48.775 --> 00:17:50.599 an independent organ and you can
NOTE Confidence: 0.9607947483333333

00:17:50.599 --> 00:17:52.600 see this sort of a trajectory of
NOTE Confidence: 0.9607947483333333

00:17:52.600 --> 00:17:54.325 peripheral blood and cord blood
NOTE Confidence: 0.9607947483333333

00:17:54.325 --> 00:17:56.446 and preterm and term infants that
NOTE Confidence: 0.9607947483333333

00:17:56.446 --> 00:17:57.439 sort of converges.
NOTE Confidence: 0.9607947483333333

00:17:57.440 --> 00:17:59.904 But you can see that cord blood
NOTE Confidence: 0.9607947483333333

00:17:59.904 --> 00:18:00.960 is completely independent.
NOTE Confidence: 0.9607947483333333

00:18:00.960 --> 00:18:02.668 And so I think studies with cord
NOTE Confidence: 0.9607947483333333

00:18:02.668 --> 00:18:03.400 blood are incredibly
NOTE Confidence: 0.836405912727273

00:18:03.447 --> 00:18:06.420 interesting, but can't just be
NOTE Confidence: 0.836405912727273

00:18:06.420 --> 00:18:08.840 extrapolated to peripheral blood.

NOTE Confidence: 0.836405912727273
00:18:08.840 --> 00:18:10.886 So we really need to investigate
NOTE Confidence: 0.836405912727273
00:18:10.886 --> 00:18:12.250 appropriate human tissue directly
NOTE Confidence: 0.836405912727273
00:18:12.305 --> 00:18:13.955 based on what questions we have.
NOTE Confidence: 0.836405912727273
00:18:13.960 --> 00:18:16.800 So what do we know about circulating fetal
NOTE Confidence: 0.836405912727273
00:18:16.800 --> 00:18:19.717 and needle immune cells directly in humans?
NOTE Confidence: 0.836405912727273
00:18:19.720 --> 00:18:22.664 Well, T cells appear incredibly early on in
NOTE Confidence: 0.836405912727273
00:18:22.664 --> 00:18:25.065 human gestation at 10 weeks of life, right?
NOTE Confidence: 0.836405912727273
00:18:25.065 --> 00:18:27.480 So barely that you know you're pregnant.
NOTE Confidence: 0.836405912727273
00:18:27.480 --> 00:18:31.197 Your fetus already has some T cells.
NOTE Confidence: 0.836405912727273
00:18:31.200 --> 00:18:35.510 They are people that have looked at
NOTE Confidence: 0.836405912727273
00:18:35.510 --> 00:18:37.956 these very early gestational T cells
NOTE Confidence: 0.836405912727273
00:18:37.956 --> 00:18:40.326 have suggested that similar to mice,
NOTE Confidence: 0.836405912727273
00:18:40.326 --> 00:18:42.860 fetal cells are more prone to differentiate
NOTE Confidence: 0.836405912727273
00:18:42.929 --> 00:18:45.020 into regulatory T cells and very
NOTE Confidence: 0.836405912727273
00:18:45.020 --> 00:18:47.120 interestingly are there regulatory T cells.
NOTE Confidence: 0.836405912727273

00:18:47.120 --> 00:18:50.560 So usually T cells are against your antigens,

NOTE Confidence: 0.836405912727273

00:18:50.560 --> 00:18:50.933 right?

NOTE Confidence: 0.836405912727273

00:18:50.933 --> 00:18:53.917 So you so you don't react to yourself.

NOTE Confidence: 0.836405912727273

00:18:53.920 --> 00:18:56.517 Fetal T cells are not only against

NOTE Confidence: 0.836405912727273

00:18:56.520 --> 00:18:58.480 they're sort of fetal antigens.

NOTE Confidence: 0.836405912727273

00:18:58.480 --> 00:19:01.045 There are also a lot of regulatory T cells

NOTE Confidence: 0.836405912727273

00:19:01.045 --> 00:19:03.029 against non inherited maternal antigens

NOTE Confidence: 0.836405912727273

00:19:03.029 --> 00:19:05.489 that are constantly crossing the placent

NOTE Confidence: 0.836405912727273

00:19:05.553 --> 00:19:07.857 and this is part of the reason that the

NOTE Confidence: 0.836405912727273

00:19:07.857 --> 00:19:10.598 fetus doesn't reject the mom as well.

NOTE Confidence: 0.836405912727273

00:19:10.600 --> 00:19:12.847 And then a lot of studies have

NOTE Confidence: 0.836405912727273

00:19:12.847 --> 00:19:14.202 suggested there's quite unique

NOTE Confidence: 0.836405912727273

00:19:14.202 --> 00:19:15.837 features of fetal T cells.

NOTE Confidence: 0.836405912727273

00:19:15.840 --> 00:19:18.108 And most of these suggest that

NOTE Confidence: 0.836405912727273

00:19:18.108 --> 00:19:20.010 there's specific cell types that

NOTE Confidence: 0.836405912727273

00:19:20.010 --> 00:19:22.044 are very abundant in that fetus.

NOTE Confidence: 0.836405912727273
00:19:22.044 --> 00:19:24.468 And early neonate infants that are
NOTE Confidence: 0.836405912727273
00:19:24.468 --> 00:19:27.138 really meant to suppress the immune
NOTE Confidence: 0.836405912727273
00:19:27.138 --> 00:19:30.200 system needs include CD 71 erythrocytes,
NOTE Confidence: 0.836405912727273
00:19:30.200 --> 00:19:32.332 myeloid derived suppressive cells,
NOTE Confidence: 0.836405912727273
00:19:32.332 --> 00:19:34.997 as well as many others.
NOTE Confidence: 0.836405912727273
00:19:35.000 --> 00:19:37.310 But there's very few studies that
NOTE Confidence: 0.836405912727273
00:19:37.310 --> 00:19:38.850 investigate directly immune development
NOTE Confidence: 0.836405912727273
00:19:38.912 --> 00:19:40.814 in human infants and there's really
NOTE Confidence: 0.836405912727273
00:19:40.814 --> 00:19:42.560 almost none in premature infants.
NOTE Confidence: 0.836405912727273
00:19:42.560 --> 00:19:44.360 And So what our group has asked is,
NOTE Confidence: 0.836405912727273
00:19:44.360 --> 00:19:46.210 can we define immune trajectories
NOTE Confidence: 0.836405912727273
00:19:46.210 --> 00:19:48.482 across the first year of life
NOTE Confidence: 0.836405912727273
00:19:48.482 --> 00:19:50.237 in term and preterm infants?
NOTE Confidence: 0.836405912727273
00:19:50.240 --> 00:19:51.340 And this is work that's
NOTE Confidence: 0.836405912727273
00:19:51.340 --> 00:19:52.440 really been led by Booney,
NOTE Confidence: 0.836405912727273

00:19:52.440 --> 00:19:55.518 who has done amazing work here.
NOTE Confidence: 0.836405912727273

00:19:55.520 --> 00:19:58.145 And what she first asked is, well,
NOTE Confidence: 0.836405912727273

00:19:58.145 --> 00:19:59.440 how do we really do these studies,
NOTE Confidence: 0.836405912727273

00:19:59.440 --> 00:20:01.560 particularly in premature infants, right?
NOTE Confidence: 0.836405912727273

00:20:01.560 --> 00:20:02.995 If you think of a premature infant,
NOTE Confidence: 0.836405912727273

00:20:03.000 --> 00:20:03.726 that's 1K,
NOTE Confidence: 0.836405912727273

00:20:03.726 --> 00:20:05.541 which is actually pretty big
NOTE Confidence: 0.836405912727273

00:20:05.541 --> 00:20:07.585 for a premature infant, right?
NOTE Confidence: 0.836405912727273

00:20:07.585 --> 00:20:08.860 There's only 100.
NOTE Confidence: 0.836405912727273

00:20:08.860 --> 00:20:11.760 Millilitres of blood that that infant has.
NOTE Confidence: 0.836405912727273

00:20:11.760 --> 00:20:13.755 And so really we can't take the
NOTE Confidence: 0.836405912727273

00:20:13.755 --> 00:20:15.894 same amount of blood that we take
NOTE Confidence: 0.836405912727273

00:20:15.894 --> 00:20:17.718 in adults to do these studies.
NOTE Confidence: 0.836405912727273

00:20:17.720 --> 00:20:20.824 And you have to really optimize what you
NOTE Confidence: 0.836405912727273

00:20:20.824 --> 00:20:23.320 can do with very limited amount of samples.
NOTE Confidence: 0.836405912727273

00:20:23.320 --> 00:20:25.392 And so Buni worked out a protocol

NOTE Confidence: 0.836405912727273
00:20:25.392 --> 00:20:27.528 where you can take just two drops
NOTE Confidence: 0.836405912727273
00:20:27.528 --> 00:20:29.372 of blood and analyze those drops
NOTE Confidence: 0.836405912727273
00:20:29.372 --> 00:20:31.560 and get a lot of information out.
NOTE Confidence: 0.836405912727273
00:20:31.560 --> 00:20:33.438 Originally we did something called Cytof,
NOTE Confidence: 0.836405912727273
00:20:33.440 --> 00:20:35.660 which is fancy facts where the
NOTE Confidence: 0.836405912727273
00:20:35.660 --> 00:20:38.153 antibodies are chelated to heavy metals
NOTE Confidence: 0.836405912727273
00:20:38.153 --> 00:20:40.518 instead of conjugated to fluorophores.
NOTE Confidence: 0.836405912727273
00:20:40.520 --> 00:20:42.865 And that allows you to combine lots
NOTE Confidence: 0.836405912727273
00:20:42.865 --> 00:20:44.440 of different antibodies together.
NOTE Confidence: 0.836405912727273
00:20:44.440 --> 00:20:46.666 And so from 1:00 and 2:00 or
NOTE Confidence: 0.836405912727273
00:20:46.666 --> 00:20:48.399 from 2 drops of blood,
NOTE Confidence: 0.836405912727273
00:20:48.400 --> 00:20:50.528 you can see a lot of different
NOTE Confidence: 0.836405912727273
00:20:50.528 --> 00:20:51.782 immune cell types. Here.
NOTE Confidence: 0.836405912727273
00:20:51.782 --> 00:20:53.834 Each dot represents an immune cell.
NOTE Confidence: 0.836405912727273
00:20:53.840 --> 00:20:55.400 So you can see there's lots
NOTE Confidence: 0.836405912727273

00:20:55.400 --> 00:20:56.440 of immune cells there.
NOTE Confidence: 0.836405912727273

00:20:56.440 --> 00:20:57.336 And interestingly,
NOTE Confidence: 0.836405912727273

00:20:57.336 --> 00:20:59.128 neutrophils are very hard
NOTE Confidence: 0.836405912727273

00:20:59.128 --> 00:21:00.920 to detect after freezing.
NOTE Confidence: 0.836405912727273

00:21:00.920 --> 00:21:02.200 But even with this protocol,
NOTE Confidence: 0.836405912727273

00:21:02.200 --> 00:21:04.440 we were able to see some neutrophils.
NOTE Confidence: 0.893989376

00:21:06.840 --> 00:21:10.800 And So what we've done is set up a study,
NOTE Confidence: 0.893989376

00:21:10.800 --> 00:21:13.254 a prospective study of really trying
NOTE Confidence: 0.893989376

00:21:13.254 --> 00:21:15.945 to analyze how does the immune
NOTE Confidence: 0.893989376

00:21:15.945 --> 00:21:18.395 system develop in premature infants.
NOTE Confidence: 0.893989376

00:21:18.400 --> 00:21:20.381 And this has really been work in
NOTE Confidence: 0.893989376

00:21:20.381 --> 00:21:21.684 collaboration with Sarah Taylor's
NOTE Confidence: 0.893989376

00:21:21.684 --> 00:21:23.944 Nourished team, who have been really
NOTE Confidence: 0.893989376

00:21:23.944 --> 00:21:26.033 instrumental in enrolling all of
NOTE Confidence: 0.893989376

00:21:26.033 --> 00:21:27.837 these patients and collecting,
NOTE Confidence: 0.893989376

00:21:27.840 --> 00:21:30.296 seeing all of the samples And then

NOTE Confidence: 0.893989376

00:21:30.296 --> 00:21:32.312 a large team from our group that

NOTE Confidence: 0.893989376

00:21:32.312 --> 00:21:34.480 have been analysing these samples.

NOTE Confidence: 0.893989376

00:21:34.480 --> 00:21:36.238 And this is really team science,

NOTE Confidence: 0.893989376

00:21:36.240 --> 00:21:38.274 what I call because every single

NOTE Confidence: 0.893989376

00:21:38.274 --> 00:21:40.586 person in our group and even people

NOTE Confidence: 0.893989376

00:21:40.586 --> 00:21:43.040 in Dean's group have helped out and

NOTE Confidence: 0.893989376

00:21:43.040 --> 00:21:44.972 process these samples and there's always

NOTE Confidence: 0.893989376

00:21:44.972 --> 00:21:47.157 somebody on call to process these 24/7.

NOTE Confidence: 0.893989376

00:21:47.157 --> 00:21:49.542 So this couldn't have been

NOTE Confidence: 0.893989376

00:21:49.542 --> 00:21:52.479 done without a lot of people.

NOTE Confidence: 0.893989376

00:21:52.480 --> 00:21:55.420 We've enrolled over 120 babies at

NOTE Confidence: 0.893989376

00:21:55.420 --> 00:21:58.500 this point and we are continuing

NOTE Confidence: 0.893989376

00:21:58.500 --> 00:22:01.488 to not only enroll in the NICU,

NOTE Confidence: 0.893989376

00:22:01.488 --> 00:22:03.560 but we're hoping to expand to the

NOTE Confidence: 0.893989376

00:22:03.628 --> 00:22:05.493 grad clinic and potentially to

NOTE Confidence: 0.893989376

00:22:05.493 --> 00:22:07.880 start enrolling a full term cohort.
NOTE Confidence: 0.893989376

00:22:07.880 --> 00:22:09.693 But in order to validate that all
NOTE Confidence: 0.893989376

00:22:09.693 --> 00:22:11.718 of this is going to work right,
NOTE Confidence: 0.893989376

00:22:11.720 --> 00:22:14.896 we first did what my group likes to
NOTE Confidence: 0.893989376

00:22:14.896 --> 00:22:18.456 call a pilot experiment, 40 samples.
NOTE Confidence: 0.893989376

00:22:18.456 --> 00:22:21.584 What we took 10 a very preterm
NOTE Confidence: 0.893989376

00:22:21.584 --> 00:22:24.480 infants ranging from 25 to 30 weeks.
NOTE Confidence: 0.893989376

00:22:24.480 --> 00:22:25.920 They're samples at one week,
NOTE Confidence: 0.893989376

00:22:25.920 --> 00:22:28.475 one month and two months of age
NOTE Confidence: 0.893989376

00:22:28.480 --> 00:22:30.916 at time point T1T2 and T3.
NOTE Confidence: 0.893989376

00:22:30.920 --> 00:22:34.880 Then we also took five preterm core bloods,
NOTE Confidence: 0.893989376

00:22:34.880 --> 00:22:37.764 eight term core bloods and then we
NOTE Confidence: 0.893989376

00:22:37.764 --> 00:22:40.478 also compared them to healthy adults.
NOTE Confidence: 0.893989376

00:22:40.480 --> 00:22:42.412 We processed all of this according
NOTE Confidence: 0.893989376

00:22:42.412 --> 00:22:44.358 to the protocol that we've created
NOTE Confidence: 0.893989376

00:22:44.358 --> 00:22:46.444 where we just try and preserve all

NOTE Confidence: 0.893989376

00:22:46.444 --> 00:22:48.818 of these cells and then when we need

NOTE Confidence: 0.893989376

00:22:48.818 --> 00:22:51.372 to analyse them we batch saw them.

NOTE Confidence: 0.893989376

00:22:51.372 --> 00:22:54.504 And for analysis we take the same

NOTE Confidence: 0.893989376

00:22:54.504 --> 00:22:57.065 sample and then we split it into three

NOTE Confidence: 0.893989376

00:22:57.065 --> 00:22:59.670 different ways of analysing just so

NOTE Confidence: 0.893989376

00:22:59.670 --> 00:23:03.035 that we can optimize what we really

NOTE Confidence: 0.893989376

00:23:03.035 --> 00:23:06.875 can get from just 100 microliters of blood.

NOTE Confidence: 0.893989376

00:23:06.880 --> 00:23:09.225 Some of these cells underwent the same

NOTE Confidence: 0.893989376

00:23:09.225 --> 00:23:11.480 cytof analysis that I showed you earlier

NOTE Confidence: 0.893989376

00:23:11.480 --> 00:23:13.920 where you were looking at protein markers.

NOTE Confidence: 0.893989376

00:23:13.920 --> 00:23:15.840 We can phenotype cells.

NOTE Confidence: 0.893989376

00:23:15.840 --> 00:23:17.940 We also looked at a lot of

NOTE Confidence: 0.893989376

00:23:17.940 --> 00:23:19.200 signaling molecules with this.

NOTE Confidence: 0.893989376

00:23:19.200 --> 00:23:21.391 Some of these cells underwent a single

NOTE Confidence: 0.893989376

00:23:21.391 --> 00:23:24.362 cell R&E SEC analysis where we can look

NOTE Confidence: 0.893989376
00:23:24.362 --> 00:23:26.327 at transcriptomics of each individual
NOTE Confidence: 0.893989376
00:23:26.394 --> 00:23:28.344 cell and that was also paired with
NOTE Confidence: 0.893989376
00:23:28.344 --> 00:23:30.927 looking at T cell receptor and B cell
NOTE Confidence: 0.893989376
00:23:30.927 --> 00:23:32.997 receptor sequencing that can allow us
NOTE Confidence: 0.893989376
00:23:33.000 --> 00:23:36.003 to know what particular TCRS and BCRS
NOTE Confidence: 0.893989376
00:23:36.003 --> 00:23:39.400 were present on the cells that are there.
NOTE Confidence: 0.893989376
00:23:39.400 --> 00:23:42.032 We also at the same time simultaneously
NOTE Confidence: 0.893989376
00:23:42.032 --> 00:23:44.880 collect blood spots and these blood spots
NOTE Confidence: 0.893989376
00:23:44.880 --> 00:23:47.362 can then be processed for proteomics.
NOTE Confidence: 0.893989376
00:23:47.362 --> 00:23:50.840 And we've used all in proteomics to do this.
NOTE Confidence: 0.893989376
00:23:50.840 --> 00:23:52.905 So can, sorry, this is just that
NOTE Confidence: 0.893989376
00:23:52.905 --> 00:23:54.840 table of the initial cohort.
NOTE Confidence: 0.893989376
00:23:54.840 --> 00:23:56.892 This is the 1st 10 infants
NOTE Confidence: 0.893989376
00:23:56.892 --> 00:23:57.918 that we've studied.
NOTE Confidence: 0.893989376
00:23:57.920 --> 00:24:00.160 As I already said, they were quite young.
NOTE Confidence: 0.893989376

00:24:00.160 --> 00:24:01.672 Their average gestational age
NOTE Confidence: 0.893989376

00:24:01.672 --> 00:24:04.293 is 28 weeks ranging from 25 to
NOTE Confidence: 0.893989376

00:24:04.293 --> 00:24:06.384 30 and they all weigh about 1K.
NOTE Confidence: 0.893989376

00:24:06.384 --> 00:24:08.688 So they all had about 100
NOTE Confidence: 0.893989376

00:24:08.688 --> 00:24:09.840 milliliters of blood.
NOTE Confidence: 0.893989376

00:24:09.840 --> 00:24:11.796 They had sort of typical complications
NOTE Confidence: 0.893989376

00:24:11.796 --> 00:24:13.720 of prematurity seen in this each
NOTE Confidence: 0.893989376

00:24:13.720 --> 00:24:15.673 group there were two babies with neck
NOTE Confidence: 0.779949344

00:24:15.680 --> 00:24:17.600 and one baby with sepsis.
NOTE Confidence: 0.784130544285714

00:24:19.680 --> 00:24:20.716 And so of course then we asked,
NOTE Confidence: 0.784130544285714

00:24:20.720 --> 00:24:22.484 can we really do this, right?
NOTE Confidence: 0.784130544285714

00:24:22.484 --> 00:24:26.120 So we took all of this blood and coordinated
NOTE Confidence: 0.784130544285714

00:24:26.205 --> 00:24:28.200 thawing all of these samples all together,
NOTE Confidence: 0.784130544285714

00:24:28.200 --> 00:24:29.880 splitting them and running
NOTE Confidence: 0.784130544285714

00:24:29.880 --> 00:24:31.560 all these separate assays.
NOTE Confidence: 0.784130544285714

00:24:31.560 --> 00:24:33.780 And we were incredibly excited to

NOTE Confidence: 0.784130544285714
00:24:33.780 --> 00:24:36.160 see that it actually didn't work.
NOTE Confidence: 0.784130544285714
00:24:36.160 --> 00:24:39.520 So this is cumulative data on the 30
NOTE Confidence: 0.784130544285714
00:24:39.520 --> 00:24:43.153 samples from the preterm peripheral blood,
NOTE Confidence: 0.784130544285714
00:24:43.153 --> 00:24:45.118 cord blood and adult samples.
NOTE Confidence: 0.784130544285714
00:24:45.120 --> 00:24:47.840 All together, the top is the site of,
NOTE Confidence: 0.784130544285714
00:24:47.840 --> 00:24:49.919 so we're looking at the proteins here.
NOTE Confidence: 0.784130544285714
00:24:49.920 --> 00:24:51.920 At the bottom is the single cell seek.
NOTE Confidence: 0.784130544285714
00:24:51.920 --> 00:24:53.696 We're looking at transcriptomics
NOTE Confidence: 0.784130544285714
00:24:53.696 --> 00:24:56.360 and this is just abundance of
NOTE Confidence: 0.784130544285714
00:24:56.433 --> 00:24:58.726 the various populations across
NOTE Confidence: 0.784130544285714
00:24:58.726 --> 00:25:01.956 longitudinally and preterm core blood,
NOTE Confidence: 0.784130544285714
00:25:01.960 --> 00:25:03.640 term core blood in adults.
NOTE Confidence: 0.784130544285714
00:25:03.640 --> 00:25:05.740 You can see that overall there's
NOTE Confidence: 0.784130544285714
00:25:05.740 --> 00:25:07.533 actually very similar representation in
NOTE Confidence: 0.784130544285714
00:25:07.533 --> 00:25:09.564 both transcriptomic part and protein
NOTE Confidence: 0.784130544285714

00:25:09.564 --> 00:25:12.074 part of the various populations.
NOTE Confidence: 0.784130544285714

00:25:12.080 --> 00:25:14.201 Things that really jump out right away
NOTE Confidence: 0.784130544285714

00:25:14.201 --> 00:25:16.708 is that the adult blood is definitely
NOTE Confidence: 0.784130544285714

00:25:16.708 --> 00:25:19.634 different from all of the neonatal blood.
NOTE Confidence: 0.784130544285714

00:25:19.634 --> 00:25:21.519 There's a much bigger population.
NOTE Confidence: 0.784130544285714

00:25:21.520 --> 00:25:23.280 These are memory CDAT cells
NOTE Confidence: 0.784130544285714

00:25:23.280 --> 00:25:25.040 and purple in both places.
NOTE Confidence: 0.784130544285714

00:25:25.040 --> 00:25:27.392 There's a much bigger
NOTE Confidence: 0.784130544285714

00:25:27.392 --> 00:25:29.156 memory population there,
NOTE Confidence: 0.784130544285714

00:25:29.160 --> 00:25:31.680 but the sort of the preterm cord blood,
NOTE Confidence: 0.784130544285714

00:25:31.680 --> 00:25:32.916 at least from the big picture,
NOTE Confidence: 0.784130544285714

00:25:32.920 --> 00:25:35.140 looks pretty similar to term cord
NOTE Confidence: 0.784130544285714

00:25:35.140 --> 00:25:37.106 blood and actually fairly similar
NOTE Confidence: 0.784130544285714

00:25:37.106 --> 00:25:39.196 to all the longitudinal samples.
NOTE Confidence: 0.784130544285714

00:25:39.200 --> 00:25:41.408 What if we zoom in on all of
NOTE Confidence: 0.784130544285714

00:25:41.408 --> 00:25:42.800 the individual populations,

NOTE Confidence: 0.784130544285714
00:25:42.800 --> 00:25:43.114 right?
NOTE Confidence: 0.784130544285714
00:25:43.114 --> 00:25:44.998 This is single cell data looking
NOTE Confidence: 0.784130544285714
00:25:44.998 --> 00:25:47.028 at just the monocytes and this
NOTE Confidence: 0.784130544285714
00:25:47.028 --> 00:25:49.080 is part of the innate immunity.
NOTE Confidence: 0.784130544285714
00:25:49.080 --> 00:25:51.103 You can see majority of the cells
NOTE Confidence: 0.784130544285714
00:25:51.103 --> 00:25:53.171 in the blood are either monocytes
NOTE Confidence: 0.784130544285714
00:25:53.171 --> 00:25:55.433 or NC is non classical monocytes.
NOTE Confidence: 0.784130544285714
00:25:55.440 --> 00:25:57.798 There's a little bit of macrophages,
NOTE Confidence: 0.784130544285714
00:25:57.800 --> 00:25:59.725 there's a little bit of DCS,
NOTE Confidence: 0.784130544285714
00:25:59.725 --> 00:26:01.915 both that's sort of the classical
NOTE Confidence: 0.784130544285714
00:26:01.915 --> 00:26:04.399 DCS and the plasma cytoid DCS.
NOTE Confidence: 0.784130544285714
00:26:04.400 --> 00:26:05.800 And then there's this population
NOTE Confidence: 0.784130544285714
00:26:05.800 --> 00:26:07.200 that I briefly mentioned before,
NOTE Confidence: 0.784130544285714
00:26:07.200 --> 00:26:08.980 which is myeloid deprive suppressive
NOTE Confidence: 0.784130544285714
00:26:08.980 --> 00:26:11.400 cells and that's a unique population
NOTE Confidence: 0.784130544285714

00:26:11.400 --> 00:26:14.190 that's really much more abundant in
NOTE Confidence: 0.784130544285714

00:26:14.190 --> 00:26:17.121 the units that's really thought to
NOTE Confidence: 0.784130544285714

00:26:17.121 --> 00:26:20.079 inhibit how the immune system responds.
NOTE Confidence: 0.784130544285714

00:26:20.080 --> 00:26:21.392 We can then, sorry,
NOTE Confidence: 0.784130544285714

00:26:21.392 --> 00:26:23.032 I'm missing all the legends.
NOTE Confidence: 0.784130544285714

00:26:23.040 --> 00:26:24.080 I'm going to do this.
NOTE Confidence: 0.784130544285714

00:26:24.080 --> 00:26:26.344 We can then look to see what is
NOTE Confidence: 0.784130544285714

00:26:26.344 --> 00:26:28.118 the progression of these cells from
NOTE Confidence: 0.784130544285714

00:26:28.120 --> 00:26:29.814 sort of pre term from cord blood
NOTE Confidence: 0.784130544285714

00:26:29.814 --> 00:26:31.757 all the way to two months of age.
NOTE Confidence: 0.784130544285714

00:26:31.760 --> 00:26:33.520 Those are the samples that we first used.
NOTE Confidence: 0.784130544285714

00:26:33.520 --> 00:26:35.599 You can see that overall there's a
NOTE Confidence: 0.784130544285714

00:26:35.599 --> 00:26:37.758 little bit of a peak at about one
NOTE Confidence: 0.784130544285714

00:26:37.758 --> 00:26:39.518 week of the monocyte populations,
NOTE Confidence: 0.784130544285714

00:26:39.518 --> 00:26:42.113 but there's two populations in
NOTE Confidence: 0.784130544285714

00:26:42.113 --> 00:26:45.100 particular that really change across

NOTE Confidence: 0.784130544285714
00:26:45.100 --> 00:26:47.240 the first two months of life.
NOTE Confidence: 0.784130544285714
00:26:47.240 --> 00:26:49.200 One of those is the dendritic cells.
NOTE Confidence: 0.784130544285714
00:26:49.200 --> 00:26:51.216 The dendritic cells are really key
NOTE Confidence: 0.784130544285714
00:26:51.216 --> 00:26:53.838 it to priming T cells and I'll show
NOTE Confidence: 0.784130544285714
00:26:53.838 --> 00:26:56.262 you in a couple of slides T cell
NOTE Confidence: 0.784130544285714
00:26:56.262 --> 00:26:58.540 data that this increase in dendritic
NOTE Confidence: 0.784130544285714
00:26:58.540 --> 00:27:00.280 cells goes beautifully with.
NOTE Confidence: 0.784130544285714
00:27:00.280 --> 00:27:03.008 And the other part that I thought was
NOTE Confidence: 0.784130544285714
00:27:03.008 --> 00:27:04.524 incredibly interesting is that for
NOTE Confidence: 0.784130544285714
00:27:04.524 --> 00:27:07.079 sure you can see that adult blood has no MDS,
NOTE Confidence: 0.784130544285714
00:27:07.079 --> 00:27:08.874 CS or myeloid derived suppressor
NOTE Confidence: 0.784130544285714
00:27:08.874 --> 00:27:11.223 cells which is sort of known term.
NOTE Confidence: 0.784130544285714
00:27:11.223 --> 00:27:13.624 Cord blood which has been previously shown
NOTE Confidence: 0.784130544285714
00:27:13.624 --> 00:27:15.759 certainly has much more of these cells.
NOTE Confidence: 0.784130544285714
00:27:15.760 --> 00:27:17.074 But if you look at pre terminal cord blood,
NOTE Confidence: 0.79366473625

00:27:17.080 --> 00:27:20.370 it's actually almost non existent in cord
NOTE Confidence: 0.79366473625

00:27:20.370 --> 00:27:23.736 blood and perhaps This is why there's so
NOTE Confidence: 0.79366473625

00:27:23.736 --> 00:27:26.312 much more inflammation in the preterm infant.
NOTE Confidence: 0.79366473625

00:27:26.320 --> 00:27:29.624 It does go up with age. It peaks at about
NOTE Confidence: 0.79366473625

00:27:29.624 --> 00:27:31.600 one month of age in these preemies,
NOTE Confidence: 0.79366473625

00:27:31.600 --> 00:27:33.133 but it actually never makes it to
NOTE Confidence: 0.79366473625

00:27:33.133 --> 00:27:34.759 the same level as in the term cord.
NOTE Confidence: 0.79366473625

00:27:34.760 --> 00:27:39.920 Look, what about some other populations?
NOTE Confidence: 0.79366473625

00:27:39.920 --> 00:27:41.960 NK cells are one of those population that
NOTE Confidence: 0.79366473625

00:27:41.960 --> 00:27:44.538 sort of lives in between the innate and the
NOTE Confidence: 0.79366473625

00:27:44.538 --> 00:27:46.600 adaptive world that I pointed out earlier.
NOTE Confidence: 0.79366473625

00:27:46.600 --> 00:27:49.078 There's various subtypes of NK populations.
NOTE Confidence: 0.79366473625

00:27:49.080 --> 00:27:50.676 I don't think that matters here,
NOTE Confidence: 0.79366473625

00:27:50.680 --> 00:27:52.150 but I think what's important here is
NOTE Confidence: 0.79366473625

00:27:52.150 --> 00:27:53.920 you can see that this is adult blood,
NOTE Confidence: 0.79366473625

00:27:53.920 --> 00:27:56.560 which is sort of this dot in black.

NOTE Confidence: 0.79366473625

00:27:56.560 --> 00:27:58.920 They're pretty low in the blood in adults.

NOTE Confidence: 0.79366473625

00:27:58.920 --> 00:27:59.988 They are much,

NOTE Confidence: 0.79366473625

00:27:59.988 --> 00:28:02.980 much higher in the blood of both in the

NOTE Confidence: 0.79366473625

00:28:02.980 --> 00:28:04.730 cord blood in particular in both term

NOTE Confidence: 0.79366473625

00:28:04.730 --> 00:28:06.778 and pre term infants and they rapidly

NOTE Confidence: 0.79366473625

00:28:06.778 --> 00:28:08.670 decline over the first two months of

NOTE Confidence: 0.79366473625

00:28:08.670 --> 00:28:10.545 age where they sort of by two months.

NOTE Confidence: 0.79366473625

00:28:10.545 --> 00:28:12.375 They're pretty much equal to what

NOTE Confidence: 0.79366473625

00:28:12.375 --> 00:28:13.760 is seen in adults.

NOTE Confidence: 0.79366473625

00:28:13.760 --> 00:28:15.740 And this population is probably

NOTE Confidence: 0.79366473625

00:28:15.740 --> 00:28:18.800 performing a lot of the functions that

NOTE Confidence: 0.79366473625

00:28:18.800 --> 00:28:22.160 classically CD8T cells would do if

NOTE Confidence: 0.79366473625

00:28:22.160 --> 00:28:25.118 because we had also transcriptional data,

NOTE Confidence: 0.79366473625

00:28:25.120 --> 00:28:27.500 we can look to see what signatures

NOTE Confidence: 0.79366473625

00:28:27.500 --> 00:28:30.033 are enriched for in the preterm cord

NOTE Confidence: 0.79366473625

00:28:30.033 --> 00:28:32.193 blood compared to term cord blood.
NOTE Confidence: 0.79366473625

00:28:32.200 --> 00:28:34.727 And all of these boxes that I
NOTE Confidence: 0.79366473625

00:28:34.727 --> 00:28:37.160 have outlined in red like CD69,
NOTE Confidence: 0.79366473625

00:28:37.160 --> 00:28:39.080 XCL one, etcetera,
NOTE Confidence: 0.79366473625

00:28:39.080 --> 00:28:41.000 they're all associated
NOTE Confidence: 0.79366473625

00:28:41.000 --> 00:28:43.644 with function of NK cells.
NOTE Confidence: 0.79366473625

00:28:43.644 --> 00:28:46.540 And it looks like the preterm cord blood
NOTE Confidence: 0.79366473625

00:28:46.614 --> 00:28:49.092 and K cells are much more activated
NOTE Confidence: 0.79366473625

00:28:49.092 --> 00:28:52.120 and much more functional than term
NOTE Confidence: 0.79366473625

00:28:52.120 --> 00:28:55.600 cord bladder or even adult cells.
NOTE Confidence: 0.79366473625

00:28:55.600 --> 00:28:56.812 We can also look,
NOTE Confidence: 0.79366473625

00:28:56.812 --> 00:28:58.327 because we have information on
NOTE Confidence: 0.79366473625

00:28:58.327 --> 00:29:00.237 so many different cell types,
NOTE Confidence: 0.79366473625

00:29:00.240 --> 00:29:02.792 we can also look to see which cells
NOTE Confidence: 0.79366473625

00:29:02.792 --> 00:29:04.927 interact with which ones and how
NOTE Confidence: 0.79366473625

00:29:04.927 --> 00:29:06.799 is that different between preemies

NOTE Confidence: 0.79366473625

00:29:06.799 --> 00:29:09.433 and adult samples or preterm cord

NOTE Confidence: 0.79366473625

00:29:09.433 --> 00:29:11.680 blood and term cord blood.

NOTE Confidence: 0.79366473625

00:29:11.680 --> 00:29:12.796 And what you can see here,

NOTE Confidence: 0.79366473625

00:29:12.800 --> 00:29:14.456 particularly for NK cells,

NOTE Confidence: 0.79366473625

00:29:14.456 --> 00:29:16.940 there's much more interaction of NK

NOTE Confidence: 0.79366473625

00:29:17.008 --> 00:29:19.480 cells with a lot of other cell types,

NOTE Confidence: 0.79366473625

00:29:19.480 --> 00:29:22.035 particularly early on in life

NOTE Confidence: 0.79366473625

00:29:22.035 --> 00:29:24.079 than compared to adults.

NOTE Confidence: 0.79366473625

00:29:24.080 --> 00:29:26.328 You can see NK cells and preemies interact

NOTE Confidence: 0.79366473625

00:29:26.328 --> 00:29:28.440 with all other cell types much more.

NOTE Confidence: 0.79366473625

00:29:28.440 --> 00:29:30.918 So something that's red is increased

NOTE Confidence: 0.79366473625

00:29:30.918 --> 00:29:33.084 interaction much more than in adults.

NOTE Confidence: 0.79366473625

00:29:33.084 --> 00:29:34.932 The graph here is showing the

NOTE Confidence: 0.79366473625

00:29:34.932 --> 00:29:36.760 the number of interactions.

NOTE Confidence: 0.79366473625

00:29:36.760 --> 00:29:38.115 The graphs here is showing

NOTE Confidence: 0.79366473625

00:29:38.115 --> 00:29:39.199 the strength of interactions.
NOTE Confidence: 0.79366473625

00:29:39.200 --> 00:29:41.286 And so there's an increase of NK
NOTE Confidence: 0.79366473625

00:29:41.286 --> 00:29:43.557 interaction both in number and in strength.
NOTE Confidence: 0.79366473625

00:29:43.560 --> 00:29:46.998 Well, what about the adaptive immune cells,
NOTE Confidence: 0.79366473625

00:29:47.000 --> 00:29:47.385 right.
NOTE Confidence: 0.79366473625

00:29:47.385 --> 00:29:49.695 And so early on it suggested
NOTE Confidence: 0.79366473625

00:29:49.695 --> 00:29:52.038 that maybe at least in mice,
NOTE Confidence: 0.79366473625

00:29:52.040 --> 00:29:55.750 there's very few memory adoptive
NOTE Confidence: 0.79366473625

00:29:55.750 --> 00:29:57.234 cells present.
NOTE Confidence: 0.79366473625

00:29:57.240 --> 00:29:58.320 If you look at blood,
NOTE Confidence: 0.79366473625

00:29:58.320 --> 00:30:01.280 this is single cell data,
NOTE Confidence: 0.79366473625

00:30:01.280 --> 00:30:03.480 certainly in term CRO blood,
NOTE Confidence: 0.79366473625

00:30:03.480 --> 00:30:05.664 almost all of it is and those
NOTE Confidence: 0.79366473625

00:30:05.664 --> 00:30:06.600 are naive cells.
NOTE Confidence: 0.79366473625

00:30:06.600 --> 00:30:09.456 So similarly to mice term CRO blood
NOTE Confidence: 0.79366473625

00:30:09.456 --> 00:30:11.718 stems will actually have very few

NOTE Confidence: 0.863752877272727
00:30:14.640 --> 00:30:16.638 memory cells in the memory cells
NOTE Confidence: 0.863752877272727
00:30:16.638 --> 00:30:18.760 here in this green population.
NOTE Confidence: 0.863752877272727
00:30:18.760 --> 00:30:20.520 But if you sort of focus on this,
NOTE Confidence: 0.863752877272727
00:30:20.520 --> 00:30:22.656 this preterm for blood actually has
NOTE Confidence: 0.863752877272727
00:30:22.656 --> 00:30:25.391 a pretty good amount of both B1 and
NOTE Confidence: 0.863752877272727
00:30:25.391 --> 00:30:27.257 those are specialized B cells that
NOTE Confidence: 0.863752877272727
00:30:27.329 --> 00:30:29.721 actually secrete antigen independent
NOTE Confidence: 0.863752877272727
00:30:29.721 --> 00:30:34.560 antibodies and memory B cells.
NOTE Confidence: 0.863752877272727
00:30:34.560 --> 00:30:36.625 If we zoom in and look at
NOTE Confidence: 0.863752877272727
00:30:36.625 --> 00:30:37.888 particular populations to see
NOTE Confidence: 0.863752877272727
00:30:37.888 --> 00:30:39.478 how this is changing overall,
NOTE Confidence: 0.863752877272727
00:30:39.480 --> 00:30:41.310 these cell numbers are actually
NOTE Confidence: 0.863752877272727
00:30:41.310 --> 00:30:43.959 very stable both in in cord blood,
NOTE Confidence: 0.863752877272727
00:30:43.960 --> 00:30:45.745 preterm cord blood and longitudinal
NOTE Confidence: 0.863752877272727
00:30:45.745 --> 00:30:48.500 sample that seems to be sort of pretty
NOTE Confidence: 0.863752877272727

00:30:48.500 --> 00:30:50.725 much defined between 5 and 10% regardless

NOTE Confidence: 0.863752877272727

00:30:50.725 --> 00:30:53.155 of what sample you're looking at.

NOTE Confidence: 0.863752877272727

00:30:53.160 --> 00:30:53.916 Plasma cells,

NOTE Confidence: 0.863752877272727

00:30:53.916 --> 00:30:55.806 those are the antibody producing

NOTE Confidence: 0.863752877272727

00:30:55.806 --> 00:30:57.960 cells similar to what we had

NOTE Confidence: 0.863752877272727

00:30:57.960 --> 00:30:59.880 thought are incredibly low at birth,

NOTE Confidence: 0.863752877272727

00:30:59.880 --> 00:31:01.456 much lower than adults.

NOTE Confidence: 0.863752877272727

00:31:01.456 --> 00:31:03.820 But then interestingly they actually go

NOTE Confidence: 0.863752877272727

00:31:03.888 --> 00:31:06.336 up pretty quickly and by one month of

NOTE Confidence: 0.863752877272727

00:31:06.336 --> 00:31:08.959 age they're fairly similar to adult levels.

NOTE Confidence: 0.863752877272727

00:31:08.960 --> 00:31:10.760 And then we found this interesting

NOTE Confidence: 0.863752877272727

00:31:10.760 --> 00:31:11.960 population that we're calling,

NOTE Confidence: 0.863752877272727

00:31:11.960 --> 00:31:13.100 sorry it's misspelled,

NOTE Confidence: 0.863752877272727

00:31:13.100 --> 00:31:15.000 we're calling immature B cells.

NOTE Confidence: 0.863752877272727

00:31:15.000 --> 00:31:17.120 These are B cell precursors.

NOTE Confidence: 0.863752877272727

00:31:17.120 --> 00:31:19.605 They are very high in term coral

NOTE Confidence: 0.863752877272727
00:31:19.605 --> 00:31:22.560 blood and they're much lower in
NOTE Confidence: 0.863752877272727
00:31:22.560 --> 00:31:24.357 peripheral preemie samples and
NOTE Confidence: 0.863752877272727
00:31:24.357 --> 00:31:26.016 when Boomi looked to see if they're
NOTE Confidence: 0.863752877272727
00:31:26.016 --> 00:31:27.239 correlate with gestational age,
NOTE Confidence: 0.863752877272727
00:31:27.240 --> 00:31:29.604 you can see this beautiful correlation
NOTE Confidence: 0.863752877272727
00:31:29.604 --> 00:31:32.520 that these cells go up with gestation.
NOTE Confidence: 0.863752877272727
00:31:32.520 --> 00:31:33.624 We don't know what the function
NOTE Confidence: 0.863752877272727
00:31:33.624 --> 00:31:34.360 of these cells are,
NOTE Confidence: 0.863752877272727
00:31:34.360 --> 00:31:36.796 but they seem to be at least
NOTE Confidence: 0.863752877272727
00:31:36.800 --> 00:31:40.040 gestationally regulated.
NOTE Confidence: 0.863752877272727
00:31:40.040 --> 00:31:42.440 If we then look at to see is
NOTE Confidence: 0.863752877272727
00:31:42.440 --> 00:31:44.256 there some increased clonality
NOTE Confidence: 0.863752877272727
00:31:44.256 --> 00:31:47.960 suggesting that there is some memory
NOTE Confidence: 0.863752877272727
00:31:47.960 --> 00:31:50.840 formation and various samples,
NOTE Confidence: 0.863752877272727
00:31:50.840 --> 00:31:53.696 it does look like there is at least
NOTE Confidence: 0.863752877272727

00:31:53.696 --> 00:31:56.108 some degree of memory formation and
NOTE Confidence: 0.863752877272727

00:31:56.108 --> 00:31:58.684 early on this is looking at the various
NOTE Confidence: 0.863752877272727

00:31:58.684 --> 00:32:00.531 cell types and how many different
NOTE Confidence: 0.863752877272727

00:32:00.531 --> 00:32:02.757 B cell clones have an expansion.
NOTE Confidence: 0.863752877272727

00:32:02.760 --> 00:32:05.272 The red here is more than 4B cells
NOTE Confidence: 0.863752877272727

00:32:05.272 --> 00:32:07.437 found with the exact same clone,
NOTE Confidence: 0.863752877272727

00:32:07.440 --> 00:32:08.860 suggesting they all come from
NOTE Confidence: 0.863752877272727

00:32:08.860 --> 00:32:09.996 the same mother cell.
NOTE Confidence: 0.863752877272727

00:32:10.000 --> 00:32:13.600 You can see that's highest than B1 cells.
NOTE Confidence: 0.863752877272727

00:32:13.600 --> 00:32:15.880 But even if we look at various samples,
NOTE Confidence: 0.863752877272727

00:32:15.880 --> 00:32:17.344 even the charcoal blood,
NOTE Confidence: 0.863752877272727

00:32:17.344 --> 00:32:20.405 the pre charcoal blood and one week samples
NOTE Confidence: 0.863752877272727

00:32:20.405 --> 00:32:23.198 all have some degree of clonal expansion.
NOTE Confidence: 0.863752877272727

00:32:23.200 --> 00:32:25.640 What about T cells?
NOTE Confidence: 0.863752877272727

00:32:25.640 --> 00:32:27.733 So it is, if you remember when
NOTE Confidence: 0.863752877272727

00:32:27.733 --> 00:32:29.759 I talked about the naive cells,

NOTE Confidence: 0.863752877272727
00:32:29.760 --> 00:32:31.880 there was a peak of D CS right
NOTE Confidence: 0.863752877272727
00:32:31.880 --> 00:32:33.319 around one month of age.
NOTE Confidence: 0.863752877272727
00:32:33.320 --> 00:32:34.704 What we see here,
NOTE Confidence: 0.863752877272727
00:32:34.704 --> 00:32:36.434 these are proliferating T cells.
NOTE Confidence: 0.863752877272727
00:32:36.440 --> 00:32:36.818 Again,
NOTE Confidence: 0.863752877272727
00:32:36.818 --> 00:32:38.330 there's a huge proliferation
NOTE Confidence: 0.863752877272727
00:32:38.330 --> 00:32:40.560 at about one month of age.
NOTE Confidence: 0.863752877272727
00:32:40.560 --> 00:32:42.592 So both the Apcs that are going to
NOTE Confidence: 0.863752877272727
00:32:42.592 --> 00:32:44.763 prime the T cells and the T cells
NOTE Confidence: 0.863752877272727
00:32:44.763 --> 00:32:46.572 themselves are sort of increasing in
NOTE Confidence: 0.863752877272727
00:32:46.572 --> 00:32:48.959 their number right around the same age.
NOTE Confidence: 0.863752877272727
00:32:48.960 --> 00:32:51.732 This is just looking at the
NOTE Confidence: 0.863752877272727
00:32:51.732 --> 00:32:53.118 various populations across.
NOTE Confidence: 0.863752877272727
00:32:53.120 --> 00:32:55.017 You can see that this is quite
NOTE Confidence: 0.863752877272727
00:32:55.017 --> 00:32:56.817 different from the B cells in the
NOTE Confidence: 0.863752877272727

00:32:56.817 --> 00:32:59.140 sense that of course there is more
NOTE Confidence: 0.863752877272727

00:32:59.140 --> 00:33:01.878 naive T cells present early on in life.
NOTE Confidence: 0.863752877272727

00:33:01.880 --> 00:33:03.985 But there's already memory formation
NOTE Confidence: 0.863752877272727

00:33:03.985 --> 00:33:07.518 both in the CD 8 and the CD4 pool,
NOTE Confidence: 0.863752877272727

00:33:07.520 --> 00:33:08.840 very early on in life,
NOTE Confidence: 0.863752877272727

00:33:08.840 --> 00:33:10.552 in the preterm cordblad
NOTE Confidence: 0.863752877272727

00:33:10.552 --> 00:33:11.836 and longitudinal samples.
NOTE Confidence: 0.863752877272727

00:33:11.840 --> 00:33:13.688 And really by about two-month of
NOTE Confidence: 0.863752877272727

00:33:13.688 --> 00:33:15.737 eight you have a pretty large
NOTE Confidence: 0.863752877272727

00:33:15.737 --> 00:33:17.999 expansion of your memory cell pool.
NOTE Confidence: 0.851232338333333

00:33:18.000 --> 00:33:20.520 Sorry, this is showing up blurry.
NOTE Confidence: 0.851232338333333

00:33:20.520 --> 00:33:22.802 But you can see sort of correlating
NOTE Confidence: 0.851232338333333

00:33:22.802 --> 00:33:25.336 with this expansion at one month of
NOTE Confidence: 0.851232338333333

00:33:25.336 --> 00:33:28.077 age of overall T cell proliferation,
NOTE Confidence: 0.851232338333333

00:33:28.080 --> 00:33:31.437 a number of different T cell subtypes go up.
NOTE Confidence: 0.851232338333333

00:33:31.440 --> 00:33:34.674 So regulatory T cells certainly go up

NOTE Confidence: 0.851232338333333
00:33:34.680 --> 00:33:36.213 and that's sort of been the predominant
NOTE Confidence: 0.851232338333333
00:33:36.213 --> 00:33:37.559 thought in the nудial immunity.
NOTE Confidence: 0.851232338333333
00:33:37.560 --> 00:33:40.188 But if you look to see their proportion is
NOTE Confidence: 0.851232338333333
00:33:40.188 --> 00:33:42.144 actually significantly higher than adults,
NOTE Confidence: 0.851232338333333
00:33:42.144 --> 00:33:45.024 right, about 6% versus 3%.
NOTE Confidence: 0.851232338333333
00:33:45.024 --> 00:33:48.720 But overall they're still quite rare.
NOTE Confidence: 0.851232338333333
00:33:48.720 --> 00:33:50.560 Majority of these are naive
NOTE Confidence: 0.851232338333333
00:33:50.560 --> 00:33:52.560 CD4T cells or effector cells,
NOTE Confidence: 0.851232338333333
00:33:52.560 --> 00:33:54.672 and those again peak at around
NOTE Confidence: 0.851232338333333
00:33:54.672 --> 00:33:56.080 one month of age.
NOTE Confidence: 0.851232338333333
00:33:56.080 --> 00:33:57.760 But if you look at memory cells,
NOTE Confidence: 0.851232338333333
00:33:57.760 --> 00:33:59.500 these are activated effector
NOTE Confidence: 0.851232338333333
00:33:59.500 --> 00:34:01.240 memory or essential memory.
NOTE Confidence: 0.851232338333333
00:34:01.240 --> 00:34:03.448 They also both go up at
NOTE Confidence: 0.851232338333333
00:34:03.448 --> 00:34:05.360 about one month of age.
NOTE Confidence: 0.851232338333333

00:34:05.360 --> 00:34:07.358 These are the same central memory
NOTE Confidence: 0.851232338333333

00:34:07.358 --> 00:34:09.592 cells that are or at least similar
NOTE Confidence: 0.851232338333333

00:34:09.592 --> 00:34:11.645 to what Tippy Mckenzie's group had
NOTE Confidence: 0.851232338333333

00:34:11.645 --> 00:34:13.520 identified in preterm cord blood.
NOTE Confidence: 0.851232338333333

00:34:13.520 --> 00:34:15.340 And you can see although our numbers
NOTE Confidence: 0.851232338333333

00:34:15.340 --> 00:34:16.759 are much smaller than cohort,
NOTE Confidence: 0.851232338333333

00:34:16.760 --> 00:34:17.786 this isn't significant.
NOTE Confidence: 0.851232338333333

00:34:17.786 --> 00:34:20.547 We see the same trend that preterm cord
NOTE Confidence: 0.851232338333333

00:34:20.547 --> 00:34:22.689 blood has almost twice as many central
NOTE Confidence: 0.851232338333333

00:34:22.689 --> 00:34:24.957 memory T cells than term cord blood.
NOTE Confidence: 0.901690894166667

00:34:27.040 --> 00:34:28.904 What about clonal expansion?
NOTE Confidence: 0.901690894166667

00:34:28.904 --> 00:34:32.754 We can see that by two-month of age, right?
NOTE Confidence: 0.901690894166667

00:34:32.754 --> 00:34:35.512 There's a this blue group here is
NOTE Confidence: 0.901690894166667

00:34:35.512 --> 00:34:37.720 the effect of memory CD8T cells.
NOTE Confidence: 0.901690894166667

00:34:37.720 --> 00:34:39.640 There's quite a lot of them.
NOTE Confidence: 0.901690894166667

00:34:39.640 --> 00:34:42.040 But if we separate out the

NOTE Confidence: 0.901690894166667
00:34:42.040 --> 00:34:43.640 preterm cord blood samples,
NOTE Confidence: 0.901690894166667
00:34:43.640 --> 00:34:45.700 there's different responses and different
NOTE Confidence: 0.901690894166667
00:34:45.700 --> 00:34:48.804 infants and some of them have a lot
NOTE Confidence: 0.901690894166667
00:34:48.804 --> 00:34:51.240 of memory T cells present at birth.
NOTE Confidence: 0.901690894166667
00:34:51.240 --> 00:34:53.195 And this particular infant here
NOTE Confidence: 0.901690894166667
00:34:53.195 --> 00:34:54.759 was exposed to chorionitis,
NOTE Confidence: 0.901690894166667
00:34:54.760 --> 00:34:57.688 suggesting that maybe the uterine infection
NOTE Confidence: 0.901690894166667
00:34:57.688 --> 00:35:00.360 is really inducing memory T cells.
NOTE Confidence: 0.82419007375
00:35:02.560 --> 00:35:05.535 And then finally we look to see
NOTE Confidence: 0.82419007375
00:35:05.535 --> 00:35:07.990 is sort of more of a concept of
NOTE Confidence: 0.82419007375
00:35:07.990 --> 00:35:09.680 trained immunity that I introduced.
NOTE Confidence: 0.82419007375
00:35:09.680 --> 00:35:12.500 Are there alterations in immune responses
NOTE Confidence: 0.82419007375
00:35:12.500 --> 00:35:15.947 in kids that had been exposed to
NOTE Confidence: 0.82419007375
00:35:15.947 --> 00:35:18.917 chorionitis versus those that have not?
NOTE Confidence: 0.82419007375
00:35:18.920 --> 00:35:21.224 And so Buni took all of the features that
NOTE Confidence: 0.82419007375

00:35:21.224 --> 00:35:23.874 we were able to identify and did APCA plot.
NOTE Confidence: 0.82419007375

00:35:23.880 --> 00:35:26.080 And you can see that the ones in
NOTE Confidence: 0.82419007375

00:35:26.080 --> 00:35:27.977 blue had no chorionitis exposure.
NOTE Confidence: 0.82419007375

00:35:27.977 --> 00:35:30.673 In the ones in green really had Choria,
NOTE Confidence: 0.82419007375

00:35:30.680 --> 00:35:32.420 the Munitis exposure,
NOTE Confidence: 0.82419007375

00:35:32.420 --> 00:35:34.160 they're separating beautifully
NOTE Confidence: 0.82419007375

00:35:34.160 --> 00:35:36.920 and that if we look at the immune
NOTE Confidence: 0.82419007375

00:35:36.920 --> 00:35:41.040 subtypes in those samples,
NOTE Confidence: 0.82419007375

00:35:41.040 --> 00:35:43.700 certainly starting at one at one week
NOTE Confidence: 0.82419007375

00:35:43.700 --> 00:35:45.920 but persisting pretty is at least by one
NOTE Confidence: 0.82419007375

00:35:45.920 --> 00:35:48.077 month age if not by two months of age.
NOTE Confidence: 0.82419007375

00:35:48.080 --> 00:35:50.192 Their immune systems are actually quite
NOTE Confidence: 0.82419007375

00:35:50.192 --> 00:35:52.639 different if they had initial exposure.
NOTE Confidence: 0.82419007375

00:35:52.640 --> 00:35:55.864 And then she could look to see what's
NOTE Confidence: 0.82419007375

00:35:55.864 --> 00:35:58.799 correlated best with coriomonitis exposure.
NOTE Confidence: 0.82419007375

00:35:58.800 --> 00:36:00.980 And the thing that came up on top is the

NOTE Confidence: 0.82419007375

00:36:01.035 --> 00:36:03.159 central membrane CD4 activated T cells.

NOTE Confidence: 0.82419007375

00:36:03.160 --> 00:36:05.602 Again the the cells that Tippy

NOTE Confidence: 0.82419007375

00:36:05.602 --> 00:36:07.781 McKenzie had first identified as

NOTE Confidence: 0.82419007375

00:36:07.781 --> 00:36:10.156 potentially important to preterm labor.

NOTE Confidence: 0.82419007375

00:36:10.160 --> 00:36:12.470 And if we look at different cell

NOTE Confidence: 0.82419007375

00:36:12.470 --> 00:36:13.980 types separated by different cell

NOTE Confidence: 0.82419007375

00:36:13.980 --> 00:36:15.160 types at different ages,

NOTE Confidence: 0.82419007375

00:36:15.160 --> 00:36:17.785 you can see that there this sort

NOTE Confidence: 0.82419007375

00:36:17.785 --> 00:36:20.086 of increase in the number of cell

NOTE Confidence: 0.82419007375

00:36:20.086 --> 00:36:21.695 types including central memory cells

NOTE Confidence: 0.82419007375

00:36:21.695 --> 00:36:23.799 is present at one week of age but

NOTE Confidence: 0.82419007375

00:36:23.799 --> 00:36:25.518 persistent throughout at least the two

NOTE Confidence: 0.82419007375

00:36:25.518 --> 00:36:28.552 months time point that we looked at.

NOTE Confidence: 0.82419007375

00:36:28.552 --> 00:36:31.000 So in summary,

NOTE Confidence: 0.82419007375

00:36:31.000 --> 00:36:32.953 I hope I've convinced you that immune

NOTE Confidence: 0.82419007375

00:36:32.953 --> 00:36:34.963 dynamics are the first two months of
NOTE Confidence: 0.82419007375

00:36:34.963 --> 00:36:37.160 life and preterm babies are highly variable.
NOTE Confidence: 0.82419007375

00:36:37.160 --> 00:36:38.510 Myeloid cells are high in
NOTE Confidence: 0.82419007375

00:36:38.510 --> 00:36:39.320 preterm peripheral blood,
NOTE Confidence: 0.82419007375

00:36:39.320 --> 00:36:41.216 then poor blood with a huge
NOTE Confidence: 0.82419007375

00:36:41.216 --> 00:36:43.369 expansion in DCS and myeloid derived
NOTE Confidence: 0.82419007375

00:36:43.369 --> 00:36:45.829 suppressor cells at one month time
NOTE Confidence: 0.82419007375

00:36:45.829 --> 00:36:48.478 point and K cells are abundant with
NOTE Confidence: 0.82419007375

00:36:48.478 --> 00:36:49.597 increased functional signature.
NOTE Confidence: 0.82419007375

00:36:49.600 --> 00:36:51.312 But although B&T cells
NOTE Confidence: 0.82419007375

00:36:51.312 --> 00:36:52.596 are predominantly naive,
NOTE Confidence: 0.82419007375

00:36:52.600 --> 00:36:55.600 there are particular memory T cells
NOTE Confidence: 0.82419007375

00:36:55.600 --> 00:36:58.839 that can be found and those really
NOTE Confidence: 0.82419007375

00:36:58.839 --> 00:37:00.904 are associated with infants that
NOTE Confidence: 0.82419007375

00:37:00.904 --> 00:37:03.000 were exposed to some infection.
NOTE Confidence: 0.82419007375

00:37:03.000 --> 00:37:05.510 So doing utero exposures really

NOTE Confidence: 0.82419007375

00:37:05.510 --> 00:37:06.990 matter functionally, right.

NOTE Confidence: 0.82419007375

00:37:06.990 --> 00:37:10.280 This is just looking at abundance data.

NOTE Confidence: 0.82419007375

00:37:10.280 --> 00:37:12.624 And so if you take the concept of

NOTE Confidence: 0.82419007375

00:37:12.624 --> 00:37:14.262 trained immunity that I introduced

NOTE Confidence: 0.82419007375

00:37:14.262 --> 00:37:16.660 earlier in in sort of the first

NOTE Confidence: 0.82419007375

00:37:16.660 --> 00:37:18.400 couple of months of life,

NOTE Confidence: 0.82419007375

00:37:18.400 --> 00:37:21.480 it's probably true in utero as well.

NOTE Confidence: 0.82419007375

00:37:21.480 --> 00:37:26.280 And this is a study where in of moms

NOTE Confidence: 0.82419007375

00:37:26.280 --> 00:37:29.252 received hepatitis BCG vaccine and you

NOTE Confidence: 0.82419007375

00:37:29.252 --> 00:37:32.489 can see that in the this this is done

NOTE Confidence: 0.82419007375

00:37:32.489 --> 00:37:35.110 in mice actually but in offsprings

NOTE Confidence: 0.82419007375

00:37:35.110 --> 00:37:39.377 that were exposed to BCG vaccine there

NOTE Confidence: 0.82419007375

00:37:39.377 --> 00:37:44.279 was significantly more response later on.

NOTE Confidence: 0.82419007375

00:37:44.280 --> 00:37:47.144 This has also been shown in mice by

NOTE Confidence: 0.82419007375

00:37:47.144 --> 00:37:49.569 beautiful paper from Yasmin Bell Gates

NOTE Confidence: 0.82419007375

00:37:49.569 --> 00:37:52.017 group that suggested that mice that

NOTE Confidence: 0.82419007375

00:37:52.087 --> 00:37:54.759 have a low level of infection in utero

NOTE Confidence: 0.82419007375

00:37:54.760 --> 00:37:56.656 actually change their offspring's

NOTE Confidence: 0.82419007375

00:37:56.656 --> 00:38:00.591 immune system in a way that if you

NOTE Confidence: 0.82419007375

00:38:00.591 --> 00:38:03.116 then challenge those offsprings with

NOTE Confidence: 0.82419007375

00:38:03.116 --> 00:38:05.878 a different infection they do better.

NOTE Confidence: 0.82419007375

00:38:05.880 --> 00:38:08.676 So in uterus exposures do matter

NOTE Confidence: 0.82419007375

00:38:08.680 --> 00:38:11.155 and not only abundance differences

NOTE Confidence: 0.82419007375

00:38:11.155 --> 00:38:14.280 but also functional, right?

NOTE Confidence: 0.82419007375

00:38:14.280 --> 00:38:16.485 So is this true just in circulation

NOTE Confidence: 0.82419007375

00:38:16.485 --> 00:38:18.811 or can we define immune trajectory

NOTE Confidence: 0.82419007375

00:38:18.811 --> 00:38:20.996 at barrier sites as well?

NOTE Confidence: 0.82419007375

00:38:21.000 --> 00:38:23.114 And what we did is we actually

NOTE Confidence: 0.82419007375

00:38:23.114 --> 00:38:23.718 took intestinal,

NOTE Confidence: 0.936645072857143

00:38:23.720 --> 00:38:25.451 small intestinal samples

NOTE Confidence: 0.936645072857143

00:38:25.451 --> 00:38:27.759 from early 2nd trimester,

NOTE Confidence: 0.936645072857143
00:38:27.760 --> 00:38:30.760 late 2nd trimester therapeutic terminations,
NOTE Confidence: 0.936645072857143
00:38:30.760 --> 00:38:32.302 an infant and subjected them to
NOTE Confidence: 0.936645072857143
00:38:32.302 --> 00:38:33.950 the same site of analysis that
NOTE Confidence: 0.936645072857143
00:38:33.950 --> 00:38:35.636 I was just showing you guys.
NOTE Confidence: 0.936645072857143
00:38:35.640 --> 00:38:38.400 And what's really drastic here
NOTE Confidence: 0.936645072857143
00:38:38.400 --> 00:38:41.956 is that about 50% of these cells
NOTE Confidence: 0.936645072857143
00:38:41.960 --> 00:38:44.720 are of the adoptive phenotype.
NOTE Confidence: 0.936645072857143
00:38:44.720 --> 00:38:46.544 And unlike the cord blood that I was
NOTE Confidence: 0.936645072857143
00:38:46.544 --> 00:38:48.480 showing you where we can see memory cells,
NOTE Confidence: 0.936645072857143
00:38:48.480 --> 00:38:50.192 but they're quite rare.
NOTE Confidence: 0.936645072857143
00:38:50.192 --> 00:38:52.760 The memory cells in the intestine
NOTE Confidence: 0.936645072857143
00:38:52.760 --> 00:38:55.032 by the time you get to about 22
NOTE Confidence: 0.936645072857143
00:38:55.032 --> 00:38:57.448 to 23 weeks make up the majority
NOTE Confidence: 0.936645072857143
00:38:57.448 --> 00:38:59.760 by far of the cells there.
NOTE Confidence: 0.936645072857143
00:38:59.760 --> 00:39:00.678 So in summary,
NOTE Confidence: 0.936645072857143

00:39:00.678 --> 00:39:02.514 maturation of the human immune system
NOTE Confidence: 0.936645072857143

00:39:02.514 --> 00:39:04.676 system occurs early in fetal development.
NOTE Confidence: 0.936645072857143

00:39:04.680 --> 00:39:06.855 Memory cells exist prenatally and
NOTE Confidence: 0.936645072857143

00:39:06.855 --> 00:39:08.595 immune system is compartmentalized,
NOTE Confidence: 0.936645072857143

00:39:08.600 --> 00:39:09.085 right.
NOTE Confidence: 0.936645072857143

00:39:09.085 --> 00:39:11.995 The cord blood is very different
NOTE Confidence: 0.936645072857143

00:39:11.995 --> 00:39:15.438 from your mucosal sites.
NOTE Confidence: 0.936645072857143

00:39:15.440 --> 00:39:17.462 This is sort of continuing work
NOTE Confidence: 0.936645072857143

00:39:17.462 --> 00:39:18.473 that Weihong do,
NOTE Confidence: 0.936645072857143

00:39:18.480 --> 00:39:20.398 Weihong Gu is doing in our group
NOTE Confidence: 0.936645072857143

00:39:20.398 --> 00:39:22.423 where she has put together this
NOTE Confidence: 0.936645072857143

00:39:22.423 --> 00:39:24.196 beautiful Atlas from really first
NOTE Confidence: 0.936645072857143

00:39:24.196 --> 00:39:26.422 trimester all the way to adults to
NOTE Confidence: 0.936645072857143

00:39:26.422 --> 00:39:28.758 look at how these cells are changing.
NOTE Confidence: 0.936645072857143

00:39:28.760 --> 00:39:30.890 And she's defined A functional signature
NOTE Confidence: 0.936645072857143

00:39:30.890 --> 00:39:33.320 of the fetal immune cells that are

NOTE Confidence: 0.936645072857143
00:39:33.320 --> 00:39:34.680 drastically different from neonatal,
NOTE Confidence: 0.936645072857143
00:39:34.680 --> 00:39:36.824 pediatric and adult cells.
NOTE Confidence: 0.936645072857143
00:39:36.824 --> 00:39:40.040 And she can actually track this
NOTE Confidence: 0.936645072857143
00:39:40.040 --> 00:39:42.532 both fetal like T cells and adult
NOTE Confidence: 0.936645072857143
00:39:42.532 --> 00:39:45.159 like T cells across the samples.
NOTE Confidence: 0.936645072857143
00:39:45.160 --> 00:39:45.680 And interestingly,
NOTE Confidence: 0.936645072857143
00:39:45.680 --> 00:39:46.720 sort of of course,
NOTE Confidence: 0.936645072857143
00:39:46.720 --> 00:39:48.008 they're very high and the fetus and
NOTE Confidence: 0.936645072857143
00:39:48.008 --> 00:39:49.519 a little bit lower and then you need,
NOTE Confidence: 0.936645072857143
00:39:49.520 --> 00:39:52.040 but even in adults we can find
NOTE Confidence: 0.936645072857143
00:39:52.040 --> 00:39:54.512 some fetal like T cells,
NOTE Confidence: 0.936645072857143
00:39:54.512 --> 00:39:57.152 suggesting they're quite long lived.
NOTE Confidence: 0.936645072857143
00:39:57.160 --> 00:39:58.678 Is this true in other surfaces?
NOTE Confidence: 0.936645072857143
00:39:58.680 --> 00:40:01.347 So work that was done by Jessica
NOTE Confidence: 0.936645072857143
00:40:01.347 --> 00:40:04.065 Tutuka in my group suggested that yes,
NOTE Confidence: 0.936645072857143

00:40:04.065 --> 00:40:05.840 that is actually exactly true.
NOTE Confidence: 0.936645072857143

00:40:05.840 --> 00:40:07.358 So she looked at the placenta,
NOTE Confidence: 0.936645072857143

00:40:07.360 --> 00:40:09.660 and this is data suggesting
NOTE Confidence: 0.936645072857143

00:40:09.660 --> 00:40:10.933 that in the placenta,
NOTE Confidence: 0.936645072857143

00:40:10.933 --> 00:40:12.559 T cells that are there are
NOTE Confidence: 0.936645072857143

00:40:12.559 --> 00:40:14.240 actually almost exclusively memory,
NOTE Confidence: 0.936645072857143

00:40:14.240 --> 00:40:16.760 so that she couldn't find any naive
NOTE Confidence: 0.936645072857143

00:40:16.760 --> 00:40:18.638 cells that were present in the placenta.
NOTE Confidence: 0.790594131176471

00:40:21.160 --> 00:40:22.288 And then Anthony Vallagalla,
NOTE Confidence: 0.790594131176471

00:40:22.288 --> 00:40:24.297 who's a NICU fellow in our group
NOTE Confidence: 0.790594131176471

00:40:24.297 --> 00:40:25.839 is following up on this work.
NOTE Confidence: 0.790594131176471

00:40:25.840 --> 00:40:28.030 And she put together a cohort
NOTE Confidence: 0.790594131176471

00:40:28.030 --> 00:40:30.404 of cases both in the mid second
NOTE Confidence: 0.790594131176471

00:40:30.404 --> 00:40:32.632 trimester and term to see how's
NOTE Confidence: 0.790594131176471

00:40:32.632 --> 00:40:34.280 the immune system changing.
NOTE Confidence: 0.790594131176471

00:40:34.280 --> 00:40:35.984 And she's done a lot of work that

NOTE Confidence: 0.790594131176471
00:40:35.984 --> 00:40:37.557 I don't have time to go into.
NOTE Confidence: 0.790594131176471
00:40:37.560 --> 00:40:39.522 But the immune system of the
NOTE Confidence: 0.790594131176471
00:40:39.522 --> 00:40:41.212 placenta is very different than
NOTE Confidence: 0.790594131176471
00:40:41.212 --> 00:40:42.797 the mid gestation and term.
NOTE Confidence: 0.790594131176471
00:40:42.800 --> 00:40:43.614 But interestingly,
NOTE Confidence: 0.790594131176471
00:40:43.614 --> 00:40:46.463 she is again able to detect memory
NOTE Confidence: 0.790594131176471
00:40:46.463 --> 00:40:49.237 T cells and these memory T cells,
NOTE Confidence: 0.790594131176471
00:40:49.240 --> 00:40:51.676 if we look at their markers or
NOTE Confidence: 0.790594131176471
00:40:51.676 --> 00:40:53.472 activation or their phosphorus
NOTE Confidence: 0.790594131176471
00:40:53.472 --> 00:40:56.200 signaling are significantly activated.
NOTE Confidence: 0.790594131176471
00:40:56.200 --> 00:40:58.272 And this is just a summary of
NOTE Confidence: 0.790594131176471
00:40:58.272 --> 00:40:59.571 everything that's been done
NOTE Confidence: 0.790594131176471
00:40:59.571 --> 00:41:02.037 in this field in the past,
NOTE Confidence: 0.790594131176471
00:41:02.040 --> 00:41:03.844 I'd say five years,
NOTE Confidence: 0.790594131176471
00:41:03.844 --> 00:41:06.332 suggesting that the diversity and
NOTE Confidence: 0.790594131176471

00:41:06.332 --> 00:41:10.294 sort of complexity of the fuel immune
NOTE Confidence: 0.790594131176471

00:41:10.294 --> 00:41:13.796 system in humans is incredibly high.
NOTE Confidence: 0.790594131176471

00:41:13.800 --> 00:41:14.346 Of course,
NOTE Confidence: 0.790594131176471

00:41:14.346 --> 00:41:15.984 that sort of begs the questions
NOTE Confidence: 0.790594131176471

00:41:15.984 --> 00:41:18.190 are what are the antigens priming
NOTE Confidence: 0.790594131176471

00:41:18.190 --> 00:41:21.266 early immune cells work from?
NOTE Confidence: 0.790594131176471

00:41:21.266 --> 00:41:22.918 Really pioneering work from
NOTE Confidence: 0.46659538

00:41:25.880 --> 00:41:29.760 Ganal, Evan, Grohd and all from Mcpherson's
NOTE Confidence: 0.46659538

00:41:29.760 --> 00:41:32.320 group suggested that it might be the bugs.
NOTE Confidence: 0.46659538

00:41:32.320 --> 00:41:34.272 They fed radioactive labeled
NOTE Confidence: 0.46659538

00:41:34.272 --> 00:41:36.712 bugs to the pregnant mice,
NOTE Confidence: 0.46659538

00:41:36.720 --> 00:41:39.240 and then they were able to detect
NOTE Confidence: 0.46659538

00:41:39.240 --> 00:41:42.360 bacterial metabolites in the offsprings,
NOTE Confidence: 0.46659538

00:41:42.360 --> 00:41:45.013 and the immune system of the offsprings
NOTE Confidence: 0.46659538

00:41:45.013 --> 00:41:47.717 was different from those that weren't fed.
NOTE Confidence: 0.46659538

00:41:47.720 --> 00:41:51.320 We have similarly done work in infant rate,

NOTE Confidence: 0.46659538

00:41:51.320 --> 00:41:53.000 and this is impossible to do in humans.

NOTE Confidence: 0.46659538

00:41:53.000 --> 00:41:55.216 But what we did is we looked at

NOTE Confidence: 0.46659538

00:41:55.216 --> 00:41:57.016 metabolites and the fetus and the

NOTE Confidence: 0.46659538

00:41:57.016 --> 00:41:58.748 infant and then adults and they

NOTE Confidence: 0.46659538

00:41:58.748 --> 00:42:00.118 cluster differently from one another

NOTE Confidence: 0.46659538

00:42:00.118 --> 00:42:01.877 with the infants being in the middle.

NOTE Confidence: 0.46659538

00:42:01.880 --> 00:42:04.640 But again, what's driving the

NOTE Confidence: 0.46659538

00:42:04.640 --> 00:42:06.848 difference predominantly are these

NOTE Confidence: 0.46659538

00:42:06.848 --> 00:42:08.990 xenobiotics and bacterial metabolites

NOTE Confidence: 0.46659538

00:42:08.990 --> 00:42:11.640 would fall into that category.

NOTE Confidence: 0.46659538

00:42:11.640 --> 00:42:14.480 That doesn't really prove that it's the bugs.

NOTE Confidence: 0.46659538

00:42:14.480 --> 00:42:17.896 So what is it really driving it?

NOTE Confidence: 0.46659538

00:42:17.896 --> 00:42:20.040 Potentially it's maternal antigen.

NOTE Confidence: 0.46659538

00:42:20.040 --> 00:42:22.392 And so Jess had looked at maternal antigens

NOTE Confidence: 0.46659538

00:42:22.392 --> 00:42:24.945 and when she stimulates cells with sort of

NOTE Confidence: 0.46659538

00:42:24.945 --> 00:42:27.518 ground up Decidua that has maternal antigens,
NOTE Confidence: 0.46659538

00:42:27.520 --> 00:42:29.200 they're certainly increased
NOTE Confidence: 0.46659538

00:42:29.200 --> 00:42:31.440 in T cells stimulation,
NOTE Confidence: 0.46659538

00:42:31.440 --> 00:42:35.019 although it's unlikely to
NOTE Confidence: 0.46659538

00:42:35.019 --> 00:42:36.798 be explaining everything.
NOTE Confidence: 0.46659538

00:42:36.800 --> 00:42:39.080 So we still think it's likely
NOTE Confidence: 0.46659538

00:42:39.080 --> 00:42:41.600 the bugs we have.
NOTE Confidence: 0.46659538

00:42:41.600 --> 00:42:43.769 A number of us in the field have put
NOTE Confidence: 0.46659538

00:42:43.769 --> 00:42:45.490 together a paper suggesting that we
NOTE Confidence: 0.46659538

00:42:45.490 --> 00:42:47.560 don't think there's a live microbiome.
NOTE Confidence: 0.46659538

00:42:47.560 --> 00:42:49.360 But what we do think is that there
NOTE Confidence: 0.46659538

00:42:49.360 --> 00:42:50.523 are bacterial components that
NOTE Confidence: 0.46659538

00:42:50.523 --> 00:42:51.839 are crossing the placenta.
NOTE Confidence: 0.46659538

00:42:51.840 --> 00:42:54.682 And when we looked at particular bacterial
NOTE Confidence: 0.46659538

00:42:54.682 --> 00:42:57.359 metabolites and there are metabolomics data,
NOTE Confidence: 0.46659538

00:42:57.360 --> 00:42:58.690 you can see both hippurate

NOTE Confidence: 0.46659538

00:42:58.690 --> 00:42:59.754 and P crasal sulfate,

NOTE Confidence: 0.46659538

00:42:59.760 --> 00:43:01.110 both that have been associated

NOTE Confidence: 0.46659538

00:43:01.110 --> 00:43:03.648 with sort of a healthy microbiome

NOTE Confidence: 0.46659538

00:43:03.648 --> 00:43:07.425 but are produced by the bugs.

NOTE Confidence: 0.46659538

00:43:07.425 --> 00:43:09.350 You can see they're significantly

NOTE Confidence: 0.46659538

00:43:09.350 --> 00:43:11.798 enriched in the four in the fetus.

NOTE Confidence: 0.46659538

00:43:11.800 --> 00:43:12.900 That doesn't directly prove

NOTE Confidence: 0.46659538

00:43:12.900 --> 00:43:14.275 that the bugs are priming,

NOTE Confidence: 0.46659538

00:43:14.280 --> 00:43:15.920 but at least it suggests

NOTE Confidence: 0.46659538

00:43:15.920 --> 00:43:17.232 that this is possible.

NOTE Confidence: 0.46659538

00:43:17.240 --> 00:43:19.550 And so work that's been ongoing and

NOTE Confidence: 0.46659538

00:43:19.550 --> 00:43:22.634 done by Tyler Rice and our group in

NOTE Confidence: 0.46659538

00:43:22.634 --> 00:43:24.250 collaboration with Sukhas Kalapur

NOTE Confidence: 0.46659538

00:43:24.250 --> 00:43:27.600 from UCLA using a non human primate

NOTE Confidence: 0.46659538

00:43:27.600 --> 00:43:29.680 model of intramniotic infection,

NOTE Confidence: 0.46659538

00:43:29.680 --> 00:43:32.104 they actually intramniotically
NOTE Confidence: 0.46659538

00:43:32.104 --> 00:43:35.152 infect these monkeys with E coli.
NOTE Confidence: 0.46659538

00:43:35.152 --> 00:43:37.679 We have then gotten the samples and
NOTE Confidence: 0.46659538

00:43:37.679 --> 00:43:40.103 so we can extract T cells from the
NOTE Confidence: 0.46659538

00:43:40.103 --> 00:43:42.545 fetus that have been exposed to these
NOTE Confidence: 0.46659538

00:43:42.545 --> 00:43:47.800 E Coli's and reprime them with E coli.
NOTE Confidence: 0.46659538

00:43:47.800 --> 00:43:50.368 And this is just these big
NOTE Confidence: 0.46659538

00:43:50.368 --> 00:43:52.080 round cells are Apcs.
NOTE Confidence: 0.46659538

00:43:52.080 --> 00:43:54.229 And then the little dots here are
NOTE Confidence: 0.46659538

00:43:54.229 --> 00:43:56.799 the T cells and what we if there is
NOTE Confidence: 0.46659538

00:43:56.800 --> 00:43:58.676 sort of if these cells are memory
NOTE Confidence: 0.46659538

00:43:58.676 --> 00:44:01.016 and it's formed memory to the coli,
NOTE Confidence: 0.46659538

00:44:01.016 --> 00:44:02.552 they should undergo blasting
NOTE Confidence: 0.46659538

00:44:02.552 --> 00:44:04.000 where colonial expansion.
NOTE Confidence: 0.46659538

00:44:04.000 --> 00:44:06.380 And you can see this beautiful clonal
NOTE Confidence: 0.46659538

00:44:06.380 --> 00:44:08.086 expansion on these pictures here.

NOTE Confidence: 0.46659538

00:44:08.086 --> 00:44:10.830 And Tyler has tracked this where you can

NOTE Confidence: 0.46659538

00:44:10.900 --> 00:44:13.020 see that there's really minimal clonal

NOTE Confidence: 0.46659538

00:44:13.020 --> 00:44:15.045 expansion without E coli stimulation

NOTE Confidence: 0.46659538

00:44:15.045 --> 00:44:17.479 and that really drastically increases.

NOTE Confidence: 0.46659538

00:44:17.480 --> 00:44:19.760 He can then send these sequences,

NOTE Confidence: 0.46659538

00:44:19.760 --> 00:44:22.448 these T cells for sequencing.

NOTE Confidence: 0.46659538

00:44:22.448 --> 00:44:24.080 You can see there's sort of

NOTE Confidence: 0.46659538

00:44:24.080 --> 00:44:26.648 enhancement in a number of different

NOTE Confidence: 0.46659538

00:44:26.648 --> 00:44:28.380 sequences in the stimulated group,

NOTE Confidence: 0.46659538

00:44:28.380 --> 00:44:29.355 and actually interestingly,

NOTE Confidence: 0.46659538

00:44:29.360 --> 00:44:31.915 a number of them have the same

NOTE Confidence: 0.46659538

00:44:31.920 --> 00:44:35.520 expansion of the same clones.

NOTE Confidence: 0.46659538

00:44:35.520 --> 00:44:38.415 This begs a lot more questions, right?

NOTE Confidence: 0.46659538

00:44:38.415 --> 00:44:40.760 Does the source of these bugs matter?

NOTE Confidence: 0.46659538

00:44:40.760 --> 00:44:43.390 Do particular Do particular bugs

NOTE Confidence: 0.46659538

00:44:43.390 --> 00:44:46.020 actually matter in the sense
NOTE Confidence: 0.8849174

00:44:46.112 --> 00:44:48.616 that are there bugs that stimulate
NOTE Confidence: 0.8849174

00:44:48.616 --> 00:44:50.660 the memory CD4 cells that are
NOTE Confidence: 0.8849174

00:44:50.660 --> 00:44:51.840 associated with preterm labour,
NOTE Confidence: 0.8849174

00:44:51.840 --> 00:44:53.667 and are those different from the ones
NOTE Confidence: 0.8849174

00:44:53.667 --> 00:44:55.280 that are associated with term labour?
NOTE Confidence: 0.8849174

00:44:55.280 --> 00:44:57.108 Does the timing matter?
NOTE Confidence: 0.8849174

00:44:57.108 --> 00:44:59.393 And how do these responses
NOTE Confidence: 0.8849174

00:44:59.393 --> 00:45:01.039 project future health?
NOTE Confidence: 0.8849174

00:45:01.040 --> 00:45:03.704 And then I will just finish with two last
NOTE Confidence: 0.8849174

00:45:03.704 --> 00:45:05.720 thoughts of where do we go from here?
NOTE Confidence: 0.8849174

00:45:05.720 --> 00:45:07.190 I hope I've convinced you that
NOTE Confidence: 0.8849174

00:45:07.190 --> 00:45:08.600 new Natal immunity is complex,
NOTE Confidence: 0.8849174

00:45:08.600 --> 00:45:10.600 dynamic and highly adoptable,
NOTE Confidence: 0.8849174

00:45:10.600 --> 00:45:14.400 but it's optimized to perform its function,
NOTE Confidence: 0.8849174

00:45:14.400 --> 00:45:17.448 and the function being protect the

NOTE Confidence: 0.8849174

00:45:17.448 --> 00:45:19.480 host and prevent overactivation.

NOTE Confidence: 0.8849174

00:45:19.480 --> 00:45:21.298 And so all of these factors

NOTE Confidence: 0.8849174

00:45:21.298 --> 00:45:23.219 actually make a huge difference in

NOTE Confidence: 0.8849174

00:45:23.219 --> 00:45:25.473 how the immune system is set up.

NOTE Confidence: 0.8849174

00:45:25.480 --> 00:45:26.257 And of course,

NOTE Confidence: 0.8849174

00:45:26.257 --> 00:45:27.811 this is making a huge difference

NOTE Confidence: 0.8849174

00:45:27.811 --> 00:45:29.720 into what diseases we're at risk for.

NOTE Confidence: 0.8849174

00:45:29.720 --> 00:45:33.472 And I think there's a huge need for

NOTE Confidence: 0.8849174

00:45:33.472 --> 00:45:36.071 large longitudinal studies to study

NOTE Confidence: 0.8849174

00:45:36.071 --> 00:45:38.681 how various factors prenatally and

NOTE Confidence: 0.8849174

00:45:38.681 --> 00:45:41.528 in early life dictate to reset the

NOTE Confidence: 0.8849174

00:45:41.528 --> 00:45:44.349 immune system and sort of put us at

NOTE Confidence: 0.8849174

00:45:44.349 --> 00:45:46.792 risk for a number of different diseases.

NOTE Confidence: 0.8849174

00:45:46.800 --> 00:45:47.586 And finally,

NOTE Confidence: 0.8849174

00:45:47.586 --> 00:45:50.300 I think we need to take all of

NOTE Confidence: 0.8849174

00:45:50.300 --> 00:45:52.560 this into account in how we design,
NOTE Confidence: 0.8849174

00:45:52.560 --> 00:45:53.880 improve vaccine strategies.
NOTE Confidence: 0.8849174

00:45:53.880 --> 00:45:56.253 And this was a beautiful illustration
NOTE Confidence: 0.8849174

00:45:56.253 --> 00:45:58.359 from the original science issue that
NOTE Confidence: 0.8849174

00:45:58.359 --> 00:46:00.805 I showed you guys from Sing Sing Wei
NOTE Confidence: 0.8849174

00:46:00.805 --> 00:46:02.856 and Commons group where if you look
NOTE Confidence: 0.8849174

00:46:02.856 --> 00:46:04.880 at this sort of infant early on,
NOTE Confidence: 0.8849174

00:46:04.880 --> 00:46:07.118 there is some pathogen specific antibodies,
NOTE Confidence: 0.8849174

00:46:07.120 --> 00:46:08.672 but they're quite low.
NOTE Confidence: 0.8849174

00:46:08.672 --> 00:46:11.000 If we immunize the mom right,
NOTE Confidence: 0.8849174

00:46:11.000 --> 00:46:15.000 we can sort of have mom's antibody cross
NOTE Confidence: 0.8849174

00:46:15.000 --> 00:46:17.520 the placenta and protect the fetus.
NOTE Confidence: 0.8849174

00:46:17.520 --> 00:46:19.326 If we sort of immunize the baby
NOTE Confidence: 0.8849174

00:46:19.326 --> 00:46:20.520 and the mom right,
NOTE Confidence: 0.8849174

00:46:20.520 --> 00:46:22.880 you get mom's humoral immunity,
NOTE Confidence: 0.8849174

00:46:22.880 --> 00:46:25.127 you get trained immunity which is sort

NOTE Confidence: 0.8849174

00:46:25.127 --> 00:46:26.893 of pathogen agnostic immunity and

NOTE Confidence: 0.8849174

00:46:26.893 --> 00:46:28.758 you get pathogen specific immunity.

NOTE Confidence: 0.8849174

00:46:28.760 --> 00:46:31.595 But what if we sort of combine the two,

NOTE Confidence: 0.8849174

00:46:31.600 --> 00:46:31.918 right?

NOTE Confidence: 0.8849174

00:46:31.918 --> 00:46:34.462 And maybe we need to find a window

NOTE Confidence: 0.8849174

00:46:34.462 --> 00:46:37.239 during pregnancy where we immunize the mom,

NOTE Confidence: 0.8849174

00:46:37.240 --> 00:46:40.320 but that also benefits the developing fetus.

NOTE Confidence: 0.8849174

00:46:40.320 --> 00:46:43.116 And maybe the fetus themselves can

NOTE Confidence: 0.8849174

00:46:43.116 --> 00:46:46.713 then mount AT cell response to the

NOTE Confidence: 0.8849174

00:46:46.713 --> 00:46:49.995 vaccine and then have double protection.

NOTE Confidence: 0.8849174

00:46:50.000 --> 00:46:51.278 I think I've mentioned all the

NOTE Confidence: 0.8849174

00:46:51.278 --> 00:46:51.917 people all along,

NOTE Confidence: 0.8849174

00:46:51.920 --> 00:46:53.928 but these are the people in our group

NOTE Confidence: 0.8849174

00:46:53.928 --> 00:46:55.650 currently that are doing all this work.

NOTE Confidence: 0.8849174

00:46:55.650 --> 00:46:57.680 And these are just all of our

NOTE Confidence: 0.8849174

00:46:57.680 --> 00:46:59.558 collaborators that I think I've mentioned.

NOTE Confidence: 0.8849174

00:46:59.560 --> 00:47:02.059 But really none of this work would

NOTE Confidence: 0.8849174

00:47:02.059 --> 00:47:04.033 have been done without Sarah's

NOTE Confidence: 0.8849174

00:47:04.033 --> 00:47:05.911 group and our partners in crime

NOTE Confidence: 0.8849174

00:47:05.911 --> 00:47:07.439 that you know my group.

NOTE Confidence: 0.8849174

00:47:07.440 --> 00:47:08.520 And I'll take any questions.

NOTE Confidence: 0.905042146

00:47:16.800 --> 00:47:18.480 Thank you so much, Lisa.

NOTE Confidence: 0.905042146

00:47:18.480 --> 00:47:21.685 Wow, that was quite a tour

NOTE Confidence: 0.905042146

00:47:21.685 --> 00:47:23.760 of of a complex system.

NOTE Confidence: 0.905042146

00:47:23.760 --> 00:47:26.336 I'm going to invite folks to send in

NOTE Confidence: 0.905042146

00:47:26.336 --> 00:47:28.015 questions through the chat and I'll

NOTE Confidence: 0.905042146

00:47:28.015 --> 00:47:30.080 read it to Lisa for her response.

NOTE Confidence: 0.905042146

00:47:30.080 --> 00:47:32.032 What was occurring to me as you were

NOTE Confidence: 0.905042146

00:47:32.032 --> 00:47:33.863 going through this whole thing aside

NOTE Confidence: 0.905042146

00:47:33.863 --> 00:47:35.892 from the incredible complexity and how

NOTE Confidence: 0.905042146

00:47:35.892 --> 00:47:38.454 much has been done to describe this

NOTE Confidence: 0.905042146

00:47:38.454 --> 00:47:41.656 Lisa was the it's it's very appealing.

NOTE Confidence: 0.905042146

00:47:41.656 --> 00:47:43.683 The notion of intervention

NOTE Confidence: 0.905042146

00:47:43.683 --> 00:47:44.772 during pregnancy actually.

NOTE Confidence: 0.905042146

00:47:44.772 --> 00:47:47.366 I mean as you started to describe

NOTE Confidence: 0.905042146

00:47:47.366 --> 00:47:49.570 all this this complex system the

NOTE Confidence: 0.905042146

00:47:49.570 --> 00:47:51.370 interventions during pregnancy that

NOTE Confidence: 0.905042146

00:47:51.370 --> 00:47:53.443 can influence the the immune system.

NOTE Confidence: 0.905042146

00:47:53.443 --> 00:47:55.130 But I I suppose that's a double

NOTE Confidence: 0.905042146

00:47:55.178 --> 00:47:56.678 edged sword too because our immune

NOTE Confidence: 0.905042146

00:47:56.678 --> 00:47:58.233 system can be our best friend

NOTE Confidence: 0.905042146

00:47:58.233 --> 00:47:59.733 or our worst enemy depending on

NOTE Confidence: 0.905042146

00:47:59.733 --> 00:48:01.044 what the particular problem is.

NOTE Confidence: 0.905042146

00:48:01.044 --> 00:48:03.892 And so you know at at at first look I

NOTE Confidence: 0.905042146

00:48:03.892 --> 00:48:05.716 think what this would be wonderful.

NOTE Confidence: 0.905042146

00:48:05.720 --> 00:48:07.246 I'd like the hepatitis B vaccine which

NOTE Confidence: 0.905042146

00:48:07.246 --> 00:48:08.666 you pointed out this is something
NOTE Confidence: 0.905042146

00:48:08.666 --> 00:48:10.118 that works really well really early.
NOTE Confidence: 0.905042146

00:48:10.120 --> 00:48:11.040 This works in the baby.
NOTE Confidence: 0.905042146

00:48:11.040 --> 00:48:13.035 So we can respond to some vaccines.
NOTE Confidence: 0.905042146

00:48:13.040 --> 00:48:14.948 So presumably there's vaccines you can
NOTE Confidence: 0.905042146

00:48:14.948 --> 00:48:16.854 give during pregnancy or other things
NOTE Confidence: 0.905042146

00:48:16.854 --> 00:48:18.582 you can give during pregnancy that
NOTE Confidence: 0.905042146

00:48:18.582 --> 00:48:20.678 are going to augment the immune system,
NOTE Confidence: 0.905042146

00:48:20.680 --> 00:48:21.436 if you will,
NOTE Confidence: 0.905042146

00:48:21.436 --> 00:48:22.696 the immune response in the
NOTE Confidence: 0.905042146

00:48:22.696 --> 00:48:24.306 fetus and the newborn, right.
NOTE Confidence: 0.905042146

00:48:24.306 --> 00:48:28.004 This I think you you you've shown us that.
NOTE Confidence: 0.905042146

00:48:28.004 --> 00:48:30.767 Then I guess what becomes a tone of
NOTE Confidence: 0.905042146

00:48:30.767 --> 00:48:32.381 caution is these interventions also are
NOTE Confidence: 0.905042146

00:48:32.381 --> 00:48:34.322 we going to find out sometime later
NOTE Confidence: 0.905042146

00:48:34.322 --> 00:48:36.458 these kids are more appropriate some

NOTE Confidence: 0.905042146

00:48:36.458 --> 00:48:38.924 intervention to reduce infections in

NOTE Confidence: 0.905042146

00:48:38.924 --> 00:48:41.088 the newborn period could ultimately

NOTE Confidence: 0.905042146

00:48:41.088 --> 00:48:42.808 to increased autoimmune disease that

NOTE Confidence: 0.905042146

00:48:42.808 --> 00:48:44.865 we hadn't only anticipated with those

NOTE Confidence: 0.905042146

00:48:44.865 --> 00:48:46.809 interventions And can you talk about

NOTE Confidence: 0.905042146

00:48:46.809 --> 00:48:48.558 that for a bit or am I off based on

NOTE Confidence: 0.8707314125

00:48:48.680 --> 00:48:50.496 that? I mean I think you hit the

NOTE Confidence: 0.8707314125

00:48:50.496 --> 00:48:52.599 nail on the head mark I think right.

NOTE Confidence: 0.8707314125

00:48:52.600 --> 00:48:55.545 I think we don't understand enough to

NOTE Confidence: 0.8707314125

00:48:55.545 --> 00:48:59.198 really know what is the best window and

NOTE Confidence: 0.8707314125

00:48:59.198 --> 00:49:02.382 what kind of responses should we be looking

NOTE Confidence: 0.8707314125

00:49:02.382 --> 00:49:05.808 for right early on versus hoping to not

NOTE Confidence: 0.8707314125

00:49:05.808 --> 00:49:08.638 induce any adverse reactions later on.

NOTE Confidence: 0.8707314125

00:49:08.640 --> 00:49:10.397 It's clear that sort of very early,

NOTE Confidence: 0.8707314125

00:49:10.400 --> 00:49:11.856 early on in pregnancy,

NOTE Confidence: 0.8707314125

00:49:11.856 --> 00:49:13.676 the immune system is really
NOTE Confidence: 0.8707314125

00:49:13.680 --> 00:49:15.395 designed to be tolerant of the mom.
NOTE Confidence: 0.8707314125

00:49:15.400 --> 00:49:19.000 And so I think interventions very
NOTE Confidence: 0.8707314125

00:49:19.000 --> 00:49:21.368 early on in pregnancy aren't
NOTE Confidence: 0.8707314125

00:49:21.368 --> 00:49:23.137 necessarily going to help prevent
NOTE Confidence: 0.8707314125

00:49:23.137 --> 00:49:24.919 any of the infections later on.
NOTE Confidence: 0.8707314125

00:49:24.920 --> 00:49:27.017 And so I think we have to find that
NOTE Confidence: 0.8707314125

00:49:27.017 --> 00:49:29.044 window sort of later on in pregnancy
NOTE Confidence: 0.8707314125

00:49:29.044 --> 00:49:31.218 where we can intervene and perhaps
NOTE Confidence: 0.8707314125

00:49:31.218 --> 00:49:34.781 sort of reset the OR develop some
NOTE Confidence: 0.8707314125

00:49:34.781 --> 00:49:37.800 memory cells that will be beneficial
NOTE Confidence: 0.8707314125

00:49:37.800 --> 00:49:40.040 in the new Natal infant period.
NOTE Confidence: 0.8707314125

00:49:40.040 --> 00:49:42.092 But I think that's sort of why I meant
NOTE Confidence: 0.8707314125

00:49:42.092 --> 00:49:43.932 we need long longitudinal cohorts
NOTE Confidence: 0.8707314125

00:49:43.932 --> 00:49:45.877 because we don't understand how,
NOTE Confidence: 0.8707314125

00:49:45.880 --> 00:49:47.105 we don't understand how that's

NOTE Confidence: 0.8707314125

00:49:47.105 --> 00:49:48.960 changing even in the new Natal period.

NOTE Confidence: 0.8707314125

00:49:48.960 --> 00:49:50.560 And we certainly don't understand

NOTE Confidence: 0.8707314125

00:49:50.560 --> 00:49:52.768 how that's going to affect children

NOTE Confidence: 0.8707314125

00:49:52.768 --> 00:49:55.200 and adults later on.

NOTE Confidence: 0.8707314125

00:49:55.200 --> 00:49:55.520 Thank

NOTE Confidence: 0.743650467142857

00:49:55.520 --> 00:49:56.204 you. Thank you.

NOTE Confidence: 0.743650467142857

00:49:56.204 --> 00:49:57.344 There's a few questions that

NOTE Confidence: 0.743650467142857

00:49:57.344 --> 00:49:58.825 have come in here with the Q&A.

NOTE Confidence: 0.743650467142857

00:49:58.825 --> 00:50:00.960 So let me read one to you.

NOTE Confidence: 0.743650467142857

00:50:00.960 --> 00:50:02.960 Very interesting and important work.

NOTE Confidence: 0.743650467142857

00:50:02.960 --> 00:50:04.340 If you looked at these immune

NOTE Confidence: 0.743650467142857

00:50:04.340 --> 00:50:05.879 markers in relation to feeding type,

NOTE Confidence: 0.743650467142857

00:50:05.880 --> 00:50:07.320 IE formula fed,

NOTE Confidence: 0.743650467142857

00:50:07.320 --> 00:50:10.680 mixed fed or breast milk fed, yes,

NOTE Confidence: 0.778511152727273

00:50:10.680 --> 00:50:13.382 well, Sarah and I have applied for

NOTE Confidence: 0.778511152727273

00:50:13.382 --> 00:50:15.640 a grant five times, but hopefully
NOTE Confidence: 0.778511152727273

00:50:15.640 --> 00:50:17.880 next time we will get it funded.
NOTE Confidence: 0.778511152727273

00:50:17.880 --> 00:50:21.080 I think that's incredibly important,
NOTE Confidence: 0.778511152727273

00:50:21.080 --> 00:50:24.120 but there's just not enough data out there.
NOTE Confidence: 0.778511152727273

00:50:24.120 --> 00:50:27.504 And I I think for sure nutrition is changing
NOTE Confidence: 0.778511152727273

00:50:27.504 --> 00:50:29.560 how the immune system is responding.
NOTE Confidence: 0.778511152727273

00:50:29.560 --> 00:50:31.480 And there's clear data, right,
NOTE Confidence: 0.778511152727273

00:50:31.480 --> 00:50:32.840 that breast milk is protective,
NOTE Confidence: 0.778511152727273

00:50:32.840 --> 00:50:34.952 whether the donor human milk is
NOTE Confidence: 0.778511152727273

00:50:34.952 --> 00:50:36.960 just as protective as unclear.
NOTE Confidence: 0.778511152727273

00:50:36.960 --> 00:50:39.172 And certainly potentially that
NOTE Confidence: 0.778511152727273

00:50:39.172 --> 00:50:42.008 formula is a little bit detrimental,
NOTE Confidence: 0.778511152727273

00:50:42.008 --> 00:50:43.917 but more work really needs to be done.
NOTE Confidence: 0.778511152727273

00:50:43.920 --> 00:50:45.300 But I think it's an incredibly
NOTE Confidence: 0.778511152727273

00:50:45.300 --> 00:50:45.760 important area.
NOTE Confidence: 0.78708636

00:50:47.080 --> 00:50:50.200 Thank you. Next question, ILC.

NOTE Confidence: 0.78708636

00:50:50.200 --> 00:50:52.657 Ilcs, excuse me, seem to play an

NOTE Confidence: 0.78708636

00:50:52.657 --> 00:50:54.213 important role connecting mediate

NOTE Confidence: 0.78708636

00:50:54.213 --> 00:50:55.957 and adaptive immune systems.

NOTE Confidence: 0.78708636

00:50:55.960 --> 00:50:58.720 What is their role Ilcs

NOTE Confidence: 0.78708636

00:50:58.720 --> 00:51:00.120 in these early stages?

NOTE Confidence: 0.897037322631579

00:51:01.200 --> 00:51:01.797 Another great question.

NOTE Confidence: 0.897037322631579

00:51:01.797 --> 00:51:03.877 So I I just didn't have time to go into

NOTE Confidence: 0.897037322631579

00:51:03.877 --> 00:51:05.155 all of the different immune components,

NOTE Confidence: 0.897037322631579

00:51:05.160 --> 00:51:08.040 but ILC that incredibly rare in the blood,

NOTE Confidence: 0.897037322631579

00:51:08.040 --> 00:51:09.786 so I don't know what role

NOTE Confidence: 0.897037322631579

00:51:09.786 --> 00:51:11.200 they would play early on.

NOTE Confidence: 0.897037322631579

00:51:11.200 --> 00:51:12.982 They're also incredibly rare in the

NOTE Confidence: 0.897037322631579

00:51:12.982 --> 00:51:14.768 blood of immunes at the mucosa side.

NOTE Confidence: 0.897037322631579

00:51:14.768 --> 00:51:15.878 I didn't go into it,

NOTE Confidence: 0.897037322631579

00:51:15.880 --> 00:51:18.250 but the ILC is actually incredibly

NOTE Confidence: 0.897037322631579

00:51:18.250 --> 00:51:21.320 abundant in the fetal intestine in humans.

NOTE Confidence: 0.897037322631579

00:51:21.320 --> 00:51:23.490 And we think they're really

NOTE Confidence: 0.897037322631579

00:51:23.490 --> 00:51:25.660 actually setting up the immune

NOTE Confidence: 0.897037322631579

00:51:25.737 --> 00:51:28.462 niche in the mucosa and they then

NOTE Confidence: 0.897037322631579

00:51:28.462 --> 00:51:30.615 drastically go down with gestation.

NOTE Confidence: 0.897037322631579

00:51:30.615 --> 00:51:33.520 So I think they're one is that

NOTE Confidence: 0.897037322631579

00:51:33.520 --> 00:51:35.795 they're needed there to set up

NOTE Confidence: 0.897037322631579

00:51:35.795 --> 00:51:37.841 how the immune system is going

NOTE Confidence: 0.897037322631579

00:51:37.920 --> 00:51:40.040 to work and they probably also do

NOTE Confidence: 0.897037322631579

00:51:40.040 --> 00:51:43.538 provide some sort of protection

NOTE Confidence: 0.897037322631579

00:51:43.538 --> 00:51:45.566 while the adaptive part of the

NOTE Confidence: 0.897037322631579

00:51:45.566 --> 00:51:47.398 immune system is being set up.

NOTE Confidence: 0.779305900625

00:51:48.880 --> 00:51:50.760 Thank you. The prevention of

NOTE Confidence: 0.779305900625

00:51:50.760 --> 00:51:53.062 neonatal tetanus relies in part on

NOTE Confidence: 0.779305900625

00:51:53.062 --> 00:51:54.837 the immunization of the mother.

NOTE Confidence: 0.779305900625

00:51:54.840 --> 00:51:56.088 Is this along the lines of

NOTE Confidence: 0.779305900625

00:51:56.088 --> 00:51:56.920 what you were speaking?

NOTE Confidence: 0.8472970575

00:51:58.280 --> 00:52:00.260 Again great question.

NOTE Confidence: 0.8472970575

00:52:00.260 --> 00:52:02.972 So you know part of the protection

NOTE Confidence: 0.8472970575

00:52:02.972 --> 00:52:04.786 that giving vaccines in pregnancy

NOTE Confidence: 0.8472970575

00:52:04.786 --> 00:52:07.078 is that you get humoral immunity,

NOTE Confidence: 0.8472970575

00:52:07.080 --> 00:52:09.080 right, Like antibody media immunity

NOTE Confidence: 0.8472970575

00:52:09.080 --> 00:52:11.080 that gets transferred to the

NOTE Confidence: 0.8472970575

00:52:11.080 --> 00:52:13.135 fetus and thereby neonates are

NOTE Confidence: 0.8472970575

00:52:13.135 --> 00:52:14.738 born with protective antibodies.

NOTE Confidence: 0.8472970575

00:52:14.738 --> 00:52:18.280 I think there is a little bit of data,

NOTE Confidence: 0.8472970575

00:52:18.280 --> 00:52:20.373 I don't, I'm not familiar with the

NOTE Confidence: 0.8472970575

00:52:20.373 --> 00:52:22.227 tetanus data that there's a paper

NOTE Confidence: 0.8472970575

00:52:22.227 --> 00:52:24.655 published on the flu vaccine that if you

NOTE Confidence: 0.8472970575

00:52:24.655 --> 00:52:26.470 give the flu vaccine during pregnancy

NOTE Confidence: 0.8472970575

00:52:26.470 --> 00:52:28.600 you can actually find flu specific

NOTE Confidence: 0.8472970575

00:52:28.600 --> 00:52:30.879 fetal T cells in the fetal blood.
NOTE Confidence: 0.8472970575

00:52:30.880 --> 00:52:32.119 That's sort of what I was suggesting.
NOTE Confidence: 0.8472970575

00:52:32.120 --> 00:52:33.440 Is there is there a window
NOTE Confidence: 0.8472970575

00:52:33.440 --> 00:52:34.600 where we can immunize that?
NOTE Confidence: 0.8472970575

00:52:34.600 --> 00:52:36.680 Not only do you get humoral immunity and
NOTE Confidence: 0.8472970575

00:52:36.680 --> 00:52:38.956 get a bump on your humoral immunity,
NOTE Confidence: 0.8472970575

00:52:38.960 --> 00:52:40.528 you also get a bump in your
NOTE Confidence: 0.8472970575

00:52:40.528 --> 00:52:41.280 T cell memory, in
NOTE Confidence: 0.740141432142857

00:52:42.960 --> 00:52:44.276 which case the possibilities
NOTE Confidence: 0.740141432142857

00:52:44.276 --> 00:52:45.921 are endless in terms of
NOTE Confidence: 0.740141432142857

00:52:45.921 --> 00:52:47.478 infection protection if you can,
NOTE Confidence: 0.740141432142857

00:52:47.480 --> 00:52:49.228 if you can do that exactly.
NOTE Confidence: 0.740141432142857

00:52:49.228 --> 00:52:51.768 Steroids are often given in
NOTE Confidence: 0.740141432142857

00:52:51.768 --> 00:52:53.800 mothers undergoing preterm labor.
NOTE Confidence: 0.740141432142857

00:52:53.800 --> 00:52:56.039 What effects do they have when they're born?
NOTE Confidence: 0.817442616666667

00:52:57.520 --> 00:52:59.758 Great question, Eduardo.

NOTE Confidence: 0.817442616666667
00:52:59.760 --> 00:53:02.920 Yes, I'm sure they do, right?
NOTE Confidence: 0.817442616666667
00:53:02.920 --> 00:53:04.452 Steroids drastically
NOTE Confidence: 0.817442616666667
00:53:04.452 --> 00:53:07.516 regulate the immune system.
NOTE Confidence: 0.817442616666667
00:53:07.520 --> 00:53:09.805 It's incredibly challenging to study
NOTE Confidence: 0.817442616666667
00:53:09.805 --> 00:53:13.090 right because almost we at least in our
NOTE Confidence: 0.817442616666667
00:53:13.090 --> 00:53:15.160 unit and especially in this cohort,
NOTE Confidence: 0.817442616666667
00:53:15.160 --> 00:53:17.452 they universally received steroids.
NOTE Confidence: 0.817442616666667
00:53:17.452 --> 00:53:19.992 And so I I don't know what effect
NOTE Confidence: 0.817442616666667
00:53:19.992 --> 00:53:21.783 they have because all of the samples
NOTE Confidence: 0.817442616666667
00:53:21.783 --> 00:53:23.397 that have been predisposed to them.
NOTE Confidence: 0.817442616666667
00:53:23.400 --> 00:53:25.560 But certainly a very important question.
NOTE Confidence: 0.494818584285714
00:53:28.280 --> 00:53:30.800 I do over the cohorts of children
NOTE Confidence: 0.494818584285714
00:53:30.800 --> 00:53:33.170 born to mothers with CBID or
NOTE Confidence: 0.494818584285714
00:53:33.170 --> 00:53:34.160 other immunity deficiencies.
NOTE Confidence: 0.887925165
00:53:35.160 --> 00:53:39.466 Yeah. So I I am not, but we have
NOTE Confidence: 0.887925165

00:53:39.466 --> 00:53:41.800 been looking for some, I think
NOTE Confidence: 0.87512131

00:53:44.000 --> 00:53:45.680 there are some at the NIH that
NOTE Confidence: 0.87512131

00:53:45.680 --> 00:53:47.464 Carrie and I have been thinking
NOTE Confidence: 0.87512131

00:53:47.464 --> 00:53:48.800 about because I think that would
NOTE Confidence: 0.87512131

00:53:48.800 --> 00:53:49.880 be super interesting. I agree. Have
NOTE Confidence: 0.960694514

00:53:52.280 --> 00:53:54.600 you found any specific differences
NOTE Confidence: 0.960694514

00:53:54.600 --> 00:53:56.184 in the functional abilities
NOTE Confidence: 0.960694514

00:53:56.184 --> 00:53:58.164 of these adaptive immune cells
NOTE Confidence: 0.960694514

00:53:58.164 --> 00:54:00.620 through through through the period?
NOTE Confidence: 0.960694514

00:54:00.620 --> 00:54:03.906 Are there transitional genetic or
NOTE Confidence: 0.960694514

00:54:03.906 --> 00:54:05.318 medicine that markers present?
NOTE Confidence: 0.73310226

00:54:07.880 --> 00:54:09.080 Sorry Mike, you were breaking up.
NOTE Confidence: 0.6872827566666666

00:54:10.200 --> 00:54:11.936 I'm sorry. I'll I'll reach this again
NOTE Confidence: 0.6872827566666666

00:54:11.936 --> 00:54:14.080 give you a second to consider it.
NOTE Confidence: 0.6872827566666666

00:54:14.080 --> 00:54:16.280 Have you found any specific
NOTE Confidence: 0.6872827566666666

00:54:16.280 --> 00:54:17.926 differences in the functional

NOTE Confidence: 0.6872827566666666
00:54:17.926 --> 00:54:19.936 abilities of these adaptive immune
NOTE Confidence: 0.6872827566666666
00:54:19.936 --> 00:54:22.079 cells through the perinatal period?
NOTE Confidence: 0.6872827566666666
00:54:22.080 --> 00:54:24.200 Are there transitional markers present,
NOTE Confidence: 0.6872827566666666
00:54:24.200 --> 00:54:24.959 genetic or otherwise?
NOTE Confidence: 0.77644047
00:54:25.400 --> 00:54:27.080 Yeah. So that's sort of the
NOTE Confidence: 0.77644047
00:54:27.080 --> 00:54:28.319 I-1 slide that I had up there.
NOTE Confidence: 0.77644047
00:54:28.320 --> 00:54:30.276 That's what Wei Hong is doing.
NOTE Confidence: 0.77644047
00:54:30.280 --> 00:54:33.080 She's looking at specific
NOTE Confidence: 0.77644047
00:54:33.080 --> 00:54:36.420 markers of fetal mucosal T cells,
NOTE Confidence: 0.77644047
00:54:36.420 --> 00:54:38.360 neonatal mucosal T cells,
NOTE Confidence: 0.77644047
00:54:38.360 --> 00:54:39.960 and adult mucosal T cells.
NOTE Confidence: 0.77644047
00:54:39.960 --> 00:54:41.480 The short answer is yes,
NOTE Confidence: 0.77644047
00:54:41.480 --> 00:54:43.058 they're certainly different.
NOTE Confidence: 0.77644047
00:54:43.058 --> 00:54:45.632 They have different functional potentials.
NOTE Confidence: 0.77644047
00:54:45.632 --> 00:54:47.120 So they proliferate.
NOTE Confidence: 0.77644047

00:54:47.120 --> 00:54:49.360 Neonatal and fetal cells proliferate
NOTE Confidence: 0.77644047

00:54:49.360 --> 00:54:51.600 drastically more than adult cells.
NOTE Confidence: 0.77644047

00:54:51.600 --> 00:54:53.320 But that work is ongoing.
NOTE Confidence: 0.87664236666667

00:54:56.240 --> 00:54:59.560 This has been quite a quite an hour,
NOTE Confidence: 0.87664236666667

00:54:59.560 --> 00:55:01.720 please. Thank you so much.
NOTE Confidence: 0.87664236666667

00:55:01.720 --> 00:55:03.960 I think among other things,
NOTE Confidence: 0.87664236666667

00:55:03.960 --> 00:55:05.200 science and teaching us all
NOTE Confidence: 0.87664236666667

00:55:05.200 --> 00:55:06.440 a lot of community biology.
NOTE Confidence: 0.87664236666667

00:55:06.440 --> 00:55:08.988 You've also shown everybody just how cool
NOTE Confidence: 0.87664236666667

00:55:08.988 --> 00:55:12.520 the section of this medicine really is.
NOTE Confidence: 0.87664236666667

00:55:12.520 --> 00:55:15.666 This is tradition for and we very
NOTE Confidence: 0.87664236666667

00:55:15.666 --> 00:55:17.200 much appreciate your sharing and
NOTE Confidence: 0.87664236666667

00:55:17.200 --> 00:55:18.800 appreciate the fact that you're
NOTE Confidence: 0.87664236666667

00:55:18.800 --> 00:55:20.880 also getting our department in our
NOTE Confidence: 0.87664236666667

00:55:20.880 --> 00:55:22.680 division more involved with others
NOTE Confidence: 0.87664236666667

00:55:22.680 --> 00:55:25.158 outside of muting this work as well.

NOTE Confidence: 0.876642366666667

00:55:25.160 --> 00:55:27.398 So thank you. Thanks to everybody.

NOTE Confidence: 0.876642366666667

00:55:27.400 --> 00:55:28.666 Cliff, is there anything else you

NOTE Confidence: 0.876642366666667

00:55:28.666 --> 00:55:30.039 need to say before we sign off?

NOTE Confidence: 0.64147525

00:55:33.160 --> 00:55:36.078 No, that was a Tour de

NOTE Confidence: 0.84712754

00:55:36.080 --> 00:55:39.160 force. Thank you. Thanks so much, everyone.

NOTE Confidence: 0.6542443675

00:55:40.240 --> 00:55:41.720 Beautiful. Bye. Bye everybody.