

WEBVTT

NOTE duration:"00:14:47.0020000"

NOTE language:en-us

NOTE Confidence: 0.85852325

00:00:00.000 --> 00:00:02.478 It's now my great pleasure to

NOTE Confidence: 0.85852325

00:00:02.478 --> 00:00:04.130 introduce Doctor Morgan Levine,

NOTE Confidence: 0.85852325

00:00:04.130 --> 00:00:06.374 who is a ladder rank assistant

NOTE Confidence: 0.85852325

00:00:06.374 --> 00:00:08.265 professor in the Department of

NOTE Confidence: 0.85852325

00:00:08.265 --> 00:00:10.568 Pathology and a member of both the

NOTE Confidence: 0.85852325

00:00:10.568 --> 00:00:12.998 Yale Combined Programs in Computational

NOTE Confidence: 0.85852325

00:00:12.998 --> 00:00:14.705 Biology and Bioinformatics,

NOTE Confidence: 0.85852325

00:00:14.710 --> 00:00:17.152 as well as the Yale Center

NOTE Confidence: 0.85852325

00:00:17.152 --> 00:00:18.780 for Research on Aging.

NOTE Confidence: 0.85852325

00:00:18.780 --> 00:00:20.725 She has extensive experience using

NOTE Confidence: 0.85852325

00:00:20.725 --> 00:00:22.670 systems level and machine learning

NOTE Confidence: 0.85852325

00:00:22.730 --> 00:00:24.478 approaches to track epigenetic,

NOTE Confidence: 0.85852325

00:00:24.480 --> 00:00:26.164 transcriptomic and proteomic changes

NOTE Confidence: 0.85852325

00:00:26.164 --> 00:00:28.269 with aging and with developing

NOTE Confidence: 0.85852325

00:00:28.269 --> 00:00:29.942 measures of risk stratification

NOTE Confidence: 0.85852325

00:00:29.942 --> 00:00:31.526 for major chronic diseases.

NOTE Confidence: 0.85852325

00:00:31.530 --> 00:00:33.007 The floor is yours up to living.

NOTE Confidence: 0.8171567

00:00:34.310 --> 00:00:35.820 Thank you so much, Nicole.

NOTE Confidence: 0.8171567

00:00:35.820 --> 00:00:38.664 So I'm going to change course a little bit

NOTE Confidence: 0.8171567

00:00:38.664 --> 00:00:41.528 and a lot of the talks they had been on.

NOTE Confidence: 0.8171567

00:00:41.530 --> 00:00:43.469 Genetics and genomics an I'm actually in

NOTE Confidence: 0.8171567

00:00:43.469 --> 00:00:45.748 talk a little bit more about epigenetics.

NOTE Confidence: 0.8171567

00:00:45.750 --> 00:00:48.261 So before I begin I do have conflict of

NOTE Confidence: 0.8171567

00:00:48.261 --> 00:00:50.558 interest so I have IP associated with some

NOTE Confidence: 0.8171567

00:00:50.558 --> 00:00:52.787 of the markers that I'm just guessing

NOTE Confidence: 0.8171567

00:00:52.787 --> 00:00:55.254 today and I'm also consultant with a

NOTE Confidence: 0.8171567

00:00:55.254 --> 00:00:58.098 biotech company called Elise Team Health.

NOTE Confidence: 0.8171567

00:00:58.100 --> 00:01:00.158 So my love is very interested in

NOTE Confidence: 0.8171567

00:01:00.158 --> 00:01:01.600 studying the biology of aging,

NOTE Confidence: 0.8171567

00:01:01.600 --> 00:01:03.696 and I think it's really important to kind

NOTE Confidence: 0.8171567

00:01:03.696 --> 00:01:05.688 of address 2 important questions there.

NOTE Confidence: 0.8171567

00:01:05.690 --> 00:01:06.578 So number one.

NOTE Confidence: 0.8171567

00:01:06.578 --> 00:01:08.650 What do we mean when we're saying

NOTE Confidence: 0.8171567

00:01:08.713 --> 00:01:10.068 we study aging and #2?

NOTE Confidence: 0.8171567

00:01:10.070 --> 00:01:11.684 Why is it actually important to

NOTE Confidence: 0.8171567

00:01:11.684 --> 00:01:13.770 study aging and I'm going to answer

NOTE Confidence: 0.8171567

00:01:13.770 --> 00:01:15.038 the second question first.

NOTE Confidence: 0.8171567

00:01:15.040 --> 00:01:17.125 'cause it's actually an easier

NOTE Confidence: 0.8171567

00:01:17.125 --> 00:01:18.376 question to address.

NOTE Confidence: 0.8171567

00:01:18.380 --> 00:01:20.998 So some people may not be aware,

NOTE Confidence: 0.8171567

00:01:21.000 --> 00:01:23.244 but aging is actually the biggest

NOTE Confidence: 0.8171567

00:01:23.244 --> 00:01:25.952 risk factor for most of the chronic

NOTE Confidence: 0.8171567

00:01:25.952 --> 00:01:27.857 diseases that people suffer and

NOTE Confidence: 0.8171567

00:01:27.857 --> 00:01:30.348 die from in the US and worldwide.

NOTE Confidence: 0.8171567

00:01:30.350 --> 00:01:32.588 So this is actually a chart.

NOTE Confidence: 0.8171567

00:01:32.590 --> 00:01:35.208 the Y axis here is actually in

NOTE Confidence: 0.8171567

00:01:35.208 --> 00:01:36.330 log incident rate.

NOTE Confidence: 0.8171567

00:01:36.330 --> 00:01:38.250 So actually what this shows is

NOTE Confidence: 0.8171567

00:01:38.250 --> 00:01:40.857 that the risk for all of these

NOTE Confidence: 0.8171567

00:01:40.857 --> 00:01:42.537 chronic diseases actually rises

NOTE Confidence: 0.8171567

00:01:42.537 --> 00:01:44.928 exponentially as a function of age,

NOTE Confidence: 0.8171567

00:01:44.930 --> 00:01:46.870 and it's actually been estimated

NOTE Confidence: 0.8171567

00:01:46.870 --> 00:01:48.034 using demographic data.

NOTE Confidence: 0.8171567

00:01:48.040 --> 00:01:50.857 That if we were to slow the aging process

NOTE Confidence: 0.8171567

00:01:50.857 --> 00:01:53.620 down by something equivalent to 7 years,

NOTE Confidence: 0.8171567

00:01:53.620 --> 00:01:55.370 so this idea of 60s,

NOTE Confidence: 0.8171567

00:01:55.370 --> 00:01:58.070 the new 50 maybe 60 is the new 53 we

NOTE Confidence: 0.8171567

00:01:58.147 --> 00:02:00.487 would actually cut the disease burden

NOTE Confidence: 0.8171567

00:02:00.487 --> 00:02:03.399 in half in the US and worldwide.

NOTE Confidence: 0.86143875

00:02:07.850 --> 00:02:10.391 So to address kind of that first

NOTE Confidence: 0.86143875

00:02:10.391 --> 00:02:13.330 question of what do I mean when I say

NOTE Confidence: 0.86143875

00:02:13.330 --> 00:02:15.455 that we study aging and also annoy

NOTE Confidence: 0.86143875

00:02:15.455 --> 00:02:18.122 me when I say if we were actually to

NOTE Confidence: 0.86143875

00:02:18.122 --> 00:02:20.690 slow the rate of aging by 7 years,

NOTE Confidence: 0.86143875

00:02:20.690 --> 00:02:22.388 I think it's important to really

NOTE Confidence: 0.86143875

00:02:22.388 --> 00:02:23.960 contrast when we're talking about

NOTE Confidence: 0.86143875

00:02:23.960 --> 00:02:25.508 something like chronological aging,

NOTE Confidence: 0.86143875

00:02:25.510 --> 00:02:26.794 which as everyone knows,

NOTE Confidence: 0.86143875

00:02:26.794 --> 00:02:28.720 is basically the time in years,

NOTE Confidence: 0.86143875

00:02:28.720 --> 00:02:30.320 months or days since birth.

NOTE Confidence: 0.86143875

00:02:30.320 --> 00:02:31.604 And actually this should

NOTE Confidence: 0.86143875

00:02:31.604 --> 00:02:32.888 have a positive connotation.

NOTE Confidence: 0.86143875

00:02:32.890 --> 00:02:34.760 It's filled with experiences and

NOTE Confidence: 0.86143875

00:02:34.760 --> 00:02:36.256 contributions back to society.

NOTE Confidence: 0.86143875

00:02:36.260 --> 00:02:38.015 But the reason that chronological

NOTE Confidence: 0.86143875

00:02:38.015 --> 00:02:39.770 age actually get such negative

NOTE Confidence: 0.86143875

00:02:39.831 --> 00:02:41.451 connotation is that it's actually

NOTE Confidence: 0.86143875

00:02:41.451 --> 00:02:43.986 tie to something that in we in the

NOTE Confidence: 0.86143875

00:02:43.986 --> 00:02:45.702 field talk about as biological aging.

NOTE Confidence: 0.86143875

00:02:45.710 --> 00:02:47.943 And there isn't a single kind of

NOTE Confidence: 0.86143875

00:02:47.943 --> 00:02:49.944 definition for what we mean when

NOTE Confidence: 0.86143875

00:02:49.944 --> 00:02:51.906 we talk about but biological aging.

NOTE Confidence: 0.86143875

00:02:51.910 --> 00:02:53.860 But at least in my lab,

NOTE Confidence: 0.86143875

00:02:53.860 --> 00:02:55.940 we like to think of this as kind

NOTE Confidence: 0.86143875

00:02:55.940 --> 00:02:58.095 of the robustness or kind of

NOTE Confidence: 0.86143875

00:02:58.095 --> 00:03:00.055 specificity of a living system.

NOTE Confidence: 0.86143875

00:03:00.060 --> 00:03:02.112 So all living systems are basically

NOTE Confidence: 0.86143875

00:03:02.112 --> 00:03:04.619 set up to function in a certain way,

NOTE Confidence: 0.86143875

00:03:04.620 --> 00:03:05.530 but overtime.

NOTE Confidence: 0.86143875

00:03:05.530 --> 00:03:08.260 That specificity tends to actually decline,

NOTE Confidence: 0.86143875

00:03:08.260 --> 00:03:10.780 and this can lead to things like

NOTE Confidence: 0.86143875

00:03:10.780 --> 00:03:12.303 manifestations of disease or
NOTE Confidence: 0.86143875

00:03:12.303 --> 00:03:14.168 basically risk of system failure,
NOTE Confidence: 0.86143875

00:03:14.170 --> 00:03:17.068 which we might describe this death.
NOTE Confidence: 0.86143875

00:03:17.070 --> 00:03:19.205 So actually what my life is very
NOTE Confidence: 0.86143875

00:03:19.205 --> 00:03:21.499 interested in doing is can we quantify
NOTE Confidence: 0.86143875

00:03:21.499 --> 00:03:23.144 biological aging and contrast that
NOTE Confidence: 0.86143875

00:03:23.144 --> 00:03:25.468 to something like chronological age?
NOTE Confidence: 0.86143875

00:03:25.470 --> 00:03:27.920 And this is important for a number
NOTE Confidence: 0.86143875

00:03:27.920 --> 00:03:28.620 of reasons,
NOTE Confidence: 0.86143875

00:03:28.620 --> 00:03:30.474 so number one as we know
NOTE Confidence: 0.86143875

00:03:30.474 --> 00:03:32.470 chronological age is not modifiable,
NOTE Confidence: 0.86143875

00:03:32.470 --> 00:03:34.570 but we think biological age is,
NOTE Confidence: 0.86143875

00:03:34.570 --> 00:03:36.320 and this is actually conserved.
NOTE Confidence: 0.86143875

00:03:36.320 --> 00:03:38.070 Therefore, as a clinical endpoint.
NOTE Confidence: 0.86143875

00:03:38.070 --> 00:03:40.408 So if there are interventions aimed at
NOTE Confidence: 0.86143875

00:03:40.408 --> 00:03:42.269 actually slowing the aging process,

NOTE Confidence: 0.86143875

00:03:42.270 --> 00:03:44.545 we wouldn't have to wait 10 or

NOTE Confidence: 0.86143875

00:03:44.545 --> 00:03:47.079 20 years to use something like.

NOTE Confidence: 0.86143875

00:03:47.080 --> 00:03:48.640 Mortality or disease incidents.

NOTE Confidence: 0.86143875

00:03:48.640 --> 00:03:49.810 As an endpoint,

NOTE Confidence: 0.86143875

00:03:49.810 --> 00:03:51.760 we can actually measure biological

NOTE Confidence: 0.86143875

00:03:51.760 --> 00:03:53.320 age in real time.

NOTE Confidence: 0.86143875

00:03:53.320 --> 00:03:55.726 It's also just important for a

NOTE Confidence: 0.86143875

00:03:55.726 --> 00:03:57.330 basic understanding of drivers

NOTE Confidence: 0.86143875

00:03:57.399 --> 00:03:58.779 of the aging process.

NOTE Confidence: 0.86143875

00:03:58.780 --> 00:04:00.730 An identification of potential therapeutics,

NOTE Confidence: 0.86143875

00:04:00.730 --> 00:04:02.788 and finally we actually think that

NOTE Confidence: 0.86143875

00:04:02.788 --> 00:04:04.655 knowing biological agent help with

NOTE Confidence: 0.86143875

00:04:04.655 --> 00:04:06.423 primary and secondary prevention

NOTE Confidence: 0.86143875

00:04:06.423 --> 00:04:07.749 through risk stratification.

NOTE Confidence: 0.86143875

00:04:07.750 --> 00:04:10.235 So understanding who in the population is

NOTE Confidence: 0.86143875

00:04:10.235 --> 00:04:13.208 most at risk of various chronic diseases.

NOTE Confidence: 0.8059414

00:04:15.240 --> 00:04:17.536 So my lab and others have actually

NOTE Confidence: 0.8059414

00:04:17.536 --> 00:04:19.599 developed things called epigenetic clocks,

NOTE Confidence: 0.8059414

00:04:19.600 --> 00:04:21.924 which is mostly what I'm going to

NOTE Confidence: 0.8059414

00:04:21.924 --> 00:04:24.447 talk about today to actually try and

NOTE Confidence: 0.8059414

00:04:24.447 --> 00:04:26.637 get at biological aging and measure

NOTE Confidence: 0.8059414

00:04:26.706 --> 00:04:29.028 it in different tissues and organs.

NOTE Confidence: 0.8059414

00:04:29.030 --> 00:04:30.848 So I think she meant clocks

NOTE Confidence: 0.8059414

00:04:30.848 --> 00:04:33.030 are based on DNA methylations,

NOTE Confidence: 0.8059414

00:04:33.030 --> 00:04:35.685 so this is the addition of a methyl group

NOTE Confidence: 0.8059414

00:04:35.685 --> 00:04:38.467 to CPG dinucleotide and DNA methylation,

NOTE Confidence: 0.8059414

00:04:38.470 --> 00:04:40.095 and epigenetics in general are

NOTE Confidence: 0.8059414

00:04:40.095 --> 00:04:41.720 really important in kind of

NOTE Confidence: 0.8059414

00:04:41.785 --> 00:04:43.189 defining cellular states.

NOTE Confidence: 0.8059414

00:04:43.190 --> 00:04:45.476 So as most of you know.

NOTE Confidence: 0.8059414

00:04:45.480 --> 00:04:48.539 Essentially, most of the cells in your.

NOTE Confidence: 0.8059414

00:04:48.540 --> 00:04:49.130 You know,

NOTE Confidence: 0.8059414

00:04:49.130 --> 00:04:51.195 in the body of the same genetics

NOTE Confidence: 0.8059414

00:04:51.195 --> 00:04:53.350 but the average genetics are going

NOTE Confidence: 0.8059414

00:04:53.350 --> 00:04:55.609 to dictate cell state and South

NOTE Confidence: 0.8059414

00:04:55.609 --> 00:04:57.991 phenotype an actually decades ago is

NOTE Confidence: 0.8059414

00:04:57.991 --> 00:04:59.926 shown that actually your epigenetic

NOTE Confidence: 0.8059414

00:04:59.926 --> 00:05:01.766 pattern can also differentiate a

NOTE Confidence: 0.8059414

00:05:01.766 --> 00:05:04.128 young cell from an old cell and

NOTE Confidence: 0.8059414

00:05:04.128 --> 00:05:05.922 using this information we and others

NOTE Confidence: 0.8059414

00:05:05.983 --> 00:05:07.707 have actually developed these.

NOTE Confidence: 0.8059414

00:05:07.710 --> 00:05:09.490 What are called epigenetic locks,

NOTE Confidence: 0.8059414

00:05:09.490 --> 00:05:11.506 where we're looking at hundreds or

NOTE Confidence: 0.8059414

00:05:11.506 --> 00:05:14.127 thousands of CPG is across the genome

NOTE Confidence: 0.8059414

00:05:14.127 --> 00:05:16.147 measuring metalation and actually from

NOTE Confidence: 0.8059414

00:05:16.147 --> 00:05:18.830 there we can get out of predicted age.

NOTE Confidence: 0.8059414

00:05:18.830 --> 00:05:20.881 So this is showing an example of
NOTE Confidence: 0.8059414

00:05:20.881 --> 00:05:23.070 one of these measures were here.
NOTE Confidence: 0.8059414

00:05:23.070 --> 00:05:25.366 We have chronological age plotted on the
NOTE Confidence: 0.8059414

00:05:25.366 --> 00:05:28.275 X axis and epigenetic age on the Y axis,
NOTE Confidence: 0.8059414

00:05:28.280 --> 00:05:29.910 and as you can see,
NOTE Confidence: 0.8059414

00:05:29.910 --> 00:05:32.052 we can get actually a very good
NOTE Confidence: 0.8059414

00:05:32.052 --> 00:05:33.830 indicator of aging based solely.
NOTE Confidence: 0.8059414

00:05:33.830 --> 00:05:37.374 This is from 513 CPG's across the genome.
NOTE Confidence: 0.8059414

00:05:37.380 --> 00:05:39.180 But far more important than just
NOTE Confidence: 0.8059414

00:05:39.180 --> 00:05:41.508 kind of this parlor trick that we
NOTE Confidence: 0.8059414

00:05:41.508 --> 00:05:43.278 can actually predict someone's age.
NOTE Confidence: 0.8059414

00:05:43.280 --> 00:05:44.920 We're really interested in kind
NOTE Confidence: 0.8059414

00:05:44.920 --> 00:05:46.560 of this variance within age,
NOTE Confidence: 0.8059414

00:05:46.560 --> 00:05:48.282 so asking the question of people
NOTE Confidence: 0.8059414

00:05:48.282 --> 00:05:50.279 who are predicted older than they
NOTE Confidence: 0.8059414

00:05:50.279 --> 00:05:51.476 actually are chronologically,

NOTE Confidence: 0.8059414
00:05:51.480 --> 00:05:53.485 or these individuals more at
NOTE Confidence: 0.8059414
00:05:53.485 --> 00:05:55.490 risk for different diseases and
NOTE Confidence: 0.8059414
00:05:55.562 --> 00:05:57.770 conditions associated with aging.
NOTE Confidence: 0.8059414
00:05:57.770 --> 00:06:00.129 So we've looked at this in a
NOTE Confidence: 0.8059414
00:06:00.129 --> 00:06:01.710 number of different issues,
NOTE Confidence: 0.8059414
00:06:01.710 --> 00:06:04.328 so first this is data from the
NOTE Confidence: 0.8059414
00:06:04.328 --> 00:06:06.720 Framingham Heart Study on that was done.
NOTE Confidence: 0.8059414
00:06:06.720 --> 00:06:09.226 The study was done by my postdoc.
NOTE Confidence: 0.8059414
00:06:09.230 --> 00:06:10.498 Albert Higgins Chen were.
NOTE Confidence: 0.8059414
00:06:10.498 --> 00:06:13.208 Basically we can look at a one V
NOTE Confidence: 0.8059414
00:06:13.208 --> 00:06:15.068 Association for one standard deviation
NOTE Confidence: 0.8059414
00:06:15.068 --> 00:06:17.364 increase in your epigenetic age based
NOTE Confidence: 0.8059414
00:06:17.364 --> 00:06:19.596 on in contrast to your chronological
NOTE Confidence: 0.8059414
00:06:19.596 --> 00:06:22.098 age and what we find is that when
NOTE Confidence: 0.8059414
00:06:22.098 --> 00:06:24.260 looking at all 'cause mortality,
NOTE Confidence: 0.8059414

00:06:24.260 --> 00:06:26.040 this one standard deviation increases
NOTE Confidence: 0.8059414

00:06:26.040 --> 00:06:28.639 associated with almost a two fold increase.
NOTE Confidence: 0.8059414

00:06:28.640 --> 00:06:31.470 Risk in all 'cause mortality.
NOTE Confidence: 0.8059414

00:06:31.470 --> 00:06:33.773 We also can look at associations with
NOTE Confidence: 0.8059414

00:06:33.773 --> 00:06:36.250 a number of different conditions,
NOTE Confidence: 0.8059414

00:06:36.250 --> 00:06:36.882 so again,
NOTE Confidence: 0.8059414

00:06:36.882 --> 00:06:38.778 we find that older epigenetic age
NOTE Confidence: 0.8059414

00:06:38.778 --> 00:06:40.817 relative to chronological age is
NOTE Confidence: 0.8059414

00:06:40.817 --> 00:06:42.609 associated with different anthropometric
NOTE Confidence: 0.8059414

00:06:42.609 --> 00:06:45.399 factors like BMI and waist circumference.
NOTE Confidence: 0.8059414

00:06:45.400 --> 00:06:47.390 Functioning factors like heart rate,
NOTE Confidence: 0.8059414

00:06:47.390 --> 00:06:48.982 systolic blood pressure associated
NOTE Confidence: 0.8059414

00:06:48.982 --> 00:06:51.347 with lipid levels, and blood glucose,
NOTE Confidence: 0.8059414

00:06:51.347 --> 00:06:53.292 different health behaviors that we
NOTE Confidence: 0.8059414

00:06:53.292 --> 00:06:55.749 think are dealing serious to health,
NOTE Confidence: 0.8059414

00:06:55.750 --> 00:06:58.138 like cigarette smoking, heavy alcohol use,

NOTE Confidence: 0.8059414

00:06:58.140 --> 00:07:00.130 and a number of diseases.

NOTE Confidence: 0.8059414

00:07:00.130 --> 00:07:00.926 Cardiovascular disease,

NOTE Confidence: 0.8059414

00:07:00.926 --> 00:07:02.876 coronary heart disease, coronary heart.

NOTE Confidence: 0.8059414

00:07:02.876 --> 00:07:04.388 Failure, depression, sleep apnea,

NOTE Confidence: 0.8059414

00:07:04.390 --> 00:07:07.094 and this is actually not an exhaustive list.

NOTE Confidence: 0.8059414

00:07:07.100 --> 00:07:09.248 We've actually associated this with a

NOTE Confidence: 0.8059414

00:07:09.248 --> 00:07:11.170 number of different diseases as well.

NOTE Confidence: 0.8059414

00:07:11.170 --> 00:07:12.860 So on the left here,

NOTE Confidence: 0.8059414

00:07:12.860 --> 00:07:14.550 this is all epigenetic gauge

NOTE Confidence: 0.8059414

00:07:14.550 --> 00:07:15.564 measured in blood.

NOTE Confidence: 0.8059414

00:07:15.570 --> 00:07:17.260 But we can also measure

NOTE Confidence: 0.8059414

00:07:17.260 --> 00:07:18.612 opportunity in specific tissues,

NOTE Confidence: 0.776605

00:07:18.620 --> 00:07:19.920 so my student care.

NOTE Confidence: 0.776605

00:07:19.920 --> 00:07:21.870 Thresh is a student in the

NOTE Confidence: 0.776605

00:07:21.943 --> 00:07:23.708 CMB program here at Yale,

NOTE Confidence: 0.776605

00:07:23.710 --> 00:07:26.076 is interested in epigenetic aging and brain.
NOTE Confidence: 0.776605

00:07:26.080 --> 00:07:28.320 So this is data from what's called
NOTE Confidence: 0.776605

00:07:28.320 --> 00:07:30.989 the Ross Mapco part where we have
NOTE Confidence: 0.776605

00:07:30.989 --> 00:07:33.455 postmortem brain samples and we've measured.
NOTE Confidence: 0.776605

00:07:33.460 --> 00:07:35.445 Gauging in dorsal lateral prefrontal
NOTE Confidence: 0.776605

00:07:35.445 --> 00:07:38.374 cortex and what we show here is
NOTE Confidence: 0.776605

00:07:38.374 --> 00:07:40.559 that higher epigenetic aging is
NOTE Confidence: 0.776605

00:07:40.559 --> 00:07:42.334 associated with postmortem diagnosis
NOTE Confidence: 0.776605

00:07:42.334 --> 00:07:44.716 of Alzheimer's disease and this is
NOTE Confidence: 0.776605

00:07:44.716 --> 00:07:46.908 based on neural pathology diagnosis.
NOTE Confidence: 0.776605

00:07:46.908 --> 00:07:49.902 But we've also shown that even
NOTE Confidence: 0.776605

00:07:49.902 --> 00:07:53.084 pre mortem this also tracks with
NOTE Confidence: 0.776605

00:07:53.084 --> 00:07:55.180 things like cognitive decline.
NOTE Confidence: 0.776605

00:07:55.180 --> 00:07:57.812 I'm so that just goes to show that
NOTE Confidence: 0.776605

00:07:57.812 --> 00:08:00.374 Abby Janicke agent can be measured
NOTE Confidence: 0.776605

00:08:00.374 --> 00:08:02.198 again across different issues,

NOTE Confidence: 0.776605

00:08:02.200 --> 00:08:04.790 so we also have a collaborations with

NOTE Confidence: 0.776605

00:08:04.790 --> 00:08:06.782 doctors whose Diane Hofstadter and

NOTE Confidence: 0.776605

00:08:06.782 --> 00:08:09.218 actually what we've looked at here,

NOTE Confidence: 0.776605

00:08:09.220 --> 00:08:11.482 is normal breast tissue from women

NOTE Confidence: 0.776605

00:08:11.482 --> 00:08:13.510 with and without breast cancer.

NOTE Confidence: 0.776605

00:08:13.510 --> 00:08:15.964 And again we show an accelerated

NOTE Confidence: 0.776605

00:08:15.964 --> 00:08:18.400 epigenetic aging phenotype in women who

NOTE Confidence: 0.776605

00:08:18.400 --> 00:08:21.304 do have breast cancer versus those who don't.

NOTE Confidence: 0.776605

00:08:21.310 --> 00:08:23.285 With the hypothesis that being

NOTE Confidence: 0.776605

00:08:23.285 --> 00:08:25.260 being that may be accelerated.

NOTE Confidence: 0.776605

00:08:25.260 --> 00:08:28.025 Aging in a given tissue may actually

NOTE Confidence: 0.776605

00:08:28.025 --> 00:08:30.057 predispose that tissue to tumorigenesis

NOTE Confidence: 0.776605

00:08:30.057 --> 00:08:32.766 and this is prior to any treatment.

NOTE Confidence: 0.776605

00:08:32.770 --> 00:08:33.510 And similarly,

NOTE Confidence: 0.776605

00:08:33.510 --> 00:08:36.100 we've looked at data in liver and

NOTE Confidence: 0.776605

00:08:36.100 --> 00:08:38.547 we find again higher epigenetic
NOTE Confidence: 0.776605

00:08:38.547 --> 00:08:41.047 aging is associated with obesity,
NOTE Confidence: 0.776605

00:08:41.050 --> 00:08:45.930 NAFLD and Nash in in the liver samples.
NOTE Confidence: 0.776605

00:08:45.930 --> 00:08:46.588 So again,
NOTE Confidence: 0.776605

00:08:46.588 --> 00:08:48.233 we can measure epigenetic aging
NOTE Confidence: 0.776605

00:08:48.233 --> 00:08:49.618 and essentially any different
NOTE Confidence: 0.776605

00:08:49.618 --> 00:08:50.958 tissue and cell type.
NOTE Confidence: 0.776605

00:08:50.960 --> 00:08:53.270 And actually we use the exact same
NOTE Confidence: 0.776605

00:08:53.270 --> 00:08:54.980 algorithm when we're doing this.
NOTE Confidence: 0.776605

00:08:54.980 --> 00:08:56.650 These aren't tissue specific algorithms,
NOTE Confidence: 0.776605

00:08:56.650 --> 00:08:59.107 so we can actually also use this to look
NOTE Confidence: 0.776605

00:08:59.107 --> 00:09:01.677 at kind of between tissue differences,
NOTE Confidence: 0.776605

00:09:01.680 --> 00:09:03.350 so there's this longstanding hypothesis
NOTE Confidence: 0.776605

00:09:03.350 --> 00:09:05.730 in aging research that even though all
NOTE Confidence: 0.776605

00:09:05.730 --> 00:09:07.370 your tissues are essentially aging,
NOTE Confidence: 0.776605

00:09:07.370 --> 00:09:09.715 they do this in an asynchronous manner,

NOTE Confidence: 0.776605

00:09:09.720 --> 00:09:12.726 so they're not all aging at the same rate.

NOTE Confidence: 0.776605

00:09:12.730 --> 00:09:14.962 So what we've done here is

NOTE Confidence: 0.776605

00:09:14.962 --> 00:09:16.450 we've looked at epigenetic.

NOTE Confidence: 0.776605

00:09:16.450 --> 00:09:18.125 In a variety of different

NOTE Confidence: 0.776605

00:09:18.125 --> 00:09:19.465 tissue and cell types,

NOTE Confidence: 0.776605

00:09:19.470 --> 00:09:21.660 and basically what we find again

NOTE Confidence: 0.776605

00:09:21.660 --> 00:09:24.059 is that your tissues and tissues do

NOTE Confidence: 0.776605

00:09:24.059 --> 00:09:26.500 not seem to age at the same rate,

NOTE Confidence: 0.776605

00:09:26.500 --> 00:09:28.510 so all these on the bottom

NOTE Confidence: 0.776605

00:09:28.510 --> 00:09:29.850 are actually from brain.

NOTE Confidence: 0.776605

00:09:29.850 --> 00:09:32.195 So it seems that brain not only

NOTE Confidence: 0.776605

00:09:32.195 --> 00:09:33.200 seems epigenetically younger,

NOTE Confidence: 0.776605

00:09:33.200 --> 00:09:35.132 but the rate of increase in

NOTE Confidence: 0.776605

00:09:35.132 --> 00:09:36.890 epigenetic aging also seems slower,

NOTE Confidence: 0.776605

00:09:36.890 --> 00:09:38.900 and then some of these more

NOTE Confidence: 0.776605

00:09:38.900 --> 00:09:40.240 proliferative tissues like colon,
NOTE Confidence: 0.776605

00:09:40.240 --> 00:09:43.888 epidermis and some of the blood cell types.
NOTE Confidence: 0.776605

00:09:43.890 --> 00:09:46.650 We can also just compare within
NOTE Confidence: 0.776605

00:09:46.650 --> 00:09:48.030 a tissue tumor.
NOTE Confidence: 0.776605

00:09:48.030 --> 00:09:50.162 Epigenetic measures from tumor
NOTE Confidence: 0.776605

00:09:50.162 --> 00:09:52.827 samples versus normal an across
NOTE Confidence: 0.776605

00:09:52.827 --> 00:09:54.547 different cancer subtypes or
NOTE Confidence: 0.776605

00:09:54.547 --> 00:09:56.767 types we find in red here.
NOTE Confidence: 0.776605

00:09:56.770 --> 00:09:59.626 The tumor samples seem to have
NOTE Confidence: 0.776605

00:09:59.626 --> 00:10:01.054 accelerated epigenetic aging
NOTE Confidence: 0.776605

00:10:01.054 --> 00:10:03.208 compared to the normal controls.
NOTE Confidence: 0.82631147

00:10:05.650 --> 00:10:07.600 So one kind of outstanding question
NOTE Confidence: 0.82631147

00:10:07.600 --> 00:10:10.082 in this field is really, you know,
NOTE Confidence: 0.82631147

00:10:10.082 --> 00:10:11.446 mechanistically what's driving up.
NOTE Confidence: 0.82631147

00:10:11.450 --> 00:10:13.634 The genetic aging, and are there
NOTE Confidence: 0.82631147

00:10:13.634 --> 00:10:15.769 actually ways to intervene and modify

NOTE Confidence: 0.82631147

00:10:15.769 --> 00:10:17.925 the rate of the Fiji night change?

NOTE Confidence: 0.82631147

00:10:17.930 --> 00:10:20.310 So one of my sons Christmas here,

NOTE Confidence: 0.82631147

00:10:20.310 --> 00:10:22.686 who's in the M2P2 program here at Yale

NOTE Confidence: 0.82631147

00:10:22.686 --> 00:10:24.491 is actually working on developing

NOTE Confidence: 0.82631147

00:10:24.491 --> 00:10:26.789 in vitro models of epigenetic aging,

NOTE Confidence: 0.82631147

00:10:26.790 --> 00:10:29.100 so we can show that.

NOTE Confidence: 0.82631147

00:10:29.100 --> 00:10:30.910 Simply by passaging different cells.

NOTE Confidence: 0.82631147

00:10:30.910 --> 00:10:32.710 We've done this in mouse

NOTE Confidence: 0.82631147

00:10:32.710 --> 00:10:33.430 embryonic fibroblasts.

NOTE Confidence: 0.82631147

00:10:33.430 --> 00:10:35.374 We've done this in human astrocytes

NOTE Confidence: 0.82631147

00:10:35.374 --> 00:10:37.121 that we can actually recapitulate

NOTE Confidence: 0.82631147

00:10:37.121 --> 00:10:39.086 the exact same epigenetic patterns

NOTE Confidence: 0.82631147

00:10:39.086 --> 00:10:41.010 that we're seeing in vivo.

NOTE Confidence: 0.82631147

00:10:41.010 --> 00:10:43.460 So this is the method that Chris

NOTE Confidence: 0.82631147

00:10:43.460 --> 00:10:45.295 generated where he can show

NOTE Confidence: 0.82631147

00:10:45.295 --> 00:10:47.080 this increase in Abidjan cage
NOTE Confidence: 0.82631147

00:10:47.080 --> 00:10:49.319 as a function of cell passage,
NOTE Confidence: 0.82631147

00:10:49.320 --> 00:10:51.777 and then it uses the exact same
NOTE Confidence: 0.82631147

00:10:51.777 --> 00:10:54.696 equation and show that we can also see
NOTE Confidence: 0.82631147

00:10:54.696 --> 00:10:57.279 these exact same changes with age in
NOTE Confidence: 0.82631147

00:10:57.279 --> 00:10:59.785 vivo in a variety of different issues,
NOTE Confidence: 0.82631147

00:10:59.790 --> 00:11:01.023 so liver long.
NOTE Confidence: 0.82631147

00:11:01.023 --> 00:11:02.667 Kidney blood adipose however
NOTE Confidence: 0.82631147

00:11:02.667 --> 00:11:04.919 lesser extent and sculpt muscle,
NOTE Confidence: 0.82631147

00:11:04.920 --> 00:11:07.368 which is perhaps not surprising 'cause
NOTE Confidence: 0.82631147

00:11:07.368 --> 00:11:10.558 it's tends to be mostly post mitotic.
NOTE Confidence: 0.82014126

00:11:12.870 --> 00:11:14.780 But then again, probably the
NOTE Confidence: 0.82014126

00:11:14.780 --> 00:11:16.308 most important question here
NOTE Confidence: 0.82014126

00:11:16.308 --> 00:11:18.479 is whether this is modifiable,
NOTE Confidence: 0.82014126

00:11:18.480 --> 00:11:21.688 so this is actually on the left here.
NOTE Confidence: 0.82014126

00:11:21.690 --> 00:11:24.567 A collaboration that we did with Doctor

NOTE Confidence: 0.82014126

00:11:24.567 --> 00:11:27.027 David Sinclair at Harvard and his

NOTE Confidence: 0.82014126

00:11:27.027 --> 00:11:29.701 then student at the time using Luann.

NOTE Confidence: 0.82014126

00:11:29.710 --> 00:11:32.380 Basically, this is.

NOTE Confidence: 0.82014126

00:11:32.380 --> 00:11:34.405 Fishing nature last year where

NOTE Confidence: 0.82014126

00:11:34.405 --> 00:11:37.810 we had a test on Ted off system.

NOTE Confidence: 0.82014126

00:11:37.810 --> 00:11:40.505 For those of you familiar with Yamanaka

NOTE Confidence: 0.82014126

00:11:40.505 --> 00:11:42.647 factors were actually doing what

NOTE Confidence: 0.82014126

00:11:42.647 --> 00:11:44.495 we call epigenetic reprogramming.

NOTE Confidence: 0.82014126

00:11:44.500 --> 00:11:48.838 So this was a three factor system with OSK.

NOTE Confidence: 0.82014126

00:11:48.840 --> 00:11:51.857 And basically what they did is they

NOTE Confidence: 0.82014126

00:11:51.857 --> 00:11:54.649 crushed the optical nerve and they show

NOTE Confidence: 0.82014126

00:11:54.649 --> 00:11:57.750 that when you turn on OSK you actually

NOTE Confidence: 0.82014126

00:11:57.750 --> 00:12:00.456 get Rigo growth of these ganglia,

NOTE Confidence: 0.82014126

00:12:00.460 --> 00:12:02.540 neural, neural neural ganglion cells.

NOTE Confidence: 0.82014126

00:12:02.540 --> 00:12:05.522 But we also see change in the

NOTE Confidence: 0.82014126

00:12:05.522 --> 00:12:07.520 epigenetic aging pattern as well,
NOTE Confidence: 0.82014126

00:12:07.520 --> 00:12:10.010 so these are to be intact.
NOTE Confidence: 0.82014126

00:12:10.010 --> 00:12:12.344 So with without the crushing but
NOTE Confidence: 0.82014126

00:12:12.344 --> 00:12:15.289 with when you get injury you see
NOTE Confidence: 0.82014126

00:12:15.289 --> 00:12:17.474 an increase in epigenetic age.
NOTE Confidence: 0.82014126

00:12:17.480 --> 00:12:19.320 But then when you.
NOTE Confidence: 0.82014126

00:12:19.320 --> 00:12:20.700 Express to SK.
NOTE Confidence: 0.82014126

00:12:20.700 --> 00:12:23.190 You get a reduction in the
NOTE Confidence: 0.82014126

00:12:23.190 --> 00:12:24.435 epigenetic age again.
NOTE Confidence: 0.82014126

00:12:24.440 --> 00:12:25.965 And we actually show this
NOTE Confidence: 0.82014126

00:12:25.965 --> 00:12:27.980 as well in an aged model,
NOTE Confidence: 0.82014126

00:12:27.980 --> 00:12:29.590 not just an injury model,
NOTE Confidence: 0.82014126

00:12:29.590 --> 00:12:31.893 where with aging we show an increase
NOTE Confidence: 0.82014126

00:12:31.893 --> 00:12:34.098 in the epigenetic age in these cells.
NOTE Confidence: 0.82014126

00:12:34.100 --> 00:12:36.740 But with OSK we we can actually show
NOTE Confidence: 0.82014126

00:12:36.740 --> 00:12:38.607 in deceleration in upper GI gauge.

NOTE Confidence: 0.82014126

00:12:38.610 --> 00:12:40.542 And we've shown in a number

NOTE Confidence: 0.82014126

00:12:40.542 --> 00:12:42.150 of different cell types too.

NOTE Confidence: 0.82014126

00:12:42.150 --> 00:12:44.374 When you look at when you take a

NOTE Confidence: 0.82014126

00:12:44.374 --> 00:12:46.450 somatic cell and convert it back

NOTE Confidence: 0.82014126

00:12:46.450 --> 00:12:48.270 to induce player problem stencil,

NOTE Confidence: 0.82014126

00:12:48.270 --> 00:12:50.650 you also get a reversion or or

NOTE Confidence: 0.82014126

00:12:50.650 --> 00:12:52.156 basically complete erase erasing

NOTE Confidence: 0.82014126

00:12:52.156 --> 00:12:54.266 of this epigenetic aging pattern.

NOTE Confidence: 0.82014126

00:12:54.270 --> 00:12:54.942 And similarly,

NOTE Confidence: 0.82014126

00:12:54.942 --> 00:12:56.958 we've also looked in studies in

NOTE Confidence: 0.82014126

00:12:56.958 --> 00:12:59.010 mice on dietary intervention,

NOTE Confidence: 0.82014126

00:12:59.010 --> 00:13:01.386 so here this is a epigenetic

NOTE Confidence: 0.82014126

00:13:01.386 --> 00:13:03.749 gauge measure and mice in blood.

NOTE Confidence: 0.82014126

00:13:03.750 --> 00:13:06.109 And here in pink we have my

NOTE Confidence: 0.82014126

00:13:06.109 --> 00:13:08.100 sister on caloric restriction,

NOTE Confidence: 0.82014126

00:13:08.100 --> 00:13:10.284 so we showed a clinically restricted
NOTE Confidence: 0.82014126

00:13:10.284 --> 00:13:13.228 mice seem to have lower epigenetic age.
NOTE Confidence: 0.82014126

00:13:13.230 --> 00:13:15.631 They were all started at the same
NOTE Confidence: 0.82014126

00:13:15.631 --> 00:13:17.580 time on choric restriction,
NOTE Confidence: 0.82014126

00:13:17.580 --> 00:13:20.604 so we actually show that it
NOTE Confidence: 0.82014126

00:13:20.604 --> 00:13:23.218 actually just also decreases the
NOTE Confidence: 0.82014126

00:13:23.218 --> 00:13:26.230 rate of epigenetic aging over time.
NOTE Confidence: 0.82014126

00:13:26.230 --> 00:13:27.571 So as takeaways,
NOTE Confidence: 0.82014126

00:13:27.571 --> 00:13:29.359 biological aging is actually
NOTE Confidence: 0.82014126

00:13:29.359 --> 00:13:31.130 distinct from chronological aging,
NOTE Confidence: 0.82014126

00:13:31.130 --> 00:13:33.668 and we can actually use things
NOTE Confidence: 0.82014126

00:13:33.668 --> 00:13:35.893 like epigenetic clocks that are
NOTE Confidence: 0.82014126

00:13:35.893 --> 00:13:38.647 based on DNA metalation to actually
NOTE Confidence: 0.82014126

00:13:38.647 --> 00:13:40.024 track biological aging,
NOTE Confidence: 0.82014126

00:13:40.030 --> 00:13:42.250 quantify it in various cells,
NOTE Confidence: 0.82014126

00:13:42.250 --> 00:13:44.185 and tissue types between person

NOTE Confidence: 0.82014126

00:13:44.185 --> 00:13:46.120 differences in the discordance between

NOTE Confidence: 0.82014126

00:13:46.180 --> 00:13:47.689 chronological inopportune engages

NOTE Confidence: 0.82014126

00:13:47.689 --> 00:13:49.701 biologically meaningful and actually

NOTE Confidence: 0.82014126

00:13:49.701 --> 00:13:52.490 has implications for things like morbidity,

NOTE Confidence: 0.82014126

00:13:52.490 --> 00:13:52.973 mortality,

NOTE Confidence: 0.82014126

00:13:52.973 --> 00:13:53.456 risk.

NOTE Confidence: 0.82014126

00:13:53.456 --> 00:13:56.354 An epigenetic clocks can be used

NOTE Confidence: 0.82014126

00:13:56.354 --> 00:13:59.154 to study asynchronous aging across

NOTE Confidence: 0.82014126

00:13:59.154 --> 00:14:02.069 different issue install States and

NOTE Confidence: 0.82014126

00:14:02.069 --> 00:14:04.768 also show distinctions in tissue

NOTE Confidence: 0.82014126

00:14:04.768 --> 00:14:07.183 state or such as acceleration

NOTE Confidence: 0.82014126

00:14:07.183 --> 00:14:08.956 at in tumor Genesis.

NOTE Confidence: 0.82014126

00:14:08.956 --> 00:14:11.374 They can also be used to

NOTE Confidence: 0.82014126

00:14:11.374 --> 00:14:13.856 facilitate in vitro aging models

NOTE Confidence: 0.82014126

00:14:13.856 --> 00:14:15.984 for discovery of therapeutics,

NOTE Confidence: 0.82014126

00:14:15.990 --> 00:14:17.890 and potentially the most important

NOTE Confidence: 0.82014126

00:14:17.890 --> 00:14:19.790 thing is that epigenetic aging

NOTE Confidence: 0.82014126

00:14:19.857 --> 00:14:21.789 phenomena is actually modifiable,

NOTE Confidence: 0.82014126

00:14:21.790 --> 00:14:25.101 but it's yet to show whether a

NOTE Confidence: 0.82014126

00:14:25.101 --> 00:14:26.520 deceleration epigenetic aging

NOTE Confidence: 0.82014126

00:14:26.599 --> 00:14:29.197 will actually manifest as as a

NOTE Confidence: 0.82014126

00:14:29.197 --> 00:14:31.585 reduced risks and things like

NOTE Confidence: 0.82014126

00:14:31.585 --> 00:14:33.298 morbidity and mortality.

NOTE Confidence: 0.82014126

00:14:33.300 --> 00:14:35.498 And with that I just want to

NOTE Confidence: 0.82014126

00:14:35.498 --> 00:14:37.119 acknowledge the people in my lab.

NOTE Confidence: 0.82014126

00:14:37.120 --> 00:14:38.264 My collaborators at Yellen

NOTE Confidence: 0.82014126

00:14:38.264 --> 00:14:39.980 elsewhere and also my funding from

NOTE Confidence: 0.8459289

00:14:40.029 --> 00:14:41.529 the National Institute on Aging,

NOTE Confidence: 0.8459289

00:14:41.530 --> 00:14:43.354 and I'm happy to take questions

NOTE Confidence: 0.8459289

00:14:43.354 --> 00:14:45.348 either via email or in the chat.

NOTE Confidence: 0.8459289

00:14:45.350 --> 00:14:47.002 Thank you so much.