WEBVTT

NOTE duration:"00:26:30.0160000"

NOTE language:en-us

NOTE Confidence: 0.9153512

00:00:00.000 --> 00:00:03.283 Morgan is an assistant professor of pathology

NOTE Confidence: 0.9153512

00:00:03.283 --> 00:00:06.347 and Epidemiology at the school of Madison.

NOTE Confidence: 0.9153512

00:00:06.350 --> 00:00:08.948 She's a member of the combined

NOTE Confidence: 0.9153512

00:00:08.948 --> 00:00:10.680 program in computational biology,

NOTE Confidence: 0.9153512

00:00:10.680 --> 00:00:13.788 environ fanatics, as well as the Center

NOTE Confidence: 0.9153512

00:00:13.788 --> 00:00:16.737 for research on Aging and her work.

NOTE Confidence: 0.9153512

00:00:16.740 --> 00:00:18.316 Her multidisciplinary work has

NOTE Confidence: 0.9153512

00:00:18.316 --> 00:00:19.892 really been integrating new

NOTE Confidence: 0.9153512

00:00:19.892 --> 00:00:21.940 methods of statistical genetics,

NOTE Confidence: 0.9153512

00:00:21.940 --> 00:00:22.806 computational biology,

NOTE Confidence: 0.9153512

00:00:22.806 --> 00:00:24.538 mathematical demography to develop,

NOTE Confidence: 0.9153512

00:00:24.540 --> 00:00:27.851 sort of a new high dimensional mix

NOTE Confidence: 0.9153512

00:00:27.851 --> 00:00:31.470 approach to aging in both humans and

NOTE Confidence: 0.9153512

00:00:31.470 --> 00:00:34.100 animal models and applying those.

NOTE Confidence: 0.9153512

00:00:34.100 --> 00:00:36.122 Efforts to a variety of major

NOTE Confidence: 0.9153512

00:00:36.122 --> 00:00:36.796 chronic disease,

NOTE Confidence: 0.9153512

00:00:36.800 --> 00:00:37.820 most notably cancer,

NOTE Confidence: 0.9153512

00:00:37.820 --> 00:00:40.200 and so Morgan really pleased to hear

NOTE Confidence: 0.9153512

00:00:40.263 --> 00:00:42.887 about your work and looking forward to talk.

NOTE Confidence: 0.9153512

00:00:42.890 --> 00:00:44.240 Thank you so much.

NOTE Confidence: 0.68500984

00:00:48.540 --> 00:00:51.190 OK, maybe we can see that yes.

NOTE Confidence: 0.9155807

00:00:55.080 --> 00:00:57.330 And let me make it bigger on my screen.

NOTE Confidence: 0.8740703

00:01:01.700 --> 00:01:04.460 OK, um, so today I'm going to talk

NOTE Confidence: 0.8740703

00:01:04.460 --> 00:01:08.001 about some of my work on in developing

NOTE Confidence: 0.8740703

00:01:08.001 --> 00:01:10.354 biomarkers using DNA methylation data

NOTE Confidence: 0.8740703

00:01:10.354 --> 00:01:13.378 to study aging and diseases like cancer.

NOTE Confidence: 0.61551213

00:01:16.750 --> 00:01:21.020 Why isn't it? I'm so I usually like to

NOTE Confidence: 0.61551213

00:01:21.020 --> 00:01:23.288 kind of remind people what the biggest

NOTE Confidence: 0.61551213

00:01:23.288 --> 00:01:25.717 risk factor for most major cancers is,

NOTE Confidence: 0.61551213

00:01:25.720 --> 00:01:27.911 and I like to illustrate this often

NOTE Confidence: 0.61551213

00:01:27.911 --> 00:01:29.579 using something like lung cancer.

NOTE Confidence: 0.61551213

00:01:29.580 --> 00:01:32.244 So a lot of times when asking students what

NOTE Confidence: 0.61551213

00:01:32.244 --> 00:01:35.060 the biggest risk factor for lung cancer is,

NOTE Confidence: 0.61551213

00:01:35.060 --> 00:01:36.986 they'll say something like cigarette smoking,

NOTE Confidence: 0.61551213

00:01:36.990 --> 00:01:38.916 which we know increases the risk.

NOTE Confidence: 0.61551213

00:01:38.920 --> 00:01:40.960 The incidence and death from lung

NOTE Confidence: 0.61551213

00:01:40.960 --> 00:01:43.110 cancer by about 15 to 30 fold.

NOTE Confidence: 0.61551213

00:01:43.110 --> 00:01:44.007 But in reality,

NOTE Confidence: 0.61551213

00:01:44.007 --> 00:01:46.100 aging itself is actually much bigger risk

NOTE Confidence: 0.61551213

00:01:46.155 --> 00:01:48.600 factor for developing lung cancer, so for

NOTE Confidence: 0.61551213

00:01:48.600 --> 00:01:51.240 individuals who are 25 to 29 years old.

NOTE Confidence: 0.61551213

00:01:51.240 --> 00:01:52.544 About one in 200,000,

NOTE Confidence: 0.61551213

00:01:52.544 --> 00:01:54.943 you have about one in 200,000 chance

NOTE Confidence: 0.61551213

00:01:54.943 --> 00:01:58.320 of Belton lung cancer, however.

NOTE Confidence: 0.61551213

00:01:58.320 --> 00:02:00.508 Nearly 400 and 100K,

NOTE Confidence: 0.61551213

00:02:00.508 --> 00:02:04.867 so it UH-80 full increase risk for the

NOTE Confidence: 0.61551213

00:02:04.867 --> 00:02:09.160 OR 800 fold increases for those 75 to 79.

NOTE Confidence: 0.61551213

00:02:09.160 --> 00:02:11.146 And this is the case across

NOTE Confidence: 0.61551213

00:02:11.146 --> 00:02:13.140 a wide variety of cancers.

NOTE Confidence: 0.61551213

00:02:13.140 --> 00:02:14.950 We see, UM, in general,

NOTE Confidence: 0.61551213

00:02:14.950 --> 00:02:17.477 an exponential increase with age in both

NOTE Confidence: 0.61551213

00:02:17.477 --> 00:02:19.658 incidents in mortality risks from cancer.

NOTE Confidence: 0.61551213

00:02:19.660 --> 00:02:20.626 And you know,

NOTE Confidence: 0.61551213

00:02:20.626 --> 00:02:22.558 some people have thought that this

NOTE Confidence: 0.61551213

00:02:22.558 --> 00:02:25.088 is just commit probability with time.

NOTE Confidence: 0.61551213

00:02:25.090 --> 00:02:27.256 So at the longer you live,

NOTE Confidence: 0.61551213

00:02:27.260 --> 00:02:29.668 the more time and the more likely

NOTE Confidence: 0.61551213

00:02:29.668 --> 00:02:31.240 they will develop cancer.

NOTE Confidence: 0.61551213

00:02:31.240 --> 00:02:31.894 But really,

NOTE Confidence: 0.61551213

00:02:31.894 --> 00:02:34.183 what we think is that it's actually

NOTE Confidence: 0.61551213

00:02:34.183 --> 00:02:35.220 the molecular.

NOTE Confidence: 0.61551213

00:02:35.220 --> 00:02:36.816 Another changes that accompanied

NOTE Confidence: 0.61551213

00:02:36.816 --> 00:02:38.811 the aging process that are

NOTE Confidence: 0.61551213

00:02:38.811 --> 00:02:40.557 actually playing a causal role.

NOTE Confidence: 0.61551213

00:02:40.560 --> 00:02:42.245 In the ideology of major

NOTE Confidence: 0.61551213

00:02:42.245 --> 00:02:43.256 diseases like cancer,

NOTE Confidence: 0.61551213

00:02:43.260 --> 00:02:46.302 so I like this kind of New Yorker Cartoon,

NOTE Confidence: 0.61551213

00:02:46.310 --> 00:02:48.565 which says you're deliberately putting

NOTE Confidence: 0.61551213

00:02:48.565 --> 00:02:52.048 yourself at risk avail help by being over 65.

NOTE Confidence: 0.61551213

00:02:52.050 --> 00:02:54.234 So one thing that my lab is really

NOTE Confidence: 0.61551213

00:02:54.234 --> 00:02:56.238 interested in is can we actually try

NOTE Confidence: 0.61551213

00:02:56.238 --> 00:02:58.040 and quantify some of these aging

NOTE Confidence: 0.61551213

00:02:58.040 --> 00:02:59.775 changes that might underlie risk

NOTE Confidence: 0.61551213

00:02:59.775 --> 00:03:02.166 for things like cancer or other

NOTE Confidence: 0.61551213

00:03:02.166 --> 00:03:03.660 major chronic diseases?

NOTE Confidence: 0.61551213

00:03:03.660 --> 00:03:05.487 And so this is where kind of

NOTE Confidence: 0.61551213

00:03:05.487 --> 00:03:06.759 biomarkers of aging come in.

NOTE Confidence: 0.61551213

00:03:06.760 --> 00:03:09.040 Uh, so aging is.

NOTE Confidence: 0.61551213

00:03:09.040 --> 00:03:10.156 Not an observable,

NOTE Confidence: 0.61551213

00:03:10.156 --> 00:03:12.016 it's it's this latent concept.

NOTE Confidence: 0.61551213

00:03:12.020 --> 00:03:14.258 So it's actually hard to define.

NOTE Confidence: 0.61551213

00:03:14.260 --> 00:03:16.702 But biomarkers can actually serve as

NOTE Confidence: 0.61551213

00:03:16.702 --> 00:03:19.066 useful proxies that we can estimate

NOTE Confidence: 0.61551213

00:03:19.066 --> 00:03:21.714 the agent Ness of a cell or tissue,

NOTE Confidence: 0.61551213

00:03:21.720 --> 00:03:23.958 or on the whole Organism level.

NOTE Confidence: 0.61551213

00:03:23.960 --> 00:03:26.564 So they serve a variety of purposes.

NOTE Confidence: 0.61551213

00:03:26.570 --> 00:03:29.552 They can be used as clinical trial

NOTE Confidence: 0.61551213

00:03:29.552 --> 00:03:31.517 endpoints for interventions to try

NOTE Confidence: 0.61551213

00:03:31.517 --> 00:03:33.652 and slow the rate of aging there.

NOTE Confidence: 0.61551213

00:03:33.660 --> 00:03:36.845 You can also be used for basic

NOTE Confidence: 0.61551213

00:03:36.845 --> 00:03:38.830 biology to understand aging.

NOTE Confidence: 0.61551213

00:03:38.830 --> 00:03:40.655 And also for risk stratification

NOTE Confidence: 0.61551213

00:03:40.655 --> 00:03:43.152 and the goals in developing some of

NOTE Confidence: 0.61551213

00:03:43.152 --> 00:03:44.976 these biomarkers is that you should

NOTE Confidence: 0.61551213

00:03:44.976 --> 00:03:46.673 have a biomarker that differentiates

NOTE Confidence: 0.61551213

00:03:46.673 --> 00:03:49.742 between a 20 year old an 8 year old,

NOTE Confidence: 0.61551213

00:03:49.742 --> 00:03:51.106 which is pretty easy.

NOTE Confidence: 0.61551213

00:03:51.110 --> 00:03:54.179 You can even use facial image to do that,

NOTE Confidence: 0.61551213

00:03:54.180 --> 00:03:56.220 but probably the harder thing is,

NOTE Confidence: 0.61551213

00:03:56.220 --> 00:03:57.488 can you actually differentiate

NOTE Confidence: 0.61551213

00:03:57.488 --> 00:03:59.073 risks among individuals of the

NOTE Confidence: 0.61551213

00:03:59.073 --> 00:04:00.310 same chronological age?

NOTE Confidence: 0.61551213

00:04:00.310 --> 00:04:02.998 So can you identify who might be aging

NOTE Confidence: 0.61551213

00:04:02.998 --> 00:04:05.427 faster or slower and then in turn,

NOTE Confidence: 0.61551213

00:04:05.430 --> 00:04:07.980 does that have implications for the

NOTE Confidence: 0.61551213

00:04:07.980 --> 00:04:11.400 risk of a future morbidity mortality?

NOTE Confidence: 0.61551213

00:04:11.400 --> 00:04:13.376 So most of the biomarkers in my lab

NOTE Confidence: 0.61551213

00:04:13.376 --> 00:04:15.586 works on a more epigenetic biomarkers

NOTE Confidence: 0.61551213

00:04:15.586 --> 00:04:18.076 and specifically involved in DNA methylation,

NOTE Confidence: 0.61551213

00:04:18.080 --> 00:04:20.600 so I like to think of the meth alone as

NOTE Confidence: 0.90098894

00:04:20.666 --> 00:04:22.988 kind of the molecular operating system

NOTE Confidence: 0.90098894

00:04:22.988 --> 00:04:25.307 it instructs else how they should

NOTE Confidence: 0.90098894

00:04:25.307 --> 00:04:27.750 behave and respond is involved in a

NOTE Confidence: 0.90098894

00:04:27.750 --> 00:04:29.836 number of different cellular processes,

NOTE Confidence: 0.90098894

00:04:29.836 --> 00:04:32.440 but a really interesting thing that

NOTE Confidence: 0.90098894

00:04:32.513 --> 00:04:34.571 was pointed out more than I think

NOTE Confidence: 0.90098894

00:04:34.571 --> 00:04:36.822 30 years ago is that there does

NOTE Confidence: 0.90098894

00:04:36.822 --> 00:04:38.778 seem to be genome wide patterns.

NOTE Confidence: 0.90098894

00:04:38.780 --> 00:04:40.940 Um that emerge in terms of

NOTE Confidence: 0.90098894

00:04:40.940 --> 00:04:42.860 changes in Maculation with aging.

NOTE Confidence: 0.90098894

00:04:42.860 --> 00:04:46.852 So you gotta change net in the maculation

NOTE Confidence: 0.90098894

00:04:46.852 --> 00:04:49.610 landscape as a function of age.

NOTE Confidence: 0.90098894

00:04:49.610 --> 00:04:51.320 And based on this, uh,

NOTE Confidence: 0.90098894

00:04:51.320 --> 00:04:52.544 a number of labs,

NOTE Confidence: 0.90098894

00:04:52.544 --> 00:04:54.074 including ours who developed what

NOTE Confidence: 0.90098894

00:04:54.074 --> 00:04:56.087 we call these epigenetic clocks.

NOTE Confidence: 0.90098894

00:04:56.090 --> 00:04:58.477 So because they have been very precise,

NOTE Confidence: 0.90098894

00:04:58.480 --> 00:05:00.520 age changes that have been observed.

NOTE Confidence: 0.90098894

00:05:00.520 --> 00:05:02.190 We actually use machine learning

NOTE Confidence: 0.90098894

00:05:02.190 --> 00:05:04.613 to predict the age of a sample

NOTE Confidence: 0.90098894

00:05:04.613 --> 00:05:06.659 based on the DNA methylation level.

NOTE Confidence: 0.90098894

00:05:06.660 --> 00:05:09.276 So you can take a sample from whole

NOTE Confidence: 0.90098894

00:05:09.276 --> 00:05:11.777 blood from tissue in a cell culture,

NOTE Confidence: 0.90098894

00:05:11.780 --> 00:05:14.060 and we often measure metalation at

NOTE Confidence: 0.90098894

00:05:14.060 --> 00:05:17.039 10s of thousands to now up to 850,000

NOTE Confidence: 0.90098894

00:05:17.039 --> 00:05:19.680 different CP G sites across the genome.

NOTE Confidence: 0.90098894

00:05:19.680 --> 00:05:22.408 And then what people have done is applied

NOTE Confidence: 0.90098894

00:05:22.408 --> 00:05:23.995 supervised machine learning methods

NOTE Confidence: 0.90098894

00:05:23.995 --> 00:05:26.105 to actually develop age predictors.

NOTE Confidence: 0.90098894

00:05:26.110 --> 00:05:28.742 So most of the early clocks were trained

NOTE Confidence: 0.90098894

00:05:28.742 --> 00:05:31.397 to predict things like chronological age,

NOTE Confidence: 0.90098894

00:05:31.400 --> 00:05:34.039 the first Clock being published in 2011.

NOTE Confidence: 0.90098894

00:05:34.040 --> 00:05:36.308 However, more recent clocks have actually,

NOTE Confidence: 0.90098894

00:05:36.310 --> 00:05:38.956 which we call the second generation at.

NOTE Confidence: 0.90098894

00:05:38.960 --> 00:05:40.468 The generic clocks were

NOTE Confidence: 0.90098894

00:05:40.468 --> 00:05:42.353 developed to predict age coral.

NOTE Confidence: 0.90098894

00:05:42.360 --> 00:05:44.250 It's so not chronological age,

NOTE Confidence: 0.90098894

00:05:44.250 --> 00:05:46.512 but things like mortality or physiological

NOTE Confidence: 0.90098894

00:05:46.512 --> 00:05:48.410 processes that change with aging.

NOTE Confidence: 0.90098894

00:05:48.410 --> 00:05:49.582 So mostly that was.

NOTE Confidence: 0.90098894

00:05:49.582 --> 00:05:51.865 Our Clock is one of the second

NOTE Confidence: 0.90098894

00:05:51.865 --> 00:05:54.607 generation clocks inside the John Clock.

NOTE Confidence: 0.90098894

00:05:54.610 --> 00:05:57.136 And the second generation clocks actually

NOTE Confidence: 0.90098894

00:05:57.136 --> 00:06:00.425 tend to be much better predictors of

NOTE Confidence: 0.90098894

00:06:00.425 --> 00:06:02.965 future disease and mortality risk.

NOTE Confidence: 0.90098894

00:06:02.970 --> 00:06:03.250 Uhm,

NOTE Confidence: 0.90098894

00:06:03.250 --> 00:06:06.284 but first I just want to show kind of how

NOTE Confidence: 0.90098894

00:06:06.284 --> 00:06:08.966 these clocks look across different tissues.

NOTE Confidence: 0.90098894

00:06:08.970 --> 00:06:12.018 So this is an example of five different

NOTE Confidence: 0.90098894

00:06:12.018 --> 00:06:14.365 epigenetic clocks in a variety of

NOTE Confidence: 0.90098894

00:06:14.365 --> 00:06:16.260 different tissue are fluid samples.

NOTE Confidence: 0.90098894

00:06:16.260 --> 00:06:17.944 On the X axis,

NOTE Confidence: 0.90098894

00:06:17.944 --> 00:06:21.130 I'm showing chronological age on the Y axis.

NOTE Confidence: 0.90098894

00:06:21.130 --> 00:06:23.965 Is this predicted at the genetic age?

NOTE Confidence: 0.90098894

00:06:23.970 --> 00:06:26.034 These two clocks by Horvath were

NOTE Confidence: 0.90098894

00:06:26.034 --> 00:06:27.990 actually trained using multiple different

NOTE Confidence: 0.90098894

00:06:27.990 --> 00:06:30.058 issues simultaneously pulled together,

NOTE Confidence: 0.90098894

00:06:30.060 --> 00:06:32.776 so that's why you get much better

NOTE Confidence: 0.90098894

00:06:32.776 --> 00:06:34.861 agreement across the tissues in

NOTE Confidence: 0.90098894

00:06:34.861 --> 00:06:36.966 terms of their predicted ages,

NOTE Confidence: 0.90098894

00:06:36.970 --> 00:06:39.352 whereas the other three clocks are

NOTE Confidence: 0.90098894

00:06:39.352 --> 00:06:41.839 actually all trained in whole blood,

NOTE Confidence: 0.90098894

00:06:41.840 --> 00:06:44.675 but still do predict still do show.

NOTE Confidence: 0.90098894

00:06:44.680 --> 00:06:46.340 Very heists age correlations.

NOTE Confidence: 0.90098894

00:06:46.340 --> 00:06:48.378 In other tissues, and actually,

NOTE Confidence: 0.90098894

00:06:48.378 --> 00:06:51.530 if we were to show this within tissue,

NOTE Confidence: 0.90098894

00:06:51.530 --> 00:06:54.206 a lot of these age correlations

NOTE Confidence: 0.90098894

00:06:54.206 --> 00:06:56.830 are above .8 two point 9.

NOTE Confidence: 0.90098894

00:06:56.830 --> 00:06:59.217 But the interesting thing is you also,

NOTE Confidence: 0.90098894

00:06:59.220 --> 00:07:01.614 if you actually took the time to

NOTE Confidence: 0.90098894

00:07:01.614 --> 00:07:04.050 map these colors out is kind of

NOTE Confidence: 0.90098894

00:07:04.050 --> 00:07:06.060 these divergent issues tend to be

NOTE Confidence: 0.90098894

00:07:06.130 --> 00:07:08.475 samples from brain or these tend to

NOTE Confidence: 0.90098894

00:07:08.475 --> 00:07:10.876 be non bring samples and we actually

NOTE Confidence: 0.90098894

00:07:10.876 --> 00:07:12.970 think that it's important to have

NOTE Confidence: 0.90098894

00:07:13.032 --> 00:07:14.897 differences in Appleton at age

NOTE Confidence: 0.90098894

00:07:14.897 --> 00:07:17.113 between tissues because we all know

NOTE Confidence: 0.90098894

00:07:17.113 --> 00:07:19.393 to choose don't age at the same rate.

NOTE Confidence: 0.90098894

00:07:19.400 --> 00:07:21.392 So we actually shouldn't be forcing

NOTE Confidence: 0.90098894

00:07:21.392 --> 00:07:23.160 similar epigenetic gauges across tissues.

NOTE Confidence: 0.91833216

00:07:26.170 --> 00:07:28.072 And then we can actually also

NOTE Confidence: 0.91833216

00:07:28.072 --> 00:07:30.205 show that epigenetic age is also

NOTE Confidence: 0.91833216

00:07:30.205 --> 00:07:32.215 differentiates normal tissue from tumor.

NOTE Confidence: 0.91833216

00:07:32.220 --> 00:07:34.356 But that is not the case

NOTE Confidence: 0.91833216

00:07:34.356 --> 00:07:35.780 across all the clocks.

NOTE Confidence: 0.91833216

00:07:35.780 --> 00:07:38.167 It tends to be the case across

NOTE Confidence: 0.91833216

00:07:38.167 --> 00:07:39.700 these second generation clocks,

NOTE Confidence: 0.91833216

00:07:39.700 --> 00:07:41.996 where we can see that in the normal

NOTE Confidence: 0.91833216

00:07:41.996 --> 00:07:43.914 tissue you get significantly lower

NOTE Confidence: 0.91833216

00:07:43.914 --> 00:07:46.458 epigenetic age compared to the tumor,

NOTE Confidence: 0.91833216

00:07:46.460 --> 00:07:48.640 and these are all adjusted

NOTE Confidence: 0.91833216

00:07:48.640 --> 00:07:49.948 for chronological age.

NOTE Confidence: 0.91833216

00:07:49.950 --> 00:07:52.479 Um, so on our Clock and also the Clock

NOTE Confidence: 0.91833216

00:07:52.479 --> 00:07:55.021 by Yang Show these differences across

NOTE Confidence: 0.91833216

00:07:55.021 --> 00:07:57.700 a variety of different tissue types.

NOTE Confidence: 0.9050141

00:08:00.000 --> 00:08:01.695 So one question that we've

NOTE Confidence: 0.9050141

00:08:01.695 --> 00:08:03.390 really been dealing with is,

NOTE Confidence: 0.9050141

00:08:03.390 --> 00:08:05.388 you know all these clocks for

NOTE Confidence: 0.9050141

00:08:05.388 --> 00:08:07.460 developed to predict the same thing.

NOTE Confidence: 0.9050141

00:08:07.460 --> 00:08:09.840 To capture this kind of epigenetic or

NOTE Confidence: 0.9050141

00:08:09.840 --> 00:08:11.529 metalation based change with aging.

NOTE Confidence: 0.9050141

00:08:11.530 --> 00:08:13.360 Yet they seem to be perhaps

NOTE Confidence: 0.9050141

00:08:13.360 --> 00:08:14.580 capturing different parts of

NOTE Confidence: 0.9050141

00:08:14.636 --> 00:08:16.268 this epigenetic aging signals.

NOTE Confidence: 0.9050141

00:08:16.270 --> 00:08:17.076 So basically,

NOTE Confidence: 0.9050141

00:08:17.076 --> 00:08:19.091 can we identify the individual

NOTE Confidence: 0.9050141

00:08:19.091 --> 00:08:20.670 components and decompose the

NOTE Confidence: 0.9050141

00:08:20.670 --> 00:08:22.494 signal to adapt to figure out

NOTE Confidence: 0.9050141

00:08:22.494 --> 00:08:24.343 what the different parts are and

NOTE Confidence: 0.9050141

00:08:24.343 --> 00:08:26.095 how they map onto disease risk?

NOTE Confidence: 0.9050141

00:08:26.100 --> 00:08:28.354 So this is kind of an illustration

NOTE Confidence: 0.9050141

00:08:28.354 --> 00:08:30.270 of taking the clocks apart.

NOTE Confidence: 0.9050141

00:08:30.270 --> 00:08:31.770 And then figuring out which each

NOTE Confidence: 0.9050141

00:08:31.770 --> 00:08:33.280 part of the Clock is doing.

NOTE Confidence: 0.855812

00:08:35.310 --> 00:08:38.496 So the way that we did this is we

NOTE Confidence: 0.855812

00:08:38.496 --> 00:08:41.020 applied something called WG CNA,

NOTE Confidence: 0.855812

00:08:41.020 --> 00:08:43.300 so it's a weighted network analysis

NOTE Confidence: 0.855812

00:08:43.300 --> 00:08:46.615 and we did this a cross using six

NOTE Confidence: 0.855812

00:08:46.615 --> 00:08:48.765 different issue in fluid datasets.

NOTE Confidence: 0.855812

00:08:48.770 --> 00:08:51.626 So we had uh samples from dermis,

NOTE Confidence: 0.855812

00:08:51.630 --> 00:08:52.854 epidermis, breast dorsolateral

NOTE Confidence: 0.855812

00:08:52.854 --> 00:08:55.295 prefrontal Cortex Colon, an full blood.

NOTE Confidence: 0.855812

00:08:55.295 --> 00:08:58.730 And the goal here was to identify Co

NOTE Confidence: 0.855812

00:08:58.730 --> 00:09:01.300 maculation modules that are shared

NOTE Confidence: 0.855812

00:09:01.300 --> 00:09:04.799 across all these tissue or sample types,

NOTE Confidence: 0.855812

00:09:04.800 --> 00:09:07.560 and from this we were able to identify

NOTE Confidence: 0.855812

00:09:07.560 --> 00:09:10.286 16 of these Co maculation modules

NOTE Confidence: 0.855812

00:09:10.286 --> 00:09:13.208 using Skeggs from the clocks which

NOTE Confidence: 0.855812

00:09:13.291 --> 00:09:15.646 word starting with about 1600.

NOTE Confidence: 0.9095152

00:09:19.070 --> 00:09:21.930 I'm so the next thing we did is we actually

NOTE Confidence: 0.9095152

00:09:21.997 --> 00:09:24.511 looked at how these different modules

NOTE Confidence: 0.9095152

00:09:24.511 --> 00:09:27.119 are impacting the overall Clock scores.

NOTE Confidence: 0.9095152

00:09:27.120 --> 00:09:29.920 So in this I've color coded all the

NOTE Confidence: 0.9095152

00:09:29.920 --> 00:09:32.624 16 modules and you can see that in

NOTE Confidence: 0.9095152

00:09:32.624 --> 00:09:35.626 our Clock and this Clock by Hannum a

NOTE Confidence: 0.9095152

00:09:35.626 --> 00:09:38.092 large proportion of this is actually

NOTE Confidence: 0.9095152

00:09:38.100 --> 00:09:39.930 driven by this yellow module,

NOTE Confidence: 0.9095152

00:09:39.930 --> 00:09:42.506 whereas the two clocks by Corvette seem

NOTE Confidence: 0.9095152

00:09:42.506 --> 00:09:45.010 to have relatively similar proportions in

NOTE Confidence: 0.9095152

00:09:45.010 --> 00:09:47.674 contributing to the overall Clock score.

NOTE Confidence: 0.9095152

00:09:47.680 --> 00:09:49.420 But the interesting module that

NOTE Confidence: 0.9095152

00:09:49.420 --> 00:09:51.550 I'm actually going to talk about

NOTE Confidence: 0.9095152

00:09:51.550 --> 00:09:53.200 today is this Brown module,

NOTE Confidence: 0.9095152

00:09:53.200 --> 00:09:55.378 which actually is shown in most

NOTE Confidence: 0.9095152

00:09:55.378 --> 00:09:58.113 of these clocks and has a pretty

NOTE Confidence: 0.9095152

00:09:58.113 --> 00:10:00.118 similar proportion of about uhm.

NOTE Confidence: 0.9095152

00:10:00.120 --> 00:10:01.723 10 to 15% in each of the

NOTE Confidence: 0.9095152

00:10:01.723 --> 00:10:03.380 clocks to the overall signal.

NOTE Confidence: 0.90328705

00:10:06.230 --> 00:10:08.651 So the other thing we can do is not

NOTE Confidence: 0.90328705

00:10:08.651 --> 00:10:11.139 just look at what proportion of the

NOTE Confidence: 0.90328705

00:10:11.139 --> 00:10:13.450 clocks is explained by each module,

NOTE Confidence: 0.90328705

00:10:13.450 --> 00:10:15.090 but whether what their capturing

NOTE Confidence: 0.90328705

00:10:15.090 --> 00:10:16.730 is actually the same signal.

NOTE Confidence: 0.90328705

00:10:16.730 --> 00:10:18.686 So this is all the modules,

NOTE Confidence: 0.90328705

00:10:18.690 --> 00:10:20.568 but I'm going to really focus

NOTE Confidence: 0.90328705

00:10:20.568 --> 00:10:22.630 just on 2 for right now,

NOTE Confidence: 0.90328705

00:10:22.630 --> 00:10:24.639 so basically this is the part of

NOTE Confidence: 0.90328705

00:10:24.639 --> 00:10:26.297 each Clock that that's represented

NOTE Confidence: 0.90328705

00:10:26.297 --> 00:10:28.859 by Stevie jobs in this Brown module.

NOTE Confidence: 0.90328705

00:10:28.860 --> 00:10:31.803 And what you can see is that for these,

NOTE Confidence: 0.90328705

00:10:31.810 --> 00:10:33.635 epigenetic clocks have really similar

NOTE Confidence: 0.90328705

00:10:33.635 --> 00:10:35.861 or high agreements in terms of

NOTE Confidence: 0.90328705

00:10:35.861 --> 00:10:37.546 their epigenetic age signal here.

NOTE Confidence: 0.90328705

00:10:37.550 --> 00:10:39.325 However, just a contrast this

NOTE Confidence: 0.90328705

00:10:39.325 --> 00:10:40.745 on this purple module,

NOTE Confidence: 0.90328705

00:10:40.750 --> 00:10:43.340 you can see that in in two of the clocks

NOTE Confidence: 0.90328705

00:10:43.406 --> 00:10:46.010 what the proper module is contributing

NOTE Confidence: 0.90328705

00:10:46.010 --> 00:10:48.200 to is considered accelerated aging,

NOTE Confidence: 0.90328705

00:10:48.200 --> 00:10:49.975 whereas in the other two

NOTE Confidence: 0.90328705

00:10:49.975 --> 00:10:51.395 clocks or three clocks,

NOTE Confidence: 0.90328705

00:10:51.400 --> 00:10:52.868 it's considered decelerated aging.

NOTE Confidence: 0.90328705

00:10:52.868 --> 00:10:56.288 So this is an example of a module is

NOTE Confidence: 0.90328705

00:10:56.288 --> 00:10:58.213 differentially waited and might be

NOTE Confidence: 0.90328705

00:10:58.213 --> 00:11:00.289 contributing to differences in the

NOTE Confidence: 0.90328705

00:11:00.289 --> 00:11:02.349 performance by the various clocks.

NOTE Confidence: 0.90328705

00:11:02.350 --> 00:11:04.240 But for the rest of the talk,

NOTE Confidence: 0.90328705

00:11:04.240 --> 00:11:06.400 I'm going to focus on this Brown module,

NOTE Confidence: 0.90328705

00:11:06.400 --> 00:11:08.227 which seems to be the one that's

NOTE Confidence: 0.90328705

00:11:08.227 --> 00:11:09.909 most important in terms of cancer.

NOTE Confidence: 0.89873034

00:11:12.150 --> 00:11:15.217 So now what we can do is we can look at

NOTE Confidence: 0.89873034

00:11:15.217 --> 00:11:18.305 instead of looking at the entire Clock score,

NOTE Confidence: 0.89873034

00:11:18.310 --> 00:11:19.930 look at the individual modules.

NOTE Confidence: 0.89873034

00:11:19.930 --> 00:11:23.170 So is there a part of the clocks for this?

NOTE Confidence: 0.89873034

00:11:23.170 --> 00:11:25.114 Actually driving this kind of these

NOTE Confidence: 0.89873034

00:11:25.114 --> 00:11:26.410 associations that we're seeing?

NOTE Confidence: 0.89873034

00:11:26.410 --> 00:11:28.818 So in this case I'm looking at just

NOTE Confidence: 0.89873034

00:11:28.818 --> 00:11:31.031 the part of our Clock that's captured

NOTE Confidence: 0.89873034

00:11:31.031 --> 00:11:33.530 by CP GS in this Brown module.

NOTE Confidence: 0.89873034

00:11:33.530 --> 00:11:36.446 So this is just 21 CP GS over all,

NOTE Confidence: 0.89873034

00:11:36.450 --> 00:11:38.700 and what we can see is we can kind of

NOTE Confidence: 0.89873034

00:11:38.770 --> 00:11:41.188 recapitulate the finding with the tumor

NOTE Confidence: 0.89873034

00:11:41.188 --> 00:11:43.900 versus normal across these different issues.

NOTE Confidence: 0.89873034

00:11:43.900 --> 00:11:45.652 However, in this case it's actually

NOTE Confidence: 0.89873034

00:11:45.652 --> 00:11:47.191 more significant when we're just

NOTE Confidence: 0.89873034

00:11:47.191 --> 00:11:48.487 considering this Brown module.

NOTE Confidence: 0.9159804

00:11:50.640 --> 00:11:53.367 We can also look up this is in normal

NOTE Confidence: 0.9159804

00:11:53.367 --> 00:11:56.345 breast tissue and we do see that this

NOTE Confidence: 0.9159804

00:11:56.345 --> 00:11:58.379 module is significantly correlated with

NOTE Confidence: 0.9159804

00:11:58.379 --> 00:12:02.170 age in normal breast, suggesting that.

NOTE Confidence: 0.9159804

00:12:02.170 --> 00:12:03.574 Perhaps as women age,

NOTE Confidence: 0.9159804

00:12:03.574 --> 00:12:05.329 their breasts as she develops.

NOTE Confidence: 0.9159804

00:12:05.330 --> 00:12:08.991 The more of this accelerated aging phenotype

NOTE Confidence: 0.9159804

00:12:08.991 --> 00:12:11.820 which could predispose them to cancer.

NOTE Confidence: 0.9159804

00:12:11.820 --> 00:12:13.750 And this is actually, uhm,

NOTE Confidence: 0.9159804

00:12:13.750 --> 00:12:15.736 what we can observe when we

NOTE Confidence: 0.9159804

00:12:15.736 --> 00:12:18.464 look at this is all data from

NOTE Confidence: 0.9159804

00:12:18.464 --> 00:12:20.674 normal breast tissue from women,

NOTE Confidence: 0.9159804

00:12:20.680 --> 00:12:22.600 either with or without breast

NOTE Confidence: 0.9159804

00:12:22.600 --> 00:12:24.136 cancer prior to treatment.

NOTE Confidence: 0.9159804

00:12:24.140 --> 00:12:26.625 This is a collaboration with others at

NOTE Confidence: 0.9159804

00:12:26.625 --> 00:12:29.655 Yale and we validated this in the original

NOTE Confidence: 0.9159804

00:12:29.655 --> 00:12:32.610 study and then also in another study.

NOTE Confidence: 0.9159804

00:12:32.610 --> 00:12:36.075 Or you can see that women with breast cancer,

NOTE Confidence: 0.9159804

00:12:36.080 --> 00:12:38.150 their normal tissues seems to

NOTE Confidence: 0.9159804

00:12:38.150 --> 00:12:39.806 be epigenetically older when

NOTE Confidence: 0.9159804

00:12:39.806 --> 00:12:42.058 we look at this Brown module.

NOTE Confidence: 0.9159804

00:12:42.060 --> 00:12:44.150 And women without breast cancer.

NOTE Confidence: 0.9159804

00:12:44.150 --> 00:12:47.230 And this is all age matched our age

NOTE Confidence: 0.9159804

00:12:47.230 --> 00:12:50.419 adjusted and adjusted for things like BMI,

NOTE Confidence: 0.9159804

00:12:50.420 --> 00:12:52.088 smoking another potential confounders.

NOTE Confidence: 0.8523743

00:12:54.830 --> 00:12:57.903 Uh, we also had a really small

NOTE Confidence: 0.8523743

00:12:57.903 --> 00:13:00.389 data set where we had, uhm,

NOTE Confidence: 0.8523743

00:13:00.389 --> 00:13:02.663 this Brown module measured in tumors

NOTE Confidence: 0.8523743

00:13:02.663 --> 00:13:05.630 and we had information on survival,

NOTE Confidence: 0.8523743

00:13:05.630 --> 00:13:09.424 so this is a data set with

NOTE Confidence: 0.8523743

00:13:09.424 --> 00:13:12.220 only 51 samples an over.

NOTE Confidence: 0.8523743

00:13:12.220 --> 00:13:15.046 I totale I are over 3471

NOTE Confidence: 0.8523743

00:13:15.046 --> 00:13:17.790 person Montes or 20 deaths.

NOTE Confidence: 0.8523743

00:13:17.790 --> 00:13:19.980 And what you can see,

NOTE Confidence: 0.8523743

00:13:19.980 --> 00:13:22.524 we need to validate this given

NOTE Confidence: 0.8523743

00:13:22.524 --> 00:13:25.115 those small sample where we do

NOTE Confidence: 0.8523743

00:13:25.115 --> 00:13:27.563 see that this Brown module 1

NOTE Confidence: 0.8523743

00:13:27.563 --> 00:13:29.387 standard deviation increase in

NOTE Confidence: 0.8523743

00:13:29.387 --> 00:13:31.697 this module it's associated with

NOTE Confidence: 0.8523743

00:13:31.697 --> 00:13:34.398 about 2.25 fold increased risk of

NOTE Confidence: 0.8523743

00:13:34.398 --> 00:13:36.578 mortality over this time period,

NOTE Confidence: 0.8523743

00:13:36.580 --> 00:13:39.639 and that's adjusting for things like age,

NOTE Confidence: 0.8523743

00:13:39.640 --> 00:13:41.384 race, ethnicity, tumor grade,

NOTE Confidence: 0.8523743

00:13:41.384 --> 00:13:43.564 ER and also chemotherapy tree.

NOTE Confidence: 0.91693026

00:13:46.550 --> 00:13:48.590 So I went looking more specifically

NOTE Confidence: 0.91693026

00:13:48.590 --> 00:13:50.860 at what's in this Brown module.

NOTE Confidence: 0.91693026

00:13:50.860 --> 00:13:53.116 Um, these are the individual CP

NOTE Confidence: 0.91693026

00:13:53.116 --> 00:13:55.908 GS in the Brown module and we

NOTE Confidence: 0.91693026

00:13:55.908 --> 00:13:58.308 can actually relate each CVG to

NOTE Confidence: 0.91693026

00:13:58.308 --> 00:14:01.036 some of the outcomes I discussed.

NOTE Confidence: 0.91693026

00:14:01.040 --> 00:14:03.763 So this first column is whether it

NOTE Confidence: 0.91693026

00:14:03.763 --> 00:14:05.919 differentiates in normal breast tissue,

NOTE Confidence: 0.91693026

00:14:05.920 --> 00:14:08.356 women with breast cancer versus controls.

NOTE Confidence: 0.91693026

00:14:08.360 --> 00:14:11.078 The second column is whether it

NOTE Confidence: 0.91693026

00:14:11.078 --> 00:14:12.890 can differentiate breast tumors

NOTE Confidence: 0.91693026

00:14:12.966 --> 00:14:14.871 from normal breast tissue and

NOTE Confidence: 0.91693026

00:14:14.871 --> 00:14:17.500 the third column is the survival.

NOTE Confidence: 0.91693026

00:14:17.500 --> 00:14:22.036 I'm finding and basically what we can see is.

NOTE Confidence: 0.91693026

00:14:22.040 --> 00:14:25.586 There's about a group of 12 CP GS for

NOTE Confidence: 0.91693026

00:14:25.586 --> 00:14:27.749 which hypermethylation so increased

NOTE Confidence: 0.91693026

00:14:27.749 --> 00:14:31.662 maculation in these 12 CP GS is

NOTE Confidence: 0.91693026

00:14:31.753 --> 00:14:34.453 associated with either cancer and

NOTE Confidence: 0.91693026

00:14:34.453 --> 00:14:37.810 normal tissue or or tumor versus

NOTE Confidence: 0.91693026

00:14:37.810 --> 00:14:41.060 normal or lower survival rate.

NOTE Confidence: 0.91693026

00:14:41.060 --> 00:14:43.948 And from the these are the jeans that

NOTE Confidence: 0.91693026

00:14:43.948 --> 00:14:46.774 these DVD's are in an there actually

NOTE Confidence: 0.91693026

00:14:46.774 --> 00:14:49.190 almost all in promoter regions in

NOTE Confidence: 0.91693026

00:14:49.190 --> 00:14:51.662 these jeans and we can use just ease

NOTE Confidence: 0.91693026

00:14:51.662 --> 00:14:53.800 12 to estimate an overall score.

NOTE Confidence: 0.91693026

00:14:53.800 --> 00:14:56.397 So we use PCA across these three

NOTE Confidence: 0.91693026

00:14:56.397 --> 00:14:59.325 samples and we can take PC one of

NOTE Confidence: 0.91693026

00:14:59.325 --> 00:15:02.169 those 12 jeans and follow up with that.

NOTE Confidence: 0.88783175

00:15:04.320 --> 00:15:06.528 So the other thing is that we also

NOTE Confidence: 0.88783175

00:15:06.528 --> 00:15:08.909 find that these 12 genius seemed

NOTE Confidence: 0.88783175

00:15:08.909 --> 00:15:10.669 to have specific characteristics,

NOTE Confidence: 0.88783175

00:15:10.670 --> 00:15:13.036 so they seem to be associated with

NOTE Confidence: 0.88783175

00:15:13.036 --> 00:15:15.209 polycomb group targets and also HT

NOTE Confidence: 0.88783175

00:15:15.209 --> 00:15:17.029 K27 trimethylation occupancy and see,

NOTE Confidence: 0.88783175

00:15:17.030 --> 00:15:19.148 and they tend to be ensues.

NOTE Confidence: 0.88783175

00:15:19.150 --> 00:15:20.209 12 pound jeans.

NOTE Confidence: 0.88783175

00:15:20.209 --> 00:15:22.680 So this is these 12 selected jeans.

NOTE Confidence: 0.88783175

00:15:22.680 --> 00:15:25.200 These were all the jeans that were

NOTE Confidence: 0.88783175

00:15:25.200 --> 00:15:27.351 in the original ground module and

NOTE Confidence: 0.88783175

00:15:27.351 --> 00:15:30.449 these are all the CP GS that we have

NOTE Confidence: 0.88783175

00:15:30.449 --> 00:15:32.555 measured in all of our samples.

NOTE Confidence: 0.88783175

00:15:32.560 --> 00:15:35.150 So about 20,000 CP GS over also.

NOTE Confidence: 0.88783175

00:15:35.150 --> 00:15:37.190 This is kind of the background.

NOTE Confidence: 0.88783175

00:15:37.190 --> 00:15:40.950 So about um 65 to 70% of them

NOTE Confidence: 0.88783175

00:15:40.950 --> 00:15:43.770 are orange juice 12 pound jeans,

NOTE Confidence: 0.88783175

00:15:43.770 --> 00:15:46.955 about 50% are Co locating with H2K27

NOTE Confidence: 0.88783175

00:15:46.955 --> 00:15:48.908 trying Appalachian and similarly

NOTE Confidence: 0.88783175

00:15:48.908 --> 00:15:53.078 50% with Polycom group targets.

NOTE Confidence: 0.88783175

00:15:53.080 --> 00:15:54.074 And Interestingly,

NOTE Confidence: 0.88783175

00:15:54.074 --> 00:15:57.056 this Association is actually not news,

NOTE Confidence: 0.88783175

00:15:57.060 --> 00:16:00.084 so there's some dating back about

NOTE Confidence: 0.88783175

00:16:00.084 --> 00:16:03.445 13 years of evidence that these

NOTE Confidence: 0.88783175

00:16:03.445 --> 00:16:05.945 polycomb mediated methylations does

NOTE Confidence: 0.88783175

00:16:05.945 --> 00:16:09.848 seem to be important in cancer and.

NOTE Confidence: 0.88783175

00:16:09.850 --> 00:16:10.264 Basically,

NOTE Confidence: 0.88783175

00:16:10.264 --> 00:16:11.920 Polycom group proteins are

NOTE Confidence: 0.88783175

00:16:11.920 --> 00:16:13.990 involved in repression of jeans

NOTE Confidence: 0.88783175

00:16:14.050 --> 00:16:15.670 that are required for salt.

NOTE Confidence: 0.88783175

00:16:15.670 --> 00:16:19.198 A stem cell differentiation.

NOTE Confidence: 0.88783175

00:16:19.200 --> 00:16:19.659 Um,

NOTE Confidence: 0.88783175

00:16:19.659 --> 00:16:22.413 so finally we also looked at

NOTE Confidence: 0.88783175

00:16:22.413 --> 00:16:26.038 these in non breast cancers again,

NOTE Confidence: 0.88783175

00:16:26.040 --> 00:16:28.740 so this is in colorectal cancer

NOTE Confidence: 0.88783175

00:16:28.740 --> 00:16:32.067 and again we find using this 12

NOTE Confidence: 0.88783175

00:16:32.067 --> 00:16:34.452 PPG DNA methylations score that

NOTE Confidence: 0.88783175

00:16:34.452 --> 00:16:37.187 we can significantly differentiate

NOTE Confidence: 0.88783175

00:16:37.187 --> 00:16:41.387 normal tissue from cancerous tissue.

NOTE Confidence: 0.88783175

00:16:41.390 --> 00:16:43.380 And Lastly, probably to me,

NOTE Confidence: 0.88783175

00:16:43.380 --> 00:16:45.365 the most interesting thing is

NOTE Confidence: 0.88783175

00:16:45.365 --> 00:16:47.350 we can look at this.

NOTE Confidence: 0.88783175

00:16:47.350 --> 00:16:49.576 A trustee PG score in completely

NOTE Confidence: 0.88783175

00:16:49.576 --> 00:16:51.568 normal tissue across a bunch

NOTE Confidence: 0.88783175

00:16:51.568 --> 00:16:53.296 of different tissue types.

NOTE Confidence: 0.88783175

00:16:53.300 --> 00:16:55.862 And basically we see really strong

NOTE Confidence: 0.88783175

00:16:55.862 --> 00:16:57.143 correlations with chronological

NOTE Confidence: 0.88783175

00:16:57.143 --> 00:16:58.858 age across all of these.

NOTE Confidence: 0.88783175

00:16:58.860 --> 00:17:01.236 So in brain whole glide colon,

NOTE Confidence: 0.88783175

00:17:01.240 --> 00:17:01.621 dermis,

NOTE Confidence: 0.88783175

00:17:01.621 --> 00:17:03.907 an epidermis which to me suggests

NOTE Confidence: 0.88783175

00:17:03.907 --> 00:17:06.642 that these might be changes that are

NOTE Confidence: 0.88783175

00:17:06.642 --> 00:17:08.547 naturally occuring with aging and

NOTE Confidence: 0.88783175

00:17:08.547 --> 00:17:10.767 that that might be predisposing.

NOTE Confidence: 0.88783175

00:17:10.770 --> 00:17:13.969 Some of these tissues to tumor Genesis.

NOTE Confidence: 0.88783175

00:17:13.970 --> 00:17:16.142 I'm so something that we're really

NOTE Confidence: 0.88783175

00:17:16.142 --> 00:17:18.448 interested now is in terms of

NOTE Confidence: 0.88783175

00:17:18.448 --> 00:17:20.818 kind of a primary or secondary

NOTE Confidence: 0.88783175

00:17:20.818 --> 00:17:21.608 prevention approach.

NOTE Confidence: 0.88783175

00:17:21.610 --> 00:17:24.052 Can you identify people who are

NOTE Confidence: 0.88783175

00:17:24.052 --> 00:17:26.804 scoring higher for their age then we

NOTE Confidence: 0.88783175

00:17:26.804 --> 00:17:29.247 would expect an are those boots are?

NOTE Confidence: 0.88783175

00:17:29.250 --> 00:17:31.380 Are those people more at risk

NOTE Confidence: 0.88783175

00:17:31.380 --> 00:17:33.290 of developing cancer in these

NOTE Confidence: 0.88783175

00:17:33.290 --> 00:17:35.360 specific tissues down the road?

NOTE Confidence: 0.88783175

00:17:35.360 --> 00:17:37.270 The other thing we're interested

NOTE Confidence: 0.88783175

00:17:37.270 --> 00:17:39.180 in is comparing across tissues.

NOTE Confidence: 0.88783175

00:17:39.180 --> 00:17:41.700 So are people who seems to be

NOTE Confidence: 0.88783175

00:17:41.700 --> 00:17:44.219 aging faster in blood also aging?

NOTE Confidence: 0.88783175

00:17:44.220 --> 00:17:46.439 Faster and something like breast or colon.

NOTE Confidence: 0.84702134

00:17:48.550 --> 00:17:50.810 And then last, um, basically,

NOTE Confidence: 0.84702134

00:17:50.810 --> 00:17:54.274 we also looked at this using a cultured

NOTE Confidence: 0.84702134

00:17:54.274 --> 00:17:56.668 fiberglass and basically we have,

NOTE Confidence: 0.84702134

00:17:56.670 --> 00:17:58.920 uhm, the early passage controls.

NOTE Confidence: 0.84702134

00:17:58.920 --> 00:18:00.925 We haven't immortalized transform fiberglass

NOTE Confidence: 0.84702134

00:18:00.925 --> 00:18:04.041 where you can see an acceleration of

NOTE Confidence: 0.84702134

00:18:04.041 --> 00:18:06.137 this epigenetic score immortalized,

NOTE Confidence: 0.84702134

00:18:06.140 --> 00:18:09.297 and we also looked in cellular senescence.

NOTE Confidence: 0.84702134

00:18:09.300 --> 00:18:12.000 So on pigeon induced, in essence,

NOTE Confidence: 0.84702134

00:18:12.000 --> 00:18:13.311 an replicative senescence,

NOTE Confidence: 0.84702134

00:18:13.311 --> 00:18:16.370 and these are near near senescence that

NOTE Confidence: 0.84702134

00:18:16.439 --> 00:18:18.889 were passage together so prohibitive.

NOTE Confidence: 0.84702134

00:18:18.890 --> 00:18:22.066 But they, uh, show high snacks and story,

NOTE Confidence: 0.84702134

00:18:22.070 --> 00:18:23.216 associated beta gal.

NOTE Confidence: 0.84702134

00:18:23.216 --> 00:18:25.890 And basically what you can see is

NOTE Confidence: 0.84702134

00:18:25.963 --> 00:18:28.435 compared to the early passes cells.

NOTE Confidence: 0.84702134

00:18:28.440 --> 00:18:30.800 We can recapitulate this

NOTE Confidence: 0.84702134

00:18:30.800 --> 00:18:32.570 Indies cultured fiberglass.

NOTE Confidence: 0.84702134

00:18:32.570 --> 00:18:33.746 So In conclusion, uhm,

NOTE Confidence: 0.84702134

00:18:33.746 --> 00:18:35.510 there are different kinds of DNA

NOTE Confidence: 0.84702134

00:18:35.566 --> 00:18:37.588 methylation changes in aging that are

NOTE Confidence: 0.84702134

00:18:37.588 --> 00:18:39.311 captured in the different epigenetic

NOTE Confidence: 0.84702134

00:18:39.311 --> 00:18:40.916 clocks and by deconstructing then

NOTE Confidence: 0.84702134

00:18:40.916 --> 00:18:42.948 we can start to understand the

NOTE Confidence: 0.84702134

00:18:42.948 --> 00:18:44.818 functionality of the signals that

NOTE Confidence: 0.84702134

00:18:44.818 --> 00:18:46.760 are captured in these clocks.

NOTE Confidence: 0.84702134

00:18:46.760 --> 00:18:47.720 And specifically,

NOTE Confidence: 0.84702134

00:18:47.720 --> 00:18:50.120 the Brown module seems particularly

NOTE Confidence: 0.84702134

00:18:50.120 --> 00:18:52.279 interesting in terms of cancer.

NOTE Confidence: 0.84702134

00:18:52.280 --> 00:18:55.234 Is one of the biggest shared signals

NOTE Confidence: 0.84702134

00:18:55.234 --> 00:18:58.124 across all the epigenetic clocks and

NOTE Confidence: 0.84702134

00:18:58.124 --> 00:19:00.689 a distinguishes tumor versus normal

NOTE Confidence: 0.84702134

00:19:00.689 --> 00:19:04.118 in a variety of different issues.

NOTE Confidence: 0.84702134

00:19:04.120 --> 00:19:04.543 Uh,

NOTE Confidence: 0.84702134

00:19:04.543 --> 00:19:06.235 differences to normal breasts

NOTE Confidence: 0.84702134

00:19:06.235 --> 00:19:08.878 are also observed for women with

NOTE Confidence: 0.84702134

00:19:08.878 --> 00:19:10.706 cancer versus those without,

NOTE Confidence: 0.84702134

00:19:10.710 --> 00:19:14.182 and the signal from these from the model

NOTE Confidence: 0.84702134

00:19:14.182 --> 00:19:17.270 and tumors associated with survival.

NOTE Confidence: 0.84702134

00:19:17.270 --> 00:19:19.727 We can that also narrow it down

NOTE Confidence: 0.84702134

00:19:19.727 --> 00:19:22.142 to $12.00 that are really driving

NOTE Confidence: 0.84702134

00:19:22.142 --> 00:19:24.704 the signal in this Brown module

NOTE Confidence: 0.84702134

00:19:24.704 --> 00:19:27.278 there mainly capturing promoters,

NOTE Confidence: 0.84702134

00:19:27.280 --> 00:19:29.360 TPG island hypermethylation that tend

NOTE Confidence: 0.84702134

00:19:29.360 --> 00:19:31.965 to be marked by Polycom extricate

NOTE Confidence: 0.84702134

00:19:31.965 --> 00:19:34.235 27 trimethylation and sues 12.

NOTE Confidence: 0.84702134

00:19:34.240 --> 00:19:36.850 We can observe acceleration in culture,

NOTE Confidence: 0.84702134

00:19:36.850 --> 00:19:37.892 fiberless, appan,

NOTE Confidence: 0.84702134

00:19:37.892 --> 00:19:38.934 immortalization transformation

NOTE Confidence: 0.84702134

00:19:38.934 --> 00:19:42.060 and also so there's no sense.

NOTE Confidence: 0.84702134

00:19:42.060 --> 00:19:43.780 But to me out again,

NOTE Confidence: 0.84702134

00:19:43.780 --> 00:19:45.922 really interesting thing is that we

NOTE Confidence: 0.84702134

00:19:45.922 --> 00:19:47.960 actually see linear changes in this

NOTE Confidence: 0.84702134

00:19:47.960 --> 00:19:49.592 signal across the adult range in

NOTE Confidence: 0.84702134

00:19:49.592 --> 00:19:51.787 a bunch of different issues which

NOTE Confidence: 0.84702134

00:19:51.787 --> 00:19:53.375 actually might be informative.

NOTE Confidence: 0.84702134

00:19:53.380 --> 00:19:54.160 So overall,

NOTE Confidence: 0.84702134

00:19:54.160 --> 00:19:56.890 I think this may represent an opinion

NOTE Confidence: 0.84702134

00:19:56.890 --> 00:19:59.245 about genetic aging change that

NOTE Confidence: 0.84702134

00:19:59.245 --> 00:20:01.610 explains the increase cancer risk.

NOTE Confidence: 0.84702134

00:20:01.610 --> 00:20:05.365 With that I want to acknowledge people

NOTE Confidence: 0.84702134

00:20:05.365 --> 00:20:08.170 in my lab and also my collaborators,

NOTE Confidence: 0.84702134

00:20:08.170 --> 00:20:10.510 both at Yale.

NOTE Confidence: 0.84702134

00:20:10.510 --> 00:20:12.337 And elsewhere, as well as my funding.

NOTE Confidence: 0.9009531

00:20:14.860 --> 00:20:16.054 Working, thank you.

NOTE Confidence: 0.9009531

00:20:16.054 --> 00:20:17.642 That's a terrific presentation

NOTE Confidence: 0.9009531

00:20:17.642 --> 00:20:19.600 in a really interesting work.

NOTE Confidence: 0.9009531

00:20:19.600 --> 00:20:22.680 And we actually have a number of

NOTE Confidence: 0.9009531

00:20:22.680 --> 00:20:25.127 questions that have been put forth

NOTE Confidence: 0.9009531

00:20:25.127 --> 00:20:28.021 on the chat or let me just run

NOTE Confidence: 0.9009531

00:20:28.021 --> 00:20:30.681 through a few Dan Demayo ask you

NOTE Confidence: 0.9009531

00:20:30.681 --> 00:20:33.046 make see that people have recently

NOTE Confidence: 0.9009531

00:20:33.046 --> 00:20:35.800 described meth elation of RNA M RNA.

NOTE Confidence: 0.9009531

00:20:35.800 --> 00:20:38.348 Specifically, does that change as well in

NOTE Confidence: 0.9009531

00:20:38.348 --> 00:20:41.328 the context of what you've been describing?

NOTE Confidence: 0.86948186

00:20:42.690 --> 00:20:44.846 So we haven't looked at that here.

NOTE Confidence: 0.86948186

00:20:44.850 --> 00:20:47.328 I know people are looking at that, um,

NOTE Confidence: 0.86948186

00:20:47.328 --> 00:20:49.952 there's a group at Harvard who is actually

NOTE Confidence: 0.86948186

00:20:49.952 --> 00:20:51.926 looking at that in terms of aging,

NOTE Confidence: 0.86948186

00:20:51.930 --> 00:20:53.981 but it for now what I'm discussing

NOTE Confidence: 0.86948186

00:20:53.981 --> 00:20:56.240 here is just CG metalation in DNA.

NOTE Confidence: 0.88106155

00:20:57.920 --> 00:21:00.068 Um, one another question sort of.

NOTE Confidence: 0.88106155

00:21:00.070 --> 00:21:02.366 Have you looked at this in the

NOTE Confidence: 0.88106155

00:21:02.366 --> 00:21:04.010 context of progeria patients,

NOTE Confidence: 0.88106155

00:21:04.010 --> 00:21:06.425 which is sort of a really interesting

NOTE Confidence: 0.88106155

00:21:06.425 --> 00:21:08.659 question as it relates to aging,

NOTE Confidence: 0.88106155

00:21:08.660 --> 00:21:11.131 is curious if if you are folks

NOTE Confidence: 0.88106155

00:21:11.131 --> 00:21:12.959 she worked with it worked

NOTE Confidence: 0.88106155

00:21:12.960 --> 00:21:15.179 in that space and so we we've

NOTE Confidence: 0.88106155

00:21:15.179 --> 00:21:17.381 looked at the overall Clock scores

NOTE Confidence: 0.88106155

00:21:17.381 --> 00:21:20.118 in progeria and not all of them,

NOTE Confidence: 0.88106155

00:21:20.120 --> 00:21:22.268 but some of them do show

NOTE Confidence: 0.88106155

00:21:22.268 --> 00:21:23.700 acceleration in fridge area.

NOTE Confidence: 0.88106155

00:21:23.700 --> 00:21:26.444 We haven't looked at this specific modules

NOTE Confidence: 0.88106155

00:21:26.444 --> 00:21:29.160 for the Brown module or the 12 PPG.

NOTE Confidence: 0.88106155

00:21:29.160 --> 00:21:31.267 Part of the Brown module in progeria,

NOTE Confidence: 0.88106155

00:21:31.270 --> 00:21:33.424 but that is actually an interesting

NOTE Confidence: 0.88106155

00:21:33.424 --> 00:21:35.168 thing and progeria something we

NOTE Confidence: 0.88106155

00:21:35.168 --> 00:21:37.184 we have plans to look at all the

NOTE Confidence: 0.88106155

00:21:37.184 --> 00:21:38.896 different modules to see if there

NOTE Confidence: 0.88106155

00:21:38.896 --> 00:21:40.852 are certain parts that are that are

NOTE Confidence: 0.88106155

00:21:40.852 --> 00:21:42.508 picking that up because again some

NOTE Confidence: 0.88106155

00:21:42.508 --> 00:21:44.725 clocks seem to pick up the progeria

NOTE Confidence: 0.88106155

00:21:44.725 --> 00:21:46.017 acceleration whereas others don't.

NOTE Confidence: 0.907711

00:21:47.090 --> 00:21:48.810 Thank you Marcus has a

NOTE Confidence: 0.907711

00:21:48.810 --> 00:21:50.890 question which as you can see,

NOTE Confidence: 0.907711

00:21:50.890 --> 00:21:53.280 he said for the for the 12 CP GS that

NOTE Confidence: 0.907711

00:21:53.353 --> 00:21:55.037 you've identified their individual

NOTE Confidence: 0.907711

00:21:55.037 --> 00:21:57.563 basis as opposed to islands in

NOTE Confidence: 0.907711

00:21:57.630 --> 00:21:59.510 any variation of those sites.

NOTE Confidence: 0.8786886

00:22:00.550 --> 00:22:02.632 Uhm, I actually haven't looked at

NOTE Confidence: 0.8786886

00:22:02.632 --> 00:22:05.019 whether there snips um at those sites,

NOTE Confidence: 0.8786886

00:22:05.020 --> 00:22:07.090 so they are individual CP GS,

NOTE Confidence: 0.8786886

00:22:07.090 --> 00:22:08.466 so 12 individuals seeking.

NOTE Confidence: 0.8786886

00:22:08.466 --> 00:22:10.162 Geez, what we're interested now

NOTE Confidence: 0.8786886

00:22:10.162 --> 00:22:12.190 is actually looking at the whole

NOTE Confidence: 0.8786886

00:22:12.250 --> 00:22:14.314 region and looking at it like

NOTE Confidence: 0.8786886

00:22:14.314 --> 00:22:15.690 variation across the regions,

NOTE Confidence: 0.8786886

00:22:15.690 --> 00:22:17.748 but we haven't done that yet.

NOTE Confidence: 0.8786886

00:22:17.750 --> 00:22:19.815 But yeah, I should go back and

NOTE Confidence: 0.8786886

00:22:19.815 --> 00:22:21.577 actually look at whether they're

NOTE Confidence: 0.8786886

00:22:21.577 --> 00:22:23.597 adjacent snips that would be.

NOTE Confidence: 0.8813521

00:22:25.750 --> 00:22:29.286 One question I have is, uhm, you know.

NOTE Confidence: 0.8813521

00:22:29.286 --> 00:22:31.878 Looking at your data and realizing

NOTE Confidence: 0.8813521

00:22:31.878 --> 00:22:34.237 that beyond aging there are,

NOTE Confidence: 0.8813521

00:22:34.240 --> 00:22:36.928 you know many sort of behaviors,

NOTE Confidence: 0.8813521

00:22:36.930 --> 00:22:39.100 environmental exposures for lack of

NOTE Confidence: 0.8813521

00:22:39.100 --> 00:22:41.840 a better phrase that drive cancer.

NOTE Confidence: 0.8813521

00:22:41.840 --> 00:22:45.895 Breast colon, certainly. And should have.

NOTE Confidence: 0.8813521

00:22:45.895 --> 00:22:48.880 Is there an opportunity to study sort of,

NOTE Confidence: 0.8813521

00:22:48.880 --> 00:22:51.876 uh, the behavior of of these individuals

NOTE Confidence: 0.8813521

00:22:51.876 --> 00:22:54.241 overtime that would drive the signature

NOTE Confidence: 0.8813521

00:22:54.241 --> 00:22:57.518 in a way that you know they are sort of.

NOTE Confidence: 0.8813521

00:22:57.520 --> 00:23:01.979 They have a greater component of that.

NOTE Confidence: 0.8813521

00:23:01.980 --> 00:23:03.745 At Methylations signature that not

NOTE Confidence: 0.8813521

00:23:03.745 --> 00:23:05.900 only is reflective of promoted aging,

NOTE Confidence: 0.8813521

00:23:05.900 --> 00:23:08.790 but increase risk of cancer. Yeah,

NOTE Confidence: 0.898412700000001

00:23:08.790 --> 00:23:11.274 so we can see we have UM shown in

NOTE Confidence: 0.898412700000001

00:23:11.274 --> 00:23:13.825 the overall Clock scores that you

NOTE Confidence: 0.898412700000001

00:23:13.825 --> 00:23:16.473 do get accelerated at genetic age

NOTE Confidence: 0.898412700000001

00:23:16.473 --> 00:23:18.711 in Association with things that we

NOTE Confidence: 0.898412700000001

00:23:18.711 --> 00:23:20.874 think of as normal risk factors,

NOTE Confidence: 0.898412700000001

00:23:20.874 --> 00:23:23.310 so cigarette smoking obesity I need in

NOTE Confidence: 0.898412700000001

00:23:23.373 --> 00:23:25.635 some socioeconomic factors seem to map

NOTE Confidence: 0.898412700000001

00:23:25.635 --> 00:23:27.919 onto differences in these aging rates.

NOTE Confidence: 0.898412700000001

00:23:27.920 --> 00:23:29.760 We haven't looked again specifically

NOTE Confidence: 0.898412700000001

00:23:29.760 --> 00:23:31.974 at this module, although I will

NOTE Confidence: 0.898412700000001

00:23:31.974 --> 00:23:34.550 say from some of our other work,

NOTE Confidence: 0.898412700000001

00:23:34.550 --> 00:23:37.175 it seems like the Brown module is

NOTE Confidence: 0.898412700000001

00:23:37.175 --> 00:23:39.080 not particularly picking up smoking.

NOTE Confidence: 0.898412700000001

00:23:39.080 --> 00:23:41.180 But that might just be when

NOTE Confidence: 0.898412700000001

00:23:41.180 --> 00:23:42.230 measured in blood,

NOTE Confidence: 0.898412700000001

00:23:42.230 --> 00:23:45.083 whether it is in long or or some other

NOTE Confidence: 0.898412700000001

00:23:45.083 --> 00:23:47.130 samples that might be different,

NOTE Confidence: 0.898412700000001

00:23:47.130 --> 00:23:49.517 whereas it seems more like that purple

NOTE Confidence: 0.898412700000001

00:23:49.517 --> 00:23:52.028 module that it didn't really go into.

NOTE Confidence: 0.898412700000001

00:23:52.030 --> 00:23:53.430 It's actually picking up

NOTE Confidence: 0.898412700000001

00:23:53.430 --> 00:23:54.830 more of those smoking,

NOTE Confidence: 0.898412700000001

00:23:54.830 --> 00:23:56.580 and the influence was smoking

NOTE Confidence: 0.898412700000001

00:23:56.580 --> 00:23:58.330 in when measured in blood.

NOTE Confidence: 0.8408731

00:24:00.150 --> 00:24:02.214 Another question is that the methyl

NOTE Confidence: 0.8408731

00:24:02.214 --> 00:24:04.956 lation that of the 12 jeans in breast

NOTE Confidence: 0.8408731

00:24:04.956 --> 00:24:07.308 and with regarding the breast in memory

NOTE Confidence: 0.8408731

00:24:07.308 --> 00:24:09.330 you can obviously the questions you

NOTE Confidence: 0.8408731

00:24:09.330 --> 00:24:13.150 can see is that breast tissue is.

NOTE Confidence: 0.8408731

00:24:13.150 --> 00:24:15.100 A combination of various cell types

NOTE Confidence: 0.8408731

00:24:15.100 --> 00:24:17.099 and have you narrowed down sort

NOTE Confidence: 0.8408731

00:24:17.099 --> 00:24:18.456 of the epithelial, fibroblast,

NOTE Confidence: 0.8408731

00:24:18.456 --> 00:24:20.436 other cell types with regard

NOTE Confidence: 0.8408731

00:24:20.436 --> 00:24:22.380 to what you're finding. Yeah,

NOTE Confidence: 0.91106963

00:24:22.380 --> 00:24:24.844 so unfortunately we just have bulk samples

NOTE Confidence: 0.91106963

00:24:24.844 --> 00:24:27.671 so we can actually narrow it down to

NOTE Confidence: 0.91106963

00:24:27.671 --> 00:24:30.250 which cell type this is coming from,

NOTE Confidence: 0.91106963

00:24:30.250 --> 00:24:32.278 but I think because breast is

NOTE Confidence: 0.91106963

00:24:32.278 --> 00:24:34.050 so heterogeneous we actually the

NOTE Confidence: 0.91106963

00:24:34.050 --> 00:24:35.855 age correlation with our measures

NOTE Confidence: 0.91106963

00:24:35.855 --> 00:24:37.770 actually much weaker and breast,

NOTE Confidence: 0.91106963

00:24:37.770 --> 00:24:39.989 I think because it's a little bit

NOTE Confidence: 0.91106963

00:24:39.989 --> 00:24:42.069 confounded by the cell composition.

NOTE Confidence: 0.91106963

00:24:42.070 --> 00:24:42.949 However, you know,

NOTE Confidence: 0.91106963

00:24:42.949 --> 00:24:45.000 part of the reason we did to

NOTE Confidence: 0.91106963

00:24:45.067 --> 00:24:47.011 follow up in the culture fiberglass

NOTE Confidence: 0.91106963

00:24:47.011 --> 00:24:49.706 was to make sure we weren't just

NOTE Confidence: 0.91106963

00:24:49.706 --> 00:24:51.478 capturing something about cell

NOTE Confidence: 0.91106963

00:24:51.478 --> 00:24:54.330 composition changes with aging.

NOTE Confidence: 0.91106963

00:24:54.330 --> 00:24:55.670 And the other interesting thing

NOTE Confidence: 0.91106963

00:24:55.670 --> 00:24:57.653 is that at least the Brown module

NOTE Confidence: 0.91106963

00:24:57.653 --> 00:24:59.417 seems to be pretty conserved across

NOTE Confidence: 0.91106963

00:24:59.417 --> 00:25:00.729 cell and tissue types,

NOTE Confidence: 0.91106963

00:25:00.730 --> 00:25:02.906 so I don't think it is picking up

NOTE Confidence: 0.91106963

00:25:02.906 --> 00:25:04.807 something from a specific tissue type.

NOTE Confidence: 0.91106963

00:25:04.810 --> 00:25:06.910 It it would be interesting to look

NOTE Confidence: 0.91106963

00:25:06.910 --> 00:25:08.138 at epithelial versus fiberglass

NOTE Confidence: 0.91106963

00:25:08.138 --> 00:25:10.274 and see if one of those is driving

NOTE Confidence: 0.91106963

00:25:10.274 --> 00:25:12.079 the signal more than the other,

NOTE Confidence: 0.91106963

00:25:12.080 --> 00:25:14.408 but right now we don't have that data.

NOTE Confidence: 0.92196023

00:25:15.020 --> 00:25:16.976 And then the last question before

NOTE Confidence: 0.92196023

00:25:16.976 --> 00:25:19.433 we break is if you looked at

NOTE Confidence: 0.92196023

00:25:19.433 --> 00:25:21.593 expression of of the individual jeans

NOTE Confidence: 0.92196023

00:25:21.593 --> 00:25:24.505 a particularly as they relate to

NOTE Confidence: 0.92196023

00:25:24.505 --> 00:25:26.489 potentially classic tumor suppressor

NOTE Confidence: 0.92196023

00:25:26.489 --> 00:25:28.590 genes or other typical mechanisms.

NOTE Confidence: 0.8860609

00:25:29.640 --> 00:25:31.880 I'm so that is the follow up that

NOTE Confidence: 0.8860609

00:25:31.880 --> 00:25:33.438 we're actually doing right now,

NOTE Confidence: 0.8860609

00:25:33.440 --> 00:25:35.760 so everything I showed today is either on

NOTE Confidence: 0.8860609

00:25:35.760 --> 00:25:38.105 the first part of the talk is impressed.

NOTE Confidence: 0.8860609

00:25:38.110 --> 00:25:39.856 The second part is in progress,

NOTE Confidence: 0.8860609

00:25:39.860 --> 00:25:42.488 so it's kind of early days still on this.

NOTE Confidence: 0.8860609

00:25:42.490 --> 00:25:44.242 But yeah, our goal is then

NOTE Confidence: 0.8860609

00:25:44.242 --> 00:25:45.410 to move to expression.

NOTE Confidence: 0.8860609

00:25:45.410 --> 00:25:47.738 We have looked at human protein at listen.

NOTE Confidence: 0.8860609

00:25:47.740 --> 00:25:51.226 Do see some associations in terms of.

NOTE Confidence: 0.8860609

00:25:51.230 --> 00:25:53.631 Answer and expression in the jeans in

NOTE Confidence: 0.8860609

00:25:53.631 --> 00:25:57.071 our 12 CG set so we are optimistic

NOTE Confidence: 0.8860609

00:25:57.071 --> 00:25:59.406 that we'll see differential expression.

NOTE Confidence: 0.917106799999999

00:26:00.670 --> 00:26:02.966 Well thank you were or just now at

NOTE Confidence: 0.917106799999999

00:26:02.966 --> 00:26:05.618 the top of the hour and I want to

NOTE Confidence: 0.917106799999999

00:26:05.618 --> 00:26:08.189 thank Morgan and Marcus for two superb

NOTE Confidence: 0.917106799999999

00:26:08.189 --> 00:26:10.239 talks that it really elucidated.

NOTE Confidence: 0.917106799999999

00:26:10.240 --> 00:26:11.560 Gray science being conducted

NOTE Confidence: 0.917106799999999

00:26:11.560 --> 00:26:12.880 at our Cancer Center.

NOTE Confidence: 0.917106799999999

00:26:12.880 --> 00:26:15.456 Thank you all for joining us again for

NOTE Confidence: 0.917106799999999

00:26:15.456 --> 00:26:17.481 virtual grand rounds and look forward

NOTE Confidence: 0.917106799999999

00:26:17.481 --> 00:26:20.139 again to seeing you all again next week.

NOTE Confidence: 0.79265245

00:26:21.180 --> 00:26:23.580 Great. Thanks, thank you.