WEBVTT

NOTE duration:"01:01:19"

NOTE recognizability:0.690

NOTE language:en-us

NOTE Confidence: 0.074070364

00:00:00.000 --> 00:00:03.225 So. Good afternoon everyone.

NOTE Confidence: 0.074070364

00:00:03.225 --> 00:00:05.682 Thank you for attending a

NOTE Confidence: 0.074070364

00:00:05.682 --> 00:00:07.090 year pathology gram one.

NOTE Confidence: 0.074070364

 $00:00:07.090 \longrightarrow 00:00:08.593$ Sending a series.

NOTE Confidence: 0.074070364

 $00:00:08.593 \rightarrow 00:00:12.100$ It's our great pleasure to invite Doctor

NOTE Confidence: 0.074070364

00:00:12.191 --> 00:00:15.647 Killer or Katie to speak at our grandma.

NOTE Confidence: 0.074070364

 $00{:}00{:}15.650 \dashrightarrow 00{:}00{:}18.611$ I met at scientific conferences and I'm

NOTE Confidence: 0.074070364

 $00:00:18.611 \rightarrow 00:00:21.299$ impressed by her outstanding mechanistic

NOTE Confidence: 0.074070364

 $00{:}00{:}21.299 \dashrightarrow 00{:}00{:}24.644$ research in immunology and cardiology.

NOTE Confidence: 0.074070364

 $00{:}00{:}24.650 \dashrightarrow 00{:}00{:}28.082$ Cloud received her pH D from the Autonomous

NOTE Confidence: 0.074070364

00:00:28.082 --> 00:00:30.756 University of Madrid, Spain, she.

NOTE Confidence: 0.074070364

 $00{:}00{:}30{.}756 \dashrightarrow 00{:}00{:}33{.}168$ Performed her postal research

NOTE Confidence: 0.074070364

00:00:33.168 --> 00:00:35.580 at Brigham Women Hospital,

 $00:00:35.580 \longrightarrow 00:00:36.984$ have a medical school.

NOTE Confidence: 0.074070364

 $00:00:36.984 \dashrightarrow 00:00:38.739$ She studied her faculty position

NOTE Confidence: 0.074070364

 $00{:}00{:}38.739 \dashrightarrow 00{:}00{:}41.157$ as an assistant professor at the

NOTE Confidence: 0.074070364

00:00:41.157 --> 00:00:43.362 Department of Medicine, Tufts University.

NOTE Confidence: 0.074070364

 $00:00:43.362 \longrightarrow 00:00:45.366$ She has been attending

NOTE Confidence: 0.074070364

 $00:00:45.366 \longrightarrow 00:00:47.454$ resources professor since 2019.

NOTE Confidence: 0.074070364

 $00{:}00{:}47{.}454 \dashrightarrow 00{:}00{:}50{.}958$ She's the program director of Immunology

NOTE Confidence: 0.074070364

 $00:00:50.958 \rightarrow 00:00:54.490$ graduate program is an endowed chemist,

NOTE Confidence: 0.074070364

 $00{:}00{:}54.490 \dashrightarrow 00{:}00{:}55.446$ and Joann,

NOTE Confidence: 0.074070364

 $00:00:55.446 \longrightarrow 00:00:57.836$ where professor and the interim

NOTE Confidence: 0.074070364

 $00:00:57.836 \longrightarrow 00:01:00.005$ vice chair of department

NOTE Confidence: 0.074070364

00:01:00.005 --> 00:01:02.744 immunology at Tufts Class Group,

NOTE Confidence: 0.074070364

 $00{:}01{:}02{.}744 \dashrightarrow 00{:}01{:}05{.}186$ has made important discoveries in the

NOTE Confidence: 0.074070364

00:01:05.186 --> 00:01:08.109 area of mechanism T cell trafficking.

NOTE Confidence: 0.074070364

 $00{:}01{:}08{.}110 \dashrightarrow 00{:}01{:}10.475$ Their research efforts are focused

NOTE Confidence: 0.074070364

 $00:01:10.475 \rightarrow 00:01:13.816$ on understanding why and how T cell

- NOTE Confidence: 0.074070364
- $00:01:13.816 \rightarrow 00:01:16.066$ subsets and in gaseous interaction.
- NOTE Confidence: 0.074070364
- $00:01:16.070 \longrightarrow 00:01:18.686$ They also study intrinsic properties of
- NOTE Confidence: 0.074070364
- $00{:}01{:}18.686 \dashrightarrow 00{:}01{:}21.907$ the vascular in the cilium that modulated
- NOTE Confidence: 0.074070364
- 00:01:21.907 --> 00:01:24.210 key cell and leukocyte recruitment
- NOTE Confidence: 0.074070364
- $00{:}01{:}24.210 \dashrightarrow 00{:}01{:}27.290$ in the T cell trafficking and survival.
- NOTE Confidence: 0.074070364
- $00{:}01{:}27{.}290 \dashrightarrow 00{:}01{:}29{.}174$ Another exciting line of risk in
- NOTE Confidence: 0.074070364
- $00:01:29.174 \rightarrow 00:01:31.270$ class group is about inflammation,
- NOTE Confidence: 0.074070364
- $00{:}01{:}31{.}270 \dashrightarrow 00{:}01{:}34{.}108$ heart failure to recent research has
- NOTE Confidence: 0.074070364
- $00{:}01{:}34.108 \dashrightarrow 00{:}01{:}36.547$ contributed significantly to your paradigm
- NOTE Confidence: 0.074070364
- $00:01:36.547 \rightarrow 00:01:39.385$ shift in understanding of heart failure.
- NOTE Confidence: 0.074070364
- $00{:}01{:}39{.}390 \dashrightarrow 00{:}01{:}42{.}407$ Putting T cell inflammation as a measure
- NOTE Confidence: 0.074070364
- $00{:}01{:}42{.}407 \dashrightarrow 00{:}01{:}45{.}979$ of player in this heart failure disease.
- NOTE Confidence: 0.074070364
- $00:01:45.980 \longrightarrow 00:01:48.710$ So exciting research program have
- NOTE Confidence: 0.074070364
- $00{:}01{:}48.710 \dashrightarrow 00{:}01{:}51.440$ led to multiple impactful papers
- NOTE Confidence: 0.074070364
- $00:01:51.530 \rightarrow 00:01:53.264$ such as circulation journal,
- NOTE Confidence: 0.074070364

 $00:01:53.264 \rightarrow 00:01:54.418$ experimental medicine,

NOTE Confidence: 0.074070364

 $00{:}01{:}54{.}418$ --> $00{:}01{:}57{.}880$ JCR inside a TVP and etc.

NOTE Confidence: 0.074070364

 $00{:}01{:}57.880 \dashrightarrow 00{:}02{:}00{.}310$ Pillars research has been has

NOTE Confidence: 0.074070364

 $00:02:00.310 \longrightarrow 00:02:03.400$ been funded by NIH one brand.

NOTE Confidence: 0.074070364

 $00{:}02{:}03{.}400 \dashrightarrow 00{:}02{:}05{.}899$ She has also showed great leadership in

NOTE Confidence: 0.074070364

 $00{:}02{:}05{.}899 \dashrightarrow 00{:}02{:}08{.}325$ science by serving our editorial board

NOTE Confidence: 0.074070364

00:02:08.325 --> 00:02:10.480 such as Junior Clinic investigation,

NOTE Confidence: 0.074070364

 $00:02:10.480 \longrightarrow 00:02:13.792$ Fast, GMC and etc.

NOTE Confidence: 0.074070364

 $00:02:13.792 \longrightarrow 00:02:14.620$ Additionally,

NOTE Confidence: 0.074070364

 $00:02:14.620 \longrightarrow 00:02:17.553$ she has been serving the American Heart

NOTE Confidence: 0.074070364

 $00{:}02{:}17.553 \dashrightarrow 00{:}02{:}19.610$ Association during past many years.

NOTE Confidence: 0.074070364

 $00:02:19.610 \dashrightarrow 00:02:22.484$ She has been the HCA basic cardiovascular

NOTE Confidence: 0.074070364

 $00:02:22.484 \dashrightarrow 00:02:25.556$ Science program chair since last year.

NOTE Confidence: 0.074070364

 $00:02:25.560 \longrightarrow 00:02:26.934$ Without further ado,

NOTE Confidence: 0.074070364

00:02:26.934 --> 00:02:28.308 let's welcome Killer.

NOTE Confidence: 0.074070364

 $00:02:28.310 \dashrightarrow 00:02:30.725$ To give us her seminar entitled T

00:02:30.725 --> 00:02:33.346 Cell Role in the passive Physiology

NOTE Confidence: 0.074070364

 $00{:}02{:}33{.}346 \dashrightarrow 00{:}02{:}35{.}698$ of heart failure, can I thank you?

NOTE Confidence: 0.67076522

 $00{:}02{:}36{.}510 \dashrightarrow 00{:}02{:}38{.}002$ Thank you very much.

NOTE Confidence: 0.67076522

 $00:02:38.002 \longrightarrow 00:02:39.867$ You ring for the invitation.

NOTE Confidence: 0.67076522

00:02:39.870 --> 00:02:44.010 It's really nice to be here and also

NOTE Confidence: 0.67076522

 $00{:}02{:}44.010 \dashrightarrow 00{:}02{:}47.962$ thank you to all those of you who

NOTE Confidence: 0.67076522

 $00{:}02{:}47.962 \dashrightarrow 00{:}02{:}49.810$ I've met with this morning because

NOTE Confidence: 0.67076522

00:02:49.874 --> 00:02:52.046 I've returned your science because I

NOTE Confidence: 0.67076522

 $00{:}02{:}52.050 \dashrightarrow 00{:}02{:}53.670$ I've been really enjoying, you know,

NOTE Confidence: 0.67076522

00:02:53.670 - 00:02:56.309 all the things that you're doing here.

NOTE Confidence: 0.67076522

 $00:02:56.310 \longrightarrow 00:02:57.998$ So as giving said,

NOTE Confidence: 0.67076522

 $00{:}02{:}57{.}998 \dashrightarrow 00{:}03{:}01{.}347$ I'm going to focus today's talk on the NOTE Confidence: 0.67076522

 $00{:}03{:}01{.}347 \dashrightarrow 00{:}03{:}04{.}268$ aspect in the lab where we study the NOTE Confidence: 0.67076522

 $00:03:04.268 \dashrightarrow 00:03:06.774$ role of T cells in the pathophysiology.

NOTE Confidence: 0.67076522

 $00:03:06.780 \dashrightarrow 00:03:10.518$ Of heart failure I have no disclosures NOTE Confidence: 0.67076522

 $00:03:10.520 \rightarrow 00:03:14.209$ and basically this is a cartoon that

NOTE Confidence: 0.67076522

 $00{:}03{:}14.209 \dashrightarrow 00{:}03{:}16.516$ summarizes the general theme of our lab,

NOTE Confidence: 0.67076522

 $00:03:16.520 \dashrightarrow 00:03:19.103$ which is how the moon system impacts

NOTE Confidence: 0.67076522

 $00:03:19.103 \longrightarrow 00:03:20.730$ cardiac and vascular health.

NOTE Confidence: 0.67076522

 $00:03:20.730 \longrightarrow 00:03:21.980$ So as you being said,

NOTE Confidence: 0.67076522

00:03:21.980 --> 00:03:24.773 I train in immunology and then I

NOTE Confidence: 0.67076522

 $00:03:24.773 \dashrightarrow 00:03:27.439$ further train in vascular biology,

NOTE Confidence: 0.67076522

 $00{:}03{:}27{.}440 \dashrightarrow 00{:}03{:}30{.}848$ but we know that immune cells

NOTE Confidence: 0.67076522

 $00{:}03{:}30{.}850 \dashrightarrow 00{:}03{:}33{.}346$ they really need to traffic into

NOTE Confidence: 0.67076522

 $00{:}03{:}33{.}346 \dashrightarrow 00{:}03{:}35{.}890$ tissues to do their functions.

NOTE Confidence: 0.67076522

 $00{:}03{:}35{.}890 \dashrightarrow 00{:}03{:}37{.}210$ But then once.

NOTE Confidence: 0.67076522

 $00{:}03{:}37{.}210 \dashrightarrow 00{:}03{:}38{.}090$ In addition,

NOTE Confidence: 0.67076522

 $00{:}03{:}38.090 \dashrightarrow 00{:}03{:}41.688$ they need to interact or crosstalk with

NOTE Confidence: 0.67076522

 $00{:}03{:}41.688 \dashrightarrow 00{:}03{:}45.769$ all the different resident cells in order

NOTE Confidence: 0.67076522

 $00:03:45.769 \longrightarrow 00:03:48.824$ to modulate homeostasis or pathology.

NOTE Confidence: 0.67076522

 $00:03:48.830 \rightarrow 00:03:50.510$ In the case of injury.

 $00:03:50.510 \rightarrow 00:03:51.670$ So for today's talk,

NOTE Confidence: 0.67076522

 $00{:}03{:}51{.}670 \dashrightarrow 00{:}03{:}53{.}787$ I will focus on what we've been

NOTE Confidence: 0.67076522

 $00{:}03{:}53.787 \dashrightarrow 00{:}03{:}55.671$ learning recently in the lab from

NOTE Confidence: 0.67076522

 $00{:}03{:}55{.}671 \dashrightarrow 00{:}03{:}57{.}834$ our work and also from the work

NOTE Confidence: 0.67076522

 $00{:}03{:}57{.}834 \dashrightarrow 00{:}04{:}00{.}578$ of others of how this interaction

NOTE Confidence: 0.67076522

 $00{:}04{:}00{.}578$ --> $00{:}04{:}03{.}288$ between adapted and innate immunity

NOTE Confidence: 0.67076522

 $00:04:03.290 \dashrightarrow 00:04:06.430$ contributes to cardiac remodeling.

NOTE Confidence: 0.67076522

 $00:04:06.430 \longrightarrow 00:04:09.764$ In hard and I I place a circle

NOTE Confidence: 0.67076522

 $00:04:09.764 \dashrightarrow 00:04:11.920$ here because this is mainly where

NOTE Confidence: 0.67076522

 $00{:}04{:}11{.}920 \dashrightarrow 00{:}04{:}13{.}728$ these interactions between adapted

NOTE Confidence: 0.67076522

 $00{:}04{:}13.728 \dashrightarrow 00{:}04{:}16.499$ and it made immune cells happen.

NOTE Confidence: 0.67076522

00:04:16.500 --> 00:04:19.152 This is what T cell antigen

NOTE Confidence: 0.67076522

 $00:04:19.152 \dashrightarrow 00:04:21.700$ recognition starts in the lymph nodes.

NOTE Confidence: 0.67076522

00:04:21.700 --> 00:04:23.652 But towards the end of the talk I

NOTE Confidence: 0.67076522

 $00{:}04{:}23.652 \dashrightarrow 00{:}04{:}25.761$ will show some new data is still

 $00{:}04{:}25{.}761 \dashrightarrow 00{:}04{:}27{.}754$ unpublished where we really find that

NOTE Confidence: 0.67076522

 $00:04:27.754 \rightarrow 00:04:29.230$ they're very similar interactions

NOTE Confidence: 0.67076522

 $00:04:29.230 \longrightarrow 00:04:31.494$ that are also happening in the

NOTE Confidence: 0.67076522

 $00{:}04{:}31{.}494 \dashrightarrow 00{:}04{:}33{.}978$ heart and that they might modulate

NOTE Confidence: 0.67076522

 $00{:}04{:}33{.}978 \dashrightarrow 00{:}04{:}35{.}560$ correct Physiology this way.

NOTE Confidence: 0.67076522

00:04:35.560 --> 00:04:37.835 So as many of you probably know,

NOTE Confidence: 0.67076522

00:04:37.840 --> 00:04:39.755 heart failure is very complex

NOTE Confidence: 0.67076522

 $00:04:39.755 \longrightarrow 00:04:40.904$ and it's multifactorial.

NOTE Confidence: 0.67076522

 $00{:}04{:}40{.}910 \dashrightarrow 00{:}04{:}42{.}354$ So to tackle mechanisms,

NOTE Confidence: 0.67076522

 $00{:}04{:}42.354 \dashrightarrow 00{:}04{:}45.780$ we need to start in a simplistic way.

NOTE Confidence: 0.67076522

 $00{:}04{:}45.780 \dashrightarrow 00{:}04{:}48.006$ But we also need to understand

NOTE Confidence: 0.67076522

 $00:04:48.006 \longrightarrow 00:04:49.119$ the full complexity.

NOTE Confidence: 0.67076522

 $00{:}04{:}49{.}120 \dashrightarrow 00{:}04{:}51{.}227$ So what do we know is that

NOTE Confidence: 0.67076522

 $00:04:51.227 \longrightarrow 00:04:52.820$ regardless of the etiology,

NOTE Confidence: 0.67076522

 $00:04:52.820 \longrightarrow 00:04:54.380$ whether it was triggered

NOTE Confidence: 0.67076522

 $00:04:54.380 \longrightarrow 00:04:55.940$ by any ischemic event,

00:04:55.940 --> 00:04:59.056 such as a myocardial infarct

NOTE Confidence: 0.67076522

 $00{:}04{:}59{.}056 \dashrightarrow 00{:}05{:}01{.}488$ or non ischemic event.

NOTE Confidence: 0.67076522

 $00{:}05{:}01{.}490 \dashrightarrow 00{:}05{:}04{.}388$ The heart remodels and the characteristics

NOTE Confidence: 0.67076522

 $00:05:04.388 \rightarrow 00:05:07.469$ of the failing heart are increased.

NOTE Confidence: 0.67076522

 $00{:}05{:}07{.}470 \dashrightarrow 00{:}05{:}11{.}000$ High level curricular pressures and

NOTE Confidence: 0.67076522

 $00:05:11.000 \dashrightarrow 00:05:13.824$ then a hypertrophic cardiomy ocytes

NOTE Confidence: 0.67076522

 $00{:}05{:}13.824 \dashrightarrow 00{:}05{:}16.770$ fibrosis and these results in

NOTE Confidence: 0.67076522

 $00{:}05{:}16.770 \dashrightarrow 00{:}05{:}19.010$ systolic and diastolic dysfunction.

NOTE Confidence: 0.67076522

 $00{:}05{:}19{.}010 \dashrightarrow 00{:}05{:}21{.}978$ And we've known since the 50s that

NOTE Confidence: 0.67076522

 $00:05:21.978 \rightarrow 00:05:23.250$ systemic chronic inflammation

NOTE Confidence: 0.67076522

 $00{:}05{:}23{.}321 \dashrightarrow 00{:}05{:}25{.}306$ is associated with pretty much

NOTE Confidence: 0.67076522

 $00{:}05{:}25{.}310 \dashrightarrow 00{:}05{:}28{.}262$ all of the causes of all of the

NOTE Confidence: 0.67076522

 $00:05:28.262 \longrightarrow 00:05:30.230$ etiologies of heart failure.

NOTE Confidence: 0.67076522

00:05:30.230 --> 00:05:31.886 I'm just going to set up my timer

NOTE Confidence: 0.67076522

 $00:05:31.886 \longrightarrow 00:05:33.417$ here to make sure that we're.

- $00:05:33.420 \longrightarrow 00:05:35.140$ Runtime here.
- NOTE Confidence: 0.67076522
- $00:05:35.140 \longrightarrow 00:05:37.180$ But unfortunately this by this knowledge,
- NOTE Confidence: 0.67076522
- $00:05:37.180 \longrightarrow 00:05:37.990$ for many,
- NOTE Confidence: 0.67076522
- $00:05:37.990 \longrightarrow 00:05:40.420$ many years today none of the
- NOTE Confidence: 0.67076522
- $00:05:40.420 \rightarrow 00:05:42.035$ anti-inflammatory therapies for clinical
- NOTE Confidence: 0.67076522
- $00:05:42.035 \rightarrow 00:05:43.875$ trials that were initially launched
- NOTE Confidence: 0.67076522
- $00:05:43.875 \rightarrow 00:05:46.709$ to tackle a pro inflammatory cytokines,
- NOTE Confidence: 0.67076522
- $00{:}05{:}46.710 \dashrightarrow 00{:}05{:}48.030$ such as TNF.
- NOTE Confidence: 0.67076522
- $00{:}05{:}48.030 \dashrightarrow 00{:}05{:}49.350$ And more recently,
- NOTE Confidence: 0.67076522
- $00:05:49.350 \longrightarrow 00:05:50.630$ with the counters trial
- NOTE Confidence: 0.67076522
- $00:05:50.630 \longrightarrow 00:05:52.550$ island bed and none of them,
- NOTE Confidence: 0.67076522
- $00{:}05{:}52{.}550 \dashrightarrow 00{:}05{:}54{.}680$ this is the anti TNF the rapies
- NOTE Confidence: 0.67076522
- $00:05:54.680 \rightarrow 00:05:57.121$ that are very efficient in treating
- NOTE Confidence: 0.67076522
- $00{:}05{:}57{.}121 \dashrightarrow 00{:}05{:}59{.}496$ out immune diseases and chronic
- NOTE Confidence: 0.67076522
- $00:05:59.496 \longrightarrow 00:06:01.252$ inflammatory diseases did not
- NOTE Confidence: 0.67076522
- $00:06:01.252 \rightarrow 00:06:03.648$ work in heart failure and there

 $00{:}06{:}03.648 \dashrightarrow 00{:}06{:}04.830$ are more recent

NOTE Confidence: 0.6007636166666667

 $00:06:04.830 \rightarrow 00:06:07.710$ promising data with the Cantor's trial,

NOTE Confidence: 0.6007636166666667

 $00:06:07.710 \longrightarrow 00:06:10.128$ although it's still early to tell

NOTE Confidence: 0.6007636166666667

 $00:06:10.130 \rightarrow 00:06:12.818$ whether it has really benefited in in

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}12.818 \dashrightarrow 00{:}06{:}16.087$ some of the outcomes of heart failure.

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}16.090 \dashrightarrow 00{:}06{:}19.267$ So what we know is that there are no

NOTE Confidence: 0.6007636166666667

 $00:06:19.267 \longrightarrow 00:06:20.718$ anti-inflammatory antifibrotic therapies

NOTE Confidence: 0.6007636166666667

 $00:06:20.718 \rightarrow 00:06:23.288$ that have been successful today,

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}23.290 \dashrightarrow 00{:}06{:}26.468$ and we know from many organ systems

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}26{.}468 \dashrightarrow 00{:}06{:}29{.}046$ that inflammation or immune cell

NOTE Confidence: 0.6007636166666667

 $00:06:29.046 \rightarrow 00:06:32.232$ activation and fibrosis go together or

NOTE Confidence: 0.6007636166666667

 $00:06:32.232 \rightarrow 00:06:35.196$ have some overlapping functions as well.

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}35{.}200 \dashrightarrow 00{:}06{:}37{.}324$ So the first question that we

NOTE Confidence: 0.6007636166666667

 $00:06:37.324 \rightarrow 00:06:39.280$ asked several years ago was is,

NOTE Confidence: 0.6007636166666667

 $00:06:39.280 \longrightarrow 00:06:41.100$ is there cardiac information?

00:06:41.100 --> 00:06:42.920 Besides systemic chronic inflammation

NOTE Confidence: 0.6007636166666667

 $00:06:42.920 \rightarrow 00:06:45.814$ again going with the concept that if the

NOTE Confidence: 0.6007636166666667

 $00:06:45.814 \rightarrow 00:06:48.313$ immune cells traffic to an inflamed issue,

NOTE Confidence: 0.6007636166666667

 $00:06:48.320 \longrightarrow 00:06:51.296$ do they exert their functions by

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}51.296 \dashrightarrow 00{:}06{:}53.280$ communicating with the tissue

NOTE Confidence: 0.6007636166666667

 $00:06:53.360 \longrightarrow 00:06:54.638$ or stroma cells?

NOTE Confidence: 0.6007636166666667

 $00:06:54.640 \longrightarrow 00:06:56.789$ And then if that was the case,

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}56{.}790 \dashrightarrow 00{:}06{:}58{.}585$ do the cardiac infiltrated muscles

NOTE Confidence: 0.6007636166666667

 $00{:}06{:}58{.}585 \dashrightarrow 00{:}07{:}00{.}021$ contribute to the hallmarks

NOTE Confidence: 0.6007636166666667

 $00:07:00.021 \rightarrow 00:07:01.726$ that we see of heart failure,

NOTE Confidence: 0.6007636166666667

 $00:07:01.730 \longrightarrow 00:07:03.030$ such as correct fibrosis?

NOTE Confidence: 0.6007636166666667

 $00:07:03.030 \longrightarrow 00:07:04.980$ And does that have any impact

NOTE Confidence: 0.6007636166666667

00:07:05.040 --> 00:07:06.399 on cardiac dysfunction?

NOTE Confidence: 0.6007636166666667

 $00:07:06.400 \longrightarrow 00:07:10.012$ And obviously we're very interested as

NOTE Confidence: 0.6007636166666667

 $00:07:10.012 \rightarrow 00:07:12.840$ basic scientists in understanding how.

NOTE Confidence: 0.6007636166666667

 $00:07:12.840 \longrightarrow 00:07:14.625$ So the first experiment that we did

- NOTE Confidence: 0.6007636166666667
- $00:07:14.625 \longrightarrow 00:07:16.460$ this this is this was published.
- NOTE Confidence: 0.6007636166666667
- 00:07:16.460 --> 00:07:18.660 This is back in 2015,
- NOTE Confidence: 0.6007636166666667
- $00{:}07{:}18.660 \dashrightarrow 00{:}07{:}21.586$ but we wanted to say whether we
- NOTE Confidence: 0.6007636166666667
- $00:07:21.586 \longrightarrow 00:07:23.950$ could see cardiac inflammation
- NOTE Confidence: 0.6007636166666667
- $00:07:23.950 \longrightarrow 00:07:25.460$ in patients with heart failure,
- NOTE Confidence: 0.6007636166666667
- $00:07:25.460 \dashrightarrow 00:07:27.609$ but we wanted to look at patients
- NOTE Confidence: 0.6007636166666667
- $00:07:27.609 \dashrightarrow 00:07:29.440$ with non ischemic heart failure.
- NOTE Confidence: 0.6007636166666667
- 00:07:29.440 --> 00:07:32.737 Antonio Barish group at VCU in Virginia.
- NOTE Confidence: 0.6007636166666667
- $00{:}07{:}32.740 \dashrightarrow 00{:}07{:}34.144$ He had elegantly demonstrated
- NOTE Confidence: 0.6007636166666667
- $00:07:34.144 \rightarrow 00:07:36.250$ years before this that in response
- NOTE Confidence: 0.6007636166666667
- 00:07:36.308 --> 00:07:37.679 to myocardial infarction,
- NOTE Confidence: 0.6007636166666667
- $00{:}07{:}37{.}680 \dashrightarrow 00{:}07{:}39{.}865$ there was decent infiltration in
- NOTE Confidence: 0.6007636166666667
- $00:07:39.865 \rightarrow 00:07:42.304$ the human heart and interestingly.
- NOTE Confidence: 0.6007636166666667
- $00{:}07{:}42.304 \dashrightarrow 00{:}07{:}45.676$ The diesels were infiltrated in the
- NOTE Confidence: 0.6007636166666667
- $00:07:45.676 \rightarrow 00:07:49.182$ in the scar zone in the infarct zone,
- NOTE Confidence: 0.6007636166666667

- 00:07:49.182 --> 00:07:49.908 but also,
- NOTE Confidence: 0.6007636166666667
- $00{:}07{:}49{.}910 \dashrightarrow 00{:}07{:}52{.}806$ so that goes along with a roll of
- NOTE Confidence: 0.6007636166666667
- $00:07:52.806 \rightarrow 00:07:55.263$ the immune system during evolution
- NOTE Confidence: 0.6007636166666667
- $00:07:55.263 \rightarrow 00:07:56.910$ to help healing.
- NOTE Confidence: 0.6007636166666667
- 00:07:56.910 --> 00:07:57.572 But interestingly,
- NOTE Confidence: 0.6007636166666667
- $00{:}07{:}57{.}572 \dashrightarrow 00{:}07{:}59{.}558$ what they had found in inference
- NOTE Confidence: 0.6007636166666667
- $00{:}07{:}59{.}558 \dashrightarrow 00{:}08{:}02{.}137$ was that there were also a lot of T
- NOTE Confidence: 0.6007636166666667
- $00{:}08{:}02.137 \dashrightarrow 00{:}08{:}03.709$ cells infiltrated and remote zones.
- NOTE Confidence: 0.6007636166666667
- $00{:}08{:}03{.}710 \dashrightarrow 00{:}08{:}05{.}870$ So we thought if we chose a patients
- NOTE Confidence: 0.6007636166666667
- $00{:}08{:}05{.}870 \dashrightarrow 00{:}08{:}08{.}126$ that did not have any impact that have
- NOTE Confidence: 0.6007636166666667
- $00:08:08.126 \rightarrow 00:08:10.550$ sort of like low chronic inflammation,
- NOTE Confidence: 0.6007636166666667
- $00:08:10.550 \longrightarrow 00:08:12.362$ where we see these as infiltrated
- NOTE Confidence: 0.6007636166666667
- $00:08:12.362 \longrightarrow 00:08:13.268$ in the heart.
- NOTE Confidence: 0.6007636166666667
- $00:08:13.270 \rightarrow 00:08:15.524$ And this is exactly what we found
- NOTE Confidence: 0.6007636166666667
- $00:08:15.524 \rightarrow 00:08:18.254$ here in Brown that they end stage
- NOTE Confidence: 0.6007636166666667
- $00:08:18.254 \rightarrow 00:08:20.018$ nonischemic heart failure and

 $00:08:20.018 \rightarrow 00:08:22.410$ heart samples which were taken as

NOTE Confidence: 0.6007636166666667

 $00{:}08{:}22{.}410 \dashrightarrow 00{:}08{:}26{.}054$ stated here from from there had

NOTE Confidence: 0.6007636166666667

 $00:08:26.054 \rightarrow 00:08:27.620$ significant diesel infiltration.

NOTE Confidence: 0.6007636166666667

 $00:08:27.620 \rightarrow 00:08:31.058$ Compared to non heart failure controls.

NOTE Confidence: 0.6007636166666667

 $00{:}08{:}31{.}060 \dashrightarrow 00{:}08{:}33{.}349$ And later on we did some experiments

NOTE Confidence: 0.6007636166666667

 $00{:}08{:}33{.}349 \dashrightarrow 00{:}08{:}36{.}200$ where we also wanted to look at what

NOTE Confidence: 0.6007636166666667

 $00:08:36.200 \rightarrow 00:08:38.460$ kind of pistols were infiltrated there,

NOTE Confidence: 0.6007636166666667

 $00:08:38.460 \longrightarrow 00:08:41.043$ and we found that many of those

NOTE Confidence: 0.6007636166666667

 $00{:}08{:}41.043 \dashrightarrow 00{:}08{:}42.932$ teachers expressed the chemo keen

NOTE Confidence: 0.6007636166666667

 $00{:}08{:}42.932 \dashrightarrow 00{:}08{:}46.280$ receptor CXCR 3 and this is shown here

NOTE Confidence: 0.6007636166666667

00:08:46.280 --> 00:08:49.100 by Red Arrows and quantified here.

NOTE Confidence: 0.6007636166666667

 $00{:}08{:}49{.}100 \dashrightarrow 00{:}08{:}51{.}991$ So this this made the basis to

NOTE Confidence: 0.6007636166666667

 $00:08:51.991 \rightarrow 00:08:53.895$ wanted to understand mechanistically

NOTE Confidence: 0.6007636166666667

 $00{:}08{:}53.895 \dashrightarrow 00{:}08{:}57.351$ what is thesis that expressed these

NOTE Confidence: 0.6007636166666667

 $00:08:57.351 \dashrightarrow 00:09:00.538$ receptors are doing within the heart.

 $00:09:00.540 \longrightarrow 00:09:02.770$ So our very broad hypothesis.

NOTE Confidence: 0.6007636166666667

 $00{:}09{:}02{.}770 \dashrightarrow 00{:}09{:}05{.}661$ 110 and Evers joined my lab as

NOTE Confidence: 0.6007636166666667

 $00:09:05.661 \rightarrow 00:09:07.528$ postdoc was asking the question,

NOTE Confidence: 0.6007636166666667

 $00:09:07.528 \rightarrow 00:09:09.604$ is this purely an association or

NOTE Confidence: 0.6007636166666667

 $00:09:09.604 \rightarrow 00:09:11.634$ are they actually contributing or

NOTE Confidence: 0.6007636166666667

 $00{:}09{:}11.634 \dashrightarrow 00{:}09{:}14.518$ doing something in the heart and her

NOTE Confidence: 0.6007636166666667

 $00:09:14.518 \rightarrow 00:09:16.440$ hypothesis was that they would be

NOTE Confidence: 0.6007636166666667

 $00:09:16.440 \rightarrow 00:09:20.115$ doing something there in the failing heart?

NOTE Confidence: 0.6007636166666667

 $00{:}09{:}20{.}120 \dashrightarrow 00{:}09{:}22{.}656$ And to start doing this we have to

NOTE Confidence: 0.6007636166666667

 $00:09:22.656 \dashrightarrow 00:09:25.144$ choose a preclinical model and knowing

NOTE Confidence: 0.6007636166666667

 $00:09:25.144 \dashrightarrow 00:09:26.716$ that heart failure is very complex,

NOTE Confidence: 0.6007636166666667

 $00{:}09{:}26.720 \dashrightarrow 00{:}09{:}30.950$ there's no optimal or perfect.

NOTE Confidence: 0.7375429225

 $00:09:30.950 \dashrightarrow 00:09:33.200$ The clinical model that mimics

NOTE Confidence: 0.7375429225

00:09:33.200 - > 00:09:35.750 all the symptoms of heart failure

NOTE Confidence: 0.7375429225

 $00:09:35.750 \longrightarrow 00:09:37.750$ or how the disease develops,

NOTE Confidence: 0.7375429225

 $00:09:37.750 \longrightarrow 00:09:39.952$ but we found that for nonischemic

- NOTE Confidence: 0.7375429225
- $00{:}09{:}39{.}952 \dashrightarrow 00{:}09{:}43{.}090$ heart failure tack or transverse or

 $00:09:43.090 \rightarrow 00:09:46.644$ reconstruction was a one where we could time,

NOTE Confidence: 0.7375429225

 $00:09:46.650 \longrightarrow 00:09:47.590$ and for certain reasons,

NOTE Confidence: 0.7375429225

 $00{:}09{:}47{.}590 \dashrightarrow 00{:}09{:}48{.}765$ that we wanted to do.

NOTE Confidence: 0.7375429225

 $00:09:48.770 \longrightarrow 00:09:51.570$ It was really a very good model to do so.

NOTE Confidence: 0.7375429225

00:09:51.570 --> 00:09:53.545 Why? Because it induces pressure

NOTE Confidence: 0.7375429225

00:09:53.545 --> 00:09:55.966 that mimics the pressure that heart

NOTE Confidence: 0.7375429225

 $00:09:55.966 \rightarrow 00:09:58.210$ failure patients have in the heart.

NOTE Confidence: 0.7375429225

 $00:09:58.210 \dashrightarrow 00:10:00.658$ Although the downside is that here.

NOTE Confidence: 0.7375429225

 $00{:}10{:}00{.}658 \dashrightarrow 00{:}10{:}03{.}514$ It induces a sudden pressure that then

NOTE Confidence: 0.7375429225

 $00:10:03.514 \longrightarrow 00:10:05.930$ is restrained versus impatience as

NOTE Confidence: 0.7375429225

 $00:10:05.930 \longrightarrow 00:10:08.480$ we know they developed progressively,

NOTE Confidence: 0.7375429225

 $00:10:08.480 \longrightarrow 00:10:09.288$ but importantly,

NOTE Confidence: 0.7375429225

00:10:09.288 --> 00:10:12.520 in this model we can basically track very

NOTE Confidence: 0.7375429225

 $00{:}10{:}12{.}592 \dashrightarrow 00{:}10{:}15{.}377$ nicely how cardiac hypertrophy develops,

 $00:10:15.380 \longrightarrow 00:10:16.872$ how cardiac fibrosis develops,

NOTE Confidence: 0.7375429225

 $00:10:16.872 \longrightarrow 00:10:19.918$ and whether we can check in per cardiac

NOTE Confidence: 0.7375429225

 $00{:}10{:}19{.}918 \dashrightarrow 00{:}10{:}22{.}138$ function and at those time points.

NOTE Confidence: 0.7375429225

 $00:10:22.140 \longrightarrow 00:10:24.884$ We could also look for diesel immune

NOTE Confidence: 0.7375429225

 $00{:}10{:}24.884 \dashrightarrow 00{:}10{:}27.084$ responses and correct diesel infiltration.

NOTE Confidence: 0.7375429225

 $00{:}10{:}27.084$ --> $00{:}10{:}30.178$ So using this model I'm showing data NOTE Confidence: 0.7375429225

 $00:10:30.178 \longrightarrow 00:10:32.405$ from 4 weeks. Play time points.

NOTE Confidence: 0.7375429225

 $00:10:32.405 \rightarrow 00:10:34.530$ That is all summarizing schematics.

NOTE Confidence: 0.7375429225

 $00{:}10{:}34{.}530 \dashrightarrow 00{:}10{:}37{.}810$ Because we published this already.

NOTE Confidence: 0.7375429225

 $00{:}10{:}37.810 \dashrightarrow 00{:}10{:}40.477$ But what we found was that it

NOTE Confidence: 0.7375429225

 $00:10:40.477 \longrightarrow 00:10:42.363$ specifically one type of thesis

NOTE Confidence: 0.7375429225

 $00:10:42.363 \longrightarrow 00:10:44.687$ that are CD 4 positive T cells

NOTE Confidence: 0.7375429225

 $00:10:44.690 \longrightarrow 00:10:46.262$ were infiltrated in the heart as

NOTE Confidence: 0.7375429225

 $00:10:46.262 \longrightarrow 00:10:47.930$ early as two weeks post stack.

NOTE Confidence: 0.7375429225

 $00:10:47.930 \longrightarrow 00:10:50.779$ And this is four weeks after Tak.

NOTE Confidence: 0.7375429225

 $00:10:50.780 \longrightarrow 00:10:51.464$ And then,

- NOTE Confidence: 0.7375429225
- $00:10:51.464 \rightarrow 00:10:53.516$ before they infiltrated in the heart,
- NOTE Confidence: 0.7375429225
- $00{:}10{:}53.520 \dashrightarrow 00{:}10{:}55.907$ we saw a significant expansion of the
- NOTE Confidence: 0.7375429225
- $00:10:55.907 \rightarrow 00:10:57.828$ medicinale draining lymph nodes that are
- NOTE Confidence: 0.7375429225
- $00:10:57.828 \longrightarrow 00:10:59.795$ the lymph nodes that drain the heart.
- NOTE Confidence: 0.7375429225
- $00{:}10{:}59{.}800 \dashrightarrow 00{:}11{:}02{.}957$ And most of those T cells express
- NOTE Confidence: 0.7375429225
- $00{:}11{:}02{.}957 \dashrightarrow 00{:}11{:}05{.}546$ interferon gamma so they were type
- NOTE Confidence: 0.7375429225
- $00{:}11{:}05{.}546 \dashrightarrow 00{:}11{:}09{.}126$ one TT cells T H1 cells which also
- NOTE Confidence: 0.7375429225
- $00:11:09.126 \rightarrow 00:11:11.018$ expressed the chemokine receptor.
- NOTE Confidence: 0.7375429225
- $00:11:11.020 \longrightarrow 00:11:13.480$ 6 year 3.
- NOTE Confidence: 0.7375429225
- $00:11:13.480 \longrightarrow 00:11:15.784$ And then we found that these
- NOTE Confidence: 0.7375429225
- $00:11:15.784 \rightarrow 00:11:18.147$ infiltration was associated with at the
- NOTE Confidence: 0.7375429225
- $00{:}11{:}18{.}147 \dashrightarrow 00{:}11{:}20{.}037$ time where mice developed fibrosis.
- NOTE Confidence: 0.7375429225
- 00:11:20.040 --> 00:11:21.356 As you can see here in pink,
- NOTE Confidence: 0.7375429225
- $00{:}11{:}21{.}360 \dashrightarrow 00{:}11{:}23{.}750$ the collagen deposition and enlargement
- NOTE Confidence: 0.7375429225
- $00:11:23.750 \rightarrow 00:11:27.410$ of the cardiac myocytes by H&E.
- NOTE Confidence: 0.7375429225

 $00:11:27.410 \rightarrow 00:11:30.098$ And what we found using this mouse

NOTE Confidence: 0.7375429225

00:11:30.098 --> 00:11:32.513 model was that if my eyes were

NOTE Confidence: 0.7375429225

00:11:32.513 --> 00:11:34.218 genetically deficient in D zones

NOTE Confidence: 0.7375429225

 $00:11:34.218 \rightarrow 00:11:36.348$ and we use different models,

NOTE Confidence: 0.7375429225

00:11:36.350 --> 00:11:39.101 diesel receptor alpha Nokia or MHC 2

NOTE Confidence: 0.7375429225

 $00{:}11{:}39{.}101 \dashrightarrow 00{:}11{:}41{.}609$ knock out or right to knock out what NOTE Confidence: 0.7375429225

 $00:11:41.609 \longrightarrow 00:11:44.415$ we found was that all the mice that

NOTE Confidence: 0.7375429225

 $00:11:44.415 \rightarrow 00:11:46.910$ did not have decent genetically they

NOTE Confidence: 0.7375429225

00:11:46.910 --> 00:11:49.070 did not develop a cardiac fibrosis.

NOTE Confidence: 0.7375429225

 $00:11:49.070 \longrightarrow 00:11:51.080$ We cannot see any College in

NOTE Confidence: 0.7375429225

 $00{:}11{:}51{.}080 \dashrightarrow 00{:}11{:}52{.}085$ the position here.

NOTE Confidence: 0.7375429225

 $00{:}11{:}52.090 \dashrightarrow 00{:}11{:}54.449$ And then when these mice were reconstituted,

NOTE Confidence: 0.7375429225

 $00:11:54.450 \longrightarrow 00:11:56.454$ we see Excel 3 positive there

NOTE Confidence: 0.7375429225

 $00{:}11{:}56{.}454 \dashrightarrow 00{:}11{:}57{.}456$ from gamma positive.

NOTE Confidence: 0.7375429225

 $00{:}11{:}57{.}460 \dashrightarrow 00{:}11{:}59{.}528$ Keystones we could partially

NOTE Confidence: 0.7375429225

 $00{:}11{:}59{.}528 \dashrightarrow 00{:}12{:}01{.}079$ reconstitute the fibrosis.

 $00{:}12{:}01.080 \dashrightarrow 00{:}12{:}02.712$ Certainly the provascular fibrosis.

NOTE Confidence: 0.7375429225

00:12:02.712 --> 00:12:04.752 As you can see here,

NOTE Confidence: 0.7375429225

 $00{:}12{:}04.760 \dashrightarrow 00{:}12{:}06.680$ and we could reconstitute and or

NOTE Confidence: 0.7375429225

 $00:12:06.680 \longrightarrow 00:12:09.460$ a lot of the cardiac dysfunction.

NOTE Confidence: 0.7375429225

00:12:09.460 --> 00:12:11.520 Although this data also suggested

NOTE Confidence: 0.7375429225

 $00{:}12{:}11.520 \dashrightarrow 00{:}12{:}14.919$ that there had to be some cardiac

NOTE Confidence: 0.7375429225

 $00:12:14.919 \longrightarrow 00:12:17.175$ antigen specificity involved to

NOTE Confidence: 0.7375429225

 $00:12:17.175 \longrightarrow 00:12:19.425$ to induce the full induction of

NOTE Confidence: 0.7375429225

 $00{:}12{:}19{.}425 \dashrightarrow 00{:}12{:}21{.}440$ cardiac fibrosis and dys function.

NOTE Confidence: 0.7375429225

00:12:21.440 --> 00:12:23.198 In these experiments, as I said,

NOTE Confidence: 0.7375429225

 $00:12:23.200 \longrightarrow 00:12:24.979$ we reconstituted fibrosis,

NOTE Confidence: 0.7375429225

00:12:24.979 --> 00:12:27.351 some parameters of systolic

NOTE Confidence: 0.7375429225

 $00:12:27.351 \longrightarrow 00:12:29.130$ and diastolic dysfunction.

NOTE Confidence: 0.7375429225

 $00{:}12{:}29{.}130 \dashrightarrow 00{:}12{:}31{.}494$ But these cells that we put

NOTE Confidence: 0.7375429225

 $00{:}12{:}31{.}494 \dashrightarrow 00{:}12{:}33{.}070$ back into these mice,

 $00:12:33.070 \rightarrow 00:12:34.830$ they were highly painful.

NOTE Confidence: 0.7375429225

 $00:12:34.830 \rightarrow 00:12:37.242$ Amatory but not antigen specific and

NOTE Confidence: 0.7375429225

00:12:37.242 --> 00:12:40.509 this will link to the second part of my

NOTE Confidence: 0.7375429225

 $00:12:40.509 \rightarrow 00:12:42.763$ talk and why that might be important.

NOTE Confidence: 0.7375429225

 $00{:}12{:}42{.}770 \dashrightarrow 00{:}12{:}46{.}721$ How we can use that in in in to

NOTE Confidence: 0.7375429225

 $00:12:46.721 \rightarrow 00:12:49.569$ understand this complex syndrome.

NOTE Confidence: 0.7375429225

 $00{:}12{:}49{.}570 \dashrightarrow 00{:}12{:}51{.}523$ So the other thing that I needed

NOTE Confidence: 0.7375429225

 $00:12:51.523 \rightarrow 00:12:52.360$ was well now

NOTE Confidence: 0.713985236956522

 $00{:}12{:}52{.}430 \dashrightarrow 00{:}12{:}55{.}058$ that we know that these T cells that express

NOTE Confidence: 0.713985236956522

 $00:12:55.058 \rightarrow 00:12:58.414$ in there from gamma are increasing the

NOTE Confidence: 0.713985236956522

 $00{:}12{:}58{.}414 \dashrightarrow 00{:}13{:}02{.}050$ lymph nodes under infiltrated in the heart.

NOTE Confidence: 0.713985236956522

 $00:13:02.050 \rightarrow 00:13:05.114$ How can we see if they actually cross

NOTE Confidence: 0.713985236956522

 $00:13:05.114 \rightarrow 00:13:07.378$ communicate with a cardiac residents?

NOTE Confidence: 0.713985236956522

 $00{:}13{:}07{.}380 \dashrightarrow 00{:}13{:}09{.}185$ Because we saw that massive

NOTE Confidence: 0.713985236956522

 $00{:}13{:}09{.}185 \dashrightarrow 00{:}13{:}10.629$ effect on cardiac fibrosis.

NOTE Confidence: 0.713985236956522

 $00:13:10.630 \longrightarrow 00:13:12.718$ We see it was a simple

00:13:12.718 --> 00:13:14.110 experiment to start with,

NOTE Confidence: 0.713985236956522

00:13:14.110 --> 00:13:15.958 which was isolating primary,

NOTE Confidence: 0.713985236956522

 $00:13:15.958 \rightarrow 00:13:18.268$ correct fiberglass from Adele mites

NOTE Confidence: 0.713985236956522

 $00:13:18.270 \rightarrow 00:13:20.628$ and then see isolated T cells.

NOTE Confidence: 0.713985236956522

 $00{:}13{:}20.630 \dashrightarrow 00{:}13{:}22.790$ From the mediastinal lymph nodes of

NOTE Confidence: 0.713985236956522

 $00:13:22.790 \rightarrow 00:13:25.190$ mice that were subjected to either sham,

NOTE Confidence: 0.713985236956522

 $00:13:25.190 \rightarrow 00:13:26.630$ so control surgery,

NOTE Confidence: 0.713985236956522

 $00:13:26.630 \longrightarrow 00:13:30.360$ I should say that some might have the

NOTE Confidence: 0.713985236956522

 $00{:}13{:}30{.}360 \dashrightarrow 00{:}13{:}33{.}300$ the open chest surgery and everything

NOTE Confidence: 0.713985236956522

 $00:13:33.300 \longrightarrow 00:13:35.888$ except for the construction to

NOTE Confidence: 0.713985236956522

 $00:13:35.888 \rightarrow 00:13:38.068$ account for possible inflammation

NOTE Confidence: 0.713985236956522

 $00{:}13{:}38.068 \dashrightarrow 00{:}13{:}40.248$ that happens during surgery.

NOTE Confidence: 0.713985236956522

 $00:13:40.250 \longrightarrow 00:13:42.738$ I know what you did is the Chico

NOTE Confidence: 0.713985236956522

 $00{:}13{:}42.738 \dashrightarrow 00{:}13{:}45.125$ culture this and then she she

NOTE Confidence: 0.713985236956522

 $00{:}13{:}45{.}125 \dashrightarrow 00{:}13{:}47{.}235$ coculture this indirect cultures or

 $00{:}13{:}47{.}235 \dashrightarrow 00{:}13{:}49{.}300$ entrance once and the idea was that

NOTE Confidence: 0.713985236956522

 $00{:}13{:}49{.}300 \dashrightarrow 00{:}13{:}51{.}330$ first he was going to see whether

NOTE Confidence: 0.713985236956522

 $00{:}13{:}51{.}330 \dashrightarrow 00{:}13{:}53{.}900$ these teasers could adhere to the

NOTE Confidence: 0.713985236956522

 $00:13:53.900 \rightarrow 00:13:56.022$ fibroblast and whether these fiberglass

NOTE Confidence: 0.713985236956522

 $00{:}13{:}56{.}022 \dashrightarrow 00{:}13{:}58{.}112$ transform to myofibroblast and to

NOTE Confidence: 0.713985236956522

 $00{:}13{:}58{.}112 \dashrightarrow 00{:}14{:}00{.}527$ do the readout for myofibroblast.

NOTE Confidence: 0.713985236956522

00:14:00.530 --> 00:14:03.716 We looked at alpha small muscle

NOTE Confidence: 0.713985236956522

 $00:14:03.716 \rightarrow 00:14:07.190$ acting which is expressed upon

NOTE Confidence: 0.713985236956522

 $00{:}14{:}07{.}190 \dashrightarrow 00{:}14{:}09{.}395$ fiber restaurants formation.

NOTE Confidence: 0.713985236956522

 $00:14:09.400 \longrightarrow 00:14:10.820$ So in those experiments,

NOTE Confidence: 0.713985236956522

 $00{:}14{:}10.820 \dashrightarrow 00{:}14{:}12.595$ this is a representative image.

NOTE Confidence: 0.713985236956522

 $00{:}14{:}12.600 \dashrightarrow 00{:}14{:}15.200$ You can see that a direct contact was

NOTE Confidence: 0.713985236956522

 $00:14:15.200 \longrightarrow 00:14:17.279$ required for these transformation,

NOTE Confidence: 0.713985236956522

 $00:14:17.280 \longrightarrow 00:14:19.560$ so these are two examples of

NOTE Confidence: 0.713985236956522

 $00{:}14{:}19.560 \dashrightarrow 00{:}14{:}21.422$ transform my fiber glass that have

NOTE Confidence: 0.713985236956522

 $00:14:21.422 \longrightarrow 00:14:23.558$ a lot of T cells bound to them.

 $00{:}14{:}23.560 \dashrightarrow 00{:}14{:}27.448$ The T cells were labeled in in green here

NOTE Confidence: 0.713985236956522

 $00{:}14{:}27{.}448 \dashrightarrow 00{:}14{:}31{.}060$ and this is the quantification of the

NOTE Confidence: 0.713985236956522

 $00:14:31.168 \rightarrow 00:14:35.290$ of the red of alpha small muscle acting.

NOTE Confidence: 0.713985236956522

 $00:14:35.290 \longrightarrow 00:14:36.840$ So the conclusion from these

NOTE Confidence: 0.713985236956522

 $00{:}14{:}36{.}840 \dashrightarrow 00{:}14{:}38{.}390$ experiments was that there was

NOTE Confidence: 0.713985236956522

 $00{:}14{:}38{.}445 \dashrightarrow 00{:}14{:}39{.}969$ these communications between.

NOTE Confidence: 0.713985236956522

 $00:14:39.970 \longrightarrow 00:14:43.138$ Pieces of fiberglass that was required

NOTE Confidence: 0.713985236956522

 $00{:}14{:}43{.}138 \dashrightarrow 00{:}14{:}45{.}843$ to induce transformation and then a

NOTE Confidence: 0.713985236956522

 $00:14:45.843 \rightarrow 00:14:47.698$ mechanistically what we found was

NOTE Confidence: 0.713985236956522

 $00:14:47.698 \rightarrow 00:14:50.089$ that this was TGF beta dependent,

NOTE Confidence: 0.713985236956522

 $00:14:50.090 \longrightarrow 00:14:51.710$ so it will block TGF beta.

NOTE Confidence: 0.713985236956522

 $00{:}14{:}51{.}710 \dashrightarrow 00{:}14{:}54{.}130$ We inhibited this transformation that

NOTE Confidence: 0.713985236956522

 $00{:}14{:}54{.}130 \dashrightarrow 00{:}14{:}57{.}266$ was not too surprising because we know

NOTE Confidence: 0.713985236956522

 $00{:}14{:}57.266 \dashrightarrow 00{:}15{:}00.164$ that PDF better was it's a classic

NOTE Confidence: 0.713985236956522

 $00{:}15{:}00{.}164 \dashrightarrow 00{:}15{:}02{.}854$ profit garlic cytokine that induces.

 $00{:}15{:}02.860 \dashrightarrow 00{:}15{:}04.605$ This transformation and that is

NOTE Confidence: 0.713985236956522

 $00{:}15{:}04.605 \dashrightarrow 00{:}15{:}06.880$ highly made by my fiber glass as well,

NOTE Confidence: 0.713985236956522

 $00:15:06.880 \rightarrow 00:15:08.800$ but what was more interesting is

NOTE Confidence: 0.713985236956522

 $00{:}15{:}08{.}800 \dashrightarrow 00{:}15{:}11{.}520$ that we found that T cells bound to

NOTE Confidence: 0.713985236956522

 $00:15:11.520 \longrightarrow 00:15:13.680$ the fiber rest through A4 integrin,

NOTE Confidence: 0.713985236956522

 $00:15:13.680 \rightarrow 00:15:16.396$ and we come one in the fiberglass

NOTE Confidence: 0.713985236956522

 $00:15:16.400 \longrightarrow 00:15:17.972$ and then once bound,

NOTE Confidence: 0.713985236956522

 $00:15:17.972 \rightarrow 00:15:20.826$ the diesels were induced and DJ better

NOTE Confidence: 0.713985236956522

 $00:15:20.826 \rightarrow 00:15:23.322$ released by the myofibrils are not

NOTE Confidence: 0.713985236956522

 $00{:}15{:}23{.}322 \dashrightarrow 00{:}15{:}26{.}256$ the other way around and this was also

NOTE Confidence: 0.713985236956522

 $00{:}15{:}26{.}256 \dashrightarrow 00{:}15{:}28{.}290$ published so I wouldn't show a lot

NOTE Confidence: 0.713985236956522

 $00{:}15{:}28{.}290 \dashrightarrow 00{:}15{:}30{.}405$ of the data there so I can focus on

NOTE Confidence: 0.713985236956522

 $00{:}15{:}30{.}468 \dashrightarrow 00{:}15{:}32{.}817$ more recent data in in our lab as well.

NOTE Confidence: 0.713985236956522

 $00:15:32.820 \longrightarrow 00:15:35.535$ We're currently working on on

NOTE Confidence: 0.713985236956522

 $00{:}15{:}35{.}535 \dashrightarrow 00{:}15{:}37{.}164$ further mechanistic insight

NOTE Confidence: 0.713985236956522

 $00:15:37.164 \longrightarrow 00:15:39.978$ into how we can prevent this.

 $00:15:39.980 \rightarrow 00:15:42.818$ They released induced by the FIBERLESS

NOTE Confidence: 0.713985236956522

 $00{:}15{:}42.818 \dashrightarrow 00{:}15{:}45.660$ upon the contact with the discus.

NOTE Confidence: 0.713985236956522

00:15:45.660 --> 00:15:47.795 So as a summary of background of

NOTE Confidence: 0.713985236956522

00:15:47.795 - 00:15:50.039 why we became interested in this,

NOTE Confidence: 0.713985236956522

 $00{:}15{:}50{.}040 \dashrightarrow 00{:}15{:}52{.}539$ we can see that in this transformation

NOTE Confidence: 0.713985236956522

 $00:15:52.539 \rightarrow 00:15:55.271$ from the healthy heart to the failing

NOTE Confidence: 0.713985236956522

 $00:15:55.271 \rightarrow 00:15:57.256$ heart using an experimental model,

NOTE Confidence: 0.713985236956522

 $00{:}15{:}57.260 \dashrightarrow 00{:}15{:}59.930$ in this case of transverse article

NOTE Confidence: 0.713985236956522

 $00{:}15{:}59{.}930 \dashrightarrow 00{:}16{:}01{.}766$ struction visit this activation,

NOTE Confidence: 0.713985236956522

 $00:16:01.766 \rightarrow 00:16:04.538$ particularly of this T cell subset.

NOTE Confidence: 0.713985236956522

 $00:16:04.540 \longrightarrow 00:16:06.628$ And then we say that these are traffic

NOTE Confidence: 0.713985236956522

 $00{:}16{:}06.628 \dashrightarrow 00{:}16{:}08.839$ to the heart and once in the heart.

NOTE Confidence: 0.713985236956522

 $00{:}16{:}08{.}840 \dashrightarrow 00{:}16{:}11{.}312$ They crossed off with a fiberglass

NOTE Confidence: 0.713985236956522

 $00{:}16{:}11.312 \dashrightarrow 00{:}16{:}12.960$ and induced cardiac fibrosis.

NOTE Confidence: 0.656873219076923

 $00{:}16{:}12{.}960 \dashrightarrow 00{:}16{:}15{.}774$ We block these by either using

 $00:16:15.774 \rightarrow 00:16:18.919$ agent mice that don't have T cells,

NOTE Confidence: 0.656873219076923

00:16:18.920 --> 00:16:21.060 or by using depletion diesel

NOTE Confidence: 0.656873219076923

 $00:16:21.060 \longrightarrow 00:16:23.200$ antibodies in wild I'm eyes.

NOTE Confidence: 0.656873219076923

 $00:16:23.200 \rightarrow 00:16:25.176$ I didn't show the data by the way.

NOTE Confidence: 0.656873219076923

 $00{:}16{:}25{.}180 \dashrightarrow 00{:}16{:}26{.}840$ We also did those studies.

NOTE Confidence: 0.656873219076923

 $00{:}16{:}26.840 \dashrightarrow 00{:}16{:}30.308$ We prevent this transformation.

NOTE Confidence: 0.656873219076923

 $00{:}16{:}30{.}310 \dashrightarrow 00{:}16{:}34{.}558$ We also found that the characters

NOTE Confidence: 0.656873219076923

 $00:16:34.558 \rightarrow 00:16:36.918$ themselves they in response to

NOTE Confidence: 0.656873219076923

 $00{:}16{:}36{.}918 \dashrightarrow 00{:}16{:}39{.}390$ pressure in response to duck even

NOTE Confidence: 0.656873219076923

 $00:16:39.473 \rightarrow 00:16:41.729$ before the T cells get there,

NOTE Confidence: 0.656873219076923

 $00:16:41.730 \longrightarrow 00:16:44.610$ they can actually make chemokines that

NOTE Confidence: 0.656873219076923

 $00{:}16{:}44.610 \dashrightarrow 00{:}16{:}47.480$ Kim attracts positive T cells and we

NOTE Confidence: 0.656873219076923

 $00{:}16{:}47{.}480 \dashrightarrow 00{:}16{:}50{.}265$ did this using a reported mice for

NOTE Confidence: 0.656873219076923

 $00:16:50.265 \rightarrow 00:16:53.441$ these schemes and and doing a time course.

NOTE Confidence: 0.656873219076923

 $00:16:53.450 \longrightarrow 00:16:55.922$ So we actually found that the

NOTE Confidence: 0.656873219076923

 $00:16:55.922 \rightarrow 00:16:57.570$ fiberglass are actually functioning

- NOTE Confidence: 0.656873219076923
- $00{:}16{:}57{.}639 \dashrightarrow 00{:}16{:}59{.}575$ as a semi immune cell because
- NOTE Confidence: 0.656873219076923
- 00:16:59.575 --> 00:17:00.940 they're releasing chemokines.
- NOTE Confidence: 0.656873219076923
- $00:17:00.940 \rightarrow 00:17:03.782$ Then they end up attracting first my
- NOTE Confidence: 0.656873219076923
- $00:17:03.782 \longrightarrow 00:17:07.157$ load cells and then T cells to the heart,
- NOTE Confidence: 0.656873219076923
- $00:17:07.160 \longrightarrow 00:17:08.876$ and then as I just showed,
- NOTE Confidence: 0.656873219076923
- $00:17:08.880 \longrightarrow 00:17:11.748$ we found that they can regulate
- NOTE Confidence: 0.656873219076923
- $00:17:11.748 \longrightarrow 00:17:13.182$ correct for groceries.
- NOTE Confidence: 0.656873219076923
- $00{:}17{:}13.190 \dashrightarrow 00{:}17{:}15.958$ So then when I question that we asked
- NOTE Confidence: 0.656873219076923
- $00:17:15.958 \rightarrow 00:17:18.978$ was well how and where this is being
- NOTE Confidence: 0.656873219076923
- $00:17:18.978 \longrightarrow 00:17:21.667$ activated in the heart and this work
- NOTE Confidence: 0.656873219076923
- 00:17:21.667 --> 00:17:24.570 was done by Jay Wanyama who was a
- NOTE Confidence: 0.656873219076923
- $00{:}17{:}24.570 \dashrightarrow 00{:}17{:}27.054$ graduate student in the lab and he
- NOTE Confidence: 0.656873219076923
- $00:17:27.054 \rightarrow 00:17:28.564$ was really interested in knowing
- NOTE Confidence: 0.656873219076923
- $00{:}17{:}28.564 \dashrightarrow 00{:}17{:}30.570$ this because he found he said well,
- NOTE Confidence: 0.656873219076923
- $00{:}17{:}30{.}570 \dashrightarrow 00{:}17{:}33{.}634$ if we found a specific antigens that might
- NOTE Confidence: 0.656873219076923

 $00{:}17{:}33{.}634 \dashrightarrow 00{:}17{:}36{.}680$ be relevant for the T cell immune response.

NOTE Confidence: 0.656873219076923

 $00{:}17{:}36{.}680 \dashrightarrow 00{:}17{:}38{.}624$ Then one could think about in

NOTE Confidence: 0.656873219076923

 $00{:}17{:}38{.}624 \dashrightarrow 00{:}17{:}39{.}920$ this in the future.

NOTE Confidence: 0.656873219076923

 $00:17:39.920 \longrightarrow 00:17:43.220$ Potentially immunizing for heart failure,

NOTE Confidence: 0.656873219076923

00:17:43.220 --> 00:17:43.588 right?

NOTE Confidence: 0.656873219076923

 $00{:}17{:}43.588 \dashrightarrow 00{:}17{:}46.900$ There will be a long term goal or at

NOTE Confidence: 0.656873219076923

 $00{:}17{:}46{.}993 \dashrightarrow 00{:}17{:}49{.}778$ least understanding whether this is

NOTE Confidence: 0.656873219076923

 $00{:}17{:}49{.}778 \dashrightarrow 00{:}17{:}53{.}146$ what was this this activation happening

NOTE Confidence: 0.656873219076923

 $00:17:53.146 \longrightarrow 00:17:57.106$ and where over time it could be prevented?

NOTE Confidence: 0.656873219076923

 $00{:}17{:}57{.}110 \dashrightarrow 00{:}17{:}59{.}998$ So to study that we use a reporter

NOTE Confidence: 0.656873219076923

 $00{:}17{:}59{.}998 \dashrightarrow 00{:}18{:}02{.}828$ mice for T cell activation or

NOTE Confidence: 0.656873219076923

 $00{:}18{:}02.828 \dashrightarrow 00{:}18{:}04.844$ T cell receptor engagement.

NOTE Confidence: 0.656873219076923

 $00{:}18{:}04.850 \dashrightarrow 00{:}18{:}07.218$ So these are in order to be activated

NOTE Confidence: 0.656873219076923

 $00:18:07.218 \longrightarrow 00:18:08.920$ by antigen presenting cells,

NOTE Confidence: 0.656873219076923

 $00:18:08.920 \longrightarrow 00:18:11.250$ they need to recognize antigen,

NOTE Confidence: 0.656873219076923

 $00{:}18{:}11{.}250 \dashrightarrow 00{:}18{:}13{.}419$ and in the case of CD 4 positive T

- NOTE Confidence: 0.656873219076923
- $00:18:13.419 \rightarrow 00:18:15.576$ cells they express the diesel receptor
- NOTE Confidence: 0.656873219076923
- $00:18:15.576 \longrightarrow 00:18:18.230$ here and then dendritic cells.
- NOTE Confidence: 0.656873219076923
- $00:18:18.230 \longrightarrow 00:18:21.346$ Are they the main antigen presenting
- NOTE Confidence: 0.656873219076923
- $00:18:21.346 \rightarrow 00:18:24.310$ cells express MHC two and they
- NOTE Confidence: 0.656873219076923
- 00:18:24.401 --> 00:18:27.365 can capture antigen and induce T
- NOTE Confidence: 0.656873219076923
- $00{:}18{:}27.365 \dashrightarrow 00{:}18{:}29.987$ cell receptor signals and these
- NOTE Confidence: 0.656873219076923
- 00:18:29.987 --> 00:18:31.649 reporter mice mimic.
- NOTE Confidence: 0.656873219076923
- 00:18:31.650 --> 00:18:33.186 They're basically reporters
- NOTE Confidence: 0.656873219076923
- $00{:}18{:}33{.}186 \dashrightarrow 00{:}18{:}35{.}234$ of diesel receptor engagement.
- NOTE Confidence: 0.656873219076923
- $00:18:35.240 \longrightarrow 00:18:38.552$ So the green are the cells are because
- NOTE Confidence: 0.656873219076923
- $00{:}18{:}38{.}552 \dashrightarrow 00{:}18{:}41{.}498$ they express N 77 which is downstream.
- NOTE Confidence: 0.656873219076923
- $00{:}18{:}41.500 \dashrightarrow 00{:}18{:}44.758$ The diesel receptor bound to GFP.
- NOTE Confidence: 0.656873219076923
- $00{:}18{:}44.760 \dashrightarrow 00{:}18{:}46.596$ So the greener the cells are.
- NOTE Confidence: 0.656873219076923
- $00{:}18{:}46{.}600 \dashrightarrow 00{:}18{:}48{.}128$ That's telling you that
- NOTE Confidence: 0.656873219076923
- $00{:}18{:}48{.}128 \dashrightarrow 00{:}18{:}49{.}274$ they're recognizing antigen.
- NOTE Confidence: 0.656873219076923

 $00:18:49.280 \longrightarrow 00:18:52.570$ This expression is also transient,

NOTE Confidence: 0.656873219076923

 $00{:}18{:}52{.}570 \dashrightarrow 00{:}18{:}55{.}696$ so if we see green cells,

NOTE Confidence: 0.656873219076923

 $00:18:55.700 \longrightarrow 00:18:57.842$ it means that at the time where

NOTE Confidence: 0.656873219076923

 $00:18:57.842 \rightarrow 00:18:59.160$ we're harvesting those cells,

NOTE Confidence: 0.656873219076923

 $00{:}18{:}59{.}160 \dashrightarrow 00{:}19{:}00{.}381$ they're recognizing antigen.

NOTE Confidence: 0.656873219076923

 $00{:}19{:}00{.}381 \dashrightarrow 00{:}19{:}03{.}230$ But it might be that they recognize

NOTE Confidence: 0.656873219076923

 $00:19:03.299 \rightarrow 00:19:05.909$ antigen and then they're not recognizing.

NOTE Confidence: 0.656873219076923

 $00:19:05.910 \longrightarrow 00:19:08.196$ Antigen at that point and then

NOTE Confidence: 0.656873219076923

 $00:19:08.196 \longrightarrow 00:19:09.339$ they lose expression.

NOTE Confidence: 0.656873219076923

 $00:19:09.340 \longrightarrow 00:19:10.796$ So in order to look at this,

NOTE Confidence: 0.656873219076923

 $00:19:10.800 \longrightarrow 00:19:12.876$ we basically did the time course

NOTE Confidence: 0.656873219076923

 $00:19:12.876 \longrightarrow 00:19:14.540$ of tag again early on,

NOTE Confidence: 0.656873219076923

 $00{:}19{:}14.540 \dashrightarrow 00{:}19{:}17.558$ where is compensatory changes and then

NOTE Confidence: 0.656873219076923

00:19:17.558 --> 00:19:20.780 once is systolic dysfunction is established,

NOTE Confidence: 0.656873219076923

 $00:19:20.780 \longrightarrow 00:19:22.516$ and then we kept them for longer.

NOTE Confidence: 0.656873219076923

 $00:19:22.520 \rightarrow 00:19:26.444$ That will mimic more chronic heart

- NOTE Confidence: 0.656873219076923
- $00{:}19{:}26{.}444 \dashrightarrow 00{:}19{:}29{.}417$ failure and what we did is we harvested
- NOTE Confidence: 0.656873219076923
- $00{:}19{:}29{.}417 \dashrightarrow 00{:}19{:}32{.}220$ the hearts and the medicinal influence.
- NOTE Confidence: 0.656873219076923
- $00:19:32.220 \longrightarrow 00:19:34.804$ And the first thing that we did here.
- NOTE Confidence: 0.656873219076923
- $00:19:34.810 \longrightarrow 00:19:37.246$ And we found that was very,
- NOTE Confidence: 0.656873219076923
- $00{:}19{:}37{.}250 \dashrightarrow 00{:}19{:}38{.}134$ very surprised,
- NOTE Confidence: 0.656873219076923
- 00:19:38.134 --> 00:19:38.576 surprising,
- NOTE Confidence: 0.656873219076923
- $00:19:38.576 \rightarrow 00:19:40.786$ and the most interesting finding.
- NOTE Confidence: 0.656873219076923
- 00:19:40.790 --> 00:19:43.580 I I I felt from from this story that we
- NOTE Confidence: 0.84957412
- $00{:}19{:}43.656 \dashrightarrow 00{:}19{:}46.218$ recently published was that we saw
- NOTE Confidence: 0.84957412
- $00:19:46.218 \longrightarrow 00:19:48.102$ this T cell receptor engagement not
- NOTE Confidence: 0.84957412
- $00{:}19{:}48.102 \dashrightarrow 00{:}19{:}50.308$ only in the cardiac lymph nodes,
- NOTE Confidence: 0.84957412
- $00{:}19{:}50{.}310 \dashrightarrow 00{:}19{:}52{.}830$ but also within the heart.
- NOTE Confidence: 0.84957412
- 00:19:52.830 --> 00:19:54.450 And as you can see here,
- NOTE Confidence: 0.84957412
- 00:19:54.450 -> 00:19:57.054 you said the very bright GFP
- NOTE Confidence: 0.84957412
- $00{:}19{:}57.054 \dashrightarrow 00{:}19{:}58.696$ cells that increase overtime.
- NOTE Confidence: 0.84957412

 $00:19:58.696 \rightarrow 00:20:01.108$ So that's telling us that once

NOTE Confidence: 0.84957412

00:20:01.108 --> 00:20:03.590 the T cells infiltrate the heart,

NOTE Confidence: 0.84957412

 $00:20:03.590 \longrightarrow 00:20:05.640$ they must be vendrick cells.

NOTE Confidence: 0.84957412

 $00{:}20{:}05{.}640 \dashrightarrow 00{:}20{:}07{.}605$ And potentially other cells that

NOTE Confidence: 0.84957412

 $00{:}20{:}07{.}605 \dashrightarrow 00{:}20{:}09{.}570$ capture the antigen and induce

NOTE Confidence: 0.84957412

 $00{:}20{:}09{.}636$ --> $00{:}20{:}11{.}541$ decent expansion within the heart NOTE Confidence: 0.84957412

00:20:11.541 --> 00:20:14.182 and that would be by passing the the

NOTE Confidence: 0.84957412

 $00{:}20{:}14.182 \dashrightarrow 00{:}20{:}16.204$ final trafficking that you need from

NOTE Confidence: 0.84957412

 $00{:}20{:}16.204 \dashrightarrow 00{:}20{:}19.460$ the lymph node into into the heart.

NOTE Confidence: 0.84957412

 $00{:}20{:}19{.}460 \dashrightarrow 00{:}20{:}21{.}917$ So we quantify this and as you can see,

NOTE Confidence: 0.84957412

 $00{:}20{:}21{.}920 \dashrightarrow 00{:}20{:}24{.}975$ there's a significant increase of

NOTE Confidence: 0.84957412

 $00{:}20{:}24.975 \dashrightarrow 00{:}20{:}27.892$ GFP positive active T cells in

NOTE Confidence: 0.84957412

 $00{:}20{:}27{.}892 \dashrightarrow 00{:}20{:}30{.}144$ the heart that correlates with

NOTE Confidence: 0.84957412

 $00:20:30.144 \longrightarrow 00:20:32.016$ decline in systolic function.

NOTE Confidence: 0.84957412

 $00{:}20{:}32.020 \dashrightarrow 00{:}20{:}35.120$ Measure here with fractions.

NOTE Confidence: 0.84957412

 $00:20:35.120 \longrightarrow 00:20:38.198$ So if we go back to how this teaser

 $00:20:38.198 \rightarrow 00:20:40.906$ activation happened in the timers,

NOTE Confidence: 0.84957412

 $00:20:40.906 \longrightarrow 00:20:45.328$ we have a lot of high T cell

NOTE Confidence: 0.84957412

00:20:45.328 --> 00:20:48.110 receptor clonal diversity because our

NOTE Confidence: 0.84957412

 $00{:}20{:}48.110 \dashrightarrow 00{:}20{:}51.740$ diesels are deciding what you know,

NOTE Confidence: 0.84957412

00:20:51.740 --> 00:20:54.030 depleting what's against self antigens

NOTE Confidence: 0.84957412

 $00{:}20{:}54.030 \dashrightarrow 00{:}20{:}56.744$ and selecting for what we might

NOTE Confidence: 0.84957412

 $00{:}20{:}56{.}744 \dashrightarrow 00{:}20{:}59{.}040$ need in the future if we get closer

NOTE Confidence: 0.84957412

 $00{:}20{:}59{.}040 \dashrightarrow 00{:}21{:}00{.}996$ to the high in the Middle East and

NOTE Confidence: 0.84957412

00:21:00.996 --> 00:21:02.802 lymph node we will have the selected

NOTE Confidence: 0.84957412

 $00{:}21{:}02{.}802 \dashrightarrow 00{:}21{:}05{.}200$ a pool of clones that will get expanded.

NOTE Confidence: 0.84957412

 $00{:}21{:}05{.}200 \dashrightarrow 00{:}21{:}07{.}360$ If there is any immune response

NOTE Confidence: 0.84957412

 $00{:}21{:}07{.}360 \dashrightarrow 00{:}21{:}08{.}872$ and then the question was what

NOTE Confidence: 0.84957412

 $00{:}21{:}08.872 \dashrightarrow 00{:}21{:}10.459$ we were seeing in the heart,

NOTE Confidence: 0.84957412

 $00{:}21{:}10.460 \dashrightarrow 00{:}21{:}12.782$ so our data using these reporter

NOTE Confidence: 0.84957412

 $00{:}21{:}12.782 \dashrightarrow 00{:}21{:}15.192$ found that indicated that there was

00:21:15.192 --> 00:21:17.556 this expansion in the correct running

NOTE Confidence: 0.84957412

 $00:21:17.556 \rightarrow 00:21:20.018$ lymph nodes as well as in the heart,

NOTE Confidence: 0.84957412

 $00:21:20.020 \longrightarrow 00:21:22.029$ and then we decided to do this

NOTE Confidence: 0.84957412

00:21:22.029 --> 00:21:23.681 receptor sequencing to get a closer

NOTE Confidence: 0.84957412

00:21:23.681 --> 00:21:25.389 look at whether these T cells or

NOTE Confidence: 0.84957412

 $00{:}21{:}25{.}444 \dashrightarrow 00{:}21{:}27{.}179$ whether it might be recognizing.

NOTE Confidence: 0.84957412

 $00:21:27.180 \longrightarrow 00:21:28.664$ So this is the structure of the

NOTE Confidence: 0.84957412

 $00:21:28.664 \rightarrow 00:21:29.300$ T cell receptor.

NOTE Confidence: 0.84957412

00:21:29.300 --> 00:21:30.580 Many of you probably know,

NOTE Confidence: 0.84957412

 $00:21:30.580 \longrightarrow 00:21:32.416$ but just as a brief reminder

NOTE Confidence: 0.84957412

00:21:32.416 --> 00:21:33.640 it has two Chainz,

NOTE Confidence: 0.84957412

 $00:21:33.640 \longrightarrow 00:21:35.620$ the alpha and the beta chain.

NOTE Confidence: 0.84957412

00:21:35.620 - 00:21:37.918 And then they recombine in many

NOTE Confidence: 0.84957412

 $00{:}21{:}37{.}918 \dashrightarrow 00{:}21{:}40{.}520$ different ways to form a specificity.

NOTE Confidence: 0.84957412

 $00{:}21{:}40{.}520 \dashrightarrow 00{:}21{:}43{.}334$ Or these pocket to many different antigens.

NOTE Confidence: 0.84957412

 $00:21:43.340 \rightarrow 00:21:46.840$ So by sequencing this Cdr three region,
- NOTE Confidence: 0.84957412
- $00:21:46.840 \longrightarrow 00:21:50.306$ which is where these two chains
- NOTE Confidence: 0.84957412
- 00:21:50.306 --> 00:21:52.982 get closer and form the pocket
- NOTE Confidence: 0.84957412
- 00:21:52.982 --> 00:21:54.320 for antigen recognition,
- NOTE Confidence: 0.84957412
- $00{:}21{:}54{.}320 \dashrightarrow 00{:}21{:}56{.}368$ we could get a sense of whether we
- NOTE Confidence: 0.84957412
- 00:21:56.368 --> 00:21:58.547 get in many different clones which
- NOTE Confidence: 0.84957412
- $00{:}21{:}58{.}547 \dashrightarrow 00{:}22{:}00{.}947$ will indicate high clonality and not
- NOTE Confidence: 0.84957412
- 00:22:01.013 --> 00:22:03.138 not really an antigen specificity.
- NOTE Confidence: 0.84957412
- $00:22:03.140 \rightarrow 00:22:05.036$ There was anything in the heart,
- NOTE Confidence: 0.84957412
- $00:22:05.040 \longrightarrow 00:22:07.744$ or whether we get.
- NOTE Confidence: 0.84957412
- $00{:}22{:}07.744 \dashrightarrow 00{:}22{:}09.608$ Enrichment so the results that
- NOTE Confidence: 0.84957412
- $00:22:09.608 \longrightarrow 00:22:11.093$ we found was as expected.
- NOTE Confidence: 0.84957412
- $00{:}22{:}11.100 \dashrightarrow 00{:}22{:}12.996$ There was a lot of clones,
- NOTE Confidence: 0.84957412
- $00{:}22{:}13.000 \dashrightarrow 00{:}22{:}15.260$ many different diesel receptors
- NOTE Confidence: 0.84957412
- $00{:}22{:}15{.}260 \dashrightarrow 00{:}22{:}17{.}520$ sequences in the timelines.
- NOTE Confidence: 0.84957412
- $00{:}22{:}17.520 \dashrightarrow 00{:}22{:}19.781$ These are the inguinal lymph nodes and
- NOTE Confidence: 0.84957412

 $00:22:19.781 \longrightarrow 00:22:22.054$ again we have a high clonal diversity

NOTE Confidence: 0.84957412

 $00:22:22.054 \longrightarrow 00:22:24.293$ and what we found was that the

NOTE Confidence: 0.84957412

 $00:22:24.293 \rightarrow 00:22:26.773$ closer that we were getting to the heart.

NOTE Confidence: 0.84957412

 $00{:}22{:}26.780 \dashrightarrow 00{:}22{:}29.215$ There more the decreased number

NOTE Confidence: 0.84957412

 $00:22:29.215 \longrightarrow 00:22:32.260$ of total clothes that we found,

NOTE Confidence: 0.84957412

 $00{:}22{:}32{.}260 \dashrightarrow 00{:}22{:}34.816$ and the highest enrichment of the NOTE Confidence: 0.84957412

00:22:34.816 --> 00:22:37.120 top 20 most represented groups.

NOTE Confidence: 0.84957412

00:22:37.120 --> 00:22:40.150 So today's my zaveri complicated

NOTE Confidence: 0.84957412

 $00{:}22{:}40{.}150 \dashrightarrow 00{:}22{:}42{.}824$ analysis and we found that there was NOTE Confidence: 0.84957412

 $00{:}22{:}42{.}824 \dashrightarrow 00{:}22{:}45{.}058$ a restricted clonal pool in the heart

NOTE Confidence: 0.84957412

 $00{:}22{:}45.060 \dashrightarrow 00{:}22{:}47.076$ and that the majority of the cells

NOTE Confidence: 0.84957412

 $00{:}22{:}47.076 \dashrightarrow 00{:}22{:}48.740$ were represented by top 20 clones.

NOTE Confidence: 0.84957412

 $00{:}22{:}48.740 \dashrightarrow 00{:}22{:}51.368$ So we started diving more into

NOTE Confidence: 0.84957412

 $00:22:51.368 \longrightarrow 00:22:53.120$ what this could be.

NOTE Confidence: 0.84957412

 $00{:}22{:}53{.}120 \dashrightarrow 00{:}22{:}54{.}610$ So what are these enrich

NOTE Confidence: 0.84957412

 $00:22:54.610 \longrightarrow 00:22:56.100$ clones responded to in the

 $00:22:56.161 \longrightarrow 00:22:58.497$ hunt and this will be the working month.

NOTE Confidence: 0.69570619444444

 $00:22:58.500 \rightarrow 00:23:01.113$ We know that this is happening and

NOTE Confidence: 0.69570619444444

 $00{:}23{:}01{.}113 \dashrightarrow 00{:}23{:}03{.}864$ then we know that there's this close

NOTE Confidence: 0.69570619444444

 $00:23:03.864 \rightarrow 00:23:06.439$ being expanded and what could those be?

NOTE Confidence: 0.69570619444444

 $00:23:06.440 \rightarrow 00:23:10.130$ So we ended up focusing on Russ and then

NOTE Confidence: 0.69570619444444

 $00:23:10.130 \rightarrow 00:23:13.399$ again because of the time limitation.

NOTE Confidence: 0.69570619444444

00:23:13.400 --> 00:23:14.448 I'm not going through

NOTE Confidence: 0.69570619444444

 $00:23:14.448 \rightarrow 00:23:15.758$ everything that we went through,

NOTE Confidence: 0.69570619444444

 $00:23:15.760 \rightarrow 00:23:17.956$ but it basically one hypothesis was

NOTE Confidence: 0.69570619444444

 $00:23:17.956 \rightarrow 00:23:20.372$ that you could have a cardiomyocyte

NOTE Confidence: 0.69570619444444

 $00:23:20.372 \rightarrow 00:23:23.018$ proteins right that the myocytes die,

NOTE Confidence: 0.69570619444444

 $00{:}23{:}23{.}020 \dashrightarrow 00{:}23{:}25{.}900$ and then the fragments are picked

NOTE Confidence: 0.69570619444444

 $00{:}23{:}25{.}900 \dashrightarrow 00{:}23{:}28{.}500$ up by adding percentage selves.

NOTE Confidence: 0.69570619444444

 $00{:}23{:}28{.}500 \dashrightarrow 00{:}23{:}30{.}428$ But it turns out that in the attack

NOTE Confidence: 0.69570619444444

 $00:23:30.428 \rightarrow 00:23:32.408$ model and like in response to my

 $00{:}23{:}32{.}408 \dashrightarrow 00{:}23{:}34{.}337$ kardelen function where you see a lot

NOTE Confidence: 0.69570619444444

 $00:23:34.337 \rightarrow 00:23:36.636$ of cell damage in the attack model.

NOTE Confidence: 0.69570619444444

00:23:36.636 --> 00:23:39.038 We don't see significant salvage early

NOTE Confidence: 0.69570619444444

 $00:23:39.038 \rightarrow 00:23:41.662$ on and even later on at four weeks.

NOTE Confidence: 0.69570619444444

00:23:41.670 --> 00:23:46.242 But what we do see is high increases of

NOTE Confidence: 0.69570619444444

00:23:46.242 --> 00:23:48.954 intramyocardial reactive oxygen oxygen NOTE Confidence: 0.69570619444444

 $00:23:48.954 \rightarrow 00:23:52.820$ species which are labeled here in green.

NOTE Confidence: 0.69570619444444

 $00:23:52.820 \rightarrow 00:23:55.908$ So we went back to literature and we

NOTE Confidence: 0.69570619444444

 $00{:}23{:}55{.}908 \dashrightarrow 00{:}23{:}58{.}446$ hypothesized that maybe Rose could modify

NOTE Confidence: 0.69570619444444

 $00{:}23{:}58{.}446 \dashrightarrow 00{:}24{:}00{.}978$ correct proteins that then form new

NOTE Confidence: 0.69570619444444

 $00{:}24{:}01{.}053 \dashrightarrow 00{:}24{:}04{.}056$ antigens that are listed AT cell response.

NOTE Confidence: 0.69570619444444

 $00:24:04.060 \rightarrow 00:24:05.002$ Why do we?

NOTE Confidence: 0.69570619444444

 $00:24:05.002 \longrightarrow 00:24:06.886$ Why would do we think that

NOTE Confidence: 0.69570619444444

 $00:24:06.886 \rightarrow 00:24:08.519$ there was a hypothesis?

NOTE Confidence: 0.69570619444444

 $00{:}24{:}08{.}520 \dashrightarrow 00{:}24{:}10{.}510$ It was because similar mechanisms

NOTE Confidence: 0.69570619444444

 $00{:}24{:}10{.}510 \dashrightarrow 00{:}24{:}13{.}058$ had been described in the vasculature

- NOTE Confidence: 0.69570619444444
- $00:24:13.058 \rightarrow 00:24:15.478$ in the context of hypertension,
- NOTE Confidence: 0.69570619444444
- $00:24:15.480 \rightarrow 00:24:19.052$ where there was this formation of ice level.
- NOTE Confidence: 0.69570619444444
- 00:24:19.052 --> 00:24:19.864 Glenda Lynn's,
- NOTE Confidence: 0.69570619444444
- $00:24:19.864 \rightarrow 00:24:23.604$ which are highly reactive intermediates by.
- NOTE Confidence: 0.69570619444444
- 00:24:23.604 --> 00:24:25.066 Lipid peroxidation.
- NOTE Confidence: 0.69570619444444
- $00{:}24{:}25{.}070 \dashrightarrow 00{:}24{:}27{.}492$ That then can adapt to self proteins
- NOTE Confidence: 0.69570619444444
- $00:24:27.492 \longrightarrow 00:24:29.450$ and create these new antigens.
- NOTE Confidence: 0.69570619444444
- $00:24:29.450 \rightarrow 00:24:32.320$ So we contacted the people who had
- NOTE Confidence: 0.69570619444444
- $00{:}24{:}32{.}320 \dashrightarrow 00{:}24{:}35{.}802$ done the scientists that had done this
- NOTE Confidence: 0.69570619444444
- 00:24:35.802 --> 00:24:37.970 very interesting research hypertension
- NOTE Confidence: 0.69570619444444
- 00:24:37.970 --> 00:24:40.210 David Harrison and Annette Kirabo,
- NOTE Confidence: 0.69570619444444
- $00{:}24{:}40{.}210 \dashrightarrow 00{:}24{:}42{.}260$ and this started a beautiful
- NOTE Confidence: 0.69570619444444
- $00:24:42.260 \rightarrow 00:24:44.772$ collaboration in which we were able
- NOTE Confidence: 0.69570619444444
- $00:24:44.772 \rightarrow 00:24:48.109$ to test this hypothesis in the heart.
- NOTE Confidence: 0.69570619444444
- $00:24:48.110 \longrightarrow 00:24:49.802$ So basically we obtain a lot
- NOTE Confidence: 0.69570619444444

00:24:49.802 --> 00:24:51.270 of reagents from their labs,

NOTE Confidence: 0.69570619444444

 $00:24:51.270 \longrightarrow 00:24:52.971$ and the first thing that we wanted

NOTE Confidence: 0.69570619444444

00:24:52.971 - > 00:24:54.662 to know is whether this matter

NOTE Confidence: 0.69570619444444

 $00:24:54.662 \rightarrow 00:24:55.866$ in the human heart.

NOTE Confidence: 0.69570619444444

 $00{:}24{:}55{.}870 \dashrightarrow 00{:}24{:}58{.}966$ So we went back or human heart failure

NOTE Confidence: 0.69570619444444

 $00:24:58.966 \rightarrow 00:25:02.101$ sections and we use this one day 11 which NOTE Confidence: 0.69570619444444

 $00:25:02.101 \longrightarrow 00:25:04.762$ is an antibody that recognizes proteins.

NOTE Confidence: 0.69570619444444

 $00:25:04.762 \longrightarrow 00:25:07.534$ Modified biologist was given to us

NOTE Confidence: 0.69570619444444

 $00{:}25{:}07{.}534 \dashrightarrow 00{:}25{:}10{.}621$ by David and Annette and as you

NOTE Confidence: 0.69570619444444

 $00{:}25{:}10.621 \dashrightarrow 00{:}25{:}13.051$ can see here we saw significant

NOTE Confidence: 0.69570619444444

 $00:25:13.135 \rightarrow 00:25:15.607$ recognition in three different

NOTE Confidence: 0.69570619444444

 $00{:}25{:}15.607 \dashrightarrow 00{:}25{:}18.079$ heart failure patient samples.

NOTE Confidence: 0.69570619444444

 $00:25:18.080 \longrightarrow 00:25:20.522$ And no signals in a non

NOTE Confidence: 0.69570619444444

 $00:25:20.522 \longrightarrow 00:25:21.743$ heart failure patient.

NOTE Confidence: 0.69570619444444

 $00:25:21.750 \longrightarrow 00:25:24.315$ We went back to the marsh model and in

NOTE Confidence: 0.69570619444444

 $00{:}25{:}24.315 \dashrightarrow 00{:}25{:}26.909$ the marsh model we went back to these

 $00:25:26.910 \rightarrow 00:25:30.599$ reporter my cells and T cell recognition.

NOTE Confidence: 0.69570619444444

00:25:30.600 --> 00:25:35.208 And we used the D1DD11 antibody

NOTE Confidence: 0.69570619444444

 $00:25:35.208 \longrightarrow 00:25:36.750$ that recognizes proteins

NOTE Confidence: 0.69570619444444

 $00:25:36.750 \longrightarrow 00:25:39.320$ modified by strategies in mouse.

NOTE Confidence: 0.69570619444444

 $00:25:39.320 \longrightarrow 00:25:41.976$ This was a different version of the antibody.

NOTE Confidence: 0.69570619444444

 $00:25:41.980 \rightarrow 00:25:44.604$ And then they also send us some ISO

NOTE Confidence: 0.69570619444444

 $00{:}25{:}44.610 \dashrightarrow 00{:}25{:}49.594$ so they can generate and I soils LG

NOTE Confidence: 0.69570619444444

 $00:25:49.594 \rightarrow 00:25:54.019$ scavengers that could be used in in mice.

NOTE Confidence: 0.69570619444444

 $00:25:54.020 \rightarrow 00:25:57.098$ So how does it work with experiments in tack?

NOTE Confidence: 0.69570619444444

 $00:25:57.100 \longrightarrow 00:25:58.636$ And then this is the structure

NOTE Confidence: 0.69570619444444

 $00:25:58.636 \rightarrow 00:26:00.180$ of the eye surgeons calendar,

NOTE Confidence: 0.69570619444444

 $00{:}26{:}00{.}180 \dashrightarrow 00{:}26{:}01{.}896$ and this is the control peptide.

NOTE Confidence: 0.69570619444444

 $00{:}26{:}01{.}900 \dashrightarrow 00{:}26{:}03{.}867$ So the two Joba that I'll be

NOTE Confidence: 0.69570619444444

 $00{:}26{:}03.867 \dashrightarrow 00{:}26{:}05.689$ showing is one with coverage.

NOTE Confidence: 0.69570619444444

 $00{:}26{:}05{.}690 \dashrightarrow 00{:}26{:}09{.}176$ Those rose reactive proteins and then

00:26:09.176 --> 00:26:12.659 we tracked this activation and T

NOTE Confidence: 0.69570619444444

 $00:26:12.659 \rightarrow 00:26:15.319$ cell receptor engagement over time.

NOTE Confidence: 0.69570619444444

 $00{:}26{:}15{.}320$ --> $00{:}26{:}18{.}032$ In some experiments we use tempo

NOTE Confidence: 0.69570619444444

00:26:18.032 --> 00:26:19.840 because it's an antioxidant,

NOTE Confidence: 0.69570619444444

 $00:26:19.840 \longrightarrow 00:26:23.608$ so it works upstream of the of the.

NOTE Confidence: 0.621444686363636

 $00{:}26{:}23.610 \dashrightarrow 00{:}26{:}27.341$ Draws formation so just to make it

NOTE Confidence: 0.621444686363636

 $00{:}26{:}27{.}341 \dashrightarrow 00{:}26{:}31{.}046$ simpler in for understanding the idea,

NOTE Confidence: 0.621444686363636

 $00:26:31.046 \rightarrow 00:26:33.350$ this is a question that we were trying

NOTE Confidence: 0.621444686363636

 $00{:}26{:}33{.}410 \dashrightarrow 00{:}26{:}35{.}678$ to ask and the idea is that in response

NOTE Confidence: 0.621444686363636

 $00{:}26{:}35{.}678 \dashrightarrow 00{:}26{:}38{.}454$ to diagnose Ross and then this Ross

NOTE Confidence: 0.621444686363636

 $00{:}26{:}38{.}454 \dashrightarrow 00{:}26{:}40{.}980$ induces the formation of this lipid

NOTE Confidence: 0.621444686363636

00:26:41.061 --> 00:26:43.556 peroxidation and this ISO, geez,

NOTE Confidence: 0.621444686363636

 $00:26:43.556 \rightarrow 00:26:47.284$ that then they adapt to a cardiac protein.

NOTE Confidence: 0.621444686363636

 $00{:}26{:}47{.}290 \dashrightarrow 00{:}26{:}49{.}498$ I'm from Disneyland pigeons that could

NOTE Confidence: 0.621444686363636

 $00{:}26{:}49{.}498 \dashrightarrow 00{:}26{:}52{.}347$ be taken by the dreaded cells and

NOTE Confidence: 0.621444686363636

 $00:26:52.347 \rightarrow 00:26:54.849$ being presented these cells to induce

- NOTE Confidence: 0.621444686363636
- $00{:}26{:}54{.}849 \dashrightarrow 00{:}26{:}57{.}450$ T cell activation and proliferation.
- NOTE Confidence: 0.621444686363636
- $00:26:57.450 \longrightarrow 00:27:00.130$ So we could block these with temple perhaps.
- NOTE Confidence: 0.621444686363636
- 00:27:00.130 00:27:02.738 And if we block this, if this was true,
- NOTE Confidence: 0.621444686363636
- $00:27:02.738 \longrightarrow 00:27:04.730$ maybe we would see less this
- NOTE Confidence: 0.621444686363636
- $00:27:04.806 \rightarrow 00:27:07.476$ activation or proliferation in heart.
- NOTE Confidence: 0.621444686363636
- $00{:}27{:}07{.}480 \dashrightarrow 00{:}27{:}09{.}804$ And if you block this with the
- NOTE Confidence: 0.621444686363636
- 00:27:09.804 --> 00:27:11.620 ISO G specific scavenger,
- NOTE Confidence: 0.621444686363636
- $00:27:11.620 \longrightarrow 00:27:13.462$ we could potentially block this and
- NOTE Confidence: 0.621444686363636
- $00:27:13.462 \longrightarrow 00:27:15.259$ block this activation in the heart,
- NOTE Confidence: 0.621444686363636
- $00:27:15.260 \rightarrow 00:27:17.460$ and then of course the final question was,
- NOTE Confidence: 0.621444686363636
- $00:27:17.460 \rightarrow 00:27:22.304$ will this have any impact incorrect function?
- NOTE Confidence: 0.621444686363636
- $00{:}27{:}22{.}310 \dashrightarrow 00{:}27{:}24{.}443$ So the first thing that we did is we
- NOTE Confidence: 0.621444686363636
- $00{:}27{:}24{.}443 \dashrightarrow 00{:}27{:}26{.}702$ did those experiments in mice and then
- NOTE Confidence: 0.621444686363636
- $00{:}27{:}26.702 \dashrightarrow 00{:}27{:}29.294$ we isolated and Rick cells from mice
- NOTE Confidence: 0.621444686363636
- $00:27:29.294 \rightarrow 00:27:32.066$ treated with these AI soldiers scavengers.
- NOTE Confidence: 0.621444686363636

 $00:27:32.070 \longrightarrow 00:27:33.666$ And as you can see here,

NOTE Confidence: 0.621444686363636

 $00{:}27{:}33.670 \dashrightarrow 00{:}27{:}36.226$ this is the antibody that detects

NOTE Confidence: 0.621444686363636

 $00:27:36.226 \longrightarrow 00:27:37.930$ the isolated protein adducts.

NOTE Confidence: 0.621444686363636

 $00:27:37.930 \rightarrow 00:27:41.170$ And as you can see with the four coma,

NOTE Confidence: 0.621444686363636

 $00:27:41.170 \longrightarrow 00:27:44.122$ which is the control and the

NOTE Confidence: 0.621444686363636

 $00:27:44.122 \longrightarrow 00:27:45.106$ control compound,

NOTE Confidence: 0.621444686363636

 $00:27:45.110 \longrightarrow 00:27:47.174$ we see that in drink cells

NOTE Confidence: 0.621444686363636

 $00{:}27{:}47.174 \dashrightarrow 00{:}27{:}49.349$ express this and take a protein.

NOTE Confidence: 0.621444686363636

00:27:49.350 --> 00:27:50.894 But this is significantly

NOTE Confidence: 0.621444686363636

 $00:27:50.894 \rightarrow 00:27:52.438$ inhibited when we scavenged.

NOTE Confidence: 0.6690343025

 $00:27:54.550 \rightarrow 00:27:56.971$ And then when we look directly in the House

NOTE Confidence: 0.6690343025

 $00:27:56.971 \rightarrow 00:27:59.246$ looking for teachers using the reporter mice,

NOTE Confidence: 0.6690343025

 $00:27:59.250 \longrightarrow 00:28:02.266$ we found that only in those miles that

NOTE Confidence: 0.6690343025

 $00{:}28{:}02{.}266 \dashrightarrow 00{:}28{:}05{.}170$ were treated with the ice berg scavengers,

NOTE Confidence: 0.6690343025

 $00:28:05.170 \rightarrow 00:28:08.020$ we were able to significantly decrease

NOTE Confidence: 0.6690343025

 $00:28:08.020 \rightarrow 00:28:10.689$ this teaser activation within the heart.

- NOTE Confidence: 0.6690343025
- 00:28:10.690 --> 00:28:12.338 This is again GFP,
- NOTE Confidence: 0.6690343025
- $00:28:12.338 \longrightarrow 00:28:14.197$ because this underreported mines and
- NOTE Confidence: 0.6690343025
- $00{:}28{:}14.197 \dashrightarrow 00{:}28{:}15.646$ I don't think I mentioned it earlier,
- NOTE Confidence: 0.6690343025
- $00:28:15.650 \longrightarrow 00:28:17.834$ but this is this receptor beta
- NOTE Confidence: 0.6690343025
- $00:28:17.834 \rightarrow 00:28:20.444$ to make sure that we're focusing
- NOTE Confidence: 0.6690343025
- $00{:}28{:}20{.}444 \dashrightarrow 00{:}28{:}23{.}329$ on the right distal population.
- NOTE Confidence: 0.6690343025
- $00:28:23.330 \longrightarrow 00:28:25.210$ So then how can OK?
- NOTE Confidence: 0.6690343025
- 00:28:25.210 --> 00:28:27.890 So now we know that under excels pick it up,
- NOTE Confidence: 0.6690343025
- $00:28:27.890 \longrightarrow 00:28:30.470$ but added functional inducing
- NOTE Confidence: 0.6690343025
- $00:28:30.470 \longrightarrow 00:28:31.760$ diesel proliferation.
- NOTE Confidence: 0.6690343025
- $00:28:31.760 \longrightarrow 00:28:34.590$ Here we found that there's
- NOTE Confidence: 0.6690343025
- 00:28:34.590 --> 00:28:36.288 less this activation,
- NOTE Confidence: 0.6690343025
- $00{:}28{:}36{.}290 \dashrightarrow 00{:}28{:}38{.}174$ so the hypothesis is that when
- NOTE Confidence: 0.6690343025
- $00{:}28{:}38{.}174 \dashrightarrow 00{:}28{:}39{.}430$ these are become activated,
- NOTE Confidence: 0.6690343025
- $00:28:39.430 \longrightarrow 00:28:42.250$ then they have to proliferate.
- NOTE Confidence: 0.6690343025

 $00:28:42.250 \rightarrow 00:28:45.008$ So we tested this hypothesis ex vivo

NOTE Confidence: 0.6690343025

 $00{:}28{:}45.008 \dashrightarrow 00{:}28{:}48.108$ and we took the genetic cells from

NOTE Confidence: 0.6690343025

 $00{:}28{:}48{.}108 \dashrightarrow 00{:}28{:}51{.}337$ control mice and loaded them with either NOTE Confidence: 0.6690343025

 $00:28:51.337 \rightarrow 00:28:54.417$ ice or GS or with a correct license

NOTE Confidence: 0.6690343025

 $00:28:54.417 \longrightarrow 00:28:57.570$ that were taken from the tag mice.

NOTE Confidence: 0.6690343025

 $00{:}28{:}57{.}570$ --> $00{:}28{:}59{.}712$ And then we coculture this and Rick NOTE Confidence: 0.6690343025

 $00{:}28{:}59{.}712 \dashrightarrow 00{:}29{:}02{.}310$ cells that were incubated with these

NOTE Confidence: 0.6690343025

 $00{:}29{:}02{.}310 \dashrightarrow 00{:}29{:}04{.}155$ characteristics with teachers that

NOTE Confidence: 0.6690343025

00:29:04.155 --> 00:29:06.330 came from medicinal lymph nodes

NOTE Confidence: 0.6690343025

 $00:29:06.330 \longrightarrow 00:29:08.616$ from either sham or tag mouse.

NOTE Confidence: 0.6690343025

 $00:29:08.620 \rightarrow 00:29:10.816$ And again we were trying to

NOTE Confidence: 0.6690343025

00:29:10.816 --> 00:29:11.914 mimic these response.

NOTE Confidence: 0.6690343025

00:29:11.920 --> 00:29:13.990 And after four days we can

NOTE Confidence: 0.6690343025

 $00{:}29{:}13.990 \dashrightarrow 00{:}29{:}16.640$ look at T cell proliferation.

NOTE Confidence: 0.6690343025

 $00:29:16.640 \rightarrow 00:29:18.899$ So the way we look at T cell proliferation

NOTE Confidence: 0.6690343025

 $00{:}29{:}18.899 \dashrightarrow 00{:}29{:}20.863$ is because the teachers are labeled

- NOTE Confidence: 0.6690343025
- $00:29:20.863 \rightarrow 00:29:22.960$ with a membrane guide that is CFC.
- NOTE Confidence: 0.6690343025
- $00{:}29{:}22{.}960 \dashrightarrow 00{:}29{:}25{.}445$ And if they proliferate as you can
- NOTE Confidence: 0.6690343025
- $00{:}29{:}25{.}445 \dashrightarrow 00{:}29{:}28{.}964$ see here to see if you see a die is
- NOTE Confidence: 0.6690343025
- $00:29:28.964 \rightarrow 00:29:31.960$ diluted and this is just one example.
- NOTE Confidence: 0.6690343025
- $00:29:31.960 \rightarrow 00:29:36.739$ If we combine some T cells with sham lysates,
- NOTE Confidence: 0.6690343025
- $00:29:36.740 \longrightarrow 00:29:37.964$ there's no proliferation,
- NOTE Confidence: 0.6690343025
- $00{:}29{:}37{.}964 \dashrightarrow 00{:}29{:}40{.}820$ and if you put tactics so there's
- NOTE Confidence: 0.6690343025
- $00{:}29{:}40.898 \dashrightarrow 00{:}29{:}42.700$ significant proliferation.
- NOTE Confidence: 0.6690343025
- 00:29:42.700 --> 00:29:44.638 But basically what we found here,
- NOTE Confidence: 0.6690343025
- $00{:}29{:}44.640 \dashrightarrow 00{:}29{:}46.860$ this is only a representative experiment.
- NOTE Confidence: 0.6690343025
- $00{:}29{:}46.860 \dashrightarrow 00{:}29{:}49.650$ Everything is quantified in the manuscript.
- NOTE Confidence: 0.6690343025
- $00{:}29{:}49{.}650 \dashrightarrow 00{:}29{:}52{.}666$ But what we found was that only when
- NOTE Confidence: 0.6690343025
- $00{:}29{:}52.666 \dashrightarrow 00{:}29{:}55.519$ the teachers came from mice with
- NOTE Confidence: 0.6690343025
- $00{:}29{:}55{.}519 \dashrightarrow 00{:}29{:}58{.}146$ experimental heart failure and the
- NOTE Confidence: 0.6690343025
- $00:29:58.146 \rightarrow 00:30:01.464$ proteins that cells were loaded with
- NOTE Confidence: 0.6690343025

 $00{:}30{:}01{.}464 \dashrightarrow 00{:}30{:}04{.}299$ cardiac proteins that came from Tak

NOTE Confidence: 0.6690343025

 $00{:}30{:}04{.}300 \dashrightarrow 00{:}30{:}06{.}466$ only this combination is when we

NOTE Confidence: 0.6690343025

 $00:30:06.466 \rightarrow 00:30:09.759$ were able to see these new antigen

NOTE Confidence: 0.6690343025

 $00:30:09.759 \rightarrow 00:30:12.119$ presentation and decent proliferation.

NOTE Confidence: 0.6690343025

 $00:30:12.120 \longrightarrow 00:30:14.591$ So did this have any impact in

NOTE Confidence: 0.6690343025

 $00:30:14.591 \longrightarrow 00:30:15.297$ cardiac function?

NOTE Confidence: 0.6690343025

 $00{:}30{:}15{.}300 \dashrightarrow 00{:}30{:}17{.}375$ And these are echoes done

NOTE Confidence: 0.6690343025

 $00:30:17.375 \longrightarrow 00:30:18.620$ by our collaborators.

NOTE Confidence: 0.6690343025

 $00{:}30{:}18.620 \dashrightarrow 00{:}30{:}21.220$ That Medical Center Rob Landon,

NOTE Confidence: 0.6690343025

 $00:30:21.220 \rightarrow 00:30:24.244$ who is a cardiologist that whom I've

NOTE Confidence: 0.6690343025

 $00:30:24.244 \rightarrow 00:30:26.620$ I've been collaborating with for many,

NOTE Confidence: 0.6690343025

 $00:30:26.620 \longrightarrow 00:30:27.328$ many years,

NOTE Confidence: 0.6690343025

 $00:30:27.328 \longrightarrow 00:30:29.452$ and what we found is that

NOTE Confidence: 0.6690343025

 $00:30:29.452 \longrightarrow 00:30:30.800$ these attack animals.

NOTE Confidence: 0.6690343025

 $00:30:30.800 \dashrightarrow 00:30:33.910$ You can see the flat line here and

NOTE Confidence: 0.6690343025

 $00:30:33.910 \rightarrow 00:30:36.560$ decrease historic function that is,

- NOTE Confidence: 0.6690343025
- $00{:}30{:}36{.}560 \dashrightarrow 00{:}30{:}38{.}510$ is quantified here.
- NOTE Confidence: 0.6690343025
- $00{:}30{:}38{.}510 \dashrightarrow 00{:}30{:}40{.}168$ Fractional shortening and
- NOTE Confidence: 0.6690343025
- $00:30:40.168 \longrightarrow 00:30:42.316$ the harsh from the two hobas.
- NOTE Confidence: 0.6690343025
- $00:30:42.320 \longrightarrow 00:30:43.460$ For them I struggle with this.
- NOTE Confidence: 0.6690343025
- 00:30:43.460 00:30:46.185 Lavender it were very healthy
- NOTE Confidence: 0.6690343025
- $00{:}30{:}46.185 \dashrightarrow 00{:}30{:}48.910$ compared to to the control.
- NOTE Confidence: 0.760014902
- $00:30:51.220 \longrightarrow 00:30:52.960$ So to summarize this part,
- NOTE Confidence: 0.760014902
- $00:30:52.960 \longrightarrow 00:30:55.431$ what we found was that in response
- NOTE Confidence: 0.760014902
- $00:30:55.431 \longrightarrow 00:30:57.899$ to high level trickler pressure.
- NOTE Confidence: 0.760014902
- 00:30:57.900 --> 00:31:00.840 There was a significant induction of
- NOTE Confidence: 0.760014902
- $00{:}31{:}00{.}840 \dashrightarrow 00{:}31{:}03{.}260$ in tramyocardial rose in the heart
- NOTE Confidence: 0.760014902
- $00{:}31{:}03.260 \dashrightarrow 00{:}31{:}06.095$ and ended in Derrick cells that are
- NOTE Confidence: 0.760014902
- 00:31:06.095 --> 00:31:08.888 here are picking up some of the
- NOTE Confidence: 0.760014902
- $00{:}31{:}08{.}888 \dashrightarrow 00{:}31{:}11{.}132$ of the proteins that are modified
- NOTE Confidence: 0.760014902
- $00:31:11.213 \dashrightarrow 00:31:13.628$ by brass induced eye surgeries.
- NOTE Confidence: 0.760014902

 $00:31:13.630 \longrightarrow 00:31:15.010$ And then in the lymph node,

NOTE Confidence: 0.760014902

 $00{:}31{:}15{.}010 \dashrightarrow 00{:}31{:}17{.}590$ we saw that these T cells respond

NOTE Confidence: 0.760014902

 $00:31:17.590 \longrightarrow 00:31:19.750$ to antigen and expand and then

NOTE Confidence: 0.760014902

 $00:31:19.750 \longrightarrow 00:31:22.207$ they can go back to the heart.

NOTE Confidence: 0.760014902

 $00{:}31{:}22{.}210 \dashrightarrow 00{:}31{:}23{.}370$ And traffic to the heart.

NOTE Confidence: 0.760014902

00:31:23.370 --> 00:31:25.800 But perhaps what was more intriguing

NOTE Confidence: 0.760014902

 $00{:}31{:}25{.}800 \dashrightarrow 00{:}31{:}28{.}928$ to us was that once in the heart.

NOTE Confidence: 0.760014902

 $00:31:28.930 \longrightarrow 00:31:31.648$ You sometimes by pass this later on

NOTE Confidence: 0.760014902

00:31:31.648 --> 00:31:34.465 within the heart because they can

NOTE Confidence: 0.760014902

 $00{:}31{:}34.465 \dashrightarrow 00{:}31{:}36.890$ actually recognize antigens within the

NOTE Confidence: 0.760014902

00:31:36.890 - 00:31:39.673 heart and be expanded there under.

NOTE Confidence: 0.760014902

 $00:31:39.673 \dashrightarrow 00:31:41.525$ This has significant effects

NOTE Confidence: 0.760014902

 $00{:}31{:}41{.}525 \dashrightarrow 00{:}31{:}42{.}914$ on cardiac fibrosis.

NOTE Confidence: 0.753394304375

00:31:45.880 --> 00:31:48.856 And I I didn't show the kind of

NOTE Confidence: 0.753394304375

 $00:31:48.856 \rightarrow 00:31:50.612$ fibroglandular also had significantly

NOTE Confidence: 0.753394304375

 $00:31:50.612 \rightarrow 00:31:53.414$ decreased fibrosis and this is going

- NOTE Confidence: 0.753394304375
- $00:31:53.414 \rightarrow 00:31:56.278$ to become more relevant for the next
- NOTE Confidence: 0.753394304375
- $00{:}31{:}56{.}278 \dashrightarrow 00{:}31{:}58{.}822$ part of the talk where I will be
- NOTE Confidence: 0.753394304375
- $00{:}31{:}58{.}822 \dashrightarrow 00{:}32{:}01{.}180$ talking about this critical antigen
- NOTE Confidence: 0.753394304375
- $00:32:01.180 \longrightarrow 00:32:04.330$ recognition that happens in heart.
- NOTE Confidence: 0.753394304375
- $00:32:04.330 \longrightarrow 00:32:07.586$ So for the last part of the talk,
- NOTE Confidence: 0.753394304375
- $00{:}32{:}07{.}590 \dashrightarrow 00{:}32{:}11{.}798$ then we I will focus about these kids
- NOTE Confidence: 0.753394304375
- $00:32:11.798 \dashrightarrow 00:32:14.510$ are correct fibroblast crosstalk.
- NOTE Confidence: 0.753394304375
- $00:32:14.510 \rightarrow 00:32:16.750$ So as I showed in the first part of the talk,
- NOTE Confidence: 0.753394304375
- $00:32:16.750 \longrightarrow 00:32:18.590$ when the diesels Infiltrator hi,
- NOTE Confidence: 0.753394304375
- $00:32:18.590 \longrightarrow 00:32:20.966$ this is an image ex vivo.
- NOTE Confidence: 0.753394304375
- $00:32:20.970 \rightarrow 00:32:23.280$ So these are fiberglass and culture
- NOTE Confidence: 0.753394304375
- $00{:}32{:}23{.}280 \dashrightarrow 00{:}32{:}26{.}196$ with T cells and you can see the
- NOTE Confidence: 0.753394304375
- $00:32:26.196 \longrightarrow 00:32:28.577$ green cells are here and the blue
- NOTE Confidence: 0.753394304375
- $00{:}32{:}28{.}577 \dashrightarrow 00{:}32{:}30{.}665$ little nuclei of the diesels and
- NOTE Confidence: 0.753394304375
- $00:32:30.665 \rightarrow 00:32:33.406$ this is a large nuclei of fiberglass.
- NOTE Confidence: 0.753394304375

 $00:32:33.406 \longrightarrow 00:32:37.000$ So we had found that with the diesels,

NOTE Confidence: 0.753394304375

 $00{:}32{:}37{.}000 \dashrightarrow 00{:}32{:}39{.}226$ either DH one cells that were

NOTE Confidence: 0.753394304375

00:32:39.226 --> 00:32:41.580 generated extra evil or T cells

NOTE Confidence: 0.753394304375

 $00:32:41.580 \longrightarrow 00:32:43.580$ isolated directly from TAC mice.

NOTE Confidence: 0.753394304375

 $00:32:43.580 \longrightarrow 00:32:45.625$ They bound to the fiber glass

NOTE Confidence: 0.753394304375

00:32:45.625 --> 00:32:48.347 and once they bound they induce NOTE Confidence: 0.753394304375

 $00{:}32{:}48{.}347 \dashrightarrow 00{:}32{:}50{.}715$ the transformation to alphasim

NOTE Confidence: 0.753394304375

00:32:50.715 --> 00:32:53.083 8 producing correct fiberglass.

NOTE Confidence: 0.753394304375

 $00{:}32{:}53{.}090 \dashrightarrow 00{:}32{:}55{.}274$ And then in the second part of

NOTE Confidence: 0.753394304375

 $00{:}32{:}55{.}274 \dashrightarrow 00{:}32{:}57{.}589$ the talk I just recently showed you

NOTE Confidence: 0.753394304375

 $00{:}32{:}57{.}590 \dashrightarrow 00{:}32{:}59{.}390$ that I didn't present themselves

NOTE Confidence: 0.753394304375

 $00:32:59.390 \longrightarrow 00:33:00.830$ and particularly in lyrics.

NOTE Confidence: 0.753394304375

 $00:33:00.830 \dashrightarrow 00:33:03.620$ Elves present antigen to T cells

NOTE Confidence: 0.753394304375

 $00:33:03.620 \rightarrow 00:33:06.577$ and there is this intramyocardial

NOTE Confidence: 0.753394304375

 $00{:}33{:}06{.}577 \dashrightarrow 00{:}33{:}09{.}577$ diesel receptor engagement.

NOTE Confidence: 0.753394304375

 $00:33:09.580 \longrightarrow 00:33:10.960$ So then we we thought,

 $00:33:10.960 \longrightarrow 00:33:11.288$ well,

NOTE Confidence: 0.753394304375

 $00:33:11.288 \rightarrow 00:33:13.256$ they're not that many dendritic cells

NOTE Confidence: 0.753394304375

 $00:33:13.256 \rightarrow 00:33:15.890$ in the heart as compared to other cells,

NOTE Confidence: 0.753394304375

 $00:33:15.890 \rightarrow 00:33:16.361$ right?

NOTE Confidence: 0.753394304375

 $00:33:16.361 \rightarrow 00:33:20.129$ Is it possible that during this T cell,

NOTE Confidence: 0.753394304375

 $00{:}33{:}20{.}130 \dashrightarrow 00{:}33{:}23{.}245$ fiberglass crosstalk not only the T cells

NOTE Confidence: 0.753394304375

 $00:33:23.245 \rightarrow 00:33:26.847$ are telling the fiberglass to to induce TGF,

NOTE Confidence: 0.753394304375

 $00:33:26.850 \rightarrow 00:33:28.248$ beta and transform?

NOTE Confidence: 0.753394304375

 $00{:}33{:}28{.}248 \dashrightarrow 00{:}33{:}31{.}044$ But may be the fiberglass because diesels

NOTE Confidence: 0.753394304375

 $00:33:31.044 \rightarrow 00:33:33.986$ are firmly adhered to the fiberglass.

NOTE Confidence: 0.753394304375

 $00:33:33.990 \rightarrow 00:33:36.846$ Maybe the fiberglass may be functioning

NOTE Confidence: 0.753394304375

 $00{:}33{:}36{.}846 \dashrightarrow 00{:}33{:}39{.}454$ as also an antigen presenting

NOTE Confidence: 0.753394304375

 $00{:}33{:}39{.}454 \dashrightarrow 00{:}33{:}41{.}790$ cell that is semi professional.

NOTE Confidence: 0.753394304375

 $00:33:41.790 \longrightarrow 00:33:44.370$ So we went back to literature,

NOTE Confidence: 0.753394304375

 $00{:}33{:}44{.}370 \dashrightarrow 00{:}33{:}46{.}770$ and in this there's this growing

00:33:46.770 --> 00:33:48.370 field of struggle immunology,

NOTE Confidence: 0.753394304375

 $00{:}33{:}48{.}370 \dashrightarrow 00{:}33{:}50{.}635$ where the concept is that antigen

NOTE Confidence: 0.753394304375

 $00:33:50.635 \longrightarrow 00:33:52.560$ presentation is no longer an

NOTE Confidence: 0.753394304375

 $00:33:52.560 \rightarrow 00:33:54.610$ exclusive domain for the lyrics.

NOTE Confidence: 0.753394304375

 $00{:}33{:}54{.}610 \dashrightarrow 00{:}33{:}56{.}975$ Also obviously then Derek cells

NOTE Confidence: 0.753394304375

00:33:56.975 --> 00:33:59.826 are antigen professional antigen

NOTE Confidence: 0.753394304375

 $00:33:59.826 \rightarrow 00:34:01.410$ presenting cells,

NOTE Confidence: 0.753394304375

 $00:34:01.410 \longrightarrow 00:34:03.360$ but they're also evidence that

NOTE Confidence: 0.753394304375

 $00{:}34{:}03{.}360 \dashrightarrow 00{:}34{:}05{.}310$ a stronger cells that support

NOTE Confidence: 0.753394304375

 $00{:}34{:}05{.}375 \dashrightarrow 00{:}34{:}07{.}999$ tissue architecture can serve as

NOTE Confidence: 0.753394304375

 $00:34:07.999 \longrightarrow 00:34:09.388$ antigen presenting cells.

NOTE Confidence: 0.753394304375

 $00:34:09.390 \longrightarrow 00:34:11.178$ Depending on the context.

NOTE Confidence: 0.753394304375

00:34:11.178 --> 00:34:12.966 So this is an.

NOTE Confidence: 0.753394304375

 $00:34:12.970 \longrightarrow 00:34:15.010$ In an example of fibroblastic

NOTE Confidence: 0.753394304375

 $00:34:15.010 \dashrightarrow 00:34:17.540$ particular cells in the lymph nodes.

NOTE Confidence: 0.753394304375

 $00:34:17.540 \rightarrow 00:34:20.717$ Timing is stomach cells can do that as well.

- NOTE Confidence: 0.753394304375
- $00{:}34{:}20.720 \dashrightarrow 00{:}34{:}21.014$ There.
- NOTE Confidence: 0.753394304375
- $00:34:21.014 \longrightarrow 00:34:22.484$ There are many reports that
- NOTE Confidence: 0.753394304375
- $00{:}34{:}22{.}484 \dashrightarrow 00{:}34{:}24{.}046$ show that two more infiltrated
- NOTE Confidence: 0.753394304375
- $00:34:24.046 \longrightarrow 00:34:25.996$ fiber blasts do that as well,
- NOTE Confidence: 0.753394304375
- $00{:}34{:}26.000 \dashrightarrow 00{:}34{:}28.086$ and it's also a recent report in
- NOTE Confidence: 0.753394304375
- $00:34:28.086 \rightarrow 00:34:30.105$ the Lang where Lang epithelial cells
- NOTE Confidence: 0.753394304375
- 00:34:30.105 00:34:32.228 in the context of inflammation,
- NOTE Confidence: 0.753394304375
- $00:34:32.228 \longrightarrow 00:34:35.060$ can actually present antigen
- NOTE Confidence: 0.753394304375
- $00{:}34{:}35{.}060 \dashrightarrow 00{:}34{:}37{.}184$ to certain diesels.
- NOTE Confidence: 0.753394304375
- $00:34:37.190 \dashrightarrow 00:34:39.350$ So we hypothesize that cardiac
- NOTE Confidence: 0.753394304375
- $00:34:39.350 \rightarrow 00:34:42.144$ fibroblasts may be functioning as antigen
- NOTE Confidence: 0.753394304375
- $00{:}34{:}42.144 \dashrightarrow 00{:}34{:}44.536$ presenting cells, and that these.
- NOTE Confidence: 0.753394304375
- $00{:}34{:}44{.}536 \dashrightarrow 00{:}34{:}47{.}068$ T cell receptor engagement that we
- NOTE Confidence: 0.753394304375
- $00{:}34{:}47.068 \dashrightarrow 00{:}34{:}49.694$ were seeing in the heart was not
- NOTE Confidence: 0.753394304375
- $00:34:49.694 \rightarrow 00:34:51.686$ exclusively due to the dirt excels,
- NOTE Confidence: 0.753394304375

 $00{:}34{:}51{.}690 \dashrightarrow 00{:}34{:}54{.}006$ but also to cut fiber breads.

NOTE Confidence: 0.753394304375

 $00{:}34{:}54{.}010 \dashrightarrow 00{:}34{:}55{.}030$ And a wind.

NOTE Confidence: 0.753394304375

 $00:34:55.030 \dashrightarrow 00:34:58.149$ Emma let this work and then called it cower.

NOTE Confidence: 0.753394304375

00:34:58.150 - 00:35:01.054 In my lab was also contributed

NOTE Confidence: 0.753394304375

 $00:35:01.054 \dashrightarrow 00:35:02.990$ significantly to this project.

NOTE Confidence: 0.753394304375

 $00:35:02.990 \dashrightarrow 00:35:05.146$ So to remind you what an antigen

NOTE Confidence: 0.753394304375

 $00:35:05.146 \dashrightarrow 00:35:07.320$ presenting cell in order to be an

NOTE Confidence: 0.753394304375

 $00:35:07.320 \rightarrow 00:35:08.800$ antigen presenting cell as poor

NOTE Confidence: 0.753394304375

 $00{:}35{:}08{.}800 \dashrightarrow 00{:}35{:}10{.}190$ as an indirect cell.

NOTE Confidence: 0.753394304375

 $00:35:10.190 \longrightarrow 00:35:13.040$ You need to efficiently internalize

NOTE Confidence: 0.753394304375

 $00{:}35{:}13.040 \dashrightarrow 00{:}35{:}14.750$ and process antigens.

NOTE Confidence: 0.824624898

 $00{:}35{:}14.750 \dashrightarrow 00{:}35{:}16.820$ You need to display them

NOTE Confidence: 0.824624898

 $00{:}35{:}16.820 \dashrightarrow 00{:}35{:}19.660$ bound to MHC 2 molecules.

NOTE Confidence: 0.824624898

 $00:35:19.660 \longrightarrow 00:35:21.574$ And then you have to present

NOTE Confidence: 0.824624898

 $00{:}35{:}21{.}574 \dashrightarrow 00{:}35{:}23{.}902$ that at the cell surface and

NOTE Confidence: 0.824624898

 $00:35:23.902 \dashrightarrow 00:35:26.312$ professional Apcs and Rick cells

 $00:35:26.312 \rightarrow 00:35:28.760$ constitutively express all of these.

NOTE Confidence: 0.824624898

 $00:35:28.760 \dashrightarrow 00:35:32.870$ MHC do is constantly expressed and then

NOTE Confidence: 0.824624898

 $00:35:32.870 \longrightarrow 00:35:35.595$ these costimulatory molecules CD80 or

NOTE Confidence: 0.824624898

 $00{:}35{:}35{.}600 \dashrightarrow 00{:}35{:}40{.}886$ CD86 that are induced upon stimulation.

NOTE Confidence: 0.824624898

 $00:35:40.890 \rightarrow 00:35:44.220$ So we started investigating whether correct,

NOTE Confidence: 0.824624898

 $00:35:44.220 \dashrightarrow 00:35:46.746$ fabulous may fit into this category.

NOTE Confidence: 0.824624898

 $00:35:46.750 \longrightarrow 00:35:49.621$ So this is a way that we select correct

NOTE Confidence: 0.824624898

 $00:35:49.621 \rightarrow 00:35:52.978$ fibrous in the heart with digest the hearts,

NOTE Confidence: 0.824624898

 $00{:}35{:}52{.}978 \dashrightarrow 00{:}35{:}56{.}200$ and then then we acquire this

NOTE Confidence: 0.824624898

 $00:35:56.308 \longrightarrow 00:35:58.375$ and all the non fraction.

NOTE Confidence: 0.824624898

00:35:58.375 --> 00:36:01.100 We're having the filial cells.

NOTE Confidence: 0.824624898

 $00{:}36{:}01{.}100 \dashrightarrow 00{:}36{:}03{.}858$ We'll have local sides and we have

NOTE Confidence: 0.824624898

 $00{:}36{:}03.860 \dashrightarrow 00{:}36{:}06.380$ a correct fiberglass here here.

NOTE Confidence: 0.824624898

 $00{:}36{:}06{.}380 \dashrightarrow 00{:}36{:}09{.}206$ Sorry so we have leukocytes here.

NOTE Confidence: 0.824624898

 $00{:}36{:}09{.}210 \dashrightarrow 00{:}36{:}12{.}096$ 3045 positives City 31 positive and

 $00:36:12.096 \longrightarrow 00:36:14.584$ killer cells within the local sides

NOTE Confidence: 0.824624898

 $00{:}36{:}14.584 \dashrightarrow 00{:}36{:}17.852$ you could look for any local side that

NOTE Confidence: 0.824624898

 $00{:}36{:}17.852 \dashrightarrow 00{:}36{:}20.091$ you're interested in and within the

NOTE Confidence: 0.824624898

 $00:36:20.091 \rightarrow 00:36:21.873$ double negatives not in the filling.

NOTE Confidence: 0.824624898

 $00{:}36{:}21.880 \dashrightarrow 00{:}36{:}23.002$ No leukocytes.

NOTE Confidence: 0.824624898

 $00{:}36{:}23.002 \dashrightarrow 00{:}36{:}26.368$ We use these marker to detect

NOTE Confidence: 0.824624898

 $00:36:26.368 \longrightarrow 00:36:29.369$ a cardiac fiberless mask 4.

NOTE Confidence: 0.824624898

 $00:36:29.370 \longrightarrow 00:36:33.066$ We also do this in Linux reporter mice,

NOTE Confidence: 0.824624898

 $00{:}36{:}33.070 \dashrightarrow 00{:}36{:}35.350$ and that's where is indicated here.

NOTE Confidence: 0.824624898

 $00:36:35.350 \longrightarrow 00:36:37.552$ So these are Linux tracing mice

NOTE Confidence: 0.824624898

 $00{:}36{:}37{.}552 \dashrightarrow 00{:}36{:}40{.}179$ where we could more more definitely

NOTE Confidence: 0.824624898

 $00:36:40.180 \longrightarrow 00:36:43.150$ get into the cardiac fiberless.

NOTE Confidence: 0.824624898

 $00:36:43.150 \longrightarrow 00:36:45.418$ So the first thing that we did is do

NOTE Confidence: 0.824624898

 $00:36:45.418 \rightarrow 00:36:47.647$ they express MHC two and a baseline?

NOTE Confidence: 0.824624898

 $00:36:47.650 \longrightarrow 00:36:48.484$ They don't.

NOTE Confidence: 0.824624898

 $00:36:48.484 \longrightarrow 00:36:51.820$ But as soon as you activate them with

- NOTE Confidence: 0.824624898
- $00{:}36{:}51{.}908 \dashrightarrow 00{:}36{:}54{.}539$ interferon gamma you induce expression

 $00:36:54.539 \rightarrow 00:36:57.220$ of MHC two and actually in the filling

NOTE Confidence: 0.824624898

 $00:36:57.220 \rightarrow 00:36:58.985$ search for instance by people here

NOTE Confidence: 0.824624898

 $00:36:58.985 \rightarrow 00:37:00.809$ at nearly the department of Pathology,

NOTE Confidence: 0.824624898

 $00{:}37{:}00{.}810 \dashrightarrow 00{:}37{:}01{.}906$ German Barber,

NOTE Confidence: 0.824624898

 $00{:}37{:}01{.}906 \dashrightarrow 00{:}37{:}05{.}194$ and others found that endothelial cells

NOTE Confidence: 0.824624898

 $00:37:05.194 \rightarrow 00:37:08.710$ can present antigens to T cells as well,

NOTE Confidence: 0.824624898

 $00:37:08.710 \rightarrow 00:37:10.635$ and they respond and express MHC two

NOTE Confidence: 0.824624898

 $00:37:10.635 \rightarrow 00:37:12.429$ in response to interferon gamma.

NOTE Confidence: 0.824624898

 $00:37:12.430 \longrightarrow 00:37:13.580$ So this would be a.

NOTE Confidence: 0.824624898

 $00{:}37{:}13.580 \dashrightarrow 00{:}37{:}17.300$ It's similar mechanism of expression.

NOTE Confidence: 0.824624898

 $00{:}37{:}17{.}300 \dashrightarrow 00{:}37{:}18{.}812$ And then what we found it was

NOTE Confidence: 0.824624898

 $00:37:18.812 \longrightarrow 00:37:20.163$ that they do express customer

NOTE Confidence: 0.824624898

 $00{:}37{:}20{.}163 \dashrightarrow 00{:}37{:}22{.}107$ little molecules that you need to

NOTE Confidence: 0.824624898

 $00{:}37{:}22.107 \dashrightarrow 00{:}37{:}23.739$ trigger that diesel activation.

 $00:37:23.740 \longrightarrow 00:37:27.324$ They do express CD 80 and

NOTE Confidence: 0.824624898

 $00:37:27.324 \longrightarrow 00:37:29.020$ is not further inducible,

NOTE Confidence: 0.824624898

 $00:37:29.020 \dashrightarrow 00:37:31.530$ induced by different comma but

NOTE Confidence: 0.824624898

 $00:37:31.530 \longrightarrow 00:37:33.538$ they don't express 86.

NOTE Confidence: 0.824624898

 $00{:}37{:}33{.}540 \dashrightarrow 00{:}37{:}35{.}694$ We collaborated with Jenn Davies and

NOTE Confidence: 0.824624898

 $00{:}37{:}35.694 \dashrightarrow 00{:}37{:}37.796$ their impact grad student in her

NOTE Confidence: 0.824624898

 $00{:}37{:}37{.}796 \dashrightarrow 00{:}37{:}39{.}620$ lab at the University of Washington

NOTE Confidence: 0.824624898

 $00:37:39.620 \rightarrow 00:37:41.805$ and exactly the same experiments

NOTE Confidence: 0.824624898

 $00{:}37{:}41.805 \dashrightarrow 00{:}37{:}44.460$ using the Linux trace in mice.

NOTE Confidence: 0.824624898

 $00:37:44.460 \rightarrow 00:37:47.274$ That is a reporter for correct fiberglass,

NOTE Confidence: 0.824624898

 $00{:}37{:}47.280 \dashrightarrow 00{:}37{:}48.560$ as shown in here.

NOTE Confidence: 0.824624898

00:37:48.560 --> 00:37:50.480 And as you can see here,

NOTE Confidence: 0.824624898

 $00{:}37{:}50{.}480 \dashrightarrow 00{:}37{:}52{.}896$ all the correct fibers that are shown here.

NOTE Confidence: 0.824624898

 $00:37:52.900 \rightarrow 00:37:54.754$ The majority of them in response to it there,

NOTE Confidence: 0.824624898

00:37:54.760 --> 00:38:00.115 from gamma, they express MHC 2 here in red,

NOTE Confidence: 0.824624898

 $00{:}38{:}00{.}120 \dashrightarrow 00{:}38{:}02{.}973$ so this is GFP and this is no inter

- NOTE Confidence: 0.824624898
- $00:38:02.973 \rightarrow 00:38:06.898$ from gamma. With their from them.
- NOTE Confidence: 0.824624898
- $00:38:06.900 \longrightarrow 00:38:08.190$ Does this matter in vivo?
- NOTE Confidence: 0.824624898
- 00:38:08.190 --> 00:38:11.169 So in vivo we did pack and we found
- NOTE Confidence: 0.824624898
- $00:38:11.169 \rightarrow 00:38:14.320$ that carrot fiberglass isolated from
- NOTE Confidence: 0.824624898
- $00:38:14.320 \longrightarrow 00:38:17.620$ from this report device expressed
- NOTE Confidence: 0.824624898
- $00:38:17.620 \longrightarrow 00:38:20.860$ MHC 2 and you can see it here.
- NOTE Confidence: 0.824624898
- $00:38:20.860 \rightarrow 00:38:24.199$ You can focus here and this is zoom vision.
- NOTE Confidence: 0.824624898
- $00:38:24.200 \longrightarrow 00:38:26.594$ So this will be all in green.
- NOTE Confidence: 0.824624898
- $00{:}38{:}26.600 \dashrightarrow 00{:}38{:}28.546$ Are cardiac fibrosis and as you can
- NOTE Confidence: 0.824624898
- $00:38:28.546 \dashrightarrow 00:38:30.571$ see there are also other cells that
- NOTE Confidence: 0.824624898
- $00:38:30.571 \longrightarrow 00:38:32.856$ could be in the filler cells in a
- NOTE Confidence: 0.824624898
- $00{:}38{:}32.856 \dashrightarrow 00{:}38{:}34.980$ small kappel Aries or the drink cells
- NOTE Confidence: 0.824624898
- $00:38:34.980 \rightarrow 00:38:37.290$ as we previously shown that Expressen EC2.
- NOTE Confidence: 0.824624898
- $00{:}38{:}37{.}290 \dashrightarrow 00{:}38{:}38{.}832$ I've been here.
- NOTE Confidence: 0.824624898
- $00:38:38.832 \rightarrow 00:38:39.346$ Definitely,
- NOTE Confidence: 0.824624898

 $00:38:39.346 \rightarrow 00:38:42.430$ the correct fiberglass are expressing MHC

NOTE Confidence: 0.636568968941177

 $00{:}38{:}42.506 \dashrightarrow 00{:}38{:}44.886$ two in response to tech as well.

NOTE Confidence: 0.636568968941177

00:38:44.890 --> 00:38:47.938 And sometimes if you look you can find

NOTE Confidence: 0.636568968941177

 $00:38:47.938 \dashrightarrow 00:38:51.540$ that T cells seem very close to this

NOTE Confidence: 0.636568968941177

 $00{:}38{:}51{.}540 \dashrightarrow 00{:}38{:}54{.}390$ MHC 2 expressing correct fiberglass.

NOTE Confidence: 0.636568968941177

 $00{:}38{:}54{.}390 \dashrightarrow 00{:}38{:}57{.}799$ We use all the models of cardiomy opathy

NOTE Confidence: 0.636568968941177

 $00{:}38{:}57{.}799 \dashrightarrow 00{:}39{:}00{.}060$ and cardiac inflammation to see

NOTE Confidence: 0.636568968941177

 $00:39:00.060 \longrightarrow 00:39:02.226$ whether this was unique or not,

NOTE Confidence: 0.636568968941177

 $00{:}39{:}02{.}230 \dashrightarrow 00{:}39{:}04{.}995$ and we used the tickers eye infection

NOTE Confidence: 0.636568968941177

 $00{:}39{:}04{.}995 \dashrightarrow 00{:}39{:}07{.}422$ model of myopathy because we know

NOTE Confidence: 0.636568968941177

 $00{:}39{:}07{.}422 \dashrightarrow 00{:}39{:}09{.}870$ that because I is a parasite,

NOTE Confidence: 0.636568968941177

00:39:09.870 --> 00:39:11.748 I didn't use his highly strong

NOTE Confidence: 0.636568968941177

 $00{:}39{:}11.748 \dashrightarrow 00{:}39{:}13.690$ in there from gamma responses,

NOTE Confidence: 0.636568968941177

00:39:13.690 - 00:39:16.084 and as you can see here in this model,

NOTE Confidence: 0.636568968941177

 $00:39{:}16.090 \dashrightarrow 00{:}39{:}18.200$ the correct fabulous also expressed

NOTE Confidence: 0.636568968941177

 $00:39:18.200 \longrightarrow 00:39:21.400$ any todo and more more of them

00:39:21.400 - > 00:39:25.080 express MHC do and then at the MFA.

NOTE Confidence: 0.636568968941177

 $00{:}39{:}25{.}080 \dashrightarrow 00{:}39{:}27{.}300$ The prizes and densities also higher.

NOTE Confidence: 0.815977051666667

 $00:39:29.490 \longrightarrow 00:39:31.008$ So then the next question was,

NOTE Confidence: 0.815977051666667

 $00:39:31.010 \longrightarrow 00:39:33.578$ well, let's see if they can.

NOTE Confidence: 0.815977051666667

 $00{:}39{:}33{.}580 \dashrightarrow 00{:}39{:}35{.}968$ Take up the antigen processor and

NOTE Confidence: 0.815977051666667

 $00:39:35.968 \rightarrow 00:39:38.940$ present that induce T cell proliferation

NOTE Confidence: 0.815977051666667

 $00{:}39{:}38{.}940 \dashrightarrow 00{:}39{:}41{.}793$ and to do that we use a reagent that

NOTE Confidence: 0.815977051666667

 $00{:}39{:}41.793 \dashrightarrow 00{:}39{:}45.088$ is do DQ of album and so this is a

NOTE Confidence: 0.8159770516666667

 $00{:}39{:}45{.}088 \dashrightarrow 00{:}39{:}47{.}721$ novel women protein that can be taken

NOTE Confidence: 0.815977051666667

00:39:47.721 - 00:39:51.286 up by proteins and if it goes in the

NOTE Confidence: 0.815977051666667

 $00:39:51.286 \rightarrow 00:39:53.292$ lysosomes with acidic lysosome pH,

NOTE Confidence: 0.815977051666667

 $00:39:53.292 \longrightarrow 00:39:55.710$ which is what you're required to

NOTE Confidence: 0.815977051666667

 $00:39:55.787 \dashrightarrow 00:39:58.066$ process antigens it costs related

NOTE Confidence: 0.815977051666667

 $00{:}39{:}58.066$ --> $00{:}39{:}59.976$ degradation and becomes for S.

NOTE Confidence: 0.815977051666667

 $00:39:59.980 \longrightarrow 00:40:01.816$ And as you can see here,

 $00:40:01.820 \longrightarrow 00:40:03.728$ regardless of the interference.

NOTE Confidence: 0.815977051666667

00:40:03.728 --> 00:40:06.113 Treatment DQ over is processed

NOTE Confidence: 0.815977051666667

 $00:40:06.113 \longrightarrow 00:40:08.059$ by cardiac fibroblast.

NOTE Confidence: 0.815977051666667

 $00:40:08.060 \rightarrow 00:40:10.601$ This is just one example of correct

NOTE Confidence: 0.815977051666667

 $00:40:10.601 \rightarrow 00:40:12.908$ fiber rest treated with equal woman,

NOTE Confidence: 0.815977051666667

 $00{:}40{:}12{.}910 \dashrightarrow 00{:}40{:}14{.}877$ but you can see here the comparison

NOTE Confidence: 0.8159770516666667

 $00:40:14.877 \longrightarrow 00:40:16.890$ of a large correct fiberglass

NOTE Confidence: 0.815977051666667

 $00:40:16.890 \longrightarrow 00:40:18.786$ and obviously a smaller in size.

NOTE Confidence: 0.815977051666667

 $00:40:18.790 \longrightarrow 00:40:21.070$ Here the bone marrow derived

NOTE Confidence: 0.815977051666667

 $00:40:21.070 \longrightarrow 00:40:24.488$ cells that a process.

NOTE Confidence: 0.815977051666667

 $00:40:24.490 \longrightarrow 00:40:26.428$ So that was very exciting too,

NOTE Confidence: 0.815977051666667

 $00:40:26.430 \longrightarrow 00:40:28.310$ because then that means that

NOTE Confidence: 0.815977051666667

 $00:40:28.310 \longrightarrow 00:40:30.470$ if they're able to process it,

NOTE Confidence: 0.815977051666667

00:40:30.470 -> 00:40:32.720 they might be able to load it into MHC

NOTE Confidence: 0.815977051666667

 $00:40:32.720 \rightarrow 00:40:34.937$ two and induce decent proliferation.

NOTE Confidence: 0.815977051666667

 $00:40:34.940 \longrightarrow 00:40:37.076$ So we did similar studies as

- NOTE Confidence: 0.815977051666667
- $00:40:37.076 \longrightarrow 00:40:39.882$ what I showed before to to look
- NOTE Confidence: 0.815977051666667
- 00:40:39.882 --> 00:40:41.190 for diesel proliferation,
- NOTE Confidence: 0.815977051666667
- $00{:}40{:}41.190 \dashrightarrow 00{:}40{:}43.726$ and we use in this case we use
- NOTE Confidence: 0.815977051666667
- $00:40:43.726 \rightarrow 00:40:45.947$ transgenic mice that are what they do,
- NOTE Confidence: 0.815977051666667
- $00{:}40{:}45{.}950 \dashrightarrow 00{:}40{:}48{.}260$ so these mice all the T cell
- NOTE Confidence: 0.815977051666667
- $00{:}40{:}48.260 \dashrightarrow 00{:}40{:}50.289$ receptors in the details express
- NOTE Confidence: 0.815977051666667
- $00:40:50.289 \longrightarrow 00:40:52.699$ a receptor for available mean.
- NOTE Confidence: 0.815977051666667
- $00:40:52.700 \longrightarrow 00:40:56.291$ And then we took this specific piece
- NOTE Confidence: 0.815977051666667
- $00{:}40{:}56.291 \dashrightarrow 00{:}40{:}58.580$ of argument and then on the other hand,
- NOTE Confidence: 0.815977051666667
- $00:40:58.580 \longrightarrow 00:40:59.750$ we took it a wild diaper.
- NOTE Confidence: 0.815977051666667
- $00:40:59.750 \longrightarrow 00:41:01.422$ Makes you do knockout.
- NOTE Confidence: 0.815977051666667
- 00:41:01.422 --> 00:41:02.676 Correct fiber rest.
- NOTE Confidence: 0.815977051666667
- $00{:}41{:}02.680 \dashrightarrow 00{:}41{:}04.626$ Three of them within their front comma
- NOTE Confidence: 0.815977051666667
- $00{:}41{:}04.626$ --> $00{:}41{:}06.640$ and treated them with normal woman.
- NOTE Confidence: 0.815977051666667
- 00:41:06.640 --> 00:41:08.940 So in this Co cultures,
- NOTE Confidence: 0.815977051666667

 $00:41:08.940 \longrightarrow 00:41:10.128$ if they carry fiberglass,

NOTE Confidence: 0.815977051666667

 $00:41:10.128 \longrightarrow 00:41:11.316$ are processing available mean?

NOTE Confidence: 0.815977051666667

 $00:41:11.320 \rightarrow 00:41:15.240$ As I I recently showed with Valve woman.

NOTE Confidence: 0.815977051666667

 $00{:}41{:}15{.}240 \dashrightarrow 00{:}41{:}17{.}814$ All these diesels with a receptor

NOTE Confidence: 0.8159770516666667

 $00{:}41{:}17.814 \dashrightarrow 00{:}41{:}20.456$ for Valve women should be able

NOTE Confidence: 0.815977051666667

 $00{:}41{:}20{.}456 \dashrightarrow 00{:}41{:}22{.}552$ to proliferate and we did other

NOTE Confidence: 0.815977051666667

 $00:41:22.552 \rightarrow 00:41:24.430$ experiments in which we use E.

NOTE Confidence: 0.815977051666667

00:41:24.430 --> 00:41:24.866 Coli,

NOTE Confidence: 0.815977051666667

 $00{:}41{:}24.866 \dashrightarrow 00{:}41{:}27.046$ a bacteria that over expresses

NOTE Confidence: 0.815977051666667

 $00:41:27.046 \longrightarrow 00:41:28.790$ about women as well.

NOTE Confidence: 0.815977051666667

00:41:28.790 --> 00:41:29.424 And again,

NOTE Confidence: 0.815977051666667

 $00:41:29.424 \rightarrow 00:41:31.326$ these are the readout of proliferation.

NOTE Confidence: 0.815977051666667

 $00:41:31.330 \rightarrow 00:41:33.122$ If there is prolific,

NOTE Confidence: 0.815977051666667

 $00{:}41{:}33{.}122 \dashrightarrow 00{:}41{:}34{.}466$ there's no proliferation.

NOTE Confidence: 0.815977051666667

00:41:34.470 --> 00:41:36.360 These teachers that I label with

NOTE Confidence: 0.815977051666667

00:41:36.360 --> 00:41:38.169 CFC will not dilute the die,

 $00:41:38.170 \rightarrow 00:41:41.970$ so we wouldn't see any peaks any dilution,

NOTE Confidence: 0.815977051666667

 $00:41:41.970 \longrightarrow 00:41:44.462$ but if there is proliferation we will

NOTE Confidence: 0.815977051666667

 $00:41:44.462 \rightarrow 00:41:46.887$ see this dilution of the membrane dye,

NOTE Confidence: 0.815977051666667

 $00:41:46.890 \rightarrow 00:41:49.774$ but that's exactly what we saw here,

NOTE Confidence: 0.8159770516666667

 $00:41:49.780 \longrightarrow 00:41:52.450$ so this is overwhelming protein.

NOTE Confidence: 0.815977051666667

 $00:41:52.450 \longrightarrow 00:41:54.560$ But here the fiberglass haven't

NOTE Confidence: 0.815977051666667

 $00:41:54.560 \rightarrow 00:41:56.670$ been treated with interferon gamma,

NOTE Confidence: 0.815977051666667

 $00:41:56.670 \longrightarrow 00:41:58.830$ so they don't express MHC 2.

NOTE Confidence: 0.8159770516666667

00:41:58.830 --> 00:41:59.838 Very little proliferation,

NOTE Confidence: 0.815977051666667

 $00{:}41{:}59{.}838 \dashrightarrow 00{:}42{:}02{.}589$ but here what you can see is that

NOTE Confidence: 0.815977051666667

 $00{:}42{:}02{.}589 \dashrightarrow 00{:}42{:}04{.}269$ when they you induce expression

NOTE Confidence: 0.815977051666667

 $00:42:04.269 \longrightarrow 00:42:06.469$ and you treat with over protein,

NOTE Confidence: 0.8159770516666667

 $00{:}42{:}06{.}470 \dashrightarrow 00{:}42{:}08{.}655$ there is a significant proliferation

NOTE Confidence: 0.815977051666667

00:42:08.655 --> 00:42:09.529 of diesel,

NOTE Confidence: 0.815977051666667

 $00{:}42{:}09{.}530 \dashrightarrow 00{:}42{:}11.658$ suggesting that the fiber glass

 $00:42:11.658 \rightarrow 00:42:13.786$ can induce diesel proliferation.

NOTE Confidence: 0.815977051666667

 $00{:}42{:}13.790 \dashrightarrow 00{:}42{:}15.895$ And here's a demonstration of

NOTE Confidence: 0.815977051666667

 $00:42:15.895 \rightarrow 00:42:18.374$ dendritic cells as a positive control,

NOTE Confidence: 0.815977051666667

 $00:42:18.374 \rightarrow 00:42:20.244$ where we see a proliferation

NOTE Confidence: 0.815977051666667

 $00{:}42{:}20{.}244 \dashrightarrow 00{:}42{:}22{.}330$ and as I said before,

NOTE Confidence: 0.815977051666667

 $00{:}42{:}22{.}330 \dashrightarrow 00{:}42{:}24.090$ these are the professional

NOTE Confidence: 0.8159770516666667

 $00:42:24.090 \rightarrow 00:42:25.410$ antigen presenting cells,

NOTE Confidence: 0.815977051666667

 $00:42:25.410 \longrightarrow 00:42:26.691$ so they don't need to be pre

NOTE Confidence: 0.815977051666667

 $00{:}42{:}26.691 \dashrightarrow 00{:}42{:}27.769$ treated within their from grammar.

NOTE Confidence: 0.815977051666667

00:42:27.770 --> 00:42:31.350 They express MHC 2. Constitutively.

NOTE Confidence: 0.815977051666667

 $00:42:31.350 \longrightarrow 00:42:32.750$ We also did these experiments,

NOTE Confidence: 0.815977051666667

 $00:42:32.750 \longrightarrow 00:42:35.186$ obviously with the MMC to knockout.

NOTE Confidence: 0.8159770516666667

 $00{:}42{:}35{.}190 \dashrightarrow 00{:}42{:}37{.}140$ Correct fiber glass to to show

NOTE Confidence: 0.815977051666667

 $00:42:37.140 \longrightarrow 00:42:41.150$ that this was a specific.

NOTE Confidence: 0.815977051666667

 $00:42:41.150 \longrightarrow 00:42:44.238$ So just to be.

NOTE Confidence: 0.815977051666667

 $00:42:44.240 \longrightarrow 00:42:46.560$ Over a convenience with this

- NOTE Confidence: 0.815977051666667
- $00:42:46.560 \longrightarrow 00:42:48.416$ we do particularly proteins.
- NOTE Confidence: 0.6989478566666667
- $00{:}42{:}48{.}420 \dashrightarrow 00{:}42{:}50{.}330$ So instead of putting a
- NOTE Confidence: 0.6989478566666667
- $00:42:50.330 \longrightarrow 00:42:51.858$ soluble of argument there,
- NOTE Confidence: 0.6989478566666667
- $00{:}42{:}51{.}860 \dashrightarrow 00{:}42{:}54{.}248$ we collaborated with Carolyn Genco and
- NOTE Confidence: 0.6989478566666667
- 00:42:54.248 --> 00:42:57.219 Robert in our floor in order Department
- NOTE Confidence: 0.6989478566666667
- $00{:}42{:}57{.}220$ --> $00{:}42{:}59{.}780$ and they just happen to have these E.
- NOTE Confidence: 0.6989478566666667
- $00:42:59.780 \longrightarrow 00:43:02.348$ Coli that over expresses,
- NOTE Confidence: 0.6989478566666667
- $00:43:02.350 \longrightarrow 00:43:04.374$ so we try to correct fiberglass with E.
- NOTE Confidence: 0.6989478566666667
- $00:43:04.380 \longrightarrow 00:43:07.278$ Coli that had an empty vehicle
- NOTE Confidence: 0.6989478566666667
- $00:43:07.278 \rightarrow 00:43:08.727$ or expressing involvement,
- NOTE Confidence: 0.6989478566666667
- $00:43:08.730 \longrightarrow 00:43:11.788$ and we saw that only when when E.
- NOTE Confidence: 0.6989478566666667
- $00{:}43{:}11.788 \dashrightarrow 00{:}43{:}14.126$ Coli was expressing about woman we saw.
- NOTE Confidence: 0.6989478566666667
- $00{:}43{:}14.130 \dashrightarrow 00{:}43{:}17.444$ Diesel is specific for ovum proliferate,
- NOTE Confidence: 0.6989478566666667
- $00{:}43{:}17{.}444 \dashrightarrow 00{:}43{:}20{.}228$ and this is all quantified here,
- NOTE Confidence: 0.6989478566666667
- $00{:}43{:}20{.}230 \dashrightarrow 00{:}43{:}21{.}775$ and this is the positive
- NOTE Confidence: 0.6989478566666667

00:43:21.775 - 00:43:23.320 control with the sender excels.

NOTE Confidence: 0.853586757142857

 $00:43:25.490 \rightarrow 00:43:28.766$ So going back to the cardiac pathophysiology,

NOTE Confidence: 0.853586757142857

 $00:43:28.770 \longrightarrow 00:43:30.108$ does this make?

NOTE Confidence: 0.853586757142857

 $00:43:30.108 \rightarrow 00:43:33.230$ Does this have any effect on correct

NOTE Confidence: 0.853586757142857

00:43:33.322 --> 00:43:36.070 dysfunction or cardiac fibrosis?

NOTE Confidence: 0.853586757142857

 $00:43:36.070 \rightarrow 00:43:37.990$ So in collaboration with Jenn Davies,

NOTE Confidence: 0.853586757142857

00:43:37.990 --> 00:43:40.194 the University of Washington,

NOTE Confidence: 0.853586757142857

 $00:43:40.194 \rightarrow 00:43:43.521$ we obtain the TCF 21 Mercury

NOTE Confidence: 0.853586757142857

00:43:43.521 --> 00:43:45.749 Mirror mice decree driver.

NOTE Confidence: 0.853586757142857

 $00:43:45.750 \longrightarrow 00:43:47.770$ Please inducible and we

NOTE Confidence: 0.853586757142857

 $00{:}43{:}47.770 \dashrightarrow 00{:}43{:}50.800$ crushed it with MHC to flux.

NOTE Confidence: 0.853586757142857

 $00{:}43{:}50{.}800 \dashrightarrow 00{:}43{:}53{.}920$ And we generated the correct

NOTE Confidence: 0.853586757142857

 $00:43:53.920 \rightarrow 00:43:57.040$ fiberglass specific deficient in MHC

NOTE Confidence: 0.853586757142857

 $00:43:57.138 \rightarrow 00:43:59.190$ do and these mice are only deficient

NOTE Confidence: 0.853586757142857

 $00:43:59.190 \longrightarrow 00:44:01.298$ if you treat them with tamoxifen

NOTE Confidence: 0.853586757142857

 $00:44:01.298 \longrightarrow 00:44:03.298$ because it's an inducible line.
- NOTE Confidence: 0.853586757142857
- $00:44:03.300 \longrightarrow 00:44:04.836$ So as you can see here,
- NOTE Confidence: 0.853586757142857
- $00{:}44{:}04{.}840 \dashrightarrow 00{:}44{:}07{.}025$ we corroborated that it when
- NOTE Confidence: 0.853586757142857
- $00:44:07.025 \longrightarrow 00:44:08.773$ we treated with tam oxifen,
- NOTE Confidence: 0.853586757142857
- $00:44:08.780 \dashrightarrow 00:44:12.868$ we decrease the expression of MHC 2.
- NOTE Confidence: 0.853586757142857
- $00:44:12.870 \rightarrow 00:44:15.390$ Here, so this this is what we will be
- NOTE Confidence: 0.853586757142857
- $00{:}44{:}15{.}390 \dashrightarrow 00{:}44{:}17{.}609$ looking at and we decrease expression.
- NOTE Confidence: 0.853586757142857
- 00:44:17.610 --> 00:44:17.966 Incorrect.
- NOTE Confidence: 0.853586757142857
- 00:44:17.966 --> 00:44:20.458 Fabulous, but not in bone marrow Dr.
- NOTE Confidence: 0.853586757142857
- $00{:}44{:}20{.}460 \dashrightarrow 00{:}44{:}23{.}214$ Dendritic cells where MHC 2 levels
- NOTE Confidence: 0.853586757142857
- $00{:}44{:}23{.}214 \dashrightarrow 00{:}44{:}25{.}602$ remain compatible in the treated
- NOTE Confidence: 0.853586757142857
- $00:44:25.602 \rightarrow 00:44:27.937$ and not treated with oxygen.
- NOTE Confidence: 0.853586757142857
- 00:44:27.940 --> 00:44:30.428 And then we looked at fibrosis and as
- NOTE Confidence: 0.853586757142857
- 00:44:30.428 --> 00:44:33.000 you can see here there was significant
- NOTE Confidence: 0.853586757142857
- $00{:}44{:}33.000 \dashrightarrow 00{:}44{:}35.640$ fibrosis in the TACK control group
- NOTE Confidence: 0.853586757142857
- $00{:}44{:}35.640 \dashrightarrow 00{:}44{:}38.039$ than non democracies untreated,
- NOTE Confidence: 0.853586757142857

 $00:44:38.040 \longrightarrow 00:44:41.351$ but when we treated with tamoxifen we

NOTE Confidence: 0.853586757142857

 $00:44:41.351 \longrightarrow 00:44:43.695$ reduce fibrosis significantly and this

NOTE Confidence: 0.853586757142857

 $00{:}44{:}43.695 \dashrightarrow 00{:}44{:}46.239$ has an impact in fractional shortening.

NOTE Confidence: 0.853586757142857

 $00:44:46.240 \rightarrow 00:44:49.966$ So here's that mouse with flattened.

NOTE Confidence: 0.853586757142857

00:44:49.970 --> 00:44:51.854 You know contraction here

NOTE Confidence: 0.853586757142857

 $00{:}44{:}51{.}854 \dashrightarrow 00{:}44{:}54{.}577$ and this is the most mice,

NOTE Confidence: 0.853586757142857

 $00{:}44{:}54{.}577 \dashrightarrow 00{:}44{:}57{.}513$ so again these are the ones that don't

NOTE Confidence: 0.853586757142857

 $00:44:57.513 \rightarrow 00:45:00.671$ have image do in the fiberglass and

NOTE Confidence: 0.853586757142857

 $00:45:00.671 \rightarrow 00:45:04.476$ they have preserved systolic function.

NOTE Confidence: 0.853586757142857

 $00:45:04.480 \longrightarrow 00:45:06.832$ So we looked in the lymph nodes

NOTE Confidence: 0.853586757142857

 $00{:}45{:}06.832 \dashrightarrow 00{:}45{:}08.966$ to right because we wanted to

NOTE Confidence: 0.853586757142857

 $00{:}45{:}08{.}966 \dashrightarrow 00{:}45{:}10{.}716$ see whether this was where.

NOTE Confidence: 0.853586757142857

 $00{:}45{:}10.720 \dashrightarrow 00{:}45{:}13.582$ Remember that we're eliminating this in

NOTE Confidence: 0.853586757142857

 $00:45:13.582 \rightarrow 00:45:17.084$ the in the cardiac fibroblast and they

NOTE Confidence: 0.853586757142857

 $00:45:17.084 \rightarrow 00:45:19.892$ might be other cells that express TCF 21,

NOTE Confidence: 0.853586757142857

 $00:45:19.892 \longrightarrow 00:45:21.020$ although it is,

- NOTE Confidence: 0.853586757142857
- $00:45:21.020 \longrightarrow 00:45:23.054$ it was described to be a
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}23.054 \dashrightarrow 00{:}45{:}24.410$ driver for collect fibers.
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}24{.}410 \dashrightarrow 00{:}45{:}26{.}804$ And what we find is that the T cell
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}26.804 \dashrightarrow 00{:}45{:}28.688$ immune response in the lymph node
- NOTE Confidence: 0.853586757142857
- $00:45:28.688 \rightarrow 00:45:31.661$ is not altered by by this intact.
- NOTE Confidence: 0.853586757142857
- $00:45:31.661 \longrightarrow 00:45:33.969$ And we also see.
- NOTE Confidence: 0.853586757142857
- $00:45:33.970 \longrightarrow 00:45:36.054$ Similar infiltration of character
- NOTE Confidence: 0.853586757142857
- $00:45:36.054 \longrightarrow 00:45:38.716$ in these mice with tam oxifen.
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}38{.}716 \dashrightarrow 00{:}45{:}42{.}004$ So working hypothesis now is that
- NOTE Confidence: 0.853586757142857
- $00:45:42.010 \rightarrow 00:45:44.470$ these are the conclusions right that
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}44{.}470 \dashrightarrow 00{:}45{:}47{.}951$ in these crosstalk we have the T cells
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}47{.}951 \dashrightarrow 00{:}45{:}49{.}719$ and the fiberglass communicating.
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}49.720 \dashrightarrow 00{:}45{:}51.604$ And in this two week crosstalk
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}51.604 \dashrightarrow 00{:}45{:}53.304$ we think there correct fibrils
- NOTE Confidence: 0.853586757142857
- $00{:}45{:}53{.}304 \dashrightarrow 00{:}45{:}55{.}759$ are Sentinel cells that can sense
- NOTE Confidence: 0.853586757142857

 $00:45:55.759 \rightarrow 00:45:57.924$ correct insults and directly boost

NOTE Confidence: 0.853586757142857

 $00{:}45{:}57{.}924 \dashrightarrow 00{:}45{:}59{.}980$ the adaptive immune response.

NOTE Confidence: 0.853586757142857

 $00{:}45{:}59{.}980 \dashrightarrow 00{:}46{:}02{.}682$ We think that there's a potential of

NOTE Confidence: 0.853586757142857

 $00:46:02.682 \rightarrow 00:46:04.480$ moderating decent immune responses

NOTE Confidence: 0.853586757142857

 $00:46:04.480 \longrightarrow 00:46:06.220$ without impairing systemic diesel

NOTE Confidence: 0.853586757142857

 $00:46:06.220 \longrightarrow 00:46:08.830$ activation by the cells which could

NOTE Confidence: 0.853586757142857

 $00:46:08.896 \rightarrow 00:46:11.416$ have undecided major suppressive effect.

NOTE Confidence: 0.853586757142857

 $00:46:11.420 \longrightarrow 00:46:13.640$ So the fact that we see.

NOTE Confidence: 0.853586757142857

 $00{:}46{:}13.640 \dashrightarrow 00{:}46{:}16.034$ Similar activation in the in the

NOTE Confidence: 0.853586757142857

 $00:46:16.034 \longrightarrow 00:46:18.679$ lymph nodes that that tells us to

NOTE Confidence: 0.853586757142857

 $00{:}46{:}18.679 \dashrightarrow 00{:}46{:}21.665$ think that these this is critical in

NOTE Confidence: 0.853586757142857

 $00{:}46{:}21.665 \dashrightarrow 00{:}46{:}24.740$ the heart for the correct fibers.

NOTE Confidence: 0.853586757142857

 $00:46:24.740 \longrightarrow 00:46:26.460$ And then the overall summary,

NOTE Confidence: 0.853586757142857

 $00:46:26.460 \longrightarrow 00:46:29.644$ just to wrap up and leave some time

NOTE Confidence: 0.853586757142857

 $00{:}46{:}29{.}644 \dashrightarrow 00{:}46{:}31{.}592$ for questions is that responses.

NOTE Confidence: 0.853586757142857

00:46:31.592 --> 00:46:33.896 I think we're pretty convinced with

- NOTE Confidence: 0.853586757142857
- 00:46:33.896 --> 00:46:36.135 our work and a lot of the work,
- NOTE Confidence: 0.853586757142857
- $00{:}46{:}36{.}140 \dashrightarrow 00{:}46{:}39{.}580$ that of others that I've cited and
- NOTE Confidence: 0.853586757142857
- $00:46:39.580 \longrightarrow 00:46:42.460$ that we we always site in in our papers,
- NOTE Confidence: 0.853586757142857
- $00{:}46{:}42.460 \dashrightarrow 00{:}46{:}44.180$ is the diesel immune responses
- NOTE Confidence: 0.853586757142857
- $00:46:44.180 \rightarrow 00:46:45.556$ contribute to the pathophysiology
- NOTE Confidence: 0.853586757142857
- $00{:}46{:}45{.}556 \dashrightarrow 00{:}46{:}47{.}399$ of nonischemic heart failure in
- NOTE Confidence: 0.853586757142857
- 00:46:47.399 --> 00:46:48.905 many different ways, right?
- NOTE Confidence: 0.853586757142857
- $00:46:48.905 \rightarrow 00:46:52.305$ So we think that eleven took blood pressure,
- NOTE Confidence: 0.853586757142857
- $00{:}46{:}52{.}310 \dashrightarrow 00{:}46{:}56{.}065$ induces a significant levels of
- NOTE Confidence: 0.853586757142857
- 00:46:56.065 --> 00:46:59.235 drugs and the formation of new
- NOTE Confidence: 0.853586757142857
- $00:46:59.235 \rightarrow 00:47:01.650$ antigens that trigger this activation
- NOTE Confidence: 0.808975422692308
- $00:47:01.736 \longrightarrow 00:47:04.662$ in the heart. Within that limited repertoire
- NOTE Confidence: 0.808975422692308
- $00{:}47{:}04.662 \dashrightarrow 00{:}47{:}08.280$ of those T cells respond to ISO LGS.
- NOTE Confidence: 0.808975422692308
- $00{:}47{:}08.280 \dashrightarrow 00{:}47{:}10.890$ Modified cardiac new antigens and contributes
- NOTE Confidence: 0.808975422692308
- $00{:}47{:}10.890 \dashrightarrow 00{:}47{:}13.450$ to cardiac fibrosis and dysfunction.
- NOTE Confidence: 0.808975422692308

 $00{:}47{:}13.450 \dashrightarrow 00{:}47{:}15.786$ But we don't think these are the early

NOTE Confidence: 0.808975422692308

 $00:47:15.786 \rightarrow 00:47:17.780$ antigens that diesels are recognizing,

NOTE Confidence: 0.808975422692308

 $00{:}47{:}17.780 \dashrightarrow 00{:}47{:}20.279$ because if you recall from our data,

NOTE Confidence: 0.808975422692308

 $00:47:20.280 \rightarrow 00:47:24.366$ even when we scavenge those icebergs

NOTE Confidence: 0.808975422692308

 $00:47:24.370 \longrightarrow 00:47:26.265$ modified proteins, we still see

NOTE Confidence: 0.808975422692308

 $00{:}47{:}26.265 \dashrightarrow 00{:}47{:}28.600$ some decent activation in the heart.

NOTE Confidence: 0.808975422692308

 $00{:}47{:}28.600 \dashrightarrow 00{:}47{:}30.787$ So we are doing a lot of more in

NOTE Confidence: 0.808975422692308

 $00:47:30.787 \longrightarrow 00:47:32.637$ depth analysis of single cell.

NOTE Confidence: 0.808975422692308

 $00:47:32.640 \rightarrow 00:47:34.260$ He's service center sequencing and

NOTE Confidence: 0.808975422692308

 $00{:}47{:}34{.}260 \dashrightarrow 00{:}47{:}36{.}943$ trying to get to what are those other

NOTE Confidence: 0.808975422692308

 $00:47:36.943 \rightarrow 00:47:39.067$ antigens that might be induced response?

NOTE Confidence: 0.808975422692308

 $00{:}47{:}39{.}067 \dashrightarrow 00{:}47{:}43{.}180$ And we also see that they're not the same.

NOTE Confidence: 0.808975422692308

00:47:43.180 --> 00:47:43.906 Backgrounds overtime,

NOTE Confidence: 0.808975422692308

00:47:43.906 --> 00:47:46.084 which might be very relevant to

NOTE Confidence: 0.808975422692308

 $00:47:46.084 \rightarrow 00:47:48.359$ see how heart failure progresses,

NOTE Confidence: 0.808975422692308

 $00:47:48.360 \longrightarrow 00:47:50.580$ at least pretty nicley.

- NOTE Confidence: 0.808975422692308
- $00{:}47{:}50{.}580 \dashrightarrow 00{:}47{:}52{.}995$ And then the last conclusion from this
- NOTE Confidence: 0.808975422692308
- $00:47:52.995 \rightarrow 00:47:55.279$ is that these bidirectional actions
- NOTE Confidence: 0.808975422692308
- 00:47:55.279 --> 00:47:57.627 between correct resident cells,
- NOTE Confidence: 0.808975422692308
- $00{:}47{:}57{.}630 \dashrightarrow 00{:}48{:}00{.}598$ in this case fiber rise and T cells
- NOTE Confidence: 0.808975422692308
- $00{:}48{:}00{.}600 \dashrightarrow 00{:}48{:}02{.}860$ contribute to correct this activation.
- NOTE Confidence: 0.808975422692308
- $00{:}48{:}02{.}860 \dashrightarrow 00{:}48{:}05{.}292$ My fibrous transformation and
- NOTE Confidence: 0.808975422692308
- $00:48:05.292 \longrightarrow 00:48:07.724$ dysfunction under the correct
- NOTE Confidence: 0.808975422692308
- $00{:}48{:}07{.}724 \dashrightarrow 00{:}48{:}11{.}499$ fabulous expression of MHC 2 molecules
- NOTE Confidence: 0.808975422692308
- $00{:}48{:}11{.}499 \dashrightarrow 00{:}48{:}15{.}364$ is central for these response.
- NOTE Confidence: 0.808975422692308
- $00:48:15.370 \longrightarrow 00:48:18.727$ So with that, I'd like to thank my lab.
- NOTE Confidence: 0.808975422692308
- 00:48:18.730 --> 00:48:21.556 I think I've mentioned everyone who's
- NOTE Confidence: 0.808975422692308
- $00{:}48{:}21.556 \dashrightarrow 00{:}48{:}26.093$ done the work who's now moved on to new
- NOTE Confidence: 0.808975422692308
- $00:48:26.093 \rightarrow 00:48:28.149$ exciting research leading positions,
- NOTE Confidence: 0.808975422692308
- $00{:}48{:}28{.}150 \dashrightarrow 00{:}48{:}30{.}294$ and then this is the new members of
- NOTE Confidence: 0.808975422692308
- $00{:}48{:}30{.}294 \dashrightarrow 00{:}48{:}32{.}460$ the lab that are trying to pick up
- NOTE Confidence: 0.808975422692308

 $00:48:32.460 \longrightarrow 00:48:34.592$ on all the good work that previous

NOTE Confidence: 0.808975422692308

 $00:48:34.592 \longrightarrow 00:48:36.626$ former members did in the lab.

NOTE Confidence: 0.808975422692308

00:48:36.630 --> 00:48:38.470 Our collaborators at the University

NOTE Confidence: 0.808975422692308

00:48:38.470 --> 00:48:39.206 of Washington,

NOTE Confidence: 0.808975422692308

 $00{:}48{:}39{.}210 \dashrightarrow 00{:}48{:}42{.}642$ Vanderbilt or collaborators at absent as

NOTE Confidence: 0.808975422692308

00:48:42.642 --> 00:48:47.170 Medical Center and our funding sources from.

NOTE Confidence: 0.808975422692308

00:48:47.170 --> 00:48:50.770 18 and also from Dallas University.

NOTE Confidence: 0.808975422692308

 $00:48:50.770 \longrightarrow 00:48:51.594$ With that,

NOTE Confidence: 0.808975422692308

00:48:51.594 --> 00:48:54.066 I'll be happy to answer questions,

NOTE Confidence: 0.808975422692308

 $00{:}48{:}54{.}070 \dashrightarrow 00{:}48{:}56{.}408$ but before that I'll make an announcement

NOTE Confidence: 0.808975422692308

00:48:56.408 --> 00:48:58.789 of a very exciting conference,

NOTE Confidence: 0.808975422692308

 $00:48:58.790 \longrightarrow 00:49:00.855$ which will hopefully happen in

NOTE Confidence: 0.808975422692308

 $00:49:00.855 \rightarrow 00:49:03.731$ person is scheduled to be in person

NOTE Confidence: 0.808975422692308

 $00:49:03.731 \longrightarrow 00:49:05.710$ in Chicago and there will be a

NOTE Confidence: 0.808975422692308

 $00:49:05.710 \longrightarrow 00:49:06.950$ lot of interest in science,

NOTE Confidence: 0.808975422692308

00:49:06.950 --> 00:49:09.806 not only in information but a lot of

- NOTE Confidence: 0.808975422692308
- $00:49:09.810 \rightarrow 00:49:14.058$ cardiology and basic and traditional science.
- NOTE Confidence: 0.808975422692308
- $00:49:14.060 \rightarrow 00:49:16.180$ So I'll be happy to take any questions.
- NOTE Confidence: 0.808975422692308
- $00:49:16.180 \longrightarrow 00:49:17.300$ Thank you for your time.
- NOTE Confidence: 0.628262262
- $00:49:20.780 \longrightarrow 00:49:23.740$ Thank you Paula for the wonderful talk.
- NOTE Confidence: 0.628262262
- $00:49:23.740 \longrightarrow 00:49:27.770$ So now we are open to questions.
- NOTE Confidence: 0.536230803333333
- $00:49:28.320 \rightarrow 00:49:32.538$ I can maybe stop sharing and.
- NOTE Confidence: 0.536230803333333
- $00:49:32.540 \longrightarrow 00:49:33.818$ Either way, would you like me?
- NOTE Confidence: 0.536230803333333
- 00:49:33.820 --> 00:49:35.038 Or maybe I can leave it open
- NOTE Confidence: 0.536230803333333
- $00{:}49{:}35{.}038 \dashrightarrow 00{:}49{:}36{.}426$ in case I need to go back to
- NOTE Confidence: 0.514669746
- 00:49:36.700 --> 00:49:40.410 good? Yeah, good idea Harold, please?
- NOTE Confidence: 0.514669746
- 00:49:40.410 --> 00:49:44.170 Yeah hi, I really enjoyed the talk.
- NOTE Confidence: 0.514669746
- $00{:}49{:}44{.}170 \dashrightarrow 00{:}49{:}45{.}150$ Wonderful stuff.
- NOTE Confidence: 0.514669746
- $00{:}49{:}45{.}150 \dashrightarrow 00{:}49{:}47{.}110$ A very simplistic question.
- NOTE Confidence: 0.514669746
- $00{:}49{:}47{.}110 \dashrightarrow 00{:}49{.}49{.}474$ So at autopsy when we see
- NOTE Confidence: 0.514669746
- $00{:}49{:}49{.}474 \dashrightarrow 00{:}49{:}51{.}689$ hearts from patients who have
- NOTE Confidence: 0.514669746

 $00:49:51.689 \longrightarrow 00:49:53.897$ really horrible heart failure.

NOTE Confidence: 0.514669746

00:49:53.900 --> 00:49:56.204 I don't ever recall seeing a

NOTE Confidence: 0.514669746

 $00:49:56.204 \rightarrow 00:49:57.740$ striking infiltrate of lymphocytes.

NOTE Confidence: 0.514669746

 $00:49:57.740 \longrightarrow 00:49:59.420$ Is it that we just get them

NOTE Confidence: 0.514669746

 $00:49:59.420 \longrightarrow 00:50:00.969$ at the end stage or or?

NOTE Confidence: 0.775912582631579

00:50:03.060 --> 00:50:05.391 I think so compared to other cells

NOTE Confidence: 0.775912582631579

 $00{:}50{:}05{.}391 \dashrightarrow 00{:}50{:}08{.}099$ T cells they you don't see massive

NOTE Confidence: 0.775912582631579

 $00{:}50{:}08.099 \dashrightarrow 00{:}50{:}10.144$ infiltration as you would see.

NOTE Confidence: 0.775912582631579

 $00{:}50{:}10.150 \dashrightarrow 00{:}50{:}12.268$ For instance post MI in the

NOTE Confidence: 0.775912582631579

 $00:50:12.268 \rightarrow 00:50:14.643$ in the in fact zone, right?

NOTE Confidence: 0.775912582631579

 $00{:}50{:}14.643 \dashrightarrow 00{:}50{:}17.814$ And I think I think you don't

NOTE Confidence: 0.775912582631579

 $00:50:17.814 \rightarrow 00:50:20.108$ need that many of them,

NOTE Confidence: 0.775912582631579

 $00{:}50{:}20{.}110 \dashrightarrow 00{:}50{:}21{.}734$ so they're definitely sparse

NOTE Confidence: 0.775912582631579

 $00:50:21.734 \rightarrow 00:50:23.764$ compared to other major cells.

NOTE Confidence: 0.775912582631579

 $00{:}50{:}23.770 \dashrightarrow 00{:}50{:}25.922$ And then the other thing that I would

NOTE Confidence: 0.775912582631579

 $00:50:25.922 \rightarrow 00:50:28.111$ say that we've seen when we take

 $00{:}50{:}28.111 \dashrightarrow 00{:}50{:}29.984$ samples from Elbert issue is that

NOTE Confidence: 0.775912582631579

00:50:29.984 --> 00:50:32.281 the human heart is very large, right?

NOTE Confidence: 0.775912582631579

 $00:50:32.281 \longrightarrow 00:50:36.369$ So it it also depends where you take

NOTE Confidence: 0.775912582631579

 $00:50:36.369 \rightarrow 00:50:40.325$ the piece from, and we've seen.

NOTE Confidence: 0.775912582631579

 $00{:}50{:}40{.}325 \dashrightarrow 00{:}50{:}43{.}150$ We've seen some samples that

NOTE Confidence: 0.775912582631579

 $00{:}50{:}43.150 \dashrightarrow 00{:}50{:}45.649$ have more than others.

NOTE Confidence: 0.775912582631579

00:50:45.650 --> 00:50:47.930 I don't think it's the timing

NOTE Confidence: 0.775912582631579

 $00:50:47.930 \longrightarrow 00:50:49.690$ because we've done. I mean,

NOTE Confidence: 0.775912582631579

 $00:50:49.690 \rightarrow 00:50:52.270$ we haven't looked at human hearts early on,

NOTE Confidence: 0.775912582631579

 $00:50:52.270 \longrightarrow 00:50:54.430$ other than those of those healthy,

NOTE Confidence: 0.775912582631579

 $00:50:54.430 \longrightarrow 00:50:57.260$ right, and those have noticed.

NOTE Confidence: 0.775912582631579

 $00{:}50{:}57{.}260 \dashrightarrow 00{:}50{:}59{.}010$ But if there was a way to

NOTE Confidence: 0.775912582631579

00:50:59.010 --> 00:51:00.130 look inhuman in mice,

NOTE Confidence: 0.775912582631579

 $00{:}51{:}00{.}130 \dashrightarrow 00{:}51{:}02{.}573$ you can track that very easily, right?

NOTE Confidence: 0.775912582631579

 $00{:}51{:}02{.}573 \dashrightarrow 00{:}51{:}05{.}840$ And one thing that we don't see is that.

 $00:51:05.840 \longrightarrow 00:51:07.960$ And in the chronic phase.

NOTE Confidence: 0.775912582631579

00:51:07.960 --> 00:51:10.256 So if you take the mice way longer,

NOTE Confidence: 0.775912582631579

 $00{:}51{:}10{.}260 \dashrightarrow 00{:}51{:}12{.}409$ we see that the diesels are more

NOTE Confidence: 0.775912582631579

 $00:51:12.409 \rightarrow 00:51:14.749$ activated when we use the reporter mice.

NOTE Confidence: 0.775912582631579

 $00{:}51{:}14.750 \dashrightarrow 00{:}51{:}17.204$ But we don't see more details

NOTE Confidence: 0.775912582631579

 $00:51:17.204 \longrightarrow 00:51:19.310$ of our own per say.

NOTE Confidence: 0.775912582631579

00:51:19.310 --> 00:51:21.005 So I think that's that's

NOTE Confidence: 0.775912582631579

00:51:21.005 --> 00:51:22.700 maybe why inhuman is tricky,

NOTE Confidence: 0.775912582631579

 $00{:}51{:}22{.}700 \dashrightarrow 00{:}51{:}24{.}345$ but definitely is not a

NOTE Confidence: 0.775912582631579

 $00:51:24.345 \longrightarrow 00:51:25.990$ dominant cell in the heart.

NOTE Confidence: 0.775912582631579

 $00{:}51{:}25{.}990 \dashrightarrow 00{:}51{:}27{.}079$ You have to.

NOTE Confidence: 0.775912582631579

00:51:27.079 --> 00:51:28.894 You'll have to find them,

NOTE Confidence: 0.775912582631579

00:51:28.900 --> 00:51:31.090 but not being dominant doesn't mean

NOTE Confidence: 0.775912582631579

 $00:51:31.090 \rightarrow 00:51:33.878$ that they don't do a lot right,

NOTE Confidence: 0.775912582631579

00:51:33.880 --> 00:51:35.060 because if they're highly

NOTE Confidence: 0.775912582631579

 $00:51:35.060 \rightarrow 00:51:36.830$ activated they can release a lot

- NOTE Confidence: 0.775912582631579
- $00:51:36.887 \dashrightarrow 00:51:38.616$ of factors and do do other things.
- NOTE Confidence: 0.775912582631579
- $00{:}51{:}38{.}620 \dashrightarrow 00{:}51{:}40{.}870$ But that's a great point, thank you.
- NOTE Confidence: 0.775912582631579
- $00:51:40.870 \longrightarrow 00:51:42.520$ Thank you for your question.
- NOTE Confidence: 0.828033891428572
- $00:51:43.890 \rightarrow 00:51:48.566$ I have a question actually 2 questions.
- NOTE Confidence: 0.828033891428572
- $00{:}51{:}48{.}570 \dashrightarrow 00{:}51{:}52{.}130$ So wonderful talk again.
- NOTE Confidence: 0.828033891428572
- $00:51:52.130 \longrightarrow 00:51:56.528$ So do you think this fibroblast
- NOTE Confidence: 0.828033891428572
- $00{:}51{:}56{.}530 \dashrightarrow 00{:}51{:}59{.}470$ CD4T cell interaction may also
- NOTE Confidence: 0.828033891428572
- 00:51:59.470 --> 00:52:03.490 induce macrophage to invade or
- NOTE Confidence: 0.828033891428572
- 00:52:03.490 --> 00:52:05.902 activate resident macrophage
- NOTE Confidence: 0.828033891428572
- $00:52:05.902 \longrightarrow 00:52:08.674$ to contribute to the fibrosis?
- NOTE Confidence: 0.828033891428572
- $00:52:08.674 \rightarrow 00:52:10.210$ That's the first question.
- NOTE Confidence: 0.828033891428572
- $00{:}52{:}10{.}210 \dashrightarrow 00{:}52{:}12{.}598$ Second question is related
- NOTE Confidence: 0.828033891428572
- $00:52:12.598 \longrightarrow 00:52:14.389$ with hardwood question,
- NOTE Confidence: 0.828033891428572
- 00:52:14.390 --> 00:52:16.554 have you considered utilizing
- NOTE Confidence: 0.828033891428572
- $00{:}52{:}16{.}554 \dashrightarrow 00{:}52{:}19{.}259$ genetic heart failure model such
- NOTE Confidence: 0.828033891428572

 $00:52:19.259 \rightarrow 00:52:22.297$ as meising heavy chain mutation?

NOTE Confidence: 0.828033891428572

 $00{:}52{:}22{.}300 \dashrightarrow 00{:}52{:}25{.}121$ Our foes reach you genetic HTM mice

NOTE Confidence: 0.828033891428572

 $00{:}52{:}25{.}121 \dashrightarrow 00{:}52{:}28{.}459$ as well as dilated cardiomy opathy like NOTE Confidence: 0.828033891428572

 $00:52:28.459 \rightarrow 00:52:31.854$ muscle Lim protein knockout mouse.

NOTE Confidence: 0.828033891428572

 $00:52:31.860 \rightarrow 00:52:33.800$ They have natural heart failure.

NOTE Confidence: 0.828033891428572

 $00{:}52{:}33{.}800 \dashrightarrow 00{:}52{:}36{.}330$ Whether your hack information could NOTE Confidence: 0.828033891428572

 $00:52:36.330 \longrightarrow 00:52:39.580$ be extended to genetic heart failure,

NOTE Confidence: 0.828033891428572

 $00{:}52{:}39{.}580 \dashrightarrow 00{:}52{:}41{.}962$ which may mimic human heart failure

NOTE Confidence: 0.828033891428572

 $00:52:41.962 \longrightarrow 00:52:43.468$ more closely. What do you think?

NOTE Confidence: 0.590237698333333

00:52:44.100 - 00:52:45.978 Yeah, those are two great questions,

NOTE Confidence: 0.590237698333333

 $00{:}52{:}45{.}980 \dashrightarrow 00{:}52{:}47{.}464$ so I'll ask for the first one.

NOTE Confidence: 0.590237698333333

 $00{:}52{:}47{.}470 \dashrightarrow 00{:}52{:}49{.}918$ The first one, you're totally right.

NOTE Confidence: 0.590237698333333

 $00{:}52{:}49{.}920 \dashrightarrow 00{:}52{:}52{.}360$ We've seen that cardiac fibroblast.

NOTE Confidence: 0.590237698333333

00:52:52.360 --> 00:52:53.924 Really, ski machines that

NOTE Confidence: 0.590237698333333

 $00:52:53.924 \rightarrow 00:52:55.488$ not only attract diesels,

NOTE Confidence: 0.590237698333333

 $00:52:55.490 \longrightarrow 00:52:57.710$ but they attract monocytes.

 $00:52:57.710 \longrightarrow 00:53:01.635$ And we we did find that actually

NOTE Confidence: 0.590237698333333

00:53:01.635 --> 00:53:05.205 before Sumanth Prabhu had now in

NOTE Confidence: 0.590237698333333

00:53:05.205 --> 00:53:08.420 Washington University of Saint Louis.

NOTE Confidence: 0.590237698333333

 $00:53:08.420 \longrightarrow 00:53:11.382$ He found that early on,

NOTE Confidence: 0.590237698333333

 $00:53:11.382 \rightarrow 00:53:14.120$ and we've corroborated that the Maya

NOTE Confidence: 0.590237698333333

00:53:14.120 --> 00:53:16.745 size the CCR 2 positive Milo itself,

NOTE Confidence: 0.590237698333333

00:53:16.750 --> 00:53:19.888 so the haematopoietic Lee derived monocytes.

NOTE Confidence: 0.590237698333333

 $00:53:19.890 \longrightarrow 00:53:21.938$ They infiltrate the hard

NOTE Confidence: 0.590237698333333

 $00:53:21.938 \longrightarrow 00:53:23.986$ before the diesels do,

NOTE Confidence: 0.590237698333333

 $00{:}53{:}23{.}990 \dashrightarrow 00{:}53{:}27{.}046$ and we found following following up on that,

NOTE Confidence: 0.590237698333333

 $00{:}53{:}27.050 \dashrightarrow 00{:}53{:}29.330$ we found that the correct fiber glass

NOTE Confidence: 0.590237698333333

 $00:53:29.330 \longrightarrow 00:53:33.098$ they make CXCL 9 and 10 that are

NOTE Confidence: 0.590237698333333

 $00{:}53{:}33{.}098 \dashrightarrow 00{:}53{:}34{.}850$ chemoattractants for diesels,

NOTE Confidence: 0.590237698333333

 $00{:}53{:}34.850 \dashrightarrow 00{:}53{:}36.954$ but they also make a lot of C, CL two.

NOTE Confidence: 0.590237698333333

 $00{:}53{:}36{.}954 \dashrightarrow 00{:}53{:}38{.}858$ So that makes a lot of sense

 $00:53:38.858 \rightarrow 00:53:40.870$ that when they sense pressure.

NOTE Confidence: 0.590237698333333

 $00{:}53{:}40.870 \dashrightarrow 00{:}53{:}42.550$ And they release the chemo kids.

NOTE Confidence: 0.590237698333333

 $00{:}53{:}42{.}550 \dashrightarrow 00{:}53{:}45{.}930$ The second thing in that related

NOTE Confidence: 0.590237698333333

 $00:53:45.930 \longrightarrow 00:53:50.730$ to that question is that.

NOTE Confidence: 0.590237698333333

 $00:53:50.730 \longrightarrow 00:53:52.164$ Once they infiltrate,

NOTE Confidence: 0.590237698333333

 $00{:}53{:}52{.}164 \dashrightarrow 00{:}53{:}53{.}120$ so we,

NOTE Confidence: 0.590237698333333

 $00:53:53.120 \rightarrow 00:53:56.464$ we've found that the major source of the

NOTE Confidence: 0.590237698333333

 $00:53:56.464 \rightarrow 00:53:58.438$ diesel chemoattractant proteins is not.

NOTE Confidence: 0.590237698333333

 $00:53:58.440 \rightarrow 00:54:01.807$ The fiberglass is actually the Milo itself.

NOTE Confidence: 0.590237698333333

 $00:54:01.810 \dashrightarrow 00:54:04.505$ So those I think it's all orchestrated.

NOTE Confidence: 0.590237698333333

 $00:54:04.510 \longrightarrow 00:54:06.578$ Basically they fibroblasts release

NOTE Confidence: 0.590237698333333

 $00:54:06.578 \dashrightarrow 00:54:09.163$ chemo treatments for innate cells.

NOTE Confidence: 0.590237698333333

 $00:54:09.170 \longrightarrow 00:54:11.535$ Then they adapted cells come

NOTE Confidence: 0.590237698333333

 $00{:}54{:}11{.}535 \dashrightarrow 00{:}54{:}13{.}386$ because there's also an interaction

NOTE Confidence: 0.590237698333333

 $00:54:13.386 \longrightarrow 00:54:15.450$ between a myeloid cells and the

NOTE Confidence: 0.590237698333333

 $00:54:15.516 \rightarrow 00:54:17.206$ fibers that we cannot ignore.

- NOTE Confidence: 0.590237698333333
- 00:54:17.210 --> 00:54:19.406 I didn't do your second question.
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}19{.}410 \dashrightarrow 00{:}54{:}22{.}406$ I would love to look at these
- NOTE Confidence: 0.590237698333333
- 00:54:22.406 --> 00:54:24.650 models of carry myopathy.
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}24.650 \dashrightarrow 00{:}54{:}27.667$ We haven't looked because we we've never.
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}27.670 \dashrightarrow 00{:}54{:}31.162$ We don't have the tools or or the mice,
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}31{.}170 \dashrightarrow 00{:}54{:}33{.}807$ but I would love to to do it because
- NOTE Confidence: 0.590237698333333
- 00:54:33.807 > 00:54:36.644 I think it's it's very important
- NOTE Confidence: 0.590237698333333
- $00:54:36.644 \rightarrow 00:54:39.109$ and especially in those mutations
- NOTE Confidence: 0.590237698333333
- $00:54:39.193 \longrightarrow 00:54:42.318$ that the myocytes are are working.
- NOTE Confidence: 0.590237698333333
- 00:54:42.318 --> 00:54:44.199 And I did,
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}44{.}200 \dashrightarrow 00{:}54{:}45{.}955$ at dysfunctional from very early
- NOTE Confidence: 0.590237698333333
- $00:54:45.955 \longrightarrow 00:54:47.359$ on it spontaneously right.
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}47{.}360 \dashrightarrow 00{:}54{:}50{.}272$ You could really track and I'm sure that
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}50{.}272 \dashrightarrow 00{:}54{:}53{.}288$ there will be other antigens involved, right?
- NOTE Confidence: 0.590237698333333
- $00{:}54{:}53{.}288 \dashrightarrow 00{:}54{:}56{.}110$ So it might be that we will need to find
- NOTE Confidence: 0.590237698333333

 $00:54:56.110 \longrightarrow 00:54:57.810$ out whether inflammation plays a role.

NOTE Confidence: 0.590237698333333

 $00{:}54{:}57{.}810 \dashrightarrow 00{:}54{:}59{.}160$ It might be that it has

NOTE Confidence: 0.590237698333333

 $00:54:59.160 \dashrightarrow 00:55:00.760$ nothing to do with information,

NOTE Confidence: 0.590237698333333

 $00:55:00.760 \longrightarrow 00:55:03.077$ but if it did, if it did,

NOTE Confidence: 0.590237698333333

 $00{:}55{:}03.080 \dashrightarrow 00{:}55{:}07.342$ it would be easier to track whether the T

NOTE Confidence: 0.590237698333333

 $00:55:07.342 \rightarrow 00:55:11.039$ cells might be recognizing proteins that are.

NOTE Confidence: 0.590237698333333

 $00:55:11.039 \rightarrow 00:55:13.697$ You know that may be misfolded,

NOTE Confidence: 0.590237698333333

 $00{:}55{:}13.700 \dashrightarrow 00{:}55{:}15.608$ or that their mutated due to

NOTE Confidence: 0.590237698333333

 $00:55:15.608 \rightarrow 00:55:17.480$ the mutation in the myocyte,

NOTE Confidence: 0.590237698333333

 $00:55:17.480 \dashrightarrow 00:55:20.075$ so that that would be a yeah, that would be.

NOTE Confidence: 0.590237698333333

 $00{:}55{:}20.075 \dashrightarrow 00{:}55{:}21.650$ That's that would be an excellent Ave.

NOTE Confidence: 0.864855594

 $00{:}55{:}23.480 \dashrightarrow 00{:}55{:}25.850$ Thank you any other questions?

NOTE Confidence: 0.650748348

00:55:32.960 --> 00:55:34.528 So yeah, I I,

NOTE Confidence: 0.650748348

 $00:55:34.528 \dashrightarrow 00:55:36.880$ I'm very excited about the talk.

NOTE Confidence: 0.650748348

 $00{:}55{:}36{.}880 \dashrightarrow 00{:}55{:}39{.}680$ I have another follow-up question.

NOTE Confidence: 0.650748348

 $00:55:39.680 \longrightarrow 00:55:42.420$ What do you think about

- NOTE Confidence: 0.650748348
- $00:55:42.420 \rightarrow 00:55:43.516$ stressed cardiomyocytes?
- NOTE Confidence: 0.650748348
- $00{:}55{:}43.520 \dashrightarrow 00{:}55{:}47.850$ They may release new entity to the
- NOTE Confidence: 0.650748348
- $00{:}55{:}47.850 \dashrightarrow 00{:}55{:}50.265$ to the identical cells or two so
- NOTE Confidence: 0.650748348
- $00:55:50.265 \dashrightarrow 00:55:52.848$ they they catch up the antigen and
- NOTE Confidence: 0.650748348
- $00{:}55{:}52{.}848 \dashrightarrow 00{:}55{:}55{.}732$ present to CD 4T cells because we
- NOTE Confidence: 0.650748348
- $00:55:55.732 \dashrightarrow 00:55:58.450$ have cardiac troponin T troponin I.
- NOTE Confidence: 0.650748348
- $00:55:58.450 \rightarrow 00:56:01.312$ Fragmented release in the injured heart
- NOTE Confidence: 0.650748348
- $00:56:01.312 \rightarrow 00:56:05.089$ and and also cardio my side when stressed.
- NOTE Confidence: 0.650748348
- $00{:}56{:}05{.}090 \dashrightarrow 00{:}56{:}06{.}802$ They may secrete teacher
- NOTE Confidence: 0.650748348
- $00{:}56{:}06{.}802 \dashrightarrow 00{:}56{:}09{.}370$ Beta 2 instead of beta one.
- NOTE Confidence: 0.650748348
- $00:56:09.370 \longrightarrow 00:56:12.410$ We adapt be interesting avenues for you to
- NOTE Confidence: 0.2591359055
- $00{:}56{:}12.420 \dashrightarrow 00{:}56{:}15.126$ yes so that so first hypothesis.
- NOTE Confidence: 0.2591359055
- $00{:}56{:}15{.}130 \dashrightarrow 00{:}56{:}17{.}916$ When we started going after the antigen
- NOTE Confidence: 0.2591359055
- 00:56:17.916 --> 00:56:21.284 when J join my lab and he really wanted
- NOTE Confidence: 0.2591359055
- $00:56:21.284 \rightarrow 00:56:24.350$ to look at this diesel drones right
- NOTE Confidence: 0.2591359055

 $00:56:24.350 \rightarrow 00:56:27.059$ and our first hypothesis was I had

NOTE Confidence: 0.2591359055

 $00{:}56{:}27.059 \dashrightarrow 00{:}56{:}30.037$ just written a commentary on a paper.

NOTE Confidence: 0.2591359055

 $00:56:30.040 \longrightarrow 00:56:32.860$ Looking at all these in altimmune

NOTE Confidence: 0.2591359055

 $00{:}56{:}32{.}860 \dashrightarrow 00{:}56{:}35{.}371$ myocarditis you know how character

NOTE Confidence: 0.2591359055

 $00{:}56{:}35{.}371 \dashrightarrow 00{:}56{:}38{.}091$ planning and myosin binding protein

NOTE Confidence: 0.2591359055

00:56:38.091 --> 00:56:41.660 C and all these proteins that

NOTE Confidence: 0.2591359055

 $00:56:41.660 \rightarrow 00:56:44.750$ that are fighting people, right?

NOTE Confidence: 0.2591359055

 $00{:}56{:}44{.}750 \dashrightarrow 00{:}56{:}47{.}445$ So we thought that that those

NOTE Confidence: 0.2591359055

00:56:47.445 --> 00:56:50.364 who were going to be the ones but NOTE Confidence: 0.2591359055

 $00{:}56{:}50{.}364 \dashrightarrow 00{:}56{:}53{.}010$ in the tag model because we didn't

NOTE Confidence: 0.2591359055

00:56:53.010 --> 00:56:55.195 see death of Carrie myocytes,

NOTE Confidence: 0.2591359055

 $00{:}56{:}55{.}200 \dashrightarrow 00{:}56{:}56{.}480$ we didn't focus on that.

NOTE Confidence: 0.2591359055

00:56:56.480 --> 00:56:58.370 But you're right, they might be.

NOTE Confidence: 0.2591359055

 $00:56:58.370 \longrightarrow 00:57:00.128$ They might be that the stretch.

NOTE Confidence: 0.2591359055

 $00:57:00.130 \longrightarrow 00:57:01.846$ Induces, as you could do that

NOTE Confidence: 0.2591359055

00:57:01.846 --> 00:57:03.270 nicely with your model, right?

 $00:57:03.270 \rightarrow 00:57:05.510$ Because you can stretch all these cells we.

NOTE Confidence: 0.2591359055

 $00:57:05.510 \rightarrow 00:57:07.150$ We don't have the ability to do that,

NOTE Confidence: 0.2591359055

 $00{:}57{:}07{.}150 \dashrightarrow 00{:}57{:}09{.}705$ but I think it's also possible because

NOTE Confidence: 0.2591359055

00:57:09.705 - 00:57:11.702 the myocytes see the fiberglass

NOTE Confidence: 0.2591359055

 $00:57:11.702 \dashrightarrow 00:57:14.391$ seed in between the myocytes, right?

NOTE Confidence: 0.2591359055

 $00:57:14.391 \rightarrow 00:57:17.997$ So there's all these literature that,

NOTE Confidence: 0.2591359055

00:57:18.000 -> 00:57:20.485 and a huge field of research that

NOTE Confidence: 0.2591359055

00:57:20.485 --> 00:57:23.008 people study kind of fiber as

NOTE Confidence: 0.2591359055

 $00{:}57{:}23.008 \dashrightarrow 00{:}57{:}24.816$ kind of myocyte communication.

NOTE Confidence: 0.2591359055

 $00{:}57{:}24.820 \dashrightarrow 00{:}57{:}27.634$ So it might be that those fragments

NOTE Confidence: 0.2591359055

 $00:57:27.634 \longrightarrow 00:57:29.548$ are actually picked up by you?

NOTE Confidence: 0.2591359055

00:57:29.548 --> 00:57:30.888 Know the Mayo side doesn't

NOTE Confidence: 0.2591359055

 $00{:}57{:}30{.}888 \dashrightarrow 00{:}57{:}31{.}960$ really need to die.

NOTE Confidence: 0.2591359055

00:57:31.960 --> 00:57:34.326 It might be that it's a stretch

NOTE Confidence: 0.2591359055

 $00{:}57{:}34{.}326 \dashrightarrow 00{:}57{:}36{.}617$ and the fiber rest pick it up.

 $00:57:36.620 \rightarrow 00:57:38.160$ And then the fiberglass percent,

NOTE Confidence: 0.2591359055

 $00:57:38.160 \dashrightarrow 00:57:40.668$ but that's purely an in speculation.

NOTE Confidence: 0.2591359055

 $00:57:40.670 \longrightarrow 00:57:41.478$ We haven't.

NOTE Confidence: 0.2591359055

 $00:57:41.478 \longrightarrow 00:57:43.498$ We haven't looked at that,

NOTE Confidence: 0.2591359055

 $00:57:43.500 \longrightarrow 00:57:46.428$ but I think it's not only.

NOTE Confidence: 0.2591359055

 $00:57:46.430 \longrightarrow 00:57:48.313$ I think this is very complex and

NOTE Confidence: 0.2591359055

 $00:57:48.313 \longrightarrow 00:57:50.154$ it's not only limited to the

NOTE Confidence: 0.2591359055

 $00:57:50.154 \longrightarrow 00:57:51.764$ T cell binding to fibroblast.

NOTE Confidence: 0.2591359055

 $00{:}57{:}51{.}770 \dashrightarrow 00{:}57{:}54{.}250$ I think there is a.

NOTE Confidence: 0.2591359055

 $00{:}57{:}54.250 \dashrightarrow 00{:}57{:}57{.}160$ Cross communication with like an

NOTE Confidence: 0.2591359055

 $00{:}57{:}57{.}160 \dashrightarrow 00{:}57{:}59{.}935$ or chestrated response there with my

NOTE Confidence: 0.2591359055

 $00{:}57{:}59{.}935 \dashrightarrow 00{:}58{:}02{.}160$ insides fiberglass and immune cells.

NOTE Confidence: 0.581264438

 $00{:}58{:}03.430 \dashrightarrow 00{:}58{:}07.178$ Yeah, so we have resident go ahead.

NOTE Confidence: 0.581264438

00:58:07.178 --> 00:58:09.748 Yeah this is Jeff Squire.

NOTE Confidence: 0.581264438

 $00{:}58{:}09{.}750 \dashrightarrow 00{:}58{:}12{.}109$ I just wonder you made a comment

NOTE Confidence: 0.581264438

 $00:58:12.109 \longrightarrow 00:58:13.996$ on your introduction that said

- NOTE Confidence: 0.581264438
- $00:58:13.996 \longrightarrow 00:58:15.608$ that no immune intervention.

00:58:15.610 --> 00:58:17.925 No trial has produced any

NOTE Confidence: 0.581264438

 $00:58:17.925 \longrightarrow 00:58:22.090$ effect on cardiac failure.

NOTE Confidence: 0.581264438

 $00:58:22.090 \rightarrow 00:58:24.493$ And I wonder whether there any

NOTE Confidence: 0.581264438

 $00:58:24.493 \rightarrow 00:58:27.298$ observations in patients who receive.

NOTE Confidence: 0.581264438

 $00:58:27.300 \longrightarrow 00:58:28.833$ Chronic immunosuppressive therapy

NOTE Confidence: 0.581264438

 $00:58:28.833 \rightarrow 00:58:31.899$ with any number of different drugs,

NOTE Confidence: 0.581264438

 $00:58:31.900 \longrightarrow 00:58:33.908$ whether there's any effect

NOTE Confidence: 0.581264438

 $00:58:33.908 \longrightarrow 00:58:35.430$ on cardiac failure.

NOTE Confidence: 0.748793660588235

 $00{:}58{:}36{.}180 \dashrightarrow 00{:}58{:}39{.}978$ Yeah, so we did actually have to look at

NOTE Confidence: 0.748793660588235

 $00:58:39.978 \longrightarrow 00:58:43.506$ that because we made a long table of.

NOTE Confidence: 0.748793660588235

 $00:58:43.510 \longrightarrow 00:58:45.826$ Exactly looking at that right of,

NOTE Confidence: 0.748793660588235

 $00{:}58{:}45{.}830 \dashrightarrow 00{:}58{:}48{.}560$ you know, these were the TNF blockers

NOTE Confidence: 0.748793660588235

 $00{:}58{:}48{.}560 \dashrightarrow 00{:}58{:}51{.}344$ and these are other immuno suppressive

NOTE Confidence: 0.748793660588235

 $00{:}58{:}51{.}344 \dashrightarrow 00{:}58{:}54{.}490$ agents and we didn't find any.

 $00{:}58{:}54{.}490 \dashrightarrow 00{:}58{:}55{.}670$ I don't think there's been.

NOTE Confidence: 0.748793660588235

 $00:58:55.670 \rightarrow 00:58:59.165$ There's been a small trials looking at that,

NOTE Confidence: 0.748793660588235

00:58:59.165 --> 00:59:01.835 and I think people have looked

NOTE Confidence: 0.748793660588235

 $00:59:01.835 \rightarrow 00:59:04.646$ at method tracks and other drugs,

NOTE Confidence: 0.748793660588235

 $00{:}59{:}04.646 \dashrightarrow 00{:}59{:}07.292$ but I don't think there's a detail

NOTE Confidence: 0.748793660588235

 $00{:}59{:}07{.}292 \dashrightarrow 00{:}59{:}09{.}001$ investigation of what having the

NOTE Confidence: 0.748793660588235

 $00:59:09.001 \dashrightarrow 00:59:10.897$ expectation would be that if you

NOTE Confidence: 0.748793660588235

 $00:59:10.963 \rightarrow 00:59:13.366$ suppress inflammation it be good, right?

NOTE Confidence: 0.748793660588235

 $00{:}59{:}13.366 \dashrightarrow 00{:}59{:}16.570$ But those drugs also have a lot of side

NOTE Confidence: 0.748793660588235

 $00:59:16.652 \dashrightarrow 00:59:19.515$ effects that may be in patients with.

NOTE Confidence: 0.748793660588235

00:59:19.520 --> 00:59:23.636 Cardiac failure are no quick right,

NOTE Confidence: 0.748793660588235

 $00{:}59{:}23.640 \dashrightarrow 00{:}59{:}26.637$ so I think we really need to dive into

NOTE Confidence: 0.748793660588235

00:59:26.640 --> 00:59:31.660 into not blocking inflammation generally

NOTE Confidence: 0.748793660588235

 $00{:}59{:}31.660 \dashrightarrow 00{:}59{:}34.978$ and try to find a smaller pathways.

NOTE Confidence: 0.854330388518518

 $00:59:36.650 \longrightarrow 00:59:38.684$ I certainly agree, but I just

NOTE Confidence: 0.854330388518518

 $00:59:38.684 \rightarrow 00:59:40.040$ wonder whether there's any

 $00:59:40.104 \longrightarrow 00:59:41.994$ evidence that you know what the

NOTE Confidence: 0.854330388518518

 $00:59:41.994 \longrightarrow 00:59:44.024$ effect of the immune system is

NOTE Confidence: 0.854330388518518

 $00:59:44.024 \longrightarrow 00:59:45.794$ on in clinically and inpatient.

NOTE Confidence: 0.854330388518518

 $00{:}59{:}45{.}800 \dashrightarrow 00{:}59{:}47{.}648$ A lot of patients who get,

NOTE Confidence: 0.854330388518518

 $00:59:47.650 \longrightarrow 00:59:49.760$ you know steroids and get

NOTE Confidence: 0.854330388518518

 $00:59:49.760 \longrightarrow 00:59:51.458$ cyclosporine and other.

NOTE Confidence: 0.79021516

00:59:53.000 - 00:59:54.575 I I don't recall all the details,

NOTE Confidence: 0.79021516

 $00:59:54.580 \rightarrow 00:59:58.873$ but there is a very elegant review by dogmen.

NOTE Confidence: 0.79021516

00:59:58.880 --> 01:00:02.394 And Luigi Adamo that they published recently?

NOTE Confidence: 0.79021516

 $01:00:02.400 \longrightarrow 01:00:03.330$ Maybe? Maybe not.

NOTE Confidence: 0.79021516

 $01{:}00{:}03.330 \dashrightarrow 01{:}00{:}06.020$ That recently, maybe a year ago in Nature,

NOTE Confidence: 0.79021516

01:00:06.020 --> 01:00:09.416 reviews, cardiology, and they have they.

NOTE Confidence: 0.79021516

 $01{:}00{:}09{.}420 \dashrightarrow 01{:}00{:}11{.}108$ They did exactly that,

NOTE Confidence: 0.79021516

 $01{:}00{:}11{.}108 \dashrightarrow 01{:}00{:}13{.}640$ and they reviewed all the literature

NOTE Confidence: 0.79021516

 $01:00:13.715 \rightarrow 01:00:16.480$ in large trials, small trials,

01:00:16.480 --> 01:00:19.720 directly tackling immune mediators,

NOTE Confidence: 0.79021516

 $01{:}00{:}19.720 \dashrightarrow 01{:}00{:}22.498$ or general immuno suppressors. And I,

NOTE Confidence: 0.79021516

01:00:22.500 --> 01:00:26.200 I recall that the conclusion is what I said,

NOTE Confidence: 0.79021516

01:00:26.200 --> 01:00:29.186 but maybe you know, maybe I mean.

NOTE Confidence: 0.79021516

01:00:29.186 --> 01:00:32.417 But I. I think yes, if you have time.

NOTE Confidence: 0.79021516

 $01{:}00{:}32.420 \dashrightarrow 01{:}00{:}35.316$ That review was very detailed and it was. NOTE Confidence: 0.79021516

 $01{:}00{:}35{.}320 \dashrightarrow 01{:}00{:}37{.}906$ It was very nice to to read and they had the

NOTE Confidence: 0.79021516

 $01:00:37.906 \rightarrow 01:00:40.090$ they reviewed the mechanistic part of it,

NOTE Confidence: 0.79021516

 $01{:}00{:}40.090 \dashrightarrow 01{:}00{:}43.420$ but then they review all the patient trials.

NOTE Confidence: 0.79021516

 $01{:}00{:}43.420 \dashrightarrow 01{:}00{:}44.710$ At the end.

NOTE Confidence: 0.79021516

01:00:44.710 --> 01:00:46.936 I believe it was in nature reviews,

NOTE Confidence: 0.79021516

 $01{:}00{:}46.936 \dashrightarrow 01{:}00{:}49.114$ cardiology for sure and I don't

NOTE Confidence: 0.79021516

 $01{:}00{:}49{.}114 \dashrightarrow 01{:}00{:}51{.}771$ know if it was 2020 or 2021.

NOTE Confidence: 0.79021516

01:00:51.771 --> 01:00:52.258 But

NOTE Confidence: 0.759341025

01:00:53.010 --> 01:00:55.278 thank you yeah. Yeah.

NOTE Confidence: 0.813786035333333

 $01{:}00{:}59{.}110 \dashrightarrow 01{:}01{:}01{.}448$ So if if there are no additional

- NOTE Confidence: 0.813786035333333
- $01:01:01.448 \longrightarrow 01:01:03.529$ questions so thank you so much
- NOTE Confidence: 0.813786035333333
- $01:01:03.529 \rightarrow 01:01:05.209$ Paula for this exciting talk.
- NOTE Confidence: 0.813786035333333
- $01{:}01{:}05{.}210 \dashrightarrow 01{:}01{:}07{.}916$ We learn a lot cardiology immunology,
- NOTE Confidence: 0.813786035333333
- $01:01:07.920 \longrightarrow 01:01:09.440$ so thank you very much.
- NOTE Confidence: 0.813786035333333
- 01:01:09.440 --> 01:01:10.920 Have a nice afternoon.
- NOTE Confidence: 0.680113662
- 01:01:11.210 --> 01:01:12.700 Thank you for the invitation.
- NOTE Confidence: 0.680113662
- 01:01:12.700 --> 01:01:15.486 I thank you all for attending bye.
- NOTE Confidence: 0.680113662
- $01:01:15.490 \longrightarrow 01:01:19.000$ Bye bye thank you.