

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 --> 00:00:08.593 Sending a series.

NOTE Confidence: 0.074070364

00:00:08.593 --> 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 --> 00:00:18.611 I met at scientific conferences and I'm

NOTE Confidence: 0.074070364

00:00:18.611 --> 00:00:21.299 impressed by her outstanding mechanistic

NOTE Confidence: 0.074070364

00:00:21.299 --> 00:00:24.644 research in immunology and cardiology.

NOTE Confidence: 0.074070364

00:00:24.650 --> 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 --> 00:00:33.168 Performed her postal research

NOTE Confidence: 0.074070364

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

NOTE Confidence: 0.074070364

00:00:35.580 --> 00:00:36.984 have a medical school.  
NOTE Confidence: 0.074070364

00:00:36.984 --> 00:00:38.739 She studied her faculty position  
NOTE Confidence: 0.074070364

00:00:38.739 --> 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 --> 00:00:45.366 She has been attending  
NOTE Confidence: 0.074070364

00:00:45.366 --> 00:00:47.454 resources professor since 2019.  
NOTE Confidence: 0.074070364

00:00:47.454 --> 00:00:50.958 She's the program director of Immunology  
NOTE Confidence: 0.074070364

00:00:50.958 --> 00:00:54.490 graduate program is an endowed chemist,  
NOTE Confidence: 0.074070364

00:00:54.490 --> 00:00:55.446 and Joann,  
NOTE Confidence: 0.074070364

00:00:55.446 --> 00:00:57.836 where professor and the interim  
NOTE Confidence: 0.074070364

00:00:57.836 --> 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 --> 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 --> 00:01:10.475 Their research efforts are focused  
NOTE Confidence: 0.074070364

00:01:10.475 --> 00:01:13.816 on understanding why and how T cell

NOTE Confidence: 0.074070364

00:01:13.816 --> 00:01:16.066 subsets and in gaseous interaction.

NOTE Confidence: 0.074070364

00:01:16.070 --> 00:01:18.686 They also study intrinsic properties of

NOTE Confidence: 0.074070364

00:01:18.686 --> 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 --> 00:01:27.290 in the T cell trafficking and survival.

NOTE Confidence: 0.074070364

00:01:27.290 --> 00:01:29.174 Another exciting line of risk in

NOTE Confidence: 0.074070364

00:01:29.174 --> 00:01:31.270 class group is about inflammation,

NOTE Confidence: 0.074070364

00:01:31.270 --> 00:01:34.108 heart failure to recent research has

NOTE Confidence: 0.074070364

00:01:34.108 --> 00:01:36.547 contributed significantly to your paradigm

NOTE Confidence: 0.074070364

00:01:36.547 --> 00:01:39.385 shift in understanding of heart failure.

NOTE Confidence: 0.074070364

00:01:39.390 --> 00:01:42.407 Putting T cell inflammation as a measure

NOTE Confidence: 0.074070364

00:01:42.407 --> 00:01:45.979 of player in this heart failure disease.

NOTE Confidence: 0.074070364

00:01:45.980 --> 00:01:48.710 So exciting research program have

NOTE Confidence: 0.074070364

00:01:48.710 --> 00:01:51.440 led to multiple impactful papers

NOTE Confidence: 0.074070364

00:01:51.530 --> 00:01:53.264 such as circulation journal,

NOTE Confidence: 0.074070364

00:01:53.264 --> 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 --> 00:02:00.310 Pillars research has been has  
NOTE Confidence: 0.074070364

00:02:00.310 --> 00:02:03.400 been funded by NIH one brand.  
NOTE Confidence: 0.074070364

00:02:03.400 --> 00:02:05.899 She has also showed great leadership in  
NOTE Confidence: 0.074070364

00:02:05.899 --> 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 --> 00:02:13.792 Fast, GMC and etc.  
NOTE Confidence: 0.074070364

00:02:13.792 --> 00:02:14.620 Additionally,  
NOTE Confidence: 0.074070364

00:02:14.620 --> 00:02:17.553 she has been serving the American Heart  
NOTE Confidence: 0.074070364

00:02:17.553 --> 00:02:19.610 Association during past many years.  
NOTE Confidence: 0.074070364

00:02:19.610 --> 00:02:22.484 She has been the HCA basic cardiovascular  
NOTE Confidence: 0.074070364

00:02:22.484 --> 00:02:25.556 Science program chair since last year.  
NOTE Confidence: 0.074070364

00:02:25.560 --> 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 --> 00:02:30.725 To give us her seminar entitled T

NOTE Confidence: 0.074070364

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

NOTE Confidence: 0.074070364

00:02:33.346 --> 00:02:35.698 of heart failure, can I thank you?

NOTE Confidence: 0.67076522

00:02:36.510 --> 00:02:38.002 Thank you very much.

NOTE Confidence: 0.67076522

00:02:38.002 --> 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 --> 00:02:47.962 thank you to all those of you who

NOTE Confidence: 0.67076522

00:02:47.962 --> 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 --> 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 --> 00:02:57.998 So as giving said,

NOTE Confidence: 0.67076522

00:02:57.998 --> 00:03:01.347 I'm going to focus today's talk on the

NOTE Confidence: 0.67076522

00:03:01.347 --> 00:03:04.268 aspect in the lab where we study the

NOTE Confidence: 0.67076522

00:03:04.268 --> 00:03:06.774 role of T cells in the pathophysiology.

NOTE Confidence: 0.67076522

00:03:06.780 --> 00:03:10.518 Of heart failure I have no disclosures

NOTE Confidence: 0.67076522

00:03:10.520 --> 00:03:14.209 and basically this is a cartoon that  
NOTE Confidence: 0.67076522

00:03:14.209 --> 00:03:16.516 summarizes the general theme of our lab,  
NOTE Confidence: 0.67076522

00:03:16.520 --> 00:03:19.103 which is how the moon system impacts  
NOTE Confidence: 0.67076522

00:03:19.103 --> 00:03:20.730 cardiac and vascular health.  
NOTE Confidence: 0.67076522

00:03:20.730 --> 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 --> 00:03:27.439 further train in vascular biology,  
NOTE Confidence: 0.67076522

00:03:27.440 --> 00:03:30.848 but we know that immune cells  
NOTE Confidence: 0.67076522

00:03:30.850 --> 00:03:33.346 they really need to traffic into  
NOTE Confidence: 0.67076522

00:03:33.346 --> 00:03:35.890 tissues to do their functions.  
NOTE Confidence: 0.67076522

00:03:35.890 --> 00:03:37.210 But then once.  
NOTE Confidence: 0.67076522

00:03:37.210 --> 00:03:38.090 In addition,  
NOTE Confidence: 0.67076522

00:03:38.090 --> 00:03:41.688 they need to interact or crosstalk with  
NOTE Confidence: 0.67076522

00:03:41.688 --> 00:03:45.769 all the different resident cells in order  
NOTE Confidence: 0.67076522

00:03:45.769 --> 00:03:48.824 to modulate homeostasis or pathology.  
NOTE Confidence: 0.67076522

00:03:48.830 --> 00:03:50.510 In the case of injury.

NOTE Confidence: 0.67076522

00:03:50.510 --> 00:03:51.670 So for today's talk,

NOTE Confidence: 0.67076522

00:03:51.670 --> 00:03:53.787 I will focus on what we've been

NOTE Confidence: 0.67076522

00:03:53.787 --> 00:03:55.671 learning recently in the lab from

NOTE Confidence: 0.67076522

00:03:55.671 --> 00:03:57.834 our work and also from the work

NOTE Confidence: 0.67076522

00:03:57.834 --> 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 --> 00:04:06.430 contributes to cardiac remodeling.

NOTE Confidence: 0.67076522

00:04:06.430 --> 00:04:09.764 In hard and I I place a circle

NOTE Confidence: 0.67076522

00:04:09.764 --> 00:04:11.920 here because this is mainly where

NOTE Confidence: 0.67076522

00:04:11.920 --> 00:04:13.728 these interactions between adapted

NOTE Confidence: 0.67076522

00:04:13.728 --> 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 --> 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 --> 00:04:25.761 will show some new data is still

NOTE Confidence: 0.67076522

00:04:25.761 --> 00:04:27.754 unpublished where we really find that

NOTE Confidence: 0.67076522

00:04:27.754 --> 00:04:29.230 they're very similar interactions

NOTE Confidence: 0.67076522

00:04:29.230 --> 00:04:31.494 that are also happening in the

NOTE Confidence: 0.67076522

00:04:31.494 --> 00:04:33.978 heart and that they might modulate

NOTE Confidence: 0.67076522

00:04:33.978 --> 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 --> 00:04:40.904 and it's multifactorial.

NOTE Confidence: 0.67076522

00:04:40.910 --> 00:04:42.354 So to tackle mechanisms,

NOTE Confidence: 0.67076522

00:04:42.354 --> 00:04:45.780 we need to start in a simplistic way.

NOTE Confidence: 0.67076522

00:04:45.780 --> 00:04:48.006 But we also need to understand

NOTE Confidence: 0.67076522

00:04:48.006 --> 00:04:49.119 the full complexity.

NOTE Confidence: 0.67076522

00:04:49.120 --> 00:04:51.227 So what do we know is that

NOTE Confidence: 0.67076522

00:04:51.227 --> 00:04:52.820 regardless of the etiology,

NOTE Confidence: 0.67076522

00:04:52.820 --> 00:04:54.380 whether it was triggered

NOTE Confidence: 0.67076522

00:04:54.380 --> 00:04:55.940 by any ischemic event,



NOTE Confidence: 0.67076522

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

NOTE Confidence: 0.67076522

00:04:59.056 --> 00:05:01.488 or non ischemic event.

NOTE Confidence: 0.67076522

00:05:01.490 --> 00:05:04.388 The heart remodels and the characteristics

NOTE Confidence: 0.67076522

00:05:04.388 --> 00:05:07.469 of the failing heart are increased.

NOTE Confidence: 0.67076522

00:05:07.470 --> 00:05:11.000 High level curricular pressures and

NOTE Confidence: 0.67076522

00:05:11.000 --> 00:05:13.824 then a hypertrophic cardiomyocytes

NOTE Confidence: 0.67076522

00:05:13.824 --> 00:05:16.770 fibrosis and these results in

NOTE Confidence: 0.67076522

00:05:16.770 --> 00:05:19.010 systolic and diastolic dysfunction.

NOTE Confidence: 0.67076522

00:05:19.010 --> 00:05:21.978 And we've known since the 50s that

NOTE Confidence: 0.67076522

00:05:21.978 --> 00:05:23.250 systemic chronic inflammation

NOTE Confidence: 0.67076522

00:05:23.321 --> 00:05:25.306 is associated with pretty much

NOTE Confidence: 0.67076522

00:05:25.310 --> 00:05:28.262 all of the causes of all of the

NOTE Confidence: 0.67076522

00:05:28.262 --> 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 --> 00:05:33.417 here to make sure that we're.

NOTE Confidence: 0.67076522

00:05:33.420 --> 00:05:35.140 Runtime here.  
NOTE Confidence: 0.67076522

00:05:35.140 --> 00:05:37.180 But unfortunately this by this knowledge,  
NOTE Confidence: 0.67076522

00:05:37.180 --> 00:05:37.990 for many,  
NOTE Confidence: 0.67076522

00:05:37.990 --> 00:05:40.420 many years today none of the  
NOTE Confidence: 0.67076522

00:05:40.420 --> 00:05:42.035 anti-inflammatory therapies for clinical  
NOTE Confidence: 0.67076522

00:05:42.035 --> 00:05:43.875 trials that were initially launched  
NOTE Confidence: 0.67076522

00:05:43.875 --> 00:05:46.709 to tackle a pro inflammatory cytokines,  
NOTE Confidence: 0.67076522

00:05:46.710 --> 00:05:48.030 such as TNF.  
NOTE Confidence: 0.67076522

00:05:48.030 --> 00:05:49.350 And more recently,  
NOTE Confidence: 0.67076522

00:05:49.350 --> 00:05:50.630 with the counters trial  
NOTE Confidence: 0.67076522

00:05:50.630 --> 00:05:52.550 island bed and none of them,  
NOTE Confidence: 0.67076522

00:05:52.550 --> 00:05:54.680 this is the anti TNF therapies  
NOTE Confidence: 0.67076522

00:05:54.680 --> 00:05:57.121 that are very efficient in treating  
NOTE Confidence: 0.67076522

00:05:57.121 --> 00:05:59.496 out immune diseases and chronic  
NOTE Confidence: 0.67076522

00:05:59.496 --> 00:06:01.252 inflammatory diseases did not  
NOTE Confidence: 0.67076522

00:06:01.252 --> 00:06:03.648 work in heart failure and there

NOTE Confidence: 0.67076522

00:06:03.648 --> 00:06:04.830 are more recent

NOTE Confidence: 0.600763616666667

00:06:04.830 --> 00:06:07.710 promising data with the Cantor's trial,

NOTE Confidence: 0.600763616666667

00:06:07.710 --> 00:06:10.128 although it's still early to tell

NOTE Confidence: 0.600763616666667

00:06:10.130 --> 00:06:12.818 whether it has really benefited in in

NOTE Confidence: 0.600763616666667

00:06:12.818 --> 00:06:16.087 some of the outcomes of heart failure.

NOTE Confidence: 0.600763616666667

00:06:16.090 --> 00:06:19.267 So what we know is that there are no

NOTE Confidence: 0.600763616666667

00:06:19.267 --> 00:06:20.718 anti-inflammatory antifibrotic therapies

NOTE Confidence: 0.600763616666667

00:06:20.718 --> 00:06:23.288 that have been successful today,

NOTE Confidence: 0.600763616666667

00:06:23.290 --> 00:06:26.468 and we know from many organ systems

NOTE Confidence: 0.600763616666667

00:06:26.468 --> 00:06:29.046 that inflammation or immune cell

NOTE Confidence: 0.600763616666667

00:06:29.046 --> 00:06:32.232 activation and fibrosis go together or

NOTE Confidence: 0.600763616666667

00:06:32.232 --> 00:06:35.196 have some overlapping functions as well.

NOTE Confidence: 0.600763616666667

00:06:35.200 --> 00:06:37.324 So the first question that we

NOTE Confidence: 0.600763616666667

00:06:37.324 --> 00:06:39.280 asked several years ago was is,

NOTE Confidence: 0.600763616666667

00:06:39.280 --> 00:06:41.100 is there cardiac information?

NOTE Confidence: 0.600763616666667

00:06:41.100 --> 00:06:42.920 Besides systemic chronic inflammation  
NOTE Confidence: 0.600763616666667

00:06:42.920 --> 00:06:45.814 again going with the concept that if the  
NOTE Confidence: 0.600763616666667

00:06:45.814 --> 00:06:48.313 immune cells traffic to an inflamed issue,  
NOTE Confidence: 0.600763616666667

00:06:48.320 --> 00:06:51.296 do they exert their functions by  
NOTE Confidence: 0.600763616666667

00:06:51.296 --> 00:06:53.280 communicating with the tissue  
NOTE Confidence: 0.600763616666667

00:06:53.360 --> 00:06:54.638 or stroma cells?  
NOTE Confidence: 0.600763616666667

00:06:54.640 --> 00:06:56.789 And then if that was the case,  
NOTE Confidence: 0.600763616666667

00:06:56.790 --> 00:06:58.585 do the cardiac infiltrated muscles  
NOTE Confidence: 0.600763616666667

00:06:58.585 --> 00:07:00.021 contribute to the hallmarks  
NOTE Confidence: 0.600763616666667

00:07:00.021 --> 00:07:01.726 that we see of heart failure,  
NOTE Confidence: 0.600763616666667

00:07:01.730 --> 00:07:03.030 such as correct fibrosis?  
NOTE Confidence: 0.600763616666667

00:07:03.030 --> 00:07:04.980 And does that have any impact  
NOTE Confidence: 0.600763616666667

00:07:05.040 --> 00:07:06.399 on cardiac dysfunction?  
NOTE Confidence: 0.600763616666667

00:07:06.400 --> 00:07:10.012 And obviously we're very interested as  
NOTE Confidence: 0.600763616666667

00:07:10.012 --> 00:07:12.840 basic scientists in understanding how.  
NOTE Confidence: 0.600763616666667

00:07:12.840 --> 00:07:14.625 So the first experiment that we did

NOTE Confidence: 0.600763616666667

00:07:14.625 --> 00:07:16.460 this this is this was published.

NOTE Confidence: 0.600763616666667

00:07:16.460 --> 00:07:18.660 This is back in 2015,

NOTE Confidence: 0.600763616666667

00:07:18.660 --> 00:07:21.586 but we wanted to say whether we

NOTE Confidence: 0.600763616666667

00:07:21.586 --> 00:07:23.950 could see cardiac inflammation

NOTE Confidence: 0.600763616666667

00:07:23.950 --> 00:07:25.460 in patients with heart failure,

NOTE Confidence: 0.600763616666667

00:07:25.460 --> 00:07:27.609 but we wanted to look at patients

NOTE Confidence: 0.600763616666667

00:07:27.609 --> 00:07:29.440 with non ischemic heart failure.

NOTE Confidence: 0.600763616666667

00:07:29.440 --> 00:07:32.737 Antonio Barish group at VCU in Virginia.

NOTE Confidence: 0.600763616666667

00:07:32.740 --> 00:07:34.144 He had elegantly demonstrated

NOTE Confidence: 0.600763616666667

00:07:34.144 --> 00:07:36.250 years before this that in response

NOTE Confidence: 0.600763616666667

00:07:36.308 --> 00:07:37.679 to myocardial infarction,

NOTE Confidence: 0.600763616666667

00:07:37.680 --> 00:07:39.865 there was decent infiltration in

NOTE Confidence: 0.600763616666667

00:07:39.865 --> 00:07:42.304 the human heart and interestingly.

NOTE Confidence: 0.600763616666667

00:07:42.304 --> 00:07:45.676 The diesels were infiltrated in the

NOTE Confidence: 0.600763616666667

00:07:45.676 --> 00:07:49.182 in the scar zone in the infarct zone,

NOTE Confidence: 0.600763616666667

00:07:49.182 --> 00:07:49.908 but also,  
NOTE Confidence: 0.600763616666667

00:07:49.910 --> 00:07:52.806 so that goes along with a roll of  
NOTE Confidence: 0.600763616666667

00:07:52.806 --> 00:07:55.263 the immune system during evolution  
NOTE Confidence: 0.600763616666667

00:07:55.263 --> 00:07:56.910 to help healing.  
NOTE Confidence: 0.600763616666667

00:07:56.910 --> 00:07:57.572 But interestingly,  
NOTE Confidence: 0.600763616666667

00:07:57.572 --> 00:07:59.558 what they had found in inference  
NOTE Confidence: 0.600763616666667

00:07:59.558 --> 00:08:02.137 was that there were also a lot of T  
NOTE Confidence: 0.600763616666667

00:08:02.137 --> 00:08:03.709 cells infiltrated and remote zones.  
NOTE Confidence: 0.600763616666667

00:08:03.710 --> 00:08:05.870 So we thought if we chose a patients  
NOTE Confidence: 0.600763616666667

00:08:05.870 --> 00:08:08.126 that did not have any impact that have  
NOTE Confidence: 0.600763616666667

00:08:08.126 --> 00:08:10.550 sort of like low chronic inflammation,  
NOTE Confidence: 0.600763616666667

00:08:10.550 --> 00:08:12.362 where we see these as infiltrated  
NOTE Confidence: 0.600763616666667

00:08:12.362 --> 00:08:13.268 in the heart.  
NOTE Confidence: 0.600763616666667

00:08:13.270 --> 00:08:15.524 And this is exactly what we found  
NOTE Confidence: 0.600763616666667

00:08:15.524 --> 00:08:18.254 here in Brown that they end stage  
NOTE Confidence: 0.600763616666667

00:08:18.254 --> 00:08:20.018 nonischemic heart failure and

NOTE Confidence: 0.600763616666667  
00:08:20.018 --> 00:08:22.410 heart samples which were taken as  
NOTE Confidence: 0.600763616666667  
00:08:22.410 --> 00:08:26.054 stated here from from there had  
NOTE Confidence: 0.600763616666667  
00:08:26.054 --> 00:08:27.620 significant diesel infiltration.  
NOTE Confidence: 0.600763616666667  
00:08:27.620 --> 00:08:31.058 Compared to non heart failure controls.  
NOTE Confidence: 0.600763616666667  
00:08:31.060 --> 00:08:33.349 And later on we did some experiments  
NOTE Confidence: 0.600763616666667  
00:08:33.349 --> 00:08:36.200 where we also wanted to look at what  
NOTE Confidence: 0.600763616666667  
00:08:36.200 --> 00:08:38.460 kind of pistols were infiltrated there,  
NOTE Confidence: 0.600763616666667  
00:08:38.460 --> 00:08:41.043 and we found that many of those  
NOTE Confidence: 0.600763616666667  
00:08:41.043 --> 00:08:42.932 teachers expressed the chemo keen  
NOTE Confidence: 0.600763616666667  
00:08:42.932 --> 00:08:46.280 receptor CXCR 3 and this is shown here  
NOTE Confidence: 0.600763616666667  
00:08:46.280 --> 00:08:49.100 by Red Arrows and quantified here.  
NOTE Confidence: 0.600763616666667  
00:08:49.100 --> 00:08:51.991 So this this made the basis to  
NOTE Confidence: 0.600763616666667  
00:08:51.991 --> 00:08:53.895 wanted to understand mechanistically  
NOTE Confidence: 0.600763616666667  
00:08:53.895 --> 00:08:57.351 what is thesis that expressed these  
NOTE Confidence: 0.600763616666667  
00:08:57.351 --> 00:09:00.538 receptors are doing within the heart.  
NOTE Confidence: 0.600763616666667

00:09:00.540 --> 00:09:02.770 So our very broad hypothesis.  
NOTE Confidence: 0.600763616666667

00:09:02.770 --> 00:09:05.661 110 and Evers joined my lab as  
NOTE Confidence: 0.600763616666667

00:09:05.661 --> 00:09:07.528 postdoc was asking the question,  
NOTE Confidence: 0.600763616666667

00:09:07.528 --> 00:09:09.604 is this purely an association or  
NOTE Confidence: 0.600763616666667

00:09:09.604 --> 00:09:11.634 are they actually contributing or  
NOTE Confidence: 0.600763616666667

00:09:11.634 --> 00:09:14.518 doing something in the heart and her  
NOTE Confidence: 0.600763616666667

00:09:14.518 --> 00:09:16.440 hypothesis was that they would be  
NOTE Confidence: 0.600763616666667

00:09:16.440 --> 00:09:20.115 doing something there in the failing heart?  
NOTE Confidence: 0.600763616666667

00:09:20.120 --> 00:09:22.656 And to start doing this we have to  
NOTE Confidence: 0.600763616666667

00:09:22.656 --> 00:09:25.144 choose a preclinical model and knowing  
NOTE Confidence: 0.600763616666667

00:09:25.144 --> 00:09:26.716 that heart failure is very complex,  
NOTE Confidence: 0.600763616666667

00:09:26.720 --> 00:09:30.950 there's no optimal or perfect.  
NOTE Confidence: 0.7375429225

00:09:30.950 --> 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 --> 00:09:37.750 or how the disease develops,  
NOTE Confidence: 0.7375429225

00:09:37.750 --> 00:09:39.952 but we found that for nonischemic



NOTE Confidence: 0.7375429225

00:09:39.952 --> 00:09:43.090 heart failure tack or transverse or

NOTE Confidence: 0.7375429225

00:09:43.090 --> 00:09:46.644 reconstruction was a one where we could time,

NOTE Confidence: 0.7375429225

00:09:46.650 --> 00:09:47.590 and for certain reasons,

NOTE Confidence: 0.7375429225

00:09:47.590 --> 00:09:48.765 that we wanted to do.

NOTE Confidence: 0.7375429225

00:09:48.770 --> 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 --> 00:09:58.210 failure patients have in the heart.

NOTE Confidence: 0.7375429225

00:09:58.210 --> 00:10:00.658 Although the downside is that here.

NOTE Confidence: 0.7375429225

00:10:00.658 --> 00:10:03.514 It induces a sudden pressure that then

NOTE Confidence: 0.7375429225

00:10:03.514 --> 00:10:05.930 is restrained versus impatience as

NOTE Confidence: 0.7375429225

00:10:05.930 --> 00:10:08.480 we know they developed progressively,

NOTE Confidence: 0.7375429225

00:10:08.480 --> 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 --> 00:10:15.377 nicely how cardiac hypertrophy develops,

NOTE Confidence: 0.7375429225

00:10:15.380 --> 00:10:16.872 how cardiac fibrosis develops,  
NOTE Confidence: 0.7375429225

00:10:16.872 --> 00:10:19.918 and whether we can check in per cardiac  
NOTE Confidence: 0.7375429225

00:10:19.918 --> 00:10:22.138 function and at those time points.  
NOTE Confidence: 0.7375429225

00:10:22.140 --> 00:10:24.884 We could also look for diesel immune  
NOTE Confidence: 0.7375429225

00:10:24.884 --> 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 --> 00:10:32.405 from 4 weeks. Play time points.  
NOTE Confidence: 0.7375429225

00:10:32.405 --> 00:10:34.530 That is all summarizing schematics.  
NOTE Confidence: 0.7375429225

00:10:34.530 --> 00:10:37.810 Because we published this already.  
NOTE Confidence: 0.7375429225

00:10:37.810 --> 00:10:40.477 But what we found was that it  
NOTE Confidence: 0.7375429225

00:10:40.477 --> 00:10:42.363 specifically one type of thesis  
NOTE Confidence: 0.7375429225

00:10:42.363 --> 00:10:44.687 that are CD 4 positive T cells  
NOTE Confidence: 0.7375429225

00:10:44.690 --> 00:10:46.262 were infiltrated in the heart as  
NOTE Confidence: 0.7375429225

00:10:46.262 --> 00:10:47.930 early as two weeks post stack.  
NOTE Confidence: 0.7375429225

00:10:47.930 --> 00:10:50.779 And this is four weeks after Tak.  
NOTE Confidence: 0.7375429225

00:10:50.780 --> 00:10:51.464 And then,

NOTE Confidence: 0.7375429225

00:10:51.464 --> 00:10:53.516 before they infiltrated in the heart,

NOTE Confidence: 0.7375429225

00:10:53.520 --> 00:10:55.907 we saw a significant expansion of the

NOTE Confidence: 0.7375429225

00:10:55.907 --> 00:10:57.828 medicinale draining lymph nodes that are

NOTE Confidence: 0.7375429225

00:10:57.828 --> 00:10:59.795 the lymph nodes that drain the heart.

NOTE Confidence: 0.7375429225

00:10:59.800 --> 00:11:02.957 And most of those T cells express

NOTE Confidence: 0.7375429225

00:11:02.957 --> 00:11:05.546 interferon gamma so they were type

NOTE Confidence: 0.7375429225

00:11:05.546 --> 00:11:09.126 one TT cells T H1 cells which also

NOTE Confidence: 0.7375429225

00:11:09.126 --> 00:11:11.018 expressed the chemokine receptor.

NOTE Confidence: 0.7375429225

00:11:11.020 --> 00:11:13.480 6 year 3.

NOTE Confidence: 0.7375429225

00:11:13.480 --> 00:11:15.784 And then we found that these

NOTE Confidence: 0.7375429225

00:11:15.784 --> 00:11:18.147 infiltration was associated with at the

NOTE Confidence: 0.7375429225

00:11:18.147 --> 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 --> 00:11:23.750 the collagen deposition and enlargement

NOTE Confidence: 0.7375429225

00:11:23.750 --> 00:11:27.410 of the cardiac myocytes by H&E.

NOTE Confidence: 0.7375429225

00:11:27.410 --> 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 --> 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 --> 00:11:41.609 knockout or right to knock out what  
NOTE Confidence: 0.7375429225

00:11:41.609 --> 00:11:44.415 we found was that all the mice that  
NOTE Confidence: 0.7375429225

00:11:44.415 --> 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 --> 00:11:51.080 We cannot see any College in  
NOTE Confidence: 0.7375429225

00:11:51.080 --> 00:11:52.085 the position here.  
NOTE Confidence: 0.7375429225

00:11:52.090 --> 00:11:54.449 And then when these mice were reconstituted,  
NOTE Confidence: 0.7375429225

00:11:54.450 --> 00:11:56.454 we see Excel 3 positive there  
NOTE Confidence: 0.7375429225

00:11:56.454 --> 00:11:57.456 from gamma positive.  
NOTE Confidence: 0.7375429225

00:11:57.460 --> 00:11:59.528 Keystones we could partially  
NOTE Confidence: 0.7375429225

00:11:59.528 --> 00:12:01.079 reconstitute the fibrosis.

NOTE Confidence: 0.7375429225  
00:12:01.080 --> 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 --> 00:12:06.680 and we could reconstitute and or  
NOTE Confidence: 0.7375429225  
00:12:06.680 --> 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 --> 00:12:14.919 that there had to be some cardiac  
NOTE Confidence: 0.7375429225  
00:12:14.919 --> 00:12:17.175 antigen specificity involved to  
NOTE Confidence: 0.7375429225  
00:12:17.175 --> 00:12:19.425 to induce the full induction of  
NOTE Confidence: 0.7375429225  
00:12:19.425 --> 00:12:21.440 cardiac fibrosis and dysfunction.  
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 --> 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 --> 00:12:29.130 and diastolic dysfunction.  
NOTE Confidence: 0.7375429225  
00:12:29.130 --> 00:12:31.494 But these cells that we put  
NOTE Confidence: 0.7375429225  
00:12:31.494 --> 00:12:33.070 back into these mice,  
NOTE Confidence: 0.7375429225

00:12:33.070 --> 00:12:34.830 they were highly painful.  
NOTE Confidence: 0.7375429225

00:12:34.830 --> 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 --> 00:12:42.763 talk and why that might be important.  
NOTE Confidence: 0.7375429225

00:12:42.770 --> 00:12:46.721 How we can use that in in in to  
NOTE Confidence: 0.7375429225

00:12:46.721 --> 00:12:49.569 understand this complex syndrome.  
NOTE Confidence: 0.7375429225

00:12:49.570 --> 00:12:51.523 So the other thing that I needed  
NOTE Confidence: 0.7375429225

00:12:51.523 --> 00:12:52.360 was well now  
NOTE Confidence: 0.713985236956522

00:12:52.430 --> 00:12:55.058 that we know that these T cells that express  
NOTE Confidence: 0.713985236956522

00:12:55.058 --> 00:12:58.414 in there from gamma are increasing the  
NOTE Confidence: 0.713985236956522

00:12:58.414 --> 00:13:02.050 lymph nodes under infiltrated in the heart.  
NOTE Confidence: 0.713985236956522

00:13:02.050 --> 00:13:05.114 How can we see if they actually cross  
NOTE Confidence: 0.713985236956522

00:13:05.114 --> 00:13:07.378 communicate with a cardiac residents?  
NOTE Confidence: 0.713985236956522

00:13:07.380 --> 00:13:09.185 Because we saw that massive  
NOTE Confidence: 0.713985236956522

00:13:09.185 --> 00:13:10.629 effect on cardiac fibrosis.  
NOTE Confidence: 0.713985236956522

00:13:10.630 --> 00:13:12.718 We see it was a simple

NOTE Confidence: 0.713985236956522  
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 --> 00:13:18.268 correct fiberglass from Adele mites  
NOTE Confidence: 0.713985236956522  
00:13:18.270 --> 00:13:20.628 and then see isolated T cells.  
NOTE Confidence: 0.713985236956522  
00:13:20.630 --> 00:13:22.790 From the mediastinal lymph nodes of  
NOTE Confidence: 0.713985236956522  
00:13:22.790 --> 00:13:25.190 mice that were subjected to either sham,  
NOTE Confidence: 0.713985236956522  
00:13:25.190 --> 00:13:26.630 so control surgery,  
NOTE Confidence: 0.713985236956522  
00:13:26.630 --> 00:13:30.360 I should say that some might have the  
NOTE Confidence: 0.713985236956522  
00:13:30.360 --> 00:13:33.300 the open chest surgery and everything  
NOTE Confidence: 0.713985236956522  
00:13:33.300 --> 00:13:35.888 except for the construction to  
NOTE Confidence: 0.713985236956522  
00:13:35.888 --> 00:13:38.068 account for possible inflammation  
NOTE Confidence: 0.713985236956522  
00:13:38.068 --> 00:13:40.248 that happens during surgery.  
NOTE Confidence: 0.713985236956522  
00:13:40.250 --> 00:13:42.738 I know what you did is the Chico  
NOTE Confidence: 0.713985236956522  
00:13:42.738 --> 00:13:45.125 culture this and then she she  
NOTE Confidence: 0.713985236956522  
00:13:45.125 --> 00:13:47.235 coculture this indirect cultures or  
NOTE Confidence: 0.713985236956522

00:13:47.235 --> 00:13:49.300 entrance once and the idea was that  
NOTE Confidence: 0.713985236956522

00:13:49.300 --> 00:13:51.330 first he was going to see whether  
NOTE Confidence: 0.713985236956522

00:13:51.330 --> 00:13:53.900 these teasers could adhere to the  
NOTE Confidence: 0.713985236956522

00:13:53.900 --> 00:13:56.022 fibroblast and whether these fiberglass  
NOTE Confidence: 0.713985236956522

00:13:56.022 --> 00:13:58.112 transform to myofibroblast and to  
NOTE Confidence: 0.713985236956522

00:13:58.112 --> 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 --> 00:14:07.190 acting which is expressed upon  
NOTE Confidence: 0.713985236956522

00:14:07.190 --> 00:14:09.395 fiber restaurants formation.  
NOTE Confidence: 0.713985236956522

00:14:09.400 --> 00:14:10.820 So in those experiments,  
NOTE Confidence: 0.713985236956522

00:14:10.820 --> 00:14:12.595 this is a representative image.  
NOTE Confidence: 0.713985236956522

00:14:12.600 --> 00:14:15.200 You can see that a direct contact was  
NOTE Confidence: 0.713985236956522

00:14:15.200 --> 00:14:17.279 required for these transformation,  
NOTE Confidence: 0.713985236956522

00:14:17.280 --> 00:14:19.560 so these are two examples of  
NOTE Confidence: 0.713985236956522

00:14:19.560 --> 00:14:21.422 transform my fiberglass that have  
NOTE Confidence: 0.713985236956522

00:14:21.422 --> 00:14:23.558 a lot of T cells bound to them.



NOTE Confidence: 0.713985236956522  
00:14:23.560 --> 00:14:27.448 The T cells were labeled in in green here  
NOTE Confidence: 0.713985236956522  
00:14:27.448 --> 00:14:31.060 and this is the quantification of the  
NOTE Confidence: 0.713985236956522  
00:14:31.168 --> 00:14:35.290 of of the red of alpha small muscle acting.  
NOTE Confidence: 0.713985236956522  
00:14:35.290 --> 00:14:36.840 So the conclusion from these  
NOTE Confidence: 0.713985236956522  
00:14:36.840 --> 00:14:38.390 experiments was that there was  
NOTE Confidence: 0.713985236956522  
00:14:38.445 --> 00:14:39.969 these communications between.  
NOTE Confidence: 0.713985236956522  
00:14:39.970 --> 00:14:43.138 Pieces of fiberglass that was required  
NOTE Confidence: 0.713985236956522  
00:14:43.138 --> 00:14:45.843 to induce transformation and then a  
NOTE Confidence: 0.713985236956522  
00:14:45.843 --> 00:14:47.698 mechanistically what we found was  
NOTE Confidence: 0.713985236956522  
00:14:47.698 --> 00:14:50.089 that this was TGF beta dependent,  
NOTE Confidence: 0.713985236956522  
00:14:50.090 --> 00:14:51.710 so it will block TGF beta.  
NOTE Confidence: 0.713985236956522  
00:14:51.710 --> 00:14:54.130 We inhibited this transformation that  
NOTE Confidence: 0.713985236956522  
00:14:54.130 --> 00:14:57.266 was not too surprising because we know  
NOTE Confidence: 0.713985236956522  
00:14:57.266 --> 00:15:00.164 that PDF better was it's a classic  
NOTE Confidence: 0.713985236956522  
00:15:00.164 --> 00:15:02.854 profit garlic cytokine that induces.  
NOTE Confidence: 0.713985236956522

00:15:02.860 --> 00:15:04.605 This transformation and that is  
NOTE Confidence: 0.713985236956522

00:15:04.605 --> 00:15:06.880 highly made by my fiberglass as well,  
NOTE Confidence: 0.713985236956522

00:15:06.880 --> 00:15:08.800 but what was more interesting is  
NOTE Confidence: 0.713985236956522

00:15:08.800 --> 00:15:11.520 that we found that T cells bound to  
NOTE Confidence: 0.713985236956522

00:15:11.520 --> 00:15:13.680 the fiber rest through A4 integrin,  
NOTE Confidence: 0.713985236956522

00:15:13.680 --> 00:15:16.396 and we come one in the fiberglass  
NOTE Confidence: 0.713985236956522

00:15:16.400 --> 00:15:17.972 and then once bound,  
NOTE Confidence: 0.713985236956522

00:15:17.972 --> 00:15:20.826 the diesels were induced and DJ better  
NOTE Confidence: 0.713985236956522

00:15:20.826 --> 00:15:23.322 released by the myofibrils are not  
NOTE Confidence: 0.713985236956522

00:15:23.322 --> 00:15:26.256 the other way around and this was also  
NOTE Confidence: 0.713985236956522

00:15:26.256 --> 00:15:28.290 published so I wouldn't show a lot  
NOTE Confidence: 0.713985236956522

00:15:28.290 --> 00:15:30.405 of the data there so I can focus on  
NOTE Confidence: 0.713985236956522

00:15:30.468 --> 00:15:32.817 more recent data in in our lab as well.  
NOTE Confidence: 0.713985236956522

00:15:32.820 --> 00:15:35.535 We're currently working on on  
NOTE Confidence: 0.713985236956522

00:15:35.535 --> 00:15:37.164 further mechanistic insight  
NOTE Confidence: 0.713985236956522

00:15:37.164 --> 00:15:39.978 into how we can prevent this.

NOTE Confidence: 0.713985236956522

00:15:39.980 --> 00:15:42.818 They released induced by the FIBERLESS

NOTE Confidence: 0.713985236956522

00:15:42.818 --> 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 --> 00:15:52.539 we can see that in this transformation

NOTE Confidence: 0.713985236956522

00:15:52.539 --> 00:15:55.271 from the healthy heart to the failing

NOTE Confidence: 0.713985236956522

00:15:55.271 --> 00:15:57.256 heart using an experimental model,

NOTE Confidence: 0.713985236956522

00:15:57.260 --> 00:15:59.930 in this case of transverse article

NOTE Confidence: 0.713985236956522

00:15:59.930 --> 00:16:01.766 struction visit this activation,

NOTE Confidence: 0.713985236956522

00:16:01.766 --> 00:16:04.538 particularly of this T cell subset.

NOTE Confidence: 0.713985236956522

00:16:04.540 --> 00:16:06.628 And then we say that these are traffic

NOTE Confidence: 0.713985236956522

00:16:06.628 --> 00:16:08.839 to the heart and once in the heart.

NOTE Confidence: 0.713985236956522

00:16:08.840 --> 00:16:11.312 They crossed off with a fiberglass

NOTE Confidence: 0.713985236956522

00:16:11.312 --> 00:16:12.960 and induced cardiac fibrosis.

NOTE Confidence: 0.656873219076923

00:16:12.960 --> 00:16:15.774 We block these by either using

NOTE Confidence: 0.656873219076923

00:16:15.774 --> 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 --> 00:16:23.200 antibodies in wild I'm eyes.  
NOTE Confidence: 0.656873219076923

00:16:23.200 --> 00:16:25.176 I didn't show the data by the way.  
NOTE Confidence: 0.656873219076923

00:16:25.180 --> 00:16:26.840 We also did those studies.  
NOTE Confidence: 0.656873219076923

00:16:26.840 --> 00:16:30.308 We prevent this transformation.  
NOTE Confidence: 0.656873219076923

00:16:30.310 --> 00:16:34.558 We also found that the characters  
NOTE Confidence: 0.656873219076923

00:16:34.558 --> 00:16:36.918 themselves they in response to  
NOTE Confidence: 0.656873219076923

00:16:36.918 --> 00:16:39.390 pressure in response to duck even  
NOTE Confidence: 0.656873219076923

00:16:39.473 --> 00:16:41.729 before the T cells get there,  
NOTE Confidence: 0.656873219076923

00:16:41.730 --> 00:16:44.610 they can actually make chemokines that  
NOTE Confidence: 0.656873219076923

00:16:44.610 --> 00:16:47.480 Kim attracts positive T cells and we  
NOTE Confidence: 0.656873219076923

00:16:47.480 --> 00:16:50.265 did this using a reported mice for  
NOTE Confidence: 0.656873219076923

00:16:50.265 --> 00:16:53.441 these schemes and and doing a time course.  
NOTE Confidence: 0.656873219076923

00:16:53.450 --> 00:16:55.922 So we actually found that the  
NOTE Confidence: 0.656873219076923

00:16:55.922 --> 00:16:57.570 fiberglass are actually functioning

NOTE Confidence: 0.656873219076923  
00:16:57.639 --> 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 --> 00:17:03.782 Then they end up attracting first my  
NOTE Confidence: 0.656873219076923  
00:17:03.782 --> 00:17:07.157 load cells and then T cells to the heart,  
NOTE Confidence: 0.656873219076923  
00:17:07.160 --> 00:17:08.876 and then as I just showed,  
NOTE Confidence: 0.656873219076923  
00:17:08.880 --> 00:17:11.748 we found that they can regulate  
NOTE Confidence: 0.656873219076923  
00:17:11.748 --> 00:17:13.182 correct for groceries.  
NOTE Confidence: 0.656873219076923  
00:17:13.190 --> 00:17:15.958 So then when I question that we asked  
NOTE Confidence: 0.656873219076923  
00:17:15.958 --> 00:17:18.978 was well how and where this is being  
NOTE Confidence: 0.656873219076923  
00:17:18.978 --> 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 --> 00:17:27.054 graduate student in the lab and he  
NOTE Confidence: 0.656873219076923  
00:17:27.054 --> 00:17:28.564 was really interested in knowing  
NOTE Confidence: 0.656873219076923  
00:17:28.564 --> 00:17:30.570 this because he found he said well,  
NOTE Confidence: 0.656873219076923  
00:17:30.570 --> 00:17:33.634 if we found a specific antigens that might  
NOTE Confidence: 0.656873219076923

00:17:33.634 --> 00:17:36.680 be relevant for the T cell immune response.

NOTE Confidence: 0.656873219076923

00:17:36.680 --> 00:17:38.624 Then one could think about in

NOTE Confidence: 0.656873219076923

00:17:38.624 --> 00:17:39.920 this in the future.

NOTE Confidence: 0.656873219076923

00:17:39.920 --> 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 --> 00:17:46.900 There will be a long term goal or at

NOTE Confidence: 0.656873219076923

00:17:46.993 --> 00:17:49.778 least understanding whether this is

NOTE Confidence: 0.656873219076923

00:17:49.778 --> 00:17:53.146 what was this this activation happening

NOTE Confidence: 0.656873219076923

00:17:53.146 --> 00:17:57.106 and where over time it could be prevented?

NOTE Confidence: 0.656873219076923

00:17:57.110 --> 00:17:59.998 So to study that we use a reporter

NOTE Confidence: 0.656873219076923

00:17:59.998 --> 00:18:02.828 mice for T cell activation or

NOTE Confidence: 0.656873219076923

00:18:02.828 --> 00:18:04.844 T cell receptor engagement.

NOTE Confidence: 0.656873219076923

00:18:04.850 --> 00:18:07.218 So these are in order to be activated

NOTE Confidence: 0.656873219076923

00:18:07.218 --> 00:18:08.920 by antigen presenting cells,

NOTE Confidence: 0.656873219076923

00:18:08.920 --> 00:18:11.250 they need to recognize antigen,

NOTE Confidence: 0.656873219076923

00:18:11.250 --> 00:18:13.419 and in the case of CD 4 positive T

NOTE Confidence: 0.656873219076923

00:18:13.419 --> 00:18:15.576 cells they express the diesel receptor

NOTE Confidence: 0.656873219076923

00:18:15.576 --> 00:18:18.230 here and then dendritic cells.

NOTE Confidence: 0.656873219076923

00:18:18.230 --> 00:18:21.346 Are they the main antigen presenting

NOTE Confidence: 0.656873219076923

00:18:21.346 --> 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 --> 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 --> 00:18:35.234 of diesel receptor engagement.

NOTE Confidence: 0.656873219076923

00:18:35.240 --> 00:18:38.552 So the green are the cells are because

NOTE Confidence: 0.656873219076923

00:18:38.552 --> 00:18:41.498 they express N 77 which is downstream.

NOTE Confidence: 0.656873219076923

00:18:41.500 --> 00:18:44.758 The diesel receptor bound to GFP.

NOTE Confidence: 0.656873219076923

00:18:44.760 --> 00:18:46.596 So the greener the cells are.

NOTE Confidence: 0.656873219076923

00:18:46.600 --> 00:18:48.128 That's telling you that

NOTE Confidence: 0.656873219076923

00:18:48.128 --> 00:18:49.274 they're recognizing antigen.

NOTE Confidence: 0.656873219076923

00:18:49.280 --> 00:18:52.570 This expression is also transient,  
NOTE Confidence: 0.656873219076923

00:18:52.570 --> 00:18:55.696 so if we see green cells,  
NOTE Confidence: 0.656873219076923

00:18:55.700 --> 00:18:57.842 it means that at the time where  
NOTE Confidence: 0.656873219076923

00:18:57.842 --> 00:18:59.160 we're harvesting those cells,  
NOTE Confidence: 0.656873219076923

00:18:59.160 --> 00:19:00.381 they're recognizing antigen.  
NOTE Confidence: 0.656873219076923

00:19:00.381 --> 00:19:03.230 But it might be that they recognize  
NOTE Confidence: 0.656873219076923

00:19:03.299 --> 00:19:05.909 antigen and then they're not recognizing.  
NOTE Confidence: 0.656873219076923

00:19:05.910 --> 00:19:08.196 Antigen at that point and then  
NOTE Confidence: 0.656873219076923

00:19:08.196 --> 00:19:09.339 they lose expression.  
NOTE Confidence: 0.656873219076923

00:19:09.340 --> 00:19:10.796 So in order to look at this,  
NOTE Confidence: 0.656873219076923

00:19:10.800 --> 00:19:12.876 we basically did the time course  
NOTE Confidence: 0.656873219076923

00:19:12.876 --> 00:19:14.540 of tag again early on,  
NOTE Confidence: 0.656873219076923

00:19:14.540 --> 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 --> 00:19:22.516 and then we kept them for longer.  
NOTE Confidence: 0.656873219076923

00:19:22.520 --> 00:19:26.444 That will mimic more chronic heart



NOTE Confidence: 0.656873219076923  
00:19:26.444 --> 00:19:29.417 failure and what we did is we harvested  
NOTE Confidence: 0.656873219076923  
00:19:29.417 --> 00:19:32.220 the hearts and the medicinal influence.  
NOTE Confidence: 0.656873219076923  
00:19:32.220 --> 00:19:34.804 And the first thing that we did here.  
NOTE Confidence: 0.656873219076923  
00:19:34.810 --> 00:19:37.246 And we found that was very,  
NOTE Confidence: 0.656873219076923  
00:19:37.250 --> 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 --> 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 --> 00:19:46.218 recently published was that we saw  
NOTE Confidence: 0.84957412  
00:19:46.218 --> 00:19:48.102 this T cell receptor engagement not  
NOTE Confidence: 0.84957412  
00:19:48.102 --> 00:19:50.308 only in the cardiac lymph nodes,  
NOTE Confidence: 0.84957412  
00:19:50.310 --> 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 --> 00:19:58.696 cells that increase overtime.  
NOTE Confidence: 0.84957412

00:19:58.696 --> 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 --> 00:20:05.640 they must be vendrick cells.  
NOTE Confidence: 0.84957412

00:20:05.640 --> 00:20:07.605 And potentially other cells that  
NOTE Confidence: 0.84957412

00:20:07.605 --> 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 bypassing the the  
NOTE Confidence: 0.84957412

00:20:14.182 --> 00:20:16.204 final trafficking that you need from  
NOTE Confidence: 0.84957412

00:20:16.204 --> 00:20:19.460 the lymph node into into the heart.  
NOTE Confidence: 0.84957412

00:20:19.460 --> 00:20:21.917 So we quantify this and as you can see,  
NOTE Confidence: 0.84957412

00:20:21.920 --> 00:20:24.975 there's a significant increase of  
NOTE Confidence: 0.84957412

00:20:24.975 --> 00:20:27.892 GFP positive active T cells in  
NOTE Confidence: 0.84957412

00:20:27.892 --> 00:20:30.144 the heart that correlates with  
NOTE Confidence: 0.84957412

00:20:30.144 --> 00:20:32.016 decline in systolic function.  
NOTE Confidence: 0.84957412

00:20:32.020 --> 00:20:35.120 Measure here with fractions.  
NOTE Confidence: 0.84957412

00:20:35.120 --> 00:20:38.198 So if we go back to how this teaser

NOTE Confidence: 0.84957412  
00:20:38.198 --> 00:20:40.906 activation happened in the timers,  
NOTE Confidence: 0.84957412  
00:20:40.906 --> 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 --> 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 --> 00:20:56.744 and selecting for what we might  
NOTE Confidence: 0.84957412  
00:20:56.744 --> 00:20:59.040 need in the future if we get closer  
NOTE Confidence: 0.84957412  
00:20:59.040 --> 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 --> 00:21:05.200 a pool of clones that will get expanded.  
NOTE Confidence: 0.84957412  
00:21:05.200 --> 00:21:07.360 If there is any immune response  
NOTE Confidence: 0.84957412  
00:21:07.360 --> 00:21:08.872 and then the question was what  
NOTE Confidence: 0.84957412  
00:21:08.872 --> 00:21:10.459 we were seeing in the heart,  
NOTE Confidence: 0.84957412  
00:21:10.460 --> 00:21:12.782 so our data using these reporter  
NOTE Confidence: 0.84957412  
00:21:12.782 --> 00:21:15.192 found that indicated that there was  
NOTE Confidence: 0.84957412

00:21:15.192 --> 00:21:17.556 this expansion in the correct running  
NOTE Confidence: 0.84957412

00:21:17.556 --> 00:21:20.018 lymph nodes as well as in the heart,  
NOTE Confidence: 0.84957412

00:21:20.020 --> 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 --> 00:21:27.179 whether it might be recognizing.  
NOTE Confidence: 0.84957412

00:21:27.180 --> 00:21:28.664 So this is the structure of the  
NOTE Confidence: 0.84957412

00:21:28.664 --> 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 --> 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 --> 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 --> 00:21:40.520 different ways to form a specificity.  
NOTE Confidence: 0.84957412

00:21:40.520 --> 00:21:43.334 Or these pocket to many different antigens.  
NOTE Confidence: 0.84957412

00:21:43.340 --> 00:21:46.840 So by sequencing this Cdr three region,

NOTE Confidence: 0.84957412  
00:21:46.840 --> 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 --> 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 --> 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 --> 00:22:05.036 There was anything in the heart,  
NOTE Confidence: 0.84957412  
00:22:05.040 --> 00:22:07.744 or whether we get.  
NOTE Confidence: 0.84957412  
00:22:07.744 --> 00:22:09.608 Enrichment so the results that  
NOTE Confidence: 0.84957412  
00:22:09.608 --> 00:22:11.093 we found was as expected.  
NOTE Confidence: 0.84957412  
00:22:11.100 --> 00:22:12.996 There was a lot of clones,  
NOTE Confidence: 0.84957412  
00:22:13.000 --> 00:22:15.260 many different diesel receptors  
NOTE Confidence: 0.84957412  
00:22:15.260 --> 00:22:17.520 sequences in the timelines.  
NOTE Confidence: 0.84957412  
00:22:17.520 --> 00:22:19.781 These are the inguinal lymph nodes and  
NOTE Confidence: 0.84957412

00:22:19.781 --> 00:22:22.054 again we have a high clonal diversity

NOTE Confidence: 0.84957412

00:22:22.054 --> 00:22:24.293 and what we found was that the

NOTE Confidence: 0.84957412

00:22:24.293 --> 00:22:26.773 closer that we were getting to the heart.

NOTE Confidence: 0.84957412

00:22:26.780 --> 00:22:29.215 There more the decreased number

NOTE Confidence: 0.84957412

00:22:29.215 --> 00:22:32.260 of total clothes that we found,

NOTE Confidence: 0.84957412

00:22:32.260 --> 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 zaverri complicated

NOTE Confidence: 0.84957412

00:22:40.150 --> 00:22:42.824 analysis and we found that there was

NOTE Confidence: 0.84957412

00:22:42.824 --> 00:22:45.058 a restricted clonal pool in the heart

NOTE Confidence: 0.84957412

00:22:45.060 --> 00:22:47.076 and that the majority of the cells

NOTE Confidence: 0.84957412

00:22:47.076 --> 00:22:48.740 were represented by top 20 clones.

NOTE Confidence: 0.84957412

00:22:48.740 --> 00:22:51.368 So we started diving more into

NOTE Confidence: 0.84957412

00:22:51.368 --> 00:22:53.120 what this could be.

NOTE Confidence: 0.84957412

00:22:53.120 --> 00:22:54.610 So what are these enrich

NOTE Confidence: 0.84957412

00:22:54.610 --> 00:22:56.100 clones responded to in the

NOTE Confidence: 0.695706194444444

00:22:56.161 --> 00:22:58.497 hunt and this will be the working month.

NOTE Confidence: 0.695706194444444

00:22:58.500 --> 00:23:01.113 We know that this is happening and

NOTE Confidence: 0.695706194444444

00:23:01.113 --> 00:23:03.864 then we know that there's this close

NOTE Confidence: 0.695706194444444

00:23:03.864 --> 00:23:06.439 being expanded and what could those be?

NOTE Confidence: 0.695706194444444

00:23:06.440 --> 00:23:10.130 So we ended up focusing on Russ and then

NOTE Confidence: 0.695706194444444

00:23:10.130 --> 00:23:13.399 again because of the time limitation.

NOTE Confidence: 0.695706194444444

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

NOTE Confidence: 0.695706194444444

00:23:14.448 --> 00:23:15.758 everything that we went through,

NOTE Confidence: 0.695706194444444

00:23:15.760 --> 00:23:17.956 but it basically one hypothesis was

NOTE Confidence: 0.695706194444444

00:23:17.956 --> 00:23:20.372 that you could have a cardiomyocyte

NOTE Confidence: 0.695706194444444

00:23:20.372 --> 00:23:23.018 proteins right that the myocytes die,

NOTE Confidence: 0.695706194444444

00:23:23.020 --> 00:23:25.900 and then the fragments are picked

NOTE Confidence: 0.695706194444444

00:23:25.900 --> 00:23:28.500 up by adding percentage selves.

NOTE Confidence: 0.695706194444444

00:23:28.500 --> 00:23:30.428 But it turns out that in the attack

NOTE Confidence: 0.695706194444444

00:23:30.428 --> 00:23:32.408 model and like in response to my

NOTE Confidence: 0.695706194444444

00:23:32.408 --> 00:23:34.337 kardelen function where you see a lot  
NOTE Confidence: 0.695706194444444

00:23:34.337 --> 00:23:36.636 of cell damage in the attack model.  
NOTE Confidence: 0.695706194444444

00:23:36.636 --> 00:23:39.038 We don't see significant salvage early  
NOTE Confidence: 0.695706194444444

00:23:39.038 --> 00:23:41.662 on and even later on at four weeks.  
NOTE Confidence: 0.695706194444444

00:23:41.670 --> 00:23:46.242 But what we do see is high increases of  
NOTE Confidence: 0.695706194444444

00:23:46.242 --> 00:23:48.954 intramyocardial reactive oxygen oxygen  
NOTE Confidence: 0.695706194444444

00:23:48.954 --> 00:23:52.820 species which are labeled here in green.  
NOTE Confidence: 0.695706194444444

00:23:52.820 --> 00:23:55.908 So we went back to literature and we  
NOTE Confidence: 0.695706194444444

00:23:55.908 --> 00:23:58.446 hypothesized that maybe Rose could modify  
NOTE Confidence: 0.695706194444444

00:23:58.446 --> 00:24:00.978 correct proteins that then form new  
NOTE Confidence: 0.695706194444444

00:24:01.053 --> 00:24:04.056 antigens that are listed AT cell response.  
NOTE Confidence: 0.695706194444444

00:24:04.060 --> 00:24:05.002 Why do we?  
NOTE Confidence: 0.695706194444444

00:24:05.002 --> 00:24:06.886 Why would do we think that  
NOTE Confidence: 0.695706194444444

00:24:06.886 --> 00:24:08.519 there was a hypothesis?  
NOTE Confidence: 0.695706194444444

00:24:08.520 --> 00:24:10.510 It was because similar mechanisms  
NOTE Confidence: 0.695706194444444

00:24:10.510 --> 00:24:13.058 had been described in the vasculature



NOTE Confidence: 0.695706194444444

00:24:13.058 --> 00:24:15.478 in the context of hypertension,

NOTE Confidence: 0.695706194444444

00:24:15.480 --> 00:24:19.052 where there was this formation of ice level.

NOTE Confidence: 0.695706194444444

00:24:19.052 --> 00:24:19.864 Glenda Lynn's,

NOTE Confidence: 0.695706194444444

00:24:19.864 --> 00:24:23.604 which are highly reactive intermediates by.

NOTE Confidence: 0.695706194444444

00:24:23.604 --> 00:24:25.066 Lipid peroxidation.

NOTE Confidence: 0.695706194444444

00:24:25.070 --> 00:24:27.492 That then can adapt to self proteins

NOTE Confidence: 0.695706194444444

00:24:27.492 --> 00:24:29.450 and create these new antigens.

NOTE Confidence: 0.695706194444444

00:24:29.450 --> 00:24:32.320 So we contacted the people who had

NOTE Confidence: 0.695706194444444

00:24:32.320 --> 00:24:35.802 done the scientists that had done this

NOTE Confidence: 0.695706194444444

00:24:35.802 --> 00:24:37.970 very interesting research hypertension

NOTE Confidence: 0.695706194444444

00:24:37.970 --> 00:24:40.210 David Harrison and Annette Kirabo,

NOTE Confidence: 0.695706194444444

00:24:40.210 --> 00:24:42.260 and this started a beautiful

NOTE Confidence: 0.695706194444444

00:24:42.260 --> 00:24:44.772 collaboration in which we were able

NOTE Confidence: 0.695706194444444

00:24:44.772 --> 00:24:48.109 to test this hypothesis in the heart.

NOTE Confidence: 0.695706194444444

00:24:48.110 --> 00:24:49.802 So basically we obtain a lot

NOTE Confidence: 0.695706194444444

00:24:49.802 --> 00:24:51.270 of reagents from their labs,  
NOTE Confidence: 0.6957061944444444

00:24:51.270 --> 00:24:52.971 and the first thing that we wanted  
NOTE Confidence: 0.6957061944444444

00:24:52.971 --> 00:24:54.662 to know is whether this matter  
NOTE Confidence: 0.6957061944444444

00:24:54.662 --> 00:24:55.866 in the human heart.  
NOTE Confidence: 0.6957061944444444

00:24:55.870 --> 00:24:58.966 So we went back or human heart failure  
NOTE Confidence: 0.6957061944444444

00:24:58.966 --> 00:25:02.101 sections and we use this one day 11 which  
NOTE Confidence: 0.6957061944444444

00:25:02.101 --> 00:25:04.762 is an antibody that recognizes proteins.  
NOTE Confidence: 0.6957061944444444

00:25:04.762 --> 00:25:07.534 Modified biologist was given to us  
NOTE Confidence: 0.6957061944444444

00:25:07.534 --> 00:25:10.621 by David and Annette and as you  
NOTE Confidence: 0.6957061944444444

00:25:10.621 --> 00:25:13.051 can see here we saw significant  
NOTE Confidence: 0.6957061944444444

00:25:13.135 --> 00:25:15.607 recognition in three different  
NOTE Confidence: 0.6957061944444444

00:25:15.607 --> 00:25:18.079 heart failure patient samples.  
NOTE Confidence: 0.6957061944444444

00:25:18.080 --> 00:25:20.522 And no signals in a non  
NOTE Confidence: 0.6957061944444444

00:25:20.522 --> 00:25:21.743 heart failure patient.  
NOTE Confidence: 0.6957061944444444

00:25:21.750 --> 00:25:24.315 We went back to the marsh model and in  
NOTE Confidence: 0.6957061944444444

00:25:24.315 --> 00:25:26.909 the marsh model we went back to these

NOTE Confidence: 0.695706194444444

00:25:26.910 --> 00:25:30.599 reporter my cells and T cell recognition.

NOTE Confidence: 0.695706194444444

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

NOTE Confidence: 0.695706194444444

00:25:35.208 --> 00:25:36.750 that recognizes proteins

NOTE Confidence: 0.695706194444444

00:25:36.750 --> 00:25:39.320 modified by strategies in mouse.

NOTE Confidence: 0.695706194444444

00:25:39.320 --> 00:25:41.976 This was a different version of the antibody.

NOTE Confidence: 0.695706194444444

00:25:41.980 --> 00:25:44.604 And then they also send us some ISO

NOTE Confidence: 0.695706194444444

00:25:44.610 --> 00:25:49.594 so they can generate and I soils LG

NOTE Confidence: 0.695706194444444

00:25:49.594 --> 00:25:54.019 scavengers that could be used in in mice.

NOTE Confidence: 0.695706194444444

00:25:54.020 --> 00:25:57.098 So how does it work with experiments in tack?

NOTE Confidence: 0.695706194444444

00:25:57.100 --> 00:25:58.636 And then this is the structure

NOTE Confidence: 0.695706194444444

00:25:58.636 --> 00:26:00.180 of the eye surgeons calendar,

NOTE Confidence: 0.695706194444444

00:26:00.180 --> 00:26:01.896 and this is the control peptide.

NOTE Confidence: 0.695706194444444

00:26:01.900 --> 00:26:03.867 So the two Joba that I'll be

NOTE Confidence: 0.695706194444444

00:26:03.867 --> 00:26:05.689 showing is one with coverage.

NOTE Confidence: 0.695706194444444

00:26:05.690 --> 00:26:09.176 Those rose reactive proteins and then

NOTE Confidence: 0.695706194444444

00:26:09.176 --> 00:26:12.659 we tracked this activation and T  
NOTE Confidence: 0.695706194444444

00:26:12.659 --> 00:26:15.319 cell receptor engagement over time.  
NOTE Confidence: 0.695706194444444

00:26:15.320 --> 00:26:18.032 In some experiments we use tempo  
NOTE Confidence: 0.695706194444444

00:26:18.032 --> 00:26:19.840 because it's an antioxidant,  
NOTE Confidence: 0.695706194444444

00:26:19.840 --> 00:26:23.608 so it works upstream of the of the.  
NOTE Confidence: 0.621444686363636

00:26:23.610 --> 00:26:27.341 Draws formation so just to make it  
NOTE Confidence: 0.621444686363636

00:26:27.341 --> 00:26:31.046 simpler in for understanding the idea,  
NOTE Confidence: 0.621444686363636

00:26:31.046 --> 00:26:33.350 this is a question that we were trying  
NOTE Confidence: 0.621444686363636

00:26:33.410 --> 00:26:35.678 to ask and the idea is that in response  
NOTE Confidence: 0.621444686363636

00:26:35.678 --> 00:26:38.454 to diagnose Ross and then this Ross  
NOTE Confidence: 0.621444686363636

00:26:38.454 --> 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 --> 00:26:47.284 that then they adapt to a cardiac protein.  
NOTE Confidence: 0.621444686363636

00:26:47.290 --> 00:26:49.498 I'm from Disneyland pigeons that could  
NOTE Confidence: 0.621444686363636

00:26:49.498 --> 00:26:52.347 be taken by the dreaded cells and  
NOTE Confidence: 0.621444686363636

00:26:52.347 --> 00:26:54.849 being presented these cells to induce

NOTE Confidence: 0.621444686363636

00:26:54.849 --> 00:26:57.450 T cell activation and proliferation.

NOTE Confidence: 0.621444686363636

00:26:57.450 --> 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 --> 00:27:04.730 maybe we would see less this

NOTE Confidence: 0.621444686363636

00:27:04.806 --> 00:27:07.476 activation or proliferation in heart.

NOTE Confidence: 0.621444686363636

00:27:07.480 --> 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 --> 00:27:13.462 we could potentially block this and

NOTE Confidence: 0.621444686363636

00:27:13.462 --> 00:27:15.259 block this activation in the heart,

NOTE Confidence: 0.621444686363636

00:27:15.260 --> 00:27:17.460 and then of course the final question was,

NOTE Confidence: 0.621444686363636

00:27:17.460 --> 00:27:22.304 will this have any impact incorrect function?

NOTE Confidence: 0.621444686363636

00:27:22.310 --> 00:27:24.443 So the first thing that we did is we

NOTE Confidence: 0.621444686363636

00:27:24.443 --> 00:27:26.702 did those experiments in mice and then

NOTE Confidence: 0.621444686363636

00:27:26.702 --> 00:27:29.294 we isolated and Rick cells from mice

NOTE Confidence: 0.621444686363636

00:27:29.294 --> 00:27:32.066 treated with these AI soldiers scavengers.

NOTE Confidence: 0.621444686363636

00:27:32.070 --> 00:27:33.666 And as you can see here,  
NOTE Confidence: 0.621444686363636

00:27:33.670 --> 00:27:36.226 this is the antibody that detects  
NOTE Confidence: 0.621444686363636

00:27:36.226 --> 00:27:37.930 the isolated protein adducts.  
NOTE Confidence: 0.621444686363636

00:27:37.930 --> 00:27:41.170 And as you can see with the four coma,  
NOTE Confidence: 0.621444686363636

00:27:41.170 --> 00:27:44.122 which is the control and the  
NOTE Confidence: 0.621444686363636

00:27:44.122 --> 00:27:45.106 control compound,  
NOTE Confidence: 0.621444686363636

00:27:45.110 --> 00:27:47.174 we see that in drink cells  
NOTE Confidence: 0.621444686363636

00:27:47.174 --> 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 --> 00:27:52.438 inhibited when we scavenged.  
NOTE Confidence: 0.6690343025

00:27:54.550 --> 00:27:56.971 And then when we look directly in the House  
NOTE Confidence: 0.6690343025

00:27:56.971 --> 00:27:59.246 looking for teachers using the reporter mice,  
NOTE Confidence: 0.6690343025

00:27:59.250 --> 00:28:02.266 we found that only in those miles that  
NOTE Confidence: 0.6690343025

00:28:02.266 --> 00:28:05.170 were treated with the iceberg scavengers,  
NOTE Confidence: 0.6690343025

00:28:05.170 --> 00:28:08.020 we were able to significantly decrease  
NOTE Confidence: 0.6690343025

00:28:08.020 --> 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 --> 00:28:14.197 because this underreported mines and

NOTE Confidence: 0.6690343025

00:28:14.197 --> 00:28:15.646 I don't think I mentioned it earlier,

NOTE Confidence: 0.6690343025

00:28:15.650 --> 00:28:17.834 but this is this receptor beta

NOTE Confidence: 0.6690343025

00:28:17.834 --> 00:28:20.444 to make sure that we're focusing

NOTE Confidence: 0.6690343025

00:28:20.444 --> 00:28:23.329 on the right distal population.

NOTE Confidence: 0.6690343025

00:28:23.330 --> 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 --> 00:28:30.470 but added functional inducing

NOTE Confidence: 0.6690343025

00:28:30.470 --> 00:28:31.760 diesel proliferation.

NOTE Confidence: 0.6690343025

00:28:31.760 --> 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 --> 00:28:38.174 so the hypothesis is that when

NOTE Confidence: 0.6690343025

00:28:38.174 --> 00:28:39.430 these are become activated,

NOTE Confidence: 0.6690343025

00:28:39.430 --> 00:28:42.250 then they have to proliferate.

NOTE Confidence: 0.6690343025

00:28:42.250 --> 00:28:45.008 So we tested this hypothesis ex vivo  
NOTE Confidence: 0.6690343025

00:28:45.008 --> 00:28:48.108 and we took the genetic cells from  
NOTE Confidence: 0.6690343025

00:28:48.108 --> 00:28:51.337 control mice and loaded them with either  
NOTE Confidence: 0.6690343025

00:28:51.337 --> 00:28:54.417 ice or GS or with a correct license  
NOTE Confidence: 0.6690343025

00:28:54.417 --> 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 --> 00:29:02.310 cells that were incubated with these  
NOTE Confidence: 0.6690343025

00:29:02.310 --> 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 --> 00:29:08.616 from either sham or tag mouse.  
NOTE Confidence: 0.6690343025

00:29:08.620 --> 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 --> 00:29:16.640 look at T cell proliferation.  
NOTE Confidence: 0.6690343025

00:29:16.640 --> 00:29:18.899 So the way we look at T cell proliferation  
NOTE Confidence: 0.6690343025

00:29:18.899 --> 00:29:20.863 is because the teachers are labeled



NOTE Confidence: 0.6690343025

00:29:20.863 --> 00:29:22.960 with a membrane guide that is CFC.

NOTE Confidence: 0.6690343025

00:29:22.960 --> 00:29:25.445 And if they proliferate as you can

NOTE Confidence: 0.6690343025

00:29:25.445 --> 00:29:28.964 see here to see if you see a die is

NOTE Confidence: 0.6690343025

00:29:28.964 --> 00:29:31.960 diluted and this is just one example.

NOTE Confidence: 0.6690343025

00:29:31.960 --> 00:29:36.739 If we combine some T cells with sham lysates,

NOTE Confidence: 0.6690343025

00:29:36.740 --> 00:29:37.964 there's no proliferation,

NOTE Confidence: 0.6690343025

00:29:37.964 --> 00:29:40.820 and if you put tactics so there's

NOTE Confidence: 0.6690343025

00:29:40.898 --> 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 --> 00:29:46.860 this is only a representative experiment.

NOTE Confidence: 0.6690343025

00:29:46.860 --> 00:29:49.650 Everything is quantified in the manuscript.

NOTE Confidence: 0.6690343025

00:29:49.650 --> 00:29:52.666 But what we found was that only when

NOTE Confidence: 0.6690343025

00:29:52.666 --> 00:29:55.519 the teachers came from mice with

NOTE Confidence: 0.6690343025

00:29:55.519 --> 00:29:58.146 experimental heart failure and the

NOTE Confidence: 0.6690343025

00:29:58.146 --> 00:30:01.464 proteins that cells were loaded with

NOTE Confidence: 0.6690343025

00:30:01.464 --> 00:30:04.299 cardiac proteins that came from Tak  
NOTE Confidence: 0.6690343025

00:30:04.300 --> 00:30:06.466 only this combination is when we  
NOTE Confidence: 0.6690343025

00:30:06.466 --> 00:30:09.759 were able to see these new antigen  
NOTE Confidence: 0.6690343025

00:30:09.759 --> 00:30:12.119 presentation and decent proliferation.  
NOTE Confidence: 0.6690343025

00:30:12.120 --> 00:30:14.591 So did this have any impact in  
NOTE Confidence: 0.6690343025

00:30:14.591 --> 00:30:15.297 cardiac function?  
NOTE Confidence: 0.6690343025

00:30:15.300 --> 00:30:17.375 And these are echoes done  
NOTE Confidence: 0.6690343025

00:30:17.375 --> 00:30:18.620 by our collaborators.  
NOTE Confidence: 0.6690343025

00:30:18.620 --> 00:30:21.220 That Medical Center Rob Landon,  
NOTE Confidence: 0.6690343025

00:30:21.220 --> 00:30:24.244 who is a cardiologist that whom I've  
NOTE Confidence: 0.6690343025

00:30:24.244 --> 00:30:26.620 I've been collaborating with for many,  
NOTE Confidence: 0.6690343025

00:30:26.620 --> 00:30:27.328 many years,  
NOTE Confidence: 0.6690343025

00:30:27.328 --> 00:30:29.452 and what we found is that  
NOTE Confidence: 0.6690343025

00:30:29.452 --> 00:30:30.800 these attack animals.  
NOTE Confidence: 0.6690343025

00:30:30.800 --> 00:30:33.910 You can see the flat line here and  
NOTE Confidence: 0.6690343025

00:30:33.910 --> 00:30:36.560 decrease historic function that is,

NOTE Confidence: 0.6690343025

00:30:36.560 --> 00:30:38.510 is quantified here.

NOTE Confidence: 0.6690343025

00:30:38.510 --> 00:30:40.168 Fractional shortening and

NOTE Confidence: 0.6690343025

00:30:40.168 --> 00:30:42.316 the harsh from the two hobas.

NOTE Confidence: 0.6690343025

00:30:42.320 --> 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 --> 00:30:48.910 compared to to the control.

NOTE Confidence: 0.760014902

00:30:51.220 --> 00:30:52.960 So to summarize this part,

NOTE Confidence: 0.760014902

00:30:52.960 --> 00:30:55.431 what we found was that in response

NOTE Confidence: 0.760014902

00:30:55.431 --> 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 --> 00:31:03.260 intramyocardial rose in the heart

NOTE Confidence: 0.760014902

00:31:03.260 --> 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 --> 00:31:11.132 of the proteins that are modified

NOTE Confidence: 0.760014902

00:31:11.213 --> 00:31:13.628 by brass induced eye surgeries.

NOTE Confidence: 0.760014902

00:31:13.630 --> 00:31:15.010 And then in the lymph node,  
NOTE Confidence: 0.760014902

00:31:15.010 --> 00:31:17.590 we saw that these T cells respond  
NOTE Confidence: 0.760014902

00:31:17.590 --> 00:31:19.750 to antigen and expand and then  
NOTE Confidence: 0.760014902

00:31:19.750 --> 00:31:22.207 they can go back to the heart.  
NOTE Confidence: 0.760014902

00:31:22.210 --> 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 --> 00:31:28.928 to us was that once in the heart.  
NOTE Confidence: 0.760014902

00:31:28.930 --> 00:31:31.648 You sometimes bypass 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 --> 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 --> 00:31:41.525 This has significant effects  
NOTE Confidence: 0.760014902

00:31:41.525 --> 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 --> 00:31:50.612 fibroglandular also had significantly  
NOTE Confidence: 0.753394304375

00:31:50.612 --> 00:31:53.414 decreased fibrosis and this is going

NOTE Confidence: 0.753394304375

00:31:53.414 --> 00:31:56.278 to become more relevant for the next

NOTE Confidence: 0.753394304375

00:31:56.278 --> 00:31:58.822 part of the talk where I will be

NOTE Confidence: 0.753394304375

00:31:58.822 --> 00:32:01.180 talking about this critical antigen

NOTE Confidence: 0.753394304375

00:32:01.180 --> 00:32:04.330 recognition that happens in heart.

NOTE Confidence: 0.753394304375

00:32:04.330 --> 00:32:07.586 So for the last part of the talk,

NOTE Confidence: 0.753394304375

00:32:07.590 --> 00:32:11.798 then we I will focus about these kids

NOTE Confidence: 0.753394304375

00:32:11.798 --> 00:32:14.510 are correct fibroblast crosstalk.

NOTE Confidence: 0.753394304375

00:32:14.510 --> 00:32:16.750 So as I showed in the first part of the talk,

NOTE Confidence: 0.753394304375

00:32:16.750 --> 00:32:18.590 when the diesels Infiltrator hi,

NOTE Confidence: 0.753394304375

00:32:18.590 --> 00:32:20.966 this is an image ex vivo.

NOTE Confidence: 0.753394304375

00:32:20.970 --> 00:32:23.280 So these are fiberglass and culture

NOTE Confidence: 0.753394304375

00:32:23.280 --> 00:32:26.196 with T cells and you can see the

NOTE Confidence: 0.753394304375

00:32:26.196 --> 00:32:28.577 green cells are here and the blue

NOTE Confidence: 0.753394304375

00:32:28.577 --> 00:32:30.665 little nuclei of the diesels and

NOTE Confidence: 0.753394304375

00:32:30.665 --> 00:32:33.406 this is a large nuclei of fiberglass.

NOTE Confidence: 0.753394304375

00:32:33.406 --> 00:32:37.000 So we had found that with the diesels,  
NOTE Confidence: 0.753394304375

00:32:37.000 --> 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 --> 00:32:43.580 isolated directly from TAC mice.  
NOTE Confidence: 0.753394304375

00:32:43.580 --> 00:32:45.625 They bound to the fiberglass  
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 --> 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 --> 00:32:55.274 And then in in the second part of  
NOTE Confidence: 0.753394304375

00:32:55.274 --> 00:32:57.589 the talk I just recently showed you  
NOTE Confidence: 0.753394304375

00:32:57.590 --> 00:32:59.390 that I didn't present themselves  
NOTE Confidence: 0.753394304375

00:32:59.390 --> 00:33:00.830 and particularly in lyrics.  
NOTE Confidence: 0.753394304375

00:33:00.830 --> 00:33:03.620 Elves present antigen to T cells  
NOTE Confidence: 0.753394304375

00:33:03.620 --> 00:33:06.577 and there is this intramyocardial  
NOTE Confidence: 0.753394304375

00:33:06.577 --> 00:33:09.577 diesel receptor engagement.  
NOTE Confidence: 0.753394304375

00:33:09.580 --> 00:33:10.960 So then we we thought,

NOTE Confidence: 0.753394304375  
00:33:10.960 --> 00:33:11.288 well,  
NOTE Confidence: 0.753394304375  
00:33:11.288 --> 00:33:13.256 they're not that many dendritic cells  
NOTE Confidence: 0.753394304375  
00:33:13.256 --> 00:33:15.890 in the heart as compared to other cells,  
NOTE Confidence: 0.753394304375  
00:33:15.890 --> 00:33:16.361 right?  
NOTE Confidence: 0.753394304375  
00:33:16.361 --> 00:33:20.129 Is it possible that during this T cell,  
NOTE Confidence: 0.753394304375  
00:33:20.130 --> 00:33:23.245 fiberglass crosstalk not only the T cells  
NOTE Confidence: 0.753394304375  
00:33:23.245 --> 00:33:26.847 are telling the fiberglass to to induce TGF,  
NOTE Confidence: 0.753394304375  
00:33:26.850 --> 00:33:28.248 beta and transform?  
NOTE Confidence: 0.753394304375  
00:33:28.248 --> 00:33:31.044 But maybe the fiberglass because diesels  
NOTE Confidence: 0.753394304375  
00:33:31.044 --> 00:33:33.986 are firmly adhered to the fiberglass.  
NOTE Confidence: 0.753394304375  
00:33:33.990 --> 00:33:36.846 Maybe the fiberglass may be functioning  
NOTE Confidence: 0.753394304375  
00:33:36.846 --> 00:33:39.454 as also an antigen presenting  
NOTE Confidence: 0.753394304375  
00:33:39.454 --> 00:33:41.790 cell that is semi professional.  
NOTE Confidence: 0.753394304375  
00:33:41.790 --> 00:33:44.370 So we went back to literature,  
NOTE Confidence: 0.753394304375  
00:33:44.370 --> 00:33:46.770 and in this there's this growing  
NOTE Confidence: 0.753394304375

00:33:46.770 --> 00:33:48.370 field of struggle immunology,  
NOTE Confidence: 0.753394304375

00:33:48.370 --> 00:33:50.635 where the concept is that antigen  
NOTE Confidence: 0.753394304375

00:33:50.635 --> 00:33:52.560 presentation is no longer an  
NOTE Confidence: 0.753394304375

00:33:52.560 --> 00:33:54.610 exclusive domain for the lyrics.  
NOTE Confidence: 0.753394304375

00:33:54.610 --> 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 --> 00:34:01.410 presenting cells,  
NOTE Confidence: 0.753394304375

00:34:01.410 --> 00:34:03.360 but they're also evidence that  
NOTE Confidence: 0.753394304375

00:34:03.360 --> 00:34:05.310 a stronger cells that support  
NOTE Confidence: 0.753394304375

00:34:05.375 --> 00:34:07.999 tissue architecture can serve as  
NOTE Confidence: 0.753394304375

00:34:07.999 --> 00:34:09.388 antigen presenting cells.  
NOTE Confidence: 0.753394304375

00:34:09.390 --> 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 --> 00:34:15.010 In an example of fibroblastic  
NOTE Confidence: 0.753394304375

00:34:15.010 --> 00:34:17.540 particular cells in the lymph nodes.  
NOTE Confidence: 0.753394304375

00:34:17.540 --> 00:34:20.717 Timing is stomach cells can do that as well.



NOTE Confidence: 0.753394304375  
00:34:20.720 --> 00:34:21.014 There.  
NOTE Confidence: 0.753394304375  
00:34:21.014 --> 00:34:22.484 There are many reports that  
NOTE Confidence: 0.753394304375  
00:34:22.484 --> 00:34:24.046 show that two more infiltrated  
NOTE Confidence: 0.753394304375  
00:34:24.046 --> 00:34:25.996 fiber blasts do that as well,  
NOTE Confidence: 0.753394304375  
00:34:26.000 --> 00:34:28.086 and it's also a recent report in  
NOTE Confidence: 0.753394304375  
00:34:28.086 --> 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 --> 00:34:35.060 can actually present antigen  
NOTE Confidence: 0.753394304375  
00:34:35.060 --> 00:34:37.184 to certain diesels.  
NOTE Confidence: 0.753394304375  
00:34:37.190 --> 00:34:39.350 So we hypothesize that cardiac  
NOTE Confidence: 0.753394304375  
00:34:39.350 --> 00:34:42.144 fibroblasts may be functioning as antigen  
NOTE Confidence: 0.753394304375  
00:34:42.144 --> 00:34:44.536 presenting cells, and that these.  
NOTE Confidence: 0.753394304375  
00:34:44.536 --> 00:34:47.068 T cell receptor engagement that we  
NOTE Confidence: 0.753394304375  
00:34:47.068 --> 00:34:49.694 were seeing in the heart was not  
NOTE Confidence: 0.753394304375  
00:34:49.694 --> 00:34:51.686 exclusively due to the dirt excels,  
NOTE Confidence: 0.753394304375

00:34:51.690 --> 00:34:54.006 but also to cut fiber breads.  
NOTE Confidence: 0.753394304375

00:34:54.010 --> 00:34:55.030 And a wind.  
NOTE Confidence: 0.753394304375

00:34:55.030 --> 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 --> 00:35:02.990 significantly to this project.  
NOTE Confidence: 0.753394304375

00:35:02.990 --> 00:35:05.146 So to remind you what an antigen  
NOTE Confidence: 0.753394304375

00:35:05.146 --> 00:35:07.320 presenting cell in order to be an  
NOTE Confidence: 0.753394304375

00:35:07.320 --> 00:35:08.800 antigen presenting cell as poor  
NOTE Confidence: 0.753394304375

00:35:08.800 --> 00:35:10.190 as an indirect cell.  
NOTE Confidence: 0.753394304375

00:35:10.190 --> 00:35:13.040 You need to efficiently internalize  
NOTE Confidence: 0.753394304375

00:35:13.040 --> 00:35:14.750 and process antigens.  
NOTE Confidence: 0.824624898

00:35:14.750 --> 00:35:16.820 You need to display them  
NOTE Confidence: 0.824624898

00:35:16.820 --> 00:35:19.660 bound to MHC 2 molecules.  
NOTE Confidence: 0.824624898

00:35:19.660 --> 00:35:21.574 And then you have to present  
NOTE Confidence: 0.824624898

00:35:21.574 --> 00:35:23.902 that at the cell surface and  
NOTE Confidence: 0.824624898

00:35:23.902 --> 00:35:26.312 professional Apcs and Rick cells

NOTE Confidence: 0.824624898

00:35:26.312 --> 00:35:28.760 constitutively express all of these.

NOTE Confidence: 0.824624898

00:35:28.760 --> 00:35:32.870 MHC do is constantly expressed and then

NOTE Confidence: 0.824624898

00:35:32.870 --> 00:35:35.595 these costimulatory molecules CD80 or

NOTE Confidence: 0.824624898

00:35:35.600 --> 00:35:40.886 CD86 that are induced upon stimulation.

NOTE Confidence: 0.824624898

00:35:40.890 --> 00:35:44.220 So we started investigating whether correct,

NOTE Confidence: 0.824624898

00:35:44.220 --> 00:35:46.746 fabulous may fit into this category.

NOTE Confidence: 0.824624898

00:35:46.750 --> 00:35:49.621 So this is a way that we select correct

NOTE Confidence: 0.824624898

00:35:49.621 --> 00:35:52.978 fibrous in the heart with digest the hearts,

NOTE Confidence: 0.824624898

00:35:52.978 --> 00:35:56.200 and then then we acquire this

NOTE Confidence: 0.824624898

00:35:56.308 --> 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 --> 00:36:03.858 We'll have local sides and we have

NOTE Confidence: 0.824624898

00:36:03.860 --> 00:36:06.380 a correct fiberglass here here.

NOTE Confidence: 0.824624898

00:36:06.380 --> 00:36:09.206 Sorry so we have leukocytes here.

NOTE Confidence: 0.824624898

00:36:09.210 --> 00:36:12.096 3045 positives City 31 positive and

NOTE Confidence: 0.824624898

00:36:12.096 --> 00:36:14.584 killer cells within the local sides  
NOTE Confidence: 0.824624898

00:36:14.584 --> 00:36:17.852 you could look for any local side that  
NOTE Confidence: 0.824624898

00:36:17.852 --> 00:36:20.091 you're interested in and within the  
NOTE Confidence: 0.824624898

00:36:20.091 --> 00:36:21.873 double negatives not in the filling.  
NOTE Confidence: 0.824624898

00:36:21.880 --> 00:36:23.002 No leukocytes.  
NOTE Confidence: 0.824624898

00:36:23.002 --> 00:36:26.368 We use these marker to detect  
NOTE Confidence: 0.824624898

00:36:26.368 --> 00:36:29.369 a cardiac fiberless mask 4.  
NOTE Confidence: 0.824624898

00:36:29.370 --> 00:36:33.066 We also do this in Linux reporter mice,  
NOTE Confidence: 0.824624898

00:36:33.070 --> 00:36:35.350 and that's where is indicated here.  
NOTE Confidence: 0.824624898

00:36:35.350 --> 00:36:37.552 So these are Linux tracing mice  
NOTE Confidence: 0.824624898

00:36:37.552 --> 00:36:40.179 where we could more more definitely  
NOTE Confidence: 0.824624898

00:36:40.180 --> 00:36:43.150 get into the cardiac fiberless.  
NOTE Confidence: 0.824624898

00:36:43.150 --> 00:36:45.418 So the first thing that we did is do  
NOTE Confidence: 0.824624898

00:36:45.418 --> 00:36:47.647 they express MHC two and a baseline?  
NOTE Confidence: 0.824624898

00:36:47.650 --> 00:36:48.484 They don't.  
NOTE Confidence: 0.824624898

00:36:48.484 --> 00:36:51.820 But as soon as you activate them with

NOTE Confidence: 0.824624898

00:36:51.908 --> 00:36:54.539 interferon gamma you induce expression

NOTE Confidence: 0.824624898

00:36:54.539 --> 00:36:57.220 of MHC two and actually in the filling

NOTE Confidence: 0.824624898

00:36:57.220 --> 00:36:58.985 search for instance by people here

NOTE Confidence: 0.824624898

00:36:58.985 --> 00:37:00.809 at nearly the department of Pathology,

NOTE Confidence: 0.824624898

00:37:00.810 --> 00:37:01.906 German Barber,

NOTE Confidence: 0.824624898

00:37:01.906 --> 00:37:05.194 and others found that endothelial cells

NOTE Confidence: 0.824624898

00:37:05.194 --> 00:37:08.710 can present antigens to T cells as well,

NOTE Confidence: 0.824624898

00:37:08.710 --> 00:37:10.635 and they respond and express MHC two

NOTE Confidence: 0.824624898

00:37:10.635 --> 00:37:12.429 in response to interferon gamma.

NOTE Confidence: 0.824624898

00:37:12.430 --> 00:37:13.580 So this would be a.

NOTE Confidence: 0.824624898

00:37:13.580 --> 00:37:17.300 It's similar mechanism of expression.

NOTE Confidence: 0.824624898

00:37:17.300 --> 00:37:18.812 And then what we found it was

NOTE Confidence: 0.824624898

00:37:18.812 --> 00:37:20.163 that they do express customer

NOTE Confidence: 0.824624898

00:37:20.163 --> 00:37:22.107 little molecules that you need to

NOTE Confidence: 0.824624898

00:37:22.107 --> 00:37:23.739 trigger that diesel activation.

NOTE Confidence: 0.824624898

00:37:23.740 --> 00:37:27.324 They do express CD 80 and  
NOTE Confidence: 0.824624898

00:37:27.324 --> 00:37:29.020 is not further inducible,  
NOTE Confidence: 0.824624898

00:37:29.020 --> 00:37:31.530 induced by different comma but  
NOTE Confidence: 0.824624898

00:37:31.530 --> 00:37:33.538 they don't express 86.  
NOTE Confidence: 0.824624898

00:37:33.540 --> 00:37:35.694 We collaborated with Jenn Davies and  
NOTE Confidence: 0.824624898

00:37:35.694 --> 00:37:37.796 their impact grad student in her  
NOTE Confidence: 0.824624898

00:37:37.796 --> 00:37:39.620 lab at the University of Washington  
NOTE Confidence: 0.824624898

00:37:39.620 --> 00:37:41.805 and exactly the same experiments  
NOTE Confidence: 0.824624898

00:37:41.805 --> 00:37:44.460 using the Linux trace in mice.  
NOTE Confidence: 0.824624898

00:37:44.460 --> 00:37:47.274 That is a reporter for correct fiberglass,  
NOTE Confidence: 0.824624898

00:37:47.280 --> 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 --> 00:37:52.896 all the correct fibers that are shown here.  
NOTE Confidence: 0.824624898

00:37:52.900 --> 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 --> 00:38:02.973 so this is GFP and this is no inter

NOTE Confidence: 0.824624898

00:38:02.973 --> 00:38:06.898 from gamma. With their from them.

NOTE Confidence: 0.824624898

00:38:06.900 --> 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 --> 00:38:14.320 that carrot fiberglass isolated from

NOTE Confidence: 0.824624898

00:38:14.320 --> 00:38:17.620 from this report device expressed

NOTE Confidence: 0.824624898

00:38:17.620 --> 00:38:20.860 MHC 2 and you can see it here.

NOTE Confidence: 0.824624898

00:38:20.860 --> 00:38:24.199 You can focus here and this is zoom vision.

NOTE Confidence: 0.824624898

00:38:24.200 --> 00:38:26.594 So this will be all in green.

NOTE Confidence: 0.824624898

00:38:26.600 --> 00:38:28.546 Are cardiac fibrosis and as you can

NOTE Confidence: 0.824624898

00:38:28.546 --> 00:38:30.571 see there are also other cells that

NOTE Confidence: 0.824624898

00:38:30.571 --> 00:38:32.856 could be in the filler cells in a

NOTE Confidence: 0.824624898

00:38:32.856 --> 00:38:34.980 small kappel Aries or the drink cells

NOTE Confidence: 0.824624898

00:38:34.980 --> 00:38:37.290 as we previously shown that Expressen EC2.

NOTE Confidence: 0.824624898

00:38:37.290 --> 00:38:38.832 I've been here.

NOTE Confidence: 0.824624898

00:38:38.832 --> 00:38:39.346 Definitely,

NOTE Confidence: 0.824624898

00:38:39.346 --> 00:38:42.430 the correct fiberglass are expressing MHC  
NOTE Confidence: 0.636568968941177

00:38:42.506 --> 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 --> 00:38:51.540 that T cells seem very close to this  
NOTE Confidence: 0.636568968941177

00:38:51.540 --> 00:38:54.390 MHC 2 expressing correct fiberglass.  
NOTE Confidence: 0.636568968941177

00:38:54.390 --> 00:38:57.799 We use all the models of cardiomyopathy  
NOTE Confidence: 0.636568968941177

00:38:57.799 --> 00:39:00.060 and cardiac inflammation to see  
NOTE Confidence: 0.636568968941177

00:39:00.060 --> 00:39:02.226 whether this was unique or not,  
NOTE Confidence: 0.636568968941177

00:39:02.230 --> 00:39:04.995 and we used the tickers eye infection  
NOTE Confidence: 0.636568968941177

00:39:04.995 --> 00:39:07.422 model of myopathy because we know  
NOTE Confidence: 0.636568968941177

00:39:07.422 --> 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 --> 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 --> 00:39:18.200 the correct fabulous also expressed  
NOTE Confidence: 0.636568968941177

00:39:18.200 --> 00:39:21.400 any todo and more more of them



NOTE Confidence: 0.636568968941177

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

NOTE Confidence: 0.636568968941177

00:39:25.080 --> 00:39:27.300 The prizes and densities also higher.

NOTE Confidence: 0.815977051666667

00:39:29.490 --> 00:39:31.008 So then the next question was,

NOTE Confidence: 0.815977051666667

00:39:31.010 --> 00:39:33.578 well, let's see if they can.

NOTE Confidence: 0.815977051666667

00:39:33.580 --> 00:39:35.968 Take up the antigen processor and

NOTE Confidence: 0.815977051666667

00:39:35.968 --> 00:39:38.940 present that induce T cell proliferation

NOTE Confidence: 0.815977051666667

00:39:38.940 --> 00:39:41.793 and to do that we use a reagent that

NOTE Confidence: 0.815977051666667

00:39:41.793 --> 00:39:45.088 is do DQ of album and so this is a

NOTE Confidence: 0.815977051666667

00:39:45.088 --> 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 --> 00:39:53.292 lysosomes with acidic lysosome pH,

NOTE Confidence: 0.815977051666667

00:39:53.292 --> 00:39:55.710 which is what you're required to

NOTE Confidence: 0.815977051666667

00:39:55.787 --> 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 --> 00:40:01.816 And as you can see here,

NOTE Confidence: 0.815977051666667

00:40:01.820 --> 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 --> 00:40:08.059 by cardiac fibroblast.  
NOTE Confidence: 0.815977051666667

00:40:08.060 --> 00:40:10.601 This is just one example of correct  
NOTE Confidence: 0.815977051666667

00:40:10.601 --> 00:40:12.908 fiber rest treated with equal woman,  
NOTE Confidence: 0.815977051666667

00:40:12.910 --> 00:40:14.877 but you can see here the comparison  
NOTE Confidence: 0.815977051666667

00:40:14.877 --> 00:40:16.890 of a large correct fiberglass  
NOTE Confidence: 0.815977051666667

00:40:16.890 --> 00:40:18.786 and obviously a smaller in size.  
NOTE Confidence: 0.815977051666667

00:40:18.790 --> 00:40:21.070 Here the bone marrow derived  
NOTE Confidence: 0.815977051666667

00:40:21.070 --> 00:40:24.488 cells that a process.  
NOTE Confidence: 0.815977051666667

00:40:24.490 --> 00:40:26.428 So that was very exciting too,  
NOTE Confidence: 0.815977051666667

00:40:26.430 --> 00:40:28.310 because then that means that  
NOTE Confidence: 0.815977051666667

00:40:28.310 --> 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 --> 00:40:34.937 two and induce decent proliferation.  
NOTE Confidence: 0.815977051666667

00:40:34.940 --> 00:40:37.076 So we did similar studies as

NOTE Confidence: 0.815977051666667

00:40:37.076 --> 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 --> 00:40:43.726 and we use in this case we use

NOTE Confidence: 0.815977051666667

00:40:43.726 --> 00:40:45.947 transgenic mice that are what they do,

NOTE Confidence: 0.815977051666667

00:40:45.950 --> 00:40:48.260 so these mice all the T cell

NOTE Confidence: 0.815977051666667

00:40:48.260 --> 00:40:50.289 receptors in the details express

NOTE Confidence: 0.815977051666667

00:40:50.289 --> 00:40:52.699 a receptor for available mean.

NOTE Confidence: 0.815977051666667

00:40:52.700 --> 00:40:56.291 And then we took this specific piece

NOTE Confidence: 0.815977051666667

00:40:56.291 --> 00:40:58.580 of argument and then on the other hand,

NOTE Confidence: 0.815977051666667

00:40:58.580 --> 00:40:59.750 we took it a wild diaper.

NOTE Confidence: 0.815977051666667

00:40:59.750 --> 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 --> 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 --> 00:41:10.128 if they carry fiberglass,  
NOTE Confidence: 0.815977051666667

00:41:10.128 --> 00:41:11.316 are processing available mean?  
NOTE Confidence: 0.815977051666667

00:41:11.320 --> 00:41:15.240 As I I recently showed with Valve woman.  
NOTE Confidence: 0.815977051666667

00:41:15.240 --> 00:41:17.814 All these diesels with a receptor  
NOTE Confidence: 0.815977051666667

00:41:17.814 --> 00:41:20.456 for Valve women should be able  
NOTE Confidence: 0.815977051666667

00:41:20.456 --> 00:41:22.552 to proliferate and we did other  
NOTE Confidence: 0.815977051666667

00:41:22.552 --> 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 --> 00:41:27.046 a bacteria that over expresses  
NOTE Confidence: 0.815977051666667

00:41:27.046 --> 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 --> 00:41:31.326 these are the readout of proliferation.  
NOTE Confidence: 0.815977051666667

00:41:31.330 --> 00:41:33.122 If there is prolific,  
NOTE Confidence: 0.815977051666667

00:41:33.122 --> 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,

NOTE Confidence: 0.815977051666667  
00:41:38.170 --> 00:41:41.970 so we wouldn't see any peaks any dilution,  
NOTE Confidence: 0.815977051666667  
00:41:41.970 --> 00:41:44.462 but if there is proliferation we will  
NOTE Confidence: 0.815977051666667  
00:41:44.462 --> 00:41:46.887 see this dilution of the membrane dye,  
NOTE Confidence: 0.815977051666667  
00:41:46.890 --> 00:41:49.774 but that's exactly what we saw here,  
NOTE Confidence: 0.815977051666667  
00:41:49.780 --> 00:41:52.450 so this is overwhelming protein.  
NOTE Confidence: 0.815977051666667  
00:41:52.450 --> 00:41:54.560 But here the fiberglass haven't  
NOTE Confidence: 0.815977051666667  
00:41:54.560 --> 00:41:56.670 been treated with interferon gamma,  
NOTE Confidence: 0.815977051666667  
00:41:56.670 --> 00:41:58.830 so they don't express MHC 2.  
NOTE Confidence: 0.815977051666667  
00:41:58.830 --> 00:41:59.838 Very little proliferation,  
NOTE Confidence: 0.815977051666667  
00:41:59.838 --> 00:42:02.589 but here what you can see is that  
NOTE Confidence: 0.815977051666667  
00:42:02.589 --> 00:42:04.269 when they you induce expression  
NOTE Confidence: 0.815977051666667  
00:42:04.269 --> 00:42:06.469 and you treat with over protein,  
NOTE Confidence: 0.815977051666667  
00:42:06.470 --> 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 --> 00:42:11.658 suggesting that the fiberglass  
NOTE Confidence: 0.815977051666667

00:42:11.658 --> 00:42:13.786 can induce diesel proliferation.  
NOTE Confidence: 0.815977051666667

00:42:13.790 --> 00:42:15.895 And here's a demonstration of  
NOTE Confidence: 0.815977051666667

00:42:15.895 --> 00:42:18.374 dendritic cells as a positive control,  
NOTE Confidence: 0.815977051666667

00:42:18.374 --> 00:42:20.244 where we see a proliferation  
NOTE Confidence: 0.815977051666667

00:42:20.244 --> 00:42:22.330 and as I said before,  
NOTE Confidence: 0.815977051666667

00:42:22.330 --> 00:42:24.090 these are the professional  
NOTE Confidence: 0.815977051666667

00:42:24.090 --> 00:42:25.410 antigen presenting cells,  
NOTE Confidence: 0.815977051666667

00:42:25.410 --> 00:42:26.691 so they don't need to be pre  
NOTE Confidence: 0.815977051666667

00:42:26.691 --> 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 --> 00:42:32.750 We also did these experiments,  
NOTE Confidence: 0.815977051666667

00:42:32.750 --> 00:42:35.186 obviously with the MMC to knockout.  
NOTE Confidence: 0.815977051666667

00:42:35.190 --> 00:42:37.140 Correct fiberglass to to show  
NOTE Confidence: 0.815977051666667

00:42:37.140 --> 00:42:41.150 that this was a specific.  
NOTE Confidence: 0.815977051666667

00:42:41.150 --> 00:42:44.238 So just to be.  
NOTE Confidence: 0.815977051666667

00:42:44.240 --> 00:42:46.560 Over a convenience with this

NOTE Confidence: 0.815977051666667

00:42:46.560 --> 00:42:48.416 we do particularly proteins.

NOTE Confidence: 0.698947856666667

00:42:48.420 --> 00:42:50.330 So instead of putting a

NOTE Confidence: 0.698947856666667

00:42:50.330 --> 00:42:51.858 soluble of argument there,

NOTE Confidence: 0.698947856666667

00:42:51.860 --> 00:42:54.248 we collaborated with Carolyn Genco and

NOTE Confidence: 0.698947856666667

00:42:54.248 --> 00:42:57.219 Robert in our floor in order Department

NOTE Confidence: 0.698947856666667

00:42:57.220 --> 00:42:59.780 and they just happen to have these E.

NOTE Confidence: 0.698947856666667

00:42:59.780 --> 00:43:02.348 Coli that over expresses,

NOTE Confidence: 0.698947856666667

00:43:02.350 --> 00:43:04.374 so we try to correct fiberglass with E.

NOTE Confidence: 0.698947856666667

00:43:04.380 --> 00:43:07.278 Coli that had an empty vehicle

NOTE Confidence: 0.698947856666667

00:43:07.278 --> 00:43:08.727 or expressing involvement,

NOTE Confidence: 0.698947856666667

00:43:08.730 --> 00:43:11.788 and we saw that only when when E.

NOTE Confidence: 0.698947856666667

00:43:11.788 --> 00:43:14.126 Coli was expressing about woman we saw.

NOTE Confidence: 0.698947856666667

00:43:14.130 --> 00:43:17.444 Diesel is specific for ovum proliferate,

NOTE Confidence: 0.698947856666667

00:43:17.444 --> 00:43:20.228 and this is all quantified here,

NOTE Confidence: 0.698947856666667

00:43:20.230 --> 00:43:21.775 and this is the positive

NOTE Confidence: 0.698947856666667

00:43:21.775 --> 00:43:23.320 control with the sender excels.  
NOTE Confidence: 0.853586757142857

00:43:25.490 --> 00:43:28.766 So going back to the cardiac pathophysiology,  
NOTE Confidence: 0.853586757142857

00:43:28.770 --> 00:43:30.108 does this make?  
NOTE Confidence: 0.853586757142857

00:43:30.108 --> 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 --> 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 --> 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 --> 00:43:47.770 Please inducible and we  
NOTE Confidence: 0.853586757142857

00:43:47.770 --> 00:43:50.800 crushed it with MHC to flux.  
NOTE Confidence: 0.853586757142857

00:43:50.800 --> 00:43:53.920 And we generated the correct  
NOTE Confidence: 0.853586757142857

00:43:53.920 --> 00:43:57.040 fiberglass specific deficient in MHC  
NOTE Confidence: 0.853586757142857

00:43:57.138 --> 00:43:59.190 do and these mice are only deficient  
NOTE Confidence: 0.853586757142857

00:43:59.190 --> 00:44:01.298 if you treat them with tamoxifen  
NOTE Confidence: 0.853586757142857

00:44:01.298 --> 00:44:03.298 because it's an inducible line.



NOTE Confidence: 0.853586757142857

00:44:03.300 --> 00:44:04.836 So as you can see here,

NOTE Confidence: 0.853586757142857

00:44:04.840 --> 00:44:07.025 we corroborated that it when

NOTE Confidence: 0.853586757142857

00:44:07.025 --> 00:44:08.773 we treated with tamoxifen,

NOTE Confidence: 0.853586757142857

00:44:08.780 --> 00:44:12.868 we decrease the expression of MHC 2.

NOTE Confidence: 0.853586757142857

00:44:12.870 --> 00:44:15.390 Here, so this this is what we will be

NOTE Confidence: 0.853586757142857

00:44:15.390 --> 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 --> 00:44:23.214 Dendritic cells where MHC 2 levels

NOTE Confidence: 0.853586757142857

00:44:23.214 --> 00:44:25.602 remain compatible in the treated

NOTE Confidence: 0.853586757142857

00:44:25.602 --> 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 --> 00:44:35.640 fibrosis in the TACK control group

NOTE Confidence: 0.853586757142857

00:44:35.640 --> 00:44:38.039 than non democracies untreated,

NOTE Confidence: 0.853586757142857

00:44:38.040 --> 00:44:41.351 but when we treated with tamoxifen we  
NOTE Confidence: 0.853586757142857

00:44:41.351 --> 00:44:43.695 reduce fibrosis significantly and this  
NOTE Confidence: 0.853586757142857

00:44:43.695 --> 00:44:46.239 has an impact in fractional shortening.  
NOTE Confidence: 0.853586757142857

00:44:46.240 --> 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 --> 00:44:54.577 and this is the most mice,  
NOTE Confidence: 0.853586757142857

00:44:54.577 --> 00:44:57.513 so again these are the ones that don't  
NOTE Confidence: 0.853586757142857

00:44:57.513 --> 00:45:00.671 have image do in the fiberglass and  
NOTE Confidence: 0.853586757142857

00:45:00.671 --> 00:45:04.476 they have preserved systolic function.  
NOTE Confidence: 0.853586757142857

00:45:04.480 --> 00:45:06.832 So we looked in the lymph nodes  
NOTE Confidence: 0.853586757142857

00:45:06.832 --> 00:45:08.966 to right because we wanted to  
NOTE Confidence: 0.853586757142857

00:45:08.966 --> 00:45:10.716 see whether this was where.  
NOTE Confidence: 0.853586757142857

00:45:10.720 --> 00:45:13.582 Remember that we're eliminating this in  
NOTE Confidence: 0.853586757142857

00:45:13.582 --> 00:45:17.084 the in the cardiac fibroblast and they  
NOTE Confidence: 0.853586757142857

00:45:17.084 --> 00:45:19.892 might be other cells that express TCF 21,  
NOTE Confidence: 0.853586757142857

00:45:19.892 --> 00:45:21.020 although it is,

NOTE Confidence: 0.853586757142857  
00:45:21.020 --> 00:45:23.054 it was described to be a  
NOTE Confidence: 0.853586757142857  
00:45:23.054 --> 00:45:24.410 driver for collect fibers.  
NOTE Confidence: 0.853586757142857  
00:45:24.410 --> 00:45:26.804 And what we find is that the T cell  
NOTE Confidence: 0.853586757142857  
00:45:26.804 --> 00:45:28.688 immune response in the lymph node  
NOTE Confidence: 0.853586757142857  
00:45:28.688 --> 00:45:31.661 is not altered by by this intact.  
NOTE Confidence: 0.853586757142857  
00:45:31.661 --> 00:45:33.969 And we also see.  
NOTE Confidence: 0.853586757142857  
00:45:33.970 --> 00:45:36.054 Similar infiltration of character  
NOTE Confidence: 0.853586757142857  
00:45:36.054 --> 00:45:38.716 in these mice with tamoxifen.  
NOTE Confidence: 0.853586757142857  
00:45:38.716 --> 00:45:42.004 So working hypothesis now is that  
NOTE Confidence: 0.853586757142857  
00:45:42.010 --> 00:45:44.470 these are the conclusions right that  
NOTE Confidence: 0.853586757142857  
00:45:44.470 --> 00:45:47.951 in these crosstalk we have the T cells  
NOTE Confidence: 0.853586757142857  
00:45:47.951 --> 00:45:49.719 and the fiberglass communicating.  
NOTE Confidence: 0.853586757142857  
00:45:49.720 --> 00:45:51.604 And in this two week crosstalk  
NOTE Confidence: 0.853586757142857  
00:45:51.604 --> 00:45:53.304 we think there correct fibrils  
NOTE Confidence: 0.853586757142857  
00:45:53.304 --> 00:45:55.759 are Sentinel cells that can sense  
NOTE Confidence: 0.853586757142857

00:45:55.759 --> 00:45:57.924 correct insults and directly boost  
NOTE Confidence: 0.853586757142857

00:45:57.924 --> 00:45:59.980 the adaptive immune response.  
NOTE Confidence: 0.853586757142857

00:45:59.980 --> 00:46:02.682 We think that there's a potential of  
NOTE Confidence: 0.853586757142857

00:46:02.682 --> 00:46:04.480 moderating decent immune responses  
NOTE Confidence: 0.853586757142857

00:46:04.480 --> 00:46:06.220 without impairing systemic diesel  
NOTE Confidence: 0.853586757142857

00:46:06.220 --> 00:46:08.830 activation by the cells which could  
NOTE Confidence: 0.853586757142857

00:46:08.896 --> 00:46:11.416 have undecided major suppressive effect.  
NOTE Confidence: 0.853586757142857

00:46:11.420 --> 00:46:13.640 So the fact that we see.  
NOTE Confidence: 0.853586757142857

00:46:13.640 --> 00:46:16.034 Similar activation in the in the  
NOTE Confidence: 0.853586757142857

00:46:16.034 --> 00:46:18.679 lymph nodes that that tells us to  
NOTE Confidence: 0.853586757142857

00:46:18.679 --> 00:46:21.665 think that these this is critical in  
NOTE Confidence: 0.853586757142857

00:46:21.665 --> 00:46:24.740 the heart for the correct fibers.  
NOTE Confidence: 0.853586757142857

00:46:24.740 --> 00:46:26.460 And then the overall summary,  
NOTE Confidence: 0.853586757142857

00:46:26.460 --> 00:46:29.644 just to wrap up and leave some time  
NOTE Confidence: 0.853586757142857

00:46:29.644 --> 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 --> 00:46:39.580 that of others that I've cited and  
NOTE Confidence: 0.853586757142857  
00:46:39.580 --> 00:46:42.460 that we we always site in in our papers,  
NOTE Confidence: 0.853586757142857  
00:46:42.460 --> 00:46:44.180 is the diesel immune responses  
NOTE Confidence: 0.853586757142857  
00:46:44.180 --> 00:46:45.556 contribute to the pathophysiology  
NOTE Confidence: 0.853586757142857  
00:46:45.556 --> 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 --> 00:46:52.305 So we think that eleven took blood pressure,  
NOTE Confidence: 0.853586757142857  
00:46:52.310 --> 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 --> 00:47:01.650 antigens that trigger this activation  
NOTE Confidence: 0.808975422692308  
00:47:01.736 --> 00:47:04.662 in the heart. Within that limited repertoire  
NOTE Confidence: 0.808975422692308  
00:47:04.662 --> 00:47:08.280 of those T cells respond to ISO LGS.  
NOTE Confidence: 0.808975422692308  
00:47:08.280 --> 00:47:10.890 Modified cardiac new antigens and contributes  
NOTE Confidence: 0.808975422692308  
00:47:10.890 --> 00:47:13.450 to cardiac fibrosis and dysfunction.  
NOTE Confidence: 0.808975422692308

00:47:13.450 --> 00:47:15.786 But we don't think these are the early

NOTE Confidence: 0.808975422692308

00:47:15.786 --> 00:47:17.780 antigens that diesels are recognizing,

NOTE Confidence: 0.808975422692308

00:47:17.780 --> 00:47:20.279 because if you recall from our data,

NOTE Confidence: 0.808975422692308

00:47:20.280 --> 00:47:24.366 even when we scavenge those icebergs

NOTE Confidence: 0.808975422692308

00:47:24.370 --> 00:47:26.265 modified proteins, we still see

NOTE Confidence: 0.808975422692308

00:47:26.265 --> 00:47:28.600 some decent activation in the heart.

NOTE Confidence: 0.808975422692308

00:47:28.600 --> 00:47:30.787 So we are doing a lot of more in

NOTE Confidence: 0.808975422692308

00:47:30.787 --> 00:47:32.637 depth analysis of single cell.

NOTE Confidence: 0.808975422692308

00:47:32.640 --> 00:47:34.260 He's service center sequencing and

NOTE Confidence: 0.808975422692308

00:47:34.260 --> 00:47:36.943 trying to get to what are those other

NOTE Confidence: 0.808975422692308

00:47:36.943 --> 00:47:39.067 antigens that might be induced response?

NOTE Confidence: 0.808975422692308

00:47:39.067 --> 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 --> 00:47:48.359 see how heart failure progresses,

NOTE Confidence: 0.808975422692308

00:47:48.360 --> 00:47:50.580 at least pretty nicely.

NOTE Confidence: 0.808975422692308  
00:47:50.580 --> 00:47:52.995 And then the last conclusion from this  
NOTE Confidence: 0.808975422692308  
00:47:52.995 --> 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 --> 00:48:00.598 in this case fiber rise and T cells  
NOTE Confidence: 0.808975422692308  
00:48:00.600 --> 00:48:02.860 contribute to correct this activation.  
NOTE Confidence: 0.808975422692308  
00:48:02.860 --> 00:48:05.292 My fibrous transformation and  
NOTE Confidence: 0.808975422692308  
00:48:05.292 --> 00:48:07.724 dysfunction under the correct  
NOTE Confidence: 0.808975422692308  
00:48:07.724 --> 00:48:11.499 fabulous expression of MHC 2 molecules  
NOTE Confidence: 0.808975422692308  
00:48:11.499 --> 00:48:15.364 is central for these response.  
NOTE Confidence: 0.808975422692308  
00:48:15.370 --> 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 --> 00:48:26.093 done the work who's now moved on to new  
NOTE Confidence: 0.808975422692308  
00:48:26.093 --> 00:48:28.149 exciting research leading positions,  
NOTE Confidence: 0.808975422692308  
00:48:28.150 --> 00:48:30.294 and then this is the new members of  
NOTE Confidence: 0.808975422692308  
00:48:30.294 --> 00:48:32.460 the lab that are trying to pick up  
NOTE Confidence: 0.808975422692308

00:48:32.460 --> 00:48:34.592 on all the good work that previous  
NOTE Confidence: 0.808975422692308

00:48:34.592 --> 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 --> 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 --> 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 --> 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 --> 00:49:00.855 which will hopefully happen in  
NOTE Confidence: 0.808975422692308

00:49:00.855 --> 00:49:03.731 person is scheduled to be in person  
NOTE Confidence: 0.808975422692308

00:49:03.731 --> 00:49:05.710 in Chicago and there will be a  
NOTE Confidence: 0.808975422692308

00:49:05.710 --> 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 --> 00:49:14.058 cardiology and basic and traditional science.  
NOTE Confidence: 0.808975422692308  
00:49:14.060 --> 00:49:16.180 So I'll be happy to take any questions.  
NOTE Confidence: 0.808975422692308  
00:49:16.180 --> 00:49:17.300 Thank you for your time.  
NOTE Confidence: 0.628262262  
00:49:20.780 --> 00:49:23.740 Thank you Paula for the wonderful talk.  
NOTE Confidence: 0.628262262  
00:49:23.740 --> 00:49:27.770 So now we are open to questions.  
NOTE Confidence: 0.536230803333333  
00:49:28.320 --> 00:49:32.538 I can maybe stop sharing and.  
NOTE Confidence: 0.536230803333333  
00:49:32.540 --> 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 --> 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 --> 00:49:45.150 Wonderful stuff.  
NOTE Confidence: 0.514669746  
00:49:45.150 --> 00:49:47.110 A very simplistic question.  
NOTE Confidence: 0.514669746  
00:49:47.110 --> 00:49:49.474 So at autopsy when we see  
NOTE Confidence: 0.514669746  
00:49:49.474 --> 00:49:51.689 hearts from patients who have  
NOTE Confidence: 0.514669746

00:49:51.689 --> 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 --> 00:49:57.740 striking infiltrate of lymphocytes.  
NOTE Confidence: 0.514669746

00:49:57.740 --> 00:49:59.420 Is it that we just get them  
NOTE Confidence: 0.514669746

00:49:59.420 --> 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 --> 00:50:08.099 T cells they you don't see massive  
NOTE Confidence: 0.775912582631579

00:50:08.099 --> 00:50:10.144 infiltration as you would see.  
NOTE Confidence: 0.775912582631579

00:50:10.150 --> 00:50:12.268 For instance post MI in the  
NOTE Confidence: 0.775912582631579

00:50:12.268 --> 00:50:14.643 in the in fact zone, right?  
NOTE Confidence: 0.775912582631579

00:50:14.643 --> 00:50:17.814 And I think I think you don't  
NOTE Confidence: 0.775912582631579

00:50:17.814 --> 00:50:20.108 need that many of them,  
NOTE Confidence: 0.775912582631579

00:50:20.110 --> 00:50:21.734 so they're definitely sparse  
NOTE Confidence: 0.775912582631579

00:50:21.734 --> 00:50:23.764 compared to other major cells.  
NOTE Confidence: 0.775912582631579

00:50:23.770 --> 00:50:25.922 And then the other thing that I would  
NOTE Confidence: 0.775912582631579

00:50:25.922 --> 00:50:28.111 say that we've seen when we take

NOTE Confidence: 0.775912582631579  
00:50:28.111 --> 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 --> 00:50:36.369 So it it also depends where you take  
NOTE Confidence: 0.775912582631579  
00:50:36.369 --> 00:50:40.325 the the piece from, and we've seen.  
NOTE Confidence: 0.775912582631579  
00:50:40.325 --> 00:50:43.150 We've seen some samples that  
NOTE Confidence: 0.775912582631579  
00:50:43.150 --> 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 --> 00:50:49.690 because we've done. I mean,  
NOTE Confidence: 0.775912582631579  
00:50:49.690 --> 00:50:52.270 we haven't looked at human hearts early on,  
NOTE Confidence: 0.775912582631579  
00:50:52.270 --> 00:50:54.430 other than those of those healthy,  
NOTE Confidence: 0.775912582631579  
00:50:54.430 --> 00:50:57.260 right, and those have noticed.  
NOTE Confidence: 0.775912582631579  
00:50:57.260 --> 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 --> 00:51:02.573 you can track that very easily, right?  
NOTE Confidence: 0.775912582631579  
00:51:02.573 --> 00:51:05.840 And one thing that we don't see is that.  
NOTE Confidence: 0.775912582631579

00:51:05.840 --> 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 --> 00:51:12.409 we see that the diesels are more  
NOTE Confidence: 0.775912582631579

00:51:12.409 --> 00:51:14.749 activated when we use the reporter mice.  
NOTE Confidence: 0.775912582631579

00:51:14.750 --> 00:51:17.204 But we don't see more details  
NOTE Confidence: 0.775912582631579

00:51:17.204 --> 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 --> 00:51:24.345 but definitely is not a  
NOTE Confidence: 0.775912582631579

00:51:24.345 --> 00:51:25.990 dominant cell in the heart.  
NOTE Confidence: 0.775912582631579

00:51:25.990 --> 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 --> 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 --> 00:51:36.830 activated they can release a lot

NOTE Confidence: 0.775912582631579

00:51:36.887 --> 00:51:38.616 of factors and do do other things.

NOTE Confidence: 0.775912582631579

00:51:38.620 --> 00:51:40.870 But that's a great point, thank you.

NOTE Confidence: 0.775912582631579

00:51:40.870 --> 00:51:42.520 Thank you for your question.

NOTE Confidence: 0.828033891428572

00:51:43.890 --> 00:51:48.566 I have a question actually 2 questions.

NOTE Confidence: 0.828033891428572

00:51:48.570 --> 00:51:52.130 So wonderful talk again.

NOTE Confidence: 0.828033891428572

00:51:52.130 --> 00:51:56.528 So do you think this fibroblast

NOTE Confidence: 0.828033891428572

00:51:56.530 --> 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 --> 00:52:08.674 to contribute to the fibrosis?

NOTE Confidence: 0.828033891428572

00:52:08.674 --> 00:52:10.210 That's the first question.

NOTE Confidence: 0.828033891428572

00:52:10.210 --> 00:52:12.598 Second question is related

NOTE Confidence: 0.828033891428572

00:52:12.598 --> 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 --> 00:52:19.259 genetic heart failure model such

NOTE Confidence: 0.828033891428572

00:52:19.259 --> 00:52:22.297 as missing heavy chain mutation?  
NOTE Confidence: 0.828033891428572

00:52:22.300 --> 00:52:25.121 Our foes reach you genetic HTM mice  
NOTE Confidence: 0.828033891428572

00:52:25.121 --> 00:52:28.459 as well as dilated cardiomyopathy like  
NOTE Confidence: 0.828033891428572

00:52:28.459 --> 00:52:31.854 muscle Lim protein knockout mouse.  
NOTE Confidence: 0.828033891428572

00:52:31.860 --> 00:52:33.800 They have natural heart failure.  
NOTE Confidence: 0.828033891428572

00:52:33.800 --> 00:52:36.330 Whether your hack information could  
NOTE Confidence: 0.828033891428572

00:52:36.330 --> 00:52:39.580 be extended to genetic heart failure,  
NOTE Confidence: 0.828033891428572

00:52:39.580 --> 00:52:41.962 which may mimic human heart failure  
NOTE Confidence: 0.828033891428572

00:52:41.962 --> 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 --> 00:52:47.464 so I'll ask for the first one.  
NOTE Confidence: 0.590237698333333

00:52:47.470 --> 00:52:49.918 The first one, you're totally right.  
NOTE Confidence: 0.590237698333333

00:52:49.920 --> 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 --> 00:52:55.488 not only attract diesels,  
NOTE Confidence: 0.590237698333333

00:52:55.490 --> 00:52:57.710 but they attract monocytes.

NOTE Confidence: 0.590237698333333  
00:52:57.710 --> 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 --> 00:53:11.382 He found that early on,  
NOTE Confidence: 0.590237698333333  
00:53:11.382 --> 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 --> 00:53:21.938 They infiltrate the hard  
NOTE Confidence: 0.590237698333333  
00:53:21.938 --> 00:53:23.986 before the diesels do,  
NOTE Confidence: 0.590237698333333  
00:53:23.990 --> 00:53:27.046 and we found following following up on that,  
NOTE Confidence: 0.590237698333333  
00:53:27.050 --> 00:53:29.330 we found that the correct fiberglass  
NOTE Confidence: 0.590237698333333  
00:53:29.330 --> 00:53:33.098 they make CXCL 9 and 10 that are  
NOTE Confidence: 0.590237698333333  
00:53:33.098 --> 00:53:34.850 chemoattractants for diesels,  
NOTE Confidence: 0.590237698333333  
00:53:34.850 --> 00:53:36.954 but they also make a lot of C, CL two.  
NOTE Confidence: 0.590237698333333  
00:53:36.954 --> 00:53:38.858 So that makes a lot of sense  
NOTE Confidence: 0.590237698333333

00:53:38.858 --> 00:53:40.870 that when they sense pressure.  
NOTE Confidence: 0.590237698333333  
00:53:40.870 --> 00:53:42.550 And they release the chemo kids.  
NOTE Confidence: 0.590237698333333  
00:53:42.550 --> 00:53:45.930 The second thing in that related  
NOTE Confidence: 0.590237698333333  
00:53:45.930 --> 00:53:50.730 to that question is that.  
NOTE Confidence: 0.590237698333333  
00:53:50.730 --> 00:53:52.164 Once they infiltrate,  
NOTE Confidence: 0.590237698333333  
00:53:52.164 --> 00:53:53.120 so we,  
NOTE Confidence: 0.590237698333333  
00:53:53.120 --> 00:53:56.464 we've found that the major source of the  
NOTE Confidence: 0.590237698333333  
00:53:56.464 --> 00:53:58.438 diesel chemoattractant proteins is not.  
NOTE Confidence: 0.590237698333333  
00:53:58.440 --> 00:54:01.807 The fiberglass is actually the Milo itself.  
NOTE Confidence: 0.590237698333333  
00:54:01.810 --> 00:54:04.505 So those I think it's all orchestrated.  
NOTE Confidence: 0.590237698333333  
00:54:04.510 --> 00:54:06.578 Basically they fibroblasts release  
NOTE Confidence: 0.590237698333333  
00:54:06.578 --> 00:54:09.163 chemo treatments for innate cells.  
NOTE Confidence: 0.590237698333333  
00:54:09.170 --> 00:54:11.535 Then they adapted cells come  
NOTE Confidence: 0.590237698333333  
00:54:11.535 --> 00:54:13.386 because there's also an interaction  
NOTE Confidence: 0.590237698333333  
00:54:13.386 --> 00:54:15.450 between a myeloid cells and the  
NOTE Confidence: 0.590237698333333  
00:54:15.516 --> 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 --> 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 --> 00:54:27.667 We haven't looked because we we've never.  
NOTE Confidence: 0.590237698333333  
00:54:27.670 --> 00:54:31.162 We don't have the tools or or the mice,  
NOTE Confidence: 0.590237698333333  
00:54:31.170 --> 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 --> 00:54:39.109 and especially in those mutations  
NOTE Confidence: 0.590237698333333  
00:54:39.193 --> 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 --> 00:54:45.955 at dysfunctional from very early  
NOTE Confidence: 0.590237698333333  
00:54:45.955 --> 00:54:47.359 on it spontaneously right.  
NOTE Confidence: 0.590237698333333  
00:54:47.360 --> 00:54:50.272 You could really track and I'm sure that  
NOTE Confidence: 0.590237698333333  
00:54:50.272 --> 00:54:53.288 there will be other antigens involved, right?  
NOTE Confidence: 0.590237698333333  
00:54:53.288 --> 00:54:56.110 So it might be that we will need to find  
NOTE Confidence: 0.590237698333333

00:54:56.110 --> 00:54:57.810 out whether inflammation plays a role.  
NOTE Confidence: 0.590237698333333

00:54:57.810 --> 00:54:59.160 It might be that it has  
NOTE Confidence: 0.590237698333333

00:54:59.160 --> 00:55:00.760 nothing to do with information,  
NOTE Confidence: 0.590237698333333

00:55:00.760 --> 00:55:03.077 but if it did, if it did,  
NOTE Confidence: 0.590237698333333

00:55:03.080 --> 00:55:07.342 it would be easier to track whether the T  
NOTE Confidence: 0.590237698333333

00:55:07.342 --> 00:55:11.039 cells might be recognizing proteins that are.  
NOTE Confidence: 0.590237698333333

00:55:11.039 --> 00:55:13.697 You know that may be misfolded,  
NOTE Confidence: 0.590237698333333

00:55:13.700 --> 00:55:15.608 or that their mutated due to  
NOTE Confidence: 0.590237698333333

00:55:15.608 --> 00:55:17.480 the mutation in the myocyte,  
NOTE Confidence: 0.590237698333333

00:55:17.480 --> 00:55:20.075 so that that would be a yeah, that would be.  
NOTE Confidence: 0.590237698333333

00:55:20.075 --> 00:55:21.650 That's that would be an excellent Ave.  
NOTE Confidence: 0.864855594

00:55:23.480 --> 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 --> 00:55:36.880 I'm very excited about the talk.  
NOTE Confidence: 0.650748348

00:55:36.880 --> 00:55:39.680 I have another follow-up question.  
NOTE Confidence: 0.650748348

00:55:39.680 --> 00:55:42.420 What do you think about

NOTE Confidence: 0.650748348

00:55:42.420 --> 00:55:43.516 stressed cardiomyocytes?

NOTE Confidence: 0.650748348

00:55:43.520 --> 00:55:47.850 They may release new entity to the

NOTE Confidence: 0.650748348

00:55:47.850 --> 00:55:50.265 to the identical cells or two so

NOTE Confidence: 0.650748348

00:55:50.265 --> 00:55:52.848 they they catch up the antigen and

NOTE Confidence: 0.650748348

00:55:52.848 --> 00:55:55.732 present to CD 4T cells because we

NOTE Confidence: 0.650748348

00:55:55.732 --> 00:55:58.450 have cardiac troponin T troponin I.

NOTE Confidence: 0.650748348

00:55:58.450 --> 00:56:01.312 Fragmented release in the injured heart

NOTE Confidence: 0.650748348

00:56:01.312 --> 00:56:05.089 and and also cardio my side when stressed.

NOTE Confidence: 0.650748348

00:56:05.090 --> 00:56:06.802 They may secrete teacher

NOTE Confidence: 0.650748348

00:56:06.802 --> 00:56:09.370 Beta 2 instead of beta one.

NOTE Confidence: 0.650748348

00:56:09.370 --> 00:56:12.410 We adapt be interesting avenues for you to

NOTE Confidence: 0.2591359055

00:56:12.420 --> 00:56:15.126 yes so that so first hypothesis.

NOTE Confidence: 0.2591359055

00:56:15.130 --> 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 --> 00:56:24.350 to look at this diesel drones right

NOTE Confidence: 0.2591359055

00:56:24.350 --> 00:56:27.059 and our first hypothesis was I had  
NOTE Confidence: 0.2591359055

00:56:27.059 --> 00:56:30.037 just written a commentary on a paper.  
NOTE Confidence: 0.2591359055

00:56:30.040 --> 00:56:32.860 Looking at all these in altimmune  
NOTE Confidence: 0.2591359055

00:56:32.860 --> 00:56:35.371 myocarditis you know how character  
NOTE Confidence: 0.2591359055

00:56:35.371 --> 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 --> 00:56:44.750 that are fighting people, right?  
NOTE Confidence: 0.2591359055

00:56:44.750 --> 00:56:47.445 So we thought that 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 --> 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 --> 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 --> 00:57:00.128 They might be that the stretch.  
NOTE Confidence: 0.2591359055

00:57:00.130 --> 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?

NOTE Confidence: 0.2591359055

00:57:03.270 --> 00:57:05.510 Because you can stretch all these cells we.

NOTE Confidence: 0.2591359055

00:57:05.510 --> 00:57:07.150 We don't have the ability to do that,

NOTE Confidence: 0.2591359055

00:57:07.150 --> 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 --> 00:57:14.391 seed in between the myocytes, right?

NOTE Confidence: 0.2591359055

00:57:14.391 --> 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 --> 00:57:24.816 kind of myocyte communication.

NOTE Confidence: 0.2591359055

00:57:24.820 --> 00:57:27.634 So it might be that those fragments

NOTE Confidence: 0.2591359055

00:57:27.634 --> 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 --> 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 --> 00:57:36.617 and the fiber rest pick it up.

NOTE Confidence: 0.2591359055

00:57:36.620 --> 00:57:38.160 And then the fiberglass percent,  
NOTE Confidence: 0.2591359055

00:57:38.160 --> 00:57:40.668 but that's purely an in speculation.  
NOTE Confidence: 0.2591359055

00:57:40.670 --> 00:57:41.478 We haven't.  
NOTE Confidence: 0.2591359055

00:57:41.478 --> 00:57:43.498 We haven't looked at that,  
NOTE Confidence: 0.2591359055

00:57:43.500 --> 00:57:46.428 but I think it's not only.  
NOTE Confidence: 0.2591359055

00:57:46.430 --> 00:57:48.313 I think this is very complex and  
NOTE Confidence: 0.2591359055

00:57:48.313 --> 00:57:50.154 it's not only limited to the  
NOTE Confidence: 0.2591359055

00:57:50.154 --> 00:57:51.764 T cell binding to fibroblast.  
NOTE Confidence: 0.2591359055

00:57:51.770 --> 00:57:54.250 I think there is a.  
NOTE Confidence: 0.2591359055

00:57:54.250 --> 00:57:57.160 Cross communication with like an  
NOTE Confidence: 0.2591359055

00:57:57.160 --> 00:57:59.935 orchestrated response there with my  
NOTE Confidence: 0.2591359055

00:57:59.935 --> 00:58:02.160 insides fiberglass and immune cells.  
NOTE Confidence: 0.581264438

00:58:03.430 --> 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 --> 00:58:12.109 I just wonder you made a comment  
NOTE Confidence: 0.581264438

00:58:12.109 --> 00:58:13.996 on your introduction that said

NOTE Confidence: 0.581264438

00:58:13.996 --> 00:58:15.608 that no immune intervention.

NOTE Confidence: 0.581264438

00:58:15.610 --> 00:58:17.925 No trial has produced any

NOTE Confidence: 0.581264438

00:58:17.925 --> 00:58:22.090 effect on cardiac failure.

NOTE Confidence: 0.581264438

00:58:22.090 --> 00:58:24.493 And I wonder whether there any

NOTE Confidence: 0.581264438

00:58:24.493 --> 00:58:27.298 observations in patients who receive.

NOTE Confidence: 0.581264438

00:58:27.300 --> 00:58:28.833 Chronic immunosuppressive therapy

NOTE Confidence: 0.581264438

00:58:28.833 --> 00:58:31.899 with any number of different drugs,

NOTE Confidence: 0.581264438

00:58:31.900 --> 00:58:33.908 whether there's any effect

NOTE Confidence: 0.581264438

00:58:33.908 --> 00:58:35.430 on cardiac failure.

NOTE Confidence: 0.748793660588235

00:58:36.180 --> 00:58:39.978 Yeah, so we did actually have to look at

NOTE Confidence: 0.748793660588235

00:58:39.978 --> 00:58:43.506 that because we made a long table of.

NOTE Confidence: 0.748793660588235

00:58:43.510 --> 00:58:45.826 Exactly looking at that right of,

NOTE Confidence: 0.748793660588235

00:58:45.830 --> 00:58:48.560 you know, these were the TNF blockers

NOTE Confidence: 0.748793660588235

00:58:48.560 --> 00:58:51.344 and these are other immunosuppressive

NOTE Confidence: 0.748793660588235

00:58:51.344 --> 00:58:54.490 agents and we didn't find any.

NOTE Confidence: 0.748793660588235

00:58:54.490 --> 00:58:55.670 I don't think there's been.  
NOTE Confidence: 0.748793660588235

00:58:55.670 --> 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 --> 00:59:04.646 at method tracks and other drugs,  
NOTE Confidence: 0.748793660588235

00:59:04.646 --> 00:59:07.292 but I don't think there's a detail  
NOTE Confidence: 0.748793660588235

00:59:07.292 --> 00:59:09.001 investigation of what having the  
NOTE Confidence: 0.748793660588235

00:59:09.001 --> 00:59:10.897 expectation would be that if you  
NOTE Confidence: 0.748793660588235

00:59:10.963 --> 00:59:13.366 suppress inflammation it be good, right?  
NOTE Confidence: 0.748793660588235

00:59:13.366 --> 00:59:16.570 But those drugs also have a lot of side  
NOTE Confidence: 0.748793660588235

00:59:16.652 --> 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 --> 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 --> 00:59:34.978 and try to find a smaller pathways.  
NOTE Confidence: 0.854330388518518

00:59:36.650 --> 00:59:38.684 I certainly agree, but I just  
NOTE Confidence: 0.854330388518518

00:59:38.684 --> 00:59:40.040 wonder whether there's any



NOTE Confidence: 0.854330388518518  
00:59:40.104 --> 00:59:41.994 evidence that you know what the  
NOTE Confidence: 0.854330388518518  
00:59:41.994 --> 00:59:44.024 effect of the immune system is  
NOTE Confidence: 0.854330388518518  
00:59:44.024 --> 00:59:45.794 on in clinically and inpatient.  
NOTE Confidence: 0.854330388518518  
00:59:45.800 --> 00:59:47.648 A lot of patients who get,  
NOTE Confidence: 0.854330388518518  
00:59:47.650 --> 00:59:49.760 you know steroids and get  
NOTE Confidence: 0.854330388518518  
00:59:49.760 --> 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 --> 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 --> 01:00:03.330 Maybe? Maybe not.  
NOTE Confidence: 0.79021516  
01:00:03.330 --> 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 --> 01:00:11.108 They did exactly that,  
NOTE Confidence: 0.79021516  
01:00:11.108 --> 01:00:13.640 and they reviewed all the literature  
NOTE Confidence: 0.79021516  
01:00:13.715 --> 01:00:16.480 in large trials, small trials,  
NOTE Confidence: 0.79021516

01:00:16.480 --> 01:00:19.720 directly tackling immune mediators,  
NOTE Confidence: 0.79021516

01:00:19.720 --> 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 --> 01:00:35.316 That review was very detailed and it was.  
NOTE Confidence: 0.79021516

01:00:35.320 --> 01:00:37.906 It was very nice to to read and they had the  
NOTE Confidence: 0.79021516

01:00:37.906 --> 01:00:40.090 they reviewed the mechanistic part of it,  
NOTE Confidence: 0.79021516

01:00:40.090 --> 01:00:43.420 but then they review all the patient trials.  
NOTE Confidence: 0.79021516

01:00:43.420 --> 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 --> 01:00:49.114 cardiology for sure and I don't  
NOTE Confidence: 0.79021516

01:00:49.114 --> 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 --> 01:01:01.448 So if if there are no additional

NOTE Confidence: 0.813786035333333

01:01:01.448 --> 01:01:03.529 questions so thank you so much

NOTE Confidence: 0.813786035333333

01:01:03.529 --> 01:01:05.209 Paula for this exciting talk.

NOTE Confidence: 0.813786035333333

01:01:05.210 --> 01:01:07.916 We learn a lot cardiology immunology,

NOTE Confidence: 0.813786035333333

01:01:07.920 --> 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 --> 01:01:19.000 Bye bye thank you.