WEBVTT

- NOTE duration:"00:59:28"
- NOTE recognizability:0.712
- NOTE language:en-us
- NOTE Confidence: 0.8969188
- 00:00:05.750 --> 00:00:07.870 OK. We are on time 12:30,
- NOTE Confidence: 0.8301440916666667
- $00:00:07.870 \longrightarrow 00:00:10.168$ so we're going to start and
- NOTE Confidence: 0.8301440916666667
- $00{:}00{:}10.170 \dashrightarrow 00{:}00{:}11.594$ so first welcome every body.
- NOTE Confidence: 0.830144091666667
- $00{:}00{:}11.594 \dashrightarrow 00{:}00{:}15.734$ This is the first in person brand grounds
- NOTE Confidence: 0.830144091666667
- $00:00:15.734 \rightarrow 00:00:18.830$ meeting and we're very happy about it.
- NOTE Confidence: 0.830144091666667
- $00:00:18.830 \longrightarrow 00:00:20.979$ So we expect to have people joining.
- NOTE Confidence: 0.830144091666667
- $00{:}00{:}20{.}980 \dashrightarrow 00{:}00{:}24.011$ We have 20 people online and may be
- NOTE Confidence: 0.830144091666667
- $00:00:24.011 \longrightarrow 00:00:26.340$ some more people to come so.
- NOTE Confidence: 0.830144091666667
- $00:00:26.340 \longrightarrow 00:00:28.350$ So it's a great pleasure
- NOTE Confidence: 0.830144091666667
- $00:00:28.350 \longrightarrow 00:00:30.360$ today to have our speaker,
- NOTE Confidence: 0.830144091666667
- $00:00:30.360 \longrightarrow 00:00:32.300$ his doctor Weiping Zou.
- NOTE Confidence: 0.830144091666667
- $00:00:32.300 \longrightarrow 00:00:34.240$ He's currently the Charles
- NOTE Confidence: 0.830144091666667
- $00:00:34.240 \longrightarrow 00:00:36.060$ Denman Creek professor.
- NOTE Confidence: 0.830144091666667

00:00:36.060 --> 00:00:37.540 He's a professor of immunology,

NOTE Confidence: 0.830144091666667

00:00:37.540 --> 00:00:37.846 pathology,

NOTE Confidence: 0.830144091666667

 $00:00:37.846 \rightarrow 00:00:39.682$ biology and surgery at the University

NOTE Confidence: 0.830144091666667

 $00:00:39.682 \longrightarrow 00:00:41.499$ of Michigan and he's also the

NOTE Confidence: 0.830144091666667

 $00{:}00{:}41.499 \dashrightarrow 00{:}00{:}43.191$ director of the Michigan Center of

NOTE Confidence: 0.830144091666667

00:00:43.191 --> 00:00:44.579 Excellence for Cancer Immunology,

NOTE Confidence: 0.830144091666667

 $00:00:44.580 \longrightarrow 00:00:44.979$ immunotherapy.

NOTE Confidence: 0.830144091666667

 $00{:}00{:}44.979 \dashrightarrow 00{:}00{:}47.772$ And he has a number of additional

NOTE Confidence: 0.830144091666667

 $00{:}00{:}47.772 \dashrightarrow 00{:}00{:}50.096$ appointments that I will omit now

NOTE Confidence: 0.830144091666667

 $00:00:50.096 \rightarrow 00:00:54.664$ because I think they just add too much.

NOTE Confidence: 0.830144091666667

 $00:00:54.664 \rightarrow 00:00:56.488$ Maybe he's training.

NOTE Confidence: 0.8301440916666667

 $00{:}00{:}56.490 \dashrightarrow 00{:}00{:}59.022$ He obtained his MD in China

NOTE Confidence: 0.830144091666667

00:00:59.022 --> 00:01:00.288 in Tongji University,

NOTE Confidence: 0.8301440916666667

 $00{:}01{:}00{.}290 \dashrightarrow 00{:}01{:}02{.}607$ and then he went on to get

NOTE Confidence: 0.830144091666667

00:01:02.607 --> 00:01:04.450 obtain a PhD in Paris.

NOTE Confidence: 0.830144091666667

 $00:01:04.450 \dashrightarrow 00:01:06.865$ That was followed by postdoctoral training in

00:01:06.865 --> 00:01:09.547 France and then postural training in Baylor,

NOTE Confidence: 0.830144091666667

 $00{:}01{:}09{.}550 \dashrightarrow 00{:}01{:}11{.}650$ Dallas.

NOTE Confidence: 0.830144091666667

 $00:01:11.650 \rightarrow 00:01:14.560$ And then from his academic career,

NOTE Confidence: 0.830144091666667

 $00:01:14.560 \longrightarrow 00:01:18.278$ he initiated his career as an

NOTE Confidence: 0.830144091666667

 $00{:}01{:}18.278 \dashrightarrow 00{:}01{:}19.502$ assistant professor in Tulane

NOTE Confidence: 0.830144091666667

00:01:19.502 --> 00:01:20.880 University in New Orleans,

NOTE Confidence: 0.830144091666667

 $00:01:20.880 \longrightarrow 00:01:23.064$ where he rose to the rank of

NOTE Confidence: 0.830144091666667

 $00:01:23.064 \rightarrow 00:01:24.480$ associate professor with tenure.

NOTE Confidence: 0.830144091666667

 $00{:}01{:}24{.}480 \dashrightarrow 00{:}01{:}26{.}736$ And then he moved to University of Michigan,

NOTE Confidence: 0.830144091666667

 $00{:}01{:}26.740 \dashrightarrow 00{:}01{:}29.260$ where he became a full professor

NOTE Confidence: 0.830144091666667

 $00:01:29.260 \longrightarrow 00:01:32.440$ and director of the program.

NOTE Confidence: 0.830144091666667

 $00:01:32.440 \dashrightarrow 00:01:34.810$ What is very interesting is that

NOTE Confidence: 0.830144091666667

 $00:01:34.810 \dashrightarrow 00:01:37.400$ he's a very productive investigator.

NOTE Confidence: 0.830144091666667

00:01:37.400 --> 00:01:39.900 He has over 190 publications.

NOTE Confidence: 0.830144091666667

 $00:01:39.900 \longrightarrow 00:01:42.312$ I could count about 35.

00:01:42.312 --> 00:01:45.602 Really high impact publications in major,

NOTE Confidence: 0.830144091666667

00:01:45.602 --> 00:01:46.959 you know, sales, science,

NOTE Confidence: 0.830144091666667

 $00{:}01{:}46.959 \dashrightarrow 00{:}01{:}47.368$ nature,

NOTE Confidence: 0.830144091666667

 $00:01:47.368 \rightarrow 00:01:50.231$ type of journals and he's also very

NOTE Confidence: 0.830144091666667

 $00{:}01{:}50{.}231 \dashrightarrow 00{:}01{:}52{.}237$ productive in the research and I

NOTE Confidence: 0.830144091666667

 $00:01:52.237 \dashrightarrow 00:01:54.130$ could count 5R1 grants at this point,

NOTE Confidence: 0.830144091666667

00:01:54.130 -> 00:01:56.834 which as you can imagine is a huge

NOTE Confidence: 0.830144091666667

 $00{:}01{:}56{.}834 \dashrightarrow 00{:}01{:}59{.}549$ amount of effort and shows to the

NOTE Confidence: 0.830144091666667

 $00{:}01{:}59{.}549 \dashrightarrow 00{:}02{:}01{.}970$ reflects the quality of his work.

NOTE Confidence: 0.8301440916666667

 $00:02:01.970 \dashrightarrow 00:02:03.310$ He has done major contributions

NOTE Confidence: 0.830144091666667

 $00:02:03.310 \dashrightarrow 00:02:05.067$ in the fields of tumor immunology

NOTE Confidence: 0.8301440916666667

 $00:02:05.067 \rightarrow 00:02:06.887$ and looking at different aspects.

NOTE Confidence: 0.8301440916666667

 $00:02:06.890 \dashrightarrow 00:02:09.050$ And recently he has focused more

NOTE Confidence: 0.830144091666667

 $00{:}02{:}09{.}050 \dashrightarrow 00{:}02{:}11.667$ on the role of the metabolism

NOTE Confidence: 0.8301440916666667

 $00:02:11.667 \rightarrow 00:02:14.397$ and how metabolism can actually

NOTE Confidence: 0.830144091666667

 $00:02:14.397 \rightarrow 00:02:16.450$ compromise adaptive immune responses

- NOTE Confidence: 0.830144091666667
- $00:02:16.450 \longrightarrow 00:02:18.450$ in the tumor microenvironment.
- NOTE Confidence: 0.830144091666667
- $00:02:18.450 \longrightarrow 00:02:20.690$ I have to also to say that he's
- NOTE Confidence: 0.830144091666667
- $00:02:20.690 \rightarrow 00:02:22.272$ a very translationally oriented,
- NOTE Confidence: 0.830144091666667
- $00:02:22.272 \rightarrow 00:02:25.168$ so his work focuses on very basic
- NOTE Confidence: 0.8301440916666667
- $00{:}02{:}25{.}170 \dashrightarrow 00{:}02{:}27{.}948$ mechanisms but also projects into
- NOTE Confidence: 0.830144091666667
- $00:02:27.948 \rightarrow 00:02:29.976$ different tumor types and he has
- NOTE Confidence: 0.830144091666667
- $00:02:29.976 \rightarrow 00:02:31.554$ done really prominent contributions
- NOTE Confidence: 0.830144091666667
- 00:02:31.554 --> 00:02:33.060 in colorectal cancer.
- NOTE Confidence: 0.830144091666667
- $00:02:33.060 \dashrightarrow 00:02:35.545$ Ovarian cancer and then also breast cancer.
- NOTE Confidence: 0.830144091666667
- 00:02:35.550 --> 00:02:39.060 So it's a very, very diverse profile.
- NOTE Confidence: 0.830144091666667
- 00:02:39.060 --> 00:02:40.760 And so without further ado,
- NOTE Confidence: 0.830144091666667
- $00{:}02{:}40.760 \dashrightarrow 00{:}02{:}43.140$ I believe Doctor Weiping Zou and his title
- NOTE Confidence: 0.830144091666667
- $00:02:43.140 \longrightarrow 00:02:45.137$ is metabolic impact on tumor
- NOTE Confidence: 0.830144091666667
- 00:02:45.137 --> 00:02:46.499 immunity and immunotherapy.
- NOTE Confidence: 0.830144091666667
- $00:02:46.500 \rightarrow 00:02:47.790$ And thank you very much.
- NOTE Confidence: 0.92904854

00:02:59.480 --> 00:03:03.945 Right. First of all I would like to.

NOTE Confidence: 0.92904854

 $00:03:03.950 \longrightarrow 00:03:08.075$ Thank God for your kind

NOTE Confidence: 0.92904854

 $00{:}03{:}08{.}075 \dashrightarrow 00{:}03{:}10{.}550$ invitation and introduction.

NOTE Confidence: 0.92904854

 $00:03:10.550 \longrightarrow 00:03:13.710$ Year is a pioneer institution

NOTE Confidence: 0.92904854

 $00:03:13.710 \longrightarrow 00:03:15.606$ of modern immunology,

NOTE Confidence: 0.92904854

 $00{:}03{:}15.610 \dashrightarrow 00{:}03{:}18.664$ particularly human immunology,

NOTE Confidence: 0.92904854

 $00:03:18.664 \dashrightarrow 00:03:23.580$ innate immunity and T cells.

NOTE Confidence: 0.92904854

 $00:03:23.580 \rightarrow 00:03:25.392$ We paid up allergy,

NOTE Confidence: 0.92904854

 $00{:}03{:}25{.}392 \dashrightarrow 00{:}03{:}28{.}411$ so in many ways this institution

NOTE Confidence: 0.92904854

 $00:03:28.411 \rightarrow 00:03:32.166$ contributed enormously to our knowledge

NOTE Confidence: 0.92904854

 $00{:}03{:}32{.}166 \dashrightarrow 00{:}03{:}35{.}170$ and also immunology translation.

NOTE Confidence: 0.92904854

 $00:03:35.170 \longrightarrow 00:03:37.894$ So this is absolutely a great

NOTE Confidence: 0.92904854

 $00:03:37.894 \rightarrow 00:03:39.580$ pleasure for me to be here.

NOTE Confidence: 0.92904854

 $00:03:39.580 \dashrightarrow 00:03:43.110$ This is the first time I'm able to give

NOTE Confidence: 0.92904854

 $00:03:43.110 \longrightarrow 00:03:45.930$ this talk to this prestigious university.

NOTE Confidence: 0.92904854

 $00:03:45.930 \rightarrow 00:03:49.586$ As I mentioned yesterday when we had dinner,

- NOTE Confidence: 0.92904854
- $00:03:49.590 \longrightarrow 00:03:52.092$ actually my old son wants to

 $00{:}03{:}52{.}092 \dashrightarrow 00{:}03{:}54{.}930$ get into the C university.

NOTE Confidence: 0.92904854

 $00:03:54.930 \longrightarrow 00:03:59.190$ He failed and I emailed him.

NOTE Confidence: 0.92904854

 $00:03:59.190 \longrightarrow 00:04:01.494$ I said, I'm going to give a talk

NOTE Confidence: 0.92904854

 $00:04:01.494 \longrightarrow 00:04:03.810$ to this university and he said,

NOTE Confidence: 0.92904854

00:04:03.810 --> 00:04:06.018 OK, you succeeded.

NOTE Confidence: 0.92904854

 $00:04:06.020 \longrightarrow 00:04:08.675$ Thank you again for this

NOTE Confidence: 0.92904854

00:04:08.675 --> 00:04:09.737 wonderful opportunity.

NOTE Confidence: 0.92904854

 $00:04:09.740 \longrightarrow 00:04:11.920$ So.

NOTE Confidence: 0.92904854

 $00:04:11.920 \longrightarrow 00:04:13.330$ See you guys.

NOTE Confidence: 0.587792848333333

00:04:22.150 --> 00:04:26.462 So use too many minorities when we

NOTE Confidence: 0.587792848333333

00:04:26.462 --> 00:04:30.409 view our cancer therapy history.

NOTE Confidence: 0.587792848333333

 $00:04:30.410 \longrightarrow 00:04:33.620$ We have come a long way.

NOTE Confidence: 0.587792848333333

 $00:04:33.620 \longrightarrow 00:04:35.796$ First we have surgery,

NOTE Confidence: 0.587792848333333

 $00:04:35.796 \rightarrow 00:04:37.011$ radiation, chemotherapy.

 $00:04:37.011 \rightarrow 00:04:39.695$ Chemotherapy and the targeted

NOTE Confidence: 0.587792848333333

 $00{:}04{:}39.695 \dashrightarrow 00{:}04{:}42.230$ the rapy for managers and rotation if

NOTE Confidence: 0.587792848333333

 $00{:}04{:}42{.}230 \dashrightarrow 00{:}04{:}45{.}230$ these days we do our immunotherapy.

NOTE Confidence: 0.587792848333333

 $00:04:45.230 \rightarrow 00:04:48.674$ As you can see from this summary.

NOTE Confidence: 0.587792848333333

 $00{:}04{:}48.680 \dashrightarrow 00{:}04{:}52.782$ Each milestone is really based on the

NOTE Confidence: 0.587792848333333

 $00{:}04{:}52.782 \dashrightarrow 00{:}04{:}55.440$ basic celebs scientific discovery.

NOTE Confidence: 0.587792848333333

 $00:04:55.440 \longrightarrow 00:05:01.070$ So people always asked what is next.

NOTE Confidence: 0.587792848333333

00:05:01.070 - 00:05:05.330 So in terms of immunotherapy,

NOTE Confidence: 0.587792848333333

 $00:05:05.330 \longrightarrow 00:05:06.870$ what we have done?

NOTE Confidence: 0.774106399333333

00:05:09.300 --> 00:05:12.846 Actually, early on we know based

NOTE Confidence: 0.774106399333333

 $00:05:12.846 \rightarrow 00:05:16.016$ on the genetic identification and

NOTE Confidence: 0.774106399333333

 $00:05:16.016 \rightarrow 00:05:18.840$ mutations people have discovered,

NOTE Confidence: 0.774106399333333

 $00:05:18.840 \longrightarrow 00:05:21.928$ it's pretty clear cancer

NOTE Confidence: 0.774106399333333

 $00:05:21.928 \longrightarrow 00:05:25.016$ is a genetic disease.

NOTE Confidence: 0.774106399333333

 $00{:}05{:}25{.}020 \dashrightarrow 00{:}05{:}29{.}570$ But all work and many others work.

NOTE Confidence: 0.774106399333333

 $00:05:29.570 \dashrightarrow 00:05:33.776$ Consider cancer is an immune disorder.

 $00{:}05{:}33.780 \dashrightarrow 00{:}05{:}37.296$ And further we have studied the

NOTE Confidence: 0.774106399333333

00:05:37.296 --> 00:05:38.468 immunosuppressive mechanisms

NOTE Confidence: 0.774106399333333

 $00:05:38.468 \rightarrow 00:05:42.295$ including the P1P1 that was in the

NOTE Confidence: 0.774106399333333

 $00:05:42.295 \rightarrow 00:05:44.419$ human tumor migraine environment.

NOTE Confidence: 0.774106399333333

 $00:05:44.420 \longrightarrow 00:05:47.708$ So we believe the human tumor

NOTE Confidence: 0.774106399333333

 $00:05:47.708 \dashrightarrow 00:05:50.292$ microenvironment holds the key to

NOTE Confidence: 0.774106399333333

00:05:50.292 --> 00:05:52.832 understanding human immunity and therapy.

NOTE Confidence: 0.774106399333333

 $00:05:52.840 \longrightarrow 00:05:54.304$ So at this stage,

NOTE Confidence: 0.774106399333333

 $00:05:54.304 \rightarrow 00:05:56.862$ when we say these two contributions,

NOTE Confidence: 0.774106399333333

00:05:56.862 --> 00:05:59.750 conceptually speaking, it's easy.

NOTE Confidence: 0.774106399333333

 $00:05:59.750 \rightarrow 00:06:03.764$ But when you talk about this 20 years ago.

NOTE Confidence: 0.774106399333333

 $00{:}06{:}03.770 \dashrightarrow 00{:}06{:}06{.}530$ It's not the same thing.

NOTE Confidence: 0.774106399333333

 $00{:}06{:}06{.}530 \dashrightarrow 00{:}06{:}09{.}716$ So we have some video articles

NOTE Confidence: 0.774106399333333

00:06:09.716 --> 00:06:12.882 in this space as we focus on

NOTE Confidence: 0.774106399333333

 $00:06:12.882 \rightarrow 00:06:13.668$ immunosuppressive mechanisms.

 $00{:}06{:}21.760 \dashrightarrow 00{:}06{:}24.550$ to terminology, as we know a lot NOTE Confidence: 0.7458623025 00:06:24.550 -> 00:06:26.960 of people getting into this area, NOTE Confidence: 0.7458623025 $00{:}06{:}26{.}960 \dashrightarrow 00{:}06{:}29{.}123$ you may see some of our work NOTE Confidence: 0.7458623025 00:06:29.123 --> 00:06:31.278 because we have not only reviewed NOTE Confidence: 0.7458623025 $00:06:31.278 \rightarrow 00:06:33.576$ the studies from our own group, NOTE Confidence: 0.7458623025 $00:06:33.580 \longrightarrow 00:06:35.580$ but also from many others. NOTE Confidence: 0.7458623025 $00:06:35.580 \rightarrow 00:06:39.038$ As you may appreciate actually at least NOTE Confidence: 0.7458623025 00:06:39.038 --> 00:06:42.456 2 high profile review articles we're NOTE Confidence: 0.7458623025 00:06:42.456 --> 00:06:45.521 done with Livingston I remarkable NOTE Confidence: 0.7458623025 00:06:45.521 --> 00:06:48.309 faculty are ADO Institution. NOTE Confidence: 0.5880662 00:06:51.670 --> 00:06:54.302 Who's good mentioned? NOTE Confidence: 0.5880662 $00:06:54.302 \rightarrow 00:06:58.350$ We are pretty much legislatively in the basic NOTE Confidence: 0.5880662 $00:06:58.437 \rightarrow 00:07:01.839$ mechanisms as well as the transformation. NOTE Confidence: 0.5880662 00:07:01.840 --> 00:07:04.630 Therefore. For all those years, NOTE Confidence: 0.5880662

00:06:19.060 - 00:06:21.760 For those who are relatively new

- NOTE Confidence: 0.5880662
- 00:07:07.620 --> 00:07:10.015 Say to again cancer microenvironment

00:07:10.015 --> 00:07:12.410 host key to understanding too

NOTE Confidence: 0.5880662

00:07:12.490 --> 00:07:14.378 many immunity and therapy.

NOTE Confidence: 0.5880662

 $00{:}07{:}14.380 \dashrightarrow 00{:}07{:}18.391$ To address this we have several research

NOTE Confidence: 0.5880662

 $00{:}07{:}18.391 \dashrightarrow 00{:}07{:}21.937$ directions or research angles you may say.

NOTE Confidence: 0.5880662

00:07:21.940 --> 00:07:24.584 For example you know

NOTE Confidence: 0.5880662

 $00:07:24.584 \rightarrow 00:07:26.567$ suppressive mechanisms network.

NOTE Confidence: 0.5880662

 $00:07:26.570 \longrightarrow 00:07:29.678$ Such as PD1PD L one OK.

NOTE Confidence: 0.5880662

 $00:07:29.680 \longrightarrow 00:07:32.744$ Then cancer athletics and

NOTE Confidence: 0.5880662

00:07:32.744 --> 00:07:34.276 epigenetic reprogramming.

NOTE Confidence: 0.5880662

 $00:07:34.280 \rightarrow 00:07:37.046$ And then a key immunologic pathways

NOTE Confidence: 0.5880662

 $00{:}07{:}37{.}046$ --> $00{:}07{:}38{.}890$ such as individual pathway,

NOTE Confidence: 0.5880662

 $00{:}07{:}38.890 \dashrightarrow 00{:}07{:}41.134$ image C and stats.

NOTE Confidence: 0.5880662

00:07:41.134 --> 00:07:42.256 And finally,

NOTE Confidence: 0.5880662

 $00{:}07{:}42.260 \dashrightarrow 00{:}07{:}45.680$ in the recent years we spent a lot of

 $00:07:45.680 \rightarrow 00:07:48.870$ time working on metabolic pathways.

NOTE Confidence: 0.5880662

00:07:48.870 --> 00:07:52.182 So I guess I'm going to spend a little

NOTE Confidence: 0.5880662

 $00{:}07{:}52.182 \dashrightarrow 00{:}07{:}55.128$ more time on the fourth direction.

NOTE Confidence: 0.5880662

 $00:07:55.130 \longrightarrow 00:07:58.094$ I will give you just one

NOTE Confidence: 0.5880662

00:07:58.094 --> 00:08:00.398 slight each for A&B&C,

NOTE Confidence: 0.5880662

 $00{:}08{:}00{.}398 \dashrightarrow 00{:}08{:}08{.}130$ just to show you where I have come from.

NOTE Confidence: 0.5880662

 $00{:}08{:}08{.}130 \dashrightarrow 00{:}08{:}10{.}314$ So and like to share this site with

NOTE Confidence: 0.5880662

 $00:08:10.314 \rightarrow 00:08:12.926$ you for the first research direction

NOTE Confidence: 0.5880662

 $00{:}08{:}12.926 \dashrightarrow 00{:}08{:}14.926$ we have immunosuppressive networks

NOTE Confidence: 0.5880662

 $00{:}08{:}14.930 \dashrightarrow 00{:}08{:}20.558$ actually almost more than 20 years ago.

NOTE Confidence: 0.5880662

 $00{:}08{:}20.560 \dashrightarrow 00{:}08{:}22.640$ Under the support and

NOTE Confidence: 0.5880662

 $00:08:22.640 \dashrightarrow 00:08:24.200$ collaboration with Millington,

NOTE Confidence: 0.5880662

 $00{:}08{:}24.200 \dashrightarrow 00{:}08{:}26.112$ we have published this

NOTE Confidence: 0.5880662

 $00:08:26.112 \longrightarrow 00:08:28.024$ paper in Nature magazine.

NOTE Confidence: 0.5880662

 $00:08:28.030 \dashrightarrow 00:08:31.270$ It was named it is time PDL one.

NOTE Confidence: 0.5880662

 $00{:}08{:}31{.}270 \dashrightarrow 00{:}08{:}32{.}510$ It's not me PDL one.

- NOTE Confidence: 0.5880662
- 00:08:32.510 --> 00:08:34.934 It's named P 781.
- NOTE Confidence: 0.5880662
- $00{:}08{:}34{.}934 \dashrightarrow 00{:}08{:}37{.}786$ These people for the first time
- NOTE Confidence: 0.5880662
- $00{:}08{:}37.786 \dashrightarrow 00{:}08{:}40.240$ demonstrating PDL one of P-70 joint
- NOTE Confidence: 0.5880662
- $00{:}08{:}40{.}325 \dashrightarrow 00{:}08{:}43{.}387$ expression recognition and profit in
- NOTE Confidence: 0.5880662
- $00{:}08{:}43.387 \dashrightarrow 00{:}08{:}45.615$ the human cancer microenvironment
- NOTE Confidence: 0.5880662
- $00{:}08{:}45.615 \dashrightarrow 00{:}08{:}48.400$ and human human chain influence.
- NOTE Confidence: 0.5880662
- $00:08:48.400 \longrightarrow 00:08:50.620$ We clearly demonstrated if you
- NOTE Confidence: 0.5880662
- $00:08:50.620 \rightarrow 00:08:53.604$ broke this pathway you can recover
- NOTE Confidence: 0.5880662
- $00:08:53.604 \longrightarrow 00:08:55.650$ the dysfunctionality cells.
- NOTE Confidence: 0.67314885
- $00{:}08{:}58{.}260 \dashrightarrow 00{:}09{:}02{.}355$ This is far before the success of
- NOTE Confidence: 0.67314885
- 00:09:02.355 --> 00:09:05.096 clinic trials, either with PD1PD1
- NOTE Confidence: 0.67314885
- $00{:}09{:}05{.}096$ --> $00{:}09{:}08{.}228$ blockade or with anti serial four.
- NOTE Confidence: 0.67314885
- $00:09:08.230 \dashrightarrow 00:09:11.030$ Of course in these days if you look NOTE Confidence: 0.67314885
- $00:09:11.030 \longrightarrow 00:09:13.536$ at the PD L1 you will not be able NOTE Confidence: 0.67314885
- 00:09:13.536 00:09:15.896 to find this table because early
- NOTE Confidence: 0.67314885

 $00:09:15.896 \dashrightarrow 00:09:19.124$ on when leaving discovered the best

NOTE Confidence: 0.67314885

 $00:09:19.124 \rightarrow 00:09:22.026$ way he named this gene as B7H1.

NOTE Confidence: 0.67314885

00:09:22.026 --> 00:09:24.042 Of course, he has many other

NOTE Confidence: 0.67314885

00:09:24.042 --> 00:09:27.180 peaceful family members, as you know.

NOTE Confidence: 0.67314885

 $00:09:27.180 \dashrightarrow 00:09:29.286$ So the second with your generation

NOTE Confidence: 0.67314885

00:09:29.286 --> 00:09:30.339 cancer at genetics,

NOTE Confidence: 0.67314885

00:09:30.340 --> 00:09:32.756 I know you have quite a few folks

NOTE Confidence: 0.67314885

 $00:09:32.756 \rightarrow 00:09:35.237$ who are interested in epigenetic

NOTE Confidence: 0.67314885

 $00{:}09{:}35{.}237 \dashrightarrow 00{:}09{:}37{.}637$ recognition in this institution,

NOTE Confidence: 0.67314885

 $00{:}09{:}37.640 \dashrightarrow 00{:}09{:}40.699$ but we look at this from the

NOTE Confidence: 0.67314885

 $00:09:40.699 \rightarrow 00:09:42.010$ immune recognition perspective.

NOTE Confidence: 0.67314885

 $00{:}09{:}42.010 \dashrightarrow 00{:}09{:}45.458$ So in the tumor microenvironment similar

NOTE Confidence: 0.67314885

 $00:09:45.458 \rightarrow 00:09:50.297$ to the TH1 and TH2 reciprocal recognition?

NOTE Confidence: 0.67314885

 $00:09:50.297 \dashrightarrow 00:09:53.642$ We have observed a reciprocal

NOTE Confidence: 0.67314885

 $00{:}09{:}53.642 \dashrightarrow 00{:}09{:}56.498$ regulation between PRC two complex

NOTE Confidence: 0.67314885

 $00:09:56.498 \rightarrow 00:09:59.823$ and Swiss sniper complex in the tumor.

 $00:09:59.830 \dashrightarrow 00:10:02.840$ So actually this recognition was

NOTE Confidence: 0.67314885

 $00{:}10{:}02{.}840 \dashrightarrow 00{:}10{:}04{.}646$ properly controlled interference

NOTE Confidence: 0.67314885

 $00:10:04.646 \rightarrow 00:10:07.532$ zeronine therefore TH one type second

NOTE Confidence: 0.67314885

 $00:10:07.532 \rightarrow 00:10:09.537$ production and T cell trafficking

NOTE Confidence: 0.67314885

00:10:09.537 --> 00:10:10.949 and human energy.

NOTE Confidence: 0.67314885

 $00:10:10.950 \longrightarrow 00:10:14.634$ We have worked out the detailed

NOTE Confidence: 0.67314885

 $00:10:14.634 \rightarrow 00:10:17.090$ biochemical and functional mechanisms.

NOTE Confidence: 0.67314885

00:10:17.090 --> 00:10:19.400 We I'm not going to show you

NOTE Confidence: 0.67314885

 $00{:}10{:}19{.}400 \dashrightarrow 00{:}10{:}21{.}389$ the details as I mentioned.

NOTE Confidence: 0.67314885

00:10:21.390 --> 00:10:23.998 Then third, research direction,

NOTE Confidence: 0.67314885

 $00{:}10{:}23.998 \dashrightarrow 00{:}10{:}27.258$ I know also several investigators

NOTE Confidence: 0.67314885

 $00:10:27.258 \longrightarrow 00:10:29.939$ including my host code is very

NOTE Confidence: 0.67314885

 $00{:}10{:}29{.}939 \dashrightarrow 00{:}10{:}33{.}145$ interested in this image C interferon

NOTE Confidence: 0.67314885

 $00{:}10{:}33.145 \dashrightarrow 00{:}10{:}35.645$ signaling sets signaling pathway.

NOTE Confidence: 0.67314885

 $00{:}10{:}35{.}650 \dashrightarrow 00{:}10{:}38{.}546$ As you know these are the key immunogenic

 $00:10:38.546 \rightarrow 00:10:40.042$ pathway in the immune responses,

NOTE Confidence: 0.67314885

00:10:40.042 --> 00:10:41.740 not only just in the tumor

NOTE Confidence: 0.67314885

00:10:41.802 --> 00:10:42.970 migraine environment.

NOTE Confidence: 0.67314885

 $00:10:42.970 \longrightarrow 00:10:44.230$ I show you one example.

NOTE Confidence: 0.67314885

 $00:10:44.230 \longrightarrow 00:10:45.256$ We have,

NOTE Confidence: 0.67314885

 $00:10:45.256 \rightarrow 00:10:48.334$ we have discovered actually you know

NOTE Confidence: 0.67314885

00:10:48.334 --> 00:10:51.577 mutations in MHC pathway and stat

NOTE Confidence: 0.67314885

 $00{:}10{:}51{.}577 \dashrightarrow 00{:}10{:}54{.}232$ and interferon pathway are considered

NOTE Confidence: 0.67314885

00:10:54.232 --> 00:10:57.509 a celebrity resistant mechanism.

NOTE Confidence: 0.67314885

 $00{:}10{:}57{.}510$ --> $00{:}11{:}00{.}342$ But we know the vast majority of the NOTE Confidence: 0.67314885

 $00:11:00.342 \rightarrow 00:11:02.969$ patients do not have those mutations.

NOTE Confidence: 0.67314885

 $00:11:02.970 \longrightarrow 00:11:05.472$ Therefore we need to find out

NOTE Confidence: 0.67314885

 $00:11:05.472 \longrightarrow 00:11:07.782$ the other pathways which may

NOTE Confidence: 0.67314885

 $00:11:07.782 \rightarrow 00:11:10.010$ contribute to safety resistance.

NOTE Confidence: 0.67314885

 $00:11:10.010 \dashrightarrow 00:11:13.640$ So one pathway we have discovered.

NOTE Confidence: 0.67314885

00:11:13.640 --> 00:11:14.292 Actually,

- NOTE Confidence: 0.67314885
- 00:11:14.292 --> 00:11:16.900 the integrity of interferon
- NOTE Confidence: 0.67314885
- $00{:}11{:}16{.}900 \dashrightarrow 00{:}11{:}21{.}610$ signaling pathway is controlled by.
- NOTE Confidence: 0.67314885
- 00:11:21.610 00:11:23.318 Jean quota of January.
- NOTE Confidence: 0.67314885
- $00:11:23.318 \dashrightarrow 00:11:26.600$ So this is a auto between septor.
- NOTE Confidence: 0.67314885
- $00{:}11{:}26.600 \dashrightarrow 00{:}11{:}29.872$ It turns out actually all of the nearing
- NOTE Confidence: 0.67314885
- $00{:}11{:}29.872 \dashrightarrow 00{:}11{:}32.695$ can control the stability and the
- NOTE Confidence: 0.67314885
- $00{:}11{:}32.695 \dashrightarrow 00{:}11{:}35.575$ degradation of the film gamma receptor.
- NOTE Confidence: 0.67314885
- $00:11:35.580 \longrightarrow 00:11:37.128$ So as a consequence,
- NOTE Confidence: 0.67314885
- $00{:}11{:}37{.}128 \dashrightarrow 00{:}11{:}39{.}918$ this controls the image C expression antigen
- NOTE Confidence: 0.67314885
- $00:11:39.918 \rightarrow 00:11:42.310$ presentation and the T cell functionality.
- NOTE Confidence: 0.67314885
- 00:11:42.310 --> 00:11:44.770 OK, I don't have time to
- NOTE Confidence: 0.67314885
- $00:11:44.770 \longrightarrow 00:11:47.159$ show you this was published.
- NOTE Confidence: 0.67314885
- $00{:}11{:}47.160 \dashrightarrow 00{:}11{:}49.057$ For those who are interested in this,
- NOTE Confidence: 0.67314885
- $00{:}11{:}49{.}060 \dashrightarrow 00{:}11{:}50{.}850$ you may have a look instead.
- NOTE Confidence: 0.67314885
- $00{:}11{:}50{.}850 \dashrightarrow 00{:}11{:}55{.}405$ Most of my time we are focused on the force
- NOTE Confidence: 0.67314885

- $00{:}11{:}55{.}405 \dashrightarrow 00{:}11{:}59{.}004$ we switch direction metabolic pathways.
- NOTE Confidence: 0.67314885
- $00{:}11{:}59{.}004 \dashrightarrow 00{:}12{:}01{.}770$ And I will.
- NOTE Confidence: 0.67314885
- $00:12:01.770 \longrightarrow 00:12:04.806$ Talk about the basically two stories.
- NOTE Confidence: 0.67314885
- 00:12:04.810 --> 00:12:09.001 One is system XC and CS4,
- NOTE Confidence: 0.67314885
- $00{:}12{:}09{.}001 \dashrightarrow 00{:}12{:}11.845$ its relationship with tumor
- NOTE Confidence: 0.67314885
- 00:12:11.845 --> 00:12:13.267 cell philippoussis.
- NOTE Confidence: 0.67314885
- $00{:}12{:}13.270 \dashrightarrow 00{:}12{:}17.006$ Another is SLC 43A2.
- NOTE Confidence: 0.67314885
- $00:12:17.006 \rightarrow 00:12:19.934$ So those ACC family members are
- NOTE Confidence: 0.67314885
- $00{:}12{:}19{.}934 \dashrightarrow 00{:}12{:}23{.}169$ nutrients or metabolite transporters.
- NOTE Confidence: 0.67314885
- $00{:}12{:}23.170 \dashrightarrow 00{:}12{:}25.366$ There are several hundreds of them.
- NOTE Confidence: 0.67314885
- 00:12:25.370 --> 00:12:27.614 Most of them are poorly understood
- NOTE Confidence: 0.67314885
- $00:12:27.614 \rightarrow 00:12:30.010$ in the field of immunology.
- NOTE Confidence: 0.67314885
- $00:12:30.010 \rightarrow 00:12:34.889$ We start to figure out some of it.
- NOTE Confidence: 0.67314885
- $00{:}12{:}34.890 \dashrightarrow 00{:}12{:}38.726$ So before that I want to introduce
- NOTE Confidence: 0.67314885
- $00:12:38.726 \longrightarrow 00:12:40.862$ the concept of ferroptosis.
- NOTE Confidence: 0.67314885
- $00:12:40.862 \longrightarrow 00:12:44.474$ So it has been defined in vitro

- NOTE Confidence: 0.67314885
- $00:12:44.480 \rightarrow 00:12:46.596$ through the synthetic compounds.
- NOTE Confidence: 0.67314885
- $00{:}12{:}46{.}596 \dashrightarrow 00{:}12{:}49{.}770$ It means the cells will die
- NOTE Confidence: 0.67314885
- 00:12:49.867 --> 00:12:53.160 through iron dependent but lipid
- NOTE Confidence: 0.67314885
- $00{:}12{:}53.160 \dashrightarrow 00{:}12{:}55.860$ peroxidation induced cell death.
- NOTE Confidence: 0.67314885
- $00:12:55.860 \longrightarrow 00:12:59.856$ There are several genes or pathways
- NOTE Confidence: 0.67314885
- $00:12:59.856 \rightarrow 00:13:03.410$ associated or regulated cell biosis.
- NOTE Confidence: 0.67314885
- 00:13:03.410 --> 00:13:04.185 So,
- NOTE Confidence: 0.67314885
- $00:13:04.185 \longrightarrow 00:13:07.285$ including this exit system
- NOTE Confidence: 0.67314885
- $00{:}13{:}07{.}290 \dashrightarrow 00{:}13{:}10{.}130$ GX4 and a CSR four.
- NOTE Confidence: 0.656827746
- 00:13:10.130 -> 00:13:13.700 However there is no CBC marker
- NOTE Confidence: 0.656827746
- $00:13:13.700 \longrightarrow 00:13:15.485$ to define Philippoussis.
- NOTE Confidence: 0.656827746
- 00:13:15.490 00:13:18.642 What we usually do we use a few
- NOTE Confidence: 0.656827746
- $00{:}13{:}18.642 \dashrightarrow 00{:}13{:}21.360$ criteria to define electrolysis,
- NOTE Confidence: 0.656827746
- $00{:}13{:}21{.}360 \dashrightarrow 00{:}13{:}24{.}230$ so one it's maybe the Rose production,
- NOTE Confidence: 0.656827746
- $00{:}13{:}24{.}230 \dashrightarrow 00{:}13{:}26{.}852$ another is expression of all states
- NOTE Confidence: 0.656827746

 $00:13:26.852 \rightarrow 00:13:29.370$ needed species on the membrane,

NOTE Confidence: 0.656827746

 $00:13:29.370 \longrightarrow 00:13:32.460$ and finally we need to see

NOTE Confidence: 0.656827746

 $00:13:32.460 \longrightarrow 00:13:34.005$ the functional activities.

NOTE Confidence: 0.656827746

 $00{:}13{:}34.010 \dashrightarrow 00{:}13{:}36.782$ So in this case we asked

NOTE Confidence: 0.656827746

 $00:13:36.782 \longrightarrow 00:13:38.630$ a very simple question.

NOTE Confidence: 0.656827746

 $00:13:38.630 \rightarrow 00:13:42.326$ We know when CDA T cells are activated,

NOTE Confidence: 0.656827746

 $00:13:42.330 \rightarrow 00:13:45.390$ engage tumor cells.

NOTE Confidence: 0.656827746

00:13:45.390 --> 00:13:47.890 CHT cells we need preparing,

NOTE Confidence: 0.656827746

 $00{:}13{:}47.890 \dashrightarrow 00{:}13{:}49.970$ makes pores on the membrane,

NOTE Confidence: 0.656827746

 $00{:}13{:}49{.}970 \dashrightarrow 00{:}13{:}51{.}155$ then grant them.

NOTE Confidence: 0.656827746

 $00{:}13{:}51{.}155 \dashrightarrow 00{:}13{:}53{.}792$ We get into the cells activated

NOTE Confidence: 0.656827746

 $00:13:53.792 \rightarrow 00:13:57.764$ caspase induce tumor cell able doses.

NOTE Confidence: 0.656827746

 $00:13:57.770 \longrightarrow 00:14:02.150$ This is text book message.

NOTE Confidence: 0.656827746

 $00{:}14{:}02{.}150 \dashrightarrow 00{:}14{:}04{.}908$ So we asked a simple question means

NOTE Confidence: 0.656827746

 $00{:}14{:}04{.}908 \dashrightarrow 00{:}14{:}08{.}687$ if CDA T cells who kills tumor cells?

NOTE Confidence: 0.656827746

 $00:14:08.690 \rightarrow 00:14:10.930$ This is a way how the tumor cells

- NOTE Confidence: 0.656827746
- 00:14:10.930 --> 00:14:13.170 die is Philippoussis involved.
- NOTE Confidence: 0.656827746
- $00:14:13.170 \longrightarrow 00:14:16.682$ So in this case we set up several
- NOTE Confidence: 0.656827746
- $00:14:16.682 \rightarrow 00:14:19.669$ experiments to test this possibility.
- NOTE Confidence: 0.656827746
- $00:14:19.670 \longrightarrow 00:14:23.806$ So one is a 88 over retention model.
- NOTE Confidence: 0.656827746
- $00:14:23.810 \rightarrow 00:14:27.450$ We do immunotherapy before you can see PD,
- NOTE Confidence: 0.656827746
- $00:14:27.450 \longrightarrow 00:14:30.696$ one can control the tumor growth.
- NOTE Confidence: 0.656827746
- $00:14:30.700 \rightarrow 00:14:33.857$ Under this condition before the tumor cells,
- NOTE Confidence: 0.656827746
- $00:14:33.860 \longrightarrow 00:14:35.862$ really it is an 8 stage before
- NOTE Confidence: 0.656827746
- $00:14:35.862 \rightarrow 00:14:37.040$ the tumor cells die,
- NOTE Confidence: 0.656827746
- 00:14:37.040 --> 00:14:38.960 you give the tumor cells out,
- NOTE Confidence: 0.656827746
- $00{:}14{:}38{.}960 \dashrightarrow 00{:}14{:}42{.}818$ you detect relative needs worse production.
- NOTE Confidence: 0.656827746
- $00{:}14{:}42.820 \dashrightarrow 00{:}14{:}45.785$ You see actually the immunotherapy
- NOTE Confidence: 0.656827746
- $00:14:45.785 \longrightarrow 00:14:48.157$ induces liberals production in
- NOTE Confidence: 0.656827746
- $00{:}14{:}48{.}157 \dashrightarrow 00{:}14{:}50{.}897$ the tumor cells in PD1 cell.
- NOTE Confidence: 0.656827746
- $00{:}14{:}50{.}900 \dashrightarrow 00{:}14{:}54{.}476$ Then we did a T cell therapy model.
- NOTE Confidence: 0.656827746

 $00:14:54.480 \longrightarrow 00:14:57.606$ Be 16 over expression cells and

NOTE Confidence: 0.656827746

 $00{:}14{:}57.606$ --> $00{:}15{:}01.299$ treated in vivo with only one cells.

NOTE Confidence: 0.656827746

 $00{:}15{:}01{.}300 \dashrightarrow 00{:}15{:}03{.}554$ It's not a surprise tumor is controlled

NOTE Confidence: 0.656827746

 $00:15:03.554 \rightarrow 00:15:06.260$ and again we see individuals production.

NOTE Confidence: 0.656827746

00:15:06.260 --> 00:15:10.068 So this suggests maybe T cells or immune

NOTE Confidence: 0.656827746

 $00{:}15{:}10.068 \dashrightarrow 00{:}15{:}13.680$ the rapy can promote liberals production.

NOTE Confidence: 0.656827746

00:15:13.680 --> 00:15:17.240 Maybe in May induce Philippoussis

NOTE Confidence: 0.656827746

 $00:15:17.240 \longrightarrow 00:15:19.376$ tumor cell paralysis.

NOTE Confidence: 0.656827746

00:15:19.380 --> 00:15:22.100 We did in vitro studies in this case

NOTE Confidence: 0.656827746

 $00{:}15{:}22.100 \dashrightarrow 00{:}15{:}24.888$ to provide direct evidence we cultured.

NOTE Confidence: 0.656827746

 $00:15:24.890 \dashrightarrow 00:15:27.515$ 41 cells with All Blacks fashion tumor NOTE Confidence: 0.656827746

00:15:27.515 --> 00:15:30.016 cells we look it's rose production

NOTE Confidence: 0.656827746

 $00{:}15{:}30{.}016 \dashrightarrow 00{:}15{:}32{.}614$ again we see rose production induced

NOTE Confidence: 0.656827746

 $00{:}15{:}32.614 \dashrightarrow 00{:}15{:}35.850$ by by only one cells and this antigen

NOTE Confidence: 0.656827746

00:15:35.850 --> 00:15:39.350 specific away can see more but if

NOTE Confidence: 0.656827746

 $00:15:39.450 \longrightarrow 00:15:42.747$ you look at the tumor cell death.

- NOTE Confidence: 0.656827746
- 00:15:42.750 --> 00:15:44.885 Of course you use a small amount
- NOTE Confidence: 0.656827746
- 00:15:44.885 --> 00:15:47.964 of T cells and in this case you can
- NOTE Confidence: 0.656827746
- $00:15:47.964 \rightarrow 00:15:50.210$ have space to manipulate the system.
- NOTE Confidence: 0.656827746
- $00{:}15{:}50{.}210 \dashrightarrow 00{:}15{:}51{.}953$ You will see you your small amount
- NOTE Confidence: 0.656827746
- $00{:}15{:}51{.}953 \dashrightarrow 00{:}15{:}55{.}690$ of T cells. You see T cell cleaning.
- NOTE Confidence: 0.656827746
- $00:15:55.690 \longrightarrow 00:15:57.410$ And under this condition,
- NOTE Confidence: 0.656827746
- $00:15:57.410 \longrightarrow 00:16:00.822$ if you use a small amount of RS3
- NOTE Confidence: 0.656827746
- $00:16:00.822 \longrightarrow 00:16:03.110$ is a dosis inducer,
- NOTE Confidence: 0.656827746
- $00:16:03.110 \longrightarrow 00:16:06.070$ you'll see some levels of human cell death.
- NOTE Confidence: 0.656827746
- $00:16:06.070 \longrightarrow 00:16:07.450$ If you put them together,
- NOTE Confidence: 0.656827746
- $00:16:07.450 \longrightarrow 00:16:09.490$ you see dramatic human cell death.
- NOTE Confidence: 0.656827746
- 00:16:09.490 --> 00:16:13.025 These tumor cells can be
- NOTE Confidence: 0.656827746
- $00:16:13.025 \longrightarrow 00:16:14.439$ completely abolished.
- NOTE Confidence: 0.656827746
- 00:16:14.440 --> 00:16:16.555 By THEODOSIS inhibitor,
- NOTE Confidence: 0.656827746
- $00{:}16{:}16{.}555 \dashrightarrow 00{:}16{:}21{.}952$ So what we have here, it means T
- NOTE Confidence: 0.656827746

- $00:16:21.952 \rightarrow 00:16:25.696$ cells can promote tumor cell factories.
- NOTE Confidence: 0.656827746
- 00:16:25.700 --> 00:16:26.237 However,
- NOTE Confidence: 0.656827746
- $00{:}16{:}26{.}237 \dashrightarrow 00{:}16{:}29{.}459$ T cells themselves are not sufficient.
- NOTE Confidence: 0.656827746
- $00:16:29.460 \rightarrow 00:16:32.099$ You need to have a trigger somewhere.
- NOTE Confidence: 0.656827746
- $00:16:32.100 \longrightarrow 00:16:35.298$ So we will explore further about
- NOTE Confidence: 0.656827746
- $00:16:35.298 \longrightarrow 00:16:36.364$ this phenomenon.
- NOTE Confidence: 0.656827746
- $00{:}16{:}36{.}370 \dashrightarrow 00{:}16{:}39{.}034$ But we studied further in vivo
- NOTE Confidence: 0.656827746
- $00:16:39.034 \longrightarrow 00:16:40.366$ in military condition.
- NOTE Confidence: 0.656827746
- 00:16:40.370 --> 00:16:42.550 So it's a classic model.
- NOTE Confidence: 0.656827746
- $00:16:42.550 \longrightarrow 00:16:44.214$ For example, with P-16,
- NOTE Confidence: 0.656827746
- $00:16:44.214 \rightarrow 00:16:46.710$ if you treat the tumor bearing
- NOTE Confidence: 0.656827746
- 00:16:46.793 --> 00:16:49.025 mice with antiscia 4 and PD1,
- NOTE Confidence: 0.656827746
- 00:16:49.030 --> 00:16:51.808 you'll see very nice tumor control.
- NOTE Confidence: 0.656827746
- 00:16:51.810 --> 00:16:54.225 But if you treat the mice under
- NOTE Confidence: 0.656827746
- $00:16:54.225 \rightarrow 00:16:56.350$ this condition with liberal statin,
- NOTE Confidence: 0.656827746
- 00:16:56.350 --> 00:16:58.798 it's a Philippoussis inhibitor.

- NOTE Confidence: 0.656827746
- $00:16:58.798 \longrightarrow 00:17:00.634$ The therapeutic efficacy
- NOTE Confidence: 0.656827746
- $00:17:00.634 \rightarrow 00:17:02.470$ is basically punished.
- NOTE Confidence: 0.656827746
- $00:17:02.470 \longrightarrow 00:17:04.470$ So this is very unusual.
- NOTE Confidence: 0.656827746
- $00:17:04.470 \rightarrow 00:17:07.034$ This is completely unexpected.
- NOTE Confidence: 0.656827746
- 00:17:07.034 --> 00:17:09.598 Because we all know
- NOTE Confidence: 0.683969263333333
- 00:17:09.600 --> 00:17:11.300 CD8T cells kill the tumor
- NOTE Confidence: 0.683969263333333
- $00:17:11.300 \longrightarrow 00:17:12.660$ cells through able process.
- NOTE Confidence: 0.683969263333333
- 00:17:12.660 00:17:15.548 How come a ferroptosis
- NOTE Confidence: 0.683969263333333
- $00:17:15.548 \longrightarrow 00:17:19.158$ inhibitor can Polish the effect?
- NOTE Confidence: 0.683969263333333
- 00:17:19.160 --> 00:17:21.760 To really ensure this possibility,
- NOTE Confidence: 0.683969263333333
- $00{:}17{:}21.760 \dashrightarrow 00{:}17{:}26.000$ we used another model means we in vitro
- NOTE Confidence: 0.683969263333333
- $00:17:26.000 \rightarrow 00:17:29.280$ generate erskin resistant tumor cells.
- NOTE Confidence: 0.683969263333333
- $00:17:29.280 \rightarrow 00:17:32.880$ It's similar to chemotherapy resistant cells.
- NOTE Confidence: 0.683969263333333
- $00{:}17{:}32.880 \dashrightarrow 00{:}17{:}35.334$ You do the individual generates the
- NOTE Confidence: 0.683969263333333
- $00{:}17{:}35{.}334 \dashrightarrow 00{:}17{:}38{.}390$ cells with this to the reverse inducer.
- NOTE Confidence: 0.683969263333333

00:17:38.390 --> 00:17:40.940 Then you do the immunotherapy.

NOTE Confidence: 0.683969263333333

00:17:40.940 --> 00:17:43.120 OK you see here,

NOTE Confidence: 0.683969263333333

 $00{:}17{:}43.120 \dashrightarrow 00{:}17{:}45.300$ parental cells are responsive

NOTE Confidence: 0.683969263333333

 $00:17:45.300 \longrightarrow 00:17:48.475$ and resistant cells are no longer

NOTE Confidence: 0.683969263333333

 $00{:}17{:}48.475 \dashrightarrow 00{:}17{:}50.050$ responsive to immunotherapy.

NOTE Confidence: 0.683969263333333

 $00{:}17{:}50.050 \dashrightarrow 00{:}17{:}54.845$ Indicating actually Ferroptosis is a

NOTE Confidence: 0.683969263333333

 $00:17:54.845 \rightarrow 00:17:59.640$ potential mechanism induced by immunotherapy.

NOTE Confidence: 0.683969263333333

00:17:59.640 --> 00:18:02.280 So we look it's Morgan mechanisms

NOTE Confidence: 0.683969263333333

 $00:18:02.280 \longrightarrow 00:18:04.639$ then to make a non story short,

NOTE Confidence: 0.683969263333333

 $00:18:04.640 \rightarrow 00:18:06.698$ we know it's interfering and other things,

NOTE Confidence: 0.683969263333333

00:18:06.700 --> 00:18:08.680 but just show you interfering here.

NOTE Confidence: 0.683969263333333

 $00{:}18{:}08{.}680 \dashrightarrow 00{:}18{:}12{.}019$ If you make a lookout receptor in

NOTE Confidence: 0.683969263333333

 $00{:}18{:}12.019 \dashrightarrow 00{:}18{:}14.700$ the knockout tumor cells and your

NOTE Confidence: 0.683969263333333

 $00{:}18{:}14.700 \dashrightarrow 00{:}18{:}17.874$ culture with only one cells you will

NOTE Confidence: 0.683969263333333

 $00:18:17.874 \rightarrow 00:18:20.109$ see actually the liberals production

NOTE Confidence: 0.683969263333333

 $00:18:20.109 \longrightarrow 00:18:23.388$ in the human cells is basically gone.

 $00:18:23.390 \longrightarrow 00:18:25.826$ Under the tumor cell death is

NOTE Confidence: 0.683969263333333

 $00:18:25.826 \longrightarrow 00:18:27.044$ also basically gone,

NOTE Confidence: 0.683969263333333

 $00:18:27.050 \rightarrow 00:18:29.648$ so indicating this tumor cell death

NOTE Confidence: 0.683969263333333

 $00:18:29.648 \rightarrow 00:18:32.160$ is controlled through the interference

NOTE Confidence: 0.683969263333333

 $00:18:32.160 \longrightarrow 00:18:34.287$ and interference signaling.

NOTE Confidence: 0.683969263333333

 $00{:}18{:}34{.}290 \dashrightarrow 00{:}18{:}37{.}645$ So then we hypothesized may be

NOTE Confidence: 0.683969263333333

 $00{:}18{:}37.645 \dashrightarrow 00{:}18{:}40.329$ interfering with your stimulate

NOTE Confidence: 0.683969263333333

 $00:18:40.330 \rightarrow 00:18:43.246$ oxygen lipid species and therefore the

NOTE Confidence: 0.683969263333333

 $00:18:43.246 \rightarrow 00:18:47.170$ cells die as we previously mentioned.

NOTE Confidence: 0.683969263333333

 $00{:}18{:}47{.}170 \dashrightarrow 00{:}18{:}51{.}088$ So we did some individual studies.

NOTE Confidence: 0.683969263333333

 $00{:}18{:}51{.}090 \dashrightarrow 00{:}18{:}54{.}191$ We cultured tumor cells with our CS

NOTE Confidence: 0.683969263333333

00:18:54.191 --> 00:18:57.038 refill processing user with or without

NOTE Confidence: 0.683969263333333

 $00{:}18{:}57{.}038 \dashrightarrow 00{:}18{:}59{.}428$ anything comma you can appreciate.

NOTE Confidence: 0.683969263333333

00:18:59.430 --> 00:19:02.988 In fact the aim is without

NOTE Confidence: 0.683969263333333

 $00{:}19{:}02{.}988 \dashrightarrow 00{:}19{:}04{.}767$ show actually interfering.

- 00:19:04.770 --> 00:19:07.820 Gamma can induce tumor cell
- NOTE Confidence: 0.683969263333333
- 00:19:07.820 --> 00:19:09.650 oxides lipid species,
- NOTE Confidence: 0.683969263333333
- 00:19:09.650 --> 00:19:13.316 so particularly USB 16P18 or induced.
- NOTE Confidence: 0.683969263333333
- $00:19:13.316 \longrightarrow 00:19:15.261$ So this is increased when
- NOTE Confidence: 0.683969263333333
- $00:19:15.261 \longrightarrow 00:19:17.476$ you have a small amount of.
- NOTE Confidence: 0.683969263333333
- 00:19:17.480 --> 00:19:19.016 ISL 3.
- NOTE Confidence: 0.683969263333333
- $00:19:19.016 \longrightarrow 00:19:23.215$ So it means actually in the film
- NOTE Confidence: 0.683969263333333
- $00:19:23.215 \longrightarrow 00:19:25.465$ gamma can properly do the job.
- NOTE Confidence: 0.683969263333333
- $00{:}19{:}25{.}470 \dashrightarrow 00{:}19{:}28{.}686$ To directly show this we used a independent
- NOTE Confidence: 0.683969263333333
- 00:19:28.686 --> 00:19:30.789 comma sensitive human tumor sauna.
- NOTE Confidence: 0.683969263333333
- 00:19:30.790 --> 00:19:32.755 It's HD human cell line
- NOTE Confidence: 0.683969263333333
- $00:19:32.755 \longrightarrow 00:19:34.327$ you treat with interferon.
- NOTE Confidence: 0.683969263333333
- 00:19:34.330 --> 00:19:36.250 You can inhibit tumor growth
- NOTE Confidence: 0.683969263333333
- $00:19:36.250 \longrightarrow 00:19:37.786$ in the English model,
- NOTE Confidence: 0.683969263333333
- $00:19:37.790 \rightarrow 00:19:40.149$ but under this condition if you use
- NOTE Confidence: 0.683969263333333
- $00:19:40.149 \longrightarrow 00:19:42.429$ liberal studying you will see the effect.

- NOTE Confidence: 0.683969263333333
- $00:19:42.430 \longrightarrow 00:19:43.507$ It's completely gone.
- NOTE Confidence: 0.683969263333333
- $00{:}19{:}43.507 \dashrightarrow 00{:}19{:}46.816$ But Earth asset in vitro if you only have
- NOTE Confidence: 0.683969263333333
- $00:19:46.816 \rightarrow 00:19:49.343$ interference or you only have 3 cells.
- NOTE Confidence: 0.683969263333333
- $00:19:49.350 \rightarrow 00:19:51.205$ The sale gas we are not having,
- NOTE Confidence: 0.683969263333333
- $00:19:51.210 \longrightarrow 00:19:53.298$ so suggesting something else,
- NOTE Confidence: 0.683969263333333
- $00:19:53.298 \longrightarrow 00:19:55.386$ not only just in.
- NOTE Confidence: 0.683969263333333
- $00:19:55.390 \rightarrow 00:19:58.567$ So but what did anything do in this case?
- NOTE Confidence: 0.683969263333333
- $00:19:58.570 \rightarrow 00:20:01.090$ We look at the molecular targets,
- NOTE Confidence: 0.683969263333333
- $00{:}20{:}01{.}090 \dashrightarrow 00{:}20{:}03{.}258$ potential molecular targets of
- NOTE Confidence: 0.683969263333333
- 00:20:03.258 --> 00:20:05.426 interferon particularly XC system.
- NOTE Confidence: 0.683969263333333
- 00:20:05.430 --> 00:20:09.224 As you know XC system can transport
- NOTE Confidence: 0.683969263333333
- $00{:}20{:}09{.}224 \dashrightarrow 00{:}20{:}12.602$ system into the cells then become
- NOTE Confidence: 0.683969263333333
- $00:20:12.602 \rightarrow 00:20:16.074$ system and GSH and this will protect
- NOTE Confidence: 0.683969263333333
- $00{:}20{:}16.074 \dashrightarrow 00{:}20{:}18.642$ the cells test from the tosis.
- NOTE Confidence: 0.683969263333333
- $00:20:18.650 \rightarrow 00:20:23.746$ So it turns out interferon actually we press,
- NOTE Confidence: 0.683969263333333

 $00:20:23.750 \longrightarrow 00:20:26.050$ we press the exit. System.

NOTE Confidence: 0.683969263333333

 $00:20:26.050 \longrightarrow 00:20:28.426$ So this is just the the among a.

NOTE Confidence: 0.683969263333333

 $00:20:28.430 \longrightarrow 00:20:30.430$ This shows you the protein.

NOTE Confidence: 0.683969263333333

00:20:30.430 --> 00:20:31.870 Not only this,

NOTE Confidence: 0.683969263333333

 $00:20:31.870 \rightarrow 00:20:34.750$ it's functionally important as shown here,

NOTE Confidence: 0.683969263333333

 $00{:}20{:}34.750 \dashrightarrow 00{:}20{:}37.792$ because the system update is reduced

NOTE Confidence: 0.683969263333333

 $00:20:37.792 \longrightarrow 00:20:40.394$ when you have independent treatment

NOTE Confidence: 0.683969263333333

 $00:20:40.394 \rightarrow 00:20:43.824$ and then the GSH synthesis is reduced,

NOTE Confidence: 0.683969263333333

00:20:43.830 --> 00:20:45.680 and particularly if you have

NOTE Confidence: 0.683969263333333

 $00:20:45.680 \longrightarrow 00:20:47.530$ again small amount of erosion.

NOTE Confidence: 0.683969263333333

 $00{:}20{:}47.530 \dashrightarrow 00{:}20{:}50.023$ This is a well known reduces GSH

NOTE Confidence: 0.683969263333333

00:20:50.023 --> 00:20:52.741 when you put them together though

NOTE Confidence: 0.683969263333333

 $00{:}20{:}52{.}741 \dashrightarrow 00{:}20{:}55{.}809$ reduction of GH is really dramatic.

NOTE Confidence: 0.683969263333333

00:20:55.810 --> 00:21:00.745 So we extend our studies to humans,

NOTE Confidence: 0.683969263333333

 $00:21:00.750 \rightarrow 00:21:03.126$ not only just we use the human cells,

NOTE Confidence: 0.683969263333333

 $00{:}21{:}03.130 \dashrightarrow 00{:}21{:}06.301$ human human cells and we meet a

- NOTE Confidence: 0.683969263333333
- $00:21:06.301 \rightarrow 00:21:07.680$ correlation with immunotherapy.
- NOTE Confidence: 0.683969263333333
- 00:21:07.680 --> 00:21:10.970 As you can see here when the
- NOTE Confidence: 0.683969263333333
- 00:21:10.970 --> 00:21:11.910 patient received
- NOTE Confidence: 0.36622321
- 00:21:11.910 --> 00:21:14.130 e-mail service called Panini Benefits,
- NOTE Confidence: 0.36622321
- $00{:}21{:}14.130 \dashrightarrow 00{:}21{:}16.958$ the XC expression is done in the
- NOTE Confidence: 0.36622321
- $00:21:16.958 \longrightarrow 00:21:19.274$ tumor of course, the interferon
- NOTE Confidence: 0.36622321
- $00:21:19.274 \dashrightarrow 00:21:22.034$ signaling and CTA is increased.
- NOTE Confidence: 0.36622321
- $00:21:22.040 \longrightarrow 00:21:23.740$ So what do we have?
- NOTE Confidence: 0.36622321
- $00{:}21{:}23{.}740 \dashrightarrow 00{:}21{:}29{.}300$ At least we can say apart from apoptosis.
- NOTE Confidence: 0.36622321
- $00{:}21{:}29{.}300 \dashrightarrow 00{:}21{:}32{.}360$ The interaction between CHT cells and
- NOTE Confidence: 0.36622321
- $00:21:32.360 \longrightarrow 00:21:35.659$ tumor cells in this context fail.
- NOTE Confidence: 0.36622321
- $00{:}21{:}35.660 \dashrightarrow 00{:}21{:}37.648$ Photos may be involved,
- NOTE Confidence: 0.36622321
- $00{:}21{:}37.648 \dashrightarrow 00{:}21{:}40.133$ and interferon gamma can target
- NOTE Confidence: 0.36622321
- $00{:}21{:}40{.}133 \dashrightarrow 00{:}21{:}42{.}958$ excision to be involved in this space.
- NOTE Confidence: 0.36622321
- 00:21:42.960 --> 00:21:44.940 This has not been previously
- NOTE Confidence: 0.36622321

- $00:21:44.940 \longrightarrow 00:21:46.920$ appreciated because we don't know.
- NOTE Confidence: 0.36622321
- $00:21:46.920 \longrightarrow 00:21:50.322$ We only think that this is able to process.
- NOTE Confidence: 0.36622321
- 00:21:50.330 --> 00:21:52.890 So now as I mentioned in the film,
- NOTE Confidence: 0.36622321
- $00:21:52.890 \rightarrow 00:21:54.298$ comma is not enough,
- NOTE Confidence: 0.36622321
- 00:21:54.298 --> 00:21:56.058 T cells are not sufficient.
- NOTE Confidence: 0.36622321
- $00:21:56.060 \longrightarrow 00:21:57.470$ So what else?
- NOTE Confidence: 0.36622321
- $00:21:57.470 \longrightarrow 00:21:58.410$ What else?
- NOTE Confidence: 0.36622321
- $00:21:58.410 \longrightarrow 00:22:01.350$ Because early on when Phil poses
- NOTE Confidence: 0.36622321
- $00{:}22{:}01{.}350 \dashrightarrow 00{:}22{:}05{.}010$ as a concept was was established,
- NOTE Confidence: 0.36622321
- $00:22:05.010 \longrightarrow 00:22:08.040$ it is basically based on the
- NOTE Confidence: 0.36622321
- $00:22:08.040 \longrightarrow 00:22:09.050$ synthetic compounds.
- NOTE Confidence: 0.36622321
- $00:22:09.050 \rightarrow 00:22:11.586$ So you treated the cells with the chemicals
- NOTE Confidence: 0.36622321
- $00{:}22{:}11.586 \dashrightarrow 00{:}22{:}13.878$ and then you see the philippoussis,
- NOTE Confidence: 0.36622321
- $00:22:13.880 \longrightarrow 00:22:15.532$ you see the pathway.
- NOTE Confidence: 0.36622321
- $00:22:15.532 \rightarrow 00:22:19.940$ So if their process is a intrinsic mechanism.
- NOTE Confidence: 0.36622321
- $00:22:19.940 \longrightarrow 00:22:21.895$ We should have a intrinsic

- NOTE Confidence: 0.36622321
- $00{:}22{:}21.895 \dashrightarrow 00{:}22{:}23.850$ mechanism to induce the fibrosis

 $00:22:23.921 \longrightarrow 00:22:26.518$ in the cells because we don't have

NOTE Confidence: 0.36622321

00:22:26.518 --> 00:22:28.299 synthetic compound in our body.

NOTE Confidence: 0.36622321

 $00:22:28.300 \longrightarrow 00:22:31.390$ So we look for the natural

NOTE Confidence: 0.36622321

 $00:22:31.390 \longrightarrow 00:22:32.935$ theodosis inducers in.

NOTE Confidence: 0.36622321

 $00{:}22{:}32{.}940 \dashrightarrow 00{:}22{:}37{.}640$ So in this case we come to a fatty acid diet.

NOTE Confidence: 0.36622321

 $00:22:37.640 \longrightarrow 00:22:39.984$ So the reason is we know they are

NOTE Confidence: 0.36622321

 $00:22:39.984 \rightarrow 00:22:42.121$ quite many publications talking about

NOTE Confidence: 0.36622321

 $00{:}22{:}42{.}121 \dashrightarrow 00{:}22{:}45{.}079$ the relationship between bias and the

NOTE Confidence: 0.36622321

 $00:22:45.079 \rightarrow 00:22:47.379$ celebrity response to immunotherapy.

NOTE Confidence: 0.36622321

 $00:22:47.380 \longrightarrow 00:22:49.555$ They are also quite some

NOTE Confidence: 0.36622321

00:22:49.555 --> 00:22:50.860 publications talking about.

NOTE Confidence: 0.36622321

 $00{:}22{:}50{.}860 \dashrightarrow 00{:}22{:}54{.}694$ Micro got microbiota and tumor cell

NOTE Confidence: 0.36622321

 $00{:}22{:}54.694 \dashrightarrow 00{:}22{:}57.250$ respond where patient responsive

NOTE Confidence: 0.36622321

 $00{:}22{:}57{.}350 \dashrightarrow 00{:}23{:}00{.}359$ responsiveness to immunotherapy.

 $00:23:00.360 \longrightarrow 00:23:02.360$ So therefore we were thinking

NOTE Confidence: 0.36622321

 $00{:}23{:}02{.}360 \dashrightarrow 00{:}23{:}04{.}360$ maybe interfering is one thing,

NOTE Confidence: 0.36622321

00:23:04.360 -> 00:23:08.075 maybe some my tablets some

NOTE Confidence: 0.36622321

 $00{:}23{:}08.075 \dashrightarrow 00{:}23{:}10.348$ metabolic nutrient will be involved.

NOTE Confidence: 0.36622321

 $00{:}23{:}10{.}348 \dashrightarrow 00{:}23{:}12{.}640$ We turned to fatty acids because

NOTE Confidence: 0.36622321

 $00{:}23{:}12.706 \dashrightarrow 00{:}23{:}15.170$ we know when the cells die through

NOTE Confidence: 0.36622321

 $00:23:15.170 \longrightarrow 00:23:15.874$ their process,

NOTE Confidence: 0.36622321

 $00:23:15.880 \longrightarrow 00:23:18.358$ it's because of oxidized lipid species.

NOTE Confidence: 0.36622321

 $00{:}23{:}18{.}360 \dashrightarrow 00{:}23{:}20{.}656$ That's why we look at the fatty acid.

NOTE Confidence: 0.36622321

00:23:20.660 - 00:23:23.340 So then I invite you to look at

NOTE Confidence: 0.36622321

 $00{:}23{:}23{.}340 \dashrightarrow 00{:}23{:}25{.}178$ several groups of fatty acids.

NOTE Confidence: 0.36622321

 $00:23:25.180 \longrightarrow 00:23:27.280$ So in fact you have short chain,

NOTE Confidence: 0.36622321

00:23:27.280 --> 00:23:27.972 medium chain,

NOTE Confidence: 0.36622321

 $00{:}23{:}27{.}972 \dashrightarrow 00{:}23{:}31{.}220$ non chain and a very long chain fatty acids.

NOTE Confidence: 0.36622321

 $00:23:31.220 \longrightarrow 00:23:33.635$ I want you to pay attention on

NOTE Confidence: 0.36622321

 $00:23:33.635 \longrightarrow 00:23:35.897$ the non gene fatty acids such

- NOTE Confidence: 0.36622321
- $00{:}23{:}35{.}897 \dashrightarrow 00{:}23{:}37{.}944$ as POAOA and a rachidonic acid.
- NOTE Confidence: 0.36622321
- $00:23:37.944 \longrightarrow 00:23:40.440$ Here we checked all of it.
- NOTE Confidence: 0.36622321
- $00{:}23{:}40{.}440 \dashrightarrow 00{:}23{:}43{.}455$ So in this case when we look at the
- NOTE Confidence: 0.36622321
- $00:23:43.455 \rightarrow 00:23:46.978$ map of fibrosis people have defined as
- NOTE Confidence: 0.36622321
- $00:23:46.978 \rightarrow 00:23:50.679$ a fibrosis involved genes and one is called.
- NOTE Confidence: 0.36622321
- 00:23:50.680 --> 00:23:51.992 A CSR 4 here.
- NOTE Confidence: 0.36622321
- $00:23:51.992 \longrightarrow 00:23:54.642$ So in fact that you prefer it's
- NOTE Confidence: 0.36622321
- $00:23:54.642 \rightarrow 00:23:57.006$ an enzyme preferred substrates,
- NOTE Confidence: 0.36622321
- 00:23:57.010 --> 00:23:58.726 it's electronic acid AA.
- NOTE Confidence: 0.36622321
- $00:23:58.726 \rightarrow 00:24:02.521$ So finally you will see the final product
- NOTE Confidence: 0.36622321
- $00{:}24{:}02{.}521 \dashrightarrow 00{:}24{:}05{.}923$ is Poly unsaturated offset lipid species.
- NOTE Confidence: 0.36622321
- $00{:}24{:}05{.}930 \dashrightarrow 00{:}24{:}08{.}186$ So in this case we are
- NOTE Confidence: 0.36622321
- $00:24:08.186 \rightarrow 00:24:10.550$ thinking it should be involved.
- NOTE Confidence: 0.36622321
- $00{:}24{:}10.550 \dashrightarrow 00{:}24{:}12.022$ So what we did,
- NOTE Confidence: 0.36622321
- $00{:}24{:}12.022 \dashrightarrow 00{:}24{:}14.987$ we cultured the tumor cells with interferon
- NOTE Confidence: 0.36622321

- $00:24:14.987 \rightarrow 00:24:17.687$ pronounced different fatty acids.
- NOTE Confidence: 0.36622321
- 00:24:17.690 --> 00:24:18.490 Long term,
- NOTE Confidence: 0.36622321
- $00{:}24{:}18{.}490 \dashrightarrow 00{:}24{:}20{.}490$ short term media change often.
- NOTE Confidence: 0.36622321
- $00:24:20.490 \longrightarrow 00:24:22.289$ Then we look at the cell desk.
- NOTE Confidence: 0.36622321
- $00{:}24{:}22{.}290 \dashrightarrow 00{:}24{:}24{.}495$ It turns out that in the presence
- NOTE Confidence: 0.36622321
- $00{:}24{:}24{.}495 \dashrightarrow 00{:}24{:}26{.}349$ of a the tumor cell,
- NOTE Confidence: 0.36622321
- $00{:}24{:}26{.}350 \dashrightarrow 00{:}24{:}28{.}194$ death is dramatically increased.
- NOTE Confidence: 0.36622321
- $00:24:28.194 \longrightarrow 00:24:30.960$ And keep in mind that these
- NOTE Confidence: 0.36622321
- $00{:}24{:}31.045 \dashrightarrow 00{:}24{:}33.650$ cell deaths can be completely
- NOTE Confidence: 0.36622321
- $00:24:33.650 \rightarrow 00:24:35.734$ blocked by THEODOSIS inhibitor.
- NOTE Confidence: 0.36622321
- $00{:}24{:}35{.}740 \dashrightarrow 00{:}24{:}38{.}337$ So it means this is really the odosis NOTE Confidence: 0.36622321
- $00:24:38.337 \rightarrow 00:24:40.458$ and this is repeated reproducible
- NOTE Confidence: 0.36622321
- $00{:}24{:}40{.}458 \dashrightarrow 00{:}24{:}43{.}242$ in P-16 and seven tumor cells
- NOTE Confidence: 0.36622321
- $00:24:43.242 \longrightarrow 00:24:45.099$ in mouse and humans.
- NOTE Confidence: 0.36622321
- $00:24:45.100 \longrightarrow 00:24:49.164$ So finally we want to see what has
- NOTE Confidence: 0.36622321
- $00:24:49.164 \rightarrow 00:24:50.970$ happened actually with electronic
$00:24:50.970 \longrightarrow 00:24:53.980$ acid in the presence of in the

NOTE Confidence: 0.800287875454545

 $00:24:54.061 \longrightarrow 00:24:57.110$ field. So we cultured human cells

NOTE Confidence: 0.800287875454545

 $00:24:57.110 \rightarrow 00:24:59.690$ with interfering with or without.

NOTE Confidence: 0.800287875454545

 $00:24:59.690 \rightarrow 00:25:03.176 \text{ E5}$ neighbored atonic acid we want

NOTE Confidence: 0.800287875454545

 $00:25:03.176 \rightarrow 00:25:06.629$ to see where electronic acid goes.

NOTE Confidence: 0.800287875454545

 $00{:}25{:}06{.}630 \dashrightarrow 00{:}25{:}09{.}666$ So in this case we made a CSL

NOTE Confidence: 0.800287875454545

 $00{:}25{:}09.666 \dashrightarrow 00{:}25{:}12.942$ knockout and the width of tumor cells.

NOTE Confidence: 0.800287875454545

 $00:25:12.950 \longrightarrow 00:25:14.868$ We treat the cells in this way.

NOTE Confidence: 0.800287875454545

 $00:25:14.870 \longrightarrow 00:25:17.510$ Then we look at different oxygenated

NOTE Confidence: 0.800287875454545

 $00:25:17.510 \rightarrow 00:25:19.708$ species because you may appreciate

NOTE Confidence: 0.800287875454545

 $00:25:19.708 \longrightarrow 00:25:22.221$ here what is the black box and

NOTE Confidence: 0.800287875454545

 $00{:}25{:}22{.}221 \dashrightarrow 00{:}25{:}24{.}709$ the red bars are all deficient.

NOTE Confidence: 0.800287875454545

 $00{:}25{:}24.710 \dashrightarrow 00{:}25{:}26.582$ It is deficient cells.

NOTE Confidence: 0.800287875454545

00:25:26.582 --> 00:25:28.922 You will see actually interfering,

NOTE Confidence: 0.800287875454545

 $00:25:28.930 \longrightarrow 00:25:30.790$ really promote.

 $00:25:30.790 \longrightarrow 00:25:34.148$ The incorporation of T5

NOTE Confidence: 0.800287875454545

 $00{:}25{:}34.148 \dashrightarrow 00{:}25{:}36.988$ neighboured electronic acid in two

NOTE Confidence: 0.800287875454545

 $00{:}25{:}36{.}988 \dashrightarrow 00{:}25{:}39{.}260$ different oxides lipid species.

NOTE Confidence: 0.800287875454545

 $00:25:39.260 \rightarrow 00:25:43.900$ So this including PE18B16 PC 18.

NOTE Confidence: 0.800287875454545

 $00:25:43.900 \longrightarrow 00:25:47.806$ You can see from the slight ACL 1400.

NOTE Confidence: 0.800287875454545

 $00{:}25{:}47.806 \dashrightarrow 00{:}25{:}49.378$ So in this case,

NOTE Confidence: 0.800287875454545

 $00{:}25{:}49{.}380 \dashrightarrow 00{:}25{:}52{.}980$ what has in the gamma Dong look at the

NOTE Confidence: 0.800287875454545

 $00:25:52.980 \rightarrow 00:25:55.853$ brooding expression of CCL 4 actually

NOTE Confidence: 0.800287875454545

 $00{:}25{:}55{.}853 \dashrightarrow 00{:}25{:}59{.}260$ in film comma stimulate its expression,

NOTE Confidence: 0.800287875454545

 $00{:}25{:}59{.}260 \dashrightarrow 00{:}26{:}02{.}015$ so this is slow transcriptional

NOTE Confidence: 0.800287875454545

 $00{:}26{:}02.015 \dashrightarrow 00{:}26{:}05.400$ recognition as the cheap essay shows.

NOTE Confidence: 0.800287875454545

00:26:05.400 --> 00:26:08.130 Actually there's a high I funding

NOTE Confidence: 0.800287875454545

 $00:26:08.130 \longrightarrow 00:26:11.440$ in the ACL 4 promoter area,

NOTE Confidence: 0.800287875454545

 $00:26:11.440 \longrightarrow 00:26:13.900$ and the cheap shows actually

NOTE Confidence: 0.800287875454545

 $00:26:13.900 \longrightarrow 00:26:15.376$ this high occupancy.

NOTE Confidence: 0.800287875454545

 $00{:}26{:}15{.}380 \dashrightarrow 00{:}26{:}17{.}893$ So we first did some in vivo

 $00{:}26{:}17.893 \dashrightarrow 00{:}26{:}20.200$ studies to show the relevance.

NOTE Confidence: 0.800287875454545

 $00{:}26{:}20{.}200 \dashrightarrow 00{:}26{:}23{.}430$ So in this case we made a ACL 4 knock out

NOTE Confidence: 0.800287875454545

 $00{:}26{:}23.512 \dashrightarrow 00{:}26{:}26.338$ tumors in several tumor cell lines.

NOTE Confidence: 0.800287875454545

 $00:26:26.340 \longrightarrow 00:26:29.409$ You see a CS4 is gone and tumors are

NOTE Confidence: 0.800287875454545

 $00:26:29.409 \longrightarrow 00:26:32.161$ getting bigger and in vivo and when

NOTE Confidence: 0.800287875454545

 $00{:}26{:}32.161 \dashrightarrow 00{:}26{:}34.799$ we did the combination therapy Ravi,

NOTE Confidence: 0.800287875454545

 $00:26:34.800 \rightarrow 00:26:37.968$ Classic way we treated mice with AA and

NOTE Confidence: 0.800287875454545

 $00:26:37.968 \longrightarrow 00:26:40.981$ AA actually can partially control the

NOTE Confidence: 0.800287875454545

 $00{:}26{:}40{.}981 \dashrightarrow 00{:}26{:}43{.}656$ tumor progression in several models,

NOTE Confidence: 0.800287875454545

 $00:26:43.660 \longrightarrow 00:26:45.736$ but keep in mind the A.

NOTE Confidence: 0.800287875454545

 $00:26:45.740 \longrightarrow 00:26:47.665$ He's a very small amount of concentration.

NOTE Confidence: 0.800287875454545

 $00{:}26{:}47.670 \dashrightarrow 00{:}26{:}49.518$ You you cannot give too much and then

NOTE Confidence: 0.800287875454545

 $00{:}26{:}49.518 \dashrightarrow 00{:}26{:}51.747$ you kill the mice because it's quite toxic.

NOTE Confidence: 0.800287875454545

 $00{:}26{:}51{.}750 \dashrightarrow 00{:}26{:}54{.}918$ So we see the combination the rapy can give

NOTE Confidence: 0.800287875454545

 $00{:}26{:}54{.}918$ --> $00{:}26{:}57{.}968$ you some benefits in the mouse model.

 $00:26:57.970 \longrightarrow 00:27:00.994$ So when you look at the patient

NOTE Confidence: 0.800287875454545

 $00:27:00.994 \longrightarrow 00:27:03.729$ with a CCL 4 expression,

NOTE Confidence: 0.800287875454545

 $00:27:03.730 \longrightarrow 00:27:07.573$ in fact high ACC for expression is

NOTE Confidence: 0.800287875454545

 $00:27:07.573 \rightarrow 00:27:10.850$ positively associated with patient survival,

NOTE Confidence: 0.800287875454545

 $00:27:10.850 \longrightarrow 00:27:15.746$ suggesting maybe it is a four is relevant in.

NOTE Confidence: 0.800287875454545

00:27:15.750 --> 00:27:17.253 The tumor microenvironment.

NOTE Confidence: 0.800287875454545

 $00{:}27{:}17.253 \dashrightarrow 00{:}27{:}22.090$ So we tested it not only like in tonic acid,

NOTE Confidence: 0.800287875454545

 $00:27:22.090 \rightarrow 00:27:24.436$ we tested them other fatty acids

NOTE Confidence: 0.800287875454545

 $00{:}27{:}24.436 \dashrightarrow 00{:}27{:}25.609$ as I mentioned,

NOTE Confidence: 0.800287875454545

 $00{:}27{:}25.610 \dashrightarrow 00{:}27{:}27.584$ but what I conclude here don't

NOTE Confidence: 0.800287875454545

 $00:27:27.584 \rightarrow 00:27:29.530$ show you all the details.

NOTE Confidence: 0.800287875454545

00:27:29.530 --> 00:27:31.483 Apart from AA,

NOTE Confidence: 0.800287875454545

 $00{:}27{:}31.483 \dashrightarrow 00{:}27{:}36.040$ OA and POA can also participate in

NOTE Confidence: 0.800287875454545

 $00{:}27{:}36.176 \dashrightarrow 00{:}27{:}40.426$ inducing the tumor cell process.

NOTE Confidence: 0.800287875454545

 $00{:}27{:}40{.}430 \dashrightarrow 00{:}27{:}43{.}720$ All these essays are in the absence

NOTE Confidence: 0.800287875454545

 $00:27:43.720 \longrightarrow 00:27:45.130$ of synthetic compound.

- NOTE Confidence: 0.800287875454545
- $00:27:45.130 \rightarrow 00:27:48.526$ So indicating what we discovered actually.
- NOTE Confidence: 0.800287875454545
- $00:27:48.530 \longrightarrow 00:27:51.728$ The effect specific fatty acids plus
- NOTE Confidence: 0.800287875454545
- $00{:}27{:}51{.}728 \dashrightarrow 00{:}27{:}54{.}591$ interferon gamma are the intrinsic
- NOTE Confidence: 0.800287875454545
- $00:27:54.591 \rightarrow 00:27:56.514$ philippoussis inducing mechanisms
- NOTE Confidence: 0.800287875454545
- $00{:}27{:}56{.}514 \dashrightarrow 00{:}27{:}59{.}719$ we are able to detect.
- NOTE Confidence: 0.800287875454545
- $00:27:59.720 \longrightarrow 00:28:02.444$ Of course all the fatty acids
- NOTE Confidence: 0.800287875454545
- $00:28:02.444 \rightarrow 00:28:04.740$ species and interference in vivo,
- NOTE Confidence: 0.800287875454545
- $00:28:04.740 \longrightarrow 00:28:06.520$ they are not synthetic combo.
- NOTE Confidence: 0.800287875454545
- $00:28:06.520 \longrightarrow 00:28:09.070$ So this is another similar to
- NOTE Confidence: 0.800287875454545
- $00:28:09.070 \longrightarrow 00:28:11.639$ the concept that we all know,
- NOTE Confidence: 0.800287875454545
- 00:28:11.640 --> 00:28:15.560 such as H170 cells, not one cytokine.
- NOTE Confidence: 0.800287875454545
- 00:28:15.560 --> 00:28:17.320 It's not enough to polarize,
- NOTE Confidence: 0.800287875454545
- $00:28:17.320 \longrightarrow 00:28:18.709$ you need several.
- NOTE Confidence: 0.800287875454545
- $00{:}28{:}18.709 \dashrightarrow 00{:}28{:}21.730$ Effectors what we have discovered, actually.
- NOTE Confidence: 0.800287875454545
- $00{:}28{:}21.730 \dashrightarrow 00{:}28{:}24.530$ Tumor cell Philippoussis needs
- NOTE Confidence: 0.800287875454545

 $00:28:24.530 \longrightarrow 00:28:25.930$ several factors,

NOTE Confidence: 0.800287875454545

 $00{:}28{:}25{.}930 \dashrightarrow 00{:}28{:}28{.}162$ and interference is one of them

NOTE Confidence: 0.800287875454545

 $00:28:28.162 \longrightarrow 00:28:30.610$ and the fatty acids are another.

NOTE Confidence: 0.800287875454545

 $00:28:30.610 \rightarrow 00:28:35.630$ So now that's the the conclusion

NOTE Confidence: 0.800287875454545

 $00{:}28{:}35{.}630 \dashrightarrow 00{:}28{:}39{.}720$ we have basically when you have the

NOTE Confidence: 0.800287875454545

 $00:28:39.720 \longrightarrow 00:28:43.360$ induction between C8 and tumor cells.

NOTE Confidence: 0.800287875454545

 $00:28:43.360 \rightarrow 00:28:45.950$ Because this is one of the founding

NOTE Confidence: 0.800287875454545

 $00:28:45.950 \longrightarrow 00:28:47.930$ father of Tosis is another.

NOTE Confidence: 0.800287875454545

 $00:28:47.930 \longrightarrow 00:28:50.090$ I hope this becomes textbook.

NOTE Confidence: 0.800287875454545

 $00:28:50.090 \longrightarrow 00:28:53.023$ So fear of loss is is mediated

NOTE Confidence: 0.800287875454545

 $00{:}28{:}53{.}023 \dashrightarrow 00{:}28{:}54{.}280$ and the recognition

NOTE Confidence: 0.637820824117647

 $00:28:54.367 \rightarrow 00:28:57.048$ through the AC system and CSL 4.

NOTE Confidence: 0.637820824117647

 $00:28:57.050 \rightarrow 00:29:00.458$ Maybe other factors will be involved as well

NOTE Confidence: 0.637820824117647

 $00:29:00.458 \longrightarrow 00:29:04.148$ and we are still working on the details.

NOTE Confidence: 0.637820824117647

 $00:29:04.150 \longrightarrow 00:29:08.374$ As you know, there are several

NOTE Confidence: 0.637820824117647

00:29:08.374 --> 00:29:12.170 philanthropic pathways people have defined.

 $00:29:12.170 \longrightarrow 00:29:16.244$ So what is the technical message here?

NOTE Confidence: 0.637820824117647

 $00:29:16.250 \longrightarrow 00:29:18.714$ You must fear of those is is

NOTE Confidence: 0.637820824117647

 $00:29:18.714 \longrightarrow 00:29:21.348$ a mode of action of Syria.

NOTE Confidence: 0.637820824117647

 $00:29:21.350 \longrightarrow 00:29:23.766$ And tumor Philippoussis is

NOTE Confidence: 0.637820824117647

 $00:29:23.766 \longrightarrow 00:29:25.292$ neural therapy mechanism.

NOTE Confidence: 0.637820824117647

 $00:29:25.292 \longrightarrow 00:29:28.519$ So if so we should think about

NOTE Confidence: 0.637820824117647

 $00:29:28.519 \longrightarrow 00:29:30.990$ the potential translation.

NOTE Confidence: 0.637820824117647

 $00:29:30.990 \longrightarrow 00:29:32.610$ We are thinking about this,

NOTE Confidence: 0.637820824117647

00:29:32.610 - 00:29:35.106 many groups are working on this.

NOTE Confidence: 0.637820824117647

 $00:29:35.110 \rightarrow 00:29:38.390$ So now we move to the second part of my talk.

NOTE Confidence: 0.637820824117647

00:29:38.390 --> 00:29:42.308 It's concerned another ACC family member,

NOTE Confidence: 0.637820824117647

00:29:42.310 --> 00:29:45.274 it's named SRC 4382.

NOTE Confidence: 0.637820824117647

 $00{:}29{:}45{.}274 \dashrightarrow 00{:}29{:}49{.}290$ So myself is a immunologist and when you

NOTE Confidence: 0.637820824117647

 $00{:}29{:}49{.}398 \dashrightarrow 00{:}29{:}53{.}514$ talk to biologists and some other people,

NOTE Confidence: 0.637820824117647

 $00{:}29{:}53{.}520 \dashrightarrow 00{:}29{:}57{.}517$ there is an idea or thought proposed

 $00:29:57.520 \rightarrow 00:30:01.090$ because the tumor cells are highly

NOTE Confidence: 0.637820824117647

 $00{:}30{:}01{.}090$ --> $00{:}30{:}02{.}875$ proliferative and invasive.

NOTE Confidence: 0.637820824117647

 $00:30:02.880 \dashrightarrow 00:30:05.360$ The tumor cells need a lot of nutrients.

NOTE Confidence: 0.637820824117647

 $00:30:05.360 \longrightarrow 00:30:07.397$ So one way to treat the patient

NOTE Confidence: 0.637820824117647

00:30:07.397 --> 00:30:09.710 that maybe we can start with the

NOTE Confidence: 0.637820824117647

00:30:09.710 --> 00:30:10.736 cancer cell death.

NOTE Confidence: 0.637820824117647

 $00:30:10.740 \longrightarrow 00:30:13.710$ So that's the way how the

NOTE Confidence: 0.637820824117647

 $00:30:13.710 \longrightarrow 00:30:15.690$ biology is maybe some.

NOTE Confidence: 0.637820824117647

00:30:15.690 --> 00:30:16.842 Pharmacologists think this way,

NOTE Confidence: 0.637820824117647

 $00:30:16.842 \longrightarrow 00:30:20.506$ I don't know, so let's see if this works.

NOTE Confidence: 0.637820824117647

 $00:30:20.510 \longrightarrow 00:30:21.329$ In that case,

NOTE Confidence: 0.637820824117647

 $00{:}30{:}21{.}329 \dashrightarrow 00{:}30{:}23{.}240$ I invite you to think about the

NOTE Confidence: 0.637820824117647

 $00{:}30{:}23{.}306 \dashrightarrow 00{:}30{:}25{.}282$ nutrients and metabolites in

NOTE Confidence: 0.637820824117647

 $00{:}30{:}25{.}282 \dashrightarrow 00{:}30{:}26{.}764$ the cancer microenvironment.

NOTE Confidence: 0.637820824117647

 $00{:}30{:}26.770 \dashrightarrow 00{:}30{:}30{.}074$ We know when the cells are exposed to

NOTE Confidence: 0.637820824117647

 $00{:}30{:}30{.}074 \dashrightarrow 00{:}30{:}31{.}996$ different metabolites and nutrients

- NOTE Confidence: 0.637820824117647
- $00:30:31.996 \longrightarrow 00:30:34.048$ in the particular environment,
- NOTE Confidence: 0.637820824117647
- $00:30:34.050 \rightarrow 00:30:36.490$ not only just human cells,
- NOTE Confidence: 0.637820824117647
- $00:30:36.490 \longrightarrow 00:30:38.584$ but also these cells and disease
- NOTE Confidence: 0.637820824117647
- $00:30:38.584 \rightarrow 00:30:40.450$ and Macy's and other cells,
- NOTE Confidence: 0.637820824117647
- $00{:}30{:}40{.}450 \dashrightarrow 00{:}30{:}42{.}562$ they must be subject to the
- NOTE Confidence: 0.637820824117647
- $00:30:42.562 \rightarrow 00:30:43.970$ regulation by the environment.
- NOTE Confidence: 0.637820824117647
- 00:30:43.970 > 00:30:45.490 Therefore, they are functional.
- NOTE Confidence: 0.637820824117647
- $00:30:45.490 \longrightarrow 00:30:47.010$ Status must be changed.
- NOTE Confidence: 0.637820824117647
- $00:30:47.010 \longrightarrow 00:30:49.768$ So it's a very simple way to
- NOTE Confidence: 0.637820824117647
- $00:30:49.768 \longrightarrow 00:30:52.099$ put so in this case.
- NOTE Confidence: 0.637820824117647
- 00:30:52.100 --> 00:30:52.858 Early on,
- NOTE Confidence: 0.637820824117647
- $00{:}30{:}52.858 \dashrightarrow 00{:}30{:}54.753$ some groups have already discovered
- NOTE Confidence: 0.637820824117647
- $00{:}30{:}54.753 \dashrightarrow 00{:}30{:}56.889$ the T cells are dysfunctional
- NOTE Confidence: 0.637820824117647
- $00{:}30{:}56.889 \dashrightarrow 00{:}30{:}59.214$ in the tumor micro environment.
- NOTE Confidence: 0.637820824117647
- $00{:}30{:}59{.}220 \dashrightarrow 00{:}31{:}01.660$ You may say the T cells are exhausted.
- NOTE Confidence: 0.637820824117647

 $00:31:01.660 \longrightarrow 00:31:02.914$ That's alright so.

NOTE Confidence: 0.637820824117647

00:31:02.914 --> 00:31:05.422 But we also know some epigenetic

NOTE Confidence: 0.637820824117647

 $00:31:05.422 \rightarrow 00:31:08.002$ pathways are involved in the regulation

NOTE Confidence: 0.637820824117647

 $00:31:08.002 \rightarrow 00:31:11.140$ of tumor cell dysfunction and T cell

NOTE Confidence: 0.637820824117647

 $00:31:11.140 \longrightarrow 00:31:13.580$ dysfunctionality in the tumor environment.

NOTE Confidence: 0.637820824117647

 $00{:}31{:}13.580 \dashrightarrow 00{:}31{:}16.373$ So we are thinking maybe in this

NOTE Confidence: 0.637820824117647

00:31:16.373 --> 00:31:19.063 case a crosstalk between metabolic

NOTE Confidence: 0.637820824117647

00:31:19.063 --> 00:31:21.166 and apologetic mechanism.

NOTE Confidence: 0.637820824117647

 $00:31:21.170 \longrightarrow 00:31:24.150$ This has, uh, evidence actually.

NOTE Confidence: 0.637820824117647

 $00:31:24.150 \rightarrow 00:31:25.848$ People have reported some of them.

NOTE Confidence: 0.637820824117647

 $00:31:25.850 \longrightarrow 00:31:26.548$ For example,

NOTE Confidence: 0.637820824117647

00:31:26.548 --> 00:31:27.246 you know,

NOTE Confidence: 0.637820824117647

00:31:27.246 --> 00:31:29.340 after H succinate and have a

NOTE Confidence: 0.637820824117647

 $00:31:29.416 \longrightarrow 00:31:31.472$ particularly succinate have has

NOTE Confidence: 0.637820824117647

 $00:31:31.472 \longrightarrow 00:31:33.528$ been studied in macrophages,

NOTE Confidence: 0.637820824117647

 $00:31:33.530 \longrightarrow 00:31:35.590$ minor cells and some others.

 $00:31:35.590 \longrightarrow 00:31:38.308$ And we are interested in Sam.

NOTE Confidence: 0.637820824117647

 $00:31:38.310 \rightarrow 00:31:40.249$ So why we are interested in them,

NOTE Confidence: 0.637820824117647

 $00:31:40.250 \rightarrow 00:31:43.330$ you will see why we're interested in them.

NOTE Confidence: 0.637820824117647

 $00:31:43.330 \longrightarrow 00:31:44.401$ So in fact,

NOTE Confidence: 0.637820824117647

 $00{:}31{:}44{.}401 \dashrightarrow 00{:}31{:}48{.}099$ in this case we look at the amino acids.

NOTE Confidence: 0.637820824117647

00:31:48.100 --> 00:31:51.796 So we did a very simple array,

NOTE Confidence: 0.637820824117647

 $00{:}31{:}51{.}800 \dashrightarrow 00{:}31{:}56{.}620$ so we cultured basically G cells with

NOTE Confidence: 0.637820824117647

 $00:31:56.620 \rightarrow 00:31:58.900$ different amino acids in the media,

NOTE Confidence: 0.637820824117647

 $00{:}31{:}58{.}900 \dashrightarrow 00{:}32{:}00{.}695$ but we manipulated the concentration

NOTE Confidence: 0.637820824117647

 $00{:}32{:}00{.}695 \dashrightarrow 00{:}32{:}03{.}760$ but we admit one by one and then we

NOTE Confidence: 0.637820824117647

00:32:03.760 - 00:32:06.020 take the functionality of the T cells,

NOTE Confidence: 0.637820824117647

 $00:32:06.020 \dashrightarrow 00:32:09.476$ basically the shell gas and the T cells.

NOTE Confidence: 0.637820824117647

00:32:09.480 --> 00:32:13.904 It turns out if you own it,

NOTE Confidence: 0.637820824117647

 $00{:}32{:}13{.}910 \dashrightarrow 00{:}32{:}14{.}858$ my theory.

NOTE Confidence: 0.637820824117647

 $00:32:14.858 \longrightarrow 00:32:17.228$ So T cells cannot stand,

 $00:32:17.230 \rightarrow 00:32:20.210$ they become very much evolution.

NOTE Confidence: 0.637820824117647

 $00{:}32{:}20{.}210 \dashrightarrow 00{:}32{:}24{.}074$ And the cells do not express much

NOTE Confidence: 0.637820824117647

 $00:32:24.074 \longrightarrow 00:32:24.626$ interference.

NOTE Confidence: 0.637820824117647

 $00:32:24.630 \rightarrow 00:32:26.961$ And then we did another way along

NOTE Confidence: 0.637820824117647

 $00:32:26.961 \rightarrow 00:32:29.270$ means we add amino acids back.

NOTE Confidence: 0.637820824117647

 $00{:}32{:}29{.}270 \dashrightarrow 00{:}32{:}31{.}550$ So it's a plus experiment.

NOTE Confidence: 0.637820824117647

 $00{:}32{:}31{.}550 \dashrightarrow 00{:}32{:}33{.}500$ So in this case we calculate

NOTE Confidence: 0.637820824117647

 $00:32:33.500 \longrightarrow 00:32:35.150$ the cells with too much

NOTE Confidence: 0.73993483

 $00{:}32{:}35{.}150 \dashrightarrow 00{:}32{:}38{.}020$ to induce the cell or

NOTE Confidence: 0.73993483

 $00:32:38.020 \rightarrow 00:32:39.168$ dysfunctionality dysfunctional.

NOTE Confidence: 0.73993483

 $00{:}32{:}39{.}170 \dashrightarrow 00{:}32{:}42{.}170$ They become embodied and reduce stereogram.

NOTE Confidence: 0.73993483

 $00:32:42.170 \dashrightarrow 00:32:45.188$ You will see under this condition

NOTE Confidence: 0.73993483

 $00:32:45.188 \longrightarrow 00:32:48.253$ if we add methionine pack we

NOTE Confidence: 0.73993483

 $00:32:48.253 \rightarrow 00:32:50.648$ will see actually the tumor.

NOTE Confidence: 0.73993483

00:32:50.650 --> 00:32:52.750 T cell F is reduced,

NOTE Confidence: 0.73993483

 $00:32:52.750 \rightarrow 00:32:55.890$ T cell function is improved.

 $00:32:55.890 \rightarrow 00:32:59.832$ So indicating actually the T cells

NOTE Confidence: 0.73993483

 $00{:}32{:}59{.}832 \dashrightarrow 00{:}33{:}03{.}706$ are very sensitive to the supply

NOTE Confidence: 0.73993483

 $00{:}33{:}03{.}706 \dashrightarrow 00{:}33{:}06{.}980$ of methionine so and then we look

NOTE Confidence: 0.73993483

 $00:33:06.980 \rightarrow 00:33:08.990$ at the methionine metabolic cycle.

NOTE Confidence: 0.73993483

 $00{:}33{:}08{.}990 \dashrightarrow 00{:}33{:}13{.}310$ So in fact my theory can become same NOTE Confidence: 0.73993483

 $00:33:13.310 \longrightarrow 00:33:18.562$ and you know Sam is a real donor for

NOTE Confidence: 0.73993483

 $00:33:18.562 \rightarrow 00:33:20.786$ methylation so history modification.

NOTE Confidence: 0.73993483

 $00:33:20.790 \longrightarrow 00:33:22.911$ So that's the reason we want to

NOTE Confidence: 0.73993483

 $00{:}33{:}22{.}911 \dashrightarrow 00{:}33{:}25{.}122$ look at some right so in this

NOTE Confidence: 0.73993483

 $00:33:25.122 \rightarrow 00:33:26.652$ case when you cut your.

NOTE Confidence: 0.73993483

00:33:26.660 --> 00:33:29.150 Have to keep cells with two

NOTE Confidence: 0.73993483

00:33:29.150 --> 00:33:30.810 measurement and you supplement

NOTE Confidence: 0.73993483

 $00{:}33{:}30{.}885 \dashrightarrow 00{:}33{:}34{.}205$ with my film and you detect all the

NOTE Confidence: 0.73993483

 $00{:}33{:}34{.}205 \dashrightarrow 00{:}33{:}35{.}725$ Internet intercellular my cabinets

NOTE Confidence: 0.73993483

00:33:35.725 --> 00:33:38.734 you will see if you do so first of

 $00:33:38.734 \rightarrow 00:33:41.393$ all you see reduced intracellular

NOTE Confidence: 0.73993483

00:33:41.393 - 00:33:44.291 methionine when you don't add in

NOTE Confidence: 0.73993483

 $00{:}33{:}44{.}291 \dashrightarrow 00{:}33{:}47{.}219$ the culture and when you add it

NOTE Confidence: 0.73993483

 $00{:}33{:}47{.}219 \dashrightarrow 00{:}33{:}49{.}714$ comes back and also you don't have

NOTE Confidence: 0.73993483

 $00{:}33{:}49{.}714 \dashrightarrow 00{:}33{:}52{.}290$ them in the SH all those things

NOTE Confidence: 0.73993483

 $00{:}33{:}52{.}290 \dashrightarrow 00{:}33{:}54{.}750$ but you supplement Matheny you can NOTE Confidence: 0.73993483

 $00:33:54.831 \rightarrow 00:33:57.336$ partially and important we cover.

NOTE Confidence: 0.73993483

 $00:33:57.340 \longrightarrow 00:34:00.120$ They are the intercellular ascend

NOTE Confidence: 0.73993483

 $00{:}34{:}00{.}120 \dashrightarrow 00{:}34{:}02{.}344$ and intercellular other metabolites

NOTE Confidence: 0.73993483

 $00:34:02.344 \longrightarrow 00:34:06.199$ of of methionine, such as SH.

NOTE Confidence: 0.73993483

 $00{:}34{:}06{.}200 \dashrightarrow 00{:}34{:}10{.}314$ So if so this must affect his notification.

NOTE Confidence: 0.73993483

 $00:34:10.314 \dashrightarrow 00:34:13.439$ So when we in this case we look at this, NOTE Confidence: 0.73993483

 $00{:}34{:}13{.}440 \dashrightarrow 00{:}34{:}15{.}516$ this is calculated with either tumor

NOTE Confidence: 0.73993483

00:34:15.516 --> 00:34:19.053 cells mouse are not human you will see

NOTE Confidence: 0.73993483

00:34:19.053 --> 00:34:22.008 actually the tumors supernatant reduce

NOTE Confidence: 0.73993483

00:34:22.008 --> 00:34:23.746 its 3K790 resonation dramatically.

- NOTE Confidence: 0.73993483
- $00:34:23.746 \rightarrow 00:34:27.398$ This is not only the case in in most cells,

 $00{:}34{:}27{.}400 \dashrightarrow 00{:}34{:}29{.}388$ in too many cells the same thing

NOTE Confidence: 0.73993483

 $00:34:29.388 \rightarrow 00:34:30.629$ and you supplement methionine

NOTE Confidence: 0.73993483

 $00:34:30.629 \rightarrow 00:34:32.299$ which you can recover it.

NOTE Confidence: 0.73993483

 $00{:}34{:}32{.}300 \dashrightarrow 00{:}34{:}35{.}996$ Other histone markers are less affected and.

NOTE Confidence: 0.73993483

00:34:36.000 --> 00:34:37.967 I I couldn't explain to you why.

NOTE Confidence: 0.73993483

 $00{:}34{:}37{.}970 \dashrightarrow 00{:}34{:}40{.}818$ Then we look at the primary cells T

NOTE Confidence: 0.73993483

 $00:34:40.818 \longrightarrow 00:34:43.660$ cells in the tumor micro in humans

NOTE Confidence: 0.73993483

 $00{:}34{:}43.660 \dashrightarrow 00{:}34{:}46.565$ and the mouse and you will see

NOTE Confidence: 0.73993483

 $00{:}34{:}46{.}565 \dashrightarrow 00{:}34{:}49{.}449$ isolated cells from the mouse system.

NOTE Confidence: 0.73993483

00:34:49.450 --> 00:34:52.496 You will see we used H3790 resonation

NOTE Confidence: 0.73993483

 $00{:}34{:}52{.}496 \dashrightarrow 00{:}34{:}56{.}923$ and so is in human CD8T cells

NOTE Confidence: 0.73993483

 $00{:}34{:}56{.}923 \dashrightarrow 00{:}34{:}59{.}287$ in the tumor microenvironment.

NOTE Confidence: 0.73993483

 $00{:}34{:}59{.}290 \dashrightarrow 00{:}35{:}00{.}618$ So in that case,

NOTE Confidence: 0.73993483

 $00{:}35{:}00{.}618 \dashrightarrow 00{:}35{:}03{.}370$ this extreme case 7 and T machination

 $00:35:03.370 \rightarrow 00:35:06.090$ must be functionally important.

NOTE Confidence: 0.73993483

 $00:35:06.090 \longrightarrow 00:35:08.110$ So to test this possibility,

NOTE Confidence: 0.73993483

 $00:35:08.110 \longrightarrow 00:35:10.329$ we made a total of 1 specific

NOTE Confidence: 0.73993483

 $00{:}35{:}10{.}329 \dashrightarrow 00{:}35{:}11{.}810$ lookout in T cells.

NOTE Confidence: 0.73993483

 $00{:}35{:}11{.}810 \dashrightarrow 00{:}35{:}14{.}918$ The reason is total one is the

NOTE Confidence: 0.73993483

 $00:35:14.918 \longrightarrow 00:35:16.400$ only endemic 8719 resolution.

NOTE Confidence: 0.73993483

 $00{:}35{:}16{.}400 \dashrightarrow 00{:}35{:}18{.}760$ So when we made it look out in

NOTE Confidence: 0.73993483

 $00{:}35{:}18.831 \dashrightarrow 00{:}35{:}21.078$ T cells and then the tumors are

NOTE Confidence: 0.73993483

00:35:21.078 --> 00:35:23.772 getting bigger than the T cells are

NOTE Confidence: 0.73993483

 $00:35:23.772 \rightarrow 00:35:25.440$ becoming apoptotic and dysfunctional.

NOTE Confidence: 0.73993483

 $00:35:25.440 \longrightarrow 00:35:28.026$ So that's one way to go.

NOTE Confidence: 0.73993483

 $00{:}35{:}28.030 \dashrightarrow 00{:}35{:}29.380$ Another way to go is.

NOTE Confidence: 0.73993483

 $00:35:29.380 \dashrightarrow 00:35:31.250$ We supplement methionine in the

NOTE Confidence: 0.73993483

 $00{:}35{:}31{.}250 \dashrightarrow 00{:}35{:}33{.}840$ tumor bearing mice in this condition.

NOTE Confidence: 0.73993483

 $00:35:33.840 \longrightarrow 00:35:36.192$ If you supplement then you reduce

NOTE Confidence: 0.73993483

 $00:35:36.192 \rightarrow 00:35:36.976$ tumor growth,

- NOTE Confidence: 0.73993483
- $00{:}35{:}36{.}980 \dashrightarrow 00{:}35{:}39{.}530$ you will cover histone modification

 $00{:}35{:}39{.}530 \dashrightarrow 00{:}35{:}43{.}321$ in T cells and also you recover

NOTE Confidence: 0.73993483

00:35:43.321 --> 00:35:45.609 the T cell functionality.

NOTE Confidence: 0.73993483

00:35:45.610 - 00:35:48.166 So we did it not only in mouse model,

NOTE Confidence: 0.73993483

 $00:35:48.170 \longrightarrow 00:35:50.270$ we did in patient with cancer.

NOTE Confidence: 0.73993483

 $00:35:50.270 \dashrightarrow 00:35:53.210$ So we supplemented methionine to the patient.

NOTE Confidence: 0.73993483

 $00:35:53.210 \longrightarrow 00:35:54.890$ Then we see the T cells.

NOTE Confidence: 0.73993483

 $00:35:54.890 \longrightarrow 00:35:58.446$ It turns out if you do so.

NOTE Confidence: 0.73993483

 $00:35:58.450 \longrightarrow 00:36:01.535$ My third supplementation can we

NOTE Confidence: 0.73993483

00:36:01.535 --> 00:36:04.030 cover each 3K79 demethylation

NOTE Confidence: 0.73993483

 $00{:}36{:}04.030 \dashrightarrow 00{:}36{:}07.810$ we cover even Step 5 expression.

NOTE Confidence: 0.73993483

 $00{:}36{:}07{.}810 \dashrightarrow 00{:}36{:}09{.}418$ We checked all the other stuff

NOTE Confidence: 0.73993483

 $00{:}36{:}09{.}418 \dashrightarrow 00{:}36{:}11{.}230$ because step five is most obvious.

NOTE Confidence: 0.73993483

 $00{:}36{:}11{.}230 \dashrightarrow 00{:}36{:}12{.}046$ And furthermore,

NOTE Confidence: 0.73993483

 $00{:}36{:}12.046 \dashrightarrow 00{:}36{:}15.310$ if you look at the second expression such

 $00:36:15.389 \longrightarrow 00:36:17.950$ as IO2, so before therapy, after,

NOTE Confidence: 0.746410053636364

 $00{:}36{:}17.950 \dashrightarrow 00{:}36{:}21.219$ before, and after, you will see I2

NOTE Confidence: 0.746410053636364

 $00:36:21.219 \rightarrow 00:36:23.639$ is largely recovered in T cells.

NOTE Confidence: 0.746410053636364

00:36:23.640 --> 00:36:26.856 You know, somehow step five really

NOTE Confidence: 0.746410053636364

 $00{:}36{:}26.856 \dashrightarrow 00{:}36{:}29.000$ controls the expression of.

NOTE Confidence: 0.746410053636364

 $00{:}36{:}29{.}000 \dashrightarrow 00{:}36{:}31{.}709$ I of O2, then we first look

NOTE Confidence: 0.746410053636364

 $00:36:31.709 \longrightarrow 00:36:33.960$ at the possible mechanisms.

NOTE Confidence: 0.746410053636364

 $00:36:33.960 \longrightarrow 00:36:37.560$ So it turns out actually it's

NOTE Confidence: 0.746410053636364

00:36:37.560 --> 00:36:39.660 379 emanation target Step 5,

NOTE Confidence: 0.746410053636364

00:36:39.660 --> 00:36:40.776 particularly step 5B,

NOTE Confidence: 0.746410053636364

 $00{:}36{:}40.776 \dashrightarrow 00{:}36{:}44.040$ and the cheaper essay shows this is the case.

NOTE Confidence: 0.746410053636364

00:36:44.040 --> 00:36:46.080 In fact, if you cut yourself

NOTE Confidence: 0.746410053636364

 $00:36:46.080 \longrightarrow 00:36:47.440$ with supernatant and with

NOTE Confidence: 0.746410053636364

 $00{:}36{:}47{.}510 \dashrightarrow 00{:}36{:}49{.}340$ the maternal supplementation,

NOTE Confidence: 0.746410053636364

 $00{:}36{:}49{.}340 \dashrightarrow 00{:}36{:}52{.}148$ methionine supplementation can recover

NOTE Confidence: 0.746410053636364

 $00:36:52.148 \rightarrow 00:36:56.360$ the occupancy in the certified model.

- NOTE Confidence: 0.746410053636364
- 00:36:56.360 --> 00:36:59.498 So this just show you again,
- NOTE Confidence: 0.746410053636364
- $00:36:59.500 \longrightarrow 00:37:03.280$ not only we cover the T cell,
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}03.280 \dashrightarrow 00{:}37{:}04.795$ the the the,
- NOTE Confidence: 0.746410053636364
- $00:37:04.795 \dashrightarrow 00:37:08.900$ the the the cheaper and also show
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}08{.}900 \dashrightarrow 00{:}37{:}11{.}498$ H3K79 nations we covered and instead
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}11{.}498 \dashrightarrow 00{:}37{:}14{.}385$ of having is recovered and I2 is
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}14.385 \dashrightarrow 00{:}37{:}16.539$ recovered in both humans and mice.
- NOTE Confidence: 0.746410053636364
- $00:37:16.540 \longrightarrow 00:37:19.516$ And finally we want to understand.
- NOTE Confidence: 0.746410053636364
- $00:37:19.520 \longrightarrow 00:37:22.080$ If methionine is there,
- NOTE Confidence: 0.746410053636364
- $00:37:22.080 \rightarrow 00:37:26.950$ why the T cells cannot get better?
- NOTE Confidence: 0.746410053636364
- $00:37:26.950 \longrightarrow 00:37:29.104$ So maybe the tumor cells all
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}29{.}104 \dashrightarrow 00{:}37{:}31{.}234$ compete T cells for methionine
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}31{.}234$ --> $00{:}37{:}33{.}690$ in the tumor microenvironment.
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}33.690 \dashrightarrow 00{:}37{:}37.717$ We turned our attention to methionine
- NOTE Confidence: 0.746410053636364
- $00{:}37{:}37{.}717 \dashrightarrow 00{:}37{:}40{.}986$ transporters so we screened all of them.
- NOTE Confidence: 0.746410053636364

00:37:40.990 - 00:37:45.330 It turns out actually you will see

NOTE Confidence: 0.746410053636364

 $00:37:45.330 \dashrightarrow 00:37:48.144$ compare tumor cells and T cells in

NOTE Confidence: 0.746410053636364

 $00{:}37{:}48.144 \dashrightarrow 00{:}37{:}50.252$ the same environment and actually

NOTE Confidence: 0.746410053636364

 $00:37:50.252 \rightarrow 00:37:53.409$ the tumor cells express quite a lot

NOTE Confidence: 0.746410053636364

 $00:37:53.409 \longrightarrow 00:37:56.750$ of ACC for 3A2 is one of methionine.

NOTE Confidence: 0.746410053636364

 $00{:}37{:}56.750 \dashrightarrow 00{:}37{:}57.422$ This product,

NOTE Confidence: 0.746410053636364

 $00:37:57.422 \dashrightarrow 00:38:00.800$ so this is among A and this is protein.

NOTE Confidence: 0.746410053636364

 $00:38:00.800 \longrightarrow 00:38:03.299$ So this is T cells and many

NOTE Confidence: 0.746410053636364

 $00{:}38{:}03{.}299 \dashrightarrow 00{:}38{:}05{.}020$ other transporters are similar,

NOTE Confidence: 0.746410053636364

 $00:38:05.020 \rightarrow 00:38:07.198$ but they are quite some differences.

NOTE Confidence: 0.746410053636364

 $00{:}38{:}07{.}200 \dashrightarrow 00{:}38{:}09{.}712$ So we are we continue to work on

NOTE Confidence: 0.746410053636364

 $00:38:09.712 \longrightarrow 00:38:11.992$ this space to define the different

NOTE Confidence: 0.746410053636364

 $00{:}38{:}11{.}992 \dashrightarrow 00{:}38{:}14{.}849$ differences we are able to see and

NOTE Confidence: 0.746410053636364

 $00:38:14.849 \longrightarrow 00:38:16.919$ then to see the functionality.

NOTE Confidence: 0.746410053636364

 $00:38:16.920 \longrightarrow 00:38:18.848$ So this suggests maybe

NOTE Confidence: 0.716931126428571

00:38:20.860 --> 00:38:22.628 AC43A2 easy transporter highly

 $00:38:22.628 \rightarrow 00:38:25.280$ expressed in the tumor cells is

NOTE Confidence: 0.716931126428571

 $00:38:25.359 \longrightarrow 00:38:27.427$ functionally important if so.

NOTE Confidence: 0.716931126428571

 $00:38:27.430 \longrightarrow 00:38:32.216$ We make a knocking down SLC 43A2.

NOTE Confidence: 0.716931126428571

 $00{:}38{:}32{.}216 \dashrightarrow 00{:}38{:}34{.}598$ In the commercials then we start to

NOTE Confidence: 0.716931126428571

 $00:38:34.598 \dashrightarrow 00:38:36.110$ capture the human cells with cells.

NOTE Confidence: 0.716931126428571

 $00:38:36.110 \dashrightarrow 00:38:38.958$ OK, so you can see actually the T

NOTE Confidence: 0.716931126428571

 $00:38:38.958 \longrightarrow 00:38:41.826$ cells are becoming less able to

NOTE Confidence: 0.716931126428571

 $00:38:41.826 \dashrightarrow 00:38:44.406$ reach the functions are recovered.

NOTE Confidence: 0.716931126428571

 $00:38:44.410 \longrightarrow 00:38:48.513$ So indicating ACC for this 382 is important.

NOTE Confidence: 0.716931126428571

 $00:38:48.513 \rightarrow 00:38:51.168$ To further demonstrate this possibility,

NOTE Confidence: 0.716931126428571

00:38:51.170 --> 00:38:52.970 we did in DEVO studies,

NOTE Confidence: 0.716931126428571

00:38:52.970 --> 00:38:55.370 if you shut down PC police

NOTE Confidence: 0.716931126428571

 $00{:}38{:}55{.}370 \dashrightarrow 00{:}38{:}57{.}430$ 382 in the tumor cells.

NOTE Confidence: 0.716931126428571

 $00{:}38{:}57{.}430 \dashrightarrow 00{:}39{:}00{.}406$ USC actually the tumor is smaller

NOTE Confidence: 0.716931126428571

 $00{:}39{:}00{.}406 \dashrightarrow 00{:}39{:}03{.}080$ in the immune competence system.

 $00:39:03.080 \longrightarrow 00:39:04.809$ The key cells in terms of their

NOTE Confidence: 0.716931126428571

 $00{:}39{:}04.809 \dashrightarrow 00{:}39{:}06.640$ number and their function are better.

NOTE Confidence: 0.716931126428571

 $00:39:06.640 \longrightarrow 00:39:08.579$ This is not only in one model.

NOTE Confidence: 0.716931126428571

 $00:39:08.580 \dashrightarrow 00:39:11.276$ In several models we can see the case.

NOTE Confidence: 0.716931126428571

 $00:39:11.280 \dashrightarrow 00:39:15.106$ So what we have here is a summary we

NOTE Confidence: 0.716931126428571

 $00{:}39{:}15.106 \dashrightarrow 00{:}39{:}17.536$ see in the tumor microenvironment,

NOTE Confidence: 0.716931126428571

 $00:39:17.540 \longrightarrow 00:39:20.465$ tumor cells express high levels

NOTE Confidence: 0.716931126428571

 $00:39:20.465 \longrightarrow 00:39:21.635$ of transporter.

NOTE Confidence: 0.716931126428571

 $00:39:21.640 \longrightarrow 00:39:25.232$ For methionine it's ACC 4382

NOTE Confidence: 0.716931126428571

 $00:39:25.232 \rightarrow 00:39:27.436$ outcompete T cells 4.

NOTE Confidence: 0.716931126428571

 $00:39:27.440 \longrightarrow 00:39:30.448$ The only surprise when T cells do not

NOTE Confidence: 0.716931126428571

 $00:39:30.448 \dashrightarrow 00:39:33.366$ get methionine and the T cells have

NOTE Confidence: 0.716931126428571

 $00:39:33.366 \rightarrow 00:39:35.645$ insufficient sense Earth myself honor.

NOTE Confidence: 0.716931126428571

 $00:39:35.645 \rightarrow 00:39:38.554$ Therefore they cannot successfully

NOTE Confidence: 0.716931126428571

 $00{:}39{:}38{.}554 \dashrightarrow 00{:}39{:}41{.}743$ do the H3K790 mace ration and

NOTE Confidence: 0.716931126428571

 $00:39:41.743 \longrightarrow 00:39:43.947$ therefore regulate stats fab.

 $00:39:43.950 \rightarrow 00:39:47.094$ And as a consequence this affect the TCL

NOTE Confidence: 0.716931126428571

 $00{:}39{:}47.094 \dashrightarrow 00{:}39{:}49.309$ functionality and the T cell survival.

NOTE Confidence: 0.716931126428571

 $00{:}39{:}49{.}310 \dashrightarrow 00{:}39{:}51{.}254$ So what we suggest here may be

NOTE Confidence: 0.716931126428571

 $00:39:51.254 \rightarrow 00:39:54.406$ you know we can either we do

NOTE Confidence: 0.716931126428571

 $00:39:54.406 \rightarrow 00:39:56.076$ mathematics supplementation, we do,

NOTE Confidence: 0.716931126428571

00:39:56.076 - 00:39:57.534 we cover the T cell immunity.

NOTE Confidence: 0.716931126428571

 $00:39:57.540 \rightarrow 00:39:59.665$ Maybe we can particularly target

NOTE Confidence: 0.716931126428571

 $00:39:59.665 \longrightarrow 00:40:03.225$ the tumor as you C for 3/8 to

NOTE Confidence: 0.716931126428571

 $00{:}40{:}03.225 \dashrightarrow 00{:}40{:}05.465$ the rescue T cell functionality.

NOTE Confidence: 0.716931126428571

 $00{:}40{:}05{.}470 \dashrightarrow 00{:}40{:}09{.}294$ So now it comes back to the question

NOTE Confidence: 0.716931126428571

 $00:40:09.294 \rightarrow 00:40:12.660$ we asked. So can we stop themselves?

NOTE Confidence: 0.716931126428571

 $00:40:12.660 \longrightarrow 00:40:14.658$ Can we stop to myself, to this?

NOTE Confidence: 0.716931126428571

 $00{:}40{:}14.658 \dashrightarrow 00{:}40{:}15.720$ Yes, we can.

NOTE Confidence: 0.716931126428571

 $00{:}40{:}15.720 \dashrightarrow 00{:}40{:}18.438$ You must ask really needed method.

NOTE Confidence: 0.716931126428571

 $00{:}40{:}18{.}440 \dashrightarrow 00{:}40{:}19{.}535$ Earth one example.

00:40:19.535 --> 00:40:22.615 But the poverty is if you stop yourself

NOTE Confidence: 0.716931126428571

 $00:40:22.615 \rightarrow 00:40:26.289$ to death, you also stop T cells to death.

NOTE Confidence: 0.716931126428571

 $00:40:26.290 \rightarrow 00:40:29.602$ Under the AIDS and who kills the tumor cells?

NOTE Confidence: 0.716931126428571

 $00{:}40{:}29.610 \dashrightarrow 00{:}40{:}30.750$ The T cells?

NOTE Confidence: 0.716931126428571

 $00{:}40{:}30.750 \dashrightarrow 00{:}40{:}31.510$ Tumor cells.

NOTE Confidence: 0.716931126428571

 $00{:}40{:}31{.}510 \dashrightarrow 00{:}40{:}33{.}010$ So that's why what we say.

NOTE Confidence: 0.716931126428571

 $00{:}40{:}33.010 \dashrightarrow 00{:}40{:}35.726$ If you want to stop human cells

NOTE Confidence: 0.716931126428571

 $00:40:35.726 \rightarrow 00:40:38.189$ to test using this approach,

NOTE Confidence: 0.716931126428571

00:40:38.190 --> 00:40:40.764 probably you kill 1000 yourself defeat

NOTE Confidence: 0.716931126428571

00:40:40.764 --> 00:40:44.229 800 and I would put the opposite way,

NOTE Confidence: 0.716931126428571

00:40:44.230 --> 00:40:49.730 you kill 800 yourself defeat defeat 101,000.

NOTE Confidence: 0.716931126428571

 $00:40:49.730 \longrightarrow 00:40:53.330$ So that's why we need to be really

NOTE Confidence: 0.716931126428571

 $00{:}40{:}53.330 \dashrightarrow 00{:}40{:}56.257$ smart to consider not only just.

NOTE Confidence: 0.716931126428571

 $00:40:56.260 \longrightarrow 00:40:57.736$ To, to the tumors,

NOTE Confidence: 0.716931126428571

 $00{:}40{:}57.736 \dashrightarrow 00{:}41{:}00.619$ but we have also considered the T cells.

NOTE Confidence: 0.716931126428571

 $00{:}41{:}00.620 \dashrightarrow 00{:}41{:}02.832$ So now we ask the question again

 $00{:}41{:}02{.}832 \dashrightarrow 00{:}41{:}05{.}398$ as I put it at the beginning.

NOTE Confidence: 0.716931126428571

 $00{:}41{:}05{.}400 \dashrightarrow 00{:}41{:}08{.}568$ So what is next in terms of telling what

NOTE Confidence: 0.716931126428571

 $00:41:08.568 \rightarrow 00:41:12.125$ is the next generation of cancer therapy?

NOTE Confidence: 0.716931126428571

00:41:12.130 --> 00:41:14.686 So in my view,

NOTE Confidence: 0.716931126428571

00:41:14.686 - 00:41:18.520 immune therapy we means the basis.

NOTE Confidence: 0.716931126428571

 $00:41:18.520 \rightarrow 00:41:20.065$ Why? Two reasons.

NOTE Confidence: 0.716931126428571

00:41:20.065 --> 00:41:22.640 Because the military has been

NOTE Confidence: 0.716931126428571

 $00:41:22.640 \rightarrow 00:41:25.358$ successful to cure some patients.

NOTE Confidence: 0.716931126428571

 $00:41:25.360 \longrightarrow 00:41:27.488$ We already know this,

NOTE Confidence: 0.716931126428571

 $00:41:27.488 \rightarrow 00:41:29.616$ indicating the powerful reason.

NOTE Confidence: 0.716931126428571

 $00:41:29.620 \longrightarrow 00:41:31.985$ The whole powerful is immune

NOTE Confidence: 0.716931126428571

 $00:41:31.985 \longrightarrow 00:41:33.877$ system could be second.

NOTE Confidence: 0.716931126428571

00:41:33.880 --> 00:41:37.366 T cells. Can kill human cells.

NOTE Confidence: 0.716931126428571

00:41:37.370 --> 00:41:38.794 It's not a surprise.

NOTE Confidence: 0.716931126428571

 $00{:}41{:}38{.}794 \dashrightarrow 00{:}41{:}41{.}633$ And the further T cells remember to kill

 $00:41:41.633 \rightarrow 00:41:44.570$ tumor cells and then nobody else can do that.

NOTE Confidence: 0.716931126428571

00:41:44.570 --> 00:41:47.055 So that's why I feel the next

NOTE Confidence: 0.716931126428571

00:41:47.055 --> 00:41:48.770 generation of cancer therapy,

NOTE Confidence: 0.716931126428571

 $00:41:48.770 \rightarrow 00:41:52.010$ immune therapy, is the basis.

NOTE Confidence: 0.716931126428571

00:41:52.010 --> 00:41:53.994 So I stop here.

NOTE Confidence: 0.716931126428571

 $00{:}41{:}53{.}994 \dashrightarrow 00{:}41{:}56{.}970$ I appreciate the contribution from several

NOTE Confidence: 0.716931126428571

 $00{:}41{:}57.062 \dashrightarrow 00{:}42{:}00.226$ very tentative federal as I did here.

NOTE Confidence: 0.716931126428571

 $00:42:00.230 \longrightarrow 00:42:01.530$ Some of them are faculty,

NOTE Confidence: 0.868589628571429

 $00:42:01.530 \longrightarrow 00:42:05.107$ some of them moved to different institutions.

NOTE Confidence: 0.868589628571429

00:42:05.110 --> 00:42:07.570 And of course I didn't particularly

NOTE Confidence: 0.868589628571429

 $00{:}42{:}07{.}570 \dashrightarrow 00{:}42{:}10{.}928$ talk about the PD1 video one study and

NOTE Confidence: 0.868589628571429

 $00{:}42{:}10{.}928 \dashrightarrow 00{:}42{:}13{.}388$ some others it was a collaboration

NOTE Confidence: 0.868589628571429

 $00:42:13.466 \longrightarrow 00:42:15.786$ with and I have quite a few,

NOTE Confidence: 0.868589628571429

 $00{:}42{:}15.790 \dashrightarrow 00{:}42{:}19.630$ some few other collaborators

NOTE Confidence: 0.868589628571429

 $00{:}42{:}19.630 \dashrightarrow 00{:}42{:}21.940$ in the United States and.

NOTE Confidence: 0.868589628571429

 $00:42:21.940 \longrightarrow 00:42:23.112$ And in other places,

- NOTE Confidence: 0.868589628571429
- $00{:}42{:}23.112 \dashrightarrow 00{:}42{:}25.300$ thank you for your attention and looking
- NOTE Confidence: 0.868589628571429
- $00{:}42{:}25{.}300 \dashrightarrow 00{:}42{:}27{.}526$ forward to your comments and questions.
- NOTE Confidence: 0.5026026
- $00:42:35.320 \longrightarrow 00:42:35.710$ Question.
- NOTE Confidence: 0.79950273111111
- $00:42:38.490 \longrightarrow 00:42:39.958$ Thank you over here.
- NOTE Confidence: 0.79950273111111
- $00:42:39.958 \longrightarrow 00:42:41.793$ So thank you very much.
- NOTE Confidence: 0.79950273111111
- $00:42:41.800 \longrightarrow 00:42:43.380$ Much appreciated.
- NOTE Confidence: 0.79950273111111
- $00:42:43.380 \rightarrow 00:42:44.854$ Presentation understood correctly,
- NOTE Confidence: 0.79950273111111
- $00:42:44.854 \longrightarrow 00:42:46.885$ you showed that the rock, correct?
- NOTE Confidence: 0.799502731111111
- $00{:}42{:}46.885 \dashrightarrow 00{:}42{:}51.210$ Doc acid was a mediator of T cell.
- NOTE Confidence: 0.75131066
- 00:42:56.560 --> 00:42:58.885 You are. Has anyone looked
- NOTE Confidence: 0.75131066
- $00:42:58.885 \longrightarrow 00:43:01.262$ inside the cell, two per cell,
- NOTE Confidence: 0.75131066
- $00:43:01.262 \longrightarrow 00:43:04.060$ that's undergoing the fructose this
- NOTE Confidence: 0.75131066
- $00{:}43{:}04{.}060 \dashrightarrow 00{:}43{:}06{.}377$ kind of objectively by the elements for
- NOTE Confidence: 0.75131066
- $00{:}43{:}06{.}377 \dashrightarrow 00{:}43{:}08{.}700$ others to see what's elevated threat?
- NOTE Confidence: 0.8264526725
- $00:43:11.100 \longrightarrow 00:43:13.555$ It is surveyed, but there
- NOTE Confidence: 0.8264526725

 $00:43:13.555 \longrightarrow 00:43:15.520$ are thousands of. Liberal.

NOTE Confidence: 0.730154073636363

 $00{:}43{:}17{.}020 \dashrightarrow 00{:}43{:}19{.}212$ Right. So in response,

NOTE Confidence: 0.730154073636363

 $00:43:19.212 \longrightarrow 00:43:23.290$ So what we have done actually we

NOTE Confidence: 0.730154073636363

 $00:43:23.290 \rightarrow 00:43:27.400$ detected electronic acids in the tumor

NOTE Confidence: 0.730154073636363

 $00{:}43{:}27{.}400 \dashrightarrow 00{:}43{:}30{.}930$ microenvironment in the tumor floats.

NOTE Confidence: 0.730154073636363

 $00:43:30.930 \longrightarrow 00:43:33.510$ So the question is very tricky.

NOTE Confidence: 0.730154073636363

 $00{:}43{:}33{.}510 \dashrightarrow 00{:}43{:}35{.}620$ You have to have sufficient

NOTE Confidence: 0.730154073636363

00:43:35.620 --> 00:43:37.308 levels of electronic acids,

NOTE Confidence: 0.730154073636363

 $00:43:37.310 \rightarrow 00:43:39.865$ but if you have very high concentration

NOTE Confidence: 0.730154073636363

 $00:43:39.865 \rightarrow 00:43:41.352$ you kill everything. Right.

NOTE Confidence: 0.730154073636363

 $00:43:41.352 \rightarrow 00:43:44.488$ So, so, so The thing is you have

NOTE Confidence: 0.730154073636363

 $00:43:44.488 \rightarrow 00:43:47.877$ to have two things simultaneously,

NOTE Confidence: 0.730154073636363

 $00{:}43{:}47{.}880 \dashrightarrow 00{:}43{:}51{.}884$ one is interfering, another is doing acid.

NOTE Confidence: 0.730154073636363

 $00:43:51.884 \rightarrow 00:43:54.940$ So that's a play you have to go.

NOTE Confidence: 0.730154073636363

 $00:43:54.940 \longrightarrow 00:43:57.844$ Yeah, we did not systemically to

NOTE Confidence: 0.730154073636363

 $00:43:57.844 \longrightarrow 00:44:00.833$ detect all the metabolites in the

- NOTE Confidence: 0.730154073636363
- 00:44:00.833 --> 00:44:03.238 tumor microenvironment by our own.
- NOTE Confidence: 0.730154073636363
- $00:44:03.240 \longrightarrow 00:44:05.417$ There are some report in that space.
- NOTE Confidence: 0.730154073636363
- $00{:}44{:}05{.}420 \dashrightarrow 00{:}44{:}07{.}268$ There are technical challenges
- NOTE Confidence: 0.730154073636363
- $00:44:07.268 \longrightarrow 00:44:09.116$ in that situation.
- NOTE Confidence: 0.730154073636363
- $00:44:09.120 \rightarrow 00:44:11.055$ I guess the question is what do you ask?
- NOTE Confidence: 0.730154073636363
- 00:44:11.060 00:44:13.382 It's a it's very annoying to to do it.
- NOTE Confidence: 0.730154073636363
- $00:44:13.390 \longrightarrow 00:44:14.726$ For example,
- NOTE Confidence: 0.730154073636363
- $00:44:14.726 \rightarrow 00:44:18.066$ we really dynamically monitor the
- NOTE Confidence: 0.730154073636363
- $00{:}44{:}18.066 \dashrightarrow 00{:}44{:}21.337$ metabolic environment when the sales
- NOTE Confidence: 0.730154073636363
- $00:44:21.337 \rightarrow 00:44:24.853$ either become able to or philanthropic
- NOTE Confidence: 0.730154073636363
- $00:44:24.853 \longrightarrow 00:44:27.489$ whether there's any difference.
- NOTE Confidence: 0.730154073636363
- $00:44:27.490 \longrightarrow 00:44:31.018$ In this case, we need to have props.
- NOTE Confidence: 0.730154073636363
- $00:44:31.018 \longrightarrow 00:44:32.650$ It's a real property.
- NOTE Confidence: 0.730154073636363
- $00:44:32.650 \longrightarrow 00:44:34.110$ We follow these people.
- NOTE Confidence: 0.730154073636363
- $00{:}44{:}34{.}110 \dashrightarrow 00{:}44{:}36{.}960$ Maybe some of you are smart and and
- NOTE Confidence: 0.730154073636363

 $00:44:36.960 \longrightarrow 00:44:39.304$ have tools we can we can do that.

NOTE Confidence: 0.730154073636363

 $00:44:39.310 \longrightarrow 00:44:41.277$ So one day it could be done.

NOTE Confidence: 0.730154073636363

 $00:44:41.280 \longrightarrow 00:44:44.234$ You know, just a trace where it

NOTE Confidence: 0.730154073636363

 $00:44:44.234 \longrightarrow 00:44:47.520$ goes and how high the levels are,

NOTE Confidence: 0.730154073636363

 $00{:}44{:}47{.}520 \dashrightarrow 00{:}44{:}49{.}020$ yeah.

NOTE Confidence: 0.730154073636363

 $00{:}44{:}49{.}020 \dashrightarrow 00{:}44{:}49{.}670$ Thanks.

NOTE Confidence: 0.7645908525

00:44:54.480 - 00:44:56.790 So I wonder if the opposite guys.

NOTE Confidence: 0.34078765

 $00:45:04.120 \longrightarrow 00:45:04.670$ Struck.

NOTE Confidence: 0.891422631

 $00:45:15.750 \longrightarrow 00:45:17.700$ Great question actually.

NOTE Confidence: 0.891422631

 $00:45:17.700 \rightarrow 00:45:22.250$ So as far as my understanding is,

NOTE Confidence: 0.891422631

 $00:45:22.250 \longrightarrow 00:45:26.514$ you know when we look at the Philippoussis.

NOTE Confidence: 0.891422631

 $00:45:26.520 \longrightarrow 00:45:28.602$ It's all the different ways how

NOTE Confidence: 0.891422631

 $00:45:28.602 \dashrightarrow 00:45:31.299$ the cells die or four for example.

NOTE Confidence: 0.891422631

00:45:31.300 --> 00:45:33.694 You know you you have some

NOTE Confidence: 0.891422631

 $00{:}45{:}33.694 \dashrightarrow 00{:}45{:}35.786$ executive genes which have been

NOTE Confidence: 0.891422631

 $00:45:35.786 \rightarrow 00:45:38.414$ well defined in enable those poses,

- NOTE Confidence: 0.891422631
- $00:45:38.414 \rightarrow 00:45:41.738$ right but for fear of nosis,
- NOTE Confidence: 0.891422631
- $00{:}45{:}41.740 \dashrightarrow 00{:}45{:}44.326$ it's really about the membrane and
- NOTE Confidence: 0.891422631
- $00:45:44.326 \rightarrow 00:45:46.605$ damage so mediated by oxygenic
- NOTE Confidence: 0.891422631
- $00:45:46.605 \rightarrow 00:45:48.980$ species that's what we know.
- NOTE Confidence: 0.891422631
- $00:45:48.980 \rightarrow 00:45:53.076$ So therefore so very direct question when you
- NOTE Confidence: 0.891422631
- $00{:}45{:}53.076 \dashrightarrow 00{:}45{:}56.626$ asked whether the factors what we studied.
- NOTE Confidence: 0.891422631
- $00:45:56.630 \longrightarrow 00:45:59.326$ Or whoever studied have
- NOTE Confidence: 0.891422631
- $00:45:59.326 \rightarrow 00:46:01.132$ directly effect on the membrane,
- NOTE Confidence: 0.891422631
- $00{:}46{:}01{.}132 \dashrightarrow 00{:}46{:}03{.}690$ let's say maybe the nails and the structures,
- NOTE Confidence: 0.891422631
- $00:46:03.690 \longrightarrow 00:46:04.599$ those things, right?
- NOTE Confidence: 0.891422631
- $00:46:04.599 \rightarrow 00:46:06.114$ We didn't go that far.
- NOTE Confidence: 0.891422631
- $00{:}46{:}06{.}120 \dashrightarrow 00{:}46{:}09{.}297$ I even don't have the expertise to do that.
- NOTE Confidence: 0.891422631
- $00{:}46{:}09{.}300 \dashrightarrow 00{:}46{:}12{.}800$ So, so I think it's very nice way to go.
- NOTE Confidence: 0.891422631
- $00:46:12.800 \longrightarrow 00:46:15.110$ So one way to to do it is we have
- NOTE Confidence: 0.891422631
- $00:46:15.183 \longrightarrow 00:46:17.633$ done a little bit means we detect
- NOTE Confidence: 0.891422631

00:46:17.633 --> 00:46:19.808 a tumor membrane if it oxidizes,

NOTE Confidence: 0.891422631

 $00{:}46{:}19.810 \dashrightarrow 00{:}46{:}21.376$ inhibit species, that's what we know.

NOTE Confidence: 0.891422631

 $00{:}46{:}21.380 \dashrightarrow 00{:}46{:}23.872$ But we don't look at the structure

NOTE Confidence: 0.891422631

 $00:46:23.872 \rightarrow 00:46:26.508$ to monitor how the sector changes

NOTE Confidence: 0.891422631

 $00{:}46{:}26{.}508 \dashrightarrow 00{:}46{:}27{.}999$ could be unacceptable.

NOTE Confidence: 0.891422631

 $00{:}46{:}28.000 \dashrightarrow 00{:}46{:}29.956$ Yeah, but we didn't know that.

NOTE Confidence: 0.891422631

 $00:46:29.960 \longrightarrow 00:46:31.560$ We even don't know how to do that.

NOTE Confidence: 0.891422631

 $00:46:31.560 \longrightarrow 00:46:34.070$ So maybe.

NOTE Confidence: 0.891422631

00:46:34.070 - 00:46:36.275 Which way we go that maybe again,

NOTE Confidence: 0.891422631

 $00:46:36.280 \longrightarrow 00:46:37.880$ if we have some proxy,

NOTE Confidence: 0.891422631

 $00:46:37.880 \longrightarrow 00:46:39.680$ it could be useful, right.

NOTE Confidence: 0.891422631

00:46:39.680 --> 00:46:40.520 So maybe you, you,

NOTE Confidence: 0.891422631

 $00:46:40.520 \rightarrow 00:46:42.100$ you have some ideas in that space.

NOTE Confidence: 0.891422631

 $00:46:42.100 \rightarrow 00:46:44.377$ We were chatting it on maybe this,

NOTE Confidence: 0.891422631

 $00{:}46{:}44{.}377 \dashrightarrow 00{:}46{:}46{.}456$ that that 's a good way to go

NOTE Confidence: 0.891422631

00:46:46.456 --> 00:46:48.391 because if people are still some

- NOTE Confidence: 0.891422631
- $00:46:48.391 \longrightarrow 00:46:50.695$ people feel or feel to see if

00:46:50.695 --> 00:46:52.675 you don't have a executive gene.

NOTE Confidence: 0.891422631

 $00:46:52.680 \longrightarrow 00:46:54.263$ So what are you talking about, right.

NOTE Confidence: 0.891422631

 $00:46:54.263 \rightarrow 00:46:57.007$ But The thing is the pathway is regulated

NOTE Confidence: 0.891422631

00:46:57.007 - 00:46:59.338 and the pathway can be inhibited,

NOTE Confidence: 0.891422631

 $00{:}46{:}59{.}340 \dashrightarrow 00{:}47{:}01{.}419$ can be activated, it can be regulated.

NOTE Confidence: 0.891422631

 $00:47:01.420 \longrightarrow 00:47:03.255$ So that's very difficult mechanism, right?

NOTE Confidence: 0.891422631

 $00{:}47{:}03.255 \dashrightarrow 00{:}47{:}04.080$ So therefore it's.

NOTE Confidence: 0.891422631

 $00{:}47{:}04.080 \dashrightarrow 00{:}47{:}05.180$ The program still this.

NOTE Confidence: 0.8401680775

 $00:47:21.780 \longrightarrow 00:47:23.100$ Yes, yes, yes.

NOTE Confidence: 0.8401680775

 $00:47:23.100 \longrightarrow 00:47:25.300$ That's also a good point.

NOTE Confidence: 0.8401680775

 $00{:}47{:}25{.}300 \dashrightarrow 00{:}47{:}27{.}554$ So you know, when you design experiments,

NOTE Confidence: 0.8401680775

 $00:47:27.560 \longrightarrow 00:47:28.560$ you want to see something,

NOTE Confidence: 0.8401680775

00:47:28.560 --> 00:47:30.370 you look at something, right?

NOTE Confidence: 0.8401680775

 $00{:}47{:}30{.}370 \dashrightarrow 00{:}47{:}33{.}205$ So therefore we didn't look

- $00:47:33.205 \longrightarrow 00:47:35.473$ at some other cells.
- NOTE Confidence: 0.8401680775
- 00:47:35.480 --> 00:47:38.350 So my. So right now we know
- NOTE Confidence: 0.8401680775
- $00:47:38.350 \longrightarrow 00:47:40.210$ different types of cells.
- NOTE Confidence: 0.8401680775
- $00{:}47{:}40{.}210 \dashrightarrow 00{:}47{:}42{.}395$ We have given the sensitivities
- NOTE Confidence: 0.8401680775
- 00:47:42.395 --> 00:47:43.706 to different stimuli,
- NOTE Confidence: 0.8401680775
- 00:47:43.710 --> 00:47:45.576 stimuli, fibrosis stimuli.
- NOTE Confidence: 0.8401680775
- $00:47:45.576 \longrightarrow 00:47:48.064$ They may have different
- NOTE Confidence: 0.8401680775
- $00{:}47{:}48.064 \dashrightarrow 00{:}47{:}49.930$ mechanisms to control.
- NOTE Confidence: 0.8401680775
- $00{:}47{:}49{.}930 \dashrightarrow 00{:}47{:}52{.}918$ So that's typically something we are
- NOTE Confidence: 0.8401680775
- $00:47:52.918 \rightarrow 00:47:55.063$ working on including for example,
- NOTE Confidence: 0.8401680775
- $00:47:55.063 \rightarrow 00:47:56.206$ how about megabytes?
- NOTE Confidence: 0.8401680775
- $00:47:56.210 \longrightarrow 00:47:58.030$ How about T cells, right?
- NOTE Confidence: 0.8401680775
- $00{:}47{:}58.030 \dashrightarrow 00{:}48{:}01.478$ So I guess this is not an mechanism
- NOTE Confidence: 0.8401680775
- $00:48:01.478 \longrightarrow 00:48:03.450$ exclusively for tumor cells.
- NOTE Confidence: 0.8401680775
- $00:48:03.450 \longrightarrow 00:48:04.810$ There is no such thing.
- NOTE Confidence: 0.8401680775
- $00:48:04.810 \longrightarrow 00:48:07.510$ So the mechanism could be functional

- NOTE Confidence: 0.8401680775
- $00:48:07.510 \longrightarrow 00:48:09.890$ for other types of cells.
- NOTE Confidence: 0.8401680775
- $00:48:09.890 \longrightarrow 00:48:11.243$ The question is?
- NOTE Confidence: 0.8401680775
- $00:48:11.243 \rightarrow 00:48:13.949$ When and how and which one?
- NOTE Confidence: 0.8401680775
- $00:48:13.950 \longrightarrow 00:48:14.685$ We are working with this
- NOTE Confidence: 0.8401680775
- $00:48:14.685 \longrightarrow 00:48:15.740$ but you can go on details.
- NOTE Confidence: 0.7144543
- $00:48:19.730 \longrightarrow 00:48:21.612$ This idea the only competition
- NOTE Confidence: 0.7144543
- $00:48:21.612 \longrightarrow 00:48:22.866$ out of competition
- NOTE Confidence: 0.73984185
- $00:48:22.870 \longrightarrow 00:48:23.659$ of tumor cells.
- NOTE Confidence: 0.8403232
- $00{:}48{:}26{.}290 \dashrightarrow 00{:}48{:}28{.}942$ Do you think it's the growth across
- NOTE Confidence: 0.8403232
- $00{:}48{:}28{.}942 \dashrightarrow 00{:}48{:}31{.}056$ towards you know we think about like
- NOTE Confidence: 0.8403232
- 00:48:31.060 00:48:33.128 lung which is sensitive to prepare
- NOTE Confidence: 0.8403232
- 00:48:33.128 --> 00:48:35.256 incorrectly that is not or for example
- NOTE Confidence: 0.8403232
- $00:48:35.256 \longrightarrow 00:48:37.268$ the location of the tool you have
- NOTE Confidence: 0.8403232
- 00:48:37.268 --> 00:48:39.112 the two reason delivered reason the
- NOTE Confidence: 0.8403232
- 00:48:39.112 --> 00:48:41.440 London or different access to metabolic
- NOTE Confidence: 0.8403232

 $00:48:41.440 \rightarrow 00:48:44.620$ substrate have you what are your thoughts

NOTE Confidence: 0.6212257266666667

 $00:48:44.630 \longrightarrow 00:48:46.256$ about that? Yes it's it's OK.

NOTE Confidence: 0.6212257266666667

 $00:48:46.260 \longrightarrow 00:48:47.388$ It's a great question.

NOTE Confidence: 0.6212257266666667

 $00:48:47.388 \longrightarrow 00:48:48.832$ It's hard to address. OK.

NOTE Confidence: 0.6212257266666667

 $00{:}48{:}48{.}832 \dashrightarrow 00{:}48{:}50{.}704$ So what we started to look

NOTE Confidence: 0.6212257266666667

 $00{:}48{:}50{.}704 \dashrightarrow 00{:}48{:}53{.}138$ at since even in the same we

NOTE Confidence: 0.6212257266666667

 $00:48:53.138 \rightarrow 00:48:54.558$ have recently paper just.

NOTE Confidence: 0.6212257266666667

00:48:54.560 --> 00:48:57.014 Eventually you even in the same

NOTE Confidence: 0.6212257266666667

 $00:48:57.014 \rightarrow 00:48:59.724$ human parent such as liver right?

NOTE Confidence: 0.6212257266666667

 $00:48:59.724 \rightarrow 00:49:03.483$ We reach locate the neighbor metastasis HCC.

NOTE Confidence: 0.6212257266666667

 $00{:}49{:}03{.}490 \dashrightarrow 00{:}49{:}06{.}210$ So in the liver microenvironment

NOTE Confidence: 0.6212257266666667

 $00:49:06.210 \longrightarrow 00:49:08.930$ you have HC and metastasis.

NOTE Confidence: 0.6212257266666667

 $00:49:08.930 \longrightarrow 00:49:12.129$ Then we look at even the same

NOTE Confidence: 0.6212257266666667

 $00:49:12.129 \longrightarrow 00:49:13.662$ macrophage subsets they are

NOTE Confidence: 0.6212257266666667

 $00{:}49{:}13.662 \dashrightarrow 00{:}49{:}14.886$ metabolic patterns are different.

NOTE Confidence: 0.85659679

00:49:17.160 - 00:49:19.632 So if they are, metabolic patterns
- NOTE Confidence: 0.85659679
- $00:49:19.632 \longrightarrow 00:49:21.556$ are different, therefore their
- NOTE Confidence: 0.85659679
- $00{:}49{:}21.556 \dashrightarrow 00{:}49{:}23.748$ metabolic needs are different.
- NOTE Confidence: 0.85659679
- $00:49:23.750 \longrightarrow 00:49:26.565$ How does it happen? Right.
- NOTE Confidence: 0.85659679
- $00:49:26.565 \rightarrow 00:49:29.290$ We have nuclear. You know,
- NOTE Confidence: 0.85659679
- $00:49:29.290 \rightarrow 00:49:31.186$ but we are still working on those things.
- NOTE Confidence: 0.85659679
- $00{:}49{:}31{.}190 \dashrightarrow 00{:}49{:}35{.}552$ So we we work more on the the way how the
- NOTE Confidence: 0.85659679
- $00:49:35.552 \rightarrow 00:49:39.688$ sales die because we believe this is this,
- NOTE Confidence: 0.85659679
- $00{:}49{:}39{.}690 \dashrightarrow 00{:}49{:}41{.}750$ these matters are not.
- NOTE Confidence: 0.85659679
- $00:49:41.750 \longrightarrow 00:49:45.620$ So so the thought is.
- NOTE Confidence: 0.85659679
- $00:49:45.620 \longrightarrow 00:49:47.813$ Different cells have
- NOTE Confidence: 0.85659679
- 00:49:47.813 --> 00:49:50.006 different metabolic pattern.
- NOTE Confidence: 0.85659679
- $00{:}49{:}50.010 \dashrightarrow 00{:}49{:}52.668$ The same cells in different metabolic
- NOTE Confidence: 0.85659679
- $00:49:52.668 \rightarrow 00:49:55.653$ environment may have to adapt this
- NOTE Confidence: 0.85659679
- $00:49:55.653 \rightarrow 00:49:58.264$ particular environmental survive #1, right?
- NOTE Confidence: 0.85659679
- $00:49:58.264 \rightarrow 00:50:00.268$ So then whether they can expand.
- NOTE Confidence: 0.85659679

 $00:50:00.270 \rightarrow 00:50:04.726$ So I guess a part from the genetic

NOTE Confidence: 0.85659679

00:50:04.726 --> 00:50:06.526 mutations which people have started

NOTE Confidence: 0.85659679

 $00{:}50{:}06{.}526$ --> $00{:}50{:}09{.}200$ or not in the space of cancer biology

NOTE Confidence: 0.85659679

 $00{:}50{:}09{.}200 \dashrightarrow 00{:}50{:}11.468$ and genetics in the recent days,

NOTE Confidence: 0.85659679

 $00{:}50{:}11.470 \dashrightarrow 00{:}50{:}13.305$ people really moved to the

NOTE Confidence: 0.85659679

 $00{:}50{:}13.305 \dashrightarrow 00{:}50{:}15.140$ field of metabolism because the

NOTE Confidence: 0.85659679

 $00{:}50{:}15{.}205 \dashrightarrow 00{:}50{:}17{.}229$ metabolism is somehow universal.

NOTE Confidence: 0.85659679

 $00:50:17.230 \longrightarrow 00:50:19.280$ It must be regulated in

NOTE Confidence: 0.85659679

 $00:50:19.280 \longrightarrow 00:50:21.330$ one way or versus another.

NOTE Confidence: 0.85659679

 $00{:}50{:}21{.}330 \dashrightarrow 00{:}50{:}23{.}498$ So that's that's why I we we have

NOTE Confidence: 0.85659679

 $00:50:23.498 \longrightarrow 00:50:24.864$ high interest in this, right.

NOTE Confidence: 0.85659679

 $00:50:24.864 \rightarrow 00:50:26.628$ But the answer is very big.

NOTE Confidence: 0.85659679

00:50:26.630 --> 00:50:28.367 I know I didn't really give you an answer,

NOTE Confidence: 0.85659679

 $00:50:28.370 \longrightarrow 00:50:29.258$ just what we have.

NOTE Confidence: 0.17853642

00:50:33.240 --> 00:50:35.800 Specificity. Signing on.

NOTE Confidence: 0.887937378

 $00:50:38.210 \longrightarrow 00:50:39.420$ So why do you think?

- NOTE Confidence: 0.7884175266666667
- 00:50:42.910 --> 00:50:43.969 Yes, that's, uh,
- NOTE Confidence: 0.7884175266666667
- 00:50:43.969 --> 00:50:46.087 it's it's a great question actually.
- NOTE Confidence: 0.7884175266666667
- $00:50:46.090 \longrightarrow 00:50:49.950$ It's. So it turns out this is a, it's a,
- NOTE Confidence: 0.7884175266666667
- $00:50:49.950 \rightarrow 00:50:52.787$ it's a, it's a biochemical question.
- NOTE Confidence: 0.7884175266666667
- 00:50:52.787 --> 00:50:57.083 OK. So if you look at the constant,
- NOTE Confidence: 0.7884175266666667
- $00{:}50{:}57{.}090 \dashrightarrow 00{:}51{:}00{.}648$ it's the lowest among all the
- NOTE Confidence: 0.7884175266666667
- $00:51:00.648 \longrightarrow 00:51:02.427$ other isomorphic modifiers.
- NOTE Confidence: 0.788417526666667
- $00:51:02.430 \longrightarrow 00:51:04.908$ So that's why it's. So it's sensitive.
- NOTE Confidence: 0.7884175266666667
- 00:51:04.910 --> 00:51:08.068 It's. Yeah, yeah, yeah. Yeah.
- NOTE Confidence: 0.7884175266666667
- 00:51:08.068 --> 00:51:10.895 Yeah. So so this actually this.
- NOTE Confidence: 0.7884175266666667
- 00:51:10.895 00:51:12.475 This information is available.
- NOTE Confidence: 0.7884175266666667
- $00:51:12.480 \longrightarrow 00:51:13.780$ It's not from us,
- NOTE Confidence: 0.7884175266666667
- $00:51:13.780 \longrightarrow 00:51:16.512$ it's from when we figured out that it's
- NOTE Confidence: 0.7884175266666667
- $00{:}51{:}16{.}512 \dashrightarrow 00{:}51{:}19{.}336$ needed on and we asked the same question,
- NOTE Confidence: 0.7884175266666667
- $00:51:19.340 \longrightarrow 00:51:21.020$ ask to ourselves why we
- NOTE Confidence: 0.7884175266666667

 $00:51:21.020 \rightarrow 00:51:22.364$ see this is predominant,

NOTE Confidence: 0.7884175266666667

 $00{:}51{:}22.370 \dashrightarrow 00{:}51{:}23.945$ the others are not so dramatic and

NOTE Confidence: 0.7884175266666667

 $00{:}51{:}23.945 \dashrightarrow 00{:}51{:}25.539$ then we know it's publications.

NOTE Confidence: 0.7884175266666667

 $00:51:25.540 \longrightarrow 00:51:27.448$ It turns out that's the case.

NOTE Confidence: 0.7884175266666667

 $00:51:27.450 \longrightarrow 00:51:27.740$ Yes.

NOTE Confidence: 0.76073954875

00:51:31.160 --> 00:51:33.000 In any of your models you're looking at.

NOTE Confidence: 0.37309444

 $00:51:35.100 \rightarrow 00:51:37.450$ The cancer cells undergoing sister type.

NOTE Confidence: 0.642862722

 $00{:}51{:}40{.}770 \dashrightarrow 00{:}51{:}44{.}000$ Um, I working on this.

NOTE Confidence: 0.642862722

 $00{:}51{:}44.000 \dashrightarrow 00{:}51{:}46.060$ We are working on this.

NOTE Confidence: 0.642862722

00:51:46.060 - 00:51:47.790 We should though I'm

NOTE Confidence: 0.778108361428571

 $00:51:47.800 \rightarrow 00:51:49.249$ not, I'm not working on the persistent.

NOTE Confidence: 0.79161745

00:51:49.990 --> 00:51:52.286 So, so yes, it's a great question.

NOTE Confidence: 0.79161745

 $00{:}51{:}52{.}290 \dashrightarrow 00{:}51{:}55{.}587$ Actually we initially I was really puzzled.

NOTE Confidence: 0.79161745

 $00{:}51{:}55{.}590 \dashrightarrow 00{:}51{:}58{.}515$ Puzzled by what when you see I show you

NOTE Confidence: 0.79161745

 $00:51:58.515 \longrightarrow 00:52:01.081$ the picture actually when you treat

NOTE Confidence: 0.79161745

 $00:52:01.081 \rightarrow 00:52:05.989$ the mice with PDL one and the CDA 4.

NOTE Confidence: 0.79161745

 $00{:}52{:}05{.}990 \dashrightarrow 00{:}52{:}08{.}822$ And under this condition you treated

NOTE Confidence: 0.79161745

 $00:52:08.822 \longrightarrow 00:52:11.600$ mice with fair process inhibitor?

NOTE Confidence: 0.79161745

 $00:52:11.600 \rightarrow 00:52:14.778$ And as the therapeutic efficacy is gone.

NOTE Confidence: 0.79161745

00:52:14.780 --> 00:52:17.608 This puzzled me so because, I mean,

NOTE Confidence: 0.79161745

 $00{:}52{:}17.608 \dashrightarrow 00{:}52{:}19.470$ we we know this is able to see

NOTE Confidence: 0.79161745

 $00{:}52{:}19{.}470 \dashrightarrow 00{:}52{:}20{.}958$ the T cells kill tumor cells.

NOTE Confidence: 0.79161745

 $00:52:20.960 \rightarrow 00:52:22.616$ It's even though this is caspase,

NOTE Confidence: 0.79161745

 $00:52:22.620 \longrightarrow 00:52:24.540$ and it's very well established,

NOTE Confidence: 0.79161745

 $00{:}52{:}24{.}540 \dashrightarrow 00{:}52{:}26{.}100$ you cannot throw away all those

NOTE Confidence: 0.79161745

 $00:52:26.100 \rightarrow 00:52:28.160$ things what people have known, right?

NOTE Confidence: 0.79161745

 $00{:}52{:}28{.}160 \dashrightarrow 00{:}52{:}32{.}920$ So the only explanation is these across.

NOTE Confidence: 0.79161745

 $00{:}52{:}32{.}920 \dashrightarrow 00{:}52{:}34{.}719$ So who is first, who is second,

NOTE Confidence: 0.79161745

 $00{:}52{:}34{.}720 \dashrightarrow 00{:}52{:}36{.}835$ who is in the middle and who initiate what?

NOTE Confidence: 0.79161745

 $00{:}52{:}36{.}840 \dashrightarrow 00{:}52{:}39{.}290$ Who emphasis what? Those kind of things.

NOTE Confidence: 0.79161745

 $00:52:39.290 \longrightarrow 00:52:40.770$ So we worked very hard,

NOTE Confidence: 0.79161745

 $00:52:40.770 \longrightarrow 00:52:42.527$ but we have no group so far.

NOTE Confidence: 0.79161745

 $00{:}52{:}42{.}530 \dashrightarrow 00{:}52{:}44{.}434$ But we know there must be a gross.

NOTE Confidence: 0.69844595625

 $00{:}52{:}44.850 \dashrightarrow 00{:}52{:}47.266$ Yeah, I'm thinking in terms of like the

NOTE Confidence: 0.69844595625

00:52:47.270 --> 00:52:49.488 paper from the green script where, you know,

NOTE Confidence: 0.69844595625

 $00:52:49.490 \rightarrow 00:52:53.340$ they show that the many monitors slight

NOTE Confidence: 0.43766722

 $00:52:56.170 \longrightarrow 00:52:56.930$ differences.

NOTE Confidence: 0.715446754

00:52:59.000 --> 00:53:01.011 Yeah, that's a possibility. Uh, actually,

NOTE Confidence: 0.715446754

00:53:01.011 --> 00:53:03.717 I just had a discussion recently.

NOTE Confidence: 0.715446754

00:53:03.720 --> 00:53:06.264 I probably will discuss with him

NOTE Confidence: 0.715446754

 $00:53:06.264 \rightarrow 00:53:09.500$ again to see which way we can we

NOTE Confidence: 0.715446754

00:53:09.500 --> 00:53:12.170 can get some insight. Yeah, yeah.

NOTE Confidence: 0.756073513333333

00:53:13.790 --> 00:53:14.945 So I have another question

NOTE Confidence: 0.756073513333333

00:53:14.945 --> 00:53:15.869 about practical you know,

NOTE Confidence: 0.756073513333333

 $00:53:15.870 \longrightarrow 00:53:18.244$ we ask pathology for always

NOTE Confidence: 0.756073513333333

 $00:53:18.244 \rightarrow 00:53:21.240$ frustrated by PO1 as a biomarker or

NOTE Confidence: 0.756073513333333

 $00:53:21.240 \longrightarrow 00:53:22.910$ TMB like there's no good biomarkers.

NOTE Confidence: 0.810907434285714

 $00{:}53{:}24{.}930 \dashrightarrow 00{:}53{:}27{.}202$ It sounds like you have about a number

NOTE Confidence: 0.810907434285714

 $00{:}53{:}27{.}202 \dashrightarrow 00{:}53{:}29{.}230$ of potential molecules that could work

NOTE Confidence: 0.810907434285714

 $00:53:29.230 \rightarrow 00:53:31.300$ as biomarkers, you know having the

NOTE Confidence: 0.810907434285714

 $00:53:31.300 \rightarrow 00:53:33.830$ right transporters in the right place.

NOTE Confidence: 0.810907434285714

 $00:53:33.830 \longrightarrow 00:53:36.942$ Do you see any, any sort of immediate

NOTE Confidence: 0.810907434285714

 $00:53:36.942 \longrightarrow 00:53:38.690$ possibility of some of these as

NOTE Confidence: 0.810907434285714

 $00:53:38.690 \rightarrow 00:53:43.830$ biomarkers for immunotherapy? Yeah, so.

NOTE Confidence: 0.815215711538462

 $00{:}53{:}43{.}830 \dashrightarrow 00{:}53{:}47{.}510$ So I I guess this is it's quite a

NOTE Confidence: 0.815215711538462

 $00{:}53{:}47.621 \dashrightarrow 00{:}53{:}50.382$ it's quite a depressing I would say.

NOTE Confidence: 0.815215711538462

 $00:53:50.382 \rightarrow 00:53:53.150$ So when you located the biomarkers right,

NOTE Confidence: 0.815215711538462

 $00:53:53.150 \rightarrow 00:53:55.942$ so it could be money you know perfectly

NOTE Confidence: 0.815215711538462

 $00{:}53{:}55{.}942 \dashrightarrow 00{:}53{:}58{.}849$ well when people started to do the PD1

NOTE Confidence: 0.815215711538462

00:53:58.849 --> 00:54:01.224 PDL 1 clinical trials and nobody knows

NOTE Confidence: 0.815215711538462

 $00{:}54{:}01{.}224 \dashrightarrow 00{:}54{:}03{.}573$ it the PD one or PDL one expression.

NOTE Confidence: 0.815215711538462

 $00{:}54{:}03{.}573 \dashrightarrow 00{:}54{:}06{.}300$ So now after that you know it is PDL

NOTE Confidence: 0.815215711538462

 $00:54:06.364 \rightarrow 00:54:08.332$ one expression and if they approve

NOTE Confidence: 0.815215711538462

 $00:54:08.332 \rightarrow 00:54:10.922$ you know you have certain levels of

NOTE Confidence: 0.815215711538462

00:54:10.922 --> 00:54:12.990 PD1 expression it's indication right.

NOTE Confidence: 0.815215711538462

 $00:54:12.990 \rightarrow 00:54:17.110$ So it's. It's not the way how how we know

NOTE Confidence: 0.815215711538462

 $00:54:17.110 \longrightarrow 00:54:20.160$ initially for it is for Philippoussis.

NOTE Confidence: 0.815215711538462

00:54:20.160 --> 00:54:22.078 I don't know which one we can

NOTE Confidence: 0.815215711538462

 $00:54:22.078 \longrightarrow 00:54:23.220$ we can really say.

NOTE Confidence: 0.815215711538462

 $00{:}54{:}23.220 \dashrightarrow 00{:}54{:}27.315$ So the best way is well check all the

NOTE Confidence: 0.815215711538462

 $00:54:27.320 \rightarrow 00:54:29.925$ social associated genes particularly protein

NOTE Confidence: 0.815215711538462

 $00:54:29.925 \rightarrow 00:54:33.520$ levels whether this will give us something.

NOTE Confidence: 0.815215711538462

 $00{:}54{:}33{.}520 \dashrightarrow 00{:}54{:}37{.}696$ You know so for example we looked at

NOTE Confidence: 0.815215711538462

 $00{:}54{:}37{.}700 \dashrightarrow 00{:}54{:}41{.}396$ a CSR four expression when you see

NOTE Confidence: 0.815215711538462

 $00{:}54{:}41{.}396 \dashrightarrow 00{:}54{:}45{.}850$ high ACR four expression may this may

NOTE Confidence: 0.815215711538462

 $00:54:45.850 \rightarrow 00:54:50.838$ help can it is for BA real bellmaker.

NOTE Confidence: 0.815215711538462

 $00:54:50.840 \rightarrow 00:54:52.952$ You get to have something to test it

NOTE Confidence: 0.815215711538462

00:54:52.952 --> 00:54:55.430 in clinic, in patient and your mouse,

- NOTE Confidence: 0.815215711538462
- $00{:}54{:}55{.}430 \dashrightarrow 00{:}54{:}57{.}614$ you know mechanism, fine.
- NOTE Confidence: 0.815215711538462
- 00:54:57.614 --> 00:55:00.016 But you if you want to see it directly
- NOTE Confidence: 0.815215711538462
- $00:55:00.016 \rightarrow 00:55:01.506$ in patient, that's another story.
- NOTE Confidence: 0.815215711538462
- $00{:}55{:}01{.}506 \dashrightarrow 00{:}55{:}03{.}558$ We need to see the patient.
- NOTE Confidence: 0.815215711538462
- $00:55:03.560 \rightarrow 00:55:05.636$ That's why we appreciate your work.
- NOTE Confidence: 0.815215711538462
- $00:55:05.640 \longrightarrow 00:55:06.816$ We need to see the patient.
- NOTE Confidence: 0.815215711538462
- $00{:}55{:}06{.}820 \dashrightarrow 00{:}55{:}08{.}850$ We need to see the tumors in
- NOTE Confidence: 0.815215711538462
- $00:55:08.850 \longrightarrow 00:55:10.849$ patient and see what's going on.
- NOTE Confidence: 0.815215711538462
- $00{:}55{:}10.850 \dashrightarrow 00{:}55{:}12.180$ Yes, but there are ways to go.
- NOTE Confidence: 0.6842294
- 00:55:56.850 -> 00:55:57.150 OK.
- NOTE Confidence: 0.8241872575
- 00:56:07.760 --> 00:56:10.032 I'm I I'm afraid I really didn't get
- NOTE Confidence: 0.8241872575
- $00{:}56{:}10.032 \dashrightarrow 00{:}56{:}11.950$ any question you asked. Maybe just.
- NOTE Confidence: 0.809215076
- $00:56:39.740 \rightarrow 00:56:43.258$ So you mean when they express the grammar?
- NOTE Confidence: 0.3403691
- 00:56:45.440 --> 00:56:45.830 Season.
- NOTE Confidence: 0.7134211
- $00:56:50.720 \longrightarrow 00:56:51.430$ Right.
- NOTE Confidence: 0.683789309

00:56:53.820 --> 00:56:57.488 So that's why. Our fear of dosis,

NOTE Confidence: 0.683789309

 $00{:}56{:}57{.}490 \dashrightarrow 00{:}57{:}01{.}246$ it's obvious when we do immunother apy.

NOTE Confidence: 0.683789309

 $00:57:01.250 \longrightarrow 00:57:02.990$ So that's the system we used.

NOTE Confidence: 0.683789309

 $00:57:02.990 \longrightarrow 00:57:05.195$ So actually in response to

NOTE Confidence: 0.683789309

 $00:57:05.195 \rightarrow 00:57:07.920$ your question early on when you

NOTE Confidence: 0.683789309

 $00:57:07.920 \longrightarrow 00:57:10.095$ just give to matoes and mice.

NOTE Confidence: 0.683789309

00:57:10.100 --> 00:57:12.683 So both you still have T cells and T

NOTE Confidence: 0.683789309

 $00:57:12.683 \rightarrow 00:57:14.958$ cells are more or less functional.

NOTE Confidence: 0.683789309

 $00{:}57{:}14.960 \dashrightarrow 00{:}57{:}17.402$ But under this condition we treated

NOTE Confidence: 0.683789309

 $00:57:17.402 \rightarrow 00:57:19.580$ myself with ferocity and crypto.

NOTE Confidence: 0.683789309

 $00:57:19.580 \longrightarrow 00:57:22.688$ We hope, we hope we can see.

NOTE Confidence: 0.683789309

 $00:57:22.690 \longrightarrow 00:57:24.940$ We thought.

NOTE Confidence: 0.683789309

00:57:24.940 --> 00:57:29.036 So you get to have sufficient levels of

NOTE Confidence: 0.683789309

 $00{:}57{:}29{.}036 \dashrightarrow 00{:}57{:}32{.}384$ interference and electronic acid and so

NOTE Confidence: 0.683789309

 $00{:}57{:}32{.}384$ --> $00{:}57{:}35{.}450$ and maybe other BOA&OA in the environment.

NOTE Confidence: 0.683789309

 $00:57:35.450 \rightarrow 00:57:39.648$ How do we do that if you don't have

NOTE Confidence: 0.683789309

 $00:57:39.648 \dashrightarrow 00:57:42.733$ a sufficient T cell infiltration?

NOTE Confidence: 0.683789309

 $00:57:42.740 \longrightarrow 00:57:46.674$ Even so, I guess we can manipulate

NOTE Confidence: 0.683789309

 $00:57:46.674 \rightarrow 00:57:48.410$ the system, for example,

NOTE Confidence: 0.683789309

00:57:48.410 - 00:57:50.240 maybe for example you have some,

NOTE Confidence: 0.683789309

 $00:57:50.240 \rightarrow 00:57:52.008$ it's not one way to go, maybe for example,

NOTE Confidence: 0.683789309

00:57:52.008 --> 00:57:54.363 if you have a card in cell therapy, right?

NOTE Confidence: 0.683789309

 $00{:}57{:}54{.}363 \dashrightarrow 00{:}57{:}56{.}554$ So not all the patients are responsive

NOTE Confidence: 0.683789309

 $00{:}57{:}56{.}554 \dashrightarrow 00{:}57{:}58{.}629$ and then we have some cells here,

NOTE Confidence: 0.683789309

00:57:58.630 - 00:58:00.790 maybe we can manipulate this

NOTE Confidence: 0.683789309

 $00:58:00.790 \longrightarrow 00:58:02.746$ specially in this, in this way,

NOTE Confidence: 0.683789309

 $00:58:02.750 \rightarrow 00:58:05.870$ another way we can do also maybe you know we

NOTE Confidence: 0.683789309

 $00:58:05.950 \rightarrow 00:58:09.149$ have ways to improve the teacher trafficking,

NOTE Confidence: 0.683789309

 $00:58:09.150 \longrightarrow 00:58:09.975$ right?

NOTE Confidence: 0.683789309

 $00:58:09.975 \longrightarrow 00:58:14.925$ So, so, so far where do?

NOTE Confidence: 0.683789309

 $00:58:14.930 \longrightarrow 00:58:16.566$ A pure airplus mechanism.

- NOTE Confidence: 0.683789309
- $00{:}58{:}16.566 \dashrightarrow 00{:}58{:}19.020$ In the absence of immune system
- NOTE Confidence: 0.683789309
- $00{:}58{:}19.098 \dashrightarrow 00{:}58{:}22.486$ whether this is a valid approach, we don't.
- NOTE Confidence: 0.683789309
- $00:58:22.486 \rightarrow 00:58:25.534$ Maybe there's a way to go?
- NOTE Confidence: 0.683789309
- $00:58:25.540 \rightarrow 00:58:29.420$ Maybe radiation or chemo or something?
- NOTE Confidence: 0.683789309
- $00{:}58{:}29{.}420 \dashrightarrow 00{:}58{:}30{.}564$ Yes and a no.
- NOTE Confidence: 0.683789309
- $00{:}58{:}30{.}564 \dashrightarrow 00{:}58{:}32{.}908$ And also we have another paper I can
- NOTE Confidence: 0.683789309
- $00:58:32.908 \longrightarrow 00:58:35.140$ mention this here and we have a paper
- NOTE Confidence: 0.683789309
- $00:58:35.214 \rightarrow 00:58:37.554$ to actually that's the first people
- NOTE Confidence: 0.683789309
- $00{:}58{:}37{.}554 \dashrightarrow 00{:}58{:}40{.}504$ talking about the effect of radiation
- NOTE Confidence: 0.683789309
- $00:58:40.504 \rightarrow 00:58:44.656$ is partially dependent on our fibrosis,
- NOTE Confidence: 0.683789309
- $00{:}58{:}44{.}660 \dashrightarrow 00{:}58{:}47{.}215$ but this fabulous especially again
- NOTE Confidence: 0.683789309
- $00{:}58{:}47.215 \dashrightarrow 00{:}58{:}49.770$ recognized by the immune system.
- NOTE Confidence: 0.683789309
- $00:58:49.770 \dashrightarrow 00:58:52.514$ So you need to have an immune system.
- NOTE Confidence: 0.683789309
- 00:58:52.520 --> 00:58:53.050 Yes,
- NOTE Confidence: 0.683789309
- $00:58:53.050 \dashrightarrow 00:58:56.760$ so that that's a cancer discovery people.
- NOTE Confidence: 0.683789309

 $00{:}58{:}56{.}760 \dashrightarrow 00{:}58{:}57{.}364$ We.

NOTE Confidence: 0.683789309

00:58:57.364 --> 00:58:59.780 Properties 4-5 years ago,

NOTE Confidence: 0.683789309

 $00{:}58{:}59{.}780 \dashrightarrow 00{:}59{:}00{.}120$ yeah.

NOTE Confidence: 0.46906483

 $00:59:02.440 \longrightarrow 00:59:02.840$ Questions?

NOTE Confidence: 0.9270984175

00:59:05.580 --> 00:59:06.268 Thank you very much

NOTE Confidence: 0.86509435

00:59:06.280 --> 00:59:07.492 again. Yeah. Thank you.

NOTE Confidence: 0.86509435

00:59:07.492 --> 00:59:08.670 Thank you. Thank you.