

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: 0.830144091666667

00:00:07.870 --> 00:00:10.168 so we're going to start and

NOTE Confidence: 0.830144091666667

00:00:10.170 --> 00:00:11.594 so first welcome everybody.

NOTE Confidence: 0.830144091666667

00:00:11.594 --> 00:00:15.734 This is the first in person brand grounds

NOTE Confidence: 0.830144091666667

00:00:15.734 --> 00:00:18.830 meeting and we're very happy about it.

NOTE Confidence: 0.830144091666667

00:00:18.830 --> 00:00:20.979 So we expect to have people joining.

NOTE Confidence: 0.830144091666667

00:00:20.980 --> 00:00:24.011 We have 20 people online and maybe

NOTE Confidence: 0.830144091666667

00:00:24.011 --> 00:00:26.340 some more people to come so.

NOTE Confidence: 0.830144091666667

00:00:26.340 --> 00:00:28.350 So it's a great pleasure

NOTE Confidence: 0.830144091666667

00:00:28.350 --> 00:00:30.360 today to have our speaker,

NOTE Confidence: 0.830144091666667

00:00:30.360 --> 00:00:32.300 his doctor Weiping Zou.

NOTE Confidence: 0.830144091666667

00:00:32.300 --> 00:00:34.240 He's currently the Charles

NOTE Confidence: 0.830144091666667

00:00:34.240 --> 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 --> 00:00:39.682 biology and surgery at the University
NOTE Confidence: 0.830144091666667

00:00:39.682 --> 00:00:41.499 of Michigan and he's also the
NOTE Confidence: 0.830144091666667

00:00:41.499 --> 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 --> 00:00:44.979 immunotherapy.
NOTE Confidence: 0.830144091666667

00:00:44.979 --> 00:00:47.772 And he has a number of additional
NOTE Confidence: 0.830144091666667

00:00:47.772 --> 00:00:50.096 appointments that I will omit now
NOTE Confidence: 0.830144091666667

00:00:50.096 --> 00:00:54.664 because I think they just add too much.
NOTE Confidence: 0.830144091666667

00:00:54.664 --> 00:00:56.488 Maybe he's training.
NOTE Confidence: 0.830144091666667

00:00:56.490 --> 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: 0.830144091666667

00:01:00.290 --> 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 --> 00:01:06.865 That was followed by postdoctoral training in

NOTE Confidence: 0.830144091666667
00:01:06.865 --> 00:01:09.547 France and then postural training in Baylor,
NOTE Confidence: 0.830144091666667
00:01:09.550 --> 00:01:11.650 Dallas.
NOTE Confidence: 0.830144091666667
00:01:11.650 --> 00:01:14.560 And then from his academic career,
NOTE Confidence: 0.830144091666667
00:01:14.560 --> 00:01:18.278 he initiated his career as an
NOTE Confidence: 0.830144091666667
00:01:18.278 --> 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 --> 00:01:23.064 where he rose to the rank of
NOTE Confidence: 0.830144091666667
00:01:23.064 --> 00:01:24.480 associate professor with tenure.
NOTE Confidence: 0.830144091666667
00:01:24.480 --> 00:01:26.736 And then he moved to University of Michigan,
NOTE Confidence: 0.830144091666667
00:01:26.740 --> 00:01:29.260 where he became a full professor
NOTE Confidence: 0.830144091666667
00:01:29.260 --> 00:01:32.440 and director of the program.
NOTE Confidence: 0.830144091666667
00:01:32.440 --> 00:01:34.810 What is very interesting is that
NOTE Confidence: 0.830144091666667
00:01:34.810 --> 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 --> 00:01:42.312 I could count about 35.
NOTE Confidence: 0.830144091666667

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 --> 00:01:47.368 nature,
NOTE Confidence: 0.830144091666667

00:01:47.368 --> 00:01:50.231 type of journals and he's also very
NOTE Confidence: 0.830144091666667

00:01:50.231 --> 00:01:52.237 productive in the research and I
NOTE Confidence: 0.830144091666667

00:01:52.237 --> 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 --> 00:01:59.549 amount of effort and shows to the
NOTE Confidence: 0.830144091666667

00:01:59.549 --> 00:02:01.970 reflects the quality of his work.
NOTE Confidence: 0.830144091666667

00:02:01.970 --> 00:02:03.310 He has done major contributions
NOTE Confidence: 0.830144091666667

00:02:03.310 --> 00:02:05.067 in the fields of tumor immunology
NOTE Confidence: 0.830144091666667

00:02:05.067 --> 00:02:06.887 and looking at different aspects.
NOTE Confidence: 0.830144091666667

00:02:06.890 --> 00:02:09.050 And recently he has focused more
NOTE Confidence: 0.830144091666667

00:02:09.050 --> 00:02:11.667 on the role of the metabolism
NOTE Confidence: 0.830144091666667

00:02:11.667 --> 00:02:14.397 and how metabolism can actually
NOTE Confidence: 0.830144091666667

00:02:14.397 --> 00:02:16.450 compromise adaptive immune responses

NOTE Confidence: 0.830144091666667
00:02:16.450 --> 00:02:18.450 in the tumor microenvironment.
NOTE Confidence: 0.830144091666667
00:02:18.450 --> 00:02:20.690 I have to also to say that he's
NOTE Confidence: 0.830144091666667
00:02:20.690 --> 00:02:22.272 a very translationally oriented,
NOTE Confidence: 0.830144091666667
00:02:22.272 --> 00:02:25.168 so his work focuses on very basic
NOTE Confidence: 0.830144091666667
00:02:25.170 --> 00:02:27.948 mechanisms but also projects into
NOTE Confidence: 0.830144091666667
00:02:27.948 --> 00:02:29.976 different tumor types and he has
NOTE Confidence: 0.830144091666667
00:02:29.976 --> 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 --> 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 --> 00:02:43.140 I believe Doctor Weiping Zou and his title
NOTE Confidence: 0.830144091666667
00:02:43.140 --> 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 --> 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 --> 00:03:08.075 Thank God for your kind
NOTE Confidence: 0.92904854

00:03:08.075 --> 00:03:10.550 invitation and introduction.
NOTE Confidence: 0.92904854

00:03:10.550 --> 00:03:13.710 Year is a pioneer institution
NOTE Confidence: 0.92904854

00:03:13.710 --> 00:03:15.606 of modern immunology,
NOTE Confidence: 0.92904854

00:03:15.610 --> 00:03:18.664 particularly human immunology,
NOTE Confidence: 0.92904854

00:03:18.664 --> 00:03:23.580 innate immunity and T cells.
NOTE Confidence: 0.92904854

00:03:23.580 --> 00:03:25.392 We paid up allergy,
NOTE Confidence: 0.92904854

00:03:25.392 --> 00:03:28.411 so in many ways this institution
NOTE Confidence: 0.92904854

00:03:28.411 --> 00:03:32.166 contributed enormously to our knowledge
NOTE Confidence: 0.92904854

00:03:32.166 --> 00:03:35.170 and also immunology translation.
NOTE Confidence: 0.92904854

00:03:35.170 --> 00:03:37.894 So this is absolutely a great
NOTE Confidence: 0.92904854

00:03:37.894 --> 00:03:39.580 pleasure for me to be here.
NOTE Confidence: 0.92904854

00:03:39.580 --> 00:03:43.110 This is the first time I'm able to give
NOTE Confidence: 0.92904854

00:03:43.110 --> 00:03:45.930 this talk to this prestigious university.
NOTE Confidence: 0.92904854

00:03:45.930 --> 00:03:49.586 As I mentioned yesterday when we had dinner,

NOTE Confidence: 0.92904854

00:03:49.590 --> 00:03:52.092 actually my old son wants to

NOTE Confidence: 0.92904854

00:03:52.092 --> 00:03:54.930 get into the C university.

NOTE Confidence: 0.92904854

00:03:54.930 --> 00:03:59.190 He failed and I emailed him.

NOTE Confidence: 0.92904854

00:03:59.190 --> 00:04:01.494 I said, I'm going to give a talk

NOTE Confidence: 0.92904854

00:04:01.494 --> 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 --> 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 --> 00:04:11.920 So.

NOTE Confidence: 0.92904854

00:04:11.920 --> 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 --> 00:04:33.620 We have come a long way.

NOTE Confidence: 0.587792848333333

00:04:33.620 --> 00:04:35.796 First we have surgery,

NOTE Confidence: 0.587792848333333

00:04:35.796 --> 00:04:37.011 radiation, chemotherapy.

NOTE Confidence: 0.587792848333333

00:04:37.011 --> 00:04:39.695 Chemotherapy and the targeted
NOTE Confidence: 0.5877928483333333

00:04:39.695 --> 00:04:42.230 therapy for managers and rotation if
NOTE Confidence: 0.5877928483333333

00:04:42.230 --> 00:04:45.230 these days we do our immunotherapy.
NOTE Confidence: 0.5877928483333333

00:04:45.230 --> 00:04:48.674 As you can see from this summary.
NOTE Confidence: 0.5877928483333333

00:04:48.680 --> 00:04:52.782 Each milestone is really based on the
NOTE Confidence: 0.5877928483333333

00:04:52.782 --> 00:04:55.440 basic celebs scientific discovery.
NOTE Confidence: 0.5877928483333333

00:04:55.440 --> 00:05:01.070 So people always asked what is next.
NOTE Confidence: 0.5877928483333333

00:05:01.070 --> 00:05:05.330 So in terms of immunotherapy,
NOTE Confidence: 0.5877928483333333

00:05:05.330 --> 00:05:06.870 what we have done?
NOTE Confidence: 0.7741063993333333

00:05:09.300 --> 00:05:12.846 Actually, early on we know based
NOTE Confidence: 0.7741063993333333

00:05:12.846 --> 00:05:16.016 on the genetic identification and
NOTE Confidence: 0.7741063993333333

00:05:16.016 --> 00:05:18.840 mutations people have discovered,
NOTE Confidence: 0.7741063993333333

00:05:18.840 --> 00:05:21.928 it's pretty clear cancer
NOTE Confidence: 0.7741063993333333

00:05:21.928 --> 00:05:25.016 is a genetic disease.
NOTE Confidence: 0.7741063993333333

00:05:25.020 --> 00:05:29.570 But all work and many others work.
NOTE Confidence: 0.7741063993333333

00:05:29.570 --> 00:05:33.776 Consider cancer is an immune disorder.

NOTE Confidence: 0.774106399333333
00:05:33.780 --> 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 --> 00:05:42.295 including the P1P1 that was in the
NOTE Confidence: 0.774106399333333
00:05:42.295 --> 00:05:44.419 human tumor migraine environment.
NOTE Confidence: 0.774106399333333
00:05:44.420 --> 00:05:47.708 So we believe the human tumor
NOTE Confidence: 0.774106399333333
00:05:47.708 --> 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 --> 00:05:54.304 So at this stage,
NOTE Confidence: 0.774106399333333
00:05:54.304 --> 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 --> 00:06:03.764 But when you talk about this 20 years ago.
NOTE Confidence: 0.774106399333333
00:06:03.770 --> 00:06:06.530 It's not the same thing.
NOTE Confidence: 0.774106399333333
00:06:06.530 --> 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 --> 00:06:13.668 immunosuppressive mechanisms.
NOTE Confidence: 0.7458623025

00:06:19.060 --> 00:06:21.760 For those who are relatively new
NOTE Confidence: 0.7458623025

00:06:21.760 --> 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 --> 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 --> 00:06:33.576 the studies from our own group,
NOTE Confidence: 0.7458623025

00:06:33.580 --> 00:06:35.580 but also from many others.
NOTE Confidence: 0.7458623025

00:06:35.580 --> 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 --> 00:06:58.350 We are pretty much legislatively in the basic
NOTE Confidence: 0.5880662

00:06:58.437 --> 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

00:07:04.630 --> 00:07:07.619 we have been working on one concept.

NOTE Confidence: 0.5880662

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

NOTE Confidence: 0.5880662

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 --> 00:07:18.391 To address this we have several research

NOTE Confidence: 0.5880662

00:07:18.391 --> 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 --> 00:07:26.567 suppressive mechanisms network.

NOTE Confidence: 0.5880662

00:07:26.570 --> 00:07:29.678 Such as PD1PD L one OK.

NOTE Confidence: 0.5880662

00:07:29.680 --> 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 --> 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 --> 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 --> 00:07:45.680 in the recent years we spent a lot of

NOTE Confidence: 0.5880662

00:07:45.680 --> 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 --> 00:07:55.128 more time on the fourth direction.
NOTE Confidence: 0.5880662

00:07:55.130 --> 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 --> 00:08:08.130 just to show you where I have come from.
NOTE Confidence: 0.5880662

00:08:08.130 --> 00:08:10.314 So and like to share this site with
NOTE Confidence: 0.5880662

00:08:10.314 --> 00:08:12.926 you for the first research direction
NOTE Confidence: 0.5880662

00:08:12.926 --> 00:08:14.926 we have immunosuppressive networks
NOTE Confidence: 0.5880662

00:08:14.930 --> 00:08:20.558 actually almost more than 20 years ago.
NOTE Confidence: 0.5880662

00:08:20.560 --> 00:08:22.640 Under the support and
NOTE Confidence: 0.5880662

00:08:22.640 --> 00:08:24.200 collaboration with Millington,
NOTE Confidence: 0.5880662

00:08:24.200 --> 00:08:26.112 we have published this
NOTE Confidence: 0.5880662

00:08:26.112 --> 00:08:28.024 paper in Nature magazine.
NOTE Confidence: 0.5880662

00:08:28.030 --> 00:08:31.270 It was named it is time PDL one.
NOTE Confidence: 0.5880662

00:08:31.270 --> 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 --> 00:08:37.786 These people for the first time

NOTE Confidence: 0.5880662

00:08:37.786 --> 00:08:40.240 demonstrating PDL one of P-70 joint

NOTE Confidence: 0.5880662

00:08:40.325 --> 00:08:43.387 expression recognition and profit in

NOTE Confidence: 0.5880662

00:08:43.387 --> 00:08:45.615 the human cancer microenvironment

NOTE Confidence: 0.5880662

00:08:45.615 --> 00:08:48.400 and human human chain influence.

NOTE Confidence: 0.5880662

00:08:48.400 --> 00:08:50.620 We clearly demonstrated if you

NOTE Confidence: 0.5880662

00:08:50.620 --> 00:08:53.604 broke this pathway you can recover

NOTE Confidence: 0.5880662

00:08:53.604 --> 00:08:55.650 the dysfunctionality cells.

NOTE Confidence: 0.67314885

00:08:58.260 --> 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 --> 00:09:11.030 Of course in these days if you look

NOTE Confidence: 0.67314885

00:09:11.030 --> 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 --> 00:09:19.124 on when leaving discovered the best
NOTE Confidence: 0.67314885

00:09:19.124 --> 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 --> 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 --> 00:09:35.237 who are interested in epigenetic
NOTE Confidence: 0.67314885

00:09:35.237 --> 00:09:37.637 recognition in this institution,
NOTE Confidence: 0.67314885

00:09:37.640 --> 00:09:40.699 but we look at this from the
NOTE Confidence: 0.67314885

00:09:40.699 --> 00:09:42.010 immune recognition perspective.
NOTE Confidence: 0.67314885

00:09:42.010 --> 00:09:45.458 So in the tumor microenvironment similar
NOTE Confidence: 0.67314885

00:09:45.458 --> 00:09:50.297 to the TH1 and TH2 reciprocal recognition?
NOTE Confidence: 0.67314885

00:09:50.297 --> 00:09:53.642 We have observed a reciprocal
NOTE Confidence: 0.67314885

00:09:53.642 --> 00:09:56.498 regulation between PRC two complex
NOTE Confidence: 0.67314885

00:09:56.498 --> 00:09:59.823 and Swiss sniper complex in the tumor.

NOTE Confidence: 0.67314885

00:09:59.830 --> 00:10:02.840 So actually this recognition was

NOTE Confidence: 0.67314885

00:10:02.840 --> 00:10:04.646 properly controlled interference

NOTE Confidence: 0.67314885

00:10:04.646 --> 00:10:07.532 zeronine therefore TH one type second

NOTE Confidence: 0.67314885

00:10:07.532 --> 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 --> 00:10:14.634 We have worked out the detailed

NOTE Confidence: 0.67314885

00:10:14.634 --> 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 --> 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 --> 00:10:27.258 I know also several investigators

NOTE Confidence: 0.67314885

00:10:27.258 --> 00:10:29.939 including my host code is very

NOTE Confidence: 0.67314885

00:10:29.939 --> 00:10:33.145 interested in this image C interferon

NOTE Confidence: 0.67314885

00:10:33.145 --> 00:10:35.645 signaling sets signaling pathway.

NOTE Confidence: 0.67314885

00:10:35.650 --> 00:10:38.546 As you know these are the key immunogenic

NOTE Confidence: 0.67314885

00:10:38.546 --> 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 --> 00:10:44.230 I show you one example.
NOTE Confidence: 0.67314885

00:10:44.230 --> 00:10:45.256 We have,
NOTE Confidence: 0.67314885

00:10:45.256 --> 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 --> 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 --> 00:11:02.969 patients do not have those mutations.
NOTE Confidence: 0.67314885

00:11:02.970 --> 00:11:05.472 Therefore we need to find out
NOTE Confidence: 0.67314885

00:11:05.472 --> 00:11:07.782 the other pathways which may
NOTE Confidence: 0.67314885

00:11:07.782 --> 00:11:10.010 contribute to safety resistance.
NOTE Confidence: 0.67314885

00:11:10.010 --> 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 --> 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 --> 00:11:26.600 So this is a auto between septor.

NOTE Confidence: 0.67314885

00:11:26.600 --> 00:11:29.872 It turns out actually all of the nearing

NOTE Confidence: 0.67314885

00:11:29.872 --> 00:11:32.695 can control the stability and the

NOTE Confidence: 0.67314885

00:11:32.695 --> 00:11:35.575 degradation of the film gamma receptor.

NOTE Confidence: 0.67314885

00:11:35.580 --> 00:11:37.128 So as a consequence,

NOTE Confidence: 0.67314885

00:11:37.128 --> 00:11:39.918 this controls the image C expression antigen

NOTE Confidence: 0.67314885

00:11:39.918 --> 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 --> 00:11:47.159 show you this was published.

NOTE Confidence: 0.67314885

00:11:47.160 --> 00:11:49.057 For those who are interested in this,

NOTE Confidence: 0.67314885

00:11:49.060 --> 00:11:50.850 you may have a look instead.

NOTE Confidence: 0.67314885

00:11:50.850 --> 00:11:55.405 Most of my time we are focused on the force

NOTE Confidence: 0.67314885

00:11:55.405 --> 00:11:59.004 we switch direction metabolic pathways.

NOTE Confidence: 0.67314885

00:11:59.004 --> 00:12:01.770 And I will.

NOTE Confidence: 0.67314885

00:12:01.770 --> 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 --> 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 --> 00:12:17.006 Another is SLC 43A2.

NOTE Confidence: 0.67314885

00:12:17.006 --> 00:12:19.934 So those ACC family members are

NOTE Confidence: 0.67314885

00:12:19.934 --> 00:12:23.169 nutrients or metabolite transporters.

NOTE Confidence: 0.67314885

00:12:23.170 --> 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 --> 00:12:30.010 in the field of immunology.

NOTE Confidence: 0.67314885

00:12:30.010 --> 00:12:34.889 We start to figure out some of it.

NOTE Confidence: 0.67314885

00:12:34.890 --> 00:12:38.726 So before that I want to introduce

NOTE Confidence: 0.67314885

00:12:38.726 --> 00:12:40.862 the concept of ferroptosis.

NOTE Confidence: 0.67314885

00:12:40.862 --> 00:12:44.474 So it has been defined in vitro

NOTE Confidence: 0.67314885

00:12:44.480 --> 00:12:46.596 through the synthetic compounds.

NOTE Confidence: 0.67314885

00:12:46.596 --> 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 --> 00:12:55.860 peroxidation induced cell death.

NOTE Confidence: 0.67314885

00:12:55.860 --> 00:12:59.856 There are several genes or pathways

NOTE Confidence: 0.67314885

00:12:59.856 --> 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 --> 00:13:07.285 including this exit system

NOTE Confidence: 0.67314885

00:13:07.290 --> 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 --> 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 --> 00:13:21.360 criteria to define electrolysis,

NOTE Confidence: 0.656827746

00:13:21.360 --> 00:13:24.230 so one it's maybe the Rose production,

NOTE Confidence: 0.656827746

00:13:24.230 --> 00:13:26.852 another is expression of all states

NOTE Confidence: 0.656827746

00:13:26.852 --> 00:13:29.370 needed species on the membrane,
NOTE Confidence: 0.656827746

00:13:29.370 --> 00:13:32.460 and finally we need to see
NOTE Confidence: 0.656827746

00:13:32.460 --> 00:13:34.005 the functional activities.
NOTE Confidence: 0.656827746

00:13:34.010 --> 00:13:36.782 So in this case we asked
NOTE Confidence: 0.656827746

00:13:36.782 --> 00:13:38.630 a very simple question.
NOTE Confidence: 0.656827746

00:13:38.630 --> 00:13:42.326 We know when CDA T cells are activated,
NOTE Confidence: 0.656827746

00:13:42.330 --> 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 --> 00:13:49.970 makes pores on the membrane,
NOTE Confidence: 0.656827746

00:13:49.970 --> 00:13:51.155 then grant them.
NOTE Confidence: 0.656827746

00:13:51.155 --> 00:13:53.792 We get into the cells activated
NOTE Confidence: 0.656827746

00:13:53.792 --> 00:13:57.764 caspase induce tumor cell able doses.
NOTE Confidence: 0.656827746

00:13:57.770 --> 00:14:02.150 This is text book message.
NOTE Confidence: 0.656827746

00:14:02.150 --> 00:14:04.908 So we asked a simple question means
NOTE Confidence: 0.656827746

00:14:04.908 --> 00:14:08.687 if CDA T cells who kills tumor cells?
NOTE Confidence: 0.656827746

00:14:08.690 --> 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 --> 00:14:16.682 So in this case we set up several

NOTE Confidence: 0.656827746

00:14:16.682 --> 00:14:19.669 experiments to test this possibility.

NOTE Confidence: 0.656827746

00:14:19.670 --> 00:14:23.806 So one is a 88 over retention model.

NOTE Confidence: 0.656827746

00:14:23.810 --> 00:14:27.450 We do immunotherapy before you can see PD,

NOTE Confidence: 0.656827746

00:14:27.450 --> 00:14:30.696 one can control the tumor growth.

NOTE Confidence: 0.656827746

00:14:30.700 --> 00:14:33.857 Under this condition before the tumor cells,

NOTE Confidence: 0.656827746

00:14:33.860 --> 00:14:35.862 really it is an 8 stage before

NOTE Confidence: 0.656827746

00:14:35.862 --> 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 --> 00:14:42.818 you detect relative needs worse production.

NOTE Confidence: 0.656827746

00:14:42.820 --> 00:14:45.785 You see actually the immunotherapy

NOTE Confidence: 0.656827746

00:14:45.785 --> 00:14:48.157 induces liberals production in

NOTE Confidence: 0.656827746

00:14:48.157 --> 00:14:50.897 the tumor cells in PD1 cell.

NOTE Confidence: 0.656827746

00:14:50.900 --> 00:14:54.476 Then we did a T cell therapy model.

NOTE Confidence: 0.656827746

00:14:54.480 --> 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 --> 00:15:03.554 It's not a surprise tumor is controlled
NOTE Confidence: 0.656827746

00:15:03.554 --> 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 --> 00:15:13.680 therapy 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 --> 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 --> 00:15:24.888 to provide direct evidence we cultured.
NOTE Confidence: 0.656827746

00:15:24.890 --> 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 --> 00:15:32.614 again we see rose production induced
NOTE Confidence: 0.656827746

00:15:32.614 --> 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 --> 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 --> 00:15:50.210 have space to manipulate the system.

NOTE Confidence: 0.656827746

00:15:50.210 --> 00:15:51.953 You will see you your small amount

NOTE Confidence: 0.656827746

00:15:51.953 --> 00:15:55.690 of T cells. You see T cell cleaning.

NOTE Confidence: 0.656827746

00:15:55.690 --> 00:15:57.410 And under this condition,

NOTE Confidence: 0.656827746

00:15:57.410 --> 00:16:00.822 if you use a small amount of RS3

NOTE Confidence: 0.656827746

00:16:00.822 --> 00:16:03.110 is a dosis inducer,

NOTE Confidence: 0.656827746

00:16:03.110 --> 00:16:06.070 you'll see some levels of human cell death.

NOTE Confidence: 0.656827746

00:16:06.070 --> 00:16:07.450 If you put them together,

NOTE Confidence: 0.656827746

00:16:07.450 --> 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 --> 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 --> 00:16:21.952 So what we have here, it means T

NOTE Confidence: 0.656827746

00:16:21.952 --> 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 --> 00:16:29.459 T cells themselves are not sufficient.

NOTE Confidence: 0.656827746

00:16:29.460 --> 00:16:32.099 You need to have a trigger somewhere.

NOTE Confidence: 0.656827746

00:16:32.100 --> 00:16:35.298 So we will explore further about

NOTE Confidence: 0.656827746

00:16:35.298 --> 00:16:36.364 this phenomenon.

NOTE Confidence: 0.656827746

00:16:36.370 --> 00:16:39.034 But we studied further in vivo

NOTE Confidence: 0.656827746

00:16:39.034 --> 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 --> 00:16:44.214 For example, with P-16,

NOTE Confidence: 0.656827746

00:16:44.214 --> 00:16:46.710 if you treat the tumor bearing

NOTE Confidence: 0.656827746

00:16:46.793 --> 00:16:49.025 mice with antisense 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 --> 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 --> 00:17:00.634 The therapeutic efficacy

NOTE Confidence: 0.656827746

00:17:00.634 --> 00:17:02.470 is basically punished.

NOTE Confidence: 0.656827746

00:17:02.470 --> 00:17:04.470 So this is very unusual.

NOTE Confidence: 0.656827746

00:17:04.470 --> 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 --> 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 --> 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 --> 00:17:26.000 we used another model means we in vitro

NOTE Confidence: 0.683969263333333

00:17:26.000 --> 00:17:29.280 generate erskin resistant tumor cells.

NOTE Confidence: 0.683969263333333

00:17:29.280 --> 00:17:32.880 It's similar to chemotherapy resistant cells.

NOTE Confidence: 0.683969263333333

00:17:32.880 --> 00:17:35.334 You do the individual generates the

NOTE Confidence: 0.683969263333333

00:17:35.334 --> 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: 0.6839692633333333

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

NOTE Confidence: 0.6839692633333333

00:17:43.120 --> 00:17:45.300 parental cells are responsive

NOTE Confidence: 0.6839692633333333

00:17:45.300 --> 00:17:48.475 and resistant cells are no longer

NOTE Confidence: 0.6839692633333333

00:17:48.475 --> 00:17:50.050 responsive to immunotherapy.

NOTE Confidence: 0.6839692633333333

00:17:50.050 --> 00:17:54.845 Indicating actually Ferroptosis is a

NOTE Confidence: 0.6839692633333333

00:17:54.845 --> 00:17:59.640 potential mechanism induced by immunotherapy.

NOTE Confidence: 0.6839692633333333

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

NOTE Confidence: 0.6839692633333333

00:18:02.280 --> 00:18:04.639 then to make a non story short,

NOTE Confidence: 0.6839692633333333

00:18:04.640 --> 00:18:06.698 we know it's interfering and other things,

NOTE Confidence: 0.6839692633333333

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

NOTE Confidence: 0.6839692633333333

00:18:08.680 --> 00:18:12.019 If you make a lookout receptor in

NOTE Confidence: 0.6839692633333333

00:18:12.019 --> 00:18:14.700 the knockout tumor cells and your

NOTE Confidence: 0.6839692633333333

00:18:14.700 --> 00:18:17.874 culture with only one cells you will

NOTE Confidence: 0.6839692633333333

00:18:17.874 --> 00:18:20.109 see actually the liberals production

NOTE Confidence: 0.6839692633333333

00:18:20.109 --> 00:18:23.388 in the human cells is basically gone.

NOTE Confidence: 0.683969263333333
00:18:23.390 --> 00:18:25.826 Under the tumor cell death is
NOTE Confidence: 0.683969263333333
00:18:25.826 --> 00:18:27.044 also basically gone,
NOTE Confidence: 0.683969263333333
00:18:27.050 --> 00:18:29.648 so indicating this tumor cell death
NOTE Confidence: 0.683969263333333
00:18:29.648 --> 00:18:32.160 is controlled through the interference
NOTE Confidence: 0.683969263333333
00:18:32.160 --> 00:18:34.287 and interference signaling.
NOTE Confidence: 0.683969263333333
00:18:34.290 --> 00:18:37.645 So then we hypothesized maybe
NOTE Confidence: 0.683969263333333
00:18:37.645 --> 00:18:40.329 interfering with your stimulate
NOTE Confidence: 0.683969263333333
00:18:40.330 --> 00:18:43.246 oxygen lipid species and therefore the
NOTE Confidence: 0.683969263333333
00:18:43.246 --> 00:18:47.170 cells die as we previously mentioned.
NOTE Confidence: 0.683969263333333
00:18:47.170 --> 00:18:51.088 So we did some individual studies.
NOTE Confidence: 0.683969263333333
00:18:51.090 --> 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 --> 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 --> 00:19:04.767 show actually interfering.
NOTE Confidence: 0.683969263333333

00:19:04.770 --> 00:19:07.820 Gamma can induce tumor cell
NOTE Confidence: 0.6839692633333333

00:19:07.820 --> 00:19:09.650 oxides lipid species,
NOTE Confidence: 0.6839692633333333

00:19:09.650 --> 00:19:13.316 so particularly USB 16P18 or induced.
NOTE Confidence: 0.6839692633333333

00:19:13.316 --> 00:19:15.261 So this is increased when
NOTE Confidence: 0.6839692633333333

00:19:15.261 --> 00:19:17.476 you have a small amount of.
NOTE Confidence: 0.6839692633333333

00:19:17.480 --> 00:19:19.016 ISL 3.
NOTE Confidence: 0.6839692633333333

00:19:19.016 --> 00:19:23.215 So it means actually in the film
NOTE Confidence: 0.6839692633333333

00:19:23.215 --> 00:19:25.465 gamma can properly do the job.
NOTE Confidence: 0.6839692633333333

00:19:25.470 --> 00:19:28.686 To directly show this we used a independent
NOTE Confidence: 0.6839692633333333

00:19:28.686 --> 00:19:30.789 comma sensitive human tumor sauna.
NOTE Confidence: 0.6839692633333333

00:19:30.790 --> 00:19:32.755 It's HD human cell line
NOTE Confidence: 0.6839692633333333

00:19:32.755 --> 00:19:34.327 you treat with interferon.
NOTE Confidence: 0.6839692633333333

00:19:34.330 --> 00:19:36.250 You can inhibit tumor growth
NOTE Confidence: 0.6839692633333333

00:19:36.250 --> 00:19:37.786 in the English model,
NOTE Confidence: 0.6839692633333333

00:19:37.790 --> 00:19:40.149 but under this condition if you use
NOTE Confidence: 0.6839692633333333

00:19:40.149 --> 00:19:42.429 liberal studying you will see the effect.

NOTE Confidence: 0.683969263333333
00:19:42.430 --> 00:19:43.507 It's completely gone.
NOTE Confidence: 0.683969263333333
00:19:43.507 --> 00:19:46.816 But Earth asset in vitro if you only have
NOTE Confidence: 0.683969263333333
00:19:46.816 --> 00:19:49.343 interference or you only have 3 cells.
NOTE Confidence: 0.683969263333333
00:19:49.350 --> 00:19:51.205 The sale gas we are not having,
NOTE Confidence: 0.683969263333333
00:19:51.210 --> 00:19:53.298 so suggesting something else,
NOTE Confidence: 0.683969263333333
00:19:53.298 --> 00:19:55.386 not only just in.
NOTE Confidence: 0.683969263333333
00:19:55.390 --> 00:19:58.567 So but what did anything do in this case?
NOTE Confidence: 0.683969263333333
00:19:58.570 --> 00:20:01.090 We look at the molecular targets,
NOTE Confidence: 0.683969263333333
00:20:01.090 --> 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 --> 00:20:12.602 system into the cells then become
NOTE Confidence: 0.683969263333333
00:20:12.602 --> 00:20:16.074 system and GSH and this will protect
NOTE Confidence: 0.683969263333333
00:20:16.074 --> 00:20:18.642 the cells test from the tosis.
NOTE Confidence: 0.683969263333333
00:20:18.650 --> 00:20:23.746 So it turns out interferon actually we press,
NOTE Confidence: 0.683969263333333

00:20:23.750 --> 00:20:26.050 we press the exit. System.
NOTE Confidence: 0.6839692633333333

00:20:26.050 --> 00:20:28.426 So this is just the the among a.
NOTE Confidence: 0.6839692633333333

00:20:28.430 --> 00:20:30.430 This shows you the protein.
NOTE Confidence: 0.6839692633333333

00:20:30.430 --> 00:20:31.870 Not only this,
NOTE Confidence: 0.6839692633333333

00:20:31.870 --> 00:20:34.750 it's functionally important as shown here,
NOTE Confidence: 0.6839692633333333

00:20:34.750 --> 00:20:37.792 because the system update is reduced
NOTE Confidence: 0.6839692633333333

00:20:37.792 --> 00:20:40.394 when you have independent treatment
NOTE Confidence: 0.6839692633333333

00:20:40.394 --> 00:20:43.824 and then the GSH synthesis is reduced,
NOTE Confidence: 0.6839692633333333

00:20:43.830 --> 00:20:45.680 and particularly if you have
NOTE Confidence: 0.6839692633333333

00:20:45.680 --> 00:20:47.530 again small amount of erosion.
NOTE Confidence: 0.6839692633333333

00:20:47.530 --> 00:20:50.023 This is a well known reduces GSH
NOTE Confidence: 0.6839692633333333

00:20:50.023 --> 00:20:52.741 when you put them together though
NOTE Confidence: 0.6839692633333333

00:20:52.741 --> 00:20:55.809 reduction of GH is really dramatic.
NOTE Confidence: 0.6839692633333333

00:20:55.810 --> 00:21:00.745 So we extend our studies to humans,
NOTE Confidence: 0.6839692633333333

00:21:00.750 --> 00:21:03.126 not only just we use the human cells,
NOTE Confidence: 0.6839692633333333

00:21:03.130 --> 00:21:06.301 human human cells and we meet a

NOTE Confidence: 0.683969263333333
00:21:06.301 --> 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 --> 00:21:16.958 the XC expression is done in the
NOTE Confidence: 0.36622321
00:21:16.958 --> 00:21:19.274 tumor of course, the interferon
NOTE Confidence: 0.36622321
00:21:19.274 --> 00:21:22.034 signaling and CTA is increased.
NOTE Confidence: 0.36622321
00:21:22.040 --> 00:21:23.740 So what do we have?
NOTE Confidence: 0.36622321
00:21:23.740 --> 00:21:29.300 At least we can say apart from apoptosis.
NOTE Confidence: 0.36622321
00:21:29.300 --> 00:21:32.360 The interaction between CHT cells and
NOTE Confidence: 0.36622321
00:21:32.360 --> 00:21:35.659 tumor cells in this context fail.
NOTE Confidence: 0.36622321
00:21:35.660 --> 00:21:37.648 Photos may be involved,
NOTE Confidence: 0.36622321
00:21:37.648 --> 00:21:40.133 and interferon gamma can target
NOTE Confidence: 0.36622321
00:21:40.133 --> 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 --> 00:21:46.920 appreciated because we don't know.
NOTE Confidence: 0.36622321

00:21:46.920 --> 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 --> 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 --> 00:21:57.470 So what else?
NOTE Confidence: 0.36622321

00:21:57.470 --> 00:21:58.410 What else?
NOTE Confidence: 0.36622321

00:21:58.410 --> 00:22:01.350 Because early on when Phil poses
NOTE Confidence: 0.36622321

00:22:01.350 --> 00:22:05.010 as a concept was was established,
NOTE Confidence: 0.36622321

00:22:05.010 --> 00:22:08.040 it is basically based on the
NOTE Confidence: 0.36622321

00:22:08.040 --> 00:22:09.050 synthetic compounds.
NOTE Confidence: 0.36622321

00:22:09.050 --> 00:22:11.586 So you treated the cells with the chemicals
NOTE Confidence: 0.36622321

00:22:11.586 --> 00:22:13.878 and then you see the philippoussis,
NOTE Confidence: 0.36622321

00:22:13.880 --> 00:22:15.532 you see the pathway.
NOTE Confidence: 0.36622321

00:22:15.532 --> 00:22:19.940 So if their process is a intrinsic mechanism.
NOTE Confidence: 0.36622321

00:22:19.940 --> 00:22:21.895 We should have a intrinsic

NOTE Confidence: 0.36622321

00:22:21.895 --> 00:22:23.850 mechanism to induce the fibrosis

NOTE Confidence: 0.36622321

00:22:23.921 --> 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 --> 00:22:31.390 So we look for the natural

NOTE Confidence: 0.36622321

00:22:31.390 --> 00:22:32.935 theodosis inducers in.

NOTE Confidence: 0.36622321

00:22:32.940 --> 00:22:37.640 So in this case we come to a fatty acid diet.

NOTE Confidence: 0.36622321

00:22:37.640 --> 00:22:39.984 So the reason is we know they are

NOTE Confidence: 0.36622321

00:22:39.984 --> 00:22:42.121 quite many publications talking about

NOTE Confidence: 0.36622321

00:22:42.121 --> 00:22:45.079 the relationship between bias and the

NOTE Confidence: 0.36622321

00:22:45.079 --> 00:22:47.379 celebrity response to immunotherapy.

NOTE Confidence: 0.36622321

00:22:47.380 --> 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 --> 00:22:54.694 Micro got microbiota and tumor cell

NOTE Confidence: 0.36622321

00:22:54.694 --> 00:22:57.250 respond where patient responsive

NOTE Confidence: 0.36622321

00:22:57.350 --> 00:23:00.359 responsiveness to immunotherapy.

NOTE Confidence: 0.36622321

00:23:00.360 --> 00:23:02.360 So therefore we were thinking
NOTE Confidence: 0.36622321

00:23:02.360 --> 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 --> 00:23:10.348 metabolic nutrient will be involved.
NOTE Confidence: 0.36622321

00:23:10.348 --> 00:23:12.640 We turned to fatty acids because
NOTE Confidence: 0.36622321

00:23:12.706 --> 00:23:15.170 we know when the cells die through
NOTE Confidence: 0.36622321

00:23:15.170 --> 00:23:15.874 their process,
NOTE Confidence: 0.36622321

00:23:15.880 --> 00:23:18.358 it's because of oxidized lipid species.
NOTE Confidence: 0.36622321

00:23:18.360 --> 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 --> 00:23:25.178 several groups of fatty acids.
NOTE Confidence: 0.36622321

00:23:25.180 --> 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 --> 00:23:31.220 non chain and a very long chain fatty acids.
NOTE Confidence: 0.36622321

00:23:31.220 --> 00:23:33.635 I want you to pay attention on
NOTE Confidence: 0.36622321

00:23:33.635 --> 00:23:35.897 the non gene fatty acids such

NOTE Confidence: 0.36622321

00:23:35.897 --> 00:23:37.944 as POAOA and arachidonic acid.

NOTE Confidence: 0.36622321

00:23:37.944 --> 00:23:40.440 Here we checked all of it.

NOTE Confidence: 0.36622321

00:23:40.440 --> 00:23:43.455 So in this case when we look at the

NOTE Confidence: 0.36622321

00:23:43.455 --> 00:23:46.978 map of fibrosis people have defined as

NOTE Confidence: 0.36622321

00:23:46.978 --> 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 --> 00:23:54.642 So in fact that you prefer it's

NOTE Confidence: 0.36622321

00:23:54.642 --> 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 --> 00:24:02.521 So finally you will see the final product

NOTE Confidence: 0.36622321

00:24:02.521 --> 00:24:05.923 is Poly unsaturated offset lipid species.

NOTE Confidence: 0.36622321

00:24:05.930 --> 00:24:08.186 So in this case we are

NOTE Confidence: 0.36622321

00:24:08.186 --> 00:24:10.550 thinking it should be involved.

NOTE Confidence: 0.36622321

00:24:10.550 --> 00:24:12.022 So what we did,

NOTE Confidence: 0.36622321

00:24:12.022 --> 00:24:14.987 we cultured the tumor cells with interferon

NOTE Confidence: 0.36622321

00:24:14.987 --> 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 --> 00:24:20.490 short term media change often.
NOTE Confidence: 0.36622321

00:24:20.490 --> 00:24:22.289 Then we look at the cell desk.
NOTE Confidence: 0.36622321

00:24:22.290 --> 00:24:24.495 It turns out that in the presence
NOTE Confidence: 0.36622321

00:24:24.495 --> 00:24:26.349 of a the tumor cell,
NOTE Confidence: 0.36622321

00:24:26.350 --> 00:24:28.194 death is dramatically increased.
NOTE Confidence: 0.36622321

00:24:28.194 --> 00:24:30.960 And keep in mind that these
NOTE Confidence: 0.36622321

00:24:31.045 --> 00:24:33.650 cell deaths can be completely
NOTE Confidence: 0.36622321

00:24:33.650 --> 00:24:35.734 blocked by THEODOSIS inhibitor.
NOTE Confidence: 0.36622321

00:24:35.740 --> 00:24:38.337 So it means this is really theodosis
NOTE Confidence: 0.36622321

00:24:38.337 --> 00:24:40.458 and this is repeated reproducible
NOTE Confidence: 0.36622321

00:24:40.458 --> 00:24:43.242 in P-16 and seven tumor cells
NOTE Confidence: 0.36622321

00:24:43.242 --> 00:24:45.099 in mouse and humans.
NOTE Confidence: 0.36622321

00:24:45.100 --> 00:24:49.164 So finally we want to see what has
NOTE Confidence: 0.36622321

00:24:49.164 --> 00:24:50.970 happened actually with electronic

NOTE Confidence: 0.36622321

00:24:50.970 --> 00:24:53.980 acid in the presence of in the

NOTE Confidence: 0.800287875454545

00:24:54.061 --> 00:24:57.110 field. So we cultured human cells

NOTE Confidence: 0.800287875454545

00:24:57.110 --> 00:24:59.690 with interfering with or without.

NOTE Confidence: 0.800287875454545

00:24:59.690 --> 00:25:03.176 E5 neighbored atonic acid we want

NOTE Confidence: 0.800287875454545

00:25:03.176 --> 00:25:06.629 to see where electronic acid goes.

NOTE Confidence: 0.800287875454545

00:25:06.630 --> 00:25:09.666 So in this case we made a CSL

NOTE Confidence: 0.800287875454545

00:25:09.666 --> 00:25:12.942 knockout and the width of tumor cells.

NOTE Confidence: 0.800287875454545

00:25:12.950 --> 00:25:14.868 We treat the cells in this way.

NOTE Confidence: 0.800287875454545

00:25:14.870 --> 00:25:17.510 Then we look at different oxygenated

NOTE Confidence: 0.800287875454545

00:25:17.510 --> 00:25:19.708 species because you may appreciate

NOTE Confidence: 0.800287875454545

00:25:19.708 --> 00:25:22.221 here what is the black box and

NOTE Confidence: 0.800287875454545

00:25:22.221 --> 00:25:24.709 the red bars are all deficient.

NOTE Confidence: 0.800287875454545

00:25:24.710 --> 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 --> 00:25:30.790 really promote.

NOTE Confidence: 0.800287875454545

00:25:30.790 --> 00:25:34.148 The incorporation of T5
NOTE Confidence: 0.800287875454545

00:25:34.148 --> 00:25:36.988 neighboured electronic acid in two
NOTE Confidence: 0.800287875454545

00:25:36.988 --> 00:25:39.260 different oxides lipid species.
NOTE Confidence: 0.800287875454545

00:25:39.260 --> 00:25:43.900 So this including PE18B16 PC 18.
NOTE Confidence: 0.800287875454545

00:25:43.900 --> 00:25:47.806 You can see from the slight ACL 1400.
NOTE Confidence: 0.800287875454545

00:25:47.806 --> 00:25:49.378 So in this case,
NOTE Confidence: 0.800287875454545

00:25:49.380 --> 00:25:52.980 what has in the gamma Dong look at the
NOTE Confidence: 0.800287875454545

00:25:52.980 --> 00:25:55.853 brooding expression of CCL 4 actually
NOTE Confidence: 0.800287875454545

00:25:55.853 --> 00:25:59.260 in film comma stimulate its expression,
NOTE Confidence: 0.800287875454545

00:25:59.260 --> 00:26:02.015 so this is slow transcriptional
NOTE Confidence: 0.800287875454545

00:26:02.015 --> 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 --> 00:26:11.440 in the ACL 4 promoter area,
NOTE Confidence: 0.800287875454545

00:26:11.440 --> 00:26:13.900 and the cheap shows actually
NOTE Confidence: 0.800287875454545

00:26:13.900 --> 00:26:15.376 this high occupancy.
NOTE Confidence: 0.800287875454545

00:26:15.380 --> 00:26:17.893 So we first did some in vivo

NOTE Confidence: 0.800287875454545
00:26:17.893 --> 00:26:20.200 studies to show the relevance.
NOTE Confidence: 0.800287875454545
00:26:20.200 --> 00:26:23.430 So in this case we made a ACL 4 knockout
NOTE Confidence: 0.800287875454545
00:26:23.512 --> 00:26:26.338 tumors in several tumor cell lines.
NOTE Confidence: 0.800287875454545
00:26:26.340 --> 00:26:29.409 You see a CS4 is gone and tumors are
NOTE Confidence: 0.800287875454545
00:26:29.409 --> 00:26:32.161 getting bigger and in vivo and when
NOTE Confidence: 0.800287875454545
00:26:32.161 --> 00:26:34.799 we did the combination therapy Ravi,
NOTE Confidence: 0.800287875454545
00:26:34.800 --> 00:26:37.968 Classic way we treated mice with AA and
NOTE Confidence: 0.800287875454545
00:26:37.968 --> 00:26:40.981 AA actually can partially control the
NOTE Confidence: 0.800287875454545
00:26:40.981 --> 00:26:43.656 tumor progression in several models,
NOTE Confidence: 0.800287875454545
00:26:43.660 --> 00:26:45.736 but keep in mind the A.
NOTE Confidence: 0.800287875454545
00:26:45.740 --> 00:26:47.665 He's a very small amount of concentration.
NOTE Confidence: 0.800287875454545
00:26:47.670 --> 00:26:49.518 You you cannot give too much and then
NOTE Confidence: 0.800287875454545
00:26:49.518 --> 00:26:51.747 you kill the mice because it's quite toxic.
NOTE Confidence: 0.800287875454545
00:26:51.750 --> 00:26:54.918 So we see the combination therapy can give
NOTE Confidence: 0.800287875454545
00:26:54.918 --> 00:26:57.968 you some benefits in the mouse model.
NOTE Confidence: 0.800287875454545

00:26:57.970 --> 00:27:00.994 So when you look at the patient
NOTE Confidence: 0.800287875454545

00:27:00.994 --> 00:27:03.729 with a CCL 4 expression,
NOTE Confidence: 0.800287875454545

00:27:03.730 --> 00:27:07.573 in fact high ACC for expression is
NOTE Confidence: 0.800287875454545

00:27:07.573 --> 00:27:10.850 positively associated with patient survival,
NOTE Confidence: 0.800287875454545

00:27:10.850 --> 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 --> 00:27:22.090 So we tested it not only like in tonic acid,
NOTE Confidence: 0.800287875454545

00:27:22.090 --> 00:27:24.436 we tested them other fatty acids
NOTE Confidence: 0.800287875454545

00:27:24.436 --> 00:27:25.609 as I mentioned,
NOTE Confidence: 0.800287875454545

00:27:25.610 --> 00:27:27.584 but what I conclude here don't
NOTE Confidence: 0.800287875454545

00:27:27.584 --> 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 --> 00:27:36.040 OA and POA can also participate in
NOTE Confidence: 0.800287875454545

00:27:36.176 --> 00:27:40.426 inducing the tumor cell process.
NOTE Confidence: 0.800287875454545

00:27:40.430 --> 00:27:43.720 All these essays are in the absence
NOTE Confidence: 0.800287875454545

00:27:43.720 --> 00:27:45.130 of synthetic compound.

NOTE Confidence: 0.800287875454545
00:27:45.130 --> 00:27:48.526 So indicating what we discovered actually.
NOTE Confidence: 0.800287875454545
00:27:48.530 --> 00:27:51.728 The effect specific fatty acids plus
NOTE Confidence: 0.800287875454545
00:27:51.728 --> 00:27:54.591 interferon gamma are the intrinsic
NOTE Confidence: 0.800287875454545
00:27:54.591 --> 00:27:56.514 philippoussis inducing mechanisms
NOTE Confidence: 0.800287875454545
00:27:56.514 --> 00:27:59.719 we are able to detect.
NOTE Confidence: 0.800287875454545
00:27:59.720 --> 00:28:02.444 Of course all the fatty acids
NOTE Confidence: 0.800287875454545
00:28:02.444 --> 00:28:04.740 species and interference in vivo,
NOTE Confidence: 0.800287875454545
00:28:04.740 --> 00:28:06.520 they are not synthetic combo.
NOTE Confidence: 0.800287875454545
00:28:06.520 --> 00:28:09.070 So this is another similar to
NOTE Confidence: 0.800287875454545
00:28:09.070 --> 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 --> 00:28:18.709 you need several.
NOTE Confidence: 0.800287875454545
00:28:18.709 --> 00:28:21.730 Effectors what we have discovered, actually.
NOTE Confidence: 0.800287875454545
00:28:21.730 --> 00:28:24.530 Tumor cell Philippoussis needs
NOTE Confidence: 0.800287875454545

00:28:24.530 --> 00:28:25.930 several factors,
NOTE Confidence: 0.800287875454545

00:28:25.930 --> 00:28:28.162 and interference is one of them
NOTE Confidence: 0.800287875454545

00:28:28.162 --> 00:28:30.610 and the fatty acids are another.
NOTE Confidence: 0.800287875454545

00:28:30.610 --> 00:28:35.630 So now that's the the the conclusion
NOTE Confidence: 0.800287875454545

00:28:35.630 --> 00:28:39.720 we have basically when you have the
NOTE Confidence: 0.800287875454545

00:28:39.720 --> 00:28:43.360 induction between C8 and tumor cells.
NOTE Confidence: 0.800287875454545

00:28:43.360 --> 00:28:45.950 Because this is one of the founding
NOTE Confidence: 0.800287875454545

00:28:45.950 --> 00:28:47.930 father of Tosis is another.
NOTE Confidence: 0.800287875454545

00:28:47.930 --> 00:28:50.090 I hope this becomes textbook.
NOTE Confidence: 0.800287875454545

00:28:50.090 --> 00:28:53.023 So fear of loss is is mediated
NOTE Confidence: 0.800287875454545

00:28:53.023 --> 00:28:54.280 and the recognition
NOTE Confidence: 0.637820824117647

00:28:54.367 --> 00:28:57.048 through the AC system and CSL 4.
NOTE Confidence: 0.637820824117647

00:28:57.050 --> 00:29:00.458 Maybe other factors will be involved as well
NOTE Confidence: 0.637820824117647

00:29:00.458 --> 00:29:04.148 and we are still working on the details.
NOTE Confidence: 0.637820824117647

00:29:04.150 --> 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.

NOTE Confidence: 0.637820824117647
00:29:12.170 --> 00:29:16.244 So what is the technical message here?
NOTE Confidence: 0.637820824117647
00:29:16.250 --> 00:29:18.714 You must fear of those is is
NOTE Confidence: 0.637820824117647
00:29:18.714 --> 00:29:21.348 a mode of action of Syria.
NOTE Confidence: 0.637820824117647
00:29:21.350 --> 00:29:23.766 And tumor Philippoussis is
NOTE Confidence: 0.637820824117647
00:29:23.766 --> 00:29:25.292 neural therapy mechanism.
NOTE Confidence: 0.637820824117647
00:29:25.292 --> 00:29:28.519 So if so we should think about
NOTE Confidence: 0.637820824117647
00:29:28.519 --> 00:29:30.990 the potential translation.
NOTE Confidence: 0.637820824117647
00:29:30.990 --> 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 --> 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 --> 00:29:49.290 So myself is a immunologist and when you
NOTE Confidence: 0.637820824117647
00:29:49.398 --> 00:29:53.514 talk to biologists and some other people,
NOTE Confidence: 0.637820824117647
00:29:53.520 --> 00:29:57.517 there is an idea or thought proposed
NOTE Confidence: 0.637820824117647

00:29:57.520 --> 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 --> 00:30:05.360 The tumor cells need a lot of nutrients.
NOTE Confidence: 0.637820824117647

00:30:05.360 --> 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 --> 00:30:13.710 So that's the way how the
NOTE Confidence: 0.637820824117647

00:30:13.710 --> 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 --> 00:30:20.506 I don't know, so let's see if this works.
NOTE Confidence: 0.637820824117647

00:30:20.510 --> 00:30:21.329 In that case,
NOTE Confidence: 0.637820824117647

00:30:21.329 --> 00:30:23.240 I invite you to think about the
NOTE Confidence: 0.637820824117647

00:30:23.306 --> 00:30:25.282 nutrients and metabolites in
NOTE Confidence: 0.637820824117647

00:30:25.282 --> 00:30:26.764 the cancer microenvironment.
NOTE Confidence: 0.637820824117647

00:30:26.770 --> 00:30:30.074 We know when the cells are exposed to
NOTE Confidence: 0.637820824117647

00:30:30.074 --> 00:30:31.996 different metabolites and nutrients

NOTE Confidence: 0.637820824117647
00:30:31.996 --> 00:30:34.048 in the particular environment,
NOTE Confidence: 0.637820824117647
00:30:34.050 --> 00:30:36.490 not only just human cells,
NOTE Confidence: 0.637820824117647
00:30:36.490 --> 00:30:38.584 but also these cells and disease
NOTE Confidence: 0.637820824117647
00:30:38.584 --> 00:30:40.450 and Macy's and other cells,
NOTE Confidence: 0.637820824117647
00:30:40.450 --> 00:30:42.562 they must be subject to the
NOTE Confidence: 0.637820824117647
00:30:42.562 --> 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 --> 00:30:47.010 Status must be changed.
NOTE Confidence: 0.637820824117647
00:30:47.010 --> 00:30:49.768 So it's a very simple way to
NOTE Confidence: 0.637820824117647
00:30:49.768 --> 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 --> 00:30:54.753 some groups have already discovered
NOTE Confidence: 0.637820824117647
00:30:54.753 --> 00:30:56.889 the T cells are dysfunctional
NOTE Confidence: 0.637820824117647
00:30:56.889 --> 00:30:59.214 in the tumor micro environment.
NOTE Confidence: 0.637820824117647
00:30:59.220 --> 00:31:01.660 You may say the T cells are exhausted.
NOTE Confidence: 0.637820824117647

00:31:01.660 --> 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 --> 00:31:08.002 pathways are involved in the regulation
NOTE Confidence: 0.637820824117647

00:31:08.002 --> 00:31:11.140 of tumor cell dysfunction and T cell
NOTE Confidence: 0.637820824117647

00:31:11.140 --> 00:31:13.580 dysfunctionality in the tumor environment.
NOTE Confidence: 0.637820824117647

00:31:13.580 --> 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 --> 00:31:24.150 This has, uh, evidence actually.
NOTE Confidence: 0.637820824117647

00:31:24.150 --> 00:31:25.848 People have reported some of them.
NOTE Confidence: 0.637820824117647

00:31:25.850 --> 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 --> 00:31:31.472 particularly succinate have has
NOTE Confidence: 0.637820824117647

00:31:31.472 --> 00:31:33.528 been studied in macrophages,
NOTE Confidence: 0.637820824117647

00:31:33.530 --> 00:31:35.590 minor cells and some others.

NOTE Confidence: 0.637820824117647
00:31:35.590 --> 00:31:38.308 And we are interested in Sam.
NOTE Confidence: 0.637820824117647
00:31:38.310 --> 00:31:40.249 So why we are interested in them,
NOTE Confidence: 0.637820824117647
00:31:40.250 --> 00:31:43.330 you will see why we're interested in them.
NOTE Confidence: 0.637820824117647
00:31:43.330 --> 00:31:44.401 So in fact,
NOTE Confidence: 0.637820824117647
00:31:44.401 --> 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 --> 00:31:56.620 so we cultured basically G cells with
NOTE Confidence: 0.637820824117647
00:31:56.620 --> 00:31:58.900 different amino acids in the media,
NOTE Confidence: 0.637820824117647
00:31:58.900 --> 00:32:00.695 but we manipulated the concentration
NOTE Confidence: 0.637820824117647
00:32:00.695 --> 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 --> 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 --> 00:32:14.858 my theory.
NOTE Confidence: 0.637820824117647
00:32:14.858 --> 00:32:17.228 So T cells cannot stand,
NOTE Confidence: 0.637820824117647

00:32:17.230 --> 00:32:20.210 they become very much evolution.
NOTE Confidence: 0.637820824117647

00:32:20.210 --> 00:32:24.074 And the cells do not express much
NOTE Confidence: 0.637820824117647

00:32:24.074 --> 00:32:24.626 interference.
NOTE Confidence: 0.637820824117647

00:32:24.630 --> 00:32:26.961 And then we did another way along
NOTE Confidence: 0.637820824117647

00:32:26.961 --> 00:32:29.270 means we add amino acids back.
NOTE Confidence: 0.637820824117647

00:32:29.270 --> 00:32:31.550 So it's a plus experiment.
NOTE Confidence: 0.637820824117647

00:32:31.550 --> 00:32:33.500 So in this case we calculate
NOTE Confidence: 0.637820824117647

00:32:33.500 --> 00:32:35.150 the cells with too much
NOTE Confidence: 0.73993483

00:32:35.150 --> 00:32:38.020 to induce the cell or
NOTE Confidence: 0.73993483

00:32:38.020 --> 00:32:39.168 dysfunctionality dysfunctional.
NOTE Confidence: 0.73993483

00:32:39.170 --> 00:32:42.170 They become embodied and reduce stereogram.
NOTE Confidence: 0.73993483

00:32:42.170 --> 00:32:45.188 You will see under this condition
NOTE Confidence: 0.73993483

00:32:45.188 --> 00:32:48.253 if we add methionine pack we
NOTE Confidence: 0.73993483

00:32:48.253 --> 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 --> 00:32:55.890 T cell function is improved.

NOTE Confidence: 0.73993483

00:32:55.890 --> 00:32:59.832 So indicating actually the T cells

NOTE Confidence: 0.73993483

00:32:59.832 --> 00:33:03.706 are very sensitive to the supply

NOTE Confidence: 0.73993483

00:33:03.706 --> 00:33:06.980 of methionine so and then we look

NOTE Confidence: 0.73993483

00:33:06.980 --> 00:33:08.990 at the methionine metabolic cycle.

NOTE Confidence: 0.73993483

00:33:08.990 --> 00:33:13.310 So in fact my theory can become same

NOTE Confidence: 0.73993483

00:33:13.310 --> 00:33:18.562 and you know Sam is a real donor for

NOTE Confidence: 0.73993483

00:33:18.562 --> 00:33:20.786 methylation so history modification.

NOTE Confidence: 0.73993483

00:33:20.790 --> 00:33:22.911 So that's the reason we want to

NOTE Confidence: 0.73993483

00:33:22.911 --> 00:33:25.122 look at some right so in this

NOTE Confidence: 0.73993483

00:33:25.122 --> 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 --> 00:33:34.205 with my film and you detect all the

NOTE Confidence: 0.73993483

00:33:34.205 --> 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

NOTE Confidence: 0.73993483

00:33:38.734 --> 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 --> 00:33:47.219 the culture and when you add it
NOTE Confidence: 0.73993483

00:33:47.219 --> 00:33:49.714 comes back and also you don't have
NOTE Confidence: 0.73993483

00:33:49.714 --> 00:33:52.290 them in the SH all those things
NOTE Confidence: 0.73993483

00:33:52.290 --> 00:33:54.750 but you supplement Matheny you can
NOTE Confidence: 0.73993483

00:33:54.831 --> 00:33:57.336 partially and important we cover.
NOTE Confidence: 0.73993483

00:33:57.340 --> 00:34:00.120 They are the intercellular ascend
NOTE Confidence: 0.73993483

00:34:00.120 --> 00:34:02.344 and intercellular other metabolites
NOTE Confidence: 0.73993483

00:34:02.344 --> 00:34:06.199 of of methionine, such as SH.
NOTE Confidence: 0.73993483

00:34:06.200 --> 00:34:10.314 So if so this must affect his notification.
NOTE Confidence: 0.73993483

00:34:10.314 --> 00:34:13.439 So when we in this case we look at this,
NOTE Confidence: 0.73993483

00:34:13.440 --> 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 --> 00:34:27.398 This is not only the case in in most cells,

NOTE Confidence: 0.73993483

00:34:27.400 --> 00:34:29.388 in too many cells the same thing

NOTE Confidence: 0.73993483

00:34:29.388 --> 00:34:30.629 and you supplement methionine

NOTE Confidence: 0.73993483

00:34:30.629 --> 00:34:32.299 which you can recover it.

NOTE Confidence: 0.73993483

00:34:32.300 --> 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 --> 00:34:40.818 Then we look at the primary cells T

NOTE Confidence: 0.73993483

00:34:40.818 --> 00:34:43.660 cells in the tumor micro in humans

NOTE Confidence: 0.73993483

00:34:43.660 --> 00:34:46.565 and the mouse and you will see

NOTE Confidence: 0.73993483

00:34:46.565 --> 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 --> 00:34:56.923 and so is in human CD8T cells

NOTE Confidence: 0.73993483

00:34:56.923 --> 00:34:59.287 in the tumor microenvironment.

NOTE Confidence: 0.73993483

00:34:59.290 --> 00:35:00.618 So in that case,

NOTE Confidence: 0.73993483

00:35:00.618 --> 00:35:03.370 this extreme case 7 and T machination

NOTE Confidence: 0.73993483

00:35:03.370 --> 00:35:06.090 must be functionally important.

NOTE Confidence: 0.73993483

00:35:06.090 --> 00:35:08.110 So to test this possibility,

NOTE Confidence: 0.73993483

00:35:08.110 --> 00:35:10.329 we made a total of 1 specific

NOTE Confidence: 0.73993483

00:35:10.329 --> 00:35:11.810 lookout in T cells.

NOTE Confidence: 0.73993483

00:35:11.810 --> 00:35:14.918 The reason is total one is the

NOTE Confidence: 0.73993483

00:35:14.918 --> 00:35:16.400 only endemic 8719 resolution.

NOTE Confidence: 0.73993483

00:35:16.400 --> 00:35:18.760 So when we made it look out in

NOTE Confidence: 0.73993483

00:35:18.831 --> 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 --> 00:35:25.440 becoming apoptotic and dysfunctional.

NOTE Confidence: 0.73993483

00:35:25.440 --> 00:35:28.026 So that's one way to go.

NOTE Confidence: 0.73993483

00:35:28.030 --> 00:35:29.380 Another way to go is.

NOTE Confidence: 0.73993483

00:35:29.380 --> 00:35:31.250 We supplement methionine in the

NOTE Confidence: 0.73993483

00:35:31.250 --> 00:35:33.840 tumor bearing mice in this condition.

NOTE Confidence: 0.73993483

00:35:33.840 --> 00:35:36.192 If you supplement then you reduce

NOTE Confidence: 0.73993483

00:35:36.192 --> 00:35:36.976 tumor growth,

NOTE Confidence: 0.73993483

00:35:36.980 --> 00:35:39.530 you will cover histone modification

NOTE Confidence: 0.73993483

00:35:39.530 --> 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 --> 00:35:50.270 we did in patient with cancer.

NOTE Confidence: 0.73993483

00:35:50.270 --> 00:35:53.210 So we supplemented methionine to the patient.

NOTE Confidence: 0.73993483

00:35:53.210 --> 00:35:54.890 Then we see the T cells.

NOTE Confidence: 0.73993483

00:35:54.890 --> 00:35:58.446 It turns out if you do so.

NOTE Confidence: 0.73993483

00:35:58.450 --> 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 --> 00:36:07.810 we cover even Step 5 expression.

NOTE Confidence: 0.73993483

00:36:07.810 --> 00:36:09.418 We checked all the other stuff

NOTE Confidence: 0.73993483

00:36:09.418 --> 00:36:11.230 because step five is most obvious.

NOTE Confidence: 0.73993483

00:36:11.230 --> 00:36:12.046 And furthermore,

NOTE Confidence: 0.73993483

00:36:12.046 --> 00:36:15.310 if you look at the second expression such

NOTE Confidence: 0.746410053636364

00:36:15.389 --> 00:36:17.950 as IO2, so before therapy, after,
NOTE Confidence: 0.746410053636364

00:36:17.950 --> 00:36:21.219 before, and after, you will see I2
NOTE Confidence: 0.746410053636364

00:36:21.219 --> 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 --> 00:36:29.000 controls the expression of.
NOTE Confidence: 0.746410053636364

00:36:29.000 --> 00:36:31.709 I of O2, then we first look
NOTE Confidence: 0.746410053636364

00:36:31.709 --> 00:36:33.960 at the possible mechanisms.
NOTE Confidence: 0.746410053636364

00:36:33.960 --> 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 --> 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 --> 00:36:47.440 with supernatant and with
NOTE Confidence: 0.746410053636364

00:36:47.510 --> 00:36:49.340 the maternal supplementation,
NOTE Confidence: 0.746410053636364

00:36:49.340 --> 00:36:52.148 methionine supplementation can recover
NOTE Confidence: 0.746410053636364

00:36:52.148 --> 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 --> 00:37:03.280 not only we cover the T cell,
NOTE Confidence: 0.746410053636364
00:37:03.280 --> 00:37:04.795 the the the,
NOTE Confidence: 0.746410053636364
00:37:04.795 --> 00:37:08.900 the the the the cheaper and also show
NOTE Confidence: 0.746410053636364
00:37:08.900 --> 00:37:11.498 H3K79 nations we covered and instead
NOTE Confidence: 0.746410053636364
00:37:11.498 --> 00:37:14.385 of having is recovered and I2 is
NOTE Confidence: 0.746410053636364
00:37:14.385 --> 00:37:16.539 recovered in both humans and mice.
NOTE Confidence: 0.746410053636364
00:37:16.540 --> 00:37:19.516 And finally we want to understand.
NOTE Confidence: 0.746410053636364
00:37:19.520 --> 00:37:22.080 If methionine is there,
NOTE Confidence: 0.746410053636364
00:37:22.080 --> 00:37:26.950 why the T cells cannot get better?
NOTE Confidence: 0.746410053636364
00:37:26.950 --> 00:37:29.104 So maybe the tumor cells all
NOTE Confidence: 0.746410053636364
00:37:29.104 --> 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 --> 00:37:37.717 We turned our attention to methionine
NOTE Confidence: 0.746410053636364
00:37:37.717 --> 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 --> 00:37:48.144 compare tumor cells and T cells in
NOTE Confidence: 0.746410053636364

00:37:48.144 --> 00:37:50.252 the same environment and actually
NOTE Confidence: 0.746410053636364

00:37:50.252 --> 00:37:53.409 the tumor cells express quite a lot
NOTE Confidence: 0.746410053636364

00:37:53.409 --> 00:37:56.750 of ACC for 3A2 is one of methionine.
NOTE Confidence: 0.746410053636364

00:37:56.750 --> 00:37:57.422 This product,
NOTE Confidence: 0.746410053636364

00:37:57.422 --> 00:38:00.800 so this is among A and this is protein.
NOTE Confidence: 0.746410053636364

00:38:00.800 --> 00:38:03.299 So this is T cells and many
NOTE Confidence: 0.746410053636364

00:38:03.299 --> 00:38:05.020 other transporters are similar,
NOTE Confidence: 0.746410053636364

00:38:05.020 --> 00:38:07.198 but they are quite some differences.
NOTE Confidence: 0.746410053636364

00:38:07.200 --> 00:38:09.712 So we are we continue to work on
NOTE Confidence: 0.746410053636364

00:38:09.712 --> 00:38:11.992 this space to define the different
NOTE Confidence: 0.746410053636364

00:38:11.992 --> 00:38:14.849 differences we are able to see and
NOTE Confidence: 0.746410053636364

00:38:14.849 --> 00:38:16.919 then to see the functionality.
NOTE Confidence: 0.746410053636364

00:38:16.920 --> 00:38:18.848 So this suggests maybe
NOTE Confidence: 0.716931126428571

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

NOTE Confidence: 0.716931126428571
00:38:22.628 --> 00:38:25.280 expressed in the tumor cells is
NOTE Confidence: 0.716931126428571
00:38:25.359 --> 00:38:27.427 functionally important if so.
NOTE Confidence: 0.716931126428571
00:38:27.430 --> 00:38:32.216 We make a knocking down SLC 43A2.
NOTE Confidence: 0.716931126428571
00:38:32.216 --> 00:38:34.598 In the commercials then we start to
NOTE Confidence: 0.716931126428571
00:38:34.598 --> 00:38:36.110 capture the human cells with cells.
NOTE Confidence: 0.716931126428571
00:38:36.110 --> 00:38:38.958 OK, so you can see actually the T
NOTE Confidence: 0.716931126428571
00:38:38.958 --> 00:38:41.826 cells are becoming less able to
NOTE Confidence: 0.716931126428571
00:38:41.826 --> 00:38:44.406 reach the functions are recovered.
NOTE Confidence: 0.716931126428571
00:38:44.410 --> 00:38:48.513 So indicating ACC for this 382 is important.
NOTE Confidence: 0.716931126428571
00:38:48.513 --> 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 --> 00:38:57.430 382 in the tumor cells.
NOTE Confidence: 0.716931126428571
00:38:57.430 --> 00:39:00.406 USC actually the tumor is smaller
NOTE Confidence: 0.716931126428571
00:39:00.406 --> 00:39:03.080 in the immune competence system.
NOTE Confidence: 0.716931126428571

00:39:03.080 --> 00:39:04.809 The key cells in terms of their
NOTE Confidence: 0.716931126428571

00:39:04.809 --> 00:39:06.640 number and their function are better.
NOTE Confidence: 0.716931126428571

00:39:06.640 --> 00:39:08.579 This is not only in one model.
NOTE Confidence: 0.716931126428571

00:39:08.580 --> 00:39:11.276 In several models we can see the case.
NOTE Confidence: 0.716931126428571

00:39:11.280 --> 00:39:15.106 So what we have here is a summary we
NOTE Confidence: 0.716931126428571

00:39:15.106 --> 00:39:17.536 see in the tumor microenvironment,
NOTE Confidence: 0.716931126428571

00:39:17.540 --> 00:39:20.465 tumor cells express high levels
NOTE Confidence: 0.716931126428571

00:39:20.465 --> 00:39:21.635 of transporter.
NOTE Confidence: 0.716931126428571

00:39:21.640 --> 00:39:25.232 For methionine it's ACC 4382
NOTE Confidence: 0.716931126428571

00:39:25.232 --> 00:39:27.436 outcompete T cells 4.
NOTE Confidence: 0.716931126428571

00:39:27.440 --> 00:39:30.448 The only surprise when T cells do not
NOTE Confidence: 0.716931126428571

00:39:30.448 --> 00:39:33.366 get methionine and the T cells have
NOTE Confidence: 0.716931126428571

00:39:33.366 --> 00:39:35.645 insufficient sense Earth myself honor.
NOTE Confidence: 0.716931126428571

00:39:35.645 --> 00:39:38.554 Therefore they cannot successfully
NOTE Confidence: 0.716931126428571

00:39:38.554 --> 00:39:41.743 do the H3K790 maceration and
NOTE Confidence: 0.716931126428571

00:39:41.743 --> 00:39:43.947 therefore regulate stats fab.

NOTE Confidence: 0.716931126428571

00:39:43.950 --> 00:39:47.094 And as a consequence this affect the TCL

NOTE Confidence: 0.716931126428571

00:39:47.094 --> 00:39:49.309 functionality and the T cell survival.

NOTE Confidence: 0.716931126428571

00:39:49.310 --> 00:39:51.254 So what we suggest here maybe

NOTE Confidence: 0.716931126428571

00:39:51.254 --> 00:39:54.406 you know we can either we do

NOTE Confidence: 0.716931126428571

00:39:54.406 --> 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 --> 00:39:59.665 Maybe we can particularly target

NOTE Confidence: 0.716931126428571

00:39:59.665 --> 00:40:03.225 the tumor as you C for 3/8 to

NOTE Confidence: 0.716931126428571

00:40:03.225 --> 00:40:05.465 the rescue T cell functionality.

NOTE Confidence: 0.716931126428571

00:40:05.470 --> 00:40:09.294 So now it comes back to the question

NOTE Confidence: 0.716931126428571

00:40:09.294 --> 00:40:12.660 we asked. So can we stop themselves?

NOTE Confidence: 0.716931126428571

00:40:12.660 --> 00:40:14.658 Can we stop to myself, to this?

NOTE Confidence: 0.716931126428571

00:40:14.658 --> 00:40:15.720 Yes, we can.

NOTE Confidence: 0.716931126428571

00:40:15.720 --> 00:40:18.438 You must ask really needed method.

NOTE Confidence: 0.716931126428571

00:40:18.440 --> 00:40:19.535 Earth one example.

NOTE Confidence: 0.716931126428571

00:40:19.535 --> 00:40:22.615 But the poverty is if you stop yourself
NOTE Confidence: 0.716931126428571

00:40:22.615 --> 00:40:26.289 to death, you also stop T cells to death.
NOTE Confidence: 0.716931126428571

00:40:26.290 --> 00:40:29.602 Under the AIDS and who kills the tumor cells?
NOTE Confidence: 0.716931126428571

00:40:29.610 --> 00:40:30.750 The T cells?
NOTE Confidence: 0.716931126428571

00:40:30.750 --> 00:40:31.510 Tumor cells.
NOTE Confidence: 0.716931126428571

00:40:31.510 --> 00:40:33.010 So that's why what we say.
NOTE Confidence: 0.716931126428571

00:40:33.010 --> 00:40:35.726 If you want to stop human cells
NOTE Confidence: 0.716931126428571

00:40:35.726 --> 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 --> 00:40:53.330 So that's why we need to be really
NOTE Confidence: 0.716931126428571

00:40:53.330 --> 00:40:56.257 smart to consider not only just.
NOTE Confidence: 0.716931126428571

00:40:56.260 --> 00:40:57.736 To, to the tumors,
NOTE Confidence: 0.716931126428571

00:40:57.736 --> 00:41:00.619 but we have also considered the T cells.
NOTE Confidence: 0.716931126428571

00:41:00.620 --> 00:41:02.832 So now we ask the question again

NOTE Confidence: 0.716931126428571

00:41:02.832 --> 00:41:05.398 as I put it at the beginning.

NOTE Confidence: 0.716931126428571

00:41:05.400 --> 00:41:08.568 So what is next in terms of telling what

NOTE Confidence: 0.716931126428571

00:41:08.568 --> 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 --> 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 --> 00:41:25.358 successful to cure some patients.

NOTE Confidence: 0.716931126428571

00:41:25.360 --> 00:41:27.488 We already know this,

NOTE Confidence: 0.716931126428571

00:41:27.488 --> 00:41:29.616 indicating the powerful reason.

NOTE Confidence: 0.716931126428571

00:41:29.620 --> 00:41:31.985 The whole powerful is immune

NOTE Confidence: 0.716931126428571

00:41:31.985 --> 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 --> 00:41:41.633 And the further T cells remember to kill

NOTE Confidence: 0.716931126428571

00:41:41.633 --> 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 --> 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 --> 00:41:56.970 I appreciate the contribution from several

NOTE Confidence: 0.716931126428571

00:41:57.062 --> 00:42:00.226 very tentative federal as I did here.

NOTE Confidence: 0.716931126428571

00:42:00.230 --> 00:42:01.530 Some of them are faculty,

NOTE Confidence: 0.868589628571429

00:42:01.530 --> 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 --> 00:42:10.928 talk about the PD1 video one study and

NOTE Confidence: 0.868589628571429

00:42:10.928 --> 00:42:13.388 some others it was a collaboration

NOTE Confidence: 0.868589628571429

00:42:13.466 --> 00:42:15.786 with and I have quite a few,

NOTE Confidence: 0.868589628571429

00:42:15.790 --> 00:42:19.630 some few other collaborators

NOTE Confidence: 0.868589628571429

00:42:19.630 --> 00:42:21.940 in the United States and.

NOTE Confidence: 0.868589628571429

00:42:21.940 --> 00:42:23.112 And in other places,

NOTE Confidence: 0.868589628571429
00:42:23.112 --> 00:42:25.300 thank you for your attention and looking
NOTE Confidence: 0.868589628571429
00:42:25.300 --> 00:42:27.526 forward to your comments and questions.
NOTE Confidence: 0.5026026
00:42:35.320 --> 00:42:35.710 Question.
NOTE Confidence: 0.799502731111111
00:42:38.490 --> 00:42:39.958 Thank you over here.
NOTE Confidence: 0.799502731111111
00:42:39.958 --> 00:42:41.793 So thank you very much.
NOTE Confidence: 0.799502731111111
00:42:41.800 --> 00:42:43.380 Much appreciated.
NOTE Confidence: 0.799502731111111
00:42:43.380 --> 00:42:44.854 Presentation understood correctly,
NOTE Confidence: 0.799502731111111
00:42:44.854 --> 00:42:46.885 you showed that the rock, correct?
NOTE Confidence: 0.799502731111111
00:42:46.885 --> 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 --> 00:43:01.262 inside the cell, two per cell,
NOTE Confidence: 0.75131066
00:43:01.262 --> 00:43:04.060 that's undergoing the fructose this
NOTE Confidence: 0.75131066
00:43:04.060 --> 00:43:06.377 kind of objectively by the elements for
NOTE Confidence: 0.75131066
00:43:06.377 --> 00:43:08.700 others to see what's elevated threat?
NOTE Confidence: 0.8264526725
00:43:11.100 --> 00:43:13.555 It is surveyed, but there
NOTE Confidence: 0.8264526725

00:43:13.555 --> 00:43:15.520 are thousands of. Liberal.
NOTE Confidence: 0.730154073636363

00:43:17.020 --> 00:43:19.212 Right. So in response,
NOTE Confidence: 0.730154073636363

00:43:19.212 --> 00:43:23.290 So what we have done actually we
NOTE Confidence: 0.730154073636363

00:43:23.290 --> 00:43:27.400 detected electronic acids in the tumor
NOTE Confidence: 0.730154073636363

00:43:27.400 --> 00:43:30.930 microenvironment in the tumor floats.
NOTE Confidence: 0.730154073636363

00:43:30.930 --> 00:43:33.510 So the question is very tricky.
NOTE Confidence: 0.730154073636363

00:43:33.510 --> 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 --> 00:43:39.865 but if you have very high concentration
NOTE Confidence: 0.730154073636363

00:43:39.865 --> 00:43:41.352 you kill everything. Right.
NOTE Confidence: 0.730154073636363

00:43:41.352 --> 00:43:44.488 So, so, so The thing is you have
NOTE Confidence: 0.730154073636363

00:43:44.488 --> 00:43:47.877 to have two things simultaneously,
NOTE Confidence: 0.730154073636363

00:43:47.880 --> 00:43:51.884 one is interfering, another is doing acid.
NOTE Confidence: 0.730154073636363

00:43:51.884 --> 00:43:54.940 So that's a play you have to go.
NOTE Confidence: 0.730154073636363

00:43:54.940 --> 00:43:57.844 Yeah, we did not systemically to
NOTE Confidence: 0.730154073636363

00:43:57.844 --> 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 --> 00:44:05.417 There are some report in that space.
NOTE Confidence: 0.730154073636363
00:44:05.420 --> 00:44:07.268 There are technical challenges
NOTE Confidence: 0.730154073636363
00:44:07.268 --> 00:44:09.116 in in that situation.
NOTE Confidence: 0.730154073636363
00:44:09.120 --> 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 --> 00:44:14.726 For example,
NOTE Confidence: 0.730154073636363
00:44:14.726 --> 00:44:18.066 we really dynamically monitor the
NOTE Confidence: 0.730154073636363
00:44:18.066 --> 00:44:21.337 metabolic environment when the sales
NOTE Confidence: 0.730154073636363
00:44:21.337 --> 00:44:24.853 either become able to or philanthropic
NOTE Confidence: 0.730154073636363
00:44:24.853 --> 00:44:27.489 whether there's any difference.
NOTE Confidence: 0.730154073636363
00:44:27.490 --> 00:44:31.018 In this case, we need to have props.
NOTE Confidence: 0.730154073636363
00:44:31.018 --> 00:44:32.650 It's a real property.
NOTE Confidence: 0.730154073636363
00:44:32.650 --> 00:44:34.110 We follow these people.
NOTE Confidence: 0.730154073636363
00:44:34.110 --> 00:44:36.960 Maybe some of you are smart and and
NOTE Confidence: 0.730154073636363

00:44:36.960 --> 00:44:39.304 have tools we can we can do that.

NOTE Confidence: 0.730154073636363

00:44:39.310 --> 00:44:41.277 So one day it could be done.

NOTE Confidence: 0.730154073636363

00:44:41.280 --> 00:44:44.234 You know, just a trace where it

NOTE Confidence: 0.730154073636363

00:44:44.234 --> 00:44:47.520 goes and how high the levels are,

NOTE Confidence: 0.730154073636363

00:44:47.520 --> 00:44:49.020 yeah.

NOTE Confidence: 0.730154073636363

00:44:49.020 --> 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 --> 00:45:04.670 Struck.

NOTE Confidence: 0.891422631

00:45:15.750 --> 00:45:17.700 Great question actually.

NOTE Confidence: 0.891422631

00:45:17.700 --> 00:45:22.250 So as far as my understanding is,

NOTE Confidence: 0.891422631

00:45:22.250 --> 00:45:26.514 you know when we look at the Philippoussis.

NOTE Confidence: 0.891422631

00:45:26.520 --> 00:45:28.602 It's all the different ways how

NOTE Confidence: 0.891422631

00:45:28.602 --> 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 --> 00:45:35.786 executive genes which have been

NOTE Confidence: 0.891422631

00:45:35.786 --> 00:45:38.414 well defined in enable those poses,

NOTE Confidence: 0.891422631

00:45:38.414 --> 00:45:41.738 right but for fear of nosis,

NOTE Confidence: 0.891422631

00:45:41.740 --> 00:45:44.326 it's really about the membrane and

NOTE Confidence: 0.891422631

00:45:44.326 --> 00:45:46.605 damage so mediated by oxygenic

NOTE Confidence: 0.891422631

00:45:46.605 --> 00:45:48.980 species that's what we know.

NOTE Confidence: 0.891422631

00:45:48.980 --> 00:45:53.076 So therefore so very direct question when you

NOTE Confidence: 0.891422631

00:45:53.076 --> 00:45:56.626 asked whether the factors what we studied.

NOTE Confidence: 0.891422631

00:45:56.630 --> 00:45:59.326 Or whoever studied have

NOTE Confidence: 0.891422631

00:45:59.326 --> 00:46:01.132 directly effect on the membrane,

NOTE Confidence: 0.891422631

00:46:01.132 --> 00:46:03.690 let's say maybe the nails and the structures,

NOTE Confidence: 0.891422631

00:46:03.690 --> 00:46:04.599 those things, right?

NOTE Confidence: 0.891422631

00:46:04.599 --> 00:46:06.114 We didn't go that far.

NOTE Confidence: 0.891422631

00:46:06.120 --> 00:46:09.297 I even don't have the expertise to do that.

NOTE Confidence: 0.891422631

00:46:09.300 --> 00:46:12.800 So, so I think it's very nice way to go.

NOTE Confidence: 0.891422631

00:46:12.800 --> 00:46:15.110 So one way to to do it is we have

NOTE Confidence: 0.891422631

00:46:15.183 --> 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 --> 00:46:21.376 inhibit species, that's what we know.
NOTE Confidence: 0.891422631

00:46:21.380 --> 00:46:23.872 But we don't look at the structure
NOTE Confidence: 0.891422631

00:46:23.872 --> 00:46:26.508 to monitor how the sector changes
NOTE Confidence: 0.891422631

00:46:26.508 --> 00:46:27.999 could be unacceptable.
NOTE Confidence: 0.891422631

00:46:28.000 --> 00:46:29.956 Yeah, but we didn't know that.
NOTE Confidence: 0.891422631

00:46:29.960 --> 00:46:31.560 We even don't know how to do that.
NOTE Confidence: 0.891422631

00:46:31.560 --> 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 --> 00:46:37.880 if we have some proxy,
NOTE Confidence: 0.891422631

00:46:37.880 --> 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 --> 00:46:42.100 you have some ideas in that space.
NOTE Confidence: 0.891422631

00:46:42.100 --> 00:46:44.377 We were chatting it on maybe this,
NOTE Confidence: 0.891422631

00:46:44.377 --> 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 --> 00:46:50.695 people feel or feel to see if

NOTE Confidence: 0.891422631

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

NOTE Confidence: 0.891422631

00:46:52.680 --> 00:46:54.263 So what are you talking about, right.

NOTE Confidence: 0.891422631

00:46:54.263 --> 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 --> 00:47:01.419 can be activated, it can be regulated.

NOTE Confidence: 0.891422631

00:47:01.420 --> 00:47:03.255 So that's very difficult mechanism, right?

NOTE Confidence: 0.891422631

00:47:03.255 --> 00:47:04.080 So therefore it's.

NOTE Confidence: 0.891422631

00:47:04.080 --> 00:47:05.180 The program still this.

NOTE Confidence: 0.8401680775

00:47:21.780 --> 00:47:23.100 Yes, yes, yes.

NOTE Confidence: 0.8401680775

00:47:23.100 --> 00:47:25.300 That's also a good point.

NOTE Confidence: 0.8401680775

00:47:25.300 --> 00:47:27.554 So you know, when you design experiments,

NOTE Confidence: 0.8401680775

00:47:27.560 --> 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 --> 00:47:33.205 So therefore we didn't look

NOTE Confidence: 0.8401680775

00:47:33.205 --> 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 --> 00:47:40.210 different types of cells.
NOTE Confidence: 0.8401680775

00:47:40.210 --> 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 --> 00:47:48.064 They may have different
NOTE Confidence: 0.8401680775

00:47:48.064 --> 00:47:49.930 mechanisms to control.
NOTE Confidence: 0.8401680775

00:47:49.930 --> 00:47:52.918 So that's typically something we are
NOTE Confidence: 0.8401680775

00:47:52.918 --> 00:47:55.063 working on including for example,
NOTE Confidence: 0.8401680775

00:47:55.063 --> 00:47:56.206 how about megabytes?
NOTE Confidence: 0.8401680775

00:47:56.210 --> 00:47:58.030 How about T cells, right?
NOTE Confidence: 0.8401680775

00:47:58.030 --> 00:48:01.478 So I guess this is not an mechanism
NOTE Confidence: 0.8401680775

00:48:01.478 --> 00:48:03.450 exclusively for tumor cells.
NOTE Confidence: 0.8401680775

00:48:03.450 --> 00:48:04.810 There is no such thing.
NOTE Confidence: 0.8401680775

00:48:04.810 --> 00:48:07.510 So the mechanism could be functional

NOTE Confidence: 0.8401680775

00:48:07.510 --> 00:48:09.890 for other types of cells.

NOTE Confidence: 0.8401680775

00:48:09.890 --> 00:48:11.243 The question is?

NOTE Confidence: 0.8401680775

00:48:11.243 --> 00:48:13.949 When and how and which one?

NOTE Confidence: 0.8401680775

00:48:13.950 --> 00:48:14.685 We are working with this

NOTE Confidence: 0.8401680775

00:48:14.685 --> 00:48:15.740 but you can go on details.

NOTE Confidence: 0.7144543

00:48:19.730 --> 00:48:21.612 This idea the only competition

NOTE Confidence: 0.7144543

00:48:21.612 --> 00:48:22.866 out of competition

NOTE Confidence: 0.73984185

00:48:22.870 --> 00:48:23.659 of tumor cells.

NOTE Confidence: 0.8403232

00:48:26.290 --> 00:48:28.942 Do you think it's the growth across

NOTE Confidence: 0.8403232

00:48:28.942 --> 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 --> 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 --> 00:48:44.620 substrate have you what are your thoughts
NOTE Confidence: 0.621225726666667

00:48:44.630 --> 00:48:46.256 about that? Yes it's it's OK.
NOTE Confidence: 0.621225726666667

00:48:46.260 --> 00:48:47.388 It's a great question.
NOTE Confidence: 0.621225726666667

00:48:47.388 --> 00:48:48.832 It's hard to address. OK.
NOTE Confidence: 0.621225726666667

00:48:48.832 --> 00:48:50.704 So what we started to look
NOTE Confidence: 0.621225726666667

00:48:50.704 --> 00:48:53.138 at since even in the same we
NOTE Confidence: 0.621225726666667

00:48:53.138 --> 00:48:54.558 have recently paper just.
NOTE Confidence: 0.621225726666667

00:48:54.560 --> 00:48:57.014 Eventually you even in the same
NOTE Confidence: 0.621225726666667

00:48:57.014 --> 00:48:59.724 human parent such as liver right?
NOTE Confidence: 0.621225726666667

00:48:59.724 --> 00:49:03.483 We reach locate the neighbor metastasis HCC.
NOTE Confidence: 0.621225726666667

00:49:03.490 --> 00:49:06.210 So in the liver microenvironment
NOTE Confidence: 0.621225726666667

00:49:06.210 --> 00:49:08.930 you have HC and metastasis.
NOTE Confidence: 0.621225726666667

00:49:08.930 --> 00:49:12.129 Then we look at even the same
NOTE Confidence: 0.621225726666667

00:49:12.129 --> 00:49:13.662 macrophage subsets they are
NOTE Confidence: 0.621225726666667

00:49:13.662 --> 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 --> 00:49:21.556 are different, therefore their

NOTE Confidence: 0.85659679

00:49:21.556 --> 00:49:23.748 metabolic needs are different.

NOTE Confidence: 0.85659679

00:49:23.750 --> 00:49:26.565 How does it happen? Right.

NOTE Confidence: 0.85659679

00:49:26.565 --> 00:49:29.290 We have nuclear. You know,

NOTE Confidence: 0.85659679

00:49:29.290 --> 00:49:31.186 but we are still working on those things.

NOTE Confidence: 0.85659679

00:49:31.190 --> 00:49:35.552 So we we work more on the the way how the

NOTE Confidence: 0.85659679

00:49:35.552 --> 00:49:39.688 sales die because we believe this is this,

NOTE Confidence: 0.85659679

00:49:39.690 --> 00:49:41.750 these matters are not.

NOTE Confidence: 0.85659679

00:49:41.750 --> 00:49:45.620 So so the thought is.

NOTE Confidence: 0.85659679

00:49:45.620 --> 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 --> 00:49:52.668 The same cells in different metabolic

NOTE Confidence: 0.85659679

00:49:52.668 --> 00:49:55.653 environment may have to adapt this

NOTE Confidence: 0.85659679

00:49:55.653 --> 00:49:58.264 particular environmental survive #1, right?

NOTE Confidence: 0.85659679

00:49:58.264 --> 00:50:00.268 So then whether they can expand.

NOTE Confidence: 0.85659679

00:50:00.270 --> 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 --> 00:50:11.468 and genetics in the recent days,
NOTE Confidence: 0.85659679

00:50:11.470 --> 00:50:13.305 people really moved to the
NOTE Confidence: 0.85659679

00:50:13.305 --> 00:50:15.140 field of metabolism because the
NOTE Confidence: 0.85659679

00:50:15.205 --> 00:50:17.229 metabolism is somehow universal.
NOTE Confidence: 0.85659679

00:50:17.230 --> 00:50:19.280 It must be regulated in
NOTE Confidence: 0.85659679

00:50:19.280 --> 00:50:21.330 one way or versus another.
NOTE Confidence: 0.85659679

00:50:21.330 --> 00:50:23.498 So that's that's why I we we have
NOTE Confidence: 0.85659679

00:50:23.498 --> 00:50:24.864 high interest in this, right.
NOTE Confidence: 0.85659679

00:50:24.864 --> 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 --> 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 --> 00:50:39.420 So why do you think?

NOTE Confidence: 0.788417526666667
00:50:42.910 --> 00:50:43.969 Yes, that's, uh,
NOTE Confidence: 0.788417526666667
00:50:43.969 --> 00:50:46.087 it's it's a great question actually.
NOTE Confidence: 0.788417526666667
00:50:46.090 --> 00:50:49.950 It's. So it turns out this is a, it's a,
NOTE Confidence: 0.788417526666667
00:50:49.950 --> 00:50:52.787 it's a, it's a biochemical question.
NOTE Confidence: 0.788417526666667
00:50:52.787 --> 00:50:57.083 OK. So if you look at the constant,
NOTE Confidence: 0.788417526666667
00:50:57.090 --> 00:51:00.648 it's the lowest among all the
NOTE Confidence: 0.788417526666667
00:51:00.648 --> 00:51:02.427 other isomorphous modifiers.
NOTE Confidence: 0.788417526666667
00:51:02.430 --> 00:51:04.908 So that's why it's. So it's sensitive.
NOTE Confidence: 0.788417526666667
00:51:04.910 --> 00:51:08.068 It's. Yeah, yeah, yeah. Yeah.
NOTE Confidence: 0.788417526666667
00:51:08.068 --> 00:51:10.895 Yeah. So so this actually this.
NOTE Confidence: 0.788417526666667
00:51:10.895 --> 00:51:12.475 This information is available.
NOTE Confidence: 0.788417526666667
00:51:12.480 --> 00:51:13.780 It's not from us,
NOTE Confidence: 0.788417526666667
00:51:13.780 --> 00:51:16.512 it's from when we figured out that it's
NOTE Confidence: 0.788417526666667
00:51:16.512 --> 00:51:19.336 needed on and we asked the same question,
NOTE Confidence: 0.788417526666667
00:51:19.340 --> 00:51:21.020 ask to ourselves why we
NOTE Confidence: 0.788417526666667

00:51:21.020 --> 00:51:22.364 see this is predominant,
NOTE Confidence: 0.788417526666667

00:51:22.370 --> 00:51:23.945 the others are not so dramatic and
NOTE Confidence: 0.788417526666667

00:51:23.945 --> 00:51:25.539 then we know it's publications.
NOTE Confidence: 0.788417526666667

00:51:25.540 --> 00:51:27.448 It turns out that's the case.
NOTE Confidence: 0.788417526666667

00:51:27.450 --> 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 --> 00:51:37.450 The cancer cells undergoing sister type.
NOTE Confidence: 0.642862722

00:51:40.770 --> 00:51:44.000 Um, I working on this.
NOTE Confidence: 0.642862722

00:51:44.000 --> 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 --> 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 --> 00:51:55.587 Actually we initially I was really puzzled.
NOTE Confidence: 0.79161745

00:51:55.590 --> 00:51:58.515 Puzzled by what when you see I show you
NOTE Confidence: 0.79161745

00:51:58.515 --> 00:52:01.081 the picture actually when you treat
NOTE Confidence: 0.79161745

00:52:01.081 --> 00:52:05.989 the mice with PDL one and the CDA 4.

NOTE Confidence: 0.79161745

00:52:05.990 --> 00:52:08.822 And under this condition you treated

NOTE Confidence: 0.79161745

00:52:08.822 --> 00:52:11.600 mice with fair process inhibitor?

NOTE Confidence: 0.79161745

00:52:11.600 --> 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 --> 00:52:19.470 we we we know this is able to see

NOTE Confidence: 0.79161745

00:52:19.470 --> 00:52:20.958 the T cells kill tumor cells.

NOTE Confidence: 0.79161745

00:52:20.960 --> 00:52:22.616 It's even though this is caspase,

NOTE Confidence: 0.79161745

00:52:22.620 --> 00:52:24.540 and it's very well established,

NOTE Confidence: 0.79161745

00:52:24.540 --> 00:52:26.100 you cannot throw away all those

NOTE Confidence: 0.79161745

00:52:26.100 --> 00:52:28.160 things what people have known, right?

NOTE Confidence: 0.79161745

00:52:28.160 --> 00:52:32.920 So the only explanation is these across.

NOTE Confidence: 0.79161745

00:52:32.920 --> 00:52:34.719 So who is first, who is second,

NOTE Confidence: 0.79161745

00:52:34.720 --> 00:52:36.835 who is in the middle and who initiate what?

NOTE Confidence: 0.79161745

00:52:36.840 --> 00:52:39.290 Who emphasis what? Those kind of things.

NOTE Confidence: 0.79161745

00:52:39.290 --> 00:52:40.770 So we worked very hard,

NOTE Confidence: 0.79161745

00:52:40.770 --> 00:52:42.527 but we have no group so far.
NOTE Confidence: 0.79161745

00:52:42.530 --> 00:52:44.434 But we know there must be a gross.
NOTE Confidence: 0.69844595625

00:52:44.850 --> 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 --> 00:52:53.340 they show that the many monitors slight
NOTE Confidence: 0.43766722

00:52:56.170 --> 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 --> 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 --> 00:53:18.244 we ask pathology for always
NOTE Confidence: 0.756073513333333

00:53:18.244 --> 00:53:21.240 frustrated by PO1 as a biomarker or
NOTE Confidence: 0.756073513333333

00:53:21.240 --> 00:53:22.910 TMB like there's no good biomarkers.

NOTE Confidence: 0.810907434285714
00:53:24.930 --> 00:53:27.202 It sounds like you have about a number
NOTE Confidence: 0.810907434285714
00:53:27.202 --> 00:53:29.230 of potential molecules that could work
NOTE Confidence: 0.810907434285714
00:53:29.230 --> 00:53:31.300 as biomarkers, you know having the
NOTE Confidence: 0.810907434285714
00:53:31.300 --> 00:53:33.830 right transporters in the right place.
NOTE Confidence: 0.810907434285714
00:53:33.830 --> 00:53:36.942 Do you see any, any sort of immediate
NOTE Confidence: 0.810907434285714
00:53:36.942 --> 00:53:38.690 possibility of some of these as
NOTE Confidence: 0.810907434285714
00:53:38.690 --> 00:53:43.830 biomarkers for immunotherapy? Yeah, so.
NOTE Confidence: 0.815215711538462
00:53:43.830 --> 00:53:47.510 So I I guess this is it's quite a
NOTE Confidence: 0.815215711538462
00:53:47.621 --> 00:53:50.382 it's quite a depressing I would say.
NOTE Confidence: 0.815215711538462
00:53:50.382 --> 00:53:53.150 So when you located the biomarkers right,
NOTE Confidence: 0.815215711538462
00:53:53.150 --> 00:53:55.942 so it could be money you know perfectly
NOTE Confidence: 0.815215711538462
00:53:55.942 --> 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 --> 00:54:03.573 it the PD one or PDL one expression.
NOTE Confidence: 0.815215711538462
00:54:03.573 --> 00:54:06.300 So now after that you know it is PDL
NOTE Confidence: 0.815215711538462

00:54:06.364 --> 00:54:08.332 one expression and if they approve
NOTE Confidence: 0.815215711538462

00:54:08.332 --> 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 --> 00:54:17.110 So it's. It's not the way how how we know
NOTE Confidence: 0.815215711538462

00:54:17.110 --> 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 --> 00:54:23.220 we can really say.
NOTE Confidence: 0.815215711538462

00:54:23.220 --> 00:54:27.315 So the best way is well check all the
NOTE Confidence: 0.815215711538462

00:54:27.320 --> 00:54:29.925 social associated genes particularly protein
NOTE Confidence: 0.815215711538462

00:54:29.925 --> 00:54:33.520 levels whether this will give us something.
NOTE Confidence: 0.815215711538462

00:54:33.520 --> 00:54:37.696 You know so for example we looked at
NOTE Confidence: 0.815215711538462

00:54:37.700 --> 00:54:41.396 a CSR four expression when you see
NOTE Confidence: 0.815215711538462

00:54:41.396 --> 00:54:45.850 high ACR four expression may this may
NOTE Confidence: 0.815215711538462

00:54:45.850 --> 00:54:50.838 help can it is for BA real bellmaker.
NOTE Confidence: 0.815215711538462

00:54:50.840 --> 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 --> 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 --> 00:55:01.506 in patient, that's another story.
NOTE Confidence: 0.815215711538462
00:55:01.506 --> 00:55:03.558 We need to see the patient.
NOTE Confidence: 0.815215711538462
00:55:03.560 --> 00:55:05.636 That's why we appreciate your work.
NOTE Confidence: 0.815215711538462
00:55:05.640 --> 00:55:06.816 We need to see the patient.
NOTE Confidence: 0.815215711538462
00:55:06.820 --> 00:55:08.850 We need to see the tumors in
NOTE Confidence: 0.815215711538462
00:55:08.850 --> 00:55:10.849 patient and see what's going on.
NOTE Confidence: 0.815215711538462
00:55:10.850 --> 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 --> 00:56:11.950 any question you asked. Maybe just.
NOTE Confidence: 0.809215076
00:56:39.740 --> 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 --> 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 --> 00:57:01.246 it's obvious when we do immunotherapy.
NOTE Confidence: 0.683789309

00:57:01.250 --> 00:57:02.990 So that's the system we used.
NOTE Confidence: 0.683789309

00:57:02.990 --> 00:57:05.195 So actually in response to
NOTE Confidence: 0.683789309

00:57:05.195 --> 00:57:07.920 your question early on when you
NOTE Confidence: 0.683789309

00:57:07.920 --> 00:57:10.095 just give tomatoes 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 --> 00:57:14.958 cells are more or less functional.
NOTE Confidence: 0.683789309

00:57:14.960 --> 00:57:17.402 But under this condition we treated
NOTE Confidence: 0.683789309

00:57:17.402 --> 00:57:19.580 myself with ferocity and crypto.
NOTE Confidence: 0.683789309

00:57:19.580 --> 00:57:22.688 We hope, we hope we can see.
NOTE Confidence: 0.683789309

00:57:22.690 --> 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 --> 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 en-
vironment.
NOTE Confidence: 0.683789309

00:57:35.450 --> 00:57:39.648 How do we do that if you don't have
NOTE Confidence: 0.683789309

00:57:39.648 --> 00:57:42.733 a sufficient T cell infiltration?
NOTE Confidence: 0.683789309

00:57:42.740 --> 00:57:46.674 Even so, I guess we can manipulate
NOTE Confidence: 0.683789309

00:57:46.674 --> 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 --> 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 --> 00:57:56.554 So not all the patients are responsive
NOTE Confidence: 0.683789309

00:57:56.554 --> 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 --> 00:58:02.746 specially in this, in this way,
NOTE Confidence: 0.683789309

00:58:02.750 --> 00:58:05.870 another way we can do also maybe you know we
NOTE Confidence: 0.683789309

00:58:05.950 --> 00:58:09.149 have ways to improve the teacher trafficking,
NOTE Confidence: 0.683789309

00:58:09.150 --> 00:58:09.975 right?
NOTE Confidence: 0.683789309

00:58:09.975 --> 00:58:14.925 So, so, so far where do?
NOTE Confidence: 0.683789309

00:58:14.930 --> 00:58:16.566 A pure airplus mechanism.

NOTE Confidence: 0.683789309

00:58:16.566 --> 00:58:19.020 In the absence of immune system

NOTE Confidence: 0.683789309

00:58:19.098 --> 00:58:22.486 whether this is a valid approach, we don't.

NOTE Confidence: 0.683789309

00:58:22.486 --> 00:58:25.534 Maybe there's a way to go?

NOTE Confidence: 0.683789309

00:58:25.540 --> 00:58:29.420 Maybe radiation or chemo or something?

NOTE Confidence: 0.683789309

00:58:29.420 --> 00:58:30.564 Yes and a no.

NOTE Confidence: 0.683789309

00:58:30.564 --> 00:58:32.908 And also we have another paper I can

NOTE Confidence: 0.683789309

00:58:32.908 --> 00:58:35.140 mention this here and we have a paper

NOTE Confidence: 0.683789309

00:58:35.214 --> 00:58:37.554 to actually that's the first people

NOTE Confidence: 0.683789309

00:58:37.554 --> 00:58:40.504 talking about the effect of radiation

NOTE Confidence: 0.683789309

00:58:40.504 --> 00:58:44.656 is partially dependent on our fibrosis,

NOTE Confidence: 0.683789309

00:58:44.660 --> 00:58:47.215 but this fabulous especially again

NOTE Confidence: 0.683789309

00:58:47.215 --> 00:58:49.770 recognized by the immune system.

NOTE Confidence: 0.683789309

00:58:49.770 --> 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 --> 00:58:56.760 so that that's a cancer discovery people.

NOTE Confidence: 0.683789309

00:58:56.760 --> 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 --> 00:59:00.120 yeah.

NOTE Confidence: 0.46906483

00:59:02.440 --> 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.