Thank you all for joining us it’s a real privilege today to welcome our new chair of pathology at Yale, Doctor Chen who joined us on March 1st? So really right into the thick of it. And in the short time he’s been here he has Collaborated with all of us, particularly in his efforts to champion the testing efforts that were essential in our response to COVID.
Chen received his training in China and received his postgraduate training at Peking Medical College, his PhD in pathology at University of Pennsylvania and most recently had served as the chair of pathology immunology and Laboratory Medicine, as well as the chair of the center of dermatology at the Robert Wood Johnson Medical School in New Jersey. Chen’s career has been focused on the work in viral hepatitis liver cancer immunotherapy graph versus host disease, as well as cancer epigenetics, where he’s made important contributions in all of these areas.
Really understanding mechanisms of carcinogenesis defining cancer biomarkers and equally importantly developing new therapeutic approaches and we’re really so privileged to have Chen not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie, note not only as the new chair, but as a member of our Cancer Center, and this really gives us, I think, really great additional expertise and strength among the talent we have here. Thank you very much Charlie,
NOTE Confidence: 0.904578924179077
00:02:27.507 --> 00:02:30.579 GI pathologist so I’m actually practicing
NOTE Confidence: 0.904578924179077
00:02:30.580 --> 00:02:32.836 in the clinical
NOTE Confidence: 0.904578924179077
00:02:32.840 --> 00:02:36.036 service and I’m also a pretty
NOTE Confidence: 0.904578924179077
00:02:36.036 --> 00:02:37.806 good mouse pathologist in general,
NOTE Confidence: 0.904578924179077
00:02:37.810 --> 00:02:40.295 so I think basically I serve
NOTE Confidence: 0.904578924179077
00:02:40.300 --> 00:02:42.645 as a sort of expert
NOTE Confidence: 0.904578924179077
00:02:42.645 --> 00:02:44.200 consultant.

00:03:29.630 --> 00:03:30.818 So today
NOTE Confidence: 0.904578924179077
00:03:30.818 --> 00:03:32.600 I would adjust the
NOTE Confidence: 0.904578924179077
00:03:32.668 --> 00:03:34.216 top one of the you know.
NOTE Confidence: 0.904578924179077
00:03:34.220 --> 00:03:36.080 You know main research project
NOTE Confidence: 0.904578924179077
00:03:36.080 --> 00:03:37.568 and you might laboratory,
NOTE Confidence: 0.904578924179077
00:03:37.570 --> 00:03:39.796 which is sort of how to divide
NOTE Confidence: 0.904578924179077
00:03:39.796 --> 00:03:42.029 up how to developer mode.
NOTE Confidence: 0.904578924179077
00:03:42.030 --> 00:03:44.910 Effective email Sara pay for
NOTE Confidence: 0.904578924179077
00:03:44.910 --> 00:03:46.638 hyper cellular carcinoma.
OK, so good. So uh, as you know a better seller cars. Nobody is very deadly disease. You know it’s actually really they will come and you know we have almost 600,000 new cases a year globally. In contrast to many other type of cancers, mostly theology is a relatively well not. Mostly theology is a relatively well not. For instance, you can see it’s almost 80% of those cases are caused by two viruses, hepatitis B and hepatitis C virus is, and then the other, so you know it’s a toxin alcohol awesome.
Recently fatty liver disease and some metabolic liver disease. You know you know all contributed to the etiology of hyper server carcinoma. I think one thing in common is in majority of the cases an there is long standing. Monitor liver disease and then develop chronic. You know you know hepatitis and also cirrhosis, which is almost like a precancerous condition, and then become my father Cellular Carcinoma because of this uniquely theology and the pathogenesis there at
least two things we can think about.

Why is the best way to eliminate it’s, you know cancer is really with it is emitted, the ideology. So in this case, if you can eliminate hepatitis B, hepatitis C with. Pretty much he limited 80% of the of the widespread you know like seen vaccination against hepatitis speed, the incidence of liver cancer indeed has seen trending down in the hepatitis B.

Prevalent regions and so the other thing is.
Question is because there is a longstanding process for, you know, from the initial lever insult to the cancer formation is you already talked? We’re talking about a 20 to 30 years and then we do have very high risk population, so we know this high risk population, so this provides a window of opportunity for us to develop ball markers or something. Therapeutic interventions. In other words, we can identify the underlying pathogenesis and hopefully we can identify targets. And to intervene to prevent out trade. Now I’ve had this order carcinoma, so currently you know.
Unfortunately the you know, liver cancer therapy is really behind too many of other solid tumors. We did not have really big progress. You know, for hyper server carcinoma therapy and there is absolutely unmet need in this cancer, so we were transplantation can be considered as a curatives therapy. If we had identified the tumor earlier and also there is a lever available for their patients, those can be considered cured. Killer and the surgical resection is,
you know,
NOTE Confidence: 0.872145533561707
has been performed by the recurrence is,
NOTE Confidence: 0.872145533561707
you know it’s almost 70% of patients
NOTE Confidence: 0.872145533561707
after the surgical resection.
NOTE Confidence: 0.872145533561707
So overall,
NOTE Confidence: 0.872145533561707
with the typical therapy currently,
NOTE Confidence: 0.872145533561707
you know the three year survival
NOTE Confidence: 0.872145533561707
is still less than 20%.
NOTE Confidence: 0.872145533561707
And, uh, in about a 10 years ago that,
NOTE Confidence: 0.872145533561707
uh, one first therapy was approved,
NOTE Confidence: 0.872145533561707
which is arrive in a, you know.
NOTE Confidence: 0.872145533561707
So resonator is terrorism Chinese
NOTE Confidence: 0.872145533561707
inhibitor and so that only showed moderate
NOTE Confidence: 0.872145533561707
effect in the small number of patients.
NOTE Confidence: 0.872145533561707
And all only the pasta two or three years
NOTE Confidence: 0.872145533561707
we have seen in another momentum which
00:07:38.988 --> 00:07:42.070 is a checkpoint inhibitors role in the
00:07:42.070 --> 00:07:44.230 treatment of other Cellular Carcinoma.
00:07:44.230 --> 00:07:47.840 So we can talk a little bit more about the
00:07:47.929 --> 00:07:51.800 checkpoint inhibitors in nice to feel slides.
00:07:51.800 --> 00:07:52.912 So first of all,
00:07:52.912 --> 00:07:55.050 these are the tires in kind is
00:07:55.050 --> 00:07:57.045 currently being tried and approved
00:07:57.045 --> 00:08:01.524 of tested in hypothetical carcinoma.
00:08:01.524 --> 00:08:03.382 neighbor which is basically another
00:08:03.382 --> 00:08:05.416 version of the revenue and then
00:08:05.416 --> 00:08:07.239 the other tools also tested.
00:08:07.240 --> 00:08:10.104 But all of those types and kindness is.
00:08:10.110 --> 00:08:11.900 It’s really more broad inhibitors
00:08:11.900 --> 00:08:13.332 rather than specific target,
so it’s been believed.

You know those kind of.

You know the haters.

But you hate this kinase activity,

and you know inconsequence surprised

play some sort of anti angiogenesis
effect so you know we have

actually also shown that you know,

for example, survivor name can also

interfere. The mitochondria is in a

particular carcinoma. In other words,

they’re probably multiple mechanism for

the tyrosine kinase mechanism of action.

We have had our cars in them and I would

like to show you this slice and this is a uh,
you know, you know, uh, the slides made by a charmer and Addison, so this tell you, you know how you know the therapy. You can see the chemotherapy, you know this is for cancer as a whole. So one thing you can tell you can see the email server which represented by this green line is, certainly is superior to any other sort of monotherapy. However, if you combine the Indian up check behind it, therapy with more targeted, you know genomically targeted agent,
you can see dramatic improvement,
so that’s probably why you know the
email therapy attract such attention.
I think as you know over the past
decade we have been talking a lot about
the clinical application of female
checkpoint inhibitor really created
this momentum for cancer therapy.
Alright, so with that background,
so this I have to say we have not much
understanding on the overall immunology
00:10:06.548 --> 00:10:14.274 So we were had. It has been considered as an immunologically tolerant organ, and that means you know there are data shows all the humans. Activity cells actually are eliminate in liver. In other words, in the liver is, well, very well protected. And the dancing in the in deliver, you know you have a wait. There are a lot of energy and presenting cells.
However, there are data shows.

Most of the antigen presenting cells actually induced or you know T ara Jennifer phenotype rather than, activate the cellular immunity and as well as I mentioned earlier majority for the hyper Cellular carcinoma is actually rising from the background of chronic viral infections, hepatitis B, hepatitis C. So this has been known.

All has been extensively studied. Long standing chronic very affection, actually rendering T cell exhaustion.
So this is another challenge is we have to think about when we talk about how to develop more effective immunotherapy for Heather Cellular Carcinoma so that you know that. Also HTC, you know it has a very higher expression of PD L1. That’s probably why this is, you know how you use.
You know you can actually use checkpoint inhibitor to block this interaction between TDLPDL One and 51.

The other aspect is there are many regulatory T cells in hypothetical carcinoma.

So we have shown you know that there is a higher number of regulatory T cell as well as myeloid derived.

The tumors surprise if TS LMDS sees, so those are the challenges we have to consider.

And then you know when put all these things together,

you know the probably we need to think about the multiple
NOTE Confidence: 0.854570984840393
00:12:20.527 --> 00:12:23.659 strategy to really develop a more
NOTE Confidence: 0.854570984840393
00:12:23.659 --> 00:12:25.600 effective immunotherapy for HTC.
NOTE Confidence: 0.854570984840393
00:12:25.600 --> 00:12:27.508 And now you know,
NOTE Confidence: 0.854570984840393
00:12:27.508 --> 00:12:29.416 staying is more broadly.
NOTE Confidence: 0.854570984840393
00:12:29.420 --> 00:12:31.324 Currently in clinical application
NOTE Confidence: 0.854570984840393
00:12:31.324 --> 00:12:33.704 also has been very exciting.
NOTE Confidence: 0.854570984840393
00:12:33.710 --> 00:12:36.278 Is a checkpoint in Hibbett are
NOTE Confidence: 0.854570984840393
00:12:36.278 --> 00:12:39.146 you see the impact will check
NOTE Confidence: 0.854570984840393
00:12:39.146 --> 00:12:41.811 component inhibitors really is act
NOTE Confidence: 0.854570984840393
00:12:41.811 --> 00:12:45.159 on multiple spy type of the middle.
NOTE Confidence: 0.854570984840393
00:12:45.160 --> 00:12:47.084 You know regulation most
NOTE Confidence: 0.854570984840393
00:12:47.084 --> 00:12:48.527 specifically blocking PDYPTL.
NOTE Confidence: 0.854570984840393
00:12:48.530 --> 00:12:49.075 Interaction.
NOTE Confidence: 0.854570984840393
00:12:49.075 --> 00:12:52.890 So the other so you can think
NOTE Confidence: 0.854570984840393
00:12:52.890 --> 00:12:56.230 about is to really eliminate.
NOTE Confidence: 0.854570984840393
Also at least inhibit regulatory T cell in the cancer, and the other is so more exciting. You know, that’s what I’m going to talk about a little bit more. Is adoptive cell transfer therapy for those adoptive transfer therapy. We really can’t think about Tuesday. Why is non antigen specific, you know? Autologous tiles, for example, in case hours, all tumor infiltrating the emphasize and then the other, emphasize and then the other, is actually another modified version of adoptive cell transfer.
Transfer therapy is engineering T cells, so this will be the car T cells.

Also, I will spend a little bit time to.

Another thing is, think about if we can identify tumor specific antigens. We can think about is to use to developers. We had done some working in this area so I will show you what we have found.

OK, this is just the introductory slide you know for what we are. You know, you know,
for this audience you probably all very well now what you know, the started for email. Check it. Check Point inhibitor therapy for example is really blocking these two inhibitory pathways under treated as a way to activate the T cells. So for liver cancer, as you know, at least right now I mean this. You know the update is I say
00:14:43.740 --> 00:14:45.120 this is updated today.
00:14:45.120 --> 00:14:46.700 Maybe it will be changed.
00:14:46.700 --> 00:14:48.596 You know very soon as well,
00:14:48.600 --> 00:14:50.322 because for right now we have
00:14:50.322 --> 00:14:52.070 at least three FDA approved.
00:14:52.070 --> 00:14:53.880 The trackpoint inhibitor is when
00:14:53.880 --> 00:14:56.002 the pipe and temporal needle and
00:14:56.002 --> 00:14:57.496 the other one is against the
00:14:57.496 --> 00:14:59.020 CTLA is I believe mad.
00:14:59.020 --> 00:15:01.232 So those are three FDA approved and
00:15:01.232 --> 00:15:03.450 certainly there are many in the pipeline.
00:15:03.450 --> 00:15:05.655 You see how busy this lies is,
00:15:05.660 --> 00:15:07.240 you know you see those.
00:15:07.240 --> 00:15:08.844 Those are the current.
00:15:08.844 --> 00:15:11.250 In Eagle trials registered away is,
you know, a clinical trial data.

And those are the space three trials with all kinds of transforming hitters, so you will notice is the most of the trials actually is looking at the combination therapy, particularly with tyrosine kinase inhibitor also entity. Eiffel you hitters as well as the combined with some, you know, a local regional therapy or surgical resection so you can see the estimated releasing date. You know complete, complete, complete completion date. It will be in the next year or two.
We’re going to see a lot about you know the results you know related to checkpoint inhibitors for HTC, so this is really exciting part of you know for the in this field right now. So now let me try to talk about a little bit more like other approach which is really adopted cell transfer, which is active investigation by quite a number of groups in the world. So which is really adopted cell transfer, for those you know this concept was in the really knew. So the first tumor,
infiltrating lymphocytes, are paid.

As you may know, it was divided decades ago by Rosenberg at NCI. So in that case you know he isolated tail. Infiltrating lymphocytes for isolated fuel from Melanoma patients and reinfused ourselves back to the patient. But now over particular, over the past few years, more and more evidence point of the really efficacy of this sort of therapy, and also most recently you can actually, you know culture. Certain cells in X-ray invaluable in Mitchell and stimulative certainty cells.
and to induce so-called settle

00:16:58.480 --> 00:17:01.240 toxic T cells and then refilled.

00:17:01.240 --> 00:17:03.766 So cells back to cancer patients.

00:17:03.770 --> 00:17:05.750 And another is really the

00:17:05.750 --> 00:17:07.334 innate immune response arm,

00:17:07.340 --> 00:17:09.330 which is in case else,

00:17:09.330 --> 00:17:11.696 you know by definition in case else

00:17:11.696 --> 00:17:13.730 it’s the main biological function

00:17:13.730 --> 00:17:16.095 is really as a surveillance.

00:17:16.100 --> 00:17:18.030 Places Seville’s role in the

00:17:18.030 --> 00:17:20.386 party at that will check out

00:17:20.386 --> 00:17:22.504 all the auto kill tumor cells.

00:17:22.510 --> 00:17:25.156 So there are a lot of attention

00:17:25.156 --> 00:17:27.029 on empty cells as well,

00:17:27.030 --> 00:17:29.870 so I will share a little bit of data we

NOTE Confidence: 0.8770107030868853
have written that down within himself

and of course the excitement coming from the engineer T cells which is part.

So those are we’ll just talk back so.

So let’s first to look at it.

This how we can induce more.

After specific immunity.

Alright,

so in this case you know

you probably won’t find out.

Is there any tumor antigen or is

there any specific tumor energy

you had asserted carcinoma?

So indeed,

you know over the years we know

Alpha fetal protein is one of the
00:18:03.257 --> 00:18:04.749 first tumor antigen associated

00:18:04.822 --> 00:18:06.818 with hypothesize are carcinoma.

00:18:06.820 --> 00:18:08.204 However with multiple different

00:18:08.204 --> 00:18:10.280 groups of trying to use Alpha

00:18:10.338 --> 00:18:12.038 F etoprotein for email therapy,

00:18:12.040 --> 00:18:14.278 the results are really mcleese mixed

00:18:14.278 --> 00:18:16.900 because maybe the Alpha fetal protein is.

00:18:16.900 --> 00:18:18.870 Really highly expressed in embryo

00:18:18.870 --> 00:18:21.476 Genesis and also in some other

00:18:21.476 --> 00:18:23.159 highly proliferating cells,

00:18:23.160 --> 00:18:25.620 so it’s great it louder challenge

00:18:25.620 --> 00:18:28.644 so this slide show that you over

00:18:28.644 --> 00:18:31.248 the years and actually for hyper

00:18:31.248 --> 00:18:32.550 disorder carcinoma.

00:18:32.550 --> 00:18:34.740 Fortunately we do with you know
we did find a variable to render gene called glide different three.

You can see this is likely country expression.

You know fairly specifically Carcinoma So what is great because it’s you know it’s an X chromosome, so it’s highly expressed in the Amber Genesis and stuff you know in adult issue and then re over express in more than 90% of hypothesized personal. So unfortunately we really do not understand the role of the life agents rate at the moment.
I mean I had two graduate students who had dedicated their season trying to figure out what is the biological role of glycogen.

After disappointing, you know we have say it looks like the gladness re somehow interact with other growth factor and to create a micro environment on the cell surface and it would direct the downstream safely to regular cell growth. Interestingly enough gladly constraint.

And now there is a general like a genetic syndrome which is a Simpson Globby, a Homer syndrome.
I have never seen temptation like this is only rated from textbook, so this is a syndrome actually. Is that loss of function of by pigments rate so you can see it in overall if you look at the syndrome is it looks like deletions of glycogen straight create some sort of overgrowth. Alright, so this you know that it has been confirmed in the now customize. Look at this. Now customize the embryo is just the much larger than the white type so this is almost the antithesis for us to think about.
If it’s a delight, beacon three can somehow as you know looks like tumor antigen mold, cancer formation but somehow during development is actually typing. Three seems to act as surprising function and to check the development. You know during the. And then if you look at it, overall expression pad network IP gains rate there, it’s really you know, three major organs expressed, blindness Ray and organize. Well, I you know the highest one
00:20:51.326 --> 00:20:53.439 actually is a play center, right?
NOTE Confidence: 0.816829929749171
00:20:53.439 --> 00:20:55.293 So the play center has highest
NOTE Confidence: 0.816829929749171
00:20:55.293 --> 00:20:56.790 expression of the clapping.
NOTE Confidence: 0.816829929749171
00:20:56.790 --> 00:20:57.436 Answer it,
NOTE Confidence: 0.816829929749171
00:20:57.436 --> 00:21:00.020 but that’s why I think that just last
NOTE Confidence: 0.816829929749171
00:21:00.090 --> 00:21:03.114 month I went to see and Harvey Doctor Harvey,
NOTE Confidence: 0.816829929749171
00:21:03.120 --> 00:21:03.491 Claimant,
NOTE Confidence: 0.816829929749171
00:21:03.491 --> 00:21:06.459 who is really the leading expert in press
NOTE Confidence: 0.816829929749171
00:21:06.459 --> 00:21:09.104 enter here at you and I talked with him.
NOTE Confidence: 0.816829929749171
00:21:09.110 --> 00:21:10.840 So I said, You know?
NOTE Confidence: 0.816829929749171
00:21:10.840 --> 00:21:13.078 Let’s figure out what is it.
NOTE Confidence: 0.816829929749171
00:21:13.080 --> 00:21:13.454 Skype,
NOTE Confidence: 0.816829929749171
00:21:13.454 --> 00:21:16.446 even serious role in place and are right.
NOTE Confidence: 0.816829929749171
00:21:16.450 --> 00:21:18.688 I know what the other organisms,
NOTE Confidence: 0.816829929749171
00:21:18.690 --> 00:21:20.178 fatal liver you see.
NOTE Confidence: 0.816829929749171
00:21:20.178 --> 00:21:21.666 This looks pretty express
and then also fatal lock.

And then I add other tissue.

Long is completely zero expression.

I thought you know like make sure they were tissue.

Now normally they do not express flight PS3 but however is expressed in.

Is the you know the email,

his chemistry, you see all the you know,

the cancer cells expressed those things.

You know the proteins on the cell

membrane and actually this is one

of the market you know in full

pathologist will liver pathology.

Sometimes when we question
about whether this is cancer or not, we tend to do email history,
chemistry to confirm, you know,
to help us to make a diagnosis of hypothesis,

so this is also we checked with all the different cancer cell lines,
the overexpressed clapping in the normal hypothesize.

So Interestingly, the mouse, iPad or cellular carcinoma does not express.

Could I pick three and only in the humans of different cell lines we have checked and the overexpressed clapping in the normal hypothesize.

But does not express, so this is a because of the mouse
had a salad or carcinoma does not express quite happy constraint.

Actually created item vantage for us to create some model to study this date. Potential human or therapy. Because when we talk about it, we want to do emails Arabic. You know we have to create a model and see how we can test some of our ideas. So this is just the last, you know, sort of a last slide of Truth demonstrated the collective Pickens Research, you know, expression and its role in, you know, You can see it so here is, you know,
almost exclusively expressed in HTC and
the same time you can see it is correlation.
It seems to be correlated with
So now, as I mentioned,
that has turned to see how we built
this model because we have over
the years and longer we built this
model which is the Bob semis totally
immune are committed and then we
original derived from optimise.
So as I mentioned earlier so this cell
line does not express any guy picking three.
So what we did is to overexpress human
00:23:46.080 --> 00:23:48.642 like Bacon three in the mouse outline

00:23:48.642 --> 00:23:50.960 and then inoculate through this minus.

00:23:50.960 --> 00:23:53.522 And it will see you know whether

00:23:53.522 --> 00:23:56.377 we can have a model to test the,

00:23:56.380 --> 00:23:58.180 you know anti tumor immunity.

00:23:58.180 --> 00:24:02.510 you know just a slide to show you here.

00:24:02.510 --> 00:24:04.634 For example whenever you introduce this

00:24:04.634 --> 00:24:07.567 cell line to the opposite minus you see.

00:24:07.570 --> 00:24:09.964 This is why type spleen and then

00:24:09.964 --> 00:24:12.761 this is the tumor. Very mouse split.

00:24:12.761 --> 00:24:14.796 This is a bother significantly

00:24:14.796 --> 00:24:16.564 large sometimes you know obvious

00:24:16.564 --> 00:24:18.034 between 3 to 5 four,

00:24:18.040 --> 00:24:19.870 so the indicating indeed the
Bobbsey might will see this.

Far into Hypersolar Carcinoma

ISO for in the summer.

Hawk trying to Mount immune response,

but at the end the tumor wins because

within two or three weeks there is.

You know, big tumor produce.

Either,

you know when we do the subq injection

or we do the also topically rejection,

you can quickly develop this HTC in the

box emails and then we look at the worst.

The cells in the privacy you know.

Certainly we have all the different type of.

Salsa peace out most of the T cells,

but actually if you will be
00:24:56.920 --> 00:24:58.810 further phenotype of those cells,
NOTE Confidence: 0.867510676383972
00:24:58.810 --> 00:25:00.976 most of those actually there is
NOTE Confidence: 0.867510676383972
00:25:00.976 --> 00:25:02.420 significant regulatory T cell
NOTE Confidence: 0.867510676383972
00:25:02.480 --> 00:25:04.670 components and also MD SC components,
NOTE Confidence: 0.865788102149963
00:25:04.670 --> 00:25:07.225 so indicating so in this box model.
NOTE Confidence: 0.865788102149963
00:25:07.230 --> 00:25:08.742 Indeed there is email,
NOTE Confidence: 0.865788102149963
00:25:08.742 --> 00:25:10.632 surprised phenotype and so that’s
NOTE Confidence: 0.865788102149963
00:25:10.632 --> 00:25:13.090 why the tumor wins and two produces.
NOTE Confidence: 0.865788102149963
00:25:13.090 --> 00:25:15.785 So we think this probably is very
NOTE Confidence: 0.865788102149963
00:25:15.785 --> 00:25:18.630 good model for us to look how we
NOTE Confidence: 0.865788102149963
00:25:18.630 --> 00:25:21.083 can develop a model to test some
NOTE Confidence: 0.865788102149963
00:25:21.083 --> 00:25:23.764 of the ideas we wanted to detach.
NOTE Confidence: 0.865788102149963
00:25:23.770 --> 00:25:25.318 ’cause I’m wiser, circular.
NOTE Confidence: 0.865788102149963
00:25:25.318 --> 00:25:26.866 I’ve seen the others.
NOTE Confidence: 0.865788102149963
00:25:26.870 --> 00:25:29.859 We want to also think about how
NOTE Confidence: 0.865788102149963
to manipulate the immune system and to check to see if we can have some more effective and the tumor immunity.

So first you know, as I mentioned, the clapping and straight, you know this highly expressed tumors. It'll specific energy.

So when we did that, go in the traditional method that you say, OK, we will just be recreated.

Called in and trying to you know, build recombinant protein both in front bacterial from the East, and then use the protein.
As you know energy and to email those mice so this data show you just show you after we immunize those mice, and then we check, you know, we did not really see any significant changes into in terms of humor and then we check the cellular immunity and humoral immunity and overall. Conclusion from that is we tried multiple times. If we just inject eclectic and straight to the mice with another really created any, I need two more community in this,
at least in this mouse model. And then we say, you know, you know.

Then we check the tumor within our really see any you know, tumor infiltrating emphasize as well.

So then we just tested this idea to see how about. We think that different approach.

So why I’m proud that we feel is maybe we should think about how to allow the light beacon St guide to the real, you know the immune organs in case like go to the split or go through the lymph node.

So one idea we did try, you know at that time sort of
00:27:09.887 --> 00:27:11.880 thought about it is you know,

00:27:11.880 --> 00:27:13.416 how about we conjugate?

00:27:13.416 --> 00:27:15.720 Collecting three with lymphocytes so using

00:27:15.778 --> 00:27:18.280 this chemical I do not try to pronounce it,

00:27:18.280 --> 00:27:19.050 you know.

00:27:19.050 --> 00:27:20.590 CC and uses conjugate.

00:27:20.590 --> 00:27:22.990 Basically we conjugated the glide Pickens,

00:27:22.990 --> 00:27:24.349 reporting with lymphocytes.

00:27:24.349 --> 00:27:27.923 So that hypothesis hypothesis was to use in

00:27:27.923 --> 00:27:30.587 the table in full size carry this protein,

00:27:30.590 --> 00:27:33.338 the energy and the lymphocytes has

00:27:33.338 --> 00:27:35.566 this natural homing capability and

00:27:35.566 --> 00:27:37.785 they will go to the right email.

00:27:37.790 --> 00:27:38.190 Oregon.

00:27:38.190 --> 00:27:40.590 Maybe that will excite, you know,
to initiate, and the tumor immunity.

So actually that’s indeed it was the case.

So this is just to show you.

You know we conjugated and emphasize with,

you know, with the protein,

and then we inject, you know,

enjoy the back.

Those info size you know to the mice,

and then we look at the tumor.

You fancy the conjugated what

so you can efficiently surprise

the tumor growth and this will

different treatment protocol.

You can see it’s really time dependent,

and so this is very exciting.

And then we say, OK,
NOTE Confidence: 0.85026603937149
00:28:13.460 --> 00:28:15.357 let’s check it was, you know all
NOTE Confidence: 0.85026603937149
00:28:15.357 --> 00:28:17.479 the cells and different components.
NOTE Confidence: 0.85026603937149
00:28:17.480 --> 00:28:20.522 So this just to show you which acted like.
NOTE Confidence: 0.85026603937149
00:28:20.530 --> 00:28:22.340 This is an ileus part,
NOTE Confidence: 0.85026603937149
00:28:22.340 --> 00:28:24.140 definitely compared to the control,
NOTE Confidence: 0.85026603937149
00:28:24.140 --> 00:28:27.389 you can see a lot of activated T cells.
NOTE Confidence: 0.85026603937149
00:28:27.390 --> 00:28:28.473 More importantly exciting
NOTE Confidence: 0.85026603937149
00:28:28.473 --> 00:28:29.917 is after this congregation.
NOTE Confidence: 0.85026603937149
00:28:29.920 --> 00:28:32.068 Actually we can see the lymphocytes
NOTE Confidence: 0.85026603937149
00:28:32.068 --> 00:28:33.890 actually infiltrated into the tumor.
NOTE Confidence: 0.85026603937149
00:28:33.890 --> 00:28:35.690 So this is a boy.
NOTE Confidence: 0.85026603937149
00:28:35.690 --> 00:28:36.378 We believe.
NOTE Confidence: 0.85026603937149
00:28:36.378 --> 00:28:39.130 This is probably why we you know this
NOTE Confidence: 0.85026603937149
00:28:39.201 --> 00:28:42.146 sortable bikes vaccination approach works.
NOTE Confidence: 0.85026603937149
00:28:42.150 --> 00:28:42.860 So again,
NOTE Confidence: 0.85026603937149
this is just another different data.

I you know to show you how this country,

you know that just this is demonstrated indeed,

although the fact that we have seen is related to the conjugation between the lymphocytes and the collective

so so for that this is but anyways summarize this data,

so we think you know later

Initially we just use the total invoice size, but now actually we test it’s just isolated.

These results and it was a tease out,

so this is a work is ongoing.
00:29:18.270 --> 00:29:20.256 So basically is what our working model of our working hypothesis.

00:29:20.256 --> 00:29:22.340 We want to continue to try.

00:29:22.340 --> 00:29:24.560 That is we are using T cell as a carrier for tumors,

00:29:26.947 --> 00:29:28.999 therapeutic vaccine delivery.

00:29:29.000 --> 00:29:30.041 So this is where we’re testing this in hypotheticals.

00:29:33.440 --> 00:29:36.464 I think there’s a possibility so those can become a sort of platform to sell.

00:29:39.730 --> 00:29:41.610 You know like you know.

00:29:43.983 --> 00:29:46.110 to get my laboratory.

00:29:46.110 --> 00:29:47.920 Now let me you know,
00:29:47.920 --> 00:29:50.773 share it with you or some of the other
NOTE Confidence: 0.85026603937149
00:29:50.773 --> 00:29:53.130 things which will also cellular therapy
NOTE Confidence: 0.85026603937149
00:29:53.130 --> 00:29:55.880 related and this one is the Carty.
NOTE Confidence: 0.85026603937149
00:29:55.880 --> 00:29:57.690 So we didn’t develop find,
NOTE Confidence: 0.85026603937149
00:29:57.690 --> 00:29:59.500 you know the valuable gladness
NOTE Confidence: 0.85026603937149
00:29:59.500 --> 00:30:02.323 riccardi cells.
NOTE Confidence: 0.85026603937149
00:30:02.323 --> 00:30:04.641 So this is just a diagram to
NOTE Confidence: 0.85026603937149
00:30:04.641 --> 00:30:06.881 show you we use the landing
NOTE Confidence: 0.85026603937149
00:30:06.881 --> 00:30:09.279 viral vector and then basically
NOTE Confidence: 0.85026603937149
00:30:09.280 --> 00:30:12.960 created this Jeep 3 car T cells.
NOTE Confidence: 0.85026603937149
00:30:12.960 --> 00:30:16.061 So right now we created both in the T cell.
NOTE Confidence: 0.85026603937149
00:30:16.061 --> 00:30:18.266 Sales and also we you know we
NOTE Confidence: 0.85026603937149
00:30:18.266 --> 00:30:21.003 created this platform using NK
NOTE Confidence: 0.85026603937149
00:30:21.003 --> 00:30:24.007 cells which I will talk a little
NOTE Confidence: 0.85026603937149
00:30:24.010 --> 00:30:26.140 bit more in the next few minutes.
NOTE Confidence: 0.85026603937149
00:30:26.140 --> 00:30:28.410 So those hasn’t been shown.
You know this is another diagram.

Other group also developed this.

Party and then they use a different regions.

They’re focusing on the sea.

Turn up the protein and then we decided to focus in on the end terminal because the end terminal is on our side of the cell membrane with believe you know, the in terminal may have better access, so this is our party.

We divided both in the lending generation that you know a platform.

We divided both in the lending and then we.
virus as well in collaboration with

another factor that rockers you know,

He has a virtual various platform.

We actually work together and also

made this construct in the

regional various platform as well.

So then you know, testing again,

So it seems to work very well.

And also we test it in the animals.

You know this just show you a different

types of satellites and this is actually

is immortalized hypothesize,

set, immortalized levers, allies,

developer in my laboratories of
the basis serve as a control. You can see though. Also the target because this tells you know does not have the 1545 cells does not have a clapping’s resort. There’s no target and the others you know the the 1545 cells does not have a clapping’s resort. There’s no target and the others you know the commonly used a cellular carcinoma cell address themselves and those type 2 so show significant killing effect. So this is this is in cell culture and then then we also decided to introduce it into into animals. And indeed you know they were treated.
Those animals this.

Our volume compared to the controls.

And at the Cardinal applicants repartee.

Indeed, so very effective,

and also lost almost two months.

You know, this is really exciting,

and I think we pretty much feel

very confident in this construct.

But now The thing is, you see,

certainly eventually will need to bring

to human trial and to see if this this,

you know construct will be actually

you know construct will be actually

showing the effectiveness in human.

So that’s certainly you know need a lot.
Effort and also some other you know funding and that will get this stuff. So this is a really you know, exciting and also we tested the similar Carty using PDX mouse model because to develop that you know that’s another thing I mentioned earlier. We are very happy to share with people you know working on hyper disorder carcinoma also. Edit cancers as well. But we build a multiple PD exercise and over the years not only we have the PDX MI, so we also have the corresponding cell card. Sterilize so you know,
for you know for both liver cancer,
NOTE Confidence: 0.847436547279358
pancreatic cancer,
NOTE Confidence: 0.847436547279358
and we also have other tumors PDX as well.
NOTE Confidence: 0.847436547279358
So this is just to give allow
NOTE Confidence: 0.847436547279358
us in future to developer mode.
NOTE Confidence: 0.847436547279358
You know, you know,
NOTE Confidence: 0.847436547279358
I would say precision of personal
NOTE Confidence: 0.847436547279358
e-mail therapy because this way
NOTE Confidence: 0.847436547279358
we can see if we can derive some.
NOTE Confidence: 0.847436547279358
More specific hydrogen,
NOTE Confidence: 0.847436547279358
and from this particular patient,
NOTE Confidence: 0.847436547279358
and then from that platform to
NOTE Confidence: 0.847436547279358
build a specific artifice, patients,
NOTE Confidence: 0.847436547279358
certainly, that’s what he,
NOTE Confidence: 0.847436547279358
what you know in the future.
NOTE Confidence: 0.847436547279358
Endeavor for that.
Alright, so the last section of my talk, you know it’s just one share the lights. Turn attention to the you know another inmate. Email cells which is encased in HTC, so you probably ask why we are so interested in today. So if you look at the. The human body. The organ contains the highest numbers in case ours is a liver. If you look at the liver almost 2% of the Leeward nucleated cells are in case of you probably say it’s very, you know, surprised you know.
Actually it’s you know, but it does. In case I’ll do indeed work is very I. I would say to say minimum is poorly understood. Alright, so however, over the years, so you see back to even 1990s. So people already shown that if that you tested. In case files from the hypothetic are still like compared to the non tumor cells, they show the empty cells. Had this dysfunctional in terms, they have lice killing effect and this also reached 2013. Another group also reported this, but very few later Richard to really show.
It’s a strong evidence. Say what is it? The NK cells function in hypo thyroid carcinoma. Alright, so as I mentioned, it’s a such a big pop. You know they have more. In case else that many other lymphocytes in the liver. So that question is how we can find that was in his house would do in that was in his house would do in those are the others, you know. So this is some people also just very reason. You know shredded. They were recently recorded.
If you expand the NK cells and then you know you feel so badly in the mouse model, actually expand it out. In case else does precise anti tumor activity in mouse models.

So this will be like an invisible experiment. So it’s just indicate you know NK cells after expansion they still maintained.

Activity I think that’s a very critical for us to talk about. You know, if we ever wanted to make in case if we ever wanted to make in case out to PSR building platform, we have to make sure the expanded engage cells would hire that function.

Right, This is, you know,
a couple years ago and this is also in collaboration with another faculty. Don’t found in rockers, and so we decided. Just let’s start, you know, some of the basics of NK cells in HTC.

you know we had a transplant program there. So we basically for any HTC transplant fever so will get the tumor and then we will, isolate NK cells from the tumor and isolated.
you know,
the Beamer tissue and also isolated the NK cells from the non tumor.
NOTE Confidence: 0.850078701972961
You know,
Mount tumor distance period I DS 5 centimeter away from the tumor and we isolate all those NK cells and then we expand it.
NOTE Confidence: 0.850078701972961
Also in case cells and that’s all what we do in the same time we get the blood.
NOTE Confidence: 0.850078701972961
You know patients per for blood in case else. And then you know to compare with different orders at least.
NOTE Confidence: 0.850078701972961
Oh groups and see what’s the function or was the basic plan in case out.
So what do you know?
After we did that so we did quite a number and yet you know the most common transplant deliveries, hepatitis C liver and also the other, alcohol induced cirrhosis? And so that’s how we literally focusing on HC deliver an also alcoholic. So with that will do the functional I say and then we did a lot of irony. Take try to see you with any changes in those cells and then later out toward you. Know quantitative PCR to determine certain specific jeans. So this. All right?
OK, thought to make a Long story short because the timing so I will not get into the killing I see.

So basically what we find is that there are significant differences between all the NK cells we isolated from different liver. So that might be interested enough. It’s TV related liver NK cells and the alcohol related liver cancer. They are also different in terms of function. You know they have light skin activity in alcohol, but how interesting they have even higher connectivity.
Which isn’t really surprising to us compared, you know. So we that suspension with it artistic and then you got all the data, but we still have sitting on large amount of data is still waiting to be analyzed, but at least right. The moment I can share, you know this really very fairly recently. Just few months ago with that we actually identify the CD 62 L of course share cell or I also liked. So this has been really significantly changed. You know, between all those different.
So here the summary.

We can see really tabley how for whatever reason in NK cells isolated from HC be related.

HTC you know the HC way related you actually have a higher expression of selected and.

However in the alcohol related NK so you have lower expression so this will be the hours they put all the guys average as a baseline.

So it’s really interesting.

You know how this dichotomy, which by itself may not be very surprising because the difference is if you look at the Histology
between the cancers arising from HCV and the cancers arising from Alcohol, the big difference is you know, in the HTV Kaiser or background deliver as well. You always have the inflammatory activity going on. In other words, you have the inflammatory Emilio within those levers, which in alcohol induced liver cancer or liver cirrhosis. You have minimum inflammatory activity. So I think this is sort of a exciting we want.
We are thinking about is right now.

It's really easy to further and you know exactly what's the actual role of the CD 62.

All out selecting the role in this in case sales particularly is, we wanted to see if the inflammatory thing all hepatitis virus itself contribute that to to that is different.

So this is our model right now, so this is a working model we are actively pursuing that.

As I mentioned, this summarize with all our current data with NK cells.

What do you see?
The in case are higher expression, what actually they are? Higher higher killing capacity. So those are mainly from the HC way steaming the HTC, right? That’s very interesting. And however, in contrast, the alcohol induced the HTC that will lower CD 62. And also lower kidding capacity. So that’s really, you know. Allow us to think about if we ever do. You know the next step in the future? If we develop a therapy? Maybe this is where if we understand.
more about the Rover LCD,

NOTE Confidence: 0.87821352481842

you know you know the CD six tool and

NOTE Confidence: 0.87821352481842

we potentially can think about is you

NOTE Confidence: 0.87821352481842

know how we can turn this CD6 tool.

NOTE Confidence: 0.87821352481842

You know, lower expression one and to

NOTE Confidence: 0.87821352481842

get together them to be more active against.

NOTE Confidence: 0.87821352481842

HTC in the alcohol siding

NOTE Confidence: 0.87821352481842

because of all the HC way.

NOTE Confidence: 0.87821352481842

However,

NOTE Confidence: 0.87821352481842

I don’t think for this stimulation

NOTE Confidence: 0.87821352481842

by CT62 will be good idea,

NOTE Confidence: 0.87821352481842

because if they already have a

NOTE Confidence: 0.87821352481842

pretty strong in as you know,

NOTE Confidence: 0.87821352481842

HC way you know for this way

NOTE Confidence: 0.87821352481842

they already have higher.

NOTE Confidence: 0.87821352481842

In case our activity and I was also
higher city 6 two expressions as well. So we may have to think about if you know what other strategies for HCA Induces.

So this is a working hypothesis. As I mentioned, we need to do more cases and then to see if we can, find something most specific and to treat you know HTC this is the tumor heterogeneity. So we can outline some of the HTC altogether. You know, apparently you know for HTC,
00:42:12.900 --> 00:42:14.512 you know differently etiology.
NOTE Confidence: 0.87821352481842
00:42:14.512 --> 00:42:17.710 It seems like to have very different.
NOTE Confidence: 0.87821352481842
00:42:17.710 --> 00:42:20.416 Biology, so we thinking about it,
NOTE Confidence: 0.87821352481842
00:42:20.420 --> 00:42:21.776 developing therapeutic strategy,
NOTE Confidence: 0.87821352481842
00:42:21.776 --> 00:42:24.940 we have to really think about it.
NOTE Confidence: 0.87821352481842
00:42:24.940 --> 00:42:28.100 Take that into a consideration.
NOTE Confidence: 0.87821352481842
00:42:28.100 --> 00:42:29.484 But on the Furthermore,
NOTE Confidence: 0.87821352481842
00:42:29.484 --> 00:42:31.560 I decide you don’t mention that
NOTE Confidence: 0.87821352481842
00:42:31.624 --> 00:42:33.289 those two testing that model
NOTE Confidence: 0.87821352481842
00:42:33.289 --> 00:42:34.954 will be the movie thing.
NOTE Confidence: 0.87821352481842
00:42:34.960 --> 00:42:37.361 It might be the HDD itself with
NOTE Confidence: 0.87821352481842
00:42:37.361 --> 00:42:39.080 somehow engage the NK cells.
NOTE Confidence: 0.87821352481842
00:42:39.080 --> 00:42:41.138 So this is our current very
NOTE Confidence: 0.87821352481842
00:42:41.138 --> 00:42:42.510 preliminary is out here.
NOTE Confidence: 0.87821352481842
00:42:42.510 --> 00:42:44.592 We basically culture the HIV positive
NOTE Confidence: 0.87821352481842
00:42:44.592 --> 00:42:46.946 because we can grow hepatitis C in
those tumor cells and then do code stimulate.

We called priming the NK cells.

You know, in this case we can just use another.

You know the NK cells and testing the targets.

In other words, it’s the priming the monkey cells with hepatitis C.

Indeed, in deals that you know NK cell functionality.

But now the question you know come to the point.
I say even you have a strong confidence: Apple cider carcinoma somehow. The HCS, you know, take CC is still prevail. So maybe this is by itself is not enough, or maybe because remember what we have so far. Test data is all in the individual isolated condition, so this is really coming to the point that there may be some other immune surprising signal type in the micro environment which even in visual you know the NK cells maintain their.
In and out, and as you know anti tumor activity.

But however in the surprising micro environment.

Those are simply just cannot function, so that's really tell us you know when we deal with HTC is causing by C virus versus you know like a narco we have to think about differently so this is really, you know, just the game with this idea in a long days and we are actively investigated the possibilities.

Alright so I think my time
00:44:27.712 --> 00:44:30.039 is almost up and I think.
NOTE Confidence: 0.856032311916351
00:44:30.040 --> 00:44:32.830 This will be the summary and I will say
NOTE Confidence: 0.856032311916351
00:44:32.830 --> 00:44:35.447 you know you can see you know this.
NOTE Confidence: 0.856032311916351
00:44:35.450 --> 00:44:36.718 From both you know,
NOTE Confidence: 0.856032311916351
00:44:36.718 --> 00:44:37.669 patients and mice,
NOTE Confidence: 0.856032311916351
00:44:37.670 --> 00:44:40.214 so there is an email response in HTC.
NOTE Confidence: 0.856032311916351
00:44:40.220 --> 00:44:41.237 That's good sign.
NOTE Confidence: 0.856032311916351
00:44:41.237 --> 00:44:43.610 That means that there is engagement between
NOTE Confidence: 0.856032311916351
00:44:43.668 --> 00:44:45.670 the tumor and then they and ominous.
NOTE Confidence: 0.856032311916351
00:44:45.670 --> 00:44:47.560 Not in the music thing,
NOTE Confidence: 0.856032311916351
00:44:47.560 --> 00:44:49.425 so this created opportunity for
NOTE Confidence: 0.856032311916351
00:44:49.425 --> 00:44:51.720 us to develop an you know,
NOTE Confidence: 0.856032311916351
00:44:51.720 --> 00:44:53.898 better therapy so that it seems
NOTE Confidence: 0.856032311916351
00:44:53.898 --> 00:44:55.783 like this email surprising cells
NOTE Confidence: 0.856032311916351
00:44:55.783 --> 00:44:57.997 are dominant in HD situation and
NOTE Confidence: 0.856032311916351
00:44:57.997 --> 00:45:00.343 about human patients and also adding
models and we demonstrate uniform.

Our own study.

Also,

many other people study also show

the tumor explanation of specifically

molasar PewDiePie scene and those car

T cells in case cells are indeed promising,

you know, a therapy.

And as you know.

Imagine that in the last section

imagine that in the last section

of other than in case also we see

the differences between the HC way

induce the HTC and alcohol induced

ACC really tell us we have to think

about a personalized email therapy approach.
We have to really see if we can separate those cancers with you according to their ideology and then see developper you know more effective therapy accordingly. So now the challenge is, you know there is another easy to get this done, but I think many are really, you know, not just in the confined within. Actually you can have this probably multi other cancers as well. I think this is one area we all need to think about how to do this. So certainly biomarker for getting service absolute liking.
So even though therapy specially but you know we’re making inroads right now. For example. Total tumor. Antigen burden, you know. Like the microsatellite instability is, as you know, has something demonstrate you know as a predictive marker for more fighter. a predictive marker for more fighter effective therapy for check for me. Hey, better so that’s the right direction. But we still need to think about more specific file markers for different cancers and see how to get everything. And then obviously we almost no. There will be some sort of
tumor resistant coming out, so that’s where you know we need to pay attention or be at least consider the possibility of the. That the veloppement of resistance and particularly women, sing about personalized email therapy. We all know that tumor Hitler genetix really does dimension as well, and the other is is really, you know. There is a very active field right now is a target and you understand you know the new energy income information because that you can induce new energy through radiation therapy.
Awesome tumor, like original local regional therapy for hyper disorder, carcinoma injecting chemotherapy, agents of radiation, you know, create a new energy and so those new editions probably will be able to serve as a target for us to develop more. Like the potential 80 factor. You know emails are paid approach OK, so with that I would say you know thanks to people who are working in my life in especially houses MD, PhD student, graduate student ID TS. Who did all this in case our work and Frank and layout with the post office.
We did also by tumor vaccine work so have a lot of collaborations tools.

Thanks from you know by you know really the priority institution University of Florida and also ruckers University and especially assigned don’t phone bill who is actually. That they did not email about, University and especially assigned you know shared his eyes, speaks parties with us, also the regional viral vector system to build better effective party and also my long term collaborator animal clinic in the. Again, you know saying You know the Funding
Agency for support our work over the years so I will stop there. and I welcome questions, ideas from the audience. Thank you. Thank you all for your attention. A chain thank you and thank you for a terrific talk as well as you know the work you’re doing in this very challenging malignancy and and folks should submit their questions on the chat button. But let me if I may start. Yeah please. You very nicely identify the potential differences in immune response between alcoholic associated legacies as the alcohol associated legacies as opposed to viral,
where given the rise in the role of non alcoholic stay out of the tightest Nash in HTC pathogenesis, where do you see that aligning compared to the models you now been studying?

Yeah, so that’s that’s a thing. There are two issues here alright. So yes, Nash Associated Hypersolar Carcinoma, you know. But these are epidemiologist study has seen the rising incidence. However, in practice seem very little of those cases, you know, because you know,
I think that’s the thing, because you know, we use in the liver transplant as our model. You know, we get those sites where it without that issue. I think this is it common. We just do not have a lot of cases. Actually human tissue cases. I would say HTC arising from the Nash patients. To really it was studied in detail, but there are, but they each center they will have a really a fuel in. The implication is very hard to do. Second point is you know if
you look at it in terms.

You look at the Histology so the alcohol related cirrhosis probably will have more resembles to the Nash Associated Cirrhosis or carcinogenesis because they both contributed. For example, how alcohol. Induce enough cirrhosis and apparel carcinoma, probably by messing up the metabolic pathway within the liver, right? So that’s the same way you know. Nice related thing. It is basically part of the metabolic syndrome, so I would think if we want to guess,
I will assume those probably more or less related to the alcohol induced the HTC, which is less information. So that's the key difference if. If we look at that issue, you have very little information in Nash or alcohol related liver injury or hepatitis C. You always have this. I'm going chronic inflammation. I think that's the key difference. I mean, it was sort of a surprise was may not be a good surprise.
Become actually see the NK cells behavior differently in there supposed to groups. Interest rates are we don’t know, so you know to complete with complete and know that yeah, so a number of our members of audience of submitting questions. I’ll start Marcus bosenberg is asking have you considered making Carty to either hepatitis B virus, hepatitis C virus antigens expressed on the cell surface? So we haven’t because the reason we haven’t you thought we really worry about that kind of therapy as a matter of fact, if you look at the viral...
distribution in the liver, we need, you know you have more very expression in the non tumor cells and tumor cells. You know, for example used in the liver. Sample I haven’t I disappear if you look at the hepatitis B. But you know, engaging expression in both the tumor tissue Anna noun tumor tissue. You tend to have higher expression. In the non timit liver tissue. So we really worry about it. You know you created this type of a target. You probably wipe out the liver instead of locating the tumor cell. So I don’t see those are really
again assumption as part of the reason we haven’t really seen.

People reporting are making those hepatitis B or C in a car key yet.

Yes, thank you so question from damper chain are the the T cell infiltrating cells in the tumor? Are they different from the T cells in the adjacent hepatitis C infected liver and related to that would be the effect of immune checkpoint therapy on the background liver vis-a-vis the tumor. If they are different.
Right, so that's you know, you know greater point, let's see first so you know, for the first part, so we didn't have to really look at the overall generic key. Infiltrating the middle size. So we basically we did not sign the whole T cells compared, you know, whole T cells compared, you know, the tumor and the non tumor liver. So we really focusing on the NK cells because we decided just focusing on K cells and for different, you know for number reasons I mentioned so we don’t know.
The total tease out difference between humor and the surrounding labor. In Hep C and also in alcohol cirrhosis. So that's what they II you know. A question is whether or not you know the for this way, the information you know driven T cell weather. You know you will be able to see in the inflammatory citing and how those are behave, so we really don't know at this one. Her thank you question from Under whose and are asking. Given the differences in tumor cell biology and immune micro environment
between HTC of different etiologies,
how do you think about modeling these ideologies in animals to more reliably test immunotherapeutic approaches?

Yeah, that’s a great point, but I think at this moment I don’t see we have a good model to test that, particularly.

You know if you look at the mouse model, a good model to test that, particularly. You know if you look at the mouse model.

I mean we we. Also created hypo these, transgender demise but we’ve never been able to recapitulate the similar similar pathogenesis.

Yes, if you have hepatitis C, you know like a transgenic mice, but somehow you do not have
all the information you would otherwise see in the human model.

The reason is when you build a transgenic mice, you basically create this tolerance for the antigen.

You know, for example, so that means that the minds of the host will trade that rise.

Transgender put in. And as a Nitro, you know, own protein, so we never be able to initiate those kind of inflammatory model.

The other model, Israel chemically induced the model.
00:55:21.726 --> 00:55:24.630 you know to look at the personal Genesis.

00:55:24.630 --> 00:55:26.737 It’s really not the same as all

00:55:26.737 --> 00:55:28.733 because in that in those cases

00:55:28.733 --> 00:55:30.773 you have more liver damage rather

00:55:30.773 --> 00:55:32.979 than actually information driven.

00:55:32.980 --> 00:55:34.428 So for that question,

00:55:34.428 --> 00:55:37.387 I don’t think you know we have really

00:55:37.387 --> 00:55:40.610 good model to to look at the email now.

00:55:40.610 --> 00:55:41.684 Check on inhibitor.

00:55:41.684 --> 00:55:43.116 So for that matter,

00:55:43.120 --> 00:55:43.480 alright,

00:55:43.480 --> 00:55:46.360 so you know the one we divided the

00:55:46.360 --> 00:55:48.624 Bobsey Miz will be good to look

00:55:48.624 --> 00:55:51.021 at the email check only hitter but

00:55:51.021 --> 00:55:53.235 again in that setting you know.

95
The difference is we don’t.

There is no hepatitis infection in that system.

We actually trying to get hepatitis C virus windows privacy, but for some reason we still cannot.

You know whether you have inflammatory. So for those you know differences.
transition alcohol induced that HTC will
be when you use trackpoint in Haverhill.
How they behave?
We don’t know for whatever the reason.
If you look at the clinical trial
they conducted the network T service
out because actually hoping serving
as a reviewer when this separated.
You know some middle ground.
I say can you tell me can
you separate this out?
Can you say alcohol, HTC patient you know?
And also HC? Wait patience when you use.
Checkpoint inhibitor,
do they behave differently?
Out behavior? Say I mean with them.

I mean, I guess probably you know the case number.

Overall, you know you’ll still have a relatively fewer numbers of people with alcohol.

HTC I think majority the patient is still like a HC way or HP way related HTC.

I think that’s really important because I think that you know.

What you got the checkpoint inhibitor should absolutely considered an I in

in the sighting of Nitro I will say in terms of the path biology,

to you know physiological difference for example whether or not
00:57:31.838 --> 00:57:33.330 they have the indulgence
00:57:33.400 --> 00:57:34.868 inflammatory milio or macro
00:57:34.868 --> 00:57:37.070 environment or not I think that
00:57:37.137 --> 00:57:39.127 could make this huge difference.
00:57:39.130 --> 00:57:41.680 I think this is actually one
00:57:41.680 --> 00:57:44.899 of the area I was saying is.
00:57:44.900 --> 00:57:47.105 We should have really look at the
00:57:47.105 --> 00:57:48.699 difference between the two groups
00:57:48.699 --> 00:57:50.750 for tumors and when we use the
00:57:50.750 --> 00:57:52.340 checkpoint inhibitor that we can
00:57:52.340 --> 00:57:54.200 probably learn a lot because one,
00:57:54.200 --> 00:57:56.060 as I said, almost no information.
00:57:56.060 --> 00:57:58.909 The others has a lot of information.
00:57:58.910 --> 00:58:01.658 Yeah I need to see more
00:58:01.660 --> 00:58:04.516 data on that. Yeah and last question
99
from Jeff Score is DPC three
expressed in Cholangio Carcinoma?
And what about cells and HTC
that show cholangiocarcinoma
不同为 cholangiocarcinoma
As a feature of HTC. No, it doesn’t.
You know a guy picking 3 does not express in Columbia Personal.
And when you know with the mic style tumor,
you know we call it the.
You know, the mix type 2 in both.
So you have hypercellular
at Michelangelo Carcinoma.
In that exciting?
Yes, some other hypercellular carcinoma
can be staying for clapping and
three so I have to say that I think this is we haven’t done that yet. So this is all this idea to the audience you know. So in the later literature they have demonstrated by email his chemistry they have seen like a certain percentage of prostate cancer. Breast cancer colon cancer also expressed like if we say 10 between 5 to 10% of those cancers also expressed clapping and three right so those are in the literature. Those really any doctor type of report out there.
We never look at it ourselves, but for some of you know anybody you know. You know if you are interested in that, it may be you can look into some of those. I mean, it’s not surprising that guy pick once we also exploiting some tumors. Because this is just one of those, you know. Amber Amber, Genesis type of property got re express and in the in cancer. So just through this information Thank you, that was really a superb talk and we’re so fortunate now to have you as a member of our.
Centers are welcome and we look forward.