Thank you all for joining us. It's a real privilege today to welcome our new chair of pathology at Yale, Doctor Chen, the Anthony N. Brady Professor of Pathology, who joined us on March 1st. So really right into the thick of it. And in the short time he's been here, he's 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. He 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 and equally importantly developing biomarkers and new therapeutic approaches.

We're really privileged to have Dr. Chen not only as the new chair but also as a member of our Cancer Center, which really gives us, I think, great additional expertise and strength among the talent we have here.

Thank you very much Charlie, for that and also more importantly, thank you for the opportunity to present this talk.

Just briefly, I am a liver...
GI pathologist so I’m actually practicing in the clinical service and I’m also a pretty good mouse pathologist in general, so I think basically I serve as a sort of expert consultant.

So today I would adjust the top one of the you know. You know main research project You know main research project and you might laboratory, which is sort of how to divide up how to developer mode. Effective email Sara pay for hyper cellular carcinoma.
00:03:46.640 --> 00:03:47.876 OK, so good.
NOTE Confidence: 0.904578924179077

00:03:47.876 --> 00:03:51.570 So uh, as you know a better seller cars.
NOTE Confidence: 0.904578924179077

00:03:51.570 --> 00:03:53.630 Nobody is very deadly disease.
NOTE Confidence: 0.904578924179077

00:03:53.630 --> 00:03:56.024 You know it’s actually really they
NOTE Confidence: 0.904578924179077

00:03:56.024 --> 00:03:59.358 will come and you know we have almost
NOTE Confidence: 0.904578924179077

00:03:59.358 --> 00:04:01.842 600,000 new cases a year globally.
NOTE Confidence: 0.904578924179077

00:04:01.850 --> 00:04:05.138 In contrast to many other type of cancers,
NOTE Confidence: 0.904578924179077

00:04:05.140 --> 00:04:05.912 you know.
NOTE Confidence: 0.904578924179077

00:04:05.912 --> 00:04:08.614 Mostly theology is a relatively well not.
NOTE Confidence: 0.904578924179077

00:04:08.620 --> 00:04:09.380 For instance,
NOTE Confidence: 0.904578924179077

00:04:09.380 --> 00:04:12.416 you can see it’s almost 80% of those
NOTE Confidence: 0.904578924179077

00:04:12.416 --> 00:04:14.684 cases are caused by two viruses,
NOTE Confidence: 0.904578924179077

00:04:14.690 --> 00:04:17.336 hepatitis B and hepatitis C virus is,
NOTE Confidence: 0.904578924179077

00:04:17.340 --> 00:04:18.652 and then the other,
NOTE Confidence: 0.904578924179077

00:04:18.652 --> 00:04:21.889 so you know it’s a toxin alcohol awesome.
NOTE Confidence: 0.904578924179077
Recently fatty liver disease and some metabolic liver disease. 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. 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 cancer, so hepatitis B vaccine has been practice of over multiple decades. I think the data is already show because 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. 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,
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, has been performed by the recurrence is, you know it’s almost 70% of patients after the surgical resection. So overall, with the typical therapy currently, you know the three year survival is still less than 20%. And, uh, in about a 10 years ago that, one first therapy was approved, which is arrive in a, you know. So resonator is terrorism Chinese inhibitor and so that only showed moderate effect in the small number of patients. And all only the pasta two or three years we have seen in another momentum which
NOTE Confidence: 0.872145533561707
00:07:38.988 --> 00:07:42.070 is a checkpoint inhibitors role in the
NOTE Confidence: 0.872145533561707
00:07:42.070 --> 00:07:44.230 treatment of other Cellular Carcinoma.
NOTE Confidence: 0.872145533561707
00:07:44.230 --> 00:07:47.840 So we can talk a little bit more about the
NOTE Confidence: 0.872145533561707
00:07:47.929 --> 00:07:51.800 checkpoint inhibitors in nice to feel slides.
NOTE Confidence: 0.872145533561707
00:07:51.800 --> 00:07:52.912 So first of all,
NOTE Confidence: 0.872145533561707
00:07:52.912 --> 00:07:55.050 these are the tires in kind is
NOTE Confidence: 0.872145533561707
00:07:55.050 --> 00:07:57.045 currently being tried and approved
NOTE Confidence: 0.872145533561707
00:07:57.045 --> 00:08:01.524 So rifle name wrecker ever made
NOTE Confidence: 0.872145533561707
00:08:01.524 --> 00:08:03.382 neighbor which is basically another
NOTE Confidence: 0.872145533561707
00:08:03.382 --> 00:08:05.416 version of the revenue and then
NOTE Confidence: 0.872145533561707
00:08:05.416 --> 00:08:08:01.524 So rifle name wrecker ever made
NOTE Confidence: 0.872145533561707
00:08:01.524 --> 00:08:03.382 neighbor which is basically another
NOTE Confidence: 0.872145533561707
00:08:03.382 --> 00:08:05.416 version of the revenue and then
NOTE Confidence: 0.872145533561707
00:08:05.416 --> 00:08:07.239 the other tools also tested.
NOTE Confidence: 0.872145533561707
00:08:07.240 --> 00:08:10.104 But all of those types and kindness is.
NOTE Confidence: 0.872145533561707
00:08:10.110 --> 00:08:11.900 It’s really more broad inhibitors
NOTE Confidence: 0.872145533561707
00:08:11.900 --> 00:08:13.332 rather than specific target,
NOTE Confidence: 0.872145533561707

11
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

to know vascularization or really

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 can see the chemotherapy,

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,

you know, certainly is superior

you know, 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, will see you how to look at the liver. So what is the unique aspect unique aspect of carcinoma?
or you know biology of the liver as well as the hypothetical question. 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. You know? P DL1 is alignment for PD one. So those engagement actually surprised that I. Activated you know anti tumor teazles. That’s probably why this is, uh, you know how you use.
You know you can actually use checkpoint inhibitor to block this interaction between TDPDL 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.
strategy to really develop a more effective immunotherapy for HTC.

And now you know, staying is more broadly. Currently in clinical application also has been very exciting. Is a checkpoint in Hibbett are you see the impact will check component inhibitors really is act on multiple spy type of the middle. You know regulation most specifically blocking PDYPTL. Interaction.

So the other so you can think about is to really eliminate.
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
NOTE Confidence: 0.854570984840393
all very well now what you know,
NOTE Confidence: 0.854570984840393
the started for email.
NOTE Confidence: 0.854570984840393
Check it.
NOTE Confidence: 0.854570984840393
Check Point inhibitor therapy for
NOTE Confidence: 0.854570984840393
every example is really blocking these two
NOTE Confidence: 0.854570984840393
inhibitory molecules PD L1 and the CD L4,
NOTE Confidence: 0.854570984840393
so those are inhibitory.
NOTE Confidence: 0.854570984840393
So basically with the variables develop
NOTE Confidence: 0.854570984840393
all kinds of Therapeutics called
NOTE Confidence: 0.854570984840393
checkpoint inhibitors is blocking those two.
NOTE Confidence: 0.854570984840393
Inhibitory pathways under treated
NOTE Confidence: 0.854570984840393
as a way to activate the T cells.
NOTE Confidence: 0.854570984840393
So for liver cancer, as you know,
NOTE Confidence: 0.854570984840393
at least right now I mean this.
NOTE Confidence: 0.854570984840393
You know the update is I say
this is updated today.

Maybe it will be changed.

You know very soon as well, because for right now we have at least three FDA approved.

The trackpoint inhibitor is when the pipe and temporal needle and the other one is against the CTLA is I believe mad.

So those are three FDA approved and certainly there are many in the pipeline.

You see how busy this lies is, you know you see those.

Those are the current.

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. EG 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 the exciting part 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, quite a number of groups in the world. So which is really adopted cell transfer, you know, therapy.

So 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 toxic T cells and then refilled. So cells back to cancer patients. And another is really the innate immune response arm, which is in case else you know by definition in case else it's the main biological function places Seville's role in the party at that will check out all the auto kill tumor cells. So there are a lot of attention on empty cells as well, so I will share a little bit of data we
have written that down within himself

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

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 highly expressed in the Amber Genesis and stuff you know 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 had dedicated their season. Trying to figure out what is the biological role of glycogen 3. After disappointing, you know we have say it looks like the gladness 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, you know 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 overall expression pad network IP gains rate there, it’s really you know, three major organs expressed, blindness Ray and organize. Well, 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.

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

35
00:21:53.176 --> 00:21:55.270 about whether this is cancer or
NOTE Confidence: 0.867510676383972
00:21:55.339 --> 00:21:57.650 not, we tend to do email history,
NOTE Confidence: 0.867510676383972
00:21:57.650 --> 00:21:59.370 chemistry to confirm, you know,
NOTE Confidence: 0.867510676383972
00:21:59.370 --> 00:22:02.475 to help us to make a diagnosis of hypothesis,
NOTE Confidence: 0.867510676383972
00:22:02.480 --> 00:22:03.776 elder personal. Alright,
NOTE Confidence: 0.867510676383972
00:22:03.776 --> 00:22:07.344 so this is also we checked with all
NOTE Confidence: 0.867510676383972
00:22:07.344 --> 00:22:09.659 the different cancer cell lines,
NOTE Confidence: 0.867510676383972
00:22:09.660 --> 00:22:12.509 tissues and both at mouse and human.
NOTE Confidence: 0.867510676383972
00:22:12.510 --> 00:22:14.074 So Interestingly, the mouse,
NOTE Confidence: 0.867510676383972
00:22:14.074 --> 00:22:16.980 iPad or cellular carcinoma does not express.
NOTE Confidence: 0.867510676383972
00:22:16.980 --> 00:22:19.460 Could I pick three and only in the
NOTE Confidence: 0.867510676383972
00:22:19.460 --> 00:22:22.044 humans of different cell lines we
NOTE Confidence: 0.867510676383972
00:22:22.044 --> 00:22:24.404 have checked and the overexpressed
NOTE Confidence: 0.867510676383972
NOTE Confidence: 0.867510676383972
00:22:26.790 --> 00:22:28.346 But does not express,
NOTE Confidence: 0.867510676383972
00:22:28.346 --> 00:22:31.652 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

have this person normal cell like

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
like Bacon three in the mouse outline and then inoculate through this minus.
And it will see you know whether we can have a model to test the, you know anti tumor immunity.

For example whenever you introduce this cell line to the opposite minus you see. This is why type spleen and then this is the tumor. Very mouse split.

This is a bother significantly large sometimes you know obvious between 3 to 5 four, so the indicating indeed the
Bobbsey might will see this.
NOTE Confidence: 0.867510676383972
Far into Hypersolar Carcinoma
NOTE Confidence: 0.867510676383972
ISO for in the summer.
NOTE Confidence: 0.867510676383972
Hawk trying to Mount immune response,
NOTE Confidence: 0.867510676383972
but at the end the tumor wins because
NOTE Confidence: 0.867510676383972
within two or three weeks there is.
NOTE Confidence: 0.867510676383972
You know, big tumor produce.
NOTE Confidence: 0.867510676383972
Either,
NOTE Confidence: 0.867510676383972
you can quickly develop this HTC in the
NOTE Confidence: 0.867510676383972
or we do the also topically rejection,
NOTE Confidence: 0.867510676383972
you can quickly develop this HTC in the
NOTE Confidence: 0.867510676383972
box emails and then we look at the worst.
NOTE Confidence: 0.867510676383972
The cells in the privacy you know.
NOTE Confidence: 0.867510676383972
Certainly we have all the different type of.
NOTE Confidence: 0.867510676383972
Salsa peace out most of the T cells,
NOTE Confidence: 0.867510676383972
but actually if you will be
00:24:56.920 --> 00:24:58.810 further phenotype of those cells,
00:24:58.810 --> 00:25:00.976 most of those actually there is
00:25:00.976 --> 00:25:02.420 significant regulatory T cell
00:25:02.480 --> 00:25:04.670 components and also MD SC components,
00:25:04.670 --> 00:25:07.225 so indicating so in this box model.
00:25:07.230 --> 00:25:08.742 Indeed there is email,
00:25:08.742 --> 00:25:10.632 surprised phenotype and so that’s
00:25:10.632 --> 00:25:13.090 why the tumor wins and two produces.
00:25:13.090 --> 00:25:15.785 So we think this probably is very
00:25:15.785 --> 00:25:18.630 good model for us to look how we
00:25:18.630 --> 00:25:21.083 can develop a model to test some
00:25:21.083 --> 00:25:23.764 of the ideas we wanted to detach.
00:25:23.770 --> 00:25:25.318 ’cause I’m wiser, circular.
00:25:25.318 --> 00:25:26.866 I’ve seen the others.
00:25:26.870 --> 00:25:29.859 We want to also think about how
to manipulate the different 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 side before and after vaccination, 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.

You know, 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 to the real, you know the immune organs in case like go through the lymph node.

So one idea we did try,

you know at that time sort of
thought about it is you know, how about we conjugate? Collecting three with lymphocytes so using this chemical I do not try to pronounce it, you know. Basically we conjugated the glide Pickens, reporting with lymphocytes. So that hypothesis was to use in the table in full size carry this protein, the energy and the lymphocytes has this natural homing capability and they will go to the right email. 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, 
and then we inject, you know, 
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,
let’s check it was, you know all the cells and different components. So this just to show you which acted like. This is an ileus part, definitely compared to the control, you can see a lot of activated T cells. More importantly exciting is after this congregation. Actually we can see the lymphocytes actually infiltrated into the tumor. So this is a boy. We believe. This is probably why we you know this sortable bikes vaccination approach works. So again,
00:28:42.860 --> 00:28:44.990 this is just another different data.
NOTE Confidence: 0.85026603937149
00:28:44.990 --> 00:28:46.904 I you know to show you
NOTE Confidence: 0.85026603937149
00:28:46.904 --> 00:28:48.900 you know how this country,
NOTE Confidence: 0.85026603937149
00:28:48.900 --> 00:28:51.024 you know that just this is
NOTE Confidence: 0.85026603937149
00:28:51.024 --> 00:28:52.086 just demonstrated indeed,
NOTE Confidence: 0.85026603937149
00:28:52.090 --> 00:28:54.183 although the fact that we have seen
NOTE Confidence: 0.85026603937149
00:28:54.183 --> 00:28:56.509 is related to the conjugation between
NOTE Confidence: 0.85026603937149
00:28:56.509 --> 00:29:01.236 the lymphocytes and the collective
NOTE Confidence: 0.85026603937149
00:29:01.236 --> 00:29:03.073 is but anyways summarize this data,
NOTE Confidence: 0.85026603937149
00:29:03.073 --> 00:29:05.071 so we think you know later
NOTE Confidence: 0.85026603937149
00:29:05.071 --> 00:29:07.000 on we actually purified we.
NOTE Confidence: 0.85026603937149
00:29:07.000 --> 00:29:09.840 Initially we just use the total invoice size,
NOTE Confidence: 0.85026603937149
00:29:09.840 --> 00:29:12.720 but now actually we test it’s just isolated.
NOTE Confidence: 0.85026603937149
00:29:12.720 --> 00:29:15.680 These results and it was a tease out,
NOTE Confidence: 0.85026603937149
00:29:15.680 --> 00:29:18.270 so this is a work is ongoing.
So basically is what our working model of our working hypothesis. We want to continue to try. That is we are using T cell as a carrier for tumors, therapeutic vaccine delivery. So this is where we’re testing this in hypotheticals. Normal, I think there’s a possibility so those can be become a sort of platform 40 sell. You know like you know. So this is a work I’m going to get my laboratory. Now let me you know.
share it with you or some of the other

00:29:50.773 --> 00:29:53.130 things which will also cellular therapy

00:29:53.130 --> 00:29:55.880 related and this one is the Carty.

00:29:55.880 --> 00:29:57.690 So we didn’t develop find,

00:29:57.690 --> 00:29:59.500 you know the valuable gladness

00:29:59.500 --> 00:30:00.224 riccardi cells.

00:30:00.230 --> 00:30:02.323 So this is just a diagram to

00:30:02.323 --> 00:30:04.641 show you we use the landing

00:30:04.641 --> 00:30:06.881 viral vector and then basically

00:30:06.881 --> 00:30:09.279 created this Jeep 3 car T cells.

00:30:09.280 --> 00:30:12.960 So right now we created both in the T cell.

00:30:12.960 --> 00:30:16.061 Sales and also we you know we

00:30:16.061 --> 00:30:18.266 created this platform using NK

00:30:18.266 --> 00:30:21.003 cells which I will talk a little

00:30:21.003 --> 00:30:24.007 bit more in the next few minutes.

00:30:24.010 --> 00:30:26.140 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 may have better access, so this is our party.

Construct and then we.

Basically this is also called a third generation that you know a platform.

We divided both in the lending
virus as well in collaboration with another factor that rockers you know, He has a virtual various platform. We actually work together and also make 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 show significant killing effect. So this is this is in cell culture and 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.

you know construct will be actually

this to human trial and to see if this this,

But now The thing is, you see,

you know, this is really exciting,

and I think we pretty much feel

very confident in this construct.

Certainly eventually will need to bring

this to human trial and to see if this this,

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 Carter 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.
NOTE Confidence: 0.847436547279358
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 of the Leeward nucleated cells are in case 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 people already shown

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 such a big pop.

You know they have more.

So that question is how we can find 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. 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.

So what the platform we use so is, 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, you know we, 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, you know we, you know we had a transplant program there.

isolate NK cells from the tumor and isolated. You know from the adjacent that you know

zone we call the adjacent alone from the,
00:36:40.010 --> 00:36:40.630 you know,
NOTE Confidence: 0.850078701972961
00:36:40.630 --> 00:36:42.490 the Beamer tissue and also isolated
NOTE Confidence: 0.850078701972961
00:36:42.490 --> 00:36:44.666 the NK cells from the non tumor.
NOTE Confidence: 0.850078701972961
00:36:44.670 --> 00:36:45.294 You know,
NOTE Confidence: 0.850078701972961
00:36:45.294 --> 00:36:46.230 like you said,
NOTE Confidence: 0.850078701972961
00:36:46.230 --> 00:36:47.910 Mount tumor distance period I
NOTE Confidence: 0.850078701972961
00:36:47.910 --> 00:36:49.941 DS 5 centimeter away from the
NOTE Confidence: 0.850078701972961
00:36:49.941 --> 00:36:51.950 tumor and we isolate all those NK
NOTE Confidence: 0.850078701972961
00:36:51.950 --> 00:36:53.689 cells and then we expand it.
NOTE Confidence: 0.850078701972961
00:36:53.690 --> 00:36:56.178 Also in case cells and that’s all what
NOTE Confidence: 0.850078701972961
00:36:56.178 --> 00:36:59.288 we do in the same time we get the blood.
NOTE Confidence: 0.850078701972961
00:36:59.290 --> 00:37:02.089 You know patients per for blood in case else.
NOTE Confidence: 0.850078701972961
00:37:02.090 --> 00:37:03.926 And then you know to compare
NOTE Confidence: 0.850078701972961
00:37:03.926 --> 00:37:05.560 with different orders at least.
NOTE Confidence: 0.850078701972961
00:37:05.560 --> 00:37:08.157 Oh groups and see what’s the function
NOTE Confidence: 0.850078701972961
00:37:08.157 --> 00:37:11.126 or was the basic plan in case out.
So what do you know?

After we did that so we did quite a number page 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 interesting 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.

HC way.
Which isn’t really surprising to us compared, you know. So we that suspension with it artistic 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 HTC 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 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 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
00:41:01.487 --> 00:41:03.350 more about the Rover LCD,
NOTE Confidence: 0.87821352481842
00:41:03.350 --> 00:41:06.194 you know you know the CD six tool and
NOTE Confidence: 0.87821352481842
00:41:06.194 --> 00:41:08.967 we potentially can think about is you
NOTE Confidence: 0.87821352481842
00:41:08.967 --> 00:41:12.139 know how we can turn this CD6 tool.
NOTE Confidence: 0.87821352481842
00:41:12.140 --> 00:41:14.744 You know, lower expression one and to
NOTE Confidence: 0.87821352481842
00:41:14.744 --> 00:41:17.697 get together them to be more active against.
NOTE Confidence: 0.87821352481842
00:41:17.700 --> 00:41:19.740 HTC in the alcohol siding
NOTE Confidence: 0.87821352481842
00:41:19.740 --> 00:41:22.220 because of all the HC way.
NOTE Confidence: 0.87821352481842
00:41:22.220 --> 00:41:25.209 I don’t think for this stimulation
NOTE Confidence: 0.87821352481842
00:41:25.209 --> 00:41:27.558 by CT62 will be good idea,
NOTE Confidence: 0.87821352481842
00:41:27.560 --> 00:41:30.026 because if they already have a
NOTE Confidence: 0.87821352481842
00:41:30.026 --> 00:41:32.499 pretty strong in as you know,
NOTE Confidence: 0.87821352481842
00:41:32.500 --> 00:41:35.195 HC way you know for this way
NOTE Confidence: 0.87821352481842
00:41:35.195 --> 00:41:37.030 they already have higher.
NOTE Confidence: 0.87821352481842
00:41:37.030 --> 00:41:39.686 In case our activity and I was also
00:41:39.686 --> 00:41:42.269 higher city 6 two expressions as well.

00:41:42.270 --> 00:41:45.130 So we may have to think about if you know

00:41:45.200 --> 00:41:47.846 what other strategies for HCA Induces.

00:41:47.850 --> 00:41:49.938 So this is a working hypothesis.

00:41:49.940 --> 00:41:51.041 As I mentioned,

00:41:51.041 --> 00:41:53.610 we need to do more cases and

00:41:53.694 --> 00:41:55.530 then to see if we can,

00:41:55.530 --> 00:41:56.328 you know,

00:41:56.328 --> 00:41:58.323 to treat you know HTC this is

00:41:58.323 --> 00:42:00.850 the bottom line is I think more

00:42:00.850 --> 00:42:03.120 you know, apparently you know for HTC,

00:42:03.120 --> 00:42:05.353 then to see this trend which

00:42:05.353 --> 00:42:06.628 is the tumor heterogeneity.

00:42:06.628 --> 00:42:09.840 So we can outline some of the HTC altogether.

00:42:09.840 --> 00:42:12.899 You know, apparently you know for HTC,
you know differently etiology.

It seems like to have very different.

Biology, so we thinking about it,

developing therapeutic strategy,

we have to really think about it.

take that into a consideration.

Furthermore, I decide you don’t mention that

those two testing that model

will be the movie thing.

It might be the HDD itself with

somehow engage the NK cells.

So this is our current very

preliminary is out here.

We basically culture the HIV positive

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.

But you know, like a 50K562 cell lines, so that sell you can

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 and creating activity in iPad.
HC, they induce Apple cider carcinoma somehow. The HCS, you know, take CC is still prevail. So in other words, 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 versus the alcohol costs the HTC. 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
is almost up and I think. This will be the summary and I will say you know you can see you know this. From both you know, patients and mice, so there is an email response in HTC. That’s good sign. That means that there is engagement between the tumor and then they and ominous. Not in the music thing, so this created opportunity for us to develop an you know; better therapy so that it seems like this email surprising cells are dominant in HD situation and 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 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 if we can develop a 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 liver cancer. 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
00:46:38.092 --> 00:46:39.480 tumor resistant coming out,
NOTE Confidence: 0.856032311916351
00:46:39.480 --> 00:46:41.832 so that’s where you know we need
NOTE Confidence: 0.856032311916351
00:46:41.832 --> 00:46:44.345 to pay attention or be at least
NOTE Confidence: 0.856032311916351
00:46:44.345 --> 00:46:46.135 consider the possibility of the.
NOTE Confidence: 0.856032311916351
00:46:46.140 --> 00:46:48.612 That the veloppement of resistance and
NOTE Confidence: 0.856032311916351
00:46:48.612 --> 00:46:51.070 its potential mechanism that causes high,
NOTE Confidence: 0.856032311916351
00:46:51.070 --> 00:46:51.892 particularly women,
NOTE Confidence: 0.856032311916351
00:46:51.892 --> 00:46:53.947 sing about personalized email therapy.
NOTE Confidence: 0.826214373111725
00:46:53.950 --> 00:46:56.939 We all know that tumor Hitler genetix
NOTE Confidence: 0.826214373111725
00:46:56.939 --> 00:46:58.880 really does dimension as well,
NOTE Confidence: 0.826214373111725
00:46:58.880 --> 00:47:02.504 but and the other is is really, you know.
NOTE Confidence: 0.826214373111725
00:47:02.504 --> 00:47:05.480 There is a very active field right now
NOTE Confidence: 0.826214373111725
00:47:05.564 --> 00:47:08.112 is a target and you understand you
NOTE Confidence: 0.826214373111725
00:47:08.112 --> 00:47:10.779 know the new energy income information
NOTE Confidence: 0.826214373111725
00:47:10.779 --> 00:47:13.755 because that you can induce new
NOTE Confidence: 0.826214373111725
00:47:13.755 --> 00:47:15.508 energy through radiation therapy.

80
Awesome tumor, like original local 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 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, you know shared his eyes, speaks parties with us, and 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 to do. The study. 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 mean, I’m going chronic inflammation. I think that’s the key difference.

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 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, uh, you know greater point, let’s see first so you know, 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, 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 you know 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. I mean we we. Also created hypothese, 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. You know,
you know to look at the personal Genesis. It's really not the same as all because in those cases you have more liver damage rather than actually information driven. So for that question, I don’t think you know we have really good model to look at the email now. Check on inhibitor. So for that matter, alright, so you know the one we divided the Bobbsey Miz will be good to look at the email check only hitter but again in that setting you know.
The difference is we don't.

There is no hepatitis infection in that system.

We actually trying to get hepatitis C virus windows privacy, HTC and trying to do that, but for some some reason we still cannot. In a, you know, recapitulate the inflammatory response. You know whether you have inflammatory changes in HTC of lice inflammatory.
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? 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 is 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 the sighting of Nitro I will say to you know physiological difference in terms of the path biology, for example whether or not
they have the indulgence inflammatory milieu or macro environment or not I think that could make this huge difference. I think this is actually one of the areas I was saying is. We should have really look at the difference between the two groups for tumors and when we use the checkpoint inhibitor that we can probably learn a lot because one, as I said, almost no information. The others has a lot of information. Yeah I need to see more data on that. Yeah and last question
from Jeff Score is DPC three

00:58:07.373 --> 00:58:09.437 expressed in Cholangio Carcinoma?

00:58:12.632 --> 00:58:14.228 And what about cells and HTC

00:58:14.228 --> 00:58:17.128 that show cholangiocarcinoma

00:58:17.130 --> 00:58:18.770 As a feature of HTC. No, it doesn’t.

00:58:21.902 --> 00:58:24.787 You know a guy picking 3 does not express in Columbia Personal.

00:58:24.790 --> 00:58:27.769 And when you know with the mic style tumor, you know we call it the.

00:58:27.770 --> 00:58:29.756 you know we call it the.

00:58:29.760 --> 00:58:32.400 You know, the mix type 2 in both.

00:58:32.400 --> 00:58:33.724 So you have hypercellular

00:58:33.724 --> 00:58:34.717 at Michelangelo Carcinoma.

00:58:34.720 --> 00:58:35.917 In that exciting?

00:58:35.917 --> 00:58:37.912 Yes, some other hypercellular carcinoma

00:58:37.912 --> 00:58:39.951 can be staying for clapping and
00:58:39.951 --> 00:58:42.638 three so I have to say that I think
00:58:42.638 --> 00:58:44.647 this is we haven’t done that yet.
00:58:44.650 --> 00:58:46.570 So this is all this idea
00:58:46.570 --> 00:58:48.290 to the audience you know.
00:58:48.290 --> 00:58:50.530 So in the later literature they have
demonstrated by email his chemistry
00:58:50.530 --> 00:58:52.181 they have seen like a certain
00:58:52.181 --> 00:58:54.071 percentage of prostate cancer.
00:58:54.071 --> 00:58:55.640 Breast cancer colon cancer also
00:58:55.640 --> 00:59:00.016 expressed clapping and three right
00:59:00.016 --> 00:59:02.166 so those are in the literature.
00:59:02.166 --> 00:59:03.886 expressed clapping and three right
00:59:03.886 --> 00:59:05.930 so those are in the literature.
00:59:05.930 --> 00:59:07.645 Those really any doctor type
00:59:07.645 --> 00:59:09.017 of report out there.
00:59:09.017 --> 00:59:10.598
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 know 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 cancer.
Centers are welcome and we look forward.