Both in cancer and obviously immunology and response to viruses.

And we'll start with our first speaker, doctor lash boost.

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And we'll start with our first speaker, doctor lash boost.

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NOTE: Confidence: 0.885055780410767
00:00:31.408 --> 00:00:33.853 Doctorate at the University of
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00:00:41.877 --> 00:00:43.901 that understanding to fundamentally
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00:00:43.901 --> 00:00:47.638 improving our way to deliver more efficient,
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00:00:47.640 --> 00:00:48.624 more effective,
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00:00:48.624 --> 00:00:51.084 and more successful clinical care.
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00:00:51.090 --> 00:00:52.076 You know,
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00:00:52.076 --> 00:00:54.048 through his laboratory work,
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00:00:55.890 --> 00:00:57.270 Medison And frankly,
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00:00:57.270 --> 00:00:58.710 His leadership of clinical
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00:00:58.710 --> 00:01:00.150 trials in clinic research,
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00:01:00.150 --> 00:01:02.280 which have not only investigated new
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drugs but also leverage new technologies to better define and predict how women will best respond to therapy. He really has been the triple thread and actually have academic Medison, and we’re pleased to have him today to share his work in translation and research in breast cancer so loud. Thank you for Evergreen speak today. Thank you Charlie, for them the opportunity to give a brief update on some of the translation of projects that we actually have been involved in the past few years here at Yale. Um? So this is my a disclosure slide and I would like to cover 3 areas.
When is exploiting the emu micro environment of a breast cancer for therapeutic purposes, some potential metabolic vulnerabilities in breast cancer I think exists and I’d like to challenge you to think and you knew very about cancer predisposition or cancer risk category cancer risk. So the road from an idea to a clinical trial or clinical trial result is really very long and often times very sort of tortuous. So as an example, about 10 years ago we published this paper very show at the presence of immune cells in primary tumors, either ER positive or triple negative,
or her two positive breast cancer service
NOTE Confidence: 0.893426477909088
usually associated with prognosis.
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Let’s outcome in patients receiving
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order surgery.
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Now the treatment and surgery so
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that people was published in 2010.
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I’d like to remind you that in 2010
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there is no effective, you know,
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therapy in any disease type.
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So we cause this the closing sentence.
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This paper was, well,
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it remains unknown whether the
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Indians selectivity is simply
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associated with with a better outcome,
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or it’s really the cause of
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the battle outcome in disease.
So around the same time in another project with a postdoc in my lab, we also looked at what sort of biological processes or gene expressions, signatures or patterns are associated with the response. Chemotherapy is really a perfect setting where you can correlate a particular biomarker with sensitive to the treatment because you can directly measure the effect of the treatment at the time of the surgery. Patients have no residual.

NOTE Confidence: 0.893426477909088
cancer after the chemo.

They tend to do really well and we call this pathological complete response.

So be selling.

This is again a number of immune signatures.

Are Indian related markers fell out so obviously the big question is so is this a mere association or a cause and effect?

Right around that time, in the second half of 2010, the 1st paper came out in the New England Journal of Medicine and eating.

manipulating an immune checkpoint,
so we’d illumi map could improve the survival of patients in metastatic Melanoma, so that really created an opportunity to test this Koziela fact versus Amir Association. 2012, which is actually the year when I joined the air. We proposed the new edgmont trial to be an S and ask them would repeal me map. It could improve the pathological complete response rate when combined with chemotherapy. So PMS said, well, now that’s a good idea, but it’s really too toxic and
00:04:20.946 --> 00:04:22.410 it’s way too early.
NOTE Confidence: 0.893426477909088

00:04:22.410 --> 00:04:24.682 So it went to look and proposed them
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00:04:24.682 --> 00:04:27.269 the same thing and you ain’t even prior,
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00:04:27.270 --> 00:04:28.790 but also for good measure,
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00:04:28.790 --> 00:04:30.578 he asked them whether they would
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00:04:30.578 --> 00:04:32.140 be interested in Edgmont Prial,
NOTE Confidence: 0.893426477909088

00:04:32.140 --> 00:04:34.114 since since a lot of immune cells
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00:04:34.114 --> 00:04:35.346 in the microenvironment predicted
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00:04:35.346 --> 00:04:36.996 better outcome of the surgery.
NOTE Confidence: 0.868568539619446

00:04:37.000 --> 00:04:38.925 So for the new regiment they actually
NOTE Confidence: 0.868568539619446

00:04:38.925 --> 00:04:41.127 sent me this lovely letter that I
NOTE Confidence: 0.868568539619446

00:04:41.127 --> 00:04:43.084 thought it’s interesting to read, right?
NOTE Confidence: 0.868568539619446

00:04:43.084 --> 00:04:44.908 So read the actual date first,
NOTE Confidence: 0.868568539619446

00:04:44.910 --> 00:04:46.728 so it’s 18th of September 2012.
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00:04:46.730 --> 00:04:47.642 The ordinary nice,
NOTE Confidence: 0.868568539619446

00:04:47.642 --> 00:04:48.858 polite rejection that well,
we are unable to provide either funding or drug for this project because of the unclear.

Either there is well, sort of tried the road for edge event registrations and they agreed to do an agent trial which led to this spoke as 1418 konnakol trial, so not as 40 actually means that it was started in 2014, so it took about two years to the NCI to really put together this large of the randomized registration trial. After Merck supported it in
2012 in principle.
So I'm kind of tenacious and not very aggressive, but I'm tenacious.
So I supposed to say my dear again to Med immune in the same year, maybe even at that time was a startup company.
They had do volume app and now they're smaller than they actually said?
Yeah, why not?
What was the single agent, I mean a single arm phase, one phase, two trial at Yale, and the randomized trial.
So the I spy consortium combined it all, so the Apple event was added to pocket back. So our study at year was just simply. Hum. So I could be presented last. There’s a historical interest because this was the first Kew Edgmont oncology trial anywhere in the world. So the first patient was enrolled in 2015. It was a phase one phase two trial, and because this has never been done in the collective setting.
combined with chemotherapy food,

though,

is chemotherapy before surgery FT

require that the first three patients

is watch for 9 months each week

for the next lot could be entered.

The results showed that the

pathological complete eradication

rate in the rest was about 44%.

The same chemotherapy regimen

in a similar trial,

and by the sea by smog.

Southwestern college group resulted

in a PCR or pathological covered
NOTE Confidence: 0.868568539619446
00:06:51.487 --> 00:06:52.907 response with different 29%.
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00:06:56.484 --> 00:06:58.680 you cancel each other higher PD
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00:07:00.772 --> 00:07:03.183 sites at a higher PCR eight more
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00:07:03.183 --> 00:07:05.358 closer to 60% rather than.
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00:07:05.358 --> 00:07:07.140 44 So remember,
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00:07:07.140 --> 00:07:10.196 parallel with this and the other study was
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00:07:10.196 --> 00:07:12.610 running through the I spy that I was so.
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00:07:12.610 --> 00:07:15.730 Lad and he showed the results of the
NOTE Confidence: 0.868568539619446
00:07:15.730 --> 00:07:18.608 Plenary session of the EC are this year on.
NOTE Confidence: 0.868568539619446
00:07:18.610 --> 00:07:20.934 The study shows 9 the randomized setting
NOTE Confidence: 0.868568539619446
00:07:20.934 --> 00:07:23.198 that indeed leave this door vulnerable.
NOTE Confidence: 0.868568539619446
00:07:23.200 --> 00:07:25.015 A product combination improved the
NOTE Confidence: 0.868568539619446
pathological can’t response rate

in both the triple negative group,

which was the results were

very eerily similar in terms of the PCI rate, 47 versus 44% in our little negative study at Yale,

and we also notice that actually this drug also work.

That is combination worked.

It was added to chemotherapy. You have to.

I mean it hormone receptor HR stands

for hormone receptor resolution,

receptor positive disease.

However, the result might this reason why this was picked for a plenary session is actually in the next slide,
so we stumbled upon a remarkably sort of simple and clear way to isolate out among the estrogen receptor positive tumors, the ones which really benefited versus those who did not. There was no editing benefit. So if you split these estrogen receptor hormone receptor positive group into two more likely subtypes, let me call your MP1 and MP2 MP one this crap sort of Mamma print. The lower end of the moment I grew up in the MP two is the Momma Prince Super High score on my printer. Similar sort of predictor that we used
to identify patients who benefit from Edgmont chemotherapy in hormone receptor positive diseases score. So what we're showing here that this core itself has a meaning and just being called high risk or or benefiting from chemotherapy is valuable, but you actually can also split this look into that really super sensitive to adding. Uh, in Indian checkpoint inhibitor to the chemotherapy. So in that group, the pathological CR equals 64% versus 22%. In the chemotherapy alone. So what is this MP group? So this NP group actually is
the group which has a very high proliferation and the relatively low estrogen receptors signaling, or estrogen receptor sort of activity. Read out that you can capture Biostar generating wearing jeans, and that's an important sort of piece of information to design the follow-up registration trial for base that we have working with. Because this guy proliferation most regions signaling group is the group that is the least likely to benefit from endocrine therapy. Gotta hand it most likely to
benefit chemotherapy, and we think that this benefit could be further augmented by adding indoor follow map. So we want to get back to this letter in September 2012 from work. So a year later, in September 30th, 2013, the FDA approved the first sort of drug to be based on pathological company response rate in breast cancer, and that was purchased. So purchasing have improved the pathological computer response rate in her two positive disease and lettered registration of this drug.
So not respecting the idea,
and they actually lounge the large randomized trial with a pathological CRS,
their endpoint, and to their credit, they invited me back.
Leadership of the trial and the results were actually published this year in the new invention of Madison because it did confirm that indeed, adding parallelism after chemotherapy improves the pathological computer education rate improved the recurrence free survival even after 18 months of median follow up.
So this is the research study that sort of was largely based on these observations. Remember 10 years ago, so it took six. It looks 40 years to actually start this study another six years to complete it. It would have been completed by now, not for the coded. So it has accrued 923 patients out of 1000 and the results probably will be become available in the next two to three years. So so some cancers that high, you know, you know. Union presence know why so often suffer numbers. Medical student at Yale took on
this project to actually look into the molecular background, or why sometimes have a lot of lymphocytes at this. Last one is now medical country fellow at Sloan Kettering. So we did these families pca let me show that many other people did before that triple negative cancer’s had a higher notation count, highly antigen mode and more cytotoxic T cells. However, when you look at the actual group On its own, like triple negative disease or ER
positive cancer, her two positive cancer.

These associations suddenly flip.

This is a correlation matrix.

I don’t expect you to see the numbers, but the colors indicate the positive correlation when it’s Brown and it’s blue, and the deeper the color, the higher the correlation value.

So you can see that the Indian signatures are highly correlated with one another.

But on the other hand, is Genomic metrics of generic complexities such as.

Mutation load or New Antigen Lord
or deletions or amplifications, loads or como complexity. We actually are inversely associated with immune Indian presence in triple negative disease and disease, so that was pretty counterintuitive. Counterintuitive in 2017. OK, so you’re moving in says you have a simpler. We can suggest the fewer than your hand surgeons are. So when I see things like this, I try to confirm it. So we reached out collaborator and friend Thomas card and ask him to
actually replicate this or with a different methodology and Thomas actually find exact same thing that in primary triple negative disease, the fewer the immune cells they hire. The Genomic heterogeneity and the worst prognosis. So worse. Prognosis means that you have a higher probability for methods. This is so and let us do this hypothesis that maybe the metastatic lesions are actually immune refugees or or escapes. So there are more immune in Earth that Michael Environment is more immune inert and these three brilliant woman took on this project
00:13:18.914 --> 00:13:20.999 or parasitically was a visiting
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00:13:20.999 --> 00:13:23.384 scientist from Hungary or so with.
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00:13:23.384 --> 00:13:26.590 Smoking baby that his lab in Charlotte.
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00:13:26.590 --> 00:13:27.724 With me and.
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00:13:27.724 --> 00:13:30.370 More Gerstein so we rounded up samples
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00:13:30.449 --> 00:13:33.249 which will pair primaries and meds and
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00:13:33.249 --> 00:13:35.940 also a separate Court of primaries.
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00:13:35.940 --> 00:13:38.299 And that’s not from the same patient,
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00:13:38.300 --> 00:13:40.911 and subjected them to a whole series
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00:13:40.911 --> 00:13:43.018 of molecular studies to test it in.
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00:13:43.020 --> 00:13:44.700 You micro environment is the
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00:13:44.700 --> 00:13:45.708 same or different,
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00:13:45.710 --> 00:13:47.095 so this is just really
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00:13:47.095 --> 00:13:48.480 examples of three sort of
NOTE Confidence: 0.843152046203613
00:13:48.540 --> 00:13:49.731 simple and straightforward
NOTE Confidence: 0.843152046203613
findings with teal comes the tumor.

Infiltrating info sites are lower in maximum primary tumors in matched and unmatched chords be dealing.

Expression is the same, it slower.

In in the matter equations and also a whole lot of different Indian signatures are all lower,

Consistently showing that there are less Indians and less activity in the breast.

Cancer metastatic micro environment.

Why don’t was really interesting though?

Is that while most of the emu markers went down, some of the Indian targets actually remain high or even increased.
in the meta static environments.

And these IO targets are potential good set of candidates for offer.

Testing them in the meta static setting, either alone or in combination.

Also in combination with established agents.

So we selected the group of this preserved IO targets for a clinical trial that we hope to conduct this support.

Clinical trials it’s called rustic and this is sort of a scheme of it.

And again, this takes this immune targets that we preserved in the meta static setting and testing in the clinic whether
they really have a functional role.

In suppressing the new Micro Hood, so because of lack of time I can’t really talk about all the other Indian projects every day, what we did compare changes in the micro environment before and after therapy and the shouts only published. This give us some ideas what to add to Pembrolizumab Order Volume app to make the treatment even more effective than you actually and setting.

Homes we also compared to same day the immune reach, triple negative and the energy or
positive Kansas to see that there is differences in their micro environments and that was done by Paso mirror medical students who is now a resident at the Harvard system the same way. So we did similar comparisons by race and King blindness. Scientists in my lab is working or not. Scientists in my lab is working or not. Of data from a number of different new agent trials that seems to do well. Map kind of what precisely defined predictors, and he rosenblit is Medical College fellow with a very nice people and actually looking at in a large pool
of data from Foundation Medicine.

And there are some really substantial differences in people like an expression depending on what site you are actually sampling.

I’m going to move on to something else that really got me excited in the past.

Many metabolic processes are catalyzed by multiple different isozymes or or proteins that really capitalizes.

Normal cells usually have many of these, and oftentimes in cancer you actually
NOTE Confidence: 0.843152046203613
00:16:31.274 --> 00:16:34.078 see that one of the isoforms become dominant,
NOTE Confidence: 0.843152046203613
00:16:34.080 --> 00:16:36.664 so that’s the schema on this figure, right?
NOTE Confidence: 0.843152046203613
00:16:36.664 --> 00:16:38.608 So normal tissue is both sides.
NOTE Confidence: 0.843152046203613
00:16:38.610 --> 00:16:41.194 When I sent to our expressed in cancer,
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00:16:41.200 --> 00:16:43.524 I just have one becomes a dominant
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00:16:43.524 --> 00:16:44.520 and the other
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00:16:44.590 --> 00:16:47.219 one is lost. So we asked how often do we
NOTE Confidence: 0.857035517692566
00:16:47.219 --> 00:16:50.565 see this in cancer and do this sort of isis
NOTE Confidence: 0.857035517692566
00:16:50.565 --> 00:16:52.960 and expression changes could could harbor.
NOTE Confidence: 0.857035517692566
00:16:52.960 --> 00:16:56.688 Or or include enzymes that we could target
NOTE Confidence: 0.857035517692566
00:16:56.688 --> 00:16:59.228 metabolically somaca March secret visiting
NOTE Confidence: 0.857035517692566
00:16:59.228 --> 00:17:02.288 scientist faculty from from a Polish
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00:17:02.288 --> 00:17:05.099 University to this project on and device.
NOTE Confidence: 0.857035517692566
00:17:05.100 --> 00:17:07.435 This sort of strategy to
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00:17:07.435 --> 00:17:09.303 look at humanizing forms.
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Isozymes managed matched primary ISOzymes managed matched primary tumors in the metastatic lesions tumors in the metastatic lesions sorry match the normal tissue. sorry match the normal tissue. The DC area across 14 different cancer The DC area across 14 different cancer types where this was available than the types where this was available than the validated the results in cell lines. validated the results in cell lines. Make sure that this is really observed in the purest system and not just an artifact of difference. observed in the purest system and not just an artifact of difference. He still different issue compositions He still different issue compositions and then says the functionality and then says the functionality in this depth map data which is in this depth map data which is basically complete knockdown of all basically complete knockdown of all human jeans in about 7 or 8 cell human jeans in about 7 or 8 cell lines and then the conference hits. lines and then the conference hits. We validated in the manual screen. We validated in the manual screen.
This is an example for you how this exactly looks. 404 Kansas so this is Csea enzyme. 2 forms ACA&B. Plots show you that how they still the ACA, which is the red and be which is the blue, had the expression a normal and an action. Cancer tissues and you can see that the Blues all go down and cancel. That means that the expression of this is lost, whereas the red remains stable and the red is the sea. So this thing this is a potentially interesting target.
So when you look at this across different cancer types and indeed app map validation data, then actually what really fell out on the top is this questionnaire carboxylase. Which show this loss of isoenzyme diversity intro different cancer types and was socially but nine different cell lines and each cancer types in in the depth map so that map has like several dozens of cell lines for a particular cancer type, like breast cancer. Nine of these showed the same loss of heterozygosity, loss of diversity as we
saw in the human data.

Different cancer types. And in this case is also validated, so most of the cell lines where the CSC was knocked out.

If it had the dominant expression, it really impact viability. But the real kicker is that when we look up what is known about this, it turns out that Pfizer has a drug that they put through phase one and phase two trials for diabetes and fatty liver, two metabolic effects that we expected. But they discontinued development.
last year or two years ago because of thrombocytopenia, which is wonderful. Because don’t beside opinion through megakaryocytes really rely on the normal lipid synthesis, because from both sides bought off and every time I turn both sides come off from the surface supermodel career site, it takes lipids. Membranes made it so we answered the proof that is really works the way it’s supposed. So the Anthony to collaboration with Pfizer to do some additional preclinical studies and bring
it in the clinic

if it validates so, we simply throw validation is pre clinical validation is falling on the shoulders of Julia fold even offer Medical College of Fellows and finish with scientists in my lab. So before the coveted broke we had a chance to look at 10 different cell lines and you see that in the human sort of achievable concentrations that you can get in the human serum. It says a pretty broad inhibitory effect. And the army is not for coffee. I could probably show you,
said the combinatorial screen results from the high throughputs combinatorial screen that we initially is doing in our core facility at the West campus and also collaborating in jacks to test this drug in PDX models. And we hope to bring this to the clinic. Maybe the year 2.

This is not our paper, this is the people from nature of it shows the distribution of different sort of mutations in large cities of Kansas. So the striking thing about this
is that there are these set of jeans that affected more than 65 cases out of close to 3000 Kansas.

And even in this sort of very modern and high sort of accuracy study, about 9% of Kansas said no driver alterations.

English challenge you to think about anyway. What you think you mean by a driver, Jean.

So is it a statistical construct from any sort of statisticians in computational biologist?

It is actually a statistical construct, but of course many of you think about this gene that caused the cancer.
The way I think about this is actually it’s just a narrative tool. To kill a good story. So this is actually from the same paper from but from the supplementary figures, but it shows you the enormous amount of model of Genomic abnormalities of any particular cancer has so retro transpositions, a few dozen number of structural variants, several dozen to several, several 1000. So these are big chunks of the DNA the thousands of in Dallas and 10s of thousands of single included variance.
you also see this actually in the CIS, which is a premalignant lesion, so these services, all the.

Well, except it’s not really cancer, but it has the same B 53 mutations clarifications or not.

Just the game keeps you big pools, better weather really.

The function of this these jeans and then the individual jeans is.

So this is a people that many years ago we did nearby Sunday.

She was that he was a medical student.
That year.

Now is a faculty at Sloan Kettering and what I want to illustrate here is that every single cancer which is a column as really a different combination of abnormalities. So if you think about it that way, maybe it’s really the reason. Because because of this combinatorial difference that they have. So if each of these contributes something then their net effect is really really heterogeneous behavior. But maybe it’s even more interesting.

Is this work with DVR? She was.
The students at that time at Yale and now it’s a medical student pad. You sequence all the human kindness ease in 90 two breast cancer, only to see whether there are any. I guess we didn’t find any, but we really observe though is that there is a very large number of high functional impact. I’m still think about for a second, so you actually carry a bunch of germ line so the mutations that inactivator overactive. It kinda seems like PSC kinase or whatnot.
So what does it mean? So please give us this idea that maybe it’s really.
He just focused too narrowly on driver mutations,
What actually would be probably also helpful is to look at the context in which this is happening and the constant Israeli hundreds of additional variants that come in from the somatic or the germ line angle.
So he proposed this idea that really functional German variance, conkle, jeans and it’s the totality of the functional impact.
High functional impact German

variants in cancer Lady Jeans.

They could actually determine cancer risk.

So we know that there are a few very high penetrance.

Cancer is chains like Bronco,

but it’s really is the minority women who carry this even very strong family history.

So what’s accounts for dismissing heredity?

You think it’s the totality of very strong family history.

So what’s accounts for dismissing heredity?

You think it’s the totality of the defects that actually are.

Embedded in a whole lot of individually non sort of.

Cannot translate that.
And then the next iteration of this, that's really the combined effect of the germline and somatic events that really lead to the malignant transformation rather than a few individually dramatic effect. And it's a project that talking visiting post doc from. And that is so if it's really true, then we would expect that woman who developed cancer the younger age will have a lot more sort of deleterious germline events in cancer jeans then people who develop cancer the later age because it's ultimately the
combined effect of the acquired and the inborn errors that lead to Kansas. So if you are born with a lot of errors to start with, it's gonna take a shorter time to get to reach this critical level. And long, behold, that's exactly what he observed in a bunch of large series like that ECA or the UK biobank and now just published this paper in Nature Communications. I want to just point out to you because time is short on this very last figure, which is the relationship between the
mutation than in the cancer versus

the variant, the German

variant burden by age groups.

So he means younger than 30 and the

other advocating speak louder than 80.

The installation ship is actually remarkable,

The patience young who are who

have cancer at a younger age and

it’s it across all the cancers that

letter TCG ahead or the UK biobank.

We also get consider the 30s, forties,

50s have a much higher germline

variant burden in cancer Lee jeans,

and this is like 5 or 6 only jeans then.

Then people who get cancer the older

age and on the other hand most
00:26:20.689 --> 00:26:22.891 folks have a much higher mutation
00:26:22.968 --> 00:26:24.978 somatic mutation so they can.
00:26:24.980 --> 00:26:27.269 So so then that led to us
00:26:27.269 --> 00:26:28.939 another idea that So what?
00:26:28.940 --> 00:26:31.580 Actually the cancer jeans are in this thing?
00:26:31.580 --> 00:26:33.506 That it’s probably a lot broader
00:26:33.506 --> 00:26:35.185 sort of repertoire then then
00:26:35.185 --> 00:26:39.786 So you could think that this study?
00:26:39.790 --> 00:26:40.537 The Dom Hussein,
00:26:40.537 --> 00:26:42.280 who is a PhD student in the
00:26:42.341 --> 00:26:43.925 computational biology program and
00:26:43.925 --> 00:26:46.301 supervised by Mian Mar Gerstein too.
00:26:46.310 --> 00:26:48.585 So how many jeans are actually connected,
00:26:48.590 --> 00:26:50.654 one step or two step or three step
NOTE Confidence: 0.870644629001617
away in a pretty important interaction

network from a cancer gene.

So if they are immediately next to it,

then they probably influence

the affective for cancer gene.

If they’re two step removed,

they still probably influence over less,

so there actually a whole lot of jeans, but.

Half of all human jeans are

actually connected.

One or two steps away from

from cancer hub gene.

Most of these are not implicated in cancer,

and if you look at their sort of

functional importance in this gap

database and it turns out that the
further away you get from the cancer hub, the less important they seem to be in survival in the depth map data. This supports the idea that there are a lot more jeans involved in cancer than what you think you see. The same when you look at weather. There is an evolutionary pressure to preserve truncating mutations in these jeans, and again the further away, the jeans which are one step away from a concert Hall gene and less and less evolutionary pressure on them into four through four to exclude truncations.
And it was so carry actually
somatic mutations. So that’s.
Personalized sort of Jim Langley scored.
That’s sums up all these effects that
people are born with cancer chains,
and that’s a project that
we actually got to ask.
Or young investigator award
to pursue together with cow.
And we say this too
gruesome pictures out here.
Just remind you guys that
this is how airplanes crash.
They actually don’t crash because
there is a statistically significant
losses of the wings or the engines
or not every single plane crashes caused by a different combination of individually nonlethal events. So they fall into groups like human error, which is almost always there, but it’s not the same human error. It’s a different kind of human error. There’s always some kind of a mechanical or instrumental failure, but it’s never the same instrument. So that’s my final slide, really studying the new micro environment. Let us to some useful ideas about clinical trials are very excited about exploring metabolic
adaptations for therapeutic targets, and we submitted the DOD grant with this with a group of other investigators, and I think I really think that the universe is functionally cancel. Event chains is much larger than we think it is interested in. More stuff at the bottom of the slide shows takes you through the list of publications by our group. So thank you, and this is my lab. Each other. Wow, thank you. That was a an impressive array of work on so many fronts. And congratulations on all of it.
I know where we're a little late on time, so let me just offer up one question. You know? I think you oppose. Obviously a very good case that it's a combination of germline asmatic events and I'm curious, do you think breast is different? Breast cancer is different than other solid to malignancy's because obviously germline and semantic events are. Install cancers, but you think breast is somehow different that respect. Yes, it's different. It's a matter of fact, so you can group really Kansas even
in this paper that I refer to be looked at different cancer types, and this Association starts to fall apart in Kansas that actually have a very high environments or customer on exposure, right? Because that in this sort of message of this new relationship. So this relationship is less strong in lung cancer, bladder cancer, and some other cancers. So the real picture of course, is nuance. It’s much more nuanced. And the same way. So the jeans we chat important so the cancer gene is probably also vary from some tissue types of tissue type.
00:30:33.030 --> 00:30:34.395 So these are the refinements
00:30:34.395 --> 00:30:35.960 that we are actually working on.
00:30:35.960 --> 00:30:38.112 Is just that I wanted to give you
00:30:38.112 --> 00:30:39.948 a repertoire of things that we do,
00:30:39.950 --> 00:30:41.570 but that’s exactly what we actually
00:30:41.570 --> 00:30:43.139 addressing in this project right now.
00:30:44.120 --> 00:30:46.184 Thank you and I know just for time
00:30:46.184 --> 00:30:47.746 will will move on, but obviously
00:30:47.746 --> 00:30:49.552 folks can certainly email allow us to.