Our second speaker today is Derrick Tom Ray, who's professor of cell biology and director of the Yale Cinema Microscopy Lab, received his PhD from University. California is an expert on quantitative live cell imaging, and he specializes in innovative approaches to microscopy, including fluorescent probes, data analysis, and spatial mapping. Received an NIH director's New Innovator Award and a coffee fellow, and today is there talk about his recent work.
which is primarily focused on spatial control of membrane trafficking during cell morphogenesis migration. In cilia formation. So, Derek, the floor is yours.

Great, so I’ll be talking about cilia which have some relevance to cancer and signaling. I’ll be talking basically about a new pathway that we’re discovering and tell you about the ramifications of this.
my conflict of interest is declared there.

So is Sherman sort of a primary?

Let me just tell you the main message in

the main message is that we're proposing

and characterizing a novel pathway.

Basically the central paradigm is

and then go on to sort of describe to

you that I think that that basically

our data suggests that we have

an alternate pathway here.

OK. Just. OK, it’s clicking differently,

so we first start off with a quick

primer here about primary cilia so you

know really sort of two aspects here.
What are they? And I suppose sort of related here, why do you care? Why should we care? So in terms of the first part, that’s relatively easy there. They’re basically present on nearly all cells. There’s a. The exceptions being red blood cells and T cells. If you go by electron microscopy. End both sort of light microscopy. You see their long and slender. The width is maybe 152 nanometers and they can extend about 10 microns long.
There's solid Terry organelles their primary cilia and let me tell you a little bit about some of the known functions. So you can sort of think of them as a specialized sensory antenna, so you have an adaptation of this for vision of your rod cells. I guess relevant to right now and coronavirus they also important for smell. And there is a loss of cilia which is causing the Syrian dysfunction of that and as well as signaling aspects. And we sort of mentioned a little bit more on that because it's really relevant to this audience. Especially in regards to cancer.
So primary slip, so why?
Why do you care in this?
And the easiest way of sort of thinking of this is thinking in terms of ciliopathies.
OK, there's a number of diseases that are basically dependent was actually sort of discovered retractively these diseases have been known for quite a long time, and then only in the last couple of decades was it really realized, in part from pioneering work at Yale.
About the sort of link between
these diseases and disruptive ciliary function so you can see this in sort of the Joubert syndrome or liver cysts kidneys. It’s quite multi organ.

But again, for this audience, I think it was particularly relevant in the context of cancer, because you actually can release vesicles from a cell which can transmit signals,
so that’s one aspect of it, but you can sort of think of it in a simple way. Simplified way of controlling this signaling on or off. Now, just to sort of just highlighting that complexity was sort of a review, that sort of indicates that it actually can go either way. You could have a certain degree of activation you could turn on or going independent that. Or you could actually do it by going independent that.
So if you look at cancer is summer activated by the presence of silly, and some are by the repression. OK, but if we sort of. Go beyond that aspect and say well, what is sort of the normal paradigm. Well, the normal paradigm here is that cilia occur once per cell cycle. So in that sense, if you think of it from that lens, you’re really not controlling except for the point of cell division.
And maybe any delays on whether you would have slid Genesis or not, and I’d like to say, change that paradigm view. So remind you again. I do a lot of imaging as you sort of heard in the intro, and this is just one example of super resolution image Ng where we can actually see this very long structure of cilia, which is, like I said, it could be you know 10 microns or so long with the resolution down to sort of 20 nanometers where you.
could actually see it as a tube. So that’s one sort of technique, but I’m going to show you another source of imaging techniques, and in short of. Exemplify that can provide new insight. Here again, this is sort of the structural aspects of this accident. Sort of in the side, which is, it’s just relatively relevant, is that they can present with this pocket Macy put the laser pointer on and in the ciliary pocket. Here, and this is the sort of shown
extra short here,

but this can be a very deep imagination.

In fact it can almost be.

Nearly entirely evaginated.

OK,

So what is sort of the key process

So the general paradigm,

in fact there's one

for epithelial cells,

which I will not sort of discuss,

but for most of the cells.

In fact the majority,

if they start with this silly

or vesicle which forms,
and then you have this double membrane membrane which should have bends in. And then you actually have this, really think of it as a super large vesicle. It’s a vesicle. This vesicle could be 7 microns long. OK, and then as a an event it actually has to go infuse the plasma membrane produce. This is a, you know, this is a standard paradigm. This happens once per cell cycle would be the standard paradigm. Now I want to bring in one other player here and this is one that we’ve worked with quite a bit,
which is called the exocyst complexes,
the tethering complex.
It was first discovered actually
at Yale in yeast,
and basically it is known to basically
drive the upstream monsters near
Fusion machinery to allow spatial
temporal control of vesicle exocytosis.
This is you can sort of see in.
This review has been thought to
for quite some while play a role
in cilia and mainly ciliogenesis
and stabilization by targeting
the vesicles right here where
they would
fuse and then basically drive let’s
say control within the accident
that is the standard paradigm.
And while I don’t want to say that is wrong,
I think it’s actually missing.
Let’s say 80% of the picture OK.
So we sort of go back to,
you know why we have this paradigm and and
and what sort of the underlying underpinning?
Well, is it? You know I want to
basically first say that is Dre.
It’s based on indirect evidence.
We’ve actually not seen the
vesicles their fusing there,
nor actually seen much of the Exorcist.
And I would say that you’re missing something
that’s really important and it’s incomplete.

But let’s sort of get beyond that and show you what I may be talking about.

But first I have to tell you.

Why, if we’re claiming to see something different, why and how are we able to do so when people been looking at Syria for quite awhile?

And so there are a number of technical aspects to the solution. The first one is we’re using a technique called total internal reflection for us. Since microscopy, let’s say axial superresolution technique and it allows us to image
just the lower surface of the cell and

actually see silly’s emergence OK.

But that actually even

without superresolution,

technique is not enough

The distance between cilia and

the surface at times is very low,

and it’s actually not clear if they

are inside the cell or actually have

emerged in or outside and think of it

again like your antenna, your antenna.

If you sort of.

Just give an analogy,

is going to respond to signals quite

differently if it’s actually outside
your car truck, what, whatever it be.

Versus pulled it inside where it cannot receive the signals.

OK, at least not the same signals.

The other technical aspect is we used a McLeod clever pH switching to identify when cilia are in or out.

We’re using this as an impulse way and we do molecular replacement of the Exorcist.

The latter was important because for a long time people were image in the Exorcist.

Or just simply overexpressing it and they would sort of see localizations like this everywhere or some accumulations, but when we did this replacement
strategy we could see it in these discrete punkte OK and this is now this is going into HeLa and other types of cells looking at vesicle excess cytosis and we could see in these kind of graphs distinct events and I just show you one trace where vesicle has arrived as we see with the Exorcist and then with another Reporter. Any Reporter here which is a floor in with the pH sensor we can actually unequivocally identify the Fusion event, so this is sort of a constitutive pathway. We know it’s coming from recycling vesicles and we can identify and study that.
OK, and we can tell the events about when The Exorcist appears and when you have the Fusion fit. This is relevant to the how we’re going to be looking at things with the cilia. So what is it that we see? In I’m really just. OK, good. OK, so here’s a short movie of what we’re seeing in terms of cilia, sort of called the Biogenesis aspects, where we see basically.
00:12:03.474 --> 00:12:05.038 exorcist recruited to cilia.
NOTE Confidence: 0.77788836
00:12:05.040 --> 00:12:07.910 So that’s sort of standard that itself
NOTE Confidence: 0.77788836
00:12:07.910 --> 00:12:10.268 is is basically showing it going
NOTE Confidence: 0.77788836
00:12:10.268 --> 00:12:13.250 through the base of a long 80 cilia,
NOTE Confidence: 0.77788836
00:12:13.250 --> 00:12:15.515 but there’s actually another phenomenon
NOTE Confidence: 0.77788836
00:12:15.515 --> 00:12:18.605 that we observed which is quite different
NOTE Confidence: 0.77788836
00:12:18.605 --> 00:12:21.613 and so now you actually see this cilia
NOTE Confidence: 0.77788836
00:12:21.689 --> 00:12:24.055 with this is the Reporter here is.
NOTE Confidence: 0.77788836
00:12:24.060 --> 00:12:26.524 Smooth and flooring or we can also
NOTE Confidence: 0.77788836
00:12:26.524 --> 00:12:29.260 use smooth and GFP so that looks
NOTE Confidence: 0.77788836
00:12:29.260 --> 00:12:31.260 to sort of characteristic curve.
NOTE Confidence: 0.77788836
00:12:31.260 --> 00:12:33.808 Linear silly and this would be in
NOTE Confidence: 0.77788836
00:12:33.808 --> 00:12:35.809 the dimensions several microns long.
NOTE Confidence: 0.77788836
00:12:35.810 --> 00:12:38.456 And what I’d like you to note,
NOTE Confidence: 0.77788836
00:12:38.460 --> 00:12:41.862 and I’m going to play this more than once,
NOTE Confidence: 0.77788836
00:12:41.870 --> 00:12:44.998 is that we actually see the red signal
NOTE Confidence: 0.77788836
00:12:44.998 --> 00:12:47.177 getting recruited to this silly boom,
NOTE Confidence: 0.77788836
00:12:47.180 --> 00:12:49.454 right there off on again off
NOTE Confidence: 0.77788836
00:12:49.454 --> 00:12:50.970 again have several times.
NOTE Confidence: 0.77788836
00:12:50.970 --> 00:12:54.638 This is the time one last time.
NOTE Confidence: 0.77788836
00:12:54.640 --> 00:12:58.213 Is in hours OK, so there’s no signal there.
NOTE Confidence: 0.77788836
00:12:58.220 --> 00:12:59.984 It appears it disappears.
NOTE Confidence: 0.77788836
00:12:59.984 --> 00:13:02.630 It appears again over the course
NOTE Confidence: 0.77788836
00:13:02.708 --> 00:13:04.990 of in this case of this movie,
NOTE Confidence: 0.77788836
00:13:04.990 --> 00:13:06.980 sort of in this minutes range,
NOTE Confidence: 0.77788836
00:13:06.980 --> 00:13:09.278 this does not fit with what you
NOTE Confidence: 0.77788836
00:13:09.278 --> 00:13:11.360 A couple of things.
NOTE Confidence: 0.77788836
00:13:11.360 --> 00:13:14.174 One is, it’s along the entire cilia,
not just the base.

Two it appears there.

Goes there and then vanish

is and then comes back.

You know an hour or two later again.

So what's going on there

and what do we know?

How can we sort of probe into that with?

I guess you can intend to punt.

So we do this by using.

Again,

we're using this exorcist and

we look after after stimulation.

See something interesting

happening here and you actually

see it quite really in the movie.
Let me just play it again and you see Pam. I realize it’s hard to catch. Bam you see that green object? That’s the vesicle flying off. OK, so we see the release of the vesicle happening as well. Now that’s actually you know that part is known, but later we actually see then the Exorcist here. OK, after that we dropped off that signal. So basically the SEK 8 which is an extra quarter decorate psyllium after serum stimulation in vesicle release OK.
And by the way I mean you know we artificially to generate cilia interesting culture, starve them. Of course the normal situation would be in syrup. OK, so. You know, per that sort of model, well, is there any evidence for this? Yes, there have been some papers here and you called it decapitation OK, where it plays off that vesicle? We actually think that the mechanism is going to happen is different? OK they are releasing it,
but you’ll see in our cartoon in the end we’re thinking that it’s happening by a different mechanism.

You can obviously see sort of the importance of that on signal transduction as I was.

Early, basically indicating earlier so.

What do we happen to our RXS reporters after we add cereal?

In this case, the FBS.

And and So what we can see here,

We’re using X-70 as our Our Exorcist Reporter I MP5 E is a silly Reporter

and a couple of different things.
One is now I should mention for soul this is endogenous. *** is no longer replaced. OK so this is sort of native conditions and what you can see is you can very clearly see it localising to cilia, but if you look carefully and I think you can see in this case here. And in this case here it actually localizes there but also forms these additional tubes which are pulling about look to pee in most movies would know are pulling out of it. So what’s going on there? I will propose to you and submit to you is that this silly is actually
inside the cell and is actually being remodeled by the X assist to pull off other membranes and remodel it through. Actually have the role of Exorcist being to tether and help fuse this monster huge, you know 510 Micron long vesicle. We we you know we basically see this in here sort of another view of that. And again there would be flooring and these large tubules that are pulling off now. Does this happen when you stimulate with steering? And the answer is yes and if you
00:16:58.710 --> 00:17:00.964 look at percent acilia you had
NOTE Confidence: 0.7813586
00:17:00.964 --> 00:17:03.680 serum they they drop down a bit.
NOTE Confidence: 0.7813586
00:17:03.680 --> 00:17:05.604 That’s that’s that’s expected.
NOTE Confidence: 0.7813586
00:17:05.604 --> 00:17:07.528 What is particularly interesting
NOTE Confidence: 0.7813586
00:17:07.528 --> 00:17:08.940 and exciting to us?
NOTE Confidence: 0.7813586
00:17:08.940 --> 00:17:12.300 Is that the colocalization with extra 70,
NOTE Confidence: 0.7813586
00:17:12.300 --> 00:17:14.700 which is usually quite low,
NOTE Confidence: 0.7813586
00:17:14.700 --> 00:17:17.145 goes up dramatically by adding
NOTE Confidence: 0.7813586
00:17:17.145 --> 00:17:19.980 serum OK so serum is is,
NOTE Confidence: 0.7813586
00:17:19.980 --> 00:17:23.340 you know going to turn over this.
NOTE Confidence: 0.7813586
00:17:23.340 --> 00:17:25.740 Also with the cell cycle.
NOTE Confidence: 0.7813586
00:17:25.740 --> 00:17:28.620 But the important thing is that’s
NOTE Confidence: 0.7813586
00:17:28.620 --> 00:17:30.540 actually driving that recruitment.
NOTE Confidence: 0.7813586
00:17:30.540 --> 00:17:33.420 Now we do some controls here.
NOTE Confidence: 0.7813586
00:17:33.420 --> 00:17:36.384 If we knocked out the other
NOTE Confidence: 0.7813586
00:17:36.384 --> 00:17:38.360 exocyst complex members OK.
Set an RX-70.

We do not see that another way of saying this is if we destabilize The Exorcist so you don’t have your entire 8 protein complex and we no longer see that localization. OK, so that’s sort of a control experiment. Then you might well ask.

Well, OK, so it’s recruited. But where is? Where is it being recruited? Relative to the Exorcist relative to the cilia? And I kind of reminded you early on that you have this ciliary sheath.

This sort of a membrane which kind
00:18:13.168 --> 00:18:16.897 of does this put the pointer on.
NOTE Confidence: 0.7813586
00:18:16.900 --> 00:18:19.717 You know we have the membrane here and then.
NOTE Confidence: 0.7813586
00:18:19.720 --> 00:18:21.280 It’s a double membrane, right?
NOTE Confidence: 0.7813586
00:18:21.280 --> 00:18:23.345 So kind of goes like that and
NOTE Confidence: 0.7813586
00:18:23.345 --> 00:18:25.039 curves all the way around.
NOTE Confidence: 0.7813586
00:18:25.040 --> 00:18:28.210 OK so or you can kind of see it here
NOTE Confidence: 0.7813586
00:18:28.304 --> 00:18:30.356 in this cartoon. And is it here?
NOTE Confidence: 0.7813586
00:18:30.356 --> 00:18:32.547 If this is there or there now?
NOTE Confidence: 0.7813586
00:18:32.550 --> 00:18:34.734 As I there’s sort of different reports,
NOTE Confidence: 0.7813586
00:18:34.740 --> 00:18:36.305 there’s obviously the ones that
NOTE Confidence: 0.7813586
00:18:36.305 --> 00:18:37.557 have done the base.
NOTE Confidence: 0.7813586
00:18:37.560 --> 00:18:39.125 There have been some reports
NOTE Confidence: 0.7813586
00:18:39.125 --> 00:18:40.377 of about being inside,
NOTE Confidence: 0.7813586
00:18:40.380 --> 00:18:42.168 but we actually believe it is
NOTE Confidence: 0.7813586
00:18:42.168 --> 00:18:43.820 actually here along the pocket.
NOTE Confidence: 0.7813586
00:18:43.820 --> 00:18:45.989 And how do we know that by using a
super resolution imaging modality?

Construction limination microscopy and I think you can sort of see it easily here.

You'd have smooth and so this would be basically your cilia Reporter,

On the inner membrane, if you like to look at it that way and we see SEK 8 or X-70 is a wider distribution.

OK, so it is on for going.

Turn off my paper airplane
00:19:19.590 --> 00:19:21.605 here for going back.
NOTE Confidence: 0.7546144
00:19:21.605 --> 00:19:24.815 It would be on the sillari
NOTE Confidence: 0.7546144
00:19:24.815 --> 00:19:26.770 pocket membrane OK.
NOTE Confidence: 0.7546144
00:19:26.770 --> 00:19:29.720 Maybe switch to pen?
NOTE Confidence: 0.7546144
00:19:29.720 --> 00:19:32.896 So we see this is tribulus emerging.
NOTE Confidence: 0.7546144
00:19:32.900 --> 00:19:35.716 As I showed you an example and we
NOTE Confidence: 0.7546144
00:19:35.716 --> 00:19:38.418 actually see it in live cell imaging
NOTE Confidence: 0.7546144
00:19:38.418 --> 00:19:40.885 as well were these tubules are
NOTE Confidence: 0.7546144
00:19:40.885 --> 00:19:43.245 dynamically pulling out of Syria?
NOTE Confidence: 0.7546144
00:19:43.250 --> 00:19:46.094 OK so we think it’s actually
NOTE Confidence: 0.7546144
00:19:46.094 --> 00:19:47.990 important for the remodeling.
NOTE Confidence: 0.7546144
00:19:47.990 --> 00:19:48.540 ****
NOTE Confidence: 0.8248625
00:19:50.900 --> 00:19:52.455 It’s a little funny and
NOTE Confidence: 0.8248625
00:19:52.455 --> 00:19:53.388 giving this presentation.
NOTE Confidence: 0.8248625
00:19:53.390 --> 00:19:55.567 Switching back between the pens or not,
NOTE Confidence: 0.8248625
00:19:55.570 --> 00:19:57.818 but let me just tell you to sort
00:19:57.818 --> 00:20:00.341 of focus on here on the point of

00:20:00.341 --> 00:20:01.998 the Arrowhead where we actually

00:20:01.998 --> 00:20:04.252 think of that as a Fusion event

00:20:04.252 --> 00:20:06.132 so you have this internal cilia,

00:20:06.132 --> 00:20:08.320 the cilia which is inside the cell.

00:20:10.130 --> 00:20:14.110 Should. And is is here and you

00:20:14.110 --> 00:20:16.080 have SEK eight there on it.

00:20:16.080 --> 00:20:18.048 We think it’s important for them,

00:20:18.050 --> 00:20:19.142 the tethering function,

00:20:19.142 --> 00:20:21.690 and at this point right here where

00:20:21.757 --> 00:20:23.906 the membrane it looks like to expand

00:20:23.906 --> 00:20:26.278 you see that little bit of a burst.

00:20:26.280 --> 00:20:28.254 At that point, the SEK 8

00:20:28.254 --> 00:20:29.570 collapses to the base,

00:20:29.570 --> 00:20:32.266 which has been sort of reported in the
literature to exist most of the time, again at a single snapshot you mainly see it at the base, but actually if you look at it live over, you know it’s called longitudinal. Earlier on these internal cilia, so we actually think it’s driving that process out.

So well, how can we actually sort of prove this unequivocal? Blee and the way that we’ve done this is basically using a pH switching experiment, and when the cilia are outside, if we switch the pH,
and we have this pH sensitive Reporter, every time we switch it, it goes on and off. OK, so we make acidify, we can turn it off, and then it goes back on again. So we basically. Switching the pH, we can tell if it’s outside here, switching, going up and down, but as you can see in this context, is not. It’s actually resistant. And why is it resistant? Because inside the cell. So it is basically inside inside, and then here you can see it switch into the purple or magenta.
00:21:47.813 --> 00:21:49.473 indicating this now outside.
NOTE Confidence: 0.8034458
00:21:49.480 --> 00:21:53.470 OK, so there we can really say.
NOTE Confidence: 0.8034458
00:21:53.470 --> 00:21:57.180 Quickly that it is is
NOTE Confidence: 0.8034458
00:21:57.180 --> 00:21:59.406 actually merging overtime.
NOTE Confidence: 0.8034458
00:21:59.410 --> 00:22:01.622 And you can sort of see these
NOTE Confidence: 0.8034458
00:22:01.622 --> 00:22:02.800 experiments were switching pH,
NOTE Confidence: 0.8034458
00:22:02.800 --> 00:22:04.648 the intensity goes up and down,
NOTE Confidence: 0.8034458
00:22:04.650 --> 00:22:05.754 the second doesn’t change.
NOTE Confidence: 0.8034458
00:22:05.754 --> 00:22:07.468 Here is a case where is
NOTE Confidence: 0.8034458
00:22:07.468 --> 00:22:08.960 actually not changing much,
NOTE Confidence: 0.8034458
00:22:08.960 --> 00:22:09.878 the thing fuses.
NOTE Confidence: 0.8197327
00:22:05.754 --> 00:22:07.410 Here is a case where is
NOTE Confidence: 0.8034458
00:22:07.468 --> 00:22:08.960 actually not changing much,
NOTE Confidence: 0.8034458
00:22:08.960 --> 00:22:09.878 the thing fuses.
NOTE Confidence: 0.8197327
00:22:12.530 --> 00:22:14.420 Right, so it’s not switching much.
NOTE Confidence: 0.8197327
00:22:14.420 --> 00:22:16.590 It fuses now start switching and then
NOTE Confidence: 0.8197327
00:22:16.590 --> 00:22:19.265 just a little bit later you see the
NOTE Confidence: 0.8197327
00:22:19.265 --> 00:22:20.940 The Exorcist is actually changing
NOTE Confidence: 0.8197327
00:22:21.005 --> 00:22:23.007 part of it and then it eventually
00:22:23.007 --> 00:22:26.645 drops off and fully into the base. OK,

00:22:26.645 --> 00:22:29.965 so we can start to identify with machinery.

00:22:29.970 --> 00:22:32.938 Is there sort of looking at who might

00:22:32.938 --> 00:22:36.210 be the players that might be engaging

00:22:36.210 --> 00:22:39.482 with The Exorcist and there is some

00:22:39.482 --> 00:22:42.450 interesting ones such as Rab 10 is a

00:22:42.450 --> 00:22:45.677 likely player and actually we see Rab

00:22:45.677 --> 00:22:48.485 10 localising there which is actually

00:22:48.485 --> 00:22:51.600 different from some of the other apps

00:22:51.688 --> 00:22:54.928 so I’d like to sort of end now and their

00:22:54.930 --> 00:22:57.070 remaining minutes with basically are.

00:22:57.070 --> 00:22:59.188 The working model and just walk

00:22:59.188 --> 00:23:01.200 you through that very briefly,

00:23:01.200 --> 00:23:03.450 so the working model is that.

00:23:03.450 --> 00:23:04.479 In this starves,
say you have cilia with these
sort of deeply emerged pockets.
The Exorcist is in the facilities
recycling endosomes and probably have
some targeting of that success here.
In the serums to stimulation,
that which is actually the normal case,
right?
If you sort of thought about
sleep in the body.
There, there actually
constantly being remodled.
constantly being remodled.
OK,
so the event of releasing the vesicles
actually different than sort of was proposed.
We believe of it sort of coming off from
one that’s fully outside this actually,
as it starts to pull in,
we believe that it was remodeling that can
actually promote this vesicle to release.
Once inside you have recruitment of
the Exorcist to this large and inside.
Which is again majority of this sort
of internalize cilia which can remodel,
pulling off tubules and consequently
then can recycle back.
So you have this entire pathway here
that can modulate the signaling.
So with sort of that this is.
Switch back to automatic.
Really this is really driven by senior
scientist in the lab Felix Riviera Molina.
NOTE Confidence: 0.79843205

Sort was reported by the people,
NOTE Confidence: 0.79843205

but really he took the lead here,
NOTE Confidence: 0.79843205

so that's where I'd like to end and
NOTE Confidence: 0.79843205

address any comments that you might have.
NOTE Confidence: 0.8779377

Thank you for very interesting talk.
NOTE Confidence: 0.8779377

Are there questions from the audience?
NOTE Confidence: 0.80636364

Let me put that you
NOTE Confidence: 0.80636364

can just type them in.
NOTE Confidence: 0.7957481

While we're waiting, yeah.
NOTE Confidence: 0.7957481

So there are a lot of genetic disorders
NOTE Confidence: 0.7957481

of cilia formation that have many
NOTE Confidence: 0.7957481

different phenotypes or anything
NOTE Confidence: 0.7957481

associated with increased cancer risk.
NOTE Confidence: 0.8162323

Yes, there have been and
NOTE Confidence: 0.8162323

there were sort of where it gets
complicated is it depends on sort of what cell types you’re looking at it. Again, again, you know pushing things up and down and sort of mentioning earlier. So yes, there are. Haven’t been sort of investigating this so much personally but but yes. Thank you. Questions for Derek. I know this zoom atmosphere makes it a little bit different. Will. So enjoy when we see people face to face again. Another question then should in. In cancer cells,
which are obviously many of them

often constantly proliferating,

do you see abnormalities of

cilia formation you could?

Do they have more cilia?

Do they turn over more rapidly?

What happens?

This is a little bit as alluding to

you can kind of push it either way,

so that’s where that’s actually where the

confusion is to cancer is that you would say,

well, do they have more silly?

Do they have less cilia and basically

the paper review had indicated that

there’s sort of the two sides on it,

so in one case you actually hyper
activate by, let’s say adding smoothing and hedgehogs signaling, so the Hedgehog is obviously a key component, as same as sort of PGF would be basically a hyper activated. The other case is where you would actually activate the signaling by the absence of the cilia. So that’s sort of where it’s you know. In some cancers are driven by having cilia, and some are driven by the absence. Sort of given the this sort of the funny paradox. Depending on that nature of which signaling pathway you’re talking about.
Is it a hedgehog sort of smoothing type of one or other signaling pathway?
And what is the activation at the Basel State?
So that’s why I think it’s given some complexity to the field because you couldn’t just simply say this is only this week, but it does.
There’s evidence for both there. Are there other any other questions in the audience? If not, thank you.
Thank you all for coming. Thank you for two speakers.
It was very interesting and
NOTE Confidence: 0.8601161
00:27:39.535 --> 00:27:41.446 everybody you have a 22 extra

NOTE Confidence: 0.8601161
00:27:41.446 --> 00:27:43.370 minutes for your day. Thank you.

NOTE Confidence: 0.8601161
00:27:43.370 --> 00:27:45.311 Thank you Dan.