WEBVTT

NOTE duration:"00:27:45.3120000"

NOTE language:en-us

NOTE Confidence: 0.7802432

00:00:00.000 --> 00:00:03.024 Our second speaker today is Derrick Tom Ray,

NOTE Confidence: 0.7802432

00:00:03.030 --> 00:00:05.082 who's professor of cell biology and

NOTE Confidence: 0.7802432

00:00:05.082 --> 00:00:07.859 director of the Yale Cinema Microscopy Lab,

NOTE Confidence: 0.7802432

00:00:07.860 --> 00:00:09.720 received his PhD from University.

NOTE Confidence: 0.7802432

00:00:09.720 --> 00:00:11.580 California is an expert on

NOTE Confidence: 0.7802432

00:00:11.580 --> 00:00:13.068 quantitative live cell imaging,

NOTE Confidence: 0.7802432

00:00:13.070 --> 00:00:14.930 and he specializes in innovative

NOTE Confidence: 0.7802432

00:00:14.930 --> 00:00:16.046 approaches to microscopy,

NOTE Confidence: 0.7802432

00:00:16.050 --> 00:00:17.166 including fluorescent probes,

NOTE Confidence: 0.7802432

00:00:17.166 --> 00:00:19.095 data analysis, and spatial mapping.

NOTE Confidence: 0.7802432

00:00:19.095 --> 00:00:21.070 Received an NIH director's New

NOTE Confidence: 0.7802432

00:00:21.070 --> 00:00:23.108 Innovator Award and a coffee fellow,

NOTE Confidence: 0.7802432

00:00:23.110 --> 00:00:24.970 and today is there talk

NOTE Confidence: 0.7802432

00:00:24.970 --> 00:00:26.458 about his recent work,

NOTE Confidence: 0.7802432

00:00:26.460 --> 00:00:28.542 which is primarily focused on spatial

NOTE Confidence: 0.7802432

00:00:28.542 --> 00:00:29.930 control of membrane trafficking

NOTE Confidence: 0.7802432

00:00:29.980 --> 00:00:31.788 during cell morphogenesis migration.

NOTE Confidence: 0.7802432

00:00:31.790 --> 00:00:32.954 In cilia formation.

NOTE Confidence: 0.7802432

00:00:32.954 --> 00:00:35.270 So Derek, the floor is yours.

NOTE Confidence: 0.8684666

00:00:48.600 --> 00:00:49.010 So.

NOTE Confidence: 0.60271686

00:00:51.670 --> 00:00:55.340 Derek, your music. Yeah

NOTE Confidence: 0.8615084

00:00:55.340 --> 00:00:58.810 OK, great. Let me go back a slide or two.

NOTE Confidence: 0.8072154

00:01:02.760 --> 00:01:05.488 Great, so I'll be talking bout cilia which

NOTE Confidence: 0.8072154

00:01:05.488 --> 00:01:08.480 have some relevance to cancer and signaling.

NOTE Confidence: 0.8072154

00:01:08.480 --> 00:01:10.965 I'll be talking basically about a new

NOTE Confidence: 0.8072154

00:01:10.965 --> 00:01:13.298 pathway that we're discovering and tell

NOTE Confidence: 0.8072154

00:01:13.298 --> 00:01:15.704 you about the ramifications of this.

NOTE Confidence: 0.8072154

00:01:15.710 --> 00:01:18.377 I not talking anybody work on SARS?

NOTE Confidence: 0.8072154

00:01:18.380 --> 00:01:21.992 Kobe 2 but I do have some work on that and

NOTE Confidence: 0.8072154

00:01:21.992 --> 00:01:25.240 my conflict of interest is declared there.

NOTE Confidence: 0.8072154

00:01:25.240 --> 00:01:27.907 So is Sherman sort of a primary?

NOTE Confidence: 0.8072154

00:01:27.910 --> 00:01:30.655 Let me just tell you the main message in

NOTE Confidence: 0.8072154

00:01:30.655 --> 00:01:33.655 the main message is that we're proposing

NOTE Confidence: 0.8072154

00:01:33.655 --> 00:01:36.030 and characterizing a novel pathway.

NOTE Confidence: 0.8072154

00:01:36.030 --> 00:01:37.770 Of cilia delivery to the surface

NOTE Confidence: 0.8072154

00:01:37.770 --> 00:01:40.028 and I will sort of tell you what.

NOTE Confidence: 0.8072154

00:01:40.030 --> 00:01:41.395 Basically the central paradigm is

NOTE Confidence: 0.8072154

00:01:41.395 --> 00:01:43.802 and then go on to sort of describe to

NOTE Confidence: 0.8072154

00:01:43.802 --> 00:01:45.666 you that I think that that basically

NOTE Confidence: 0.8072154

00:01:45.666 --> 00:01:47.628 our data suggests that we have

NOTE Confidence: 0.8072154

00:01:47.628 --> 00:01:48.900 an alternate pathway here.

NOTE Confidence: 0.89520365

00:01:51.330 --> 00:01:55.639 OK. Just. OK, it's clicking differently,

NOTE Confidence: 0.89520365

00:01:55.639 --> 00:01:59.192 so we first start off with a quick

NOTE Confidence: 0.89520365

00:01:59.192 --> 00:02:02.279 primer here about primary cilia so you

NOTE Confidence: 0.89520365

00:02:02.279 --> 00:02:05.206 know really sort of two aspects here.

NOTE Confidence: 0.89520365

00:02:05.210 --> 00:02:06.515 What are they?

NOTE Confidence: 0.89520365

00:02:06.515 --> 00:02:09.560 And I suppose sort of related here,

NOTE Confidence: 0.89520365

00:02:09.560 --> 00:02:13.040 why do you care? Why should we care?

NOTE Confidence: 0.89520365

00:02:13.040 --> 00:02:16.085 So in terms of the first part,

NOTE Confidence: 0.89520365

00:02:16.090 --> 00:02:17.830 that's relatively easy there

NOTE Confidence: 0.89520365

00:02:17.830 --> 00:02:19.570 long slender cellular antenna.

NOTE Confidence: 0.89520365

00:02:19.570 --> 00:02:21.306 They're basically present on

NOTE Confidence: 0.89520365

00:02:21.306 --> 00:02:23.534 nearly all cells. There's a.

NOTE Confidence: 0.89520365

00:02:23.534 --> 00:02:25.382 The exceptions being red

NOTE Confidence: 0.89520365

00:02:25.382 --> 00:02:27.850 blood cells and T cells.

NOTE Confidence: 0.89520365

00:02:27.850 --> 00:02:31.270 If you go by electron microscopy.

NOTE Confidence: 0.89520365

00:02:31.270 --> 00:02:33.526 End both sort of light microscopy.

NOTE Confidence: 0.89520365

00:02:33.530 --> 00:02:35.786 You see their long and slender.

NOTE Confidence: 0.89520365

00:02:35.790 --> 00:02:38.366 The width is maybe 152 nanometers and

NOTE Confidence: 0.89520365

00:02:38.366 --> 00:02:41.070 they can extend about 10 microns long.

NOTE Confidence: 0.89520365

00:02:41.070 --> 00:02:43.215 There's solid Terry organelles their

NOTE Confidence: 0.89520365

00:02:43.215 --> 00:02:46.707 primary cilia and let me tell you a little

NOTE Confidence: 0.89520365

00:02:46.707 --> 00:02:50.700 bit about some of the known functions.

NOTE Confidence: 0.89520365

00:02:50.700 --> 00:02:53.778 So you can sort of think of them

NOTE Confidence: 0.89520365

00:02:53.778 --> 00:02:55.970 as a specialized sensory antenna,

NOTE Confidence: 0.89520365

00:02:55.970 --> 00:02:58.665 so you have a adaption of this

NOTE Confidence: 0.89520365

00:02:58.665 --> 00:03:01.229 for vision of your rod cells.

NOTE Confidence: 0.89520365

00:03:01.230 --> 00:03:04.286 I guess relevant to right now and and

NOTE Confidence: 0.89520365

00:03:04.286 --> 00:03:06.900 coronavirus they also important for smell.

NOTE Confidence: 0.89520365

00:03:06.900 --> 00:03:09.684 And there is a loss of cilia which

NOTE Confidence: 0.89520365

00:03:09.684 --> 00:03:12.159 is causing the Syrian dysfunction of

NOTE Confidence: 0.89520365

00:03:12.159 --> 00:03:15.410 that and as well as signaling aspects.

NOTE Confidence: 0.89520365

00:03:15.410 --> 00:03:17.804 And we sort of mentioned a little

NOTE Confidence: 0.89520365

00:03:17.804 --> 00:03:20.370 bit more on that because it's

NOTE Confidence: 0.89520365

00:03:20.370 --> 00:03:22.795 really relevant to this audience.

NOTE Confidence: 0.89520365

00:03:22.800 --> 00:03:26.470 Especially in regards to cancer.

NOTE Confidence: 0.89520365

00:03:26.470 --> 00:03:28.550 So primary slip, so why?

NOTE Confidence: 0.89520365

00:03:28.550 --> 00:03:31.040 Why do you care in this?

NOTE Confidence: 0.89520365

00:03:31.040 --> 00:03:33.672 And the easiest way of sort of

NOTE Confidence: 0.89520365

00:03:33.672 --> 00:03:35.799 thinking of this is thinking

NOTE Confidence: 0.89520365

00:03:35.799 --> 00:03:38.084 of in terms of ciliopathies.

NOTE Confidence: 0.89520365

00:03:38.090 --> 00:03:38.501 OK,

NOTE Confidence: 0.89520365

00:03:38.501 --> 00:03:40.967 there's a number of diseases that

NOTE Confidence: 0.89520365

00:03:40.967 --> 00:03:43.201 are basically dependent was actually

NOTE Confidence: 0.89520365

00:03:43.201 --> 00:03:45.061 sort of discovered retractively

NOTE Confidence: 0.89520365

00:03:45.061 --> 00:03:47.306 these diseases have been known

NOTE Confidence: 0.89520365

00:03:47.306 --> 00:03:48.876 for quite a long time,

NOTE Confidence: 0.89520365

00:03:48.880 --> 00:03:51.526 and then only in the last couple

NOTE Confidence: 0.89520365

00:03:51.526 --> 00:03:54.279 of decades was it really realized,

NOTE Confidence: 0.89520365

00:03:54.280 --> 00:03:57.430 in part from pioneering work at Yale.

NOTE Confidence: 0.89520365

00:03:57.430 --> 00:04:00.070 About the sort of link between

NOTE Confidence: 0.89520365

00:04:00.070 --> 00:04:01.830 these diseases and disruptive

NOTE Confidence: 0.89520365

00:04:01.907 --> 00:04:04.322 ciliary function so you can see this

NOTE Confidence: 0.89520365

00:04:04.322 --> 00:04:06.813 in sort of the Joubert syndrome

NOTE Confidence: 0.89520365

00:04:06.813 --> 00:04:08.657 or liver cysts kidneys.

NOTE Confidence: 0.89520365

00:04:08.660 --> 00:04:12.250 It's quite multi multi organal.

NOTE Confidence: 0.89520365

00:04:12.250 --> 00:04:13.960 But again, for this audience,

NOTE Confidence: 0.89520365

00:04:13.960 --> 00:04:16.078 I think it was particularly relevant

NOTE Confidence: 0.89520365

00:04:16.078 --> 00:04:18.408 is in the context of of cancer,

NOTE Confidence: 0.89520365

00:04:18.410 --> 00:04:20.970 and you can sort of think of it

NOTE Confidence: 0.89520365

00:04:20.970 --> 00:04:23.536 in terms of sort of two aspects,

NOTE Confidence: 0.89520365

00:04:23.540 --> 00:04:24.626 one aberrant signaling,

NOTE Confidence: 0.89520365

00:04:24.626 --> 00:04:27.541 and then your cilia being part of that

NOTE Confidence: 0.89520365

00:04:27.541 --> 00:04:30.029 rule that would turn things on and off.

NOTE Confidence: 0.89520365

00:04:30.030 --> 00:04:32.298 It gets a little more complex here

NOTE Confidence: 0.89520365

00:04:32.298 --> 00:04:34.391 because you actually can release vesicles

NOTE Confidence: 0.89520365

00:04:34.391 --> 00:04:36.862 from a cell which can transmit signals,

NOTE Confidence: 0.89520365

00:04:36.870 --> 00:04:39.875 so that's one aspect of it, but you can

NOTE Confidence: 0.89520365

00:04:39.875 --> 00:04:43.129 sort of think of it in a simple way.

NOTE Confidence: 0.89520365

00:04:43.130 --> 00:04:45.770 Simplified way of controlling

NOTE Confidence: 0.89520365

00:04:45.770 --> 00:04:49.070 this signaling on or off.

NOTE Confidence: 0.89520365

00:04:49.070 --> 00:04:49.448 Now,

NOTE Confidence: 0.89520365

00:04:49.448 --> 00:04:51.716 just to sort of just highlighting

NOTE Confidence: 0.89520365

00:04:51.716 --> 00:04:54.029 that complexity was sort of a review,

NOTE Confidence: 0.89520365

00:04:54.030 --> 00:04:56.160 that sort of indicates that it

NOTE Confidence: 0.89520365

00:04:56.160 --> 00:04:57.920 actually can go either way.

NOTE Confidence: 0.89520365

00:04:57.920 --> 00:05:00.044 You could have a certain degree

NOTE Confidence: 0.89520365

00:05:00.044 --> 00:05:02.260 of activation you could turn on

NOTE Confidence: 0.89520365

00:05:02.260 --> 00:05:04.095 hedgehog by activation of this

NOTE Confidence: 0.89520365

00:05:04.095 --> 00:05:06.417 receptor level and sort of pathway B.

NOTE Confidence: 0.89520365

00:05:06.420 --> 00:05:08.898 Or you could actually do it by

NOTE Confidence: 0.89520365

00:05:08.898 --> 00:05:09.960 going independent that.

NOTE Confidence: 0.89520365

00:05:09.960 --> 00:05:12.616 So if you look at cancer is summer

NOTE Confidence: 0.89520365

00:05:12.616 --> 00:05:14.910 activated by the presence of silly,

NOTE Confidence: 0.89520365

00:05:14.910 --> 00:05:17.040 and some are by the repression.

NOTE Confidence: 0.8284338

00:05:17.040 --> 00:05:19.236 OK, but if we sort of.

NOTE Confidence: 0.8284338

00:05:19.240 --> 00:05:21.858 Go beyond that aspect and say well,

NOTE Confidence: 0.8284338

00:05:21.860 --> 00:05:24.478 what is sort of the normal paradigm.

NOTE Confidence: 0.8284338

00:05:24.480 --> 00:05:26.736 Well, the normal paradigm here is

NOTE Confidence: 0.8284338

00:05:26.736 --> 00:05:29.339 that cilia occur once per cell cycle.

NOTE Confidence: 0.8284338

00:05:29.340 --> 00:05:31.545 OK, so you generate them and during

NOTE Confidence: 0.8284338

00:05:31.545 --> 00:05:34.034 G and G1G0 there sort of present

NOTE Confidence: 0.8284338

00:05:34.034 --> 00:05:35.879 throughout and then they have

NOTE Confidence: 0.8284338

00:05:35.879 --> 00:05:38.308 to be assembled during division.

NOTE Confidence: 0.8284338

00:05:38.310 --> 00:05:39.726 So in that sense,

NOTE Confidence: 0.8284338

00:05:39.726 --> 00:05:42.799 if you think of it from that lens,

NOTE Confidence: 0.8284338

00:05:42.800 --> 00:05:45.140 you're really not controlling except

NOTE Confidence: 0.8284338

00:05:45.140 --> 00:05:48.739 for to the point of cell division.

NOTE Confidence: 0.8284338

00:05:48.740 --> 00:05:51.078 And maybe any delays on whether you

NOTE Confidence: 0.8284338

00:05:51.078 --> 00:05:53.128 would have slid Genesis or not,

NOTE Confidence: 0.8284338

00:05:53.130 --> 00:05:54.820 and I'd like to say,

NOTE Confidence: 0.8284338

00:05:54.820 --> 00:05:57.360 change that paradigm view.

NOTE Confidence: 0.8284338

00:05:57.360 --> 00:05:58.604 So remind you again.

NOTE Confidence: 0.8284338

00:05:58.604 --> 00:06:01.179 I do a lot of imaging as you

NOTE Confidence: 0.8284338

00:06:01.179 --> 00:06:03.069 sort of heard in the intro,

NOTE Confidence: 0.8284338

00:06:03.070 --> 00:06:05.303 and this is just one example of

NOTE Confidence: 0.8284338

00:06:05.303 --> 00:06:07.258 super resolution image Ng where we

NOTE Confidence: 0.8284338

00:06:07.258 --> 00:06:09.136 can actually see this very long

NOTE Confidence: 0.8284338

00:06:09.136 --> 00:06:10.676 structure of cilia, which is,

NOTE Confidence: 0.8284338

00:06:10.676 --> 00:06:11.630 like I said,

NOTE Confidence: 0.8284338

00:06:11.630 --> 00:06:13.838 it could be you know 10 microns or

NOTE Confidence: 0.8284338

00:06:13.838 --> 00:06:15.899 so long with the resolution down

NOTE Confidence: 0.8284338

00:06:15.899 --> 00:06:18.430 to sort of 20 nanometers where you

NOTE Confidence: 0.8284338

00:06:18.430 --> 00:06:20.495 could actually see it as a tube.

NOTE Confidence: 0.8284338

00:06:20.500 --> 00:06:22.396 So that's one sort of technique,

NOTE Confidence: 0.8284338

00:06:22.400 --> 00:06:24.374 but I'm going to show you another

NOTE Confidence: 0.8284338

00:06:24.374 --> 00:06:25.890 source of imaging techniques,

NOTE Confidence: 0.8284338

00:06:25.890 --> 00:06:27.474 and in short of.

NOTE Confidence: 0.8284338

00:06:27.474 --> 00:06:29.850 Exemplify that can provide new insight.

NOTE Confidence: 0.8284338

00:06:29.850 --> 00:06:30.620 Here again,

NOTE Confidence: 0.8284338

00:06:30.620 --> 00:06:32.930 this is sort of the structural

NOTE Confidence: 0.8284338

00:06:32.930 --> 00:06:34.799 aspects of this accident.

NOTE Confidence: 0.8284338

00:06:34.800 --> 00:06:37.696 Sort of in the side, which is,

NOTE Confidence: 0.8284338

00:06:37.696 --> 00:06:39.348 it's just relatively relevant,

NOTE Confidence: 0.8284338

00:06:39.350 --> 00:06:42.150 is that they can present with this

NOTE Confidence: 0.8284338

00:06:42.150 --> 00:06:44.681 pocket Macy put the laser pointer

NOTE Confidence: 0.8284338

00:06:44.681 --> 00:06:47.183 on and in the ciliary pocket.

NOTE Confidence: 0.8284338

00:06:47.190 --> 00:06:47.593 Here,

NOTE Confidence: 0.8284338

00:06:47.593 --> 00:06:50.414 and this is the sort of shown

NOTE Confidence: 0.8284338

00:06:50.414 --> 00:06:51.740 extra short here,

NOTE Confidence: 0.8284338

00:06:51.740 --> 00:06:55.036 but this can be a very deep imagination.

NOTE Confidence: 0.8284338

00:06:55.040 --> 00:06:57.638 In fact it can almost be.

NOTE Confidence: 0.8284338

00:06:57.640 --> 00:06:58.702 Nearly entirely evaginated.

NOTE Confidence: 0.8284338

00:06:58.702 --> 00:06:59.056 OK,

NOTE Confidence: 0.8284338

00:06:59.056 --> 00:07:01.870 So what is sort of the key process

NOTE Confidence: 0.8284338

00:07:01.870 --> 00:07:03.736 of how they how they form?

NOTE Confidence: 0.8284338

00:07:03.740 --> 00:07:04.972 So the general paradigm,

NOTE Confidence: 0.8284338

00:07:04.972 --> 00:07:06.512 in fact there's there's one

NOTE Confidence: 0.8284338

00:07:06.512 --> 00:07:07.809 for epithelial cells,

NOTE Confidence: 0.8284338

00:07:07.810 --> 00:07:10.176 which I will not sort of discuss,

NOTE Confidence: 0.8284338

00:07:10.180 --> 00:07:12.220 but for most of the cells.

NOTE Confidence: 0.8284338

00:07:12.220 --> 00:07:13.508 In fact the majority,

NOTE Confidence: 0.8284338

00:07:13.508 --> 00:07:15.440 if they start with this silly

NOTE Confidence: 0.8284338

00:07:15.506 --> 00:07:16.958 or vesicle which forms,

NOTE Confidence: 0.8284338

00:07:16.960 --> 00:07:19.424 and then you have this double membrane

NOTE Confidence: 0.8284338

00:07:19.424 --> 00:07:21.369 membrane which should have bends in.

NOTE Confidence: 0.8284338

00:07:21.370 --> 00:07:23.398 And then you actually have this,

NOTE Confidence: 0.8284338

00:07:23.400 --> 00:07:26.460 really think of it as a super large vesicle.

NOTE Confidence: 0.8284338

00:07:26.460 --> 00:07:27.711 It's a vesicle.

NOTE Confidence: 0.8284338

00:07:27.711 --> 00:07:30.630 This vesicle could be 7 microns long,

NOTE Confidence: 0.8284338

00:07:30.630 --> 00:07:31.084 OK,

NOTE Confidence: 0.8284338

00:07:31.084 --> 00:07:35.170 and then as a an event it actually has

NOTE Confidence: 0.8284338

00:07:35.278 --> 00:07:39.709 to go infuse the plasma membrane produce.

NOTE Confidence: 0.8284338

00:07:39.710 --> 00:07:41.330 This is a, you know,

NOTE Confidence: 0.8284338

00:07:41.330 --> 00:07:42.940 this is a standard paradigm.

NOTE Confidence: 0.8284338

00:07:42.940 --> 00:07:45.526 This happens once per cell cycle

NOTE Confidence: 0.8284338

00:07:45.526 --> 00:07:48.050 would be the standard paradigm.

NOTE Confidence: 0.8284338

00:07:48.050 --> 00:07:51.570 Now I want to bring in one other

NOTE Confidence: 0.8284338

00:07:51.570 --> 00:07:54.850 player here and this is one that

NOTE Confidence: 0.8284338

00:07:54.850 --> 00:07:57.650 we've worked with quite a bit,

NOTE Confidence: 0.8284338

00:07:57.650 --> 00:08:00.386 which is called the exocyst complexes,

NOTE Confidence: 0.8284338

00:08:00.390 --> 00:08:01.806 the tethering complex.

NOTE Confidence: 0.8284338

00:08:01.806 --> 00:08:04.166 It was first discovered actually

NOTE Confidence: 0.8284338

00:08:04.166 --> 00:08:05.870 at Yale in yeast,

NOTE Confidence: 0.8284338

00:08:05.870 --> 00:08:09.055 and basically it is known to basically

NOTE Confidence: 0.8284338

00:08:09.055 --> 00:08:11.576 drive the upstream monsters near

NOTE Confidence: 0.8284338

00:08:11.576 --> 00:08:14.251 Fusion machinery to allow spatial

NOTE Confidence: 0.8284338

00:08:14.251 --> 00:08:17.459 temporal control of vesicle exocytosis.

NOTE Confidence: 0.8284338

00:08:17.460 --> 00:08:20.588 This is you can sort of see in.

NOTE Confidence: 0.8284338

00:08:20.590 --> 00:08:22.702 This review has been thought to

NOTE Confidence: 0.8284338

00:08:22.702 --> 00:08:25.240 for quite some while play a role

NOTE Confidence: 0.8284338

00:08:25.240 --> 00:08:27.000 in cilia and mainly ciliogenesis

NOTE Confidence: 0.8284338

00:08:27.000 --> 00:08:29.139 and and stabilization by targeting

NOTE Confidence: 0.8284338

00:08:29.139 --> 00:08:31.409 the vesicles right here where

NOTE Confidence: 0.8284338

00:08:31.409 --> 00:08:32.317 they would

NOTE Confidence: 0.8069569

00:08:32.320 --> 00:08:34.534 fuse and then basically drive let's

NOTE Confidence: 0.8069569

00:08:34.534 --> 00:08:36.497 say control within the accident

NOTE Confidence: 0.8069569

00:08:36.497 --> 00:08:38.567 that is the standard paradigm.

NOTE Confidence: 0.8069569

00:08:38.570 --> 00:08:42.480 And while I don't want to say that is wrong,

NOTE Confidence: 0.8069569

00:08:42.480 --> 00:08:44.440 I think it's actually missing.

NOTE Confidence: 0.8069569

00:08:44.440 --> 00:08:48.500 Let's say 80% of the picture OK.

NOTE Confidence: 0.8069569

00:08:48.500 --> 00:08:50.635 So we sort of go back to,

NOTE Confidence: 0.8069569

00:08:50.640 --> 00:08:52.944 you know why we have this paradigm and and

NOTE Confidence: 0.8069569

00:08:52.944 --> 00:08:55.537 and what sort of the underlying underpinning?

NOTE Confidence: 0.8069569

00:08:55.540 --> 00:08:58.052 Well, is it? You know I want to

NOTE Confidence: 0.8069569

00:08:58.052 --> 00:08:59.818 basically first say that is Dre.

NOTE Confidence: 0.8069569

00:08:59.820 --> 00:09:01.350 It's based on indirect evidence.

NOTE Confidence: 0.8069569

00:09:01.350 --> 00:09:02.880 We've actually not seen the

NOTE Confidence: 0.8069569

00:09:02.880 --> 00:09:04.104 vesicles their fusing there,

NOTE Confidence: 0.8069569

00:09:04.110 --> 00:09:06.245 nor actually seen much of the Exorcist.

NOTE Confidence: 0.8069569

00:09:06.250 --> 00:09:08.490 And I would say that you're missing something

NOTE Confidence: 0.8069569

00:09:08.490 --> 00:09:10.527 that's really important and it's incomplete.

NOTE Confidence: 0.8069569

00:09:10.530 --> 00:09:12.930 But let's sort of get beyond that and

NOTE Confidence: 0.8069569

00:09:12.930 --> 00:09:15.425 show you what I may be talking about.

NOTE Confidence: 0.8069569

00:09:15.430 --> 00:09:17.677 But first I have to tell you.

NOTE Confidence: 0.8069569

00:09:17.680 --> 00:09:19.655 Why, if we're claiming to

NOTE Confidence: 0.8069569

00:09:19.655 --> 00:09:20.840 see something different,

NOTE Confidence: 0.8069569

00:09:20.840 --> 00:09:24.542 why and how are we able to do so when people

NOTE Confidence: 0.8069569

00:09:24.542 --> 00:09:27.944 been looking at Syria for quite awhile?

NOTE Confidence: 0.8069569

00:09:27.950 --> 00:09:30.526 And so there are a number of

NOTE Confidence: 0.8069569

00:09:30.526 --> 00:09:32.690 technical aspects to the solution.

NOTE Confidence: 0.8069569

00:09:32.690 --> 00:09:35.578 The first one is we're using a technique

NOTE Confidence: 0.8069569

00:09:35.578 --> 00:09:38.217 called total internal reflection for us.

NOTE Confidence: 0.8069569

00:09:38.220 --> 00:09:39.214 Since microscopy,

NOTE Confidence: 0.8069569

00:09:39.214 --> 00:09:41.202 let's say axial superresolution

NOTE Confidence: 0.8069569

00:09:41.202 --> 00:09:44.199 technique and it allows us to image

NOTE Confidence: 0.8069569

00:09:44.199 --> 00:09:46.893 just the lower surface of the cell and

NOTE Confidence: 0.8069569

00:09:46.893 --> 00:09:49.048 actually see silly's emergence OK.

NOTE Confidence: 0.8069569

00:09:49.050 --> 00:09:50.522 But that actually even

NOTE Confidence: 0.8069569

00:09:50.522 --> 00:09:51.258 without superresolution,

NOTE Confidence: 0.8069569

00:09:51.260 --> 00:09:52.728 technique is not enough

NOTE Confidence: 0.8069569

00:09:52.728 --> 00:09:54.196 to be unequivocal there.

NOTE Confidence: 0.8069569

00:09:54.200 --> 00:09:56.060 The distance between cilia and

NOTE Confidence: 0.8069569

00:09:56.060 --> 00:09:58.620 the surface at times is very low,

NOTE Confidence: 0.8069569

00:09:58.620 --> 00:10:01.098 and it's actually not clear if they

NOTE Confidence: 0.8069569

00:10:01.098 --> 00:10:03.735 are inside the cell or actually have

NOTE Confidence: 0.8069569

00:10:03.735 --> 00:10:06.771 emerged in or outside and think of it

NOTE Confidence: 0.8069569

00:10:06.771 --> 00:10:08.922 again like your antenna, your antenna.

NOTE Confidence: 0.8069569

00:10:08.922 --> 00:10:10.386 If you sort of.

NOTE Confidence: 0.8069569

00:10:10.390 --> 00:10:11.698 Just give an analogy,

NOTE Confidence: 0.8069569

00:10:11.698 --> 00:10:14.138 is going to respond to signals quite

NOTE Confidence: 0.8069569

00:10:14.138 --> 00:10:16.168 differently if it's actually outside

NOTE Confidence: 0.8069569

00:10:16.168 --> 00:10:18.766 your car truck, what, whatever it be.

NOTE Confidence: 0.8069569

00:10:18.766 --> 00:10:20.486 Versus pulled it inside where

NOTE Confidence: 0.8069569

00:10:20.486 --> 00:10:22.618 it cannot receive the signals.

NOTE Confidence: 0.8069569

00:10:22.620 --> 00:10:25.140 OK, at least not the same signals.

NOTE Confidence: 0.8069569

00:10:25.140 --> 00:10:27.373 The other technical aspect is is we

NOTE Confidence: 0.8069569

00:10:27.373 --> 00:10:30.034 used a a McLeod clever pH switching

NOTE Confidence: 0.8069569

00:10:30.034 --> 00:10:33.059 to identify when cilia are in or out.

NOTE Confidence: 0.8069569

00:10:33.060 --> 00:10:35.348 We're using this as an impulse way and

NOTE Confidence: 0.8069569

00:10:35.348 --> 00:10:38.458 we do molecular replacement of the Exorcist.

NOTE Confidence: 0.8069569

00:10:38.460 --> 00:10:42.012 The latter was important because for a long

NOTE Confidence: 0.8069569

00:10:42.012 --> 00:10:45.167 time people were image in the Exorcist.

NOTE Confidence: 0.8069569

00:10:45.170 --> 00:10:47.214 Or just simply overexpressing it and they

NOTE Confidence: 0.8069569

00:10:47.214 --> 00:10:49.370 would sort of see localizations like

NOTE Confidence: 0.8069569

00:10:49.370 --> 00:10:51.400 this everywhere or some accumulations,

NOTE Confidence: 0.8069569

00:10:51.400 --> 00:10:53.638 but when we did this replacement

NOTE Confidence: 0.8069569

00:10:53.638 --> 00:10:56.160 strategy we could see it in these

NOTE Confidence: 0.8069569

00:10:56.160 --> 00:10:58.386 discrete punkte OK and this is now

NOTE Confidence: 0.8069569

00:10:58.458 --> 00:11:00.782 this is going into HeLa and other

NOTE Confidence: 0.8069569

00:11:00.782 --> 00:11:02.836 types of cells looking at vesicle

NOTE Confidence: 0.8069569

00:11:02.836 --> 00:11:05.300 excess cytosis and we could see in

NOTE Confidence: 0.8069569

00:11:05.373 --> 00:11:07.449 these kind of graphs distinct events

NOTE Confidence: 0.8069569

00:11:07.449 --> 00:11:10.204 and I just show you one trace where

NOTE Confidence: 0.8069569

00:11:10.204 --> 00:11:12.852 vesicle has arrived as we see with the

NOTE Confidence: 0.8069569

00:11:12.852 --> 00:11:14.928 Exorcist and then with another Reporter.

NOTE Confidence: 0.8069569

00:11:14.930 --> 00:11:16.150 And this is a.

NOTE Confidence: 0.8069569

00:11:16.150 --> 00:11:18.863 Any Reporter here which is a floor in

NOTE Confidence: 0.8069569

00:11:18.863 --> 00:11:21.691 with the pH sensor we can actually

NOTE Confidence: 0.8069569

00:11:21.691 --> 00:11:24.018 unequivocally identify the Fusion event,

NOTE Confidence: 0.8069569

00:11:24.020 --> 00:11:27.076 so this is sort of a constitutive pathway.

NOTE Confidence: 0.8069569

00:11:27.080 --> 00:11:30.083 We know it's coming from recycling vesicles

NOTE Confidence: 0.8069569

00:11:30.083 --> 00:11:33.360 and we can identify and study that.

NOTE Confidence: 0.8069569

00:11:33.360 --> 00:11:33.592 OK,

NOTE Confidence: 0.8069569

00:11:33.592 --> 00:11:35.216 and we can tell the events about

NOTE Confidence: 0.8069569

00:11:35.216 --> 00:11:35.680 when The

NOTE Confidence: 0.813769

00:11:35.737 --> 00:11:36.885 Exorcist appears and when

NOTE Confidence: 0.813769

00:11:36.885 --> 00:11:38.320 you have the Fusion fit.

NOTE Confidence: 0.813769

00:11:38.320 --> 00:11:39.748 This is relevant to the how

NOTE Confidence: 0.813769

00:11:39.748 --> 00:11:41.045 we're going to be looking

NOTE Confidence: 0.813769

00:11:41.045 --> 00:11:42.500 at things with the cilia.

NOTE Confidence: 0.813769

00:11:42.500 --> 00:11:45.559 So what is it that we see?

NOTE Confidence: 0.813769

00:11:45.560 --> 00:11:48.200 In I'm really just.

NOTE Confidence: 0.7963002

00:11:52.750 --> 00:11:55.260 OK, good. OK, so here's

NOTE Confidence: 0.77788836

00:11:55.260 --> 00:11:57.997 a short movie of what we're seeing

NOTE Confidence: 0.77788836

00:11:58.000 --> 00:11:59.564 in terms of cilia,

NOTE Confidence: 0.77788836

00:11:59.564 --> 00:12:01.910 sort of called the Biogenesis aspects,

NOTE Confidence: 0.77788836

00:12:01.910 --> 00:12:03.474 where we see basically

NOTE Confidence: 0.77788836

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 which is basically 4 hours.

NOTE Confidence: 0.77788836

00:13:06.980 --> 00:13:09.278 So in appearing there in this

NOTE Confidence: 0.77788836

00:13:09.278 --> 00:13:11.360 sort of the minutes range,

NOTE Confidence: 0.77788836

00:13:11.360 --> 00:13:14.174 this does not fit with what you

NOTE Confidence: 0.77788836

00:13:14.174 --> 00:13:16.929 would expect of sort of the well.

NOTE Confidence: 0.77788836

00:13:16.930 --> 00:13:18.522 A couple of things.

NOTE Confidence: 0.77788836

00:13:18.522 --> 00:13:21.310 One is, it's along the entire cilia,

NOTE Confidence: 0.77788836

00:13:21.310 --> 00:13:22.954 not just the base.

NOTE Confidence: 0.77788836

00:13:22.954 --> 00:13:25.009 Two is it appears there.

NOTE Confidence: 0.77788836

00:13:25.010 --> 00:13:26.440 Goes there and then vanish

NOTE Confidence: 0.77788836

00:13:26.440 --> 00:13:27.870 is and then comes back.

NOTE Confidence: 0.77788836

00:13:27.870 --> 00:13:30.158 You know an hour or two later again.

NOTE Confidence: 0.77788836

00:13:30.160 --> 00:13:31.535 So what's going on there

NOTE Confidence: 0.77788836

00:13:31.535 --> 00:13:33.300 and what do we you know?

NOTE Confidence: 0.77788836

00:13:33.300 --> 00:13:35.874 How can we sort of probe into that with?

NOTE Confidence: 0.77788836

00:13:35.880 --> 00:13:39.310 I guess you can intend to punt.

NOTE Confidence: 0.77788836

00:13:39.310 --> 00:13:41.938 So we do this by using.

NOTE Confidence: 0.77788836

00:13:41.940 --> 00:13:42.456 Again,

NOTE Confidence: 0.77788836

00:13:42.456 --> 00:13:45.036 we're using this exorcist and

NOTE Confidence: 0.77788836

00:13:45.036 --> 00:13:48.300 we look after after stimulation.

NOTE Confidence: 0.77788836

00:13:48.300 --> 00:13:49.431 See something interesting

NOTE Confidence: 0.77788836

00:13:49.431 --> 00:13:51.316 happening here and you actually

NOTE Confidence: 0.77788836

00:13:51.316 --> 00:13:53.666 see it quite really in the movie.

NOTE Confidence: 0.77788836

00:13:53.670 --> 00:13:57.250 Let me just play it again and you see Pam.

NOTE Confidence: 0.77788836

00:13:57.250 --> 00:13:58.321 Let me just.

NOTE Confidence: 0.77788836

00:13:58.321 --> 00:14:00.463 I realize it's hard to catch.

NOTE Confidence: 0.77788836

00:14:00.470 --> 00:14:02.618 Bam you see that green object?

NOTE Confidence: 0.77788836

00:14:02.620 --> 00:14:04.410 That's the vesicle flying off.

NOTE Confidence: 0.77788836

00:14:04.410 --> 00:14:06.958 OK, so we see the release of

NOTE Confidence: 0.77788836

00:14:06.958 --> 00:14:08.709 the vesicle happening as well.

NOTE Confidence: 0.77788836

00:14:08.710 --> 00:14:10.495 Now that's actually you know

NOTE Confidence: 0.77788836

00:14:10.495 --> 00:14:11.923 that part is known,

NOTE Confidence: 0.77788836

00:14:11.930 --> 00:14:13.715 but later we actually see

NOTE Confidence: 0.77788836

00:14:13.715 --> 00:14:15.143 then the Exorcist here.

NOTE Confidence: 0.77788836

00:14:15.150 --> 00:14:18.590 OK, after that we dropped off that signal.

NOTE Confidence: 0.77788836

00:14:18.590 --> 00:14:21.206 So basically the SEK 8 which is an

NOTE Confidence: 0.77788836

00:14:21.206 --> 00:14:23.388 extra quarter decorate psyllium after

NOTE Confidence: 0.77788836

00:14:23.388 --> 00:14:26.298 serum stimulation in vesicle release OK.

NOTE Confidence: 0.77788836

00:14:26.300 --> 00:14:29.261 And by the way I mean you know we

NOTE Confidence: 0.77788836

00:14:29.261 --> 00:14:31.299 artificially to generate cilia

NOTE Confidence: 0.77788836

00:14:31.299 --> 00:14:33.374 interesting culture, starve them.

NOTE Confidence: 0.77788836

00:14:33.374 --> 00:14:35.834 Of course the normal situation

NOTE Confidence: 0.77788836

00:14:35.834 --> 00:14:37.940 would be in syrup.

NOTE Confidence: 0.77788836

00:14:37.940 --> 00:14:40.560 OK, so.

NOTE Confidence: 0.77788836

00:14:40.560 --> 00:14:42.828 You know, per that sort of model,

NOTE Confidence: 0.77788836

00:14:42.830 --> 00:14:45.098 well, is there any evidence for this?

NOTE Confidence: 0.77788836

00:14:45.100 --> 00:14:46.954 Yes, there have been some some

NOTE Confidence: 0.77788836

00:14:46.954 --> 00:14:49.310 papers here and you called it called.

NOTE Confidence: 0.77788836

00:14:49.310 --> 00:14:49.958 The word.

NOTE Confidence: 0.77788836

00:14:49.958 --> 00:14:51.578 Is it called decapitation OK,

NOTE Confidence: 0.77788836

00:14:51.580 --> 00:14:53.518 where it plays off that vesicle?

NOTE Confidence: 0.77788836

00:14:53.520 --> 00:14:55.512 We actually think that the mechanism

NOTE Confidence: 0.77788836

00:14:55.512 --> 00:14:58.058 is going to happen is is is different?

NOTE Confidence: 0.77788836

00:14:58.060 --> 00:14:59.680 OK they are releasing it,

NOTE Confidence: 0.77788836

00:14:59.680 --> 00:15:01.535 but you'll see in our cartoon in

NOTE Confidence: 0.77788836

00:15:01.535 --> 00:15:03.560 the end we're thinking that it's

NOTE Confidence: 0.77788836

00:15:03.560 --> 00:15:05.505 happening by a different mechanism.

NOTE Confidence: 0.77788836

00:15:05.510 --> 00:15:07.454 You can obviously see sort of

NOTE Confidence: 0.77788836

00:15:07.454 --> 00:15:09.479 the importance of that on signal

NOTE Confidence: 0.77788836

00:15:09.479 --> 00:15:10.807 transduction as I was.

NOTE Confidence: 0.67264396

00:15:10.810 --> 00:15:16.540 Early, basically indicating earlier so.

NOTE Confidence: 0.67264396

00:15:16.540 --> 00:15:19.550 What do we happens to our RXS

NOTE Confidence: 0.67264396

00:15:19.550 --> 00:15:21.920 reporters after we add cereal?

NOTE Confidence: 0.67264396

00:15:21.920 --> 00:15:24.740 In this case, the FBS.

NOTE Confidence: 0.67264396

00:15:24.740 --> 00:15:27.476 And and So what we can see here,

NOTE Confidence: 0.67264396

00:15:27.480 --> 00:15:29.888 and you're sort of the overview slide.

NOTE Confidence: 0.67264396

00:15:29.890 --> 00:15:32.626 We're using X-70 as as our Our Exorcist

NOTE Confidence: 0.67264396

00:15:32.626 --> 00:15:35.072 Reporter I MP5 E is a silly Reporter

NOTE Confidence: 0.67264396

00:15:35.072 --> 00:15:37.429 and a couple of different things.

NOTE Confidence: 0.67264396

00:15:37.430 --> 00:15:39.206 One is now I should mention

NOTE Confidence: 0.67264396

00:15:39.206 --> 00:15:41.200 for soul this is endogenous.

NOTE Confidence: 0.67264396

00:15:41.200 --> 00:15:42.920 *** is no longer replaced.

NOTE Confidence: 0.67264396

00:15:42.920 --> 00:15:45.624 OK so this is sort of native conditions

NOTE Confidence: 0.67264396

00:15:45.624 --> 00:15:48.437 and what you can see is you can very

NOTE Confidence: 0.67264396

00:15:48.437 --> 00:15:50.808 clearly see it localising to cilia,

NOTE Confidence: 0.67264396

00:15:50.810 --> 00:15:53.239 but if you look carefully and I

NOTE Confidence: 0.67264396

00:15:53.239 --> 00:15:56.056 think you can see in this case here.

NOTE Confidence: 0.67264396

00:15:56.060 --> 00:15:58.615 And in this case here it actually.

NOTE Confidence: 0.67264396

00:15:58.620 --> 00:16:01.546 It localizes there but also forms these

NOTE Confidence: 0.67264396

00:16:01.546 --> 00:16:03.548 additional tubes which are pulling

NOTE Confidence: 0.67264396

00:16:03.548 --> 00:16:05.907 about look to pee in most movies

NOTE Confidence: 0.67264396

00:16:05.907 --> 00:16:08.135 would know are pulling out of it.

NOTE Confidence: 0.67264396

00:16:08.140 --> 00:16:11.320 So what's going on there?

NOTE Confidence: 0.67264396

00:16:11.320 --> 00:16:14.304 I will propose to you and submit to

NOTE Confidence: 0.67264396

00:16:14.304 --> 00:16:17.366 you is that this silly is actually

NOTE Confidence: 0.67264396

00:16:17.366 --> 00:16:20.607 inside the cell and is actually being

NOTE Confidence: 0.67264396

00:16:20.607 --> 00:16:24.303 remodeled by the X assist to pull off

NOTE Confidence: 0.67264396

00:16:24.310 --> 00:16:26.908 other membranes and remodel it through.

NOTE Confidence: 0.67264396

00:16:26.910 --> 00:16:29.864 Actually have the role of Exorcist being

NOTE Confidence: 0.67264396

00:16:29.864 --> 00:16:33.396 to tether and help fuse this monster huge,

NOTE Confidence: 0.67264396

00:16:33.400 --> 00:16:35.998 you know 510 Micron long vesicle.

NOTE Confidence: 0.7813586

00:16:38.120 --> 00:16:40.816 We we you know we basically see this

NOTE Confidence: 0.7813586

00:16:40.816 --> 00:16:43.800 in here sort of another view of that.

NOTE Confidence: 0.7813586

00:16:43.800 --> 00:16:45.900 And again there would be flooring

NOTE Confidence: 0.7813586

00:16:45.900 --> 00:16:47.710 smooth in there as well.

NOTE Confidence: 0.7813586

00:16:47.710 --> 00:16:50.527 So you smooth in IPP in 5E and these

NOTE Confidence: 0.7813586

00:16:50.527 --> 00:16:53.390 large tubules that are pulling off now.

NOTE Confidence: 0.7813586

00:16:53.390 --> 00:16:55.165 Does this happen when you

NOTE Confidence: 0.7813586

00:16:55.165 --> 00:16:56.230 stimulate with steering?

NOTE Confidence: 0.7813586

00:16:56.230 --> 00:16:58.710 And the answer is yes and if you

NOTE Confidence: 0.7813586

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.

NOTE Confidence: 0.7813586

00:17:38.360 --> 00:17:39.356 Set an RX-70.

NOTE Confidence: 0.7813586

00:17:39.356 --> 00:17:42.147 We do not see that another way of

NOTE Confidence: 0.7813586

00:17:42.147 --> 00:17:44.457 saying this is if we destabilize

NOTE Confidence: 0.7813586

00:17:44.457 --> 00:17:47.234 The Exorcist so you don't have your

NOTE Confidence: 0.7813586

00:17:47.234 --> 00:17:49.544 entire 8 protein complex and we

NOTE Confidence: 0.7813586

00:17:49.550 --> 00:17:51.420 no longer see that localization.

NOTE Confidence: 0.7813586

00:17:51.420 --> 00:17:54.396 OK, so that's sort of a control experiment.

NOTE Confidence: 0.7813586

00:17:54.400 --> 00:17:56.260 Then you might well ask.

NOTE Confidence: 0.7813586

00:17:56.260 --> 00:17:58.130 Well, OK, so it's recruited.

NOTE Confidence: 0.7813586

00:17:58.130 --> 00:18:01.106 But where is? Where is it being recruited?

NOTE Confidence: 0.7813586

00:18:01.110 --> 00:18:02.975 Relative to the Exorcist relative

NOTE Confidence: 0.7813586

00:18:02.975 --> 00:18:04.094 to the cilia?

NOTE Confidence: 0.7813586

00:18:04.100 --> 00:18:06.844 And I kind of reminded you early on

NOTE Confidence: 0.7813586

00:18:06.844 --> 00:18:09.568 that you have this ciliary sheath.

NOTE Confidence: 0.7813586

00:18:09.570 --> 00:18:13.168 This sort of a membrane which kind

NOTE Confidence: 0.7813586

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

NOTE Confidence: 0.7813586

00:18:45.989 --> 00:18:47.978 super resolution imaging modality?

NOTE Confidence: 0.7813586

00:18:47.980 --> 00:18:51.854 Construction limination microscopy and I

NOTE Confidence: 0.7813586

00:18:51.854 --> 00:18:54.670 think you can sort of see it easily here.

NOTE Confidence: 0.7813586

00:18:54.670 --> 00:18:56.665 You'd have smooth and so this would

NOTE Confidence: 0.7813586

00:18:56.665 --> 00:18:58.389 be basically your cilia Reporter,

NOTE Confidence: 0.7813586

00:18:58.390 --> 00:19:00.202 which would be on the extracellular

NOTE Confidence: 0.7813586

00:19:00.202 --> 00:19:01.800 side where I should write.

NOTE Confidence: 0.7813586

00:19:01.800 --> 00:19:04.299 So would be.

NOTE Confidence: 0.7813586

00:19:04.300 --> 00:19:05.736 On the inner membrane,

NOTE Confidence: 0.7813586

00:19:05.736 --> 00:19:08.545 if you like to look at it that

NOTE Confidence: 0.7813586

00:19:08.545 --> 00:19:11.403 way and we see SEK 8 or X-70 is

NOTE Confidence: 0.7813586

00:19:11.403 --> 00:19:12.840 a wider distribution.

NOTE Confidence: 0.7813586

00:19:12.840 --> 00:19:13.197 OK,

NOTE Confidence: 0.7813586

00:19:13.197 --> 00:19:15.339 so it is on for going.

NOTE Confidence: 0.7546144

00:19:17.530 --> 00:19:19.590 Turn off my paper airplane

NOTE Confidence: 0.7546144

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 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

NOTE Confidence: 0.8248625

00:19:57.818 --> 00:20:00.341 of focus on here on the point of

NOTE Confidence: 0.8248625

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

NOTE Confidence: 0.8248625

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

NOTE Confidence: 0.8248625

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

NOTE Confidence: 0.8248625

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

NOTE Confidence: 0.5048806

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

NOTE Confidence: 0.5048806

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

NOTE Confidence: 0.8060176

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

NOTE Confidence: 0.8060176

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

NOTE Confidence: 0.8060176

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

NOTE Confidence: 0.8060176

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

NOTE Confidence: 0.8060176

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

NOTE Confidence: 0.8060176

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

NOTE Confidence: 0.8060176

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

NOTE Confidence: 0.8060176

00:20:29.570 --> 00:20:32.266 which has been sort of reported in the

NOTE Confidence: 0.8060176

00:20:32.266 --> 00:20:34.498 literature to exist most of the time,

NOTE Confidence: 0.8060176

00:20:34.500 --> 00:20:36.450 again at a single snapshot you

NOTE Confidence: 0.8060176

00:20:36.450 --> 00:20:38.450 mainly see it at the base,

NOTE Confidence: 0.8060176

00:20:38.450 --> 00:20:41.402 but actually if you look at it live over,

NOTE Confidence: 0.8060176

00:20:41.410 --> 00:20:43.490 you know it's called longitudinal.

NOTE Confidence: 0.8060176

00:20:43.490 --> 00:20:47.700 You would actually see it.

NOTE Confidence: 0.8060176

00:20:47.700 --> 00:20:49.470 Earlier on these internal cilia,

NOTE Confidence: 0.8060176

00:20:49.470 --> 00:20:51.240 so we actually think it's

NOTE Confidence: 0.8060176

00:20:51.240 --> 00:20:52.656 driving that process out.

NOTE Confidence: 0.7073801

00:20:56.110 --> 00:20:56.600 OK.

NOTE Confidence: 0.8034458

00:20:59.540 --> 00:21:01.586 So well, how can we actually

NOTE Confidence: 0.8034458

00:21:01.586 --> 00:21:03.900 sort of prove this unequivocal?

NOTE Confidence: 0.8034458

00:21:03.900 --> 00:21:07.113 Blee and the way that we've done this is

NOTE Confidence: 0.8034458

00:21:07.113 --> 00:21:09.840 basically using a pH switching experiment,

NOTE Confidence: 0.8034458

00:21:09.840 --> 00:21:12.210 and when the cilia are outside,

NOTE Confidence: 0.8034458

00:21:12.210 --> 00:21:14.190 if we switch the pH,

NOTE Confidence: 0.8034458

00:21:14.190 --> 00:21:16.955 and we have this pH sensitive Reporter,

NOTE Confidence: 0.8034458

00:21:16.960 --> 00:21:20.920 every time we switch it, it goes on and off.

NOTE Confidence: 0.8034458

00:21:20.920 --> 00:21:24.880 OK, so we make acidify, we can turn it off,

NOTE Confidence: 0.8034458

00:21:24.880 --> 00:21:27.659 and then it goes back on again.

NOTE Confidence: 0.8034458

00:21:27.660 --> 00:21:28.809 So we basically.

NOTE Confidence: 0.8034458

00:21:28.809 --> 00:21:29.958 Switching the pH,

NOTE Confidence: 0.8034458

00:21:29.960 --> 00:21:32.228 we can tell if it's outside here,

NOTE Confidence: 0.8034458

00:21:32.230 --> 00:21:33.860 switching, going up and down,

NOTE Confidence: 0.8034458

00:21:33.860 --> 00:21:37.108 but as you can see in this context, is not.

NOTE Confidence: 0.8034458

00:21:37.108 --> 00:21:38.080 It's actually resistant.

NOTE Confidence: 0.8034458

00:21:38.080 --> 00:21:39.710 And why is it resistant?

NOTE Confidence: 0.8034458

00:21:39.710 --> 00:21:41.010 Because inside the cell.

NOTE Confidence: 0.8034458

00:21:41.010 --> 00:21:42.960 So it is basically inside inside,

NOTE Confidence: 0.8034458

00:21:42.960 --> 00:21:45.456 inside and then here you can see it

NOTE Confidence: 0.8034458

00:21:45.456 --> 00:21:47.813 switch into the purple or magenta

NOTE Confidence: 0.8034458

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 --> 00:22:07.410 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

NOTE Confidence: 0.8197327

00:22:23.007 --> 00:22:26.645 drops off and fully into the base. OK,

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

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

NOTE Confidence: 0.8197327

00:23:03.450 --> 00:23:04.479 In this starves,

NOTE Confidence: 0.8197327

00:23:04.479 --> 00:23:06.537 say you have cilia with these

NOTE Confidence: 0.8197327

00:23:06.537 --> 00:23:08.698 sort of deeply emerged pockets.

NOTE Confidence: 0.8197327

00:23:08.700 --> 00:23:11.382 The Exorcist is in the facilities

NOTE Confidence: 0.8197327

00:23:11.382 --> 00:23:13.638 recycling endosomes and probably have

NOTE Confidence: 0.8197327

00:23:13.638 --> 00:23:16.020 some targeting of that success here.

NOTE Confidence: 0.8197327

00:23:16.020 --> 00:23:17.550 In the serums to stimulation,

NOTE Confidence: 0.8197327

00:23:17.550 --> 00:23:19.678 that which is actually the normal case,

NOTE Confidence: 0.8197327

00:23:19.680 --> 00:23:20.142 right?

NOTE Confidence: 0.8197327

00:23:20.142 --> 00:23:22.914 If you sort of thought about

NOTE Confidence: 0.8197327

00:23:22.914 --> 00:23:24.880 sleep in the body.

NOTE Confidence: 0.8197327

00:23:24.880 --> 00:23:26.604 There, there there actually

NOTE Confidence: 0.8197327

00:23:26.604 --> 00:23:27.897 constantly being remodled.

NOTE Confidence: 0.8197327

00:23:27.900 --> 00:23:28.347 OK,

NOTE Confidence: 0.8197327

00:23:28.347 --> 00:23:31.476 so the event of releasing the vesicles

NOTE Confidence: 0.8197327

00:23:31.476 --> 00:23:34.356 actually different than sort of was proposed.

NOTE Confidence: 0.8197327

00:23:34.360 --> 00:23:37.555 We believe of it sort of coming off from

NOTE Confidence: 0.8197327

00:23:37.555 --> 00:23:40.829 one that's fully outside this actually,

NOTE Confidence: 0.8197327

00:23:40.830 --> 00:23:43.410 as it starts to pull in,

NOTE Confidence: 0.8197327

00:23:43.410 --> 00:23:46.802 we believe that it was remodeling that can

NOTE Confidence: 0.8197327

00:23:46.802 --> 00:23:49.448 actually promote this vesicle to release.

NOTE Confidence: 0.8197327

00:23:49.450 --> 00:23:52.174 Once inside you have recruitment of

NOTE Confidence: 0.8197327

00:23:52.174 --> 00:23:55.449 the Exorcist to this large and inside.

NOTE Confidence: 0.8197327

00:23:55.450 --> 00:23:58.768 Which is again majority of this sort

NOTE Confidence: 0.8197327

00:23:58.768 --> 00:24:01.770 of internalize cilia which can remodel,

NOTE Confidence: 0.8197327

00:24:01.770 --> 00:24:04.195 pulling off tubules and consequently

NOTE Confidence: 0.8197327

00:24:04.195 --> 00:24:06.135 then can recycle back.

NOTE Confidence: 0.8197327

00:24:06.140 --> 00:24:09.332 So you have this entire pathway here

NOTE Confidence: 0.8197327

00:24:09.332 --> 00:24:11.969 that can modulate the signaling.

NOTE Confidence: 0.8197327

00:24:11.970 --> 00:24:15.379 So with sort of that this is.

NOTE Confidence: 0.79843205

00:24:17.920 --> 00:24:19.420 Switch back to automatic.

NOTE Confidence: 0.79843205

00:24:19.420 --> 00:24:22.139 Really this is really driven by senior

NOTE Confidence: 0.79843205

00:24:22.139 --> 00:24:24.960 scientist in the lab Felix Riviera Molina.

NOTE Confidence: 0.79843205

00:24:24.960 --> 00:24:27.300 Sort was reported by the people,

NOTE Confidence: 0.79843205

00:24:27.300 --> 00:24:30.037 but really he took the lead here,

NOTE Confidence: 0.79843205

00:24:30.040 --> 00:24:32.904 so that's where I'd like to end and

NOTE Confidence: 0.79843205

00:24:32.904 --> 00:24:35.909 address any comments that you might have.

NOTE Confidence: 0.8779377

00:24:37.760 --> 00:24:39.518 Thank you for very interesting talk.

NOTE Confidence: 0.8779377

00:24:39.520 --> 00:24:41.290 Are there questions from the audience?

NOTE Confidence: 0.80636364

00:24:42.480 --> 00:24:43.540 Let me put that you

NOTE Confidence: 0.80636364

00:24:43.540 --> 00:24:44.590 can just type them in.

NOTE Confidence: 0.7957481

00:24:46.790 --> 00:24:48.163 While we're waiting, yeah.

NOTE Confidence: 0.7957481

00:24:48.163 --> 00:24:50.905 So there are a lot of genetic disorders

NOTE Confidence: 0.7957481

00:24:50.905 --> 00:24:53.485 of cilia formation that have many

NOTE Confidence: 0.7957481

00:24:53.485 --> 00:24:55.345 different phenotypes or anything

NOTE Confidence: 0.7957481

00:24:55.345 --> 00:24:57.860 associated with increased cancer risk.

NOTE Confidence: 0.8162323

00:24:59.950 --> 00:25:02.098 Yes, there there have been and

NOTE Confidence: 0.8162323

00:25:02.098 --> 00:25:04.707 there were sort of where it gets

NOTE Confidence: 0.8162323

00:25:04.707 --> 00:25:07.269 complicated is it depends on sort of

NOTE Confidence: 0.8162323

00:25:07.342 --> 00:25:10.044 what cell types you're looking at it.

NOTE Confidence: 0.8162323

00:25:10.050 --> 00:25:12.444 Again, again, you know pushing things up

NOTE Confidence: 0.8162323

00:25:12.444 --> 00:25:15.277 and down and sort of mentioning earlier.

NOTE Confidence: 0.8162323

00:25:15.280 --> 00:25:16.824 So yes, there are.

NOTE Confidence: 0.8162323

00:25:16.824 --> 00:25:18.754 Haven't been sort of investigating

NOTE Confidence: 0.8162323

00:25:18.754 --> 00:25:21.265 this so much personally but but yes.

NOTE Confidence: 0.9135724

00:25:22.970 --> 00:25:23.520 Thank you.

NOTE Confidence: 0.87619084

00:25:26.840 --> 00:25:28.349 Questions for Derek.

NOTE Confidence: 0.7930513

00:25:30.430 --> 00:25:31.690 I know this zoom atmosphere

NOTE Confidence: 0.7930513

00:25:31.690 --> 00:25:33.520 makes it a little bit different.

NOTE Confidence: 0.7930513

00:25:33.520 --> 00:25:36.875 Will. So enjoy when we see

NOTE Confidence: 0.7930513

00:25:36.875 --> 00:25:38.180 people face to face again.

NOTE Confidence: 0.7807439

00:25:47.870 --> 00:25:50.350 Another question then should in.

NOTE Confidence: 0.76829845

00:25:51.560 --> 00:25:52.463 In cancer cells,

NOTE Confidence: 0.76829845

00:25:52.463 --> 00:25:54.269 which are obviously many of them

NOTE Confidence: 0.76829845

00:25:54.269 --> 00:25:56.000 often constantly proliferating,

NOTE Confidence: 0.76829845

00:25:56.000 --> 00:25:57.850 do you see abnormalities of

NOTE Confidence: 0.76829845

00:25:57.850 --> 00:25:59.330 cilia formation you could?

NOTE Confidence: 0.76829845

00:25:59.330 --> 00:26:01.180 Do they have more cilia?

NOTE Confidence: 0.76829845

00:26:01.180 --> 00:26:03.400 Do they turn over more rapidly?

NOTE Confidence: 0.76829845

00:26:03.400 --> 00:26:04.140 What happens?

NOTE Confidence: 0.7792757

00:26:05.690 --> 00:26:08.194 This is a little bit as alluding to

NOTE Confidence: 0.7792757

00:26:08.194 --> 00:26:10.856 you can kind of push it either way,

NOTE Confidence: 0.7792757

00:26:10.860 --> 00:26:13.226 so that's where that's actually where the

NOTE Confidence: 0.7792757

00:26:13.226 --> 00:26:16.029 confusion is to cancer is that you would say,

NOTE Confidence: 0.7792757

00:26:16.030 --> 00:26:17.956 well, do they have more silly?

NOTE Confidence: 0.7792757

00:26:17.960 --> 00:26:20.291 Do they have less cilia and basically

NOTE Confidence: 0.7792757

00:26:20.291 --> 00:26:22.297 the paper review had indicated that

NOTE Confidence: 0.7792757

00:26:22.297 --> 00:26:24.750 there's sort of the two sides on it,

NOTE Confidence: 0.7792757

00:26:24.750 --> 00:26:27.004 so in one case you actually hyper

NOTE Confidence: 0.7792757

00:26:27.004 --> 00:26:28.622 activate by, let's say adding

NOTE Confidence: 0.7792757

00:26:28.622 --> 00:26:29.918 smoothing and hedgehogs signaling,

NOTE Confidence: 0.7792757

00:26:29.920 --> 00:26:32.496 so the Hedgehog is obviously a key component,

NOTE Confidence: 0.7792757

00:26:32.500 --> 00:26:34.516 as same as sort of PGF would

NOTE Confidence: 0.7792757

00:26:34.516 --> 00:26:36.520 be basically a hyper activated.

NOTE Confidence: 0.7792757

00:26:36.520 --> 00:26:39.621 The other case is where you would

NOTE Confidence: 0.7792757

00:26:39.621 --> 00:26:41.473 actually activate the signaling

NOTE Confidence: 0.7792757

00:26:41.473 --> 00:26:44.095 by the absence of the cilia.

NOTE Confidence: 0.7792757

00:26:44.100 --> 00:26:47.668 So that's sort of where it's you know.

NOTE Confidence: 0.7792757

00:26:47.670 --> 00:26:51.238 In some cancers are driven by having cilia,

NOTE Confidence: 0.7792757

00:26:51.240 --> 00:26:55.944 and some are driven by the absence.

NOTE Confidence: 0.7792757

00:26:55.950 --> 00:26:57.594 Sort of given the this sort

NOTE Confidence: 0.7792757

00:26:57.594 --> 00:26:59.260 of the the funny paradox.

NOTE Confidence: 0.7792757

00:26:59.260 --> 00:27:01.054 Depending on that nature of which

NOTE Confidence: 0.7792757

00:27:01.054 --> 00:27:02.570 signaling pathway you're talking about.

NOTE Confidence: 0.7792757

00:27:02.570 --> 00:27:04.404 Is it a hedgehog sort of smoothing

NOTE Confidence: 0.7792757

00:27:04.404 --> 00:27:06.790 type of one or other signaling pathway?

NOTE Confidence: 0.7792757

00:27:06.790 --> 00:27:08.295 And what is the activation

NOTE Confidence: 0.7792757

00:27:08.295 --> 00:27:09.499 at the Basel State?

NOTE Confidence: 0.7792757

00:27:09.500 --> 00:27:11.812 So that's why I think it's given some

NOTE Confidence: 0.7792757

00:27:11.812 --> 00:27:13.980 complexity to the field because you couldn't

NOTE Confidence: 0.7792757

00:27:13.980 --> 00:27:16.418 just simply say this is only this week,

NOTE Confidence: 0.7792757

00:27:16.420 --> 00:27:18.949 but it does.

NOTE Confidence: 0.7792757

00:27:18.950 --> 00:27:20.830 Yeah, yeah.

NOTE Confidence: 0.7792757

00:27:20.830 --> 00:27:22.550 There's evidence for both there.

NOTE Confidence: 0.88823843

00:27:23.800 --> 00:27:25.120 Are there other any other

NOTE Confidence: 0.88823843

00:27:25.120 --> 00:27:26.176 questions in the audience?

NOTE Confidence: 0.8601161

00:27:33.600 --> 00:27:34.860 If not, thank you.

NOTE Confidence: 0.8601161

00:27:34.860 --> 00:27:36.435 Thank you all for coming.

NOTE Confidence: 0.8601161

00:27:36.440 --> 00:27:38.010 Thank you for two speakers.

NOTE Confidence: 0.8601161

00:27:38.010 --> 00:27:39.535 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.