WEBVTT

NOTE duration:”00:59:13”

NOTE recognizability:0.859

NOTE language:en-us

NOTE Confidence: 0.8928436375

00:00:00.000 --> 00:00:02.064 So it's a couple minutes after the hour,

NOTE Confidence: 0.8928436375

00:00:02.070 --> 00:00:04.206 so why don't we get started?

NOTE Confidence: 0.8928436375

00:00:04.210 --> 00:00:07.706 Welcome to grand rounds.

NOTE Confidence: 0.8928436375

00:00:07.706 --> 00:00:12.186 We have two really interesting talks today.

NOTE Confidence: 0.8928436375

00:00:12.186 --> 00:00:15.690 For those of you who don't know me,

NOTE Confidence: 0.8928436375

00:00:15.690 --> 00:00:17.580 I'll just.

NOTE Confidence: 0.8928436375

00:00:17.580 --> 00:00:19.316 Point out that my name is Ryan Crop.

NOTE Confidence: 0.8928436375

00:00:19.320 --> 00:00:23.577 I'm very new to Yale as the new medical

NOTE Confidence: 0.8928436375

00:00:23.577 --> 00:00:27.208 director for the Clinical Trials Office.

NOTE Confidence: 0.8928436375

00:00:27.210 --> 00:00:30.927 And it's pleasure to start meeting everyone.

NOTE Confidence: 0.8928436375

00:00:30.930 --> 00:00:32.460 So we have two took off.

NOTE Confidence: 0.8928436375

00:00:32.460 --> 00:00:35.700 As I mentioned the 1st.

NOTE Confidence: 0.8928436375

00:00:35.700 --> 00:00:38.770 Benjamin Turk has been

NOTE Confidence: 0.8928436375

00:00:38.770 --> 00:00:40.170 kind enough to join us.

NOTE Confidence: 0.8928436375

00:00:40.170 --> 00:00:42.055 He's an associate professor of

NOTE Confidence: 0.8928436375

00:00:42.055 --> 00:00:43.563 pharmacology and director of

NOTE Confidence: 0.8928436375

00:00:43.563 --> 00:00:45.408 Medical Studies and pharmacology.

NOTE Confidence: 0.8928436375

00:00:45.410 --> 00:00:48.644 He's a member of the CSN program.

NOTE Confidence: 0.8928436375

00:00:48.650 --> 00:00:51.668 His graduate work was in biological

NOTE Confidence: 0.8928436375

00:00:51.668 --> 00:00:55.212 chemistry at MIT and then a postdoc

NOTE Confidence: 0.8928436375

00:00:55.212 --> 00:00:58.086 with Luke Cantley also in Boston,

NOTE Confidence: 0.8928436375

00:00:58.090 --> 00:01:00.370 and he works understanding

NOTE Confidence: 0.8928436375

00:01:00.370 --> 00:01:02.080 molecular mechanisms underlying

NOTE Confidence: 0.8928436375

00:01:02.080 --> 00:01:04.856 signaling pathways and how they're

NOTE Confidence: 0.8928436375

00:01:04.856 --> 00:01:06.828 organized into large networks,

NOTE Confidence: 0.8928436375

00:01:06.830 --> 00:01:08.320 and his lab has been.

NOTE Confidence: 0.8928436375

00:01:08.320 --> 00:01:10.572 Setting protein modifying enzymes

NOTE Confidence: 0.8928436375

00:01:10.572 --> 00:01:12.770 and particularly kinase and

NOTE Confidence: 0.8928436375

00:01:12.770 --> 00:01:15.445 proteases that are important in

NOTE Confidence: 0.8928436375

00:01:15.445 --> 00:01:18.322 in signaling networks and today he

NOTE Confidence: 0.8928436375

00:01:18.322 --> 00:01:20.866 will be talking about the aquaponic

NOTE Confidence: 0.8928436375

00:01:20.866 --> 00:01:23.418 not kinase signaling network.

NOTE Confidence: 0.8928436375

00:01:23.420 --> 00:01:24.428 Thank you Doctor Turk.

NOTE Confidence: 0.933292344

00:01:25.800 --> 00:01:29.848 OK, thank you. I will share my screen.

NOTE Confidence: 0.4755459

00:01:32.410 --> 00:01:33.300 See.

NOTE Confidence: 0.92828127

00:01:36.230 --> 00:01:39.398 OK can you see my screen in the pointer?

NOTE Confidence: 0.92828127

00:01:39.400 --> 00:01:41.314 Yeah perfect OK great.

NOTE Confidence: 0.92828127

00:01:41.314 --> 00:01:44.443 Well thank you for that introduction and

NOTE Confidence: 0.92828127

00:01:44.443 --> 00:01:47.517 also for the invitation to present our

NOTE Confidence: 0.92828127

00:01:47.517 --> 00:01:50.839 work on MAP kinase signaling networks.

NOTE Confidence: 0.92828127

00:01:50.840 --> 00:01:52.220 So as we all know,

NOTE Confidence: 0.92828127

00:01:52.220 --> 00:01:55.230 one of the hallmarks of cancer is

NOTE Confidence: 0.92828127

00:01:55.230 --> 00:01:56.983 uncontrolled cell proliferation and

NOTE Confidence: 0.92828127

00:01:56.983 --> 00:02:00.160 survival and cancer cells accomplish this,

NOTE Confidence: 0.92828127

00:02:00.160 --> 00:02:02.878 at least in part through Co

NOTE Confidence: 0.92828127

00:02:02.878 --> 00:02:05.368 opting signaling pathways that are

NOTE Confidence: 0.92828127

00:02:05.368 --> 00:02:07.764 normally activated downstream of

NOTE Confidence: 0.92828127

00:02:07.764 --> 00:02:10.160 peptide growth factor receptors.

NOTE Confidence: 0.92828127

00:02:10.160 --> 00:02:12.008 I'm gonna be talking about one of

NOTE Confidence: 0.92828127

00:02:12.008 --> 00:02:13.902 the major arms of growth factor

NOTE Confidence: 0.92828127

00:02:13.902 --> 00:02:16.214 signaling the wrasse, RAF, MEK,

NOTE Confidence: 0.92828127

00:02:16.214 --> 00:02:18.110 Erk, signaling cascade.

NOTE Confidence: 0.92828127

00:02:18.110 --> 00:02:20.540 So owing to high frequency mutations

NOTE Confidence: 0.92828127

00:02:20.540 --> 00:02:23.469 in rosanky genes as well as mutation,

NOTE Confidence: 0.92828127

00:02:23.470 --> 00:02:26.050 amplification of growth factor receptors,

NOTE Confidence: 0.92828127

00:02:26.050 --> 00:02:28.498 this pathway is amongst the most

NOTE Confidence: 0.92828127

00:02:28.500 --> 00:02:31.734 highly hyper activated in or more

NOTE Confidence: 0.92828127

00:02:31.734 --> 00:02:33.890 frequent most frequently hyperactivated

NOTE Confidence: 0.92828127

00:02:33.973 --> 00:02:35.230 in human cancers.

NOTE Confidence: 0.92828127

00:02:35.230 --> 00:02:38.398 And though the pathway has been the

NOTE Confidence: 0.92828127

00:02:38.398 --> 00:02:40.542 subject of intense study for for decades now,

NOTE Confidence: 0.92828127

00:02:40.550 --> 00:02:41.854 there are still some.

NOTE Confidence: 0.92828127

00:02:41.854 --> 00:02:44.086 Open questions in the field that our

NOTE Confidence: 0.92828127

00:02:44.086 --> 00:02:46.018 lab and of course many others are,

NOTE Confidence: 0.92828127

00:02:46.020 --> 00:02:48.043 are trying to understand and to to

NOTE Confidence: 0.92828127

00:02:48.043 --> 00:02:50.510 sum up some of these questions that

NOTE Confidence: 0.92828127

00:02:50.510 --> 00:02:52.430 I'm really talking about today.

NOTE Confidence: 0.92828127

00:02:52.430 --> 00:02:53.294 One question,

NOTE Confidence: 0.92828127

00:02:53.294 --> 00:02:55.454 what are the functionally important

NOTE Confidence: 0.92828127

00:02:55.454 --> 00:02:58.498 components of MAP kinase signaling networks?

NOTE Confidence: 0.92828127

00:02:58.500 --> 00:03:00.690 So obviously the kinases that form

NOTE Confidence: 0.92828127

00:03:00.690 --> 00:03:03.360 the core cascade are are have been

NOTE Confidence: 0.92828127

00:03:03.360 --> 00:03:05.265 well studied or well understood,

NOTE Confidence: 0.92828127

00:03:05.270 --> 00:03:07.088 but we have less understanding of

NOTE Confidence: 0.92828127

00:03:07.088 --> 00:03:08.780 other regulators of the pathway.

NOTE Confidence: 0.92828127

00:03:08.780 --> 00:03:11.558 So for example the protein phosphatases.

NOTE Confidence: 0.92828127

00:03:11.560 --> 00:03:13.550 That act on these kinases,

NOTE Confidence: 0.92828127

00:03:13.550 --> 00:03:15.800 and thus attenuate signaling through

NOTE Confidence: 0.92828127

00:03:15.800 --> 00:03:19.728 the pathway and it in addition.

NOTE Confidence: 0.92828127

00:03:19.730 --> 00:03:22.424 We don't have a complete catalogue

NOTE Confidence: 0.92828127

00:03:22.424 --> 00:03:26.105 of the substrates of Erk that act as

NOTE Confidence: 0.92828127

00:03:26.105 --> 00:03:28.350 the critical effectors in mediating

NOTE Confidence: 0.92828127

00:03:28.350 --> 00:03:31.404 the cancer cell phone. It type.

NOTE Confidence: 0.92828127

00:03:31.404 --> 00:03:32.970 So in addition,

NOTE Confidence: 0.92828127

00:03:32.970 --> 00:03:35.262 one question we're interested in is

NOTE Confidence: 0.92828127

00:03:35.262 --> 00:03:37.220 how specific connections are made

NOTE Confidence: 0.92828127

00:03:37.220 --> 00:03:39.404 between the kinases and the regulators

NOTE Confidence: 0.92828127

00:03:39.404 --> 00:03:41.339 and substrates in this pathway.

NOTE Confidence: 0.92828127

00:03:41.340 --> 00:03:43.836 So there's been a lot of really beautiful

NOTE Confidence: 0.92828127

00:03:43.836 --> 00:03:45.615 structural work emerging recently on

NOTE Confidence: 0.92828127

00:03:45.615 --> 00:03:47.805 the upstream components of the pathway,

NOTE Confidence: 0.92828127

00:03:47.810 --> 00:03:48.564 in particular,

NOTE Confidence: 0.92828127

00:03:48.564 --> 00:03:51.203 how Rask connects to RAF and MEK.

NOTE Confidence: 0.92828127

00:03:51.210 --> 00:03:52.040 But again,

NOTE Confidence: 0.92828127

00:03:52.040 --> 00:03:54.530 our understanding of the more downstream

NOTE Confidence: 0.92828127

00:03:54.530 --> 00:03:57.042 components where where we have these

NOTE Confidence: 0.92828127

00:03:57.042 --> 00:03:59.057 critical effector kinases and their

NOTE Confidence: 0.92828127

00:03:59.057 --> 00:04:01.179 substrates is is less well understood.

NOTE Confidence: 0.92828127

00:04:01.180 --> 00:04:02.311 And then lastly,

NOTE Confidence: 0.92828127

00:04:02.311 --> 00:04:04.950 one thing we know is that the

NOTE Confidence: 0.92828127

00:04:05.033 --> 00:04:07.493 persistent high level of activation

NOTE Confidence: 0.92828127

00:04:07.493 --> 00:04:11.231 of this pathway that one gets with

NOTE Confidence: 0.92828127

00:04:11.231 --> 00:04:14.221 new genic activation really doesn't

NOTE Confidence: 0.92828127

00:04:14.221 --> 00:04:16.382 faithfully recapitulate the sort

NOTE Confidence: 0.92828127

00:04:16.382 --> 00:04:18.192 of normal dynamics of activation

NOTE Confidence: 0.92828127

00:04:18.192 --> 00:04:20.724 when we'd see in response to a

NOTE Confidence: 0.92828127

00:04:20.724 --> 00:04:22.740 growth factor in a normal cell.

NOTE Confidence: 0.92828127

00:04:22.740 --> 00:04:25.792 And this can lead to a phenomenon

NOTE Confidence: 0.92828127

00:04:25.792 --> 00:04:27.676 that someone sometimes called

NOTE Confidence: 0.92828127

00:04:27.676 --> 00:04:29.668 network rewiring and how.

NOTE Confidence: 0.92828127

00:04:29.670 --> 00:04:31.518 New or which new connections are

NOTE Confidence: 0.92828127

00:04:31.518 --> 00:04:33.532 made in these networks and which

NOTE Confidence: 0.92828127

00:04:33.532 --> 00:04:35.498 connections are broken is is is

NOTE Confidence: 0.92828127

00:04:35.498 --> 00:04:36.682 something that's important to

NOTE Confidence: 0.92828127

00:04:36.682 --> 00:04:39.075 know in terms of having a complete

NOTE Confidence: 0.92828127

00:04:39.075 --> 00:04:40.880 understanding of tumor cell biology.

NOTE Confidence: 0.92828127

00:04:40.880 --> 00:04:44.100 So I'm I'm gonna tell two stories

NOTE Confidence: 0.92828127

00:04:44.100 --> 00:04:45.020 briefly today.

NOTE Confidence: 0.92828127

00:04:45.020 --> 00:04:48.335 The first has to do with the oncogenic

NOTE Confidence: 0.92828127

00:04:48.335 --> 00:04:51.845 map kinase signaling in in Melanoma.

NOTE Confidence: 0.92828127

00:04:51.850 --> 00:04:52.286 OK,

NOTE Confidence: 0.92828127

00:04:52.286 --> 00:04:55.338 so as many of you probably know,

NOTE Confidence: 0.92828127

00:04:55.340 --> 00:04:57.308 malignant melanomas are really

NOTE Confidence: 0.92828127

00:04:57.308 --> 00:04:59.276 driven by hyperactive Erk,

NOTE Confidence: 0.92828127

00:04:59.280 --> 00:05:02.808 MAP kinase signaling and so about half of

NOTE Confidence: 0.92828127

00:05:02.808 --> 00:05:05.817 melanomas Harbor mutations in the BRAF gene.

NOTE Confidence: 0.811468077142857

00:05:05.820 --> 00:05:08.660 Most frequently the V 600 year Leal that

NOTE Confidence: 0.811468077142857

00:05:08.660 --> 00:05:11.980 leads to high level constitutive activation.

NOTE Confidence: 0.811468077142857

00:05:11.980 --> 00:05:15.256 And the remaining tumors have mutations.

NOTE Confidence: 0.811468077142857

00:05:15.260 --> 00:05:17.258 Most of them have mutations either

NOTE Confidence: 0.811468077142857

00:05:17.258 --> 00:05:21.680 in the NRAS, GTP ace, the NF One Ras.

NOTE Confidence: 0.811468077142857

00:05:21.680 --> 00:05:24.794 GTP is activating protein that negatively

NOTE Confidence: 0.811468077142857

00:05:24.794 --> 00:05:27.759 regulates the pathway or gain of

NOTE Confidence: 0.811468077142857

00:05:27.759 --> 00:05:30.177 function mutations in in MEK MEK,

NOTE Confidence: 0.811468077142857

00:05:30.180 --> 00:05:33.796 one which is just around stream of UVB

NOTE Confidence: 0.811468077142857

00:05:33.796 --> 00:05:37.330 graph and and of course the dependence of

NOTE Confidence: 0.811468077142857

00:05:37.330 --> 00:05:40.585 melanomas on this pathway has really driven

NOTE Confidence: 0.811468077142857

00:05:40.585 --> 00:05:44.026 the development and eventual FDA approval.

NOTE Confidence: 0.811468077142857

00:05:44.030 --> 00:05:46.406 Of kinase inhibitors that target both

NOTE Confidence: 0.811468077142857

00:05:46.406 --> 00:05:49.472 B RAF and MEK that are currently

NOTE Confidence: 0.811468077142857

00:05:49.472 --> 00:05:51.336 used to treat Melanoma,

NOTE Confidence: 0.811468077142857

00:05:51.340 --> 00:05:54.724 and while there is a high response rate

NOTE Confidence: 0.811468077142857

00:05:54.724 --> 00:05:58.106 for tumors that harbor be RAF mutations,

NOTE Confidence: 0.811468077142857

00:05:58.110 --> 00:05:59.874 the the problem with these drugs

NOTE Confidence: 0.811468077142857

00:05:59.874 --> 00:06:01.739 and really all targeted therapies is

NOTE Confidence: 0.811468077142857

00:06:01.739 --> 00:06:03.629 that the responses are not durable

NOTE Confidence: 0.811468077142857

00:06:03.629 --> 00:06:05.059 and patients will relapse within

NOTE Confidence: 0.811468077142857

00:06:05.059 --> 00:06:08.800 a few months to a couple of years.

NOTE Confidence: 0.811468077142857

00:06:08.800 --> 00:06:11.544 And the most common way that one sees

NOTE Confidence: 0.811468077142857

00:06:11.544 --> 00:06:13.814 resistance to these inhibitors is through

NOTE Confidence: 0.811468077142857

00:06:13.814 --> 00:06:17.159 re activation of the Erk MAP kinase pathway.

NOTE Confidence: 0.811468077142857

00:06:17.160 --> 00:06:19.075 Despite the continued presence of

NOTE Confidence: 0.811468077142857

00:06:19.075 --> 00:06:21.407 inhibitor but one can also see

NOTE Confidence: 0.811468077142857

00:06:21.407 --> 00:06:23.477 activation of bypass pathways like the

NOTE Confidence: 0.811468077142857

00:06:23.477 --> 00:06:26.192 P I3 kinase mtor pathway leading to

NOTE Confidence: 0.811468077142857

00:06:26.192 --> 00:06:28.207 resistance and obviously there's been

NOTE Confidence: 0.811468077142857

00:06:28.207 --> 00:06:30.020 a lot of interest in understanding

NOTE Confidence: 0.811468077142857

00:06:30.020 --> 00:06:31.815 these mechanisms of of tumor cell

NOTE Confidence: 0.811468077142857

00:06:31.815 --> 00:06:33.510 resistance to these therapeutic agents.

NOTE Confidence: 0.811468077142857

00:06:33.510 --> 00:06:35.421 With the idea that if you understand

NOTE Confidence: 0.811468077142857

00:06:35.421 --> 00:06:37.402 how cells become resistant you might

NOTE Confidence: 0.811468077142857

00:06:37.402 --> 00:06:38.686 be able to devise.

NOTE Confidence: 0.811468077142857

00:06:38.690 --> 00:06:39.181 Addition,

NOTE Confidence: 0.811468077142857

00:06:39.181 --> 00:06:41.145 new therapeutic strategies that

NOTE Confidence: 0.811468077142857

00:06:41.145 --> 00:06:43.109 might be more durable.

NOTE Confidence: 0.811468077142857

00:06:43.110 --> 00:06:45.798 So we got into this area through a

NOTE Confidence: 0.811468077142857

00:06:45.798 --> 00:06:48.258 genetic loss of function screen and SH

NOTE Confidence: 0.811468077142857

00:06:48.258 --> 00:06:51.548 RNA screen that one of my graduate students,

NOTE Confidence: 0.811468077142857

00:06:51.550 --> 00:06:54.305 Eunice Cho conducted to identify

NOTE Confidence: 0.811468077142857

00:06:54.305 --> 00:06:57.060 genes that modulate sensitivity to

NOTE Confidence: 0.811468077142857

00:06:57.147 --> 00:07:00.105 MEK inhibitors in Melanoma cells and

NOTE Confidence: 0.811468077142857

00:07:00.105 --> 00:07:02.989 this work was published last year.

NOTE Confidence: 0.811468077142857

00:07:02.990 --> 00:07:04.440 People are interested in getting

NOTE Confidence: 0.811468077142857

00:07:04.440 --> 00:07:06.484 more of the details before I talk

NOTE Confidence: 0.811468077142857

00:07:06.484 --> 00:07:08.104 about the specifics of this research,

NOTE Confidence: 0.811468077142857

00:07:08.110 --> 00:07:10.902 I have to briefly plug the Yale Cancer

NOTE Confidence: 0.811468077142857

00:07:10.902 --> 00:07:12.766 Center Functional Genomics core that

NOTE Confidence: 0.811468077142857

00:07:12.766 --> 00:07:14.968 I Co direct with David Calderwood.

NOTE Confidence: 0.811468077142857

00:07:14.970 --> 00:07:15.576 And really,

NOTE Confidence: 0.811468077142857

00:07:15.576 --> 00:07:17.697 the the the the mission of this

NOTE Confidence: 0.811468077142857

00:07:17.697 --> 00:07:20.024 core is to facilitate these loss

NOTE Confidence: 0.811468077142857

00:07:20.024 --> 00:07:21.592 of function genetic screens.

NOTE Confidence: 0.811468077142857

00:07:21.600 --> 00:07:23.640 CRISPR CAS 9 screens or SH RNA screens

NOTE Confidence: 0.811468077142857

00:07:23.640 --> 00:07:25.875 like I'm going to talk about and so

NOTE Confidence: 0.811468077142857

00:07:25.875 --> 00:07:27.716 hopefully this talk will give you a

NOTE Confidence: 0.811468077142857

00:07:27.716 --> 00:07:29.216 flavor of the kinds of information

NOTE Confidence: 0.811468077142857

00:07:29.216 --> 00:07:31.848 you can get out of these screens

NOTE Confidence: 0.811468077142857

00:07:31.848 --> 00:07:34.085 and inspire you to contact us and

NOTE Confidence: 0.811468077142857

00:07:34.085 --> 00:07:35.495 and set up your own.

NOTE Confidence: 0.811468077142857

00:07:35.500 --> 00:07:37.250 So I don't have a lot of time to talk

NOTE Confidence: 0.811468077142857

00:07:37.300 --> 00:07:39.284 about the details of how the screen works.

NOTE Confidence: 0.811468077142857

00:07:39.290 --> 00:07:42.390 Needless to say, we.

NOTE Confidence: 0.811468077142857

00:07:42.390 --> 00:07:44.605 In introduce Melanoma cell line

NOTE Confidence: 0.811468077142857

00:07:44.605 --> 00:07:47.590 with a pooled SH RNA library.

NOTE Confidence: 0.811468077142857

00:07:47.590 --> 00:07:48.439 In this one.

NOTE Confidence: 0.811468077142857

00:07:48.439 --> 00:07:49.288 In this case,

NOTE Confidence: 0.811468077142857

00:07:49.290 --> 00:07:50.662 one targeting kinases and

NOTE Confidence: 0.811468077142857

00:07:50.662 --> 00:07:52.377 phosphatases and then we propagate

NOTE Confidence: 0.811468077142857

00:07:52.377 --> 00:07:54.470 in either the presence or absence.

NOTE Confidence: 0.811468077142857

00:07:54.470 --> 00:07:56.234 One of two MEK inhibitors tromette

NOTE Confidence: 0.811468077142857

00:07:56.234 --> 00:07:58.767 never sell you met in IB and then we

NOTE Confidence: 0.811468077142857

00:07:58.767 --> 00:08:00.500 look at which hairpins become enriched

NOTE Confidence: 0.811468077142857

00:08:00.500 --> 00:08:03.072 or depleted from the population at the

NOTE Confidence: 0.811468077142857

00:08:03.072 --> 00:08:05.960 end of the screen and and what this

NOTE Confidence: 0.811468077142857

00:08:06.047 --> 00:08:09.399 will should tell us our our what jeans.

NOTE Confidence: 0.811468077142857

00:08:09.400 --> 00:08:13.054 Impact the sensitivity mekan hitters and

NOTE Confidence: 0.811468077142857

00:08:13.054 --> 00:08:15.490 hopefully identify additional genetic

NOTE Confidence: 0.811468077142857

00:08:15.570 --> 00:08:18.456 modifiers of of map kinase signaling.

NOTE Confidence: 0.904180252631579

00:08:18.460 --> 00:08:20.140 So I'm going to jump to the

NOTE Confidence: 0.904180252631579

00:08:20.140 --> 00:08:22.200 top hit that came out of this

NOTE Confidence: 0.904180252631579

00:08:22.200 --> 00:08:23.800 screen which was a phosphatase.

NOTE Confidence: 0.904180252631579

00:08:23.800 --> 00:08:26.000 Assyrian threonine phosphatase called

NOTE Confidence: 0.904180252631579

00:08:26.000 --> 00:08:28.805 PPP six seed, and what you can see

NOTE Confidence: 0.904180252631579

00:08:28.805 --> 00:08:30.498 here is that amongst all of the

NOTE Confidence: 0.904180252631579

00:08:30.498 --> 00:08:32.178 hair pins that were in our library,

NOTE Confidence: 0.904180252631579

00:08:32.180 --> 00:08:34.610 those that target PPP succeed were

NOTE Confidence: 0.904180252631579

00:08:34.610 --> 00:08:36.624 specifically enriched in the presence

NOTE Confidence: 0.904180252631579

00:08:36.624 --> 00:08:39.200 of either Solomon if or trim it nib.

NOTE Confidence: 0.904180252631579

00:08:39.200 --> 00:08:40.530 But under control conditions they

NOTE Confidence: 0.904180252631579

00:08:40.530 --> 00:08:42.420 were not enriched in the population.

NOTE Confidence: 0.904180252631579

00:08:42.420 --> 00:08:44.268 And what that means is that when you

NOTE Confidence: 0.904180252631579

00:08:44.268 --> 00:08:45.798 treat cells with a MEK inhibitor,

NOTE Confidence: 0.904180252631579

00:08:45.800 --> 00:08:48.810 they grow better if you knock down.

NOTE Confidence: 0.904180252631579

00:08:48.810 --> 00:08:50.868 PPP 6C OK.

NOTE Confidence: 0.904180252631579

00:08:50.868 --> 00:08:54.396 So seeing PPP 6C as a hit in the

NOTE Confidence: 0.904180252631579

00:08:54.396 --> 00:08:56.799 screen really caught our eye and the

NOTE Confidence: 0.904180252631579

00:08:56.799 --> 00:08:58.905 reason for that is that something

NOTE Confidence: 0.904180252631579

00:08:58.980 --> 00:09:01.488 like 7 to 9% of melanomas have been

NOTE Confidence: 0.904180252631579

00:09:01.488 --> 00:09:03.136 shown through genomic analysis.

NOTE Confidence: 0.904180252631579

00:09:03.140 --> 00:09:06.070 Whole exome sequencing to harbor

NOTE Confidence: 0.904180252631579

00:09:06.070 --> 00:09:08.020 what are thought to be loss

NOTE Confidence: 0.904180252631579

00:09:08.020 --> 00:09:09.814 of function mutations in PP6C.

NOTE Confidence: 0.904180252631579

00:09:09.814 --> 00:09:12.284 So we thought identifying this

NOTE Confidence: 0.904180252631579

00:09:12.284 --> 00:09:14.610 phosphatase in the screen for modulators

NOTE Confidence: 0.904180252631579

00:09:14.610 --> 00:09:16.871 of drug sensitivity in Melanoma cell

NOTE Confidence: 0.904180252631579

00:09:16.871 --> 00:09:19.067 lines was probably not a coincidence.

NOTE Confidence: 0.904180252631579

00:09:19.070 --> 00:09:20.780 So first thing we did was to try to.

NOTE Confidence: 0.904180252631579

00:09:20.780 --> 00:09:22.928 Verify this result.

NOTE Confidence: 0.904180252631579

00:09:22.928 --> 00:09:26.160 So we derived PDP60 knockout cells

NOTE Confidence: 0.904180252631579

00:09:26.160 --> 00:09:28.320 through CRISPR CAS 9 gene editing,

NOTE Confidence: 0.904180252631579

00:09:28.320 --> 00:09:29.226 and sure enough,

NOTE Confidence: 0.904180252631579

00:09:29.226 --> 00:09:31.340 if we titrate in MEK inhibitor in

NOTE Confidence: 0.904180252631579

00:09:31.409 --> 00:09:33.479 this case a trim it and if you can

NOTE Confidence: 0.904180252631579

00:09:33.479 --> 00:09:35.850 see that knocking out PPP6C leads to

NOTE Confidence: 0.904180252631579

00:09:35.850 --> 00:09:37.600 substantial resistance to the inhibitor

NOTE Confidence: 0.904180252631579

00:09:37.600 --> 00:09:40.217 and the other thing that we're observing,

NOTE Confidence: 0.904180252631579

00:09:40.220 --> 00:09:41.680 which is kind of interesting,

NOTE Confidence: 0.904180252631579

00:09:41.680 --> 00:09:45.196 is that actually sells deleted for

NOTE Confidence: 0.904180252631579

00:09:45.200 --> 00:09:48.875 PPP6C grow more poorly than wild type

NOTE Confidence: 0.904180252631579

00:09:48.880 --> 00:09:51.376 cell line than the wild type cell line.

NOTE Confidence: 0.904180252631579

00:09:51.380 --> 00:09:54.396 But that growth is at growth effect is

NOTE Confidence: 0.904180252631579

00:09:54.396 --> 00:09:56.328 actually rescued by low concentrations

NOTE Confidence: 0.904180252631579

00:09:56.328 --> 00:09:58.918 of the MEK inhibitor and this is

NOTE Confidence: 0.904180252631579

00:09:58.988 --> 00:10:00.998 reminiscent of a phenomenon that's

NOTE Confidence: 0.904180252631579

00:10:00.998 --> 00:10:04.280 been seen in in preclinical models,

NOTE Confidence: 0.904180252631579

00:10:04.280 --> 00:10:07.730 that's called inhibitor addiction and

NOTE Confidence: 0.904180252631579

00:10:07.730 --> 00:10:11.326 basically what what this means is that

NOTE Confidence: 0.904180252631579

00:10:11.330 --> 00:10:13.070 it's it's typically characterized

NOTE Confidence: 0.904180252631579

00:10:13.070 --> 00:10:15.245 by cells having hyperactive map

NOTE Confidence: 0.904180252631579

00:10:15.245 --> 00:10:16.906 kinase signaling and hyperactive

NOTE Confidence: 0.904180252631579

00:10:16.906 --> 00:10:19.228 map kinase signaling is toxic to

NOTE Confidence: 0.904180252631579

00:10:19.228 --> 00:10:21.428 cells and they can be brought back.

NOTE Confidence: 0.904180252631579

00:10:21.430 --> 00:10:24.027 Down into the range that's optimal for

NOTE Confidence: 0.904180252631579

00:10:24.027 --> 00:10:26.152 cell growth with low concentrations

NOTE Confidence: 0.904180252631579

00:10:26.152 --> 00:10:27.568 of an inhibitor,

NOTE Confidence: 0.904180252631579

00:10:27.570 --> 00:10:29.950 and so that was it in a sort of a

NOTE Confidence: 0.904180252631579

00:10:30.026 --> 00:10:32.234 immediate clue that of what might

NOTE Confidence: 0.904180252631579

00:10:32.234 --> 00:10:33.706 be going on here.

NOTE Confidence: 0.904180252631579

00:10:33.710 --> 00:10:36.265 That if loss of PPP6C caused hyper

NOTE Confidence: 0.904180252631579

00:10:36.265 --> 00:10:38.629 activation of MAP kinase signaling,

NOTE Confidence: 0.904180252631579

00:10:38.630 --> 00:10:40.916 that would explain why you get

NOTE Confidence: 0.904180252631579

00:10:40.916 --> 00:10:42.905 resistance because it requires higher

NOTE Confidence: 0.904180252631579

00:10:42.905 --> 00:10:45.269 concentrations of drug to suppress the

NOTE Confidence: 0.904180252631579

00:10:45.269 --> 00:10:47.769 pathway enough to inhibit cell growth.

NOTE Confidence: 0.904180252631579

00:10:47.770 --> 00:10:50.355 And also explain this drug

NOTE Confidence: 0.904180252631579

00:10:50.355 --> 00:10:51.389 addiction phenotype.

NOTE Confidence: 0.904180252631579

00:10:51.390 --> 00:10:52.846 And sure enough, that's what we see.

NOTE Confidence: 0.904180252631579

00:10:52.850 --> 00:10:53.782 So basically,

NOTE Confidence: 0.904180252631579

00:10:53.782 --> 00:10:57.044 if we look at a number of

NOTE Confidence: 0.904180252631579

00:10:57.044 --> 00:11:00.206 distinct PPP 60 knockout clones,

NOTE Confidence: 0.904180252631579

00:11:00.206 --> 00:11:03.576 we can see profound hyperphosphorylation

NOTE Confidence: 0.904180252631579

00:11:03.576 --> 00:11:06.254 hyperactivation of of MEK and of Erk

NOTE Confidence: 0.904180252631579

00:11:06.254 --> 00:11:08.613 and we can rescue that hyperactivation

NOTE Confidence: 0.904180252631579

00:11:08.613 --> 00:11:12.092 by re expressing a wild type allele

NOTE Confidence: 0.904180252631579

00:11:12.092 --> 00:11:15.908 of PPP 6C but not a phosphatase dead

NOTE Confidence: 0.904180252631579

00:11:15.908 --> 00:11:18.110 allele that's catalytically inactive.

NOTE Confidence: 0.904180252631579

00:11:18.110 --> 00:11:18.502 OK,

NOTE Confidence: 0.904180252631579

00:11:18.502 --> 00:11:20.462 and we extended these observations

NOTE Confidence: 0.904180252631579

00:11:20.462 --> 00:11:23.098 to a whole panel of cell lines.

NOTE Confidence: 0.904180252631579

00:11:23.100 --> 00:11:25.404 I'm only showing a few of them here,

NOTE Confidence: 0.904180252631579

00:11:25.410 --> 00:11:25.895 basically,

NOTE Confidence: 0.904180252631579

00:11:25.895 --> 00:11:28.805 regardless of lineages we lookin cell

NOTE Confidence: 0.904180252631579

00:11:28.805 --> 00:11:31.950 lines that either harbor BRAF mutations,

NOTE Confidence: 0.904180252631579

00:11:31.950 --> 00:11:34.300 or crass Oren RAST mutations

NOTE Confidence: 0.904180252631579

00:11:34.300 --> 00:11:36.650 with a couple of exceptions.

NOTE Confidence: 0.786400669166667

00:11:36.650 --> 00:11:39.546 We see that when we knock down PPP

NOTE Confidence: 0.786400669166667

00:11:39.546 --> 00:11:42.736 60 by SH RNA, we get increased mech

NOTE Confidence: 0.786400669166667

00:11:42.736 --> 00:11:44.906 and or increased ORC phosphorylation.

NOTE Confidence: 0.786400669166667

00:11:44.910 --> 00:11:46.944 So we do think this is a general phenomenon,

NOTE Confidence: 0.786400669166667

00:11:46.950 --> 00:11:48.498 at least in the context of

NOTE Confidence: 0.786400669166667

00:11:48.498 --> 00:11:50.870 oncogenic map kinase. Signaling so.

NOTE Confidence: 0.681916948571429

00:11:53.210 --> 00:11:57.134 PPP succeed is a phosphatase and

NOTE Confidence: 0.681916948571429

00:11:57.134 --> 00:11:59.176 in experiments that I I I won't

NOTE Confidence: 0.681916948571429

00:11:59.176 --> 00:12:00.660 have time to tell you about.

NOTE Confidence: 0.681916948571429

00:12:00.660 --> 00:12:04.223 We had ruled out activation of upstream

NOTE Confidence: 0.681916948571429

00:12:04.223 --> 00:12:07.082 components of the pathway and had

NOTE Confidence: 0.681916948571429

00:12:07.082 --> 00:12:09.826 a good handle on this PB6C acting

NOTE Confidence: 0.681916948571429

00:12:09.826 --> 00:12:12.729 at the level of MEK because it's a

NOTE Confidence: 0.681916948571429

00:12:12.729 --> 00:12:14.341 phosphatase may most straightforward

NOTE Confidence: 0.681916948571429

00:12:14.341 --> 00:12:16.337 explanation would be that it directly

NOTE Confidence: 0.681916948571429

00:12:16.337 --> 00:12:18.022 dephosphorylates Mac and we we

NOTE Confidence: 0.681916948571429

00:12:18.022 --> 00:12:19.920 do think that's what's going on.

NOTE Confidence: 0.681916948571429

00:12:19.920 --> 00:12:21.762 So in in vitro phosphatase assays

NOTE Confidence: 0.681916948571429

00:12:21.762 --> 00:12:22.990 we could show that.

NOTE Confidence: 0.681916948571429

00:12:22.990 --> 00:12:26.554 Purified PP6P6C complexes.

NOTE Confidence: 0.681916948571429

00:12:26.554 --> 00:12:28.030 Candy phosphorylate MEK,

NOTE Confidence: 0.681916948571429

00:12:28.030 --> 00:12:29.926 but they don't be phosphorylate Erk,

NOTE Confidence: 0.681916948571429

00:12:29.930 --> 00:12:32.149 so there seems to be some substrate

NOTE Confidence: 0.681916948571429

00:12:32.149 --> 00:12:34.062 specificity for the upstream component

NOTE Confidence: 0.681916948571429

00:12:34.062 --> 00:12:36.664 and probably more compelling we could

NOTE Confidence: 0.681916948571429

00:12:36.664 --> 00:12:39.046 detect at least an indirect physical

NOTE Confidence: 0.681916948571429

00:12:39.046 --> 00:12:41.302 interaction between Mac and PPP 6C.

NOTE Confidence: 0.681916948571429

00:12:41.302 --> 00:12:43.732 So PP6C is the catalytic

NOTE Confidence: 0.681916948571429

00:12:43.732 --> 00:12:46.009 subunit of holoenzyme that is,

NOTE Confidence: 0.681916948571429

00:12:46.010 --> 00:12:46.515 heterotrimeric,

NOTE Confidence: 0.681916948571429

00:12:46.515 --> 00:12:48.535 that includes regulatory subunits

NOTE Confidence: 0.681916948571429

00:12:48.535 --> 00:12:51.644 that have ascribed roles and binding

NOTE Confidence: 0.681916948571429

00:12:51.644 --> 00:12:53.716 to substrates and recruiting

NOTE Confidence: 0.681916948571429

00:12:53.716 --> 00:12:55.270 them for dephosphorylation.

NOTE Confidence: 0.681916948571429

00:12:55.270 --> 00:12:58.707 And we could see in komuna precipitation

NOTE Confidence: 0.681916948571429

00:12:58.707 --> 00:13:01.741 assays that pulling down any of

NOTE Confidence: 0.681916948571429

00:13:01.741 --> 00:13:03.705 the three regulatory subunits.

NOTE Confidence: 0.681916948571429

00:13:03.710 --> 00:13:06.022 I will bring down Mac but not so

NOTE Confidence: 0.681916948571429

00:13:06.022 --> 00:13:08.189 much with the catalytic subunit,

NOTE Confidence: 0.681916948571429

00:13:08.190 --> 00:13:10.780 sort of confirming a role for these

NOTE Confidence: 0.681916948571429

00:13:10.780 --> 00:13:12.850 regulatory subunits in in recruiting.

NOTE Confidence: 0.681916948571429

00:13:12.850 --> 00:13:16.190 MEC two to the complex.

NOTE Confidence: 0.681916948571429

00:13:16.190 --> 00:13:18.528 So I mentioned that PPP 6C is

NOTE Confidence: 0.681916948571429

00:13:18.528 --> 00:13:19.929 recurrently mutated in melanomas

NOTE Confidence: 0.681916948571429

00:13:19.929 --> 00:13:22.553 and so we wanted to look at whether

NOTE Confidence: 0.681916948571429

00:13:22.553 --> 00:13:24.394 these mutations affected signaling

NOTE Confidence: 0.681916948571429

00:13:24.394 --> 00:13:26.804 through the MAP kinase pathway.

NOTE Confidence: 0.681916948571429

00:13:26.810 --> 00:13:29.366 And so we perform rescue experiments

NOTE Confidence: 0.681916948571429

00:13:29.366 --> 00:13:32.690 where we re expressed series of the

NOTE Confidence: 0.681916948571429

00:13:32.690 --> 00:13:35.390 the most frequently observed mutants

NOTE Confidence: 0.681916948571429

00:13:35.390 --> 00:13:39.038 in our PP60 knockout cells and what we

NOTE Confidence: 0.681916948571429

00:13:39.038 --> 00:13:42.209 observed is with a single exception

NOTE Confidence: 0.681916948571429

00:13:42.210 --> 00:13:45.230 that these mutants were either

NOTE Confidence: 0.681916948571429

00:13:45.230 --> 00:13:47.646 entirely or partially defective.

NOTE Confidence: 0.681916948571429

00:13:47.650 --> 00:13:50.705 In their ability to mediate

NOTE Confidence: 0.681916948571429

00:13:50.705 --> 00:13:51.927 mech dephosphorylation,

NOTE Confidence: 0.681916948571429

00:13:51.930 --> 00:13:54.528 so we conclude that these are

NOTE Confidence: 0.681916948571429

00:13:54.530 --> 00:13:56.955 likely partial loss of function

NOTE Confidence: 0.681916948571429

00:13:56.955 --> 00:14:00.040 mutations and it sort of makes

NOTE Confidence: 0.681916948571429

00:14:00.040 --> 00:14:02.860 sense that they're functioning to

NOTE Confidence: 0.681916948571429

00:14:02.860 --> 00:14:05.465 increase signaling through the core

NOTE Confidence: 0.681916948571429

00:14:05.465 --> 00:14:07.549 pathway that drives melanomas.

NOTE Confidence: 0.681916948571429

00:14:07.550 --> 00:14:10.427 That is, the map kinase signaling pathway.

NOTE Confidence: 0.681916948571429

00:14:10.430 --> 00:14:11.396 So, unfortunately,

NOTE Confidence: 0.681916948571429

00:14:11.396 --> 00:14:14.777 PPP 60 mutations are are rare enough

NOTE Confidence: 0.681916948571429

00:14:14.777 --> 00:14:17.600 that we we really don't know the.

NOTE Confidence: 0.681916948571429

00:14:17.600 --> 00:14:20.108 Clinical relevance of these

NOTE Confidence: 0.681916948571429

00:14:20.108 --> 00:14:22.616 mutations to pathway activation,

NOTE Confidence: 0.681916948571429

00:14:22.620 --> 00:14:25.374 but we were able to mine some data from

NOTE Confidence: 0.681916948571429

00:14:25.374 --> 00:14:28.383 C bio portal and it did appear as if

NOTE Confidence: 0.681916948571429

00:14:28.383 --> 00:14:30.532 there was a significant correlation

NOTE Confidence: 0.681916948571429

00:14:30.532 --> 00:14:33.352 between the M RNA expression level

NOTE Confidence: 0.681916948571429

00:14:33.352 --> 00:14:35.810 of PPP6C and the level of either

NOTE Confidence: 0.681916948571429

00:14:35.810 --> 00:14:38.248 phospho Erk or Phospho MEK as seen

NOTE Confidence: 0.681916948571429

00:14:38.248 --> 00:14:39.993 in reverse phase protein arrays.

NOTE Confidence: 0.681916948571429

00:14:40.000 --> 00:14:43.207 So we do believe that PPP 6C is

NOTE Confidence: 0.681916948571429

00:14:43.207 --> 00:14:45.781 modulating flux through the pathway in

NOTE Confidence: 0.681916948571429

00:14:45.781 --> 00:14:49.025 tumors and and may be a factor that

NOTE Confidence: 0.681916948571429

00:14:49.025 --> 00:14:50.418 influences. Therapeutic response.

NOTE Confidence: 0.681916948571429

00:14:50.418 --> 00:14:50.917 OK,

NOTE Confidence: 0.681916948571429

00:14:50.917 --> 00:14:54.410 so in conclusion of this first part

NOTE Confidence: 0.681916948571429

00:14:54.499 --> 00:14:57.225 we've identified PPP 6C as a new

NOTE Confidence: 0.681916948571429

00:14:57.225 --> 00:14:58.640 player in restraining oncogenic map

NOTE Confidence: 0.681916948571429

00:14:58.702 --> 00:15:00.170 kinase signaling through dephosphorylation

NOTE Confidence: 0.681916948571429

00:15:00.170 --> 00:15:02.930 of MEK and that loss of function.

NOTE Confidence: 0.681916948571429

00:15:02.930 --> 00:15:06.297 Mutations of PPP 60 lead to hyper

NOTE Confidence: 0.681916948571429

00:15:06.297 --> 00:15:08.439 activated Erk signaling some of the

NOTE Confidence: 0.681916948571429

00:15:08.439 --> 00:15:10.070 open questions that we're trying to pursue.

NOTE Confidence: 0.681916948571429

00:15:10.070 --> 00:15:10.510 Now,

NOTE Confidence: 0.681916948571429

00:15:10.510 --> 00:15:12.710 how is PPP 6C regulated?

NOTE Confidence: 0.681916948571429

00:15:12.710 --> 00:15:15.839 So this phenomenon where PPP 6C is

NOTE Confidence: 0.681916948571429

00:15:15.839 --> 00:15:18.410 required to restrain MEK activation

NOTE Confidence: 0.681916948571429

00:15:18.410 --> 00:15:19.844 has has something that we really

NOTE Confidence: 0.681916948571429

00:15:19.844 --> 00:15:21.860 only see in the setting of oncogenic

NOTE Confidence: 0.681916948571429

00:15:21.860 --> 00:15:23.200 activation of the pathway.

NOTE Confidence: 0.681916948571429

00:15:23.200 --> 00:15:25.804 And that suggests to us that maybe

NOTE Confidence: 0.681916948571429

00:15:25.804 --> 00:15:26.920 there's a negative

NOTE Confidence: 0.950039684210526

00:15:26.994 --> 00:15:29.374 feedback loop where pathway activation

NOTE Confidence: 0.950039684210526

00:15:29.374 --> 00:15:31.693 leads to activation of PPP6C

NOTE Confidence: 0.950039684210526

00:15:31.693 --> 00:15:33.758 towards the phosphorylation of MEK,

NOTE Confidence: 0.950039684210526

00:15:33.760 --> 00:15:36.160 and we'd like to understand how that happens.

NOTE Confidence: 0.950039684210526

00:15:36.160 --> 00:15:38.368 And of course, it may be that there

NOTE Confidence: 0.950039684210526

00:15:38.368 --> 00:15:40.180 are other signaling outputs substrates

NOTE Confidence: 0.950039684210526

00:15:40.180 --> 00:15:42.700 other than mech that are functionally

NOTE Confidence: 0.950039684210526

00:15:42.700 --> 00:15:44.914 important for tumors where you see lots

NOTE Confidence: 0.950039684210526

00:15:44.914 --> 00:15:47.285 of people pay 60 and we're interested

NOTE Confidence: 0.950039684210526

00:15:47.285 --> 00:15:49.875 in trying to identify those as well.

NOTE Confidence: 0.950039684210526

00:15:49.880 --> 00:15:51.390 So for the remaining time,

NOTE Confidence: 0.950039684210526

00:15:51.390 --> 00:15:53.446 I'm going to switch gears a little bit

NOTE Confidence: 0.950039684210526

00:15:53.446 --> 00:15:55.425 and move downstream in the pathway to

NOTE Confidence: 0.950039684210526

00:15:55.425 --> 00:15:58.013 do the the the kinase in the bottom

NOTE Confidence: 0.950039684210526

00:15:58.013 --> 00:16:00.619 of the map kinase cascade IIRC,

NOTE Confidence: 0.950039684210526

00:16:00.620 --> 00:16:03.469 and here the we're going to be

NOTE Confidence: 0.950039684210526

00:16:03.469 --> 00:16:06.359 talking a little bit more about the

NOTE Confidence: 0.950039684210526

00:16:06.359 --> 00:16:08.204 structural basis for how connections

NOTE Confidence: 0.950039684210526

00:16:08.204 --> 00:16:10.319 in the pathway is are made,

NOTE Confidence: 0.950039684210526

00:16:10.320 --> 00:16:12.756 and also some of these network rewiring

NOTE Confidence: 0.950039684210526

00:16:12.756 --> 00:16:14.343 phenomena they introduced at the

NOTE Confidence: 0.950039684210526

00:16:14.343 --> 00:16:16.030 beginning and so the work I'm going

NOTE Confidence: 0.950039684210526

00:16:16.030 --> 00:16:18.505 to talk about is the work of really

NOTE Confidence: 0.950039684210526

00:16:18.505 --> 00:16:19.874 talented graduate student who's.

NOTE Confidence: 0.950039684210526

00:16:19.874 --> 00:16:22.478 Currently in the lab Julissa Torres

NOTE Confidence: 0.950039684210526

00:16:22.478 --> 00:16:25.627 Robles and what she was interested in

NOTE Confidence: 0.950039684210526

00:16:25.627 --> 00:16:28.653 in looking at our oncogenic mutations in

NOTE Confidence: 0.950039684210526

00:16:28.653 --> 00:16:31.677 in Erk 2 itself or encoded by the map K1G.

NOTE Confidence: 0.950039684210526

00:16:31.677 --> 00:16:33.966 So as I said at the outset,

NOTE Confidence: 0.950039684210526

00:16:33.970 --> 00:16:36.178 you have high frequency mutations in

NOTE Confidence: 0.950039684210526

00:16:36.178 --> 00:16:38.714 multiple cancer types of Rasen draft but

NOTE Confidence: 0.950039684210526

00:16:38.714 --> 00:16:41.038 at lower frequency you do see mutations

NOTE Confidence: 0.950039684210526

00:16:41.103 --> 00:16:43.335 in some of the downstream components.

NOTE Confidence: 0.950039684210526

00:16:43.340 --> 00:16:45.266 The Erk mutations in particular are

NOTE Confidence: 0.950039684210526

00:16:45.266 --> 00:16:47.080 sort of interesting because you don't

NOTE Confidence: 0.950039684210526

00:16:47.080 --> 00:16:48.753 see them in the same tumor types

NOTE Confidence: 0.950039684210526

00:16:48.753 --> 00:16:50.675 that you do the Rasen draft mutation.

NOTE Confidence: 0.950039684210526

00:16:50.680 --> 00:16:53.039 So where, where as Rasen rap mutations

NOTE Confidence: 0.950039684210526

00:16:53.039 --> 00:16:55.000 you you see in melanomas,

NOTE Confidence: 0.950039684210526

00:16:55.000 --> 00:16:57.052 lung cancers, colorectal cancers,

NOTE Confidence: 0.950039684210526

00:16:57.052 --> 00:16:58.078 pancreatic cancer,

NOTE Confidence: 0.950039684210526

00:16:58.080 --> 00:16:58.840 the Erk.

NOTE Confidence: 0.950039684210526

00:16:58.840 --> 00:17:00.740 2 mutations are largely restricted

NOTE Confidence: 0.950039684210526

00:17:00.740 --> 00:17:02.640 to squamous cell carcinomas,

NOTE Confidence: 0.950039684210526

00:17:02.640 --> 00:17:05.965 so about 8% of cervical squamous cell

NOTE Confidence: 0.950039684210526

00:17:05.965 --> 00:17:08.199 carcinomas have recurrent or two

NOTE Confidence: 0.950039684210526

00:17:08.199 --> 00:17:11.232 mutations and about 2% of head and neck.

NOTE Confidence: 0.950039684210526

00:17:11.232 --> 00:17:13.197 Squamous cell carcinomas have these

NOTE Confidence: 0.950039684210526

00:17:13.197 --> 00:17:15.066 mutations and they've attracted some

NOTE Confidence: 0.950039684210526

00:17:15.066 --> 00:17:16.911 attention in that setting because

NOTE Confidence: 0.950039684210526

00:17:16.911 --> 00:17:18.706 of potential association between

NOTE Confidence: 0.950039684210526

00:17:18.706 --> 00:17:20.976 the presence of those mutations.

NOTE Confidence: 0.950039684210526

00:17:20.980 --> 00:17:25.135 And clinical responses to EGF

NOTE Confidence: 0.950039684210526

00:17:25.135 --> 00:17:26.797 receptor inhibitors.

NOTE Confidence: 0.950039684210526

00:17:26.800 --> 00:17:28.732 So one of the things that kind

NOTE Confidence: 0.950039684210526

00:17:28.732 --> 00:17:30.820 of attracted us to this is the

NOTE Confidence: 0.950039684210526

00:17:30.820 --> 00:17:32.320 the nature of these mutations.

NOTE Confidence: 0.950039684210526

00:17:32.320 --> 00:17:35.041 They're sort of unusual when you compare

NOTE Confidence: 0.950039684210526

00:17:35.041 --> 00:17:37.387 them to other activating mutations and

NOTE Confidence: 0.950039684210526

00:17:37.387 --> 00:17:39.679 protein kinases that you see in cancer.

NOTE Confidence: 0.950039684210526

00:17:39.680 --> 00:17:41.039 So unlike say,

NOTE Confidence: 0.950039684210526

00:17:41.039 --> 00:17:43.757 BRAF mutations or EGF receptor mutations,

NOTE Confidence: 0.950039684210526

00:17:43.760 --> 00:17:45.580 these mutations don't intrinsically

NOTE Confidence: 0.950039684210526

00:17:45.580 --> 00:17:48.310 hyper activate the kinase and they

NOTE Confidence: 0.950039684210526

00:17:48.383 --> 00:17:50.567 all map at least in three dimensional

NOTE Confidence: 0.950039684210526

00:17:50.567 --> 00:17:52.504 space to a really interesting

NOTE Confidence: 0.950039684210526

00:17:52.504 --> 00:17:54.829 region of the kinase catalytic.

NOTE Confidence: 0.950039684210526

00:17:54.830 --> 00:17:56.496 So this is a region that falls

NOTE Confidence: 0.950039684210526

00:17:56.496 --> 00:17:58.110 outside of the catalytic cleft.

NOTE Confidence: 0.950039684210526

00:17:58.110 --> 00:18:00.567 That's known as the common docking group,

NOTE Confidence: 0.950039684210526

00:18:00.570 --> 00:18:02.215 and it's called that because

NOTE Confidence: 0.950039684210526

00:18:02.215 --> 00:18:04.850 it serves as a hub for protein

NOTE Confidence: 0.950039684210526

00:18:04.850 --> 00:18:07.150 protein interactions with ERP two,

NOTE Confidence: 0.950039684210526

00:18:07.150 --> 00:18:10.024 so this docking groove binds to

NOTE Confidence: 0.950039684210526

00:18:10.024 --> 00:18:12.649 a number of substrates of Erk,

NOTE Confidence: 0.950039684210526

00:18:12.650 --> 00:18:15.009 but it also binds to irks regulators,

NOTE Confidence: 0.950039684210526

00:18:15.010 --> 00:18:18.574 so the Mach one and Mach 2 which are

NOTE Confidence: 0.950039684210526

00:18:18.574 --> 00:18:20.334 the positive regulars that phosphorylate

NOTE Confidence: 0.950039684210526

00:18:20.334 --> 00:18:22.870 and turn on or combined at this site,

NOTE Confidence: 0.950039684210526

00:18:22.870 --> 00:18:26.032 and the dual specificity phosphatase that

NOTE Confidence: 0.950039684210526

00:18:26.032 --> 00:18:29.178 dephosphorylates find it this site as well.

NOTE Confidence: 0.950039684210526

00:18:29.180 --> 00:18:31.752 So this sort of presents a little

NOTE Confidence: 0.950039684210526

00:18:31.752 --> 00:18:33.736 bit of a conundrum because I just,

NOTE Confidence: 0.950039684210526

00:18:33.736 --> 00:18:34.312 you know,

NOTE Confidence: 0.950039684210526

00:18:34.312 --> 00:18:36.040 told you that this is a

NOTE Confidence: 0.9346002125

00:18:36.116 --> 00:18:37.424 really functionally important

NOTE Confidence: 0.9346002125

00:18:37.424 --> 00:18:40.476 part of the of the molecule yet,

NOTE Confidence: 0.9346002125

00:18:40.480 --> 00:18:42.034 and so you might expect that mutations

NOTE Confidence: 0.9346002125

00:18:42.034 --> 00:18:43.877 at this site would be loss of function.

NOTE Confidence: 0.9346002125

00:18:43.880 --> 00:18:46.046 But of course just logically it

NOTE Confidence: 0.9346002125

00:18:46.046 --> 00:18:48.201 would seem that mutations in, IIRC,

NOTE Confidence: 0.9346002125

00:18:48.201 --> 00:18:50.700 that you find in cancer should be

NOTE Confidence: 0.9346002125

00:18:50.767 --> 00:18:52.979 gain of function and and the reason

NOTE Confidence: 0.9346002125

00:18:52.979 --> 00:18:55.832 why this is is that these mutations

NOTE Confidence: 0.9346002125

00:18:55.832 --> 00:18:58.122 actually cause selective disruption of

NOTE Confidence: 0.9346002125

00:18:58.122 --> 00:19:00.644 these protein protein interactions.

NOTE Confidence: 0.9346002125

00:19:00.644 --> 00:19:02.708 So for example,

NOTE Confidence: 0.9346002125

00:19:02.710 --> 00:19:04.756 we know that these cancer associated

NOTE Confidence: 0.9346002125

00:19:04.756 --> 00:19:06.718 Earth mutants are still able to

NOTE Confidence: 0.9346002125

00:19:06.718 --> 00:19:08.580 interact with MEK one and MEK two,

NOTE Confidence: 0.9346002125

00:19:08.580 --> 00:19:10.666 and so they can be activated normally,

NOTE Confidence: 0.9346002125

00:19:10.670 --> 00:19:12.878 but they no longer interact with

NOTE Confidence: 0.9346002125

00:19:12.878 --> 00:19:14.350 the dual specificity phosphatase.

NOTE Confidence: 0.9346002125

00:19:14.350 --> 00:19:16.961 So incels, this leads to an imbalance

NOTE Confidence: 0.9346002125

00:19:16.961 --> 00:19:19.170 between their activation and inactivation,

NOTE Confidence: 0.9346002125

00:19:19.170 --> 00:19:21.355 and you accumulate the hyper

NOTE Confidence: 0.9346002125

00:19:21.355 --> 00:19:24.110 phosphorylated active form of the kinase,

NOTE Confidence: 0.9346002125

00:19:24.110 --> 00:19:26.297 but that's not all there is to it because

NOTE Confidence: 0.9346002125

00:19:26.297 --> 00:19:28.809 it turns out that at least one of the

NOTE Confidence: 0.9346002125

00:19:28.809 --> 00:19:31.027 major signaling outputs of Earth that is the.

NOTE Confidence: 0.9346002125

00:19:31.030 --> 00:19:32.818 Chinese risk is also

NOTE Confidence: 0.9346002125

00:19:32.818 --> 00:19:34.606 broken by these mutations,

NOTE Confidence: 0.9346002125

00:19:34.610 --> 00:19:36.188 so these mutants don't interact with

NOTE Confidence: 0.9346002125

00:19:36.188 --> 00:19:38.189 risk and they don't phosphorylate risk,

NOTE Confidence: 0.9346002125

00:19:38.190 --> 00:19:40.422 and so that makes you raised

NOTE Confidence: 0.9346002125

00:19:40.422 --> 00:19:42.710 a few questions in our mind.

NOTE Confidence: 0.9346002125

00:19:42.710 --> 00:19:44.566 So first of all,

NOTE Confidence: 0.9346002125

00:19:44.566 --> 00:19:47.350 what is the scope of interactions

NOTE Confidence: 0.9346002125

00:19:47.447 --> 00:19:49.363 with Erk that are selectively

NOTE Confidence: 0.9346002125

00:19:49.363 --> 00:19:50.927 disrupted by her mutations?

NOTE Confidence: 0.9346002125

00:19:50.930 --> 00:19:52.834 We simply don't know this at this

NOTE Confidence: 0.9346002125

00:19:52.834 --> 00:19:55.222 point and and from a kind of

NOTE Confidence: 0.9346002125

00:19:55.222 --> 00:19:56.730 structural or biochemical standpoint.

NOTE Confidence: 0.9346002125

00:19:56.730 --> 00:19:58.760 Why are some interactions broken

NOTE Confidence: 0.9346002125

00:19:58.760 --> 00:20:00.790 and some spared something that

NOTE Confidence: 0.9346002125

00:20:00.855 --> 00:20:02.660 we we also don't understand?

NOTE Confidence: 0.9346002125

00:20:02.660 --> 00:20:03.540 And so.

NOTE Confidence: 0.9346002125

00:20:03.540 --> 00:20:06.180 In order to address this question,

NOTE Confidence: 0.9346002125

00:20:06.180 --> 00:20:08.652 Jay Lisa conducted a proteome wide

NOTE Confidence: 0.9346002125

00:20:08.652 --> 00:20:11.108 screen to identify sequences that can

NOTE Confidence: 0.9346002125

00:20:11.108 --> 00:20:13.316 interact with the Erk docking group,

NOTE Confidence: 0.9346002125

00:20:13.320 --> 00:20:15.090 and again I don't have time

NOTE Confidence: 0.9346002125

00:20:15.090 --> 00:20:16.790 to explain this in detail.

NOTE Confidence: 0.9346002125

00:20:16.790 --> 00:20:19.373 What we did was mine the human

NOTE Confidence: 0.9346002125

00:20:19.373 --> 00:20:21.509 proteome for short amino acid

NOTE Confidence: 0.9346002125

00:20:21.509 --> 00:20:23.879 stretches of amino acid sequence.

NOTE Confidence: 0.9346002125

00:20:23.880 --> 00:20:27.306 That sort of had sequence similarity

NOTE Confidence: 0.9346002125

00:20:27.306 --> 00:20:30.410 to known interacting sequences like you

NOTE Confidence: 0.9346002125

00:20:30.410 --> 00:20:33.600 would find in in Mach one and Mach 2.

NOTE Confidence: 0.9346002125

00:20:33.600 --> 00:20:35.375 And prepared a genetically encoded

NOTE Confidence: 0.9346002125

00:20:35.375 --> 00:20:37.204 library of about 12,000 sequences.

NOTE Confidence: 0.9346002125

00:20:37.204 --> 00:20:39.114 So these are short sequences,

NOTE Confidence: 0.9346002125

00:20:39.120 --> 00:20:40.955 fragments of proteins that are

NOTE Confidence: 0.9346002125

00:20:40.955 --> 00:20:42.423 14 amino acids long.

NOTE Confidence: 0.9346002125

00:20:42.430 --> 00:20:44.719 And then we use those in a

NOTE Confidence: 0.9346002125

00:20:44.719 --> 00:20:45.700 pooled competitive yeast.

NOTE Confidence: 0.9346002125

00:20:45.700 --> 00:20:47.430 Two hybrid screening format and

NOTE Confidence: 0.9346002125

00:20:47.430 --> 00:20:50.000 and the the bottom line is that you

NOTE Confidence: 0.9346002125

00:20:50.000 --> 00:20:52.587 know similar to sort of an SH RNA or

NOTE Confidence: 0.9346002125

00:20:52.587 --> 00:20:55.093 crisper screen if we have a successful

NOTE Confidence: 0.9346002125

00:20:55.093 --> 00:20:57.660 interaction between Erk and the interactor,

NOTE Confidence: 0.9346002125

00:20:57.660 --> 00:20:58.900 this will become enriched

NOTE Confidence: 0.9346002125

00:20:58.900 --> 00:21:00.140 in the population overtime,

NOTE Confidence: 0.9346002125

00:21:00.140 --> 00:21:02.380 and we can detect this by next

NOTE Confidence: 0.9346002125

00:21:02.380 --> 00:21:03.020 generation sequencing.

NOTE Confidence: 0.9346002125

00:21:03.020 --> 00:21:05.090 So when we do this screen with wild type.

NOTE Confidence: 0.9346002125

00:21:05.090 --> 00:21:08.730 Work we can see that on gratifyingly,

NOTE Confidence: 0.9346002125

00:21:08.730 --> 00:21:10.655 all of the known interactors

NOTE Confidence: 0.9346002125

00:21:10.655 --> 00:21:12.580 interacting fragments that were in

NOTE Confidence: 0.9346002125

00:21:12.649 --> 00:21:14.669 the library actually scores hits.

NOTE Confidence: 0.9346002125

00:21:14.670 --> 00:21:16.326 They become enriched,

NOTE Confidence: 0.9346002125

00:21:16.326 --> 00:21:17.430 and furthermore,

NOTE Confidence: 0.9346002125

00:21:17.430 --> 00:21:19.789 if we align all of these sequences,

NOTE Confidence: 0.9346002125

00:21:19.790 --> 00:21:21.866 we can see a sequence motif.

NOTE Confidence: 0.9346002125

00:21:21.870 --> 00:21:23.420 A signature sequence that emerges

NOTE Confidence: 0.9346002125

00:21:23.420 --> 00:21:25.790 that seems to be a common feature

NOTE Confidence: 0.9346002125

00:21:25.790 --> 00:21:28.070 of sequences that interact with Erk.

NOTE Confidence: 0.9346002125

00:21:28.070 --> 00:21:30.170 So a cluster of proline residues and

NOTE Confidence: 0.9346002125

00:21:30.170 --> 00:21:32.769 a couple of leucine residues close by,

NOTE Confidence: 0.9346002125

00:21:32.770 --> 00:21:34.681 and this is interesting in its own

NOTE Confidence: 0.9346002125

00:21:34.681 --> 00:21:36.899 right because it tells us something about.

NOTE Confidence: 0.9346002125

00:21:36.900 --> 00:21:40.698 How Erk recruits it's interacting proteins,

NOTE Confidence: 0.889380216

00:21:40.700 --> 00:21:42.918 but what about the mutants? So J.

NOTE Confidence: 0.889380216

00:21:42.918 --> 00:21:45.710 Lisa conducted this same screen with the two

NOTE Confidence: 0.889380216

00:21:45.785 --> 00:21:48.790 most recurrent cancer associated mutations,

NOTE Confidence: 0.889380216

00:21:48.790 --> 00:21:51.875 D321 and E322K and what we saw

NOTE Confidence: 0.889380216

00:21:51.875 --> 00:21:54.280 was kind of what we expected,

NOTE Confidence: 0.889380216

00:21:54.280 --> 00:21:56.814 which is that most of the interactions

NOTE Confidence: 0.889380216

00:21:56.814 --> 00:21:59.237 are preserved about 2/3 of the the

NOTE Confidence: 0.889380216

00:21:59.237 --> 00:22:01.555 interactors that scored his hits for wild

NOTE Confidence: 0.889380216

00:22:01.555 --> 00:22:03.956 type or also interact with the mutants,

NOTE Confidence: 0.889380216

00:22:03.960 --> 00:22:06.809 but about a third of them interacted.

NOTE Confidence: 0.889380216

00:22:06.810 --> 00:22:09.450 Only with the wild type kinase,

NOTE Confidence: 0.889380216

00:22:09.450 --> 00:22:10.288 and furthermore,

NOTE Confidence: 0.889380216

00:22:10.288 --> 00:22:13.221 when we look at the the sequences

NOTE Confidence: 0.889380216

00:22:13.221 --> 00:22:15.929 that interact only with wild type,

NOTE Confidence: 0.889380216

00:22:15.930 --> 00:22:18.430 we actually lose this sequence

NOTE Confidence: 0.889380216

00:22:18.430 --> 00:22:20.430 motif that's characteristic of

NOTE Confidence: 0.889380216

00:22:20.430 --> 00:22:23.046 of of Erk binders in general.

NOTE Confidence: 0.889380216

00:22:23.050 --> 00:22:25.125 And actually there's very little

NOTE Confidence: 0.889380216

00:22:25.125 --> 00:22:26.370 distinguishing feature here,

NOTE Confidence: 0.889380216

00:22:26.370 --> 00:22:28.995 save for the significant selection of a

NOTE Confidence: 0.889380216

00:22:28.995 --> 00:22:31.148 single arching residue in the sequence.

NOTE Confidence: 0.889380216

00:22:31.150 --> 00:22:32.482 So we were a little bit

NOTE Confidence: 0.889380216

00:22:32.482 --> 00:22:33.730 flummoxed by this at first,

NOTE Confidence: 0.889380216

00:22:33.730 --> 00:22:35.776 but first we just wanted to

NOTE Confidence: 0.889380216

00:22:35.776 --> 00:22:37.140 do some basic validation.

NOTE Confidence: 0.889380216

00:22:37.140 --> 00:22:39.723 I I'm I'm starting to run short on time,

NOTE Confidence: 0.889380216

00:22:39.730 --> 00:22:41.314 so I'm going to go through this briefly.

NOTE Confidence: 0.889380216

00:22:41.320 --> 00:22:41.653 Basically,

NOTE Confidence: 0.889380216

00:22:41.653 --> 00:22:43.318 we could confirm that a

NOTE Confidence: 0.889380216

00:22:43.318 --> 00:22:45.320 sensually all of the sequences,

NOTE Confidence: 0.889380216

00:22:45.320 --> 00:22:48.288 but if we if we made synthetic peptides

NOTE Confidence: 0.889380216

00:22:48.288 --> 00:22:49.833 corresponding to these sequences

NOTE Confidence: 0.889380216

00:22:49.833 --> 00:22:52.409 that scored as hits in the screen,

NOTE Confidence: 0.889380216

00:22:52.410 --> 00:22:55.594 we could see that where we expected we

NOTE Confidence: 0.889380216

00:22:55.594 --> 00:22:58.030 saw differential binding in vitro to

NOTE Confidence: 0.889380216

00:22:58.030 --> 00:23:00.740 wild type versus mutant alleles of Erk,

NOTE Confidence: 0.889380216

00:23:00.740 --> 00:23:02.702 one of them in particular peptide

NOTE Confidence: 0.889380216

00:23:02.702 --> 00:23:05.030 coming from the protein ISG 20 had

NOTE Confidence: 0.889380216

00:23:05.030 --> 00:23:06.956 particularly high affinity for Erk and

NOTE Confidence: 0.889380216

00:23:06.956 --> 00:23:09.229 showed the biggest differential binding.

NOTE Confidence: 0.889380216

00:23:09.230 --> 00:23:11.768 Between wild type and mutant forms.

NOTE Confidence: 0.889380216

00:23:11.770 --> 00:23:13.674 So we decided to take a structural

NOTE Confidence: 0.889380216

00:23:13.674 --> 00:23:15.043 biology approach to understand what

NOTE Confidence: 0.889380216

00:23:15.043 --> 00:23:17.019 was going on here in terms of how

NOTE Confidence: 0.889380216

00:23:17.075 --> 00:23:18.734 this interacted with her and with a

NOTE Confidence: 0.889380216

00:23:18.734 --> 00:23:20.870 lot of help from Titus Boggins lab

NOTE Confidence: 0.889380216

00:23:20.870 --> 00:23:22.645 here in the pharmacology department,

NOTE Confidence: 0.889380216

00:23:22.650 --> 00:23:25.298 Jay Lisa was able to solve the X-ray

NOTE Confidence: 0.889380216

00:23:25.298 --> 00:23:27.327 cocrystal structure of wild type work too.

NOTE Confidence: 0.889380216

00:23:27.330 --> 00:23:29.829 In complex with this fragment of the

NOTE Confidence: 0.889380216

00:23:29.829 --> 00:23:32.370 ISG 20 protein and I'm just going to

NOTE Confidence: 0.889380216

00:23:32.370 --> 00:23:35.156 zoom in on the key feature at the

NOTE Confidence: 0.889380216

00:23:35.156 --> 00:23:38.460 region of ISG 20 that binds to IRK.

NOTE Confidence: 0.889380216

00:23:38.460 --> 00:23:41.161 That is close to the hot spot for

NOTE Confidence: 0.889380216

00:23:41.161 --> 00:23:43.267 these mutations we see that the

NOTE Confidence: 0.889380216

00:23:43.267 --> 00:23:45.640 peptide forms a single turn of an

NOTE Confidence: 0.889380216

00:23:45.640 --> 00:23:47.668 alpha Helix and that is enforced.

NOTE Confidence: 0.889380216

00:23:47.668 --> 00:23:49.958 That motive interaction is enforced

NOTE Confidence: 0.889380216

00:23:49.958 --> 00:23:53.299 by a sequence motif that involves a

NOTE Confidence: 0.889380216

00:23:53.299 --> 00:23:55.215 hydrophobic isoleucine residue and

NOTE Confidence: 0.889380216

00:23:55.215 --> 00:23:57.815 then two arginine residues position

NOTE Confidence: 0.889380216

00:23:57.815 --> 00:24:00.965 close by that actually make direct

NOTE Confidence: 0.889380216

00:24:00.965 --> 00:24:04.060 polar contacts to the acidic residues

NOTE Confidence: 0.889380216

00:24:04.060 --> 00:24:06.928 that are mutated in in cancer.

NOTE Confidence: 0.889380216

00:24:06.930 --> 00:24:09.658 And sure enough, if we then go back.

NOTE Confidence: 0.889380216

00:24:09.660 --> 00:24:11.780 And look at our sequences.

NOTE Confidence: 0.889380216

00:24:11.780 --> 00:24:13.835 That bound most preferentially to

NOTE Confidence: 0.889380216

00:24:13.835 --> 00:24:16.335 wild type the the top 9 sequences

NOTE Confidence: 0.889380216

00:24:16.335 --> 00:24:18.535 in the original used to hybrid

NOTE Confidence: 0.889380216

00:24:18.535 --> 00:24:21.211 screening data all have this sequence

NOTE Confidence: 0.889380216

00:24:21.211 --> 00:24:24.800 motif and we could further confirm

NOTE Confidence: 0.889380216

00:24:24.800 --> 00:24:26.786 that this motif was important for

NOTE Confidence: 0.889380216

00:24:26.786 --> 00:24:28.480 binding to wild type IIRC,

NOTE Confidence: 0.889380216

00:24:28.480 --> 00:24:30.790 but not to mutant forms of work

NOTE Confidence: 0.889380216

00:24:30.790 --> 00:24:32.727 through in vitro binding assays

NOTE Confidence: 0.889380216

00:24:32.727 --> 00:24:35.355 that we did with synthetic peptides.

NOTE Confidence: 0.889380216

00:24:35.360 --> 00:24:35.996 So basically,

NOTE Confidence: 0.889380216

00:24:35.996 --> 00:24:37.904 if we if we mutate any

NOTE Confidence: 0.889380216

00:24:37.904 --> 00:24:39.670 of these three residues.

NOTE Confidence: 0.889380216

00:24:39.670 --> 00:24:41.930 We greatly reduce the binding

NOTE Confidence: 0.889380216

00:24:41.930 --> 00:24:44.190 affinity with wild type IIRC,

NOTE Confidence: 0.889380216

00:24:44.190 --> 00:24:46.255 but we have no effect on the

NOTE Confidence: 0.889380216

00:24:46.255 --> 00:24:47.536 already weak binding affinity

NOTE Confidence: 0.889380216

00:24:47.536 --> 00:24:49.546 with the mutant forms of FERC,

NOTE Confidence: 0.935739000909091

00:24:49.550 --> 00:24:51.400 presumably because the damage had

NOTE Confidence: 0.935739000909091

00:24:51.400 --> 00:24:53.810 already been done by those mutants.

NOTE Confidence: 0.935739000909091

00:24:53.810 --> 00:24:55.950 So we think we have a good handle on why

NOTE Confidence: 0.935739000909091

00:24:56.012 --> 00:24:57.384 some sequences interact specifically

NOTE Confidence: 0.935739000909091

00:24:57.384 --> 00:24:59.880 with wild type work and are broken.

NOTE Confidence: 0.935739000909091

00:24:59.880 --> 00:25:02.134 The interactions are broken with the mutants,

NOTE Confidence: 0.935739000909091

00:25:02.140 --> 00:25:04.282 but we're now trying to do is sort of

NOTE Confidence: 0.935739000909091

00:25:04.282 --> 00:25:06.035 understand a little bit more about how

NOTE Confidence: 0.935739000909091

00:25:06.035 --> 00:25:07.709 this relates to tumor cell biology,

NOTE Confidence: 0.935739000909091

00:25:07.710 --> 00:25:09.698 and this is my last data slide.

NOTE Confidence: 0.935739000909091

00:25:09.700 --> 00:25:11.492 And So what we've been doing is looking

NOTE Confidence: 0.935739000909091

00:25:11.492 --> 00:25:13.543 at some of the full length proteins

NOTE Confidence: 0.935739000909091

00:25:13.543 --> 00:25:15.093 that corresponds to its corresponding

NOTE Confidence: 0.935739000909091

00:25:15.147 --> 00:25:16.870 hits from the screen, and one that

NOTE Confidence: 0.935739000909091

00:25:16.870 --> 00:25:18.310 in particular that caught our eye,

NOTE Confidence: 0.935739000909091

00:25:18.310 --> 00:25:21.705 is the row GTPS exchange factor def.

NOTE Confidence: 0.935739000909091

00:25:21.710 --> 00:25:25.422 H1, which has been implicated in a positive

NOTE Confidence: 0.935739000909091

00:25:25.422 --> 00:25:28.876 feedback loop for the Erk signaling pathway.

NOTE Confidence: 0.935739000909091

00:25:28.880 --> 00:25:31.344 It's a known substrate of of work,

NOTE Confidence: 0.935739000909091

00:25:31.350 --> 00:25:33.210 and we can confirm that indietro,

NOTE Confidence: 0.935739000909091

00:25:33.210 --> 00:25:36.066 but also also confirm that these

NOTE Confidence: 0.935739000909091

00:25:36.066 --> 00:25:39.146 cancer mutated forms of Erk are

NOTE Confidence: 0.935739000909091

00:25:39.146 --> 00:25:40.778 unable to phosphorylate.

NOTE Confidence: 0.935739000909091

00:25:40.780 --> 00:25:42.280 FH1, at least in vitro,

NOTE Confidence: 0.935739000909091

00:25:42.280 --> 00:25:44.740 and we're now following up.

NOTE Confidence: 0.935739000909091

00:25:44.740 --> 00:25:48.100 On these studies in head and neck

NOTE Confidence: 0.935739000909091

00:25:48.100 --> 00:25:50.062 squamous cell carcinoma cell lines

NOTE Confidence: 0.935739000909091

00:25:50.062 --> 00:25:52.150 to see if we can verify this result

NOTE Confidence: 0.935739000909091

00:25:52.214 --> 00:25:53.919 and understand what this means

NOTE Confidence: 0.935739000909091

00:25:53.920 --> 00:25:57.420 for for tumor cell biology.

NOTE Confidence: 0.935739000909091

00:25:57.420 --> 00:26:00.540 So to sum up this part,

NOTE Confidence: 0.935739000909091

00:26:00.540 --> 00:26:04.210 we've identified that cancer associated

NOTE Confidence: 0.935739000909091

00:26:04.210 --> 00:26:07.871 mutations that map to these common docking

NOTE Confidence: 0.935739000909091

00:26:07.871 --> 00:26:11.606 groove of Earth 2 disrupt a subset of

NOTE Confidence: 0.935739000909091

00:26:11.606 --> 00:26:13.619 interactions and specifically those

NOTE Confidence: 0.935739000909091

00:26:13.619 --> 00:26:16.419 involving a particular sequence motif.

NOTE Confidence: 0.935739000909091

00:26:16.420 --> 00:26:18.124 And what we're trying to figure out now,

NOTE Confidence: 0.935739000909091

00:26:18.130 --> 00:26:18.842 of course,

NOTE Confidence: 0.935739000909091

00:26:18.842 --> 00:26:20.978 is if selective engagement of these

NOTE Confidence: 0.935739000909091

00:26:20.978 --> 00:26:23.382 substrates is important for the phenotypic

NOTE Confidence: 0.935739000909091

00:26:23.382 --> 00:26:25.422 consequences of work to mutation.

NOTE Confidence: 0.935739000909091

00:26:25.430 --> 00:26:26.513 So with that.

NOTE Confidence: 0.935739000909091

00:26:26.513 --> 00:26:29.040 I will stop and thank the people

NOTE Confidence: 0.935739000909091

00:26:29.128 --> 00:26:31.408 who did the work I mentioned,

NOTE Confidence: 0.935739000909091

00:26:31.410 --> 00:26:32.306 Eunice Cho,

NOTE Confidence: 0.935739000909091

00:26:32.306 --> 00:26:34.994 who recently left the lab graduated

NOTE Confidence: 0.935739000909091

00:26:34.994 --> 00:26:38.174 last year who had done all the work on

NOTE Confidence: 0.935739000909091

00:26:38.180 --> 00:26:41.460 PPP 6C and the work on Earth mutants

NOTE Confidence: 0.935739000909091

00:26:41.460 --> 00:26:44.419 was conducted by Julissa Torres Robles.

NOTE Confidence: 0.935739000909091

00:26:44.420 --> 00:26:46.260 I also like to point out my collaborators,

NOTE Confidence: 0.935739000909091

00:26:46.260 --> 00:26:47.172 David Calderwood,

NOTE Confidence: 0.935739000909091

00:26:47.172 --> 00:26:49.908 who's my partner in all the

NOTE Confidence: 0.935739000909091

00:26:49.908 --> 00:26:51.320 functional genomics stuff.

NOTE Confidence: 0.935739000909091

00:26:51.320 --> 00:26:53.574 Tice Boggins lab who helped us with

NOTE Confidence: 0.935739000909091

00:26:53.574 --> 00:26:55.155 the crystallography and Mark Gerstein

NOTE Confidence: 0.935739000909091

00:26:55.155 --> 00:26:57.108 lab that helped us with the the.

NOTE Confidence: 0.935739000909091

00:26:57.110 --> 00:27:01.020 Library design and computational analysis.

NOTE Confidence: 0.935739000909091

00:27:01.020 --> 00:27:02.770 And with that I'm happy to take

NOTE Confidence: 0.935739000909091

00:27:02.770 --> 00:27:04.248 any questions if we have time.

NOTE Confidence: 0.93107848

00:27:05.610 --> 00:27:07.969 Thank you that that that was great

NOTE Confidence: 0.93107848

00:27:07.969 --> 00:27:10.529 and really nice work and and and a

NOTE Confidence: 0.93107848

00:27:10.529 --> 00:27:12.272 good advertisement for the functional

NOTE Confidence: 0.93107848

00:27:12.272 --> 00:27:14.788 genomics core 'cause it looks like some

NOTE Confidence: 0.93107848

00:27:14.788 --> 00:27:16.696 really impressive data we have maybe

NOTE Confidence: 0.93107848

00:27:16.696 --> 00:27:19.009 two or three minutes for questions.

NOTE Confidence: 0.93107848

00:27:19.010 --> 00:27:21.466 If you wouldn't mind just putting him in

NOTE Confidence: 0.93107848

00:27:21.466 --> 00:27:23.570 the chat while people are doing that,

NOTE Confidence: 0.93107848

00:27:23.570 --> 00:27:26.898 can I just ask you a quick question

NOTE Confidence: 0.93107848

00:27:26.898 --> 00:27:31.190 about the the PP6C study?

NOTE Confidence: 0.93107848

00:27:31.190 --> 00:27:33.689 Is it worth you think going back

NOTE Confidence: 0.93107848

00:27:33.689 --> 00:27:36.008 and trying to redo your your.

NOTE Confidence: 0.93107848

00:27:36.010 --> 00:27:39.652 Knock down screen in a background

NOTE Confidence: 0.93107848

00:27:39.652 --> 00:27:43.536 of the the PPP mutant contacts

NOTE Confidence: 0.93107848

00:27:43.536 --> 00:27:46.366 to see if there's other.

NOTE Confidence: 0.93107848

00:27:46.370 --> 00:27:48.802 Targets that could restore

NOTE Confidence: 0.93107848

00:27:48.802 --> 00:27:50.280 sensitivity to the inhibitors.

NOTE Confidence: 0.900493566666667

00:27:50.630 --> 00:27:52.430 Yeah, I I do believe so.

NOTE Confidence: 0.900493566666667

00:27:52.430 --> 00:27:54.670 And actually one of the things that

NOTE Confidence: 0.900493566666667

00:27:54.670 --> 00:27:56.920 we have planned is is such a screen.

NOTE Confidence: 0.900493566666667

00:27:56.920 --> 00:27:58.949 So the screen that we did before

NOTE Confidence: 0.900493566666667

00:27:58.949 --> 00:28:01.405 was a focus SH RNA library and what

NOTE Confidence: 0.900493566666667

00:28:01.405 --> 00:28:03.892 we're gearing up to do is a genome

NOTE Confidence: 0.900493566666667

00:28:03.892 --> 00:28:05.997 wide CRISPR screen where we compare

NOTE Confidence: 0.900493566666667

00:28:05.997 --> 00:28:08.391 wildtype cells with the PPP 60

NOTE Confidence: 0.900493566666667

00:28:08.391 --> 00:28:10.497 knockout cells in the presence or

NOTE Confidence: 0.900493566666667

00:28:10.497 --> 00:28:13.210 absence of the of the MEK inhibitor,

NOTE Confidence: 0.900493566666667

00:28:13.210 --> 00:28:15.002 and so we're hoping to get out

NOTE Confidence: 0.900493566666667

00:28:15.002 --> 00:28:16.440 of that are basically.

NOTE Confidence: 0.900493566666667

00:28:16.440 --> 00:28:18.300 We should get genetic modifiers

NOTE Confidence: 0.900493566666667

00:28:18.300 --> 00:28:21.137 that affect the growth of the PPP 60

NOTE Confidence: 0.900493566666667

00:28:21.137 --> 00:28:23.244 knockout cells and one of the hopes

NOTE Confidence: 0.900493566666667

00:28:23.309 --> 00:28:25.524 is that we'll identify potentially

NOTE Confidence: 0.900493566666667

00:28:25.524 --> 00:28:27.574 other signaling outputs of PP6C

NOTE Confidence: 0.900493566666667

00:28:27.574 --> 00:28:29.218 that are important for growth and

NOTE Confidence: 0.900493566666667

00:28:29.218 --> 00:28:30.450 maybe drug sensitivity as well.

NOTE Confidence: 0.776560158

00:28:31.960 --> 00:28:34.600 You know, it seems like it makes that

NOTE Confidence: 0.776560158

00:28:34.600 --> 00:28:37.990 make sense in just one other question.

NOTE Confidence: 0.776560158

00:28:37.990 --> 00:28:39.362 I got a little,

NOTE Confidence: 0.776560158

00:28:39.362 --> 00:28:41.770 maybe I misunderstood in terms of the.

NOTE Confidence: 0.776560158

00:28:41.770 --> 00:28:44.070 The prevalence of these mutations

NOTE Confidence: 0.776560158

00:28:44.070 --> 00:28:48.029 in the in the in that phosphatase,

NOTE Confidence: 0.776560158

00:28:48.030 --> 00:28:50.270 and they I I thought you had said

NOTE Confidence: 0.776560158

00:28:50.270 --> 00:28:52.400 that they were relatively common.

NOTE Confidence: 0.624400154

00:28:54.030 --> 00:28:56.834 It's it's 7 to 9% depending on

NOTE Confidence: 0.624400154

00:28:56.834 --> 00:28:59.244 the study, so they're they're.

NOTE Confidence: 0.624400154

00:28:59.250 --> 00:29:00.636 They're not as common it it's.

NOTE Confidence: 0.624400154

00:29:00.640 --> 00:29:01.108 It's actually interesting

NOTE Confidence: 0.624400154

00:29:01.108 --> 00:29:02.044 if you look at the data,

NOTE Confidence: 0.624400154

00:29:02.050 --> 00:29:03.514 they're sort of the I guess

NOTE Confidence: 0.624400154

00:29:03.514 --> 00:29:04.490 the fifth most common,

NOTE Confidence: 0.624400154

00:29:04.490 --> 00:29:07.186 you know after the big guys and Ranson.

NOTE Confidence: 0.624400154

00:29:07.186 --> 00:29:09.097 If one and I think P 53

NOTE Confidence: 0.624400154

00:29:09.097 --> 00:29:10.680 they they're their next

NOTE Confidence: 0.901823112

00:29:10.850 --> 00:29:13.384 and do they get enriched? Have you do?

NOTE Confidence: 0.901823112

00:29:13.384 --> 00:29:15.890 Are there any databases of MEK resistant

NOTE Confidence: 0.901823112

00:29:15.964 --> 00:29:18.046 MEK inhibitor resistant samples that

NOTE Confidence: 0.901823112

00:29:18.046 --> 00:29:19.887 you can look to see whether it's

NOTE Confidence: 0.901823112

00:29:19.887 --> 00:29:21.460 enrichment for that mutation? Yeah,

NOTE Confidence: 0.923248665

00:29:21.470 --> 00:29:23.326 that hasn't really come out of those studies.

NOTE Confidence: 0.923248665

00:29:23.330 --> 00:29:25.500 A lot of those studies have been.

NOTE Confidence: 0.923248665

00:29:25.500 --> 00:29:29.130 Looking at sort of individual

NOTE Confidence: 0.923248665

00:29:29.130 --> 00:29:30.888 patients and you know people

NOTE Confidence: 0.923248665

00:29:30.888 --> 00:29:31.916 have made patients right.

NOTE Confidence: 0.923248665

00:29:31.920 --> 00:29:33.044 Zena graphs and things

NOTE Confidence: 0.923248665

00:29:33.044 --> 00:29:34.449 like that and and done.

NOTE Confidence: 0.923248665

00:29:34.450 --> 00:29:37.732 You know whole exome saying there's no.

NOTE Confidence: 0.923248665

00:29:37.732 --> 00:29:39.902 I mean because they're not

NOTE Confidence: 0.923248665

00:29:39.902 --> 00:29:41.512 particularly common that it really

NOTE Confidence: 0.923248665

00:29:41.512 --> 00:29:44.174 has not come up as a bonafide

NOTE Confidence: 0.923248665

00:29:44.174 --> 00:29:45.485 clinical resistance mechanism.

NOTE Confidence: 0.7960527

00:29:47.040 --> 00:29:50.230 OK, alright thank. Thank you again.

NOTE Confidence: 0.7960527

00:29:50.230 --> 00:29:53.464 Really nice work so why don't we

NOTE Confidence: 0.7960527

00:29:53.464 --> 00:29:56.434 move on to our next presenter?

NOTE Confidence: 0.7960527

00:29:56.434 --> 00:29:58.890 Is Doctor Grace Kang,

NOTE Confidence: 0.7960527

00:29:58.890 --> 00:30:01.205 who's an assistant professor in

NOTE Confidence: 0.7960527

00:30:01.205 --> 00:30:03.520 Department of Psychiatry and a

NOTE Confidence: 0.7960527

00:30:03.595 --> 00:30:06.125 member of our cancer Prevention

NOTE Confidence: 0.7960527

00:30:06.125 --> 00:30:08.149 and Control research program.

NOTE Confidence: 0.7960527

00:30:08.150 --> 00:30:11.209 She did her graduate work in clinical

NOTE Confidence: 0.7960527

00:30:11.209 --> 00:30:14.281 psychology at Saint Johns and in postdoc

NOTE Confidence: 0.7960527

00:30:14.281 --> 00:30:17.580 in adolescent addictions in the in the Yale.

NOTE Confidence: 0.7960527

00:30:17.580 --> 00:30:19.448 A school of Medicine's

NOTE Confidence: 0.7960527

00:30:19.448 --> 00:30:21.316 division of substance abuse.

NOTE Confidence: 0.7960527

00:30:21.320 --> 00:30:23.224 Her current research interests

NOTE Confidence: 0.7960527

00:30:23.224 --> 00:30:25.120 include understanding, substance use,

NOTE Confidence: 0.7960527

00:30:25.120 --> 00:30:27.000 health disparities among youth,

NOTE Confidence: 0.7960527

00:30:27.000 --> 00:30:29.023 and the use of social media for

NOTE Confidence: 0.7960527

00:30:29.023 --> 00:30:30.639 tobacco marketing and and novel

NOTE Confidence: 0.7960527

00:30:30.639 --> 00:30:32.354 tobacco use behaviors among youth,

NOTE Confidence: 0.7960527

00:30:32.360 --> 00:30:34.976 and I think she'll be talking

NOTE Confidence: 0.7960527

00:30:34.976 --> 00:30:36.284 about that today.

NOTE Confidence: 0.7960527

00:30:36.290 --> 00:30:38.972 Her title is leveraging social media

NOTE Confidence: 0.7960527

00:30:38.972 --> 00:30:41.620 analysis to inform tobacco prevention.

NOTE Confidence: 0.7960527

00:30:41.620 --> 00:30:44.148 Dr Kang thank you for for joining us.

NOTE Confidence: 0.694307386666667

00:30:52.250 --> 00:30:53.606 And I think you're on mute.

NOTE Confidence: 0.942003116666667

00:30:57.030 --> 00:30:58.566 OK, can you hear me now?

NOTE Confidence: 0.942003116666667

00:30:58.570 --> 00:31:01.870 Yep perfect OK great thanks.

NOTE Confidence: 0.942003116666667

00:31:01.870 --> 00:31:02.752 And you could hear you could

NOTE Confidence: 0.942003116666667

00:31:02.752 --> 00:31:03.890 see my slice here, right?

NOTE Confidence: 0.942003116666667

00:31:03.890 --> 00:31:06.260 Yeah, OK, awesome, thank you.

NOTE Confidence: 0.942003116666667

00:31:06.260 --> 00:31:08.310 Well, thank you so much

NOTE Confidence: 0.942003116666667

00:31:08.310 --> 00:31:10.280 for having me here today.

NOTE Confidence: 0.942003116666667

00:31:10.280 --> 00:31:12.175 We're gonna really switch gears

NOTE Confidence: 0.942003116666667

00:31:12.175 --> 00:31:14.070 and talk about social media

NOTE Confidence: 0.942003116666667

00:31:14.143 --> 00:31:16.007 and youth tobacco prevention,

NOTE Confidence: 0.942003116666667

00:31:16.010 --> 00:31:19.610 so I will give a brief outline of what

NOTE Confidence: 0.942003116666667

00:31:19.610 --> 00:31:22.749 we'll what I will talk about today.

NOTE Confidence: 0.791336816190476

00:31:24.880 --> 00:31:26.452 So I'll first given out overview

NOTE Confidence: 0.791336816190476

00:31:26.452 --> 00:31:28.500 of why we should care about East

NOTE Confidence: 0.791336816190476

00:31:28.500 --> 00:31:30.075 figure prevention in the context

NOTE Confidence: 0.791336816190476

00:31:30.075 --> 00:31:32.068 of tobacco prevention and and,

NOTE Confidence: 0.791336816190476

00:31:32.068 --> 00:31:34.372 and then the importance of leveraging

NOTE Confidence: 0.791336816190476

00:31:34.372 --> 00:31:36.528 social media to understand Easter

NOTE Confidence: 0.791336816190476

00:31:36.528 --> 00:31:39.109 youth behaviors and promotion and and

NOTE Confidence: 0.791336816190476

00:31:39.109 --> 00:31:41.383 then talk about limitations on current

NOTE Confidence: 0.791336816190476

00:31:41.383 --> 00:31:43.670 methods to analyze social media and

NOTE Confidence: 0.791336816190476

00:31:43.670 --> 00:31:46.362 then introduce how advances in new

NOTE Confidence: 0.791336816190476

00:31:46.362 --> 00:31:49.566 computational methods could be used to.

NOTE Confidence: 0.791336816190476

00:31:49.570 --> 00:31:51.808 To overcome some of these limitations,

NOTE Confidence: 0.791336816190476

00:31:51.810 --> 00:31:53.952 and then I'm going to talk about

NOTE Confidence: 0.791336816190476

00:31:53.952 --> 00:31:55.941 two specific studies in our group

NOTE Confidence: 0.791336816190476

00:31:55.941 --> 00:31:58.083 using YouTube data to understand E,

NOTE Confidence: 0.791336816190476

00:31:58.090 --> 00:31:59.740 cigarette content and social media.

NOTE Confidence: 0.851875136666667

00:32:02.790 --> 00:32:04.908 So cigarette smoking is a leading

NOTE Confidence: 0.851875136666667

00:32:04.908 --> 00:32:06.910 cause of preventable cause of death,

NOTE Confidence: 0.851875136666667

00:32:06.910 --> 00:32:08.465 disease, disability and death in

NOTE Confidence: 0.851875136666667

00:32:08.465 --> 00:32:10.717 the United States and we also know

NOTE Confidence: 0.851875136666667

00:32:10.717 --> 00:32:12.434 that smoking causes cancer's of

NOTE Confidence: 0.851875136666667

00:32:12.434 --> 00:32:15.108 a variety of charts in the body.

NOTE Confidence: 0.851875136666667

00:32:15.110 --> 00:32:17.060 However, cigarette is just one type

NOTE Confidence: 0.851875136666667

00:32:17.060 --> 00:32:19.050 of tobacco product in the market.

NOTE Confidence: 0.851875136666667

00:32:19.050 --> 00:32:20.874 There are other types of tobacco

NOTE Confidence: 0.851875136666667

00:32:20.874 --> 00:32:22.090 products such as cigars,

NOTE Confidence: 0.851875136666667

00:32:22.090 --> 00:32:23.370 smokeless tobacco, E cigarettes,

NOTE Confidence: 0.851875136666667

00:32:23.370 --> 00:32:27.450 just to name a few, that Berry in harm.

NOTE Confidence: 0.851875136666667

00:32:27.450 --> 00:32:29.506 And here what you see is this is

NOTE Confidence: 0.851875136666667

00:32:29.506 --> 00:32:31.638 a graph from CDC and this shows.

NOTE Confidence: 0.851875136666667

00:32:31.640 --> 00:32:33.775 Different tobacco products and use

NOTE Confidence: 0.851875136666667

00:32:33.775 --> 00:32:36.696 rates across the decade and what you

NOTE Confidence: 0.851875136666667

00:32:36.696 --> 00:32:39.202 see is overall this decrease in tobacco

NOTE Confidence: 0.851875136666667

00:32:39.202 --> 00:32:41.899 use right and but this dotted green

NOTE Confidence: 0.851875136666667

00:32:41.899 --> 00:32:44.092 line here is increasing E cigarette

NOTE Confidence: 0.851875136666667

00:32:44.092 --> 00:32:46.200 use over the years since 2014,

NOTE Confidence: 0.851875136666667

00:32:46.200 --> 00:32:48.860 E cigarettes have been the most commonly

NOTE Confidence: 0.851875136666667

00:32:48.860 --> 00:32:51.376 used tobacco product use among youth

NOTE Confidence: 0.851875136666667

00:32:51.380 --> 00:32:54.450 and in 2020 more than 4.5 million of

NOTE Confidence: 0.851875136666667

00:32:54.450 --> 00:32:57.600 the US youth are are using E cigarettes.

NOTE Confidence: 0.851875136666667

00:32:57.600 --> 00:32:59.370 And so when you take E

NOTE Confidence: 0.851875136666667

00:32:59.370 --> 00:33:00.255 cigarettes into consideration,

NOTE Confidence: 0.851875136666667

00:33:00.260 --> 00:33:01.740 the overall tobacco use rates.

NOTE Confidence: 0.851875136666667

00:33:01.740 --> 00:33:04.550 Is increasing among US youth?

NOTE Confidence: 0.751896954545455

00:33:07.170 --> 00:33:08.773 So for those who are not that

NOTE Confidence: 0.751896954545455

00:33:08.773 --> 00:33:10.020 familiar with E cigarette,

NOTE Confidence: 0.751896954545455

00:33:10.020 --> 00:33:11.905 I'll just provide an overview

NOTE Confidence: 0.751896954545455

00:33:11.905 --> 00:33:14.090 of what a E cigarette is.

NOTE Confidence: 0.751896954545455

00:33:14.090 --> 00:33:15.185 There are many different types

NOTE Confidence: 0.751896954545455

00:33:15.185 --> 00:33:16.610 of E cigarettes on the market.

NOTE Confidence: 0.751896954545455

00:33:16.610 --> 00:33:18.740 These devices are not regulated,

NOTE Confidence: 0.751896954545455

00:33:18.740 --> 00:33:21.596 so there is a rapid innovation such

NOTE Confidence: 0.751896954545455

00:33:21.596 --> 00:33:23.664 different product characteristics and E

NOTE Confidence: 0.751896954545455

00:33:23.664 --> 00:33:25.609 cigarette devices have evolved overtime.

NOTE Confidence: 0.751896954545455

00:33:25.610 --> 00:33:27.937 It first started out with Cigalikes,

NOTE Confidence: 0.751896954545455

00:33:27.937 --> 00:33:31.279 which is a which resembles cigarettes.

NOTE Confidence: 0.751896954545455

00:33:31.280 --> 00:33:33.050 And then evolve into second

NOTE Confidence: 0.751896954545455

00:33:33.050 --> 00:33:35.180 generation on devices like vape pens,

NOTE Confidence: 0.751896954545455

00:33:35.180 --> 00:33:37.420 which resembles like a pen.

NOTE Confidence: 0.751896954545455

00:33:37.420 --> 00:33:40.726 Third generations are these mods which

NOTE Confidence: 0.751896954545455

00:33:40.726 --> 00:33:43.870 vary in how they're it could be really

NOTE Confidence: 0.751896954545455

00:33:43.870 --> 00:33:46.120 customized in very different ways,

NOTE Confidence: 0.751896954545455

00:33:46.120 --> 00:33:49.480 and it could also excel large

NOTE Confidence: 0.751896954545455

00:33:49.480 --> 00:33:51.720 amounts of excelled aerosol,

NOTE Confidence: 0.751896954545455

00:33:51.720 --> 00:33:54.488 and then there is this pod mods here

NOTE Confidence: 0.751896954545455

00:33:54.488 --> 00:33:57.298 that sort of varies and how it looks.

NOTE Confidence: 0.751896954545455

00:33:57.300 --> 00:33:58.755 The most notable device you

NOTE Confidence: 0.751896954545455

00:33:58.755 --> 00:34:00.640 may have heard of is Jewel.

NOTE Confidence: 0.751896954545455

00:34:00.640 --> 00:34:02.500 They recently got popular because.

NOTE Confidence: 0.751896954545455

00:34:02.500 --> 00:34:04.936 They use nicotine salt instead of freebase.

NOTE Confidence: 0.751896954545455

00:34:04.940 --> 00:34:06.595 So Freebase nicotine is manipulated

NOTE Confidence: 0.751896954545455

00:34:06.595 --> 00:34:08.958 so that it has more of the

NOTE Confidence: 0.751896954545455

00:34:08.958 --> 00:34:12.300 harshness or kick the smokers likes.

NOTE Confidence: 0.751896954545455

00:34:12.300 --> 00:34:14.226 The nicotine salt is manipulated by

NOTE Confidence: 0.751896954545455

00:34:14.226 --> 00:34:16.688 lower the pH level so that it's not

NOTE Confidence: 0.751896954545455

00:34:16.688 --> 00:34:18.736 as harsh and allows for higher levels

NOTE Confidence: 0.751896954545455

00:34:18.736 --> 00:34:20.899 of nicotine and so the the problem

NOTE Confidence: 0.751896954545455

00:34:20.899 --> 00:34:23.720 with using nicotine salt is that

NOTE Confidence: 0.751896954545455

00:34:23.720 --> 00:34:27.020 because it's easier to to debate,

NOTE Confidence: 0.751896954545455

00:34:27.020 --> 00:34:29.617 you know higher levels of nicotine could

NOTE Confidence: 0.751896954545455

00:34:29.617 --> 00:34:32.688 be included in this products and therefore.

NOTE Confidence: 0.751896954545455

00:34:32.690 --> 00:34:34.622 You know the initiation among youth

NOTE Confidence: 0.751896954545455

00:34:34.622 --> 00:34:36.641 could could be a risk because

NOTE Confidence: 0.751896954545455

00:34:36.641 --> 00:34:38.639 of his high level of nicotine.

NOTE Confidence: 0.751896954545455

00:34:38.640 --> 00:34:40.968 So once Jewel started really hitting

NOTE Confidence: 0.751896954545455

00:34:40.968 --> 00:34:43.580 the market and getting really popular,

NOTE Confidence: 0.751896954545455

00:34:43.580 --> 00:34:45.560 this fifth generation of devices

NOTE Confidence: 0.751896954545455

00:34:45.560 --> 00:34:47.540 started entering the market and

NOTE Confidence: 0.751896954545455

00:34:47.606 --> 00:34:49.646 these are disposable pod devices.

NOTE Confidence: 0.751896954545455

00:34:49.650 --> 00:34:51.456 They're meant to be single use

NOTE Confidence: 0.751896954545455

00:34:51.456 --> 00:34:52.660 sometimes with multiple packs.

NOTE Confidence: 0.751896954545455

00:34:52.660 --> 00:34:54.080 They're small, they're discrete,

NOTE Confidence: 0.751896954545455

00:34:54.080 --> 00:34:56.120 they look like jewel they contain.

NOTE Confidence: 0.751896954545455

00:34:56.120 --> 00:34:57.980 They also contain they contain salt,

NOTE Confidence: 0.751896954545455

00:34:57.980 --> 00:34:59.828 so which has high levels of nicotine

NOTE Confidence: 0.751896954545455

00:34:59.828 --> 00:35:01.760 and it comes in multiple flavors.

NOTE Confidence: 0.751896954545455

00:35:01.760 --> 00:35:04.376 And there's a widely and importantly,

NOTE Confidence: 0.751896954545455

00:35:04.380 --> 00:35:04.930 they're cheap,

NOTE Confidence: 0.751896954545455

00:35:04.930 --> 00:35:07.910 so you might see a lot of these products on.

NOTE Confidence: 0.751896954545455

00:35:07.910 --> 00:35:10.115 Come in in your gas stations and

NOTE Confidence: 0.751896954545455

00:35:10.115 --> 00:35:11.510 other store convenience stores.

NOTE Confidence: 0.806130926666667

00:35:13.670 --> 00:35:15.050 So how do you cigarettes work?

NOTE Confidence: 0.806130926666667

00:35:15.050 --> 00:35:16.935 You know, even though these

NOTE Confidence: 0.806130926666667

00:35:16.935 --> 00:35:19.240 cigarettes vary in how they look,

NOTE Confidence: 0.806130926666667

00:35:19.240 --> 00:35:22.229 so the anatomy is is the same.

NOTE Confidence: 0.806130926666667

00:35:22.230 --> 00:35:25.122 So it has a component that

NOTE Confidence: 0.806130926666667

00:35:25.122 --> 00:35:27.050 holds that you liquid.

NOTE Confidence: 0.806130926666667

00:35:27.050 --> 00:35:28.920 It has a heating element.

NOTE Confidence: 0.806130926666667

00:35:28.920 --> 00:35:31.312 Any of the power power source in the

NOTE Confidence: 0.806130926666667

00:35:31.312 --> 00:35:33.783 form of batteries and is a mouthpiece

NOTE Confidence: 0.806130926666667

00:35:33.783 --> 00:35:36.598 in which the user could use to inhale

NOTE Confidence: 0.806130926666667

00:35:36.598 --> 00:35:38.789 the aerosol from from the of the

NOTE Confidence: 0.806130926666667

00:35:38.790 --> 00:35:41.576 vape and in some in some devices,

NOTE Confidence: 0.806130926666667

00:35:41.580 --> 00:35:44.490 just inhaling could activate the device.

NOTE Confidence: 0.806130926666667

00:35:44.490 --> 00:35:47.566 So what's in E liquid is made

NOTE Confidence: 0.806130926666667

00:35:47.566 --> 00:35:49.178 up of nicotine flavorings.

NOTE Confidence: 0.806130926666667

00:35:49.180 --> 00:35:51.092 The base is made up of proper link

NOTE Confidence: 0.806130926666667

00:35:51.092 --> 00:35:52.880 like coal and vegetable glycerin,

NOTE Confidence: 0.806130926666667

00:35:52.880 --> 00:35:54.440 as well as other additives.

NOTE Confidence: 0.806130926666667

00:35:54.440 --> 00:35:55.980 So in terms of nicotine,

NOTE Confidence: 0.806130926666667

00:35:55.980 --> 00:35:57.890 that's that's the main drug.

NOTE Confidence: 0.806130926666667

00:35:57.890 --> 00:35:59.422 So it stimulates the,

NOTE Confidence: 0.806130926666667

00:35:59.422 --> 00:36:01.337 stimulates the central nervous system.

NOTE Confidence: 0.806130926666667

00:36:01.340 --> 00:36:02.700 It raises blood pressure,

NOTE Confidence: 0.806130926666667

00:36:02.700 --> 00:36:04.345 respiration, heart heart rate,

NOTE Confidence: 0.806130926666667

00:36:04.345 --> 00:36:06.955 and releases a feeling of pleasure.

NOTE Confidence: 0.806130926666667

00:36:06.960 --> 00:36:09.276 And the the E cigarette that

NOTE Confidence: 0.806130926666667

00:36:09.276 --> 00:36:11.754 comes in Freebase comes in zero

NOTE Confidence: 0.806130926666667

00:36:11.754 --> 00:36:13.879 to 36 milligrams per milliliter.

NOTE Confidence: 0.806130926666667

00:36:13.880 --> 00:36:15.905 The nicotine salt on their

NOTE Confidence: 0.806130926666667

00:36:15.905 --> 00:36:17.120 marketed as percentage.

NOTE Confidence: 0.806130926666667

00:36:17.120 --> 00:36:18.872 So so for example,

NOTE Confidence: 0.806130926666667

00:36:18.872 --> 00:36:21.500 Jewel come as come as 5%,

NOTE Confidence: 0.806130926666667

00:36:21.500 --> 00:36:23.515 which is equivalent to about

NOTE Confidence: 0.806130926666667

00:36:23.515 --> 00:36:25.127 59 milligrams per milliliter.

NOTE Confidence: 0.806130926666667

00:36:25.130 --> 00:36:27.160 And you know the the issue with

NOTE Confidence: 0.806130926666667

00:36:27.160 --> 00:36:28.999 labeling is also very important,

NOTE Confidence: 0.806130926666667

00:36:29.000 --> 00:36:31.496 because you know 5% of anything

NOTE Confidence: 0.806130926666667

00:36:31.496 --> 00:36:33.160 just sounds little right.

NOTE Confidence: 0.806130926666667

00:36:33.160 --> 00:36:35.162 But if you actually look at the

NOTE Confidence: 0.806130926666667

00:36:35.162 --> 00:36:36.659 milligram per milliliter is actually

NOTE Confidence: 0.806130926666667

00:36:36.659 --> 00:36:38.119 very high level of nicotine.

NOTE Confidence: 0.806130926666667

00:36:38.120 --> 00:36:39.554 And this is what makes the

NOTE Confidence: 0.806130926666667

00:36:39.554 --> 00:36:41.050 nicotine is what makes addictive.

NOTE Confidence: 0.806130926666667

00:36:41.050 --> 00:36:44.200 There are zero level of eliquids

NOTE Confidence: 0.806130926666667

00:36:44.200 --> 00:36:46.220 and E cigarettes available.

NOTE Confidence: 0.806130926666667

00:36:46.220 --> 00:36:46.660 However,

NOTE Confidence: 0.806130926666667

00:36:46.660 --> 00:36:48.860 I should say that that's

NOTE Confidence: 0.806130926666667

00:36:48.860 --> 00:36:51.159 not that's not very common.

NOTE Confidence: 0.806130926666667

00:36:51.160 --> 00:36:52.440 These E cigarettes come in

NOTE Confidence: 0.806130926666667

00:36:52.440 --> 00:36:53.208 many different flavors.

NOTE Confidence: 0.806130926666667

00:36:53.210 --> 00:36:55.650 There's more than 7000 flavors.

NOTE Confidence: 0.806130926666667

00:36:55.650 --> 00:36:57.561 You know it comes in the typical

NOTE Confidence: 0.806130926666667

00:36:57.561 --> 00:36:58.800 like menthol tobacco flavor,

NOTE Confidence: 0.806130926666667

00:36:58.800 --> 00:37:00.956 but what's really popular or you know,

NOTE Confidence: 0.806130926666667

00:37:00.960 --> 00:37:02.840 fruit candy store that desert

NOTE Confidence: 0.806130926666667

00:37:02.840 --> 00:37:03.968 kind of flavors.

NOTE Confidence: 0.806130926666667

00:37:03.970 --> 00:37:06.962 And also there's also a lot of names

NOTE Confidence: 0.806130926666667

00:37:06.962 --> 00:37:09.500 that does not allude to actual,

NOTE Confidence: 0.806130926666667

00:37:09.500 --> 00:37:10.751 you know food,

NOTE Confidence: 0.806130926666667

00:37:10.751 --> 00:37:12.836 but like obscure names like

NOTE Confidence: 0.806130926666667

00:37:12.836 --> 00:37:14.820 you know Unicorn milk,

NOTE Confidence: 0.806130926666667

00:37:14.820 --> 00:37:16.660 or you know vampire blood

NOTE Confidence: 0.806130926666667

00:37:16.660 --> 00:37:18.132 or things like that.

NOTE Confidence: 0.806130926666667

00:37:18.140 --> 00:37:21.080 That gets people's attention.

NOTE Confidence: 0.806130926666667

00:37:21.080 --> 00:37:23.786 It is made up of chemicals.

NOTE Confidence: 0.806130926666667

00:37:23.790 --> 00:37:24.990 And the people in glycol,

NOTE Confidence: 0.806130926666667

00:37:24.990 --> 00:37:26.630 vegetable glycerin and the

NOTE Confidence: 0.806130926666667

00:37:26.630 --> 00:37:29.090 combination of the two is used.

NOTE Confidence: 0.806130926666667

00:37:29.090 --> 00:37:31.786 The ratio of the two is to create

NOTE Confidence: 0.806130926666667

00:37:31.786 --> 00:37:34.185 either more aerosol or less aerosol

NOTE Confidence: 0.806130926666667

00:37:34.185 --> 00:37:37.132 is used to intensify flavors or or

NOTE Confidence: 0.806130926666667

00:37:37.132 --> 00:37:39.925 a lower the intensity of flavors and

NOTE Confidence: 0.806130926666667

00:37:39.925 --> 00:37:41.650 nicotine or other chemicals added

NOTE Confidence: 0.806130926666667

00:37:41.650 --> 00:37:44.310 such as other water and other chemicals.

NOTE Confidence: 0.806130926666667

00:37:44.310 --> 00:37:46.590 So in addition to you know

NOTE Confidence: 0.806130926666667

00:37:46.590 --> 00:37:47.730 nicotine flavor flavorings,

NOTE Confidence: 0.806130926666667

00:37:47.730 --> 00:37:48.105 PG,

NOTE Confidence: 0.806130926666667

00:37:48.105 --> 00:37:48.480 VG,

NOTE Confidence: 0.806130926666667

00:37:48.480 --> 00:37:50.730 and other chemicals E cigarette aerosol

NOTE Confidence: 0.806130926666667

00:37:50.730 --> 00:37:53.515 have known or are shown to have

NOTE Confidence: 0.806130926666667

00:37:53.515 --> 00:37:55.485 heavy metals volatile organic compounds,

NOTE Confidence: 0.806130926666667

00:37:55.490 --> 00:37:57.080 and fine and ultrafine particles

NOTE Confidence: 0.806130926666667

00:37:57.080 --> 00:37:59.186 that can be inhaled deeply into the

NOTE Confidence: 0.806130926666667

00:37:59.186 --> 00:38:01.650 lungs by both by users as well as bystanders.

NOTE Confidence: 0.806130926666667

00:38:01.650 --> 00:38:04.680 The long term effects of this

NOTE Confidence: 0.806130926666667

00:38:04.680 --> 00:38:06.700 vaping is currently unknown.

NOTE Confidence: 0.806130926666667

00:38:06.700 --> 00:38:07.640 So why?

NOTE Confidence: 0.806130926666667

00:38:07.640 --> 00:38:11.325 Why should we care right about E cigarettes?

NOTE Confidence: 0.806130926666667

00:38:11.325 --> 00:38:13.995 So nicotine use among youth increases

NOTE Confidence: 0.806130926666667

00:38:13.995 --> 00:38:17.077 the risk of lifelong tobacco addiction.

NOTE Confidence: 0.806130926666667

00:38:17.080 --> 00:38:19.698 And it could also increase the risk

NOTE Confidence: 0.806130926666667

00:38:19.698 --> 00:38:22.427 for future addiction to other drugs as well.

NOTE Confidence: 0.806130926666667

00:38:22.430 --> 00:38:23.850 This is this E sticker.

NOTE Confidence: 0.493515865

00:38:23.850 --> 00:38:26.398 Use is considered an epidemic

NOTE Confidence: 0.493515865

00:38:26.398 --> 00:38:28.430 in the United States,

NOTE Confidence: 0.493515865

00:38:28.430 --> 00:38:30.770 so it's NIH, including NCIS.

NOTE Confidence: 0.493515865

00:38:30.770 --> 00:38:32.760 Research priority priority is to

NOTE Confidence: 0.493515865

00:38:32.760 --> 00:38:35.070 prevent you thicker E cigarette use.

NOTE Confidence: 0.493515865

00:38:35.070 --> 00:38:38.196 In fact SCI has RFA specifically

NOTE Confidence: 0.493515865

00:38:38.196 --> 00:38:41.587 focus on preventing E cigarette use

NOTE Confidence: 0.493515865

00:38:41.587 --> 00:38:45.205 among youth and has a collaborative.

NOTE Confidence: 0.493515865

00:38:45.210 --> 00:38:47.815 A grant that's interested in

NOTE Confidence: 0.493515865

00:38:47.815 --> 00:38:49.860 in particularly interested in E

NOTE Confidence: 0.493515865

00:38:49.860 --> 00:38:51.760 cigarette preventing E cigarette use,

NOTE Confidence: 0.493515865

00:38:51.760 --> 00:38:54.742 and then lastly they also have

NOTE Confidence: 0.493515865

00:38:54.742 --> 00:38:56.730 invested considerable resources into

NOTE Confidence: 0.785546605

00:38:59.000 --> 00:38:59.382 developingsmokefree.gov,

NOTE Confidence: 0.785546605

00:38:59.382 --> 00:39:01.292 which has resources to help

NOTE Confidence: 0.785546605

00:39:01.292 --> 00:39:03.670 youth to quit E cigarette use.

NOTE Confidence: 0.785546605

00:39:03.670 --> 00:39:05.240 So we're thinking of how

NOTE Confidence: 0.785546605

00:39:05.240 --> 00:39:06.810 to prevent E cigarette use.

NOTE Confidence: 0.785546605

00:39:06.810 --> 00:39:08.772 We've got to consider a lot of factors right,

NOTE Confidence: 0.785546605

00:39:08.780 --> 00:39:10.700 so there are social,

NOTE Confidence: 0.785546605

00:39:10.700 --> 00:39:11.582 environmental, cognitive,

NOTE Confidence: 0.785546605

00:39:11.582 --> 00:39:13.592 and genetic influences that plays

NOTE Confidence: 0.785546605

00:39:13.592 --> 00:39:16.540 a role in in youth tobacco use.

NOTE Confidence: 0.785546605

00:39:16.540 --> 00:39:19.076 But we also know is that tobacco promotion,

NOTE Confidence: 0.785546605

00:39:19.080 --> 00:39:20.724 marketing, advertising is causally

NOTE Confidence: 0.785546605

00:39:20.724 --> 00:39:23.190 related to youth tobacco use and

NOTE Confidence: 0.785546605

00:39:23.259 --> 00:39:24.979 this has been well established

NOTE Confidence: 0.785546605

00:39:24.979 --> 00:39:27.100 and has been talked about in

NOTE Confidence: 0.785546605

00:39:27.100 --> 00:39:28.790 in in surgeon general reports.

NOTE Confidence: 0.785546605

00:39:28.790 --> 00:39:31.526 So I'm going to focus on social media

NOTE Confidence: 0.785546605

00:39:31.526 --> 00:39:34.026 because now with the advent of social media,

NOTE Confidence: 0.785546605

00:39:34.030 --> 00:39:36.952 tobacco promotion really faces a unique

NOTE Confidence: 0.785546605

00:39:36.952 --> 00:39:39.529 challenge because social media is fast,

NOTE Confidence: 0.785546605

00:39:39.530 --> 00:39:40.186 it's cheap,

NOTE Confidence: 0.785546605

00:39:40.186 --> 00:39:43.588 you could reach a lot of people at a quick

NOTE Confidence: 0.785546605

00:39:43.588 --> 00:39:46.150 speed and it doesn't have sufficient to.

NOTE Confidence: 0.785546605

00:39:46.150 --> 00:39:50.060 To to control its content.

NOTE Confidence: 0.785546605

00:39:50.060 --> 00:39:52.097 So it might not be that surprising

NOTE Confidence: 0.785546605

00:39:52.097 --> 00:39:54.585 to you to hear that you know social

NOTE Confidence: 0.785546605

00:39:54.585 --> 00:39:56.160 media is popular among youth.

NOTE Confidence: 0.785546605

00:39:56.160 --> 00:39:58.855 90% of youth have used social media,

NOTE Confidence: 0.785546605

00:39:58.860 --> 00:40:01.464 75% have at least one active social

NOTE Confidence: 0.785546605

00:40:01.464 --> 00:40:03.954 media profile and 93% report visiting

NOTE Confidence: 0.785546605

00:40:03.954 --> 00:40:07.160 on social media site at least daily.

NOTE Confidence: 0.785546605

00:40:07.160 --> 00:40:09.645 When it comes to understanding how E

NOTE Confidence: 0.785546605

00:40:09.645 --> 00:40:11.763 cigarettes are promoted to youth is

NOTE Confidence: 0.785546605

00:40:11.763 --> 00:40:13.749 so important to understand how it's

NOTE Confidence: 0.785546605

00:40:13.749 --> 00:40:15.737 promoted so pro E cigarette content.

NOTE Confidence: 0.785546605

00:40:15.740 --> 00:40:19.100 Is on social media through paid ads

NOTE Confidence: 0.785546605

00:40:19.100 --> 00:40:21.372 through influencers promoting the

NOTE Confidence: 0.785546605

00:40:21.372 --> 00:40:23.728 products and on post from a share

NOTE Confidence: 0.785546605

00:40:23.728 --> 00:40:25.899 by their peers and other people?

NOTE Confidence: 0.785546605

00:40:25.900 --> 00:40:28.294 And recent studies have or are finding

NOTE Confidence: 0.785546605

00:40:28.294 --> 00:40:31.032 that use of social media among youth

NOTE Confidence: 0.785546605

00:40:31.032 --> 00:40:33.492 is associated with E cigarette use?

NOTE Confidence: 0.785546605

00:40:33.500 --> 00:40:35.378 So while there are many different

NOTE Confidence: 0.785546605

00:40:35.378 --> 00:40:37.207 types of social media platforms in

NOTE Confidence: 0.785546605

00:40:37.207 --> 00:40:39.255 our in our group or I'm going to

NOTE Confidence: 0.785546605

00:40:39.320 --> 00:40:40.712 present research findings specific

NOTE Confidence: 0.785546605

00:40:40.712 --> 00:40:43.107 to YouTube and I'm and I'm sure

NOTE Confidence: 0.785546605

00:40:43.107 --> 00:40:45.256 all of you have used YouTube so

NOTE Confidence: 0.785546605

00:40:45.256 --> 00:40:46.409 you're familiar with it.

NOTE Confidence: 0.785546605

00:40:46.410 --> 00:40:49.920 YouTube is free online streaming service.

NOTE Confidence: 0.785546605

00:40:49.920 --> 00:40:52.320 Is used by 1.9 billion users,

NOTE Confidence: 0.785546605

00:40:52.320 --> 00:40:54.496 which is a third of all Internet users

NOTE Confidence: 0.785546605

00:40:54.496 --> 00:40:57.034 and people spend about a billion hours a

NOTE Confidence: 0.785546605

00:40:57.034 --> 00:40:59.219 day watching watching online YouTube videos.

NOTE Confidence: 0.785546605

00:40:59.220 --> 00:41:01.999 So the the data on the right.

NOTE Confidence: 0.785546605

00:41:02.000 --> 00:41:04.952 The graph here shows this is data from 2018,

NOTE Confidence: 0.785546605

00:41:04.960 --> 00:41:06.380 so it's a bit old,

NOTE Confidence: 0.785546605

00:41:06.380 --> 00:41:09.068 but it shows that among teens YouTube

NOTE Confidence: 0.785546605

00:41:09.068 --> 00:41:11.131 is still popular and actually

NOTE Confidence: 0.785546605

00:41:11.131 --> 00:41:13.639 there's a recent data that's done.

NOTE Confidence: 0.785546605

00:41:13.640 --> 00:41:16.128 I think this year last year that showed

NOTE Confidence: 0.785546605

00:41:16.128 --> 00:41:18.987 that You Tube is still popular among

NOTE Confidence: 0.785546605

00:41:18.987 --> 00:41:21.157 youth despite newer platforms entering.

NOTE Confidence: 0.785546605

00:41:21.160 --> 00:41:22.416 That's popular among youth.

NOTE Confidence: 0.785546605

00:41:22.416 --> 00:41:25.031 We could also see that among those people

NOTE Confidence: 0.785546605

00:41:25.031 --> 00:41:27.383 who use they they're using YouTube often.

NOTE Confidence: 0.7472244125

00:41:30.630 --> 00:41:33.640 So E cigarettes have been

NOTE Confidence: 0.7472244125

00:41:33.640 --> 00:41:35.446 identified on YouTube.

NOTE Confidence: 0.7472244125

00:41:35.450 --> 00:41:36.826 And people have examined.

NOTE Confidence: 0.7472244125

00:41:36.826 --> 00:41:38.546 Researchers have examined E cigarette

NOTE Confidence: 0.7472244125

00:41:38.546 --> 00:41:40.496 content on YouTube to inform prevention.

NOTE Confidence: 0.7472244125

00:41:40.500 --> 00:41:41.588 They have identified certain

NOTE Confidence: 0.7472244125

00:41:41.588 --> 00:41:43.220 themes that appear in this video,

NOTE Confidence: 0.7472244125

00:41:43.220 --> 00:41:47.210 such as bait tricks that appeal to you and

NOTE Confidence: 0.7472244125

00:41:47.210 --> 00:41:49.720 as well as unorthodox or modify users.

NOTE Confidence: 0.7472244125

00:41:49.720 --> 00:41:51.974 So how people might hack these devices

NOTE Confidence: 0.7472244125

00:41:51.974 --> 00:41:54.300 and use for unintended purposes,

NOTE Confidence: 0.7472244125

00:41:54.300 --> 00:41:56.575 people are examine Instagram videos

NOTE Confidence: 0.7472244125

00:41:56.575 --> 00:41:58.573 to understand whether there's health

NOTE Confidence: 0.7472244125

00:41:58.573 --> 00:42:00.378 warning labels associated with them,

NOTE Confidence: 0.7472244125

00:42:00.380 --> 00:42:04.126 as well as how do these videos explain

NOTE Confidence: 0.7472244125

00:42:04.126 --> 00:42:06.106 health effects of E cigarettes?

NOTE Confidence: 0.7472244125

00:42:06.110 --> 00:42:08.930 And nicotine use as well as

NOTE Confidence: 0.7472244125

00:42:08.930 --> 00:42:10.340 the marketing content.

NOTE Confidence: 0.7472244125

00:42:10.340 --> 00:42:12.657 These are just some examples of what's

NOTE Confidence: 0.7472244125

00:42:12.657 --> 00:42:14.620 been examined on YouTube videos.

NOTE Confidence: 0.7472244125

00:42:14.620 --> 00:42:16.444 However, there is a lot of

NOTE Confidence: 0.7472244125

00:42:16.444 --> 00:42:17.660 limitation in current methods,

NOTE Confidence: 0.7472244125

00:42:17.660 --> 00:42:19.400 so all of these prior studies

NOTE Confidence: 0.7472244125

00:42:19.400 --> 00:42:20.560 have used human coding,

NOTE Confidence: 0.7472244125

00:42:20.560 --> 00:42:22.018 which means that you know we

NOTE Confidence: 0.7472244125

00:42:22.018 --> 00:42:23.833 have humans going in and and and

NOTE Confidence: 0.7472244125

00:42:23.833 --> 00:42:25.411 watching a video to identify these

NOTE Confidence: 0.7472244125

00:42:25.411 --> 00:42:26.991 themes and really limit the number

NOTE Confidence: 0.7472244125

00:42:26.991 --> 00:42:28.620 of videos that could be examined.

NOTE Confidence: 0.7472244125

00:42:28.620 --> 00:42:30.780 So in these studies they examine

NOTE Confidence: 0.7472244125

00:42:30.780 --> 00:42:32.470 about 50 to 350 videos,

NOTE Confidence: 0.7472244125

00:42:32.470 --> 00:42:34.300 but in our previous study we

NOTE Confidence: 0.7472244125

00:42:34.300 --> 00:42:36.298 examined big trip videos on YouTube.

NOTE Confidence: 0.7472244125

00:42:36.300 --> 00:42:38.722 We found that there is like 156,000

NOTE Confidence: 0.7472244125

00:42:38.722 --> 00:42:41.340 videos just on vape tricks along and

NOTE Confidence: 0.7472244125

00:42:41.340 --> 00:42:43.168 other studies have found that 2200

NOTE Confidence: 0.7472244125

00:42:43.168 --> 00:42:44.536 new E cigarette videos are being.

NOTE Confidence: 0.7472244125

00:42:44.540 --> 00:42:46.748 Upload every month.

NOTE Confidence: 0.7472244125

00:42:46.750 --> 00:42:47.124 So,

NOTE Confidence: 0.7472244125

00:42:47.124 --> 00:42:48.620 advances in computational methods

NOTE Confidence: 0.7472244125

00:42:48.620 --> 00:42:50.927 can enhance the methods used to

NOTE Confidence: 0.7472244125

00:42:50.927 --> 00:42:52.797 analyze social media data to

NOTE Confidence: 0.7472244125

00:42:52.797 --> 00:42:54.293 inform tobacco regulatory science.

NOTE Confidence: 0.912790375294118

00:42:56.800 --> 00:42:59.206 So the other issue with social

NOTE Confidence: 0.912790375294118

00:42:59.206 --> 00:43:01.838 media is that social media custom

NOTE Confidence: 0.912790375294118

00:43:01.838 --> 00:43:04.198 tailors the content to users.

NOTE Confidence: 0.912790375294118

00:43:04.200 --> 00:43:06.790 So we know that there is a lot of E

NOTE Confidence: 0.912790375294118

00:43:06.869 --> 00:43:09.401 cigarette content and this I should

NOTE Confidence: 0.912790375294118

00:43:09.401 --> 00:43:12.590 say this algorithm of how social media

NOTE Confidence: 0.912790375294118

00:43:12.590 --> 00:43:15.064 content tailors the users is proprietary

NOTE Confidence: 0.912790375294118

00:43:15.064 --> 00:43:17.774 and we really don't know what kind

NOTE Confidence: 0.912790375294118

00:43:17.774 --> 00:43:20.008 of content user being exposed to,

NOTE Confidence: 0.912790375294118

00:43:20.008 --> 00:43:22.300 so understanding the types of content

NOTE Confidence: 0.912790375294118

00:43:22.364 --> 00:43:25.060 that you would mute or exposed to is

NOTE Confidence: 0.912790375294118

00:43:25.060 --> 00:43:27.138 really important to inform regulations

NOTE Confidence: 0.912790375294118

00:43:27.140 --> 00:43:30.192 as well as how to create prevention

NOTE Confidence: 0.912790375294118

00:43:30.192 --> 00:43:33.039 strategies such as counter marketing.

NOTE Confidence: 0.912790375294118

00:43:33.040 --> 00:43:34.970 And no study has yet.

NOTE Confidence: 0.912790375294118

00:43:34.970 --> 00:43:36.638 Try to mimic youth conducting the

NOTE Confidence: 0.912790375294118

00:43:36.638 --> 00:43:38.488 search and then apply machine learning

NOTE Confidence: 0.912790375294118

00:43:38.488 --> 00:43:40.534 to understand all the data retrieved.

NOTE Confidence: 0.97449684

00:43:43.870 --> 00:43:47.248 So. So advanced computational

NOTE Confidence: 0.97449684

00:43:47.248 --> 00:43:49.684 methods can be applied to overcome

NOTE Confidence: 0.97449684

00:43:49.684 --> 00:43:51.688 these limitations and and gaps,

NOTE Confidence: 0.97449684

00:43:51.690 --> 00:43:53.856 or another limitation is getting more.

NOTE Confidence: 0.97449684

00:43:53.860 --> 00:43:58.660 How do we get these data or videos

NOTE Confidence: 0.97449684

00:43:58.660 --> 00:44:01.136 rapidly so some platforms provide

NOTE Confidence: 0.97449684

00:44:01.136 --> 00:44:03.012 access via application programming

NOTE Confidence: 0.97449684

00:44:03.012 --> 00:44:05.199 interfaces APIs while other platforms

NOTE Confidence: 0.97449684

00:44:05.199 --> 00:44:07.174 require more involved coding to

NOTE Confidence: 0.97449684

00:44:07.174 --> 00:44:09.779 build data scrapers and API's could

NOTE Confidence: 0.97449684

00:44:09.779 --> 00:44:11.531 potentially deliver thousands or

NOTE Confidence: 0.97449684

00:44:11.531 --> 00:44:14.358 even millions of posts per day.

NOTE Confidence: 0.97449684

00:44:14.358 --> 00:44:16.306 And additionally computational methods.

NOTE Confidence: 0.97449684

00:44:16.310 --> 00:44:18.614 Can be used to understand topics

NOTE Confidence: 0.97449684

00:44:18.614 --> 00:44:20.150 related to tobacco prevention

NOTE Confidence: 0.97449684

00:44:20.213 --> 00:44:22.318 using large social media datasets.

NOTE Confidence: 0.97449684

00:44:22.320 --> 00:44:25.371 So now I will sort of switch gear to

NOTE Confidence: 0.97449684

00:44:25.371 --> 00:44:27.534 talk about two studies that we've

NOTE Confidence: 0.97449684

00:44:27.534 --> 00:44:29.189 used to analyze YouTube content

NOTE Confidence: 0.97449684

00:44:29.189 --> 00:44:31.590 on E cigarettes and these studies

NOTE Confidence: 0.97449684

00:44:31.590 --> 00:44:33.194 use unsupervised machine learning

NOTE Confidence: 0.97449684

00:44:33.194 --> 00:44:34.880 rule based classification,

NOTE Confidence: 0.97449684

00:44:34.880 --> 00:44:37.565 network analysis as well as

NOTE Confidence: 0.97449684

00:44:37.565 --> 00:44:39.176 supervised machine learning.

NOTE Confidence: 0.97449684

00:44:39.180 --> 00:44:41.630 The study one we wanted to understand

NOTE Confidence: 0.97449684

00:44:41.630 --> 00:44:43.201 whether E cigarette content

NOTE Confidence: 0.97449684

00:44:43.201 --> 00:44:45.943 on YouTube differs by U2 youth

NOTE Confidence: 0.97449684

00:44:45.943 --> 00:44:46.857 demographic characteristics.

NOTE Confidence: 0.97449684

00:44:46.860 --> 00:44:48.828 To understand whether you think content

NOTE Confidence: 0.97449684

00:44:48.828 --> 00:44:50.959 is being tailored to certain views.

NOTE Confidence: 0.97449684

00:44:50.960 --> 00:44:52.196 To do this,

NOTE Confidence: 0.97449684

00:44:52.196 --> 00:44:54.668 we create a 16 fictitious viewer

NOTE Confidence: 0.97449684

00:44:54.668 --> 00:44:56.556 profiles and these viewer

NOTE Confidence: 0.97449684

00:44:56.556 --> 00:44:58.886 profiles were separated by age.

NOTE Confidence: 0.97449684

00:44:58.890 --> 00:45:01.590 So 16 year olds and 24 year olds by

NOTE Confidence: 0.97449684

00:45:01.590 --> 00:45:03.817 gender as well as race ethnicity.

NOTE Confidence: 0.97449684

00:45:03.820 --> 00:45:05.000 We may profile for white,

NOTE Confidence: 0.97449684

00:45:05.000 --> 00:45:05.391 black,

NOTE Confidence: 0.97449684

00:45:05.391 --> 00:45:07.737 Hispanic youth and we used factory

NOTE Confidence: 0.97449684

00:45:07.737 --> 00:45:09.750 reset Android phone with Orbot

NOTE Confidence: 0.97449684

00:45:09.750 --> 00:45:11.675 app to delete all personalization

NOTE Confidence: 0.97449684

00:45:11.675 --> 00:45:13.410 based on search results.

NOTE Confidence: 0.97449684

00:45:13.410 --> 00:45:15.066 And these are the search results

NOTE Confidence: 0.97449684

00:45:15.066 --> 00:45:16.844 are words that we use related

NOTE Confidence: 0.97449684

00:45:16.844 --> 00:45:18.698 to E cigarettes and we conducted

NOTE Confidence: 0.97449684

00:45:18.698 --> 00:45:19.979 this search inmate 720.

NOTE Confidence: 0.97449684

00:45:19.980 --> 00:45:22.440 And we obtain 140 videos which

NOTE Confidence: 0.97449684

00:45:22.440 --> 00:45:24.700 is equivalent to about 7 pages

NOTE Confidence: 0.97449684

00:45:24.700 --> 00:45:27.366 of 20 videos per page for each

NOTE Confidence: 0.97449684

00:45:27.366 --> 00:45:29.652 search word and fix your profile.

NOTE Confidence: 0.97449684

00:45:29.652 --> 00:45:32.564 And so after we remove all the

NOTE Confidence: 0.97449684

00:45:32.564 --> 00:45:35.200 duplicates we had 4201 non duplicate

NOTE Confidence: 0.97449684

00:45:35.200 --> 00:45:38.000 videos in our search result.

NOTE Confidence: 0.97449684

00:45:38.000 --> 00:45:40.106 The first we wanted to understand,

NOTE Confidence: 0.97449684

00:45:40.110 --> 00:45:42.522 you know we had to develop a cool bug

NOTE Confidence: 0.97449684

00:45:42.522 --> 00:45:45.010 to understand what we're examining.

NOTE Confidence: 0.97449684

00:45:45.010 --> 00:45:46.660 So what we're interested in examining

NOTE Confidence: 0.97449684

00:45:46.660 --> 00:45:48.686 was like what are the videos being

NOTE Confidence: 0.97449684

00:45:48.686 --> 00:45:50.166 related to E cigarettes, right?

NOTE Confidence: 0.97449684

00:45:50.166 --> 00:45:51.696 So were they product reviews,

NOTE Confidence: 0.97449684

00:45:51.700 --> 00:45:53.700 vape tricks, health information?

NOTE Confidence: 0.97449684

00:45:53.700 --> 00:45:54.700 You know?

NOTE Confidence: 0.97449684

00:45:54.700 --> 00:45:57.628 What were these videos talking about?

NOTE Confidence: 0.97449684

00:45:57.630 --> 00:45:59.151 And then we want to know who are the

NOTE Confidence: 0.97449684

00:45:59.151 --> 00:46:00.587 people who are uploading these videos,

NOTE Confidence: 0.97449684

00:46:00.590 --> 00:46:03.022 where they private users,

NOTE Confidence: 0.97449684

00:46:03.022 --> 00:46:05.130 retailers and we want to know what

NOTE Confidence: 0.97449684

00:46:05.130 --> 00:46:06.938 types of E cigarette products are

NOTE Confidence: 0.97449684

00:46:06.938 --> 00:46:08.710 being featured or the eliquids

NOTE Confidence: 0.97449684

00:46:08.710 --> 00:46:10.750 box mod pods and so on.

NOTE Confidence: 0.97449684

00:46:10.750 --> 00:46:13.318 We also want to see if there were

NOTE Confidence: 0.97449684

00:46:13.318 --> 00:46:14.930 actually selling these products

NOTE Confidence: 0.97449684

00:46:14.930 --> 00:46:17.117 to youth and so we buy we look to

NOTE Confidence: 0.97449684

00:46:17.117 --> 00:46:19.235 see whether this external links

NOTE Confidence: 0.97449684

00:46:19.235 --> 00:46:21.495 for purchasing and discount codes.

NOTE Confidence: 0.97449684

00:46:21.500 --> 00:46:23.830 So once we quoted this book, I'll catbug.

NOTE Confidence: 0.97449684

00:46:23.830 --> 00:46:25.690 We're two independent reviewers

NOTE Confidence: 0.97449684

00:46:25.690 --> 00:46:28.060 randomly review the finalizer themes,

NOTE Confidence: 0.97449684

00:46:28.060 --> 00:46:31.410 and then we establish integrative

NOTE Confidence: 0.97449684

00:46:31.410 --> 00:46:32.080 reliability.

NOTE Confidence: 0.97449684

00:46:32.080 --> 00:46:34.426 And then after that one quarter

NOTE Confidence: 0.97449684

00:46:34.426 --> 00:46:35.599 labeled 1000 videos,

NOTE Confidence: 0.97449684

00:46:35.600 --> 00:46:38.366 which was used to train supervised

NOTE Confidence: 0.97449684

00:46:38.366 --> 00:46:40.569 machine learning algorithms for study one,

NOTE Confidence: 0.97449684

00:46:40.569 --> 00:46:42.480 I'm going to focus on video themes

NOTE Confidence: 0.97449684

00:46:42.544 --> 00:46:44.488 because our goal was to understand

NOTE Confidence: 0.97449684

00:46:44.488 --> 00:46:46.220 whether the video theme content

NOTE Confidence: 0.97449684

00:46:46.220 --> 00:46:47.740 was different among users.

NOTE Confidence: 0.97449684

00:46:47.740 --> 00:46:48.167 However,

NOTE Confidence: 0.97449684

00:46:48.167 --> 00:46:51.583 the methods are the same for both studies.

NOTE Confidence: 0.97449684

00:46:51.590 --> 00:46:53.708 So using network analysis we plotted

NOTE Confidence: 0.97449684

00:46:53.708 --> 00:46:56.018 exposure similarities as a network of

NOTE Confidence: 0.97449684

00:46:56.018 --> 00:46:57.698 demographic attributes and videos.

NOTE Confidence: 0.97449684

00:46:57.700 --> 00:47:00.150 So what you see here is a graph of male,

NOTE Confidence: 0.864424234

00:47:00.150 --> 00:47:02.390 female and by different age groups and

NOTE Confidence: 0.864424234

00:47:02.390 --> 00:47:04.829 the thickness of this purple line indicate

NOTE Confidence: 0.864424234

00:47:04.829 --> 00:47:06.959 the normal number of common videos.

NOTE Confidence: 0.864424234

00:47:06.960 --> 00:47:10.281 So what we see that both 24 year old

NOTE Confidence: 0.864424234

00:47:10.281 --> 00:47:12.748 profiles have the most most videos

NOTE Confidence: 0.864424234

00:47:12.748 --> 00:47:15.575 in common and then it's 24 year

NOTE Confidence: 0.864424234

00:47:15.575 --> 00:47:18.130 old male and 16 year old female.

NOTE Confidence: 0.864424234

00:47:18.130 --> 00:47:20.069 And we also use K means clustering,

NOTE Confidence: 0.864424234

00:47:20.070 --> 00:47:22.644 which is a powerful unsupervised machine

NOTE Confidence: 0.864424234

00:47:22.644 --> 00:47:24.834 learning algorithm that finds similarity

NOTE Confidence: 0.864424234

00:47:24.834 --> 00:47:27.294 between items and grouped them into

NOTE Confidence: 0.864424234

00:47:27.294 --> 00:47:29.330 clusters without the human input.

NOTE Confidence: 0.864424234

00:47:29.330 --> 00:47:32.638 And then we used human data.

NOTE Confidence: 0.864424234

00:47:32.638 --> 00:47:35.630 A human labeled data as an input to

NOTE Confidence: 0.864424234

00:47:35.713 --> 00:47:38.678 graph convolutional network for machine

NOTE Confidence: 0.864424234

00:47:38.678 --> 00:47:42.074 based classification of the 4201 videos,

NOTE Confidence: 0.864424234

00:47:42.074 --> 00:47:43.610 titles and descriptions.

NOTE Confidence: 0.864424234

00:47:43.610 --> 00:47:46.658 And we found that just north of high

NOTE Confidence: 0.864424234

00:47:46.658 --> 00:47:51.450 accuracy and using GCN we were able to

NOTE Confidence: 0.864424234

00:47:51.450 --> 00:47:54.566 identify what the video themes were.

NOTE Confidence: 0.864424234

00:47:54.566 --> 00:47:58.845 So 49% of the videos were product reviews,

NOTE Confidence: 0.864424234

00:47:58.850 --> 00:47:59.588 26.9 videos.

NOTE Confidence: 0.864424234

00:47:59.588 --> 00:48:01.433 Or informational or or modifying

NOTE Confidence: 0.864424234

00:48:01.433 --> 00:48:03.602 so these are videos that teaches

NOTE Confidence: 0.864424234

00:48:03.602 --> 00:48:06.261 people how to use an E cigarette or

NOTE Confidence: 0.864424234

00:48:06.261 --> 00:48:08.469 how to modify or hack in E cigarette

NOTE Confidence: 0.864424234

00:48:08.470 --> 00:48:10.366 15% or health information.

NOTE Confidence: 0.864424234

00:48:10.366 --> 00:48:13.555 Videos about E cigarettes and 9% were

NOTE Confidence: 0.864424234

00:48:13.555 --> 00:48:15.625 just like other types of videos.

NOTE Confidence: 0.947678246666667

00:48:18.890 --> 00:48:21.355 And so after performing clustering

NOTE Confidence: 0.947678246666667

00:48:21.355 --> 00:48:23.011 classification, we calculate the

NOTE Confidence: 0.947678246666667

00:48:23.011 --> 00:48:25.333 percentage of each video type in

NOTE Confidence: 0.947678246666667

00:48:25.333 --> 00:48:28.044 each category by demographic groups.

NOTE Confidence: 0.947678246666667

00:48:28.044 --> 00:48:31.950 So what we find here is that.

NOTE Confidence: 0.947678246666667

00:48:31.950 --> 00:48:33.798 The green color is the product of you,

NOTE Confidence: 0.947678246666667

00:48:33.800 --> 00:48:35.728 so these are videos that talk about you

NOTE Confidence: 0.947678246666667

00:48:35.728 --> 00:48:37.535 know like give product reviews on the

NOTE Confidence: 0.947678246666667

00:48:37.535 --> 00:48:39.437 product and we find that the product

NOTE Confidence: 0.947678246666667

00:48:39.437 --> 00:48:41.147 reviews represented by the green color

NOTE Confidence: 0.947678246666667

00:48:41.147 --> 00:48:44.540 is more common among 24 year old profiles.

NOTE Confidence: 0.947678246666667

00:48:44.540 --> 00:48:46.975 Health health is represented by

NOTE Confidence: 0.947678246666667

00:48:46.975 --> 00:48:50.388 Orange is similar or cross a little

NOTE Confidence: 0.947678246666667

00:48:50.388 --> 00:48:52.608 bit more common among males.

NOTE Confidence: 0.947678246666667

00:48:52.610 --> 00:48:54.300 And what you what's interesting

NOTE Confidence: 0.947678246666667

00:48:54.300 --> 00:48:56.430 here is that the lighter bluish

NOTE Confidence: 0.947678246666667

00:48:56.430 --> 00:48:58.330 purplish color here is informational

NOTE Confidence: 0.947678246666667

00:48:58.330 --> 00:49:00.858 videos where how to use an Instagram

NOTE Confidence: 0.947678246666667

00:49:00.858 --> 00:49:02.748 or how to modify an Instagram.

NOTE Confidence: 0.947678246666667

00:49:02.750 --> 00:49:05.486 And that's a lot more common

NOTE Confidence: 0.947678246666667

00:49:05.486 --> 00:49:07.310 among underage female group.

NOTE Confidence: 0.947678246666667

00:49:07.310 --> 00:49:09.886 And other other videos are more common,

NOTE Confidence: 0.947678246666667

00:49:09.890 --> 00:49:11.660 represented by the darker purple

NOTE Confidence: 0.947678246666667

00:49:11.660 --> 00:49:13.830 here for male 16 year olds,

NOTE Confidence: 0.947678246666667

00:49:13.830 --> 00:49:15.700 which is concerning because these

NOTE Confidence: 0.947678246666667

00:49:15.700 --> 00:49:17.989 videos had content like you know

NOTE Confidence: 0.947678246666667

00:49:17.989 --> 00:49:19.739 related to cannabis vaping and

NOTE Confidence: 0.947678246666667

00:49:19.739 --> 00:49:21.569 other vape tricks and so on.

NOTE Confidence: 0.947678246666667

00:49:21.570 --> 00:49:23.780 So there is concerning content

NOTE Confidence: 0.947678246666667

00:49:23.780 --> 00:49:25.990 that shows that more tailored

NOTE Confidence: 0.947678246666667

00:49:26.068 --> 00:49:28.280 towards younger younger youth.

NOTE Confidence: 0.947678246666667

00:49:28.280 --> 00:49:30.892 So our results show that demographic

NOTE Confidence: 0.947678246666667

00:49:30.892 --> 00:49:33.260 attributes does factor into

NOTE Confidence: 0.947678246666667

00:49:33.260 --> 00:49:35.036 YouTube algorithmic systems.

NOTE Confidence: 0.947678246666667

00:49:35.040 --> 00:49:36.920 In the context of esseker

NOTE Confidence: 0.947678246666667

00:49:36.920 --> 00:49:38.424 related queries on YouTube,

NOTE Confidence: 0.947678246666667

00:49:38.430 --> 00:49:40.590 we found that the similarities between

NOTE Confidence: 0.947678246666667

00:49:40.590 --> 00:49:43.270 exposure for male and female 24 year

NOTE Confidence: 0.947678246666667

00:49:43.270 --> 00:49:45.504 olds and actually higher than than

NOTE Confidence: 0.947678246666667

00:49:45.504 --> 00:49:47.039 the connection between other pairs.

NOTE Confidence: 0.947678246666667

00:49:47.040 --> 00:49:48.670 We also found that underage

NOTE Confidence: 0.947678246666667

00:49:48.670 --> 00:49:50.872 users work more exposed to more

NOTE Confidence: 0.947678246666667

00:49:50.872 --> 00:49:52.918 instructional videos on E cigarettes,

NOTE Confidence: 0.947678246666667

00:49:52.918 --> 00:49:54.994 while all the age groups were

NOTE Confidence: 0.947678246666667

00:49:54.994 --> 00:49:57.240 most exposed to product reviews.

NOTE Confidence: 0.947678246666667

00:49:57.240 --> 00:50:00.467 So all of this is concerning because.

NOTE Confidence: 0.947678246666667

00:50:00.470 --> 00:50:03.690 We because this shows that underage profiles,

NOTE Confidence: 0.947678246666667

00:50:03.690 --> 00:50:06.390 right so 16 year olds are able to or

NOTE Confidence: 0.947678246666667

00:50:06.390 --> 00:50:09.029 are exposed to E cigarette content

NOTE Confidence: 0.947678246666667

00:50:09.030 --> 00:50:11.758 despite YouTube having policies

NOTE Confidence: 0.947678246666667

00:50:11.758 --> 00:50:14.486 about prohibiting Easter great

NOTE Confidence: 0.947678246666667

00:50:14.486 --> 00:50:16.362 content to their underage viewers,

NOTE Confidence: 0.947678246666667

00:50:16.362 --> 00:50:17.554 such as product reviews.

NOTE Confidence: 0.87126529125

00:50:19.650 --> 00:50:23.578 So now I'll talk about our second study.

NOTE Confidence: 0.87126529125

00:50:23.580 --> 00:50:25.561 So we identify we have four areas

NOTE Confidence: 0.87126529125

00:50:25.561 --> 00:50:27.138 of interest, which is, you know,

NOTE Confidence: 0.87126529125

00:50:27.138 --> 00:50:28.398 what are the video themes?

NOTE Confidence: 0.87126529125

00:50:28.400 --> 00:50:30.696 Who are the people uploading these videos?

NOTE Confidence: 0.87126529125

00:50:30.700 --> 00:50:32.464 You know what types of E cigarette

NOTE Confidence: 0.87126529125

00:50:32.464 --> 00:50:34.133 products are being featured and is

NOTE Confidence: 0.87126529125

00:50:34.133 --> 00:50:35.849 their presence of sales and discounts.

NOTE Confidence: 0.87126529125

00:50:35.850 --> 00:50:37.936 So what we want to do is we you know we

NOTE Confidence: 0.87126529125

00:50:37.936 --> 00:50:39.784 could use human coders to identify them,

NOTE Confidence: 0.87126529125

00:50:39.790 --> 00:50:42.782 but we wanted to know can we use

NOTE Confidence: 0.87126529125

00:50:42.782 --> 00:50:44.428 supervised machine learning to

NOTE Confidence: 0.87126529125

00:50:44.428 --> 00:50:46.894 identify these key areas that could

NOTE Confidence: 0.87126529125

00:50:46.894 --> 00:50:49.329 inform E cigarette prevention?

NOTE Confidence: 0.87126529125

00:50:49.330 --> 00:50:50.500 So what is machine learning?

NOTE Confidence: 0.87126529125

00:50:50.500 --> 00:50:52.180 Machine learning is powerful and it could

NOTE Confidence: 0.87126529125

00:50:52.180 --> 00:50:54.096 be used to examine a large data set.

NOTE Confidence: 0.87126529125

00:50:54.100 --> 00:50:55.340 So in this case large,

NOTE Confidence: 0.87126529125

00:50:55.340 --> 00:50:56.812 many videos machine learning

NOTE Confidence: 0.87126529125

00:50:56.812 --> 00:50:59.020 has been used to examine social

NOTE Confidence: 0.87126529125

00:50:59.084 --> 00:51:01.109 media content around tobacco use.

NOTE Confidence: 0.87126529125

00:51:01.110 --> 00:51:01.616 However,

NOTE Confidence: 0.87126529125

00:51:01.616 --> 00:51:04.194 no studies have examined YouTube

NOTE Confidence: 0.87126529125

00:51:04.194 --> 00:51:06.410 videos using machine learning.

NOTE Confidence: 0.87126529125

00:51:06.410 --> 00:51:08.643 So this is a quick overview of

NOTE Confidence: 0.87126529125

00:51:08.643 --> 00:51:10.670 what a machine learning does,

NOTE Confidence: 0.87126529125

00:51:10.670 --> 00:51:14.586 so using an algorithm to it uses

NOTE Confidence: 0.87126529125

00:51:14.586 --> 00:51:16.126 an algorithm to predict something.

NOTE Confidence: 0.87126529125

00:51:16.130 --> 00:51:17.138 So in this case,

NOTE Confidence: 0.87126529125

00:51:17.138 --> 00:51:19.170 if we're interested in it saying you know,

NOTE Confidence: 0.87126529125

00:51:19.170 --> 00:51:21.434 can we use machine learning to to to

NOTE Confidence: 0.87126529125

00:51:21.434 --> 00:51:23.514 identify if a video featuring an E

NOTE Confidence: 0.87126529125

00:51:23.514 --> 00:51:25.662 cigarette first we need to teach the

NOTE Confidence: 0.87126529125

00:51:25.662 --> 00:51:27.920 algorithm what an E cigarette is, right?

NOTE Confidence: 0.87126529125

00:51:27.920 --> 00:51:30.465 So we we teach it, if it's jewel,

NOTE Confidence: 0.87126529125

00:51:30.465 --> 00:51:32.244 if it's east, sick, if it's vape,

NOTE Confidence: 0.87126529125

00:51:32.244 --> 00:51:33.720 then it's considered an E cigarette

NOTE Confidence: 0.87126529125

00:51:33.766 --> 00:51:34.928 and this is A and this is,

NOTE Confidence: 0.87126529125

00:51:34.930 --> 00:51:36.610 this data set is now.

NOTE Confidence: 0.87126529125

00:51:36.610 --> 00:51:39.712 Used to train the machine learning

NOTE Confidence: 0.87126529125

00:51:39.712 --> 00:51:41.762 algorithm and the algorithm learns

NOTE Confidence: 0.87126529125

00:51:41.762 --> 00:51:44.519 from this example data set and later

NOTE Confidence: 0.87126529125

00:51:44.519 --> 00:51:46.962 uses a different data set to predict

NOTE Confidence: 0.87126529125

00:51:46.962 --> 00:51:49.590 whether they could identify an E cigarette.

NOTE Confidence: 0.87126529125

00:51:49.590 --> 00:51:51.190 So if it correctly identify

NOTE Confidence: 0.87126529125

00:51:51.190 --> 00:51:52.790 that there is an issue,

NOTE Confidence: 0.87126529125

00:51:52.790 --> 00:51:55.130 regret that he's a successful model.

NOTE Confidence: 0.87126529125

00:51:55.130 --> 00:51:57.116 If it fails to identify where

NOTE Confidence: 0.87126529125

00:51:57.116 --> 00:51:59.010 if an E cigarette exists,

NOTE Confidence: 0.87126529125

00:51:59.010 --> 00:52:00.009 when it doesn't,

NOTE Confidence: 0.87126529125

00:52:00.009 --> 00:52:02.007 then we reach train this machine

NOTE Confidence: 0.87126529125

00:52:02.007 --> 00:52:04.101 article rhythm until we could

NOTE Confidence: 0.87126529125

00:52:04.101 --> 00:52:05.797 achieve a successful classification.

NOTE Confidence: 0.8682599155

00:52:08.630 --> 00:52:10.838 So in our study, this is a model

NOTE Confidence: 0.8682599155

00:52:10.838 --> 00:52:12.516 performance of our machine learning

NOTE Confidence: 0.8682599155

00:52:12.516 --> 00:52:14.987 models for each of the four categories,

NOTE Confidence: 0.8682599155

00:52:14.990 --> 00:52:17.790 F1 score is a measure of test accuracy.

NOTE Confidence: 0.8682599155

00:52:17.790 --> 00:52:19.114 It's calculated from the

NOTE Confidence: 0.8682599155

00:52:19.114 --> 00:52:21.100 precision and recall of a test.

NOTE Confidence: 0.827493696842105

00:52:23.200 --> 00:52:25.280 And this is a like a pretty good

NOTE Confidence: 0.827493696842105

00:52:25.280 --> 00:52:26.793 score considering the complexity of

NOTE Confidence: 0.827493696842105

00:52:26.793 --> 00:52:28.665 the themes that we were identifying.

NOTE Confidence: 0.92218714

00:52:31.180 --> 00:52:32.430 So what do we find?

NOTE Confidence: 0.92218714

00:52:32.430 --> 00:52:34.747 So this is a little more detailed

NOTE Confidence: 0.92218714

00:52:34.747 --> 00:52:37.107 look into video themes that we use

NOTE Confidence: 0.92218714

00:52:37.107 --> 00:52:39.530 in this case study versus our study.

NOTE Confidence: 0.92218714

00:52:39.530 --> 00:52:41.746 One that's what we have more themes here,

NOTE Confidence: 0.92218714

00:52:41.750 --> 00:52:43.544 and we also similarly identify the

NOTE Confidence: 0.92218714

00:52:43.544 --> 00:52:45.429 product views were the most common.

NOTE Confidence: 0.92218714

00:52:45.430 --> 00:52:47.366 And if you see a picture image here,

NOTE Confidence: 0.92218714

00:52:47.370 --> 00:52:48.833 this is an example of what a

NOTE Confidence: 0.92218714

00:52:48.833 --> 00:52:50.133 product review look like, right?

NOTE Confidence: 0.92218714

00:52:50.133 --> 00:52:52.148 This is Jewel starter Kit

NOTE Confidence: 0.92218714

00:52:52.148 --> 00:52:53.357 unboxing and review.

NOTE Confidence: 0.92218714

00:52:53.360 --> 00:52:55.918 And we also found that 72nd highest

NOTE Confidence: 0.92218714

00:52:55.918 --> 00:52:58.552 video theme was modified video that

NOTE Confidence: 0.92218714

00:52:58.552 --> 00:53:00.954 teaches people how to modify and

NOTE Confidence: 0.92218714

00:53:00.954 --> 00:53:03.126 informational videos on how to use

NOTE Confidence: 0.92218714

00:53:03.205 --> 00:53:05.860 health information was 11% other

NOTE Confidence: 0.92218714

00:53:05.860 --> 00:53:08.660 themes that were still ysaguirre.

NOTE Confidence: 0.92218714

00:53:08.660 --> 00:53:11.060 9% of marijuana related things

NOTE Confidence: 0.92218714

00:53:11.060 --> 00:53:13.616 was 6% and other irrelevant theme

NOTE Confidence: 0.92218714

00:53:13.616 --> 00:53:16.010 which is like non E cigarette

NOTE Confidence: 0.92218714

00:53:16.089 --> 00:53:18.306 theme for five percent 5.6% and

NOTE Confidence: 0.92218714

00:53:18.306 --> 00:53:20.244 vape chicks was one point 1%.

NOTE Confidence: 0.86880266

00:53:22.500 --> 00:53:24.460 So product type, so this is so this

NOTE Confidence: 0.86880266

00:53:24.460 --> 00:53:26.945 is all the different types of products

NOTE Confidence: 0.86880266

00:53:26.945 --> 00:53:28.875 that we identified through machine

NOTE Confidence: 0.86880266

00:53:28.934 --> 00:53:30.842 learning and and what this actually

NOTE Confidence: 0.86880266

00:53:30.842 --> 00:53:33.555 shows is that there are a variety of

NOTE Confidence: 0.86880266

00:53:33.555 --> 00:53:35.771 different types of E cigarette products

NOTE Confidence: 0.86880266

00:53:35.771 --> 00:53:38.494 that are being featured on on YouTube.

NOTE Confidence: 0.86880266

00:53:38.500 --> 00:53:40.906 So who are the people who

NOTE Confidence: 0.86880266

00:53:40.906 --> 00:53:42.510 are uploading these videos?

NOTE Confidence: 0.86880266

00:53:42.510 --> 00:53:44.030 54% were weighed enthusiasm,

NOTE Confidence: 0.86880266

00:53:44.030 --> 00:53:45.930 so who are big enthusiasts?

NOTE Confidence: 0.86880266

00:53:45.930 --> 00:53:48.750 These are independent users who post

NOTE Confidence: 0.86880266

00:53:48.750 --> 00:53:50.630 almost exclusively about bathing.

NOTE Confidence: 0.86880266

00:53:50.630 --> 00:53:52.560 So when you go to the channel page to see

NOTE Confidence: 0.86880266

00:53:52.608 --> 00:53:54.348 what kind of videos they've uploaded,

NOTE Confidence: 0.86880266

00:53:54.350 --> 00:53:56.066 it was mostly related to vaping,

NOTE Confidence: 0.86880266

00:53:56.070 --> 00:53:58.080 but they were not directly

NOTE Confidence: 0.86880266

00:53:58.080 --> 00:53:59.688 connected to vaping company,

NOTE Confidence: 0.86880266

00:53:59.690 --> 00:54:01.265 so we cannot verify that

NOTE Confidence: 0.86880266

00:54:01.265 --> 00:54:02.525 their influences or not.

NOTE Confidence: 0.86880266

00:54:02.530 --> 00:54:05.379 So these are some examples of like

NOTE Confidence: 0.86880266

00:54:05.379 --> 00:54:07.906 account of people who've a person.

NOTE Confidence: 0.86880266

00:54:07.906 --> 00:54:09.796 Vape enthusiasts of channel page.

NOTE Confidence: 0.86880266

00:54:09.800 --> 00:54:11.052 As you could see,

NOTE Confidence: 0.86880266

00:54:11.052 --> 00:54:12.930 all the contents related to vaping.

NOTE Confidence: 0.86880266

00:54:12.930 --> 00:54:14.965 This is problematic because when

NOTE Confidence: 0.86880266

00:54:14.965 --> 00:54:17.000 it comes to regulating content,

NOTE Confidence: 0.86880266

00:54:17.000 --> 00:54:20.616 you cannot regulate private users, right?

NOTE Confidence: 0.86880266

00:54:20.616 --> 00:54:21.796 You can't tell the regular

NOTE Confidence: 0.86880266

00:54:21.796 --> 00:54:23.020 person to say you know.

NOTE Confidence: 0.86880266

00:54:23.020 --> 00:54:24.820 Don't post things about vaping.

NOTE Confidence: 0.86880266

00:54:24.820 --> 00:54:25.181 However,

NOTE Confidence: 0.86880266

00:54:25.181 --> 00:54:26.625 you could regulate influencers

NOTE Confidence: 0.86880266

00:54:26.625 --> 00:54:29.167 who get paid by the industry to

NOTE Confidence: 0.86880266

00:54:29.167 --> 00:54:31.183 post their products and the the.

NOTE Confidence: 0.86880266

00:54:31.190 --> 00:54:32.595 The difficulty with vape enthusiasts

NOTE Confidence: 0.86880266

00:54:32.595 --> 00:54:34.561 is that there's no way to tell

NOTE Confidence: 0.86880266

00:54:34.561 --> 00:54:35.577 who are vape enthusiast,

NOTE Confidence: 0.86880266

00:54:35.580 --> 00:54:39.668 who are influencers and her regular users.

NOTE Confidence: 0.86880266

00:54:39.670 --> 00:54:41.044 21% are stores,

NOTE Confidence: 0.86880266

00:54:41.044 --> 00:54:45.014 12% is other sources and six point 4% of

NOTE Confidence: 0.86880266

00:54:45.014 --> 00:54:47.838 medical community and 6% of private users.

NOTE Confidence: 0.918577972727273

00:54:51.550 --> 00:54:54.430 So 59% of video did not have any

NOTE Confidence: 0.918577972727273

00:54:54.430 --> 00:54:57.598 discount or links 34% of the videos

NOTE Confidence: 0.918577972727273

00:54:57.598 --> 00:55:00.033 had external links for purchasing

NOTE Confidence: 0.918577972727273

00:55:00.040 --> 00:55:02.539 and 5% or have other discount methods

NOTE Confidence: 0.918577972727273

00:55:02.539 --> 00:55:04.490 and one point 7% had discount.

NOTE Confidence: 0.918577972727273

00:55:04.490 --> 00:55:07.520 So this is a screenshot of of of

NOTE Confidence: 0.918577972727273

00:55:07.520 --> 00:55:09.620 instructional videos like beginning

NOTE Confidence: 0.918577972727273

00:55:09.620 --> 00:55:12.539 beginners vaping tip that also had

NOTE Confidence: 0.918577972727273

00:55:12.539 --> 00:55:14.747 a link that you could purchase

NOTE Confidence: 0.918577972727273

00:55:14.747 --> 00:55:16.899 as well as a coupon code.

NOTE Confidence: 0.918577972727273

00:55:16.900 --> 00:55:17.930 For purchasing,

NOTE Confidence: 0.918577972727273

00:55:17.930 --> 00:55:22.050 So what do we find in this study?

NOTE Confidence: 0.918577972727273

00:55:22.050 --> 00:55:25.008 We found that I complicated things

NOTE Confidence: 0.918577972727273

00:55:25.008 --> 00:55:27.802 relevant to E cigarettes could be

NOTE Confidence: 0.918577972727273

00:55:27.802 --> 00:55:29.857 identified using machine learning and

NOTE Confidence: 0.918577972727273

00:55:29.857 --> 00:55:32.330 fictitious youth viewer profiles on YouTube.

NOTE Confidence: 0.918577972727273

00:55:32.330 --> 00:55:34.830 We identified videos that violated

NOTE Confidence: 0.918577972727273

00:55:34.830 --> 00:55:36.830 YouTube tobacco policy restricting

NOTE Confidence: 0.918577972727273

00:55:36.830 --> 00:55:39.068 promotional content to underage minors,

NOTE Confidence: 0.918577972727273

00:55:39.070 --> 00:55:41.744 such as product reviews and purchasing links.

NOTE Confidence: 0.918577972727273

00:55:41.750 --> 00:55:43.460 Again, there was a high level

NOTE Confidence: 0.918577972727273

00:55:43.460 --> 00:55:44.960 of industry presence and such

NOTE Confidence: 0.918577972727273

00:55:44.960 --> 00:55:46.495 as faith enthusiast at stores.

NOTE Confidence: 0.816114232

00:55:49.040 --> 00:55:51.420 So overall conclusions, you know.

NOTE Confidence: 0.816114232

00:55:51.420 --> 00:55:53.575 Mixed methods such as qualitative

NOTE Confidence: 0.816114232

00:55:53.575 --> 00:55:55.730 analysis using human labellers and

NOTE Confidence: 0.816114232

00:55:55.801 --> 00:55:57.896 computational methods can really reveal

NOTE Confidence: 0.816114232

00:55:57.896 --> 00:56:00.879 E cigarette use content to inform youth,

NOTE Confidence: 0.816114232

00:56:00.880 --> 00:56:03.868 tobacco prevention and social media has

NOTE Confidence: 0.816114232

00:56:03.868 --> 00:56:09.488 really a really rich data and has a good.

NOTE Confidence: 0.816114232

00:56:09.490 --> 00:56:11.890 You know you could have a really good

NOTE Confidence: 0.816114232

00:56:11.890 --> 00:56:14.140 understanding of youth behaviors as well as

NOTE Confidence: 0.816114232

00:56:14.140 --> 00:56:16.399 promotion and sales that youth can access.

NOTE Confidence: 0.816114232

00:56:16.400 --> 00:56:18.170 And again, this is our current

NOTE Confidence: 0.816114232

00:56:18.170 --> 00:56:20.438 occurring a lot on YouTube as well

NOTE Confidence: 0.816114232

00:56:20.438 --> 00:56:22.484 as on other social media platforms.

NOTE Confidence: 0.816114232

00:56:22.490 --> 00:56:25.129 And to prevent youth E cigarette uptake,

NOTE Confidence: 0.816114232

00:56:25.130 --> 00:56:26.990 regulation of social media,

NOTE Confidence: 0.816114232

00:56:26.990 --> 00:56:29.315 a promotion that occurs in

NOTE Confidence: 0.816114232

00:56:29.315 --> 00:56:31.620 social media is really needed.

NOTE Confidence: 0.816114232

00:56:31.620 --> 00:56:33.732 So you know this is one example of

NOTE Confidence: 0.816114232

00:56:33.732 --> 00:56:35.928 how social media could be leveraged

NOTE Confidence: 0.816114232

00:56:35.928 --> 00:56:37.528 using qualitative and computation

NOTE Confidence: 0.816114232

00:56:37.528 --> 00:56:39.280 method to understand certain

NOTE Confidence: 0.816114232

00:56:39.280 --> 00:56:41.505 behaviors that could prevent KENS.

NOTE Confidence: 0.816114232

00:56:41.510 --> 00:56:42.920 Has cancer prevention

NOTE Confidence: 0.816114232

00:56:42.920 --> 00:56:44.800 implications like tobacco use?

NOTE Confidence: 0.816114232

00:56:44.800 --> 00:56:47.624 But certainly this this type of methods could

NOTE Confidence: 0.816114232

00:56:47.624 --> 00:56:50.794 be used to understand other behaviors that

NOTE Confidence: 0.816114232

00:56:50.794 --> 00:56:53.730 has direct implications to preventing cancer,

NOTE Confidence: 0.816114232

00:56:53.730 --> 00:56:54.942 such as, you know,

NOTE Confidence: 0.816114232

00:56:54.942 --> 00:56:55.548 physical activity,

NOTE Confidence: 0.816114232

00:56:55.550 --> 00:56:56.758 diet, obesity as well.

NOTE Confidence: 0.820818150526316

00:56:59.010 --> 00:57:01.614 So I'd like to acknowledge our funding

NOTE Confidence: 0.820818150526316

00:57:01.614 --> 00:57:04.233 stores as well as Yale Tobacco Center

NOTE Confidence: 0.820818150526316

00:57:04.233 --> 00:57:06.635 of the Study on Tobacco Regulation,

NOTE Confidence: 0.820818150526316

00:57:06.635 --> 00:57:10.723 tobacco product of Youth in addiction and

NOTE Confidence: 0.820818150526316

00:57:10.723 --> 00:57:13.962 also our team in University, Texas Austin,

NOTE Confidence: 0.820818150526316

00:57:13.962 --> 00:57:16.878 who is leading the computational methods.

NOTE Confidence: 0.89424739

00:57:18.980 --> 00:57:20.468 So thank you for your attention.

NOTE Confidence: 0.897111616666667

00:57:22.480 --> 00:57:24.152 Thanks Doctor Kang that

NOTE Confidence: 0.897111616666667

00:57:24.152 --> 00:57:26.242 that was that was great.

NOTE Confidence: 0.897111616666667

00:57:26.250 --> 00:57:28.740 And it's open for questions,

NOTE Confidence: 0.897111616666667

00:57:28.740 --> 00:57:29.880 please put him in the chat.

NOTE Confidence: 0.897111616666667

00:57:29.880 --> 00:57:31.328 I know we only have a few minutes,

NOTE Confidence: 0.897111616666667

00:57:31.330 --> 00:57:32.985 but maybe we could stay

NOTE Confidence: 0.897111616666667

00:57:32.985 --> 00:57:35.020 over for a minute or two.

NOTE Confidence: 0.897111616666667

00:57:35.020 --> 00:57:36.160 If people have questions.

NOTE Confidence: 0.73515178

00:57:38.670 --> 00:57:44.755 Have you? Reached out to YouTube and showed

NOTE Confidence: 0.73515178

00:57:44.755 --> 00:57:47.380 them your data and asked whether they,

NOTE Confidence: 0.73515178

00:57:47.380 --> 00:57:49.515 I mean it does sound like there's

NOTE Confidence: 0.73515178

00:57:49.515 --> 00:57:51.788 clear you have clear evidence that

NOTE Confidence: 0.73515178

00:57:51.788 --> 00:57:53.933 their policies are being violated.

NOTE Confidence: 0.73515178

00:57:53.940 --> 00:57:56.165 Presumably they have the computational

NOTE Confidence: 0.73515178

00:57:56.165 --> 00:57:59.760 firepower to be able to do similar things.

NOTE Confidence: 0.73515178

00:57:59.760 --> 00:58:01.530 Is it something that they may

NOTE Confidence: 0.73515178

00:58:01.530 --> 00:58:03.070 be convinced to look into?

NOTE Confidence: 0.71717041

00:58:03.850 --> 00:58:05.390 Yeah, that's a great question.

NOTE Confidence: 0.71717041

00:58:05.390 --> 00:58:07.448 You know, I have a paper cut

NOTE Confidence: 0.71717041

00:58:07.448 --> 00:58:08.690 currently under review that's

NOTE Confidence: 0.71717041

00:58:08.690 --> 00:58:10.804 looking at all of the self imposed.

NOTE Confidence: 0.71717041

00:58:10.810 --> 00:58:11.830 Social media policy.

NOTE Confidence: 0.71717041

00:58:11.830 --> 00:58:14.673 Across all the all the social media platforms

NOTE Confidence: 0.71717041

00:58:14.673 --> 00:58:17.067 on tobacco and and not surprisingly,

NOTE Confidence: 0.71717041

00:58:17.070 --> 00:58:19.268 you know all of the social media

NOTE Confidence: 0.71717041

00:58:19.268 --> 00:58:21.528 platforms that do have these policies.

NOTE Confidence: 0.71717041

00:58:21.530 --> 00:58:22.850 They're not being enforced,

NOTE Confidence: 0.71717041

00:58:22.850 --> 00:58:25.266 so so hopefully you know this will

NOTE Confidence: 0.71717041

00:58:25.266 --> 00:58:27.146 bring some more greater attention.

NOTE Confidence: 0.71717041

00:58:27.150 --> 00:58:28.342 Aside from You Tube.

NOTE Confidence: 0.71717041

00:58:28.342 --> 00:58:30.895 But just looking at all the social media

NOTE Confidence: 0.71717041

00:58:30.895 --> 00:58:33.352 platforms and what more could be done.

NOTE Confidence: 0.71717041

00:58:33.360 --> 00:58:34.788 Yeah, and I think could get,

NOTE Confidence: 0.71717041

00:58:34.790 --> 00:58:35.422 you know,

NOTE Confidence: 0.71717041

00:58:35.422 --> 00:58:36.992 I think 1 translational component

NOTE Confidence: 0.71717041

00:58:36.992 --> 00:58:39.169 is that we publish in peer review

NOTE Confidence: 0.71717041

00:58:39.169 --> 00:58:40.887 journals and a lot of this information

NOTE Confidence: 0.71717041

00:58:40.887 --> 00:58:42.506 don't get out into the bigger world

NOTE Confidence: 0.71717041

00:58:42.506 --> 00:58:44.053 and I think just doing some of

NOTE Confidence: 0.71717041

00:58:44.060 --> 00:58:45.728 that legwork might be important in

NOTE Confidence: 0.71717041

00:58:45.728 --> 00:58:47.238 getting some of these attention

NOTE Confidence: 0.71717041

00:58:47.238 --> 00:58:48.938 for two social media platforms.

NOTE Confidence: 0.87706414

00:58:50.980 --> 00:58:53.668 It's important work.

NOTE Confidence: 0.87706414

00:58:53.670 --> 00:58:55.128 So it's it's a few minutes

NOTE Confidence: 0.87706414

00:58:55.128 --> 00:58:56.771 after the hour doesn't look like

NOTE Confidence: 0.87706414

00:58:56.771 --> 00:58:57.995 there's any more questions.

NOTE Confidence: 0.87706414

00:58:58.000 --> 00:59:00.244 So again, thank you to both

NOTE Confidence: 0.87706414

00:59:00.244 --> 00:59:02.421 the the presenters for very

NOTE Confidence: 0.87706414

00:59:02.421 --> 00:59:04.218 interesting discussion and.

NOTE Confidence: 0.87706414

00:59:04.220 --> 00:59:06.388 We'll see you at the next grand rounds.

NOTE Confidence: 0.87706414

00:59:06.390 --> 00:59:07.260 Thank thank you.

NOTE Confidence: 0.891741095

00:59:08.510 --> 00:59:09.170 Thank you.