WEBVTT 2 NOTE duration:"00:29:00"

NOTE recognizability:0.912

NOTE language:en-us

NOTE Confidence: 0.928458502727273

00:00:00.000 --> 00:00:02.196 Funding for Yale Cancer Answers is

NOTE Confidence: 0.928458502727273

00:00:02.196 --> 00:00:04.280 provided by Smilo Cancer Hospital.

NOTE Confidence: 0.9610672

00:00:06.600 --> 00:00:08.840 Welcome to Yale Cancer Answers

NOTE Confidence: 0.9610672

00:00:08.840 --> 00:00:10.600 with Doctor Aneesh Chagpar.

NOTE Confidence: 0.9610672

00:00:10.600 --> 00:00:12.510 Yale Cancer Answers features the

NOTE Confidence: 0.9610672

00:00:12.510 --> 00:00:14.360 latest information on cancer care

NOTE Confidence: 0.9610672

00:00:14.360 --> 00:00:15.817 by welcoming oncologists and

NOTE Confidence: 0.9610672

00:00:15.817 --> 00:00:17.773 specialists who are on the forefront

NOTE Confidence: 0.9610672

00:00:17.773 --> 00:00:19.759 of the battle to fight cancer.

NOTE Confidence: 0.9610672

00:00:19.760 --> 00:00:21.495 This week it's a conversation

NOTE Confidence: 0.9610672

00:00:21.495 --> 00:00:23.230 about research into new methods

NOTE Confidence: 0.9610672

00:00:23.288 --> 00:00:25.024 for targeting pancreatic cancer

NOTE Confidence: 0.9610672

00:00:25.024 --> 00:00:26.760 with Doctor Moi Bhattacharya.

NOTE Confidence: 0.9610672

00:00:26.760 --> 00:00:28.760 Doctor Bhattacharya is an assistant

NOTE Confidence: 0.9610672

00:00:28.760 --> 00:00:30.360 professor of pharmacology at

NOTE Confidence: 0.9610672

00:00:30.360 --> 00:00:32.238 the Yale School of Medicine,

NOTE Confidence: 0.9610672

00:00:32.240 --> 00:00:34.060 where Doctor Chagpar is a

NOTE Confidence: 0.9610672

00:00:34.060 --> 00:00:35.516 professor of surgical oncology.

NOTE Confidence: 0.902785351304348

00:00:36.440 --> 00:00:38.496 So wait, maybe we can start off by

NOTE Confidence: 0.902785351304348

00:00:38.496 --> 00:00:40.387 you telling us a little bit more

NOTE Confidence: 0.902785351304348

00:00:40.387 --> 00:00:42.318 about yourself and what it is you do.

NOTE Confidence: 0.851798856666667

00:00:42.760 --> 00:00:47.398 I am a biophysicist by training.

NOTE Confidence: 0.851798856666667

00:00:47.400 --> 00:00:51.120 My lab is very multidisciplinary.

NOTE Confidence: 0.851798856666667

00:00:51.120 --> 00:00:54.465 We study membrane localized cell

NOTE Confidence: 0.851798856666667

00:00:54.465 --> 00:00:57.141 signaling from different perspectives

NOTE Confidence: 0.851798856666667

00:00:57.141 --> 00:00:59.995 starting from pancreatic cancer which

NOTE Confidence: 0.851798856666667

00:00:59.995 --> 00:01:02.320 is what we are focused on today,

NOTE Confidence: 0.851798856666667

00:01:02.320 --> 00:01:05.446 but also from the direction of

NOTE Confidence: 0.851798856666667

00:01:05.446 --> 00:01:08.560 psychiatric disorders and pain perception.

NOTE Confidence: 0.851798856666667

00:01:08.560 --> 00:01:11.248 And we bring in various techniques

NOTE Confidence: 0.851798856666667

00:01:11.248 --> 00:01:13.040 to answer the question.

NOTE Confidence: 0.851798856666667

00:01:13.040 --> 00:01:14.840 We are very question centric,

NOTE Confidence: 0.851798856666667

00:01:14.840 --> 00:01:17.190 problem centric where the biology

NOTE Confidence: 0.851798856666667

00:01:17.190 --> 00:01:20.615 is decided 1st and then we just

NOTE Confidence: 0.851798856666667

00:01:20.615 --> 00:01:22.595 bring in various methodologies

NOTE Confidence: 0.851798856666667

00:01:22.595 --> 00:01:25.597 that are available or we make

NOTE Confidence: 0.851798856666667

00:01:25.597 --> 00:01:27.947 new technologies to answer the

NOTE Confidence: 0.851798856666667

00:01:27.947 --> 00:01:30.608 questions that are important to us.

NOTE Confidence: 0.851798856666667

00:01:30.608 --> 00:01:34.063 So we are at the Sterling Hall of

NOTE Confidence: 0.851798856666667

00:01:34.063 --> 00:01:37.234 Medicine and I'm a relatively new lab.

NOTE Confidence: 0.851798856666667

00:01:37.240 --> 00:01:39.625 I have been at Yale only for about 3

NOTE Confidence: 0.851798856666667

00:01:39.625 --> 00:01:42.157 1/2 years and it's been great so far.

NOTE Confidence: 0.77413603

00:01:43.240 --> 00:01:46.484 OK. So we, you know, kind of set

NOTE Confidence: 0.77413603

00:01:46.484 --> 00:01:48.942 the stage for us in terms of how

NOTE Confidence: 0.77413603

00:01:48.942 --> 00:01:50.452 you got interested in pancreatic

NOTE Confidence: 0.77413603

00:01:50.452 --> 00:01:52.368 cancer and what exactly are the

NOTE Confidence: 0.77413603

00:01:52.368 --> 00:01:53.676 questions that you're studying,

NOTE Confidence: 0.957862474

00:01:54.720 --> 00:01:58.440 right. So you know I,

NOTE Confidence: 0.957862474

00:01:58.440 --> 00:02:02.220 when I was looking into as I said

NOTE Confidence: 0.957862474

00:02:02.220 --> 00:02:03.720 I'm a biophysicist by training,

NOTE Confidence: 0.957862474

00:02:03.720 --> 00:02:08.040 but we have a really interesting,

NOTE Confidence: 0.957862474

00:02:08.040 --> 00:02:10.815 you know, we love approaching

NOTE Confidence: 0.957862474

00:02:10.815 --> 00:02:12.480 interesting biological problems,

NOTE Confidence: 0.957862474

00:02:12.480 --> 00:02:14.433 outstanding biological problems

NOTE Confidence: 0.957862474

00:02:14.433 --> 00:02:17.037 with our biophysical technologies.

NOTE Confidence: 0.957862474

00:02:17.040 --> 00:02:19.212 And when I was looking into

NOTE Confidence: 0.957862474

00:02:19.212 --> 00:02:21.080 the literature it seemed like,

NOTE Confidence: 0.957862474

00:02:21.080 --> 00:02:24.629 I mean there are pancreatic cancer is

NOTE Confidence: 0.957862474

00:02:24.629 --> 00:02:28.247 probably one with the lowest five year

NOTE Confidence: 0.957862474

00:02:28.247 --> 00:02:31.674 survival rates and there are so many

NOTE Confidence: 0.957862474

00:02:31.674 --> 00:02:33.959 outstanding questions that still exist.

NOTE Confidence: 0.957862474

00:02:33.960 --> 00:02:37.650 I think one of the biggest one is we know

NOTE Confidence: 0.957862474

00:02:37.745 --> 00:02:41.075 that this particular gene called Ras,

NOTE Confidence: 0.957862474

00:02:41.080 --> 00:02:44.596 specifically K Ras for pancreatic cancer,

NOTE Confidence: 0.957862474

00:02:44.600 --> 00:02:47.264 that is a well known marker

NOTE Confidence: 0.957862474

00:02:47.264 --> 00:02:48.596 for pancreatic cancer.

NOTE Confidence: 0.957862474

00:02:48.600 --> 00:02:51.888 It's mutated in pancreatic cancer more

NOTE Confidence: 0.957862474

00:02:51.888 --> 00:02:55.280 than 95% of all screened patients.

NOTE Confidence: 0.957862474

00:02:55.280 --> 00:02:59.018 So immediately one would think that

NOTE Confidence: 0.957862474

00:02:59.018 --> 00:03:01.664 this would be a fantastic target to

NOTE Confidence: 0.957862474

00:03:01.664 --> 00:03:04.146 you know inhibit or pharmacologically

NOTE Confidence: 0.957862474

00:03:04.146 --> 00:03:06.886 target to treat pancreatic cancer

NOTE Confidence: 0.957862474

00:03:06.886 --> 00:03:09.667 and this knowledge has been out

NOTE Confidence: 0.957862474

00:03:09.667 --> 00:03:12.073 there for last 20 plus years.

NOTE Confidence: 0.957862474

00:03:12.080 --> 00:03:12.748 However,

NOTE Confidence: 0.957862474

00:03:12.748 --> 00:03:16.756 in pancreatic cancer there is no

NOTE Confidence: 0.957862474

00:03:16.756 --> 00:03:19.939 chaos targeted therapies that exist

NOTE Confidence: 0.957862474

00:03:19.939 --> 00:03:23.108 still And the key reason for that

NOTE Confidence: 0.957862474

00:03:23.108 --> 00:03:25.600 is chaos has been traditionally

NOTE Confidence: 0.957862474

00:03:25.600 --> 00:03:29.440 a very difficult to drug target.

NOTE Confidence: 0.957862474

00:03:29.440 --> 00:03:32.068 And we were really interested in

NOTE Confidence: 0.957862474

00:03:32.068 --> 00:03:34.869 this because this is here is a

NOTE Confidence: 0.957862474

00:03:34.869 --> 00:03:37.257 protein or a gene that is immediately

NOTE Confidence: 0.957862474

00:03:37.257 --> 00:03:38.628 correlated statistically with

NOTE Confidence: 0.957862474

00:03:38.628 --> 00:03:40.913 a particular form of cancer,

NOTE Confidence: 0.957862474

00:03:40.920 --> 00:03:41.880 pancreatic cancer.

NOTE Confidence: 0.957862474

00:03:41.880 --> 00:03:45.240 Why are we not targeting that protein?

NOTE Confidence: 0.957862474

00:03:45.240 --> 00:03:47.215 And then when we delved

NOTE Confidence: 0.957862474

00:03:47.215 --> 00:03:48.795 deeper into the literature,

NOTE Confidence: 0.957862474

00:03:48.800 --> 00:03:50.882 it became obvious to us that

NOTE Confidence: 0.957862474

00:03:50.882 --> 00:03:52.760 why it was not done.

NOTE Confidence: 0.957862474

00:03:52.760 --> 00:03:55.518 And we wanted to study this protein

NOTE Confidence: 0.957862474

00:03:55.518 --> 00:03:57.850 from a molecular standpoint to see

NOTE Confidence: 0.957862474

00:03:57.850 --> 00:04:00.803 if we can expose some new you know

NOTE Confidence: 0.957862474

00:04:00.803 --> 00:04:03.077 a pain points for the protein,

NOTE Confidence: 0.957862474

00:04:03.080 --> 00:04:05.208 some new Achilles heel in the protein

NOTE Confidence: 0.957862474

00:04:05.208 --> 00:04:07.920 that can be pharmacl logically targeted.

NOTE Confidence: 0.957862474

00:04:07.920 --> 00:04:11.315 And that is what kind of motivated

NOTE Confidence: 0.957862474

00:04:11.320 --> 00:04:13.560 our looking into this particular

NOTE Confidence: 0.957862474

00:04:13.560 --> 00:04:15.352 protein with our biophysical,

NOTE Confidence: 0.957862474

00:04:15.360 --> 00:04:17.560 newly developed biophysical techniques.

NOTE Confidence: 0.870727518846154

00:04:18.360 --> 00:04:20.824 So I mean it's it makes sense that

NOTE Confidence: 0.870727518846154

00:04:20.824 --> 00:04:23.638 if KRAS is mutated in the vast

NOTE Confidence: 0.870727518846154

00:04:23.638 --> 00:04:25.763 majority of pancreatic cancers that

NOTE Confidence: 0.870727518846154

00:04:25.840 --> 00:04:28.036 it would be an obvious target.

NOTE Confidence: 0.870727518846154

00:04:28.040 --> 00:04:33.290 Tell us more about why exactly previous

NOTE Confidence: 0.870727518846154

00:04:33.290 --> 00:04:35.870 labs found it so difficult to come

NOTE Confidence: 0.870727518846154

00:04:35.870 --> 00:04:38.396 up with a Ras targeted protein and

NOTE Confidence: 0.870727518846154

00:04:38.396 --> 00:04:40.862 and what the techniques that you

NOTE Confidence: 0.870727518846154

00:04:40.862 --> 00:04:43.564 have are that made you feel more

NOTE Confidence: 0.870727518846154

00:04:43.564 --> 00:04:45.736 confident that you could approach

NOTE Confidence: 0.870727518846154

00:04:45.736 --> 00:04:49.280 this task that others failed at.

NOTE Confidence: 0.893374011428572

00:04:50.160 --> 00:04:52.890 Right. So I'll answer the first question

NOTE Confidence: 0.893374011428572

00:04:52.890 --> 00:04:55.678 like why has it been so difficult?

NOTE Confidence: 0.893374011428572

00:04:55.680 --> 00:04:59.996 First, Ras is a very small protein.

NOTE Confidence: 0.893374011428572

00:05:00.000 --> 00:05:01.830 It doesn't have a lot of

NOTE Confidence: 0.893374011428572

00:05:01.830 --> 00:05:03.440 pockets where drugs can bind.

NOTE Confidence: 0.893374011428572

00:05:03.440 --> 00:05:05.800 It's a very shallow protein,

NOTE Confidence: 0.893374011428572

00:05:05.800 --> 00:05:08.400 small shallow protein with not

NOTE Confidence: 0.893374011428572

00:05:08.400 --> 00:05:11.680 very many deep pockets which are

NOTE Confidence: 0.893374011428572

00:05:11.680 --> 00:05:14.032 traditionally targeted by drugs.

NOTE Confidence: 0.893374011428572

00:05:14.032 --> 00:05:19.652 At the same time, Ras actually binds GTP.

NOTE Confidence: 0.893374011428572

00:05:19.652 --> 00:05:22.680 The nucleotide and it's affinity

NOTE Confidence: 0.893374011428572

00:05:22.680 --> 00:05:25.320 for GTP is also very tight.

NOTE Confidence: 0.893374011428572

00:05:25.320 --> 00:05:28.477 It is very difficult to make a

NOTE Confidence: 0.893374011428572

00:05:28.477 --> 00:05:30.559 GTP competitive inhibitor for Ras.

NOTE Confidence: 0.893374011428572

00:05:30.560 --> 00:05:33.038 I think as a function of that,

NOTE Confidence: 0.893374011428572

00:05:33.040 --> 00:05:36.118 because of these two main reasons,

NOTE Confidence: 0.893374011428572

00:05:36.120 --> 00:05:39.720 Ras has remained difficult to drug for long.

NOTE Confidence: 0.893374011428572

00:05:39.720 --> 00:05:41.880 Recently over the last five years,

NOTE Confidence: 0.893374011428572

00:05:41.880 --> 00:05:44.562 there had been new drugs against

NOTE Confidence: 0.893374011428572

00:05:44.562 --> 00:05:47.410 Ras which take the advantage of

NOTE Confidence: 0.893374011428572

00:05:47.410 --> 00:05:49.820 certain Ras mutants in cancer

NOTE Confidence: 0.893374011428572

00:05:49.820 --> 00:05:52.853 which can be covalently bound to

NOTE Confidence: 0.893374011428572

00:05:52.853 --> 00:05:55.835 drugs like the mutation at G12.

NOTE Confidence: 0.893374011428572

00:05:55.840 --> 00:05:58.294 The possession glycine 12 into a

NOTE Confidence: 0.893374011428572

00:05:58.294 --> 00:06:00.604 cysteine where the cysteine could be

NOTE Confidence: 0.893374011428572

00:06:00.604 --> 00:06:03.004 used as a covalent kind of prong to

NOTE Confidence: 0.893374011428572

00:06:03.076 --> 00:06:05.476 bring in a drug and bind it because

NOTE Confidence: 0.893374011428572

00:06:05.476 --> 00:06:08.902 there is no deep pockets to bind you

NOTE Confidence: 0.893374011428572

00:06:08.902 --> 00:06:11.194 know otherwise bind drug in Ross.

NOTE Confidence: 0.893374011428572

00:06:11.200 --> 00:06:11.992 However,

NOTE Confidence: 0.893374011428572

00:06:11.992 --> 00:06:15.513 in pancreatic cancer the G12C

NOTE Confidence: 0.893374011428572

00:06:15.513 --> 00:06:17.278 mutation is not that common.

NOTE Confidence: 0.893374011428572

00:06:17.280 --> 00:06:19.648 The most common mutations

NOTE Confidence: 0.893374011428572

00:06:19.648 --> 00:06:22.616 are G12VG12D which are not,

NOTE Confidence: 0.893374011428572

00:06:22.616 --> 00:06:25.438 you know capable of being targeted

NOTE Confidence: 0.893374011428572

00:06:25.438 --> 00:06:27.514 by this drug because they cannot

NOTE Confidence: 0.893374011428572

00:06:27.514 --> 00:06:29.240 be covalently modified.

NOTE Confidence: 0.893374011428572

00:06:29.240 --> 00:06:32.600 So there lies these open,

NOTE Confidence: 0.893374011428572

00:06:32.600 --> 00:06:36.045 you know, area a gap where OK,

NOTE Confidence: 0.893374011428572

00:06:36.045 --> 00:06:38.475 it can be used for certain

NOTE Confidence: 0.893374011428572

00:06:38.475 --> 00:06:40.508 cancers showing the G12C mutation.

NOTE Confidence: 0.893374011428572

00:06:40.508 --> 00:06:42.543 But what about pancreatic cancer

NOTE Confidence: 0.893374011428572

00:06:42.543 --> 00:06:44.520 where that mutation doesn't appear

NOTE Confidence: 0.893374011428572

00:06:44.520 --> 00:06:46.776 and the ones that appear cannot

NOTE Confidence: 0.893374011428572

00:06:46.839 --> 00:06:48.784 be targeted by covalent drugs.

NOTE Confidence: 0.893374011428572

00:06:48.784 --> 00:06:50.800 So what we did,

NOTE Confidence: 0.893374011428572

00:06:50.800 --> 00:06:53.200 we asked a different question.

NOTE Confidence: 0.893374011428572

00:06:53.200 --> 00:06:54.568 We asked that, OK,

NOTE Confidence: 0.893374011428572

00:06:54.568 --> 00:06:56.278 Ras doesn't have deep pockets,

NOTE Confidence: 0.893374011428572

00:06:56.280 --> 00:06:59.328 but can Ras actually form an

NOTE Confidence: 0.893374011428572

00:06:59.328 --> 00:07:01.360 oligomer or a dimer?

NOTE Confidence: 0.893374011428572

00:07:01.360 --> 00:07:04.650 And does that dimer actually have or

NOTE Confidence: 0.893374011428572

00:07:04.650 --> 00:07:06.727 dimerization or formation basically

NOTE Confidence: 0.893374011428572

00:07:06.727 --> 00:07:10.237 having multiple rust subunits come together,

NOTE Confidence: 0.893374011428572

00:07:10.240 --> 00:07:13.810 Does that have an impact on

NOTE Confidence: 0.893374011428572

00:07:13.810 --> 00:07:16.152 downstream signaling in physiological

NOTE Confidence: 0.893374011428572

00:07:16.152 --> 00:07:17.880 and oncogenic conditions?

NOTE Confidence: 0.893374011428572

00:07:17.880 --> 00:07:21.720 Because if that connection is established,

NOTE Confidence: 0.893374011428572

00:07:21.720 --> 00:07:25.302 then that oligomeric interface now becomes

NOTE Confidence: 0.893374011428572

00:07:25.302 --> 00:07:28.960 a target for pharmacological interventions.

NOTE Confidence: 0.893374011428572

00:07:28.960 --> 00:07:32.038 So with that kind of motivating

NOTE Confidence: 0.893374011428572

00:07:32.040 --> 00:07:33.604 factor as our guide,

NOTE Confidence: 0.893374011428572

00:07:33.604 --> 00:07:36.459 we asked the question that can we

NOTE Confidence: 0.893374011428572

00:07:36.459 --> 00:07:39.476 actually look at oligomeric status of Ras?

NOTE Confidence: 0.893374011428572

00:07:39.480 --> 00:07:42.216 But there lies a problem because

NOTE Confidence: 0.893374011428572

00:07:42.216 --> 00:07:44.040 looking at membrane protein,

NOTE Confidence: 0.893374011428572

00:07:44.040 --> 00:07:47.080 oligomeric organization has long remained

NOTE Confidence: 0.893374011428572

00:07:47.080 --> 00:07:50.120 A challenging problem in biophysics.

NOTE Confidence: 0.893374011428572

00:07:50.120 --> 00:07:53.000 It is a solved problem for soluble proteins,

NOTE Confidence: 0.893374011428572

00:07:53.000 --> 00:07:55.808 but with membrane proteins it is

NOTE Confidence: 0.893374011428572

00:07:55.808 --> 00:07:57.212 challenging primarily because

NOTE Confidence: 0.893374011428572

00:07:57.212 --> 00:07:58.760 of three reasons.

NOTE Confidence: 0.893374011428572

00:07:58.760 --> 00:08:01.904 The first reason is it is difficult to

NOTE Confidence: 0.893374011428572

00:08:01.904 --> 00:08:03.241 distinguish oligomeric organization

NOTE Confidence: 0.893374011428572

00:08:03.241 --> 00:08:06.103 from subunits that are just hanging

NOTE Confidence: 0.893374011428572

00:08:06.103 --> 00:08:08.639 around spatially proximal on the membrane.

NOTE Confidence: 0.893374011428572

00:08:08.640 --> 00:08:10.744 So we don't know that is are the

NOTE Confidence: 0.893374011428572

00:08:10.744 --> 00:08:12.412 two subunits of rust coming together

NOTE Confidence: 0.893374011428572

00:08:12.412 --> 00:08:14.840 to form a dimer on the membrane or

NOTE Confidence: 0.893374011428572

00:08:14.840 --> 00:08:17.090 the two subunits are just spatially

NOTE Confidence: 0.893374011428572

00:08:17.090 --> 00:08:19.112 proximal because of the technologies

NOTE Confidence: 0.893374011428572

00:08:19.112 --> 00:08:22.080 that were available to us till date.

NOTE Confidence: 0.893374011428572

00:08:22.080 --> 00:08:24.824 So my lab first developed a new

NOTE Confidence: 0.893374011428572

00:08:24.824 --> 00:08:26.000 technology to look,

NOTE Confidence: 0.893374011428572

00:08:26.000 --> 00:08:28.740 a generalized technology to look

NOTE Confidence: 0.893374011428572

00:08:28.740 --> 00:08:31.480 at membrane protein oligomeric organization.

NOTE Confidence: 0.893374011428572

00:08:31.480 --> 00:08:34.456 And then we applied that technology

NOTE Confidence: 0.893374011428572

00:08:34.456 --> 00:08:37.210 after having validated it to Ras

NOTE Confidence: 0.893374011428572

00:08:37.210 --> 00:08:39.905 to ask the question that can this

NOTE Confidence: 0.893374011428572

00:08:39.905 --> 00:08:40.290 hallmark

NOTE Confidence: 0.814819159

00:08:40.375 --> 00:08:42.850 oncogene form dimers or higher

NOTE Confidence: 0.814819159

00:08:42.850 --> 00:08:45.325 order oligomers on membranes and

NOTE Confidence: 0.814819159

00:08:45.411 --> 00:08:48.161 does oncogenic mutations alter this

NOTE Confidence: 0.814819159

00:08:48.161 --> 00:08:50.361 distribution because that will

NOTE Confidence: 0.814819159

00:08:50.361 --> 00:08:52.510 now expose an Achilles heel for

NOTE Confidence: 0.814819159

00:08:52.510 --> 00:08:55.548 Ras and we did this for K Ras in

NOTE Confidence: 0.814819159

00:08:55.548 --> 00:08:57.273 the context of pancreatic cancer.

NOTE Confidence: 0.9549015525

00:08:59.320 --> 00:09:02.000 And so, you know,

NOTE Confidence: 0.9549015525

00:09:02.000 --> 00:09:05.036 help me to understand, you know,

NOTE Confidence: 0.9549015525

00:09:05.040 --> 00:09:08.706 how exactly you take advantage of

NOTE Confidence: 0.9549015525

00:09:08.706 --> 00:09:13.718 this dimerization or oligomerization.

NOTE Confidence: 0.9549015525

00:09:13.720 --> 00:09:16.960 Does this happen in nature?

NOTE Confidence: 0.9549015525

00:09:16.960 --> 00:09:19.440 Does this happen in cancers?

NOTE Confidence: 0.9549015525

00:09:19.440 --> 00:09:22.600 Is this something that's inducible?

NOTE Confidence: 0.9549015525

00:09:22.600 --> 00:09:24.160 How does that work exactly?

NOTE Confidence: 0.92881205

00:09:24.960 --> 00:09:26.560 That's a great question actually.

NOTE Confidence: 0.92881205

00:09:26.560 --> 00:09:32.370 So what we realized is chaos in its

NOTE Confidence: 0.92881205

00:09:32.370 --> 00:09:35.065 wild type in its native state exists

NOTE Confidence: 0.92881205

00:09:35.065 --> 00:09:37.879 as a monomer dimer equilibrium.

NOTE Confidence: 0.92881205

00:09:37.880 --> 00:09:41.120 However, upon introduction of well

NOTE Confidence: 0.92881205

00:09:41.120 --> 00:09:43.712 known prominent oncogenic mutations,

NOTE Confidence: 0.92881205

00:09:43.720 --> 00:09:47.590 we saw that the population of dimers went up

NOTE Confidence: 0.92881205

00:09:47.590 --> 00:09:51.437 and the population of monomers went down.

NOTE Confidence: 0.92881205

00:09:51.440 --> 00:09:54.404 And the hypothesis here is with

NOTE Confidence: 0.92881205

00:09:54.404 --> 00:09:56.800 increased dimerization of K Ras,

NOTE Confidence: 0.92881205

00:09:56.800 --> 00:10:00.468 it may be now able to hyperactivate

NOTE Confidence: 0.92881205

00:10:00.468 --> 00:10:02.720 the downstream MAP K Ras,

NOTE Confidence: 0.92881205

00:10:02.720 --> 00:10:05.996 MAP K signaling pathway that has

NOTE Confidence: 0.92881205

00:10:06.000 --> 00:10:08.592 a huge role in cell proliferation

NOTE Confidence: 0.92881205

00:10:08.592 --> 00:10:10.320 and differentiation and that

NOTE Confidence: 0.92881205

00:10:10.396 --> 00:10:13.273 could be you know connected to the

NOTE Confidence: 0.92881205

00:10:13.273 --> 00:10:15.280 uncontrolled cell growth in cancer.

NOTE Confidence: 0.92881205

00:10:15.280 --> 00:10:19.488 So the connection is that increased

NOTE Confidence: 0.92881205

00:10:19.488 --> 00:10:22.896 dimers of chaos in the oncogenic

NOTE Confidence: 0.92881205

00:10:22.896 --> 00:10:26.108 mutation case actually may now trigger

NOTE Confidence: 0.92881205

00:10:26.108 --> 00:10:28.693 increased MAP case signaling which

NOTE Confidence: 0.92881205

00:10:28.693 --> 00:10:31.520 leads to uncontrolled cell growth.

NOTE Confidence: 0.92881205

00:10:31.520 --> 00:10:34.411 So we have shown that there is

NOTE Confidence: 0.92881205

00:10:34.411 --> 00:10:36.240 increased dimerization in cancer.

NOTE Confidence: 0.92881205

00:10:36.240 --> 00:10:38.944 Our next goal is to connect this with

NOTE Confidence: 0.92881205

00:10:38.944 --> 00:10:40.799 the downstream signaling aspect.

NOTE Confidence: 0.92881205

00:10:40.800 --> 00:10:43.800 And then we can say that, OK,

NOTE Confidence: 0.92881205

00:10:43.800 --> 00:10:45.360 great, increase dimer,

NOTE Confidence: 0.92881205

00:10:45.360 --> 00:10:47.440 increase signaling in cancer,

NOTE Confidence: 0.92881205

00:10:47.440 --> 00:10:49.880 if we break the dimer by a small

NOTE Confidence: 0.92881205

00:10:49.880 --> 00:10:51.600 molecule or by a mono body,

NOTE Confidence: 0.92881205

00:10:51.600 --> 00:10:54.246 a nano body that will reverted back

NOTE Confidence: 0.92881205

00:10:54.246 --> 00:10:56.916 to its wild type or native status

NOTE Confidence: 0.92881205

00:10:56.916 --> 00:11:00.624 and that may be able to stop the

NOTE Confidence: 0.92881205

00:11:00.624 --> 00:11:02.799 hyperactivated downstream signaling.

NOTE Confidence: 0.969051042

00:11:04.480 --> 00:11:06.904 And so tell us more about

NOTE Confidence: 0.969051042

00:11:06.904 --> 00:11:09.576 how that that works. I mean,

NOTE Confidence: 0.969051042

00:11:09.576 --> 00:11:12.744 because it sounds like you've already

NOTE Confidence: 0.969051042

00:11:12.744 --> 00:11:15.882 established that when this equilibrium,

NOTE Confidence: 0.969051042

00:11:15.882 --> 00:11:19.352 this monomer dimer equilibrium shifts

NOTE Confidence: 0.969051042

00:11:19.352 --> 00:11:22.466 towards dimerization that you have more

NOTE Confidence: 0.969051042

00:11:22.466 --> 00:11:24.945 of this downstream signaling, right?

NOTE Confidence: 0.969051042

00:11:24.945 --> 00:11:30.400 That is more like the oncogenic state and so.

NOTE Confidence: 0.969051042

00:11:30.400 --> 00:11:32.880 So I guess there's a couple of questions.

NOTE Confidence: 0.969051042

00:11:32.880 --> 00:11:36.520 One, is it possible in fact to break

NOTE Confidence: 0.969051042

00:11:36.520 --> 00:11:40.125 that and to shift these cells to

NOTE Confidence: 0.969051042

00:11:40.125 --> 00:11:43.570 a more monomeric state And two,

NOTE Confidence: 0.969051042

00:11:43.570 --> 00:11:48.140 does the monomeric state have have less

NOTE Confidence: 0.969051042

00:11:48.140 --> 00:11:51.560 downstream signaling that is less oncogenic?

NOTE Confidence: 0.969051042

00:11:51.560 --> 00:11:55.024 So tell us more about how you you

NOTE Confidence: 0.969051042

00:11:55.024 --> 00:11:57.415 can kind of revert these dimers

NOTE Confidence: 0.969051042

00:11:57.415 --> 00:12:01.240 back to a monomeric state, right.

NOTE Confidence: 0.969051042

00:12:01.240 --> 00:12:02.400 So

NOTE Confidence: 0.903965220769231

00:12:02.400 --> 00:12:04.176 with our new technology,

NOTE Confidence: 0.903965220769231

00:12:04.176 --> 00:12:07.615 the native nano bleach where we can look

NOTE Confidence: 0.903965220769231

00:12:07.615 --> 00:12:10.672 into redistribution of oligomeric assemblies,

NOTE Confidence: 0.903965220769231

00:12:10.672 --> 00:12:15.413 we can now start screening for small

NOTE Confidence: 0.903965220769231

00:12:15.413 --> 00:12:18.220 molecules or set antibody or a mono

NOTE Confidence: 0.903965220769231

00:12:18.220 --> 00:12:20.440 body that will revert the states.

NOTE Confidence: 0.903965220769231

00:12:20.440 --> 00:12:23.080 So this is not published in unpublished data.

NOTE Confidence: 0.903965220769231

00:12:23.080 --> 00:12:27.627 We have some early kind of indications

NOTE Confidence: 0.903965220769231

00:12:27.627 --> 00:12:31.953 that there is a mono body which when we

NOTE Confidence: 0.903965220769231

00:12:31.953 --> 00:12:35.229 screened using our technology can actually

NOTE Confidence: 0.903965220769231

00:12:35.229 --> 00:12:38.275 revert back the increased dimeric state

NOTE Confidence: 0.903965220769231

00:12:38.275 --> 00:12:41.820 of chaos back to its wild type levels.

NOTE Confidence: 0.903965220769231

00:12:41.820 --> 00:12:44.780 So we have evidence that that mono body

NOTE Confidence: 0.903965220769231

00:12:44.851 --> 00:12:47.840 exists and that existed in the literature,

NOTE Confidence: 0.903965220769231

00:12:47.840 --> 00:12:51.445 but there was not a good understanding

NOTE Confidence: 0.903965220769231

00:12:51.445 --> 00:12:54.473 of the mechanism of how it was

NOTE Confidence: 0.903965220769231

00:12:54.473 --> 00:12:56.534 able to kill oncogenic signaling.

NOTE Confidence: 0.903965220769231

00:12:56.534 --> 00:12:59.576 And now we have provided A

NOTE Confidence: 0.903965220769231

00:12:59.576 --> 00:13:01.240 mechanistic explanation that OK,

NOTE Confidence: 0.903965220769231

00:13:01.240 --> 00:13:04.240 that is happening by actually

NOTE Confidence: 0.903965220769231

00:13:04.240 --> 00:13:06.640 reducing the dimeric population.

NOTE Confidence: 0.903965220769231

00:13:06.640 --> 00:13:09.088 So that is our first indication

NOTE Confidence: 0.903965220769231

00:13:09.088 --> 00:13:12.240 that it can be actually broken.

NOTE Confidence: 0.903965220769231

00:13:12.240 --> 00:13:15.340 It can be reverted back to the OR you know

NOTE Confidence: 0.903965220769231

00:13:15.414 --> 00:13:18.438 to the wild type status of monomer dimer.

NOTE Confidence: 0.903965220769231

00:13:18.440 --> 00:13:20.615 The increased dimer can be

NOTE Confidence: 0.903965220769231

00:13:20.615 --> 00:13:23.255 actually pushed back and that is

NOTE Confidence: 0.903965220769231

00:13:23.255 --> 00:13:25.035 connected to decreased signaling.

NOTE Confidence: 0.903965220769231

00:13:25.040 --> 00:13:27.798 So that is a very exciting Ave.

NOTE Confidence: 0.903965220769231

00:13:27.800 --> 00:13:30.152 that we are exploring in our

NOTE Confidence: 0.903965220769231

00:13:30.152 --> 00:13:31.720 next set of studies.

NOTE Confidence: 0.913003154285714

00:13:32.520 --> 00:13:34.998 Fantastic. Well, we need to take a

NOTE Confidence: 0.913003154285714

00:13:34.998 --> 00:13:37.599 short break here for a medical minute.

NOTE Confidence: 0.913003154285714

00:13:37.600 --> 00:13:39.568 Please stay tuned to learn more

NOTE Confidence: 0.913003154285714

00:13:39.568 --> 00:13:41.389 about new methods in targeting

NOTE Confidence: 0.913003154285714

00:13:41.389 --> 00:13:43.599 pancreatic cancer with my guest,

NOTE Confidence: 0.913003154285714

00:13:43.600 --> 00:13:45.838 Doctor Moi Bhattacharya.

NOTE Confidence: 0.860036734

00:13:46.360 --> 00:13:48.380 Funding for Yale Cancer Answers

NOTE Confidence: 0.860036734

00:13:48.380 --> 00:13:50.400 comes from Smilo Cancer Hospital,

NOTE Confidence: 0.860036734

00:13:50.400 --> 00:13:52.200 where their Cancer Genetics and

NOTE Confidence: 0.860036734

00:13:52.200 --> 00:13:53.280 Prevention program includes

NOTE Confidence: 0.860036734

00:13:53.280 --> 00:13:55.395 a Colon Cancer Genetics and

NOTE Confidence: 0.860036734

00:13:55.395 --> 00:13:57.179 Prevention Program that provides

NOTE Confidence: 0.860036734

00:13:57.179 --> 00:13:58.517 comprehensive risk assessment,

NOTE Confidence: 0.860036734

00:13:58.520 --> 00:14:00.038 education and screening

NOTE Confidence: 0.8679131

00:14:02.280 --> 00:14:02.640 milocancerhospital.org

NOTE Confidence: 0.96481156

00:14:04.920 --> 00:14:06.800 Breast cancer is one of the

NOTE Confidence: 0.96481156

00:14:06.800 --> 00:14:08.320 most common cancers in women.

NOTE Confidence: 0.96481156

00:14:08.320 --> 00:14:09.640 In Connecticut alone,

NOTE Confidence: 0.96481156

00:14:09.640 --> 00:14:11.840 approximately 3500 women will be

NOTE Confidence: 0.96481156

00:14:11.840 --> 00:14:14.320 diagnosed with breast cancer this year,

NOTE Confidence: 0.96481156

00:14:14.320 --> 00:14:15.870 but there is hope thanks

NOTE Confidence: 0.96481156

00:14:15.870 --> 00:14:16.800 to earlier detection,

NOTE Confidence: 0.96481156

00:14:16.800 --> 00:14:17.919 non invasive treatments,

NOTE Confidence: 0.96481156

00:14:17.919 --> 00:14:20.157 and the development of novel therapies.

NOTE Confidence: 0.96481156

00:14:20.160 --> 00:14:21.804 To fight breast cancer,

NOTE Confidence: 0.96481156

00:14:21.804 --> 00:14:24.270 women should schedule a baseline mammogram

NOTE Confidence: 0.96481156

00:14:24.339 --> 00:14:27.030 beginning at age 40 or earlier if they have

NOTE Confidence: 0.96481156

00:14:27.030 --> 00:14:29.640 risk factors associated with the disease.

NOTE Confidence: 0.96481156

00:14:29.640 --> 00:14:31.260 With screening, early detection,

NOTE Confidence: 0.96481156

00:14:31.260 --> 00:14:32.880 and a healthy lifestyle,

NOTE Confidence: 0.96481156

00:14:32.880 --> 00:14:35.080 breast cancer can be defeated.

NOTE Confidence: 0.96481156

00:14:35.080 --> 00:14:36.884 Clinical trials are currently

NOTE Confidence: 0.96481156

00:14:36.884 --> 00:14:38.688 underway at federally designated

NOTE Confidence: 0.96481156

00:14:38.688 --> 00:14:40.080 comprehensive cancer centers,

NOTE Confidence: 0.96481156

00:14:40.080 --> 00:14:41.980 such as Yale Cancer Center

NOTE Confidence: 0.96481156

00:14:41.980 --> 00:14:43.880 and its Mylo Cancer Hospital,

NOTE Confidence: 0.96481156

00:14:43.880 --> 00:14:45.930 to make innovative new treatments

NOTE Confidence: 0.96481156

00:14:45.930 --> 00:14:47.160 available to patients.

NOTE Confidence: 0.96481156

00:14:47.160 --> 00:14:48.672 Digital breast tomosynthesis,

NOTE Confidence: 0.96481156

00:14:48.672 --> 00:14:51.696 or 3D mammography is also transforming

NOTE Confidence: 0.96481156

00:14:51.696 --> 00:14:54.472 breast cancer screening by significantly

NOTE Confidence: 0.96481156

00:14:54.472 --> 00:14:56.125 reducing unnecessary procedures

NOTE Confidence: 0.96481156

00:14:56.125 --> 00:14:58.720 while picking up more cancers.

NOTE Confidence: 0.96481156

00:14:58.720 --> 00:15:00.992 More information is available

NOTE Confidence: 0.96481156

00:15:00.992 --> 00:15:01.994 at yalecancercenter.org.

NOTE Confidence: 0.96481156

00:15:01.994 --> 00:15:04.598 You're listening to Connecticut Public Radio.

NOTE Confidence: 0.954169555

00:15:05.560 --> 00:15:07.798 Welcome back to Yale Cancer Answers.

NOTE Confidence: 0.954169555

00:15:07.800 --> 00:15:09.880 This is Doctor Aneesh Jagpar,

NOTE Confidence: 0.954169555

00:15:09.880 --> 00:15:11.637 and I'm joined tonight by my guest,

NOTE Confidence: 0.954169555

00:15:11.640 --> 00:15:13.041 Doctor Moi Bhattacharya.

NOTE Confidence: 0.954169555

00:15:13.041 --> 00:15:15.376 We're talking about new methods

NOTE Confidence: 0.954169555

00:15:15.376 --> 00:15:17.599 in targeting pancreatic cancer.

NOTE Confidence: 0.954169555

00:15:17.600 --> 00:15:19.120 And right before the break,

NOTE Confidence: 0.954169555

00:15:19.120 --> 00:15:21.346 Moi was telling us about some work

NOTE Confidence: 0.954169555

00:15:21.346 --> 00:15:23.160 that's been going on in her lab

NOTE Confidence: 0.954169555

00:15:23.160 --> 00:15:25.956 that looks at a new technology.

NOTE Confidence: 0.954169555

00:15:25.960 --> 00:15:28.000 Basically, the idea is that

NOTE Confidence: 0.954169555

00:15:28.000 --> 00:15:29.632 for most pancreatic cancers,

NOTE Confidence: 0.954169555

00:15:29.640 --> 00:15:32.676 there's a mutation in K Ras.

NOTE Confidence: 0.954169555

00:15:32.680 --> 00:15:36.280 And what she was able to discover was that

NOTE Confidence: 0.954169555

00:15:36.280 --> 00:15:39.160 these K Ras molecules sometimes dimerize.

NOTE Confidence: 0.954169555

00:15:39.160 --> 00:15:41.890 There's this, there's this balance

NOTE Confidence: 0.954169555

00:15:41.890 --> 00:15:44.074 between monomers and dimers.

NOTE Confidence: 0.954169555

00:15:44.080 --> 00:15:47.797 And when K Ras is in that dimeric state,

NOTE Confidence: 0.954169555

00:15:47.800 --> 00:15:51.196 that's when the oncogenic signaling happens.

NOTE Confidence: 0.954169555

00:15:51.200 --> 00:15:54.210 Well, it turns out that although we've

NOTE Confidence: 0.954169555

00:15:54.210 --> 00:15:57.240 known about K Ras for a long time,

NOTE Confidence: 0.954169555

00:15:57.240 --> 00:15:58.596 2 decades or so,

NOTE Confidence: 0.954169555

00:15:58.596 --> 00:16:00.291 nobody's ever been really able

NOTE Confidence: 0.954169555

00:16:00.291 --> 00:16:02.199 to target it effectively.

NOTE Confidence: 0.954169555

00:16:02.200 --> 00:16:04.685 Well, now there's new technology

NOTE Confidence: 0.954169555

00:16:04.685 --> 00:16:08.729 that might end up pushing K Ras to be

NOTE Confidence: 0.954169555

00:16:08.729 --> 00:16:11.557 more in its Monomeric state and have

NOTE Confidence: 0.954169555

00:16:11.557 --> 00:16:14.754 less of that oncogenic signaling and

NOTE Confidence: 0.954169555

00:16:14.754 --> 00:16:18.078 potentially that can be really exciting.

NOTE Confidence: 0.954169555

00:16:18.080 --> 00:16:20.272 So Moya, I want to pick up the

NOTE Confidence: 0.954169555

00:16:20.272 --> 00:16:21.518 discussion where we left it.

NOTE Confidence: 0.954169555

00:16:21.520 --> 00:16:25.916 So when you use this new technology,

NOTE Confidence: 0.954169555

00:16:25.920 --> 00:16:28.800 I think you called it nano bleach, right?

NOTE Confidence: 0.954169555

00:16:28.800 --> 00:16:30.240 Native nano bleach,

NOTE Confidence: 0.954169555

00:16:30.240 --> 00:16:31.690 native nano bleach.

NOTE Confidence: 0.954169555

00:16:31.690 --> 00:16:35.680 It's a first of all interesting name.

NOTE Confidence: 0.954169555

00:16:35.680 --> 00:16:37.360 I guess the first question is how

NOTE Confidence: 0.954169555

00:16:37.360 --> 00:16:39.600 did you come up with that name?

NOTE Confidence: 0.954169555

00:16:39.600 --> 00:16:42.528 But the other question is and

NOTE Confidence: 0.954169555

00:16:42.528 --> 00:16:44.480 maybe tied to this,

NOTE Confidence: 0.954169555

00:16:44.480 --> 00:16:47.476 can you talk a little bit about

NOTE Confidence: 0.954169555

00:16:47.480 --> 00:16:50.560 how exactly this is delivered

NOTE Confidence: 0.954169555

00:16:50.560 --> 00:16:52.360 and what the side effects are,

NOTE Confidence: 0.82080306625

00:16:53.320 --> 00:16:57.130 right. So the native nano bleach

NOTE Confidence: 0.82080306625

00:16:57.130 --> 00:17:00.405 technology is basically a way to look

NOTE Confidence: 0.82080306625

00:17:00.405 --> 00:17:03.078 into the changes in the oligomeric

NOTE Confidence: 0.82080306625

00:17:03.078 --> 00:17:05.978 organization of membrane proteins in

NOTE Confidence: 0.82080306625

00:17:05.978 --> 00:17:09.839 the context of their native membranes.

NOTE Confidence: 0.82080306625

00:17:09.840 --> 00:17:13.375 So the way we develop this technology

NOTE Confidence: 0.82080306625

00:17:13.375 --> 00:17:15.920 is it has remained A challenging problem

NOTE Confidence: 0.82080306625

00:17:15.920 --> 00:17:17.723 to look at oligomeric organization

NOTE Confidence: 0.82080306625

00:17:17.723 --> 00:17:19.997 of membrane proteins due to many,

NOTE Confidence: 0.82080306625

00:17:20.000 --> 00:17:21.623 many different reasons.

NOTE Confidence: 0.82080306625

00:17:21.623 --> 00:17:25.960 I think the most prominent reason of those

NOTE Confidence: 0.82080306625

00:17:25.960 --> 00:17:28.858 is the fact that the membrane proteins

NOTE Confidence: 0.82080306625

00:17:28.858 --> 00:17:32.480 sit in the in a pool of native lipids,

NOTE Confidence: 0.82080306625

00:17:32.480 --> 00:17:35.000 so their buffering media

NOTE Confidence: 0.82080306625

00:17:35.000 --> 00:17:37.520 is comprised of lipids.

NOTE Confidence: 0.82080306625

00:17:37.520 --> 00:17:41.080 Now most preparations of looking

NOTE Confidence: 0.82080306625

00:17:41.080 --> 00:17:43.928 biophysically into membrane proteins

NOTE Confidence: 0.82080306625

00:17:43.928 --> 00:17:46.890 erase this native membrane context.

NOTE Confidence: 0.82080306625

00:17:46.890 --> 00:17:49.840 Their native milieu is gone,

NOTE Confidence: 0.82080306625

00:17:49.840 --> 00:17:52.120 and more often than not,

NOTE Confidence: 0.82080306625

00:17:52.120 --> 00:17:55.186 this native locale of the membrane

NOTE Confidence: 0.82080306625

00:17:55.186 --> 00:17:57.989 proteins is really important in

NOTE Confidence: 0.82080306625

00:17:57.989 --> 00:17:59.999 templating their organization,

NOTE Confidence: 0.82080306625

00:18:00.000 --> 00:18:02.760 their function, the downstream signaling,

NOTE Confidence: 0.82080306625

00:18:02.760 --> 00:18:04.044 and so on.

NOTE Confidence: 0.82080306625

00:18:04.044 --> 00:18:06.184 But there exists really no

NOTE Confidence: 0.82080306625

00:18:06.184 --> 00:18:08.474 technology to look at, you know,

NOTE Confidence: 0.82080306625

00:18:08.474 --> 00:18:09.485 membrane proteins without

NOTE Confidence: 0.82080306625

00:18:09.485 --> 00:18:10.833 the use of detergents,

NOTE Confidence: 0.82080306625

00:18:10.840 --> 00:18:13.374 which is what is commonly used that

NOTE Confidence: 0.82080306625

00:18:13.374 --> 00:18:16.239 strips off this native membrane context.

NOTE Confidence: 0.82080306625

00:18:16.240 --> 00:18:17.924 That's the first problem.

NOTE Confidence: 0.82080306625

00:18:17.924 --> 00:18:20.918 The second problem is often when we

NOTE Confidence: 0.82080306625

00:18:20.918 --> 00:18:22.878 are looking at membrane proteins

NOTE Confidence: 0.82080306625

00:18:22.878 --> 00:18:25.320 we are using light microscopy.

NOTE Confidence: 0.82080306625

00:18:25.320 --> 00:18:27.612 And using light microscopy,

NOTE Confidence: 0.82080306625

00:18:27.612 --> 00:18:31.440 it is very difficult to distinguish if

NOTE Confidence: 0.82080306625

00:18:31.440 --> 00:18:34.700 two subunits of the protein are, say,

NOTE Confidence: 0.82080306625

00:18:34.700 --> 00:18:37.360 at 100 nanometer apart from each other,

NOTE Confidence: 0.82080306625

00:18:37.360 --> 00:18:40.251 or 10 nanometer apart or five nanometer

NOTE Confidence: 0.82080306625

00:18:40.251 --> 00:18:43.280 apart when they're truly forming a complex.

NOTE Confidence: 0.82080306625

00:18:43.280 --> 00:18:45.772 And this is because something that is

NOTE Confidence: 0.82080306625

00:18:45.772 --> 00:18:47.799 called the diffraction limit of light,

NOTE Confidence: 0.82080306625

00:18:47.800 --> 00:18:51.517 which does not allow us to distinguish

NOTE Confidence: 0.82080306625

00:18:51.520 --> 00:18:54.327 2 or more particles as you know

NOTE Confidence: 0.82080306625

00:18:54.327 --> 00:18:56.539 individual ones when they're closer

NOTE Confidence: 0.82080306625

00:18:56.539 --> 00:18:59.317 than 200 nanometer of each other.

NOTE Confidence: 0.82080306625

00:18:59.320 --> 00:19:01.438 So that is the second challenge.

NOTE Confidence: 0.82080306625

00:19:01.440 --> 00:19:03.890 So we didn't have a technology to

NOTE Confidence: 0.82080306625

00:19:03.890 --> 00:19:05.923 look into organization of membrane

NOTE Confidence: 0.82080306625

00:19:05.923 --> 00:19:07.755 proteins using light microscopy.

NOTE Confidence: 0.82080306625

00:19:07.760 --> 00:19:08.646 And finally,

NOTE Confidence: 0.82080306625

00:19:08.646 --> 00:19:11.304 any technique that looks into this

NOTE Confidence: 0.82080306625

00:19:11.304 --> 00:19:13.777 question has to work with proteins

NOTE Confidence: 0.82080306625

00:19:13.777 --> 00:19:16.541 at a wide range of expression levels

NOTE Confidence: 0.82080306625

00:19:16.541 --> 00:19:19.109 including proteins as they are produced

NOTE Confidence: 0.82080306625

00:19:19.109 --> 00:19:21.990 in the cell without over expressing

NOTE Confidence: 0.82080306625

00:19:21.990 --> 00:19:24.640 them without with minimal manipulation

NOTE Confidence: 0.82080306625

00:19:24.640 --> 00:19:27.400 basically to the native environment.

NOTE Confidence: 0.82080306625

00:19:27.400 --> 00:19:30.992 So we realized that we have now we

NOTE Confidence: 0.82080306625

00:19:30.992 --> 00:19:34.894 used up an antipathic copolymer to

NOTE Confidence: 0.82080306625

00:19:34.894 --> 00:19:38.514 basically cut out membrane protein

NOTE Confidence: 0.82080306625

00:19:38.520 --> 00:19:41.256 from you know circular patches of

NOTE Confidence: 0.82080306625

00:19:41.256 --> 00:19:43.080 the native membrane environment.

NOTE Confidence: 0.82080306625

00:19:43.080 --> 00:19:45.831 Think of it as cutting out cookies

NOTE Confidence: 0.82080306625

00:19:45.831 --> 00:19:48.320 out of native membrane dough.

NOTE Confidence: 0.82080306625

00:19:48.320 --> 00:19:49.880 So you have the membrane.

NOTE Confidence: 0.82080306625

00:19:49.880 --> 00:19:51.360 You're cutting out this cookies.

NOTE Confidence: 0.82080306625

00:19:51.360 --> 00:19:52.132 Each cookie,

NOTE Confidence: 0.82080306625

00:19:52.132 --> 00:19:54.834 which is about 10 nanometer in diameter,

NOTE Confidence: 0.82080306625

00:19:54.840 --> 00:19:57.768 contains all the subunits of a

NOTE Confidence: 0.82080306625

00:19:57.768 --> 00:19:59.720 membrane protein of interest.

NOTE Confidence: 0.82080306625

00:19:59.720 --> 00:20:02.258 Then you count how many subunits

NOTE Confidence: 0.82080306625

00:20:02.258 --> 00:20:04.942 are of the membrane protein of

NOTE Confidence: 0.82080306625

00:20:04.942 --> 00:20:07.672 your interest is present in that

NOTE Confidence: 0.82080306625

00:20:07.672 --> 00:20:10.078 10 nanometer cookie. So now.

NOTE Confidence: 0.82080306625

00:20:10.078 --> 00:20:13.011 We have overcome the problem of the

NOTE Confidence: 0.82080306625

00:20:13.011 --> 00:20:15.210 diffraction limit of light because

NOTE Confidence: 0.82080306625

00:20:15.210 --> 00:20:17.766 we are imposing A lateral spatial

NOTE Confidence: 0.82080306625

00:20:17.848 --> 00:20:20.323 resolution of 10 nanometer physically

NOTE Confidence: 0.82080306625

00:20:20.323 --> 00:20:23.248 using our sample because we are

NOTE Confidence: 0.82080306625

00:20:23.248 --> 00:20:25.488 counting the number of subunits

NOTE Confidence: 0.82080306625

00:20:25.488 --> 00:20:28.140 within each native nano disk which

NOTE Confidence: 0.82080306625

00:20:28.140 --> 00:20:30.474 is what we call these cookies.

NOTE Confidence: 0.82080306625

00:20:30.480 --> 00:20:34.805 So that is the reason why we named

NOTE Confidence: 0.82080306625

00:20:34.805 --> 00:20:36.959 our technology native nano bleach,

NOTE Confidence: 0.82080306625

00:20:36.960 --> 00:20:39.648 because it is native nano disk

NOTE Confidence: 0.82080306625

00:20:39.648 --> 00:20:41.943 photo bleaching technology where we

NOTE Confidence: 0.82080306625

00:20:41.943 --> 00:20:44.078 are counting using photo bleaching

NOTE Confidence: 0.82080306625

00:20:44.078 --> 00:20:45.786 analysis the number of

NOTE Confidence: 0.872879619

00:20:45.858 --> 00:20:47.708 subunits of a protein that

NOTE Confidence: 0.872879619

00:20:47.708 --> 00:20:49.558 is within each nano disk.

NOTE Confidence: 0.872879619

00:20:49.560 --> 00:20:52.000 Now from this point on,

NOTE Confidence: 0.872879619

00:20:52.000 --> 00:20:54.520 we have now a generalized technique

NOTE Confidence: 0.872879619

00:20:54.520 --> 00:20:57.375 that actually can look into oligomeric

NOTE Confidence: 0.872879619

00:20:57.375 --> 00:21:00.120 organization of any membrane protein,

NOTE Confidence: 0.872879619

00:21:00.120 --> 00:21:03.040 not just KRAS, but any,

NOTE Confidence: 0.872879619

00:21:03.040 --> 00:21:05.476 any of your favorite membrane protein.

NOTE Confidence: 0.872879619

00:21:05.480 --> 00:21:08.600 And that is how we developed a new

NOTE Confidence: 0.872879619

00:21:08.600 --> 00:21:10.869 technology that made asking this

NOTE Confidence: 0.872879619

00:21:10.869 --> 00:21:13.677 question that does actually you know

NOTE Confidence: 0.872879619

00:21:13.677 --> 00:21:16.535 Kairos form dimers or higher order

NOTE Confidence: 0.872879619

00:21:16.535 --> 00:21:18.840 oligomers and what happens upon

NOTE Confidence: 0.872879619

00:21:18.840 --> 00:21:20.872 oncogenic mutations even possible

NOTE Confidence: 0.872879619

00:21:20.872 --> 00:21:23.412 because this question was intractable

NOTE Confidence: 0.872879619

00:21:23.412 --> 00:21:25.919 without the advent of this technology.

NOTE Confidence: 0.961936302

00:21:27.920 --> 00:21:29.840 And so this is great.

NOTE Confidence: 0.961936302

00:21:29.840 --> 00:21:31.884 I mean it sounds really exciting that

NOTE Confidence: 0.961936302

00:21:31.884 --> 00:21:34.571 you know you found a way to look at

NOTE Confidence: 0.961936302

00:21:34.571 --> 00:21:36.440 these membrane proteins and study them.

NOTE Confidence: 0.961936302

00:21:36.440 --> 00:21:40.862 You've found a way to get the

NOTE Confidence: 0.961936302

00:21:40.862 --> 00:21:43.717 dimers to separate into monomers.

NOTE Confidence: 0.961936302

00:21:43.720 --> 00:21:46.198 So you know shifting that balance

NOTE Confidence: 0.961936302

00:21:46.198 --> 00:21:48.608 and and you've demonstrated at least

NOTE Confidence: 0.961936302

00:21:48.608 --> 00:21:50.333 in early unpublished work that

NOTE Confidence: 0.961936302

00:21:50.333 --> 00:21:52.612 there is in the monomeric state

NOTE Confidence: 0.961936302

00:21:52.612 --> 00:21:54.958 which you're able to shift these

NOTE Confidence: 0.961936302

00:21:54.960 --> 00:21:57.760 these molecules cules too there's

NOTE Confidence: 0.961936302

00:21:57.760 --> 00:22:00.560 less of that downstream signaling.

NOTE Confidence: 0.961936302

00:22:00.560 --> 00:22:03.180 So then the question becomes

NOTE Confidence: 0.961936302

00:22:03.180 --> 00:22:05.800 that's great in the lab,

NOTE Confidence: 0.961936302

00:22:05.800 --> 00:22:09.275 how do you get that into people and

NOTE Confidence: 0.961936302

00:22:09.275 --> 00:22:11.760 what are the side effects of this

NOTE Confidence: 0.965653216666667

00:22:12.320 --> 00:22:15.332 right. So you know,

NOTE Confidence: 0.965653216666667

00:22:15.332 --> 00:22:18.706 we are approaching this question

NOTE Confidence: 0.965653216666667

00:22:18.706 --> 00:22:21.194 from a molecular framework,

NOTE Confidence: 0.965653216666667

00:22:21.200 --> 00:22:22.655 you know perspective.

NOTE Confidence: 0.965653216666667

00:22:22.655 --> 00:22:26.758 And I think the next steps to moving

NOTE Confidence: 0.965653216666667

00:22:26.758 --> 00:22:29.194 towards more translational research

NOTE Confidence: 0.965653216666667

00:22:29.194 --> 00:22:33.502 with this would be to actually scream

NOTE Confidence: 0.965653216666667

00:22:33.502 --> 00:22:37.000 now that we have established that

NOTE Confidence: 0.965653216666667

00:22:37.000 --> 00:22:39.610 Dimer's actually may be connected

NOTE Confidence: 0.965653216666667

00:22:39.610 --> 00:22:42.220 to the hyperactive signaling in

NOTE Confidence: 0.965653216666667

00:22:42.307 --> 00:22:44.960 Ras mutant cancers and it can be,

NOTE Confidence: 0.965653216666667

00:22:44.960 --> 00:22:48.256 you know when that is reverted back that

NOTE Confidence: 0.965653216666667

00:22:48.256 --> 00:22:50.459 hyperactive signaling is ameliorated 1.

NOTE Confidence: 0.965653216666667

00:22:50.459 --> 00:22:53.112 Can think of using this as a

NOTE Confidence: 0.965653216666667

00:22:53.112 --> 00:22:55.104 screening platform for say small

NOTE Confidence: 0.965653216666667

00:22:55.104 --> 00:22:57.420 molecules that will now break the

NOTE Confidence: 0.965653216666667

00:22:57.420 --> 00:23:00.570 Ras dimers or other form of drugs

NOTE Confidence: 0.965653216666667

00:23:00.570 --> 00:23:02.358 like antibodies or nanobodies

NOTE Confidence: 0.965653216666667

00:23:02.360 --> 00:23:04.640 that will break this Ras dimer.

NOTE Confidence: 0.965653216666667

00:23:04.640 --> 00:23:08.465 So that'll I think be the step one to

NOTE Confidence: 0.965653216666667

00:23:08.465 --> 00:23:10.484 identify new new molecular competence

NOTE Confidence: 0.965653216666667

00:23:10.484 --> 00:23:13.438 that's going to now break this dimer.

NOTE Confidence: 0.965653216666667

00:23:13.440 --> 00:23:15.400 Once we have identified that,

NOTE Confidence: 0.965653216666667

00:23:15.400 --> 00:23:16.918 then we go to Step 2.

NOTE Confidence: 0.965653216666667

00:23:16.920 --> 00:23:18.792 Are these molecular components

NOTE Confidence: 0.965653216666667

00:23:18.792 --> 00:23:21.600 that are capable of breaking the

NOTE Confidence: 0.965653216666667

00:23:21.674 --> 00:23:24.470 dimers actually work in the setup

NOTE Confidence: 0.965653216666667

00:23:24.470 --> 00:23:26.972 of animal models And then of

NOTE Confidence: 0.965653216666667

00:23:26.972 --> 00:23:29.520 course move that on to trials and

NOTE Confidence: 0.965653216666667

00:23:29.607 --> 00:23:32.197 patients and so on and so forth.

NOTE Confidence: 0.965653216666667

00:23:32.200 --> 00:23:36.440 I think the this is going to be one approach.

NOTE Confidence: 0.965653216666667

00:23:36.440 --> 00:23:39.051 The other approach is to go back

NOTE Confidence: 0.965653216666667

00:23:39.051 --> 00:23:41.956 and look into the literature and see

NOTE Confidence: 0.965653216666667

00:23:41.956 --> 00:23:44.680 that if there were other already

NOTE Confidence: 0.965653216666667

00:23:44.680 --> 00:23:47.080 existing monobodies or antibodies

NOTE Confidence: 0.965653216666667

00:23:47.080 --> 00:23:50.521 that were shown to reduce hyperactive

NOTE Confidence: 0.965653216666667

00:23:50.521 --> 00:23:52.726 signaling in Ras mutant cancer

NOTE Confidence: 0.965653216666667

00:23:52.726 --> 00:23:55.578 and can be actually explain their

NOTE Confidence: 0.965653216666667

00:23:55.578 --> 00:23:58.118 function using the Ras dimerization.

NOTE Confidence: 0.965653216666667

00:23:58.120 --> 00:24:00.472 You know decrease in in the

NOTE Confidence: 0.965653216666667

00:24:00.472 --> 00:24:02.040 in the cancer setup.

NOTE Confidence: 0.965653216666667

00:24:02.040 --> 00:24:04.126 So I think the first step would

NOTE Confidence: 0.965653216666667

00:24:04.126 --> 00:24:05.908 be discovery of these molecular

NOTE Confidence: 0.965653216666667

00:24:05.908 --> 00:24:08.380 components that can break the dimers

NOTE Confidence: 0.965653216666667

00:24:08.380 --> 00:24:10.684 and decrease signaling and then

NOTE Confidence: 0.965653216666667

00:24:10.684 --> 00:24:13.216 the second component will be moving

NOTE Confidence: 0.965653216666667

00:24:13.216 --> 00:24:16.451 this along to the next steps more

NOTE Confidence: 0.965653216666667

00:24:16.451 --> 00:24:18.756 translational steps side effect wise.

NOTE Confidence: 0.965653216666667

00:24:18.760 --> 00:24:21.909 The one thing I can think of is you

NOTE Confidence: 0.965653216666667

00:24:21.909 --> 00:24:24.690 know Ras as we found K Ras exists as

NOTE Confidence: 0.965653216666667

00:24:24.771 --> 00:24:27.396 a monomer and dimer to begin with.

NOTE Confidence: 0.965653216666667

00:24:27.400 --> 00:24:30.400 It has an equilibrium roughly 5050,

NOTE Confidence: 0.965653216666667

00:24:30.400 --> 00:24:32.680 sixty, forty I would say.

NOTE Confidence: 0.965653216666667

00:24:32.680 --> 00:24:35.866 And then only in the oncogenic setup

NOTE Confidence: 0.965653216666667

00:24:35.866 --> 00:24:40.190 the dimers go up up to like 70% and

NOTE Confidence: 0.965653216666667

00:24:40.190 --> 00:24:43.235 the monomers go down to say 30%.

NOTE Confidence: 0.965653216666667

00:24:43.240 --> 00:24:47.520 We have to revert the dimers back

NOTE Confidence: 0.965653216666667

00:24:47.520 --> 00:24:49.520 to wild type levels,

NOTE Confidence: 0.965653216666667

00:24:49.520 --> 00:24:51.620 but we don't want to break maybe

NOTE Confidence: 0.965653216666667

00:24:51.620 --> 00:24:53.544 the entirety of the dimers because

NOTE Confidence: 0.965653216666667

00:24:53.544 --> 00:24:56.173 we know that in the native state it

NOTE Confidence: 0.965653216666667

00:24:56.173 --> 00:24:58.159 already exists as a monomer dimer

NOTE Confidence: 0.965653216666667

00:24:58.159 --> 00:25:00.564 and breaking the entire dimeric

NOTE Confidence: 0.965653216666667

00:25:00.564 --> 00:25:04.074 population may actually be detrimental.

NOTE Confidence: 0.965653216666667

00:25:04.080 --> 00:25:06.465 So it's like, you know, an Abacus scale.

NOTE Confidence: 0.965653216666667

00:25:06.465 --> 00:25:08.595 We are trying to move it,

NOTE Confidence: 0.965653216666667

00:25:08.600 --> 00:25:11.064 tune it to the perfect level where the

NOTE Confidence: 0.965653216666667

00:25:11.064 --> 00:25:13.879 dimers are brought back to the native levels,

NOTE Confidence: 0.965653216666667

00:25:13.880 --> 00:25:16.784 but not like completely ablated because

NOTE Confidence: 0.965653216666667

00:25:16.784 --> 00:25:20.287 I can foresee that that might actually

NOTE Confidence: 0.965653216666667

00:25:20.287 --> 00:25:23.239 have some side effects like some,

NOTE Confidence: 0.965653216666667

00:25:23.240 --> 00:25:24.168 you know,

NOTE Confidence: 0.965653216666667

00:25:24.168 --> 00:25:26.952 negative effects because Ross signaling is

NOTE Confidence: 0.965653216666667

00:25:26.952 --> 00:25:29.238 absolutely critical for our cell growth,

NOTE Confidence: 0.965653216666667

00:25:29.240 --> 00:25:30.509 maintenance and proliferation

NOTE Confidence: 0.965653216666667

00:25:30.509 --> 00:25:33.047 and we have to just recalibrate

NOTE Confidence: 0.965653216666667

00:25:33.047 --> 00:25:35.160 things back to the native levels.

NOTE Confidence: 0.7678646

00:25:37.400 --> 00:25:42.200 So can you, I mean it sounds like the,

NOTE Confidence: 0.7678646

00:25:42.200 --> 00:25:45.168 you know we are at the beginning stages

NOTE Confidence: 0.7678646

00:25:45.168 --> 00:25:48.355 of what might be a really exciting Rd.

NOTE Confidence: 0.7678646

00:25:48.360 --> 00:25:50.663 Can you talk a little bit about

NOTE Confidence: 0.7678646

00:25:50.663 --> 00:25:52.350 how this technology might be

NOTE Confidence: 0.7678646

00:25:52.350 --> 00:25:54.240 used in other cancers as well,

NOTE Confidence: 0.7678646

00:25:54.240 --> 00:25:55.925 I mean Ras doesn't exist

NOTE Confidence: 0.7678646

00:25:55.925 --> 00:25:57.273 just in pancreatic cancer,

NOTE Confidence: 0.956451538333333

00:25:57.640 --> 00:25:59.780 absolutely, that's a great question

NOTE Confidence: 0.956451538333333

00:25:59.780 --> 00:26:02.560 because we are actually starting to study.

NOTE Confidence: 0.956451538333333

00:26:02.560 --> 00:26:07.215 So Ras actually comes in as like four

NOTE Confidence: 0.956451538333333

00:26:07.215 --> 00:26:09.640 different isoforms and splice variants.

NOTE Confidence: 0.956451538333333

00:26:09.640 --> 00:26:10.900 There's K Ras,

NOTE Confidence: 0.956451538333333

00:26:10.900 --> 00:26:13.840 4A and 4B which are splice variants,

NOTE Confidence: 0.956451538333333

00:26:13.840 --> 00:26:17.476 and then there is H Ras and N Ras.

NOTE Confidence: 0.956451538333333

00:26:17.480 --> 00:26:19.680 Now it was shown very,

NOTE Confidence: 0.956451538333333

00:26:19.680 --> 00:26:22.296 very nicely over the last, you know,

NOTE Confidence: 0.956451538333333

00:26:22.296 --> 00:26:25.012 a beautiful work over the last three

NOTE Confidence: 0.956451538333333

00:26:25.012 --> 00:26:28.680 decades that each of the Ras isoform

NOTE Confidence: 0.956451538333333

00:26:28.680 --> 00:26:32.724 seems to have a prominent role in

NOTE Confidence: 0.956451538333333

00:26:32.724 --> 00:26:35.636 a given type of cancer or a given,

NOTE Confidence: 0.956451538333333

00:26:35.640 --> 00:26:37.080 you know, set of cancers.

NOTE Confidence: 0.956451538333333

00:26:37.080 --> 00:26:39.500 For example, Keras is really

NOTE Confidence: 0.956451538333333

00:26:39.500 --> 00:26:41.436 prominent in pancreatic cancer,

NOTE Confidence: 0.956451538333333

00:26:41.440 --> 00:26:45.570 lung cancer, whereas Enras mutations

NOTE Confidence: 0.956451538333333

00:26:45.570 --> 00:26:48.874 really prominent in melanomas.

NOTE Confidence: 0.956451538333333

00:26:48.880 --> 00:26:51.172 So what is this?

NOTE Confidence: 0.956451538333333

00:26:51.172 --> 00:26:52.318 You know,

NOTE Confidence: 0.956451538333333

00:26:52.320 --> 00:26:54.858 what is the connection between different

NOTE Confidence: 0.956451538333333

00:26:54.858 --> 00:26:57.022 Ras isoforms and their connection

NOTE Confidence: 0.956451538333333

00:26:57.022 --> 00:26:59.440 to a particular type of cancer?

NOTE Confidence: 0.956451538333333

00:26:59.440 --> 00:27:01.560 How are these isoforms different?

NOTE Confidence: 0.956451538333333

00:27:01.560 --> 00:27:03.525 And that's actually an important

NOTE Confidence: 0.956451538333333

00:27:03.525 --> 00:27:06.402 question because if you look at sequence

NOTE Confidence: 0.956451538333333

00:27:06.402 --> 00:27:08.517 identity between the Ras isoforms,

NOTE Confidence: 0.956451538333333

00:27:08.520 --> 00:27:10.578 which is often what you know

NOTE Confidence: 0.956451538333333

00:27:10.578 --> 00:27:13.079 biologists look at to see if the

NOTE Confidence: 0.956451538333333

00:27:13.079 --> 00:27:14.839 two proteins are very similar,

NOTE Confidence: 0.956451538333333

00:27:14.840 --> 00:27:16.595 different or if they're very

NOTE Confidence: 0.956451538333333

00:27:16.595 --> 00:27:17.999 different from each other,

NOTE Confidence: 0.956451538333333

00:27:18.000 --> 00:27:21.032 you will see that the Ras isoforms are

NOTE Confidence: 0.956451538333333

00:27:21.032 --> 00:27:22.759 remarkably identical to each other.

NOTE Confidence: 0.956451538333333

00:27:22.760 --> 00:27:24.920 They actually have about 90%

NOTE Confidence: 0.956451538333333

00:27:24.920 --> 00:27:27.600 sequence identity with each other.

NOTE Confidence: 0.956451538333333

00:27:27.600 --> 00:27:30.554 Despite that, despite being so you know,

NOTE Confidence: 0.956451538333333

00:27:30.560 --> 00:27:32.285 similar in sequence,

NOTE Confidence: 0.956451538333333

00:27:32.285 --> 00:27:35.160 they are actually playing out.

NOTE Confidence: 0.956451538333333

00:27:35.160 --> 00:27:38.520 They seem to be having different,

NOTE Confidence: 0.956451538333333

00:27:38.520 --> 00:27:39.891 you know, prominence,

NOTE Confidence: 0.956451538333333

00:27:39.891 --> 00:27:41.719 different levels of prominence,

NOTE Confidence: 0.956451538333333

00:27:41.720 --> 00:27:44.318 prominence in different types of cancers,

NOTE Confidence: 0.956451538333333

00:27:44.320 --> 00:27:46.435 different oncogenic mutations

NOTE Confidence: 0.956451538333333

00:27:46.435 --> 00:27:49.960 are playing different roles in

NOTE Confidence: 0.956451538333333

00:27:49.960 --> 00:27:51.548 different types of cancers.

NOTE Confidence: 0.956451538333333

00:27:51.548 --> 00:27:55.145 So there is I think a lot of mystery

NOTE Confidence: 0.956451538333333

00:27:55.145 --> 00:27:57.825 that is still unsolved that where

NOTE Confidence: 0.956451538333333

00:27:57.825 --> 00:28:00.915 is all this fidelity coming from?

NOTE Confidence: 0.956451538333333

00:28:00.920 --> 00:28:02.660 How are these isoforms,

NOTE Confidence: 0.956451538333333

00:28:02.660 --> 00:28:04.835 which are apparently very similar,

NOTE Confidence: 0.956451538333333

00:28:04.840 --> 00:28:05.800 playing, you know,

NOTE Confidence: 0.956451538333333

00:28:05.800 --> 00:28:07.400 very distinct roles in different

NOTE Confidence: 0.956451538333333

00:28:07.400 --> 00:28:08.520 types of cancers.

NOTE Confidence: 0.956451538333333

00:28:08.520 --> 00:28:10.676 So those are the kind of questions,

NOTE Confidence: 0.956451538333333

00:28:10.680 --> 00:28:12.660 like basic science questions,

NOTE Confidence: 0.956451538333333

00:28:12.660 --> 00:28:15.416 We are trying to, you know,

NOTE Confidence: 0.956451538333333

00:28:15.416 --> 00:28:17.356 approach next with our studies.

NOTE Confidence: 0.878970626

00:28:17.960 --> 00:28:19.975 Doctor Moi Bhattacharya is an

NOTE Confidence: 0.878970626

00:28:19.975 --> 00:28:21.587 assistant professor of pharmacology

NOTE Confidence: 0.878970626

00:28:21.587 --> 00:28:23.717 at the Yale School of Medicine.

NOTE Confidence: 0.878970626

00:28:23.720 --> 00:28:25.708 If you have questions,

NOTE Confidence: 0.878970626

00:28:25.708 --> 00:28:27.660 the address is canceranswers@yale.edu,

NOTE Confidence: 0.878970626

00:28:27.660 --> 00:28:30.420 and past editions of the program

NOTE Confidence: 0.878970626

00:28:30.420 --> 00:28:32.809 are available in audio and written

NOTE Confidence: 0.878970626

00:28:32.809 --> 00:28:33.745 form at yalecancercenter.org.

NOTE Confidence: 0.878970626

00:28:33.745 --> 00:28:36.185 We hope you'll join us next week to

NOTE Confidence: 0.878970626

00:28:36.185 --> 00:28:38.039 learn more about the fight against

NOTE Confidence: 0.878970626

00:28:38.039 --> 00:28:39.880 cancer here on Connecticut Public Radio.

NOTE Confidence: 0.878970626

00:28:39.880 --> 00:28:41.950 Funding for Yale Cancer Answers is

NOTE Confidence: 0.878970626

00:28:41.950 --> 00:28:43.920 provided by Smilo Cancer Hospital.