WEBVTT

NOTE duration:"00:29:00" NOTE recognizability:0.848

NOTE language:en-us

NOTE Confidence: 0.895326650909091

 $00:00:00.000 \longrightarrow 00:00:02.154$ Funding for Yale Cancer Answers is

NOTE Confidence: 0.895326650909091

00:00:02.154 --> 00:00:04.190 provided by Smilow Cancer Hospital.

NOTE Confidence: 0.8923836

 $00:00:06.410 \dashrightarrow 00:00:08.954$ Welcome to Yale Cancer answers with your

NOTE Confidence: 0.8923836

 $00:00:08.954 \longrightarrow 00:00:11.618$ host doctor in East JGP are Yale Cancer

NOTE Confidence: 0.8923836

 $00:00:11.618 \longrightarrow 00:00:13.488$ answers features the latest information

NOTE Confidence: 0.8923836

 $00:00:13.488 \longrightarrow 00:00:15.771$ on cancer care by welcoming oncologists

NOTE Confidence: 0.8923836

 $00{:}00{:}15.771 \dashrightarrow 00{:}00{:}18.347$ and specialists who are on the forefront

NOTE Confidence: 0.8923836

 $00:00:18.407 \dashrightarrow 00:00:20.774$ of the battle to fight cancer this week.

NOTE Confidence: 0.8923836

 $00:00:20.774 \longrightarrow 00:00:22.946$ It's a conversation about the molecular

NOTE Confidence: 0.8923836

 $00:00:22.946 \longrightarrow 00:00:25.488$ mechanisms of cancer with Doctor Daryl Klein.

NOTE Confidence: 0.8923836

 $00:00:25.490 \longrightarrow 00:00:27.744$ Doctor Klein is an assistant professor of

NOTE Confidence: 0.8923836

 $00:00:27.744 \longrightarrow 00:00:30.027$ pharmacology at the Yale School of Medicine,

NOTE Confidence: 0.8923836

 $00:00:30.030 \longrightarrow 00:00:32.076$ where Doctor Chad Power as a

00:00:32.076 --> 00:00:33.440 professor of surgical oncology.

NOTE Confidence: 0.9258690608

 $00{:}00{:}34.810 \dashrightarrow 00{:}00{:}36.406$ So Darrell maybe we can start

NOTE Confidence: 0.9258690608

 $00:00:36.406 \longrightarrow 00:00:38.305$ off by you telling us a little

NOTE Confidence: 0.9258690608

 $00:00:38.305 \longrightarrow 00:00:39.605$ bit more about yourself and

NOTE Confidence: 0.9258690608

 $00:00:39.605 \longrightarrow 00:00:41.460$ what it is exactly that you do.

NOTE Confidence: 0.737310321

 $00:00:42.070 \longrightarrow 00:00:43.870$ Yeah, I mean I think.

NOTE Confidence: 0.737310321

 $00:00:43.870 \longrightarrow 00:00:46.894$ My path to become a medical

NOTE Confidence: 0.737310321

00:00:46.894 --> 00:00:49.423 researcher involves my personal back

NOTE Confidence: 0.737310321

 $00{:}00{:}49.423 \dashrightarrow 00{:}00{:}52.590$ story and my love of competition.

NOTE Confidence: 0.737310321

00:00:52.590 --> 00:00:54.918 In some ways, I feel like I've been

NOTE Confidence: 0.737310321

 $00{:}00{:}54.918 \dashrightarrow 00{:}00{:}57.360$ destined to study kinases and cancer and

NOTE Confidence: 0.737310321

00:00:57.360 --> 00:01:00.547 their mechanisms and and with the hope of

NOTE Confidence: 0.737310321

 $00:01:00.547 \longrightarrow 00:01:02.315$ developing useful cancer therapeutics.

NOTE Confidence: 0.737310321

00:01:02.320 --> 00:01:05.260 And my career trajectory if you will.

NOTE Confidence: 0.737310321

 $00:01:05.260 \longrightarrow 00:01:06.908$ As a medical scientist,

NOTE Confidence: 0.737310321

 $00:01:06.908 \longrightarrow 00:01:10.100$ began long before my formal training.

00:01:10.100 --> 00:01:12.724 I grew up in New Jersey just outside

NOTE Confidence: 0.737310321

 $00{:}01{:}12.724 \dashrightarrow 00{:}01{:}14.840$ of Philadelphia, and at a young age.

NOTE Confidence: 0.737310321

 $00:01:14.840 \longrightarrow 00:01:18.466$ My my sister was diagnosed with cancer.

NOTE Confidence: 0.737310321

00:01:18.470 --> 00:01:21.300 Kimberly, my sister, was diagnosed

NOTE Confidence: 0.737310321

 $00{:}01{:}21.300 \dashrightarrow 00{:}01{:}25.050$ with MLE or chronic myeloid leukemia.

NOTE Confidence: 0.737310321

 $00:01:25.050 \longrightarrow 00:01:28.230$ It's a blood cancer that's rare

NOTE Confidence: 0.737310321

 $00:01:28.230 \longrightarrow 00:01:30.565$ in children at that time.

NOTE Confidence: 0.737310321

00:01:30.565 --> 00:01:32.690 Over 40 years ago now,

NOTE Confidence: 0.737310321

00:01:32.690 --> 00:01:35.468 Peter Noel at the University of

NOTE Confidence: 0.737310321

00:01:35.468 --> 00:01:37.835 Pennsylvania in Philadelphia was studying

NOTE Confidence: 0.737310321

 $00:01:37.835 \longrightarrow 00:01:40.873$ the driving mutations that lead to CML.

NOTE Confidence: 0.737310321

 $00{:}01{:}40.880 \dashrightarrow 00{:}01{:}43.142$ And he discovered a chromosome alteration

NOTE Confidence: 0.737310321

 $00{:}01{:}43.142 \dashrightarrow 00{:}01{:}45.437$ that he dubbed the Philadelphia

NOTE Confidence: 0.737310321

00:01:45.437 --> 00:01:47.243 chromosome and kmle patients,

NOTE Confidence: 0.737310321

 $00:01:47.243 \longrightarrow 00:01:49.770$ like my sister and and the results

 $00:01:49.838 \longrightarrow 00:01:50.858$ of that change.

NOTE Confidence: 0.737310321

 $00{:}01{:}50.860 \to 00{:}01{:}53.479$ Is that a new protein is made a fusion

NOTE Confidence: 0.737310321

00:01:53.479 --> 00:01:56.398 of a tyrosine kinase signaling protein?

NOTE Confidence: 0.737310321

00:01:56.400 --> 00:01:58.696 That's that's stuck in the on position,

NOTE Confidence: 0.737310321

 $00:01:58.700 \longrightarrow 00:02:00.780$ and that instructs cells to.

NOTE Confidence: 0.737310321

 $00:02:00.780 \longrightarrow 00:02:03.867$ To divide and grow and thus cancer.

NOTE Confidence: 0.737310321

 $00:02:03.870 \longrightarrow 00:02:06.110$ And that protein became a target for

NOTE Confidence: 0.737310321

00:02:06.110 --> 00:02:08.179 drug discovery and it really heralded

NOTE Confidence: 0.737310321

 $00{:}02{:}08.180 \dashrightarrow 00{:}02{:}10.664$ the era of precision medicine that

NOTE Confidence: 0.737310321

 $00:02:10.664 \longrightarrow 00:02:12.860$ is specifically targeting a single.

NOTE Confidence: 0.737310321

 $00:02:12.860 \longrightarrow 00:02:15.004$ You know bad protein with a drug and

NOTE Confidence: 0.737310321

 $00:02:15.004 \longrightarrow 00:02:17.099$ that and that was really exciting.

NOTE Confidence: 0.737310321

 $00:02:17.100 \longrightarrow 00:02:20.430$ And in 2001 there was this huge success with.

NOTE Confidence: 0.737310321

 $00{:}02{:}20.430 \dashrightarrow 00{:}02{:}22.490$ The mat neighbor or Gleevec,

NOTE Confidence: 0.737310321

 $00:02:22.490 \longrightarrow 00:02:24.668$ and that became the first drug

NOTE Confidence: 0.737310321

00:02:24.670 --> 00:02:26.386 that was developed to target a

00:02:26.386 --> 00:02:28.109 specific kinase to treat a disease,

NOTE Confidence: 0.737310321

 $00:02:28.110 \longrightarrow 00:02:30.170$ and in this case, someone.

NOTE Confidence: 0.737310321

 $00:02:30.170 \longrightarrow 00:02:33.110$ And patients treated with this drug can

NOTE Confidence: 0.737310321

 $00:02:33.110 \longrightarrow 00:02:36.290$ live long lives with controlled disease.

NOTE Confidence: 0.737310321

00:02:36.290 --> 00:02:38.690 Unfortunately for you know, Kimberly,

NOTE Confidence: 0.737310321

 $00:02:38.690 \longrightarrow 00:02:40.426$ my sister, at that time it was.

NOTE Confidence: 0.737310321

 $00:02:40.430 \longrightarrow 00:02:42.926$ It was just the beginning of

NOTE Confidence: 0.737310321

 $00:02:42.926 \longrightarrow 00:02:44.174$ understanding this disease.

NOTE Confidence: 0.737310321

 $00:02:44.180 \longrightarrow 00:02:45.560$ And there were no therapeutics,

NOTE Confidence: 0.737310321

00:02:45.560 --> 00:02:46.700 and that meant you know,

NOTE Confidence: 0.737310321

 $00:02:46.700 \longrightarrow 00:02:48.620$ little could be done, and.

NOTE Confidence: 0.737310321

 $00:02:48.620 \longrightarrow 00:02:50.867$ In this powerlessness drives me to find

NOTE Confidence: 0.737310321

 $00{:}02{:}50.867 \dashrightarrow 00{:}02{:}53.351$ ways to spare other families similar

NOTE Confidence: 0.737310321

 $00:02:53.351 \longrightarrow 00:02:57.017$ devastation and to better understand cancer.

NOTE Confidence: 0.737310321

00:02:57.020 --> 00:02:57.506 You know,

 $00:02:57.506 \longrightarrow 00:03:00.000$ I really have spent a large part of my career

NOTE Confidence: 0.737310321

 $00:03:00.000 \longrightarrow 00:03:02.840$ investigating the molecular basis for,

NOTE Confidence: 0.737310321

 $00:03:02.840 \longrightarrow 00:03:04.127$ for oncogenic signaling.

NOTE Confidence: 0.73731032100:03:04.127 --> 00:03:04.556 And. NOTE Confidence: 0.737310321

 $00:03:04.556 \longrightarrow 00:03:07.796$ You know on that path I attended

NOTE Confidence: 0.737310321

00:03:07.796 --> 00:03:10.116 the University of Pennsylvania

NOTE Confidence: 0.737310321

00:03:10.116 --> 00:03:12.520 for my undergrad in my PhD,

NOTE Confidence: 0.737310321

 $00:03:12.520 \longrightarrow 00:03:13.944$ and my medical degree,

NOTE Confidence: 0.737310321

 $00:03:13.944 \longrightarrow 00:03:16.651$ and I did clinical rotations at the

NOTE Confidence: 0.737310321

00:03:16.651 --> 00:03:19.126 Children's Hospital of Philadelphia Chop.

NOTE Confidence: 0.737310321

00:03:19.130 --> 00:03:21.659 So I was walking the same halls as Peter,

NOTE Confidence: 0.737310321

 $00:03:21.660 \longrightarrow 00:03:24.552$ Noel and my parents and my

NOTE Confidence: 0.737310321

00:03:24.552 --> 00:03:25.998 sister years before.

NOTE Confidence: 0.737310321

 $00:03:26.000 \longrightarrow 00:03:29.072$ I joined the MSTP or medical

NOTE Confidence: 0.737310321

 $00:03:29.072 \longrightarrow 00:03:31.120$ Scientist training program and.

NOTE Confidence: 0.737310321

 $00:03:31.120 \longrightarrow 00:03:33.238$ This was funded by the NIH,

00:03:33.240 --> 00:03:35.250 the National Institutes of Health,

NOTE Confidence: 0.737310321

 $00{:}03{:}35.250 \dashrightarrow 00{:}03{:}37.858$ to grant to train a group of physicians,

NOTE Confidence: 0.737310321

 $00:03:37.860 \longrightarrow 00:03:39.180$ also to be researchers,

NOTE Confidence: 0.737310321

 $00:03:39.180 \longrightarrow 00:03:41.350$ and the goal of that program is

NOTE Confidence: 0.737310321

 $00:03:41.350 \longrightarrow 00:03:43.385$ basically to link basic science

NOTE Confidence: 0.737310321

 $00:03:43.385 \longrightarrow 00:03:45.013$ findings to the clinic.

NOTE Confidence: 0.737310321

 $00:03:45.020 \longrightarrow 00:03:48.184$ The bench to the bedside and to

NOTE Confidence: 0.737310321

 $00{:}03{:}48.184 \dashrightarrow 00{:}03{:}50.944$ Brig lab progress into useful

NOTE Confidence: 0.737310321

 $00:03:50.944 \longrightarrow 00:03:52.812$ therapeutics as rapidly as possible.

NOTE Confidence: 0.737310321

 $00{:}03{:}52.812 \dashrightarrow 00{:}03{:}56.033$ And I think the success of Leave Act was

NOTE Confidence: 0.737310321

 $00:03:56.033 \longrightarrow 00:03:58.397$ just the beginning of targeting kinases.

NOTE Confidence: 0.737310321

 $00{:}03{:}58.400 \dashrightarrow 00{:}04{:}00.485$ These these tires and kinases

NOTE Confidence: 0.737310321

 $00{:}04{:}00.485 --> 00{:}04{:}02.153$ other kinases and cancer.

NOTE Confidence: 0.737310321

 $00:04:02.160 \longrightarrow 00:04:03.518$ And so when I was at Penn,

NOTE Confidence: 0.932154455

 $00:04:03.520 \longrightarrow 00:04:06.880$ I studied under Professor Mark Lemon.

 $00:04:06.880 \longrightarrow 00:04:09.092$ He was working on those other kinases

NOTE Confidence: 0.932154455

 $00{:}04{:}09.092 \dashrightarrow 00{:}04{:}11.250$ that lead to different cancers.

NOTE Confidence: 0.932154455

00:04:11.250 --> 00:04:14.450 And you know, to see how they might

NOTE Confidence: 0.932154455

00:04:14.450 --> 00:04:16.998 cause cancer and how we might leverage

NOTE Confidence: 0.932154455

 $00:04:16.998 \longrightarrow 00:04:18.090$ understanding their mechanisms

NOTE Confidence: 0.932154455

 $00:04:18.142 \longrightarrow 00:04:21.900$ to develop new therapeutics.

NOTE Confidence: 0.932154455

00:04:21.900 --> 00:04:24.875 I also mentioned you know my my

NOTE Confidence: 0.932154455

00:04:24.875 --> 00:04:28.778 desire for you know competition.

NOTE Confidence: 0.932154455

 $00:04:28.780 \longrightarrow 00:04:31.428$ And so one thing I I'm not sure

NOTE Confidence: 0.932154455

 $00:04:31.428 \longrightarrow 00:04:33.839$ that people really understand is

NOTE Confidence: 0.932154455

 $00:04:33.839 \longrightarrow 00:04:35.620$ how competitive research compete.

NOTE Confidence: 0.932154455

00:04:35.620 --> 00:04:36.960 And I, you know,

NOTE Confidence: 0.932154455

 $00{:}04{:}36.960 \dashrightarrow 00{:}04{:}38.668$ I grew up playing sports in college

NOTE Confidence: 0.932154455

00:04:38.668 --> 00:04:40.916 and I love competing and and track and

NOTE Confidence: 0.932154455

 $00:04:40.916 \longrightarrow 00:04:43.120$ field and crew and football and baseball.

NOTE Confidence: 0.932154455

 $00:04:43.120 \longrightarrow 00:04:46.397$ And when I first joined Mark's

00:04:46.397 --> 00:04:48.056 lab at Penn and was first

NOTE Confidence: 0.932154455

00:04:48.056 --> 00:04:49.199 introduced to lab research,

NOTE Confidence: 0.932154455

 $00:04:49.200 \longrightarrow 00:04:51.408$ I realized there that.

NOTE Confidence: 0.932154455

 $00:04:51.410 \longrightarrow 00:04:53.246$ Scientific researches is intensely

NOTE Confidence: 0.932154455

 $00{:}04{:}53.246 \dashrightarrow 00{:}04{:}56.467$ competitive and I think it makes Olympic

NOTE Confidence: 0.932154455

 $00:04:56.467 \longrightarrow 00:04:59.255$ sport seem safe by comparison and I

NOTE Confidence: 0.932154455

 $00:04:59.255 \longrightarrow 00:05:02.500$ love that and I loved everything about that.

NOTE Confidence: 0.932154455

 $00:05:02.500 \longrightarrow 00:05:04.852$ And then the problem is in

NOTE Confidence: 0.932154455

 $00:05:04.852 \longrightarrow 00:05:06.028$ sensually in science.

NOTE Confidence: 0.932154455

 $00{:}05{:}06.030 \dashrightarrow 00{:}05{:}08.042$ You're competing with unknown

NOTE Confidence: 0.932154455

 $00:05:08.042 \longrightarrow 00:05:11.060$ competitors and and an unknown number

NOTE Confidence: 0.932154455

 $00:05:11.142 \longrightarrow 00:05:13.685$ of of teams and and the rules of the

NOTE Confidence: 0.932154455

 $00{:}05{:}13.685 \dashrightarrow 00{:}05{:}15.957$ game are undefined and you don't even

NOTE Confidence: 0.932154455

 $00:05:15.957 \longrightarrow 00:05:17.937$ know when the conversation started.

NOTE Confidence: 0.932154455 00:05:17.940 --> 00:05:18.302 So, NOTE Confidence: 0.932154455 $00:05:18.302 \longrightarrow 00:05:20.112$ and certainly your competitors have

NOTE Confidence: 0.932154455

 $00:05:20.112 \longrightarrow 00:05:22.299$ more money and resources than you do,

NOTE Confidence: 0.932154455

 $00:05:22.300 \longrightarrow 00:05:25.208$ so you're always the underdog and and

NOTE Confidence: 0.932154455

 $00:05:25.208 \longrightarrow 00:05:28.100$ that excites me and I and I like that.

NOTE Confidence: 0.932154455

 $00:05:28.100 \longrightarrow 00:05:29.336$ You know an example.

NOTE Confidence: 0.932154455

 $00:05:29.336 \longrightarrow 00:05:31.490$ When we started the project will chat

NOTE Confidence: 0.932154455

 $00:05:31.490 \longrightarrow 00:05:33.402$ more about in a in a little bit.

NOTE Confidence: 0.932154455

00:05:33.410 --> 00:05:35.419 We were certain that that you know

NOTE Confidence: 0.932154455

 $00{:}05{:}35.419 \dashrightarrow 00{:}05{:}37.927$ half a dozen other groups in the world

NOTE Confidence: 0.932154455

00:05:37.927 --> 00:05:40.440 were already working on it and and we

NOTE Confidence: 0.932154455

 $00:05:40.440 \longrightarrow 00:05:42.449$ didn't know how far along they were.

NOTE Confidence: 0.932154455

 $00:05:42.450 \longrightarrow 00:05:44.370$ And so all you know is what you don't know.

NOTE Confidence: 0.932154455

00:05:44.370 --> 00:05:45.546 And if you want to win,

NOTE Confidence: 0.932154455

 $00:05:45.550 \longrightarrow 00:05:48.278$ you have to work nonstop like 24/7.

NOTE Confidence: 0.932154455

00:05:48.278 --> 00:05:51.950 I once spent 50 hours straight in the lab

NOTE Confidence: 0.932154455

 $00:05:51.950 \longrightarrow 00:05:54.350$ when I was a grad student without sleeping.

 $00:05:54.350 \longrightarrow 00:05:57.284$ And then you know that was exciting to me.

NOTE Confidence: 0.932154455

 $00{:}05{:}57.290 \dashrightarrow 00{:}05{:}59.570$ That's something you can't do in.

NOTE Confidence: 0.932154455

00:05:59.570 --> 00:06:02.864 In sport after the game you you go home,

NOTE Confidence: 0.932154455

 $00:06:02.870 \longrightarrow 00:06:05.845$ but science is a years long competition

NOTE Confidence: 0.932154455

 $00:06:05.850 \longrightarrow 00:06:08.442$ with no timeouts and the

NOTE Confidence: 0.932154455

 $00:06:08.442 \longrightarrow 00:06:11.520$ intensity is is off the charts so.

NOTE Confidence: 0.932154455

00:06:11.520 --> 00:06:14.425 I think that that frames kind of.

NOTE Confidence: 0.932154455

 $00:06:14.430 \longrightarrow 00:06:16.926$ Why I became a medical researcher

NOTE Confidence: 0.932154455

00:06:16.926 --> 00:06:18.590 and and and why?

NOTE Confidence: 0.932154455

 $00:06:18.590 \dashrightarrow 00:06:21.173$ Why I love doing the work that I do.

NOTE Confidence: 0.88524498777778

 $00:06:22.860 \longrightarrow 00:06:25.479$ So let's take a step back for a bit.

NOTE Confidence: 0.885244987777778

 $00:06:25.480 \longrightarrow 00:06:27.856$ I mean, that sounds really inspiring

NOTE Confidence: 0.885244987777778

 $00{:}06{:}27.856 \dashrightarrow 00{:}06{:}30.153$ and and interesting in terms of

NOTE Confidence: 0.88524498777778

 $00:06:30.153 \longrightarrow 00:06:32.400$ how this kind of came full circle.

NOTE Confidence: 0.885244987777778

 $00{:}06{:}32.400 \dashrightarrow 00{:}06{:}34.175$ How you? Had this experience

00:06:34.175 --> 00:06:36.753 with your sister and then went on

NOTE Confidence: 0.88524498777778

 $00{:}06{:}36.753 \dashrightarrow 00{:}06{:}38.961$ to to become a scientist that's

NOTE Confidence: 0.88524498777778

00:06:38.961 --> 00:06:41.157 hopefully making a difference in the

NOTE Confidence: 0.88524498777778

 $00{:}06{:}41.157 \dashrightarrow 00{:}06{:}43.245$ lives of other patients like her.

NOTE Confidence: 0.885244987777778

00:06:43.250 --> 00:06:44.694 But for our audience,

NOTE Confidence: 0.88524498777778

00:06:44.694 --> 00:06:47.643 maybe you can take a step back and

NOTE Confidence: 0.88524498777778

 $00:06:47.643 \longrightarrow 00:06:50.467$ tell us exactly like what is a kinase

NOTE Confidence: 0.88524498777778

 $00:06:50.548 \longrightarrow 00:06:53.390$ and why are they important in cancer?

NOTE Confidence: 0.80161613

00:06:54.420 --> 00:06:55.578 Sure, sure, yeah.

NOTE Confidence: 0.80161613

 $00{:}06{:}55.578 \dashrightarrow 00{:}06{:}57.894$ I mean I should also mention

NOTE Confidence: 0.80161613

 $00{:}06{:}57.894 \dashrightarrow 00{:}07{:}00.409$ that while I trained as A and

NOTE Confidence: 0.80161613

00:07:00.409 --> 00:07:02.610 MDP MD PhD physician scientist,

NOTE Confidence: 0.80161613

 $00:07:02.610 \longrightarrow 00:07:05.780$ I've actually chosen a path

NOTE Confidence: 0.80161613

 $00{:}07{:}05.780 \dashrightarrow 00{:}07{:}08.142$ devoted entirely to research.

NOTE Confidence: 0.80161613

00:07:08.142 --> 00:07:11.088 So during training, when I you know,

NOTE Confidence: 0.80161613

 $00{:}07{:}11.088 \dashrightarrow 00{:}07{:}12.723$ find myself engaging with patients

 $00:07:12.723 \longrightarrow 00:07:15.574$ and and talking to them about the

NOTE Confidence: 0.80161613

 $00{:}07{:}15.574 \dashrightarrow 00{:}07{:}17.400$ unfortunately limited treatment options I,

NOTE Confidence: 0.80161613

 $00:07:17.400 \longrightarrow 00:07:19.080$ I found that difficult and frustrating

NOTE Confidence: 0.80161613

 $00:07:19.080 \longrightarrow 00:07:21.364$ and all I wanted to do was rush

NOTE Confidence: 0.80161613

 $00:07:21.364 \longrightarrow 00:07:23.611$ back to the lab and and find

NOTE Confidence: 0.80161613

 $00:07:23.611 \longrightarrow 00:07:25.059$ new potential therapeutic avenues.

NOTE Confidence: 0.80161613

 $00:07:25.060 \longrightarrow 00:07:27.342$ So I made a choice to devote

NOTE Confidence: 0.80161613

 $00:07:27.342 \longrightarrow 00:07:29.078$ myself entirely to lab work,

NOTE Confidence: 0.80161613

 $00{:}07{:}29.078 \dashrightarrow 00{:}07{:}31.392$ but at the same time I'm still

NOTE Confidence: 0.80161613

 $00:07:31.392 \longrightarrow 00:07:32.496$ working with other physicians,

NOTE Confidence: 0.80161613

 $00:07:32.500 \longrightarrow 00:07:34.356$ scientists and clinicians to

NOTE Confidence: 0.80161613

 $00{:}07{:}34.356 \dashrightarrow 00{:}07{:}36.676$ help bridge our our discoveries.

NOTE Confidence: 0.80161613

 $00:07:36.680 \longrightarrow 00:07:39.209$ To the bedside.

NOTE Confidence: 0.80161613

 $00:07:39.210 \longrightarrow 00:07:42.710$ Kinases are often drivers of

NOTE Confidence: 0.80161613

 $00:07:42.710 \longrightarrow 00:07:45.201$ cancers and and the one that I've

00:07:45.201 --> 00:07:47.566 been working on recently ALK and

NOTE Confidence: 0.80161613

00:07:47.566 --> 00:07:50.302 a plastic lymphoma kinases is a

NOTE Confidence: 0.80161613

 $00{:}07{:}50.302 \dashrightarrow 00{:}07{:}53.140$ well known cancer related protein.

NOTE Confidence: 0.80161613

 $00:07:53.140 \longrightarrow 00:07:55.162$ And much like the protein involved

NOTE Confidence: 0.80161613

 $00:07:55.162 \longrightarrow 00:07:56.840$ in my sisters of Mle,

NOTE Confidence: 0.80161613

 $00:07:56.840 \longrightarrow 00:07:59.300$ it's a tyrosine kinase and

NOTE Confidence: 0.80161613

 $00:07:59.300 \longrightarrow 00:08:01.372$ basically tyrosine kinases instruct

NOTE Confidence: 0.80161613

 $00:08:01.372 \longrightarrow 00:08:04.480$ the cells to grow and divide,

NOTE Confidence: 0.80161613

 $00{:}08{:}04.480 --> 00{:}08{:}07.040$ and if this is unregulated

NOTE Confidence: 0.80161613

 $00:08:07.040 \longrightarrow 00:08:09.908$ that leads to cancer.

NOTE Confidence: 0.80161613

 $00:08:09.910 \longrightarrow 00:08:15.290$ So ALK well, unlike the Siml case, ALK is.

NOTE Confidence: 0.80161613

 $00{:}08{:}15.290 \dashrightarrow 00{:}08{:}18.006$ Is A is a receptor tyrosine kinase.

NOTE Confidence: 0.80161613

 $00:08:18.010 \longrightarrow 00:08:19.774$ So what that means is ALK is

NOTE Confidence: 0.80161613

 $00:08:19.774 \longrightarrow 00:08:21.549$ located in a different part of

NOTE Confidence: 0.80161613

 $00:08:21.549 \longrightarrow 00:08:24.314$ the cell than the CML kinase.

NOTE Confidence: 0.80161613

 $00:08:24.314 \longrightarrow 00:08:27.470$ So if it if a cell were an ocean,

 $00:08:27.470 \longrightarrow 00:08:29.766$ the CML kinase would be a submarine

NOTE Confidence: 0.80161613

 $00:08:29.766 \longrightarrow 00:08:32.566$ and ALK would be more like an aircraft

NOTE Confidence: 0.80161613

 $00:08:32.566 \longrightarrow 00:08:35.833$ carrier at the surface and so this.

NOTE Confidence: 0.80161613

00:08:35.833 --> 00:08:37.696 Localization difference has

NOTE Confidence: 0.80161613

 $00{:}08{:}37.696 \dashrightarrow 00{:}08{:}38.938$ the rapeutic implications.

NOTE Confidence: 0.80161613

00:08:38.940 --> 00:08:40.060 As you might imagine,

NOTE Confidence: 0.80161613

00:08:40.060 --> 00:08:42.084 you can't target a submarine the same

NOTE Confidence: 0.80161613

00:08:42.084 --> 00:08:44.348 way you would target in an aircraft carrier.

NOTE Confidence: 0.80161613

 $00{:}08{:}44.350 \dashrightarrow 00{:}08{:}46.806$ So in the clinic we use small molecule.

NOTE Confidence: 0.80161613

 $00{:}08{:}46.810 \dashrightarrow 00{:}08{:}49.306$ You know missile like drugs that can dive

NOTE Confidence: 0.80161613

 $00{:}08{:}49.306 \dashrightarrow 00{:}08{:}51.770$ deep into the ocean to reach that kmle.

NOTE Confidence: 0.80161613

 $00{:}08{:}51.770 \dashrightarrow 00{:}08{:}54.272$ Kinase submarine whereas for ALK we

NOTE Confidence: 0.80161613

 $00{:}08{:}54.272 \dashrightarrow 00{:}08{:}56.798$ have an opportunity to use antibodies

NOTE Confidence: 0.80161613

 $00:08:56.798 \longrightarrow 00:08:59.910$ that can target it at the cell surface,

NOTE Confidence: 0.80161613

 $00:08:59.910 \longrightarrow 00:09:01.330$ so more like a.

 $00:09:01.330 \longrightarrow 00:09:05.160$ You know a B52 bomber.

NOTE Confidence: 0.80161613

 $00{:}09{:}05.160 \dashrightarrow 00{:}09{:}06.906$ It's been known for years that

NOTE Confidence: 0.80161613

 $00:09:06.906 \longrightarrow 00:09:09.158$ ALK is a driver of neuroblastoma.

NOTE Confidence: 0.80161613

00:09:09.158 --> 00:09:12.422 Now neuroblastoma is a cancer of

NOTE Confidence: 0.80161613

 $00:09:12.422 \longrightarrow 00:09:14.850$ the peripheral nervous system.

NOTE Confidence: 0.80161613

00:09:14.850 --> 00:09:17.419 It's one of the more common pediatric

NOTE Confidence: 0.80161613

00:09:17.419 --> 00:09:19.385 cancers that accounts for more than

NOTE Confidence: 0.80161613

00:09:19.385 --> 00:09:23.289 10% of childhood cancer mortality.

NOTE Confidence: 0.80161613

 $00:09:23.289 \longrightarrow 00:09:26.061$ But clinically useful the rapeutics

NOTE Confidence: 0.80161613

 $00:09:26.061 \longrightarrow 00:09:29.058$ have been slow to develop,

NOTE Confidence: 0.80161613

00:09:29.058 --> 00:09:32.194 and I think you know one of the key

NOTE Confidence: 0.80161613

00:09:32.194 --> 00:09:33.900 reasons for this slow development of

NOTE Confidence: 0.80161613

 $00:09:33.900 \longrightarrow 00:09:36.098$ treatments is likely the lack of a.

NOTE Confidence: 0.80161613

 $00:09:36.100 \longrightarrow 00:09:39.280$ Structural framework for the target alcc.

NOTE Confidence: 0.80161613

00:09:39.280 --> 00:09:39.760 Simply put,

NOTE Confidence: 0.80161613

00:09:39.760 --> 00:09:41.680 we have you know no idea what it

 $00:09:41.738 \longrightarrow 00:09:43.538$ looked like or how it functioned.

NOTE Confidence: 0.80161613

 $00{:}09{:}43.540 \dashrightarrow 00{:}09{:}47.185$ It was a complete mystery before our work.

NOTE Confidence: 0.80161613

 $00{:}09{:}47.190 \dashrightarrow 00{:}09{:}50.853$ I mean the fact that ALK is expressed on

NOTE Confidence: 0.80161613

 $00:09:50.853 \longrightarrow 00:09:53.228$ neuroblastoma cells but is not present.

NOTE Confidence: 0.80161613

 $00{:}09{:}53.230 \dashrightarrow 00{:}09{:}56.340$ On healthy tissue makes Alka

NOTE Confidence: 0.80161613

00:09:56.340 --> 00:09:58.206 veritable oncogenic beacon.

NOTE Confidence: 0.80161613

 $00:09:58.210 \longrightarrow 00:10:00.630$ That's a perfect target

NOTE Confidence: 0.80161613

 $00:10:00.630 \longrightarrow 00:10:02.445$ for precision medicine.

NOTE Confidence: 0.80161613

00:10:02.450 --> 00:10:04.405 It's much like the novel

NOTE Confidence: 0.80161613

00:10:04.405 --> 00:10:05.969 fusion protein and kmle.

NOTE Confidence: 0.80161613

 $00:10:05.970 \longrightarrow 00:10:09.720$ In each case the protein.

NOTE Confidence: 0.80161613

00:10:09.720 --> 00:10:10.105 Specifically,

NOTE Confidence: 0.80161613

 $00:10:10.105 \longrightarrow 00:10:12.415$ if you're targeting the protein specifically,

NOTE Confidence: 0.80161613

00:10:12.420 --> 00:10:14.328 it should have little side effects

NOTE Confidence: 0.80161613

 $00:10:14.328 \longrightarrow 00:10:16.060$ outside of the cancer itself.

00:10:16.060 --> 00:10:19.237 And the hope is that if we can target

NOTE Confidence: 0.80161613

 $00{:}10{:}19.237 \dashrightarrow 00{:}10{:}21.949$ this kinase alken neuroblastoma.

NOTE Confidence: 0.891430347647059

 $00:10:21.950 \longrightarrow 00:10:24.561$ That we might have the same positive

NOTE Confidence: 0.891430347647059

 $00:10:24.561 \longrightarrow 00:10:26.041$ outcomes for neuroblastoma that

NOTE Confidence: 0.891430347647059

00:10:26.041 --> 00:10:27.817 we see for patients with KMLE.

NOTE Confidence: 0.79956105

00:10:29.260 --> 00:10:32.420 So you know one of the things that

NOTE Confidence: 0.79956105

 $00:10:32.420 \longrightarrow 00:10:34.220$ always fascinates me is how you

NOTE Confidence: 0.79956105

 $00:10:34.220 \longrightarrow 00:10:35.870$ find these things to begin with.

NOTE Confidence: 0.79956105

 $00{:}10{:}35.870 \dashrightarrow 00{:}10{:}39.014$ I mean, how do we know that these

NOTE Confidence: 0.79956105

 $00:10:39.014 \longrightarrow 00:10:41.350$ kinases play a role in cancer?

NOTE Confidence: 0.79956105

00:10:41.350 --> 00:10:43.906 How does that? How do you figure that out?

NOTE Confidence: 0.79956105

00:10:43.910 --> 00:10:46.864 How do you know which kinases are

NOTE Confidence: 0.79956105

 $00:10:46.864 \longrightarrow 00:10:49.370$ submarines and which kinases are

NOTE Confidence: 0.79956105

00:10:49.370 --> 00:10:51.968 our aircraft carriers, I mean.

NOTE Confidence: 0.79956105

00:10:51.968 --> 00:10:54.551 And how did you figure out that

NOTE Confidence: 0.79956105

 $00:10:54.551 \longrightarrow 00:10:56.900$ these were important anyways?

 $00:10:56.900 \longrightarrow 00:10:57.968$ How does that happen?

NOTE Confidence: 0.82554652

 $00:10:59.730 \longrightarrow 00:11:01.230$ That's a good question.

NOTE Confidence: 0.82554652

 $00:11:01.230 \longrightarrow 00:11:02.355$ That's certainly outside

NOTE Confidence: 0.82554652

 $00:11:02.355 \longrightarrow 00:11:06.780$ of my lab's expertise.

NOTE Confidence: 0.82554652

 $00{:}11{:}06.780 \dashrightarrow 00{:}11{:}10.260$ A lot of that is done through genomic

NOTE Confidence: 0.82554652

 $00:11:10.260 \longrightarrow 00:11:13.806$ work and associating certain genes

NOTE Confidence: 0.82554652

00:11:13.806 --> 00:11:16.878 with certain disease phenotypes,

NOTE Confidence: 0.82554652

 $00:11:16.880 \longrightarrow 00:11:19.178$ and so where my labs expertise

NOTE Confidence: 0.82554652

 $00{:}11{:}19.178 \dashrightarrow 00{:}11{:}21.920$ comes in pretty much after the fact.

NOTE Confidence: 0.82554652

 $00{:}11{:}21.920 \dashrightarrow 00{:}11{:}25.910$ Once these associations are known.

NOTE Confidence: 0.82554652

00:11:25.910 --> 00:11:28.774 That's where we come in to help define

NOTE Confidence: 0.82554652

00:11:28.774 --> 00:11:30.709 bio physically and structurally,

NOTE Confidence: 0.82554652

 $00{:}11{:}30.710 \dashrightarrow 00{:}11{:}32.930$ exactly how these kinases

NOTE Confidence: 0.82554652

 $00:11:32.930 \longrightarrow 00:11:35.705$ and uncle genes are acting,

NOTE Confidence: 0.82554652

 $00:11:35.710 \longrightarrow 00:11:37.670$ and hopefully if we have a molecular

00:11:37.670 --> 00:11:40.654 picture of that how we might design

NOTE Confidence: 0.82554652

 $00:11:40.654 \longrightarrow 00:11:42.798$ and develop therapeutics to.

NOTE Confidence: 0.82554652

 $00:11:42.800 \longrightarrow 00:11:46.167$ To stall that and and prevent disease.

NOTE Confidence: 0.890860507142857

 $00:11:47.890 \longrightarrow 00:11:50.730$ So when you say that it it kind of all

NOTE Confidence: 0.890860507142857

 $00:11:50.806 \longrightarrow 00:11:53.196$ starts with understanding what genes

NOTE Confidence: 0.890860507142857

00:11:53.196 --> 00:11:56.190 are expressed in what genes aren't.

NOTE Confidence: 0.890860507142857

 $00:11:56.190 \longrightarrow 00:11:59.404$ I mean it, it sounds like the progress

NOTE Confidence: 0.890860507142857

 $00:11:59.404 \longrightarrow 00:12:02.568$ that we make in terms of cancer

NOTE Confidence: 0.890860507142857

 $00{:}12{:}02.568 {\:\raisebox{--}{\text{--}}}{\:\raisebox{--}{\text{--}}}{\:\raisebox{--}{\text{--}}} 00{:}12{:}04.574$ medicine is really investigators.

NOTE Confidence: 0.890860507142857

00:12:04.574 --> 00:12:06.646 Building on other investigators

NOTE Confidence: 0.890860507142857

 $00{:}12{:}06.646 \dashrightarrow 00{:}12{:}09.600$ building on other investigators work.

NOTE Confidence: 0.890860507142857

 $00:12:09.600 \longrightarrow 00:12:12.442$ So somebody you know maybe was sequencing

NOTE Confidence: 0.890860507142857

 $00:12:12.442 \longrightarrow 00:12:16.025$ some genes and found that some genes were

NOTE Confidence: 0.890860507142857

 $00:12:16.025 \longrightarrow 00:12:18.680$ overexpressed in some cancers versus not.

NOTE Confidence: 0.890860507142857

 $00:12:18.680 \longrightarrow 00:12:21.848$ And then other people kind of discovered that

NOTE Confidence: 0.890860507142857

 $00:12:21.848 \longrightarrow 00:12:25.237$ that gene was associated with a protein like.

 $00:12:25.240 \longrightarrow 00:12:27.557$ A kinase and then you look at

NOTE Confidence: 0.890860507142857

 $00:12:27.557 \longrightarrow 00:12:29.552$ that kinase and say well where

NOTE Confidence: 0.890860507142857

 $00:12:29.552 \longrightarrow 00:12:32.010$ is it and how can we target it?

NOTE Confidence: 0.890860507142857

00:12:32.010 --> 00:12:34.537 Is that kind of how that works?

NOTE Confidence: 0.890860507142857 00:12:34.540 --> 00:12:34.900 That's

NOTE Confidence: 0.929737544

00:12:34.910 --> 00:12:36.980 exactly right, right? I mean,

NOTE Confidence: 0.929737544

00:12:36.980 --> 00:12:40.494 it's it's work of a tremendous number

NOTE Confidence: 0.929737544

 $00:12:40.494 \longrightarrow 00:12:43.850$ of individuals with differing expertise.

NOTE Confidence: 0.929737544

 $00{:}12{:}43.850 \dashrightarrow 00{:}12{:}46.220$ Certainly the approach my lab takes

NOTE Confidence: 0.929737544

 $00:12:46.220 \longrightarrow 00:12:49.119$ is just one cog in that machine,

NOTE Confidence: 0.929737544

 $00:12:49.120 \longrightarrow 00:12:50.686$ one that's a bit further down,

NOTE Confidence: 0.929737544

 $00:12:50.690 \longrightarrow 00:12:52.447$ and probably less than the discovery stage.

NOTE Confidence: 0.929737544

 $00:12:52.450 \longrightarrow 00:12:54.784$ But one one that is keenly

NOTE Confidence: 0.929737544

 $00:12:54.784 \longrightarrow 00:12:56.340$ important to understand the

NOTE Confidence: 0.929737544

00:12:56.414 --> 00:12:58.719 mechanism of how molecules work,

 $00:12:58.720 \longrightarrow 00:13:00.544$ which can then give us insight

NOTE Confidence: 0.929737544

 $00:13:00.544 \longrightarrow 00:13:02.785$ into how we might target these

NOTE Confidence: 0.929737544

 $00:13:02.785 \longrightarrow 00:13:04.228$ and develop therapeutics.

NOTE Confidence: 0.929737544

 $00:13:04.230 \longrightarrow 00:13:05.550$ Around their function.

NOTE Confidence: 0.915260749090909

 $00:13:06.960 \longrightarrow 00:13:08.900$ And then the other question

NOTE Confidence: 0.915260749090909

 $00:13:08.900 \longrightarrow 00:13:11.160$ that that I often have is.

NOTE Confidence: 0.915260749090909

 $00:13:11.160 \longrightarrow 00:13:14.994$ OK, so you know you discover this kinase and

NOTE Confidence: 0.915260749090909

 $00:13:14.994 \longrightarrow 00:13:18.965$ you discover that it's important in cancer.

NOTE Confidence: 0.915260749090909

 $00{:}13{:}18.970 \dashrightarrow 00{:}13{:}22.226$ Why is it that some kinases are important

NOTE Confidence: 0.915260749090909

 $00:13:22.226 \longrightarrow 00:13:25.288$ in some cancers but not in others?

NOTE Confidence: 0.915260749090909

 $00:13:25.290 \longrightarrow 00:13:27.210$ I mean, how do these kinases?

NOTE Confidence: 0.915260749090909

 $00:13:27.210 \longrightarrow 00:13:30.451$ Why? Why do you have these genes

NOTE Confidence: 0.915260749090909

 $00:13:30.451 \longrightarrow 00:13:33.229$ for these kinases to begin with?

NOTE Confidence: 0.915260749090909

00:13:33.230 --> 00:13:36.338 And why are they differentially expressed?

NOTE Confidence: 0.872277651666666

 $00:13:37.490 \longrightarrow 00:13:41.750$ Cancer often recapitulates the the paradigms

NOTE Confidence: 0.872277651666666

 $00{:}13{:}41.750 \dashrightarrow 00{:}13{:}46.710$ that are important and during development.

 $00:13:46.710 \longrightarrow 00:13:49.440$ So all of these kinases are crucially

NOTE Confidence: 0.872277651666666

 $00:13:49.440 \longrightarrow 00:13:52.849$ important in the in the stages of development

NOTE Confidence: 0.872277651666666

 $00:13:52.849 \longrightarrow 00:13:55.670$ and help patterning and complex tissues.

NOTE Confidence: 0.872277651666666

00:13:55.670 --> 00:13:58.575 After that, they they often kind of

NOTE Confidence: 0.872277651666666

00:13:58.575 --> 00:14:01.609 are aren't used so much in adulthood,

NOTE Confidence: 0.872277651666666

 $00:14:01.610 \longrightarrow 00:14:04.330$ and it's only during cancer.

NOTE Confidence: 0.872277651666666

 $00:14:04.330 \longrightarrow 00:14:07.984$ In the the oncogenic process that a lot of

NOTE Confidence: 0.872277651666666

 $00:14:07.984 \longrightarrow 00:14:11.687$ these developmental pathways are reawakened,

NOTE Confidence: 0.872277651666666

 $00:14:11.690 \longrightarrow 00:14:14.203$ and they can be reawakened in different

NOTE Confidence: 0.872277651666666

00:14:14.203 --> 00:14:16.459 tissues and and different places,

NOTE Confidence: 0.87227765166666600:14:16.460 --> 00:14:17.225 but they all.

NOTE Confidence: 0.872277651666666

 $00:14:17.225 \longrightarrow 00:14:18.500$ Lead to the same thing.

NOTE Confidence: 0.872277651666666

 $00{:}14{:}18.500 \longrightarrow 00{:}14{:}20.880$ Basically once you turn return

NOTE Confidence: 0.872277651666666

 $00:14:20.880 \longrightarrow 00:14:24.023$ a kinase on your turning on

NOTE Confidence: 0.872277651666666

 $00:14:24.023 \longrightarrow 00:14:27.172$ the the growth instructions and

00:14:27.172 --> 00:14:30.036 when that's not counterbalanced,

NOTE Confidence: 0.872277651666666

 $00:14:30.040 \longrightarrow 00:14:31.988$ that's how cancer develops.

NOTE Confidence: 0.8382126625

 $00:14:32.840 \longrightarrow 00:14:34.316$ Well, we're going to take a

NOTE Confidence: 0.8382126625

00:14:34.316 --> 00:14:36.179 short break for a medical minute,

NOTE Confidence: 0.8382126625

 $00:14:36.180 \longrightarrow 00:14:37.780$ but when we come back,

NOTE Confidence: 0.8382126625

 $00:14:37.780 \longrightarrow 00:14:40.270$ let's learn more about the molecular

NOTE Confidence: 0.8382126625

00:14:40.270 --> 00:14:42.714 mechanisms of cancer and how exactly

NOTE Confidence: 0.8382126625

 $00:14:42.714 \longrightarrow 00:14:44.430$ we target these differentially

NOTE Confidence: 0.8382126625

 $00:14:44.430 \longrightarrow 00:14:46.430$ expressed kinases to actually

NOTE Confidence: 0.8382126625

 $00:14:46.430 \longrightarrow 00:14:49.130$ make a difference for patients,

NOTE Confidence: 0.8382126625

 $00{:}14{:}49.130 \mathrel{--}{>} 00{:}14{:}50.972$ please stay tuned for more with

NOTE Confidence: 0.8382126625

00:14:50.972 --> 00:14:52.550 my guest doctor Daryl Klein

NOTE Confidence: 0.884235398214286

 $00:14:53.060 \longrightarrow 00:14:55.340$ funding for Yale Cancer Answers comes

NOTE Confidence: 0.884235398214286

 $00:14:55.340 \longrightarrow 00:14:57.715$ from Smilow Cancer Hospital with an

NOTE Confidence: 0.884235398214286

 $00:14:57.715 \longrightarrow 00:15:00.097$ event focused on nutrition for cancer

NOTE Confidence: 0.884235398214286

 $00:15:00.097 \longrightarrow 00:15:01.944$ survivorship presented by the Smilow

 $00:15:01.944 \longrightarrow 00:15:03.589$ Cancer Care Center in Trumbull.

NOTE Confidence: 0.884235398214286

 $00{:}15{:}03.590 \dashrightarrow 00{:}15{:}06.894$ April 14th Register at Yale Cancer Center.

NOTE Confidence: 0.884235398214286

 $00:15:06.900 \longrightarrow 00:15:09.658$ Org or email cancer answers at Yale.

NOTE Confidence: 0.838554415

00:15:11.920 --> 00:15:13.832 The American Cancer Society

NOTE Confidence: 0.838554415

 $00:15:13.832 \longrightarrow 00:15:16.368$ estimates that nearly 150,000 people

NOTE Confidence: 0.838554415

 $00:15:16.368 \longrightarrow 00:15:18.986$ in the US will be diagnosed with

NOTE Confidence: 0.838554415

 $00:15:18.986 \longrightarrow 00:15:20.917$ colorectal cancer this year alone.

NOTE Confidence: 0.838554415

 $00:15:20.920 \longrightarrow 00:15:23.070$ When detected, early colorectal cancer

NOTE Confidence: 0.838554415

 $00{:}15{:}23.070 \dashrightarrow 00{:}15{:}25.800$ is easily treated and highly curable,

NOTE Confidence: 0.838554415

00:15:25.800 --> 00:15:27.864 and men and women over the age of

NOTE Confidence: 0.838554415

 $00:15:27.864 \longrightarrow 00:15:29.643$ 45 should have regular colonoscopies

NOTE Confidence: 0.838554415

 $00:15:29.643 \longrightarrow 00:15:31.633$ to screen for the disease.

NOTE Confidence: 0.838554415

 $00{:}15{:}31.640 \dashrightarrow 00{:}15{:}33.088$ Patients with colorectal cancer

NOTE Confidence: 0.838554415

 $00:15:33.088 \longrightarrow 00:15:35.260$ have more hope than ever before,

NOTE Confidence: 0.838554415

 $00:15:35.260 \longrightarrow 00:15:38.080$ thanks to increased access to advanced

 $00:15:38.080 \longrightarrow 00:15:39.960$ therapies and specialized care.

NOTE Confidence: 0.838554415

 $00{:}15{:}39.960 \dashrightarrow 00{:}15{:}41.816$ Clinical trials are currently

NOTE Confidence: 0.838554415

 $00:15:41.816 \longrightarrow 00:15:43.672$ underway at federally designated

NOTE Confidence: 0.838554415

 $00:15:43.672 \longrightarrow 00:15:45.110$ Comprehensive Cancer Centers.

NOTE Confidence: 0.838554415

 $00{:}15{:}45.110 \dashrightarrow 00{:}15{:}47.990$ Such as Yale Cancer Center and its Milo

NOTE Confidence: 0.838554415

 $00{:}15{:}47.990 \dashrightarrow 00{:}15{:}50.583$ Cancer Hospital to test innovative new

NOTE Confidence: 0.838554415

 $00:15:50.583 \longrightarrow 00:15:52.856$ treatments for colorectal cancer tumor.

NOTE Confidence: 0.838554415

 $00:15:52.856 \longrightarrow 00:15:55.186$ Gene analysis has helped improve

NOTE Confidence: 0.838554415

 $00{:}15{:}55.186 \dashrightarrow 00{:}15{:}57.050$ management of colorectal cancer

NOTE Confidence: 0.838554415

00:15:57.115 --> 00:15:59.345 by identifying the patients most

NOTE Confidence: 0.838554415

 $00{:}15{:}59.345 \dashrightarrow 00{:}16{:}01.575$ likely to benefit from chemotherapy

NOTE Confidence: 0.838554415

00:16:01.644 --> 00:16:03.348 and newer targeted agents,

NOTE Confidence: 0.838554415

 $00:16:03.350 \longrightarrow 00:16:06.170$ resulting in more patient specific treatment.

NOTE Confidence: 0.838554415

00:16:06.170 --> 00:16:09.230 More information is available at

NOTE Confidence: 0.838554415

00:16:09.230 --> 00:16:10.532 yalecancercenter.org you're listening

NOTE Confidence: 0.838554415

 $00:16:10.532 \longrightarrow 00:16:12.268$ to Connecticut Public Radio.

 $00:16:13.040 \longrightarrow 00:16:15.056$ Welcome back to Yale Cancer answers.

NOTE Confidence: 0.895207821666667

 $00:16:15.060 \longrightarrow 00:16:16.356$ This is doctor in East Egg

NOTE Confidence: 0.895207821666667

00:16:16.356 --> 00:16:17.778 part and I'm joined to night by

NOTE Confidence: 0.895207821666667

00:16:17.778 --> 00:16:19.294 my guest doctor, Daryl Klein.

NOTE Confidence: 0.895207821666667

 $00:16:19.294 \longrightarrow 00:16:21.556$ We're learning more about the molecular

NOTE Confidence: 0.895207821666667

 $00:16:21.556 \longrightarrow 00:16:23.610$ mechanisms of cancer and right before

NOTE Confidence: 0.895207821666667

 $00:16:23.610 \longrightarrow 00:16:25.852$ the break Daryl was telling us about

NOTE Confidence: 0.895207821666667

 $00:16:25.852 \longrightarrow 00:16:27.507$ this profoundly inspiring story of

NOTE Confidence: 0.895207821666667

00:16:27.507 --> 00:16:30.025 his sister who is diagnosed with CML,

NOTE Confidence: 0.895207821666667

 $00:16:30.025 \longrightarrow 00:16:32.000$ which really started his journey

NOTE Confidence: 0.895207821666667

00:16:32.000 --> 00:16:34.219 on becoming a physician scientist,

NOTE Confidence: 0.895207821666667

 $00:16:34.220 \longrightarrow 00:16:37.298$ and one who is particularly interested

NOTE Confidence: 0.895207821666667

 $00{:}16{:}37.300 \dashrightarrow 00{:}16{:}41.300$ in these molecules called kinases,

NOTE Confidence: 0.895207821666667

 $00:16:41.300 \longrightarrow 00:16:43.334$ which really work.

NOTE Confidence: 0.895207821666667

 $00:16:43.334 \longrightarrow 00:16:48.080$ To activate the growth of of cancer

 $00{:}16{:}48.212 \dashrightarrow 00{:}16{:}51.192$ cells and so you know Darrell before

NOTE Confidence: 0.895207821666667

 $00:16:51.192 \longrightarrow 00:16:53.775$ the break you were mentioning that

NOTE Confidence: 0.895207821666667

00:16:53.775 --> 00:16:56.559 eurolab really after we know that

NOTE Confidence: 0.895207821666667

 $00:16:56.559 \longrightarrow 00:17:00.154$ you know a kinase is involved in a

NOTE Confidence: 0.895207821666667

 $00:17:00.154 \longrightarrow 00:17:02.706$ particular cancer is really involved

NOTE Confidence: 0.895207821666667

 $00:17:02.706 \longrightarrow 00:17:05.692$ in looking at its its structure

NOTE Confidence: 0.895207821666667

 $00:17:05.692 \longrightarrow 00:17:08.254$ and kind of how to target it.

NOTE Confidence: 0.895207821666667

 $00:17:08.260 \longrightarrow 00:17:09.949$ Is that right?

NOTE Confidence: 0.895207821666667 00:17:09.950 --> 00:17:10.720 Exactly,

NOTE Confidence: 0.904520128571429

00:17:11.550 --> 00:17:14.525 my lab is a structural biology lab,

NOTE Confidence: 0.904520128571429

 $00:17:14.530 \longrightarrow 00:17:18.418$ so you know, we're sensually photographers.

NOTE Confidence: 0.904520128571429

 $00:17:18.420 \longrightarrow 00:17:20.240$ But we take pictures of of very,

NOTE Confidence: 0.904520128571429

00:17:20.240 --> 00:17:23.798 very tiny things, molecules and proteins,

NOTE Confidence: 0.904520128571429

 $00:17:23.800 \longrightarrow 00:17:26.085$ and so this. Requires specialized

NOTE Confidence: 0.904520128571429

00:17:26.085 --> 00:17:28.370 equipment cameras if you will.

NOTE Confidence: 0.904520128571429

 $00:17:28.370 \longrightarrow 00:17:32.430$ That use X rays and electrons rather

 $00:17:32.430 \longrightarrow 00:17:34.670$ than light in the in the visual

NOTE Confidence: 0.904520128571429

 $00:17:34.670 \longrightarrow 00:17:36.550$ spectrum that that we're used to.

NOTE Confidence: 0.904520128571429

00:17:36.550 --> 00:17:39.760 Uhm? You know, many people know.

NOTE Confidence: 0.904520128571429

 $00:17:39.760 \longrightarrow 00:17:41.970$ DNA, so let's start there.

NOTE Confidence: 0.904520128571429

 $00{:}17{:}41.970 \dashrightarrow 00{:}17{:}44.749$ People have heard of DNA and Watson

NOTE Confidence: 0.904520128571429

 $00:17:44.749 \longrightarrow 00:17:48.058$ and Crick and and they're double Helix.

NOTE Confidence: 0.904520128571429

00:17:48.060 --> 00:17:51.084 And DNA is is basically a cookbook

NOTE Confidence: 0.904520128571429

00:17:51.084 --> 00:17:54.458 with 10s of thousands of recipes,

NOTE Confidence: 0.904520128571429

 $00{:}17{:}54.460 \rightarrow 00{:}17{:}57.320$ and they're mostly protein recipes,

NOTE Confidence: 0.904520128571429

 $00{:}17{:}57.320 \dashrightarrow 00{:}18{:}01.604$ so I guess it's a keto or Paleo cookbook.

NOTE Confidence: 0.904520128571429

 $00:18:01.610 \longrightarrow 00:18:04.508$ ALK is one of these recipes.

NOTE Confidence: 0.904520128571429

 $00{:}18{:}04.510 \dashrightarrow 00{:}18{:}08.245$ And the recipe in the DNA cookbook tells us

NOTE Confidence: 0.904520128571429

 $00{:}18{:}08.250 \longrightarrow 00{:}18{:}12.290$ the ingredients and the order to make alcc.

NOTE Confidence: 0.904520128571429

 $00:18:12.290 \longrightarrow 00:18:16.754$ But one big problem with this DNA cookbook.

NOTE Confidence: 0.904520128571429

 $00:18:16.760 \longrightarrow 00:18:18.120$ Is it's not illustrated,

 $00:18:18.120 \longrightarrow 00:18:20.628$ so we have no idea what the

NOTE Confidence: 0.904520128571429

00:18:20.628 --> 00:18:22.578 final product will look like.

NOTE Confidence: 0.904520128571429

00:18:22.580 --> 00:18:25.775 So you know my lab follows the recipe to

NOTE Confidence: 0.904520128571429

 $00:18:25.775 \longrightarrow 00:18:28.630$ take pictures of the final products to.

NOTE Confidence: 0.904520128571429

 $00:18:28.630 \longrightarrow 00:18:32.008$ To illustrate this, this DNA cookbook.

NOTE Confidence: 0.904520128571429

00:18:32.010 --> 00:18:35.335 So we take molecular photographs

NOTE Confidence: 0.904520128571429

 $00:18:35.335 \longrightarrow 00:18:38.838$ of the protein and also the mutants

NOTE Confidence: 0.904520128571429

 $00:18:38.838 \longrightarrow 00:18:40.723$ that are found in cancer.

NOTE Confidence: 0.904520128571429

 $00:18:40.730 \longrightarrow 00:18:44.090$ And in these pictures give us a better

NOTE Confidence: 0.904520128571429

00:18:44.090 --> 00:18:46.174 understanding of how things supposed

NOTE Confidence: 0.904520128571429

 $00:18:46.174 \longrightarrow 00:18:49.330$ to look like and how it changes in cancer.

NOTE Confidence: 0.904520128571429

 $00:18:49.330 \longrightarrow 00:18:51.826$ And in this can inform us

NOTE Confidence: 0.904520128571429

 $00:18:51.826 \longrightarrow 00:18:53.074$ about approaches to.

NOTE Confidence: 0.904520128571429

 $00:18:53.080 \longrightarrow 00:18:57.529$ Designing targeted therapeutics.

NOTE Confidence: 0.904520128571429

00:18:57.530 --> 00:19:01.233 So my lab just reported the structure

NOTE Confidence: 0.904520128571429

00:19:01.233 --> 00:19:05.409 of of the protein ALK in nature.

 $00:19:05.410 \longrightarrow 00:19:08.335$ That's the tyrosine kinase that's

NOTE Confidence: 0.904520128571429

 $00:19:08.335 \longrightarrow 00:19:10.090$ important in neuroblastoma.

NOTE Confidence: 0.904520128571429

 $00:19:10.090 \longrightarrow 00:19:12.726$ And this gave us a first look at

NOTE Confidence: 0.904520128571429

00:19:12.726 --> 00:19:15.544 this unique uncle Gene and it's,

NOTE Confidence: 0.904520128571429

00:19:15.544 --> 00:19:18.183 you know it's going to be impossible

NOTE Confidence: 0.904520128571429

 $00:19:18.183 \longrightarrow 00:19:21.210$ for me to relay the complexities here.

NOTE Confidence: 0.904520128571429

 $00:19:21.210 \longrightarrow 00:19:23.196$ But if we stick to our.

NOTE Confidence: 0.904520128571429

 $00:19:23.200 \longrightarrow 00:19:25.758$ Analogy of the the cell is an ocean, it's.

NOTE Confidence: 0.904520128571429

 $00:19:25.758 \longrightarrow 00:19:28.026$ It's not unreasonable to say that

NOTE Confidence: 0.904520128571429

 $00{:}19{:}28.026 \to 00{:}19{:}30.935$ Alcc did actually look a bit like an

NOTE Confidence: 0.904520128571429

00:19:30.935 --> 00:19:33.880 aircraft carrier. I mean it had this.

NOTE Confidence: 0.904520128571429

 $00:19:33.880 \longrightarrow 00:19:37.380$ Unusual a long gated structure and it

NOTE Confidence: 0.904520128571429

 $00{:}19{:}37.380 \dashrightarrow 00{:}19{:}40.796$ probably lies parallel to the to the surface,

NOTE Confidence: 0.904520128571429

 $00:19:40.800 \longrightarrow 00:19:42.900$ so it's like an aircraft carrier

NOTE Confidence: 0.904520128571429

 $00:19:42.900 \longrightarrow 00:19:44.448$ floating on the water.

 $00:19:44.448 \longrightarrow 00:19:46.770$ Or the surface of a cell.

NOTE Confidence: 0.904520128571429

 $00:19:46.770 \longrightarrow 00:19:48.228$ And and furthermore,

NOTE Confidence: 0.904520128571429

 $00:19:48.228 \longrightarrow 00:19:52.430$ we can see how it actually gets activated.

NOTE Confidence: 0.904520128571429

 $00:19:52.430 \longrightarrow 00:19:54.716$ Basically two of these aircraft carriers

NOTE Confidence: 0.904520128571429

00:19:54.716 --> 00:19:57.840 line up next to one another and in

NOTE Confidence: 0.904520128571429

00:19:57.840 --> 00:20:00.126 that position they're then capable to

NOTE Confidence: 0.904520128571429

00:20:00.203 --> 00:20:02.926 sell to send their their growth signals,

NOTE Confidence: 0.904520128571429

00:20:02.930 --> 00:20:05.120 which ultimately end up being

NOTE Confidence: 0.904520128571429

 $00{:}20{:}05.120 \dashrightarrow 00{:}20{:}06.434$ cancerous growth signals.

NOTE Confidence: 0.904520128571429

 $00:20:06.440 \longrightarrow 00:20:08.588$ To the neuroblastoma cell.

NOTE Confidence: 0.904520128571429

 $00{:}20{:}08.588 \to 00{:}20{:}10.736$ Uncontrolled ALK activation like

NOTE Confidence: 0.904520128571429

 $00:20:10.736 \longrightarrow 00:20:13.948$ this leads to cancer and it and it

NOTE Confidence: 0.904520128571429

 $00:20:13.948 \longrightarrow 00:20:16.432$ results from the tumor continuing to

NOTE Confidence: 0.904520128571429

 $00:20:16.432 \longrightarrow 00:20:18.960$ express this developmental out gene

NOTE Confidence: 0.904520128571429

 $00:20:18.960 \longrightarrow 00:20:23.930$ along with its stimulatory ligand.

NOTE Confidence: 0.904520128571429

 $00{:}20{:}23.930 \dashrightarrow 00{:}20{:}26.090$ Our research reveals an approach

 $00:20:26.090 \longrightarrow 00:20:29.229$ to shutting off ALK and and that

NOTE Confidence: 0.904520128571429

 $00:20:29.229 \longrightarrow 00:20:31.484$ it can be quite straightforward.

NOTE Confidence: 0.904520128571429

 $00{:}20{:}31.490 \dashrightarrow 00{:}20{:}34.550$ Potentially if we use our structure

NOTE Confidence: 0.904520128571429

 $00:20:34.550 \longrightarrow 00:20:35.790$ as a sa blueprint,

NOTE Confidence: 0.904520128571429

 $00:20:35.790 \longrightarrow 00:20:37.536$ we can see clear areas where

NOTE Confidence: 0.904520128571429

 $00:20:37.536 \longrightarrow 00:20:39.550$ we would want to target this.

NOTE Confidence: 0.904520128571429

 $00:20:39.550 \longrightarrow 00:20:41.470$ This aircraft like molecule.

NOTE Confidence: 0.904520128571429

 $00:20:41.470 \longrightarrow 00:20:43.731$ I mean there's certain vulnerabilities

NOTE Confidence: 0.904520128571429

 $00:20:43.731 \longrightarrow 00:20:46.118$ that are revealed in the structure that

NOTE Confidence: 0.904520128571429

 $00:20:46.118 \longrightarrow 00:20:48.283$ we can strategically target and and

NOTE Confidence: 0.904520128571429

00:20:48.283 --> 00:20:50.425 you know sync this aircraft carrier,

NOTE Confidence: 0.904520128571429

 $00{:}20{:}50.430 \dashrightarrow 00{:}20{:}53.310$ and so my lab now is designing potent

NOTE Confidence: 0.7377237425

 $00{:}20{:}53.310 \dashrightarrow 00{:}20{:}54.924$ antibodies. That specifically

NOTE Confidence: 0.7377237425

00:20:54.924 --> 00:20:57.614 target these regions in ALK,

NOTE Confidence: 0.7377237425

 $00:20:57.620 \longrightarrow 00:21:00.014$ and you know there's there's small

 $00:21:00.014 \longrightarrow 00:21:02.358$ molecules currently out there in use for.

NOTE Confidence: 0.7377237425

 $00:21:02.360 \longrightarrow 00:21:04.820$ Neuroblastoma, as well as many other

NOTE Confidence: 0.7377237425

 $00:21:04.820 \longrightarrow 00:21:07.119$ different cancers that are driven or

NOTE Confidence: 0.7377237425

00:21:07.120 --> 00:21:10.528 or partially dependent on on kinases.

NOTE Confidence: 0.7377237425

 $00{:}21{:}10.530 \dashrightarrow 00{:}21{:}12.855$ And compared to small molecule

NOTE Confidence: 0.7377237425

00:21:12.855 --> 00:21:13.785 therapeutics antibodies,

NOTE Confidence: 0.7377237425

 $00{:}21{:}13.790 \dashrightarrow 00{:}21{:}16.674$ I think can offer a great benefit.

NOTE Confidence: 0.7377237425

 $00:21:16.680 \longrightarrow 00:21:18.845$ The small molecule drugs that

NOTE Confidence: 0.7377237425

 $00{:}21{:}18.845 {\:\raisebox{--}{\text{--}}}{\:\raisebox{--}{\text{--}}}{\:\raisebox{--}{\text{--}}} 00{:}21{:}21.527$ are now currently in use like

NOTE Confidence: 0.7377237425

00:21:21.527 --> 00:21:23.667 prison and learn Latin.

NOTE Confidence: 0.7377237425

 $00{:}21{:}23.670 \dashrightarrow 00{:}21{:}25.450$ They target the intracellular.

NOTE Confidence: 0.7377237425

 $00:21:25.450 \longrightarrow 00:21:29.060$ The actual kinase domain of the protein out.

NOTE Confidence: 0.7377237425

 $00:21:29.060 \longrightarrow 00:21:31.734$ And one problem with these types of

NOTE Confidence: 0.7377237425

 $00:21:31.734 \longrightarrow 00:21:33.510$ inhibitors is that you can't keep

NOTE Confidence: 0.7377237425

 $00:21:33.510 \longrightarrow 00:21:35.240$ fooling the cancer for very long.

NOTE Confidence: 0.7377237425

 $00:21:35.240 \longrightarrow 00:21:37.322$ They the cancer figures out this

 $00{:}21{:}37.322 \dashrightarrow 00{:}21{:}39.446$ trip quite fast that you're trying

NOTE Confidence: 0.7377237425

00:21:39.446 --> 00:21:42.118 to inhibit it in this in this domain,

NOTE Confidence: 0.7377237425

 $00:21:42.120 \longrightarrow 00:21:44.745$ and they and the cancer makes changes

NOTE Confidence: 0.7377237425

 $00:21:44.745 \longrightarrow 00:21:46.829$ that diminish the drugs impact.

NOTE Confidence: 0.7377237425

 $00:21:46.830 \longrightarrow 00:21:48.690$ Whereas I think the antibody

NOTE Confidence: 0.7377237425

 $00:21:48.690 \longrightarrow 00:21:51.599$ approach is is a more brute

NOTE Confidence: 0.7377237425

00:21:51.599 --> 00:21:53.770 force approach and it's harder for

NOTE Confidence: 0.7377237425

 $00:21:53.770 \longrightarrow 00:21:55.270$ the cancer to overcome this,

NOTE Confidence: 0.7377237425

 $00{:}21{:}55.270 \dashrightarrow 00{:}21{:}57.194$ the strategy of inhibition.

NOTE Confidence: 0.7377237425

 $00{:}21{:}57.194 \dashrightarrow 00{:}22{:}00.080$ I think the the therapeutic future

NOTE Confidence: 0.7377237425

 $00:22:00.163 \longrightarrow 00:22:02.373$ will likely use a combination

NOTE Confidence: 0.7377237425

 $00:22:02.373 \longrightarrow 00:22:04.583$ of these two to completely.

NOTE Confidence: 0.7377237425

 $00:22:04.590 \longrightarrow 00:22:08.660$ Dismantle the the out machinery.

NOTE Confidence: 0.7377237425

 $00{:}22{:}08.660 \dashrightarrow 00{:}22{:}10.940$ In some ways you know cancer can be

NOTE Confidence: 0.7377237425

 $00:22:10.940 \longrightarrow 00:22:13.157$ feod viewed as having some of the

00:22:13.157 --> 00:22:15.445 similar challenges that we see for SARS,

NOTE Confidence: 0.7377237425

 $00:22:15.445 \longrightarrow 00:22:18.235$ Co V2 and both use similar

NOTE Confidence: 0.7377237425

 $00{:}22{:}18.235 \dashrightarrow 00{:}22{:}20.400$ strategies to overcome disease.

NOTE Confidence: 0.7377237425

 $00:22:20.400 \longrightarrow 00:22:23.280$ Both you know cancer and

NOTE Confidence: 0.7377237425

 $00:22:23.280 \longrightarrow 00:22:25.008$ viruses mutate rapidly.

NOTE Confidence: 0.7377237425

 $00:22:25.010 \longrightarrow 00:22:27.885$ And they can evolve to

NOTE Confidence: 0.7377237425

 $00:22:27.885 \longrightarrow 00:22:29.610$ different inhibitor approaches.

NOTE Confidence: 0.7377237425

 $00:22:29.610 \longrightarrow 00:22:32.220$ And just as we use antibodies

NOTE Confidence: 0.7377237425

 $00{:}22{:}32.220 \dashrightarrow 00{:}22{:}35.312$ through vaccination or or directly

NOTE Confidence: 0.7377237425

 $00:22:35.312 \longrightarrow 00:22:37.964$ injecting recombinant antibodies and

NOTE Confidence: 0.7377237425

 $00:22:37.964 \longrightarrow 00:22:40.890$ small molecules to overcome COVID.

NOTE Confidence: 0.7377237425

00:22:40.890 --> 00:22:44.299 Now we have a new blueprint for ALK to

NOTE Confidence: 0.7377237425

 $00:22:44.299 \longrightarrow 00:22:46.244$ help us overcome similar challenges

NOTE Confidence: 0.7377237425

 $00:22:46.244 \longrightarrow 00:22:48.742$ that are encountered in in cancer

NOTE Confidence: 0.7377237425

 $00:22:48.742 \longrightarrow 00:22:50.498$ and in particular neuroblastoma.

NOTE Confidence: 0.900451000714286

 $00:22:51.520 \longrightarrow 00:22:55.003$ And it sounds like when you know the the

 $00:22:55.003 \longrightarrow 00:22:57.568$ structure of these aircraft carriers.

NOTE Confidence: 0.900451000714286

 $00{:}22{:}57.570 \longrightarrow 00{:}23{:}00.377$ But you can be very specific about

NOTE Confidence: 0.900451000714286

 $00:23:00.377 \longrightarrow 00:23:02.682$ you know targeting those particular

NOTE Confidence: 0.900451000714286

 $00:23:02.682 \longrightarrow 00:23:05.748$ molecules as opposed to normal cells.

NOTE Confidence: 0.900451000714286

00:23:05.750 --> 00:23:08.156 So you might have you know

NOTE Confidence: 0.900451000714286

 $00:23:08.156 \longrightarrow 00:23:10.570$ a bomber that only targets,

NOTE Confidence: 0.900451000714286

 $00:23:10.570 \longrightarrow 00:23:12.616$ you know that flatbed where the

NOTE Confidence: 0.900451000714286

 $00:23:12.616 \longrightarrow 00:23:15.149$ aircraft lands on the aircraft carrier.

NOTE Confidence: 0.900451000714286

 $00{:}23{:}15.150 \dashrightarrow 00{:}23{:}18.918$ Or you can have some sort of a.

NOTE Confidence: 0.900451000714286

 $00:23:18.920 \longrightarrow 00:23:21.728$ A mechanism whereby these two aircraft

NOTE Confidence: 0.900451000714286

 $00{:}23{:}21.728 \longrightarrow 00{:}23{:}24.986$ carriers can't line up together that really

NOTE Confidence: 0.900451000714286

00:23:24.986 --> 00:23:27.074 wouldn't apply in any other situation,

NOTE Confidence: 0.900451000714286

 $00{:}23{:}27.080 \dashrightarrow 00{:}23{:}29.712$ so you can try to get more precise

NOTE Confidence: 0.900451000714286

 $00:23:29.712 \longrightarrow 00:23:31.939$ or more targeted the rapies.

NOTE Confidence: 0.900451000714286

 $00:23:31.940 \longrightarrow 00:23:32.468$ Is that right?

00:23:33.820 --> 00:23:34.912 That's exactly right,

NOTE Confidence: 0.931961159090909

 $00:23:34.912 \longrightarrow 00:23:37.860$ and remember that I said that you know,

NOTE Confidence: 0.931961159090909

 $00:23:37.860 \longrightarrow 00:23:40.025$ since alpha is expressed only

NOTE Confidence: 0.931961159090909

00:23:40.025 --> 00:23:42.190 on neuroblastoma cells but not

NOTE Confidence: 0.931961159090909

00:23:42.263 --> 00:23:44.139 present on healthy tissue,

NOTE Confidence: 0.931961159090909

 $00:23:44.140 \longrightarrow 00:23:45.668$ it really makes targeting

NOTE Confidence: 0.931961159090909

00:23:45.668 --> 00:23:47.960 ALK the perfect for you know.

NOTE Confidence: 0.931961159090909

00:23:47.960 --> 00:23:49.410 Set up for precision medicine

NOTE Confidence: 0.931961159090909

 $00:23:49.410 \longrightarrow 00:23:51.639$ and then a layer on top of that,

NOTE Confidence: 0.931961159090909

00:23:51.640 --> 00:23:53.992 which I think you were just referring

NOTE Confidence: 0.931961159090909

 $00:23:53.992 \longrightarrow 00:23:57.177$ to is now that we know the detailed

NOTE Confidence: 0.931961159090909

 $00:23:57.177 \longrightarrow 00:23:59.282$ structure and blueprints of this.

NOTE Confidence: 0.931961159090909

 $00:23:59.290 \longrightarrow 00:24:00.434$ And that's exactly what we're trying to do.

NOTE Confidence: 0.931961159090909

00:24:00.440 --> 00:24:02.240 We're trying to design

NOTE Confidence: 0.931961159090909

 $00:24:02.240 \longrightarrow 00:24:03.590$ antibodies that specifically.

NOTE Confidence: 0.931961159090909

 $00:24:03.590 \longrightarrow 00:24:07.210$ Block areas on the protein that are

 $00:24:07.210 \longrightarrow 00:24:09.850$ involved in important for it's activation.

NOTE Confidence: 0.931961159090909

 $00:24:09.850 \longrightarrow 00:24:12.754$ That is precisely where the ligand

NOTE Confidence: 0.931961159090909

 $00:24:12.754 \longrightarrow 00:24:17.150$ binds to activate the receptor and

NOTE Confidence: 0.931961159090909

00:24:17.150 --> 00:24:19.990 getting back to how it's activated.

NOTE Confidence: 0.931961159090909

 $00:24:19.990 \longrightarrow 00:24:22.762$ Where we see the two molecules

NOTE Confidence: 0.931961159090909

00:24:22.762 --> 00:24:24.998 lining up side-by-side to each other,

NOTE Confidence: 0.931961159090909

00:24:25.000 --> 00:24:27.085 we're designing antibodies that can

NOTE Confidence: 0.931961159090909

 $00{:}24{:}27.085 \dashrightarrow 00{:}24{:}29.624$ block that interface to prevent it

NOTE Confidence: 0.931961159090909

00:24:29.624 --> 00:24:31.940 from being activated that is being

NOTE Confidence: 0.931961159090909

 $00:24:31.940 \longrightarrow 00:24:33.600$ activated independent of ligand.

NOTE Confidence: 0.931961159090909

00:24:33.600 --> 00:24:36.197 Which could be caused by certain mutations,

NOTE Confidence: 0.931961159090909

 $00:24:36.200 \longrightarrow 00:24:38.780$ which is further research that we're

NOTE Confidence: 0.931961159090909

 $00:24:38.780 \longrightarrow 00:24:41.900$ doing now or or with the ligand.

NOTE Confidence: 0.931961159090909

 $00:24:41.900 \longrightarrow 00:24:45.278$ So we're using all this information

NOTE Confidence: 0.931961159090909

00:24:45.278 --> 00:24:47.530 to specifically design antibodies

 $00:24:47.614 \longrightarrow 00:24:50.062$ that are tailored to this molecule

NOTE Confidence: 0.931961159090909

 $00{:}24{:}50.062 \dashrightarrow 00{:}24{:}53.342$ and the and the type of mutations

NOTE Confidence: 0.931961159090909

00:24:53.342 --> 00:24:55.952 or mechanisms that activate it

NOTE Confidence: 0.931961159090909

 $00:24:55.952 \longrightarrow 00:24:58.300$ specifically in in neuroblastoma.

NOTE Confidence: 0.913035372

 $00:24:59.530 \longrightarrow 00:25:02.470$ And so as you design these

NOTE Confidence: 0.913035372

 $00:25:02.470 \longrightarrow 00:25:04.430$ antibodies in these treatments,

NOTE Confidence: 0.913035372

 $00:25:04.430 \longrightarrow 00:25:06.716$ you're doing that in the lab. How?

NOTE Confidence: 0.913035372

00:25:06.716 --> 00:25:08.998 How does it actually get into patients?

NOTE Confidence: 0.913035372

00:25:09.000 --> 00:25:11.760 How does it affect people like your sister?

NOTE Confidence: 0.913035372

 $00:25:11.760 \longrightarrow 00:25:14.415$ Because that's where the story

NOTE Confidence: 0.913035372

 $00:25:14.415 \longrightarrow 00:25:16.473$ really started and how long

NOTE Confidence: 0.913035372

 $00{:}25{:}16.473 \dashrightarrow 00{:}25{:}18.128$ does that whole process take?

NOTE Confidence: 0.796460149

00:25:19.720 --> 00:25:21.772 You're right, that's a that's certainly

NOTE Confidence: 0.796460149

 $00{:}25{:}21.772 \dashrightarrow 00{:}25{:}24.452$ is is a long process and you know

NOTE Confidence: 0.796460149

 $00:25:24.452 \longrightarrow 00:25:26.851$ Cancer Research is is so matured and

NOTE Confidence: 0.796460149

 $00:25:26.851 \longrightarrow 00:25:29.041$ specialized now that it really requires

 $00:25:29.041 \longrightarrow 00:25:31.664$ you know effort to put these discoveries

NOTE Confidence: 0.796460149

 $00{:}25{:}31.664 \dashrightarrow 00{:}25{:}33.854$ into usable formats and for others

NOTE Confidence: 0.796460149

 $00:25:33.860 \longrightarrow 00:25:36.986$ to build upon and meaningful ways.

NOTE Confidence: 0.796460149

00:25:36.990 --> 00:25:39.790 And just as the NIH created that MSTP

NOTE Confidence: 0.796460149

 $00:25:39.790 \longrightarrow 00:25:42.702$ program to link basic science and patient

NOTE Confidence: 0.796460149

 $00:25:42.702 \longrightarrow 00:25:45.496$ Care now I think we need similar links

NOTE Confidence: 0.796460149

 $00:25:45.496 \longrightarrow 00:25:47.310$ between basic science researchers.

NOTE Confidence: 0.796460149

 $00{:}25{:}47.310 \dashrightarrow 00{:}25{:}50.572$ I mean, the you know RNA biologist

NOTE Confidence: 0.796460149

 $00:25:50.572 \longrightarrow 00:25:52.360$ and chromosome researcher and.

NOTE Confidence: 0.796460149

00:25:52.360 --> 00:25:54.388 And in the biophysicist like me

NOTE Confidence: 0.796460149

00:25:54.388 --> 00:25:56.871 trying to link up with the model

NOTE Confidence: 0.796460149

 $00:25:56.871 \longrightarrow 00:25:59.335$ Organism biologist to test the a lot

NOTE Confidence: 0.796460149

 $00{:}25{:}59.409 \dashrightarrow 00{:}26{:}01.619$ of these and preclinical setups.

NOTE Confidence: 0.796460149

 $00{:}26{:}01.620 \dashrightarrow 00{:}26{:}04.168$ We all speak a different scientific dialect

NOTE Confidence: 0.796460149

 $00:26:04.168 \longrightarrow 00:26:06.300$ and we have different perspectives,

 $00:26:06.300 \longrightarrow 00:26:10.460$ so you know how do we work together

NOTE Confidence: 0.796460149

00:26:10.555 --> 00:26:12.577 and in one answer to that is is,

NOTE Confidence: 0.796460149

 $00:26:12.580 \longrightarrow 00:26:14.996$ you know being part of the Yale Cancer

NOTE Confidence: 0.796460149

 $00{:}26{:}14.996 \to 00{:}26{:}17.377$ Biol Biology Institute that I'm a part of.

NOTE Confidence: 0.796460149

00:26:17.380 --> 00:26:19.942 You know we we really bring

NOTE Confidence: 0.796460149

 $00{:}26{:}19.942 \dashrightarrow 00{:}26{:}21.650$ together desperate researchers among

NOTE Confidence: 0.796460149

 $00:26:21.718 \longrightarrow 00:26:23.518$ those interested in cancer.

NOTE Confidence: 0.796460149

00:26:23.520 --> 00:26:26.310 And so you know now I have and and

NOTE Confidence: 0.796460149

 $00{:}26{:}26.310 {\:{\circ}{\circ}{\circ}}>00{:}26{:}29.380$ being a physician scientist so you know

NOTE Confidence: 0.796460149

 $00:26:29.380 \longrightarrow 00:26:32.250$ now there's a cohort of people and

NOTE Confidence: 0.796460149

 $00{:}26{:}32.250 \dashrightarrow 00{:}26{:}35.024$ colleagues that I can work with that

NOTE Confidence: 0.796460149

 $00{:}26{:}35.024 \dashrightarrow 00{:}26{:}37.148$ can bring our developing antibodies

NOTE Confidence: 0.796460149

 $00:26:37.148 \longrightarrow 00:26:40.292$ that we have into preclinical testing

NOTE Confidence: 0.796460149

 $00:26:40.292 \longrightarrow 00:26:43.850$ quite rapidly to see if they do.

NOTE Confidence: 0.796460149

00:26:43.850 --> 00:26:48.230 So good activity in vivo and then that

NOTE Confidence: 0.796460149

 $00:26:48.230 \longrightarrow 00:26:50.430$ hopefully can be rapidly leveraged

 $00:26:50.430 \longrightarrow 00:26:53.169$ into reaching the the patients that

NOTE Confidence: 0.796460149

 $00{:}26{:}53.169 \dashrightarrow 00{:}26{:}55.180$ desperately need these treatments.

NOTE Confidence: 0.90850388875

00:26:56.680 --> 00:26:58.490 Sounds very much like you

NOTE Confidence: 0.90850388875

00:26:58.490 --> 00:26:59.576 had mentioned earlier,

NOTE Confidence: 0.90850388875

 $00:26:59.580 \longrightarrow 00:27:02.396$ but this is kind of a microcosm for

NOTE Confidence: 0.90850388875

00:27:02.396 --> 00:27:04.680 the macrocosm of how science works,

NOTE Confidence: 0.90850388875

 $00:27:04.680 \longrightarrow 00:27:06.960$ that that your lab puts together.

NOTE Confidence: 0.90850388875

 $00:27:06.960 \longrightarrow 00:27:09.284$ People who all kind of come at

NOTE Confidence: 0.90850388875

 $00:27:09.284 \longrightarrow 00:27:12.099$ the problem of of ALK from a

NOTE Confidence: 0.90850388875

 $00:27:12.099 \longrightarrow 00:27:13.835$ slightly different vantage point.

NOTE Confidence: 0.90850388875

 $00:27:13.840 \longrightarrow 00:27:17.574$ But the work in your lab kind of builds

NOTE Confidence: 0.90850388875

 $00:27:17.574 \longrightarrow 00:27:19.800$ on the work of other people's labs,

NOTE Confidence: 0.90850388875

 $00{:}27{:}19.800 \dashrightarrow 00{:}27{:}22.572$ and so may be in in the last

NOTE Confidence: 0.90850388875

 $00:27:22.572 \longrightarrow 00:27:24.580$ few minutes that we have,

NOTE Confidence: 0.90850388875

 $00:27:24.580 \longrightarrow 00:27:26.810$ you could tell us kind of a little bit about.

00:27:26.810 --> 00:27:29.357 How that works in the grand scheme of things?

NOTE Confidence: 0.90850388875

 $00{:}27{:}29.360 --> 00{:}27{:}31.150$ I mean, it sounds like.

NOTE Confidence: 0.90850388875

 $00:27:31.150 \longrightarrow 00:27:33.230$ One of the things that we've realized with

NOTE Confidence: 0.90850388875

00:27:33.230 --> 00:27:35.266 the pandemic is that the world is shrinking,

NOTE Confidence: 0.90850388875

 $00:27:35.270 \longrightarrow 00:27:38.015$ and hopefully the scientific discovery

NOTE Confidence: 0.90850388875

 $00:27:38.015 \longrightarrow 00:27:41.559$ from one lab to another kind of.

NOTE Confidence: 0.90850388875

00:27:41.560 --> 00:27:43.240 Bounces around fairly easily.

NOTE Confidence: 0.90850388875

 $00:27:43.240 \longrightarrow 00:27:45.340$ How does that collaboration work?

NOTE Confidence: 0.882697558

00:27:46.130 --> 00:27:49.136 I think it is. It is certainly a challenge

NOTE Confidence: 0.882697558

00:27:49.136 --> 00:27:51.664 and I think you know getting getting

NOTE Confidence: 0.882697558

 $00{:}27{:}51.664 \dashrightarrow 00{:}27{:}54.656$ researchers to to talk to each other and

NOTE Confidence: 0.882697558

 $00:27:54.656 \longrightarrow 00:27:57.786$ work together is an important part of that.

NOTE Confidence: 0.882697558

00:27:57.790 --> 00:28:00.940 And like you said, I think you know

NOTE Confidence: 0.882697558

 $00{:}28{:}00.940 \to 00{:}28{:}03.550$ during the pandemic and having people

NOTE Confidence: 0.882697558

 $00:28:03.550 \longrightarrow 00:28:06.008$ communicate in different ways like we

NOTE Confidence: 0.882697558

 $00:28:06.008 \longrightarrow 00:28:08.850$ are now through zoom and other things.

 $00{:}28{:}08.850 \dashrightarrow 00{:}28{:}11.424$ Maybe the world is shrinking a bit and I

NOTE Confidence: 0.882697558

 $00{:}28{:}11.424 \dashrightarrow 00{:}28{:}13.944$ think that's a good thing for science and

NOTE Confidence: 0.882697558

 $00:28:13.944 \longrightarrow 00:28:16.520$ that's a good thing for research because.

NOTE Confidence: 0.882697558

00:28:16.520 --> 00:28:19.472 Of course, all of us working

NOTE Confidence: 0.882697558

 $00:28:19.472 \longrightarrow 00:28:21.440$ independently and making advances.

NOTE Confidence: 0.882697558

 $00:28:21.440 \longrightarrow 00:28:23.169$ We don't want them to go unnoticed

NOTE Confidence: 0.882697558

 $00:28:23.169 \longrightarrow 00:28:25.033$ by the people next in that chain

NOTE Confidence: 0.882697558

 $00:28:25.033 \longrightarrow 00:28:26.373$ that you were talking about.

NOTE Confidence: 0.882697558

 $00:28:26.380 \longrightarrow 00:28:28.495$ That's necessary to make the

NOTE Confidence: 0.882697558

 $00{:}28{:}28.495 \dashrightarrow 00{:}28{:}30.610$ leap to bring these discoveries

NOTE Confidence: 0.882697558

 $00{:}28{:}30.683 \dashrightarrow 00{:}28{:}32.867$ to their the rapeutic potential.

NOTE Confidence: 0.772678952866667

 $00{:}28{:}33.480 \dashrightarrow 00{:}28{:}35.670$ Doctor Daryl Klein is an assistant

NOTE Confidence: 0.772678952866667

 $00{:}28{:}35.670 \dashrightarrow 00{:}28{:}37.130$ professor of pharmacology at

NOTE Confidence: 0.772678952866667

00:28:37.195 --> 00:28:38.820 the Yale School of Medicine.

NOTE Confidence: 0.772678952866667

 $00:28:38.820 \longrightarrow 00:28:40.852$ If you have questions,

 $00{:}28{:}40.852 \dashrightarrow 00{:}28{:}42.747$ the address is canceranswers@yale.edu

NOTE Confidence: 0.772678952866667

 $00{:}28{:}42.747 \dashrightarrow 00{:}28{:}44.949$ and past editions of the program

NOTE Confidence: 0.772678952866667

 $00{:}28{:}44.949 \dashrightarrow 00{:}28{:}47.028$ are available in audio and written.

NOTE Confidence: 0.772678952866667

00:28:47.030 --> 00:28:48.968 Farm at yalecancercenter.org.

NOTE Confidence: 0.772678952866667

 $00{:}28{:}48.968 \dashrightarrow 00{:}28{:}51.512$ We hope you'll join us next week to

NOTE Confidence: 0.772678952866667

 $00{:}28{:}51.512 \dashrightarrow 00{:}28{:}53.449$ learn more about the fight against

NOTE Confidence: 0.772678952866667

 $00:28:53.449 \longrightarrow 00:28:55.014$ cancer here on Connecticut Public

NOTE Confidence: 0.772678952866667

 $00:28:55.068 \longrightarrow 00:28:56.856$ radio funding for Yale Cancer Answers

NOTE Confidence: 0.772678952866667

00:28:56.856 --> 00:29:00.000 is provided by Smilow Cancer Hospital.