WEBVTT

NOTE duration:"00:29:00"

NOTE recognizability:0.848

NOTE language:en-us

NOTE Confidence: 0.895326650909091

 $00:00:00.000 \rightarrow 00:00:02.154$  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 --> 00:00:11.618 host doctor in East JGP are Yale Cancer

NOTE Confidence: 0.8923836

 $00{:}00{:}11.618 \dashrightarrow 00{:}00{:}13.488$  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

 $00{:}00{:}20{.}774 \dashrightarrow 00{:}00{:}22{.}946$  It's a conversation about the molecular

NOTE Confidence: 0.8923836

 $00{:}00{:}22.946 \dashrightarrow 00{:}00{:}25.488$  mechanisms of cancer with Doctor Daryl Klein.

NOTE Confidence: 0.8923836

 $00{:}00{:}25{.}490 \dashrightarrow 00{:}00{:}27{.}744$ Doctor Klein is an assistant professor of

NOTE Confidence: 0.8923836

00:00:27.744 --> 00:00:30.027 pharmacology at the Yale School of Medicine,

NOTE Confidence: 0.8923836

 $00{:}00{:}30{.}030 \dashrightarrow 00{:}00{:}32{.}076$  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 --> 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 --> 00:00:39.605 bit more about yourself and

NOTE Confidence: 0.9258690608

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

NOTE Confidence: 0.737310321

 $00{:}00{:}42.070 \dashrightarrow 00{:}00{:}43.870$  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

 $00:00:46.894 \rightarrow 00:00:49.423$  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

 $00:00:52.590 \rightarrow 00:00:54.918$  In some ways, I feel like I've been

NOTE Confidence: 0.737310321

 $00{:}00{:}54{.}918$  -->  $00{:}00{:}57{.}360$  destined to study kinases and cancer and

NOTE Confidence: 0.737310321

 $00:00:57.360 \rightarrow 00:01:00.547$  their mechanisms and and with the hope of

NOTE Confidence: 0.737310321

 $00{:}01{:}00{.}547 \dashrightarrow 00{:}01{:}02{.}315$  developing useful cancer the rapeutics.

NOTE Confidence: 0.737310321

 $00:01:02.320 \longrightarrow 00:01:05.260$  And my career trajectory if you will.

NOTE Confidence: 0.737310321

00:01:05.260 --> 00:01:06.908 As a medical scientist,

NOTE Confidence: 0.737310321

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

- NOTE Confidence: 0.737310321
- 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
- $00:01:14.840 \rightarrow 00:01:18.466$  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
- $00{:}01{:}25{.}050 \dashrightarrow 00{:}01{:}28{.}230$  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
- $00{:}01{:}32.690 \dashrightarrow 00{:}01{:}35.468$  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
- $00:01:37.835 \rightarrow 00:01:40.873$  the driving mutations that lead to CML.
- NOTE Confidence: 0.737310321
- $00{:}01{:}40.880$  -->  $00{:}01{:}43.142$  And he discovered a chromosome alteration NOTE Confidence: 0.737310321
- 00:01:43.142 --> 00:01:45.437 that he dubbed the Philadelphia
- NOTE Confidence: 0.737310321
- $00{:}01{:}45{.}437 \dashrightarrow 00{:}01{:}47{.}243$  chromosome and kmle patients,
- NOTE Confidence: 0.737310321
- $00:01:47.243 \dashrightarrow 00:01:49.770$  like my sister and and the results
- NOTE Confidence: 0.737310321

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

NOTE Confidence: 0.737310321

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

NOTE Confidence: 0.737310321

 $00:01:53.479 \dashrightarrow 00:01:56.398$  of a tyrosine kinase signaling protein?

NOTE Confidence: 0.737310321

 $00:01:56.400 \rightarrow 00:01:58.696$  That's stuck in the on position,

NOTE Confidence: 0.737310321

 $00{:}01{:}58{.}700 \dashrightarrow 00{:}02{:}00{.}780$  and that instructs cells to.

NOTE Confidence: 0.737310321

 $00{:}02{:}00{.}780 \dashrightarrow 00{:}02{:}03.867$  To divide and grow and thus cancer.

NOTE Confidence: 0.737310321

 $00{:}02{:}03.870 \dashrightarrow 00{:}02{:}06.110$  And that protein became a target for

NOTE Confidence: 0.737310321

 $00:02:06.110 \longrightarrow 00:02:08.179$  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

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

NOTE Confidence: 0.737310321

 $00{:}02{:}12.860 \dashrightarrow 00{:}02{:}15.004$  You know bad protein with a drug and

NOTE Confidence: 0.737310321

 $00:02:15.004 \dashrightarrow 00:02:17.099$  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

 $00:02:20.430 \longrightarrow 00:02:22.490$  The mat neighbor or Gleevec,

NOTE Confidence: 0.737310321

 $00{:}02{:}22{.}490 \dashrightarrow 00{:}02{:}24{.}668$  and that became the first drug

NOTE Confidence: 0.737310321

 $00:02:24.670 \longrightarrow 00:02:26.386$  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

 $00{:}02{:}30{.}170 \dashrightarrow 00{:}02{:}33{.}110$  And patients treated with this drug can

NOTE Confidence: 0.737310321

 $00:02:33.110 \rightarrow 00:02:36.290$  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

 $00:02:45.560 \longrightarrow 00:02:46.700$  and that meant you know,

NOTE Confidence: 0.737310321

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

NOTE Confidence: 0.737310321

 $00{:}02{:}48.620 \dashrightarrow 00{:}02{:}50.867$  In this powerlessness drives me to find

NOTE Confidence: 0.737310321

 $00:02:50.867 \rightarrow 00:02:53.351$  ways to spare other families similar

NOTE Confidence: 0.737310321

 $00{:}02{:}53{.}351 \dashrightarrow 00{:}02{:}57{.}017$  devastation and to better understand cancer.

NOTE Confidence: 0.737310321

 $00:02:57.020 \rightarrow 00:02:57.506$  You know,

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

NOTE Confidence: 0.737310321

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

NOTE Confidence: 0.737310321

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

NOTE Confidence: 0.737310321

 $00:03:04.127 \longrightarrow 00:03:04.556$  And.

NOTE Confidence: 0.737310321

 $00{:}03{:}04.556 \dashrightarrow 00{:}03{:}07.796$  You know on that path I attended

NOTE Confidence: 0.737310321

 $00:03:07.796 \dashrightarrow 00:03:10.116$  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 --> 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

 $00{:}03{:}19{.}130 \dashrightarrow 00{:}03{:}21.659$  So I was walking the same halls as Peter,

NOTE Confidence: 0.737310321

00:03:21.660 --> 00:03:24.552 Noel and my parents and my

NOTE Confidence: 0.737310321

 $00:03:24.552 \longrightarrow 00:03:25.998$  sister years before.

NOTE Confidence: 0.737310321

00:03:26.000 --> 00:03:29.072 I joined the MSTP or medical

NOTE Confidence: 0.737310321

00:03:29.072 --> 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,

- NOTE Confidence: 0.737310321
- 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
- $00{:}03{:}41{.}350 \dashrightarrow 00{:}03{:}43{.}385$  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
- $00:03:50.944 \dashrightarrow 00:03:52.812$  the rapeutics 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
- $00:03:56.033 \rightarrow 00:03:58.397$  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
- $00{:}04{:}00{.}485 \dashrightarrow 00{:}04{:}02{.}153$  other kinases and cancer.
- NOTE Confidence: 0.737310321
- $00{:}04{:}02{.}160 \dashrightarrow 00{:}04{:}03{.}518$  And so when I was at Penn,
- NOTE Confidence: 0.932154455
- $00{:}04{:}03.520 \dashrightarrow 00{:}04{:}06.880$ I studied under Professor Mark Lemon.
- NOTE Confidence: 0.932154455

 $00{:}04{:}06{.}880 \dashrightarrow 00{:}04{:}09{.}092$  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

 $00{:}04{:}11{.}250 \dashrightarrow 00{:}04{:}14{.}450$  And you know, to see how they might

NOTE Confidence: 0.932154455

 $00{:}04{:}14.450 \dashrightarrow 00{:}04{:}16.998$  cause cancer and how we might leverage

NOTE Confidence: 0.932154455

 $00{:}04{:}16.998 \dashrightarrow 00{:}04{:}18.090$  understanding their mechanisms

NOTE Confidence: 0.932154455

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

NOTE Confidence: 0.932154455

 $00{:}04{:}21{.}900 \dashrightarrow 00{:}04{:}24{.}875$  I also mentioned you know my my

NOTE Confidence: 0.932154455

 $00:04:24.875 \rightarrow 00:04:28.778$  desire for you know competition.

NOTE Confidence: 0.932154455

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

NOTE Confidence: 0.932154455

 $00{:}04{:}31{.}428 \dashrightarrow 00{:}04{:}33{.}839$  that people really understand is

NOTE Confidence: 0.932154455

 $00{:}04{:}33{.}839 \dashrightarrow 00{:}04{:}35{.}620$  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 --> 00:04:38.668 I grew up playing sports in college

NOTE Confidence: 0.932154455

 $00{:}04{:}38.668 \dashrightarrow 00{:}04{:}40.916$  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 --> 00:04:46.397 And when I first joined Mark's

- NOTE Confidence: 0.932154455
- $00{:}04{:}46.397 \dashrightarrow 00{:}04{:}48.056$  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
- $00{:}04{:}49{.}200 \dashrightarrow 00{:}04{:}51{.}408$  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
- $00{:}04{:}56{.}467 \dashrightarrow 00{:}04{:}59{.}255$  sport seem safe by comparison and and I
- NOTE Confidence: 0.932154455
- $00:04:59.255 \rightarrow 00:05:02.500$  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
- $00:05:04.852 \rightarrow 00:05:06.028$  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
- $00:05:08.042 \rightarrow 00:05:11.060$  competitors and and an unknown number
- NOTE Confidence: 0.932154455
- $00{:}05{:}11.142 \dashrightarrow 00{:}05{:}13.685$  of of teams and and the rules of the
- NOTE Confidence: 0.932154455
- $00:05:13.685 \rightarrow 00:05:15.957$  game are undefined and you don't even
- NOTE Confidence: 0.932154455
- $00{:}05{:}15{.}957 \dashrightarrow 00{:}05{:}17{.}937$  know when the conversation started.
- NOTE Confidence: 0.932154455
- 00:05:17.940 --> 00:05:18.302 So,
- NOTE Confidence: 0.932154455

 $00:05:18.302 \rightarrow 00:05:20.112$  and certainly your competitors have

NOTE Confidence: 0.932154455

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

NOTE Confidence: 0.932154455

00:05:22.300 --> 00:05:25.208 so you're always the underdog and and NOTE Confidence: 0.932154455

00:05:25.208 --> 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

 $00:05:29.336 \dashrightarrow 00:05:31.490$  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

 $00{:}05{:}33{.}410 \dashrightarrow 00{:}05{:}35{.}419$  We were certain that that you know

NOTE Confidence: 0.932154455

 $00{:}05{:}35{.}419$  -->  $00{:}05{:}37{.}927$  half a dozen other groups in the world

NOTE Confidence: 0.932154455

 $00{:}05{:}37{.}927 \dashrightarrow 00{:}05{:}40{.}440$  were already working on it and and we

NOTE Confidence: 0.932154455

 $00{:}05{:}40{.}440 \dashrightarrow 00{:}05{:}42{.}449$  didn't know how far along they were.

NOTE Confidence: 0.932154455

00:05:42.450 --> 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

 $00{:}05{:}48.278 \dashrightarrow 00{:}05{:}51.950$  I once spent 50 hours straight in the lab

NOTE Confidence: 0.932154455

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

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

NOTE Confidence: 0.932154455

00:05:57.290 --> 00:05:59.570 That's something you can't do in.

NOTE Confidence: 0.932154455

 $00:05:59.570 \rightarrow 00:06:02.864$  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

 $00{:}06{:}05{.}850 \dashrightarrow 00{:}06{:}08{.}442$  with no time outs 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

 $00:06:11.520 \longrightarrow 00:06:14.425$  I think 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 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: 0.885244987777778

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

NOTE Confidence: 0.885244987777778

 $00{:}06{:}25{.}480 \dashrightarrow 00{:}06{:}27{.}856$  I mean, that sounds really inspiring

NOTE Confidence: 0.885244987777778

 $00{:}06{:}27.856$  -->  $00{:}06{:}30.153$  and and interesting in terms of

NOTE Confidence: 0.885244987777778

 $00{:}06{:}30{.}153 \dashrightarrow 00{:}06{:}32{.}400$  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: 0.885244987777778

 $00{:}06{:}36{.}753 \dashrightarrow 00{:}06{:}38{.}961$  to to become a scientist that's

NOTE Confidence: 0.885244987777778

 $00:06:38.961 \longrightarrow 00:06:41.157$  hopefully making a difference in the

NOTE Confidence: 0.885244987777778

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

NOTE Confidence: 0.88524498777778

 $00{:}06{:}43.250 \dashrightarrow 00{:}06{:}44.694$  But for our audience,

NOTE Confidence: 0.885244987777778

 $00{:}06{:}44{.}694 \dashrightarrow 00{:}06{:}47{.}643$  maybe you can take a step back and

NOTE Confidence: 0.885244987777778

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

NOTE Confidence: 0.885244987777778

 $00:06:50.548 \rightarrow 00:06:53.390$  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 --> 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

 $00{:}07{:}02.610 \dashrightarrow 00{:}07{:}05.780$  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

 $00:07:11.088 \rightarrow 00:07:12.723$  find myself engaging with patients

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

NOTE Confidence: 0.80161613

00:07:15.574 --> 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

 $00{:}07{:}19{.}080 \dashrightarrow 00{:}07{:}21{.}364$  and and all I wanted to do was rush

NOTE Confidence: 0.80161613

 $00{:}07{:}21.364 \dashrightarrow 00{:}07{:}23.611$  back to the lab and and find

NOTE Confidence: 0.80161613

 $00{:}07{:}23.611 \dashrightarrow 00{:}07{:}25.059$  new potential the rapeutic avenues.

NOTE Confidence: 0.80161613

00:07:25.060 --> 00:07:27.342 So I made a choice to devote

NOTE Confidence: 0.80161613

00:07:27.342 --> 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

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

NOTE Confidence: 0.80161613

 $00{:}07{:}32.500 \dashrightarrow 00{:}07{:}34.356$  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

 $00{:}07{:}36{.}680 \dashrightarrow 00{:}07{:}39{.}209$  To the bed side.

NOTE Confidence: 0.80161613

00:07:39.210 --> 00:07:42.710 Kinases are often drivers of

NOTE Confidence: 0.80161613

 $00{:}07{:}42.710 \dashrightarrow 00{:}07{:}45.201$  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

 $00{:}07{:}56.840 \dashrightarrow 00{:}07{:}59.300$  it's a tyrosine kinase and

NOTE Confidence: 0.80161613

 $00:07:59.300 \rightarrow 00:08:01.372$  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

 $00{:}08{:}04{.}480 \dashrightarrow 00{:}08{:}07{.}040$  and if this is unregulated

NOTE Confidence: 0.80161613

 $00{:}08{:}07{.}040 \dashrightarrow 00{:}08{:}09{.}908$  that leads to cancer.

NOTE Confidence: 0.80161613

 $00{:}08{:}09{.}910 \dashrightarrow 00{:}08{:}15{.}290$  So ALK well, unlike the Siml case, ALK is.

NOTE Confidence: 0.80161613

00:08:15.290 --> 00:08:18.006 Is A is a receptor tyrosine kinase.

NOTE Confidence: 0.80161613

 $00{:}08{:}18{.}010 \dashrightarrow 00{:}08{:}19{.}774$  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

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

 $00{:}08{:}27{.}470 \dashrightarrow 00{:}08{:}29{.}766$  the CML kinase would be a submarine

NOTE Confidence: 0.80161613

 $00{:}08{:}29.766 \dashrightarrow 00{:}08{:}32.566$  and ALK would be more like an aircraft

NOTE Confidence: 0.80161613

 $00:08:32.566 \dashrightarrow 00:08:35.833$  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 --> 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

 $00:08:40.060 \longrightarrow 00:08:42.084$  you can't target a submarine the same

NOTE Confidence: 0.80161613

 $00:08:42.084 \rightarrow 00:08:44.348$  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

 $00{:}08{:}51{.}770$  -->  $00{:}08{:}54{.}272$  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

 $00:08:56.798 \dashrightarrow 00:08:59.910$  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 --> 00:09:06.906 It's been known for years that

NOTE Confidence: 0.80161613

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

NOTE Confidence: 0.80161613

 $00{:}09{:}09{.}158 \dashrightarrow 00{:}09{:}12.422$  Now neuroblastoma is a cancer of

NOTE Confidence: 0.80161613

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

NOTE Confidence: 0.80161613

 $00{:}09{:}14.850 \dashrightarrow 00{:}09{:}17.419$  It's one of the more common pediatric

NOTE Confidence: 0.80161613

 $00{:}09{:}17{.}419 \dashrightarrow 00{:}09{:}19{.}385$  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 --> 00:09:26.061 But clinically useful the rapeutics

NOTE Confidence: 0.80161613

00:09:26.061 -> 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

 $00{:}09{:}32{.}194 \dashrightarrow 00{:}09{:}33{.}900$  reasons for this slow development of

NOTE Confidence: 0.80161613

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

NOTE Confidence: 0.80161613

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

NOTE Confidence: 0.80161613

 $00:09:39.280 \longrightarrow 00:09:39.760$  Simply put,

NOTE Confidence: 0.80161613

 $00:09:39.760 \longrightarrow 00:09:41.680$  we have you know no idea what it

- NOTE Confidence: 0.80161613
- 00:09:41.738 --> 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 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
- $00:09:50.853 \rightarrow 00:09:53.228$  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
- $00:09:56.340 \dashrightarrow 00:09:58.206$  veritable on cogenic beacon.
- NOTE Confidence: 0.80161613
- $00:09:58.210 \longrightarrow 00:10:00.630$  That's a perfect target
- NOTE Confidence: 0.80161613
- $00{:}10{:}00{.}630 \dashrightarrow 00{:}10{:}02{.}445$  for precision medicine.
- NOTE Confidence: 0.80161613
- $00:10:02.450 \longrightarrow 00:10:04.405$  It's much like the novel
- NOTE Confidence: 0.80161613
- $00:10:04.405 \longrightarrow 00:10:05.969$  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
- $00:10:09.720 \longrightarrow 00:10:10.105$  Specifically,
- NOTE Confidence: 0.80161613
- $00:10:10.105 \rightarrow 00:10:12.415$  if you're targeting the protein specifically,
- NOTE Confidence: 0.80161613
- $00{:}10{:}12{.}420 \dashrightarrow 00{:}10{:}14{.}328$  it should have little side effects
- NOTE Confidence: 0.80161613
- $00:10:14.328 \rightarrow 00:10:16.060$  outside of the cancer itself.
- NOTE Confidence: 0.80161613

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

 $00{:}10{:}21{.}950 \dashrightarrow 00{:}10{:}24{.}561$  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

 $00:10:26.041 \dashrightarrow 00:10:27.817$  we see for patients with KMLE.

NOTE Confidence: 0.79956105

 $00{:}10{:}29{.}260 \dashrightarrow 00{:}10{:}32{.}420$  So you know one of the things that

NOTE Confidence: 0.79956105

 $00{:}10{:}32{.}420 \dashrightarrow 00{:}10{:}34{.}220$  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 --> 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

 $00{:}10{:}41{.}350 \dashrightarrow 00{:}10{:}43{.}906$  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

 $00{:}10{:}46.864 \dashrightarrow 00{:}10{:}49.370$  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

 $00{:}10{:}51{.}968 \dashrightarrow 00{:}10{:}54{.}551$  And how did you figure out that

NOTE Confidence: 0.79956105

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

- NOTE Confidence: 0.79956105
- $00:10:56.900 \longrightarrow 00:10:57.968$  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
- $00{:}11{:}02{.}355 \dashrightarrow 00{:}11{:}06{.}780$  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
- $00{:}11{:}10.260 \dashrightarrow 00{:}11{:}13.806$  work and associating certain genes
- NOTE Confidence: 0.82554652
- $00:11:13.806 \rightarrow 00:11:16.878$  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
- $00:11:30.710 \longrightarrow 00:11:32.930$  exactly how these kinases
- NOTE Confidence: 0.82554652
- $00{:}11{:}32{.}930 \dashrightarrow 00{:}11{:}35{.}705$  and uncle genes are acting,
- NOTE Confidence: 0.82554652
- $00{:}11{:}35{.}710 \dashrightarrow 00{:}11{:}37{.}670$  and hopefully if we have a molecular
- NOTE Confidence: 0.82554652

 $00:11:37.670 \longrightarrow 00:11:40.654$  picture of that how we might design

NOTE Confidence: 0.82554652

 $00:11:40.654 \rightarrow 00:11:42.798$  and develop the rapeutics to.

NOTE Confidence: 0.82554652

 $00{:}11{:}42.800 \dashrightarrow 00{:}11{:}46.167$  To stall that and and prevent disease.

NOTE Confidence: 0.890860507142857

 $00{:}11{:}47{.}890 \dashrightarrow 00{:}11{:}50{.}730$  So when you say that it it kind of all

NOTE Confidence: 0.890860507142857

 $00{:}11{:}50{.}806 \dashrightarrow 00{:}11{:}53{.}196$  starts with understanding what genes

NOTE Confidence: 0.890860507142857

 $00:11:53.196 \rightarrow 00:11:56.190$  are expressed in what genes aren't.

NOTE Confidence: 0.890860507142857

 $00{:}11{:}56{.}190 \dashrightarrow 00{:}11{:}59{.}404$  I mean it, it sounds like the progress

NOTE Confidence: 0.890860507142857

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

NOTE Confidence: 0.890860507142857

 $00{:}12{:}02.568 \dashrightarrow 00{:}12{:}04.574$  medicine is really investigators.

NOTE Confidence: 0.890860507142857

 $00{:}12{:}04{.}574 \dashrightarrow 00{:}12{:}06{.}646$  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

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

NOTE Confidence: 0.890860507142857

 $00{:}12{:}12{.}442 \dashrightarrow 00{:}12{:}16{.}025$  some genes and found that some genes were

NOTE Confidence: 0.890860507142857

 $00:12:16.025 \rightarrow 00:12:18.680$  over expressed in some cancers versus not.

NOTE Confidence: 0.890860507142857

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

NOTE Confidence: 0.890860507142857

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

- NOTE Confidence: 0.890860507142857
- $00:12:25.240 \longrightarrow 00:12:27.557$  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
- $00:12:29.552 \rightarrow 00:12:32.010$  is it and how can we target it?
- NOTE Confidence: 0.890860507142857
- $00:12:32.010 \longrightarrow 00:12:34.537$  Is that kind of how that works?
- NOTE Confidence: 0.890860507142857
- $00{:}12{:}34{.}540 \dashrightarrow 00{:}12{:}34{.}900$  That's
- NOTE Confidence: 0.929737544
- 00:12:34.910 --> 00:12:36.980 exactly right, right? I mean,
- NOTE Confidence: 0.929737544
- $00{:}12{:}36{.}980 \dashrightarrow 00{:}12{:}40{.}494$  it's it's work of a tremendous number
- NOTE Confidence: 0.929737544
- $00:12:40.494 \rightarrow 00:12:43.850$  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
- $00:12:46.220 \rightarrow 00:12:49.119$  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
- $00:12:50.690 \rightarrow 00:12:52.447$  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
- $00{:}12{:}54{.}784 \dashrightarrow 00{:}12{:}56{.}340$  important to understand the
- NOTE Confidence: 0.929737544
- 00:12:56.414 --> 00:12:58.719 mechanism of how molecules work,
- NOTE Confidence: 0.929737544

 $00:12:58.720 \longrightarrow 00:13:00.544$  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 the rapeutics.

NOTE Confidence: 0.929737544

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

NOTE Confidence: 0.915260749090909

 $00{:}13{:}06{.}960 \dashrightarrow 00{:}13{:}08{.}900$  And then the other question

NOTE Confidence: 0.915260749090909

 $00{:}13{:}08{.}900 \dashrightarrow 00{:}13{:}11{.}160$  that that I often have is.

NOTE Confidence: 0.915260749090909

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

NOTE Confidence: 0.915260749090909

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

NOTE Confidence: 0.915260749090909

00:13:18.970 --> 00:13:22.226 Why is it that some kinases are important

NOTE Confidence: 0.915260749090909

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

NOTE Confidence: 0.915260749090909

00:13:25.290 --> 00:13:27.210 I mean, how do these kinases?

NOTE Confidence: 0.915260749090909

00:13:27.210 --> 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

 $00:13:33.230 \rightarrow 00:13:36.338$  And why are they differentially expressed?

NOTE Confidence: 0.872277651666666

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

NOTE Confidence: 0.872277651666666

 $00:13:41.750 \rightarrow 00:13:46.710$  that are important and during development.

00:13:46.710 --> 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

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

NOTE Confidence: 0.872277651666666

 $00:13:55.670 \rightarrow 00:13:58.575$  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

 $00{:}14{:}04{.}330 \dashrightarrow 00{:}14{:}07{.}984$  In the the oncogenic process that a lot of

NOTE Confidence: 0.872277651666666

00:14:07.984 --> 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: 0.872277651666666

 $00:14:16.460 \longrightarrow 00:14:17.225$  but they all.

NOTE Confidence: 0.872277651666666

 $00{:}14{:}17.225 \dashrightarrow 00{:}14{:}18.500$  Lead to the same thing.

NOTE Confidence: 0.872277651666666

00:14:18.500 --> 00:14:20.880 Basically once you turn return

NOTE Confidence: 0.872277651666666

00:14:20.880 --> 00:14:24.023 a kinase on your turning on

NOTE Confidence: 0.872277651666666

 $00{:}14{:}24{.}023 \dashrightarrow 00{:}14{:}27{.}172$  the the growth instructions and

 $00:14:27.172 \rightarrow 00:14:30.036$  when that's not counterbalanced,

NOTE Confidence: 0.872277651666666

 $00{:}14{:}30{.}040 \dashrightarrow 00{:}14{:}31{.}988$  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

 $00:14:34.316 \rightarrow 00:14:36.179$  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 --> 00:14:40.270 let's learn more about the molecular

NOTE Confidence: 0.8382126625

 $00:14:40.270 \longrightarrow 00:14:42.714$  mechanisms of cancer and how exactly

NOTE Confidence: 0.8382126625

 $00:14:42.714 \rightarrow 00:14:44.430$  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 --> 00:14:49.130 make a difference for patients,

NOTE Confidence: 0.8382126625

 $00{:}14{:}49{.}130 \dashrightarrow 00{:}14{:}50{.}972$  please stay tuned for more with

NOTE Confidence: 0.8382126625

 $00:14:50.972 \longrightarrow 00:14:52.550$  my guest doctor Daryl Klein

NOTE Confidence: 0.884235398214286

 $00{:}14{:}53.060 \dashrightarrow 00{:}14{:}55.340$  funding for Yale Cancer Answers comes

NOTE Confidence: 0.884235398214286

 $00{:}14{:}55{.}340 \dashrightarrow 00{:}14{:}57{.}715$  from Smilow Cancer Hospital with an

NOTE Confidence: 0.884235398214286

 $00{:}14{:}57{.}715 \dashrightarrow 00{:}15{:}00{.}097$  event focused on nutrition for cancer

NOTE Confidence: 0.884235398214286

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

- NOTE Confidence: 0.884235398214286
- 00:15:01.944 --> 00:15:03.589 Cancer Care Center in Trumbull.
- NOTE Confidence: 0.884235398214286
- 00:15:03.590 --> 00:15:06.894 April 14th Register at Yale Cancer Center.
- NOTE Confidence: 0.884235398214286
- 00:15:06.900 --> 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
- $00:15:13.832 \rightarrow 00:15:16.368$  estimates that nearly 150,000 people
- NOTE Confidence: 0.838554415
- $00{:}15{:}16{.}368 \dashrightarrow 00{:}15{:}18{.}986$  in the US will be diagnosed with
- NOTE Confidence: 0.838554415
- $00:15:18.986 \rightarrow 00:15:20.917$  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
- $00:15:27.864 \rightarrow 00:15:29.643$  45 should have regular colonoscopies
- NOTE Confidence: 0.838554415
- $00{:}15{:}29.643 \dashrightarrow 00{:}15{:}31.633$  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
- $00:15:33.088 \rightarrow 00:15:35.260$  have more hope than ever before,
- NOTE Confidence: 0.838554415
- $00{:}15{:}35{.}260 \dashrightarrow 00{:}15{:}38{.}080$  thanks to increased access to advanced
- NOTE Confidence: 0.838554415

 $00:15:38.080 \rightarrow 00:15:39.960$  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

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

NOTE Confidence: 0.838554415

00:15:45.110 --> 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

 $00{:}15{:}50{.}583 \dashrightarrow 00{:}15{:}52{.}856$  treatments for colorectal cancer tumor.

NOTE Confidence: 0.838554415

 $00{:}15{:}52.856 \dashrightarrow 00{:}15{:}55.186$  Gene analysis has helped improve

NOTE Confidence: 0.838554415

00:15:55.186 --> 00:15:57.050 management of colorectal cancer

NOTE Confidence: 0.838554415

 $00{:}15{:}57{.}115 \dashrightarrow 00{:}15{:}59{.}345$  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

 $00{:}16{:}01{.}644 \dashrightarrow 00{:}16{:}03{.}348$  and newer targeted agents,

NOTE Confidence: 0.838554415

00:16:03.350 --> 00:16:06.170 resulting in more patient specific treatment.

NOTE Confidence: 0.838554415

 $00{:}16{:}06{.}170 \dashrightarrow 00{:}16{:}09{.}230$  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

 $00{:}16{:}10.532 \dashrightarrow 00{:}16{:}12.268$  to Connecticut Public Radio.

- NOTE Confidence: 0.895207821666667
- $00:16:13.040 \longrightarrow 00:16:15.056$  Welcome back to Yale Cancer answers.
- NOTE Confidence: 0.895207821666667
- 00:16:15.060 --> 00:16:16.356 This is doctor in East Egg
- NOTE Confidence: 0.895207821666667
- $00{:}16{:}16{.}356 \dashrightarrow 00{:}16{:}17{.}778$  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: 0.8952078216666667
- $00:16:19.294 \rightarrow 00:16:21.556$  We're learning more about the molecular
- NOTE Confidence: 0.895207821666667
- $00{:}16{:}21.556 \dashrightarrow 00{:}16{:}23.610$  mechanisms of cancer and right before
- NOTE Confidence: 0.8952078216666667
- $00:16:23.610 \longrightarrow 00:16:25.852$  the break Daryl was telling us about
- NOTE Confidence: 0.895207821666667
- 00:16:25.852 --> 00:16:27.507 this profoundly inspiring story of
- NOTE Confidence: 0.8952078216666667
- $00:16:27.507 \rightarrow 00:16:30.025$  his sister who is diagnosed with CML,
- NOTE Confidence: 0.895207821666667
- 00:16:30.025 --> 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
- $00:16:34.220 \rightarrow 00:16:37.298$  and one who is particularly interested
- NOTE Confidence: 0.895207821666667
- 00:16:37.300 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
- $00:16:43.334 \rightarrow 00:16:48.080$  To activate the growth of of cancer
- NOTE Confidence: 0.895207821666667

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

NOTE Confidence: 0.895207821666667

 $00{:}16{:}51{.}192 \dashrightarrow 00{:}16{:}53{.}775$  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

 $00:16:56.559 \rightarrow 00:17:00.154$  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

 $00{:}17{:}02.706 \dashrightarrow 00{:}17{:}05.692$  in looking at its its structure

NOTE Confidence: 0.8952078216666667

 $00:17:05.692 \longrightarrow 00:17:08.254$  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

 $00:17:11.550 \rightarrow 00:17:14.525$  my lab is a structural biology lab,

NOTE Confidence: 0.904520128571429

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

NOTE Confidence: 0.904520128571429

00:17:18.420 --> 00:17:20.240 But we take pictures of of very,

NOTE Confidence: 0.904520128571429

 $00:17:20.240 \rightarrow 00:17:23.798$  very tiny things, molecules and proteins,

NOTE Confidence: 0.904520128571429

 $00{:}17{:}23.800 \dashrightarrow 00{:}17{:}26.085$  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

 $00{:}17{:}28.370 \dashrightarrow 00{:}17{:}32.430$  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

 $00{:}17{:}44.749 \dashrightarrow 00{:}17{:}48.058$  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

 $00:17:51.084 \rightarrow 00:17:54.458$  with 10s of thousands of recipes,

NOTE Confidence: 0.904520128571429

00:17:54.460 - 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

 $00{:}18{:}01{.}610 \dashrightarrow 00{:}18{:}04{.}508$  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

 $00{:}18{:}08{.}250 \dashrightarrow 00{:}18{:}12{.}290$  the ingredients and the order to make alcc.

NOTE Confidence: 0.904520128571429

 $00{:}18{:}12.290 \dashrightarrow 00{:}18{:}16.754$  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,

 $00{:}18{:}18{.}120 \dashrightarrow 00{:}18{:}20{.}628$  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

 $00{:}18{:}22{.}580 \dashrightarrow 00{:}18{:}25{.}775$  So you know my lab follows the recipe to

NOTE Confidence: 0.904520128571429

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

NOTE Confidence: 0.904520128571429

 $00{:}18{:}28.630 \dashrightarrow 00{:}18{:}32.008$  To illustrate this, this DNA cookbook.

NOTE Confidence: 0.904520128571429

 $00{:}18{:}32.010 \dashrightarrow 00{:}18{:}35.335$  So we take molecular photographs

NOTE Confidence: 0.904520128571429

 $00{:}18{:}35{.}335 \dashrightarrow 00{:}18{:}38{.}838$  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

 $00{:}18{:}40{.}730 \dashrightarrow 00{:}18{:}44{.}090$  And in these pictures give us a better

NOTE Confidence: 0.904520128571429

 $00:18:44.090 \rightarrow 00:18:46.174$  understanding of how things supposed

NOTE Confidence: 0.904520128571429

 $00{:}18{:}46{.}174 \dashrightarrow 00{:}18{:}49{.}330$  to look like and how it changes in cancer.

NOTE Confidence: 0.904520128571429

 $00{:}18{:}49{.}330 \dashrightarrow 00{:}18{:}51{.}826$  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

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

NOTE Confidence: 0.904520128571429

 $00:18:57.530 \rightarrow 00:19:01.233$  So my lab just reported the structure

NOTE Confidence: 0.904520128571429

 $00:19:01.233 \rightarrow 00:19:05.409$  of of the protein ALK in nature.

00:19:05.410 - > 00:19:08.335 That's the tyrosine kinase that's

NOTE Confidence: 0.904520128571429

 $00{:}19{:}08{.}335 \dashrightarrow 00{:}19{:}10{.}090$  important in neuroblastoma.

NOTE Confidence: 0.904520128571429

 $00{:}19{:}10.090 \dashrightarrow 00{:}19{:}12.726$  And this gave us a first look at

NOTE Confidence: 0.904520128571429

 $00:19:12.726 \longrightarrow 00:19:15.544$  this unique uncle Gene and it's,

NOTE Confidence: 0.904520128571429

 $00:19:15.544 \rightarrow 00:19:18.183$  you know it's going to be impossible

NOTE Confidence: 0.904520128571429

 $00:19:18.183 \rightarrow 00:19:21.210$  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

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

NOTE Confidence: 0.904520128571429

 $00{:}19{:}25{.}758 \dashrightarrow 00{:}19{:}28{.}026$  It's not unreasonable to say that

NOTE Confidence: 0.904520128571429

 $00:19:28.026 \rightarrow 00:19:30.935$  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

 $00{:}19{:}33.880 \dashrightarrow 00{:}19{:}37.380$  Unusual a long gated structure and it

NOTE Confidence: 0.904520128571429

 $00:19:37.380 \rightarrow 00:19:40.796$  probably lies parallel to the to the surface,

NOTE Confidence: 0.904520128571429

00:19:40.800 --> 00:19:42.900 so it's like an aircraft carrier

NOTE Confidence: 0.904520128571429

 $00{:}19{:}42{.}900 \dashrightarrow 00{:}19{:}44{.}448$  floating on the water.

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

NOTE Confidence: 0.904520128571429

 $00{:}19{:}46{.}770 \dashrightarrow 00{:}19{:}48{.}228$  And and furthermore,

NOTE Confidence: 0.904520128571429

 $00:19:48.228 \rightarrow 00:19:52.430$  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

 $00{:}19{:}54.716 \dashrightarrow 00{:}19{:}57.840$  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

 $00:20:00.203 \rightarrow 00:20:02.926$  sell to send their their growth signals,

NOTE Confidence: 0.904520128571429

 $00:20:02.930 \rightarrow 00:20:05.120$  which ultimately end up being

NOTE Confidence: 0.904520128571429

 $00:20:05.120 \longrightarrow 00:20:06.434$  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 --> 00:20:10.736 Uncontrolled ALK activation like

NOTE Confidence: 0.904520128571429

 $00{:}20{:}10.736 \dashrightarrow 00{:}20{:}13.948$  this leads to cancer and it and it

NOTE Confidence: 0.904520128571429

 $00{:}20{:}13.948 \dashrightarrow 00{:}20{:}16.432$  results from the tumor continuing to

NOTE Confidence: 0.904520128571429

 $00{:}20{:}16.432 \dashrightarrow 00{:}20{:}18.960$  express this developmental out gene

NOTE Confidence: 0.904520128571429

 $00:20:18.960 \rightarrow 00:20:23.930$  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 --> 00:20:29.229 to shutting off ALK and that

NOTE Confidence: 0.904520128571429

00:20:29.229 --> 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

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

NOTE Confidence: 0.904520128571429

 $00{:}20{:}35{.}790 \dashrightarrow 00{:}20{:}37{.}536$  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

 $00{:}20{:}43.731 \dashrightarrow 00{:}20{:}46.118$  that are revealed in the structure that

NOTE Confidence: 0.904520128571429

 $00:20:46.118 \rightarrow 00:20:48.283$  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

 $00:20:53.310 \longrightarrow 00:20:54.924$  antibodies. That specifically

NOTE Confidence: 0.7377237425

 $00:20:54.924 \rightarrow 00:20:57.614$  target these regions in ALK,

NOTE Confidence: 0.7377237425

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

 $00:21:00.014 \rightarrow 00:21:02.358$  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

 $00{:}21{:}04{.}820 \dashrightarrow 00{:}21{:}07{.}119$  different cancers that are driven or

NOTE Confidence: 0.7377237425

 $00:21:07.120 \rightarrow 00:21:10.528$  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

 $00:21:12.855 \longrightarrow 00:21:13.785$  the rapeutics 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 --> 00:21:21.527 are now currently in use like

NOTE Confidence: 0.7377237425

 $00:21:21.527 \longrightarrow 00:21:23.667$  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

 $00{:}21{:}29.060 \dashrightarrow 00{:}21{:}31.734$  And one problem with these types of

NOTE Confidence: 0.7377237425

 $00:21:31.734 \rightarrow 00:21:33.510$  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

- NOTE Confidence: 0.7377237425
- 00:21:37.322 --> 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
- $00{:}21{:}51{.}599 \dashrightarrow 00{:}21{:}53{.}770$  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
- $00:21:55.270 \longrightarrow 00:21:57.194$  the strategy of inhibition.
- NOTE Confidence: 0.7377237425
- $00{:}21{:}57{.}194 \dashrightarrow 00{:}22{:}00{.}080$  I think the the the rapeutic future
- NOTE Confidence: 0.7377237425
- $00:22:00.163 \longrightarrow 00:22:02.373$  will likely use a combination
- NOTE Confidence: 0.7377237425
- $00{:}22{:}02{.}373 \dashrightarrow 00{:}22{:}04{.}583$  of these two to completely.
- NOTE Confidence: 0.7377237425
- $00{:}22{:}04.590 \dashrightarrow 00{:}22{:}08.660$  Dismantle the the out machinery.
- NOTE Confidence: 0.7377237425
- 00:22:08.660 --> 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
- NOTE Confidence: 0.7377237425

 $00:22:13.157 \rightarrow 00:22:15.445$  similar challenges that we see for SARS,

NOTE Confidence: 0.7377237425

 $00{:}22{:}15{.}445 \dashrightarrow 00{:}22{:}18{.}235$  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

 $00{:}22{:}27.885 \dashrightarrow 00{:}22{:}29.610$  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

 $00{:}22{:}35{.}312 \dashrightarrow 00{:}22{:}37{.}964$  injecting recombinant antibodies and

NOTE Confidence: 0.7377237425

 $00{:}22{:}37{.}964 \dashrightarrow 00{:}22{:}40{.}890$  small molecules to overcome COVID.

NOTE Confidence: 0.7377237425

 $00{:}22{:}40{.}890 \dashrightarrow 00{:}22{:}44{.}299$  Now we have a new blueprint for ALK to

NOTE Confidence: 0.7377237425

 $00:22:44.299 \rightarrow 00:22:46.244$  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

 $00{:}22{:}48.742 \dashrightarrow 00{:}22{:}50.498$  and in particular neuroblastoma.

NOTE Confidence: 0.900451000714286

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

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

NOTE Confidence: 0.900451000714286

00:22:57.570 --> 00:23:00.377 But you can be very specific about

NOTE Confidence: 0.900451000714286

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

NOTE Confidence: 0.900451000714286

 $00:23:02.682 \rightarrow 00:23:05.748$  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

 $00{:}23{:}12.616 \dashrightarrow 00{:}23{:}15.149$  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

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

NOTE Confidence: 0.900451000714286

 $00{:}23{:}21.728 \dashrightarrow 00{:}23{:}24.986$  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

 $00:23:27.080 \longrightarrow 00:23:29.712$  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
- $00:23:34.912 \rightarrow 00:23:37.860$  and remember that I said that you know,
- NOTE Confidence: 0.931961159090909
- 00:23:37.860 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
- $00:23:42.263 \longrightarrow 00:23:44.139$  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
- $00:23:51.640 \rightarrow 00:23:53.992$  which I think you were just referring
- NOTE Confidence: 0.931961159090909
- $00{:}23{:}53{.}992 \dashrightarrow 00{:}23{:}57{.}177$  to is now that we know the detailed
- NOTE Confidence: 0.931961159090909
- $00{:}23{:}57{.}177 \dashrightarrow 00{:}23{:}59{.}282$  structure and blueprints of this.
- NOTE Confidence: 0.931961159090909
- $00:23:59.290 \rightarrow 00:24:00.434$  And that's exactly what we're trying to do.
- NOTE Confidence: 0.931961159090909
- $00:24:00.440 \longrightarrow 00:24:02.240$  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
- $00:24:03.590 \rightarrow 00:24:07.210$  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

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

NOTE Confidence: 0.931961159090909

 $00:24:12.754 \rightarrow 00:24:17.150$  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

 $00{:}24{:}19{.}990 \dashrightarrow 00{:}24{:}22{.}762$  Where we see the 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

 $00:24:25.000 \rightarrow 00:24:27.085$  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 --> 00:24:33.600 activated independent of ligand.

NOTE Confidence: 0.931961159090909

 $00:24:33.600 \rightarrow 00:24:36.197$  Which could be caused by certain mutations,

NOTE Confidence: 0.931961159090909

 $00{:}24{:}36{.}200 \dashrightarrow 00{:}24{:}38{.}780$  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

 $00{:}24{:}41{.}900 \dashrightarrow 00{:}24{:}45{.}278$  So we're using all this information

NOTE Confidence: 0.931961159090909

 $00{:}24{:}45{.}278 \dashrightarrow 00{:}24{:}47{.}530$  to specifically design antibodies

 $00:24:47.614 \rightarrow 00:24:50.062$  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

 $00{:}24{:}53{.}342 \dashrightarrow 00{:}24{:}55{.}952$  or mechanisms that activate it

NOTE Confidence: 0.931961159090909

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

NOTE Confidence: 0.913035372

 $00{:}24{:}59{.}530 \dashrightarrow 00{:}25{:}02{.}470$  And so as you design these

NOTE Confidence: 0.913035372

 $00{:}25{:}02{.}470 \dashrightarrow 00{:}25{:}04{.}430$  antibodies in these treatments,

NOTE Confidence: 0.913035372

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

NOTE Confidence: 0.913035372

 $00:25:06.716 \rightarrow 00:25:08.998$  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

 $00:25:19.720 \longrightarrow 00:25:21.772$  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

 $00{:}25{:}24{.}452 \dashrightarrow 00{:}25{:}26{.}851$  Cancer Research is is so matured and

NOTE Confidence: 0.796460149

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

 $00:25:29.041 \rightarrow 00:25:31.664$  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 --> 00:25:36.986 to build upon and meaningful ways.

NOTE Confidence: 0.796460149

 $00{:}25{:}36{.}990 \dashrightarrow 00{:}25{:}39{.}790$  And just as the NIH created that MSTP NOTE Confidence: 0.796460149

 $00{:}25{:}39{.}790 \dashrightarrow 00{:}25{:}42{.}702$  program to link basic science and patient NOTE Confidence: 0.796460149

 $00{:}25{:}42.702 \dashrightarrow 00{:}25{:}45.496$  Care now I think we need similar links

NOTE Confidence: 0.796460149

 $00{:}25{:}45{.}496 \dashrightarrow 00{:}25{:}47{.}310$  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

 $00{:}25{:}50{.}572 \dashrightarrow 00{:}25{:}52{.}360$  and chromosome researcher and.

NOTE Confidence: 0.796460149

 $00:25:52.360 \longrightarrow 00:25:54.388$  And in the biophysicist like me

NOTE Confidence: 0.796460149

 $00:25:54.388 \rightarrow 00:25:56.871$  trying to link up with the model

NOTE Confidence: 0.796460149

00:25:56.871 --> 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

 $00{:}26{:}04.168 \dashrightarrow 00{:}26{:}06.300$  and we have different perspectives,

00:26:06.300 --> 00:26:10.460 so you know how do we work together

NOTE Confidence: 0.796460149

 $00{:}26{:}10.555 \dashrightarrow 00{:}26{:}12.577$  and in one answer to that is is,

NOTE Confidence: 0.796460149

 $00{:}26{:}12.580 \dashrightarrow 00{:}26{:}14.996$  you know being part of the Yale Cancer NOTE Confidence: 0.796460149

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

NOTE Confidence: 0.796460149

 $00:26:17.380 \longrightarrow 00:26:19.942$  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

 $00:26:21.718 \rightarrow 00:26:23.518$  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

 $00{:}26{:}26{.}310 \dashrightarrow 00{:}26{:}29{.}380$  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

 $00{:}26{:}37.148 \dashrightarrow 00{:}26{:}40.292$  that we have into preclinical testing

NOTE Confidence: 0.796460149

 $00{:}26{:}40{.}292 \dashrightarrow 00{:}26{:}43{.}850$  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

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

- NOTE Confidence: 0.796460149
- $00:26:50.430 \rightarrow 00:26:53.169$  into reaching the the patients that

 $00:26:53.169 \longrightarrow 00:26:55.180$  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

 $00:26:58.490 \longrightarrow 00:26:59.576$  had mentioned earlier,

NOTE Confidence: 0.90850388875

 $00{:}26{:}59{.}580 \dashrightarrow 00{:}27{:}02{.}396$  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

 $00{:}27{:}09{.}284 \dashrightarrow 00{:}27{:}12{.}099$  the problem of of ALK from a

NOTE Confidence: 0.90850388875

00:27:12.099 --> 00:27:13.835 slightly different vantage point.

NOTE Confidence: 0.90850388875

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

NOTE Confidence: 0.90850388875

 $00{:}27{:}17{.}574 \dashrightarrow 00{:}27{:}19{.}800$  on the work of other people's labs,

NOTE Confidence: 0.90850388875

 $00:27:19.800 \longrightarrow 00:27:22.572$  and so maybe in the last

NOTE Confidence: 0.90850388875

 $00{:}27{:}22{.}572 \dashrightarrow 00{:}27{:}24{.}580$  few minutes that we have,

NOTE Confidence: 0.90850388875

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

 $00:27:26.810 \rightarrow 00:27:29.357$  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

 $00{:}27{:}31{.}150 \dashrightarrow 00{:}27{:}33{.}230$  One of the things that we've realized with

NOTE Confidence: 0.90850388875

 $00:27:33.230 \rightarrow 00:27:35.266$  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

 $00:27:43.240 \rightarrow 00:27:45.340$  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

 $00{:}27{:}49{.}136 \dashrightarrow 00{:}27{:}51{.}664$  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

 $00{:}27{:}54.656 \dashrightarrow 00{:}27{:}57.786$  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 --> 00:28:03.550 during the pandemic and having people

NOTE Confidence: 0.882697558

 $00{:}28{:}03{.}550 \dashrightarrow 00{:}28{:}06{.}008$  communicate in different ways like we

NOTE Confidence: 0.882697558

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

00:28:08.850 --> 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

 $00:28:13.944 \rightarrow 00:28:16.520$  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

 $00{:}28{:}19.472 \dashrightarrow 00{:}28{:}21.440$  independently and making advances.

NOTE Confidence: 0.882697558

 $00{:}28{:}21{.}440 \dashrightarrow 00{:}28{:}23{.}169$  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

 $00:28:25.033 \rightarrow 00:28:26.373$  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

 $00:28:28.495 \rightarrow 00:28:30.610$  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 --> 00:28:35.670 Doctor Daryl Klein is an assistant

NOTE Confidence: 0.772678952866667

 $00:28:35.670 \longrightarrow 00:28:37.130$  professor of pharmacology at

NOTE Confidence: 0.772678952866667

 $00{:}28{:}37{.}195 \dashrightarrow 00{:}28{:}38{.}820$  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

 $00{:}28{:}47.030 \dashrightarrow 00{:}28{:}48.968$  Farm at yale cancercenter.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 --> 00:28:53.449 learn more about the fight against

NOTE Confidence: 0.772678952866667

00:28:53.449 --> 00:28:55.014 cancer here on Connecticut Public

NOTE Confidence: 0.772678952866667

 $00{:}28{:}55{.}068 \dashrightarrow 00{:}28{:}56{.}856$  radio funding for Yale Cancer Answers

NOTE Confidence: 0.772678952866667

 $00:28:56.856 \rightarrow 00:29:00.000$  is provided by Smilow Cancer Hospital.