

WEBVTT

NOTE duration: "00:05:41.162"

NOTE Confidence: 0.9467436

00:00:04.559 --> 00:00:06.000 In general, a tumor grows

NOTE Confidence: 0.9467436

00:00:06.000 --> 00:00:06.799 when we have one of

NOTE Confidence: 0.9467436

00:00:06.799 --> 00:00:08.320 two types of mutations. Either

NOTE Confidence: 0.9467436

00:00:08.320 --> 00:00:09.840 mutation that's telling the cells

NOTE Confidence: 0.9467436

00:00:09.840 --> 00:00:10.980 to grow out of control

NOTE Confidence: 0.9467436

00:00:11.039 --> 00:00:12.400 or the opposite, where we've

NOTE Confidence: 0.9467436

00:00:12.400 --> 00:00:13.440 got a mutation that is

NOTE Confidence: 0.9467436

00:00:13.440 --> 00:00:14.639 tamped down the genes that

NOTE Confidence: 0.9467436

00:00:14.639 --> 00:00:15.975 tell it not to grow.

NOTE Confidence: 0.9484063

00:00:16.535 --> 00:00:17.655 And so with a brain

NOTE Confidence: 0.9484063

00:00:17.655 --> 00:00:19.015 tumor, with with any tumor,

NOTE Confidence: 0.9484063

00:00:19.015 --> 00:00:20.135 when we have these mutations,

NOTE Confidence: 0.9484063

00:00:20.135 --> 00:00:22.295 it's disrupting the normal flow

NOTE Confidence: 0.9484063

00:00:22.295 --> 00:00:24.135 of growth and apoptosis or

NOTE Confidence: 0.9484063

00:00:24.135 --> 00:00:25.114 or natural death.
NOTE Confidence: 0.962756

00:00:25.975 --> 00:00:27.815 Normal cells, cancer cells are
NOTE Confidence: 0.962756

00:00:27.815 --> 00:00:29.494 fascinating that every eight hours
NOTE Confidence: 0.962756

00:00:29.494 --> 00:00:31.035 when they divide, there's billions
NOTE Confidence: 0.962756

00:00:31.095 --> 00:00:32.450 of DNA that needs to
NOTE Confidence: 0.962756

00:00:32.450 --> 00:00:33.150 be repaired.
NOTE Confidence: 0.95560986

00:00:33.690 --> 00:00:35.130 When they're replicated there'll be
NOTE Confidence: 0.95560986

00:00:35.130 --> 00:00:36.430 mistakes that are made
NOTE Confidence: 0.97273153

00:00:36.810 --> 00:00:38.570 and the DNA damage response
NOTE Confidence: 0.97273153

00:00:38.570 --> 00:00:40.650 pathways are responsible for fixing
NOTE Confidence: 0.97273153

00:00:40.650 --> 00:00:42.409 those errors. Now normal cells
NOTE Confidence: 0.97273153

00:00:42.409 --> 00:00:43.530 don't divide that often so
NOTE Confidence: 0.97273153

00:00:43.530 --> 00:00:44.250 they don't make a lot
NOTE Confidence: 0.97273153

00:00:44.250 --> 00:00:46.165 of errors, But cancer cells
NOTE Confidence: 0.97273153

00:00:46.165 --> 00:00:48.005 are rapidly dividing and rapidly
NOTE Confidence: 0.97273153

00:00:48.005 --> 00:00:49.445 growing, and such that there

NOTE Confidence: 0.97273153
00:00:49.445 --> 00:00:50.965 are many mistakes that occur,
NOTE Confidence: 0.97273153
00:00:50.965 --> 00:00:52.485 and the DNA damage response
NOTE Confidence: 0.97273153
00:00:52.485 --> 00:00:54.345 pathways help them survive,
NOTE Confidence: 0.99580234
00:00:54.805 --> 00:00:56.585 through those replication cycles.
NOTE Confidence: 0.90166694
00:00:57.925 --> 00:00:59.685 Often they have defects or
NOTE Confidence: 0.90166694
00:00:59.685 --> 00:01:00.180 they have
NOTE Confidence: 0.967055
00:01:00.740 --> 00:01:02.740 dysfunctional ways that they run
NOTE Confidence: 0.967055
00:01:02.740 --> 00:01:03.560 those pathways.
NOTE Confidence: 0.9749349
00:01:04.500 --> 00:01:06.180 And central to that is
NOTE Confidence: 0.9749349
00:01:06.180 --> 00:01:07.800 one protein called PARP
NOTE Confidence: 0.9470387
00:01:08.180 --> 00:01:09.000 that's implicated
NOTE Confidence: 0.9971273
00:01:09.300 --> 00:01:10.680 in brain tumor survival.
NOTE Confidence: 0.955703
00:01:11.060 --> 00:01:12.180 If we can target those
NOTE Confidence: 0.955703
00:01:12.180 --> 00:01:13.540 proteins that aren't supposed to
NOTE Confidence: 0.955703
00:01:13.540 --> 00:01:14.884 be there, then we've got
NOTE Confidence: 0.955703

00:01:14.884 --> 00:01:16.164 to target a therapy. And
NOTE Confidence: 0.955703

00:01:16.164 --> 00:01:17.125 we can fight what we
NOTE Confidence: 0.955703

00:01:17.125 --> 00:01:18.164 call the driver of the
NOTE Confidence: 0.955703

00:01:18.164 --> 00:01:19.204 tumor and make it stop
NOTE Confidence: 0.955703

00:01:19.204 --> 00:01:19.704 growing.
NOTE Confidence: 0.95566195

00:01:25.685 --> 00:01:27.125 In about two thousand fifteen,
NOTE Confidence: 0.95566195

00:01:27.125 --> 00:01:28.244 when our lab had just
NOTE Confidence: 0.95566195

00:01:28.244 --> 00:01:29.870 started at Yale, about three
NOTE Confidence: 0.95566195

00:01:29.870 --> 00:01:31.410 years into my faculty,
NOTE Confidence: 0.9985726

00:01:31.790 --> 00:01:32.750 we made a series of
NOTE Confidence: 0.9985726

00:01:32.750 --> 00:01:33.250 discoveries
NOTE Confidence: 0.9803354

00:01:33.630 --> 00:01:35.490 where we found that certain
NOTE Confidence: 0.9803354

00:01:35.550 --> 00:01:36.930 tumor associated mutations
NOTE Confidence: 0.9455607

00:01:37.230 --> 00:01:39.230 found in adults, but more
NOTE Confidence: 0.9455607

00:01:39.230 --> 00:01:40.990 often pediatric and what we
NOTE Confidence: 0.9455607

00:01:40.990 --> 00:01:41.470 call the,

NOTE Confidence: 0.91529775

00:01:42.165 --> 00:01:44.245 adolescent young adult population or

NOTE Confidence: 0.91529775

00:01:44.245 --> 00:01:45.465 the AYA population,

NOTE Confidence: 0.9844025

00:01:45.925 --> 00:01:46.965 we found that there was

NOTE Confidence: 0.9844025

00:01:46.965 --> 00:01:49.145 mutations specifically in those tumors

NOTE Confidence: 0.93746555

00:01:49.605 --> 00:01:51.625 that caused DNA repair defects.

NOTE Confidence: 0.9499147

00:01:53.045 --> 00:01:54.405 What was very interesting is

NOTE Confidence: 0.9499147

00:01:54.405 --> 00:01:55.945 that in my early faculty,

NOTE Confidence: 0.9499147

00:01:56.005 --> 00:01:57.600 I won a Cureshurt Young

NOTE Confidence: 0.9499147

00:01:57.600 --> 00:01:58.740 Investigator Award.

NOTE Confidence: 0.99655324

00:01:59.040 --> 00:02:00.240 And this was a three

NOTE Confidence: 0.99655324

00:02:00.240 --> 00:02:02.560 year award that really provided

NOTE Confidence: 0.99655324

00:02:02.560 --> 00:02:03.300 the infrastructure

NOTE Confidence: 0.9860049

00:02:03.680 --> 00:02:04.720 for us to make the

NOTE Confidence: 0.9860049

00:02:04.720 --> 00:02:06.320 discovery, which was the link

NOTE Confidence: 0.9860049

00:02:06.320 --> 00:02:07.700 between IDH mutations

NOTE Confidence: 0.99595594

00:02:08.319 --> 00:02:09.620 and DNA repair.
NOTE Confidence: 0.9918982

00:02:10.875 --> 00:02:12.334 We were able to treat
NOTE Confidence: 0.9918982

00:02:12.474 --> 00:02:13.674 cells that have the IDH
NOTE Confidence: 0.9918982

00:02:13.674 --> 00:02:15.034 mutation with a class of
NOTE Confidence: 0.9918982

00:02:15.034 --> 00:02:16.234 drugs that are FDA approved
NOTE Confidence: 0.9918982

00:02:16.234 --> 00:02:17.215 called PARP inhibitors.
NOTE Confidence: 0.9774505

00:02:17.594 --> 00:02:19.674 PARP inhibitors work against tumor
NOTE Confidence: 0.9774505

00:02:19.674 --> 00:02:21.135 cells that have this defect,
NOTE Confidence: 0.9774505

00:02:21.355 --> 00:02:22.394 and we realized that we
NOTE Confidence: 0.9774505

00:02:22.394 --> 00:02:23.594 could use the FDA approved
NOTE Confidence: 0.9774505

00:02:23.594 --> 00:02:25.200 PARP inhibitors and try them
NOTE Confidence: 0.9774505

00:02:25.200 --> 00:02:27.520 in young adult pediatric patients
NOTE Confidence: 0.9774505

00:02:27.520 --> 00:02:28.960 that have these IDH mutant
NOTE Confidence: 0.9774505

00:02:28.960 --> 00:02:29.460 gliomas.
NOTE Confidence: 0.9938236

00:02:30.320 --> 00:02:31.360 So you've got a very
NOTE Confidence: 0.9938236

00:02:31.360 --> 00:02:33.200 small population with very specific

NOTE Confidence: 0.9938236
00:02:33.200 --> 00:02:33.700 mutations
NOTE Confidence: 0.9805115
00:02:34.000 --> 00:02:35.120 that need to be studied
NOTE Confidence: 0.9805115
00:02:35.120 --> 00:02:36.240 on their own. As you
NOTE Confidence: 0.9805115
00:02:36.240 --> 00:02:38.080 can imagine, very difficult to
NOTE Confidence: 0.9805115
00:02:38.080 --> 00:02:39.280 get funding for this sort
NOTE Confidence: 0.9805115
00:02:39.280 --> 00:02:40.695 of trial. And that's when
NOTE Confidence: 0.9805115
00:02:40.695 --> 00:02:42.075 we went back to Curesearch
NOTE Confidence: 0.95666635
00:02:42.615 --> 00:02:43.655 and were able to take
NOTE Confidence: 0.95666635
00:02:43.655 --> 00:02:45.435 advantage of the Curesearch Catapult
NOTE Confidence: 0.95666635
00:02:45.495 --> 00:02:47.095 award. And this award allowed
NOTE Confidence: 0.95666635
00:02:47.095 --> 00:02:48.875 us to essentially take this
NOTE Confidence: 0.95666635
00:02:49.014 --> 00:02:49.835 bench discovery
NOTE Confidence: 0.98401326
00:02:50.215 --> 00:02:51.815 and move it directly into
NOTE Confidence: 0.98401326
00:02:51.815 --> 00:02:52.395 the bedside.
NOTE Confidence: 0.93980265
00:02:53.150 --> 00:02:54.270 The trial that doctor Bindra
NOTE Confidence: 0.93980265

00:02:54.270 --> 00:02:55.070 and I worked on has
NOTE Confidence: 0.93980265

00:02:55.070 --> 00:02:56.350 many components to it. And
NOTE Confidence: 0.93980265

00:02:56.350 --> 00:02:57.710 so it takes many different
NOTE Confidence: 0.93980265

00:02:57.710 --> 00:02:58.210 experts,
NOTE Confidence: 0.9719778

00:02:58.670 --> 00:02:59.630 and it takes a large
NOTE Confidence: 0.9719778

00:02:59.630 --> 00:03:01.390 amount of funding sources to
NOTE Confidence: 0.9719778

00:03:01.390 --> 00:03:02.530 make it all come together.
NOTE Confidence: 0.9719778

00:03:02.590 --> 00:03:04.530 We are always grateful to
NOTE Confidence: 0.9719778

00:03:04.750 --> 00:03:06.590 our donors, the foundations that
NOTE Confidence: 0.9719778

00:03:06.590 --> 00:03:07.090 support
NOTE Confidence: 0.9762128

00:03:07.905 --> 00:03:09.825 this really difficult work. And
NOTE Confidence: 0.9762128

00:03:09.825 --> 00:03:10.785 so we looked at other
NOTE Confidence: 0.9762128

00:03:10.785 --> 00:03:12.865 consortiums like the Pacific Neuro
NOTE Confidence: 0.9762128

00:03:12.865 --> 00:03:14.005 Oncology Consortium,
NOTE Confidence: 0.97520167

00:03:14.625 --> 00:03:16.065 who actually then allowed us
NOTE Confidence: 0.97520167

00:03:16.065 --> 00:03:17.345 to run our trial across

NOTE Confidence: 0.97520167
00:03:17.345 --> 00:03:18.625 a broader network of sites,
NOTE Confidence: 0.97520167
00:03:18.625 --> 00:03:19.905 and they also provided their
NOTE Confidence: 0.97520167
00:03:19.905 --> 00:03:21.505 own funding. And so working
NOTE Confidence: 0.97520167
00:03:21.505 --> 00:03:23.010 together with the Curessearch and
NOTE Confidence: 0.97520167
00:03:23.010 --> 00:03:23.669 the PNOG,
NOTE Confidence: 0.9467693
00:03:24.050 --> 00:03:25.010 group, we were able to
NOTE Confidence: 0.9467693
00:03:25.010 --> 00:03:27.010 do a national trial in
NOTE Confidence: 0.9467693
00:03:27.010 --> 00:03:28.130 a role of fairly large
NOTE Confidence: 0.9467693
00:03:28.130 --> 00:03:29.010 number of patients in a
NOTE Confidence: 0.9467693
00:03:29.010 --> 00:03:30.150 short period of time.
NOTE Confidence: 0.9809421
00:03:34.530 --> 00:03:35.650 I think this trial is
NOTE Confidence: 0.9809421
00:03:35.650 --> 00:03:37.835 helping us be more cognizant
NOTE Confidence: 0.9809421
00:03:37.975 --> 00:03:40.475 of specific mutations and unique,
NOTE Confidence: 0.9971083
00:03:41.175 --> 00:03:42.535 targets that we can look
NOTE Confidence: 0.9971083
00:03:42.535 --> 00:03:44.055 at in adolescent and young
NOTE Confidence: 0.9971083

00:03:44.055 --> 00:03:44.875 adult tumors.
NOTE Confidence: 0.9987285

00:03:45.495 --> 00:03:47.175 Priscilla was a really interesting
NOTE Confidence: 0.9987285

00:03:47.175 --> 00:03:48.475 and unique case.
NOTE Confidence: 0.9996834

00:03:49.010 --> 00:03:49.829 Her tumor
NOTE Confidence: 0.96451795

00:03:50.129 --> 00:03:51.409 was a high grade tumor,
NOTE Confidence: 0.96451795

00:03:51.409 --> 00:03:52.370 at the same time it
NOTE Confidence: 0.96451795

00:03:52.370 --> 00:03:54.370 carried a specific mutation that
NOTE Confidence: 0.96451795

00:03:54.370 --> 00:03:55.090 we thought that we could
NOTE Confidence: 0.96451795

00:03:55.090 --> 00:03:56.769 target. Obviously, I was dealing
NOTE Confidence: 0.96451795

00:03:56.769 --> 00:03:57.989 with this new diagnosis
NOTE Confidence: 0.97100604

00:03:58.450 --> 00:03:59.829 that came out of nowhere.
NOTE Confidence: 0.97100604

00:03:59.890 --> 00:04:01.750 It was an inoperable tumor.
NOTE Confidence: 0.90149176

00:04:02.105 --> 00:04:03.705 So from the beginning they
NOTE Confidence: 0.90149176

00:04:03.705 --> 00:04:04.745 told me we're gonna start
NOTE Confidence: 0.90149176

00:04:04.745 --> 00:04:05.245 radiation.
NOTE Confidence: 0.92349577

00:04:05.705 --> 00:04:06.345 I was,

NOTE Confidence: 0.9514756
00:04:06.745 --> 00:04:08.665 twenty three and living on
NOTE Confidence: 0.9514756
00:04:08.665 --> 00:04:09.325 my own,
NOTE Confidence: 0.99622023
00:04:10.265 --> 00:04:11.545 and where I needed to
NOTE Confidence: 0.99622023
00:04:11.545 --> 00:04:12.285 get radiation
NOTE Confidence: 0.9248073
00:04:12.825 --> 00:04:14.040 was two and a half
NOTE Confidence: 0.9248073
00:04:14.040 --> 00:04:15.800 hours away and then during
NOTE Confidence: 0.9248073
00:04:15.800 --> 00:04:17.320 radiation they said a few
NOTE Confidence: 0.9248073
00:04:17.320 --> 00:04:18.680 days after you finish radiation
NOTE Confidence: 0.9248073
00:04:18.680 --> 00:04:19.960 we're gonna start the chemo
NOTE Confidence: 0.9248073
00:04:19.960 --> 00:04:20.620 but then,
NOTE Confidence: 0.9968267
00:04:21.000 --> 00:04:22.360 I wasn't even finished with
NOTE Confidence: 0.9968267
00:04:22.360 --> 00:04:23.339 the first cycle
NOTE Confidence: 0.9869528
00:04:23.640 --> 00:04:24.440 when I had to go
NOTE Confidence: 0.9869528
00:04:24.440 --> 00:04:25.339 into the hospital
NOTE Confidence: 0.9186846
00:04:25.640 --> 00:04:27.104 and after after testing they
NOTE Confidence: 0.9186846

00:04:27.104 --> 00:04:29.285 saw the bad brain inflammation.

NOTE Confidence: 0.8821073

00:04:30.305 --> 00:04:31.525 And so thankfully,

NOTE Confidence: 0.95644444

00:04:32.384 --> 00:04:33.444 we reevaluated

NOTE Confidence: 0.87714547

00:04:33.904 --> 00:04:35.425 and I was I I

NOTE Confidence: 0.87714547

00:04:35.425 --> 00:04:37.345 was referred to you over

NOTE Confidence: 0.87714547

00:04:37.345 --> 00:04:38.724 here. Well, the initial,

NOTE Confidence: 0.9386224

00:04:39.025 --> 00:04:40.145 work out at Binger's lab

NOTE Confidence: 0.9386224

00:04:40.145 --> 00:04:42.200 informed the trial. The trial

NOTE Confidence: 0.9386224

00:04:42.260 --> 00:04:43.779 has given us confidence in

NOTE Confidence: 0.9386224

00:04:43.779 --> 00:04:46.040 treating patients with this particular

NOTE Confidence: 0.9386224

00:04:46.180 --> 00:04:47.160 class of drug,

NOTE Confidence: 0.9801112

00:04:47.540 --> 00:04:49.080 in this particular mutation.

NOTE Confidence: 0.9853165

00:04:49.380 --> 00:04:50.260 And so when we saw

NOTE Confidence: 0.9853165

00:04:50.260 --> 00:04:52.020 Priscilla's mutation, we had the

NOTE Confidence: 0.9853165

00:04:52.020 --> 00:04:53.620 confidence to go ahead and

NOTE Confidence: 0.9853165

00:04:53.620 --> 00:04:55.140 try this treatment course. Feeling

NOTE Confidence: 0.9853165
00:04:55.140 --> 00:04:56.040 more confident
NOTE Confidence: 0.9825122
00:04:56.395 --> 00:04:57.275 in the care I was
NOTE Confidence: 0.9825122
00:04:57.275 --> 00:04:58.735 receiving made a big difference
NOTE Confidence: 0.9825122
00:04:59.034 --> 00:05:00.074 because even though I was
NOTE Confidence: 0.9825122
00:05:00.074 --> 00:05:00.875 sick, even though I was
NOTE Confidence: 0.9825122
00:05:00.875 --> 00:05:01.914 not feeling well, as long
NOTE Confidence: 0.9825122
00:05:01.914 --> 00:05:02.794 as I felt like we
NOTE Confidence: 0.9825122
00:05:02.794 --> 00:05:05.115 were truly fighting the the
NOTE Confidence: 0.9825122
00:05:05.115 --> 00:05:05.615 disease,
NOTE Confidence: 0.92662466
00:05:06.235 --> 00:05:08.154 then I saw an end
NOTE Confidence: 0.92662466
00:05:08.154 --> 00:05:08.974 in InSite,
NOTE Confidence: 0.9695525
00:05:09.370 --> 00:05:10.490 and that helped that helped
NOTE Confidence: 0.9695525
00:05:10.490 --> 00:05:12.009 a lot. We've gotten control
NOTE Confidence: 0.9695525
00:05:12.009 --> 00:05:13.850 of Priscilla's tumor. She is
NOTE Confidence: 0.9695525
00:05:13.850 --> 00:05:15.130 still tumor free despite the
NOTE Confidence: 0.9695525

00:05:15.130 --> 00:05:16.410 fact that she's off medication
NOTE Confidence: 0.9695525

00:05:16.410 --> 00:05:17.770 and she's doing great. So
NOTE Confidence: 0.9695525

00:05:17.770 --> 00:05:19.229 even though we had treated
NOTE Confidence: 0.9722935

00:05:19.610 --> 00:05:21.225 fifty, sixty patients in this
NOTE Confidence: 0.9722935

00:05:21.385 --> 00:05:23.545 trial, we already saw evidence,
NOTE Confidence: 0.9722935

00:05:23.545 --> 00:05:25.225 early evidence of efficacy in
NOTE Confidence: 0.9722935

00:05:25.225 --> 00:05:27.145 response, which then allows us
NOTE Confidence: 0.9722935

00:05:27.145 --> 00:05:28.345 to treat patients with the
NOTE Confidence: 0.9722935

00:05:28.345 --> 00:05:29.785 same tumor. And that's what's
NOTE Confidence: 0.9722935

00:05:29.785 --> 00:05:30.985 the beauty of these small
NOTE Confidence: 0.9722935

00:05:30.985 --> 00:05:32.765 trials having a massive impact
NOTE Confidence: 0.9722935

00:05:32.904 --> 00:05:34.445 on pediatric cancer research.