WEBVTT

NOTE duration: ”01:05:21.578”

NOTE Confidence: 0.9918325

00:00:00.080 --> 00:00:01.680 Good afternoon, everyone. Thank you

NOTE Confidence: 0.9918325

00:00:01.680 --> 00:00:02.740 so much for coming.

NOTE Confidence: 0.91192275

00:00:04.000 --> 00:00:06.899 Today is, our annual William

NOTE Confidence: 0.755229

00:00:07.279 --> 00:00:08.420 McAllister Junior,

NOTE Confidence: 0.73152614

00:00:08.880 --> 00:00:10.019 Memorial Lecture.

NOTE Confidence: 0.9576838

00:00:10.719 --> 00:00:11.119 And,

NOTE Confidence: 0.9995151

00:00:11.599 --> 00:00:12.500 we are very

NOTE Confidence: 0.91315085

00:00:13.134 --> 00:00:15.054 honored to have, doctor Jason

NOTE Confidence: 0.91315085

00:00:15.054 --> 00:00:15.855 Hornick as,

NOTE Confidence: 0.936629

00:00:16.414 --> 00:00:17.954 a recipient of this lectureship

NOTE Confidence: 0.936629

00:00:18.015 --> 00:00:18.515 award.

NOTE Confidence: 0.88280123

00:00:19.454 --> 00:00:21.134 Doctor Hornick is a professor

NOTE Confidence: 0.88280123

00:00:21.134 --> 00:00:22.735 of pathology at Harvard Medical

NOTE Confidence: 0.88280123

00:00:22.735 --> 00:00:24.494 School, and our cancer chair

NOTE Confidence: 0.88280123

00:00:24.494 --> 00:00:26.035 at Brigham at Women's Hospital,

NOTE Confidence: 0.9478917

00:00:26.520 --> 00:00:27.960 director of anatomic pathology and

NOTE Confidence: 0.9478917

00:00:27.960 --> 00:00:28.460 immunohistochemistry

NOTE Confidence: 0.9587953

00:00:28.920 --> 00:00:30.380 at Brigham and Women's Hospital,

NOTE Confidence: 0.9587953

00:00:30.600 --> 00:00:31.720 and chief of soft tissue

NOTE Confidence: 0.9587953

00:00:31.720 --> 00:00:33.960 and bone pathology at, Mass

NOTE Confidence: 0.9587953

00:00:33.960 --> 00:00:35.640 General Brigham. So it's a

NOTE Confidence: 0.9587953

00:00:35.640 --> 00:00:36.460 great honor,

NOTE Confidence: 0.9332162

00:00:37.000 --> 00:00:38.280 to have doctor Hornick with

NOTE Confidence: 0.9332162

00:00:38.280 --> 00:00:39.320 us today. And,

NOTE Confidence: 0.9703248

00:00:40.065 --> 00:00:41.265 just a few words about

NOTE Confidence: 0.9703248

00:00:41.265 --> 00:00:42.085 this lectureship,

NOTE Confidence: 0.9597459

00:00:42.465 --> 00:00:42.784 and,

NOTE Confidence: 0.9749811

00:00:43.345 --> 00:00:44.485 I have to tell to

NOTE Confidence: 0.9749811

00:00:44.545 --> 00:00:46.705 to Jason, actually, our faculty

NOTE Confidence: 0.9749811

00:00:46.705 --> 00:00:47.825 voted for you to receive

NOTE Confidence: 0.9749811

00:00:47.825 --> 00:00:49.585 this lectureship award. It was

NOTE Confidence: 0.9749811

00:00:49.585 --> 00:00:51.025 a nomination process, and it

NOTE Confidence: 0.9749811

00:00:51.025 --> 00:00:52.700 was a vote. So it's

NOTE Confidence: 0.9749811

00:00:52.700 --> 00:00:54.000 really, you know, we wanna

NOTE Confidence: 0.9749811

00:00:54.060 --> 00:00:55.180 express how much we actually

NOTE Confidence: 0.9749811

00:00:55.180 --> 00:00:56.540 appreciate what you did for

NOTE Confidence: 0.9749811

00:00:56.540 --> 00:00:58.320 the field of surgical pathology.

NOTE Confidence: 0.936216

00:00:58.860 --> 00:01:00.640 But back to doctor McAllister,

NOTE Confidence: 0.99801743

00:01:00.940 --> 00:01:01.600 who was

NOTE Confidence: 0.9463828

00:01:01.980 --> 00:01:03.680 a graduate of Yale College

NOTE Confidence: 0.9463828

00:01:03.900 --> 00:01:06.080 and John Hopkins Medical School

NOTE Confidence: 0.9463828

00:01:06.365 --> 00:01:08.045 and Department of Pathology. He

NOTE Confidence: 0.9463828

00:01:08.045 --> 00:01:09.165 actually came back to New

NOTE Confidence: 0.9463828

00:01:09.165 --> 00:01:09.665 Haven

NOTE Confidence: 0.92626023

00:01:09.965 --> 00:01:11.005 and served as the chief

NOTE Confidence: 0.92626023

00:01:11.005 --> 00:01:12.445 of surgical pathology for the

NOTE Confidence: 0.92626023

00:01:12.445 --> 00:01:12.765 new year,

NOTE Confidence: 0.9511618

00:01:13.485 --> 00:01:15.345 for the New Haven, hospital

NOTE Confidence: 0.9511618

00:01:15.405 --> 00:01:16.705 for twenty five years

NOTE Confidence: 0.9500757

00:01:17.005 --> 00:01:18.685 from, nineteen fifty three to

NOTE Confidence: 0.9500757

00:01:18.685 --> 00:01:20.065 nineteen seventy eight.

NOTE Confidence: 0.9908763

00:01:20.579 --> 00:01:21.079 And,

NOTE Confidence: 0.89369637

00:01:21.939 --> 00:01:24.119 he was diagnostic pathologist

NOTE Confidence: 0.64033854

00:01:24.659 --> 00:01:25.159 educator,

NOTE Confidence: 0.9813045

00:01:25.939 --> 00:01:26.259 and,

NOTE Confidence: 0.9156734

00:01:26.819 --> 00:01:28.340 his teaching including the science

NOTE Confidence: 0.9156734

00:01:28.340 --> 00:01:29.700 of medicine, also the art

NOTE Confidence: 0.9156734

00:01:29.700 --> 00:01:30.979 of living. He was an

NOTE Confidence: 0.9156734

00:01:30.979 --> 00:01:31.479 extraordinary

NOTE Confidence: 0.88798213

00:01:31.859 --> 00:01:33.000 mentor, adviser,

NOTE Confidence: 0.9360155

00:01:33.795 --> 00:01:35.975 friend to students, residents, coworkers,

NOTE Confidence: 0.9360155

00:01:36.115 --> 00:01:37.735 and physicians from all discipline.

NOTE Confidence: 0.9360155

00:01:37.955 --> 00:01:38.915 And I think this also

NOTE Confidence: 0.9360155

00:01:38.915 --> 00:01:40.915 described doctor Jason Hornick. So,

NOTE Confidence: 0.9360155

00:01:41.235 --> 00:01:42.435 I don't think doctor Jason

NOTE Confidence: 0.9360155

00:01:42.435 --> 00:01:44.194 Hornick needs any introduction, but

NOTE Confidence: 0.9360155

00:01:44.194 --> 00:01:45.235 just going to say a

NOTE Confidence: 0.9360155

00:01:45.235 --> 00:01:46.680 few words about you.

NOTE Confidence: 0.6273749

00:01:47.319 --> 00:01:48.860 Doctor Horney has started,

NOTE Confidence: 0.888093

00:01:49.360 --> 00:01:49.860 his,

NOTE Confidence: 0.89256895

00:01:50.360 --> 00:01:51.800 medical school and completed his

NOTE Confidence: 0.89256895

00:01:51.800 --> 00:01:53.640 medical training at University of

NOTE Confidence: 0.89256895

00:01:53.640 --> 00:01:55.480 California, where she obtained his

NOTE Confidence: 0.89256895

00:01:55.480 --> 00:01:57.180 MD and the PhD degree.

NOTE Confidence: 0.9021696

00:01:57.480 --> 00:01:58.680 From West Coast to he

NOTE Confidence: 0.9021696

00:01:58.680 --> 00:02:00.200 moved to East Coast to,

NOTE Confidence: 0.9021696

00:02:00.440 --> 00:02:02.460 Harvard Medical School, where he

NOTE Confidence: 0.95958084

00:02:02.775 --> 00:02:04.295 did a training in anatomic

NOTE Confidence: 0.95958084

00:02:04.295 --> 00:02:04.795 pathology

NOTE Confidence: 0.72723603

00:02:05.495 --> 00:02:05.815 and,

NOTE Confidence: 0.9623362

00:02:06.295 --> 00:02:09.275 impressive fellowships in GYN, anatomic

NOTE Confidence: 0.9623362

00:02:09.335 --> 00:02:11.435 pathology, soft tissue pathology, hematopathology,

NOTE Confidence: 0.794998

00:02:11.735 --> 00:02:12.794 and the gastrointestinal pathology.

NOTE Confidence: 0.94853127

00:02:13.495 --> 00:02:14.455 I don't see, I don't

NOTE Confidence: 0.94853127

00:02:14.455 --> 00:02:15.995 think we see that anymore.

NOTE Confidence: 0.94853127

00:02:16.055 --> 00:02:17.310 So, he's, like, one of

NOTE Confidence: 0.94853127

00:02:17.310 --> 00:02:18.690 the last, I would say,

NOTE Confidence: 0.9253968

00:02:19.310 --> 00:02:20.830 pathologist who actually went through

NOTE Confidence: 0.9253968

00:02:20.830 --> 00:02:22.110 such extensive training and is

NOTE Confidence: 0.9253968

00:02:22.110 --> 00:02:23.330 actually able to do

NOTE Confidence: 0.9175434

00:02:23.790 --> 00:02:25.470 ex excellent job in all

NOTE Confidence: 0.9175434

00:02:25.470 --> 00:02:26.210 of the areas.

NOTE Confidence: 0.937031

00:02:26.590 --> 00:02:27.790 But what he is most

NOTE Confidence: 0.937031

00:02:27.790 --> 00:02:29.310 known for is certainly the

NOTE Confidence: 0.937031

00:02:29.310 --> 00:02:30.255 area of bone and soft

NOTE Confidence: 0.937031

00:02:30.255 --> 00:02:31.855 tissue pathology and GI as

NOTE Confidence: 0.937031

00:02:31.855 --> 00:02:32.895 well, but bone and soft

NOTE Confidence: 0.937031

00:02:32.895 --> 00:02:33.875 tissue in particular,

NOTE Confidence: 0.9412102

00:02:34.255 --> 00:02:35.855 where he really defined multiple

NOTE Confidence: 0.9412102

00:02:35.855 --> 00:02:37.555 entities and actually help us

NOTE Confidence: 0.9412102

00:02:37.694 --> 00:02:39.535 to develop many diagnostic tests

NOTE Confidence: 0.9412102

00:02:39.535 --> 00:02:40.895 that we routinely use. So

NOTE Confidence: 0.9412102

00:02:40.895 --> 00:02:41.855 it's all thanks to you,

NOTE Confidence: 0.9412102

00:02:41.855 --> 00:02:42.895 Jason. So thank you so

NOTE Confidence: 0.9412102

00:02:42.895 --> 00:02:43.200 much.

NOTE Confidence: 0.89370525

00:02:44.400 --> 00:02:46.239 Numerous publications needed to say

NOTE Confidence: 0.89370525

00:02:46.239 --> 00:02:47.760 were five hundred. It's just

NOTE Confidence: 0.89370525

00:02:47.840 --> 00:02:49.519 I I stopped counting, actually,

NOTE Confidence: 0.89370525

00:02:49.519 --> 00:02:50.500 in your CV.

NOTE Confidence: 0.937185

00:02:50.959 --> 00:02:52.340 But, other notable,

NOTE Confidence: 0.8444878

00:02:52.879 --> 00:02:53.379 contributions,

NOTE Confidence: 0.95862585

00:02:53.760 --> 00:02:55.519 he's been, editor of the

NOTE Confidence: 0.95862585

00:02:55.519 --> 00:02:57.120 WHO for the last three

NOTE Confidence: 0.95862585

00:02:57.120 --> 00:02:57.620 editions,

NOTE Confidence: 0.9898602

00:02:58.725 --> 00:03:00.885 and, he's currently serving as

NOTE Confidence: 0.9898602

00:03:00.885 --> 00:03:02.485 the president of the United

NOTE Confidence: 0.9898602

00:03:02.485 --> 00:03:03.565 States and the Canadian Academy

NOTE Confidence: 0.9898602

00:03:03.565 --> 00:03:04.264 of Pathology

NOTE Confidence: 0.9122148

00:03:04.725 --> 00:03:06.505 and is immediate past president

NOTE Confidence: 0.9122148

00:03:06.645 --> 00:03:08.084 of the Arthur Purdes South

NOTE Confidence: 0.9122148

00:03:08.084 --> 00:03:10.105 Society of Surgical Pathologists. So,

NOTE Confidence: 0.9122148

00:03:10.300 --> 00:03:11.580 Jason, thank you so much

NOTE Confidence: 0.9122148

00:03:11.580 --> 00:03:13.180 for, coming to us today

NOTE Confidence: 0.9122148

00:03:13.180 --> 00:03:15.200 and accepting this Lectureship Award.

NOTE Confidence: 0.9122148

00:03:15.340 --> 00:03:16.080 Thank you.

NOTE Confidence: 0.92793417

00:03:20.459 --> 00:03:21.660 Thank you so much, Sonia.

NOTE Confidence: 0.92793417

00:03:21.660 --> 00:03:22.620 And it's really such a

NOTE Confidence: 0.92793417

00:03:22.620 --> 00:03:23.740 pleasure to be here back

NOTE Confidence: 0.92793417

00:03:23.740 --> 00:03:24.375 at Yale.

NOTE Confidence: 0.997562

00:03:24.775 --> 00:03:25.975 And I very much appreciate

NOTE Confidence: 0.997562

00:03:25.975 --> 00:03:27.255 the faculty voting for me

NOTE Confidence: 0.997562

00:03:27.255 --> 00:03:27.915 to come.

NOTE Confidence: 0.9749457

00:03:28.455 --> 00:03:29.415 I feel like I come

NOTE Confidence: 0.9749457

00:03:29.415 --> 00:03:30.695 about every ten years. It's

NOTE Confidence: 0.9749457

00:03:30.695 --> 00:03:31.655 been a while, but it's

NOTE Confidence: 0.9749457

00:03:31.655 --> 00:03:32.794 so nice to be back.

NOTE Confidence: 0.9379332

00:03:33.895 --> 00:03:34.935 I thought I'd come south

NOTE Confidence: 0.9379332

00:03:34.935 --> 00:03:35.815 and the weather would be

NOTE Confidence: 0.9379332

00:03:35.815 --> 00:03:37.815 amazing. But surprisingly, it's very

NOTE Confidence: 0.9379332

00:03:37.815 --> 00:03:38.795 similar to Boston.

NOTE Confidence: 0.99130696

00:03:40.300 --> 00:03:42.220 So, you know, throughout my

NOTE Confidence: 0.99130696

00:03:42.220 --> 00:03:43.920 career and throughout my

NOTE Confidence: 0.8901768

00:03:44.220 --> 00:03:45.840 kind of pathology years,

NOTE Confidence: 0.9627802

00:03:46.300 --> 00:03:47.420 I've really had a big

NOTE Confidence: 0.9627802

00:03:47.420 --> 00:03:49.600 interest in diagnostic immunistic chemistry.

NOTE Confidence: 0.99008584

00:03:50.380 --> 00:03:51.580 In my PhD, I worked

NOTE Confidence: 0.99008584

00:03:51.580 --> 00:03:52.800 on antibody engineering

NOTE Confidence: 0.9886447

00:03:54.015 --> 00:03:55.375 where, I was working on

NOTE Confidence: 0.9886447

00:03:55.375 --> 00:03:57.394 various constructs for tumor targeting

NOTE Confidence: 0.92937905

00:03:57.855 --> 00:03:59.135 before we had drugs that

NOTE Confidence: 0.92937905

00:03:59.135 --> 00:04:01.135 were antibodies, before Rituxan and

NOTE Confidence: 0.92937905

00:04:01.135 --> 00:04:01.635 Herceptin,

NOTE Confidence: 0.94714963

00:04:02.894 --> 00:04:03.555 and others.

NOTE Confidence: 0.91660076

00:04:04.254 --> 00:04:05.310 And I knew nothing nothing

NOTE Confidence: 0.91660076

00:04:05.310 --> 00:04:06.470 about pathology, but I knew

NOTE Confidence: 0.91660076

00:04:06.470 --> 00:04:08.130 a lot about antibodies. So

NOTE Confidence: 0.91660076

00:04:08.350 --> 00:04:09.470 it was sort of easy

NOTE Confidence: 0.91660076

00:04:09.470 --> 00:04:10.130 to become

NOTE Confidence: 0.9540078

00:04:10.750 --> 00:04:12.370 interested in immunohistochemistry.

NOTE Confidence: 0.99786395

00:04:13.230 --> 00:04:14.270 And in this session, I'm

NOTE Confidence: 0.99786395

00:04:14.270 --> 00:04:16.029 really gonna focus on how

NOTE Confidence: 0.99786395

00:04:16.029 --> 00:04:16.529 immunohistochemistry

NOTE Confidence: 0.9988265

00:04:17.070 --> 00:04:18.430 has changed over the last

NOTE Confidence: 0.9988265

00:04:18.430 --> 00:04:19.250 twenty years.

NOTE Confidence: 0.8738898

00:04:20.350 --> 00:04:20.850 I'm

NOTE Confidence: 0.96877605

00:04:21.464 --> 00:04:22.504 I like to kind of

NOTE Confidence: 0.96877605

00:04:22.504 --> 00:04:24.185 pretend there's a separation between

NOTE Confidence: 0.96877605

00:04:24.185 --> 00:04:25.544 the twentieth century and twenty

NOTE Confidence: 0.96877605

00:04:25.544 --> 00:04:26.284 first century.

NOTE Confidence: 0.97786176

00:04:26.585 --> 00:04:27.544 It's not, of course, a

NOTE Confidence: 0.97786176

00:04:27.544 --> 00:04:29.145 nice line there. But for

NOTE Confidence: 0.97786176

00:04:29.145 --> 00:04:30.344 the first twenty five to

NOTE Confidence: 0.97786176

00:04:30.344 --> 00:04:32.044 thirty years, we use this

NOTE Confidence: 0.9995448

00:04:32.425 --> 00:04:32.925 technology

NOTE Confidence: 0.9975131

00:04:33.750 --> 00:04:34.870 to try to define a

NOTE Confidence: 0.9975131

00:04:34.870 --> 00:04:35.850 line of differentiation.

NOTE Confidence: 0.9906512

00:04:36.710 --> 00:04:37.990 What do the tumor cells

NOTE Confidence: 0.9906512

00:04:37.990 --> 00:04:39.990 most closely resemble? And this

NOTE Confidence: 0.9906512

00:04:39.990 --> 00:04:42.070 still is critically important for

NOTE Confidence: 0.9906512

00:04:42.070 --> 00:04:42.810 us in

NOTE Confidence: 0.98090917

00:04:43.110 --> 00:04:45.610 oncologic surgical pathology and hematopathology.

NOTE Confidence: 0.982191

00:04:47.115 --> 00:04:48.475 But now we have so

NOTE Confidence: 0.982191

00:04:48.475 --> 00:04:49.455 many examples

NOTE Confidence: 0.99968874

00:04:49.875 --> 00:04:50.375 of

NOTE Confidence: 0.999826

00:04:50.795 --> 00:04:52.815 using antibodies to recognize

NOTE Confidence: 0.99412745

00:04:53.355 --> 00:04:55.275 the protein correlates of molecular

NOTE Confidence: 0.99412745

00:04:55.275 --> 00:04:56.335 genetic alterations.

NOTE Confidence: 0.98717463

00:04:56.955 --> 00:04:58.415 So this is really a

NOTE Confidence: 0.98432964

00:04:58.875 --> 00:05:00.420 whole new way of using

NOTE Confidence: 0.98432964

00:05:00.500 --> 00:05:01.700 this technology, and I know

NOTE Confidence: 0.98432964

00:05:01.700 --> 00:05:03.460 there's many people here who

NOTE Confidence: 0.98432964

00:05:03.460 --> 00:05:04.820 are expert in this field

NOTE Confidence: 0.98432964

00:05:04.820 --> 00:05:05.480 as well.

NOTE Confidence: 0.9899971

00:05:05.940 --> 00:05:07.540 But I'm really gonna talk

NOTE Confidence: 0.9899971

00:05:07.540 --> 00:05:09.800 about molecular genetics, but only

NOTE Confidence: 0.98695666

00:05:10.340 --> 00:05:12.040 as what the protein

NOTE Confidence: 0.9899688

00:05:12.340 --> 00:05:14.360 surrogates are, the protein consequences

NOTE Confidence: 0.80324334

00:05:15.425 --> 00:05:16.245 for immunoskemetry.

NOTE Confidence: 0.96359456

00:05:16.865 --> 00:05:17.365 And,

NOTE Confidence: 0.9834845

00:05:17.985 --> 00:05:19.265 you know, we still use

NOTE Confidence: 0.9834845

00:05:19.265 --> 00:05:20.785 all the time so many

NOTE Confidence: 0.9834845

00:05:20.785 --> 00:05:22.805 antibodies that are helpful to

NOTE Confidence: 0.84830755

00:05:24.145 --> 00:05:25.125 to sub classify

NOTE Confidence: 0.9995687

00:05:25.425 --> 00:05:26.725 tumors that we can't

NOTE Confidence: 0.9579785

00:05:27.025 --> 00:05:28.404 diagnose down the microscope.

NOTE Confidence: 0.99906445

00:05:28.889 --> 00:05:29.389 Undifferentiated

NOTE Confidence: 0.98205125

00:05:29.850 --> 00:05:30.910 malignant neoplasms

NOTE Confidence: 0.965618

00:05:31.690 --> 00:05:33.870 or narrowing down various diagnostic

NOTE Confidence: 0.965618

00:05:33.930 --> 00:05:35.529 categories. But I'm not gonna

NOTE Confidence: 0.965618

00:05:35.529 --> 00:05:36.810 talk about this. I'm gonna

NOTE Confidence: 0.965618

00:05:36.810 --> 00:05:38.490 talk about what some people

NOTE Confidence: 0.965618

00:05:38.490 --> 00:05:39.529 have liked to call next

NOTE Confidence: 0.965618

00:05:39.529 --> 00:05:40.509 generation immunohistochemistry.

NOTE Confidence: 0.9871646

00:05:42.195 --> 00:05:44.435 And I've listed six different

NOTE Confidence: 0.9871646

00:05:44.435 --> 00:05:46.195 topics here, and I'm just

NOTE Confidence: 0.9871646

00:05:46.195 --> 00:05:47.315 gonna give one or two

NOTE Confidence: 0.9871646

00:05:47.315 --> 00:05:48.514 examples in each of these

NOTE Confidence: 0.9871646

00:05:48.514 --> 00:05:49.014 areas

NOTE Confidence: 0.9692956

00:05:49.555 --> 00:05:50.915 by way of introduction to

NOTE Confidence: 0.9692956

00:05:50.915 --> 00:05:51.654 this field.

NOTE Confidence: 0.9631774

00:05:52.354 --> 00:05:53.555 Some of you will be

NOTE Confidence: 0.9631774

00:05:53.555 --> 00:05:54.755 familiar with some of these

NOTE Confidence: 0.9631774

00:05:54.755 --> 00:05:56.695 antibodies, others will be new.

NOTE Confidence: 0.98742735

00:05:57.480 --> 00:05:59.000 And all the antibodies I'm

NOTE Confidence: 0.98742735

00:05:59.000 --> 00:06:01.420 talking about today are antibodies

NOTE Confidence: 0.98742735

00:06:01.560 --> 00:06:03.000 we use routinely in our

NOTE Confidence: 0.98742735

00:06:03.000 --> 00:06:04.860 clinical practice in my department.

NOTE Confidence: 0.98054737

00:06:06.279 --> 00:06:07.400 And I'm not gonna read

NOTE Confidence: 0.98054737

00:06:07.400 --> 00:06:08.600 this list because I'm gonna

NOTE Confidence: 0.98054737

00:06:08.600 --> 00:06:09.800 give examples as we go

NOTE Confidence: 0.98054737

00:06:09.800 --> 00:06:11.185 through them. But you can

NOTE Confidence: 0.98054737

00:06:11.185 --> 00:06:12.544 see the really broad range

NOTE Confidence: 0.98054737

00:06:12.544 --> 00:06:13.365 of applications

NOTE Confidence: 0.9745086

00:06:14.145 --> 00:06:15.264 this has opened up for

NOTE Confidence: 0.9745086

00:06:15.264 --> 00:06:17.185 us. In some cases, these

NOTE Confidence: 0.9745086

00:06:17.185 --> 00:06:18.785 antibodies can really help narrow

NOTE Confidence: 0.9745086

00:06:18.785 --> 00:06:20.324 down a differential diagnosis.

NOTE Confidence: 0.9980431

00:06:21.025 --> 00:06:22.085 But in other cases,

NOTE Confidence: 0.9945184

00:06:22.464 --> 00:06:24.065 they are perfect surrogates for

NOTE Confidence: 0.9945184

00:06:24.065 --> 00:06:25.125 molecular genetics,

NOTE Confidence: 0.9933177

00:06:25.720 --> 00:06:27.240 allowing us to perform a

NOTE Confidence: 0.9933177

00:06:27.240 --> 00:06:29.100 single antibody test for immunohistochemistry

NOTE Confidence: 0.9668536

00:06:30.120 --> 00:06:31.400 instead of any form of

NOTE Confidence: 0.9668536

00:06:31.400 --> 00:06:33.400 molecular genetic testing. And this

NOTE Confidence: 0.9668536

00:06:33.400 --> 00:06:34.920 is really valuable both for

NOTE Confidence: 0.9668536

00:06:34.920 --> 00:06:36.700 the turnaround time, the expense,

NOTE Confidence: 0.99925745

00:06:37.240 --> 00:06:38.835 and for practices throughout the

NOTE Confidence: 0.99925745

00:06:38.835 --> 00:06:40.375 world that don't have access

NOTE Confidence: 0.984519

00:06:40.995 --> 00:06:43.395 to expensive next generation sequencing

NOTE Confidence: 0.984519

00:06:43.395 --> 00:06:44.375 and other technologies.

NOTE Confidence: 0.9699694

00:06:44.835 --> 00:06:46.035 So that's in part been

NOTE Confidence: 0.9699694

00:06:46.035 --> 00:06:47.635 one of my goals of

NOTE Confidence: 0.9699694

00:06:47.635 --> 00:06:48.835 working in this field is

NOTE Confidence: 0.9699694

00:06:48.835 --> 00:06:49.895 to make it easy

NOTE Confidence: 0.99496967

00:06:50.275 --> 00:06:52.595 for pathologists to diagnose rare

NOTE Confidence: 0.99496967

00:06:52.595 --> 00:06:53.095 cancers

NOTE Confidence: 0.997033

00:06:53.580 --> 00:06:55.020 in a very straightforward and

NOTE Confidence: 0.997033

00:06:55.020 --> 00:06:55.919 rapid fashion.

NOTE Confidence: 0.98766345

00:06:56.779 --> 00:06:58.699 So probably the oldest example

NOTE Confidence: 0.98766345

00:06:58.699 --> 00:06:59.980 I'm gonna talk about today

NOTE Confidence: 0.98766345

00:06:59.980 --> 00:07:01.820 is an example where we

NOTE Confidence: 0.98766345

00:07:01.820 --> 00:07:03.919 can look for abnormal protein

NOTE Confidence: 0.98766345

00:07:04.060 --> 00:07:04.560 localization,

NOTE Confidence: 0.9975458

00:07:05.339 --> 00:07:06.779 and that is for beta

NOTE Confidence: 0.9975458

00:07:06.779 --> 00:07:07.279 catenin.

NOTE Confidence: 0.9839458

00:07:08.025 --> 00:07:09.065 I'm sure you all know

NOTE Confidence: 0.9839458

00:07:09.065 --> 00:07:10.585 about beta catenin, which is

NOTE Confidence: 0.9839458

00:07:10.585 --> 00:07:11.245 the protein,

NOTE Confidence: 0.9872891

00:07:12.264 --> 00:07:13.865 that is encoded by CTN

NOTE Confidence: 0.9872891

00:07:13.865 --> 00:07:15.005 and B1 gene

NOTE Confidence: 0.95352983

00:07:15.465 --> 00:07:17.485 involved along with the APC

NOTE Confidence: 0.95352983

00:07:17.705 --> 00:07:18.205 protein

NOTE Confidence: 0.987385

00:07:18.745 --> 00:07:20.845 in the Wnt signaling pathway.

NOTE Confidence: 0.99812084

00:07:21.870 --> 00:07:22.850 And mutations

NOTE Confidence: 0.96784246

00:07:23.230 --> 00:07:24.770 in CTN and B1

NOTE Confidence: 0.935618

00:07:25.470 --> 00:07:27.710 or biallelic inactivation of the

NOTE Confidence: 0.935618

00:07:27.710 --> 00:07:30.130 adenomatous polyposis coli gene,

NOTE Confidence: 0.9790983

00:07:30.590 --> 00:07:32.030 most often in patients who

NOTE Confidence: 0.9790983

00:07:32.030 --> 00:07:34.850 have FAP, familial adenomatous polyposis,

NOTE Confidence: 0.9958782

00:07:35.715 --> 00:07:37.735 results in an aberrant localization

NOTE Confidence: 0.9958782

00:07:37.875 --> 00:07:38.935 of beta catenin

NOTE Confidence: 0.99602365

00:07:39.635 --> 00:07:40.935 from the cell membrane

NOTE Confidence: 0.9950717

00:07:41.235 --> 00:07:42.595 inside the cell to the

NOTE Confidence: 0.9950717

00:07:42.595 --> 00:07:44.135 cytoplasm and the nucleus.

NOTE Confidence: 0.9998493

00:07:44.755 --> 00:07:46.215 This is very helpful

NOTE Confidence: 0.99947476

00:07:46.755 --> 00:07:48.135 to support the diagnosis

NOTE Confidence: 0.9992318

00:07:48.595 --> 00:07:49.495 of a select

NOTE Confidence: 0.9997245

00:07:50.170 --> 00:07:51.630 group of tumor types

NOTE Confidence: 0.9989627

00:07:51.930 --> 00:07:53.150 that have mutations

NOTE Confidence: 0.99726003

00:07:53.530 --> 00:07:54.910 in one of these genes.

NOTE Confidence: 0.99726003

00:07:55.130 --> 00:07:56.570 And I've listed them here

NOTE Confidence: 0.99726003

00:07:56.570 --> 00:07:57.230 on this

NOTE Confidence: 0.95530033

00:07:57.930 --> 00:07:59.530 slide. And I'm just gonna

NOTE Confidence: 0.95530033

00:07:59.530 --> 00:08:00.750 show you two examples.

NOTE Confidence: 0.94564617

00:08:01.370 --> 00:08:02.730 So the first, a very

NOTE Confidence: 0.94564617

00:08:02.730 --> 00:08:03.550 old example.

NOTE Confidence: 0.97550327

00:08:04.095 --> 00:08:05.375 In nineteen ninety nine, it

NOTE Confidence: 0.97550327

00:08:05.375 --> 00:08:06.115 was discovered

NOTE Confidence: 0.99770176

00:08:06.575 --> 00:08:08.515 that beta catenin mutations

NOTE Confidence: 0.99952334

00:08:09.295 --> 00:08:10.915 are the most common drivers

NOTE Confidence: 0.98658323

00:08:11.535 --> 00:08:12.835 of desmoid fibromatosis.

NOTE Confidence: 0.9912681

00:08:13.775 --> 00:08:14.975 You know, so called deep

NOTE Confidence: 0.9912681

00:08:14.975 --> 00:08:15.475 fibromatosis

NOTE Confidence: 0.98654705

00:08:16.460 --> 00:08:18.060 that's a locally aggressive soft

NOTE Confidence: 0.98654705

00:08:18.060 --> 00:08:20.060 tissue tumor that arises fairly

NOTE Confidence: 0.98654705

00:08:20.060 --> 00:08:20.560 commonly,

NOTE Confidence: 0.96981984

00:08:21.740 --> 00:08:23.260 extra abdominal sites in the

NOTE Confidence: 0.96981984

00:08:23.260 --> 00:08:24.400 abdominal cavity.

NOTE Confidence: 0.92890024

00:08:25.020 --> 00:08:27.260 And, Liz Montgomery and colleagues

NOTE Confidence: 0.92890024

00:08:27.260 --> 00:08:28.000 showed us,

NOTE Confidence: 0.9449904

00:08:28.540 --> 00:08:30.275 twenty years ago now that

NOTE Confidence: 0.9449904

00:08:30.275 --> 00:08:31.655 we could use immunohistochemistry

NOTE Confidence: 0.9955034

00:08:32.755 --> 00:08:34.535 to look for aberrant localization

NOTE Confidence: 0.9955034

00:08:34.834 --> 00:08:36.035 of this protein as a

NOTE Confidence: 0.9955034

00:08:36.035 --> 00:08:37.815 very good diagnostic surrogate.

NOTE Confidence: 0.9977948

00:08:39.154 --> 00:08:41.075 It's not perfect. It's only

NOTE Confidence: 0.9977948

00:08:41.075 --> 00:08:42.295 about eighty percent

NOTE Confidence: 0.96186125

00:08:42.755 --> 00:08:44.774 sensitive for desmoid fibromatosis.

NOTE Confidence: 0.8967158

00:08:45.929 --> 00:08:48.090 So but fortunately it's negative

NOTE Confidence: 0.8967158

00:08:48.090 --> 00:08:49.370 in many other tumors we

NOTE Confidence: 0.8967158

00:08:49.370 --> 00:08:50.110 would consider

NOTE Confidence: 0.9912021

00:08:50.490 --> 00:08:51.950 in the differential diagnosis.

NOTE Confidence: 0.99176085

00:08:52.570 --> 00:08:54.910 But because specificity and sensitivity

NOTE Confidence: 0.99176085

00:08:55.130 --> 00:08:56.110 are not perfect,

NOTE Confidence: 0.99913913

00:08:56.570 --> 00:08:58.170 it must be interpreted in

NOTE Confidence: 0.99913913

00:08:58.170 --> 00:08:59.950 the context of morphology

NOTE Confidence: 0.99091446

00:09:00.410 --> 00:09:01.070 and clinical

NOTE Confidence: 0.8765874

00:09:01.875 --> 00:09:02.375 details.

NOTE Confidence: 0.9914243

00:09:02.995 --> 00:09:04.295 And at the same time,

NOTE Confidence: 0.9914243

00:09:04.595 --> 00:09:06.054 the lack of this pattern

NOTE Confidence: 0.9914243

00:09:06.195 --> 00:09:08.375 certainly does not preclude diagnosis.

NOTE Confidence: 0.99781615

00:09:08.995 --> 00:09:10.115 But this is great when

NOTE Confidence: 0.99781615

00:09:10.115 --> 00:09:11.155 you're dealing with a small

NOTE Confidence: 0.99781615

00:09:11.155 --> 00:09:11.975 core biopsy

NOTE Confidence: 0.9840919

00:09:12.355 --> 00:09:13.475 and you're feeling a little

NOTE Confidence: 0.9840919

00:09:13.475 --> 00:09:14.835 bit uncomfortable to make a

NOTE Confidence: 0.9840919

00:09:14.835 --> 00:09:16.695 firm diagnosis of this tumor,

NOTE Confidence: 0.9840919

00:09:16.959 --> 00:09:18.559 which obviously has very huge

NOTE Confidence: 0.9840919

00:09:18.559 --> 00:09:19.059 implications

NOTE Confidence: 0.9986423

00:09:19.679 --> 00:09:21.220 for management of the patient.

NOTE Confidence: 0.98550355

00:09:22.000 --> 00:09:23.620 So this is desmoid fibromatosis.

NOTE Confidence: 0.9652123

00:09:24.640 --> 00:09:26.080 This tumor is composed of

NOTE Confidence: 0.9652123

00:09:26.080 --> 00:09:26.899 these bland,

NOTE Confidence: 0.99956757

00:09:27.519 --> 00:09:28.019 uniform

NOTE Confidence: 0.9082682

00:09:28.399 --> 00:09:28.899 myofibroblastic

NOTE Confidence: 0.9908182

00:09:29.519 --> 00:09:30.980 spindle cells with

NOTE Confidence: 0.9887104

00:09:31.315 --> 00:09:33.655 tapering nuclei and indistinct cytoplasm

NOTE Confidence: 0.9296576

00:09:34.675 --> 00:09:36.775 arranged in long sweeping fascicles

NOTE Confidence: 0.9296576

00:09:36.915 --> 00:09:39.815 within a often collagenous stroma.

NOTE Confidence: 0.996823

00:09:40.275 --> 00:09:41.315 One of the clues to

NOTE Confidence: 0.996823

00:09:41.315 --> 00:09:43.015 the diagnosis is the presence

NOTE Confidence: 0.996823

00:09:43.075 --> 00:09:43.735 of these

NOTE Confidence: 0.97573

00:09:44.350 --> 00:09:46.210 relatively thick walled muscularized

NOTE Confidence: 0.99962795

00:09:46.590 --> 00:09:47.090 vessels

NOTE Confidence: 0.9919918

00:09:47.870 --> 00:09:49.490 that have variable perivascular

NOTE Confidence: 0.9985252

00:09:49.870 --> 00:09:51.710 edema between the bundles of

NOTE Confidence: 0.9985252

00:09:51.710 --> 00:09:52.690 spindle cells.

NOTE Confidence: 0.9459961

00:09:53.790 --> 00:09:55.250 And this is beta catenin.

NOTE Confidence: 0.9459961

00:09:55.309 --> 00:09:57.309 We get again, aberrant nuclear

NOTE Confidence: 0.9459961

00:09:57.309 --> 00:09:57.809 localization

NOTE Confidence: 0.99948996

00:09:58.795 --> 00:10:00.495 as a very helpful finding

NOTE Confidence: 0.97039086

00:10:00.875 --> 00:10:02.575 to diagnose desmoid fibromatosis.

NOTE Confidence: 0.97140956

00:10:04.315 --> 00:10:05.755 One other example is a

NOTE Confidence: 0.97140956

00:10:05.755 --> 00:10:07.355 tumor type that arises in

NOTE Confidence: 0.97140956

00:10:07.355 --> 00:10:09.515 the, sino nasal region that's

NOTE Confidence: 0.97140956

00:10:09.515 --> 00:10:11.135 called glomangio pericytoma.

NOTE Confidence: 0.9920389

00:10:12.260 --> 00:10:13.300 We used to refer to

NOTE Confidence: 0.9920389

00:10:13.300 --> 00:10:14.839 it as sino nasal hemangioparicytoma.

NOTE Confidence: 0.97963923

00:10:16.500 --> 00:10:17.620 This is a lesion that

NOTE Confidence: 0.97963923

00:10:17.620 --> 00:10:19.540 presents as a polypoid mass,

NOTE Confidence: 0.97963923

00:10:19.540 --> 00:10:21.399 most often in the ethmoid

NOTE Confidence: 0.97963923

00:10:21.460 --> 00:10:23.080 sinus or the nasal cavity.

NOTE Confidence: 0.9609415

00:10:23.540 --> 00:10:24.980 It can recur locally, but

NOTE Confidence: 0.9609415

00:10:24.980 --> 00:10:26.645 it's entirely benign. So certainly

NOTE Confidence: 0.9609415

00:10:26.645 --> 00:10:27.845 you don't wanna mistake this

NOTE Confidence: 0.9609415

00:10:27.845 --> 00:10:29.545 tumor for a sarcoma.

NOTE Confidence: 0.9984984

00:10:30.165 --> 00:10:31.525 This is a true tumor

NOTE Confidence: 0.9984984

00:10:31.525 --> 00:10:32.345 of perivascular

NOTE Confidence: 0.96013165

00:10:32.725 --> 00:10:34.985 contractile cells or pericytes,

NOTE Confidence: 0.9974448

00:10:35.605 --> 00:10:36.505 and it often

NOTE Confidence: 0.84257007

00:10:37.045 --> 00:10:38.585 expresses actin filaments.

NOTE Confidence: 0.965623

00:10:40.070 --> 00:10:41.190 This is how they look.

NOTE Confidence: 0.965623

00:10:41.190 --> 00:10:42.550 They often have these thin

NOTE Confidence: 0.965623

00:10:42.550 --> 00:10:44.170 walled branching blood vessels.

NOTE Confidence: 0.9953555

00:10:44.550 --> 00:10:45.350 As you see in the

NOTE Confidence: 0.9953555

00:10:45.350 --> 00:10:46.330 middle of the field,

NOTE Confidence: 0.9962173

00:10:46.710 --> 00:10:48.150 the tumor cells are these

NOTE Confidence: 0.9962173

00:10:48.150 --> 00:10:50.650 very uniform and evenly distributed

NOTE Confidence: 0.9962173

00:10:50.790 --> 00:10:51.770 oval cells

NOTE Confidence: 0.9854999

00:10:52.150 --> 00:10:53.690 with very fine chromatin.

NOTE Confidence: 0.98936504

00:10:56.025 --> 00:10:57.405 In twenty fifteen,

NOTE Confidence: 0.99800986

00:10:58.025 --> 00:10:59.165 two groups simultaneously

NOTE Confidence: 0.99876666

00:10:59.705 --> 00:11:00.205 discovered

NOTE Confidence: 0.92450976

00:11:00.745 --> 00:11:03.005 that sino nasal glomangioparicitoma

NOTE Confidence: 0.95745414

00:11:05.145 --> 00:11:05.645 harbors

NOTE Confidence: 0.90931076

00:11:06.345 --> 00:11:08.265 activating mutations in beta catenin

NOTE Confidence: 0.90931076

00:11:08.265 --> 00:11:09.565 and CTN and B1,

NOTE Confidence: 0.9416871

00:11:09.865 --> 00:11:11.460 just like desmoid fibromatosis.

NOTE Confidence: 0.97536904

00:11:12.400 --> 00:11:13.440 And all of a sudden

NOTE Confidence: 0.97536904

00:11:13.440 --> 00:11:14.900 it became very easy

NOTE Confidence: 0.9974971

00:11:15.360 --> 00:11:17.040 to confirm the diagnosis with

NOTE Confidence: 0.9974971

00:11:17.040 --> 00:11:18.100 a single antibody.

NOTE Confidence: 0.99814814

00:11:18.880 --> 00:11:20.559 And it's much more impressive

NOTE Confidence: 0.99814814

00:11:20.559 --> 00:11:21.779 than desmoid tumors

NOTE Confidence: 0.92567253

00:11:22.080 --> 00:11:24.020 where you'll have really intense

NOTE Confidence: 0.99546725

00:11:24.705 --> 00:11:25.684 nuclear and cytoplasmic

NOTE Confidence: 0.99976295

00:11:25.985 --> 00:11:26.485 staining

NOTE Confidence: 0.95812994

00:11:26.865 --> 00:11:28.385 and essentially one hundred percent

NOTE Confidence: 0.95812994

00:11:28.385 --> 00:11:29.425 of the tumors of this

NOTE Confidence: 0.95812994

00:11:29.425 --> 00:11:29.925 class.

NOTE Confidence: 0.9822794

00:11:30.385 --> 00:11:31.665 So this is the way

NOTE Confidence: 0.9822794

00:11:31.665 --> 00:11:32.725 we now diagnose

NOTE Confidence: 0.9972194

00:11:33.184 --> 00:11:35.045 this uncommon tumor type.

NOTE Confidence: 0.9398789

00:11:36.705 --> 00:11:38.530 So moving on to cert

NOTE Confidence: 0.9398789

00:11:38.610 --> 00:11:40.309 looking for protein loss

NOTE Confidence: 0.98532

00:11:40.850 --> 00:11:42.690 due to inactivation of tumor

NOTE Confidence: 0.98532

00:11:42.690 --> 00:11:43.750 suppressor genes.

NOTE Confidence: 0.9745779

00:11:44.210 --> 00:11:45.330 This is not a complete

NOTE Confidence: 0.9745779

00:11:45.330 --> 00:11:46.870 list. There are many examples.

NOTE Confidence: 0.9427574

00:11:47.410 --> 00:11:48.470 You know, TP53

NOTE Confidence: 0.94104046

00:11:49.010 --> 00:11:50.450 obviously is an example we've

NOTE Confidence: 0.94104046

00:11:50.450 --> 00:11:51.830 known about for decades.

NOTE Confidence: 0.9907958

00:11:52.445 --> 00:11:53.645 That's a little bit different

NOTE Confidence: 0.9907958

00:11:53.645 --> 00:11:55.245 because of stabilization of the

NOTE Confidence: 0.9907958

00:11:55.245 --> 00:11:57.165 protein. We often get what

NOTE Confidence: 0.9907958

00:11:57.165 --> 00:11:58.304 looks like overexpression,

NOTE Confidence: 0.99631023

00:11:59.005 --> 00:12:00.365 but sometimes when you have

NOTE Confidence: 0.99631023

00:12:00.365 --> 00:12:01.425 truncating mutations,

NOTE Confidence: 0.9982895

00:12:01.885 --> 00:12:03.084 you do get a complete

NOTE Confidence: 0.9982895

00:12:03.084 --> 00:12:04.145 loss of the protein.

NOTE Confidence: 0.9703742

00:12:04.520 --> 00:12:06.200 But here's examples where we

NOTE Confidence: 0.9703742

00:12:06.200 --> 00:12:08.220 do find consistent complete loss.

NOTE Confidence: 0.97810584

00:12:08.600 --> 00:12:09.800 And again, I'm just gonna

NOTE Confidence: 0.97810584

00:12:09.800 --> 00:12:11.179 give you two examples.

NOTE Confidence: 0.89176154

00:12:11.960 --> 00:12:12.679 The first,

NOTE Confidence: 0.9663277

00:12:13.320 --> 00:12:14.620 example is BAP1.

NOTE Confidence: 0.9922541

00:12:15.320 --> 00:12:17.100 This is a nuclear deubiquitinase

NOTE Confidence: 0.9790098

00:12:18.355 --> 00:12:19.955 that was found in twenty

NOTE Confidence: 0.9790098

00:12:19.955 --> 00:12:20.455 eleven

NOTE Confidence: 0.9976911

00:12:20.995 --> 00:12:22.135 to be inactivated

NOTE Confidence: 0.9994974

00:12:23.075 --> 00:12:24.295 in the vast majority

NOTE Confidence: 0.93216956

00:12:25.475 --> 00:12:27.415 of pleural diffuse mesotheliomas,

NOTE Confidence: 0.99356383

00:12:28.675 --> 00:12:30.455 both in the sporadic setting

NOTE Confidence: 0.97902906

00:12:30.915 --> 00:12:32.355 and in patients who have

NOTE Confidence: 0.97902906

00:12:32.355 --> 00:12:33.495 germline mutations

NOTE Confidence: 0.98631746

00:12:34.110 --> 00:12:35.390 in BAP1, which is a

NOTE Confidence: 0.98631746

00:12:35.390 --> 00:12:36.290 very uncommon

NOTE Confidence: 0.99322873

00:12:37.070 --> 00:12:38.050 cancer predisposition

NOTE Confidence: 0.99623936

00:12:38.429 --> 00:12:38.929 syndrome.

NOTE Confidence: 0.89198387

00:12:40.110 --> 00:12:41.890 And since then, several groups,

NOTE Confidence: 0.89198387

00:12:42.029 --> 00:12:42.990 one of the first was

NOTE Confidence: 0.89198387

00:12:42.990 --> 00:12:44.690 led by Andy Cherg from

NOTE Confidence: 0.89198387

00:12:44.910 --> 00:12:46.210 Vancouver in Canada,

NOTE Confidence: 0.99958634

00:12:46.670 --> 00:12:47.710 showed us how we can

NOTE Confidence: 0.99958634

00:12:47.710 --> 00:12:48.770 use this antibody

NOTE Confidence: 0.99892247

00:12:49.315 --> 00:12:50.915 as a very helpful marker

NOTE Confidence: 0.99892247

00:12:50.915 --> 00:12:52.215 to diagnose mesothelioma

NOTE Confidence: 0.99274915

00:12:53.395 --> 00:12:55.075 when we don't have very

NOTE Confidence: 0.99274915

00:12:55.075 --> 00:12:55.975 clear invasion

NOTE Confidence: 0.995098

00:12:56.675 --> 00:12:58.435 of adipose tissue of the

NOTE Confidence: 0.995098

00:12:58.435 --> 00:13:00.215 parietal pleura and other structures.

NOTE Confidence: 0.9979289

00:13:00.595 --> 00:13:01.475 And those of you who

NOTE Confidence: 0.9979289

00:13:01.475 --> 00:13:03.415 work in surgical pathology know

NOTE Confidence: 0.9979289

00:13:03.679 --> 00:13:04.800 that that's really what you

NOTE Confidence: 0.9979289

00:13:04.800 --> 00:13:06.740 need to diagnose malignancy

NOTE Confidence: 0.97185105

00:13:07.519 --> 00:13:08.899 in atypical mesothelial

NOTE Confidence: 0.9583562

00:13:09.279 --> 00:13:09.779 proliferations.

NOTE Confidence: 0.9545319

00:13:12.079 --> 00:13:13.779 The BAP1 tumor predisposition

NOTE Confidence: 0.9995486

00:13:14.319 --> 00:13:14.819 syndrome

NOTE Confidence: 0.9898496

00:13:15.519 --> 00:13:16.019 predisposes

NOTE Confidence: 0.9812015

00:13:16.399 --> 00:13:17.860 not only to the development

NOTE Confidence: 0.9812015

00:13:18.079 --> 00:13:18.819 of mesothelioma,

NOTE Confidence: 0.9542208

00:13:19.815 --> 00:13:20.934 but to a range of

NOTE Confidence: 0.9542208

00:13:20.934 --> 00:13:23.115 very unusual melanocytic tumors,

NOTE Confidence: 0.9927626

00:13:23.495 --> 00:13:24.855 as well as renal cell

NOTE Confidence: 0.9927626

00:13:24.855 --> 00:13:25.355 carcinoma.

NOTE Confidence: 0.99129725

00:13:25.975 --> 00:13:27.895 And the sporadic counterparts of

NOTE Confidence: 0.99129725

00:13:27.895 --> 00:13:28.875 all these tumors

NOTE Confidence: 0.96730006

00:13:29.415 --> 00:13:31.035 can also harbor mutations,

NOTE Confidence: 0.996231

00:13:31.495 --> 00:13:32.395 that are somatic.

NOTE Confidence: 0.9722956

00:13:35.010 --> 00:13:35.970 So this was a case

NOTE Confidence: 0.9722956

00:13:35.970 --> 00:13:36.610 I had a couple of

NOTE Confidence: 0.9722956

00:13:36.610 --> 00:13:37.570 years ago, which is a

NOTE Confidence: 0.9722956

00:13:37.570 --> 00:13:39.429 really nice illustration of this,

NOTE Confidence: 0.9950788

00:13:39.890 --> 00:13:40.390 finding.

NOTE Confidence: 0.97589093

00:13:41.010 --> 00:13:42.290 This was a patient who

NOTE Confidence: 0.97589093

00:13:42.290 --> 00:13:42.770 was,

NOTE Confidence: 0.9809401

00:13:43.090 --> 00:13:44.450 a seventy five year old

NOTE Confidence: 0.9809401

00:13:44.450 --> 00:13:45.429 man who had

NOTE Confidence: 0.8447664

00:13:45.735 --> 00:13:48.135 a plural effusion. Going like

NOTE Confidence: 0.8447664

00:13:48.135 --> 00:13:49.334 two thousand two thousand two

NOTE Confidence: 0.8447664

00:13:49.334 --> 00:13:50.855 thousand. Now it's just like

NOTE Confidence: 0.8447664

00:13:50.934 --> 00:13:52.535 we kind of We have

NOTE Confidence: 0.8447664

00:13:52.774 --> 00:13:54.315 can can someone please mute?

NOTE Confidence: 0.8447664

00:13:54.375 --> 00:13:55.815 Yeah. Two thousand total over

NOTE Confidence: 0.8447664

00:13:55.815 --> 00:13:57.894 four years. So with Someone

NOTE Confidence: 0.8447664

00:13:57.894 --> 00:13:59.334 help me mute them? Maybe

NOTE Confidence: 0.8447664

00:13:59.334 --> 00:13:59.834 not.

NOTE Confidence: 0.98872596

00:14:00.295 --> 00:14:01.035 Oh, well.

NOTE Confidence: 0.9745906

00:14:03.329 --> 00:14:05.009 And when the surgeon went

NOTE Confidence: 0.9745906

00:14:05.009 --> 00:14:06.209 in to look into the

NOTE Confidence: 0.9745906

00:14:06.209 --> 00:14:07.110 pleural cavity,

NOTE Confidence: 0.998161

00:14:07.569 --> 00:14:09.649 she saw nothing abnormal. So

NOTE Confidence: 0.998161

00:14:09.649 --> 00:14:11.509 she took these arbitrary biopsies

NOTE Confidence: 0.97909325

00:14:11.970 --> 00:14:13.829 all over the parietal pleura,

NOTE Confidence: 0.98168254

00:14:14.135 --> 00:14:15.255 and this was the only

NOTE Confidence: 0.98168254

00:14:15.255 --> 00:14:17.095 biopsy that had abnormality. You

NOTE Confidence: 0.98168254

00:14:17.095 --> 00:14:18.475 can see we have these

NOTE Confidence: 0.8744558

00:14:18.934 --> 00:14:21.355 uniform mildly atypical epithelioid

NOTE Confidence: 0.71704495

00:14:21.735 --> 00:14:22.235 cells,

NOTE Confidence: 0.85093814

00:14:22.615 --> 00:14:24.774 whether they're barely trickling into

NOTE Confidence: 0.85093814

00:14:24.774 --> 00:14:25.435 the fat,

NOTE Confidence: 0.99850047

00:14:25.895 --> 00:14:27.310 which would be how we

NOTE Confidence: 0.99850047

00:14:27.310 --> 00:14:28.990 would confirm the diagnosis of

NOTE Confidence: 0.99850047

00:14:28.990 --> 00:14:29.490 mesothelioma.

NOTE Confidence: 0.99792707

00:14:30.350 --> 00:14:31.149 But if this is all

NOTE Confidence: 0.99792707

00:14:31.149 --> 00:14:32.029 you get, it's a little

NOTE Confidence: 0.99792707

00:14:32.029 --> 00:14:33.889 bit scary to diagnose this

NOTE Confidence: 0.9516446

00:14:34.750 --> 00:14:37.310 almost uniformly fatal tumor. So

NOTE Confidence: 0.9516446

00:14:37.310 --> 00:14:38.769 let's look at BAP1 immunoscedochemistry.

NOTE Confidence: 0.98904425

00:14:39.945 --> 00:14:40.905 This was such a nice

NOTE Confidence: 0.98904425

00:14:40.905 --> 00:14:42.025 example. You can see the

NOTE Confidence: 0.98904425

00:14:42.025 --> 00:14:42.845 normal mesothelium

NOTE Confidence: 0.98576945

00:14:43.465 --> 00:14:44.985 on the upper and lower

NOTE Confidence: 0.98576945

00:14:44.985 --> 00:14:45.945 parts of the image on

NOTE Confidence: 0.98576945

00:14:45.945 --> 00:14:47.145 the right. And then we

NOTE Confidence: 0.98576945

00:14:47.145 --> 00:14:48.505 have the neoplasia in the

NOTE Confidence: 0.98576945

00:14:48.505 --> 00:14:49.005 middle

NOTE Confidence: 0.913981

00:14:49.385 --> 00:14:50.505 and you see this really

NOTE Confidence: 0.913981

00:14:50.505 --> 00:14:51.565 beautiful transition

NOTE Confidence: 0.99950206

00:14:52.480 --> 00:14:54.500 between normal nuclear staining

NOTE Confidence: 0.9913966

00:14:54.800 --> 00:14:56.160 and tumor cells that have

NOTE Confidence: 0.9913966

00:14:56.160 --> 00:14:57.700 a complete loss of BAP1.

NOTE Confidence: 0.9996192

00:14:58.160 --> 00:14:59.360 So this is a beautiful

NOTE Confidence: 0.9996192

00:14:59.360 --> 00:14:59.860 surrogate

NOTE Confidence: 0.9616619

00:15:00.400 --> 00:15:02.480 for biallelic inactivation of the

NOTE Confidence: 0.9616619

00:15:02.480 --> 00:15:03.540 BAP1 gene.

NOTE Confidence: 0.894248

00:15:04.255 --> 00:15:06.495 And, my colleague, Lynette Scholl,

NOTE Confidence: 0.894248

00:15:06.495 --> 00:15:08.014 along with David Chaple, who's

NOTE Confidence: 0.894248

00:15:08.014 --> 00:15:08.255 now,

NOTE Confidence: 0.9857627

00:15:09.135 --> 00:15:10.415 works on faculty at the

NOTE Confidence: 0.9857627

00:15:10.415 --> 00:15:11.555 University of Michigan,

NOTE Confidence: 0.94797343

00:15:12.495 --> 00:15:14.514 evaluated a panel of different,

NOTE Confidence: 0.90708965

00:15:15.214 --> 00:15:16.595 antibodies that recognize,

NOTE Confidence: 0.95594394

00:15:17.375 --> 00:15:19.154 protein products of tumor suppressors

NOTE Confidence: 0.9613028

00:15:19.830 --> 00:15:21.210 and found that the combination

NOTE Confidence: 0.9613028

00:15:21.510 --> 00:15:22.950 not only of BAP1, but

NOTE Confidence: 0.9613028

00:15:22.950 --> 00:15:24.010 also of MTAP

NOTE Confidence: 0.9650866

00:15:24.470 --> 00:15:26.630 and Merlin, the NF2 gene

NOTE Confidence: 0.9650866

00:15:26.630 --> 00:15:27.530 protein product

NOTE Confidence: 0.92735255

00:15:28.070 --> 00:15:29.990 together can be very helpful

NOTE Confidence: 0.92735255

00:15:29.990 --> 00:15:30.730 to diagnose

NOTE Confidence: 0.9576022

00:15:31.350 --> 00:15:31.850 mesothelioma.

NOTE Confidence: 0.99862474

00:15:32.310 --> 00:15:33.190 And this has become a

NOTE Confidence: 0.99862474

00:15:33.190 --> 00:15:35.315 routine part of our diagnostic

NOTE Confidence: 0.99862474

00:15:35.455 --> 00:15:35.955 practice.

NOTE Confidence: 0.9960471

00:15:37.215 --> 00:15:38.735 One other marker I'm gonna

NOTE Confidence: 0.9960471

00:15:38.735 --> 00:15:40.835 mention is a tumor suppressor

NOTE Confidence: 0.9960471

00:15:41.135 --> 00:15:41.795 that is

NOTE Confidence: 0.9989362

00:15:42.095 --> 00:15:42.595 inactivated

NOTE Confidence: 0.9552269

00:15:42.975 --> 00:15:44.595 in a very rare aggressive

NOTE Confidence: 0.9552269

00:15:44.655 --> 00:15:45.155 cancer

NOTE Confidence: 0.9962639

00:15:45.615 --> 00:15:47.375 that occurs predominantly in the

NOTE Confidence: 0.9962639

00:15:47.375 --> 00:15:49.530 ovary of adolescent girls and

NOTE Confidence: 0.9962639

00:15:49.530 --> 00:15:50.270 young women

NOTE Confidence: 0.9533513

00:15:50.650 --> 00:15:51.770 that goes by this very

NOTE Confidence: 0.9533513

00:15:51.770 --> 00:15:53.630 long name, small cell carcinoma

NOTE Confidence: 0.9533513

00:15:53.850 --> 00:15:54.590 of the ovary

NOTE Confidence: 0.96847785

00:15:54.970 --> 00:15:55.790 of hypercalcemic

NOTE Confidence: 0.9935131

00:15:56.490 --> 00:15:56.990 type.

NOTE Confidence: 0.9453497

00:15:57.450 --> 00:15:58.490 It's a it's a long

NOTE Confidence: 0.9453497

00:15:58.490 --> 00:16:00.010 descriptive name. We often call

NOTE Confidence: 0.9453497

00:16:00.010 --> 00:16:01.610 it SCUT because it's easier

NOTE Confidence: 0.9453497

00:16:01.610 --> 00:16:03.470 than saying all these words.

NOTE Confidence: 0.99177814

00:16:03.995 --> 00:16:05.035 And we call it this

NOTE Confidence: 0.99177814

00:16:05.035 --> 00:16:06.235 name because in about two

NOTE Confidence: 0.99177814

00:16:06.235 --> 00:16:07.214 thirds of cases,

NOTE Confidence: 0.99933624

00:16:07.755 --> 00:16:09.695 patients present with quite profound

NOTE Confidence: 0.99604595

00:16:10.315 --> 00:16:10.815 hypercalcemia.

NOTE Confidence: 0.99837863

00:16:11.915 --> 00:16:13.834 And even with early stage

NOTE Confidence: 0.99837863

00:16:13.834 --> 00:16:15.774 disease localized to the ovary,

NOTE Confidence: 0.9993557

00:16:16.235 --> 00:16:18.154 their survival is very poor

NOTE Confidence: 0.9993557

00:16:18.154 --> 00:16:19.770 for this aggressive cancer type.

NOTE Confidence: 0.9821343

00:16:20.890 --> 00:16:22.810 Many cases have focal areas

NOTE Confidence: 0.9821343

00:16:22.810 --> 00:16:24.810 with these dilated follicle like

NOTE Confidence: 0.9821343

00:16:24.810 --> 00:16:25.310 spaces.

NOTE Confidence: 0.9994988

00:16:25.850 --> 00:16:27.610 That's very characteristic of this

NOTE Confidence: 0.9994988

00:16:27.610 --> 00:16:28.590 aggressive tumor

NOTE Confidence: 0.935535

00:16:29.050 --> 00:16:30.250 and we call it small

NOTE Confidence: 0.935535

00:16:30.250 --> 00:16:31.950 cell because most examples

NOTE Confidence: 0.96866816

00:16:32.685 --> 00:16:34.785 are dominated by fairly uniform

NOTE Confidence: 0.96866816

00:16:34.845 --> 00:16:36.285 small round blue cells with

NOTE Confidence: 0.96866816

00:16:36.285 --> 00:16:37.425 a little bit of cytoplasm.

NOTE Confidence: 0.97661763

00:16:38.445 --> 00:16:39.805 This is not really a

NOTE Confidence: 0.97661763

00:16:39.805 --> 00:16:41.405 small cell carcinoma as you

NOTE Confidence: 0.97661763

00:16:41.405 --> 00:16:43.345 think of small cell carcinomas

NOTE Confidence: 0.97661763

00:16:43.485 --> 00:16:44.490 of any other site.

NOTE Confidence: 0.94788086

00:16:44.970 --> 00:16:46.170 In fact, some people have

NOTE Confidence: 0.94788086

00:16:46.170 --> 00:16:47.690 proposed this is probably better

NOTE Confidence: 0.94788086

00:16:47.690 --> 00:16:48.910 aligned with a sarcoma,

NOTE Confidence: 0.9902642

00:16:49.370 --> 00:16:50.330 but we still call it

NOTE Confidence: 0.9902642

00:16:50.330 --> 00:16:51.870 this long descriptive name.

NOTE Confidence: 0.9852283

00:16:52.330 --> 00:16:53.770 In about fifty percent of

NOTE Confidence: 0.9852283

00:16:53.770 --> 00:16:54.270 cases,

NOTE Confidence: 0.99149466

00:16:54.810 --> 00:16:56.170 there is a large cell

NOTE Confidence: 0.99149466

00:16:56.170 --> 00:16:56.670 component

NOTE Confidence: 0.9818552

00:16:57.325 --> 00:16:59.584 which often has rhabdoid cytoplasmic

NOTE Confidence: 0.98414165

00:16:59.964 --> 00:17:00.464 inclusions,

NOTE Confidence: 0.99962926

00:17:01.005 --> 00:17:02.225 which are these intermediate

NOTE Confidence: 0.9094198

00:17:02.605 --> 00:17:03.584 filament containing

NOTE Confidence: 0.596726

00:17:04.285 --> 00:17:04.785 perinuclear

NOTE Confidence: 0.97237456

00:17:05.165 --> 00:17:06.865 inclusions that look all hyaline.

NOTE Confidence: 0.98241115

00:17:07.165 --> 00:17:09.325 And that's looks very similar

NOTE Confidence: 0.98241115

00:17:09.325 --> 00:17:11.085 to malignant rhabdoid tumors of

NOTE Confidence: 0.98241115

00:17:11.085 --> 00:17:12.705 the of infancy.

NOTE Confidence: 0.983296

00:17:14.260 --> 00:17:15.780 And again, we have multiple

NOTE Confidence: 0.983296

00:17:15.780 --> 00:17:17.220 groups that essentially at the

NOTE Confidence: 0.983296

00:17:17.220 --> 00:17:18.580 same time published in the

NOTE Confidence: 0.983296

00:17:18.580 --> 00:17:19.400 same issue

NOTE Confidence: 0.92811966

00:17:19.700 --> 00:17:21.480 of Nature Genetics discovered

NOTE Confidence: 0.92935145

00:17:22.100 --> 00:17:22.760 that inactivating

NOTE Confidence: 0.84023494

00:17:23.060 --> 00:17:24.280 mutations in SMARCA4,

NOTE Confidence: 0.9842051

00:17:25.375 --> 00:17:26.815 which encodes a protein that's

NOTE Confidence: 0.9842051

00:17:26.815 --> 00:17:27.875 also called BRG1,

NOTE Confidence: 0.99081045

00:17:28.734 --> 00:17:30.975 are the defining genomic feature

NOTE Confidence: 0.99081045

00:17:30.975 --> 00:17:32.835 of this aggressive cancer type.

NOTE Confidence: 0.99081045

00:17:33.054 --> 00:17:34.575 And otherwise, they have a

NOTE Confidence: 0.99081045

00:17:34.575 --> 00:17:35.075 very

NOTE Confidence: 0.8738775

00:17:35.455 --> 00:17:37.294 flat genome. It's really a

NOTE Confidence: 0.8738775

00:17:37.375 --> 00:17:38.755 this isolated event

NOTE Confidence: 0.998486

00:17:39.090 --> 00:17:40.630 can lead to this incredibly

NOTE Confidence: 0.998486

00:17:40.770 --> 00:17:42.770 aggressive cancer type. And in

NOTE Confidence: 0.998486

00:17:42.770 --> 00:17:43.270 fact,

NOTE Confidence: 0.9994793

00:17:43.650 --> 00:17:44.309 in about

NOTE Confidence: 0.99942386

00:17:44.609 --> 00:17:46.070 fifty percent of patients,

NOTE Confidence: 0.9870138

00:17:46.609 --> 00:17:48.470 even without a family history,

NOTE Confidence: 0.9870138

00:17:48.690 --> 00:17:49.650 they will be found to

NOTE Confidence: 0.9870138

00:17:49.650 --> 00:17:51.330 have a germline mutation. So

NOTE Confidence: 0.9870138

00:17:51.330 --> 00:17:53.350 the penetrance is quite variable.

NOTE Confidence: 0.98999757

00:17:53.945 --> 00:17:55.145 But this has now become

NOTE Confidence: 0.98999757

00:17:55.145 --> 00:17:56.665 an easy way to diagnose

NOTE Confidence: 0.98999757

00:17:56.665 --> 00:17:57.725 this rare cancer.

NOTE Confidence: 0.99961406

00:17:58.025 --> 00:17:59.145 We no longer have to

NOTE Confidence: 0.99961406

00:17:59.145 --> 00:18:00.365 send it to an expert

NOTE Confidence: 0.9524645

00:18:00.665 --> 00:18:01.945 to help us decide that

NOTE Confidence: 0.9524645

00:18:01.945 --> 00:18:03.465 this is in fact one

NOTE Confidence: 0.9524645

00:18:03.465 --> 00:18:04.605 of these rare cancers.

NOTE Confidence: 0.94729155

00:18:06.710 --> 00:18:08.150 And just like we saw,

NOTE Confidence: 0.94729155

00:18:08.390 --> 00:18:09.130 in BAP1,

NOTE Confidence: 0.999574

00:18:09.590 --> 00:18:10.950 we have a complete loss

NOTE Confidence: 0.999574

00:18:10.950 --> 00:18:12.170 of the normal nuclear

NOTE Confidence: 0.7953948

00:18:12.710 --> 00:18:13.210 reactivities

NOTE Confidence: 0.89442945

00:18:13.590 --> 00:18:15.369 for SMARCA4 or BRG1,

NOTE Confidence: 0.98359096

00:18:16.150 --> 00:18:17.590 and this is found in

NOTE Confidence: 0.98359096

00:18:17.590 --> 00:18:19.050 almost a hundred percent

NOTE Confidence: 0.99751395

00:18:19.430 --> 00:18:20.970 of tumors of this class.

NOTE Confidence: 0.9772378

00:18:22.605 --> 00:18:23.885 One example of a really

NOTE Confidence: 0.9772378

00:18:23.885 --> 00:18:24.945 nice epigenetic

NOTE Confidence: 0.84918064

00:18:25.325 --> 00:18:27.185 alteration we can assess for

NOTE Confidence: 0.84918064

00:18:27.244 --> 00:18:27.905 by immunoskemetry,

NOTE Confidence: 0.9918764

00:18:28.445 --> 00:18:29.484 and I talked about this

NOTE Confidence: 0.9918764

00:18:29.484 --> 00:18:31.025 with the trainees this morning,

NOTE Confidence: 0.9363137

00:18:31.325 --> 00:18:32.925 is a malignant peripheral nerve

NOTE Confidence: 0.9363137

00:18:32.925 --> 00:18:33.665 sheath tumor.

NOTE Confidence: 0.9975376

00:18:34.080 --> 00:18:35.200 As many of you know,

NOTE Confidence: 0.9975376

00:18:35.200 --> 00:18:36.340 about fifty percent

NOTE Confidence: 0.9919969

00:18:36.799 --> 00:18:37.539 of MPNSTs

NOTE Confidence: 0.9757435

00:18:38.080 --> 00:18:39.679 arise in patients with NF

NOTE Confidence: 0.9757435

00:18:39.679 --> 00:18:40.179 one,

NOTE Confidence: 0.99376094

00:18:40.799 --> 00:18:42.260 forty percent are sporadic,

NOTE Confidence: 0.999285

00:18:42.720 --> 00:18:44.799 and ten percent arise following

NOTE Confidence: 0.999285

00:18:44.799 --> 00:18:46.340 therapeutic radiation therapy.

NOTE Confidence: 0.9991556

00:18:47.345 --> 00:18:48.965 If you have a malignant

NOTE Confidence: 0.9991556

00:18:49.105 --> 00:18:50.325 spindle cell neoplasm

NOTE Confidence: 0.9766078

00:18:51.185 --> 00:18:52.645 in a patient with NF1

NOTE Confidence: 0.96965814

00:18:53.505 --> 00:18:54.945 or arising from a large

NOTE Confidence: 0.96965814

00:18:54.945 --> 00:18:55.445 nerve

NOTE Confidence: 0.99094

00:18:55.825 --> 00:18:56.865 or coming out of a

NOTE Confidence: 0.99094

00:18:56.865 --> 00:18:57.685 benign neurofibroma,

NOTE Confidence: 0.99735224

00:18:58.145 --> 00:18:59.845 the diagnosis is pretty easy.

NOTE Confidence: 0.99735224

00:19:00.145 --> 00:19:01.925 But outside of those associations,

NOTE Confidence: 0.9880617

00:19:02.659 --> 00:19:04.119 this is a really difficult

NOTE Confidence: 0.9880617

00:19:04.179 --> 00:19:04.679 diagnosis,

NOTE Confidence: 0.99699146

00:19:05.539 --> 00:19:06.760 especially because

NOTE Confidence: 0.9953742

00:19:07.619 --> 00:19:09.380 our markers of nerve sheath

NOTE Confidence: 0.9953742

00:19:09.380 --> 00:19:09.880 differentiation,

NOTE Confidence: 0.8727272

00:19:10.740 --> 00:19:12.519 the Schwann cell markers S100

NOTE Confidence: 0.8727272

00:19:12.740 --> 00:19:13.399 and Sox10,

NOTE Confidence: 0.95240355

00:19:14.179 --> 00:19:15.765 are only positive in just

NOTE Confidence: 0.95240355

00:19:15.845 --> 00:19:17.225 under half of the cases,

NOTE Confidence: 0.98641145

00:19:17.605 --> 00:19:18.965 and they're focal and weak

NOTE Confidence: 0.98641145

00:19:18.965 --> 00:19:20.565 and unimpressive when they are

NOTE Confidence: 0.98641145

00:19:20.565 --> 00:19:21.065 positive.

NOTE Confidence: 0.99940896

00:19:21.445 --> 00:19:22.665 So it really relies

NOTE Confidence: 0.84997463

00:19:23.045 --> 00:19:23.545 on,

NOTE Confidence: 0.99617547

00:19:24.484 --> 00:19:26.244 excluding other tumors you might

NOTE Confidence: 0.99617547

00:19:26.244 --> 00:19:28.105 consider in the differential diagnosis

NOTE Confidence: 0.852979

00:19:28.645 --> 00:19:30.665 and pay paying close attention

NOTE Confidence: 0.9829855

00:19:31.210 --> 00:19:32.910 to the often very distinctive

NOTE Confidence: 0.9829855

00:19:32.970 --> 00:19:33.470 histology.

NOTE Confidence: 0.9892467

00:19:34.890 --> 00:19:36.810 Many examples of malignant peripheral

NOTE Confidence: 0.9892467

00:19:36.810 --> 00:19:37.710 nerve sheath tumor

NOTE Confidence: 0.9982629

00:19:38.090 --> 00:19:39.950 have these abrupt transitions

NOTE Confidence: 0.9544411

00:19:40.890 --> 00:19:43.470 between very highly cellular fascicular

NOTE Confidence: 0.9544411

00:19:43.690 --> 00:19:44.190 areas

NOTE Confidence: 0.94004995

00:19:44.734 --> 00:19:46.815 and slightly less cellular areas

NOTE Confidence: 0.94004995

00:19:46.815 --> 00:19:48.755 with a scant myxoid stroma,

NOTE Confidence: 0.97043014

00:19:49.375 --> 00:19:50.915 typically with this perivascular

NOTE Confidence: 0.9710152

00:19:51.935 --> 00:19:52.435 hypercellularity

NOTE Confidence: 0.988452

00:19:53.055 --> 00:19:53.795 or condensation

NOTE Confidence: 0.9990521

00:19:54.095 --> 00:19:54.915 of the cells

NOTE Confidence: 0.99735105

00:19:55.295 --> 00:19:56.515 around the blood vessels.

NOTE Confidence: 0.9838871

00:19:56.940 --> 00:19:58.139 And if you see classic

NOTE Confidence: 0.9838871

00:19:58.139 --> 00:19:59.500 histology, that can be very

NOTE Confidence: 0.9838871

00:19:59.500 --> 00:20:00.000 helpful,

NOTE Confidence: 0.97512084

00:20:00.379 --> 00:20:01.740 but many cases don't look

NOTE Confidence: 0.97512084

00:20:01.740 --> 00:20:02.799 as good as this.

NOTE Confidence: 0.9139671

00:20:04.940 --> 00:20:07.580 Mentioning another chromatin remodeling complex,

NOTE Confidence: 0.9139671

00:20:07.580 --> 00:20:09.759 this is the polychrome repressive

NOTE Confidence: 0.9139671

00:20:09.820 --> 00:20:10.960 complex two.

NOTE Confidence: 0.97649133

00:20:11.615 --> 00:20:13.635 PRC two has multiple subunits,

NOTE Confidence: 0.97649133

00:20:13.695 --> 00:20:14.575 as you can see in

NOTE Confidence: 0.97649133

00:20:14.575 --> 00:20:16.195 this this nice diagram,

NOTE Confidence: 0.8974127

00:20:16.815 --> 00:20:18.835 including SUS12 and EED.

NOTE Confidence: 0.9985501

00:20:19.615 --> 00:20:20.115 And

NOTE Confidence: 0.9982682

00:20:20.494 --> 00:20:21.935 we've known for quite some

NOTE Confidence: 0.9982682

00:20:21.935 --> 00:20:22.435 time

NOTE Confidence: 0.99786586

00:20:22.735 --> 00:20:24.210 that this complex

NOTE Confidence: 0.983652

00:20:24.830 --> 00:20:26.750 is a methylating enzyme that's

NOTE Confidence: 0.983652

00:20:26.750 --> 00:20:28.049 recruited to chromatin

NOTE Confidence: 0.92729443

00:20:28.750 --> 00:20:29.570 to trimethylate

NOTE Confidence: 0.9845731

00:20:30.029 --> 00:20:31.409 histone h three

NOTE Confidence: 0.98783726

00:20:31.789 --> 00:20:33.470 at the lysine twenty seven

NOTE Confidence: 0.98783726

00:20:33.470 --> 00:20:33.970 residue.

NOTE Confidence: 0.9947009

00:20:34.669 --> 00:20:36.210 And we call that moiety

NOTE Confidence: 0.93523157

00:20:37.005 --> 00:20:38.765 h three k twenty seven

NOTE Confidence: 0.93523157

00:20:38.765 --> 00:20:39.665 m e three.

NOTE Confidence: 0.9862578

00:20:40.205 --> 00:20:41.165 And if you say it

NOTE Confidence: 0.9862578

00:20:41.165 --> 00:20:42.125 under your breath a few

NOTE Confidence: 0.9862578

00:20:42.125 --> 00:20:43.965 times, you'll learn to repeat

NOTE Confidence: 0.9862578

00:20:43.965 --> 00:20:44.945 it very easily.

NOTE Confidence: 0.9772769

00:20:45.484 --> 00:20:47.165 H three k twenty seven

NOTE Confidence: 0.9772769

00:20:47.165 --> 00:20:47.984 m e three,

NOTE Confidence: 0.9960275

00:20:48.285 --> 00:20:49.325 and now you know my

NOTE Confidence: 0.9960275

00:20:49.325 --> 00:20:50.305 iPhone password.

NOTE Confidence: 0.9982534

00:20:51.679 --> 00:20:53.059 So this modification

NOTE Confidence: 0.97455007

00:20:53.919 --> 00:20:54.880 is a way that we

NOTE Confidence: 0.97455007

00:20:54.880 --> 00:20:56.559 kinda keep our transcription in

NOTE Confidence: 0.97455007

00:20:56.559 --> 00:20:57.059 check,

NOTE Confidence: 0.99267083

00:20:57.359 --> 00:20:59.299 but modifications or dysregulation

NOTE Confidence: 0.99918777

00:21:00.080 --> 00:21:01.600 can lead to cancer of

NOTE Confidence: 0.99918777

00:21:01.600 --> 00:21:02.580 various types.

NOTE Confidence: 0.95684737

00:21:03.359 --> 00:21:04.740 And in two thousand fourteen,

NOTE Confidence: 0.9993121

00:21:05.440 --> 00:21:06.820 several groups discovered

NOTE Confidence: 0.99911606

00:21:07.425 --> 00:21:08.645 that mutations

NOTE Confidence: 0.98554623

00:21:09.105 --> 00:21:10.385 in one of the genes

NOTE Confidence: 0.98554623

00:21:10.385 --> 00:21:11.765 that encodes PRC2

NOTE Confidence: 0.9914694

00:21:12.865 --> 00:21:15.045 are found in most examples

NOTE Confidence: 0.97116476

00:21:15.665 --> 00:21:17.345 of high grade malignant peripheral

NOTE Confidence: 0.97116476

00:21:17.345 --> 00:21:18.325 nerve sheath tumor.

NOTE Confidence: 0.9981459

00:21:18.785 --> 00:21:20.085 And these alterations

NOTE Confidence: 0.85844445

00:21:20.625 --> 00:21:21.685 either in SUS12

NOTE Confidence: 0.857295

00:21:22.220 --> 00:21:23.660 most often or sometimes an

NOTE Confidence: 0.857295

00:21:23.660 --> 00:21:24.160 EED

NOTE Confidence: 0.7657403

00:21:25.020 --> 00:21:25.520 lead

NOTE Confidence: 0.9989176

00:21:26.140 --> 00:21:26.880 to inactivation

NOTE Confidence: 0.9847544

00:21:27.180 --> 00:21:28.080 of the enzyme.

NOTE Confidence: 0.9445133

00:21:28.540 --> 00:21:29.359 So PRC2

NOTE Confidence: 0.87201905

00:21:29.660 --> 00:21:32.000 can no longer trimethylt histone

NOTE Confidence: 0.87201905

00:21:32.140 --> 00:21:32.640 three

NOTE Confidence: 0.9710728

00:21:32.940 --> 00:21:34.425 at lysine twenty seven.

NOTE Confidence: 0.99791807

00:21:34.905 --> 00:21:36.744 And remarkably, there were already

NOTE Confidence: 0.99791807

00:21:36.744 --> 00:21:38.445 commercial antibodies available

NOTE Confidence: 0.90866804

00:21:38.825 --> 00:21:41.244 that only recognized histone three

NOTE Confidence: 0.998796

00:21:41.545 --> 00:21:42.445 when it has

NOTE Confidence: 0.9880825

00:21:42.985 --> 00:21:44.525 lysine twenty seven trimethylation.

NOTE Confidence: 0.99257505

00:21:45.305 --> 00:21:46.905 So we're looking for loss

NOTE Confidence: 0.99257505

00:21:46.905 --> 00:21:49.244 of this normal trimethylation mark

NOTE Confidence: 0.8673157

00:21:49.669 --> 00:21:50.330 by immunoskechemistry.

NOTE Confidence: 0.99981964

00:21:51.190 --> 00:21:52.490 And this works best

NOTE Confidence: 0.99837655

00:21:53.109 --> 00:21:54.789 in intermediate to high grade

NOTE Confidence: 0.99837655

00:21:54.789 --> 00:21:56.150 examples, which are the ones

NOTE Confidence: 0.99837655

00:21:56.150 --> 00:21:57.690 we encounter most often

NOTE Confidence: 0.93536985

00:21:57.990 --> 00:21:59.350 in the sporadic setting in

NOTE Confidence: 0.93536985

00:21:59.350 --> 00:22:01.030 our clinical practice and surgical

NOTE Confidence: 0.93536985

00:22:01.030 --> 00:22:01.530 pathology.

NOTE Confidence: 0.9537383

00:22:02.054 --> 00:22:03.734 In low grade MPNST, we're

NOTE Confidence: 0.9537383

00:22:03.734 --> 00:22:04.695 really trying to decide is

NOTE Confidence: 0.9537383

00:22:04.695 --> 00:22:05.274 it malignant

NOTE Confidence: 0.9010681

00:22:05.894 --> 00:22:07.274 in a patient with NF1

NOTE Confidence: 0.9010681

00:22:07.414 --> 00:22:09.595 who's gets a atypical neurofibroma

NOTE Confidence: 0.64834666

00:22:09.975 --> 00:22:10.634 in transformation.

NOTE Confidence: 0.9720848

00:22:11.174 --> 00:22:12.294 We're not trying to decide

NOTE Confidence: 0.9720848

00:22:12.294 --> 00:22:13.174 is it a nerve sheath

NOTE Confidence: 0.9720848

00:22:13.174 --> 00:22:13.674 tumor.

NOTE Confidence: 0.99907225

00:22:14.570 --> 00:22:15.470 The specificity

NOTE Confidence: 0.9982999

00:22:15.770 --> 00:22:16.830 is also excellent.

NOTE Confidence: 0.9973478

00:22:17.530 --> 00:22:18.970 Almost all the tumors you

NOTE Confidence: 0.9973478

00:22:18.970 --> 00:22:20.350 would consider in the differential

NOTE Confidence: 0.9973478

00:22:20.410 --> 00:22:20.910 diagnosis

NOTE Confidence: 0.9899664

00:22:21.690 --> 00:22:22.590 show consistent

NOTE Confidence: 0.88852257

00:22:22.970 --> 00:22:23.470 normal

NOTE Confidence: 0.9936905

00:22:23.850 --> 00:22:25.550 staining with this antibody.

NOTE Confidence: 0.973896

00:22:26.170 --> 00:22:27.850 The only two exceptions are

NOTE Confidence: 0.973896

00:22:27.850 --> 00:22:28.875 dedifferentiated liposarcoma

NOTE Confidence: 0.905575

00:22:31.755 --> 00:22:33.595 melanoma. That's a very small

NOTE Confidence: 0.905575

00:22:33.595 --> 00:22:34.095 percentage.

NOTE Confidence: 0.82475895

00:22:35.195 --> 00:22:36.234 As you many of you

NOTE Confidence: 0.82475895

00:22:36.234 --> 00:22:38.155 know, Ddiff liposarq has MDM

NOTE Confidence: 0.82475895

00:22:38.155 --> 00:22:38.734 two amplification.

NOTE Confidence: 0.9722072

00:22:39.435 --> 00:22:40.555 So that's an easy way

NOTE Confidence: 0.9722072

00:22:40.555 --> 00:22:41.695 to make that diagnosis.

NOTE Confidence: 0.9901209

00:22:42.409 --> 00:22:44.250 And spindle cell melanomas arise

NOTE Confidence: 0.9901209

00:22:44.250 --> 00:22:45.289 in the skin. They spread

NOTE Confidence: 0.9901209

00:22:45.289 --> 00:22:46.270 to lymph nodes.

NOTE Confidence: 0.97669834

00:22:46.650 --> 00:22:48.730 They're strongly and diffusely SOX10

NOTE Confidence: 0.97669834

00:22:48.730 --> 00:22:50.250 and S100 positive in most

NOTE Confidence: 0.97669834

00:22:50.250 --> 00:22:52.010 cases. So it's usually not

NOTE Confidence: 0.97669834

00:22:52.010 --> 00:22:52.909 really a problem

NOTE Confidence: 0.9986531

00:22:53.210 --> 00:22:55.015 in differential diagnosis for a

NOTE Confidence: 0.9986531

00:22:55.015 --> 00:22:55.515 deep

NOTE Confidence: 0.9896872

00:22:55.975 --> 00:22:57.755 seated malignant spindle cell neoplasm

NOTE Confidence: 0.9896872

00:22:57.975 --> 00:22:59.355 with limited or no

NOTE Confidence: 0.65985394

00:22:59.655 --> 00:23:00.715 Sox ten expression.

NOTE Confidence: 0.98347676

00:23:01.494 --> 00:23:02.375 So this is what it

NOTE Confidence: 0.98347676

00:23:02.375 --> 00:23:03.335 looks like. It looks just

NOTE Confidence: 0.98347676

00:23:03.335 --> 00:23:05.015 like a tumor suppressor protein

NOTE Confidence: 0.98347676

00:23:05.015 --> 00:23:06.695 loss, but we're looking for

NOTE Confidence: 0.98347676

00:23:06.855 --> 00:23:08.054 we're seeing a loss of

NOTE Confidence: 0.98347676

00:23:08.054 --> 00:23:09.869 the trimethyl mark. And it

NOTE Confidence: 0.98347676

00:23:09.869 --> 00:23:11.710 works beautifully. We now use

NOTE Confidence: 0.98347676

00:23:11.710 --> 00:23:13.330 this daily in my practice,

NOTE Confidence: 0.94168705

00:23:13.790 --> 00:23:14.850 in our laboratory.

NOTE Confidence: 0.9949464

00:23:15.390 --> 00:23:16.350 And this was a case

NOTE Confidence: 0.9949464

00:23:16.350 --> 00:23:17.710 that would be impossible to

NOTE Confidence: 0.9949464

00:23:17.710 --> 00:23:18.210 recognize.

NOTE Confidence: 0.99086016

00:23:18.750 --> 00:23:19.869 It just looks like a

NOTE Confidence: 0.99086016

00:23:19.869 --> 00:23:20.369 fibrosarcoma

NOTE Confidence: 0.9834167

00:23:20.990 --> 00:23:21.490 like

NOTE Confidence: 0.9170228

00:23:21.790 --> 00:23:24.130 fascicular spindle cell malignant neoplasm,

NOTE Confidence: 0.9891651

00:23:24.765 --> 00:23:25.725 but we know this is

NOTE Confidence: 0.9891651

00:23:25.725 --> 00:23:27.165 MPNST because it arose in

NOTE Confidence: 0.9891651

00:23:27.165 --> 00:23:28.545 a patient with NF one.

NOTE Confidence: 0.9983121

00:23:29.965 --> 00:23:31.005 And one of the tumors

NOTE Confidence: 0.9983121

00:23:31.005 --> 00:23:32.845 that is most difficult to

NOTE Confidence: 0.9983121

00:23:32.845 --> 00:23:34.625 distinguish is synovial sarcoma.

NOTE Confidence: 0.99968433

00:23:35.405 --> 00:23:37.425 These tumors have normal staining

NOTE Confidence: 0.942423

00:23:37.805 --> 00:23:39.345 for the trinephile antibody.

NOTE Confidence: 0.9551455

00:23:44.700 --> 00:23:45.900 So now we're gonna shift

NOTE Confidence: 0.9551455

00:23:45.900 --> 00:23:47.119 and talk a little bit

NOTE Confidence: 0.8533304

00:23:47.660 --> 00:23:48.160 about

NOTE Confidence: 0.9921802

00:23:48.780 --> 00:23:51.260 looking for protein correlates of

NOTE Confidence: 0.9921802

00:23:51.260 --> 00:23:52.080 gene fusions

NOTE Confidence: 0.9876788

00:23:52.940 --> 00:23:55.040 as predictive testing for targeted

NOTE Confidence: 0.9876788

00:23:55.100 --> 00:23:55.600 therapies.

NOTE Confidence: 0.985031

00:23:56.385 --> 00:23:57.744 You all know about ALK.

NOTE Confidence: 0.985031

00:23:57.744 --> 00:23:59.125 This is a very

NOTE Confidence: 0.9940538

00:23:59.905 --> 00:24:01.365 exciting topic in

NOTE Confidence: 0.95712405

00:24:01.665 --> 00:24:03.285 oncology, medical oncology,

NOTE Confidence: 0.9726521

00:24:03.905 --> 00:24:05.265 and ROS1, which is a

NOTE Confidence: 0.9726521

00:24:05.265 --> 00:24:07.505 very similar receptor tyrosine kinase

NOTE Confidence: 0.9726521

00:24:07.505 --> 00:24:08.005 gene.

NOTE Confidence: 0.9969546

00:24:08.609 --> 00:24:10.530 And about four percent of

NOTE Confidence: 0.9969546

00:24:10.530 --> 00:24:11.350 lung adenocarcinomas

NOTE Confidence: 0.9667575

00:24:11.970 --> 00:24:13.990 have gene fusions involving ALK.

NOTE Confidence: 0.9590297

00:24:14.290 --> 00:24:16.230 One percent have ROS1 fusions.

NOTE Confidence: 0.99849087

00:24:16.609 --> 00:24:18.210 And these alterations are much

NOTE Confidence: 0.99849087

00:24:18.210 --> 00:24:19.990 more common in inflammatory

NOTE Confidence: 0.9613399

00:24:20.290 --> 00:24:20.790 myofibroblastic

NOTE Confidence: 0.85334224

00:24:21.330 --> 00:24:21.830 tumors,

NOTE Confidence: 0.9983059

00:24:23.024 --> 00:24:24.565 within which they were identified

NOTE Confidence: 0.9983059

00:24:24.625 --> 00:24:25.744 before they were in lung

NOTE Confidence: 0.9983059

00:24:25.744 --> 00:24:26.244 cancer.

NOTE Confidence: 0.999403

00:24:27.825 --> 00:24:28.325 This

NOTE Confidence: 0.88760024

00:24:29.585 --> 00:24:31.524 gene was named after

NOTE Confidence: 0.9748209

00:24:31.984 --> 00:24:33.684 lymphoma, as you all know.

NOTE Confidence: 0.9748209

00:24:33.904 --> 00:24:35.764 This is the anaplastic lymphoma

NOTE Confidence: 0.9748209

00:24:35.904 --> 00:24:36.404 kinase.

NOTE Confidence: 0.95588666

00:24:37.210 --> 00:24:38.570 Way back in nineteen ninety

NOTE Confidence: 0.95588666

00:24:38.570 --> 00:24:39.070 four,

NOTE Confidence: 0.87975603

00:24:39.530 --> 00:24:40.750 Morris and Look

NOTE Confidence: 0.99289167

00:24:41.210 --> 00:24:41.710 discovered

NOTE Confidence: 0.99835604

00:24:42.090 --> 00:24:43.230 that ALK fusions

NOTE Confidence: 0.999706

00:24:43.930 --> 00:24:45.710 are a very common driver

NOTE Confidence: 0.998247

00:24:46.170 --> 00:24:47.630 in a very uncommon

NOTE Confidence: 0.66963

00:24:48.330 --> 00:24:48.830 aggressive

NOTE Confidence: 0.95493126

00:24:49.685 --> 00:24:51.545 t cell non Hodgkin lymphoma

NOTE Confidence: 0.95493126

00:24:51.605 --> 00:24:53.845 that's now called anaplastic large

NOTE Confidence: 0.95493126

00:24:53.845 --> 00:24:54.585 cell lymphoma,

NOTE Confidence: 0.9537316

00:24:55.045 --> 00:24:55.865 ALK rearranged.

NOTE Confidence: 0.9683645

00:24:56.645 --> 00:24:57.925 It was two thousand and

NOTE Confidence: 0.9683645

00:24:57.925 --> 00:24:59.525 seven that Souda and colleagues

NOTE Confidence: 0.9683645

00:24:59.525 --> 00:25:00.265 from Japan

NOTE Confidence: 0.9669514

00:25:01.045 --> 00:25:03.045 discovered the first gene fusions

NOTE Confidence: 0.9669514

00:25:03.045 --> 00:25:04.885 in lung cancer involving ALK.

NOTE Confidence: 0.9669514

00:25:04.885 --> 00:25:07.100 This was the EML4 ALK

NOTE Confidence: 0.9669514

00:25:07.100 --> 00:25:07.600 fusion.

NOTE Confidence: 0.9974174

00:25:08.059 --> 00:25:09.419 Many of these cases are

NOTE Confidence: 0.9974174

00:25:09.419 --> 00:25:09.919 mucinous

NOTE Confidence: 0.9823335

00:25:10.539 --> 00:25:11.840 or poorly differentiated

NOTE Confidence: 0.99153185

00:25:12.220 --> 00:25:12.720 adenocarcinomas

NOTE Confidence: 0.97995955

00:25:13.179 --> 00:25:14.720 with a signet ring cell

NOTE Confidence: 0.97995955

00:25:14.859 --> 00:25:16.780 component, although not invariably. They

NOTE Confidence: 0.97995955

00:25:16.780 --> 00:25:17.760 can have a range

NOTE Confidence: 0.9993978

00:25:18.375 --> 00:25:20.375 of histology within the spectrum

NOTE Confidence: 0.9993978

00:25:20.375 --> 00:25:21.035 of adenocarcinomas.

NOTE Confidence: 0.9652592

00:25:22.535 --> 00:25:24.375 And then remarkably, in only

NOTE Confidence: 0.9652592

00:25:24.375 --> 00:25:26.315 three years between that publication

NOTE Confidence: 0.9678739

00:25:27.095 --> 00:25:28.455 and the publication of this

NOTE Confidence: 0.9678739

00:25:28.455 --> 00:25:30.315 first phase one clinical trial,

NOTE Confidence: 0.8766043

00:25:31.335 --> 00:25:32.155 this group,

NOTE Confidence: 0.924153

00:25:32.600 --> 00:25:34.920 predominantly from Massachusetts General Hospital

NOTE Confidence: 0.924153

00:25:34.920 --> 00:25:35.580 in Boston,

NOTE Confidence: 0.96859854

00:25:36.280 --> 00:25:37.560 showed us that we can

NOTE Confidence: 0.96859854

00:25:37.560 --> 00:25:38.060 target,

NOTE Confidence: 0.9856592

00:25:38.920 --> 00:25:39.420 this

NOTE Confidence: 0.86937475

00:25:39.880 --> 00:25:40.380 fusion

NOTE Confidence: 0.901186

00:25:41.000 --> 00:25:43.020 in advanced lung adenocarcinomas

NOTE Confidence: 0.99290574

00:25:43.720 --> 00:25:45.100 with ALK gene rearrangements

NOTE Confidence: 0.99847335

00:25:45.904 --> 00:25:47.424 as a very effective way

NOTE Confidence: 0.99847335

00:25:47.424 --> 00:25:49.365 of treating these unfortunate patients.

NOTE Confidence: 0.96823066

00:25:49.825 --> 00:25:50.625 And I just have to

NOTE Confidence: 0.96823066

00:25:50.625 --> 00:25:51.505 give a shout out to

NOTE Confidence: 0.96823066

00:25:51.505 --> 00:25:52.725 my friend, John Iefrady.

NOTE Confidence: 0.99484193

00:25:53.345 --> 00:25:54.625 The senior author is a

NOTE Confidence: 0.99484193

00:25:54.625 --> 00:25:55.764 molecular pathologist.

NOTE Confidence: 0.98313946

00:25:56.544 --> 00:25:57.664 I actually trained him in

NOTE Confidence: 0.98313946

00:25:57.664 --> 00:25:58.865 surgical pathology. He was a

NOTE Confidence: 0.98313946

00:25:58.865 --> 00:25:59.744 first year when I was

NOTE Confidence: 0.98313946

00:25:59.744 --> 00:26:01.230 a second year. John likes

NOTE Confidence: 0.98313946

00:26:01.230 --> 00:26:02.270 to say it didn't take

NOTE Confidence: 0.98313946

00:26:02.270 --> 00:26:03.550 because he doesn't do surgical

NOTE Confidence: 0.98313946

00:26:03.550 --> 00:26:04.050 pathology,

NOTE Confidence: 0.9279041

00:26:04.510 --> 00:26:05.890 but he's a brilliant molecular

NOTE Confidence: 0.9279041

00:26:05.950 --> 00:26:08.530 pathologist who actually developed Archer

NOTE Confidence: 0.9279041

00:26:08.830 --> 00:26:10.130 in his research lab,

NOTE Confidence: 0.99355364

00:26:10.590 --> 00:26:11.790 and he was a senior

NOTE Confidence: 0.99355364

00:26:11.790 --> 00:26:13.090 in this paper.

NOTE Confidence: 0.9515288

00:26:14.065 --> 00:26:14.945 And you can see from

NOTE Confidence: 0.9515288

00:26:14.945 --> 00:26:16.545 the waterfall plot, this had

NOTE Confidence: 0.9515288

00:26:16.545 --> 00:26:18.145 really dramatic benefit to these

NOTE Confidence: 0.9515288

00:26:18.145 --> 00:26:18.645 patients.

NOTE Confidence: 0.9919083

00:26:19.185 --> 00:26:20.145 I'm sure many of you

NOTE Confidence: 0.9919083

00:26:20.145 --> 00:26:21.045 know that crizotinib

NOTE Confidence: 0.9915207

00:26:21.425 --> 00:26:23.365 alone doesn't last very long.

NOTE Confidence: 0.96937627

00:26:23.665 --> 00:26:26.325 Patients develop secondary resistance mutations

NOTE Confidence: 0.9930756

00:26:27.160 --> 00:26:28.600 within the kinase domain of

NOTE Confidence: 0.9930756

00:26:28.600 --> 00:26:30.119 ALK, but now we have

NOTE Confidence: 0.9930756

00:26:30.119 --> 00:26:31.100 many different

NOTE Confidence: 0.953109

00:26:31.480 --> 00:26:32.619 targeted therapeutics,

NOTE Confidence: 0.96028

00:26:32.920 --> 00:26:34.460 second, third, fourth generation,

NOTE Confidence: 0.9786029

00:26:34.920 --> 00:26:36.460 and this has really transformed

NOTE Confidence: 0.9758313

00:26:37.160 --> 00:26:39.320 thoracic oncology practice, not only

NOTE Confidence: 0.9758313

00:26:39.320 --> 00:26:41.685 against ALK, but against ROS1

NOTE Confidence: 0.9758313

00:26:41.744 --> 00:26:42.725 and many other,

NOTE Confidence: 0.9970455

00:26:43.345 --> 00:26:44.485 kinase alterations.

NOTE Confidence: 0.9940996

00:26:46.705 --> 00:26:48.145 Beyond the tumors I've mentioned,

NOTE Confidence: 0.9940996

00:26:48.145 --> 00:26:49.105 we now know that ALK

NOTE Confidence: 0.9940996

00:26:49.105 --> 00:26:50.305 fusions are found in a

NOTE Confidence: 0.9940996

00:26:50.305 --> 00:26:52.165 wide range of tumor types.

NOTE Confidence: 0.9610537

00:26:52.545 --> 00:26:53.925 Some are highly aggressive,

NOTE Confidence: 0.9995127

00:26:54.409 --> 00:26:55.789 Some of them are usually

NOTE Confidence: 0.9589423

00:26:56.330 --> 00:26:57.690 indolent, and some of them

NOTE Confidence: 0.9589423

00:26:57.690 --> 00:26:58.990 are entirely benign.

NOTE Confidence: 0.977165

00:26:59.450 --> 00:27:01.070 Even in these very trivial

NOTE Confidence: 0.977165

00:27:01.130 --> 00:27:03.049 benign skin tumors that we

NOTE Confidence: 0.977165

00:27:03.049 --> 00:27:03.549 call

NOTE Confidence: 0.989696

00:27:03.850 --> 00:27:04.350 epithelioid

NOTE Confidence: 0.8005384

00:27:04.650 --> 00:27:05.150 fibrocystiocytomas.

NOTE Confidence: 0.9705149

00:27:06.250 --> 00:27:07.289 And they can have the

NOTE Confidence: 0.9705149

00:27:07.289 --> 00:27:08.590 exact same fusions

NOTE Confidence: 0.999691

00:27:09.105 --> 00:27:10.804 as highly aggressive cancers.

NOTE Confidence: 0.96901053

00:27:12.785 --> 00:27:15.045 The ALK fusion partner sometimes

NOTE Confidence: 0.96901053

00:27:15.184 --> 00:27:16.965 results in a distinctive pattern

NOTE Confidence: 0.69555795

00:27:17.905 --> 00:27:18.645 by immunohistochemistry

NOTE Confidence: 0.99480236

00:27:19.025 --> 00:27:20.385 down the microscope, which is

NOTE Confidence: 0.99480236

00:27:20.385 --> 00:27:21.525 really quite amazing.

NOTE Confidence: 0.97395617

00:27:22.190 --> 00:27:23.710 The most common fusion in

NOTE Confidence: 0.97395617

00:27:23.710 --> 00:27:25.710 anaplastic large cell lymphoma with

NOTE Confidence: 0.97395617

00:27:25.710 --> 00:27:26.210 nucleophosmin

NOTE Confidence: 0.9946076

00:27:27.230 --> 00:27:28.530 results in this combined

NOTE Confidence: 0.9993637

00:27:29.150 --> 00:27:29.650 cytoplasmic

NOTE Confidence: 0.998792

00:27:30.109 --> 00:27:31.490 and nuclear pattern.

NOTE Confidence: 0.9824553

00:27:32.190 --> 00:27:34.270 There's a very distinctive pattern

NOTE Confidence: 0.9824553

00:27:34.270 --> 00:27:36.095 we see in an aggressive

NOTE Confidence: 0.9824553

00:27:36.234 --> 00:27:37.615 variant of inflammatory

NOTE Confidence: 0.96087265

00:27:37.915 --> 00:27:38.415 myofibroblastic

NOTE Confidence: 0.9918595

00:27:38.955 --> 00:27:39.455 tumor

NOTE Confidence: 0.9660235

00:27:39.835 --> 00:27:41.135 that's called epithelioid

NOTE Confidence: 0.99033433

00:27:41.755 --> 00:27:42.255 inflammatory

NOTE Confidence: 0.9791508

00:27:42.635 --> 00:27:43.135 myofibroblastic

NOTE Confidence: 0.9018534

00:27:43.755 --> 00:27:44.255 sarcoma,

NOTE Confidence: 0.9893175

00:27:44.635 --> 00:27:45.934 and that is a nuclear

NOTE Confidence: 0.9893175

00:27:45.994 --> 00:27:47.615 membrane pattern of ALK.

NOTE Confidence: 0.9983069

00:27:47.920 --> 00:27:49.200 And this is all based

NOTE Confidence: 0.9983069

00:27:49.200 --> 00:27:50.580 on what the fusion partner

NOTE Confidence: 0.9857559

00:27:51.040 --> 00:27:52.000 is. Many of the other

NOTE Confidence: 0.9857559

00:27:52.000 --> 00:27:53.859 fusions result in a cytoplasmic

NOTE Confidence: 0.9991358

00:27:54.640 --> 00:27:55.619 pattern of staining.

NOTE Confidence: 0.9531555

00:27:56.560 --> 00:27:58.580 This is ALCL with nucleophosmin.

NOTE Confidence: 0.97962064

00:27:58.960 --> 00:28:00.415 You can see that kind

NOTE Confidence: 0.97962064

00:28:00.415 --> 00:28:02.275 of complex pattern of localization

NOTE Confidence: 0.99924564

00:28:02.975 --> 00:28:04.035 within the cells.

NOTE Confidence: 0.99494123

00:28:05.055 --> 00:28:06.515 This is lung adenocarcinoma

NOTE Confidence: 0.97316307

00:28:06.975 --> 00:28:08.734 with EML4 ALK fusion, a

NOTE Confidence: 0.97316307

00:28:08.734 --> 00:28:09.234 granular

NOTE Confidence: 0.9856335

00:28:09.775 --> 00:28:11.635 pattern of cytoplasmic staining.

NOTE Confidence: 0.99579865

00:28:12.109 --> 00:28:13.410 And this is that aggressive

NOTE Confidence: 0.99579865

00:28:13.470 --> 00:28:14.609 variant of IMT

NOTE Confidence: 0.86176497

00:28:15.470 --> 00:28:17.650 where the Ran binding protein

NOTE Confidence: 0.86176497

00:28:17.710 --> 00:28:18.450 two fusion

NOTE Confidence: 0.96056825

00:28:19.070 --> 00:28:20.690 brings ALK to the nuclear

NOTE Confidence: 0.96056825

00:28:20.830 --> 00:28:21.730 pore complex

NOTE Confidence: 0.89740825

00:28:22.109 --> 00:28:23.230 and it looks like this

NOTE Confidence: 0.89740825

00:28:23.230 --> 00:28:24.850 really distinctive, beautiful

NOTE Confidence: 0.9810774

00:28:25.230 --> 00:28:26.850 nuclear membrane pattern.

NOTE Confidence: 0.9923747

00:28:28.765 --> 00:28:30.525 For clinical practice, it's also

NOTE Confidence: 0.9923747

00:28:30.525 --> 00:28:32.785 very important to know that

NOTE Confidence: 0.9976946

00:28:33.085 --> 00:28:33.984 which antibody

NOTE Confidence: 0.9981125

00:28:34.285 --> 00:28:36.065 clone you're using is important

NOTE Confidence: 0.96716976

00:28:36.845 --> 00:28:38.125 in terms of what you're

NOTE Confidence: 0.96716976

00:28:38.125 --> 00:28:40.330 using the application for. The

NOTE Confidence: 0.96716976

00:28:40.330 --> 00:28:41.769 ALK one clone we've had

NOTE Confidence: 0.96716976

00:28:41.769 --> 00:28:43.129 for more than thirty years,

NOTE Confidence: 0.96716976

00:28:43.129 --> 00:28:44.350 and it works beautifully

NOTE Confidence: 0.9709258

00:28:45.049 --> 00:28:46.429 for lymphoma diagnosis,

NOTE Confidence: 0.9775549

00:28:46.889 --> 00:28:48.889 but it's rather insensitive. It's

NOTE Confidence: 0.9775549

00:28:48.889 --> 00:28:49.710 not a very,

NOTE Confidence: 0.9996253

00:28:50.330 --> 00:28:51.389 powerful antibody

NOTE Confidence: 0.60402685

00:28:52.090 --> 00:28:52.590 and

NOTE Confidence: 0.99570346

00:28:53.085 --> 00:28:53.905 lung adenocarcinomas

NOTE Confidence: 0.98539454

00:28:54.765 --> 00:28:56.284 with ALK fusions actually have

NOTE Confidence: 0.98539454

00:28:56.284 --> 00:28:57.485 a pretty low level of

NOTE Confidence: 0.98539454

00:28:57.485 --> 00:28:58.385 protein expression.

NOTE Confidence: 0.9847775

00:28:58.924 --> 00:29:00.684 So ALK one is usually

NOTE Confidence: 0.9847775

00:29:00.684 --> 00:29:02.125 negative, and it doesn't help

NOTE Confidence: 0.9847775

00:29:02.125 --> 00:29:04.044 you as a screen for

NOTE Confidence: 0.9847775

00:29:04.044 --> 00:29:05.905 EML four or other ALK

NOTE Confidence: 0.9847775

00:29:05.965 --> 00:29:06.784 gene fusions.

NOTE Confidence: 0.9986299

00:29:07.620 --> 00:29:08.360 In contrast,

NOTE Confidence: 0.9985971

00:29:09.060 --> 00:29:10.180 in the last ten years

NOTE Confidence: 0.9985971

00:29:10.180 --> 00:29:11.300 or so, there have been

NOTE Confidence: 0.9985971

00:29:11.300 --> 00:29:11.800 two

NOTE Confidence: 0.9656338

00:29:12.340 --> 00:29:14.600 highly sensitive anti ALK antibodies

NOTE Confidence: 0.9656338

00:29:14.740 --> 00:29:15.240 developed,

NOTE Confidence: 0.984297

00:29:15.700 --> 00:29:17.460 which are beautiful surrogates for

NOTE Confidence: 0.984297

00:29:17.460 --> 00:29:18.120 the fusions.

NOTE Confidence: 0.9692591

00:29:18.660 --> 00:29:20.180 And now they can be

NOTE Confidence: 0.9692591

00:29:20.180 --> 00:29:22.040 used as a standalone test

NOTE Confidence: 0.99496824

00:29:22.485 --> 00:29:24.245 to identify what patients with

NOTE Confidence: 0.99496824

00:29:24.245 --> 00:29:25.065 lung adenocarcinoma

NOTE Confidence: 0.9066661

00:29:26.245 --> 00:29:28.025 can be treated with targeted

NOTE Confidence: 0.9066661

00:29:28.165 --> 00:29:28.665 therapies.

NOTE Confidence: 0.8285534

00:29:29.925 --> 00:29:30.425 Inflammatory

NOTE Confidence: 0.9238028

00:29:30.805 --> 00:29:31.305 myofibroblastic

NOTE Confidence: 0.9880176

00:29:31.765 --> 00:29:32.805 tumors are kind of in

NOTE Confidence: 0.9880176

00:29:32.805 --> 00:29:34.325 the middle. The level of

NOTE Confidence: 0.9880176

00:29:34.325 --> 00:29:35.705 expression is usually

NOTE Confidence: 0.9987564

00:29:36.059 --> 00:29:36.559 sufficient

NOTE Confidence: 0.95515984

00:29:37.019 --> 00:29:39.019 for ALK1 to detect the

NOTE Confidence: 0.95515984

00:29:39.019 --> 00:29:40.159 ALK in IMTs,

NOTE Confidence: 0.98756504

00:29:40.700 --> 00:29:41.980 but you'll miss about five

NOTE Confidence: 0.98756504

00:29:41.980 --> 00:29:43.600 percent of cases that way.

NOTE Confidence: 0.98756504

00:29:43.659 --> 00:29:45.580 The newer antibodies, you'll pick

NOTE Confidence: 0.98756504

00:29:45.580 --> 00:29:46.960 up all the ALK fusions.

NOTE Confidence: 0.9504277

00:29:48.715 --> 00:29:49.835 And we were very lucky.

NOTE Confidence: 0.9504277

00:29:49.835 --> 00:29:51.135 We were able to piggyback

NOTE Confidence: 0.98025763

00:29:51.515 --> 00:29:52.815 along with that really

NOTE Confidence: 0.76148707

00:29:53.434 --> 00:29:53.934 fundamental,

NOTE Confidence: 0.9891588

00:29:54.715 --> 00:29:55.215 like

NOTE Confidence: 0.91462904

00:29:55.755 --> 00:29:57.674 practice changing paper on lung

NOTE Confidence: 0.91462904

00:29:57.674 --> 00:29:58.174 adenocarcinoma

NOTE Confidence: 0.94697464

00:29:59.115 --> 00:30:00.335 with crizotinib

NOTE Confidence: 0.9279592

00:30:00.635 --> 00:30:01.455 that I mentioned.

NOTE Confidence: 0.97822464

00:30:02.190 --> 00:30:03.470 Because of that paper, we

NOTE Confidence: 0.97822464

00:30:03.470 --> 00:30:04.929 could publish a case report,

NOTE Confidence: 0.9621162

00:30:05.389 --> 00:30:06.750 snuck into the same issue

NOTE Confidence: 0.9621162

00:30:06.750 --> 00:30:07.710 of the New England Journal

NOTE Confidence: 0.9621162

00:30:07.710 --> 00:30:08.370 of Medicine,

NOTE Confidence: 0.99249995

00:30:08.830 --> 00:30:10.110 the first patient with one

NOTE Confidence: 0.99249995

00:30:10.110 --> 00:30:11.630 of these aggressive variants of

NOTE Confidence: 0.99249995

00:30:11.630 --> 00:30:12.130 IMT

NOTE Confidence: 0.95322245

00:30:12.590 --> 00:30:14.049 who had a really dramatic

NOTE Confidence: 0.98883224

00:30:14.825 --> 00:30:16.045 response to crizotinib.

NOTE Confidence: 0.9485412

00:30:16.425 --> 00:30:18.185 And this was from this

NOTE Confidence: 0.9485412

00:30:18.185 --> 00:30:18.685 study.

NOTE Confidence: 0.9409334

00:30:19.145 --> 00:30:21.245 My former colleague, James Butrinsky,

NOTE Confidence: 0.93472356

00:30:21.945 --> 00:30:24.445 who's a medical oncologist specializing

NOTE Confidence: 0.93472356

00:30:24.585 --> 00:30:25.325 in sarcoma,

NOTE Confidence: 0.9799306

00:30:25.865 --> 00:30:27.005 treated this patient

NOTE Confidence: 0.98512554

00:30:27.465 --> 00:30:28.685 who had a pelvic

NOTE Confidence: 0.96023065

00:30:29.380 --> 00:30:31.400 epithelioid inflammatory myofibroblastic

NOTE Confidence: 0.9882928

00:30:32.020 --> 00:30:32.520 sarcoma.

NOTE Confidence: 0.9801465

00:30:33.059 --> 00:30:35.080 It recurred locally with multifocal

NOTE Confidence: 0.9801465

00:30:35.299 --> 00:30:36.200 disease, including

NOTE Confidence: 0.82806003

00:30:36.659 --> 00:30:38.200 a metastasis of the liver.

NOTE Confidence: 0.9804831

00:30:38.580 --> 00:30:39.940 The patient went on therapy.

NOTE Confidence: 0.9804831

00:30:39.940 --> 00:30:41.220 After three months, there was

NOTE Confidence: 0.9804831

00:30:41.220 --> 00:30:42.840 a dramatic partial response.

NOTE Confidence: 0.9872135

00:30:43.455 --> 00:30:44.835 Then a surgical oncologist

NOTE Confidence: 0.9502511

00:30:45.615 --> 00:30:46.735 by the name of Monica

NOTE Confidence: 0.9502511

00:30:46.735 --> 00:30:47.235 Bertinoli,

NOTE Confidence: 0.98677593

00:30:47.695 --> 00:30:48.894 who actually moved on to

NOTE Confidence: 0.98677593

00:30:48.894 --> 00:30:49.855 become the head of the

NOTE Confidence: 0.98677593

00:30:49.855 --> 00:30:50.355 NCI,

NOTE Confidence: 0.99551773

00:30:50.815 --> 00:30:51.615 and then she was the

NOTE Confidence: 0.99551773

00:30:51.615 --> 00:30:52.595 head of the NIH.

NOTE Confidence: 0.96069336

00:30:53.054 --> 00:30:54.095 So my claim to fame

NOTE Confidence: 0.96069336

00:30:54.095 --> 00:30:55.455 is I briefly worked with

NOTE Confidence: 0.96069336

00:30:55.455 --> 00:30:56.835 Monica, who's a brilliant

NOTE Confidence: 0.9918743

00:30:57.215 --> 00:30:57.715 scientist

NOTE Confidence: 0.80510247

00:30:58.414 --> 00:30:58.995 and a

NOTE Confidence: 0.95368445

00:30:59.510 --> 00:31:00.410 surgical oncologist.

NOTE Confidence: 0.966434

00:31:01.270 --> 00:31:02.550 She did debulking of this

NOTE Confidence: 0.966434

00:31:02.550 --> 00:31:03.050 patient,

NOTE Confidence: 0.99374753

00:31:03.350 --> 00:31:04.710 and he survived for more

NOTE Confidence: 0.99374753

00:31:04.710 --> 00:31:05.990 than ten years on oral

NOTE Confidence: 0.99374753

00:31:05.990 --> 00:31:08.230 crizotinib therapy after this. So

NOTE Confidence: 0.99374753

00:31:08.230 --> 00:31:10.330 this is not only transformative

NOTE Confidence: 0.99374753

00:31:10.470 --> 00:31:11.850 for patients with carcinomas,

NOTE Confidence: 0.9987651

00:31:12.470 --> 00:31:13.770 but there are some

NOTE Confidence: 0.9781989

00:31:14.595 --> 00:31:15.095 aggressive

NOTE Confidence: 0.9994981

00:31:15.635 --> 00:31:16.855 mesenchymal tumors

NOTE Confidence: 0.95009995

00:31:17.475 --> 00:31:19.235 that are targetable because of

NOTE Confidence: 0.95009995

00:31:19.235 --> 00:31:19.895 these alterations.

NOTE Confidence: 0.9800415

00:31:21.715 --> 00:31:22.755 And just a few words

NOTE Confidence: 0.9800415

00:31:22.755 --> 00:31:24.115 about ROS1. So this is

NOTE Confidence: 0.9800415

00:31:24.115 --> 00:31:25.095 ROS1 immunohistochemistry

NOTE Confidence: 0.96911854

00:31:26.195 --> 00:31:27.155 in one of the lung

NOTE Confidence: 0.96911854

00:31:27.155 --> 00:31:27.655 adenocarcinomas

NOTE Confidence: 0.96129894

00:31:28.275 --> 00:31:29.575 with a ROS1 fusion.

NOTE Confidence: 0.976849

00:31:30.409 --> 00:31:32.330 But unfortunately, the antibody we

NOTE Confidence: 0.976849

00:31:32.330 --> 00:31:33.470 have against ROS1

NOTE Confidence: 0.99047893

00:31:34.090 --> 00:31:35.390 is highly sensitive,

NOTE Confidence: 0.9993461

00:31:35.929 --> 00:31:36.909 but the specificity

NOTE Confidence: 0.99790895

00:31:37.210 --> 00:31:38.750 is less than the ones

NOTE Confidence: 0.9011462

00:31:40.010 --> 00:31:41.309 against ALK.

NOTE Confidence: 0.99441487

00:31:41.610 --> 00:31:42.809 So it's a very good

NOTE Confidence: 0.99441487

00:31:42.809 --> 00:31:43.309 screen,

NOTE Confidence: 0.9503795

00:31:43.654 --> 00:31:44.774 but we can't use it

NOTE Confidence: 0.9503795

00:31:44.774 --> 00:31:46.955 as a standalone predictive test

NOTE Confidence: 0.9942165

00:31:47.255 --> 00:31:48.315 for lung adenocarcinoma.

NOTE Confidence: 0.9688704

00:31:49.174 --> 00:31:50.375 So in our practice, we

NOTE Confidence: 0.9688704

00:31:50.375 --> 00:31:52.154 do run ALK and ROS1

NOTE Confidence: 0.9688704

00:31:52.294 --> 00:31:52.955 as routine

NOTE Confidence: 0.9974464

00:31:53.575 --> 00:31:54.955 screening for lung adenocarcinomas.

NOTE Confidence: 0.9774773

00:31:56.070 --> 00:31:57.590 If ALK is positive, that's

NOTE Confidence: 0.9774773

00:31:57.590 --> 00:31:59.130 enough information for treatment.

NOTE Confidence: 0.99645215

00:31:59.669 --> 00:32:01.049 But ROS1 requires

NOTE Confidence: 0.5556337

00:32:01.429 --> 00:32:01.929 confirmation

NOTE Confidence: 0.98208094

00:32:02.710 --> 00:32:04.730 by gene fusion testing or

NOTE Confidence: 0.98208094

00:32:04.870 --> 00:32:05.370 FISH.

NOTE Confidence: 0.9552054

00:32:07.835 --> 00:32:09.195 One other example I'm just

NOTE Confidence: 0.9552054

00:32:09.195 --> 00:32:10.395 gonna mention because it's been

NOTE Confidence: 0.9552054

00:32:10.395 --> 00:32:11.515 such a hot topic in

NOTE Confidence: 0.9552054

00:32:11.515 --> 00:32:12.015 oncology

NOTE Confidence: 0.95346606

00:32:12.555 --> 00:32:13.995 and that's NTRK, which I'm

NOTE Confidence: 0.95346606

00:32:13.995 --> 00:32:14.955 sure many of you know

NOTE Confidence: 0.95346606

00:32:14.955 --> 00:32:15.455 about.

NOTE Confidence: 0.9881432

00:32:15.915 --> 00:32:17.915 Three different NTRK genes result

NOTE Confidence: 0.9881432

00:32:17.915 --> 00:32:19.215 in three different proteins.

NOTE Confidence: 0.94679934

00:32:20.110 --> 00:32:21.549 One, two, and three becomes

NOTE Confidence: 0.94679934

00:32:21.549 --> 00:32:22.990 A, B, and C. And

NOTE Confidence: 0.94679934

00:32:22.990 --> 00:32:24.769 we have antibodies available

NOTE Confidence: 0.95181334

00:32:25.230 --> 00:32:27.570 that recognize a conserved sequence

NOTE Confidence: 0.91612875

00:32:28.110 --> 00:32:29.649 in all three of these

NOTE Confidence: 0.91612875

00:32:29.789 --> 00:32:30.690 Turk proteins.

NOTE Confidence: 0.9714985

00:32:31.389 --> 00:32:33.010 It's a very nice antibody.

NOTE Confidence: 0.9714985

00:32:33.149 --> 00:32:34.465 And why do we care

NOTE Confidence: 0.9714985

00:32:34.465 --> 00:32:36.304 about NTRK? Because very similar

NOTE Confidence: 0.9714985

00:32:36.304 --> 00:32:37.745 to what we saw in

NOTE Confidence: 0.9714985

00:32:37.745 --> 00:32:39.365 ALK prearranged lung cancers,

NOTE Confidence: 0.90909123

00:32:40.625 --> 00:32:41.125 NTRK,

NOTE Confidence: 0.99034405

00:32:42.304 --> 00:32:44.225 tumors with NTRK fusions that

NOTE Confidence: 0.99034405

00:32:44.225 --> 00:32:45.125 are very aggressive

NOTE Confidence: 0.93388635

00:32:45.585 --> 00:32:47.284 can be effectively treated

NOTE Confidence: 0.9924768

00:32:47.620 --> 00:32:48.279 with larotrectinib

NOTE Confidence: 0.9835815

00:32:48.980 --> 00:32:51.140 and other NTRK inhibitors. And

NOTE Confidence: 0.9835815

00:32:51.140 --> 00:32:52.659 in fact, in this first

NOTE Confidence: 0.9835815

00:32:52.659 --> 00:32:54.520 paper that was published almost

NOTE Confidence: 0.9646894

00:32:54.980 --> 00:32:56.200 eight years ago now,

NOTE Confidence: 0.9814701

00:32:56.580 --> 00:32:58.100 the waterfall plot looks even

NOTE Confidence: 0.9814701

00:32:58.100 --> 00:32:59.080 better than crizotinib,

NOTE Confidence: 0.9725028

00:32:59.735 --> 00:33:00.855 And as you'll notice from

NOTE Confidence: 0.9725028

00:33:00.855 --> 00:33:02.315 the top of this graph,

NOTE Confidence: 0.99659806

00:33:02.855 --> 00:33:05.015 this was agnostic to tumor

NOTE Confidence: 0.99659806

00:33:05.015 --> 00:33:06.875 type. So we had carcinomas,

NOTE Confidence: 0.79372877

00:33:07.895 --> 00:33:08.395 GIST,

NOTE Confidence: 0.99753946

00:33:09.655 --> 00:33:10.955 salivary gland tumors,

NOTE Confidence: 0.9797067

00:33:11.415 --> 00:33:11.915 melanoma,

NOTE Confidence: 0.94609773

00:33:13.095 --> 00:33:14.715 all a couple of sarcomas.

NOTE Confidence: 0.9569739

00:33:15.540 --> 00:33:17.400 Irrespective of the tumor type.

NOTE Confidence: 0.99872446

00:33:17.780 --> 00:33:19.000 If it was metastatic

NOTE Confidence: 0.97446126

00:33:20.100 --> 00:33:22.100 malignancy with an NTRK fusion,

NOTE Confidence: 0.97446126

00:33:22.100 --> 00:33:23.640 they had really good responses

NOTE Confidence: 0.97446126

00:33:23.700 --> 00:33:24.600 in most cases.

NOTE Confidence: 0.99886894

00:33:25.780 --> 00:33:27.880 The antibody works really well

NOTE Confidence: 0.99086165

00:33:28.455 --> 00:33:30.135 to identify tumors that are

NOTE Confidence: 0.99086165

00:33:30.135 --> 00:33:31.914 defined by NTRK fusions.

NOTE Confidence: 0.99402314

00:33:32.534 --> 00:33:33.835 For example, in

NOTE Confidence: 0.8770778

00:33:35.414 --> 00:33:36.554 infantile fibrosarcoma,

NOTE Confidence: 0.9371752

00:33:37.495 --> 00:33:39.434 this antibody, the Pentract antibodies

NOTE Confidence: 0.9371752

00:33:39.575 --> 00:33:40.855 become a very easy way

NOTE Confidence: 0.9371752

00:33:40.855 --> 00:33:41.835 to make the diagnosis.

NOTE Confidence: 0.9885987

00:33:42.600 --> 00:33:43.880 The same thing goes for

NOTE Confidence: 0.9885987

00:33:43.880 --> 00:33:46.059 secretory carcinomas of the breast

NOTE Confidence: 0.93423194

00:33:46.440 --> 00:33:48.200 or salivary gland or rarely

NOTE Confidence: 0.93423194

00:33:48.200 --> 00:33:49.580 in skin and other sites.

NOTE Confidence: 0.9355813

00:33:50.040 --> 00:33:50.860 These have,

NOTE Confidence: 0.9255755

00:33:51.400 --> 00:33:53.180 NTRK fusions as a defining

NOTE Confidence: 0.9255755

00:33:53.240 --> 00:33:54.700 feature and immunohistochemistry

NOTE Confidence: 0.9912275

00:33:55.320 --> 00:33:56.600 works beautifully. You see the

NOTE Confidence: 0.9912275

00:33:56.600 --> 00:33:57.660 nuclear staining

NOTE Confidence: 0.8561805

00:33:57.985 --> 00:33:58.804 in these secretory

NOTE Confidence: 0.95469403

00:33:59.105 --> 00:33:59.605 carcinomas.

NOTE Confidence: 0.96539754

00:34:01.184 --> 00:34:03.205 And several groups have actually

NOTE Confidence: 0.96539754

00:34:03.264 --> 00:34:03.764 evaluated,

NOTE Confidence: 0.8505144

00:34:04.625 --> 00:34:05.684 PennTrak immunostochemistry

NOTE Confidence: 0.99180025

00:34:06.784 --> 00:34:08.385 as a surrogate for NTRK

NOTE Confidence: 0.99180025

00:34:08.385 --> 00:34:08.885 fusions

NOTE Confidence: 0.98871756

00:34:09.425 --> 00:34:10.864 in tumor types where the

NOTE Confidence: 0.98871756

00:34:10.864 --> 00:34:11.844 NTRK rearrangements

NOTE Confidence: 0.98705006

00:34:12.224 --> 00:34:13.685 are much less common.

NOTE Confidence: 0.9948126

00:34:14.040 --> 00:34:14.920 And as I'll show you

NOTE Confidence: 0.9948126

00:34:14.920 --> 00:34:16.280 in a minute, sometimes these

NOTE Confidence: 0.9948126

00:34:16.280 --> 00:34:17.900 are very, very rare events.

NOTE Confidence: 0.9817949

00:34:18.360 --> 00:34:19.239 Many of these were led

NOTE Confidence: 0.9817949

00:34:19.239 --> 00:34:20.760 by Jacqueline Heckman from New

NOTE Confidence: 0.9817949

00:34:20.760 --> 00:34:21.260 York.

NOTE Confidence: 0.9728687

00:34:21.719 --> 00:34:23.180 Really beautiful papers,

NOTE Confidence: 0.83054775

00:34:23.880 --> 00:34:24.940 trying to decide

NOTE Confidence: 0.99926025

00:34:25.480 --> 00:34:26.600 whether we could use the

NOTE Confidence: 0.99926025

00:34:26.600 --> 00:34:27.980 antibody as a surrogate.

NOTE Confidence: 0.99804205

00:34:28.635 --> 00:34:29.594 And as you see from

NOTE Confidence: 0.99804205

00:34:29.594 --> 00:34:30.555 the left side of this

NOTE Confidence: 0.99804205

00:34:30.555 --> 00:34:31.055 panel,

NOTE Confidence: 0.90202975

00:34:31.675 --> 00:34:32.175 unfortunately,

NOTE Confidence: 0.992613

00:34:32.555 --> 00:34:33.995 in many cancers that are

NOTE Confidence: 0.992613

00:34:33.995 --> 00:34:34.975 much more common,

NOTE Confidence: 0.9195226

00:34:35.435 --> 00:34:37.455 the fusions are really rare,

NOTE Confidence: 0.961088

00:34:37.755 --> 00:34:39.114 zero point one percent, zero

NOTE Confidence: 0.961088

00:34:39.114 --> 00:34:40.655 point three percent of tumors.

NOTE Confidence: 0.9732844

00:34:42.210 --> 00:34:43.410 And Lynette and I did

NOTE Confidence: 0.9732844

00:34:43.410 --> 00:34:43.910 this

NOTE Confidence: 0.83544934

00:34:44.210 --> 00:34:44.710 prospective,

NOTE Confidence: 0.9643207

00:34:45.170 --> 00:34:46.609 very small screening study a

NOTE Confidence: 0.9643207

00:34:46.609 --> 00:34:47.670 couple of years ago

NOTE Confidence: 0.9255552

00:34:47.969 --> 00:34:48.930 just to kind of test

NOTE Confidence: 0.9255552

00:34:48.930 --> 00:34:49.910 out this hypothesis.

NOTE Confidence: 0.9986496

00:34:50.609 --> 00:34:51.890 We were using all the

NOTE Confidence: 0.9986496

00:34:51.890 --> 00:34:53.090 cases for which we were

NOTE Confidence: 0.9986496

00:34:53.090 --> 00:34:53.989 already doing

NOTE Confidence: 0.9962353

00:34:54.965 --> 00:34:56.665 testing for lung cancer,

NOTE Confidence: 0.99714476

00:34:57.045 --> 00:34:57.545 endometrial

NOTE Confidence: 0.9417599

00:34:57.844 --> 00:34:59.705 cancer, colon cancer for MMR,

NOTE Confidence: 0.9211091

00:35:00.245 --> 00:35:01.625 and we used one antibody

NOTE Confidence: 0.9211091

00:35:01.685 --> 00:35:02.825 to do a pen track

NOTE Confidence: 0.9211091

00:35:03.045 --> 00:35:04.245 over the course of, like,

NOTE Confidence: 0.9211091

00:35:04.245 --> 00:35:05.705 six months. And we found

NOTE Confidence: 0.97601414

00:35:06.085 --> 00:35:07.844 that four out of almost

NOTE Confidence: 0.97601414

00:35:07.844 --> 00:35:09.785 five hundred cases were positive.

NOTE Confidence: 0.97761416

00:35:10.460 --> 00:35:11.980 But by testing, only one

NOTE Confidence: 0.97761416

00:35:11.980 --> 00:35:12.940 of these had an NTRK

NOTE Confidence: 0.97761416

00:35:12.940 --> 00:35:13.440 fusion.

NOTE Confidence: 0.96451056

00:35:13.819 --> 00:35:15.099 So clearly, this is not

NOTE Confidence: 0.96451056

00:35:15.099 --> 00:35:16.559 a great method to screen,

NOTE Confidence: 0.9912974

00:35:16.859 --> 00:35:18.219 and it probably is not

NOTE Confidence: 0.9912974

00:35:18.219 --> 00:35:18.960 gonna solve

NOTE Confidence: 0.9953966

00:35:19.339 --> 00:35:21.180 the problem to identify these

NOTE Confidence: 0.9953966

00:35:21.180 --> 00:35:23.900 very rare NTRK rearranged aggressive

NOTE Confidence: 0.9953966

00:35:23.900 --> 00:35:24.400 cancers.

NOTE Confidence: 0.93362135

00:35:25.015 --> 00:35:25.895 And if you look at

NOTE Confidence: 0.93362135

00:35:25.895 --> 00:35:27.575 this other study by Rosen

NOTE Confidence: 0.93362135

00:35:27.575 --> 00:35:29.195 from Clinical Cancer Research

NOTE Confidence: 0.8850298

00:35:29.734 --> 00:35:31.275 from twenty twenty,

NOTE Confidence: 0.99760544

00:35:31.575 --> 00:35:32.955 you see that the sensitivity

NOTE Confidence: 0.99760544

00:35:33.255 --> 00:35:33.994 and specificity

NOTE Confidence: 0.8871919

00:35:34.295 --> 00:35:35.035 are imperfect.

NOTE Confidence: 0.9983078

00:35:35.415 --> 00:35:36.795 And that's really the problem.

NOTE Confidence: 0.9995424

00:35:37.170 --> 00:35:37.910 The sensitivity

NOTE Confidence: 0.963667

00:35:38.290 --> 00:35:40.290 for NTRK3 is almost eighty

NOTE Confidence: 0.963667

00:35:40.290 --> 00:35:42.050 percent, so you're gonna miss

NOTE Confidence: 0.963667

00:35:42.050 --> 00:35:43.270 twenty percent of cases.

NOTE Confidence: 0.9916955

00:35:44.050 --> 00:35:45.510 And at the same time,

NOTE Confidence: 0.9916955

00:35:45.809 --> 00:35:47.650 the specificity overall is only

NOTE Confidence: 0.9916955

00:35:47.650 --> 00:35:48.710 about eighty percent.

NOTE Confidence: 0.9292215

00:35:49.010 --> 00:35:50.690 So, unfortunately, it looks like

NOTE Confidence: 0.9292215

00:35:50.690 --> 00:35:52.290 immuno stick chemistry doesn't save

NOTE Confidence: 0.9292215

00:35:52.290 --> 00:35:53.845 us as a screen for

NOTE Confidence: 0.9292215

00:35:53.845 --> 00:35:55.045 these patients and you really

NOTE Confidence: 0.9292215

00:35:55.045 --> 00:35:55.785 have to do

NOTE Confidence: 0.91761553

00:35:56.085 --> 00:35:58.185 fusion testing, which obviously in,

NOTE Confidence: 0.9156513

00:35:59.045 --> 00:36:00.645 resource poor settings, is it

NOTE Confidence: 0.9156513

00:36:00.645 --> 00:36:01.145 possible?

NOTE Confidence: 0.9870693

00:36:01.445 --> 00:36:02.725 So it's still a problem

NOTE Confidence: 0.9870693

00:36:02.725 --> 00:36:04.165 that we're trying to, figure

NOTE Confidence: 0.9870693

00:36:04.165 --> 00:36:04.665 out.

NOTE Confidence: 0.9958086

00:36:06.830 --> 00:36:07.710 Next, I'm going to show

NOTE Confidence: 0.9958086

00:36:07.710 --> 00:36:08.750 you a couple of really

NOTE Confidence: 0.9958086

00:36:08.750 --> 00:36:11.170 nice examples of mutant oncoprotein

NOTE Confidence: 0.99777466

00:36:11.550 --> 00:36:12.530 specific antibodies.

NOTE Confidence: 0.9920586

00:36:13.390 --> 00:36:14.670 We've had these for many

NOTE Confidence: 0.9920586

00:36:14.670 --> 00:36:15.550 years. Some of them are

NOTE Confidence: 0.9920586

00:36:15.550 --> 00:36:17.010 newer and some are older.

NOTE Confidence: 0.99604344

00:36:20.015 --> 00:36:21.135 I suspect many of you

NOTE Confidence: 0.99604344

00:36:21.135 --> 00:36:22.275 know about the IDH1

NOTE Confidence: 0.8025827

00:36:23.375 --> 00:36:23.875 R132H

NOTE Confidence: 0.982615

00:36:24.735 --> 00:36:26.355 mutation specific antibody.

NOTE Confidence: 0.994497

00:36:26.895 --> 00:36:28.735 This has become routine practice

NOTE Confidence: 0.994497

00:36:28.735 --> 00:36:30.275 for diagnosis of gliomas.

NOTE Confidence: 0.8765614

00:36:31.055 --> 00:36:32.275 It's really a remarkably

NOTE Confidence: 0.99839556

00:36:32.575 --> 00:36:33.635 powerful way

NOTE Confidence: 0.9577069

00:36:34.930 --> 00:36:36.610 for classification of gliomas and

NOTE Confidence: 0.9577069

00:36:36.610 --> 00:36:37.110 prognostication.

NOTE Confidence: 0.9760022

00:36:38.130 --> 00:36:38.630 Fortunately,

NOTE Confidence: 0.9582754

00:36:39.250 --> 00:36:40.930 it's the most common IDH

NOTE Confidence: 0.9582754

00:36:40.930 --> 00:36:42.530 mutation by far in glial

NOTE Confidence: 0.9582754

00:36:42.530 --> 00:36:43.030 neoplasms.

NOTE Confidence: 0.9041813

00:36:44.210 --> 00:36:45.730 Only about six or seven

NOTE Confidence: 0.9041813

00:36:45.730 --> 00:36:46.230 percent

NOTE Confidence: 0.9981027

00:36:46.530 --> 00:36:48.070 of gliomas have mutations

NOTE Confidence: 0.91723555

00:36:48.614 --> 00:36:50.135 in IDH one or IDH

NOTE Confidence: 0.91723555

00:36:50.135 --> 00:36:52.055 two that are different amino

NOTE Confidence: 0.91723555

00:36:52.055 --> 00:36:52.875 acids substitutions.

NOTE Confidence: 0.9593618

00:36:53.975 --> 00:36:54.935 And I'm gonna show you

NOTE Confidence: 0.9593618

00:36:54.935 --> 00:36:56.375 a couple other nice examples

NOTE Confidence: 0.9593618

00:36:56.375 --> 00:36:57.975 here. So this is, this

NOTE Confidence: 0.9593618

00:36:57.975 --> 00:36:59.175 is the first example I

NOTE Confidence: 0.9593618

00:36:59.175 --> 00:37:00.375 just mentioned, the high grade

NOTE Confidence: 0.9593618

00:37:00.375 --> 00:37:00.875 glioma,

NOTE Confidence: 0.99035203

00:37:01.489 --> 00:37:02.450 and you can see that

NOTE Confidence: 0.99035203

00:37:02.450 --> 00:37:03.750 really beautiful immunoreactivity.

NOTE Confidence: 0.98275167

00:37:04.770 --> 00:37:06.290 If IDH1 is wild type,

NOTE Confidence: 0.98275167

00:37:06.290 --> 00:37:07.589 it's entirely negative.

NOTE Confidence: 0.9763212

00:37:07.969 --> 00:37:09.089 And this is done now

NOTE Confidence: 0.9763212

00:37:09.089 --> 00:37:10.230 every day in neuropathology

NOTE Confidence: 0.9540014

00:37:11.089 --> 00:37:11.589 practice

NOTE Confidence: 0.6666032

00:37:12.290 --> 00:37:12.790 everywhere,

NOTE Confidence: 0.9856492

00:37:13.410 --> 00:37:15.349 where you're diagnosing glial neoplasms.

NOTE Confidence: 0.99489295

00:37:16.575 --> 00:37:17.614 To show you one other

NOTE Confidence: 0.99489295

00:37:17.614 --> 00:37:18.435 nice example,

NOTE Confidence: 0.9620613

00:37:18.815 --> 00:37:20.255 I'm gonna just present this

NOTE Confidence: 0.9620613

00:37:20.255 --> 00:37:21.075 as an unknown.

NOTE Confidence: 0.9956374

00:37:21.614 --> 00:37:22.974 This is from an elderly

NOTE Confidence: 0.9956374

00:37:22.974 --> 00:37:24.415 man who presented with small

NOTE Confidence: 0.9956374

00:37:24.415 --> 00:37:25.234 bowel obstruction.

NOTE Confidence: 0.9745541

00:37:25.855 --> 00:37:26.895 When the surgeon went in

NOTE Confidence: 0.9745541

00:37:26.895 --> 00:37:28.415 and took out the segment

NOTE Confidence: 0.9745541

00:37:28.415 --> 00:37:29.395 of small bowel,

NOTE Confidence: 0.9600947

00:37:29.770 --> 00:37:30.890 you can see why there

NOTE Confidence: 0.9600947

00:37:30.890 --> 00:37:32.270 was this very large

NOTE Confidence: 0.9789675

00:37:32.890 --> 00:37:34.810 ulcerated mass that was kinking

NOTE Confidence: 0.9789675

00:37:34.810 --> 00:37:35.470 the bowel,

NOTE Confidence: 0.9693167

00:37:36.010 --> 00:37:37.230 growing into the lumen,

NOTE Confidence: 0.989873

00:37:37.610 --> 00:37:39.370 involving the submucosa and the

NOTE Confidence: 0.989873

00:37:39.370 --> 00:37:39.870 mucosa.

NOTE Confidence: 0.99104375

00:37:40.570 --> 00:37:41.450 And if you look at

NOTE Confidence: 0.99104375

00:37:41.450 --> 00:37:42.830 high power at this tumor,

NOTE Confidence: 0.99943197

00:37:43.925 --> 00:37:45.385 it has a really undifferentiated

NOTE Confidence: 0.79941916

00:37:45.765 --> 00:37:46.265 appearance,

NOTE Confidence: 0.9959844

00:37:46.805 --> 00:37:47.625 a sheet

NOTE Confidence: 0.9863061

00:37:48.005 --> 00:37:48.985 of epithelioid

NOTE Confidence: 0.99474937

00:37:49.445 --> 00:37:51.205 or oval cells with abundant

NOTE Confidence: 0.99474937

00:37:51.205 --> 00:37:52.025 pale cytoplasm

NOTE Confidence: 0.98486596

00:37:52.725 --> 00:37:54.185 and a very high mitotic

NOTE Confidence: 0.98486596

00:37:54.244 --> 00:37:54.744 rate.

NOTE Confidence: 0.98830926

00:37:55.285 --> 00:37:56.645 So now we're dealing with

NOTE Confidence: 0.98830926

00:37:56.645 --> 00:37:57.900 kind of the classic problem.

NOTE Confidence: 0.98830926

00:37:57.900 --> 00:37:59.680 Here's a very poorly differentiated

NOTE Confidence: 0.98677945

00:38:00.700 --> 00:38:01.200 malignancy.

NOTE Confidence: 0.98863816

00:38:01.500 --> 00:38:02.940 What could it be? Is

NOTE Confidence: 0.98863816

00:38:02.940 --> 00:38:05.739 it carcinoma, melanoma, sarcoma, something

NOTE Confidence: 0.98863816

00:38:05.739 --> 00:38:06.239 else?

NOTE Confidence: 0.9403031

00:38:06.540 --> 00:38:07.520 We do immunohistochemistry

NOTE Confidence: 0.83663577

00:38:08.619 --> 00:38:10.079 and everything is negative.

NOTE Confidence: 0.9994285

00:38:10.755 --> 00:38:11.654 So we're stuck.

NOTE Confidence: 0.9994288

00:38:12.355 --> 00:38:13.575 We have an undifferentiated

NOTE Confidence: 0.9957263

00:38:14.275 --> 00:38:15.335 malignant neoplasm,

NOTE Confidence: 0.9845759

00:38:16.035 --> 00:38:17.714 which is the oncologist's favorite

NOTE Confidence: 0.9845759

00:38:17.714 --> 00:38:18.214 diagnosis.

NOTE Confidence: 0.93844956

00:38:19.394 --> 00:38:20.694 When you make the diagnosis,

NOTE Confidence: 0.97484857

00:38:21.234 --> 00:38:22.515 they're totally fine. They know

NOTE Confidence: 0.97484857

00:38:22.515 --> 00:38:23.394 what to do. That's a

NOTE Confidence: 0.97484857

00:38:23.394 --> 00:38:24.994 joke because it's a really

NOTE Confidence: 0.97484857

00:38:24.994 --> 00:38:25.734 big problem.

NOTE Confidence: 0.9752313

00:38:26.520 --> 00:38:28.040 But in this case, we

NOTE Confidence: 0.9752313

00:38:28.040 --> 00:38:29.180 did one other marker,

NOTE Confidence: 0.9774338

00:38:29.800 --> 00:38:31.820 which was the BRAF V600E

NOTE Confidence: 0.97773373

00:38:32.360 --> 00:38:33.260 specific antibody.

NOTE Confidence: 0.9853409

00:38:33.640 --> 00:38:34.600 And as you can see,

NOTE Confidence: 0.9853409

00:38:34.600 --> 00:38:36.440 it's beautifully positive in the

NOTE Confidence: 0.9853409

00:38:36.440 --> 00:38:38.219 cytoplasm of these tumor cells.

NOTE Confidence: 0.94320536

00:38:38.680 --> 00:38:39.800 And this is in fact

NOTE Confidence: 0.94320536

00:38:39.800 --> 00:38:41.020 metastatic dedifferentiated

NOTE Confidence: 0.99871683

00:38:41.400 --> 00:38:41.900 melanoma.

NOTE Confidence: 0.9984833

00:38:42.675 --> 00:38:43.875 And what the surgeon didn't

NOTE Confidence: 0.9984833

00:38:43.875 --> 00:38:45.155 know is this patient actually

NOTE Confidence: 0.9984833

00:38:45.155 --> 00:38:45.975 had a history

NOTE Confidence: 0.9501989

00:38:46.515 --> 00:38:48.135 of a locally advanced melanoma,

NOTE Confidence: 0.9501989

00:38:48.275 --> 00:38:49.555 like fifteen years ago, I

NOTE Confidence: 0.9501989

00:38:49.555 --> 00:38:51.075 think, on the back, but

NOTE Confidence: 0.9501989

00:38:51.075 --> 00:38:52.675 nobody knew, but we're able

NOTE Confidence: 0.9501989

00:38:52.675 --> 00:38:53.875 to solve it by this

NOTE Confidence: 0.9501989

00:38:53.875 --> 00:38:54.375 antibody.

NOTE Confidence: 0.9995425

00:38:54.880 --> 00:38:56.099 And this is a relatively

NOTE Confidence: 0.9995425

00:38:56.239 --> 00:38:56.739 new

NOTE Confidence: 0.9996835

00:38:57.119 --> 00:38:57.619 discovery

NOTE Confidence: 0.99214244

00:38:58.239 --> 00:39:00.320 that there are a small

NOTE Confidence: 0.99214244

00:39:00.320 --> 00:39:00.820 subset

NOTE Confidence: 0.9127447

00:39:01.440 --> 00:39:03.680 of melanomas, usually metastatic but

NOTE Confidence: 0.9127447

00:39:03.680 --> 00:39:04.820 occasionally primary,

NOTE Confidence: 0.9716564

00:39:05.200 --> 00:39:07.515 that are entirely negative for

NOTE Confidence: 0.9716564

00:39:07.515 --> 00:39:09.434 all the lineage markers. They

NOTE Confidence: 0.9716564

00:39:09.434 --> 00:39:11.355 don't express any neural crest

NOTE Confidence: 0.9716564

00:39:11.355 --> 00:39:12.815 markers or any melanoma

NOTE Confidence: 0.9444219

00:39:13.434 --> 00:39:14.494 restricted antibodies.

NOTE Confidence: 0.9422948

00:39:14.954 --> 00:39:15.454 S100,

NOTE Confidence: 0.8862963

00:39:15.755 --> 00:39:18.155 Sox10, HMB, Melanate, tyrosines, they're

NOTE Confidence: 0.8862963

00:39:18.155 --> 00:39:18.815 all negative.

NOTE Confidence: 0.9988643

00:39:19.290 --> 00:39:20.810 And that's really difficult. This

NOTE Confidence: 0.9988643

00:39:20.810 --> 00:39:22.190 is a challenging diagnosis.

NOTE Confidence: 0.99914604

00:39:22.969 --> 00:39:23.710 If they're

NOTE Confidence: 0.9998896

00:39:24.090 --> 00:39:25.310 entirely undifferentiated

NOTE Confidence: 0.9981116

00:39:25.690 --> 00:39:26.730 from the beginning, then we

NOTE Confidence: 0.9981116

00:39:26.730 --> 00:39:27.630 call them undifferentiated

NOTE Confidence: 0.9978704

00:39:28.010 --> 00:39:28.510 melanoma.

NOTE Confidence: 0.96809983

00:39:29.210 --> 00:39:30.330 If they started off with

NOTE Confidence: 0.96809983

00:39:30.330 --> 00:39:31.630 a conventional melanoma

NOTE Confidence: 0.98972815

00:39:32.105 --> 00:39:33.224 and then it recurred or

NOTE Confidence: 0.98972815

00:39:33.224 --> 00:39:35.065 metastasized and lost its markers,

NOTE Confidence: 0.98972815

00:39:35.065 --> 00:39:35.724 we call

NOTE Confidence: 0.9930247

00:39:36.025 --> 00:39:36.605 them dedifferentiated

NOTE Confidence: 0.99848795

00:39:37.145 --> 00:39:37.645 melanoma.

NOTE Confidence: 0.9788813

00:39:38.744 --> 00:39:39.944 And one of the best

NOTE Confidence: 0.9788813

00:39:39.944 --> 00:39:41.305 early studies on this topic

NOTE Confidence: 0.9788813

00:39:41.305 --> 00:39:43.244 was from Abbas Agami from

NOTE Confidence: 0.9788813

00:39:43.305 --> 00:39:43.805 Germany

NOTE Confidence: 0.98937833

00:39:44.400 --> 00:39:45.680 who published a series of

NOTE Confidence: 0.98937833

00:39:45.680 --> 00:39:46.960 these tumors and really talked

NOTE Confidence: 0.98937833

00:39:46.960 --> 00:39:47.460 about

NOTE Confidence: 0.99258393

00:39:47.839 --> 00:39:49.200 how we can recognize them

NOTE Confidence: 0.99258393

00:39:49.200 --> 00:39:50.960 in surgical pathology, what testing

NOTE Confidence: 0.99258393

00:39:50.960 --> 00:39:51.859 we can do

NOTE Confidence: 0.9915722

00:39:52.160 --> 00:39:53.059 to help us.

NOTE Confidence: 0.98088634

00:39:53.599 --> 00:39:55.380 There was a nice genomic

NOTE Confidence: 0.98088634

00:39:55.520 --> 00:39:56.900 study by David Adams,

NOTE Confidence: 0.7589676

00:39:57.520 --> 00:39:58.900 from United Kingdom,

NOTE Confidence: 0.9991392

00:39:59.344 --> 00:40:01.285 which had very similar observations

NOTE Confidence: 0.9991392

00:40:01.344 --> 00:40:02.964 with some more genomic testing.

NOTE Confidence: 0.974294

00:40:04.704 --> 00:40:06.385 And as I mentioned, until

NOTE Confidence: 0.974294

00:40:06.385 --> 00:40:08.005 we had this concept,

NOTE Confidence: 0.99017864

00:40:08.625 --> 00:40:10.065 we're often left with this

NOTE Confidence: 0.99017864

00:40:10.065 --> 00:40:12.404 descriptive, horrible, unhelpful diagnosis.

NOTE Confidence: 0.99867356

00:40:13.410 --> 00:40:14.869 The clues to the diagnosis

NOTE Confidence: 0.9880514

00:40:15.329 --> 00:40:17.430 sometimes are the anatomic site.

NOTE Confidence: 0.9860608

00:40:17.809 --> 00:40:19.329 The axilla is a very

NOTE Confidence: 0.9860608

00:40:19.329 --> 00:40:20.790 rare site for sarcomas,

NOTE Confidence: 0.9986993

00:40:21.489 --> 00:40:22.849 but it's a very common

NOTE Confidence: 0.9986993

00:40:22.849 --> 00:40:24.309 site for the first presentation

NOTE Confidence: 0.98866314

00:40:25.010 --> 00:40:27.170 of metastatic melanoma to a

NOTE Confidence: 0.98866314

00:40:27.170 --> 00:40:27.989 lymph node.

NOTE Confidence: 0.96253747

00:40:28.795 --> 00:40:30.895 Sometimes these tumors have rhabdoid

NOTE Confidence: 0.96253747

00:40:31.035 --> 00:40:32.415 cytology. In fact,

NOTE Confidence: 0.997718

00:40:32.875 --> 00:40:34.815 in adult malignant neoplasms,

NOTE Confidence: 0.9958935

00:40:35.594 --> 00:40:37.275 the most common tumor with

NOTE Confidence: 0.9958935

00:40:37.275 --> 00:40:39.695 rhabdoid cytoplasmic inclusions is metastatic

NOTE Confidence: 0.9958935

00:40:39.835 --> 00:40:40.335 melanoma.

NOTE Confidence: 0.9908932

00:40:40.715 --> 00:40:41.515 So that can be a

NOTE Confidence: 0.9908932

00:40:41.515 --> 00:40:42.015 clue.

NOTE Confidence: 0.99955976

00:40:42.700 --> 00:40:44.800 If you do genomic testing,

NOTE Confidence: 0.9983843

00:40:45.500 --> 00:40:47.040 you can find the characteristic

NOTE Confidence: 0.9444835

00:40:47.340 --> 00:40:48.560 mutations of melanoma.

NOTE Confidence: 0.91234934

00:40:49.260 --> 00:40:52.000 BRAF, NRAS, KIT, NF one,

NOTE Confidence: 0.95685476

00:40:52.460 --> 00:40:53.120 the other,

NOTE Confidence: 0.98554194

00:40:53.580 --> 00:40:55.200 alterations you see in melanoma.

NOTE Confidence: 0.9629334

00:40:55.864 --> 00:40:56.744 And if you use a

NOTE Confidence: 0.9629334

00:40:56.744 --> 00:40:58.265 large panel that in part

NOTE Confidence: 0.9629334

00:40:58.265 --> 00:40:59.545 of the algorithms, they will

NOTE Confidence: 0.9629334

00:40:59.545 --> 00:41:02.364 read out particular mutation signatures.

NOTE Confidence: 0.94248295

00:41:03.065 --> 00:41:04.184 You can find a UV

NOTE Confidence: 0.94248295

00:41:04.184 --> 00:41:05.785 signature and you know that

NOTE Confidence: 0.94248295

00:41:05.785 --> 00:41:07.625 it's metastatic melanoma and it's

NOTE Confidence: 0.94248295

00:41:07.625 --> 00:41:08.444 not a sarcoma.

NOTE Confidence: 0.9631529

00:41:09.510 --> 00:41:10.469 And I've shown you how

NOTE Confidence: 0.9631529

00:41:10.469 --> 00:41:12.330 we have mutation specific immunohistochemistry.

NOTE Confidence: 0.99071026

00:41:13.350 --> 00:41:14.550 Just a few more quick

NOTE Confidence: 0.99071026

00:41:14.550 --> 00:41:15.050 examples.

NOTE Confidence: 0.9862411

00:41:15.430 --> 00:41:17.110 This was an axillary mass

NOTE Confidence: 0.9862411

00:41:17.110 --> 00:41:18.310 in a patient with no

NOTE Confidence: 0.9862411

00:41:18.310 --> 00:41:18.810 known

NOTE Confidence: 0.9541857

00:41:19.110 --> 00:41:19.610 history,

NOTE Confidence: 0.99762964

00:41:20.150 --> 00:41:20.969 an undifferentiated

NOTE Confidence: 0.95694214

00:41:21.670 --> 00:41:22.489 sheet like

NOTE Confidence: 0.9761764

00:41:22.994 --> 00:41:26.114 epithelioid malignant neoplasm with open

NOTE Confidence: 0.9761764

00:41:26.114 --> 00:41:28.035 chromatin, small nucleoli, and lots

NOTE Confidence: 0.9761764

00:41:28.035 --> 00:41:29.255 of mitotic activity.

NOTE Confidence: 0.9274202

00:41:30.914 --> 00:41:32.194 The only stain that was

NOTE Confidence: 0.9274202

00:41:32.194 --> 00:41:33.714 positive was CAM five point

NOTE Confidence: 0.9274202

00:41:33.714 --> 00:41:34.214 two.

NOTE Confidence: 0.99722254

00:41:34.515 --> 00:41:36.035 This is a monoclonal antibody

NOTE Confidence: 0.99722254

00:41:36.035 --> 00:41:38.349 that recognizes keratin eight. It

NOTE Confidence: 0.99722254

00:41:38.349 --> 00:41:39.550 wasn't very strong, but there

NOTE Confidence: 0.99722254

00:41:39.550 --> 00:41:40.270 was a little bit of

NOTE Confidence: 0.99722254

00:41:40.270 --> 00:41:41.469 staining. So you could say,

NOTE Confidence: 0.99722254

00:41:41.469 --> 00:41:43.170 well, maybe it's an undifferentiated

NOTE Confidence: 0.9983886

00:41:43.469 --> 00:41:43.969 carcinoma.

NOTE Confidence: 0.96710455

00:41:44.270 --> 00:41:45.070 We got a little bit

NOTE Confidence: 0.96710455

00:41:45.070 --> 00:41:45.730 of keratin,

NOTE Confidence: 0.9453546

00:41:46.349 --> 00:41:48.030 but, unfortunately, that was wrong.

NOTE Confidence: 0.9453546

00:41:48.030 --> 00:41:49.329 It had PRAME expression

NOTE Confidence: 0.94979846

00:41:49.869 --> 00:41:51.310 as well as RAS q

NOTE Confidence: 0.94979846

00:41:51.310 --> 00:41:53.055 sixty one r, and this

NOTE Confidence: 0.94979846

00:41:53.055 --> 00:41:55.474 is a metastatic undifferentiated melanoma.

NOTE Confidence: 0.8909919

00:41:55.855 --> 00:41:56.755 And occasionally,

NOTE Confidence: 0.99755144

00:41:57.535 --> 00:41:59.454 metastatic melanomas can have some

NOTE Confidence: 0.99755144

00:41:59.454 --> 00:42:00.594 expression of keratins.

NOTE Confidence: 0.98105884

00:42:01.055 --> 00:42:02.515 It's a well known diagnostic

NOTE Confidence: 0.98105884

00:42:02.575 --> 00:42:03.714 pitfall for dometopathologists,

NOTE Confidence: 0.99927014

00:42:04.734 --> 00:42:06.255 but it's definitely a source

NOTE Confidence: 0.99927014

00:42:06.255 --> 00:42:06.755 of

NOTE Confidence: 0.9994369

00:42:07.210 --> 00:42:09.050 challenge for us in surgical

NOTE Confidence: 0.9994369

00:42:09.050 --> 00:42:09.550 pathology.

NOTE Confidence: 0.98912007

00:42:11.130 --> 00:42:12.489 One other example, this was

NOTE Confidence: 0.98912007

00:42:12.489 --> 00:42:14.330 an undifferentiated melanoma in an

NOTE Confidence: 0.98912007

00:42:14.330 --> 00:42:16.750 axillary lymph node. This tumor

NOTE Confidence: 0.98912007

00:42:16.969 --> 00:42:18.590 had some rhabdoid cytoplasmic

NOTE Confidence: 0.81191534

00:42:18.969 --> 00:42:19.469 conclusions.

NOTE Confidence: 0.83624464

00:42:19.844 --> 00:42:21.364 By meus to chemistry, it

NOTE Confidence: 0.83624464

00:42:21.364 --> 00:42:23.065 reacted with absolutely nothing

NOTE Confidence: 0.9234909

00:42:23.525 --> 00:42:25.305 except for BRAF V600E.

NOTE Confidence: 0.9801072

00:42:28.165 --> 00:42:29.545 One other nice example,

NOTE Confidence: 0.9676424

00:42:30.005 --> 00:42:31.864 Adrian Flanagan from London

NOTE Confidence: 0.86323225

00:42:32.369 --> 00:42:33.989 discovered in two thousand thirteen,

NOTE Confidence: 0.979964

00:42:34.690 --> 00:42:36.130 the giant cell tumors of

NOTE Confidence: 0.979964

00:42:36.130 --> 00:42:36.630 bone

NOTE Confidence: 0.89960176

00:42:37.170 --> 00:42:38.230 and chondroblastoma.

NOTE Confidence: 0.9984535

00:42:38.769 --> 00:42:39.829 These are the two

NOTE Confidence: 0.99464566

00:42:40.130 --> 00:42:41.269 very well known

NOTE Confidence: 0.9399475

00:42:41.730 --> 00:42:43.569 locally aggressive tumors that arise

NOTE Confidence: 0.9399475

00:42:43.569 --> 00:42:44.930 in the epiphysis of long

NOTE Confidence: 0.9399475

00:42:44.930 --> 00:42:45.430 bones,

NOTE Confidence: 0.9972344

00:42:46.395 --> 00:42:47.135 harbor mutations

NOTE Confidence: 0.932762

00:42:48.075 --> 00:42:49.935 in histone H3 genes,

NOTE Confidence: 0.9871683

00:42:50.395 --> 00:42:52.075 the same gene that encodes

NOTE Confidence: 0.9871683

00:42:52.075 --> 00:42:53.455 the histone three protein

NOTE Confidence: 0.97525793

00:42:53.835 --> 00:42:54.815 that is trimethylated

NOTE Confidence: 0.94723326

00:42:55.915 --> 00:42:56.415 in

NOTE Confidence: 0.89343584

00:42:57.275 --> 00:42:58.715 loss of the trimethylation in

NOTE Confidence: 0.89343584

00:42:58.715 --> 00:43:00.270 malignant peripheral nerve root tumor.

NOTE Confidence: 0.95811385

00:43:00.750 --> 00:43:02.030 But in this case, there's

NOTE Confidence: 0.95811385

00:43:02.030 --> 00:43:03.410 amino acid substitutions.

NOTE Confidence: 0.97431546

00:43:04.430 --> 00:43:06.750 One particular substitution, g thirty

NOTE Confidence: 0.97431546

00:43:06.750 --> 00:43:07.570 four w,

NOTE Confidence: 0.995947

00:43:07.950 --> 00:43:09.310 is found in eighty five

NOTE Confidence: 0.995947

00:43:09.310 --> 00:43:10.670 to ninety percent of giant

NOTE Confidence: 0.995947

00:43:10.670 --> 00:43:12.510 cell tumors of bone. There's

NOTE Confidence: 0.995947

00:43:12.510 --> 00:43:13.489 a different substitution

NOTE Confidence: 0.99768966

00:43:13.790 --> 00:43:14.530 in chondroblastoma.

NOTE Confidence: 0.98712796

00:43:15.945 --> 00:43:17.645 In most cases, the diagnosis

NOTE Confidence: 0.98712796

00:43:17.785 --> 00:43:18.685 is pretty easy.

NOTE Confidence: 0.8752647

00:43:18.985 --> 00:43:20.364 Radiology is distinctive.

NOTE Confidence: 0.9993636

00:43:20.825 --> 00:43:21.965 We have mononuclear

NOTE Confidence: 0.98973656

00:43:22.265 --> 00:43:23.864 cells and huge numbers of

NOTE Confidence: 0.98973656

00:43:23.864 --> 00:43:26.285 osteoclasts that have very impressive

NOTE Confidence: 0.98973656

00:43:26.344 --> 00:43:27.405 numbers of nuclei.

NOTE Confidence: 0.9926728

00:43:27.945 --> 00:43:29.145 But if you're dealing with

NOTE Confidence: 0.9926728

00:43:29.145 --> 00:43:30.205 a small biopsy

NOTE Confidence: 0.99817175

00:43:30.670 --> 00:43:32.190 or the radiology is not

NOTE Confidence: 0.99817175

00:43:32.190 --> 00:43:33.250 entirely definitive,

NOTE Confidence: 0.99942476

00:43:33.550 --> 00:43:34.989 it's very useful to have

NOTE Confidence: 0.99942476

00:43:34.989 --> 00:43:35.650 a surrogate

NOTE Confidence: 0.9944157

00:43:35.950 --> 00:43:37.010 for these mutations.

NOTE Confidence: 0.90432817

00:43:37.550 --> 00:43:38.910 So now we use this

NOTE Confidence: 0.90432817

00:43:38.910 --> 00:43:39.890 histone H3G34W

NOTE Confidence: 0.9927224

00:43:41.870 --> 00:43:43.950 mutation specific antibody for giant

NOTE Confidence: 0.9927224

00:43:43.950 --> 00:43:45.170 cell tumor of bone.

NOTE Confidence: 0.9784479

00:43:45.545 --> 00:43:46.585 As you can see, the

NOTE Confidence: 0.9784479

00:43:46.585 --> 00:43:48.985 osteoclasts are not neoplastic, they're

NOTE Confidence: 0.9784479

00:43:48.985 --> 00:43:49.485 reactive.

NOTE Confidence: 0.99528605

00:43:49.945 --> 00:43:50.905 Even though we call it

NOTE Confidence: 0.99528605

00:43:50.905 --> 00:43:52.585 giant cell tumor, the giant

NOTE Confidence: 0.99528605

00:43:52.585 --> 00:43:54.045 cells are actually non neoplastic.

NOTE Confidence: 0.99528605

00:43:54.185 --> 00:43:55.785 It's the mononuclear cells that

NOTE Confidence: 0.99528605

00:43:55.785 --> 00:43:56.525 are positive,

NOTE Confidence: 0.99881655

00:43:56.905 --> 00:43:58.265 but it's really a very

NOTE Confidence: 0.99881655

00:43:58.265 --> 00:43:59.385 easy way to make the

NOTE Confidence: 0.99881655

00:43:59.385 --> 00:43:59.885 diagnosis.

NOTE Confidence: 0.99188435

00:44:01.050 --> 00:44:01.870 Very rarely,

NOTE Confidence: 0.930961

00:44:02.730 --> 00:44:04.170 giant cell tumors of bone

NOTE Confidence: 0.930961

00:44:04.170 --> 00:44:04.989 can transform

NOTE Confidence: 0.9749481

00:44:05.450 --> 00:44:06.750 to high grade sarcomas.

NOTE Confidence: 0.9968545

00:44:07.370 --> 00:44:08.590 They still retain

NOTE Confidence: 0.9924709

00:44:09.130 --> 00:44:09.870 the G34W

NOTE Confidence: 0.978687

00:44:10.570 --> 00:44:12.110 or other histone H3

NOTE Confidence: 0.97512513

00:44:12.650 --> 00:44:13.150 substitutions.

NOTE Confidence: 0.6872134

00:44:16.565 --> 00:44:17.045 Now,

NOTE Confidence: 0.948385

00:44:17.364 --> 00:44:18.805 mentioning again something that I

NOTE Confidence: 0.948385

00:44:18.885 --> 00:44:19.925 that we talked about this

NOTE Confidence: 0.948385

00:44:19.925 --> 00:44:21.204 morning in the resident slide

NOTE Confidence: 0.948385

00:44:21.204 --> 00:44:21.704 seminar.

NOTE Confidence: 0.99888355

00:44:22.085 --> 00:44:23.685 This is a fusion specific

NOTE Confidence: 0.99888355

00:44:23.685 --> 00:44:25.125 antibody that was developed for

NOTE Confidence: 0.99888355

00:44:25.125 --> 00:44:26.185 synovial sarcoma.

NOTE Confidence: 0.9958148

00:44:29.280 --> 00:44:31.200 Synovial sarcoma is quite common.

NOTE Confidence: 0.9958148

00:44:31.440 --> 00:44:32.400 As you all know, it's

NOTE Confidence: 0.9958148

00:44:32.400 --> 00:44:33.280 one of the ten most

NOTE Confidence: 0.9958148

00:44:33.280 --> 00:44:34.100 common sarcomas.

NOTE Confidence: 0.9915344

00:44:34.720 --> 00:44:35.860 It's quite aggressive.

NOTE Confidence: 0.9299283

00:44:36.320 --> 00:44:37.520 The ten year survival is

NOTE Confidence: 0.9299283

00:44:37.520 --> 00:44:38.660 about fifty percent,

NOTE Confidence: 0.9557999

00:44:39.815 --> 00:44:41.174 and it's defined by a

NOTE Confidence: 0.9557999

00:44:41.174 --> 00:44:42.634 pathic mnemonic translocation

NOTE Confidence: 0.9757592

00:44:43.494 --> 00:44:45.515 between chromosomes X and eighteen.

NOTE Confidence: 0.994082

00:44:46.134 --> 00:44:47.894 This results in fusions of

NOTE Confidence: 0.994082

00:44:47.894 --> 00:44:49.654 genes that have changed their

NOTE Confidence: 0.994082

00:44:49.654 --> 00:44:50.614 names a bit over the

NOTE Confidence: 0.994082

00:44:50.614 --> 00:44:51.114 years.

NOTE Confidence: 0.9679881

00:44:51.430 --> 00:44:53.110 They're now named after the

NOTE Confidence: 0.9679881

00:44:53.110 --> 00:44:54.790 tumor type and the chromosome.

NOTE Confidence: 0.9679881

00:44:54.790 --> 00:44:56.010 So they're easy to remember.

NOTE Confidence: 0.9064367

00:44:56.630 --> 00:44:57.130 SS18

NOTE Confidence: 0.92965305

00:44:57.590 --> 00:44:59.530 and SSX. Synovial sarcoma

NOTE Confidence: 0.9261647

00:44:59.910 --> 00:45:01.930 on chromosomes eighteen and chromosomes

NOTE Confidence: 0.9261647

00:45:02.070 --> 00:45:02.570 X.

NOTE Confidence: 0.9576171

00:45:03.110 --> 00:45:04.730 We have three different variants,

NOTE Confidence: 0.9576171

00:45:04.994 --> 00:45:06.515 monophasic, which is a spindle

NOTE Confidence: 0.9576171

00:45:06.515 --> 00:45:07.335 cell neoplasm,

NOTE Confidence: 0.9679735

00:45:08.114 --> 00:45:10.134 biphasic that contains epithelial

NOTE Confidence: 0.8124651

00:45:10.434 --> 00:45:10.934 glands,

NOTE Confidence: 0.99734324

00:45:11.474 --> 00:45:13.474 and poorly differentiated that has

NOTE Confidence: 0.99734324

00:45:13.474 --> 00:45:14.535 round cell morphology

NOTE Confidence: 0.96819496

00:45:15.234 --> 00:45:16.594 that can be very difficult

NOTE Confidence: 0.96819496

00:45:16.594 --> 00:45:17.255 to distinguish

NOTE Confidence: 0.97490877

00:45:17.714 --> 00:45:19.315 from Ewing's sarcoma and other

NOTE Confidence: 0.97490877

00:45:19.315 --> 00:45:20.454 round cell sarcomas.

NOTE Confidence: 0.9956168

00:45:20.980 --> 00:45:23.140 And conventional markers are really

NOTE Confidence: 0.9956168

00:45:23.140 --> 00:45:24.120 not very helpful

NOTE Confidence: 0.9714346

00:45:24.500 --> 00:45:26.280 to diagnose synovial sarcoma.

NOTE Confidence: 0.9512323

00:45:26.660 --> 00:45:28.260 And until quite recently in

NOTE Confidence: 0.9512323

00:45:28.260 --> 00:45:29.160 most practices,

NOTE Confidence: 0.98459524

00:45:29.860 --> 00:45:31.400 we would confirm the diagnosis

NOTE Confidence: 0.98459524

00:45:31.620 --> 00:45:33.400 by sequencing or by FISH

NOTE Confidence: 0.98459524

00:45:33.695 --> 00:45:34.815 to look for the fusion

NOTE Confidence: 0.98459524

00:45:34.815 --> 00:45:36.515 or the SS18 rearrangement.

NOTE Confidence: 0.89967203

00:45:37.855 --> 00:45:38.815 And a couple of years

NOTE Confidence: 0.89967203

00:45:38.815 --> 00:45:39.935 ago, we worked with a

NOTE Confidence: 0.89967203

00:45:39.935 --> 00:45:41.955 colleague, Segal Kadoch, who's a

NOTE Confidence: 0.89967203

00:45:42.175 --> 00:45:42.675 scientist,

NOTE Confidence: 0.97219735

00:45:42.975 --> 00:45:44.415 at the Dana Farber Cancer

NOTE Confidence: 0.97219735

00:45:44.415 --> 00:45:44.915 Institute.

NOTE Confidence: 0.9207768

00:45:45.295 --> 00:45:46.494 When Segal was a post

NOTE Confidence: 0.9207768

00:45:46.494 --> 00:45:47.935 doc at Stanford before she

NOTE Confidence: 0.9207768

00:45:47.935 --> 00:45:49.750 joined the faculty at Dana

NOTE Confidence: 0.9207768

00:45:49.750 --> 00:45:50.250 Farber,

NOTE Confidence: 0.99955815

00:45:50.550 --> 00:45:52.570 she discovered the mechanism of

NOTE Confidence: 0.83850795

00:45:52.870 --> 00:45:54.250 transformation of cells

NOTE Confidence: 0.966845

00:45:54.710 --> 00:45:56.470 by the synovial sarcoma fusion

NOTE Confidence: 0.966845

00:45:56.470 --> 00:45:56.970 protein,

NOTE Confidence: 0.956243

00:45:57.350 --> 00:45:58.470 and she's become one of

NOTE Confidence: 0.956243

00:45:58.470 --> 00:45:59.830 the world experts in the

NOTE Confidence: 0.956243

00:45:59.830 --> 00:46:00.330 SWISNF

NOTE Confidence: 0.98380035

00:46:00.950 --> 00:46:02.650 chromatin remodeling complex.

NOTE Confidence: 0.9975591

00:46:03.110 --> 00:46:03.770 And she

NOTE Confidence: 0.9991617

00:46:05.015 --> 00:46:05.515 recommended

NOTE Confidence: 0.98703414

00:46:05.895 --> 00:46:07.655 amino acid sequences to use

NOTE Confidence: 0.98703414

00:46:07.655 --> 00:46:08.875 to immunize animals

NOTE Confidence: 0.9575839

00:46:09.335 --> 00:46:11.335 to develop these monoclonal antibodies.

NOTE Confidence: 0.9575839

00:46:11.335 --> 00:46:12.855 And, essentially, we were just

NOTE Confidence: 0.9575839

00:46:12.855 --> 00:46:13.895 a test lab for these

NOTE Confidence: 0.9575839

00:46:13.895 --> 00:46:14.395 antibodies.

NOTE Confidence: 0.9852993

00:46:14.775 --> 00:46:16.055 The company she worked with

NOTE Confidence: 0.9852993

00:46:16.055 --> 00:46:17.655 kept sending us aliquots of

NOTE Confidence: 0.9852993

00:46:17.655 --> 00:46:18.315 the antibodies

NOTE Confidence: 0.9790722

00:46:18.849 --> 00:46:20.450 that worked beautifully in Western

NOTE Confidence: 0.9790722

00:46:20.450 --> 00:46:21.890 blot, but most of them

NOTE Confidence: 0.9790722

00:46:21.890 --> 00:46:22.849 didn't work at all. We

NOTE Confidence: 0.9790722

00:46:22.849 --> 00:46:24.210 couldn't optimize them to get

NOTE Confidence: 0.9790722

00:46:24.210 --> 00:46:24.950 any signal

NOTE Confidence: 0.8559023

00:46:25.250 --> 00:46:26.609 in formal and fixed paraffin

NOTE Confidence: 0.8559023

00:46:26.609 --> 00:46:28.150 embedded tissue administered chemistry.

NOTE Confidence: 0.9357127

00:46:28.609 --> 00:46:29.349 And eventually,

NOTE Confidence: 0.99883753

00:46:30.369 --> 00:46:31.190 in late

NOTE Confidence: 0.666649

00:46:31.489 --> 00:46:31.989 nineteen,

NOTE Confidence: 0.7954393

00:46:32.849 --> 00:46:33.910 two thousand nineteen,

NOTE Confidence: 0.9553844

00:46:34.445 --> 00:46:35.265 we finally,

NOTE Confidence: 0.9935638

00:46:35.645 --> 00:46:37.085 uncovered two of their antibodies

NOTE Confidence: 0.9935638

00:46:37.085 --> 00:46:37.985 that worked beautifully.

NOTE Confidence: 0.9809722

00:46:38.605 --> 00:46:39.325 One of them is a

NOTE Confidence: 0.9809722

00:46:39.325 --> 00:46:41.485 fusion antibody that recognizes the

NOTE Confidence: 0.9809722

00:46:41.485 --> 00:46:42.705 sequence that crosses

NOTE Confidence: 0.93139654

00:46:43.244 --> 00:46:44.605 the break point between the

NOTE Confidence: 0.93139654

00:46:44.605 --> 00:46:45.344 two genes,

NOTE Confidence: 0.9712576

00:46:45.965 --> 00:46:47.725 which was ninety five percent

NOTE Confidence: 0.9712576

00:46:47.725 --> 00:46:49.265 sensitive and a hundred percent

NOTE Confidence: 0.9712576

00:46:49.325 --> 00:46:49.825 specific

NOTE Confidence: 0.99634886

00:46:50.180 --> 00:46:51.620 in this study that included

NOTE Confidence: 0.99634886

00:46:51.620 --> 00:46:52.520 a range of

NOTE Confidence: 0.99052614

00:46:52.820 --> 00:46:54.520 potential histologic mimics.

NOTE Confidence: 0.99687725

00:46:54.980 --> 00:46:56.340 And we also found one

NOTE Confidence: 0.99687725

00:46:56.340 --> 00:46:57.239 of their antibodies

NOTE Confidence: 0.9735649

00:46:57.860 --> 00:46:59.880 directed against a conserved sequence

NOTE Confidence: 0.97839385

00:47:00.340 --> 00:47:01.860 at the C terminus of

NOTE Confidence: 0.97839385

00:47:01.860 --> 00:47:03.765 all the SSX proteins was

NOTE Confidence: 0.95864826

00:47:04.305 --> 00:47:06.485 the opposite. Hundred percent sensitive

NOTE Confidence: 0.95864826

00:47:06.785 --> 00:47:08.065 and a little bit less

NOTE Confidence: 0.95864826

00:47:08.065 --> 00:47:08.565 specific.

NOTE Confidence: 0.99630857

00:47:09.185 --> 00:47:10.325 And it works beautifully.

NOTE Confidence: 0.9803285

00:47:11.105 --> 00:47:12.545 So this is genetic testing.

NOTE Confidence: 0.9803285

00:47:12.545 --> 00:47:14.225 We're looking for the fusion

NOTE Confidence: 0.9803285

00:47:14.225 --> 00:47:14.725 protein.

NOTE Confidence: 0.98029995

00:47:15.359 --> 00:47:16.960 And every single nucleus is

NOTE Confidence: 0.98029995

00:47:16.960 --> 00:47:18.420 positive because it's a genomic

NOTE Confidence: 0.98029995

00:47:18.559 --> 00:47:19.059 alteration

NOTE Confidence: 0.99714607

00:47:19.680 --> 00:47:20.660 in these cells.

NOTE Confidence: 0.9939049

00:47:20.960 --> 00:47:23.059 This is classic monophasic synovial

NOTE Confidence: 0.9939049

00:47:23.119 --> 00:47:23.619 sarcoma,

NOTE Confidence: 0.9861662

00:47:24.239 --> 00:47:26.259 very cellular spindle cell neoplasm

NOTE Confidence: 0.9861662

00:47:26.400 --> 00:47:27.440 that, as one of the

NOTE Confidence: 0.9861662

00:47:27.440 --> 00:47:29.059 residents described this morning,

NOTE Confidence: 0.9830437

00:47:29.364 --> 00:47:31.364 very little cytoplasm. They're almost

NOTE Confidence: 0.9830437

00:47:31.364 --> 00:47:32.425 overlapping nuclei.

NOTE Confidence: 0.99316657

00:47:32.805 --> 00:47:34.085 They often have these little

NOTE Confidence: 0.99316657

00:47:34.085 --> 00:47:34.985 wiry collagen

NOTE Confidence: 0.97071505

00:47:35.285 --> 00:47:36.825 bundles between the cells.

NOTE Confidence: 0.9998387

00:47:37.364 --> 00:47:38.425 Beautiful reactivity

NOTE Confidence: 0.99698114

00:47:39.125 --> 00:47:39.785 with the

NOTE Confidence: 0.84883237

00:47:40.325 --> 00:47:40.825 SS18SSX

NOTE Confidence: 0.9511017

00:47:41.605 --> 00:47:43.065 fusion specific antibody.

NOTE Confidence: 0.99891084

00:47:43.520 --> 00:47:45.140 And this is poorly differentiated

NOTE Confidence: 0.99891084

00:47:45.280 --> 00:47:46.420 synovial sarcoma

NOTE Confidence: 0.94408965

00:47:46.800 --> 00:47:48.400 that can look very similar

NOTE Confidence: 0.94408965

00:47:48.400 --> 00:47:50.239 to other high grade round

NOTE Confidence: 0.94408965

00:47:50.239 --> 00:47:51.060 cell sarcomas.

NOTE Confidence: 0.97665083

00:47:51.520 --> 00:47:53.040 And the fusion antibody is,

NOTE Confidence: 0.97665083

00:47:53.040 --> 00:47:54.420 again, beautifully positive.

NOTE Confidence: 0.98913926

00:47:56.744 --> 00:47:58.025 And finally, before I end,

NOTE Confidence: 0.98913926

00:47:58.025 --> 00:47:59.404 I'm just gonna talk about

NOTE Confidence: 0.91383624

00:47:59.704 --> 00:48:00.605 using immunohistochemistry

NOTE Confidence: 0.9983351

00:48:01.224 --> 00:48:01.964 to screen

NOTE Confidence: 0.9939105

00:48:02.344 --> 00:48:04.525 for familial predisposition syndromes.

NOTE Confidence: 0.97264814

00:48:05.145 --> 00:48:06.525 You all know about mismatch

NOTE Confidence: 0.97264814

00:48:06.664 --> 00:48:07.964 repair protein immunohistochemistry.

NOTE Confidence: 0.9994504

00:48:08.825 --> 00:48:09.944 We've been doing this for

NOTE Confidence: 0.9994504

00:48:09.944 --> 00:48:10.444 decades.

NOTE Confidence: 0.97664815

00:48:10.850 --> 00:48:12.210 This is a very useful

NOTE Confidence: 0.97664815

00:48:12.210 --> 00:48:13.410 way to screen for Lynch

NOTE Confidence: 0.97664815

00:48:13.410 --> 00:48:13.910 syndrome

NOTE Confidence: 0.87500906

00:48:14.370 --> 00:48:16.630 in colorectal endometrial adenocarcinoma,

NOTE Confidence: 0.99074167

00:48:17.730 --> 00:48:19.430 upper urinary tract adenocarcinomas,

NOTE Confidence: 0.97231305

00:48:19.969 --> 00:48:20.710 for example,

NOTE Confidence: 0.9765116

00:48:21.010 --> 00:48:22.130 the tumor types that are

NOTE Confidence: 0.9765116

00:48:22.130 --> 00:48:23.330 most common in patients with

NOTE Confidence: 0.9765116

00:48:23.330 --> 00:48:25.030 Lynch syndrome with germline mutations.

NOTE Confidence: 0.9759434

00:48:25.635 --> 00:48:26.755 And now that's become a

NOTE Confidence: 0.9759434

00:48:26.755 --> 00:48:28.614 huge area of surgical pathology

NOTE Confidence: 0.9759434

00:48:28.755 --> 00:48:29.255 practice.

NOTE Confidence: 0.995542

00:48:29.715 --> 00:48:30.775 Now that we have

NOTE Confidence: 0.99124163

00:48:31.155 --> 00:48:33.475 immune checkpoint inhibitor therapy, which

NOTE Confidence: 0.99124163

00:48:33.475 --> 00:48:34.614 is most effective

NOTE Confidence: 0.9927478

00:48:35.155 --> 00:48:36.835 for cancers that have mismatch

NOTE Confidence: 0.9927478

00:48:36.835 --> 00:48:37.815 repair deficiency

NOTE Confidence: 0.9464971

00:48:38.739 --> 00:48:39.940 outside of Lynch syndrome as

NOTE Confidence: 0.9464971

00:48:39.940 --> 00:48:41.800 well when they're sporadically inactivated

NOTE Confidence: 0.95922667

00:48:42.420 --> 00:48:43.700 either by methylation of the

NOTE Confidence: 0.95922667

00:48:43.700 --> 00:48:45.940 MLH1 promoter or by somatic

NOTE Confidence: 0.95922667

00:48:45.940 --> 00:48:47.239 mutations, for example.

NOTE Confidence: 0.99403405

00:48:47.540 --> 00:48:48.580 But we have a couple

NOTE Confidence: 0.99403405

00:48:48.580 --> 00:48:49.940 other examples of how we

NOTE Confidence: 0.99403405

00:48:49.940 --> 00:48:51.000 can use antibodies

NOTE Confidence: 0.99891216

00:48:51.780 --> 00:48:54.120 to screen for the potential

NOTE Confidence: 0.92437184

00:48:55.425 --> 00:48:57.185 alterations that that belies some

NOTE Confidence: 0.92437184

00:48:57.185 --> 00:48:58.005 of these other

NOTE Confidence: 0.8040544

00:48:58.625 --> 00:48:59.844 tumor syndromes.

NOTE Confidence: 0.97698426

00:49:00.385 --> 00:49:01.505 The one I'm gonna mention

NOTE Confidence: 0.97698426

00:49:01.505 --> 00:49:02.885 is succinate dehydrogenase.

NOTE Confidence: 0.97053

00:49:03.985 --> 00:49:05.425 We've known for quite some

NOTE Confidence: 0.97053

00:49:05.425 --> 00:49:07.665 time that patients with Kearney

NOTE Confidence: 0.97053

00:49:07.665 --> 00:49:08.165 Triad

NOTE Confidence: 0.94609046

00:49:08.850 --> 00:49:10.130 described by Aden Kearney at

NOTE Confidence: 0.94609046

00:49:10.130 --> 00:49:11.490 the Mayo Clinic in nineteen

NOTE Confidence: 0.94609046

00:49:11.490 --> 00:49:12.390 seventy seven,

NOTE Confidence: 0.93639445

00:49:13.010 --> 00:49:14.930 developed these three distinctive tumor

NOTE Confidence: 0.93639445

00:49:14.930 --> 00:49:15.430 types,

NOTE Confidence: 0.9896623

00:49:16.050 --> 00:49:17.750 unusual form of gastric

NOTE Confidence: 0.97196794

00:49:18.130 --> 00:49:18.630 gastrointestinal

NOTE Confidence: 0.948765

00:49:18.930 --> 00:49:20.310 stromal tumor or GIST,

NOTE Confidence: 0.9591624

00:49:20.934 --> 00:49:22.315 extra adrenal paraganglioma,

NOTE Confidence: 0.9945137

00:49:23.174 --> 00:49:24.635 and pulmonary chondroma.

NOTE Confidence: 0.98721963

00:49:25.414 --> 00:49:26.614 And we didn't really know

NOTE Confidence: 0.98721963

00:49:26.614 --> 00:49:27.815 why for many years. This

NOTE Confidence: 0.98721963

00:49:27.815 --> 00:49:29.355 is not a familial syndrome.

NOTE Confidence: 0.98721963

00:49:29.654 --> 00:49:31.174 It's sporadic, and it usually

NOTE Confidence: 0.98721963

00:49:31.174 --> 00:49:32.315 affects young women.

NOTE Confidence: 0.97867477

00:49:33.739 --> 00:49:34.859 About ten years ago, it

NOTE Confidence: 0.97867477

00:49:34.859 --> 00:49:35.599 was discovered

NOTE Confidence: 0.9941287

00:49:35.980 --> 00:49:37.599 that this is caused by

NOTE Confidence: 0.9791394

00:49:37.900 --> 00:49:38.400 hypermethylation

NOTE Confidence: 0.9447772

00:49:38.940 --> 00:49:40.480 of the SDHC promoter.

NOTE Confidence: 0.9987516

00:49:41.500 --> 00:49:42.940 There is a much more

NOTE Confidence: 0.9987516

00:49:42.940 --> 00:49:43.440 common

NOTE Confidence: 0.98004955

00:49:43.900 --> 00:49:45.039 familial paraganglioma

NOTE Confidence: 0.99495715

00:49:45.579 --> 00:49:47.805 syndrome, which is responsible for

NOTE Confidence: 0.99495715

00:49:47.805 --> 00:49:49.485 about twenty percent of all

NOTE Confidence: 0.99495715

00:49:49.485 --> 00:49:49.985 paragangliomas,

NOTE Confidence: 0.9825478

00:49:51.165 --> 00:49:52.945 which is caused by germline

NOTE Confidence: 0.9825478

00:49:53.005 --> 00:49:53.505 mutations

NOTE Confidence: 0.98820686

00:49:54.205 --> 00:49:55.425 in either SDHB,

NOTE Confidence: 0.9709856

00:49:55.805 --> 00:49:57.185 SDHC, or SDHD.

NOTE Confidence: 0.9793558

00:49:58.380 --> 00:50:00.000 This has very high penetrance,

NOTE Confidence: 0.9732753

00:50:00.539 --> 00:50:01.920 and you could use immunohistochemistry

NOTE Confidence: 0.95718217

00:50:02.380 --> 00:50:03.339 as a screen as I'll

NOTE Confidence: 0.95718217

00:50:03.339 --> 00:50:04.140 come back to in a

NOTE Confidence: 0.95718217

00:50:04.140 --> 00:50:04.799 few minutes.

NOTE Confidence: 0.9413435

00:50:05.260 --> 00:50:06.779 One other syndrome is called

NOTE Confidence: 0.9413435

00:50:06.779 --> 00:50:09.099 Kearney Stratakis, which is very

NOTE Confidence: 0.9413435

00:50:09.099 --> 00:50:11.025 similar to Kearney triad, except

NOTE Confidence: 0.9413435

00:50:11.265 --> 00:50:12.944 these patients do not develop

NOTE Confidence: 0.9413435

00:50:12.944 --> 00:50:14.085 pulmonary chondromas.

NOTE Confidence: 0.98872524

00:50:14.625 --> 00:50:15.825 And this is essentially just

NOTE Confidence: 0.98872524

00:50:15.825 --> 00:50:17.105 a variant of the familial

NOTE Confidence: 0.98872524

00:50:17.105 --> 00:50:17.605 paraganglioma

NOTE Confidence: 0.9608532

00:50:17.984 --> 00:50:19.904 syndrome where they also develop

NOTE Confidence: 0.9608532

00:50:19.904 --> 00:50:21.204 these distinctive gists.

NOTE Confidence: 0.9954162

00:50:22.944 --> 00:50:23.984 I'm sure many of you

NOTE Confidence: 0.9954162

00:50:23.984 --> 00:50:25.285 know in surgical pathology

NOTE Confidence: 0.9998867

00:50:25.890 --> 00:50:27.589 that we really can't predict

NOTE Confidence: 0.9828882

00:50:27.969 --> 00:50:28.869 which paragangliomas

NOTE Confidence: 0.9435438

00:50:29.250 --> 00:50:30.309 are going to be malignant.

NOTE Confidence: 0.99959445

00:50:30.690 --> 00:50:32.130 That's been something we've tried

NOTE Confidence: 0.99959445

00:50:32.130 --> 00:50:33.170 to deal with for many

NOTE Confidence: 0.99959445

00:50:33.170 --> 00:50:34.450 decades without a lot of

NOTE Confidence: 0.99959445

00:50:34.450 --> 00:50:34.950 success.

NOTE Confidence: 0.9995621

00:50:35.650 --> 00:50:36.710 It turns out

NOTE Confidence: 0.9818777

00:50:37.010 --> 00:50:37.750 the most

NOTE Confidence: 0.9135926

00:50:38.385 --> 00:50:40.545 powerful predictor of malignancy in

NOTE Confidence: 0.9135926

00:50:40.545 --> 00:50:41.045 paragangliomas

NOTE Confidence: 0.92106247

00:50:42.065 --> 00:50:43.125 is SDHB

NOTE Confidence: 0.6534275

00:50:43.425 --> 00:50:43.925 mutation,

NOTE Confidence: 0.92880166

00:50:44.545 --> 00:50:45.605 germline mutations.

NOTE Confidence: 0.9946749

00:50:46.305 --> 00:50:47.745 Patients with this syndrome who

NOTE Confidence: 0.9946749

00:50:47.745 --> 00:50:49.205 have that particular alteration

NOTE Confidence: 0.9713294

00:50:49.825 --> 00:50:51.125 have a risk of metastasis

NOTE Confidence: 0.9713294

00:50:51.185 --> 00:50:52.645 that's about fifty percent.

NOTE Confidence: 0.9975091

00:50:53.040 --> 00:50:54.820 There's also a very unusual

NOTE Confidence: 0.9853814

00:50:55.440 --> 00:50:57.620 kind of narrow anatomic distribution

NOTE Confidence: 0.95085895

00:50:58.480 --> 00:50:59.860 based on what the underlying,

NOTE Confidence: 0.9779932

00:51:00.960 --> 00:51:02.560 genetic alteration is, as you

NOTE Confidence: 0.9779932

00:51:02.560 --> 00:51:03.860 can see from this table.

NOTE Confidence: 0.99577624

00:51:07.065 --> 00:51:09.225 So it turns out that

NOTE Confidence: 0.99577624

00:51:09.225 --> 00:51:10.905 irrespective of which gene is

NOTE Confidence: 0.99577624

00:51:10.905 --> 00:51:11.405 mutated

NOTE Confidence: 0.9375665

00:51:12.025 --> 00:51:14.344 or if SDHC has promoter

NOTE Confidence: 0.9375665

00:51:14.344 --> 00:51:14.844 hypermethylation,

NOTE Confidence: 0.99288434

00:51:15.864 --> 00:51:16.685 the SDHB

NOTE Confidence: 0.99811155

00:51:16.985 --> 00:51:18.505 part of this enzyme complex

NOTE Confidence: 0.99811155

00:51:18.505 --> 00:51:19.244 gets degraded.

NOTE Confidence: 0.9830602

00:51:19.560 --> 00:51:21.239 It requires stability of all

NOTE Confidence: 0.9830602

00:51:21.239 --> 00:51:22.520 the elements in order for

NOTE Confidence: 0.9830602

00:51:22.520 --> 00:51:23.500 it to sit there.

NOTE Confidence: 0.9796809

00:51:23.800 --> 00:51:25.160 So you can use one

NOTE Confidence: 0.9796809

00:51:25.160 --> 00:51:26.460 antibody for SDHB

NOTE Confidence: 0.9746047

00:51:27.160 --> 00:51:28.520 as a surrogate for an

NOTE Confidence: 0.9746047

00:51:28.520 --> 00:51:30.060 inactivation of the complex.

NOTE Confidence: 0.9878289

00:51:30.360 --> 00:51:31.480 So this has now become

NOTE Confidence: 0.9878289

00:51:31.480 --> 00:51:32.780 a very easy way

NOTE Confidence: 0.9986869

00:51:33.114 --> 00:51:33.855 to screen

NOTE Confidence: 0.8750364

00:51:34.155 --> 00:51:35.614 for the familial paraganglioma

NOTE Confidence: 0.98953706

00:51:36.075 --> 00:51:36.575 syndrome.

NOTE Confidence: 0.9955769

00:51:37.114 --> 00:51:38.815 The first nice paper demonstrating

NOTE Confidence: 0.9955769

00:51:38.875 --> 00:51:39.835 how you might do this

NOTE Confidence: 0.9955769

00:51:39.835 --> 00:51:40.895 in clinical practice

NOTE Confidence: 0.96118456

00:51:41.355 --> 00:51:42.975 was published in Lancet Oncology

NOTE Confidence: 0.96118456

00:51:43.114 --> 00:51:43.835 by a group from the

NOTE Confidence: 0.96118456

00:51:43.835 --> 00:51:44.335 Netherlands,

NOTE Confidence: 0.9924756

00:51:45.114 --> 00:51:46.175 and this has become

NOTE Confidence: 0.99154925

00:51:46.780 --> 00:51:48.140 standard of practice for us

NOTE Confidence: 0.99154925

00:51:48.140 --> 00:51:48.640 now,

NOTE Confidence: 0.9245548

00:51:49.020 --> 00:51:51.340 in collaboration with, Justine Barletta,

NOTE Confidence: 0.9245548

00:51:51.340 --> 00:51:52.960 our head of endocrine pathology,

NOTE Confidence: 0.97380906

00:51:53.340 --> 00:51:54.620 and our colleagues at the

NOTE Confidence: 0.97380906

00:51:54.620 --> 00:51:55.120 genetics

NOTE Confidence: 0.9853055

00:51:55.740 --> 00:51:56.940 clinic at the Dana Farber

NOTE Confidence: 0.9853055

00:51:56.940 --> 00:51:57.840 Cancer Institute.

NOTE Confidence: 0.9741076

00:51:58.220 --> 00:51:59.680 Every patient with periganglioma

NOTE Confidence: 0.98506546

00:52:00.140 --> 00:52:00.800 or pheochromocytoma

NOTE Confidence: 0.9449445

00:52:01.935 --> 00:52:02.594 gets immunohistochemistry

NOTE Confidence: 0.96302736

00:52:03.135 --> 00:52:04.835 for SDHB as a screen

NOTE Confidence: 0.94897354

00:52:05.135 --> 00:52:06.415 to direct them for,

NOTE Confidence: 0.8008907

00:52:07.055 --> 00:52:08.114 germline testing.

NOTE Confidence: 0.9886994

00:52:08.975 --> 00:52:10.275 This is a pheochromocytoma

NOTE Confidence: 0.9817472

00:52:10.975 --> 00:52:12.094 of the adrenal gland with

NOTE Confidence: 0.9817472

00:52:12.094 --> 00:52:12.995 normal staining.

NOTE Confidence: 0.97250056

00:52:13.455 --> 00:52:14.594 It's this mitochondrial

NOTE Confidence: 0.9499714

00:52:14.975 --> 00:52:16.890 granular cytoplasmic pattern, as you

NOTE Confidence: 0.9499714

00:52:16.890 --> 00:52:17.869 can see here.

NOTE Confidence: 0.9887589

00:52:18.329 --> 00:52:19.630 This is an SDHB

NOTE Confidence: 0.732965

00:52:20.089 --> 00:52:21.069 mutants paraganglioma.

NOTE Confidence: 0.995165

00:52:22.329 --> 00:52:24.270 In contrast, the tumor cells

NOTE Confidence: 0.99899423

00:52:24.650 --> 00:52:26.089 show a complete loss of

NOTE Confidence: 0.99899423

00:52:26.089 --> 00:52:27.069 the normal cytoplasmic

NOTE Confidence: 0.9477281

00:52:27.450 --> 00:52:27.950 staining,

NOTE Confidence: 0.99239826

00:52:28.329 --> 00:52:29.549 whereas the endothelial

NOTE Confidence: 0.9974233

00:52:29.849 --> 00:52:30.349 cells

NOTE Confidence: 0.9504233

00:52:31.525 --> 00:52:32.344 and the sustentacular

NOTE Confidence: 0.98356164

00:52:32.805 --> 00:52:33.305 cells,

NOTE Confidence: 0.99434847

00:52:33.765 --> 00:52:35.605 those specialized Schwann cells that

NOTE Confidence: 0.99434847

00:52:35.605 --> 00:52:36.905 invest the individual

NOTE Confidence: 0.8748953

00:52:37.525 --> 00:52:39.065 zelbollen of the paraganglioma,

NOTE Confidence: 0.9911165

00:52:39.925 --> 00:52:41.864 show normal granular staining.

NOTE Confidence: 0.95575154

00:52:43.329 --> 00:52:44.690 As I mentioned, the gist

NOTE Confidence: 0.95575154

00:52:44.690 --> 00:52:46.210 that arise in the context

NOTE Confidence: 0.95575154

00:52:46.210 --> 00:52:47.510 of STH deficiency

NOTE Confidence: 0.9952724

00:52:48.290 --> 00:52:49.510 are really special.

NOTE Confidence: 0.89334965

00:52:50.130 --> 00:52:51.910 They have this multi nodular

NOTE Confidence: 0.89334965

00:52:52.050 --> 00:52:53.349 plexiform architecture,

NOTE Confidence: 0.99508125

00:52:53.969 --> 00:52:54.849 as you can see in

NOTE Confidence: 0.99508125

00:52:54.849 --> 00:52:56.210 the scanning images on the

NOTE Confidence: 0.99508125

00:52:56.210 --> 00:52:56.950 left and

NOTE Confidence: 0.99606943

00:52:57.305 --> 00:52:58.125 the intermediate power

NOTE Confidence: 0.97458696

00:52:58.425 --> 00:53:00.205 on the right, they're usually

NOTE Confidence: 0.97458696

00:53:00.345 --> 00:53:00.845 epithelioid

NOTE Confidence: 0.9814931

00:53:01.385 --> 00:53:02.505 and they have a very

NOTE Confidence: 0.9814931

00:53:02.505 --> 00:53:03.785 high rate of spreading to

NOTE Confidence: 0.9814931

00:53:03.785 --> 00:53:05.005 regional lymph nodes.

NOTE Confidence: 0.9995977

00:53:05.465 --> 00:53:07.405 About thirty percent of patients

NOTE Confidence: 0.9894635

00:53:07.705 --> 00:53:08.765 will have perigastric

NOTE Confidence: 0.8082768

00:53:09.065 --> 00:53:09.565 lymphometastases

NOTE Confidence: 0.9985092

00:53:10.665 --> 00:53:11.625 at the time of their

NOTE Confidence: 0.9985092

00:53:11.625 --> 00:53:12.605 partial gastrectomy.

NOTE Confidence: 0.9544411

00:53:13.359 --> 00:53:14.640 And this is in contrast

NOTE Confidence: 0.9544411

00:53:14.640 --> 00:53:16.020 to KIT mutant GIS,

NOTE Confidence: 0.9844458

00:53:16.320 --> 00:53:17.599 which spread to lymph nodes

NOTE Confidence: 0.9844458

00:53:17.599 --> 00:53:18.719 in about zero point one

NOTE Confidence: 0.9844458

00:53:18.719 --> 00:53:20.160 percent of cases. That's an

NOTE Confidence: 0.9844458

00:53:20.160 --> 00:53:21.460 incredibly rare event.

NOTE Confidence: 0.9981481

00:53:22.400 --> 00:53:23.219 These tumors

NOTE Confidence: 0.9769249

00:53:23.760 --> 00:53:25.219 very frequently metastasize

NOTE Confidence: 0.9792624

00:53:26.079 --> 00:53:27.599 to the perineal cavity or

NOTE Confidence: 0.9792624

00:53:27.599 --> 00:53:29.244 the liver, but they have

NOTE Confidence: 0.9792624

00:53:29.244 --> 00:53:31.165 a relatively indolent growth, and

NOTE Confidence: 0.9792624

00:53:31.165 --> 00:53:32.545 some patients can survive

NOTE Confidence: 0.99127346

00:53:33.244 --> 00:53:35.885 for years without therapy, without

NOTE Confidence: 0.99127346

00:53:35.885 --> 00:53:36.385 getting

NOTE Confidence: 0.9966565

00:53:36.844 --> 00:53:38.925 really sick. Unfortunately, many of

NOTE Confidence: 0.9966565

00:53:38.925 --> 00:53:40.285 them eventually succumb, but they

NOTE Confidence: 0.9966565

00:53:40.285 --> 00:53:41.985 can have a protracted course,

NOTE Confidence: 0.93897986

00:53:42.300 --> 00:53:43.900 which is totally different from

NOTE Confidence: 0.93897986

00:53:43.900 --> 00:53:44.880 KIT mutant GIS

NOTE Confidence: 0.93784356

00:53:45.180 --> 00:53:47.100 without targeted therapy. Once they

NOTE Confidence: 0.93784356

00:53:47.100 --> 00:53:47.600 metastasize,

NOTE Confidence: 0.9916759

00:53:48.380 --> 00:53:49.820 patients die of disease within

NOTE Confidence: 0.9916759

00:53:49.820 --> 00:53:51.360 about twelve to eighteen months.

NOTE Confidence: 0.9916759

00:53:51.500 --> 00:53:53.260 So totally different biology. They

NOTE Confidence: 0.9916759

00:53:53.260 --> 00:53:54.400 don't respond to

NOTE Confidence: 0.9197922

00:53:54.785 --> 00:53:56.545 kit inhibitors, obviously, because they're

NOTE Confidence: 0.9197922

00:53:56.545 --> 00:53:58.085 driven by a totally different

NOTE Confidence: 0.9258152

00:53:58.465 --> 00:53:58.965 pathway.

NOTE Confidence: 0.995965

00:53:59.745 --> 00:54:00.965 And at the same time,

NOTE Confidence: 0.995965

00:54:01.185 --> 00:54:02.245 we can't predict

NOTE Confidence: 0.9990098

00:54:02.785 --> 00:54:04.145 which patients are going to

NOTE Confidence: 0.9990098

00:54:04.145 --> 00:54:04.645 metastasize

NOTE Confidence: 0.9944412

00:54:05.425 --> 00:54:07.205 for our risk stratification criteria.

NOTE Confidence: 0.9699071

00:54:07.770 --> 00:54:08.890 So this is a special

NOTE Confidence: 0.9699071

00:54:08.890 --> 00:54:10.730 tumor type which is being

NOTE Confidence: 0.9699071

00:54:10.730 --> 00:54:12.010 separated from the rest of

NOTE Confidence: 0.9699071

00:54:12.010 --> 00:54:12.670 the GISTS

NOTE Confidence: 0.94930685

00:54:12.969 --> 00:54:14.730 in the twenty twenty six

NOTE Confidence: 0.94930685

00:54:14.730 --> 00:54:15.790 WHO classification,

NOTE Confidence: 0.94229764

00:54:16.650 --> 00:54:18.330 both the digestive disease volume

NOTE Confidence: 0.94229764

00:54:18.330 --> 00:54:19.870 and the soft tissue volume

NOTE Confidence: 0.94229764

00:54:20.010 --> 00:54:21.130 which will come out later

NOTE Confidence: 0.94229764

00:54:21.130 --> 00:54:21.950 this year.

NOTE Confidence: 0.9682928

00:54:22.864 --> 00:54:24.724 Anthony Gill from Sydney, Australia

NOTE Confidence: 0.9682928

00:54:24.864 --> 00:54:25.744 first showed us how we

NOTE Confidence: 0.9682928

00:54:25.744 --> 00:54:26.484 can use

NOTE Confidence: 0.89741516

00:54:26.864 --> 00:54:27.364 immunohistochemistry

NOTE Confidence: 0.99443465

00:54:27.905 --> 00:54:29.825 for SDHB to identify these

NOTE Confidence: 0.99443465

00:54:29.825 --> 00:54:30.325 tumors.

NOTE Confidence: 0.9938806

00:54:30.864 --> 00:54:32.224 This is very easy to

NOTE Confidence: 0.9938806

00:54:32.224 --> 00:54:33.844 apply. It works very well.

NOTE Confidence: 0.99375165

00:54:34.145 --> 00:54:35.184 And similar to what we

NOTE Confidence: 0.99375165

00:54:35.184 --> 00:54:36.244 saw with the paragangliomas,

NOTE Confidence: 0.99942714

00:54:37.260 --> 00:54:38.700 we have a complete loss

NOTE Confidence: 0.99942714

00:54:38.700 --> 00:54:39.760 of normal cytoplasmic

NOTE Confidence: 0.9999069

00:54:40.060 --> 00:54:40.560 staining

NOTE Confidence: 0.97806036

00:54:40.860 --> 00:54:42.540 in the tumor cells. And

NOTE Confidence: 0.97806036

00:54:42.540 --> 00:54:43.900 again, we have an internal

NOTE Confidence: 0.97806036

00:54:43.900 --> 00:54:44.400 control,

NOTE Confidence: 0.99686235

00:54:45.020 --> 00:54:45.520 endothelium

NOTE Confidence: 0.61516565

00:54:46.060 --> 00:54:46.560 or

NOTE Confidence: 0.99885285

00:54:46.940 --> 00:54:47.440 mucosa

NOTE Confidence: 0.9345064

00:54:48.060 --> 00:54:49.660 or the smooth muscle of

NOTE Confidence: 0.9345064

00:54:49.660 --> 00:54:50.960 the muscularis propria.

NOTE Confidence: 0.93683064

00:54:52.985 --> 00:54:54.445 So my closing comments,

NOTE Confidence: 0.9634522

00:54:54.825 --> 00:54:56.025 I've shown you we have

NOTE Confidence: 0.9634522

00:54:56.025 --> 00:54:57.545 this rapid evolution of a

NOTE Confidence: 0.9634522

00:54:57.545 --> 00:54:59.085 new generation of markers,

NOTE Confidence: 0.67722666

00:54:59.545 --> 00:55:00.685 femininistic chemistry,

NOTE Confidence: 0.9992312

00:55:01.065 --> 00:55:02.585 that are making it really

NOTE Confidence: 0.9992312

00:55:02.585 --> 00:55:03.725 easy to identify

NOTE Confidence: 0.99088055

00:55:04.344 --> 00:55:06.585 the molecular genetic alterations that

NOTE Confidence: 0.99088055

00:55:06.585 --> 00:55:08.400 define various cancer types,

NOTE Confidence: 0.997643

00:55:08.960 --> 00:55:10.239 helping us in our surgical

NOTE Confidence: 0.997643

00:55:10.239 --> 00:55:11.380 pathology practice,

NOTE Confidence: 0.9886547

00:55:12.160 --> 00:55:14.319 replacing molecular genetic testing in

NOTE Confidence: 0.9886547

00:55:14.319 --> 00:55:15.059 many cases.

NOTE Confidence: 0.99870634

00:55:15.599 --> 00:55:16.339 In addition,

NOTE Confidence: 0.9961368

00:55:16.719 --> 00:55:17.839 this is a nice form

NOTE Confidence: 0.9961368

00:55:17.839 --> 00:55:19.219 of rapid and inexpensive

NOTE Confidence: 0.9650423

00:55:19.760 --> 00:55:22.020 predictive testing for targeted therapies.

NOTE Confidence: 0.94238126

00:55:22.545 --> 00:55:23.905 And finally, just showed you

NOTE Confidence: 0.94238126

00:55:23.905 --> 00:55:24.645 one example

NOTE Confidence: 0.9423069

00:55:25.105 --> 00:55:26.065 of how we can use

NOTE Confidence: 0.9423069

00:55:26.065 --> 00:55:26.885 this technique

NOTE Confidence: 0.9933063

00:55:27.344 --> 00:55:29.285 as broad screening for familial

NOTE Confidence: 0.9933063

00:55:29.425 --> 00:55:30.724 cancer predisposition

NOTE Confidence: 0.9994447

00:55:31.105 --> 00:55:31.605 syndromes.

NOTE Confidence: 0.94696397

00:55:32.224 --> 00:55:33.585 Thank you again for inviting

NOTE Confidence: 0.94696397

00:55:33.585 --> 00:55:35.665 me to share this session

NOTE Confidence: 0.94696397

00:55:35.665 --> 00:55:36.944 with you today, and I'm

NOTE Confidence: 0.94696397

00:55:36.944 --> 00:55:38.219 happy to answer any questions.

NOTE Confidence: 0.93810767

00:55:52.045 --> 00:55:54.225 Yes. Great talk. Thank you.

NOTE Confidence: 0.8637527

00:55:55.005 --> 00:55:56.605 I just have a question

NOTE Confidence: 0.8637527

00:55:56.605 --> 00:55:58.545 about the the first example.

NOTE Confidence: 0.88265234

00:56:02.125 --> 00:56:02.925 Because when I was a

NOTE Confidence: 0.88265234

00:56:02.925 --> 00:56:03.425 resident,

NOTE Confidence: 0.91687113

00:56:03.725 --> 00:56:05.005 I was looking at this

NOTE Confidence: 0.91687113

00:56:05.005 --> 00:56:06.180 at the NIH, and I

NOTE Confidence: 0.91687113

00:56:06.339 --> 00:56:08.099 had no idea. I'm tired.

NOTE Confidence: 0.91687113

00:56:08.099 --> 00:56:09.540 This is tumor. I actually

NOTE Confidence: 0.91687113

00:56:09.540 --> 00:56:10.920 asked the attending

NOTE Confidence: 0.8381006

00:56:11.219 --> 00:56:12.339 who's trying to teach me

NOTE Confidence: 0.8381006

00:56:12.339 --> 00:56:12.839 already.

NOTE Confidence: 0.51497704

00:56:13.700 --> 00:56:14.599 That's all situated.

NOTE Confidence: 0.7756829

00:56:15.540 --> 00:56:16.119 Exactly. And,

NOTE Confidence: 0.7804823

00:56:17.660 --> 00:56:19.400 I I it's the specific

NOTE Confidence: 0.9056303

00:56:20.265 --> 00:56:21.005 form of pericyclinoma

NOTE Confidence: 0.89161396

00:56:21.944 --> 00:56:23.565 that's that's responsive to that,

NOTE Confidence: 0.91386914

00:56:24.984 --> 00:56:26.265 that marker, is it just

NOTE Confidence: 0.91386914

00:56:26.265 --> 00:56:27.464 present in the nose, or

NOTE Confidence: 0.91386914

00:56:27.464 --> 00:56:28.785 does that occur also for

NOTE Confidence: 0.91386914

00:56:28.785 --> 00:56:30.605 for Yeah. No. It's amazing.

NOTE Confidence: 0.91386914

00:56:30.664 --> 00:56:32.045 This is only sinonasal.

NOTE Confidence: 0.99895126

00:56:32.344 --> 00:56:33.385 So this is a very

NOTE Confidence: 0.99895126

00:56:33.385 --> 00:56:34.204 special tumor

NOTE Confidence: 0.99702764

00:56:34.760 --> 00:56:36.200 that only arises in the

NOTE Confidence: 0.99702764

00:56:36.200 --> 00:56:38.119 sinonasal tract. All the other

NOTE Confidence: 0.99702764

00:56:38.119 --> 00:56:39.480 parasitic tumors in the rest

NOTE Confidence: 0.99702764

00:56:39.480 --> 00:56:40.599 of the body have totally

NOTE Confidence: 0.99702764

00:56:40.599 --> 00:56:41.099 different

NOTE Confidence: 0.9416814

00:56:41.400 --> 00:56:43.400 genetics. Like, glomus tumors and

NOTE Confidence: 0.9416814

00:56:43.400 --> 00:56:44.140 some myoperacytomas

NOTE Confidence: 0.82991457

00:56:45.319 --> 00:56:47.020 have notch gene fusions.

NOTE Confidence: 0.99195474

00:56:47.415 --> 00:56:48.235 Totally different.

NOTE Confidence: 0.9846394

00:56:48.695 --> 00:56:50.055 It's really it's amazing. This

NOTE Confidence: 0.9846394

00:56:50.055 --> 00:56:51.515 is only sino nasal.

NOTE Confidence: 0.97870445

00:56:51.975 --> 00:56:53.415 And, you know, it's such

NOTE Confidence: 0.97870445

00:56:53.415 --> 00:56:54.075 a beautiful,

NOTE Confidence: 0.99862623

00:56:54.935 --> 00:56:55.594 you know,

NOTE Confidence: 0.9089191

00:56:56.135 --> 00:56:57.815 example of fleshing out all

NOTE Confidence: 0.9089191

00:56:57.815 --> 00:56:59.495 of these very, you know,

NOTE Confidence: 0.9089191

00:56:59.495 --> 00:57:01.255 rare things, but with very

NOTE Confidence: 0.9089191

00:57:01.255 --> 00:57:02.795 specific genetic alteration.

NOTE Confidence: 0.9983208

00:57:03.200 --> 00:57:03.860 Is it

NOTE Confidence: 0.9106155

00:57:04.320 --> 00:57:05.920 your sense that this is

NOTE Confidence: 0.9106155

00:57:05.920 --> 00:57:07.600 gonna continue, and and this

NOTE Confidence: 0.9106155

00:57:07.600 --> 00:57:09.040 is gonna play out building

NOTE Confidence: 0.9106155

00:57:09.040 --> 00:57:09.540 an?

NOTE Confidence: 0.9381029

00:57:10.080 --> 00:57:11.600 Yeah. And we we so

NOTE Confidence: 0.9381029

00:57:11.600 --> 00:57:13.300 the question is, you know,

NOTE Confidence: 0.9381029

00:57:13.360 --> 00:57:14.180 using chemistry

NOTE Confidence: 0.98100334

00:57:14.560 --> 00:57:15.600 to look for the genetic

NOTE Confidence: 0.98100334

00:57:15.600 --> 00:57:17.120 alterations, is this gonna kinda

NOTE Confidence: 0.98100334

00:57:17.120 --> 00:57:18.465 continue? And, you know, we

NOTE Confidence: 0.98100334

00:57:18.465 --> 00:57:19.825 still are working on more

NOTE Confidence: 0.98100334

00:57:19.825 --> 00:57:21.525 antibodies to identify fusions.

NOTE Confidence: 0.9750082

00:57:22.705 --> 00:57:23.505 I think we have a

NOTE Confidence: 0.9750082

00:57:23.505 --> 00:57:24.465 long way to go to

NOTE Confidence: 0.9750082

00:57:24.465 --> 00:57:25.825 make it useful, but, you

NOTE Confidence: 0.9750082

00:57:25.825 --> 00:57:27.185 know, many people kinda struggle

NOTE Confidence: 0.9750082

00:57:27.185 --> 00:57:28.625 with, well, in a practice

NOTE Confidence: 0.9750082

00:57:28.625 --> 00:57:30.145 that has very easy assets

NOTE Confidence: 0.9750082

00:57:30.145 --> 00:57:32.065 to to fusion testing by

NOTE Confidence: 0.9750082

00:57:32.065 --> 00:57:33.205 RNA NGS,

NOTE Confidence: 0.9821901

00:57:33.720 --> 00:57:34.440 should we just do that

NOTE Confidence: 0.9821901

00:57:34.440 --> 00:57:35.880 instead of developing these new

NOTE Confidence: 0.9821901

00:57:35.880 --> 00:57:37.240 antibodies? And it sort of

NOTE Confidence: 0.9821901

00:57:37.240 --> 00:57:38.840 depends on volume and your

NOTE Confidence: 0.9821901

00:57:38.840 --> 00:57:39.740 practice models.

NOTE Confidence: 0.9729652

00:57:40.920 --> 00:57:42.280 Some of the relatively common

NOTE Confidence: 0.9729652

00:57:42.280 --> 00:57:43.240 ones that we do see

NOTE Confidence: 0.9729652

00:57:43.240 --> 00:57:44.780 with some frequency, I think

NOTE Confidence: 0.9729652

00:57:44.920 --> 00:57:45.420 immunohistochemistry

NOTE Confidence: 0.9814837

00:57:45.800 --> 00:57:46.815 makes a lot of sense.

NOTE Confidence: 0.9814837

00:57:47.214 --> 00:57:48.095 Probably if you work at

NOTE Confidence: 0.9814837

00:57:48.095 --> 00:57:49.214 a cancer center that doesn't

NOTE Confidence: 0.9814837

00:57:49.214 --> 00:57:50.015 have as many of a

NOTE Confidence: 0.9814837

00:57:50.015 --> 00:57:51.395 particular group of tumors,

NOTE Confidence: 0.9989528

00:57:51.855 --> 00:57:53.474 sequencing is probably preferable.

NOTE Confidence: 0.78355116

00:57:54.335 --> 00:57:55.234 Yes. Yeah.

NOTE Confidence: 0.9829093

00:57:55.694 --> 00:57:57.474 Very nice talk. Thank you.

NOTE Confidence: 0.872715

00:57:57.935 --> 00:57:59.454 This is slightly peripheral and

NOTE Confidence: 0.872715

00:57:59.454 --> 00:58:00.835 maybe somewhat of a trivial

NOTE Confidence: 0.872715

00:58:00.974 --> 00:58:02.095 question, but since you were

NOTE Confidence: 0.872715

00:58:02.095 --> 00:58:03.240 the head of the, you

NOTE Confidence: 0.872715

00:58:03.240 --> 00:58:04.780 know, that little while,

NOTE Confidence: 0.8439863

00:58:05.960 --> 00:58:07.500 how do you manage the

NOTE Confidence: 0.8439863

00:58:07.720 --> 00:58:09.160 logistics of this other than

NOTE Confidence: 0.8439863

00:58:09.160 --> 00:58:10.040 getting, you know, like a

NOTE Confidence: 0.8439863

00:58:10.040 --> 00:58:11.480 not your old woman to

NOTE Confidence: 0.8439863

00:58:11.480 --> 00:58:12.520 go in every day and

NOTE Confidence: 0.8439863

00:58:12.520 --> 00:58:14.040 hand singing stuff? Like, you're

NOTE Confidence: 0.8439863

00:58:14.040 --> 00:58:15.340 having all these additional

NOTE Confidence: 0.7850584

00:58:15.720 --> 00:58:17.580 things added in all Yeah.

NOTE Confidence: 0.97160274

00:58:19.425 --> 00:58:20.465 Yeah. So the question is

NOTE Confidence: 0.97160274

00:58:20.465 --> 00:58:21.145 sort of how do you

NOTE Confidence: 0.97160274

00:58:21.185 --> 00:58:22.385 logistically, how do you deal

NOTE Confidence: 0.97160274

00:58:22.385 --> 00:58:23.665 with this? And he was

NOTE Confidence: 0.97160274

00:58:23.665 --> 00:58:25.025 referring to our now retired

NOTE Confidence: 0.97160274

00:58:25.025 --> 00:58:25.845 head of hematopathology

NOTE Confidence: 0.91909057

00:58:26.865 --> 00:58:27.825 who liked to do her

NOTE Confidence: 0.91909057

00:58:27.825 --> 00:58:28.865 own pipetting and her own

NOTE Confidence: 0.91909057

00:58:28.865 --> 00:58:29.765 lab for hematopathology,

NOTE Confidence: 0.8842925

00:58:30.385 --> 00:58:32.620 Jerry Pincus, who's amazing, brilliant

NOTE Confidence: 0.9927691

00:58:33.000 --> 00:58:33.500 hematopathologist

NOTE Confidence: 0.95347387

00:58:33.880 --> 00:58:34.840 and one of the pioneers

NOTE Confidence: 0.95347387

00:58:34.840 --> 00:58:35.500 of immunohistochemistry,

NOTE Confidence: 0.9810793

00:58:36.200 --> 00:58:37.160 when they were all frozen

NOTE Confidence: 0.9810793

00:58:37.160 --> 00:58:38.280 sections, she was doing that

NOTE Confidence: 0.9810793

00:58:38.280 --> 00:58:39.420 as well. She's amazing.

NOTE Confidence: 0.9884771

00:58:40.760 --> 00:58:41.880 You definitely have to have

NOTE Confidence: 0.9884771

00:58:41.880 --> 00:58:43.580 a very good technical group.

NOTE Confidence: 0.9884771

00:58:43.800 --> 00:58:45.240 I'm very lucky. My lab

NOTE Confidence: 0.9884771

00:58:45.240 --> 00:58:45.740 supervisor,

NOTE Confidence: 0.9448066

00:58:46.415 --> 00:58:47.955 she's a an immunohistochemical

NOTE Confidence: 0.9412074

00:58:48.734 --> 00:58:49.935 technologist who'd been doing it

NOTE Confidence: 0.9412074

00:58:49.935 --> 00:58:50.835 for thirty years.

NOTE Confidence: 0.9735655

00:58:51.214 --> 00:58:53.155 She's really adept at optimizing

NOTE Confidence: 0.9735655

00:58:53.295 --> 00:58:54.355 antibodies. So

NOTE Confidence: 0.9969207

00:58:54.974 --> 00:58:56.095 I work with her to

NOTE Confidence: 0.9969207

00:58:56.095 --> 00:58:58.435 identify a commercially available source

NOTE Confidence: 0.9364364

00:58:58.850 --> 00:58:59.810 where it's a company that

NOTE Confidence: 0.9364364

00:58:59.810 --> 00:59:01.010 I pretty much trust that

NOTE Confidence: 0.9364364

00:59:01.010 --> 00:59:02.210 I think they've validated enough

NOTE Confidence: 0.9364364

00:59:02.210 --> 00:59:03.270 that I believe them,

NOTE Confidence: 0.9934697

00:59:03.570 --> 00:59:04.790 that it works in FFPE.

NOTE Confidence: 0.95183975

00:59:05.250 --> 00:59:06.690 Sometimes they're still lying and

NOTE Confidence: 0.95183975

00:59:06.690 --> 00:59:08.050 it's wrong, but often they

NOTE Confidence: 0.95183975

00:59:08.050 --> 00:59:09.490 work. So I'll order an

NOTE Confidence: 0.95183975

00:59:09.490 --> 00:59:11.090 antibody and I'll just have

NOTE Confidence: 0.95183975

00:59:11.090 --> 00:59:12.530 a hypothesis. I'll test it

NOTE Confidence: 0.95183975

00:59:12.530 --> 00:59:13.410 in a tumor with a

NOTE Confidence: 0.95183975

00:59:13.410 --> 00:59:14.150 known alteration.

NOTE Confidence: 0.96209306

00:59:14.775 --> 00:59:15.575 If it works, then I

NOTE Confidence: 0.96209306

00:59:15.575 --> 00:59:16.615 just do a small pilot

NOTE Confidence: 0.96209306

00:59:16.615 --> 00:59:17.815 with a resident or fellow.

NOTE Confidence: 0.96209306

00:59:17.815 --> 00:59:19.174 So they'll have a nice

NOTE Confidence: 0.96209306

00:59:19.174 --> 00:59:20.375 project to present at one

NOTE Confidence: 0.96209306

00:59:20.375 --> 00:59:21.974 of our use cap meetings

NOTE Confidence: 0.96209306

00:59:21.974 --> 00:59:23.414 and a nice proof of

NOTE Confidence: 0.96209306

00:59:23.414 --> 00:59:25.095 principle paper. And then I

NOTE Confidence: 0.96209306

00:59:25.095 --> 00:59:25.734 bring it on as a

NOTE Confidence: 0.96209306

00:59:25.734 --> 00:59:27.494 clinical test. But it definitely

NOTE Confidence: 0.96209306

00:59:27.494 --> 00:59:28.795 takes a lot of legwork,

NOTE Confidence: 0.9621128

00:59:29.300 --> 00:59:31.320 takes technical expertise, it takes

NOTE Confidence: 0.9621128

00:59:31.540 --> 00:59:33.619 energy for a trainee or

NOTE Confidence: 0.9621128

00:59:33.619 --> 00:59:35.080 a junior colleague to

NOTE Confidence: 0.9813892

00:59:36.100 --> 00:59:37.300 pull a bunch of cases

NOTE Confidence: 0.9813892

00:59:37.300 --> 00:59:38.580 with known genetics and the

NOTE Confidence: 0.9813892

00:59:38.580 --> 00:59:39.640 differential diagnosis,

NOTE Confidence: 0.9666652

00:59:40.100 --> 00:59:40.980 you know, so that you

NOTE Confidence: 0.9666652

00:59:40.980 --> 00:59:41.960 can make sure

NOTE Confidence: 0.95726264

00:59:42.444 --> 00:59:44.365 that the specificity is enough

NOTE Confidence: 0.95726264

00:59:44.365 --> 00:59:45.085 for it to be a

NOTE Confidence: 0.95726264

00:59:45.085 --> 00:59:46.065 valuable in practice.

NOTE Confidence: 0.89622

00:59:46.525 --> 00:59:47.345 It is not

NOTE Confidence: 0.9038112

00:59:47.885 --> 00:59:49.484 it is not straightforward unless

NOTE Confidence: 0.9038112

00:59:49.484 --> 00:59:50.765 you have the infrastructure to

NOTE Confidence: 0.9038112

00:59:50.765 --> 00:59:52.125 support that. And then I

NOTE Confidence: 0.9038112

00:59:52.125 --> 00:59:53.724 guess I'm curious on the

NOTE Confidence: 0.9038112

00:59:53.724 --> 00:59:55.250 latter half. Once you've established

NOTE Confidence: 0.9038112

00:59:55.569 --> 00:59:56.369 Yeah. How do you get

NOTE Confidence: 0.9038112

00:59:56.369 --> 00:59:57.730 it into your workflows? You're

NOTE Confidence: 0.9038112

00:59:57.730 --> 00:59:58.630 getting the turnaround

NOTE Confidence: 0.96355224

00:59:59.010 --> 00:59:59.990 of such a large

NOTE Confidence: 0.8288107

01:00:00.450 --> 01:00:01.810 panel panel of tests so

NOTE Confidence: 0.8288107

01:00:01.810 --> 01:00:03.569 many places have been. Yeah.

NOTE Confidence: 0.8288107

01:00:03.569 --> 01:00:04.930 The question is about turnaround

NOTE Confidence: 0.8288107

01:00:04.930 --> 01:00:05.810 and bringing it into the

NOTE Confidence: 0.8288107

01:00:05.810 --> 01:00:06.710 clinical armamentarium.

NOTE Confidence: 0.98175645

01:00:08.285 --> 01:00:09.325 We we only do one

NOTE Confidence: 0.98175645

01:00:09.325 --> 01:00:10.545 run a day still.

NOTE Confidence: 0.9701034

01:00:11.965 --> 01:00:13.165 Yeah. We we do one

NOTE Confidence: 0.9701034

01:00:13.165 --> 01:00:14.605 immunosy chemistry run a day.

NOTE Confidence: 0.9701034

01:00:14.605 --> 01:00:15.605 Every morning, they come out

NOTE Confidence: 0.9701034

01:00:15.605 --> 01:00:17.085 at, like, two o'clock, and

NOTE Confidence: 0.9701034

01:00:17.085 --> 01:00:19.025 we just have enough machines

NOTE Confidence: 0.9701034

01:00:19.085 --> 01:00:20.525 that we can run a

NOTE Confidence: 0.9701034

01:00:20.525 --> 01:00:21.345 bunch of tests.

NOTE Confidence: 0.9753651

01:00:21.920 --> 01:00:23.360 I don't know. It's like,

NOTE Confidence: 0.9753651

01:00:23.360 --> 01:00:24.160 you need a lot of

NOTE Confidence: 0.9753651

01:00:24.160 --> 01:00:25.040 machines. If you have a

NOTE Confidence: 0.9753651

01:00:25.040 --> 01:00:26.480 very high volume practice, we

NOTE Confidence: 0.9753651

01:00:26.480 --> 01:00:28.340 run probably seven hundred

NOTE Confidence: 0.98123664

01:00:28.640 --> 01:00:30.000 tests a day. It's a

NOTE Confidence: 0.98123664

01:00:30.000 --> 01:00:30.500 lot

NOTE Confidence: 0.90390193

01:00:30.960 --> 01:00:31.940 of lot of machines.

NOTE Confidence: 0.7733568

01:00:34.755 --> 01:00:35.255 Yes.

NOTE Confidence: 0.51153827

01:00:35.555 --> 01:00:36.994 The few statements are not

NOTE Confidence: 0.51153827

01:00:36.994 --> 01:00:38.674 the UPR and Yes. Not

NOTE Confidence: 0.51153827

01:00:38.994 --> 01:00:40.355 but the central plastic. It's

NOTE Confidence: 0.51153827

01:00:40.355 --> 01:00:41.395 very hard dealing with the

NOTE Confidence: 0.51153827

01:00:41.395 --> 01:00:41.895 setting.

NOTE Confidence: 0.8591863

01:00:43.954 --> 01:00:45.555 Yes. How do you handle

NOTE Confidence: 0.8591863

01:00:45.555 --> 01:00:47.015 this with this IFC?

NOTE Confidence: 0.97632104

01:00:48.119 --> 01:00:49.000 Yeah. I think you have

NOTE Confidence: 0.97632104

01:00:49.000 --> 01:00:50.280 to make sure that your

NOTE Confidence: 0.97632104

01:00:50.280 --> 01:00:51.640 sort of signal to noise

NOTE Confidence: 0.97632104

01:00:51.640 --> 01:00:53.640 ratio is is enough. And

NOTE Confidence: 0.97632104

01:00:53.640 --> 01:00:55.559 when it's a universally expressed

NOTE Confidence: 0.97632104

01:00:55.559 --> 01:00:56.700 protein, for example,

NOTE Confidence: 0.96946317

01:00:57.079 --> 01:00:58.280 if you really crank it

NOTE Confidence: 0.96946317

01:00:58.280 --> 01:00:58.920 as it were and you

NOTE Confidence: 0.96946317

01:00:58.920 --> 01:01:00.119 get a very strong signal

NOTE Confidence: 0.96946317

01:01:00.119 --> 01:01:01.500 and you're looking for loss,

NOTE Confidence: 0.96946317

01:01:01.625 --> 01:01:02.744 then you can feel confident

NOTE Confidence: 0.96946317

01:01:02.744 --> 01:01:03.785 there is true loss. I

NOTE Confidence: 0.96946317

01:01:03.785 --> 01:01:04.605 think the problem

NOTE Confidence: 0.93346554

01:01:05.145 --> 01:01:06.825 is when you've optimized an

NOTE Confidence: 0.93346554

01:01:06.825 --> 01:01:07.325 antibody

NOTE Confidence: 0.94208336

01:01:07.785 --> 01:01:09.385 and the signal's weak and

NOTE Confidence: 0.94208336

01:01:09.385 --> 01:01:11.224 everything, then it's very hard

NOTE Confidence: 0.94208336

01:01:11.224 --> 01:01:12.345 to decide if there's loss,

NOTE Confidence: 0.94208336

01:01:12.345 --> 01:01:13.560 especially as you said if

NOTE Confidence: 0.94208336

01:01:13.560 --> 01:01:15.427 it's cytoplasmic. So you have

NOTE Confidence: 0.94208336

01:01:15.427 --> 01:01:17.294 to make sure the signal's

NOTE Confidence: 0.94208336

01:01:17.294 --> 01:01:19.160 really strong. So we we

NOTE Confidence: 0.94208336

01:01:19.160 --> 01:01:21.027 actually use some antibody detection

NOTE Confidence: 0.94208336

01:01:21.027 --> 01:01:22.894 kits where the chemistry really

NOTE Confidence: 0.94208336

01:01:22.894 --> 01:01:24.761 boosts the signal even if

NOTE Confidence: 0.94208336

01:01:24.761 --> 01:01:26.628 it's not kinda standard practice

NOTE Confidence: 0.94208336

01:01:26.628 --> 01:01:28.175 when you're dealing with some

NOTE Confidence: 0.94208336

01:01:28.175 --> 01:01:29.795 antibodies that have pretty weak

NOTE Confidence: 0.94906557

01:01:30.095 --> 01:01:30.595 results.

NOTE Confidence: 0.9412257

01:01:31.055 --> 01:01:31.855 And some of them are

NOTE Confidence: 0.9412257

01:01:31.855 --> 01:01:32.735 the ones that we really

NOTE Confidence: 0.9412257

01:01:32.735 --> 01:01:34.095 like to use, like the

NOTE Confidence: 0.9412257

01:01:34.095 --> 01:01:35.855 highly sensitive ALK and ROS1

NOTE Confidence: 0.9412257

01:01:35.855 --> 01:01:37.215 and BRAF e six hundred

NOTE Confidence: 0.9412257

01:01:37.215 --> 01:01:38.495 d. The antibodies aren't that

NOTE Confidence: 0.9412257

01:01:38.495 --> 01:01:39.455 strong, so you really have

NOTE Confidence: 0.9412257

01:01:39.455 --> 01:01:40.860 to boost the signal so

NOTE Confidence: 0.9412257

01:01:40.860 --> 01:01:41.900 you can believe it that

NOTE Confidence: 0.9412257

01:01:41.900 --> 01:01:43.100 it when it's positive, it's

NOTE Confidence: 0.9412257

01:01:43.100 --> 01:01:44.860 real. And with loss, it's

NOTE Confidence: 0.9412257

01:01:44.860 --> 01:01:45.760 the same problem.

NOTE Confidence: 0.96331644

01:01:46.140 --> 01:01:46.940 So a lot of it's

NOTE Confidence: 0.96331644

01:01:46.940 --> 01:01:48.380 just kind of validation and

NOTE Confidence: 0.96331644

01:01:48.380 --> 01:01:50.140 optimization and feeling comfortable with

NOTE Confidence: 0.96331644

01:01:50.140 --> 01:01:50.800 the results.

NOTE Confidence: 0.89235306

01:01:51.420 --> 01:01:51.920 Yeah.

NOTE Confidence: 0.7043392

01:01:52.935 --> 01:01:53.435 Thanks.

NOTE Confidence: 0.73361707

01:01:53.815 --> 01:01:54.315 Thanks.

NOTE Confidence: 0.61829203

01:01:55.095 --> 01:01:56.795 I think I've seen those,

NOTE Confidence: 0.68412125

01:01:57.735 --> 01:01:59.575 platforms, like, moving form, code

NOTE Confidence: 0.68412125

01:01:59.575 --> 01:02:00.775 expedite to a ton of

NOTE Confidence: 0.68412125

01:02:00.775 --> 01:02:02.255 things that once it's Yeah.

NOTE Confidence: 0.68412125

01:02:02.455 --> 01:02:04.055 Even that color is. So,

NOTE Confidence: 0.68412125

01:02:04.055 --> 01:02:05.175 you know, you really have

NOTE Confidence: 0.68412125

01:02:05.175 --> 01:02:06.535 that, you know, talk sort

NOTE Confidence: 0.68412125

01:02:06.535 --> 01:02:08.310 of look. Yeah. So, like,

NOTE Confidence: 0.68412125

01:02:08.310 --> 01:02:09.430 doing all of these on

NOTE Confidence: 0.68412125

01:02:09.430 --> 01:02:10.250 one session.

NOTE Confidence: 0.99146396

01:02:10.550 --> 01:02:11.450 Do you think

NOTE Confidence: 0.90007424

01:02:11.830 --> 01:02:13.670 we're pretty close, somewhat close

NOTE Confidence: 0.90007424

01:02:13.670 --> 01:02:14.870 to doing that instead of

NOTE Confidence: 0.90007424

01:02:14.870 --> 01:02:15.530 our HC?

NOTE Confidence: 0.9984135

01:02:16.230 --> 01:02:17.350 Yeah. I mean, I so

NOTE Confidence: 0.9984135

01:02:17.350 --> 01:02:18.490 the question is about

NOTE Confidence: 0.9611221

01:02:18.790 --> 01:02:20.070 the technologies that are sort

NOTE Confidence: 0.9611221

01:02:20.070 --> 01:02:21.830 of multiplexing in really impressive

NOTE Confidence: 0.9611221

01:02:21.830 --> 01:02:23.154 ways, often using kind of

NOTE Confidence: 0.9611221

01:02:23.154 --> 01:02:23.654 digital,

NOTE Confidence: 0.9668858

01:02:24.674 --> 01:02:26.674 and artificial intelligence can be

NOTE Confidence: 0.9668858

01:02:26.674 --> 01:02:28.194 very supportive of that. You

NOTE Confidence: 0.9668858

01:02:28.194 --> 01:02:29.315 have people in your department

NOTE Confidence: 0.9668858

01:02:29.315 --> 01:02:29.875 who know a lot more

NOTE Confidence: 0.9668858

01:02:29.875 --> 01:02:30.674 about that than I do.

NOTE Confidence: 0.9668858

01:02:30.674 --> 01:02:31.474 I don't do any of

NOTE Confidence: 0.9668858

01:02:31.474 --> 01:02:33.075 that. I do like very

NOTE Confidence: 0.9668858

01:02:33.075 --> 01:02:34.835 old school immunosystem chemistry, and

NOTE Confidence: 0.9668858

01:02:34.835 --> 01:02:36.180 I don't really, I don't

NOTE Confidence: 0.9668858

01:02:36.180 --> 01:02:37.640 keep abreast of that technology

NOTE Confidence: 0.9668858

01:02:37.700 --> 01:02:38.740 enough to know how close

NOTE Confidence: 0.9668858

01:02:38.740 --> 01:02:40.200 we are to routine implementation.

NOTE Confidence: 0.7805465

01:02:41.060 --> 01:02:41.859 But you had a question

NOTE Confidence: 0.7805465

01:02:41.859 --> 01:02:43.859 or comment? Yes. I guess.

NOTE Confidence: 0.7805465

01:02:43.859 --> 01:02:45.619 Thanks. So everything you should

NOTE Confidence: 0.7805465

01:02:45.619 --> 01:02:46.980 list today was really fascinating,

NOTE Confidence: 0.7805465

01:02:46.980 --> 01:02:48.705 but it's all minor. Yes.

NOTE Confidence: 0.7805465

01:02:49.025 --> 01:02:50.965 The following that continuous expression

NOTE Confidence: 0.9588304

01:02:52.465 --> 01:02:53.745 Yes. Yeah. The question is,

NOTE Confidence: 0.9588304

01:02:53.745 --> 01:02:55.185 these are all binary, and

NOTE Confidence: 0.9588304

01:02:55.185 --> 01:02:57.105 that's exactly right. So for

NOTE Confidence: 0.9588304

01:02:57.105 --> 01:02:58.085 me, colorimetric,

NOTE Confidence: 0.7536712

01:02:59.265 --> 01:03:00.885 right field, immuno chemistry,

NOTE Confidence: 0.99766666

01:03:01.585 --> 01:03:02.725 unless it's binary,

NOTE Confidence: 0.9866367

01:03:03.025 --> 01:03:04.140 I don't really know how

NOTE Confidence: 0.9866367

01:03:04.140 --> 01:03:05.260 to do it. And I

NOTE Confidence: 0.9866367

01:03:05.260 --> 01:03:06.539 know that you are doing

NOTE Confidence: 0.9866367

01:03:06.539 --> 01:03:07.660 a lot of great techniques

NOTE Confidence: 0.9866367

01:03:07.660 --> 01:03:09.180 to try to get readouts

NOTE Confidence: 0.9866367

01:03:09.180 --> 01:03:10.799 that are much more granular

NOTE Confidence: 0.9866367

01:03:10.940 --> 01:03:12.619 along a spectrum. But for

NOTE Confidence: 0.9866367

01:03:12.619 --> 01:03:14.960 me, I think using these

NOTE Confidence: 0.9866367

01:03:15.019 --> 01:03:16.160 old school techniques,

NOTE Confidence: 0.9917714

01:03:17.175 --> 01:03:18.775 you can't really get very

NOTE Confidence: 0.9917714

01:03:18.775 --> 01:03:20.535 good gradations of intensity of

NOTE Confidence: 0.9917714

01:03:20.535 --> 01:03:22.055 staining. So I am really

NOTE Confidence: 0.9917714

01:03:22.055 --> 01:03:24.215 just looking for genetic alterations

NOTE Confidence: 0.9917714

01:03:24.215 --> 01:03:25.675 that are plus minus. And

NOTE Confidence: 0.9917714

01:03:25.815 --> 01:03:27.675 you definitely need other methods

NOTE Confidence: 0.9990028

01:03:28.295 --> 01:03:29.595 to be able to get

NOTE Confidence: 0.9453934

01:03:30.430 --> 01:03:31.550 a a much more kinda

NOTE Confidence: 0.9453934

01:03:31.550 --> 01:03:33.230 active range of expression of

NOTE Confidence: 0.9453934

01:03:33.230 --> 01:03:33.730 proteins.

NOTE Confidence: 0.981103

01:03:35.310 --> 01:03:37.230 Yeah. And, obviously, your department

NOTE Confidence: 0.981103

01:03:37.230 --> 01:03:37.950 has done a lot on

NOTE Confidence: 0.981103

01:03:37.950 --> 01:03:39.470 this, and I I've read

NOTE Confidence: 0.981103

01:03:39.470 --> 01:03:40.110 a lot of it, and

NOTE Confidence: 0.981103

01:03:40.110 --> 01:03:41.390 it's very impressive, but I

NOTE Confidence: 0.981103

01:03:41.390 --> 01:03:42.450 don't do that stuff.

NOTE Confidence: 0.93482417

01:03:43.630 --> 01:03:44.450 Yeah. Please.

NOTE Confidence: 0.92385125

01:04:07.360 --> 01:04:07.860 Yeah.

NOTE Confidence: 0.96701163

01:04:08.560 --> 01:04:09.760 Yeah. Yeah. The question is

NOTE Confidence: 0.96701163

01:04:09.760 --> 01:04:11.460 in in sort of resource

NOTE Confidence: 0.96701163

01:04:11.600 --> 01:04:12.420 poor settings

NOTE Confidence: 0.97058403

01:04:12.880 --> 01:04:14.355 that really are don't or

NOTE Confidence: 0.97058403

01:04:14.355 --> 01:04:15.715 might never have access to

NOTE Confidence: 0.97058403

01:04:15.715 --> 01:04:17.335 genomic testing of any kind,

NOTE Confidence: 0.9386117

01:04:17.875 --> 01:04:19.155 does do these forms of

NOTE Confidence: 0.9386117

01:04:19.155 --> 01:04:19.655 immunohistochemistry,

NOTE Confidence: 0.96986896

01:04:20.035 --> 01:04:21.635 is that a possibility? And

NOTE Confidence: 0.96986896

01:04:21.635 --> 01:04:22.775 again, I think that's

NOTE Confidence: 0.94581014

01:04:23.155 --> 01:04:24.935 this is still not inexpensive.

NOTE Confidence: 0.99066395

01:04:25.715 --> 01:04:26.755 So I know that in

NOTE Confidence: 0.99066395

01:04:26.755 --> 01:04:28.135 many countries, even immunohistochemistry

NOTE Confidence: 0.9334368

01:04:28.515 --> 01:04:29.950 is impossible. But, you know,

NOTE Confidence: 0.9334368

01:04:29.950 --> 01:04:30.990 for example, you know, we

NOTE Confidence: 0.9334368

01:04:30.990 --> 01:04:32.030 do a lot of outreach

NOTE Confidence: 0.9334368

01:04:32.030 --> 01:04:33.630 with some countries through the

NOTE Confidence: 0.9334368

01:04:33.630 --> 01:04:35.230 Partners in Health kind of,

NOTE Confidence: 0.9334368

01:04:35.230 --> 01:04:37.470 you know, organization, including, like,

NOTE Confidence: 0.9334368

01:04:37.470 --> 01:04:38.290 in in Rwanda.

NOTE Confidence: 0.99306494

01:04:38.750 --> 01:04:39.710 And we've helped set up

NOTE Confidence: 0.99306494

01:04:39.710 --> 01:04:40.830 a laboratory there where they

NOTE Confidence: 0.99306494

01:04:40.830 --> 01:04:41.490 do immunohistochemistry.

NOTE Confidence: 0.92696255

01:04:42.510 --> 01:04:43.870 We kinda help advise the

NOTE Confidence: 0.92696255

01:04:43.870 --> 01:04:45.285 panel and some of the

NOTE Confidence: 0.92696255

01:04:45.525 --> 01:04:47.305 relatively common sarcomas

NOTE Confidence: 0.95714295

01:04:47.845 --> 01:04:48.964 that they see in their

NOTE Confidence: 0.95714295

01:04:48.964 --> 01:04:50.325 population, they actually get some

NOTE Confidence: 0.95714295

01:04:50.325 --> 01:04:52.085 of these antibodies. So I

NOTE Confidence: 0.95714295

01:04:52.085 --> 01:04:53.224 think that certainly,

NOTE Confidence: 0.9688389

01:04:54.005 --> 01:04:55.285 you need to have some

NOTE Confidence: 0.9688389

01:04:55.285 --> 01:04:56.645 level of expertise by the

NOTE Confidence: 0.9688389

01:04:56.645 --> 01:04:58.164 pathologist, which is another big

NOTE Confidence: 0.9688389

01:04:58.164 --> 01:04:58.984 problem because

NOTE Confidence: 0.96381176

01:04:59.310 --> 01:05:00.590 not all countries have the

NOTE Confidence: 0.96381176

01:05:00.590 --> 01:05:01.630 kinds of training that the

NOTE Confidence: 0.96381176

01:05:01.630 --> 01:05:03.170 Western world does for

NOTE Confidence: 0.77146053

01:05:03.550 --> 01:05:04.530 diagnostic immunoistochemistry

NOTE Confidence: 0.98075783

01:05:05.310 --> 01:05:07.790 and surgical pathology. But, I

NOTE Confidence: 0.98075783

01:05:07.790 --> 01:05:08.910 mean, really, I hope that

NOTE Confidence: 0.98075783

01:05:08.910 --> 01:05:10.290 this is helpful for

NOTE Confidence: 0.99310696

01:05:10.670 --> 01:05:11.790 settings where they don't have

NOTE Confidence: 0.99310696

01:05:11.790 --> 01:05:13.070 any genetic or or, you

NOTE Confidence: 0.99310696

01:05:13.070 --> 01:05:14.690 know, molecular genetic testing.

NOTE Confidence: 0.9936444

01:05:17.693 --> 01:05:18.893 Well, thank you again so

NOTE Confidence: 0.9936444

01:05:18.893 --> 01:05:20.353 much for for the invitation.