WEBVTT

NOTE duration:"01:06:24"

NOTE recognizability:0.861

NOTE language:en-us

NOTE Confidence: 0.31098902

00:00:00.000 --> 00:00:04.470 Well. While people are still

NOTE Confidence: 0.31098902

00:00:04.470 --> 00:00:08.365 logging in, we have 60, so I'll

NOTE Confidence: 0.31098902

00:00:08.365 --> 00:00:11.380 get started with the introduction.

NOTE Confidence: 0.795379901111111

00:00:13.400 --> 00:00:16.809 Most people don't need an introduction to

NOTE Confidence: 0.795379901111111

00:00:16.809 --> 00:00:20.440 Doctor Gibson, Doctor Gibson, but so my

NOTE Confidence: 0.795379901111111

00:00:20.440 --> 00:00:24.320 introduction is going to be very brief.

NOTE Confidence: 0.795379901111111

00:00:24.320 --> 00:00:28.359 Dr Gibson did her bachelor's in science

NOTE Confidence: 0.795379901111111

00:00:28.359 --> 00:00:32.062 from University of Minnesota and then

NOTE Confidence: 0.795379901111111

00:00:32.062 --> 00:00:37.230 went on to do MD PhD at the Mayo Clinic's

NOTE Confidence: 0.795379901111111

00:00:37.230 --> 00:00:40.230 School of Medicine. Following that,

NOTE Confidence: 0.795379901111111

00:00:40.230 --> 00:00:44.046 she went to Brigham and women.

NOTE Confidence: 0.795379901111111

00:00:44.050 --> 00:00:46.438 For a pathology residency,

NOTE Confidence: 0.795379901111111

00:00:46.438 --> 00:00:50.765 and she must have liked the northeast

NOTE Confidence: 0.795379901111111

00:00:50.765 --> 00:00:54.820 so much that she decided to pursue

NOTE Confidence: 0.795379901111111

00:00:54.820 --> 00:00:57.620 further career in the Northeast,

NOTE Confidence: 0.795379901111111

00:00:57.620 --> 00:01:00.826 finishing up with a chief residency at

NOTE Confidence: 0.795379901111111

00:01:00.826 --> 00:01:05.040 Brigham and Women's and then a GI Fellowship.

NOTE Confidence: 0.795379901111111

00:01:05.040 --> 00:01:07.700 She followed this with a brief stint

NOTE Confidence: 0.795379901111111

00:01:07.700 --> 00:01:10.534 back at Mayo Clinic and came right

NOTE Confidence: 0.795379901111111

00:01:10.534 --> 00:01:14.044 back and joined our department.

NOTE Confidence: 0.795379901111111

00:01:14.044 --> 00:01:18.275 In 2011, as assistant professor and

NOTE Confidence: 0.795379901111111

00:01:18.275 --> 00:01:22.305 now Joanna Gibson is an associate

NOTE Confidence: 0.795379901111111

00:01:22.305 --> 00:01:24.923 professor in GI pathology.

NOTE Confidence: 0.795379901111111

00:01:24.923 --> 00:01:29.214 She serves on many committees and is

NOTE Confidence: 0.795379901111111

00:01:29.214 --> 00:01:32.262 currently the director of Quality

NOTE Confidence: 0.795379901111111

00:01:32.262 --> 00:01:34.098 and Patient Safety.

NOTE Confidence: 0.795379901111111

00:01:34.098 --> 00:01:36.026 In Joanne's practice,

NOTE Confidence: 0.795379901111111

00:01:36.026 --> 00:01:38.658 she combines molecular pathology

NOTE Confidence: 0.795379901111111

00:01:38.658 --> 00:01:40.632 and GI pathology,

NOTE Confidence: 0.795379901111111

00:01:40.640 --> 00:01:43.165 and today Doctor Gibson will

NOTE Confidence: 0.795379901111111

00:01:43.165 --> 00:01:45.948 share her insights. Indu.

NOTE Confidence: 0.795379901111111

00:01:45.948 --> 00:01:51.020 Oncology and molecular pathology.

NOTE Confidence: 0.795379901111111

00:01:51.020 --> 00:01:55.297 A brief housekeeping notice that from today.

NOTE Confidence: 0.795379901111111

00:01:55.300 --> 00:01:55.876 Unfortunately,

NOTE Confidence: 0.795379901111111

00:01:55.876 --> 00:01:59.908 there has been a change to how

NOTE Confidence: 0.795379901111111

00:01:59.908 --> 00:02:03.975 CMA credit is given when you text

NOTE Confidence: 0.795379901111111

00:02:03.975 --> 00:02:06.012 your CMA credit number.

NOTE Confidence: 0.795379901111111

00:02:06.012 --> 00:02:10.129 If your CMA profile is up to date

NOTE Confidence: 0.795379901111111

00:02:10.129 --> 00:02:13.219 with regards to disclosure of

NOTE Confidence: 0.795379901111111

00:02:13.219 --> 00:02:17.040 conflicts of interest and other stuff,

NOTE Confidence: 0.795379901111111

00:02:17.040 --> 00:02:19.800 you would get CMA credit.

NOTE Confidence: 0.795379901111111

00:02:19.800 --> 00:02:20.370 Otherwise,

NOTE Confidence: 0.795379901111111

00:02:20.370 --> 00:02:21.510 you may.

NOTE Confidence: 0.795379901111111

00:02:21.510 --> 00:02:25.500 Get a message that your profile is

NOTE Confidence: 0.795379901111111

00:02:25.613 --> 00:02:29.584 not up to date and Susanna has now

NOTE Confidence: 0.795379901111111

00:02:29.584 --> 00:02:33.180 found this out just today and she sent

NOTE Confidence: 0.795379901111111

00:02:33.180 --> 00:02:36.270 an email to the entire department.

NOTE Confidence: 0.795379901111111

00:02:36.270 --> 00:02:38.730 So it's a simple fix.

NOTE Confidence: 0.795379901111111

00:02:38.730 --> 00:02:42.030 Just update your CMA profile.

NOTE Confidence: 0.795379901111111

00:02:42.030 --> 00:02:45.038 With that, I'll let Joanna take it away.

NOTE Confidence: 0.790206436666667

00:02:46.190 --> 00:02:49.238 Thank you Manju. Share my screen.

NOTE Confidence: 0.895555935

00:02:54.350 --> 00:02:56.420 Go to presentation mode. Hopefully you

NOTE Confidence: 0.895555935

00:02:56.420 --> 00:02:58.979 guys can see that presentation mode.

NOTE Confidence: 0.777844734545454

00:03:01.130 --> 00:03:03.044 Yes, great. I'm going to try

NOTE Confidence: 0.777844734545454

00:03:03.044 --> 00:03:04.950 to use this laser pointer.

NOTE Confidence: 0.777844734545454

00:03:04.950 --> 00:03:08.275 See if that works for highlighting things.

NOTE Confidence: 0.777844734545454

00:03:08.280 --> 00:03:10.611 So Andrew, thank you so much for

NOTE Confidence: 0.777844734545454

00:03:10.611 --> 00:03:12.598 the introduction and thank you so

NOTE Confidence: 0.777844734545454

00:03:12.598 --> 00:03:14.446 much for the opportunity to come

NOTE Confidence: 0.777844734545454

00:03:14.446 --> 00:03:16.839 and give Brian Rounds and in our

NOTE Confidence: 0.777844734545454

00:03:16.839 --> 00:03:18.435 own department it's definitely a

NOTE Confidence: 0.777844734545454

00:03:18.435 --> 00:03:20.570 privilege to be able to do that.

NOTE Confidence: 0.777844734545454

00:03:20.570 --> 00:03:24.167 So I just want to come back to my early

NOTE Confidence: 0.777844734545454

00:03:24.167 --> 00:03:26.729 education and pathology and sort of

NOTE Confidence: 0.777844734545454

00:03:26.729 --> 00:03:29.639 explain a few things that sort of.

NOTE Confidence: 0.777844734545454

00:03:29.640 --> 00:03:33.312 Have led to where I am today so my

NOTE Confidence: 0.777844734545454

00:03:33.312 --> 00:03:35.898 interested oncology started early.

NOTE Confidence: 0.777844734545454

00:03:35.900 --> 00:03:37.820 In my, you know when I got to the Mayo

NOTE Confidence: 0.777844734545454

00:03:37.871 --> 00:03:39.735 Clinic for my for my MD PhD training.

NOTE Confidence: 0.922901777

00:03:41.940 --> 00:03:43.536 You know, I started to get

NOTE Confidence: 0.922901777

00:03:43.536 --> 00:03:44.600 interested in cancer biology,

NOTE Confidence: 0.922901777

00:03:44.600 --> 00:03:47.696 and I succinctly remember a lecture

NOTE Confidence: 0.922901777

00:03:47.696 --> 00:03:50.462 that Doctor Brookhart gave when he was

NOTE Confidence: 0.922901777

00:03:50.462 --> 00:03:52.332 there at that time, and I I really,

NOTE Confidence: 0.922901777

00:03:52.332 --> 00:03:54.239 he was my first example of sort of,

NOTE Confidence: 0.922901777

00:03:54.240 --> 00:03:55.738 you know, how do you study cancer?

NOTE Confidence: 0.922901777

00:03:55.740 --> 00:03:57.030 How do you look at it?

NOTE Confidence: 0.922901777

00:03:57.030 --> 00:03:59.706 I think it triggered my interest

NOTE Confidence: 0.922901777

00:03:59.706 --> 00:04:02.697 in pathology and once I got to

NOTE Confidence: 0.922901777

00:04:02.697 --> 00:04:04.506 residency and into my fellowship,

NOTE Confidence: 0.922901777

00:04:04.506 --> 00:04:07.556 I started to sort of submit my interest

NOTE Confidence: 0.922901777

00:04:07.556 --> 00:04:09.766 specifically more in GI cancers

NOTE Confidence: 0.922901777

00:04:09.766 --> 00:04:12.030 and specifically colorectal cancer.

NOTE Confidence: 0.922901777

00:04:12.030 --> 00:04:12.840 And so yes,

NOTE Confidence: 0.922901777

00:04:12.840 --> 00:04:15.098 I kind of went back and forth the

NOTE Confidence: 0.922901777

00:04:15.098 --> 00:04:17.552 East and West Coast and just going

NOTE Confidence: 0.922901777

00:04:17.552 --> 00:04:20.736 to do one thing here and move now,

NOTE Confidence: 0.922901777

00:04:20.736 --> 00:04:23.310 I can't do it just one second here guys.

NOTE Confidence: 0.890193559090909

00:04:28.240 --> 00:04:30.921 The zoom window is interfering with my

NOTE Confidence: 0.890193559090909

00:04:30.921 --> 00:04:34.037 view of the slides and it was I didn't

NOTE Confidence: 0.890193559090909

00:04:34.037 --> 00:04:38.460 move it out of the way. And so I.

NOTE Confidence: 0.952518356666667

00:04:41.150 --> 00:04:42.416 So when I arrived at Yale,

NOTE Confidence: 0.952518356666667

00:04:42.420 --> 00:04:44.856 I already had a very strong

NOTE Confidence: 0.952518356666667

00:04:44.856 --> 00:04:47.650 interest in oncology and cancer,

NOTE Confidence: 0.952518356666667

00:04:47.650 --> 00:04:49.630 specifically colorectal cancer.

NOTE Confidence: 0.952518356666667

00:04:49.630 --> 00:04:51.408 And you know, when I got into

NOTE Confidence: 0.952518356666667

00:04:51.408 --> 00:04:53.175 the Yale practice, that's sort of

NOTE Confidence: 0.952518356666667

00:04:53.175 --> 00:04:55.732 where I focused my efforts and so.

NOTE Confidence: 0.952518356666667

00:04:55.732 --> 00:04:57.937 Hopefully throughout this talk you'll

NOTE Confidence: 0.952518356666667

00:04:57.937 --> 00:05:00.772 get to see how that intersection.

NOTE Confidence: 0.952518356666667

00:05:00.772 --> 00:05:03.752 Of oncology pathology molecular pathology

NOTE Confidence: 0.952518356666667

00:05:03.752 --> 00:05:07.427 occurred for one GI pathologists practice

NOTE Confidence: 0.952518356666667

00:05:07.427 --> 00:05:10.985 myself and specifically how does the

NOTE Confidence: 0.952518356666667

00:05:10.985 --> 00:05:14.860 intersection sort of lead to patient?

NOTE Confidence: 0.952518356666667

00:05:14.860 --> 00:05:17.285 Management changes and and you

NOTE Confidence: 0.952518356666667

00:05:17.285 --> 00:05:20.230 know how we impact patient care.

NOTE Confidence: 0.952518356666667

00:05:20.230 --> 00:05:22.246 So conceptually, this is how I'm going

NOTE Confidence: 0.952518356666667

00:05:22.246 --> 00:05:24.774 to sort of present my grand rounds.

NOTE Confidence: 0.952518356666667

00:05:24.774 --> 00:05:27.162 I'm going to use patient examples

NOTE Confidence: 0.952518356666667

00:05:27.162 --> 00:05:29.968 to highlight different biomarkers,

NOTE Confidence: 0.952518356666667

00:05:29.970 --> 00:05:31.116 different technologies,

NOTE Confidence: 0.952518356666667

00:05:31.116 --> 00:05:34.554 and different effects on patient impact.

NOTE Confidence: 0.952518356666667

00:05:34.560 --> 00:05:36.378 So hopefully throughout this entire talk,

NOTE Confidence: 0.952518356666667

00:05:36.380 --> 00:05:38.925 they'll be sort of a common theme of

NOTE Confidence: 0.952518356666667

00:05:38.925 --> 00:05:42.975 that progression of of data sharing.

NOTE Confidence: 0.952518356666667

00:05:42.980 --> 00:05:43.378 Alright,

NOTE Confidence: 0.952518356666667

00:05:43.378 --> 00:05:45.766 so starting with patient number one

NOTE Confidence: 0.952518356666667

00:05:45.770 --> 00:05:47.678 this was a 45 year old man who had

NOTE Confidence: 0.952518356666667

00:05:47.678 --> 00:05:49.474 his first screening colonoscopy and

NOTE Confidence: 0.952518356666667

00:05:49.474 --> 00:05:51.754 was diagnosed with colon cancer that

NOTE Confidence: 0.952518356666667

00:05:51.818 --> 00:05:53.876 you can see here on the endoscopic

NOTE Confidence: 0.952518356666667

00:05:53.876 --> 00:05:57.850 picture and on the Histology image,

NOTE Confidence: 0.952518356666667

00:05:57.850 --> 00:06:01.714 and so I'll invite the residents to

NOTE Confidence: 0.952518356666667

00:06:01.714 --> 00:06:05.548 use the chat if they want to and what

NOTE Confidence: 0.952518356666667

00:06:05.548 --> 00:06:08.238 molecular tests should be ordered and why.

NOTE Confidence: 0.91240495

00:06:11.080 --> 00:06:13.456 Open the check my other screen.

NOTE Confidence: 0.8473419

00:06:17.940 --> 00:06:18.930 And.

NOTE Confidence: 0.8890275325

00:06:21.960 --> 00:06:24.660 So the answer should be MSI

NOTE Confidence: 0.8890275325

00:06:24.660 --> 00:06:26.390 testing exactly excellent.

NOTE Confidence: 0.95840699125

00:06:32.340 --> 00:06:34.575 Somehow something is getting stuck

NOTE Confidence: 0.95840699125

00:06:34.575 --> 00:06:38.760 in my PowerPoint, I apologize.

NOTE Confidence: 0.95840699125

00:06:38.760 --> 00:06:40.657 I have to quit one more time.

NOTE Confidence: 0.95840699125

00:06:40.660 --> 00:06:47.340 There we go alright? So.

NOTE Confidence: 0.95840699125

00:06:47.340 --> 00:06:49.945 Colon cancer remains one of

NOTE Confidence: 0.95840699125

00:06:49.945 --> 00:06:51.415 the most common cancers.

NOTE Confidence: 0.95840699125

00:06:51.415 --> 00:06:52.990 That's third common in both

NOTE Confidence: 0.95840699125

00:06:52.990 --> 00:06:54.870 men and women after prostate,

NOTE Confidence: 0.95840699125

00:06:54.870 --> 00:06:56.865 in Latin or breast and lung cancers,

NOTE Confidence: 0.95840699125

00:06:56.870 --> 00:07:00.180 and it also remains a.

NOTE Confidence: 0.95840699125

00:07:00.180 --> 00:07:03.342 You know high high contributor to

NOTE Confidence: 0.95840699125

00:07:03.342 --> 00:07:06.200 cancer deaths in both men and women,

NOTE Confidence: 0.95840699125

00:07:06.200 --> 00:07:11.105 and so it still remains a major problem in.

NOTE Confidence: 0.95840699125

00:07:11.110 --> 00:07:13.288 In the United States and worldwide,

NOTE Confidence: 0.95840699125

00:07:13.290 --> 00:07:15.180 and I wanted to make the patient

NOTE Confidence: 0.95840699125

00:07:15.180 --> 00:07:17.149 the age at 45 because recent

NOTE Confidence: 0.95840699125

00:07:17.149 --> 00:07:19.333 reports have shown that there's a

NOTE Confidence: 0.95840699125

00:07:19.333 --> 00:07:21.340 rising incident saying patients,

NOTE Confidence: 0.95840699125

00:07:21.340 --> 00:07:23.034 and I I really wanted to bring

NOTE Confidence: 0.95840699125

00:07:23.034 --> 00:07:24.200 this into this presentation

NOTE Confidence: 0.95840699125

00:07:24.200 --> 00:07:26.085 to just make everybody aware.

NOTE Confidence: 0.95840699125

00:07:26.090 --> 00:07:29.410 And although we have done a

NOTE Confidence: 0.95840699125

00:07:29.410 --> 00:07:31.050 really good job in decreasing

NOTE Confidence: 0.95840699125

00:07:31.120 --> 00:07:33.230 cancer rates in older populations,

NOTE Confidence: 0.95840699125

00:07:33.230 --> 00:07:36.926 we it had been noted that the younger

NOTE Confidence: 0.95840699125

00:07:36.926 --> 00:07:41.360 patients are having increasing rates and.

NOTE Confidence: 0.95840699125

00:07:41.360 --> 00:07:42.552 And the problem is,

NOTE Confidence: 0.95840699125

00:07:42.552 --> 00:07:44.630 is that the young populations are not,

NOTE Confidence: 0.95840699125

00:07:44.630 --> 00:07:45.384 you know,

NOTE Confidence: 0.95840699125

00:07:45.384 --> 00:07:47.646 not being screened as screening age

NOTE Confidence: 0.95840699125

00:07:47.646 --> 00:07:50.000 was greater than 50 for many years,

NOTE Confidence: 0.95840699125

00:07:50.000 --> 00:07:52.296 and most recently because of this data,

NOTE Confidence: 0.95840699125

00:07:52.300 --> 00:07:54.165 the American Cancer Society has

NOTE Confidence: 0.95840699125

00:07:54.165 --> 00:07:56.518 recommended that people at age 45

NOTE Confidence: 0.95840699125

00:07:56.518 --> 00:07:58.230 start undergo regular screening

NOTE Confidence: 0.95840699125

00:07:58.230 --> 00:07:59.514 for colorectal cancer.

NOTE Confidence: 0.95840699125

00:07:59.520 --> 00:08:00.942 And this is true for patients

NOTE Confidence: 0.95840699125

00:08:00.942 --> 00:08:01.653 with average risk.

NOTE Confidence: 0.95840699125

00:08:01.660 --> 00:08:02.121 Obviously,

NOTE Confidence: 0.95840699125

00:08:02.121 --> 00:08:05.348 if there's any other risk factors that

NOTE Confidence: 0.95840699125

00:08:05.348 --> 00:08:09.395 age of of screening might might also change.

NOTE Confidence: 0.95840699125

00:08:09.400 --> 00:08:11.630 And so diagnosis in colorectal

NOTE Confidence: 0.95840699125

00:08:11.630 --> 00:08:13.900 cancer is something that we do

NOTE Confidence: 0.95840699125

00:08:13.900 --> 00:08:15.720 every day as GI pathologists.

NOTE Confidence: 0.95840699125

00:08:15.720 --> 00:08:18.387 Here I have an example of a

NOTE Confidence: 0.95840699125

00:08:18.387 --> 00:08:20.877 malignant polyp that shows a little

NOTE Confidence: 0.95840699125

00:08:20.877 --> 00:08:23.394 bit of residual benign adenoma on

NOTE Confidence: 0.95840699125

00:08:23.394 --> 00:08:26.313 the side of this of this tumor.

NOTE Confidence: 0.95840699125

00:08:26.320 --> 00:08:28.440 But bulk of this small,

NOTE Confidence: 0.95840699125

00:08:28.440 --> 00:08:30.124 malignant polyp is composed

NOTE Confidence: 0.95840699125

00:08:30.124 --> 00:08:31.387 of invasive adenocarcinoma,

NOTE Confidence: 0.95840699125

00:08:31.390 --> 00:08:34.180 so we recognize the Mulligan glands,

NOTE Confidence: 0.95840699125

00:08:34.180 --> 00:08:36.408 but they're atypia irregularity,

NOTE Confidence: 0.95840699125

00:08:36.408 --> 00:08:39.193 and it doesn't plastic stroma.

NOTE Confidence: 0.95840699125

00:08:39.200 --> 00:08:42.256 And when I see a slide of cancer,

NOTE Confidence: 0.95840699125

00:08:42.260 --> 00:08:44.645 I automatically just my mind

NOTE Confidence: 0.95840699125

00:08:44.645 --> 00:08:47.030 comes to the molecular pathways

NOTE Confidence: 0.95840699125

00:08:47.111 --> 00:08:50.489 of colorectal carcinoma and.

NOTE Confidence: 0.95840699125

00:08:50.490 --> 00:08:52.170 What's exciting about colorectal personal.

NOTE Confidence: 0.95840699125

00:08:52.170 --> 00:08:55.789 It's it's one of the first examples

NOTE Confidence: 0.95840699125

00:08:55.789 --> 00:08:58.910 of a carcinogenesis pathway of of

NOTE Confidence: 0.95840699125

00:08:58.910 --> 00:09:02.333 showing how cancer can go from benign.

NOTE Confidence: 0.95840699125

00:09:02.340 --> 00:09:06.060 Lesions to invasive lesions that impact

NOTE Confidence: 0.95840699125

00:09:06.060 --> 00:09:09.580 patient health and patient mortality,

NOTE Confidence: 0.95840699125

00:09:09.580 --> 00:09:12.015 and there are multiple pathways

NOTE Confidence: 0.95840699125

00:09:12.015 --> 00:09:14.062 that colorectal cancer can form,

NOTE Confidence: 0.95840699125

00:09:14.062 --> 00:09:16.099 and so when I'm sitting and looking

NOTE Confidence: 0.95840699125

00:09:16.099 --> 00:09:18.520 at these slides of colorectal cancer,

NOTE Confidence: 0.95840699125

00:09:18.520 --> 00:09:20.740 I'm always thinking is this a,

NOTE Confidence: 0.95840699125

00:09:20.740 --> 00:09:22.320 you know, conventional pathways.

NOTE Confidence: 0.95840699125

00:09:22.320 --> 00:09:25.720 This is the rate of pathway and for the

NOTE Confidence: 0.95840699125

00:09:25.720 --> 00:09:27.912 purpose of MSI testing of why that's there,

NOTE Confidence: 0.95840699125

00:09:27.912 --> 00:09:29.717 it's because we do have a familial

NOTE Confidence: 0.95840699125

00:09:29.717 --> 00:09:31.229 pathway of colorectal cancer.

NOTE Confidence: 0.95840699125

00:09:31.230 --> 00:09:32.526 And there's two main.

NOTE Confidence: 0.95840699125

00:09:32.526 --> 00:09:32.850 Pathways,

NOTE Confidence: 0.95840699125

00:09:32.850 --> 00:09:34.950 Faps and Lynch Syndrome FAP is

NOTE Confidence: 0.95840699125

00:09:34.950 --> 00:09:36.807 generally fairly easy to diagnose

NOTE Confidence: 0.95840699125

00:09:36.807 --> 00:09:38.767 once you get to colonoscopy.

NOTE Confidence: 0.95840699125

00:09:38.770 --> 00:09:42.530 This is a phenotype that is quite dramatic.

NOTE Confidence: 0.95840699125

00:09:42.530 --> 00:09:44.840 There's hundreds and hundreds of

NOTE Confidence: 0.95840699125

00:09:44.840 --> 00:09:47.198 turbulent moments within the colon,

NOTE Confidence: 0.95840699125

00:09:47.198 --> 00:09:49.910 and so when patients get their

NOTE Confidence: 0.95840699125

00:09:49.910 --> 00:09:50.590 first colonoscopy,

NOTE Confidence: 0.95840699125

00:09:50.590 --> 00:09:53.050 the diagnosis can be made relatively easily.

NOTE Confidence: 0.95840699125

00:09:53.050 --> 00:09:54.736 Lynch syndrome, on the other hand,

NOTE Confidence: 0.95840699125

00:09:54.740 --> 00:09:55.990 does not have a polyposis.

NOTE Confidence: 0.95840699125

00:09:55.990 --> 00:09:58.706 The old name for Lynch syndrome was

NOTE Confidence: 0.95840699125

00:09:58.706 --> 00:10:01.725 non polyposis colorectal carcinoma.

NOTE Confidence: 0.95840699125

00:10:01.725 --> 00:10:07.530 And. And so this.

NOTE Confidence: 0.95840699125

00:10:07.530 --> 00:10:07.810 So,

NOTE Confidence: 0.95840699125

00:10:07.810 --> 00:10:09.210 so being able to recognize

NOTE Confidence: 0.95840699125

00:10:09.210 --> 00:10:10.330 Lynch syndrome is an

NOTE Confidence: 0.919879264285714

00:10:10.393 --> 00:10:11.877 important component to try.

NOTE Confidence: 0.919879264285714

00:10:11.880 --> 00:10:13.910 You know, to try to identify whether

NOTE Confidence: 0.919879264285714

00:10:13.910 --> 00:10:15.855 the patients that we are seeing

NOTE Confidence: 0.919879264285714

00:10:15.855 --> 00:10:17.207 have a genetic predisposition,

NOTE Confidence: 0.919879264285714

00:10:17.210 --> 00:10:19.580 which then will impact not just

NOTE Confidence: 0.919879264285714

00:10:19.580 --> 00:10:22.210 that patient but also their family.

NOTE Confidence: 0.919879264285714

00:10:22.210 --> 00:10:25.192 And Lynch syndrome is the most common

NOTE Confidence: 0.919879264285714

00:10:25.192 --> 00:10:27.950 form of heritable colorectal cancer.

NOTE Confidence: 0.919879264285714

00:10:27.950 --> 00:10:29.834 Probably accounts up to two to

NOTE Confidence: 0.919879264285714

00:10:29.834 --> 00:10:31.626 3% of all colorectal cancer.

NOTE Confidence: 0.919879264285714

00:10:31.626 --> 00:10:33.840 It has an autosomal dominant inheritance

NOTE Confidence: 0.919879264285714

00:10:33.905 --> 00:10:35.529 pattern and most importantly,

NOTE Confidence: 0.919879264285714

00:10:35.530 --> 00:10:37.005 it is associated with cancers

NOTE Confidence: 0.919879264285714

00:10:37.005 --> 00:10:38.990 outside of the GI tract as well,

NOTE Confidence: 0.919879264285714

00:10:38.990 --> 00:10:41.470 primarily in the mutual cancer,

NOTE Confidence: 0.919879264285714

00:10:41.470 --> 00:10:44.390 but various other ones to a lesser degree.

NOTE Confidence: 0.919879264285714

00:10:44.390 --> 00:10:46.842 And for many years,

NOTE Confidence: 0.919879264285714

00:10:46.842 --> 00:10:49.348 diagnostic criteria or based on

NOTE Confidence: 0.919879264285714

00:10:49.348 --> 00:10:50.997 the Amsterdam features which.

NOTE Confidence: 0.919879264285714

00:10:50.997 --> 00:10:53.199 Which really mostly looked at family

NOTE Confidence: 0.919879264285714

00:10:53.199 --> 00:10:56.228 history to be able to make a diagnosis

NOTE Confidence: 0.919879264285714

00:10:56.228 --> 00:10:58.412 at this particular syndrome and what

NOTE Confidence: 0.919879264285714

00:10:58.412 --> 00:11:01.180 happened in the 90s and into the 2000s,

NOTE Confidence: 0.919879264285714

00:11:01.180 --> 00:11:04.340 which is kind of when I was getting my PhD.

NOTE Confidence: 0.919879264285714

00:11:04.340 --> 00:11:05.956 Some of you know,

NOTE Confidence: 0.919879264285714

00:11:05.956 --> 00:11:08.380 some really important discoveries were made.

NOTE Confidence: 0.919879264285714

00:11:08.380 --> 00:11:11.240 One was that Lynch syndrome.

NOTE Confidence: 0.919879264285714

00:11:11.240 --> 00:11:13.110 Was.

NOTE Confidence: 0.919879264285714

00:11:13.110 --> 00:11:16.160 Was discovered to be related

NOTE Confidence: 0.919879264285714

00:11:16.160 --> 00:11:17.990 to microsatellite instability

NOTE Confidence: 0.919879264285714

00:11:17.990 --> 00:11:21.187 in the tumor cells and the.

NOTE Confidence: 0.919879264285714

00:11:21.190 --> 00:11:24.274 Set of four mismatch repair proteins

NOTE Confidence: 0.919879264285714

00:11:24.274 --> 00:11:27.943 were identified as the genetic cause of

NOTE Confidence: 0.919879264285714

00:11:27.943 --> 00:11:30.690 large syndrome and in at least one study,

NOTE Confidence: 0.919879264285714

00:11:30.690 --> 00:11:33.222 the most common mutation that's found

NOTE Confidence: 0.919879264285714

00:11:33.222 --> 00:11:36.618 in Lindstrom is MSH 2 and MLH 1 being

NOTE Confidence: 0.919879264285714

00:11:36.618 --> 00:11:39.026 a close second common with the other

NOTE Confidence: 0.919879264285714

00:11:39.026 --> 00:11:41.870 two being less frequent and just to

NOTE Confidence: 0.919879264285714

00:11:41.870 --> 00:11:44.010 remind everybody what are microsatellites.

NOTE Confidence: 0.919879264285714

00:11:44.010 --> 00:11:45.252 Microsatellites are

NOTE Confidence: 0.919879264285714

00:11:45.252 --> 00:11:47.736 repetitive regions of DNA.

NOTE Confidence: 0.919879264285714

00:11:47.740 --> 00:11:49.462 They can be found through they're

NOTE Confidence: 0.919879264285714

00:11:49.462 --> 00:11:50.610 found throughout the genome,

NOTE Confidence: 0.919879264285714

00:11:50.610 --> 00:11:51.191 including.

NOTE Confidence: 0.919879264285714

00:11:51.191 --> 00:11:54.677 Within exons of of important genes

NOTE Confidence: 0.919879264285714

00:11:54.680 --> 00:11:57.110 and they are particularly sensitive

NOTE Confidence: 0.919879264285714

00:11:57.110 --> 00:11:59.540 to replication errors to mismatches.

NOTE Confidence: 0.919879264285714

00:11:59.540 --> 00:12:04.230 So here you can see a mismatch occurred in

NOTE Confidence: 0.919879264285714

00:12:04.230 --> 00:12:07.620 this particular area and these proteins.

NOTE Confidence: 0.919879264285714

00:12:07.620 --> 00:12:09.995 These mismatch repair proteins repair

NOTE Confidence: 0.919879264285714

00:12:09.995 --> 00:12:12.760 that mismatch and if they are absent.

NOTE Confidence: 0.919879264285714

00:12:12.760 --> 00:12:15.128 If these proteins are not able to function,

NOTE Confidence: 0.919879264285714

00:12:15.130 --> 00:12:17.139 this mismatch is not repaired and you

NOTE Confidence: 0.919879264285714

00:12:17.139 --> 00:12:19.584 get you end up with variably sized

NOTE Confidence: 0.919879264285714

00:12:19.584 --> 00:12:21.870 alleles at that particular Microsoft like.

NOTE Confidence: 0.919879264285714

00:12:21.870 --> 00:12:25.726 So focus which can then be seen an

NOTE Confidence: 0.919879264285714

00:12:25.726 --> 00:12:28.786 old-fashioned gels which you know don't

NOTE Confidence: 0.919879264285714

00:12:28.786 --> 00:12:32.340 don't get done really anymore that much.

NOTE Confidence: 0.919879264285714

00:12:32.340 --> 00:12:34.752 So how does that you know

NOTE Confidence: 0.919879264285714

00:12:34.752 --> 00:12:37.070 really occur in more detail?

NOTE Confidence: 0.919879264285714

00:12:37.070 --> 00:12:40.085 So basically the mismatch is

NOTE Confidence: 0.919879264285714

00:12:40.085 --> 00:12:42.497 originally recognized by a

NOTE Confidence: 0.919879264285714

00:12:42.497 --> 00:12:44.908 heterodimer of MSH 2 and MSH 6.

NOTE Confidence: 0.919879264285714

00:12:44.910 --> 00:12:46.394 Which then recruits another

NOTE Confidence: 0.919879264285714

00:12:46.394 --> 00:12:48.940 heterodimer of MLH one and PMS two,

NOTE Confidence: 0.919879264285714

00:12:48.940 --> 00:12:49.843 and these heterodimer

NOTE Confidence: 0.919879264285714

00:12:49.843 --> 00:12:51.047 formations are really important.

NOTE Confidence: 0.919879264285714

00:12:51.050 --> 00:12:54.508 And once once this mismatch is recognized,

NOTE Confidence: 0.919879264285714

00:12:54.510 --> 00:12:56.634 other proteins get recruited to the

NOTE Confidence: 0.919879264285714

00:12:56.634 --> 00:12:58.890 site of this particular DNA mismatch,

NOTE Confidence: 0.919879264285714

00:12:58.890 --> 00:13:02.040 which then excised the region of the

NOTE Confidence: 0.919879264285714

00:13:02.040 --> 00:13:07.300 DNA that is involved and that gets re.

NOTE Confidence: 0.919879264285714

00:13:07.300 --> 00:13:11.549 Be synthesized and the heterodimers can be.

NOTE Confidence: 0.74578455

00:13:13.660 --> 00:13:14.520 Can be.

NOTE Confidence: 0.842628699333333

00:13:17.970 --> 00:13:21.030 And the reason that the heterodimers

NOTE Confidence: 0.842628699333333

00:13:21.030 --> 00:13:24.308 are important is because when you have

NOTE Confidence: 0.842628699333333

00:13:24.308 --> 00:13:26.308 a missing part of the heterodimers.

NOTE Confidence: 0.842628699333333

00:13:26.308 --> 00:13:28.759 So let's say there's a mutation and one

NOTE Confidence: 0.842628699333333

00:13:28.759 --> 00:13:30.684 of the genes that forms a heterodimer.

NOTE Confidence: 0.842628699333333

00:13:30.690 --> 00:13:33.972 The heterodimer is unstable and both

NOTE Confidence: 0.842628699333333

00:13:33.972 --> 00:13:37.080 proteins end up getting degraded.

NOTE Confidence: 0.842628699333333

00:13:37.080 --> 00:13:39.110 So if you have like a truncating

NOTE Confidence: 0.842628699333333

00:13:39.110 --> 00:13:40.838 mutation or something like that of 1,

NOTE Confidence: 0.842628699333333

00:13:40.840 --> 00:13:43.717 the other protein becomes unstable as well,

NOTE Confidence: 0.842628699333333

00:13:43.720 --> 00:13:45.988 and so we can see this.

NOTE Confidence: 0.842628699333333

00:13:45.990 --> 00:13:49.626 In the IHC that we do every day for

NOTE Confidence: 0.842628699333333

00:13:49.630 --> 00:13:52.269 four MMR proteins that we see the

NOTE Confidence: 0.842628699333333

00:13:52.269 --> 00:13:54.118 predominant pattern that we see

NOTE Confidence: 0.842628699333333

00:13:54.118 --> 00:13:56.068 is the paired loss of expression,

NOTE Confidence: 0.842628699333333

00:13:56.070 --> 00:14:00.790 and that's because of this biologic.

NOTE Confidence: 0.842628699333333

00:14:00.790 --> 00:14:03.620 Process of of the heterodimers

NOTE Confidence: 0.842628699333333

00:14:03.620 --> 00:14:07.350 being unstable when one is mutated.

NOTE Confidence: 0.842628699333333

00:14:07.350 --> 00:14:07.874 And conversely,

NOTE Confidence: 0.842628699333333

00:14:07.874 --> 00:14:09.708 when we see paired loss of expression,

NOTE Confidence: 0.842628699333333

00:14:09.710 --> 00:14:10.838 you know the other.

NOTE Confidence: 0.842628699333333

00:14:10.838 --> 00:14:12.248 The other header dimers usually

NOTE Confidence: 0.842628699333333

00:14:12.248 --> 00:14:13.630 shows preserved expression,

NOTE Confidence: 0.842628699333333

00:14:13.630 --> 00:14:15.295 although there are rare examples

NOTE Confidence: 0.842628699333333

00:14:15.295 --> 00:14:17.500 where all four might be missing.

NOTE Confidence: 0.842628699333333

00:14:17.500 --> 00:14:19.798 And so how does colorectal cancer

NOTE Confidence: 0.842628699333333

00:14:19.798 --> 00:14:21.330 develop and Lynch syndrome?

NOTE Confidence: 0.842628699333333

00:14:21.330 --> 00:14:24.612 There the model is an accelerated

NOTE Confidence: 0.842628699333333

00:14:24.612 --> 00:14:26.800 carcinogenesis model that adheres

NOTE Confidence: 0.842628699333333

00:14:26.882 --> 00:14:29.244 to nuisance hypothesis for the first

NOTE Confidence: 0.842628699333333

00:14:29.244 --> 00:14:31.806 hit is the germline mutation in one

NOTE Confidence: 0.842628699333333

00:14:31.806 --> 00:14:34.158 of the four at the margins and the

NOTE Confidence: 0.842628699333333

00:14:34.158 --> 00:14:36.920 second hit is a acquired somatic

NOTE Confidence: 0.842628699333333

00:14:36.920 --> 00:14:40.220 mutation of the paired MMR gene,

NOTE Confidence: 0.842628699333333

00:14:40.220 --> 00:14:43.112 usually within a adenoma that forms

NOTE Confidence: 0.842628699333333

00:14:43.112 --> 00:14:45.040 sporadically within within these

NOTE Confidence: 0.842628699333333

00:14:45.111 --> 00:14:47.445 patients and the thought is that.

NOTE Confidence: 0.842628699333333

00:14:47.450 --> 00:14:48.842 Sporadic I don't know.

NOTE Confidence: 0.842628699333333

00:14:48.842 --> 00:14:51.476 Must have formed an Ellis in a

NOTE Confidence: 0.842628699333333

00:14:51.476 --> 00:14:52.907 Lynch syndrome background.

NOTE Confidence: 0.842628699333333

00:14:52.910 --> 00:14:54.715 Will progress the cancer much

NOTE Confidence: 0.842628699333333

00:14:54.715 --> 00:14:57.355 faster than they would in a non

NOTE Confidence: 0.842628699333333

00:14:57.355 --> 00:14:58.498 Lynch syndrome patient.

NOTE Confidence: 0.787858124565217

00:15:00.540 --> 00:15:02.380 And here you can see an example of

NOTE Confidence: 0.787858124565217

00:15:02.380 --> 00:15:04.048 an adenoma that has lost so that

NOTE Confidence: 0.787858124565217

00:15:04.048 --> 00:15:05.820 knowledge one and PMS 2 not all of.

NOTE Confidence: 0.787858124565217

00:15:05.820 --> 00:15:07.948 Not all adenomas will show that in

NOTE Confidence: 0.787858124565217

00:15:07.948 --> 00:15:09.820 Lynch syndrome it's partly depends on

NOTE Confidence: 0.787858124565217

00:15:09.820 --> 00:15:12.680 the extent of you know of the pathway.

NOTE Confidence: 0.787858124565217

00:15:12.680 --> 00:15:14.051 That's that's progressed,

NOTE Confidence: 0.787858124565217

00:15:14.051 --> 00:15:17.880 at which time we actually see the biopsy.

NOTE Confidence: 0.787858124565217

00:15:17.880 --> 00:15:21.696 And so the current guidelines have been

NOTE Confidence: 0.787858124565217

00:15:21.696 --> 00:15:24.832 refined over the last decade or so,

NOTE Confidence: 0.787858124565217

00:15:24.840 --> 00:15:26.130 and now there's, you know,

NOTE Confidence: 0.787858124565217

00:15:26.130 --> 00:15:27.684 very strong recommendation.

NOTE Confidence: 0.787858124565217

00:15:27.684 --> 00:15:30.274 That there should be universal

NOTE Confidence: 0.787858124565217

00:15:30.274 --> 00:15:32.918 screening of all colorectal carcinomas

NOTE Confidence: 0.787858124565217

00:15:32.918 --> 00:15:35.966 to maximize the ability to identify

NOTE Confidence: 0.787858124565217

00:15:35.966 --> 00:15:38.280 patients with lips syndrome.

NOTE Confidence: 0.787858124565217

00:15:38.280 --> 00:15:41.628 And you know, and the mutual carcinomas

NOTE Confidence: 0.787858124565217

00:15:41.628 --> 00:15:43.570 are part of this recommendation.

NOTE Confidence: 0.787858124565217

00:15:43.570 --> 00:15:44.306 And I'm, you know,

NOTE Confidence: 0.787858124565217

00:15:44.306 --> 00:15:45.684 I'm going to leave it to others

NOTE Confidence: 0.787858124565217

00:15:45.684 --> 00:15:46.359 to talk about.

NOTE Confidence: 0.787858124565217

00:15:46.360 --> 00:15:49.290 End of mutual adenocarcinoma and

NOTE Confidence: 0.787858124565217

00:15:49.290 --> 00:15:51.634 and those you know.

NOTE Confidence: 0.787858124565217

00:15:51.640 --> 00:15:53.540 Special features that are

NOTE Confidence: 0.787858124565217

00:15:53.540 --> 00:15:55.915 associated with that tumor type.

NOTE Confidence: 0.887828775

00:15:58.100 --> 00:15:59.699 But more recently,

NOTE Confidence: 0.887828775

00:15:59.699 --> 00:16:02.364 the guidelines have also expanded

NOTE Confidence: 0.887828775

00:16:02.364 --> 00:16:05.170 the tumor types that should be

NOTE Confidence: 0.887828775

00:16:05.170 --> 00:16:07.145 included in that screening process,

NOTE Confidence: 0.887828775

00:16:07.150 --> 00:16:10.900 and that those tumors you know.

NOTE Confidence: 0.887828775

00:16:10.900 --> 00:16:13.316 Consider doing screening for

NOTE Confidence: 0.887828775

00:16:13.316 --> 00:16:15.532 other GI tractors. Small bowel,

NOTE Confidence: 0.887828775

00:16:15.532 --> 00:16:17.728 gastric pancreas, and you know, etc.

NOTE Confidence: 0.887828775

00:16:17.728 --> 00:16:19.463 And another important aspect of

NOTE Confidence: 0.887828775

00:16:19.463 --> 00:16:21.911 the new recommendations is that an

NOTE Confidence: 0.887828775

00:16:21.911 --> 00:16:24.280 infrastructure needs to be in place

NOTE Confidence: 0.887828775

00:16:24.280 --> 00:16:26.130 to handle the screening results.

NOTE Confidence: 0.904293453

00:16:28.270 --> 00:16:30.562 And the guidelines are actually interesting

NOTE Confidence: 0.904293453

00:16:30.562 --> 00:16:33.491 because they don't really come down on

NOTE Confidence: 0.904293453

00:16:33.491 --> 00:16:35.826 any particular method of screening.

NOTE Confidence: 0.904293453

00:16:35.830 --> 00:16:38.336 The two methods that are discussed in

NOTE Confidence: 0.904293453

00:16:38.336 --> 00:16:39.962 those guidelines are immunohistochemistry

NOTE Confidence: 0.904293453

00:16:39.962 --> 00:16:41.906 and the preliminary chain

NOTE Confidence: 0.904293453

00:16:41.906 --> 00:16:46.400 reaction or PCR, and you know.

NOTE Confidence: 0.904293453

00:16:46.400 --> 00:16:49.430 So both are accepted methods of

NOTE Confidence: 0.904293453

00:16:49.430 --> 00:16:52.377 screening and both have their own.

NOTE Confidence: 0.904293453

00:16:52.380 --> 00:16:55.110 Pluses and minuses in terms of what

NOTE Confidence: 0.904293453

00:16:55.110 --> 00:16:57.239 information and how sensitive they

NOTE Confidence: 0.904293453

00:16:57.239 --> 00:16:59.897 are for for capturing the patients.

NOTE Confidence: 0.904293453

00:16:59.900 --> 00:17:02.180 Immunohistochemistry is really the

NOTE Confidence: 0.904293453

00:17:02.180 --> 00:17:05.200 preferred initial method in practice,

NOTE Confidence: 0.904293453

00:17:05.200 --> 00:17:08.792 so most labs have ability to do

NOTE Confidence: 0.904293453

00:17:08.792 --> 00:17:11.060 immunostains that so this is an expensive

NOTE Confidence: 0.904293453

00:17:11.120 --> 00:17:13.130 and it's widely available and it's

NOTE Confidence: 0.904293453

00:17:13.130 --> 00:17:15.473 fairly easy to express to assess for

NOTE Confidence: 0.904293453

00:17:15.473 --> 00:17:17.657 the expression of them are proteins the

NOTE Confidence: 0.904293453

00:17:17.660 --> 00:17:19.830 turn around time is also very quick,

NOTE Confidence: 0.904293453

00:17:19.830 --> 00:17:23.685 and and as we'll see the pattern of MMR loss.

NOTE Confidence: 0.904293453

00:17:23.690 --> 00:17:27.360 And also suggest Lynch syndrome.

NOTE Confidence: 0.904293453

00:17:27.360 --> 00:17:27.970 And.

NOTE Confidence: 0.70450518

00:17:31.020 --> 00:17:32.975 And guide any additional testing

NOTE Confidence: 0.70450518

00:17:32.975 --> 00:17:34.930 manshu I see your question.

NOTE Confidence: 0.897152508333333

00:17:37.330 --> 00:17:41.173 So I do not know specific associations

NOTE Confidence: 0.897152508333333

00:17:41.173 --> 00:17:44.200 with head and neck tumors.

NOTE Confidence: 0.897152508333333

00:17:44.200 --> 00:17:46.028 With Lynch syndrome specifically,

NOTE Confidence: 0.897152508333333

00:17:46.028 --> 00:17:48.991 but if you do, you know I'm.

NOTE Confidence: 0.897152508333333

00:17:48.991 --> 00:17:51.253 I'm sure there have been reports,

NOTE Confidence: 0.897152508333333

00:17:51.260 --> 00:17:52.370 but I'm not aware of any,

NOTE Confidence: 0.897152508333333

00:17:52.370 --> 00:17:54.080 and if anybody else knows,

NOTE Confidence: 0.897152508333333

00:17:54.080 --> 00:17:55.050 feel free to chime in.

NOTE Confidence: 0.861887121111111

00:17:58.590 --> 00:18:00.963 The PCR method is used mostly at

NOTE Confidence: 0.861887121111111

00:18:00.963 --> 00:18:03.529 least in the realm of colorectal

NOTE Confidence: 0.861887121111111

00:18:03.529 --> 00:18:05.979 cancer as a confirmatory method,

NOTE Confidence: 0.861887121111111

00:18:05.980 --> 00:18:06.760 complementary method.

NOTE Confidence: 0.861887121111111

00:18:06.760 --> 00:18:09.490 It's not the primary method of screening,

NOTE Confidence: 0.861887121111111

00:18:09.490 --> 00:18:12.500 and it does require a

NOTE Confidence: 0.861887121111111

00:18:12.500 --> 00:18:14.366 molecular laboratory ability,

NOTE Confidence: 0.861887121111111

00:18:14.366 --> 00:18:18.490 so this limits its its availability,

NOTE Confidence: 0.861887121111111

00:18:18.490 --> 00:18:20.740 although these days.

NOTE Confidence: 0.861887121111111

00:18:20.740 --> 00:18:22.744 Most academic centers have a molecular

NOTE Confidence: 0.861887121111111

00:18:22.744 --> 00:18:24.596 laboratory where this can be done

NOTE Confidence: 0.861887121111111

00:18:24.596 --> 00:18:26.428 the turn around time is a little bit

NOTE Confidence: 0.861887121111111

00:18:26.490 --> 00:18:28.429 longer because there is a step of

NOTE Confidence: 0.861887121111111

00:18:28.429 --> 00:18:30.036 DNA extraction that needs to be done

NOTE Confidence: 0.861887121111111

00:18:30.036 --> 00:18:31.929 and and for a long time people sort

NOTE Confidence: 0.861887121111111

00:18:31.929 --> 00:18:33.963 of argued in literature about which

NOTE Confidence: 0.861887121111111

00:18:33.963 --> 00:18:35.676 microsatellite markers are the best, etc.

NOTE Confidence: 0.861887121111111

00:18:35.676 --> 00:18:38.098 And you know, I'm not going to

NOTE Confidence: 0.861887121111111

00:18:38.098 --> 00:18:40.649 go into those kind of details,

NOTE Confidence: 0.861887121111111

00:18:40.650 --> 00:18:43.914 but usually at least five microsatellite

NOTE Confidence: 0.861887121111111

00:18:43.914 --> 00:18:47.372 markers are tested to look for instability.

NOTE Confidence: 0.861887121111111

00:18:47.372 --> 00:18:48.336 And, importantly,

NOTE Confidence: 0.861887121111111

00:18:48.336 --> 00:18:51.710 the PCR reaction will not be able

NOTE Confidence: 0.861887121111111

00:18:51.789 --> 00:18:54.049 to distinguish inherited forms

NOTE Confidence: 0.861887121111111

00:18:54.050 --> 00:18:56.090 and sporadic forms of MSI cancer.

NOTE Confidence: 0.861887121111111

00:18:56.090 --> 00:18:57.629 And we'll look at that a little bit more.

NOTE Confidence: 0.861887121111111

00:18:57.630 --> 00:18:58.464 So here's result.

NOTE Confidence: 0.861887121111111

00:18:58.464 --> 00:18:59.020 Number one.

NOTE Confidence: 0.861887121111111

00:18:59.020 --> 00:19:02.396 Here we have an add no carcinoma that

NOTE Confidence: 0.861887121111111

00:19:02.396 --> 00:19:05.564 shows clearly shows loss of MSH 6 at MSH.

NOTE Confidence: 0.861887121111111

00:19:05.570 --> 00:19:07.400 2 in the tumor with preservation

NOTE Confidence: 0.861887121111111

00:19:07.400 --> 00:19:09.080 of MLH one and PMS 2.

NOTE Confidence: 0.861887121111111

00:19:09.080 --> 00:19:12.815 One important aspect of interpreting

NOTE Confidence: 0.861887121111111

00:19:12.815 --> 00:19:16.134 MMR stains is that you should

NOTE Confidence: 0.861887121111111

00:19:16.134 --> 00:19:18.414 look for intervening benign cells

NOTE Confidence: 0.861887121111111

00:19:18.414 --> 00:19:20.880 that have preserved staining.

NOTE Confidence: 0.861887121111111

00:19:20.880 --> 00:19:24.520 So in the MSH 16 that's a little bit faint,

NOTE Confidence: 0.861887121111111

00:19:24.520 --> 00:19:26.560 but you can see that there's some brown

NOTE Confidence: 0.861887121111111

00:19:26.560 --> 00:19:28.630 staining of the intervening stromal cells,

NOTE Confidence: 0.861887121111111

00:19:28.630 --> 00:19:30.740 mostly lymphocytes it looks like,

NOTE Confidence: 0.861887121111111

00:19:30.740 --> 00:19:32.378 and in the MSH 2 stain that

NOTE Confidence: 0.861887121111111

00:19:32.378 --> 00:19:33.920 is a little bit stronger,

NOTE Confidence: 0.861887121111111

00:19:33.920 --> 00:19:38.216 so there is some variability in in these.

NOTE Confidence: 0.861887121111111

00:19:38.220 --> 00:19:40.061 And and how you know what this

NOTE Confidence: 0.861887121111111

00:19:40.061 --> 00:19:41.370 looks like with results?

NOTE Confidence: 0.861887121111111

00:19:41.370 --> 00:19:44.496 And So what should happen next?

NOTE Confidence: 0.861887121111111

00:19:44.500 --> 00:19:45.588 Anybody have an idea?

NOTE Confidence: 0.870500851

00:19:48.100 --> 00:19:49.705 I'll give residents half a

NOTE Confidence: 0.870500851

00:19:49.705 --> 00:19:51.310 second to think about it.

NOTE Confidence: 0.967368852

00:19:56.520 --> 00:20:02.135 So the next step is well, so you can look

NOTE Confidence: 0.967368852

00:20:02.135 --> 00:20:04.893 for any algorithms that there's many,

NOTE Confidence: 0.967368852

00:20:04.893 --> 00:20:07.350 many algorithms that exist to help you

NOTE Confidence: 0.967368852

00:20:07.414 --> 00:20:09.934 figure out what to do with those results.

NOTE Confidence: 0.967368852

00:20:09.940 --> 00:20:12.924 So with the loss of MSH 2 and

NOTE Confidence: 0.967368852

00:20:12.924 --> 00:20:16.556 MSH 6 or isolated loss of PMS 2.

NOTE Confidence: 0.967368852

00:20:16.560 --> 00:20:18.490 The patients should be referred

NOTE Confidence: 0.967368852

00:20:18.490 --> 00:20:19.648 to cancer genetics.

NOTE Confidence: 0.967368852

00:20:19.650 --> 00:20:21.280 No additional testing is needed.

NOTE Confidence: 0.967368852

00:20:21.280 --> 00:20:22.300 They should just go to cancer,

NOTE Confidence: 0.967368852

00:20:22.300 --> 00:20:23.110 genetics and cancer.

NOTE Confidence: 0.967368852

00:20:23.110 --> 00:20:25.000 Genetics will take care of the rest.

NOTE Confidence: 0.967368852

00:20:25.000 --> 00:20:28.360 We don't need to worry about it.

NOTE Confidence: 0.967368852

00:20:28.360 --> 00:20:31.426 And we are really lucky at

NOTE Confidence: 0.967368852

00:20:31.426 --> 00:20:34.605 Yale because we do have that

NOTE Confidence: 0.967368852

00:20:34.605 --> 00:20:36.950 infrastructure in place that.

NOTE Confidence: 0.815315428181818

00:20:40.380 --> 00:20:42.980 That sorry, somebody is direct

NOTE Confidence: 0.815315428181818

00:20:42.980 --> 00:20:46.150 messaging me for the CMU code.

NOTE Confidence: 0.815315428181818

00:20:46.150 --> 00:20:47.938 That should be, uh, that's already

NOTE Confidence: 0.815315428181818

00:20:47.938 --> 00:20:49.699 been sent a couple of times.

NOTE Confidence: 0.3385651594

00:20:49.710 --> 00:20:52.710 Yeah, just just ignore. Ignore, yes.

NOTE Confidence: 0.892753072222222

00:20:55.010 --> 00:20:58.718 And so we do have an infrastructure in place.

NOTE Confidence: 0.892753072222222

00:20:58.720 --> 00:21:00.310 We do have a cancer genetics

NOTE Confidence: 0.892753072222222

00:21:00.310 --> 00:21:01.105 and prevention program.

NOTE Confidence: 0.892753072222222

00:21:01.110 --> 00:21:03.728 They're located at on the SRC campus,

NOTE Confidence: 0.892753072222222

00:21:03.730 --> 00:21:05.922 and the one of the directors of the

NOTE Confidence: 0.892753072222222

00:21:05.922 --> 00:21:09.942 program is Shabbir Lor, who's endoscopist.

NOTE Confidence: 0.892753072222222

00:21:09.942 --> 00:21:13.010 And and so, like I said,

NOTE Confidence: 0.892753072222222

00:21:13.010 --> 00:21:14.606 we're lucky that we have this infrastructure,

NOTE Confidence: 0.892753072222222

00:21:14.610 --> 00:21:17.952 and they've actually at Yale.

NOTE Confidence: 0.892753072222222

00:21:17.952 --> 00:21:19.496 This infrastructure has actually

NOTE Confidence: 0.892753072222222

00:21:19.496 --> 00:21:21.470 changed over over the years.

NOTE Confidence: 0.892753072222222

00:21:21.470 --> 00:21:23.984 Initially, you know, we had universal

NOTE Confidence: 0.892753072222222

00:21:23.984 --> 00:21:26.245 testing for colorectal cancer for a

NOTE Confidence: 0.892753072222222

00:21:26.245 --> 00:21:30.840 number of years now and initially.

NOTE Confidence: 0.892753072222222

00:21:30.840 --> 00:21:34.028 But it was dependent on the provider,

NOTE Confidence: 0.892753072222222

00:21:34.028 --> 00:21:34.636 you know.

NOTE Confidence: 0.892753072222222

00:21:34.636 --> 00:21:37.240 So we see the biopsy of the cancer.

NOTE Confidence: 0.892753072222222

00:21:37.240 --> 00:21:38.680 We do the immunostains.

NOTE Confidence: 0.892753072222222

00:21:38.680 --> 00:21:40.840 We write a report of that,

NOTE Confidence: 0.892753072222222

00:21:40.840 --> 00:21:44.192 and it goes back to the endoscopist to have,

NOTE Confidence: 0.892753072222222

00:21:44.192 --> 00:21:44.764 you know,

NOTE Confidence: 0.892753072222222

00:21:44.764 --> 00:21:46.861 to have that result and then it

NOTE Confidence: 0.892753072222222

00:21:46.861 --> 00:21:48.727 depended on that endoscopist to be

NOTE Confidence: 0.892753072222222

00:21:48.727 --> 00:21:51.189 able to refer the patient to genetics.

NOTE Confidence: 0.892753072222222

00:21:51.190 --> 00:21:53.645 Well, this this genetics clinic

NOTE Confidence: 0.892753072222222

00:21:53.645 --> 00:21:55.609 decided you know what?

NOTE Confidence: 0.892753072222222

00:21:55.610 --> 00:21:56.214 Screw that.

NOTE Confidence: 0.892753072222222

00:21:56.214 --> 00:21:58.630 Let's let's see if we can get to

NOTE Confidence: 0.892753072222222

00:21:58.706 --> 00:22:00.967 this data a little bit more a

NOTE Confidence: 0.892753072222222

00:22:00.967 --> 00:22:03.040 little bit faster and so they've.

NOTE Confidence: 0.892753072222222

00:22:03.040 --> 00:22:05.284 They've you know,

NOTE Confidence: 0.892753072222222

00:22:05.284 --> 00:22:08.199 created some automated review at

NOTE Confidence: 0.892753072222222

00:22:08.199 --> 00:22:10.564 First pathologist review and now

NOTE Confidence: 0.892753072222222

00:22:10.564 --> 00:22:13.110 an automated review for colorectal

NOTE Confidence: 0.892753072222222

00:22:13.110 --> 00:22:15.570 cancer and and it's turned out

NOTE Confidence: 0.892753072222222

00:22:15.570 --> 00:22:17.990 that with this strategy where they

NOTE Confidence: 0.892753072222222

00:22:17.990 --> 00:22:20.720 get an automated report of all the

NOTE Confidence: 0.892753072222222

00:22:20.720 --> 00:22:22.977 patients that meet certain criteria

NOTE Confidence: 0.892753072222222

00:22:22.977 --> 00:22:25.685 with the results they've been able

NOTE Confidence: 0.892753072222222

00:22:25.685 --> 00:22:27.860 to identify eleven additional Lynch

NOTE Confidence: 0.892753072222222

00:22:27.860 --> 00:22:30.648 syndrome patients in in this time frame.

NOTE Confidence: 0.892753072222222

00:22:30.648 --> 00:22:31.680 And it it.

NOTE Confidence: 0.892753072222222

00:22:31.680 --> 00:22:33.780 Seems to be a cost effective way

NOTE Confidence: 0.892753072222222

00:22:33.780 --> 00:22:36.199 of doing this material and this

NOTE Confidence: 0.892753072222222

00:22:36.199 --> 00:22:38.655 this data had been presented at

NOTE Confidence: 0.892753072222222

00:22:38.655 --> 00:22:41.880 a couple of different meetings.

NOTE Confidence: 0.892753072222222

00:22:41.880 --> 00:22:43.956 Over the last couple of years,

NOTE Confidence: 0.892753072222222

00:22:43.960 --> 00:22:45.620 and so we you know,

NOTE Confidence: 0.892753072222222

00:22:45.620 --> 00:22:48.284 we again all we need to worry as

NOTE Confidence: 0.892753072222222

00:22:48.284 --> 00:22:50.992 well exists is that we report the

NOTE Confidence: 0.892753072222222

00:22:50.992 --> 00:22:53.644 results and those results will be

NOTE Confidence: 0.892753072222222

00:22:53.644 --> 00:22:55.534 automatically sent over to the

NOTE Confidence: 0.892753072222222

00:22:55.534 --> 00:22:57.460 genetics clinic for them to be

NOTE Confidence: 0.892753072222222

00:22:57.533 --> 00:22:59.591 able to reach out to the patient

NOTE Confidence: 0.892753072222222

00:22:59.591 --> 00:23:02.115 and to the provider of the patient

NOTE Confidence: 0.892753072222222

00:23:02.115 --> 00:23:04.758 to create that genetic consult.

NOTE Confidence: 0.892753072222222

00:23:04.758 --> 00:23:09.030 For confirmation of diagnosis.

NOTE Confidence: 0.892753072222222

00:23:09.030 --> 00:23:13.119 And MRI is usually pretty

NOTE Confidence: 0.892753072222222

00:23:13.119 --> 00:23:14.958 straightforward to interpret.

NOTE Confidence: 0.892753072222222

00:23:14.960 --> 00:23:16.759 There's you know it's really just as

NOTE Confidence: 0.892753072222222

00:23:16.759 --> 00:23:18.848 the is there standing as they're not,

NOTE Confidence: 0.892753072222222

00:23:18.850 --> 00:23:22.930 but there are a couple of cautious

NOTE Confidence: 0.892753072222222

00:23:22.930 --> 00:23:24.967 caveats that should be kept in mind.

NOTE Confidence: 0.892753072222222

00:23:24.970 --> 00:23:27.985 If you have a very small amount of tumor,

NOTE Confidence: 0.892753072222222

00:23:27.990 --> 00:23:29.320 you know,

NOTE Confidence: 0.892753072222222

00:23:29.320 --> 00:23:33.310 be cognizant that limited tumor samples.

NOTE Confidence: 0.892753072222222

00:23:33.310 --> 00:23:35.130 May have, you know,

NOTE Confidence: 0.892753072222222

00:23:35.130 --> 00:23:36.950 maybe under you know,

NOTE Confidence: 0.892753072222222

00:23:36.950 --> 00:23:39.351 maybe over called for absence of tumor

NOTE Confidence: 0.892753072222222

00:23:39.351 --> 00:23:41.482 staining if you're only looking at a

NOTE Confidence: 0.892753072222222

00:23:41.482 --> 00:23:43.890 a few glance of tumor and also some

NOTE Confidence: 0.892753072222222

00:23:43.890 --> 00:23:45.870 unusual patterns have been reported.

NOTE Confidence: 0.892753072222222

00:23:45.870 --> 00:23:48.618 Some of those are things like

NOTE Confidence: 0.892753072222222

00:23:48.618 --> 00:23:50.450 this dot like powder.

NOTE Confidence: 0.892753072222222

00:23:50.450 --> 00:23:52.075 Majority of these are associated

NOTE Confidence: 0.892753072222222

00:23:52.075 --> 00:23:53.375 with lots of protein.

NOTE Confidence: 0.892753072222222

00:23:53.380 --> 00:23:55.060 It's an abnormal expression pattern

NOTE Confidence: 0.892753072222222

00:23:55.060 --> 00:23:57.628 and so if if you're ever in doubt

NOTE Confidence: 0.892753072222222

00:23:57.628 --> 00:23:59.553 you can always order the PCR to

NOTE Confidence: 0.892753072222222

00:23:59.615 --> 00:24:02.100 confirm that there's presence of

NOTE Confidence: 0.892753072222222

00:24:02.100 --> 00:24:04.140 microsatellite stability and false

NOTE Confidence: 0.892753072222222

00:24:04.140 --> 00:24:06.740 negative results are pretty rare.

NOTE Confidence: 0.892753072222222

00:24:06.740 --> 00:24:10.370 They will occur in less than 10% of.

NOTE Confidence: 0.892753072222222

00:24:10.370 --> 00:24:12.778 Of patients and that can occur because

NOTE Confidence: 0.892753072222222

00:24:12.778 --> 00:24:14.760 depending on the mutation type,

NOTE Confidence: 0.892753072222222

00:24:14.760 --> 00:24:15.660 it may not be.

NOTE Confidence: 0.892753072222222

00:24:15.660 --> 00:24:16.785 Activity can still be preserved

NOTE Confidence: 0.892753072222222

00:24:16.785 --> 00:24:18.163 even though there is actual

NOTE Confidence: 0.892753072222222

00:24:18.163 --> 00:24:19.267 dysfunction of the protein,

NOTE Confidence: 0.947275824

00:24:19.270 --> 00:24:20.690 so it it can happen.

NOTE Confidence: 0.947275824

00:24:20.690 --> 00:24:23.175 It's a biological phenomenon that's

NOTE Confidence: 0.947275824

00:24:23.175 --> 00:24:25.722 quite possible and more recently with

NOTE Confidence: 0.947275824

00:24:25.722 --> 00:24:28.050 one of our residents not allowed.

NOTE Confidence: 0.947275824

00:24:28.050 --> 00:24:32.435 Smote. Oh, I have done a small study to

NOTE Confidence: 0.947275824

00:24:32.435 --> 00:24:36.350 look at our MMR staining here at Yale,

NOTE Confidence: 0.947275824

00:24:36.350 --> 00:24:38.765 and we looked at 150 patients who

NOTE Confidence: 0.947275824

00:24:38.765 --> 00:24:41.530 had two or more MMR IHC results.

NOTE Confidence: 0.947275824

00:24:41.530 --> 00:24:44.050 And it turns out that most of those

NOTE Confidence: 0.947275824

00:24:44.050 --> 00:24:46.300 MMR results are quite reproducible,

NOTE Confidence: 0.947275824

00:24:46.300 --> 00:24:47.746 and so it's a robust test,

NOTE Confidence: 0.947275824

00:24:47.750 --> 00:24:50.487 and we did find this coordinate MRI

NOTE Confidence: 0.947275824

00:24:50.487 --> 00:24:53.978 HC patterns and 6% of patients and.

NOTE Confidence: 0.9217447

00:24:56.240 --> 00:25:01.030 And. Those 6% primarily were

NOTE Confidence: 0.9217447

00:25:01.030 --> 00:25:02.785 independent primary tumor,

NOTE Confidence: 0.9217447

00:25:02.790 --> 00:25:04.846 so if a patient had a primary of,

NOTE Confidence: 0.9217447

00:25:04.850 --> 00:25:06.830 you know colon and a primary,

NOTE Confidence: 0.9217447

00:25:06.830 --> 00:25:09.224 you know of breast, they might show

NOTE Confidence: 0.9217447

00:25:09.224 --> 00:25:11.591 different patterns of IHC because they

NOTE Confidence: 0.9217447

00:25:11.591 --> 00:25:13.726 will arise through different mechanisms.

NOTE Confidence: 0.9217447

00:25:13.730 --> 00:25:16.862 And then I have a question from Doctor Robert

NOTE Confidence: 0.9217447

00:25:16.862 --> 00:25:20.850 about utility of them are in adenomas.

NOTE Confidence: 0.9217447

00:25:20.850 --> 00:25:26.238 And so yes, adenomas can show loss

NOTE Confidence: 0.9217447

00:25:26.238 --> 00:25:29.368 of of MMR proteins, but not always.

NOTE Confidence: 0.9217447

00:25:29.370 --> 00:25:31.610 It's, you know, if you find loss,

NOTE Confidence: 0.9217447

00:25:31.610 --> 00:25:32.430 that's great,

NOTE Confidence: 0.9217447

00:25:32.430 --> 00:25:35.604 and you can certainly use that

NOTE Confidence: 0.9217447

00:25:35.604 --> 00:25:38.766 information to suggest genetic counseling.

NOTE Confidence: 0.9217447

00:25:38.766 --> 00:25:42.140 But if you find preserved IHC,

NOTE Confidence: 0.9217447

00:25:42.140 --> 00:25:44.120 it does not rule out the

NOTE Confidence: 0.9217447

00:25:44.120 --> 00:25:45.770 possibility of Lynch syndrome.

NOTE Confidence: 0.9217447

00:25:45.770 --> 00:25:46.544 In that case,

NOTE Confidence: 0.9217447

00:25:46.544 --> 00:25:48.092 I don't have a slide specifically

NOTE Confidence: 0.9217447

00:25:48.092 --> 00:25:49.019 addressing this question.

NOTE Confidence: 0.898589208333333

00:25:52.160 --> 00:25:54.380 Alright, so here is another result,

NOTE Confidence: 0.898589208333333

00:25:54.380 --> 00:25:55.976 so this is another possible outcome.

NOTE Confidence: 0.898589208333333

00:25:55.980 --> 00:25:59.616 Here we have a mucinous adenocarcinoma.

NOTE Confidence: 0.898589208333333

00:25:59.620 --> 00:26:02.149 You can see a lot of you know mucin

NOTE Confidence: 0.898589208333333

00:26:02.149 --> 00:26:03.645 production with the malignant lens

NOTE Confidence: 0.898589208333333

00:26:03.645 --> 00:26:06.243 here and we see loss of MLH one and

NOTE Confidence: 0.898589208333333

00:26:06.243 --> 00:26:08.126 PMS two and again we always want

NOTE Confidence: 0.898589208333333

00:26:08.130 --> 00:26:10.656 to look for positive staining in

NOTE Confidence: 0.898589208333333

00:26:10.656 --> 00:26:12.892 the intervening normal cells that

NOTE Confidence: 0.898589208333333

00:26:12.892 --> 00:26:15.157 are present within the around.

NOTE Confidence: 0.898589208333333

00:26:15.160 --> 00:26:16.540 The tumor within the tumor.

NOTE Confidence: 0.898589208333333

00:26:16.540 --> 00:26:18.860 And we have preservation of MSH 2 and MSH 6.

NOTE Confidence: 0.898589208333333

00:26:18.860 --> 00:26:20.534 So what's the?

NOTE Confidence: 0.898589208333333

00:26:20.534 --> 00:26:22.766 Next step here anybody.

NOTE Confidence: 0.945369157142857

00:26:29.120 --> 00:26:30.926 So I'll just move on to that,

NOTE Confidence: 0.945369157142857

00:26:30.930 --> 00:26:34.298 let's see. There you go.

NOTE Confidence: 0.945369157142857

00:26:34.298 --> 00:26:36.090 So the answer is that we should

NOTE Confidence: 0.945369157142857

00:26:36.147 --> 00:26:37.939 go to MLH 1 methylation and the

NOTE Confidence: 0.945369157142857

00:26:37.939 --> 00:26:40.185 reason why we need to do that is

NOTE Confidence: 0.945369157142857

00:26:40.185 --> 00:26:41.605 because we need to distinguish.

NOTE Confidence: 0.945369157142857

00:26:41.610 --> 00:26:43.714 Tumors that occur in the setting of Lynch

NOTE Confidence: 0.945369157142857

00:26:43.714 --> 00:26:45.729 syndrome from those that occur sporadically.

NOTE Confidence: 0.945369157142857

00:26:45.730 --> 00:26:48.286 So here is our algorithm and

NOTE Confidence: 0.945369157142857

00:26:48.286 --> 00:26:49.868 so now we have lots of MLH,

NOTE Confidence: 0.945369157142857

00:26:49.870 --> 00:26:52.915 one with or without loss of PMS

NOTE Confidence: 0.945369157142857

00:26:52.915 --> 00:26:55.948 two this should trigger.

NOTE Confidence: 0.945369157142857

00:26:55.950 --> 00:26:59.718 Ordering MLH 1 metalation PCR to

NOTE Confidence: 0.945369157142857

00:26:59.718 --> 00:27:03.118 determine what happens and the MLH 1

NOTE Confidence: 0.945369157142857

00:27:03.118 --> 00:27:05.003 methylation specific PCR is performed

NOTE Confidence: 0.945369157142857

00:27:05.003 --> 00:27:07.899 in our Yale Molecular Diagnostics Lab,

NOTE Confidence: 0.945369157142857

00:27:07.900 --> 00:27:11.724 so it's pretty easy to to do that

NOTE Confidence: 0.945369157142857

00:27:11.724 --> 00:27:15.960 ordering and depending on what the MLH

NOTE Confidence: 0.945369157142857

00:27:15.960 --> 00:27:20.650 1 methylation results show you would

NOTE Confidence: 0.945369157142857

00:27:20.650 --> 00:27:23.856 you would refer the patient to genetics,

NOTE Confidence: 0.945369157142857

00:27:23.860 --> 00:27:26.770 so if no methylation is seen.

NOTE Confidence: 0.945369157142857

00:27:26.770 --> 00:27:29.262 Of MLH one, then the patient should

NOTE Confidence: 0.945369157142857

00:27:29.262 --> 00:27:31.539 be referred to cancer genetics,

NOTE Confidence: 0.945369157142857

00:27:31.540 --> 00:27:32.780 and so that's the reason.

NOTE Confidence: 0.945369157142857

00:27:32.780 --> 00:27:34.808 Why is because there's two pathways

NOTE Confidence: 0.945369157142857

00:27:34.808 --> 00:27:36.640 to MSI and colorectal cancer,

NOTE Confidence: 0.945369157142857

00:27:36.640 --> 00:27:38.140 and they're actually both quite different.

NOTE Confidence: 0.945369157142857

00:27:38.140 --> 00:27:41.094 So we've talked at length about Lynch

NOTE Confidence: 0.945369157142857

00:27:41.094 --> 00:27:44.117 syndrome and I wish I see your answer.

NOTE Confidence: 0.945369157142857

00:27:44.120 --> 00:27:46.830 I I, you know, I, I didn't.

NOTE Confidence: 0.945369157142857

00:27:46.830 --> 00:27:49.190 I didn't see it fast enough to read

NOTE Confidence: 0.945369157142857

00:27:49.263 --> 00:27:51.759 it as I started to explain the answer.

NOTE Confidence: 0.945369157142857

00:27:51.760 --> 00:27:54.064 But you're absolutely correct,

NOTE Confidence: 0.945369157142857

00:27:54.064 --> 00:27:54.640 methylation.

NOTE Confidence: 0.945369157142857

00:27:54.640 --> 00:27:56.770 So the Lynch syndrome we've already

NOTE Confidence: 0.945369157142857

00:27:56.770 --> 00:27:57.480 talked about.

NOTE Confidence: 0.945369157142857

00:27:57.480 --> 00:28:00.096 We talked about how patients have

NOTE Confidence: 0.945369157142857

00:28:00.096 --> 00:28:02.490 germline mutations and they get a

NOTE Confidence: 0.945369157142857

00:28:02.490 --> 00:28:05.010 second hit in their adenoma which can

NOTE Confidence: 0.945369157142857

00:28:05.091 --> 00:28:08.019 then lead to deficient mismatch repair.

NOTE Confidence: 0.945369157142857

00:28:08.020 --> 00:28:08.574 Ultimately,

NOTE Confidence: 0.945369157142857

00:28:08.574 --> 00:28:10.236 microsatellite stability and

NOTE Confidence: 0.945369157142857

00:28:10.236 --> 00:28:11.898 with microsatellite stability

NOTE Confidence: 0.945369157142857

00:28:11.898 --> 00:28:14.403 come secondary mutations and a

NOTE Confidence: 0.945369157142857

00:28:14.403 --> 00:28:15.959 variety of coding microsatellites.

NOTE Confidence: 0.945369157142857

00:28:15.960 --> 00:28:18.298 And it can lead to and all

NOTE Confidence: 0.945369157142857

00:28:18.298 --> 00:28:20.118 of that leads to cancer.

NOTE Confidence: 0.945369157142857

00:28:20.120 --> 00:28:23.857 Sporadic MSI cancers are quite different,

NOTE Confidence: 0.945369157142857

00:28:23.857 --> 00:28:26.776 although the end result is very similar

NOTE Confidence: 0.945369157142857

00:28:26.776 --> 00:28:29.498 meaning that they do end up with

NOTE Confidence: 0.945369157142857

00:28:29.498 --> 00:28:31.318 the same deficient mismatch repair.

NOTE Confidence: 0.945369157142857

00:28:31.320 --> 00:28:34.218 But the mechanism and the process is

NOTE Confidence: 0.945369157142857

00:28:34.218 --> 00:28:38.810 very different and so MSI high sporadic.

NOTE Confidence: 0.945369157142857

00:28:38.810 --> 00:28:41.630 Cancers occur through the serrated pathway

NOTE Confidence: 0.945369157142857

00:28:41.630 --> 00:28:44.499 of carcinogenesis and in this pathway,

NOTE Confidence: 0.945369157142857

00:28:44.500 --> 00:28:46.944 sessile strated polyps are

NOTE Confidence: 0.945369157142857

00:28:46.944 --> 00:28:49.500 thoughts develop a intermediate,

NOTE Confidence: 0.945369157142857

00:28:49.500 --> 00:28:50.830 dysplastic steps.

NOTE Confidence: 0.945369157142857

00:28:50.830 --> 00:28:52.825 Most SSPS will.

NOTE Confidence: 0.945369157142857

00:28:52.830 --> 00:28:56.687 This will have beer after 600 imitation,

NOTE Confidence: 0.945369157142857

00:28:56.690 --> 00:29:00.062 so these tumors also very commonly

NOTE Confidence: 0.945369157142857

00:29:00.062 --> 00:29:03.080 have fee 600 mutations and then

NOTE Confidence: 0.945369157142857

00:29:03.080 --> 00:29:05.005 what happens and you know.

NOTE Confidence: 0.945369157142857

00:29:05.010 --> 00:29:06.845 It's it's really unclear how

NOTE Confidence: 0.945369157142857

00:29:06.845 --> 00:29:09.398 this starts or why you know what

NOTE Confidence: 0.945369157142857

00:29:09.398 --> 00:29:11.659 is it within an SSP that allows

NOTE Confidence: 0.945369157142857

00:29:11.659 --> 00:29:13.787 for this mechanism to occur.

NOTE Confidence: 0.945369157142857

00:29:13.790 --> 00:29:16.072 But what is that to happen is

NOTE Confidence: 0.945369157142857

00:29:16.072 --> 00:29:19.083 that the MLH 1 gene is silenced

NOTE Confidence: 0.945369157142857

00:29:19.083 --> 00:29:21.528 in an epigenetic fashion through

NOTE Confidence: 0.945369157142857

00:29:21.528 --> 00:29:24.188 methylation of the promoter of MLH one.

NOTE Confidence: 0.945369157142857

00:29:24.190 --> 00:29:26.024 So here's all of these CPG islands

NOTE Confidence: 0.945369157142857

00:29:26.024 --> 00:29:27.950 that end up getting methylated,

NOTE Confidence: 0.945369157142857

00:29:27.950 --> 00:29:31.786 and once it is methylated the chromatin

NOTE Confidence: 0.945369157142857

00:29:31.786 --> 00:29:36.147 closes up and is inaccessible to being.

NOTE Confidence: 0.945369157142857

00:29:36.150 --> 00:29:38.014 Transcribed and the protein

NOTE Confidence: 0.945369157142857

00:29:38.014 --> 00:29:40.344 can no longer be expressed.

NOTE Confidence: 0.945369157142857

00:29:40.350 --> 00:29:46.698 So virtually all cases of sporadic.

NOTE Confidence: 0.945369157142857

00:29:46.700 --> 00:29:49.420 MSI high cancers will have

NOTE Confidence: 0.945369157142857

00:29:49.420 --> 00:29:51.284 MLH 1 promoter methylation,

NOTE Confidence: 0.945369157142857

00:29:51.284 --> 00:29:55.174 which we can test for and the result

NOTE Confidence: 0.945369157142857

00:29:55.174 --> 00:29:58.813 is that patients get MSI high cancers.

NOTE Confidence: 0.945369157142857

00:29:58.813 --> 00:30:01.939 These tend to be poorly differentiated

NOTE Confidence: 0.945369157142857

00:30:01.939 --> 00:30:04.228 or mucinous in nature.

NOTE Confidence: 0.945369157142857

00:30:04.230 --> 00:30:06.218 They also have other associations such as

NOTE Confidence: 0.945369157142857

00:30:06.218 --> 00:30:08.236 more commonly being found on the right side,

NOTE Confidence: 0.919368495

00:30:08.240 --> 00:30:10.958 more commonly being found in older

NOTE Confidence: 0.919368495

00:30:10.958 --> 00:30:12.770 patients and female patients.

NOTE Confidence: 0.919368495

00:30:12.770 --> 00:30:15.443 They do tend to have a good prognosis and

NOTE Confidence: 0.919368495

00:30:15.443 --> 00:30:19.670 there are some specific. Therapeutic?

NOTE Confidence: 0.919368495

00:30:19.670 --> 00:30:23.570 Options for these patients. And so.

NOTE Confidence: 0.914795324

00:30:26.430 --> 00:30:28.860 Going back to our paradigm,

NOTE Confidence: 0.914795324

00:30:28.860 --> 00:30:30.624 this is where we would determine

NOTE Confidence: 0.914795324

00:30:30.624 --> 00:30:32.522 if if a patient needed referral

NOTE Confidence: 0.914795324

00:30:32.522 --> 00:30:34.832 to genetics or if they have a

NOTE Confidence: 0.914795324

00:30:34.832 --> 00:30:36.608 sporadic form of MSI high cancer

NOTE Confidence: 0.914795324

00:30:36.608 --> 00:30:38.818 when it comes to loss of MLH 1.

NOTE Confidence: 0.866319956666667

00:30:46.740 --> 00:30:50.225 And so moving out patient two patient

NOTE Confidence: 0.866319956666667

00:30:50.225 --> 00:30:52.970 two is a 50 year old woman she had.

NOTE Confidence: 0.866319956666667

00:30:52.970 --> 00:30:55.679 She was diagnosed with a right sided add no

NOTE Confidence: 0.866319956666667

00:30:55.679 --> 00:30:59.076 carcinoma and we already had testing done.

NOTE Confidence: 0.866319956666667

00:30:59.080 --> 00:31:02.016 She had MLH one and PMS two loss.

NOTE Confidence: 0.866319956666667

00:31:02.020 --> 00:31:04.450 So you can see those there.

NOTE Confidence: 0.866319956666667

00:31:04.450 --> 00:31:07.838 She was positive for MLH 1 methylation.

NOTE Confidence: 0.866319956666667

00:31:07.840 --> 00:31:10.820 So we think it's sporadic.

NOTE Confidence: 0.866319956666667

00:31:10.820 --> 00:31:11.600 It's a sporadic I'm.

NOTE Confidence: 0.866319956666667

00:31:11.600 --> 00:31:12.816 It's like I can't, Sir,

NOTE Confidence: 0.866319956666667

00:31:12.816 --> 00:31:15.868 but the note was that she had

NOTE Confidence: 0.866319956666667

00:31:15.868 --> 00:31:18.970 greater than 50 polyps in her colon.

NOTE Confidence: 0.866319956666667

00:31:18.970 --> 00:31:20.811 So what is a possible diagnosis and

NOTE Confidence: 0.866319956666667

00:31:20.811 --> 00:31:23.057 the hint is that she ended up with a.

NOTE Confidence: 0.6918929376

00:31:25.840 --> 00:31:28.235 Total colectomy and majority of

NOTE Confidence: 0.6918929376

00:31:28.235 --> 00:31:30.630 her polyps versus ulcerated polyps.

NOTE Confidence: 0.917919565

00:31:32.670 --> 00:31:35.682 And if any of the residents

NOTE Confidence: 0.917919565

00:31:35.682 --> 00:31:38.998 have an idea of. Of a diagnosis.

NOTE Confidence: 0.851673578448276

00:31:44.790 --> 00:31:46.926 Alright, so the possible diagnosis is

NOTE Confidence: 0.851673578448276

00:31:46.926 --> 00:31:49.260 that the patient has severe polyposis

NOTE Confidence: 0.851673578448276

00:31:49.260 --> 00:31:52.221 syndrome and this continues to be an

NOTE Confidence: 0.851673578448276

00:31:52.221 --> 00:31:53.818 underrecognized colorectal predisposition

NOTE Confidence: 0.851673578448276

00:31:53.818 --> 00:31:56.578 polyposis syndrome that is specifically

NOTE Confidence: 0.851673578448276

00:31:56.578 --> 00:32:00.690 associated with MSI high MLH one loss

NOTE Confidence: 0.851673578448276

00:32:00.690 --> 00:32:06.650 and MLH 1 methylated carcinomas, and.

NOTE Confidence: 0.851673578448276

00:32:06.650 --> 00:32:09.498 Men and women tend to get this equally.

NOTE Confidence: 0.851673578448276

00:32:09.500 --> 00:32:12.188 This can be seen at any age.

NOTE Confidence: 0.851673578448276

00:32:12.190 --> 00:32:14.910 And it's usually diagnosed unexpectedly

NOTE Confidence: 0.851673578448276

00:32:14.910 --> 00:32:17.950 at screening colonoscopy or or at.

NOTE Confidence: 0.851673578448276

00:32:17.950 --> 00:32:21.643 Or colectomy, there's two main variants.

NOTE Confidence: 0.851673578448276

00:32:21.643 --> 00:32:23.108 Type one and Type 2,

NOTE Confidence: 0.851673578448276

00:32:23.110 --> 00:32:25.147 based on sort of the location and

NOTE Confidence: 0.851673578448276

00:32:25.147 --> 00:32:27.243 number of polyps that are found in

NOTE Confidence: 0.851673578448276

00:32:27.243 --> 00:32:28.989 and these sort of correlate with

NOTE Confidence: 0.851673578448276

00:32:28.990 --> 00:32:34.000 The Who criteria for SPS diagnosis,

NOTE Confidence: 0.851673578448276

00:32:34.000 --> 00:32:35.626 so criterion one is, you know,

NOTE Confidence: 0.851673578448276

00:32:35.630 --> 00:32:37.652 more than five strated polyps proximal

NOTE Confidence: 0.851673578448276

00:32:37.652 --> 00:32:39.410 to the ****** and they have to be,

NOTE Confidence: 0.851673578448276

00:32:39.410 --> 00:32:40.929 you know, greater than 5 millimeters and

NOTE Confidence: 0.851673578448276

00:32:40.929 --> 00:32:42.786 two of them have to be greater than one.

NOTE Confidence: 0.851673578448276

00:32:42.790 --> 00:32:44.590 I mean that gets a little bit wordy.

NOTE Confidence: 0.851673578448276

00:32:44.590 --> 00:32:46.110 Where's the Criterion 2 is,

NOTE Confidence: 0.851673578448276

00:32:46.110 --> 00:32:48.810 you know greater than.

NOTE Confidence: 0.851673578448276

00:32:48.810 --> 00:32:52.386 23 polyps anywhere in the colon with no

NOTE Confidence: 0.851673578448276

00:32:52.386 --> 00:32:55.337 particular size criteria and you know,

NOTE Confidence: 0.851673578448276

00:32:55.337 --> 00:32:57.971 even though this is a fairly

NOTE Confidence: 0.851673578448276

00:32:57.971 --> 00:33:00.140 distinct polyposis syndrome,

NOTE Confidence: 0.851673578448276

00:33:00.140 --> 00:33:04.628 genetics are not understood, not known.

NOTE Confidence: 0.851673578448276

00:33:04.630 --> 00:33:06.060 Have not been, you know,

NOTE Confidence: 0.851673578448276

00:33:06.060 --> 00:33:08.358 specific Gene has not been discovered.

NOTE Confidence: 0.851673578448276

00:33:08.360 --> 00:33:09.600 That sort of explains

NOTE Confidence: 0.851673578448276

00:33:09.600 --> 00:33:10.840 majority of these cases,

NOTE Confidence: 0.851673578448276

00:33:10.840 --> 00:33:14.308 although some some have been proposed.

NOTE Confidence: 0.851673578448276

00:33:14.310 --> 00:33:15.470 At the Scopic Lee,

NOTE Confidence: 0.851673578448276

00:33:15.470 --> 00:33:17.210 these patients just have multiple polyps

NOTE Confidence: 0.851673578448276

00:33:17.263 --> 00:33:19.118 and they tend to have this characteristic

NOTE Confidence: 0.851673578448276

00:33:19.118 --> 00:33:21.250 mucus cap so so they can be recognized,

NOTE Confidence: 0.851673578448276

00:33:21.250 --> 00:33:23.470 and the scopic Lee somewhat.

NOTE Confidence: 0.851673578448276

00:33:23.470 --> 00:33:25.402 If there is ability to do

NOTE Confidence: 0.851673578448276

00:33:25.402 --> 00:33:26.368 confocal laser endoscopy,

NOTE Confidence: 0.851673578448276

00:33:26.370 --> 00:33:28.050 which you know most places

NOTE Confidence: 0.851673578448276

00:33:28.050 --> 00:33:29.394 don't have that ability,

NOTE Confidence: 0.851673578448276

00:33:29.400 --> 00:33:31.505 there are some unique features

NOTE Confidence: 0.851673578448276

00:33:31.505 --> 00:33:34.634 that can be that can be detected,

NOTE Confidence: 0.851673578448276

00:33:34.634 --> 00:33:36.964 such as these thin branching.

NOTE Confidence: 0.851673578448276

00:33:36.970 --> 00:33:39.730 ***** and dystrophic goblet cells.

NOTE Confidence: 0.851673578448276

00:33:39.730 --> 00:33:41.946 When you look at the specimens grossly again,

NOTE Confidence: 0.851673578448276

00:33:41.950 --> 00:33:43.094 there's no distinctive features.

NOTE Confidence: 0.851673578448276

00:33:43.094 --> 00:33:44.810 The polyps tend to be sessile,

NOTE Confidence: 0.851673578448276

00:33:44.810 --> 00:33:45.677 and you know,

NOTE Confidence: 0.851673578448276

00:33:45.677 --> 00:33:48.441 so if you notice one of these types of

NOTE Confidence: 0.851673578448276

00:33:48.441 --> 00:33:51.162 phenomena in the in the colon cancers

NOTE Confidence: 0.851673578448276

00:33:51.162 --> 00:33:53.270 that you gross sampling of multiple

NOTE Confidence: 0.851673578448276

00:33:53.270 --> 00:33:56.030 polyps is crucial for the deduction of SPS,

NOTE Confidence: 0.851673578448276

00:33:56.030 --> 00:33:57.030 and the reason why is,

NOTE Confidence: 0.851673578448276

00:33:57.030 --> 00:33:59.070 if you have a partial colectomy and a

NOTE Confidence: 0.851673578448276

00:33:59.070 --> 00:34:01.088 patient has serrated polyposis syndrome,

NOTE Confidence: 0.851673578448276

00:34:01.090 --> 00:34:02.650 it might be that they are,

NOTE Confidence: 0.851673578448276

00:34:02.650 --> 00:34:04.393 you know, continues to be a high

NOTE Confidence: 0.851673578448276

00:34:04.393 --> 00:34:05.530 risk for developing cancer,

NOTE Confidence: 0.851673578448276

00:34:05.530 --> 00:34:07.226 and their remaining colon.

NOTE Confidence: 0.851673578448276

00:34:07.226 --> 00:34:09.924 That they have and in one small

NOTE Confidence: 0.851673578448276

00:34:09.924 --> 00:34:12.999 study that had done a few years ago,

NOTE Confidence: 0.851673578448276

00:34:13.000 --> 00:34:16.140 we found in a cohort of 22 patients who had

NOTE Confidence: 0.851673578448276

00:34:16.217 --> 00:34:19.360 colectomy and were found to have polyposis,

NOTE Confidence: 0.851673578448276

00:34:19.360 --> 00:34:22.416 we actually found SPS as the cause of

NOTE Confidence: 0.851673578448276

00:34:22.416 --> 00:34:24.839 the polyposis in about 1/4 of them.

NOTE Confidence: 0.851673578448276

00:34:24.840 --> 00:34:26.046 And furthermore,

NOTE Confidence: 0.851673578448276

00:34:26.046 --> 00:34:28.458 in a separate study,

NOTE Confidence: 0.851673578448276

00:34:28.460 --> 00:34:31.028 we looked at a population of

NOTE Confidence: 0.851673578448276

00:34:31.028 --> 00:34:33.799 over 2000 patients who had at

NOTE Confidence: 0.851673578448276

00:34:33.799 --> 00:34:35.767 least one pseudopolyps diognosed.

NOTE Confidence: 0.851673578448276

00:34:35.767 --> 00:34:40.306 And we found that one point 4% or 32

NOTE Confidence: 0.851673578448276

00:34:40.306 --> 00:34:42.771 patients met criteria for serrated

NOTE Confidence: 0.851673578448276

00:34:42.771 --> 00:34:45.530 polyps syndrome and these patients

NOTE Confidence: 0.851673578448276

00:34:45.530 --> 00:34:49.070 had a variety of polyp types.

NOTE Confidence: 0.851673578448276

00:34:49.070 --> 00:34:52.052 Many of them had advanced neoplastic

NOTE Confidence: 0.851673578448276

00:34:52.052 --> 00:34:53.490 features, so they either had,

NOTE Confidence: 0.851673578448276

00:34:53.490 --> 00:34:53.960 you know,

NOTE Confidence: 0.851673578448276

00:34:53.960 --> 00:34:56.020 dysplasia within their serrated polyp,

NOTE Confidence: 0.851673578448276

00:34:56.020 --> 00:34:58.350 or frank invasive carcinoma and

NOTE Confidence: 0.851673578448276

00:34:58.350 --> 00:35:00.680 what's interesting is that these

NOTE Confidence: 0.851673578448276

00:35:00.757 --> 00:35:02.942 carcinomas actually had a variety

NOTE Confidence: 0.851673578448276

00:35:02.942 --> 00:35:04.319 of augmentations within them.

NOTE Confidence: 0.851673578448276

00:35:04.319 --> 00:35:06.510 So even though the prevalent thought is

NOTE Confidence: 0.907215903333333

00:35:06.567 --> 00:35:08.968 that these. Cancers all lead to you know,

NOTE Confidence: 0.907215903333333

00:35:08.970 --> 00:35:11.454 one type of MSI high tumor

NOTE Confidence: 0.907215903333333

00:35:11.454 --> 00:35:12.696 with direct mutations.

NOTE Confidence: 0.907215903333333

00:35:12.700 --> 00:35:14.450 We actually did find that there's you

NOTE Confidence: 0.907215903333333

00:35:14.450 --> 00:35:16.232 know one with a key reputation among

NOTE Confidence: 0.907215903333333

00:35:16.232 --> 00:35:18.490 these and some did not have the reputation,

NOTE Confidence: 0.907215903333333

00:35:18.490 --> 00:35:20.320 so it's sort of an interesting

NOTE Confidence: 0.907215903333333

00:35:20.320 --> 00:35:22.190 question still.

NOTE Confidence: 0.907215903333333

00:35:22.190 --> 00:35:26.306 And so all of this together,

NOTE Confidence: 0.907215903333333

00:35:26.310 --> 00:35:28.249 you know we can put together a

NOTE Confidence: 0.907215903333333

00:35:28.249 --> 00:35:29.080 basic molecular classification

NOTE Confidence: 0.907215903333333

00:35:29.126 --> 00:35:30.080 of colorectal cancer.

NOTE Confidence: 0.938062296470588

00:35:32.530 --> 00:35:34.914 OK, so now kind of going to shift

NOTE Confidence: 0.938062296470588

00:35:34.914 --> 00:35:37.047 gears and start talking a little

NOTE Confidence: 0.938062296470588

00:35:37.047 --> 00:35:39.072 bit more about mutation testing.

NOTE Confidence: 0.938062296470588

00:35:39.072 --> 00:35:40.916 So here's another patient.

NOTE Confidence: 0.938062296470588

00:35:40.920 --> 00:35:42.786 Newly diagnosed metastatic

NOTE Confidence: 0.938062296470588

00:35:42.786 --> 00:35:46.262 colorectal cancer to the liver.

NOTE Confidence: 0.938062296470588

00:35:46.262 --> 00:35:49.982 Prior testing showed microsatellite stable

NOTE Confidence: 0.938062296470588

00:35:49.982 --> 00:35:52.920 tumor and what should you order next?

NOTE Confidence: 0.907137524

00:35:57.940 --> 00:35:59.966 And so in order to, you know.

NOTE Confidence: 0.907137524

00:35:59.966 --> 00:36:02.579 So this is where we come back to the

NOTE Confidence: 0.907137524

00:36:02.579 --> 00:36:04.727 NCCN guidelines and sort of start

NOTE Confidence: 0.907137524

00:36:04.727 --> 00:36:06.333 to understand how is information

NOTE Confidence: 0.907137524

00:36:06.333 --> 00:36:08.331 used and what sort of information

NOTE Confidence: 0.907137524

00:36:08.331 --> 00:36:10.520 is needed for continued treatment,

NOTE Confidence: 0.907137524

00:36:10.520 --> 00:36:13.244 and so patients who have metastatic

NOTE Confidence: 0.907137524

00:36:13.244 --> 00:36:15.060 colorectal cancer should have

NOTE Confidence: 0.907137524

00:36:15.134 --> 00:36:17.718 genotyping forreston draft mutations.

NOTE Confidence: 0.907137524

00:36:17.720 --> 00:36:20.588 And the reason for that is

NOTE Confidence: 0.907137524

00:36:20.588 --> 00:36:22.820 is because there is a.

NOTE Confidence: 0.907137524

00:36:22.820 --> 00:36:26.108 Antibody that's frequently used as part

NOTE Confidence: 0.907137524

00:36:26.108 --> 00:36:28.740 of chemotherapy for colorectal cancer.

NOTE Confidence: 0.907137524

00:36:28.740 --> 00:36:31.396 The targets. The rest raft pathway,

NOTE Confidence: 0.907137524

00:36:31.396 --> 00:36:35.379 and so in order for this antibody to work,

NOTE Confidence: 0.907137524

00:36:35.380 --> 00:36:40.090 rest, and draft have to be wild type.

NOTE Confidence: 0.907137524

00:36:40.090 --> 00:36:42.456 And so this is where this is

NOTE Confidence: 0.907137524

00:36:42.456 --> 00:36:44.189 where this pathway comes in.

NOTE Confidence: 0.907137524

00:36:44.190 --> 00:36:48.744 So here we have EGFR, which then

NOTE Confidence: 0.907137524

00:36:48.744 --> 00:36:52.266 signals downstream into grass and RAF.

NOTE Confidence: 0.907137524

00:36:52.270 --> 00:36:54.804 RAF happens to be the most mutated

NOTE Confidence: 0.907137524

00:36:54.804 --> 00:36:56.510 gene in colorectal cancers.

NOTE Confidence: 0.907137524

00:36:56.510 --> 00:36:57.782 Approximately, you know,

NOTE Confidence: 0.907137524

00:36:57.782 --> 00:37:00.516 up to even 50% of colorectal

NOTE Confidence: 0.907137524

00:37:00.516 --> 00:37:02.992 cancers will have RASK mutations,

NOTE Confidence: 0.907137524

00:37:02.992 --> 00:37:07.354 and they're in order to use setx map as

NOTE Confidence: 0.907137524

00:37:07.354 --> 00:37:10.239 a component of the chemotherapeutic.

NOTE Confidence: 0.907137524

00:37:10.240 --> 00:37:12.020 Regimen.

NOTE Confidence: 0.907137524

00:37:12.020 --> 00:37:15.028 We have to rule out mutations in the

NOTE Confidence: 0.907137524

00:37:15.028 --> 00:37:18.092 tumor because this this antibody will

NOTE Confidence: 0.907137524

00:37:18.092 --> 00:37:22.003 have no efficacy of downstream of that

NOTE Confidence: 0.907137524

00:37:22.003 --> 00:37:26.706 of of of EGFR is an activating mutation.

NOTE Confidence: 0.907137524

00:37:26.710 --> 00:37:29.265 But you can see that we also have,

NOTE Confidence: 0.907137524

00:37:29.265 --> 00:37:30.840 you know there's mutations in

NOTE Confidence: 0.907137524

00:37:30.840 --> 00:37:32.308 various other genes as well,

NOTE Confidence: 0.907137524

00:37:32.310 --> 00:37:33.906 some of which may be targetable

NOTE Confidence: 0.907137524

00:37:33.906 --> 00:37:34.970 and others are not.

NOTE Confidence: 0.907137524

00:37:34.970 --> 00:37:38.638 So how do we test for driver

NOTE Confidence: 0.907137524

00:37:38.638 --> 00:37:40.750 driver for forreston ref?

NOTE Confidence: 0.907137524

00:37:40.750 --> 00:37:42.958 Mutations in colorectal cancer.

NOTE Confidence: 0.907137524

00:37:42.958 --> 00:37:45.166 This has evolved overtime.

NOTE Confidence: 0.907137524

00:37:45.170 --> 00:37:45.964 You know,

NOTE Confidence: 0.907137524

00:37:45.964 --> 00:37:47.949 ten years ago would have

NOTE Confidence: 0.907137524

00:37:47.949 --> 00:37:50.099 been PCR of some sort.

NOTE Confidence: 0.907137524

00:37:50.100 --> 00:37:51.675 And you know,

NOTE Confidence: 0.907137524

00:37:51.675 --> 00:37:56.210 but that has evolved quickly through.

NOTE Confidence: 0.907137524

00:37:56.210 --> 00:37:59.080 Into real time PCR and now primarily

NOTE Confidence: 0.907137524

00:37:59.080 --> 00:38:01.098 next generation sequencing being the

NOTE Confidence: 0.907137524

00:38:01.098 --> 00:38:03.625 standard for doing this type of testing.

NOTE Confidence: 0.907137524

00:38:03.630 --> 00:38:06.166 And so I so after coming to Yale,

NOTE Confidence: 0.907137524

00:38:06.170 --> 00:38:08.510 I got interested in colorectal

NOTE Confidence: 0.907137524

00:38:08.510 --> 00:38:10.382 molecular testing at Yale,

NOTE Confidence: 0.907137524

00:38:10.390 --> 00:38:12.534 and I, you know,

NOTE Confidence: 0.907137524

00:38:12.534 --> 00:38:13.606 sort of.

NOTE Confidence: 0.907137524

00:38:13.610 --> 00:38:15.545 Intersected with with our molecular

NOTE Confidence: 0.907137524

00:38:15.545 --> 00:38:18.382 labs and try to find out like what

NOTE Confidence: 0.907137524

00:38:18.382 --> 00:38:20.989 is going on and so we have two main

NOTE Confidence: 0.907137524

00:38:20.989 --> 00:38:23.355 labs that do CRC molecular testing

NOTE Confidence: 0.907137524

00:38:23.355 --> 00:38:25.863 and they don't overlap too much

NOTE Confidence: 0.907137524

00:38:25.863 --> 00:38:28.002 with each other in terms of the

NOTE Confidence: 0.907137524

00:38:28.002 --> 00:38:29.550 the specific test that they do.

NOTE Confidence: 0.907137524

00:38:29.550 --> 00:38:31.262 So the molecular diagnostics

NOTE Confidence: 0.907137524

00:38:31.262 --> 00:38:33.830 lab does a lot of PCR.

NOTE Confidence: 0.907137524

00:38:33.830 --> 00:38:36.494 For MSI and also single gene

NOTE Confidence: 0.907137524

00:38:36.494 --> 00:38:38.720 testing like graph 4K Ras,

NOTE Confidence: 0.907137524

00:38:38.720 --> 00:38:40.766 they also performed the MLH fund

NOTE Confidence: 0.907137524

00:38:40.766 --> 00:38:42.728 methylation and I'm here just focusing

NOTE Confidence: 0.907137524

00:38:42.728 --> 00:38:45.420 on the role of this lab and CRC testing.

NOTE Confidence: 0.907137524

00:38:45.420 --> 00:38:47.260 I'm not at all going to talk about,

NOTE Confidence: 0.907137524

00:38:47.260 --> 00:38:49.288 you know all the other wonderful

NOTE Confidence: 0.907137524

00:38:49.288 --> 00:38:51.743 things that that lab does and has

NOTE Confidence: 0.907137524

00:38:51.743 --> 00:38:53.482 developed in recent years and

NOTE Confidence: 0.907137524

00:38:53.482 --> 00:38:55.594 then we have the tumor profiling

NOTE Confidence: 0.907137524

00:38:55.594 --> 00:38:57.652 laboratory and the tumor profiling

NOTE Confidence: 0.907137524

00:38:57.652 --> 00:38:59.520 laboratory primarily uses next

NOTE Confidence: 0.907137524

00:38:59.520 --> 00:39:02.319 generation sequencing as a method for

NOTE Confidence: 0.907137524

00:39:02.319 --> 00:39:04.469 detecting mutations and tumor cells.

NOTE Confidence: 0.907137524

00:39:04.470 --> 00:39:06.129 And I'll talk in a lot more

NOTE Confidence: 0.907137524

00:39:06.129 --> 00:39:07.527 detail about that lab, so.

NOTE Confidence: 0.907137524

00:39:07.527 --> 00:39:10.029 You know when I first arrived

NOTE Confidence: 0.907137524

00:39:10.029 --> 00:39:11.850 at Yale in 2011,

NOTE Confidence: 0.907137524

00:39:11.850 --> 00:39:14.350 this was our GI Group back then and

NOTE Confidence: 0.907137524

00:39:14.350 --> 00:39:17.186 I was primarily doing GI pathology,

NOTE Confidence: 0.907137524

00:39:17.186 --> 00:39:21.330 but I I really wanted to expand my

NOTE Confidence: 0.907137524

00:39:21.330 --> 00:39:23.255 clinical practice and I started

NOTE Confidence: 0.907137524

00:39:23.255 --> 00:39:26.278 thinking about maybe I I could join the,

NOTE Confidence: 0.907137524

00:39:26.280 --> 00:39:27.002 you know,

NOTE Confidence: 0.907137524

00:39:27.002 --> 00:39:29.168 one of the molecular labs and

NOTE Confidence: 0.907137524

00:39:29.168 --> 00:39:29.890 after discussing

NOTE Confidence: 0.871654207647059

00:39:29.961 --> 00:39:32.474 with various people I got support from.

NOTE Confidence: 0.872011747142857

00:39:39.290 --> 00:39:42.623 There we go. I got support from Doctor

NOTE Confidence: 0.872011747142857

00:39:42.623 --> 00:39:45.041 Walter and the tumor profiling lab

NOTE Confidence: 0.872011747142857

00:39:45.041 --> 00:39:47.856 and with doctor Marrows and Doctor so

NOTE Confidence: 0.872011747142857

00:39:47.856 --> 00:39:51.108 Nards and Doctor James support as well.

NOTE Confidence: 0.872011747142857

00:39:51.110 --> 00:39:54.206 I was able to join the tumor profiling

NOTE Confidence: 0.872011747142857

00:39:54.206 --> 00:39:56.328 laboratory as a faculty member.

NOTE Confidence: 0.872011747142857

00:39:56.330 --> 00:39:58.770 And you know, how did I do this?

NOTE Confidence: 0.872011747142857

00:39:58.770 --> 00:40:01.020 I mean, this was not something

NOTE Confidence: 0.872011747142857

00:40:01.020 --> 00:40:02.145 that happened overnight.

NOTE Confidence: 0.872011747142857

00:40:02.150 --> 00:40:04.006 I joined the laboratories

NOTE Confidence: 0.872011747142857

00:40:04.006 --> 00:40:05.398 Case Review conference.

NOTE Confidence: 0.872011747142857

00:40:05.400 --> 00:40:08.250 Just sort of a consensus

NOTE Confidence: 0.872011747142857

00:40:08.250 --> 00:40:10.772 conference type review of cases.

NOTE Confidence: 0.872011747142857

00:40:10.772 --> 00:40:13.700 I went to the precision Medicine

NOTE Confidence: 0.872011747142857

00:40:13.793 --> 00:40:15.790 tumor board for, you know,

NOTE Confidence: 0.872011747142857

00:40:15.790 --> 00:40:17.990 a while before then joining the roster of

NOTE Confidence: 0.872011747142857

00:40:18.051 --> 00:40:20.158 people who present at that tumor board,

NOTE Confidence: 0.872011747142857

00:40:20.160 --> 00:40:23.436 I shadowed the faculty at that time in the

NOTE Confidence: 0.872011747142857

00:40:23.436 --> 00:40:26.176 German profiling lab and then finally.

NOTE Confidence: 0.872011747142857

00:40:26.180 --> 00:40:28.898 I was able to get a block of six

NOTE Confidence: 0.872011747142857

00:40:28.898 --> 00:40:31.405 weeks to be able to do a rotation

NOTE Confidence: 0.872011747142857

00:40:31.405 --> 00:40:33.594 sort of identical to what a fellow

NOTE Confidence: 0.872011747142857

00:40:33.594 --> 00:40:37.075 would do and learned all the different

NOTE Confidence: 0.872011747142857

00:40:37.075 --> 00:40:40.460 aspects of the tumor profiling lab.

NOTE Confidence: 0.872011747142857

00:40:40.460 --> 00:40:43.518 And so primarily next generation

NOTE Confidence: 0.872011747142857

00:40:43.518 --> 00:40:45.474 sequencing is the platform that is

NOTE Confidence: 0.872011747142857

00:40:45.474 --> 00:40:47.260 used by the tumor profiling lab and

NOTE Confidence: 0.872011747142857

00:40:47.260 --> 00:40:49.060 this is an ultra high throughput,

NOTE Confidence: 0.872011747142857

00:40:49.060 --> 00:40:52.000 scalable, fast method of sequencing DNA,

NOTE Confidence: 0.872011747142857

00:40:52.000 --> 00:40:54.468 and it's, you know.

NOTE Confidence: 0.872011747142857

00:40:54.470 --> 00:40:56.662 I I fit the whole sequence of events

NOTE Confidence: 0.872011747142857

00:40:56.662 --> 00:40:58.533 of how next generation sequencing

NOTE Confidence: 0.872011747142857

00:40:58.533 --> 00:41:00.209 works on one slide,

NOTE Confidence: 0.872011747142857

00:41:00.210 --> 00:41:02.738 but it's it's it's a very busy slide

NOTE Confidence: 0.872011747142857

00:41:02.740 --> 00:41:04.090 and so there's there's different

NOTE Confidence: 0.872011747142857

00:41:04.090 --> 00:41:05.740 steps that have to be done.

NOTE Confidence: 0.872011747142857

00:41:05.740 --> 00:41:07.528 First sample has to be prepared,

NOTE Confidence: 0.872011747142857

00:41:07.530 --> 00:41:09.740 DNA has to be extracted.

NOTE Confidence: 0.872011747142857

00:41:09.740 --> 00:41:12.156 Library preparation and templating

NOTE Confidence: 0.872011747142857

00:41:12.156 --> 00:41:13.968 has to occur.

NOTE Confidence: 0.872011747142857

00:41:13.970 --> 00:41:15.884 Sequencing has to occur in the

NOTE Confidence: 0.872011747142857

00:41:15.884 --> 00:41:18.426 sequencing is sort of a bit of a

NOTE Confidence: 0.872011747142857

00:41:18.426 --> 00:41:21.760 magical step where it's actually, you know.

NOTE Confidence: 0.872011747142857

00:41:21.760 --> 00:41:22.430 It's a.

NOTE Confidence: 0.572236422

00:41:24.990 --> 00:41:26.430 Electric, you know it's a.

NOTE Confidence: 0.572236422

00:41:26.430 --> 00:41:28.418 It's a electronic signaling

NOTE Confidence: 0.572236422

00:41:28.418 --> 00:41:29.909 or electronic sequencing.

NOTE Confidence: 0.572236422

00:41:29.910 --> 00:41:31.800 Basically that that occurs and

NOTE Confidence: 0.572236422

00:41:31.800 --> 00:41:34.570 it generates a ton of information

NOTE Confidence: 0.572236422

00:41:34.570 --> 00:41:36.526 by informatics is a big big

NOTE Confidence: 0.572236422

00:41:36.526 --> 00:41:38.949 step and we have several people

NOTE Confidence: 0.572236422

00:41:38.950 --> 00:41:42.290 working on that who actually.

NOTE Confidence: 0.572236422

00:41:42.290 --> 00:41:44.082 Go through all of these steps and

NOTE Confidence: 0.572236422

00:41:44.082 --> 00:41:45.994 give us the annotated mutations that

NOTE Confidence: 0.572236422

00:41:45.994 --> 00:41:47.686 are found in a particular tumor,

NOTE Confidence: 0.572236422

00:41:47.690 --> 00:41:50.378 and then we have to interpret

NOTE Confidence: 0.572236422

00:41:50.378 --> 00:41:52.780 those those variants and we use

NOTE Confidence: 0.572236422

00:41:52.780 --> 00:41:55.081 different types of databases to to

NOTE Confidence: 0.572236422

00:41:55.081 --> 00:41:57.273 do that and just to sort of make

NOTE Confidence: 0.572236422

00:41:57.273 --> 00:41:59.469 sure that everyone sort of knows

NOTE Confidence: 0.572236422

00:41:59.470 --> 00:42:01.339 most of the stuff happens in the

NOTE Confidence: 0.572236422

00:42:01.339 --> 00:42:02.610 Department of Laboratory Medicine.

NOTE Confidence: 0.572236422

00:42:02.610 --> 00:42:04.053 The variant interpretation

NOTE Confidence: 0.572236422

00:42:04.053 --> 00:42:06.458 is what the faculty do,

NOTE Confidence: 0.572236422

00:42:06.460 --> 00:42:09.556 and we do that and and it's the

NOTE Confidence: 0.572236422

00:42:09.556 --> 00:42:11.360 pathology faculty who do that.

NOTE Confidence: 0.572236422

00:42:11.360 --> 00:42:12.388 And so.

NOTE Confidence: 0.572236422

00:42:12.388 --> 00:42:14.958 How is NGS actually used,

NOTE Confidence: 0.572236422

00:42:14.960 --> 00:42:16.520 and what are the advantages

NOTE Confidence: 0.572236422

00:42:16.520 --> 00:42:18.080 of it so you know,

NOTE Confidence: 0.572236422

00:42:18.080 --> 00:42:20.545 with NGS you can sequence

NOTE Confidence: 0.572236422

00:42:20.545 --> 00:42:24.460 really any area that you know.

NOTE Confidence: 0.572236422

00:42:24.460 --> 00:42:27.043 Almost any area that is of interest

NOTE Confidence: 0.572236422

00:42:27.043 --> 00:42:28.969 and the advantages that multiple

NOTE Confidence: 0.572236422

00:42:28.969 --> 00:42:31.573 areas can be sequenced all at once,

NOTE Confidence: 0.572236422

00:42:31.580 --> 00:42:32.264 like massively,

NOTE Confidence: 0.572236422

00:42:32.264 --> 00:42:35.500 and so you know when you look at crass.

NOTE Confidence: 0.572236422

00:42:35.500 --> 00:42:35.905 Yes,

NOTE Confidence: 0.572236422

00:42:35.905 --> 00:42:37.930 there are some common hotspots

NOTE Confidence: 0.572236422

00:42:37.930 --> 00:42:39.550 that are really interesting

NOTE Confidence: 0.572236422

00:42:39.621 --> 00:42:41.357 and recur quite frequently,

NOTE Confidence: 0.572236422

00:42:41.360 --> 00:42:43.075 like a code on 12 or 13,

NOTE Confidence: 0.572236422

00:42:43.080 --> 00:42:45.397 but there's a lot of other smaller

NOTE Confidence: 0.572236422

00:42:45.397 --> 00:42:48.380 hotspots at 146 at 1:17 at 61,

NOTE Confidence: 0.572236422

00:42:48.380 --> 00:42:50.620 and so with NGS we're able to sequence

NOTE Confidence: 0.572236422

00:42:50.620 --> 00:42:52.618 all of the hot spots at once,

NOTE Confidence: 0.572236422

00:42:52.620 --> 00:42:55.488 and so we have one panel.

NOTE Confidence: 0.572236422

00:42:55.490 --> 00:42:57.630 For.

NOTE Confidence: 0.572236422

00:42:57.630 --> 00:42:59.922 That looks at 50 different hotspots

NOTE Confidence: 0.572236422

00:42:59.922 --> 00:43:03.298 or I should say looks at 50 genes

NOTE Confidence: 0.572236422

00:43:03.298 --> 00:43:07.452 at various hotspots and this is the

NOTE Confidence: 0.572236422

00:43:07.452 --> 00:43:10.117 panel that's used for diagnosing.

NOTE Confidence: 0.572236422

00:43:10.120 --> 00:43:13.714 Metastatic colorectal cancer and how

NOTE Confidence: 0.572236422

00:43:13.714 --> 00:43:16.770 does the entry of data come back to us?

NOTE Confidence: 0.572236422

00:43:16.770 --> 00:43:19.100 It's actually.

NOTE Confidence: 0.572236422

00:43:19.100 --> 00:43:21.554 Comes back in an Excel style

NOTE Confidence: 0.572236422

00:43:21.554 --> 00:43:23.673 spreadsheet which can be somewhere

NOTE Confidence: 0.572236422

00:43:23.673 --> 00:43:26.055 you know this is a simple.

NOTE Confidence: 0.572236422

00:43:26.060 --> 00:43:27.468 Summary of that result.

NOTE Confidence: 0.572236422

00:43:27.468 --> 00:43:30.676 So here we have, you know, for example,

NOTE Confidence: 0.572236422

00:43:30.676 --> 00:43:35.136 TP 53 has a C DNA mutation that

NOTE Confidence: 0.572236422

00:43:35.136 --> 00:43:39.980 replaces G2AG to an A at nucleotide 818,

NOTE Confidence: 0.572236422

00:43:39.980 --> 00:43:43.500 which then leads to a change in the

NOTE Confidence: 0.572236422

00:43:43.595 --> 00:43:46.944 protein of arginine to 73 to a histidine.

NOTE Confidence: 0.572236422

00:43:46.950 --> 00:43:49.986 And what's also important is that

NOTE Confidence: 0.572236422

00:43:49.986 --> 00:43:53.540 this particular position was.

NOTE Confidence: 0.572236422

00:43:53.540 --> 00:43:54.215 Stop.

NOTE Confidence: 0.572236422

00:43:54.215 --> 00:43:58.265 It was read almost 2000 times,

NOTE Confidence: 0.572236422

00:43:58.270 --> 00:44:02.598 so this position was was found in 2000.

NOTE Confidence: 0.572236422

00:44:02.600 --> 00:44:04.968 Let's look was seen at least 2000 times,

NOTE Confidence: 0.572236422

00:44:04.970 --> 00:44:09.626 and 20% of those reads showed this variant,

NOTE Confidence: 0.572236422

00:44:09.630 --> 00:44:12.638 and so here you can see what that

NOTE Confidence: 0.572236422

00:44:12.638 --> 00:44:16.970 looks like in in the I GB program.

NOTE Confidence: 0.572236422

00:44:16.970 --> 00:44:19.034 So this is the genomics viewer that we

NOTE Confidence: 0.572236422

00:44:19.034 --> 00:44:21.190 used to look at the actual mutation.

NOTE Confidence: 0.572236422

00:44:21.190 --> 00:44:23.190 So here we have the K rest gene.

NOTE Confidence: 0.572236422

00:44:23.190 --> 00:44:25.246 With this particular mutation,

NOTE Confidence: 0.572236422

00:44:25.246 --> 00:44:28.330 and there's each of these bars

NOTE Confidence: 0.572236422

00:44:28.419 --> 00:44:30.864 represents one of these reads

NOTE Confidence: 0.572236422

00:44:30.864 --> 00:44:33.309 that forms the coverage and.

NOTE Confidence: 0.572236422

00:44:33.310 --> 00:44:35.614 That she represents the change at

NOTE Confidence: 0.572236422

00:44:35.614 --> 00:44:38.015 that particular meeting, and we have.

NOTE Confidence: 0.572236422

00:44:38.015 --> 00:44:40.090 And they're color coded for

NOTE Confidence: 0.572236422

00:44:40.090 --> 00:44:42.130 reverse sent forward reads.

NOTE Confidence: 0.802340514307692

00:44:44.210 --> 00:44:47.586 And so this is what a cancer mutation

NOTE Confidence: 0.802340514307692

00:44:47.586 --> 00:44:50.010 hotspot panel result looks like.

NOTE Confidence: 0.802340514307692

00:44:50.010 --> 00:44:52.315 There's an add no carcinoma

NOTE Confidence: 0.802340514307692

00:44:52.315 --> 00:44:55.622 estimated 30% malignant cells and

NOTE Confidence: 0.802340514307692

00:44:55.622 --> 00:45:00.890 we have a BRAF V600E mutation.

NOTE Confidence: 0.802340514307692

00:45:00.890 --> 00:45:03.330 And our other pathology records

NOTE Confidence: 0.802340514307692

00:45:03.330 --> 00:45:06.880 show that this was an MSS cancer,

NOTE Confidence: 0.802340514307692

00:45:06.880 --> 00:45:09.827 and so this brings up an interesting

NOTE Confidence: 0.802340514307692

00:45:09.827 --> 00:45:12.659 subject of the reputation in MSS.

NOTE Confidence: 0.802340514307692

00:45:12.660 --> 00:45:13.428 Colorectal cancers.

NOTE Confidence: 0.802340514307692

00:45:13.428 --> 00:45:16.116 And this is an interesting subtype of

NOTE Confidence: 0.802340514307692

00:45:16.116 --> 00:45:18.396 cancer that does not neatly fit into

NOTE Confidence: 0.802340514307692

00:45:18.396 --> 00:45:20.700 our current models of personal genesis.

NOTE Confidence: 0.802340514307692

00:45:20.700 --> 00:45:25.028 These tumor types are.

NOTE Confidence: 0.802340514307692

00:45:25.030 --> 00:45:27.370 Relatively rare on the order of,

NOTE Confidence: 0.802340514307692

00:45:27.370 --> 00:45:30.226 you know, maybe 5-4 to 7% depending

NOTE Confidence: 0.802340514307692

00:45:30.226 --> 00:45:34.202 on what study you read, and you know.

NOTE Confidence: 0.802340514307692

00:45:34.202 --> 00:45:36.410 Unlike other tumor types,

NOTE Confidence: 0.802340514307692

00:45:36.410 --> 00:45:38.650 that kind of neatly fit into our

NOTE Confidence: 0.802340514307692

00:45:38.650 --> 00:45:40.860 knowledge of of precursor lesions, etc.

NOTE Confidence: 0.802340514307692

00:45:40.860 --> 00:45:43.510 We don't really know how these tumors

NOTE Confidence: 0.802340514307692

00:45:43.510 --> 00:45:46.389 arise and what is the what is the primary

NOTE Confidence: 0.802340514307692

00:45:46.389 --> 00:45:48.618 sort of starting point for those.

NOTE Confidence: 0.802340514307692

00:45:48.618 --> 00:45:51.435 But the most interesting thing is that

NOTE Confidence: 0.802340514307692

00:45:51.435 --> 00:45:53.969 they do now have a therapeutic option,

NOTE Confidence: 0.802340514307692

00:45:53.970 --> 00:45:55.610 and so recognizing these tumors.

NOTE Confidence: 0.802340514307692

00:45:55.610 --> 00:45:58.670 Is important and I'm working

NOTE Confidence: 0.802340514307692

00:45:58.670 --> 00:46:02.400 with our current fellow Dr each,

NOTE Confidence: 0.802340514307692

00:46:02.400 --> 00:46:04.400 as well as some others and looking at.

NOTE Confidence: 0.824044827142857

00:46:07.630 --> 00:46:09.828 MSS CRC's. Looking at some of those

NOTE Confidence: 0.824044827142857

00:46:09.828 --> 00:46:12.050 molecular features to add to this knowledge,

NOTE Confidence: 0.824044827142857

00:46:12.050 --> 00:46:15.354 and this is this is the most recent.

NOTE Confidence: 0.8939981275

00:46:18.760 --> 00:46:21.552 This is that this is a study that

NOTE Confidence: 0.8939981275

00:46:21.552 --> 00:46:23.420 described that tablet therapy,

NOTE Confidence: 0.8939981275

00:46:23.420 --> 00:46:26.300 the doublet therapy includes

NOTE Confidence: 0.8939981275

00:46:26.300 --> 00:46:28.408 this EGFR targeted treatment,

NOTE Confidence: 0.8939981275

00:46:28.408 --> 00:46:30.078 such as a tax map,

NOTE Confidence: 0.8939981275

00:46:30.080 --> 00:46:32.240 combined with a BYREF inhibitor.

NOTE Confidence: 0.8939981275

00:46:32.240 --> 00:46:34.274 Initially, this was also had a

NOTE Confidence: 0.8939981275

00:46:34.274 --> 00:46:36.400 component of a MEK inhibitor,

NOTE Confidence: 0.8939981275

00:46:36.400 --> 00:46:39.376 but within a few months of

NOTE Confidence: 0.8939981275

00:46:39.376 --> 00:46:41.360 this paper being published,

NOTE Confidence: 0.8939981275

00:46:41.360 --> 00:46:42.852 they've they've decided that

NOTE Confidence: 0.8939981275

00:46:42.852 --> 00:46:45.090 the doublet has just as much

NOTE Confidence: 0.8939981275

00:46:45.156 --> 00:46:47.246 efficacy as the triplet therapy.

NOTE Confidence: 0.8939981275

00:46:47.250 --> 00:46:49.903 And so this is now becoming a

NOTE Confidence: 0.8939981275

00:46:49.903 --> 00:46:52.338 standard of of care for BRAF.

NOTE Confidence: 0.85856925

00:46:54.550 --> 00:46:58.498 Mutated by MSS tumors.

NOTE Confidence: 0.85856925

00:46:58.500 --> 00:47:00.988 Alright, so moving on to a different patient.

NOTE Confidence: 0.85856925

00:47:00.990 --> 00:47:04.131 This was a patient #4 who had a combined

NOTE Confidence: 0.85856925

00:47:04.131 --> 00:47:05.760 hepatocellular cholangiocarcinoma.

NOTE Confidence: 0.85856925

00:47:05.760 --> 00:47:08.892 It was MSS and now his

NOTE Confidence: 0.85856925

00:47:08.892 --> 00:47:10.458 progressive disease and.

NOTE Confidence: 0.85856925

00:47:10.460 --> 00:47:13.134 As a pathologist, do you order anything?

NOTE Confidence: 0.85856925

00:47:13.140 --> 00:47:15.816 The answer is no, you don't.

NOTE Confidence: 0.85856925

00:47:15.820 --> 00:47:17.878 It's kind of a trick question.

NOTE Confidence: 0.85856925

00:47:17.880 --> 00:47:20.352 It's the oncologist who may order

NOTE Confidence: 0.85856925

00:47:20.352 --> 00:47:22.397 a comprehensive NGS panel and

NOTE Confidence: 0.85856925

00:47:22.397 --> 00:47:24.658 that panel at Yale is on combine.

NOTE Confidence: 0.85856925

00:47:24.660 --> 00:47:26.958 And so the anchor mine is

NOTE Confidence: 0.85856925

00:47:26.958 --> 00:47:29.110 a much bigger panel.

NOTE Confidence: 0.85856925

00:47:29.110 --> 00:47:34.218 It sequences 87 jeans at various hotspots.

NOTE Confidence: 0.85856925

00:47:34.220 --> 00:47:36.304 There's also 48 genes

NOTE Confidence: 0.85856925

00:47:36.304 --> 00:47:38.388 that are fully sequenced.

NOTE Confidence: 0.85856925

00:47:38.390 --> 00:47:40.520 These are mostly the tumor supressors.

NOTE Confidence: 0.85856925

00:47:40.520 --> 00:47:42.704 We were also able to look at

NOTE Confidence: 0.85856925

00:47:42.704 --> 00:47:44.566 amplification of a number of genes

NOTE Confidence: 0.85856925

00:47:44.566 --> 00:47:46.968 as well as a number of gene fusions

NOTE Confidence: 0.85856925

00:47:46.968 --> 00:47:49.476 and so the anchor mine panel is

NOTE Confidence: 0.85856925

00:47:49.476 --> 00:47:51.591 used primarily in patients who

NOTE Confidence: 0.85856925

00:47:51.591 --> 00:47:54.420 have stage four disease and have.

NOTE Confidence: 0.85856925

00:47:54.420 --> 00:47:56.300 Failed conventional chemotherapy and

NOTE Confidence: 0.85856925

00:47:56.300 --> 00:47:59.370 it's really to identify mutations that

NOTE Confidence: 0.85856925

00:47:59.370 --> 00:48:01.610 may be therapeutic therapeutically.

NOTE Confidence: 0.85856925

00:48:01.610 --> 00:48:04.030 Targetable in a specific manner,

NOTE Confidence: 0.85856925

00:48:04.030 --> 00:48:07.020 or may may have implications

NOTE Confidence: 0.85856925

00:48:07.020 --> 00:48:10.010 for clinical trials as well,

NOTE Confidence: 0.85856925

00:48:10.010 --> 00:48:12.460 and we what what's unique about the

NOTE Confidence: 0.85856925

00:48:12.460 --> 00:48:14.816 Yale practices that we use a germ

NOTE Confidence: 0.85856925

00:48:14.816 --> 00:48:16.858 line control to determine the somatic

NOTE Confidence: 0.85856925

00:48:16.858 --> 00:48:18.454 status versus hereditary status

NOTE Confidence: 0.85856925

00:48:18.454 --> 00:48:20.870 of any variance that we identify.

NOTE Confidence: 0.85856925

00:48:20.870 --> 00:48:21.538 And so,

NOTE Confidence: 0.85856925

00:48:21.538 --> 00:48:23.542 so this was actually two patients

NOTE Confidence: 0.85856925

00:48:23.542 --> 00:48:25.655 with in this example, and.

NOTE Confidence: 0.85856925

00:48:25.655 --> 00:48:28.080 And we ended up publishing

NOTE Confidence: 0.85856925

00:48:28.080 --> 00:48:31.080 this short case series.

NOTE Confidence: 0.85856925

00:48:31.080 --> 00:48:33.618 With a former fellow at Yale,

NOTE Confidence: 0.85856925

00:48:33.620 --> 00:48:36.338 so one of the patients was at 59 year

NOTE Confidence: 0.85856925

00:48:36.338 --> 00:48:40.080 old woman and she had a combined

NOTE Confidence: 0.85856925

00:48:40.080 --> 00:48:41.346 cholangio carcinoma carcinoma.

NOTE Confidence: 0.85856925

00:48:41.346 --> 00:48:44.300 You can see that HTC component here.

NOTE Confidence: 0.85856925

00:48:44.300 --> 00:48:45.812 The collector component there.

NOTE Confidence: 0.85856925

00:48:45.812 --> 00:48:48.080 She had a personal history of

NOTE Confidence: 0.85856925

00:48:48.146 --> 00:48:50.072 breast cancer in the past and

NOTE Confidence: 0.85856925

00:48:50.072 --> 00:48:51.740 the thyroid cancer as well,

NOTE Confidence: 0.85856925

00:48:51.740 --> 00:48:53.973 and then she had a fairly extensive

NOTE Confidence: 0.85856925

00:48:53.973 --> 00:48:56.029 family history of cancer of various

NOTE Confidence: 0.85856925

00:48:56.029 --> 00:48:57.759 cancers and then patient #2,

NOTE Confidence: 0.85856925

00:48:57.760 --> 00:49:00.152 excuse me is a 62 year old man

NOTE Confidence: 0.85856925

00:49:00.152 --> 00:49:02.940 and he didn't have prior cancers.

NOTE Confidence: 0.85856925

00:49:02.940 --> 00:49:04.636 But he did have a sister who had

NOTE Confidence: 0.85856925

00:49:04.636 --> 00:49:06.080 both breast and uterine cancers,

NOTE Confidence: 0.85856925

00:49:06.080 --> 00:49:09.650 who had died of those cancers.

NOTE Confidence: 0.85856925

00:49:09.650 --> 00:49:11.966 And these are the alkaline results

NOTE Confidence: 0.85856925

00:49:11.966 --> 00:49:13.510 for those two patients.

NOTE Confidence: 0.85856925

00:49:13.510 --> 00:49:15.995 Both patients ended up having

NOTE Confidence: 0.85856925

00:49:15.995 --> 00:49:20.100 a bracket 2 mutation.

NOTE Confidence: 0.85856925

00:49:20.100 --> 00:49:22.370 And.

NOTE Confidence: 0.85856925

00:49:22.370 --> 00:49:24.506 Patient one has this

NOTE Confidence: 0.85856925

00:49:24.506 --> 00:49:26.108 pathogenic nonsense mutation,

NOTE Confidence: 0.85856925

00:49:26.110 --> 00:49:28.234 so it's premature leads to premature

NOTE Confidence: 0.85856925

00:49:28.234 --> 00:49:29.650 termination of the protein,

NOTE Confidence: 0.85856925

00:49:29.650 --> 00:49:32.539 and this was found to be both in the

NOTE Confidence: 0.85856925

00:49:32.539 --> 00:49:35.194 germline and in the tumor and patient.

NOTE Confidence: 0.85856925

00:49:35.194 --> 00:49:37.979 Two had two Broadcom mutations.

NOTE Confidence: 0.85856925

00:49:37.980 --> 00:49:40.458 One of these mutations is a

NOTE Confidence: 0.85856925

00:49:40.458 --> 00:49:42.344 pathogenic splice site mutation and

NOTE Confidence: 0.85856925

00:49:42.344 --> 00:49:44.216 this was found to be again in the

NOTE Confidence: 0.85856925

00:49:44.216 --> 00:49:45.566 patients germline sample as well

NOTE Confidence: 0.85856925

00:49:45.566 --> 00:49:47.478 as the tumor sample and then there

NOTE Confidence: 0.85856925

00:49:47.478 --> 00:49:49.098 was a second somatic mutation in

NOTE Confidence: 0.85856925

00:49:49.098 --> 00:49:51.210 bracket two as well and so based

NOTE Confidence: 0.85856925

00:49:51.210 --> 00:49:53.160 on these results a diagnosis of

NOTE Confidence: 0.85856925

00:49:53.226 --> 00:49:55.150 heritage Terry breast cancer.

NOTE Confidence: 0.85856925

00:49:55.150 --> 00:49:56.350 In a variant,

NOTE Confidence: 0.85856925

00:49:56.350 --> 00:49:58.750 syndrome can be made in both

NOTE Confidence: 0.85856925

00:49:58.750 --> 00:50:00.956 patients and you know it's it's one

NOTE Confidence: 0.85856925

00:50:00.956 --> 00:50:02.749 of these situations where I'm like,

NOTE Confidence: 0.85856925

00:50:02.750 --> 00:50:03.566 well, you know people,

NOTE Confidence: 0.85856925

00:50:03.566 --> 00:50:04.790 could you know maybe the patient

NOTE Confidence: 0.85856925

00:50:04.832 --> 00:50:06.170 with breast cancer should have been,

NOTE Confidence: 0.85856925

00:50:06.170 --> 00:50:08.207 you know, found to have this previously.

NOTE Confidence: 0.85856925

00:50:08.210 --> 00:50:11.450 I don't know. Not really sure.

NOTE Confidence: 0.85856925

00:50:11.450 --> 00:50:13.240 You know what, you know.

NOTE Confidence: 0.85856925

00:50:13.240 --> 00:50:15.380 When patients get screened for

NOTE Confidence: 0.85856925

00:50:15.380 --> 00:50:16.664 breast cancer exactly.

NOTE Confidence: 0.859277637777778

00:50:16.670 --> 00:50:19.750 For the syndrome, but looking at you

NOTE Confidence: 0.859277637777778

00:50:19.750 --> 00:50:22.325 know malignancy risks and patients

NOTE Confidence: 0.859277637777778

00:50:22.325 --> 00:50:24.665 with this particular syndrome

NOTE Confidence: 0.859277637777778

00:50:24.665 --> 00:50:27.005 combined cholangiocarcinoma HCC or

NOTE Confidence: 0.859277637777778

00:50:27.084 --> 00:50:29.814 is not really anywhere on that list.

NOTE Confidence: 0.859277637777778

00:50:29.820 --> 00:50:31.260 So you know, maybe they're related,

NOTE Confidence: 0.859277637777778

00:50:31.260 --> 00:50:32.388 you know, pancreatic.

NOTE Confidence: 0.859277637777778

00:50:32.388 --> 00:50:35.020 You know it's a biliary type cancer.

NOTE Confidence: 0.859277637777778

00:50:35.020 --> 00:50:36.966 Maybe that that that might be a

NOTE Confidence: 0.859277637777778

00:50:36.966 --> 00:50:39.078 hint that that could be part of it.

NOTE Confidence: 0.859277637777778

00:50:39.080 --> 00:50:42.727 So here's an example where we can

NOTE Confidence: 0.859277637777778

00:50:42.727 --> 00:50:46.050 really impact patient results,

NOTE Confidence: 0.859277637777778

00:50:46.050 --> 00:50:51.750 patient families by detecting mutations.

NOTE Confidence: 0.859277637777778

00:50:51.750 --> 00:50:53.214 And you know what?

NOTE Confidence: 0.859277637777778

00:50:53.214 --> 00:50:55.044 The risks that are associated

NOTE Confidence: 0.859277637777778

00:50:55.044 --> 00:50:57.849 with them in tumors that are not

NOTE Confidence: 0.859277637777778

00:50:57.849 --> 00:51:00.120 necessarily expected for that syndrome.

NOTE Confidence: 0.859277637777778

00:51:00.120 --> 00:51:02.510 And in addition to that,

NOTE Confidence: 0.859277637777778

00:51:02.510 --> 00:51:04.946 this also leads to the possibility

NOTE Confidence: 0.859277637777778

00:51:04.946 --> 00:51:07.608 of a specific type of therapy,

NOTE Confidence: 0.859277637777778

00:51:07.608 --> 00:51:10.380 and so in brocco mutated tumors,

NOTE Confidence: 0.859277637777778

00:51:10.380 --> 00:51:13.638 the use of carp inhibitors is.

NOTE Confidence: 0.859277637777778

00:51:13.640 --> 00:51:15.848 Is a possibility where you know.

NOTE Confidence: 0.742855642

00:51:18.650 --> 00:51:22.260 Where you know if you Park is an

NOTE Confidence: 0.742855642

00:51:22.260 --> 00:51:25.900 enzyme that is involved in DNA repair

NOTE Confidence: 0.742855642

00:51:26.010 --> 00:51:29.345 and if you include if you add up our

NOTE Confidence: 0.742855642

00:51:29.345 --> 00:51:31.591 PIN hitter and hit this enzyme in

NOTE Confidence: 0.742855642

00:51:31.591 --> 00:51:33.877 tumors that have a mutated BRACA.

NOTE Confidence: 0.742855642

00:51:33.880 --> 00:51:36.496 2 homologous recombination cannot

NOTE Confidence: 0.742855642

00:51:36.496 --> 00:51:40.420 be done and these patients undergo.

NOTE Confidence: 0.742855642

00:51:40.420 --> 00:51:42.716 You know these tumors undergo cell death

NOTE Confidence: 0.742855642

00:51:42.716 --> 00:51:44.840 and something called synthetic lethality.

NOTE Confidence: 0.742855642

00:51:44.840 --> 00:51:46.779 And there are now a lot of

NOTE Confidence: 0.742855642

00:51:46.779 --> 00:51:47.920 carpet hitters that are.

NOTE Confidence: 0.742855642

00:51:47.920 --> 00:51:49.812 Clinical use primarily for

NOTE Confidence: 0.742855642

00:51:49.812 --> 00:51:51.704 ovarian and breast cancers,

NOTE Confidence: 0.742855642

00:51:51.710 --> 00:51:53.738 but they definitely would be an

NOTE Confidence: 0.742855642

00:51:53.738 --> 00:51:55.921 option for both of these patients

NOTE Confidence: 0.742855642

00:51:55.921 --> 00:51:57.806 if if they should recur.

NOTE Confidence: 0.742855642

00:51:57.810 --> 00:52:01.026 For their tumor, and this is another example.

NOTE Confidence: 0.742855642

00:52:01.030 --> 00:52:03.040 That was a different publication

NOTE Confidence: 0.742855642

00:52:03.040 --> 00:52:04.144 that was also interesting,

NOTE Confidence: 0.742855642

00:52:04.144 --> 00:52:06.732 and this was a 63 year old man who

NOTE Confidence: 0.742855642

00:52:06.732 --> 00:52:08.192 had a gallbladder respected and

NOTE Confidence: 0.742855642

00:52:08.192 --> 00:52:10.704 this was initially seen else not at

NOTE Confidence: 0.742855642

00:52:10.704 --> 00:52:12.852 not centrally Yale and the initial

NOTE Confidence: 0.742855642

00:52:12.852 --> 00:52:15.390 diagnosis that was made was Edna carcinoma.

NOTE Confidence: 0.742855642

00:52:15.390 --> 00:52:18.280 Several, you know months later.

NOTE Confidence: 0.742855642

00:52:18.280 --> 00:52:20.868 The page you know,

NOTE Confidence: 0.742855642

00:52:20.868 --> 00:52:23.456 the clinician oncologist ordered,

NOTE Confidence: 0.742855642

00:52:23.460 --> 00:52:25.497 and she S testing and MSI testing,

NOTE Confidence: 0.742855642

00:52:25.500 --> 00:52:27.810 and it came to us.

NOTE Confidence: 0.742855642

00:52:27.810 --> 00:52:31.878 For assessment and between the morphology

NOTE Confidence: 0.742855642

00:52:31.878 --> 00:52:36.998 and the results from the oncoming testing,

NOTE Confidence: 0.742855642

00:52:37.000 --> 00:52:38.806 the diagnosis was revised to Miso,

NOTE Confidence: 0.742855642

00:52:38.810 --> 00:52:40.280 thi Lio Ma,

NOTE Confidence: 0.742855642

00:52:40.280 --> 00:52:42.641 and that's because this particular tumor,

NOTE Confidence: 0.742855642

00:52:42.641 --> 00:52:44.720 one of the reasons was that this

NOTE Confidence: 0.742855642

00:52:44.775 --> 00:52:46.989 particular tumor showed about 1 mutation,

NOTE Confidence: 0.742855642

00:52:46.990 --> 00:52:48.550 and again there's two of them.

NOTE Confidence: 0.742855642

00:52:48.550 --> 00:52:50.461 There's one mutation that was seen both

NOTE Confidence: 0.742855642

00:52:50.461 --> 00:52:52.759 in the tumor and in the patient's blood,

NOTE Confidence: 0.742855642

00:52:52.760 --> 00:52:54.072 and a second back,

NOTE Confidence: 0.742855642

00:52:54.072 --> 00:52:55.456 one mutation that was found

NOTE Confidence: 0.742855642

00:52:55.456 --> 00:52:56.424 in just the tumor.

NOTE Confidence: 0.742855642

00:52:56.430 --> 00:52:58.537 So here's an example of somebody again.

NOTE Confidence: 0.742855642

00:52:58.540 --> 00:53:01.468 Has a germline first hit and that one

NOTE Confidence: 0.742855642

00:53:01.468 --> 00:53:04.675 and the tumor there's a second hit in

NOTE Confidence: 0.742855642

00:53:04.675 --> 00:53:07.150 in the in the second allele of BAP one.

NOTE Confidence: 0.81358908

00:53:12.340 --> 00:53:13.858 Doctor Shelper I see your question.

NOTE Confidence: 0.81358908

00:53:13.860 --> 00:53:15.960 I can come back to it a little bit later

NOTE Confidence: 0.81358908

00:53:15.960 --> 00:53:18.018 and so for this particular patient we

NOTE Confidence: 0.81358908

00:53:18.018 --> 00:53:20.924 can make a diagnosis of Bab 1 trimmer

NOTE Confidence: 0.81358908

00:53:20.924 --> 00:53:22.970 for Disposition syndrome and you know,

NOTE Confidence: 0.81358908

00:53:22.970 --> 00:53:24.420 looking at this patient pedigree,

NOTE Confidence: 0.81358908

00:53:24.420 --> 00:53:26.219 there was actually quite a lot of

NOTE Confidence: 0.81358908

00:53:26.219 --> 00:53:27.960 cancer in this patient syndrome.

NOTE Confidence: 0.81358908

00:53:27.960 --> 00:53:28.972 And you know, again,

NOTE Confidence: 0.81358908

00:53:28.972 --> 00:53:31.065 you know we can sort of allow this

NOTE Confidence: 0.81358908

00:53:31.065 --> 00:53:33.512 family to be able to be tested for it

NOTE Confidence: 0.81358908

00:53:33.512 --> 00:53:35.724 and and now they can start potentially

NOTE Confidence: 0.81358908

00:53:35.724 --> 00:53:40.680 screening for some of these cancers, etc.

NOTE Confidence: 0.81358908

00:53:40.680 --> 00:53:43.290 And and so.

NOTE Confidence: 0.81358908

00:53:43.290 --> 00:53:45.474 You know the concept of being able

NOTE Confidence: 0.81358908

00:53:45.474 --> 00:53:47.934 to do genetic findings that are

NOTE Confidence: 0.81358908

00:53:47.934 --> 00:53:49.870 discovered through online testing.

NOTE Confidence: 0.81358908

00:53:49.870 --> 00:53:52.586 Is is something that we are working

NOTE Confidence: 0.81358908

00:53:52.586 --> 00:53:55.101 on in collaboration again with our

NOTE Confidence: 0.81358908

00:53:55.101 --> 00:53:58.878 genetics clinic and we looked at 123

NOTE Confidence: 0.81358908

00:53:58.878 --> 00:54:02.226 patients who had a known pathogenic

NOTE Confidence: 0.81358908

00:54:02.226 --> 00:54:07.668 variant and you know 2/3 of them.

NOTE Confidence: 0.81358908

00:54:07.670 --> 00:54:09.938 We're not known prior to the testing

NOTE Confidence: 0.81358908

00:54:09.938 --> 00:54:11.915 with alkaline that that that they

NOTE Confidence: 0.81358908

00:54:11.915 --> 00:54:14.438 had in pathogenic mutation in their

NOTE Confidence: 0.81358908

00:54:14.438 --> 00:54:17.594 germ line that will impact either

NOTE Confidence: 0.81358908

00:54:17.600 --> 00:54:19.652 their family members or options for

NOTE Confidence: 0.81358908

00:54:19.652 --> 00:54:21.550 therapy and then doctor Shelper.

NOTE Confidence: 0.81358908

00:54:21.550 --> 00:54:25.335 You mentioned that in this case the

NOTE Confidence: 0.81358908

00:54:25.335 --> 00:54:27.630 germ line was it is a little bit low.

NOTE Confidence: 0.81358908

00:54:27.630 --> 00:54:30.395 It would be expected to be at.

NOTE Confidence: 0.81358908

00:54:30.400 --> 00:54:33.456 40% or 50% if it was a heterozygous

NOTE Confidence: 0.81358908

00:54:33.456 --> 00:54:34.220 germline variant,

NOTE Confidence: 0.81358908

00:54:34.220 --> 00:54:38.660 it's within range of what we see with.

NOTE Confidence: 0.81358908

00:54:38.660 --> 00:54:40.360 With.

NOTE Confidence: 0.81358908

00:54:40.360 --> 00:54:41.602 With MGS testing,

NOTE Confidence: 0.81358908

00:54:41.602 --> 00:54:44.500 so sometimes there can be a little

NOTE Confidence: 0.81358908

00:54:44.588 --> 00:54:47.458 bit of skewing that happens with NGS

NOTE Confidence: 0.81358908

00:54:47.460 --> 00:54:49.828 and you may not get a perfect number,

NOTE Confidence: 0.81358908

00:54:49.830 --> 00:54:53.806 but we we typically accept these results.

NOTE Confidence: 0.63366647

00:54:57.400 --> 00:54:59.356 And Doctor Robert asked another question.

NOTE Confidence: 0.63366647

00:54:59.360 --> 00:55:01.160 The diagnosis of change from the

NOTE Confidence: 0.63366647

00:55:01.160 --> 00:55:02.996 adenocarcinoma to miso, thi Lio Ma?

NOTE Confidence: 0.63366647

00:55:02.996 --> 00:55:04.556 It was based by both.

NOTE Confidence: 0.63366647

00:55:04.560 --> 00:55:06.918 Really it was based on both.

NOTE Confidence: 0.63366647

00:55:06.920 --> 00:55:09.881 So when they add note when this

NOTE Confidence: 0.63366647

00:55:09.881 --> 00:55:12.508 gallbladder came over we were able to.

NOTE Confidence: 0.63366647

00:55:12.510 --> 00:55:15.885 So I'll say this was all Doctor Ilkay who

NOTE Confidence: 0.63366647

00:55:15.885 --> 00:55:18.759 initially raised alarm about the diagnosis.

NOTE Confidence: 0.63366647

00:55:18.760 --> 00:55:21.226 She she thought it was an odd looking add,

NOTE Confidence: 0.63366647

00:55:21.230 --> 00:55:22.720 no carcinoma, quote, UN quote,

NOTE Confidence: 0.63366647

00:55:22.720 --> 00:55:24.655 and so she ordered additional

NOTE Confidence: 0.63366647

00:55:24.655 --> 00:55:25.816 immunostains to check.

NOTE Confidence: 0.63366647

00:55:25.820 --> 00:55:28.692 And and at the same time NGS was

NOTE Confidence: 0.63366647

00:55:28.692 --> 00:55:30.918 being done with anchor mine.

NOTE Confidence: 0.63366647

00:55:30.920 --> 00:55:31.924 So basically,

NOTE Confidence: 0.63366647

00:55:31.924 --> 00:55:35.438 when all of those results came out,

NOTE Confidence: 0.63366647

00:55:35.440 --> 00:55:37.590 you know it was coordinated

NOTE Confidence: 0.63366647

00:55:37.590 --> 00:55:39.740 and the change was made.

NOTE Confidence: 0.63366647

00:55:39.740 --> 00:55:41.080 So sort of a combination.

NOTE Confidence: 0.63366647

00:55:41.080 --> 00:55:42.627 It was not one or the other.

NOTE Confidence: 0.92627313

00:55:46.250 --> 00:55:49.431 OK, so in the last three minutes last

NOTE Confidence: 0.92627313

00:55:49.431 --> 00:55:51.328 patient, so this was a patient who

NOTE Confidence: 0.92627313

00:55:51.328 --> 00:55:53.566 had a new diagnosis of metastatic

NOTE Confidence: 0.92627313

00:55:53.566 --> 00:55:55.611 non different carcinoma and the

NOTE Confidence: 0.92627313

00:55:55.611 --> 00:55:57.350 question is what do you order?

NOTE Confidence: 0.92627313

00:55:57.350 --> 00:56:00.276 And really again it's a tricky question

NOTE Confidence: 0.92627313

00:56:00.276 --> 00:56:03.005 because NGS does not really have a

NOTE Confidence: 0.92627313

00:56:03.005 --> 00:56:05.771 huge role in the diagnosis of any

NOTE Confidence: 0.92627313

00:56:05.771 --> 00:56:08.099 neuroendocrine tumors or neoplasms.

NOTE Confidence: 0.92627313

00:56:08.100 --> 00:56:09.905 Neurocrine tumors tend to be

NOTE Confidence: 0.92627313

00:56:09.905 --> 00:56:12.293 diagnosed by morphology as either well

NOTE Confidence: 0.92627313

00:56:12.293 --> 00:56:14.389 differentiated or poorly differentiated.

NOTE Confidence: 0.92627313

00:56:14.390 --> 00:56:16.995 And you know, poorly differentiated

NOTE Confidence: 0.92627313

00:56:16.995 --> 00:56:20.795 ones tend to have a lot of P53RB

NOTE Confidence: 0.92627313

00:56:20.795 --> 00:56:23.420 mutations or CDKN 2A mutations,

NOTE Confidence: 0.92627313

00:56:23.420 --> 00:56:25.766 whereas the mtor pathway tends to

NOTE Confidence: 0.92627313

00:56:25.766 --> 00:56:28.306 be altered in the wild if tumors,

NOTE Confidence: 0.92627313

00:56:28.306 --> 00:56:30.798 and so NGS that targeted therapy does

NOTE Confidence: 0.92627313

00:56:30.798 --> 00:56:33.169 not really have a huge role in this.

NOTE Confidence: 0.92627313

00:56:33.170 --> 00:56:33.702 Nevertheless,

NOTE Confidence: 0.92627313

00:56:33.702 --> 00:56:37.426 on combine was ordered for this patient.

NOTE Confidence: 0.92627313

00:56:37.430 --> 00:56:39.929 And so this is from the hepatitis

NOTE Confidence: 0.92627313

00:56:39.929 --> 00:56:42.498 specimen and we estimated 90% malignant

NOTE Confidence: 0.92627313

00:56:42.498 --> 00:56:45.778 cells within this tumor sample and over

NOTE Confidence: 0.92627313

00:56:45.778 --> 00:56:48.886 150 mutations right outside in this tumor.

NOTE Confidence: 0.92627313

00:56:48.890 --> 00:56:51.088 And you know, this is something that,

NOTE Confidence: 0.92627313

00:56:51.090 --> 00:56:53.602 like when we get one of these results

NOTE Confidence: 0.92627313

00:56:53.602 --> 00:56:56.035 on the tumor profiling lab service.

NOTE Confidence: 0.92627313

00:56:56.035 --> 00:56:59.320 We just like want to start crying because how

NOTE Confidence: 0.92627313

00:56:59.391 --> 00:57:03.170 do you assess 150 importations in one tumor?

NOTE Confidence: 0.92627313

00:57:03.170 --> 00:57:05.690 And you know you've got like 20 other

NOTE Confidence: 0.92627313

00:57:05.690 --> 00:57:07.982 tumors to look at, so you kind of.

NOTE Confidence: 0.92627313

00:57:07.982 --> 00:57:10.019 You know you sort of gain experience

NOTE Confidence: 0.92627313

00:57:10.019 --> 00:57:12.552 and you figure things out anyway,

NOTE Confidence: 0.92627313

00:57:12.552 --> 00:57:16.164 so we had 15 mutations there.

NOTE Confidence: 0.92627313

00:57:16.170 --> 00:57:17.290 That were, you know,

NOTE Confidence: 0.92627313

00:57:17.290 --> 00:57:18.130 sort of significant.

NOTE Confidence: 0.92627313

00:57:18.130 --> 00:57:20.890 There's 140 others that were maybe

NOTE Confidence: 0.92627313

00:57:20.890 --> 00:57:23.816 like a little bit more vus types,

NOTE Confidence: 0.92627313

00:57:23.820 --> 00:57:26.900 and so basically this is a tumor that's

NOTE Confidence: 0.92627313

00:57:26.900 --> 00:57:29.970 consistent with hypermutation and.

NOTE Confidence: 0.92627313

00:57:29.970 --> 00:57:32.876 How does hyper mutation occur in cancer?

NOTE Confidence: 0.92627313

00:57:32.876 --> 00:57:35.206 There's multiple causes of it.

NOTE Confidence: 0.92627313

00:57:35.210 --> 00:57:38.058 MSI is one of those we've already spoken

NOTE Confidence: 0.92627313

00:57:38.058 --> 00:57:40.985 about MSI quite a bit and others could

NOTE Confidence: 0.92627313

00:57:40.985 --> 00:57:44.040 be mutations and pull or pull D and

NOTE Confidence: 0.92627313

00:57:44.040 --> 00:57:48.590 Neurocrine tumors are not commonly.

NOTE Confidence: 0.92627313

00:57:48.590 --> 00:57:51.530 Do not commonly show MSI high status.

NOTE Confidence: 0.92627313

00:57:51.530 --> 00:57:54.869 Maybe only a handful of those cases.

NOTE Confidence: 0.92627313

00:57:54.870 --> 00:57:58.380 And maturity of.

NOTE Confidence: 0.92627313

00:57:58.380 --> 00:58:00.402 You know MSI high tumors are

NOTE Confidence: 0.92627313

00:58:00.402 --> 00:58:01.413 sporadic in nature,

NOTE Confidence: 0.92627313

00:58:01.420 --> 00:58:03.364 so you know we want to execute lynchings.

NOTE Confidence: 0.92627313

00:58:03.370 --> 00:58:04.595 M in this patient and

NOTE Confidence: 0.92627313

00:58:04.595 --> 00:58:05.575 thankfully none of these.

NOTE Confidence: 0.92627313

00:58:05.580 --> 00:58:07.692 None of these mutations were germ

NOTE Confidence: 0.92627313

00:58:07.692 --> 00:58:10.260 line in this particular patient and

NOTE Confidence: 0.92627313

00:58:10.260 --> 00:58:13.560 just looking deeper into literature

NOTE Confidence: 0.92627313

00:58:13.560 --> 00:58:16.480 you know what do we know about

NOTE Confidence: 0.92627313

00:58:16.480 --> 00:58:18.080 hypermutation and nerve tumors you

NOTE Confidence: 0.92627313

00:58:18.142 --> 00:58:20.256 know and does MSI contribute to that?

NOTE Confidence: 0.92627313

00:58:20.260 --> 00:58:22.116 And at least then one study there seems

NOTE Confidence: 0.92627313

00:58:22.116 --> 00:58:24.140 to be a contribution of them aside,

NOTE Confidence: 0.92627313

00:58:24.140 --> 00:58:26.305 hypermutation in our consumers and

NOTE Confidence: 0.92627313

00:58:26.305 --> 00:58:28.999 another study also found a fairly

NOTE Confidence: 0.92627313

00:58:28.999 --> 00:58:32.588 high number. Tumors that had.

NOTE Confidence: 0.92627313

00:58:32.590 --> 00:58:33.056 Mr.

NOTE Confidence: 0.92627313

00:58:33.056 --> 00:58:35.852 That was unstable but not a

NOTE Confidence: 0.92627313

00:58:35.852 --> 00:58:38.289 lot of detail about it,

NOTE Confidence: 0.92627313

00:58:38.290 --> 00:58:40.602 and the point is that maybe it doesn't

NOTE Confidence: 0.92627313

00:58:40.602 --> 00:58:42.743 really matter what the cause of the MSI

NOTE Confidence: 0.92627313

00:58:42.743 --> 00:58:45.720 in this patient is, but now we know that.

NOTE Confidence: 0.92627313

00:58:45.720 --> 00:58:46.623 Or the hypermutation.

NOTE Confidence: 0.92627313

00:58:46.623 --> 00:58:48.730 But now we know that there's a

NOTE Confidence: 0.92627313

00:58:48.795 --> 00:58:50.246 response to PD one inhibition.

NOTE Confidence: 0.92627313

00:58:50.246 --> 00:58:52.276 That's an option for him,

NOTE Confidence: 0.92627313

00:58:52.280 --> 00:58:55.108 and this is an example of a

NOTE Confidence: 0.92627313

00:58:55.108 --> 00:58:58.980 patient who responded to Pembroke.

NOTE Confidence: 0.92627313

00:58:58.980 --> 00:59:02.850 You know who had a MSI High Nordic rent

NOTE Confidence: 0.92627313

00:59:02.850 --> 00:59:05.640 tumor and this is something that's,

NOTE Confidence: 0.92627313

00:59:05.640 --> 00:59:07.059 you know this.

NOTE Confidence: 0.92627313

00:59:07.059 --> 00:59:10.370 This expanding utility for using MSI to

NOTE Confidence: 0.8851997185

00:59:10.463 --> 00:59:13.511 predict response to PD one is

NOTE Confidence: 0.8851997185

00:59:13.511 --> 00:59:15.543 a relatively recent finding.

NOTE Confidence: 0.8851997185

00:59:15.550 --> 00:59:20.856 And we can also think about MSI.

NOTE Confidence: 0.8851997185

00:59:20.860 --> 00:59:21.936 As measured by NGS,

NOTE Confidence: 0.8851997185

00:59:21.936 --> 00:59:23.900 this is an emerging by informatics tools.

NOTE Confidence: 0.8851997185

00:59:23.900 --> 00:59:25.545 There are numerous computational methods

NOTE Confidence: 0.8851997185

00:59:25.545 --> 00:59:27.950 that can be used for NGS detection

NOTE Confidence: 0.8851997185

00:59:27.950 --> 00:59:29.774 and just in the interest of time I'm

NOTE Confidence: 0.8851997185

00:59:29.774 --> 00:59:31.647 going to skip through some of these.

NOTE Confidence: 0.8851997185

00:59:31.650 --> 00:59:32.846 We did look at.

NOTE Confidence: 0.8851997185

00:59:32.846 --> 00:59:36.185 We did look at one of these methods to be

NOTE Confidence: 0.8851997185

00:59:36.185 --> 00:59:39.590 able to tell NGS with our former fellow,

NOTE Confidence: 0.8851997185

00:59:39.590 --> 00:59:41.942 and we did find that this is a

NOTE Confidence: 0.8851997185

00:59:41.942 --> 00:59:43.972 specific but non sensitive method,

NOTE Confidence: 0.8851997185

00:59:43.972 --> 00:59:48.310 at least using the oncoming NGS data and so.

NOTE Confidence: 0.8851997185

00:59:48.310 --> 00:59:49.830 In this particular patient,

NOTE Confidence: 0.8851997185

00:59:49.830 --> 00:59:52.410 although the mantis was negative for MSI,

NOTE Confidence: 0.8851997185

00:59:52.410 --> 00:59:54.960 you know we still have questions

NOTE Confidence: 0.8851997185

00:59:54.960 --> 00:59:56.960 about you know what might have

NOTE Confidence: 0.8851997185

00:59:56.960 --> 00:59:59.200 been the cause of this patience.

NOTE Confidence: 0.8851997185

00:59:59.200 --> 01:00:01.168 Anyway, I'm going to skip the next couple

NOTE Confidence: 0.8851997185

01:00:01.168 --> 01:00:03.117 of slides here and just get to the end.

NOTE Confidence: 0.8851997185

01:00:03.120 --> 01:00:04.450 If any of you are interested in

NOTE Confidence: 0.8851997185

01:00:04.450 --> 01:00:06.020 in more of these types of cases,

NOTE Confidence: 0.8851997185

01:00:06.020 --> 01:00:08.180 please come to the precision Medicine

NOTE Confidence: 0.8851997185

01:00:08.180 --> 01:00:10.490 tumor board where we review all kinds

NOTE Confidence: 0.8851997185

01:00:10.490 --> 01:00:12.520 of tumors with all sorts of findings,

NOTE Confidence: 0.8851997185

01:00:12.520 --> 01:00:14.384 both germline and somatic,

NOTE Confidence: 0.8851997185

01:00:14.384 --> 01:00:17.180 and determine what best causes are.

NOTE Confidence: 0.8851997185

01:00:17.180 --> 01:00:18.023 So, in summary,

NOTE Confidence: 0.8851997185

01:00:18.023 --> 01:00:20.374 I hope you guys have seen how I've

NOTE Confidence: 0.8851997185

01:00:20.374 --> 01:00:21.964 gone through this mandering path

NOTE Confidence: 0.8851997185

01:00:21.964 --> 01:00:24.749 of being a GI and liver surgical

NOTE Confidence: 0.8851997185

01:00:24.749 --> 01:00:26.673 pathologist into incorporating molecular

NOTE Confidence: 0.8851997185

01:00:26.673 --> 01:00:30.620 pathology into my practice and into my.

NOTE Confidence: 0.8851997185

01:00:30.620 --> 01:00:33.120 Research and focusing on

NOTE Confidence: 0.8851997185

01:00:33.120 --> 01:00:36.400 patients results and.

NOTE Confidence: 0.8851997185

01:00:36.400 --> 01:00:37.298 And outcomes,

NOTE Confidence: 0.8851997185

01:00:37.298 --> 01:00:39.543 and hopefully in the future

NOTE Confidence: 0.8851997185

01:00:39.543 --> 01:00:42.404 we can coordinate some of this

NOTE Confidence: 0.8851997185

01:00:42.404 --> 01:00:44.320 information more seamlessly and

NOTE Confidence: 0.8851997185

01:00:44.320 --> 01:00:46.980 have an integrated practice where.

NOTE Confidence: 0.8851997185

01:00:46.980 --> 01:00:49.940 This information flow happens easily

NOTE Confidence: 0.8851997185

01:00:49.940 --> 01:00:54.470 and accessibly to everyone and so.

NOTE Confidence: 0.8851997185

01:00:54.470 --> 01:00:58.013 I'd like to thank everyone I you know, AM.

NOTE Confidence: 0.8851997185

01:00:58.013 --> 01:01:01.486 Moving on to some new new things

NOTE Confidence: 0.8851997185

01:01:01.486 --> 01:01:03.454 in the department as the Director

NOTE Confidence: 0.8851997185

01:01:03.454 --> 01:01:05.482 of Quality and Patient Safety cell

NOTE Confidence: 0.8851997185

01:01:05.482 --> 01:01:07.450 be leaving behind some of this,

NOTE Confidence: 0.8851997185

01:01:07.450 --> 01:01:09.266 some of this research that I'm doing here,

NOTE Confidence: 0.8851997185

01:01:09.270 --> 01:01:14.854 but I'm sticking around and I'm looking for.

NOTE Confidence: 0.8851997185

01:01:14.860 --> 01:01:18.120 You know collaboration with everybody,

NOTE Confidence: 0.8851997185

01:01:18.120 --> 01:01:20.990 and in this new endeavor.

NOTE Confidence: 0.8851997185

01:01:20.990 --> 01:01:21.662 And that's it.

NOTE Confidence: 0.8851997185

01:01:21.662 --> 01:01:22.110 That's yeah,

NOTE Confidence: 0.8851997185

01:01:22.110 --> 01:01:24.966 I'm sorry for going over a little bit,

NOTE Confidence: 0.8851997185

01:01:24.970 --> 01:01:26.626 but I'm happy to take some

NOTE Confidence: 0.8851997185

01:01:26.626 --> 01:01:28.040 additional questions at this time.

NOTE Confidence: 0.636027378181818

01:01:30.150 --> 01:01:33.350 So we have about 84 people logged in

NOTE Confidence: 0.636027378181818

01:01:33.350 --> 01:01:37.506 and we are well over the time limit,

NOTE Confidence: 0.636027378181818

01:01:37.506 --> 01:01:41.790 but maybe a quick one or two questions.

NOTE Confidence: 0.636027378181818

01:01:41.790 --> 01:01:44.280 Please unmute yourself and ask.

NOTE Confidence: 0.823035436666667

01:01:47.110 --> 01:01:50.096 So I can start with Joanne, you know?

NOTE Confidence: 0.823035436666667

01:01:50.096 --> 01:01:52.126 Joanne, thank you for this.

NOTE Confidence: 0.823035436666667

01:01:52.126 --> 01:01:54.506 Very interesting you know seminar.

NOTE Confidence: 0.823035436666667

01:01:54.510 --> 01:01:56.688 I think this is you as your last set.

NOTE Confidence: 0.823035436666667

01:01:56.690 --> 01:01:59.448 So I point out this is exactly

NOTE Confidence: 0.823035436666667

01:01:59.450 --> 01:02:01.436 probably the future direction of

NOTE Confidence: 0.823035436666667

01:02:01.436 --> 01:02:03.418 future practice of our pathologies.

NOTE Confidence: 0.745086356363636

01:02:03.820 --> 01:02:05.990 So my question to you is if we are from from

NOTE Confidence: 0.878107091428571

01:02:06.000 --> 01:02:09.178 your personal experience and do you feel?

NOTE Confidence: 0.878107091428571

01:02:09.180 --> 01:02:12.664 I mean if whatever you can share with us,

NOTE Confidence: 0.878107091428571

01:02:12.670 --> 01:02:14.130 some of your personal experience,

NOTE Confidence: 0.878107091428571

01:02:14.130 --> 01:02:16.110 you know when you are not about

NOTE Confidence: 0.878107091428571

01:02:16.110 --> 01:02:17.435 certain that you did not.

NOTE Confidence: 0.878107091428571

01:02:17.440 --> 01:02:18.904 Through the Molecular Pathology

NOTE Confidence: 0.878107091428571

01:02:18.904 --> 01:02:21.266 fellowship you are just, you know,

NOTE Confidence: 0.878107091428571

01:02:21.266 --> 01:02:23.954 surgical pathologists and then decided to.

NOTE Confidence: 0.878107091428571

01:02:23.960 --> 01:02:25.332 You know to practice molecular

NOTE Confidence: 0.878107091428571

01:02:25.332 --> 01:02:26.660 pathology what you know.

NOTE Confidence: 0.878107091428571

01:02:26.660 --> 01:02:28.536 What's your experience you think is doable?

NOTE Confidence: 0.878107091428571

01:02:28.540 --> 01:02:29.640 I mean certainly it's doable.

NOTE Confidence: 0.878107091428571

01:02:29.640 --> 01:02:30.540 You prove it.

NOTE Confidence: 0.878107091428571

01:02:30.540 --> 01:02:32.216 But what I'm saying and it obviously

NOTE Confidence: 0.878107091428571

01:02:32.216 --> 01:02:34.760 you know and it hurdles any sort of

NOTE Confidence: 0.878107091428571

01:02:34.834 --> 01:02:37.480 insights you may have for other sort

NOTE Confidence: 0.878107091428571

01:02:37.480 --> 01:02:39.548 of aspiring surgical pathologies that

NOTE Confidence: 0.878107091428571

01:02:39.548 --> 01:02:42.134 may thinking that goes through the,

NOTE Confidence: 0.878107091428571

01:02:42.140 --> 01:02:43.968 you know, the way you have guns.

NOTE Confidence: 0.878107091428571

01:02:43.968 --> 01:02:45.480 Yeah, yeah, absolutely.

NOTE Confidence: 0.878107091428571

01:02:45.480 --> 01:02:47.256 I mean, I hope other pathologists

NOTE Confidence: 0.878107091428571

01:02:47.256 --> 01:02:49.740 can join me in in this way as well.

NOTE Confidence: 0.878107091428571

01:02:49.740 --> 01:02:52.062 I I think challenge is that

NOTE Confidence: 0.878107091428571

01:02:52.062 --> 01:02:54.070 there is more molecular work.

NOTE Confidence: 0.878107091428571

01:02:54.070 --> 01:02:56.126 Then there are molecular

NOTE Confidence: 0.878107091428571

01:02:56.126 --> 01:02:57.668 trained molecular pathologists,

NOTE Confidence: 0.878107091428571

01:02:57.670 --> 01:03:01.478 so there is need for you know additional

NOTE Confidence: 0.878107091428571

01:03:01.478 --> 01:03:04.408 expertise in this area and I think

NOTE Confidence: 0.878107091428571

01:03:04.410 --> 01:03:06.810 in addition the world of molecular

NOTE Confidence: 0.878107091428571

01:03:06.810 --> 01:03:09.628 pathology I think is changing rapidly

NOTE Confidence: 0.878107091428571

01:03:09.628 --> 01:03:12.418 more rapidly than the fellowship

NOTE Confidence: 0.878107091428571

01:03:12.418 --> 01:03:15.842 training can sort of keep up with

NOTE Confidence: 0.878107091428571

01:03:15.842 --> 01:03:19.063 and you know a lot of these end results.

NOTE Confidence: 0.878107091428571

01:03:19.063 --> 01:03:22.150 You know this is all in the last five years.

NOTE Confidence: 0.878107091428571

01:03:22.150 --> 01:03:23.374 Fellowships can change fast

NOTE Confidence: 0.878107091428571

01:03:23.374 --> 01:03:24.904 enough to sort of incorporate.

NOTE Confidence: 0.878107091428571

01:03:24.910 --> 01:03:29.160 That aspect, and.

NOTE Confidence: 0.878107091428571

01:03:29.160 --> 01:03:30.918 And you know, I you know,

NOTE Confidence: 0.878107091428571

01:03:30.920 --> 01:03:33.280 I personally had a strong interest in cancer.

NOTE Confidence: 0.878107091428571

01:03:33.280 --> 01:03:35.240 That I, you know, goes back to you,

NOTE Confidence: 0.878107091428571

01:03:35.240 --> 01:03:36.756 know my PhD days.

NOTE Confidence: 0.878107091428571

01:03:36.756 --> 01:03:39.697 So I was sort of primed to

NOTE Confidence: 0.878107091428571

01:03:39.697 --> 01:03:41.989 learn this material quickly.

NOTE Confidence: 0.878107091428571

01:03:41.990 --> 01:03:46.348 But it can be done, I think with.

NOTE Confidence: 0.878107091428571

01:03:46.350 --> 01:03:46.965 You know what?

NOTE Confidence: 0.878107091428571

01:03:46.965 --> 01:03:49.116 So one thing that I did I I always like

NOTE Confidence: 0.878107091428571

01:03:49.116 --> 01:03:51.252 to think I always like to say that I

NOTE Confidence: 0.878107091428571

01:03:51.252 --> 01:03:53.128 actually did exactly what a fellow does.

NOTE Confidence: 0.878107091428571

01:03:53.130 --> 01:03:55.500 I did a six week rotation at TPL at that's

NOTE Confidence: 0.878107091428571

01:03:55.558 --> 01:03:57.924 what a fellow in molecular pathology does.

NOTE Confidence: 0.878107091428571

01:03:57.930 --> 01:04:00.289 They do a six week rotation in

NOTE Confidence: 0.878107091428571

01:04:00.289 --> 01:04:02.922 TPL and I'm focusing on just that

NOTE Confidence: 0.878107091428571

01:04:02.922 --> 01:04:04.450 aspect of molecular pathology.

NOTE Confidence: 0.878107091428571

01:04:04.450 --> 01:04:05.602 I'm not, you know,

NOTE Confidence: 0.878107091428571

01:04:05.602 --> 01:04:07.650 I I let others worry about you,

NOTE Confidence: 0.878107091428571

01:04:07.650 --> 01:04:09.216 know the fish.

NOTE Confidence: 0.878107091428571

01:04:09.216 --> 01:04:12.348 The MLH 1 methylation the PCR,

NOTE Confidence: 0.878107091428571

01:04:12.350 --> 01:04:14.638 you know, I, I trust the you know

NOTE Confidence: 0.878107091428571

01:04:14.638 --> 01:04:16.838 other labs to do their part so I'm.

NOTE Confidence: 0.878107091428571

01:04:16.840 --> 01:04:17.696 You know,

NOTE Confidence: 0.878107091428571

01:04:17.696 --> 01:04:20.264 with a narrow focus like that,

NOTE Confidence: 0.878107091428571

01:04:20.270 --> 01:04:22.321 I think it's quite possible for many

NOTE Confidence: 0.878107091428571

01:04:22.321 --> 01:04:24.228 pathologists sort of interact with this,

NOTE Confidence: 0.878107091428571

01:04:24.230 --> 01:04:25.530 and I think in addition,

NOTE Confidence: 0.878107091428571

01:04:25.530 --> 01:04:28.050 we really need to expand our teaching

NOTE Confidence: 0.878107091428571

01:04:28.050 --> 01:04:31.500 so that everybody can sort of chip in

NOTE Confidence: 0.878107091428571

01:04:31.500 --> 01:04:36.098 small things in in this in this endeavor.

NOTE Confidence: 0.878107091428571

01:04:36.100 --> 01:04:38.380 So just by increasing our,

NOTE Confidence: 0.878107091428571

01:04:38.380 --> 01:04:40.908 you know our ability to teach the future

NOTE Confidence: 0.878107091428571

01:04:40.908 --> 01:04:42.539 generations some of this material.

NOTE Confidence: 0.878107091428571

01:04:42.540 --> 01:04:43.518 I think it's just it's a.

NOTE Confidence: 0.878107091428571

01:04:43.520 --> 01:04:47.250 It's a rapidly evolving field.

NOTE Confidence: 0.878107091428571

01:04:47.250 --> 01:04:48.938 And and I think we need to be.

NOTE Confidence: 0.913217235384615

01:04:51.350 --> 01:04:53.506 Creative and how we approach all the

NOTE Confidence: 0.913217235384615

01:04:53.506 --> 01:04:55.698 work that this field is generating.

NOTE Confidence: 0.905584825

01:04:58.190 --> 01:04:58.660 Thank you.

NOTE Confidence: 0.928757385

01:05:07.620 --> 01:05:13.760 Well, if there are no questions. I'll let.

NOTE Confidence: 0.928757385

01:05:13.760 --> 01:05:16.830 It was a great shock Joanna I I think

NOTE Confidence: 0.930157747142857

01:05:16.840 --> 01:05:18.520 as a surgical pathologist,

NOTE Confidence: 0.930157747142857

01:05:18.520 --> 01:05:21.206 I really appreciate the bringing in

NOTE Confidence: 0.930157747142857

01:05:21.206 --> 01:05:23.766 of integration with molecular and I.

NOTE Confidence: 0.930157747142857

01:05:23.766 --> 01:05:25.610 I think we would all welcome

NOTE Confidence: 0.916243268333333

01:05:25.920 --> 01:05:28.160 that integrated report and

NOTE Confidence: 0.916243268333333

01:05:28.160 --> 01:05:30.490 the learning that we can gain

NOTE Confidence: 0.916243268333333

01:05:30.490 --> 01:05:32.440 from you and your colleagues.

NOTE Confidence: 0.916243268333333

01:05:32.440 --> 01:05:34.676 So I I think that we will be

NOTE Confidence: 0.916243268333333

01:05:34.676 --> 01:05:36.128 very supportive of this and

NOTE Confidence: 0.951481355454545

01:05:36.240 --> 01:05:38.214 I want to thank you for giving

NOTE Confidence: 0.951481355454545

01:05:38.214 --> 01:05:39.400 such an interesting talk.

NOTE Confidence: 0.951481355454545

01:05:39.400 --> 01:05:42.700 So patient focused. That I think,

NOTE Confidence: 0.951481355454545

01:05:42.700 --> 01:05:45.643 makes it quite clear that the time is now

NOTE Confidence: 0.931565046875

01:05:45.700 --> 01:05:48.103 to do this, yes, so you and I will

NOTE Confidence: 0.931565046875

01:05:48.103 --> 01:05:50.556 have to talk about the colon cancer,

NOTE Confidence: 0.931565046875

01:05:50.560 --> 01:05:52.450 integrated reports and how we can

NOTE Confidence: 0.931565046875

01:05:52.450 --> 01:05:54.828 bring that to our service for sure.

NOTE Confidence: 0.649894767777778

01:05:57.280 --> 01:05:59.926 And we also want to talk

NOTE Confidence: 0.649894767777778

01:05:59.926 --> 01:06:01.249 about integrated report.

NOTE Confidence: 0.649894767777778

01:06:01.250 --> 01:06:03.840 In reports in head and neck cancers,

NOTE Confidence: 0.889952935

01:06:03.870 --> 01:06:05.510 absolutely all of them.

NOTE Confidence: 0.943713785

01:06:06.490 --> 01:06:07.698 Thank you so much.

NOTE Confidence: 0.886903056666667

01:06:10.380 --> 01:06:12.972 Alright, thank you everybody,

NOTE Confidence: 0.886903056666667

01:06:12.972 --> 01:06:14.800 thank you. Thank you.