WEBVTT

NOTE duration:"01:12:03"

NOTE recognizability:0.828

NOTE language:en-us

NOTE Confidence: 0.733418249090909

00:00:00.000 --> 00:00:02.574 Part so today I'm so happy

NOTE Confidence: 0.733418249090909

00:00:02.574 --> 00:00:05.010 to introduce our term policy.

NOTE Confidence: 0.733418249090909

00:00:05.010 --> 00:00:08.190 He's from university Iowa notice grant.

NOTE Confidence: 0.733418249090909

00:00:08.190 --> 00:00:11.198 Grant Grant Speaker invited by GI pathology

NOTE Confidence: 0.733418249090909

00:00:11.198 --> 00:00:13.284 and the middle of the Country Life.

NOTE Confidence: 0.733418249090909

00:00:13.284 --> 00:00:14.753 So hard copies here.

NOTE Confidence: 0.733418249090909

00:00:14.753 --> 00:00:17.630 We in collaboration invite him to come

NOTE Confidence: 0.8083981925

00:00:17.640 --> 00:00:19.700 here for talk so.

NOTE Confidence: 0.67658304625

00:00:21.120 --> 00:00:23.212 Directly from University Northwestern

NOTE Confidence: 0.67658304625

00:00:23.212 --> 00:00:28.388 University of Chicago in 2004. I'm Diana.

NOTE Confidence: 0.67658304625

00:00:28.390 --> 00:00:31.460 University of Virginia from 2004,

NOTE Confidence: 0.67658304625

00:00:31.460 --> 00:00:33.917 2008 and then after that he did

NOTE Confidence: 0.67658304625

00:00:33.917 --> 00:00:36.568 one-year GFL in Ohio University.

NOTE Confidence: 0.67658304625

00:00:36.570 --> 00:00:38.795 After that in 2019,

NOTE Confidence: 0.67658304625

00:00:38.795 --> 00:00:41.654 2009 right he moved to Harvard Medical

NOTE Confidence: 0.67658304625

00:00:41.654 --> 00:00:43.910 School for instructor for two years

NOTE Confidence: 0.67658304625

00:00:43.910 --> 00:00:46.185 and then he moved to University Iowa

NOTE Confidence: 0.67658304625

00:00:46.185 --> 00:00:48.422 and then from a senior professor as

NOTE Confidence: 0.67658304625

00:00:48.422 --> 00:00:51.478 a professor and I'm full professor.

NOTE Confidence: 0.67658304625

00:00:51.480 --> 00:00:53.742 And that the policy he published

NOTE Confidence: 0.67658304625

00:00:53.742 --> 00:00:56.145 more than 150 papers and then also

NOTE Confidence: 0.67658304625

00:00:56.145 --> 00:00:58.589 book book chapters and most of the

NOTE Confidence: 0.67658304625

00:00:58.589 --> 00:01:00.424 papers published and which chapters

NOTE Confidence: 0.67658304625

00:01:00.424 --> 00:01:02.635 in GI pathology even though chemistry

NOTE Confidence: 0.67658304625

00:01:02.635 --> 00:01:06.264 and the new tumor and that's why his

NOTE Confidence: 0.67658304625

00:01:06.264 --> 00:01:09.202 research focuses on immuno markers,

NOTE Confidence: 0.67658304625

00:01:09.202 --> 00:01:11.939 you know for for all the diseases

NOTE Confidence: 0.67658304625

00:01:11.939 --> 00:01:14.664 and also he has his research

NOTE Confidence: 0.67658304625

00:01:14.664 --> 00:01:16.020 in neuroendocrine tumor.

NOTE Confidence: 0.67658304625

00:01:16.020 --> 00:01:18.456 He has been joining a lot,

NOTE Confidence: 0.67658304625

00:01:18.460 --> 00:01:20.060 a lot of collaborative studies

NOTE Confidence: 0.67658304625

00:01:20.060 --> 00:01:21.721 you know for H.

NOTE Confidence: 0.67658304625

00:01:21.721 --> 00:01:23.429 OK, for Edge grants,

NOTE Confidence: 0.67658304625

00:01:23.430 --> 00:01:25.840 you know his collaborator for the

NOTE Confidence: 0.67658304625

00:01:25.840 --> 00:01:27.680 studies therefore you are consumer.

NOTE Confidence: 0.67658304625

00:01:27.680 --> 00:01:30.152 That's why you know he involves so many

NOTE Confidence: 0.67658304625

00:01:30.152 --> 00:01:33.374 professional societies especially for cap,

NOTE Confidence: 0.67658304625

00:01:33.374 --> 00:01:36.286 US cap and ASAP for cab.

NOTE Confidence: 0.67658304625

00:01:36.286 --> 00:01:39.072 He has been the even though his

NOTE Confidence: 0.67658304625

00:01:39.072 --> 00:01:41.066 country committee from member,

NOTE Confidence: 0.67658304625

00:01:41.066 --> 00:01:44.778 vice chair and chair and also he's a

NOTE Confidence: 0.67658304625

00:01:44.778 --> 00:01:46.988 international even though his commentary

NOTE Confidence: 0.67658304625

00:01:46.988 --> 00:01:49.374 Society Board of directors and also

NOTE Confidence: 0.67658304625

00:01:49.374 --> 00:01:51.490 involve other lot of committees.

NOTE Confidence: 0.67658304625

00:01:51.490 --> 00:01:52.850 US CAP and cap.

NOTE Confidence: 0.67658304625

00:01:52.850 --> 00:01:55.390 I will not mention all of them.

NOTE Confidence: 0.67658304625

00:01:55.390 --> 00:01:58.318 Or he has.

NOTE Confidence: 0.67658304625

00:01:58.320 --> 00:01:59.880 I have so many publications I

NOTE Confidence: 0.67658304625

00:01:59.880 --> 00:02:01.698 mentioned and I gave so many talks.

NOTE Confidence: 0.67658304625

00:02:01.700 --> 00:02:03.332 Also, you know you watch the talks

NOTE Confidence: 0.67658304625

00:02:03.332 --> 00:02:05.860 everywhere you ask cap cap SP.

NOTE Confidence: 0.67658304625

00:02:05.860 --> 00:02:08.380 So I cannot mention how many hits,

NOTE Confidence: 0.67658304625

00:02:08.380 --> 00:02:09.920 more than 100 pages.

NOTE Confidence: 0.67658304625

00:02:09.920 --> 00:02:14.388 So it's better to ask him to talk so.

NOTE Confidence: 0.67658304625

00:02:14.390 --> 00:02:16.022 So Andrew, test your.

NOTE Confidence: 0.67658304625

00:02:16.022 --> 00:02:16.838 Thank you.

NOTE Confidence: 0.67658304625

00:02:16.840 --> 00:02:17.260 Yes,

NOTE Confidence: 0.67658304625

00:02:17.330 --> 00:02:17.720 yeah.

NOTE Confidence: 0.933795031538461

00:02:31.930 --> 00:02:35.302 This is this is literally my

NOTE Confidence: 0.933795031538461

00:02:35.302 --> 00:02:39.159 favorite thing to do in the world.

4

NOTE Confidence: 0.933795031538461

00:02:39.160 --> 00:02:42.065 Is to is to interact with folks,

NOTE Confidence: 0.933795031538461

00:02:42.070 --> 00:02:43.950 with folks like you.

NOTE Confidence: 0.933795031538461

00:02:43.950 --> 00:02:47.850 And I'm so privileged to to have this,

NOTE Confidence: 0.933795031538461

00:02:47.850 --> 00:02:50.062 to have this position.

NOTE Confidence: 0.933795031538461

00:02:50.062 --> 00:02:53.594 You know, the single most important

NOTE Confidence: 0.933795031538461

00:02:53.594 --> 00:02:57.783 take home point from any talk is

NOTE Confidence: 0.933795031538461

00:02:57.783 --> 00:03:02.207 that the purpose of this talk is to

NOTE Confidence: 0.933795031538461

00:03:02.207 --> 00:03:06.749 make a connection with each of you.

NOTE Confidence: 0.933795031538461

00:03:06.750 --> 00:03:11.244 I'm here for you and I

NOTE Confidence: 0.933795031538461

00:03:11.244 --> 00:03:14.240 became whatever you want.

NOTE Confidence: 0.933795031538461

00:03:14.240 --> 00:03:16.100 If you know me from Twitter,

NOTE Confidence: 0.933795031538461

00:03:16.100 --> 00:03:18.168 I became IHC guy.

NOTE Confidence: 0.933795031538461

00:03:18.168 --> 00:03:20.236 From from you here,

NOTE Confidence: 0.933795031538461

00:03:20.240 --> 00:03:22.627 you know I and this talk is

NOTE Confidence: 0.933795031538461

00:03:22.627 --> 00:03:24.880 gonna be about how to become,

NOTE Confidence: 0.933795031538461

00:03:24.880 --> 00:03:25.770 how to become an act,

NOTE Confidence: 0.933795031538461

00:03:25.770 --> 00:03:26.950 how to become an expert.

NOTE Confidence: 0.933795031538461

00:03:26.950 --> 00:03:28.462 And the way to become an expert

NOTE Confidence: 0.933795031538461

00:03:28.462 --> 00:03:30.328 is to say that you're an expert.

NOTE Confidence: 0.933795031538461

00:03:30.330 --> 00:03:32.026 That's one of the, that's one of the,

NOTE Confidence: 0.933795031538461

00:03:32.030 --> 00:03:34.088 that's one of the cheat codes.

NOTE Confidence: 0.933795031538461

00:03:34.090 --> 00:03:36.688 Uh, I'm a pretty informal guy,

NOTE Confidence: 0.933795031538461

00:03:36.690 --> 00:03:39.792 so I invite everybody to relax

NOTE Confidence: 0.933795031538461

00:03:39.792 --> 00:03:43.270 and to try to be present.

NOTE Confidence: 0.933795031538461

00:03:43.270 --> 00:03:45.490 And actually the hardest thing for

NOTE Confidence: 0.933795031538461

00:03:45.490 --> 00:03:49.062 me as I get going is to be present

NOTE Confidence: 0.933795031538461

00:03:49.062 --> 00:03:50.938 because it's it's it's anxiety

NOTE Confidence: 0.933795031538461

00:03:50.938 --> 00:03:53.610 provoking to be to be in front of,

NOTE Confidence: 0.933795031538461

00:03:53.610 --> 00:03:55.386 in front of all you guys.

NOTE Confidence: 0.933795031538461

00:03:55.390 --> 00:03:58.064 One thing that I'll say is it

NOTE Confidence: 0.933795031538461

00:03:58.064 --> 00:04:00.364 always astounds me that I have

NOTE Confidence: 0.933795031538461

00:04:00.364 --> 00:04:02.512 this platform and that we all

NOTE Confidence: 0.933795031538461

00:04:02.512 --> 00:04:05.016 and that we all come together.

NOTE Confidence: 0.933795031538461

00:04:05.020 --> 00:04:07.450 Because I had a problematic

NOTE Confidence: 0.933795031538461

00:04:07.450 --> 00:04:09.394 relationship with my father,

NOTE Confidence: 0.933795031538461

00:04:09.400 --> 00:04:11.500 and if it wasn't for that,

NOTE Confidence: 0.933795031538461

00:04:11.500 --> 00:04:15.161 I would probably be in fourth period

NOTE Confidence: 0.933795031538461

00:04:15.161 --> 00:04:17.160 teaching chemistry right now.

NOTE Confidence: 0.933795031538461

00:04:17.160 --> 00:04:19.216 And you know, I need to do it.

NOTE Confidence: 0.933795031538461

00:04:19.220 --> 00:04:22.514 I need to do it better because of that.

NOTE Confidence: 0.933795031538461

00:04:22.520 --> 00:04:27.826 Ohh boy. We lost. Somebody's.

NOTE Confidence: 0.933795031538461

00:04:27.826 --> 00:04:31.256 Somebody's moving the screen around.

NOTE Confidence: 0.933795031538461

00:04:31.260 --> 00:04:32.874 And the the other thing I'll

NOTE Confidence: 0.933795031538461

00:04:32.874 --> 00:04:34.230 the other thing I'll say.

NOTE Confidence: 0.89931188

00:04:37.890 --> 00:04:40.953 I've given this talk multiple times. And.

NOTE Confidence: 0.89931188

00:04:40.953 --> 00:04:44.460 And the the last time I gave it was at

NOTE Confidence: 0.89931188

00:04:44.460 --> 00:04:47.900 Mayo and I wanted to and I wanted to say,

NOTE Confidence: 0.89931188

00:04:47.900 --> 00:04:50.468 but I was so dumbstruck by

NOTE Confidence: 0.89931188

00:04:50.468 --> 00:04:52.720 what I encountered at Mayo,

NOTE Confidence: 0.89931188

00:04:52.720 --> 00:04:54.976 which I'll briefly relate to you,

NOTE Confidence: 0.89931188

00:04:54.980 --> 00:04:59.546 that this talk is, you know, if I gave

NOTE Confidence: 0.89931188

00:04:59.546 --> 00:05:02.180 the talk that I actually came to give,

NOTE Confidence: 0.89931188

00:05:02.180 --> 00:05:04.434 which I'm not sure that I will,

NOTE Confidence: 0.89931188

00:05:04.440 --> 00:05:07.387 this talk is my love letter to

NOTE Confidence: 0.89931188

00:05:07.387 --> 00:05:09.782 immunohistochemistry and I give lots

NOTE Confidence: 0.89931188

00:05:09.782 --> 00:05:11.898 of kinds of immunohistochemistry.

NOTE Confidence: 0.89931188

00:05:11.900 --> 00:05:13.019 Box I give.

NOTE Confidence: 0.89931188

00:05:13.019 --> 00:05:15.630 I give ones that are love letters.

NOTE Confidence: 0.89931188

00:05:15.630 --> 00:05:17.450 I give ones that are.

NOTE Confidence: 0.89931188

00:05:17.450 --> 00:05:20.075 I call myself an immuno optimist and

NOTE Confidence: 0.89931188

00:05:20.075 --> 00:05:22.448 immuno pessimist and an immune realist.

NOTE Confidence: 0.89931188

00:05:22.450 --> 00:05:25.018 I give an immuno pessimist talk

NOTE Confidence: 0.89931188

00:05:25.018 --> 00:05:27.810 this past weekend to the CAP CSA.

NOTE Confidence: 0.89931188

00:05:27.810 --> 00:05:30.222 The title of the talk was

NOTE Confidence: 0.89931188

00:05:30.222 --> 00:05:31.830 immunohistochemistry is in the

NOTE Confidence: 0.89931188

00:05:31.906 --> 00:05:34.349 midst of a quality crisis and low.

NOTE Confidence: 0.89931188

00:05:34.350 --> 00:05:36.852 Her two is a symptom and most of the

NOTE Confidence: 0.89931188

00:05:36.852 --> 00:05:38.942 talks that I give are immuno realists

NOTE Confidence: 0.89931188

00:05:38.942 --> 00:05:41.629 and I give a lot of nuts and bolts.

NOTE Confidence: 0.89931188

00:05:41.630 --> 00:05:42.468 Didactic.

NOTE Confidence: 0.89931188

00:05:42.468 --> 00:05:44.982 About diagnostic applications

NOTE Confidence: 0.89931188

00:05:44.982 --> 00:05:46.658 of immunohistochemistry.

NOTE Confidence: 0.891022443846154

00:05:50.070 --> 00:05:52.342 So this is this is the title of

NOTE Confidence: 0.891022443846154

00:05:52.342 --> 00:05:55.063 the talk that I submitted next

NOTE Confidence: 0.891022443846154

00:05:55.063 --> 00:05:56.620 generation immunohistochemistry how

NOTE Confidence: 0.891022443846154

00:05:56.620 --> 00:05:59.415 to build highly effective diagnostic

NOTE Confidence: 0.891022443846154

00:05:59.415 --> 00:06:01.739 tests in anatomic pathology.

NOTE Confidence: 0.891022443846154

00:06:01.740 --> 00:06:04.140 But I think maybe this is this is

NOTE Confidence: 0.891022443846154

00:06:04.140 --> 00:06:06.816 the talk that I'd like to to that I'd

NOTE Confidence: 0.891022443846154

00:06:06.816 --> 00:06:09.390 like to try to give simultaneously.

NOTE Confidence: 0.891022443846154

00:06:09.390 --> 00:06:11.826 On the invitation and advice of Zuchen,

NOTE Confidence: 0.891022443846154

00:06:11.830 --> 00:06:14.086 who actually invited me to give

NOTE Confidence: 0.891022443846154

00:06:14.086 --> 00:06:15.950 this talk three years ago,

NOTE Confidence: 0.891022443846154

00:06:15.950 --> 00:06:19.100 and he said that my target audience

NOTE Confidence: 0.891022443846154

00:06:19.100 --> 00:06:21.750 was trainees and young faculty.

NOTE Confidence: 0.891022443846154

00:06:21.750 --> 00:06:24.578 And so how about to the next

NOTE Confidence: 0.891022443846154

00:06:24.578 --> 00:06:25.790 generation of pathologists,

NOTE Confidence: 0.891022443846154

00:06:25.790 --> 00:06:28.898 how to cultivate a highly successful

NOTE Confidence: 0.891022443846154

00:06:28.898 --> 00:06:30.944 career in anatomic pathology?

NOTE Confidence: 0.891022443846154

00:06:30.944 --> 00:06:33.484 You, you have the tools,

NOTE Confidence: 0.891022443846154

00:06:33.490 --> 00:06:34.594 the most important,

NOTE Confidence: 0.891022443846154

00:06:34.594 --> 00:06:36.434 the most important insight that

NOTE Confidence: 0.891022443846154

00:06:36.434 --> 00:06:38.730 I can give you is to do this.

NOTE Confidence: 0.891022443846154

00:06:38.730 --> 00:06:39.874 You have to know.

NOTE Confidence: 0.891022443846154

00:06:39.874 --> 00:06:40.160 Yourself.

NOTE Confidence: 0.870742597142857

00:06:42.980 --> 00:06:45.339 So if I give the straight talk,

NOTE Confidence: 0.870742597142857

00:06:45.340 --> 00:06:48.040 this is the elevator pitch.

NOTE Confidence: 0.870742597142857

00:06:48.040 --> 00:06:50.370 I can build an immunohistochemical

NOTE Confidence: 0.870742597142857

00:06:50.370 --> 00:06:52.700 test to virtually any target,

NOTE Confidence: 0.870742597142857

00:06:52.700 --> 00:06:54.400 and these 150 publications

NOTE Confidence: 0.870742597142857

00:06:54.400 --> 00:06:56.540 are predicated in that,

NOTE Confidence: 0.870742597142857

00:06:56.540 --> 00:06:59.942 and the value proposition is for all of you.

NOTE Confidence: 0.870742597142857

00:06:59.950 --> 00:07:03.217 What ioffer you is at the end of this

NOTE Confidence: 0.870742597142857

00:07:03.217 --> 00:07:05.758 lecture is probably too ambitious,

NOTE Confidence: 0.870742597142857

00:07:05.760 --> 00:07:07.748 but my goal is to begin to

NOTE Confidence: 0.870742597142857

00:07:07.748 --> 00:07:10.337 provide you the tools to be able

NOTE Confidence: 0.870742597142857

00:07:10.337 --> 00:07:11.997 to build an immunohistochemical.

NOTE Confidence: 0.870742597142857

00:07:12.000 --> 00:07:14.416 Test to any target every time I go

NOTE Confidence: 0.870742597142857

00:07:14.416 --> 00:07:17.543 to a meeting and I've introduced

NOTE Confidence: 0.870742597142857

00:07:17.543 --> 00:07:19.983 the new immunohistochemical marker.

NOTE Confidence: 0.870742597142857

00:07:19.990 --> 00:07:22.654 The most common question that I

NOTE Confidence: 0.870742597142857

00:07:22.654 --> 00:07:25.658 get from from you know world expert

NOTE Confidence: 0.870742597142857

00:07:25.658 --> 00:07:27.326 end user diagnostic pathologist

NOTE Confidence: 0.870742597142857

00:07:27.326 --> 00:07:29.348 is how did you do this?

NOTE Confidence: 0.870742597142857

00:07:29.350 --> 00:07:30.934 Is this commercially,

NOTE Confidence: 0.870742597142857

00:07:30.934 --> 00:07:33.046 is this commercially available?

NOTE Confidence: 0.870742597142857

00:07:33.050 --> 00:07:35.586 Where do I get this and and the

NOTE Confidence: 0.870742597142857

00:07:35.586 --> 00:07:38.258 answer is that there are dozens

NOTE Confidence: 0.870742597142857

00:07:38.258 --> 00:07:40.698 if not hundreds of commercially

NOTE Confidence: 0.870742597142857

00:07:40.698 --> 00:07:42.120 available antibodies.

NOTE Confidence: 0.870742597142857

00:07:42.120 --> 00:07:46.200 To virtually every target,

NOTE Confidence: 0.870742597142857

00:07:46.200 --> 00:07:51.303 because science is a $160 billion industry.

NOTE Confidence: 0.870742597142857

00:07:51.303 --> 00:07:55.440 I can't remember David where I resourced it,

NOTE Confidence: 0.870742597142857

00:07:55.440 --> 00:07:58.086 but Google, Google, I know the NIH.

NOTE Confidence: 0.870742597142857

00:07:58.090 --> 00:08:01.510 The NIH, for example,

NOTE Confidence: 0.870742597142857

00:08:01.510 --> 00:08:07.860 grants $40 billion of of award every year.

NOTE Confidence: 0.870742597142857

00:08:07.860 --> 00:08:10.398 And so there's a good jillion

NOTE Confidence: 0.870742597142857

00:08:10.398 --> 00:08:12.540 antibody companies and they make.

NOTE Confidence: 0.870742597142857

00:08:12.540 --> 00:08:13.050 Immunohistology,

NOTE Confidence: 0.870742597142857

00:08:13.050 --> 00:08:15.090 they make primary antibodies

NOTE Confidence: 0.870742597142857

00:08:15.090 --> 00:08:17.130 to everything because some,

NOTE Confidence: 0.870742597142857

00:08:17.130 --> 00:08:19.874 somewhere in some corner of the world,

NOTE Confidence: 0.870742597142857

00:08:19.880 --> 00:08:22.640 somebody is studying, studying.

NOTE Confidence: 0.870742597142857

00:08:22.640 --> 00:08:24.674 And so you can make an

NOTE Confidence: 0.870742597142857

00:08:24.674 --> 00:08:26.540 immunohistochemical test at any target.

NOTE Confidence: 0.866492543333333

00:08:29.930 --> 00:08:31.586 The biography, you know this is.

NOTE Confidence: 0.866492543333333

00:08:31.590 --> 00:08:33.876 This is important because this is.

NOTE Confidence: 0.866492543333333

00:08:33.880 --> 00:08:35.938 This is to answer the question

NOTE Confidence: 0.866492543333333

00:08:35.938 --> 00:08:37.946 how to cultivate a successful

NOTE Confidence: 0.866492543333333

00:08:37.946 --> 00:08:40.186 career in anatomic pathology,

NOTE Confidence: 0.866492543333333

00:08:40.190 --> 00:08:43.628 and I'll say more specifically how

NOTE Confidence: 0.866492543333333

00:08:43.628 --> 00:08:47.147 to cultivate a successful career in

NOTE Confidence: 0.866492543333333

00:08:47.147 --> 00:08:50.513 anatomic pathology in the context of.

NOTE Confidence: 0.866492543333333

00:08:50.520 --> 00:08:51.334 Constrained resources.

NOTE Confidence: 0.866492543333333

00:08:51.334 --> 00:08:54.590 You know, I've worked at a bunch of

NOTE Confidence: 0.866492543333333

00:08:54.667 --> 00:08:57.761 different places and there are very few

NOTE Confidence: 0.866492543333333

00:08:57.761 --> 00:09:00.198 exceptional places with the best people

NOTE Confidence: 0.866492543333333

00:09:00.198 --> 00:09:03.171 and the best cohorts and the best resources,

NOTE Confidence: 0.866492543333333

00:09:03.171 --> 00:09:04.854 the vast majority.

NOTE Confidence: 0.866492543333333

00:09:04.854 --> 00:09:09.630 The central mass of places are lovely places.

NOTE Confidence: 0.866492543333333

00:09:09.630 --> 00:09:12.150 Iowa is a lovely place,

NOTE Confidence: 0.866492543333333

00:09:12.150 --> 00:09:14.340 but even within the constraints,

NOTE Confidence: 0.866492543333333

00:09:14.340 --> 00:09:17.268 the constraints of a lovely place

NOTE Confidence: 0.866492543333333

00:09:17.268 --> 00:09:20.790 if you are smart and passionate.

NOTE Confidence: 0.866492543333333

00:09:20.790 --> 00:09:22.788 And have a point of view.

00:09:22.790 --> 00:09:25.730 You can have a wildly successful

00:09:25.730 --> 00:09:27.690 career in anatomic pathology.

00:09:27.690 --> 00:09:30.588 And So what did I decide to lean into?

00:09:30.590 --> 00:09:33.968 I decided to lean into immunohistochemistry.

00:09:33.970 --> 00:09:35.950 I started out in GI pathology.

00:09:35.950 --> 00:09:38.010 I am a GI pathologist,

00:09:38.010 --> 00:09:40.338 but I decided to lean into

00:09:40.338 --> 00:09:42.490 immunohistochemistry for so many reasons.

00:09:42.490 --> 00:09:44.989 And then another thing Zuchen mentioned is

00:09:44.989 --> 00:09:48.350 I'm also a neuroendocrine tumor pathologist.

00:09:48.350 --> 00:09:50.562 Every lovely place is.

00:09:50.562 --> 00:09:54.670 Exceptional at something or a few things.

00:09:54.670 --> 00:09:56.848 And the reason that I'm a

00:09:56.848 --> 00:09:57.937 neuroendocrine tumor pathologist

00:09:57.937 --> 00:09:59.907 is at the University of Iowa,

00:09:59.910 --> 00:10:02.182 the most special group,

NOTE Confidence: 0.866492543333333

00:10:02.182 --> 00:10:05.022 the most successful multidisciplinary group,

NOTE Confidence: 0.866492543333333

00:10:05.030 --> 00:10:07.190 the most highly funded group is

NOTE Confidence: 0.866492543333333

00:10:07.190 --> 00:10:08.630 the neuroendocrine tumor group.

NOTE Confidence: 0.866492543333333

00:10:08.630 --> 00:10:10.583 And so if you go to a place and

NOTE Confidence: 0.866492543333333

00:10:10.583 --> 00:10:12.412 you want to study pancreas cancer

NOTE Confidence: 0.866492543333333

00:10:12.412 --> 00:10:14.830 or you want to study colon cancer,

NOTE Confidence: 0.866492543333333

00:10:14.830 --> 00:10:16.655 I've studied all these different

NOTE Confidence: 0.866492543333333

00:10:16.655 --> 00:10:18.805 things in different phases of my

NOTE Confidence: 0.866492543333333

00:10:18.805 --> 00:10:20.798 career and they're the they're.

NOTE Confidence: 0.866492543333333

00:10:20.798 --> 00:10:25.238 See or a B minus group in that tumor type,

NOTE Confidence: 0.866492543333333

00:10:25.240 --> 00:10:27.220 it's a it's a losing proposition.

NOTE Confidence: 0.866492543333333

00:10:27.220 --> 00:10:29.872 So one of the recommendations is

NOTE Confidence: 0.866492543333333

00:10:29.872 --> 00:10:32.715 to survey the scene and identify

NOTE Confidence: 0.866492543333333

00:10:32.715 --> 00:10:34.695 the the most talented,

NOTE Confidence: 0.866492543333333

00:10:34.700 --> 00:10:36.500 most passionate individuals and

NOTE Confidence: 0.866492543333333

00:10:36.500 --> 00:10:38.750 allow yourself with that group.

NOTE Confidence: 0.887869394

00:10:40.830 --> 00:10:42.540 So I think you've already

NOTE Confidence: 0.887869394

00:10:42.540 --> 00:10:44.250 gotten a sense of this.

NOTE Confidence: 0.887869394

00:10:44.250 --> 00:10:48.252 I'm anybody is anybody familiar with

NOTE Confidence: 0.887869394

00:10:48.252 --> 00:10:52.050 the Myers Briggs personality inventory.

NOTE Confidence: 0.887869394

00:10:52.050 --> 00:10:57.466 I'm a union psychologist on the side and.

NOTE Confidence: 0.887869394

00:10:57.470 --> 00:11:00.830 I'm an ENFP and ENFP's

NOTE Confidence: 0.887869394

00:11:00.830 --> 00:11:03.518 are like functional ADHD.

NOTE Confidence: 0.887869394

00:11:03.520 --> 00:11:06.138 And so this is how a normal

NOTE Confidence: 0.887869394

00:11:06.138 --> 00:11:07.850 person tells this story.

NOTE Confidence: 0.887869394

00:11:07.850 --> 00:11:09.670 And this is how I this is

NOTE Confidence: 0.887869394

00:11:09.670 --> 00:11:11.249 how I tell the story.

NOTE Confidence: 0.887869394

00:11:11.250 --> 00:11:13.128 It's I tell lots of stories.

NOTE Confidence: 0.887869394

00:11:13.130 --> 00:11:14.402 It's very iterative.

NOTE Confidence: 0.887869394

00:11:14.402 --> 00:11:16.946 I say that my my communication

NOTE Confidence: 0.887869394

00:11:16.946 --> 00:11:19.340 is at times circumlocutory.

NOTE Confidence: 0.887869394

00:11:19.340 --> 00:11:22.188 But it always comes around to a point.

NOTE Confidence: 0.887869394

00:11:22.190 --> 00:11:24.080 So the value proposition and I and

NOTE Confidence: 0.887869394

00:11:24.080 --> 00:11:26.390 I speak to lots of audiences today,

NOTE Confidence: 0.887869394

00:11:26.390 --> 00:11:28.358 I'm mostly talking to

NOTE Confidence: 0.887869394

00:11:28.358 --> 00:11:29.834 diagnostic pathology trainees,

NOTE Confidence: 0.887869394

00:11:29.840 --> 00:11:32.416 but I also talked to base to

NOTE Confidence: 0.887869394

00:11:32.416 --> 00:11:35.299 basic scientists quite a bit about

NOTE Confidence: 0.887869394

00:11:35.299 --> 00:11:36.997 challenges in immunohistochemistry.

NOTE Confidence: 0.887869394

00:11:37.000 --> 00:11:38.790 And I'll say that everybody

NOTE Confidence: 0.887869394

00:11:38.790 --> 00:11:39.864 benefits from smart,

NOTE Confidence: 0.887869394

00:11:39.870 --> 00:11:41.754 technically sound immunohistochemistry

NOTE Confidence: 0.887869394

00:11:41.754 --> 00:11:45.522 and I'm offering to be your

NOTE Confidence: 0.887869394

00:11:45.522 --> 00:11:46.950 immunohistochemistry concierge.

NOTE Confidence: 0.887869394

00:11:46.950 --> 00:11:50.430 I I I warmly invite you to reach out to me.

NOTE Confidence: 0.887869394

00:11:50.430 --> 00:11:52.130 I'm deeply interested in what.

NOTE Confidence: 0.887869394

00:11:52.130 --> 00:11:53.564 You're interested in,

NOTE Confidence: 0.887869394

00:11:53.564 --> 00:11:56.432 I'm deeply interested in helping to

NOTE Confidence: 0.887869394

00:11:56.432 --> 00:11:58.814 advance your academic careers because

NOTE Confidence: 0.887869394

00:11:58.814 --> 00:12:00.458 I want to interact with bright,

NOTE Confidence: 0.887869394

00:12:00.460 --> 00:12:01.705 talented, passionate individuals.

NOTE Confidence: 0.887869394

00:12:01.705 --> 00:12:04.195 And so this talk is really,

NOTE Confidence: 0.887869394

00:12:04.200 --> 00:12:05.656 it's directed at everybody.

NOTE Confidence: 0.887869394

00:12:05.656 --> 00:12:07.476 It's mainly directed at trainees.

NOTE Confidence: 0.887869394

00:12:07.480 --> 00:12:10.077 I love to interact with local IHC

NOTE Confidence: 0.887869394

00:12:10.077 --> 00:12:12.061 lab directors because I benefited

NOTE Confidence: 0.887869394

00:12:12.061 --> 00:12:14.051 so much from interaction with

NOTE Confidence: 0.887869394

00:12:14.051 --> 00:12:16.496 IHC lab directors when I was

NOTE Confidence: 0.887869394

00:12:16.496 --> 00:12:18.848 a junior member on the CAP

NOTE Confidence: 0.887869394

00:12:18.848 --> 00:12:19.643 Immunohistochemistry committee.

NOTE Confidence: 0.887869394

00:12:19.643 --> 00:12:22.464 I I love interacting with clinical fact.

NOTE Confidence: 0.887869394

00:12:22.470 --> 00:12:22.906 Faculty,

NOTE Confidence: 0.887869394

00:12:22.906 --> 00:12:24.650 especially junior faculty who

NOTE Confidence: 0.887869394

00:12:24.650 --> 00:12:27.344 want to do scholarship but have

NOTE Confidence: 0.887869394

00:12:27.344 --> 00:12:29.579 limited time and limited resources.

NOTE Confidence: 0.887869394

00:12:29.580 --> 00:12:31.925 And I have a tried and true

NOTE Confidence: 0.887869394

00:12:31.925 --> 00:12:34.716 method to have a positive study

NOTE Confidence: 0.887869394

00:12:34.716 --> 00:12:38.118 using what I call next generation

NOTE Confidence: 0.887869394

00:12:38.118 --> 00:12:40.234 immunohistochemistry as a function of

NOTE Confidence: 0.887869394

00:12:40.234 --> 00:12:43.640 what my chair at Brigham told me to be,

NOTE Confidence: 0.887869394

00:12:43.640 --> 00:12:45.240 which was a translational

NOTE Confidence: 0.887869394

00:12:45.240 --> 00:12:46.040 molecular pathologist.

NOTE Confidence: 0.887869394

00:12:46.040 --> 00:12:47.800 And I also love to I love to

NOTE Confidence: 0.887869394

00:12:47.800 --> 00:12:49.917 talk to scientists and I love

NOTE Confidence: 0.887869394

00:12:49.917 --> 00:12:51.533 to collaborate with scientists.

NOTE Confidence: 0.887869394

00:12:51.540 --> 00:12:54.165 For the scientists in the in the

NOTE Confidence: 0.887869394

00:12:54.165 --> 00:12:56.493 room if you were going to read two

NOTE Confidence: 0.887869394

00:12:56.493 --> 00:12:59.047 papers about if you were going to

NOTE Confidence: 0.887869394

00:12:59.047 --> 00:13:01.112 read one paper about immunohistochemistry.

NOTE Confidence: 0.887869394

00:13:01.120 --> 00:13:03.066 So this is and thank you David

NOTE Confidence: 0.887869394

00:13:03.066 --> 00:13:04.479 for your work on this.

NOTE Confidence: 0.887869394

00:13:04.480 --> 00:13:07.182 This is a this is a paper

NOTE Confidence: 0.887869394

00:13:07.182 --> 00:13:08.912 that discusses validation of

NOTE Confidence: 0.887869394

00:13:08.912 --> 00:13:10.880 immunohistochemical markers in the

NOTE Confidence: 0.887869394

00:13:10.880 --> 00:13:13.852 research space and it's all about

NOTE Confidence: 0.887869394

00:13:13.852 --> 00:13:16.438 diet it's all about specificity of

NOTE Confidence: 0.887869394

00:13:16.438 --> 00:13:18.622 the antibody now for clinicians

NOTE Confidence: 0.887869394

00:13:18.622 --> 00:13:21.709 like myself that don't have access to.

NOTE Confidence: 0.887869394

00:13:21.710 --> 00:13:24.070 Gene editing technologies, for example,

NOTE Confidence: 0.887869394

00:13:24.070 --> 00:13:25.958 to validate their immunostains.

NOTE Confidence: 0.887869394

00:13:25.958 --> 00:13:28.790 How do I validate my immunostains?

NOTE Confidence: 0.887869394

00:13:28.790 --> 00:13:29.336 Clinically,

NOTE Confidence: 0.887869394

00:13:29.336 --> 00:13:30.974 diagnostically with with

NOTE Confidence: 0.887869394

00:13:30.974 --> 00:13:33.704 large cohorts of of tumors,

NOTE Confidence: 0.887869394

00:13:33.710 --> 00:13:35.942 gold standard diagnosis, H&E.

NOTE Confidence: 0.887869394

00:13:35.942 --> 00:13:38.174 But for basic scientists

NOTE Confidence: 0.887869394

00:13:38.174 --> 00:13:40.640 this is the way to go.

NOTE Confidence: 0.887869394

00:13:40.640 --> 00:13:42.380 And then this paper is wonderful.

NOTE Confidence: 0.887869394

00:13:42.380 --> 00:13:45.062 It's from my friend Angelo Dimarzo

NOTE Confidence: 0.887869394

00:13:45.062 --> 00:13:47.658 that that really applies many of

NOTE Confidence: 0.887869394

00:13:47.658 --> 00:13:50.206 the principles in the in the Yulin

NOTE Confidence: 0.887869394

00:13:50.206 --> 00:13:52.767 paper and does it in a case based.

NOTE Confidence: 0.905802405789474

00:13:56.820 --> 00:13:59.136 This is an incredibly important concept

NOTE Confidence: 0.905802405789474

00:13:59.136 --> 00:14:02.205 and I talked about this in the in

NOTE Confidence: 0.905802405789474

00:14:02.205 --> 00:14:04.020 the teaching session this morning.

NOTE Confidence: 0.905802405789474

00:14:04.020 --> 00:14:05.754 This concept of fit for purpose

NOTE Confidence: 0.905802405789474

00:14:05.754 --> 00:14:07.779 I and I stated it slightly

NOTE Confidence: 0.905802405789474

00:14:07.779 --> 00:14:09.794 different in the unknown session.

NOTE Confidence: 0.905802405789474

00:14:09.800 --> 00:14:14.180 I said that immunohistochemical assays are

NOTE Confidence: 0.905802405789474

00:14:14.180 --> 00:14:17.100 not interchangeable between laboratories

NOTE Confidence: 0.905802405789474

00:14:17.196 --> 00:14:19.330 and the quantity of the analyte,

NOTE Confidence: 0.905802405789474

00:14:19.330 --> 00:14:21.178 which is something that we rarely measure,

NOTE Confidence: 0.905802405789474

00:14:21.180 --> 00:14:22.520 and David's working on it

NOTE Confidence: 0.905802405789474

00:14:22.520 --> 00:14:24.550 and my goal is to take that.

NOTE Confidence: 0.905802405789474

00:14:24.550 --> 00:14:26.266 Of the clinical laboratory.

NOTE Confidence: 0.905802405789474

00:14:26.266 --> 00:14:29.584 But the quantity of the analyte that

NOTE Confidence: 0.905802405789474

00:14:29.584 --> 00:14:32.252 we're measuring by immunohistochemistry

NOTE Confidence: 0.905802405789474

00:14:32.252 --> 00:14:34.380 indirectly is very variable among

NOTE Confidence: 0.905802405789474

00:14:34.380 --> 00:14:36.977 tumor types that you might use the

NOTE Confidence: 0.905802405789474

00:14:36.977 --> 00:14:39.294 same immuno for the example that I

NOTE Confidence: 0.905802405789474

00:14:39.294 --> 00:14:41.818 gave this morning was got a got a 3,

NOTE Confidence: 0.905802405789474

00:14:41.820 --> 00:14:44.204 there's a tiny amount of got a 3IN

NOTE Confidence: 0.905802405789474

00:14:44.204 --> 00:14:46.388 para Feo relative to the amount

NOTE Confidence: 0.905802405789474

00:14:46.388 --> 00:14:48.626 of peripheral got it 3IN breast

NOTE Confidence: 0.905802405789474

00:14:48.626 --> 00:14:50.411 cancer in urothelial cancer and

NOTE Confidence: 0.905802405789474

00:14:50.411 --> 00:14:52.694 so for immunohistochemistry to be

NOTE Confidence: 0.905802405789474

00:14:52.694 --> 00:14:55.184 successful and the reason that.

NOTE Confidence: 0.905802405789474

00:14:55.190 --> 00:14:57.980 Published studies vary so much is

NOTE Confidence: 0.905802405789474

00:14:57.980 --> 00:14:59.375 that immunohistochemical assays

NOTE Confidence: 0.905802405789474

00:14:59.375 --> 00:15:00.938 should be conceived of,

NOTE Confidence: 0.905802405789474

00:15:00.940 --> 00:15:03.088 optimized and validated to

NOTE Confidence: 0.905802405789474

00:15:03.088 --> 00:15:05.236 meet a specific purpose.

NOTE Confidence: 0.905802405789474

00:15:05.240 --> 00:15:08.275 A single immunohistochemical assay is

NOTE Confidence: 0.905802405789474

00:15:08.275 --> 00:15:11.310 generally poorly positioned to meet

NOTE Confidence: 0.905802405789474

00:15:11.395 --> 00:15:14.185 multiple purposes and the the current

NOTE Confidence: 0.905802405789474

00:15:14.185 --> 00:15:17.548 her two problem is an is an example.

NOTE Confidence: 0.905802405789474

00:15:17.550 --> 00:15:19.800 And here's another wonderful example.

NOTE Confidence: 0.905802405789474

00:15:19.800 --> 00:15:25.446 ER clinical IHC assays are optimized.

NOTE Confidence: 0.905802405789474

00:15:25.450 --> 00:15:28.348 To select patients for endocrine therapy,

00:15:28.350 --> 00:15:30.150 that's how they're optimized and

00:15:30.150 --> 00:15:32.833 if you wanted to build an ER

00:15:32.833 --> 00:15:34.863 assay to distinguish luminal from

00:15:34.863 --> 00:15:36.610 triple negative breast cancer,

00:15:36.610 --> 00:15:38.980 it would be a fundamentally

00:15:38.980 --> 00:15:41.350 different assay and that's why.

00:15:41.350 --> 00:15:43.278 Triple negative breast cancers

00:15:43.278 --> 00:15:45.206 by gene expression profiling

00:15:45.206 --> 00:15:47.462 sometimes maybe 5% of the time.

00:15:47.462 --> 00:15:51.524 7% of the time they have ER 1 + 1, two 310%.

00:15:51.524 --> 00:15:54.583 This low ER problem that was addressed

00:15:54.583 --> 00:15:57.509 in the last ASCO CAP guideline.

00:15:57.510 --> 00:15:59.678 The original immunohistochemical assays

00:15:59.678 --> 00:16:03.690 for ER were optimized to predict survival,

00:16:03.690 --> 00:16:05.466 so they were they were prognostic.

00:16:05.470 --> 00:16:08.380 But the the current immunohistochemical

NOTE Confidence: 0.905802405789474

00:16:08.380 --> 00:16:11.290 assays optimized for this purpose.

NOTE Confidence: 0.905802405789474

00:16:11.290 --> 00:16:14.040 Predict response to endocrine therapy

NOTE Confidence: 0.905802405789474

00:16:14.040 --> 00:16:16.938 do pretty good but imperfectly for

NOTE Confidence: 0.905802405789474

00:16:16.938 --> 00:16:19.594 this application and then this

NOTE Confidence: 0.905802405789474

00:16:19.594 --> 00:16:22.170 application is disappears entirely.

NOTE Confidence: 0.799350865

00:16:25.790 --> 00:16:27.478 Skip this. Everybody loves.

NOTE Confidence: 0.799350865

00:16:27.478 --> 00:16:28.744 Everybody loves immunohistochemistry

NOTE Confidence: 0.799350865

00:16:28.744 --> 00:16:30.010 because it's cheap.

NOTE Confidence: 0.799350865

00:16:30.010 --> 00:16:30.946 It's widely available.

NOTE Confidence: 0.799350865

00:16:30.946 --> 00:16:33.478 This is an important point that I want

NOTE Confidence: 0.799350865

00:16:33.478 --> 00:16:35.501 to emphasize to people that want to

NOTE Confidence: 0.799350865

00:16:35.501 --> 00:16:36.812 do research in immunohistochemistry

NOTE Confidence: 0.799350865

00:16:36.812 --> 00:16:39.484 is there is a near endless supply of

NOTE Confidence: 0.799350865

00:16:39.490 --> 00:16:40.866 commercially available primary antibodies.

NOTE Confidence: 0.799350865

00:16:40.866 --> 00:16:42.930 You just have to be patient.

NOTE Confidence: 0.799350865

00:16:42.930 --> 00:16:44.490 The first one might not work,

NOTE Confidence: 0.799350865

00:16:44.490 --> 00:16:46.146 the second one might not work,

NOTE Confidence: 0.799350865

00:16:46.150 --> 00:16:47.350 the fifth one might not work,

NOTE Confidence: 0.799350865

00:16:47.350 --> 00:16:48.616 and then you have to decide

NOTE Confidence: 0.799350865

00:16:48.616 --> 00:16:49.850 when to cut your losses.

NOTE Confidence: 0.799350865

00:16:49.850 --> 00:16:51.565 These are the these are the advantages.

NOTE Confidence: 0.799350865

00:16:51.570 --> 00:16:54.209 These are a lot of the challenges.

NOTE Confidence: 0.799350865

00:16:54.210 --> 00:16:56.400 Yeah, it's not typically quantitative.

NOTE Confidence: 0.799350865

00:16:56.400 --> 00:16:58.857 And David, it is work is working on this.

NOTE Confidence: 0.799350865

00:16:58.860 --> 00:16:59.940 This is from my,

NOTE Confidence: 0.799350865

00:16:59.940 --> 00:17:02.669 as the Chair of the College of American

NOTE Confidence: 0.799350865

00:17:02.669 --> 00:17:03.713 Pathologists Immunohistochemistry

NOTE Confidence: 0.799350865

00:17:03.713 --> 00:17:06.323 Committee responsible for putting out

NOTE Confidence: 0.799350865

00:17:06.323 --> 00:17:09.086 a national and really international

NOTE Confidence: 0.799350865

00:17:09.086 --> 00:17:10.718 proficiency testing program.

NOTE Confidence: 0.799350865

00:17:10.720 --> 00:17:11.821 There's lack of,

NOTE Confidence: 0.799350865

00:17:11.821 --> 00:17:14.023 there's lack of high quality material

NOTE Confidence: 0.799350865

00:17:14.023 --> 00:17:16.230 for external quality assessment.

NOTE Confidence: 0.799350865

00:17:16.230 --> 00:17:18.814 And then as a local IHC lab director,

NOTE Confidence: 0.799350865

00:17:18.820 --> 00:17:21.112 this impacts my ability to have

NOTE Confidence: 0.799350865

00:17:21.112 --> 00:17:22.640 high quality control material

NOTE Confidence: 0.799350865

00:17:22.704 --> 00:17:24.516 and then this is the promise.

NOTE Confidence: 0.799350865

00:17:24.520 --> 00:17:26.512 We want homogeneous,

NOTE Confidence: 0.799350865

00:17:26.512 --> 00:17:29.168 controlled material of known

NOTE Confidence: 0.799350865

00:17:29.170 --> 00:17:30.128 analyte concentration.

NOTE Confidence: 0.799350865

00:17:30.128 --> 00:17:32.523 And there's a couple different

NOTE Confidence: 0.799350865

00:17:32.523 --> 00:17:34.690 ways to skin this cat.

NOTE Confidence: 0.799350865

00:17:34.690 --> 00:17:38.060 David working with my friend

NOTE Confidence: 0.799350865

00:17:38.060 --> 00:17:41.288 Regan Fulton in Sausalito, CA.

NOTE Confidence: 0.799350865

00:17:41.288 --> 00:17:44.223 You can combine isagenix cell lines

NOTE Confidence: 0.799350865

00:17:44.223 --> 00:17:45.978 and you get the quantification

NOTE Confidence: 0.799350865

00:17:45.978 --> 00:17:47.969 from however you do quantification.

NOTE Confidence: 0.799350865

00:17:47.970 --> 00:17:49.602 Mass spec, for example.

NOTE Confidence: 0.799350865

00:17:49.602 --> 00:17:51.642 And then there's another paradigm.

NOTE Confidence: 0.799350865

00:17:51.650 --> 00:17:54.068 There's a guy called Steve Bogan,

NOTE Confidence: 0.799350865

00:17:54.070 --> 00:17:55.674 and he has a.

NOTE Confidence: 0.799350865

00:17:55.674 --> 00:17:57.679 Company called Boston Cell Standards

NOTE Confidence: 0.799350865

00:17:57.679 --> 00:18:00.609 and he coats glass microbeads with

NOTE Confidence: 0.799350865

00:18:00.609 --> 00:18:02.569 known concentrations of analyte

NOTE Confidence: 0.799350865

00:18:02.569 --> 00:18:05.370 and that's traceable to to a

NOTE Confidence: 0.799350865

00:18:05.370 --> 00:18:07.600 reference standard and I mentioned,

NOTE Confidence: 0.799350865

00:18:07.600 --> 00:18:09.530 I said the immuno pessimist

NOTE Confidence: 0.799350865

00:18:09.530 --> 00:18:10.688 talks immunohistochemistry is

NOTE Confidence: 0.799350865

00:18:10.688 --> 00:18:13.037 in the midst of equality crisis.

NOTE Confidence: 0.799350865

00:18:13.040 --> 00:18:15.824 It's mainly because of lack of

NOTE Confidence: 0.799350865

00:18:15.824 --> 00:18:17.216 quantifiable reference material

NOTE Confidence: 0.799350865

00:18:17.216 --> 00:18:19.332 and we are actively working on

NOTE Confidence: 0.799350865

00:18:19.332 --> 00:18:21.936 this at the at the at the national

NOTE Confidence: 0.799350865

00:18:21.936 --> 00:18:23.516 level and this is 1.

NOTE Confidence: 0.62878126

00:18:31.070 --> 00:18:33.980 As next generation Immuno Histochemistry,

NOTE Confidence: 0.62878126

00:18:33.980 --> 00:18:37.240 we'll talk about selection, optimization

NOTE Confidence: 0.62878126

00:18:37.240 --> 00:18:39.810 and validation depending on time.

NOTE Confidence: 0.771372466363637

00:18:43.600 --> 00:18:45.332 Presented a dry challenge.

NOTE Confidence: 0.771372466363637

00:18:45.332 --> 00:18:48.520 One of my friends on your Roden,

NOTE Confidence: 0.771372466363637

00:18:48.520 --> 00:18:50.860 who's a wonderful long, she's also

NOTE Confidence: 0.771372466363637

00:18:50.860 --> 00:18:53.658 the director of the IHC lab at Mayo.

NOTE Confidence: 0.771372466363637

00:18:53.660 --> 00:18:56.060 She said, Andrew, there's this,

NOTE Confidence: 0.771372466363637

00:18:56.060 --> 00:18:58.540 she's a she loves thymoma.

NOTE Confidence: 0.771372466363637

00:18:58.540 --> 00:19:00.220 There's this wonderful immunohistochemical

NOTE Confidence: 0.771372466363637

00:19:00.220 --> 00:19:03.064 marker that was published in a paper

NOTE Confidence: 0.771372466363637

00:19:03.064 --> 00:19:04.877 in MJ Surge Path 10 years ago,

NOTE Confidence: 0.771372466363637

00:19:04.880 --> 00:19:06.248 and it's not commercially

00:19:06.248 --> 00:19:08.550 available and I want to study it.

00:19:08.550 --> 00:19:11.662 But we're stuck, and I and I can

00:19:11.662 --> 00:19:14.770 solve her problem by finding many,

00:19:14.770 --> 00:19:16.654 many commercially available

00:19:16.654 --> 00:19:19.794 antibodies that target my babies.

00:19:19.800 --> 00:19:22.528 So I do lots and lots of research

00:19:22.528 --> 00:19:23.210 and immunohistochemistry,

00:19:23.210 --> 00:19:26.522 and my favorite fun thing to do is make

00:19:26.522 --> 00:19:30.009 novel diagnostic markers from from scratch.

00:19:30.010 --> 00:19:33.174 And so OTC is in my lab,

00:19:33.180 --> 00:19:35.264 the most sensitive Pato

00:19:35.264 --> 00:19:36.827 cellular differentiation marker.

00:19:36.830 --> 00:19:39.296 The other thing I like to do is repurpose.

00:19:39.300 --> 00:19:39.731 Antibodies.

00:19:39.731 --> 00:19:43.610 So IGF two which had emerged as a diagnostic

00:19:43.692 --> 00:19:46.617 marker for adrenal cortical carcinoma.

NOTE Confidence: 0.771372466363637

00:19:46.620 --> 00:19:51.084 I found a novel diagnostic application

NOTE Confidence: 0.771372466363637

00:19:51.084 --> 00:19:53.757 in paraganglioma pheochromocytoma packs.

NOTE Confidence: 0.771372466363637

00:19:53.757 --> 00:19:55.942 One, we talked about cross

NOTE Confidence: 0.771372466363637

00:19:55.942 --> 00:19:57.253 reactivity this morning.

NOTE Confidence: 0.771372466363637

00:19:57.260 --> 00:19:59.759 I said polyclonal packs 8 cross reacts

NOTE Confidence: 0.771372466363637

00:19:59.759 --> 00:20:01.744 with other packs family transcription

NOTE Confidence: 0.771372466363637

00:20:01.744 --> 00:20:04.276 factors including pack 6 and that's

NOTE Confidence: 0.771372466363637

00:20:04.276 --> 00:20:07.334 why it's an adequate diagnostic marker

NOTE Confidence: 0.771372466363637

00:20:07.334 --> 00:20:09.478 in pancreatic neuroendocrine tumors.

NOTE Confidence: 0.771372466363637

00:20:09.480 --> 00:20:11.526 And I was actually having dinner

NOTE Confidence: 0.771372466363637

00:20:11.526 --> 00:20:14.276 with Anya at a Kappa HC committee

NOTE Confidence: 0.771372466363637

00:20:14.276 --> 00:20:16.020 meeting four years ago.

NOTE Confidence: 0.771372466363637

00:20:16.020 --> 00:20:18.054 And she said I want to do a course

NOTE Confidence: 0.771372466363637

00:20:18.054 --> 00:20:20.157 about pitfalls and thoracic pathology.

NOTE Confidence: 0.771372466363637

00:20:20.160 --> 00:20:21.465 Like, you know,

00:20:21.465 --> 00:20:24.075 polyclonal Paxata is positive in thymomas,

00:20:24.080 --> 00:20:26.340 but monoclonal paxata is negative.

00:20:26.340 --> 00:20:27.204 And she said that.

00:20:27.204 --> 00:20:27.636 And I,

00:20:27.640 --> 00:20:29.896 from the example that I knew

00:20:29.896 --> 00:20:32.280 from PAX 5 and pack six,

00:20:32.280 --> 00:20:35.160 I knew that that there was some other

00:20:35.160 --> 00:20:36.976 PAX family transcription factor

00:20:36.976 --> 00:20:40.018 that was expressed in the thymus.

00:20:40.020 --> 00:20:42.520 And I all you have to do is have pub,

00:20:42.520 --> 00:20:42.919 pub,

00:20:42.919 --> 00:20:45.313 Med and a few bioinformatics tools

00:20:45.313 --> 00:20:47.900 that I will share with you to

00:20:47.900 --> 00:20:50.500 be able to solve this in silico.

00:20:50.500 --> 00:20:52.684 And then doing the clinical study

00:20:52.684 --> 00:20:55.422 is a formality angler one is a

NOTE Confidence: 0.771372466363637

00:20:55.422 --> 00:20:57.038 diagnostic marker for chondromyxoid

NOTE Confidence: 0.771372466363637

00:20:57.038 --> 00:20:59.854 fibroma and it's based on the the

NOTE Confidence: 0.771372466363637

00:20:59.854 --> 00:21:01.390 defining molecular genetic event

NOTE Confidence: 0.771372466363637

00:21:01.390 --> 00:21:04.990 and that lesion hey one and then

NOTE Confidence: 0.771372466363637

00:21:04.990 --> 00:21:07.254 specifically hay one immunohistochemistry

NOTE Confidence: 0.771372466363637

00:21:07.254 --> 00:21:10.573 directed to the end terminus of the hay one.

NOTE Confidence: 0.771372466363637

00:21:10.580 --> 00:21:13.836 Gene or I should say protein as a

NOTE Confidence: 0.771372466363637

00:21:13.836 --> 00:21:15.822 diagnostic marker for mesenchymal

NOTE Confidence: 0.771372466363637

00:21:15.822 --> 00:21:17.994 chondrosarcoma where a diagnostic

NOTE Confidence: 0.771372466363637

00:21:17.994 --> 00:21:21.609 marker did not cry previously exist.

NOTE Confidence: 0.771372466363637

00:21:21.610 --> 00:21:24.210 And then the last one got a four,

NOTE Confidence: 0.771372466363637

00:21:24.210 --> 00:21:27.535 which I've brought up as a pan

NOTE Confidence: 0.771372466363637

00:21:27.535 --> 00:21:29.666 GI marker expressed in the upper

NOTE Confidence: 0.771372466363637

00:21:29.666 --> 00:21:31.430 tract and not in the colon.

NOTE Confidence: 0.771372466363637

00:21:31.430 --> 00:21:34.166 So very complementary to SAP B2,

NOTE Confidence: 0.771372466363637

00:21:34.170 --> 00:21:36.322 which is more of a lower GI colon

NOTE Confidence: 0.771372466363637

00:21:36.322 --> 00:21:37.882 specific marker and I don't know

NOTE Confidence: 0.771372466363637

00:21:37.882 --> 00:21:39.328 that we'll get to all these

NOTE Confidence: 0.771372466363637

00:21:39.391 --> 00:21:41.256 specific examples and that's fine.

NOTE Confidence: 0.771372466363637

00:21:41.260 --> 00:21:42.895 The concepts more important than

NOTE Confidence: 0.771372466363637

00:21:42.895 --> 00:21:44.203 the than the detail.

NOTE Confidence: 0.899225165714286

00:21:46.440 --> 00:21:48.376 So next generation immunohistochemistry,

NOTE Confidence: 0.899225165714286

00:21:48.376 --> 00:21:51.562 this is my, this is my stick.

NOTE Confidence: 0.899225165714286

00:21:51.562 --> 00:21:55.830 And this term I, I sort of Co developed

NOTE Confidence: 0.899225165714286

00:21:55.830 --> 00:21:59.070 with with my very close friend that I

NOTE Confidence: 0.899225165714286

00:21:59.070 --> 00:22:01.659 worked with incredibly closely at Brigham.

NOTE Confidence: 0.899225165714286

00:22:01.660 --> 00:22:04.999 Jason hornick. Jason and I do next

NOTE Confidence: 0.899225165714286

00:22:04.999 --> 00:22:05.953 generation immunohistochemistry.

NOTE Confidence: 0.899225165714286

00:22:05.960 --> 00:22:07.838 He does it almost exclusively in

NOTE Confidence: 0.899225165714286

00:22:07.838 --> 00:22:10.691 sarcoma and I do it in pan cancer

NOTE Confidence: 0.899225165714286

00:22:10.691 --> 00:22:12.223 diagnostic applications because I'm

NOTE Confidence: 0.899225165714286

00:22:12.223 --> 00:22:14.656 at Iowa right because he's at Brigham

NOTE Confidence: 0.899225165714286

00:22:14.656 --> 00:22:17.250 and he could do next generation of.

NOTE Confidence: 0.899225165714286

00:22:17.250 --> 00:22:20.220 Sarcoma and Iowa has a lovely

NOTE Confidence: 0.899225165714286

00:22:20.220 --> 00:22:21.210 sarcoma program,

NOTE Confidence: 0.899225165714286

00:22:21.210 --> 00:22:23.330 but it does not have an exceptional one.

NOTE Confidence: 0.899225165714286

00:22:23.330 --> 00:22:26.672 And so I do next generation

NOTE Confidence: 0.899225165714286

00:22:26.672 --> 00:22:28.370 immunohistochemistry and I'm not going

NOTE Confidence: 0.899225165714286

00:22:28.370 --> 00:22:30.430 to restrict myself to any tumor type.

NOTE Confidence: 0.899225165714286

00:22:30.430 --> 00:22:32.662 I'm going to pick off anything

NOTE Confidence: 0.899225165714286

00:22:32.662 --> 00:22:34.520 that anything that I can.

NOTE Confidence: 0.899225165714286

00:22:34.520 --> 00:22:36.656 And how do I find markers?

NOTE Confidence: 0.899225165714286

00:22:36.660 --> 00:22:41.091 And I had lovely discussions this morning

NOTE Confidence: 0.899225165714286

00:22:41.091 --> 00:22:44.232 about my passions for developmental biology.

NOTE Confidence: 0.899225165714286

00:22:44.232 --> 00:22:47.074 I spend many Saturdays in the library

NOTE Confidence: 0.899225165714286

00:22:47.074 --> 00:22:49.280 reading developmental biology papers,

NOTE Confidence: 0.899225165714286

00:22:49.280 --> 00:22:50.285 trying to understand.

NOTE Confidence: 0.899225165714286

00:22:50.285 --> 00:22:53.079 First thing I told you guys this morning

NOTE Confidence: 0.899225165714286

00:22:53.079 --> 00:22:55.383 is tumors recapitulate cells and tissues

NOTE Confidence: 0.899225165714286

00:22:55.383 --> 00:22:58.216 native to the organ in which they arise.

NOTE Confidence: 0.899225165714286

00:22:58.220 --> 00:23:00.943 And so it behooves me to understand

NOTE Confidence: 0.899225165714286

00:23:00.943 --> 00:23:02.835 the developmental biology of those

NOTE Confidence: 0.899225165714286

00:23:02.835 --> 00:23:04.797 cells and tissues and from them.

NOTE Confidence: 0.899225165714286

00:23:04.800 --> 00:23:06.930 I derive my diagnostic markers those

NOTE Confidence: 0.899225165714286

00:23:06.930 --> 00:23:10.001 are my favorite are are querying the

NOTE Confidence: 0.899225165714286

00:23:10.001 --> 00:23:11.585 developmental biology literature.

NOTE Confidence: 0.899225165714286

00:23:11.590 --> 00:23:13.972 We also do protein correlates of

NOTE Confidence: 0.899225165714286

00:23:13.972 --> 00:23:15.918 molecular genetic events and you

NOTE Confidence: 0.899225165714286

00:23:15.918 --> 00:23:18.178 know we did we talked about TP53

NOTE Confidence: 0.899225165714286

00:23:18.178 --> 00:23:20.818 and P53 immunohistochemistry RV one

NOTE Confidence: 0.899225165714286

00:23:20.818 --> 00:23:22.930 and RV immunohistochemistry this

NOTE Confidence: 0.899225165714286

00:23:23.009 --> 00:23:24.530 morning is exemplars.

NOTE Confidence: 0.899225165714286

00:23:24.530 --> 00:23:26.876 And then you can also identify

NOTE Confidence: 0.899225165714286

00:23:26.876 --> 00:23:28.931 markers identified by gene expression

NOTE Confidence: 0.899225165714286

00:23:28.931 --> 00:23:31.439 profiling and I say that's cheating

NOTE Confidence: 0.899225165714286

00:23:31.439 --> 00:23:34.346 and the reason I say it's cheating is.

NOTE Confidence: 0.899225165714286

00:23:34.350 --> 00:23:35.220 Well, I can't do it.

NOTE Confidence: 0.899225165714286

00:23:35.220 --> 00:23:36.120 I don't have the.

NOTE Confidence: 0.899225165714286

00:23:36.120 --> 00:23:37.470 I don't have the resources to

NOTE Confidence: 0.899225165714286

00:23:37.526 --> 00:23:38.918 do gene expression profiling.

NOTE Confidence: 0.899225165714286

00:23:38.920 --> 00:23:41.881 I would rather use my brain to identify a

NOTE Confidence: 0.899225165714286

00:23:41.881 --> 00:23:44.674 target than have something come up as the,

NOTE Confidence: 0.899225165714286

00:23:44.680 --> 00:23:47.206 you know the the most differentially

NOTE Confidence: 0.899225165714286

00:23:47.206 --> 00:23:50.059 expressed marker in some in some experiment

NOTE Confidence: 0.899225165714286

00:23:50.059 --> 00:23:52.436 though I have used markers identify,

NOTE Confidence: 0.899225165714286

00:23:52.436 --> 00:23:54.726 I have used that strategy

NOTE Confidence: 0.899225165714286

00:23:54.726 --> 00:23:56.100 to identify markers.

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NOTE Confidence: 0.899225165714286

00:23:56.100 --> 00:23:56.628 You know,

NOTE Confidence: 0.899225165714286

00:23:56.628 --> 00:23:58.476 this is me being an immuno optimist.

NOTE Confidence: 0.899225165714286

00:23:58.480 --> 00:24:01.264 Our diagnostic markers keep getting better

NOTE Confidence: 0.899225165714286

00:24:01.264 --> 00:24:04.498 and better and better and you know this.

NOTE Confidence: 0.899225165714286

00:24:04.500 --> 00:24:07.460 I'm a sort of a goodwill hunting pathologist.

NOTE Confidence: 0.899225165714286

00:24:07.460 --> 00:24:08.240 You wasted

NOTE Confidence: 0.877195167777778

00:24:10.250 --> 00:24:14.275 $150,000 on an education or some some

NOTE Confidence: 0.877195167777778

00:24:14.275 --> 00:24:16.480 fancy experiments for an education.

NOTE Confidence: 0.877195167777778

00:24:16.480 --> 00:24:19.012 You could have got for $1.50 in

NOTE Confidence: 0.877195167777778

00:24:19.012 --> 00:24:21.358 late fees at the Public Library.

NOTE Confidence: 0.877195167777778

00:24:21.360 --> 00:24:23.823 So this is how I find diagnostic

NOTE Confidence: 0.877195167777778

00:24:23.823 --> 00:24:25.401 markers and this is and I'll

NOTE Confidence: 0.877195167777778

00:24:25.401 --> 00:24:27.207 say you know this is an example.

NOTE Confidence: 0.877195167777778

00:24:27.210 --> 00:24:30.612 This is How I Met cute got a 3.

NOTE Confidence: 0.877195167777778

00:24:30.620 --> 00:24:33.036 So this was the 1st paper that was

NOTE Confidence: 0.877195167777778

00:24:33.036 --> 00:24:34.812 published in the diagnostic pathology

NOTE Confidence: 0.877195167777778

00:24:34.812 --> 00:24:37.877 space that identified got a 3 as a

NOTE Confidence: 0.877195167777778

00:24:37.877 --> 00:24:40.032 urothelial cancer diagnostic marker and

NOTE Confidence: 0.877195167777778

00:24:40.032 --> 00:24:42.170 this used gene expression profiling.

NOTE Confidence: 0.877195167777778

00:24:42.170 --> 00:24:44.220 This came out of Stanford.

NOTE Confidence: 0.877195167777778

00:24:44.220 --> 00:24:46.338 John Higgins was the first author.

NOTE Confidence: 0.877195167777778

00:24:46.340 --> 00:24:48.710 This is Rob West and Matt

NOTE Confidence: 0.877195167777778

00:24:48.710 --> 00:24:51.120 Vander Reines work and they did.

NOTE Confidence: 0.877195167777778

00:24:51.120 --> 00:24:53.166 Gene expression profiling of Gu tumor,

NOTE Confidence: 0.877195167777778

00:24:53.170 --> 00:24:55.710 so they did kidney,

NOTE Confidence: 0.877195167777778

00:24:55.710 --> 00:24:57.396 black bladder and and prostate and

NOTE Confidence: 0.877195167777778

00:24:57.396 --> 00:24:59.707 got a three was identified as a

NOTE Confidence: 0.877195167777778

00:24:59.707 --> 00:25:01.211 highly differentially expressed gene

NOTE Confidence: 0.877195167777778

00:25:01.211 --> 00:25:04.004 in those tumor types and then you

NOTE Confidence: 0.877195167777778

00:25:04.004 --> 00:25:05.604 validate it with immunohistochemistry.

NOTE Confidence: 0.873888986666667

00:25:07.670 --> 00:25:10.109 Here's another one.

NOTE Confidence: 0.873888986666667

00:25:10.110 --> 00:25:12.100 And the defining molecular genetic

NOTE Confidence: 0.873888986666667

00:25:12.100 --> 00:25:14.687 event of a tumor is identified

NOTE Confidence: 0.873888986666667

00:25:14.687 --> 00:25:17.267 through and through whole genome

NOTE Confidence: 0.873888986666667

00:25:17.267 --> 00:25:19.675 or whole exome sequencing, Jason.

NOTE Confidence: 0.873888986666667

00:25:19.675 --> 00:25:22.690 And I say the tumor type has been solved

NOTE Confidence: 0.873888986666667

00:25:22.765 --> 00:25:25.613 and when the tumor type has been solved,

NOTE Confidence: 0.873888986666667

00:25:25.620 --> 00:25:28.200 this is such fertile ground to

NOTE Confidence: 0.873888986666667

00:25:28.200 --> 00:25:29.920 identify a diagnostic marker.

NOTE Confidence: 0.873888986666667

00:25:29.920 --> 00:25:32.908 So, so, so this defining molecular

NOTE Confidence: 0.873888986666667

00:25:32.908 --> 00:25:35.455 genetic event of solitary fibrous

NOTE Confidence: 0.873888986666667

00:25:35.455 --> 00:25:37.805 tumor was described and within

NOTE Confidence: 0.873888986666667

00:25:37.805 --> 00:25:40.510 a few months Jason and Chris.

NOTE Confidence: 0.873888986666667

00:25:40.510 --> 00:25:42.660 Chris. Butcher and Leona Doyle,

NOTE Confidence: 0.873888986666667

00:25:42.660 --> 00:25:45.810 wonderful junior now middle faculty,

NOTE Confidence: 0.873888986666667

00:25:45.810 --> 00:25:47.868 used to be my resident and fellow

NOTE Confidence: 0.873888986666667

00:25:47.868 --> 00:25:49.830 can published a diagnostic study,

NOTE Confidence: 0.873888986666667

00:25:49.830 --> 00:25:51.910 and when the immunohistochemical

NOTE Confidence: 0.873888986666667

00:25:51.910 --> 00:25:55.030 markers are identified in this fashion,

NOTE Confidence: 0.873888986666667

00:25:55.030 --> 00:25:57.690 they are so damn specific.

NOTE Confidence: 0.873888986666667

00:25:57.690 --> 00:25:59.970 They're so damn sensitive and specific.

NOTE Confidence: 0.873888986666667

00:25:59.970 --> 00:26:04.119 So this is how stat six came to be.

NOTE Confidence: 0.873888986666667

00:26:04.120 --> 00:26:06.172 And then I can take it to my lab.

NOTE Confidence: 0.873888986666667

00:26:06.180 --> 00:26:07.600 So this was a case,

NOTE Confidence: 0.873888986666667

00:26:07.600 --> 00:26:09.805 a spinal lesion that had a little

NOTE Confidence: 0.873888986666667

00:26:09.805 --> 00:26:11.786 bit of carrot and positivity that

NOTE Confidence: 0.873888986666667

00:26:11.786 --> 00:26:14.040 sat in the file for 10 years

NOTE Confidence: 0.873888986666667

00:26:14.107 --> 00:26:16.119 diagnosed as synovial sarcoma.

NOTE Confidence: 0.873888986666667

00:26:16.120 --> 00:26:17.300 I had identified this case.

NOTE Confidence: 0.873888986666667

00:26:17.300 --> 00:26:19.768 I was doing a TLE one validation

NOTE Confidence: 0.873888986666667

00:26:19.768 --> 00:26:21.616 several years ago and it was

NOTE Confidence: 0.873888986666667

00:26:21.616 --> 00:26:23.659 TLE one negative and I looked at

00:26:23.659 --> 00:26:25.243 this tumor and I actually didn't

00:26:25.306 --> 00:26:26.956 think it was synovial sarcoma.

00:26:26.960 --> 00:26:29.795 I thought it was a poorly differentiated

00:26:29.795 --> 00:26:32.137 solitary fibrous tumor and in fact it is

00:26:32.137 --> 00:26:34.678 and I and I say using next generation.

00:26:34.680 --> 00:26:35.397 Immunohistochemistry.

00:26:35.397 --> 00:26:39.699 You can elevate the ability of

00:26:39.699 --> 00:26:41.850 already strong morphologist,

00:26:41.850 --> 00:26:43.434 already strong diagnostic

00:26:43.434 --> 00:26:44.490 surgical pathologists.

00:26:44.490 --> 00:26:46.225 You give them incredibly sharp

00:26:46.225 --> 00:26:47.960 tools and they can become

00:26:48.025 --> 00:26:49.699 exceptional diagnostically.

00:26:52.220 --> 00:26:56.392 And then hit my love letter to

00:26:56.392 --> 00:26:58.180 transcription factors history.

00:26:58.180 --> 00:27:00.236 Historically, our diagnostic armamentarium

00:27:00.236 --> 00:27:02.806 was geared toward cytoplasmic and

00:27:02.806 --> 00:27:04.511 membranous differentiation markers

00:27:04.511 --> 00:27:06.759 that were empirically discovered.

00:27:06.760 --> 00:27:09.147 We would like mince up some tissue

00:27:09.147 --> 00:27:12.107 and put it in A and put it in a

00:27:12.107 --> 00:27:14.578 rabbit and see and see what's stuck.

00:27:14.580 --> 00:27:16.060 And so, you know,

00:27:16.060 --> 00:27:18.280 here's a breast cancer with mammaglobin

00:27:18.347 --> 00:27:20.879 and gross cystic disease fluid protein.

00:27:20.880 --> 00:27:22.266 And remember this,

00:27:22.266 --> 00:27:24.576 inside of plasmic differentiation markers,

00:27:24.580 --> 00:27:26.995 their expression tends to be

00:27:26.995 --> 00:27:28.927 markedly reduced in poorly

00:27:28.927 --> 00:27:31.442 differentiated tumors as opposed to

00:27:31.442 --> 00:27:32.912 lineage restricted transcription

NOTE Confidence: 0.866198558

00:27:32.912 --> 00:27:35.419 factors that tend to not always,

NOTE Confidence: 0.866198558

00:27:35.420 --> 00:27:37.742 but tend to be diffusely strongly

NOTE Confidence: 0.866198558

00:27:37.742 --> 00:27:39.290 expressed independent of the

NOTE Confidence: 0.866198558

00:27:39.355 --> 00:27:42.037 differentiation state status of the marker.

NOTE Confidence: 0.866198558

00:27:42.040 --> 00:27:44.353 And I like to coin a lot of terms

NOTE Confidence: 0.866198558

00:27:44.353 --> 00:27:46.915 and this is what I call the primacy.

NOTE Confidence: 0.866198558

00:27:46.920 --> 00:27:48.936 Primacy either means first or best.

NOTE Confidence: 0.866198558

00:27:48.940 --> 00:27:51.406 So this is for me the primacy because best.

NOTE Confidence: 0.866198558

00:27:51.410 --> 00:27:53.730 Primacy of lineage restricted

NOTE Confidence: 0.866198558

00:27:53.730 --> 00:27:54.890 transcription factors.

NOTE Confidence: 0.866198558

00:27:54.890 --> 00:27:56.615 And immuno optimists,

NOTE Confidence: 0.866198558

00:27:56.615 --> 00:27:59.490 immuno pessimists and immuno realists,

NOTE Confidence: 0.866198558

00:27:59.490 --> 00:28:02.666 and really we should all be immuno realist.

NOTE Confidence: 0.866198558

00:28:02.670 --> 00:28:04.368 Every new immunohistochemical

NOTE Confidence: 0.866198558

00:28:04.368 --> 00:28:07.764 test is like a new technology.

NOTE Confidence: 0.866198558

00:28:07.770 --> 00:28:10.108 This you may be familiar with is

NOTE Confidence: 0.866198558

00:28:10.108 --> 00:28:12.556 the Gartner Hype cycle that's used

NOTE Confidence: 0.866198558

00:28:12.556 --> 00:28:14.388 to describe new technologies.

NOTE Confidence: 0.866198558

00:28:14.390 --> 00:28:16.690 When new technologies are described,

NOTE Confidence: 0.866198558

00:28:16.690 --> 00:28:18.910 we're incredibly enthusiastic about them

NOTE Confidence: 0.866198558

00:28:18.910 --> 00:28:21.130 and overly enthusiastic about them.

NOTE Confidence: 0.866198558

00:28:21.130 --> 00:28:23.080 And then they start failing a

NOTE Confidence: 0.866198558

00:28:23.080 --> 00:28:24.990 bit and then we keep studying.

NOTE Confidence: 0.866198558

00:28:24.990 --> 00:28:27.146 Studying and studying and we've learned more,

NOTE Confidence: 0.866198558

00:28:27.150 --> 00:28:28.990 and we learn advantages,

NOTE Confidence: 0.866198558

00:28:28.990 --> 00:28:29.843 disadvantages, limitations,

NOTE Confidence: 0.866198558

00:28:29.843 --> 00:28:30.236 pitfalls,

NOTE Confidence: 0.866198558

00:28:30.236 --> 00:28:32.987 and we end up with this plateau

NOTE Confidence: 0.866198558

00:28:32.987 --> 00:28:34.350 of productivity.

NOTE Confidence: 0.866198558

00:28:34.350 --> 00:28:38.934 And I will say the reason that many

NOTE Confidence: 0.866198558

00:28:38.934 --> 00:28:40.791 immunohistochemical tests historically

NOTE Confidence: 0.866198558

00:28:40.791 --> 00:28:44.457 or new analytes have suffered from

NOTE Confidence: 0.866198558

00:28:44.457 --> 00:28:47.810 this is from poor experimental design.

NOTE Confidence: 0.866198558

00:28:47.810 --> 00:28:49.822 Immunohistochemical when you're introducing

NOTE Confidence: 0.866198558

00:28:49.822 --> 00:28:53.310 a new diagnostic marker into the space,

NOTE Confidence: 0.866198558

00:28:53.310 --> 00:28:56.080 it behooves one to examine.

NOTE Confidence: 0.866198558

00:28:56.080 --> 00:28:57.880 All the lesions in the

NOTE Confidence: 0.866198558

00:28:57.880 --> 00:28:58.600 differential diagnosis,

NOTE Confidence: 0.866198558

00:28:58.600 --> 00:29:02.552 if it behooves one to look for potential

NOTE Confidence: 0.866198558

00:29:02.552 --> 00:29:04.420 additional diagnostic utilities,

NOTE Confidence: 0.866198558

00:29:04.420 --> 00:29:06.107 and you can do that by staining

NOTE Confidence: 0.866198558

00:29:06.107 --> 00:29:07.240 a bunch of cases.

NOTE Confidence: 0.866198558

00:29:07.240 --> 00:29:09.802 But you can also use publicly

NOTE Confidence: 0.866198558

00:29:09.802 --> 00:29:11.510 available gene expression data

NOTE Confidence: 0.866198558

00:29:11.590 --> 00:29:13.798 to do the experiment in silico,

NOTE Confidence: 0.866198558

00:29:13.800 --> 00:29:16.400 and then and then to confirm it with

NOTE Confidence: 0.866198558

00:29:16.400 --> 00:29:18.359 parents paraffin and this is these

NOTE Confidence: 0.866198558

00:29:18.359 --> 00:29:20.231 are all papers published by Marku

NOTE Confidence: 0.866198558

00:29:20.299 --> 00:29:23.408 Marku Miettinen, who's a personal hero,

NOTE Confidence: 0.866198558

00:29:23.408 --> 00:29:26.068 and he bombs every new.

NOTE Confidence: 0.866198558

00:29:26.070 --> 00:29:26.916 Immunohistochemical marker,

NOTE Confidence: 0.866198558

00:29:26.916 --> 00:29:29.031 he studies them in thousands

NOTE Confidence: 0.866198558

00:29:29.031 --> 00:29:30.770 and thousands of tumors.

NOTE Confidence: 0.866198558

00:29:30.770 --> 00:29:31.862 So you know,

NOTE Confidence: 0.866198558

00:29:31.862 --> 00:29:36.520 got a 3 and 2500 tumors 4 for example.

NOTE Confidence: 0.866198558

00:29:36.520 --> 00:29:39.289 And again, exceptional,

NOTE Confidence: 0.866198558

00:29:39.289 --> 00:29:42.058 lovely, you know,

NOTE Confidence: 0.866198558

00:29:42.060 --> 00:29:44.769 doing what you can within the constraints

NOTE Confidence: 0.866198558

00:29:44.769 --> 00:29:47.138 of the resources at your disposal.

NOTE Confidence: 0.866198558

00:29:47.140 --> 00:29:50.119 And So what I've done at Iowa over the

NOTE Confidence: 0.866198558

00:29:50.119 --> 00:29:52.839 last 11 years is do what Marku did.

NOTE Confidence: 0.866198558

00:29:52.840 --> 00:29:55.240 And so I've developed tissue microarrays.

NOTE Confidence: 0.866198558

00:29:55.240 --> 00:29:55.824 I, I,

NOTE Confidence: 0.866198558

00:29:55.824 --> 00:29:56.408 you know,

NOTE Confidence: 0.866198558

00:29:56.408 --> 00:29:58.607 boasted this morning that I have hundreds

NOTE Confidence: 0.866198558

00:29:58.607 --> 00:30:00.522 of tissue microarrays of thousands

NOTE Confidence: 0.866198558

00:30:00.522 --> 00:30:03.392 of tumors of every, of every type.

NOTE Confidence: 0.866198558

00:30:03.392 --> 00:30:06.056 And I'm now able to do,

NOTE Confidence: 0.866198558

00:30:06.060 --> 00:30:08.504 able to do this.

NOTE Confidence: 0.866198558

00:30:08.504 --> 00:30:11.526 And so instead of doing this,

NOTE Confidence: 0.866198558

00:30:11.526 --> 00:30:15.510 we start at the plateau of productivity.

NOTE Confidence: 0.866198558

00:30:15.510 --> 00:30:17.650 We start with an informed

NOTE Confidence: 0.866198558

00:30:17.650 --> 00:30:18.934 new diagnostic marker.

NOTE Confidence: 0.760002003

00:30:24.040 --> 00:30:27.351 So stains I love most are oligo

NOTE Confidence: 0.760002003

00:30:27.351 --> 00:30:28.770 specific transcription factors.

NOTE Confidence: 0.760002003

00:30:28.770 --> 00:30:30.970 That, and I think a lot of people

NOTE Confidence: 0.760002003

00:30:30.970 --> 00:30:33.054 expect to transcription factor to

NOTE Confidence: 0.760002003

00:30:33.054 --> 00:30:35.494 have a single diagnostic application.

NOTE Confidence: 0.760002003

00:30:35.500 --> 00:30:38.260 And I think that's entirely unrealistic

NOTE Confidence: 0.760002003

00:30:38.260 --> 00:30:41.568 that the body is too efficient to

NOTE Confidence: 0.760002003

00:30:41.568 --> 00:30:43.868 use a single transcription factor

NOTE Confidence: 0.760002003

00:30:43.868 --> 00:30:46.684 for a single application it it

NOTE Confidence: 0.760002003

00:30:46.684 --> 00:30:49.755 reuses things you know and and so.

NOTE Confidence: 0.760002003

00:30:49.755 --> 00:30:52.240 It just behooves us to know the

NOTE Confidence: 0.760002003

00:30:52.240 --> 00:30:53.497 different diagnostic applications

NOTE Confidence: 0.760002003

00:30:53.497 --> 00:30:55.877 for all these different markers.

NOTE Confidence: 0.760002003

00:30:55.880 --> 00:30:57.796 And so I say stains, I lovers,

NOTE Confidence: 0.760002003

00:30:57.796 --> 00:31:00.838 Swiss army knives and sappy 2 is, you know,

NOTE Confidence: 0.760002003

00:31:00.838 --> 00:31:03.176 an example that I'll share with you.

NOTE Confidence: 0.760002003

00:31:03.180 --> 00:31:04.180 You know,

NOTE Confidence: 0.760002003

00:31:04.180 --> 00:31:07.180 my approach to every diagnostic marker,

NOTE Confidence: 0.760002003

00:31:07.180 --> 00:31:08.512 mainly transcription factors,

NOTE Confidence: 0.760002003

00:31:08.512 --> 00:31:12.270 is I dig very deeply into the basic

00:31:12.270 --> 00:31:14.558 science underpinning the marker,

00:31:14.560 --> 00:31:17.070 especially the developmental biology because

00:31:17.070 --> 00:31:20.619 that's my hop hobby and so sappy too.

00:31:20.620 --> 00:31:21.296 You know,

00:31:21.296 --> 00:31:22.986 pathologists learned about it about

00:31:22.986 --> 00:31:25.441 10 years ago because it was actually

00:31:25.441 --> 00:31:28.203 identified as a colon cancer marker in the

00:31:28.203 --> 00:31:30.422 context of the human protein Atlas effort.

00:31:30.430 --> 00:31:31.934 But every new diagnostic

00:31:31.934 --> 00:31:34.590 marker if you go to Pub Med,

00:31:34.590 --> 00:31:35.997 has a rich,

00:31:35.997 --> 00:31:38.811 generally decades long history in the

00:31:38.811 --> 00:31:40.769 developmental biology literature.

00:31:40.770 --> 00:31:44.690 And so even though we met SAT B2 in 2011,

00:31:44.690 --> 00:31:46.550 this was this was studied by

00:31:46.625 --> 00:31:48.590 developmental biologists that's

NOTE Confidence: 0.760002003

00:31:48.590 --> 00:31:51.210 involved in neuronal development.

NOTE Confidence: 0.760002003

00:31:51.210 --> 00:31:52.506 Craniofacial development

NOTE Confidence: 0.760002003

00:31:52.506 --> 00:31:54.450 and skeletal development.

NOTE Confidence: 0.760002003

00:31:54.450 --> 00:31:56.298 And from the developmental

NOTE Confidence: 0.760002003

00:31:56.298 --> 00:31:58.146 biology of the marker,

NOTE Confidence: 0.760002003

00:31:58.150 --> 00:31:59.850 you can infer diagnostic applications

NOTE Confidence: 0.760002003

00:31:59.850 --> 00:32:01.900 and then you can test them.

NOTE Confidence: 0.760002003

00:32:01.900 --> 00:32:05.164 You can design the study to test them.

NOTE Confidence: 0.760002003

00:32:05.170 --> 00:32:08.229 And so here's sat B2 doing the

NOTE Confidence: 0.760002003

00:32:08.229 --> 00:32:10.162 most familiar SAT B2 thing.

NOTE Confidence: 0.760002003

00:32:10.162 --> 00:32:12.027 This is a mucinous adenocarcinoma

NOTE Confidence: 0.760002003

00:32:12.027 --> 00:32:14.221 that before I had sat B2 I would

NOTE Confidence: 0.760002003

00:32:14.221 --> 00:32:16.319 have said had a lower GI phenotype.

NOTE Confidence: 0.760002003

00:32:16.320 --> 00:32:17.110 It's homogeneous.

NOTE Confidence: 0.760002003

00:32:17.110 --> 00:32:19.085 I say homogeneous for diffuse,

NOTE Confidence: 0.760002003

00:32:19.090 --> 00:32:23.260 strong for CK20 and CDX 2.

NOTE Confidence: 0.760002003

00:32:23.260 --> 00:32:25.948 And I would have said adenocarcinoma with

NOTE Confidence: 0.760002003

00:32:25.948 --> 00:32:28.320 mucinous features and lower GI phenotype.

NOTE Confidence: 0.760002003

00:32:28.320 --> 00:32:29.600 And this one's actually sappy,

NOTE Confidence: 0.760002003

00:32:29.600 --> 00:32:30.564 too negative,

NOTE Confidence: 0.760002003

00:32:30.564 --> 00:32:33.456 and this is actually an ampullary

NOTE Confidence: 0.760002003

00:32:33.456 --> 00:32:33.938 adenocarcinoma.

NOTE Confidence: 0.760002003

00:32:33.940 --> 00:32:36.730 So this is SATB 2 conferring

NOTE Confidence: 0.760002003

00:32:36.730 --> 00:32:38.125 lower GI specificity.

NOTE Confidence: 0.772248778571429

00:32:40.160 --> 00:32:41.315 Here's another diagnostic

NOTE Confidence: 0.772248778571429

00:32:41.315 --> 00:32:42.855 application of SAT V2.

NOTE Confidence: 0.772248778571429

00:32:42.860 --> 00:32:45.632 This is an undifferentiated

NOTE Confidence: 0.772248778571429

00:32:45.632 --> 00:32:47.018 undifferentiated carcinoma.

NOTE Confidence: 0.772248778571429

00:32:47.020 --> 00:32:49.402 Here's a carrot and in the

NOTE Confidence: 0.772248778571429

00:32:49.402 --> 00:32:51.320 colon it's MLH 1 deficient.

NOTE Confidence: 0.772248778571429

00:32:51.320 --> 00:32:55.866 So this is a this is a not quite a medullary.

NOTE Confidence: 0.772248778571429

00:32:55.870 --> 00:32:57.850 It's an undifferentiated MSI high

NOTE Confidence: 0.772248778571429

00:32:57.850 --> 00:33:00.460 cancer and it's CDX two negative

NOTE Confidence: 0.772248778571429

00:33:00.460 --> 00:33:02.812 and MSI high colon cancers are

NOTE Confidence: 0.772248778571429

00:33:02.812 --> 00:33:05.293 often CDX two negative because CDX

NOTE Confidence: 0.772248778571429

00:33:05.293 --> 00:33:07.783 2 actually has micro satellites in

NOTE Confidence: 0.772248778571429

00:33:07.783 --> 00:33:10.317 its exons and is susceptible to.

NOTE Confidence: 0.772248778571429

00:33:10.320 --> 00:33:12.404 Frameshift mutation and then

NOTE Confidence: 0.772248778571429

00:33:12.404 --> 00:33:15.530 nonsense mediated decay so that it's.

NOTE Confidence: 0.772248778571429

00:33:15.530 --> 00:33:18.806 It also explains why the tumors

NOTE Confidence: 0.772248778571429

00:33:18.806 --> 00:33:19.898 are undifferentiated.

NOTE Confidence: 0.772248778571429

00:33:19.900 --> 00:33:21.776 And here's sappy 2 in this case.

NOTE Confidence: 0.772248778571429

00:33:21.780 --> 00:33:25.098 So SAP two has an additional diagnostic

NOTE Confidence: 0.772248778571429

00:33:25.098 --> 00:33:28.504 application as an increased it adds

NOTE Confidence: 0.772248778571429

00:33:28.504 --> 00:33:31.664 increased sensitivity to the detection

NOTE Confidence: 0.772248778571429

00:33:31.664 --> 00:33:34.100 of undifferentiated colon cancer.

NOTE Confidence: 0.772248778571429

00:33:34.100 --> 00:33:35.102 Here's another one.

NOTE Confidence: 0.772248778571429

00:33:35.102 --> 00:33:36.772 This Jason did because he

NOTE Confidence: 0.772248778571429

00:33:36.772 --> 00:33:38.000 was positioned to do it.

NOTE Confidence: 0.772248778571429

00:33:38.000 --> 00:33:39.768 He's a sarcoma pathologist.

NOTE Confidence: 0.772248778571429

00:33:39.768 --> 00:33:42.860 He did it with my resident Jay

NOTE Confidence: 0.772248778571429

00:33:42.860 --> 00:33:44.990 Connor who's now the chief of

NOTE Confidence: 0.772248778571429

00:33:44.990 --> 00:33:48.400 GI at at at Sinai in Toronto.

NOTE Confidence: 0.772248778571429

00:33:48.400 --> 00:33:50.934 Is this so this was age-old question.

NOTE Confidence: 0.772248778571429

00:33:50.940 --> 00:33:54.041 Is this osteoid or is it just

NOTE Confidence: 0.772248778571429

00:33:54.041 --> 00:33:57.848 hyalinized stroma and sappy 2 is an

NOTE Confidence: 0.772248778571429

00:33:57.848 --> 00:33:59.636 osteoblast differentiation marker.

NOTE Confidence: 0.772248778571429

00:33:59.640 --> 00:34:01.999 We knew that from the developmental biology

NOTE Confidence: 0.772248778571429

00:34:01.999 --> 00:34:04.269 literature and now this age-old question.

NOTE Confidence: 0.772248778571429

00:34:04.270 --> 00:34:06.290 I can say emphatically yes,

NOTE Confidence: 0.772248778571429

00:34:06.290 --> 00:34:07.974 this is an Austin.

NOTE Confidence: 0.772248778571429

00:34:07.974 --> 00:34:09.237 This is osteoid.

NOTE Confidence: 0.772248778571429

00:34:09.240 --> 00:34:10.600 Here's another diagnostic application

NOTE Confidence: 0.772248778571429

00:34:10.600 --> 00:34:13.423 and this is where I had the opportunity

NOTE Confidence: 0.772248778571429

00:34:13.423 --> 00:34:15.233 to contribute to literature because

NOTE Confidence: 0.772248778571429

00:34:15.233 --> 00:34:17.716 this is where I was the best position.

NOTE Confidence: 0.772248778571429

00:34:17.720 --> 00:34:19.834 I was best positioned to study this

NOTE Confidence: 0.772248778571429

00:34:19.834 --> 00:34:22.099 marker in the neuroendocrine space.

NOTE Confidence: 0.772248778571429

00:34:22.100 --> 00:34:24.515 And I had presented this morning that

NOTE Confidence: 0.772248778571429

00:34:24.515 --> 00:34:27.758 SAT B2 is a wonderful marker of rectal,

NOTE Confidence: 0.772248778571429

00:34:27.760 --> 00:34:29.872 also expressed by appendiceal

NOTE Confidence: 0.772248778571429

00:34:29.872 --> 00:34:31.456 well differentiated neuroendocrine

NOTE Confidence: 0.772248778571429

00:34:31.456 --> 00:34:34.765 tumors and it's not expressed by

NOTE Confidence: 0.772248778571429

00:34:34.765 --> 00:34:36.415 pancreatic neuroendocrine tumors.

NOTE Confidence: 0.772248778571429

00:34:36.420 --> 00:34:38.520 And then I had also shared that

NOTE Confidence: 0.772248778571429

00:34:38.520 --> 00:34:39.420 this is important.

NOTE Confidence: 0.772248778571429

00:34:39.420 --> 00:34:42.150 Because a lot of the transcriptional

00:34:42.150 --> 00:34:44.480 machinery that drives pancreas net

00:34:44.480 --> 00:34:47.090 development namely Pack 6 and islet

00:34:47.090 --> 00:34:49.451 one that transcriptional machinery is

00:34:49.451 --> 00:34:52.409 also operant in rectal neuroendocrine tumors.

00:34:52.410 --> 00:34:53.268 And so this,

00:34:53.268 --> 00:34:55.961 this gave me a tool to clearly distinguish

00:34:55.961 --> 00:34:59.066 pancreatic and rectal neuroendocrine tumors.

00:34:59.070 --> 00:35:00.729 And then I showed you the morphology,

00:35:00.730 --> 00:35:01.281 right.

00:35:01.281 --> 00:35:04.036 Everybody can everybody after this

00:35:04.036 --> 00:35:07.099 morning's discussion could tell me that

00:35:07.099 --> 00:35:10.235 this is type B trabecular paper clip rectal.

00:35:10.240 --> 00:35:12.532 And then here's here's another diagnostic

00:35:12.532 --> 00:35:14.859 application I shared this this morning.

00:35:14.860 --> 00:35:16.288 How about PD neck?

00:35:16.288 --> 00:35:17.716 And in PD neck,

NOTE Confidence: 0.772248778571429

00:35:17.720 --> 00:35:20.780 sat B2 is a reasonably sensitive,

NOTE Confidence: 0.772248778571429

00:35:20.780 --> 00:35:23.990 highly specific marker of cutaneous

NOTE Confidence: 0.772248778571429

00:35:23.990 --> 00:35:25.274 neuroendocrine carcinoma,

NOTE Confidence: 0.772248778571429

00:35:25.280 --> 00:35:27.458 Merkel cell carcinoma.

NOTE Confidence: 0.828534414

00:35:29.590 --> 00:35:31.530 And, and there's more, right.

NOTE Confidence: 0.828534414

00:35:31.530 --> 00:35:33.942 So here I'm being like a, you know,

NOTE Confidence: 0.828534414

00:35:33.942 --> 00:35:35.606 immunohistochemistry used car salesman.

NOTE Confidence: 0.828534414

00:35:35.610 --> 00:35:38.080 There's one more diagnostic application.

NOTE Confidence: 0.828534414

00:35:38.080 --> 00:35:41.045 This is, this is a, this is an

NOTE Confidence: 0.828534414

00:35:41.045 --> 00:35:43.086 undifferentiated round cell sarcoma.

NOTE Confidence: 0.828534414

00:35:43.086 --> 00:35:46.270 That's Ewing sarcoma. Ish.

NOTE Confidence: 0.828534414

00:35:46.270 --> 00:35:49.454 It's a little too pleomorphic to be a

NOTE Confidence: 0.828534414

00:35:49.454 --> 00:35:52.520 Ewing sarcoma and it's CD 99 negative and

NOTE Confidence: 0.828534414

00:35:52.520 --> 00:35:56.335 before I had the opportunity to validate

NOTE Confidence: 0.828534414

00:35:56.335 --> 00:35:59.839 becor immunohistochemistry in my lab.

NOTE Confidence: 0.828534414

00:35:59.840 --> 00:36:01.947 Because it was hard to come across

NOTE Confidence: 0.828534414

00:36:01.950 --> 00:36:03.434 10B core rearranged sarcomas,

NOTE Confidence: 0.828534414

00:36:03.434 --> 00:36:07.342 I use SAP B2 as a surrogate for B

NOTE Confidence: 0.828534414

00:36:07.342 --> 00:36:10.007 core rearranged sarcomas because about

NOTE Confidence: 0.828534414

00:36:10.010 --> 00:36:12.140 70% of B core rearranged sarcomas

NOTE Confidence: 0.828534414

00:36:12.140 --> 00:36:14.084 are strongly sappy, too positive.

NOTE Confidence: 0.828534414

00:36:14.084 --> 00:36:16.269 This was demonstrated by Christina

NOTE Confidence: 0.828534414

00:36:16.269 --> 00:36:18.563 Antonescu in gene expression profiling

NOTE Confidence: 0.828534414

00:36:18.563 --> 00:36:21.293 experiments and sort of tucked in,

NOTE Confidence: 0.828534414

00:36:21.300 --> 00:36:23.834 you know, as a supplementary fig figure

NOTE Confidence: 0.828534414

00:36:23.834 --> 00:36:27.145 in one of her papers from 10 years ago.

NOTE Confidence: 0.828534414

00:36:27.150 --> 00:36:27.696 All right.

NOTE Confidence: 0.828534414

00:36:27.696 --> 00:36:29.880 So I always ask will it Swiss army

NOTE Confidence: 0.828534414

00:36:29.945 --> 00:36:31.884 knife and and the answer is yes.

NOTE Confidence: 0.828534414

00:36:31.890 --> 00:36:35.364 Yes I want more more value with fewer mark,

NOTE Confidence: 0.828534414

00:36:35.370 --> 00:36:36.590 fewer markers.

NOTE Confidence: 0.828534414

00:36:36.590 --> 00:36:37.262 All right.

NOTE Confidence: 0.828534414

00:36:37.262 --> 00:36:40.558 So that's next generation

NOTE Confidence: 0.828534414

00:36:40.558 --> 00:36:43.516 immunohistochemistry onto optimization.

NOTE Confidence: 0.828534414

00:36:43.520 --> 00:36:46.808 It's maybe we could say selection

NOTE Confidence: 0.828534414

00:36:46.808 --> 00:36:49.340 optimization and validation and so,

NOTE Confidence: 0.828534414

00:36:49.340 --> 00:36:52.724 so there's Twitter, so am I HC guy.

NOTE Confidence: 0.828534414

00:36:52.730 --> 00:36:55.762 And the reason that I'm IHC guy is

NOTE Confidence: 0.828534414

00:36:55.762 --> 00:36:58.063 I'm passionate about being connected

NOTE Confidence: 0.828534414

00:36:58.063 --> 00:37:00.985 with people and having the opportunity

NOTE Confidence: 0.828534414

00:37:00.985 --> 00:37:04.008 to share things that I'm passionate

NOTE Confidence: 0.828534414

00:37:04.008 --> 00:37:05.560 about mainly immunohistochemistry.

NOTE Confidence: 0.828534414

00:37:05.560 --> 00:37:10.731 I'm kind of a nerd and and so I use

NOTE Confidence: 0.828534414

00:37:10.731 --> 00:37:13.643 this platform to to mentor IHC lab.

NOTE Confidence: 0.828534414

00:37:13.650 --> 00:37:15.290 Directorship and different directors

NOTE Confidence: 0.828534414

00:37:15.290 --> 00:37:18.340 are at different levels and I give

60

NOTE Confidence: 0.828534414

00:37:18.340 --> 00:37:20.428 different directors different advice.

NOTE Confidence: 0.828534414

00:37:20.430 --> 00:37:23.314 So this is my friend Frank Ingram,

NOTE Confidence: 0.828534414

00:37:23.320 --> 00:37:25.384 who's Chuck Town MG,

NOTE Confidence: 0.828534414

00:37:25.384 --> 00:37:29.027 very popular on Twitter and he took

NOTE Confidence: 0.828534414

00:37:29.027 --> 00:37:32.587 over as a local icy lab director in

NOTE Confidence: 0.828534414

00:37:32.587 --> 00:37:35.743 his community practice in Charlotte,

NOTE Confidence: 0.828534414

00:37:35.743 --> 00:37:39.607 NC and he had no training in in

NOTE Confidence: 0.828534414

00:37:39.607 --> 00:37:41.479 Immunohistochemistry Lab directorship.

NOTE Confidence: 0.828534414

00:37:41.480 --> 00:37:43.846 Just like me, I had no formal.

NOTE Confidence: 0.828534414

00:37:43.850 --> 00:37:45.236 Training in Immunohistochemistry

NOTE Confidence: 0.828534414

00:37:45.236 --> 00:37:48.008 lab directorship and he said I

NOTE Confidence: 0.828534414

00:37:48.008 --> 00:37:50.450 want to bring up God up, 3 packs,

NOTE Confidence: 0.828534414

00:37:50.450 --> 00:37:51.060 8 socks,

NOTE Confidence: 0.828534414

00:37:51.060 --> 00:37:54.219 10 and erg to which I said Hallelujah,

NOTE Confidence: 0.828534414

00:37:54.220 --> 00:37:56.380 like you must have those markers.

NOTE Confidence: 0.828534414

00:37:56.380 --> 00:37:58.180 And I provide you know I I talk

NOTE Confidence: 0.828534414

00:37:58.180 --> 00:38:00.155 a lot right and I write a lot.

NOTE Confidence: 0.828534414

00:38:00.160 --> 00:38:03.292 So I provided him very detailed

NOTE Confidence: 0.828534414

00:38:03.292 --> 00:38:06.780 instructions about how I would go about

NOTE Confidence: 0.828534414

00:38:06.780 --> 00:38:08.865 value optimizing and then validating

NOTE Confidence: 0.828534414

00:38:08.865 --> 00:38:12.100 what I consider to be pretty routine.

NOTE Confidence: 0.828534414

00:38:12.100 --> 00:38:15.844 Tried and true robust.

NOTE Confidence: 0.828534414

00:38:15.844 --> 00:38:17.716 Immunohistochemical markers.

NOTE Confidence: 0.828534414

00:38:17.720 --> 00:38:19.281 And then here's another one of my

NOTE Confidence: 0.828534414

00:38:19.281 --> 00:38:20.954 close friends. This is Phil Reese.

NOTE Confidence: 0.828534414

00:38:20.954 --> 00:38:22.484 Phil Reese is operating at

NOTE Confidence: 0.828534414

00:38:22.484 --> 00:38:24.319 A at a much higher level.

NOTE Confidence: 0.828534414

00:38:24.320 --> 00:38:25.852 He's an IC lab.

NOTE Confidence: 0.828534414

00:38:25.852 --> 00:38:27.767 He's the IHC lab director

NOTE Confidence: 0.828534414

00:38:27.767 --> 00:38:29.718 at OHSU in Portland.

NOTE Confidence: 0.828534414

00:38:29.720 --> 00:38:31.960 He took the lab over from Megan Troxell,

00:38:31.960 --> 00:38:34.860 who's a Jedi Master of

00:38:34.860 --> 00:38:36.600 Immunohistochemistry lab directorship.

00:38:36.600 --> 00:38:39.088 And she and I have taught each other

00:38:39.088 --> 00:38:41.177 a tremendous amount over the years.

00:38:41.180 --> 00:38:43.875 And Phil was looking for something very,

00:38:43.880 --> 00:38:45.544 very specific.

00:38:45.544 --> 00:38:48.040 He wanted immunohistochemistry.

00:38:48.040 --> 00:38:51.148 For Toxoplasma, which is a really,

00:38:51.150 --> 00:38:54.408 really niche application and I said,

00:38:54.410 --> 00:38:54.942 well,

00:38:54.942 --> 00:38:57.070 I certainly don't do

00:38:57.070 --> 00:38:58.666 immunohistochemistry for Toxoplasma.

00:38:58.670 --> 00:39:01.183 But the one person in the world

00:39:01.183 --> 00:39:04.819 that's the best person to talk to you

00:39:04.819 --> 00:39:06.307 about Toxoplasma immunohistochemistry

00:39:06.307 --> 00:39:08.788 is an unfortunately he passed

NOTE Confidence: 0.828534414

00:39:08.788 --> 00:39:11.128 away about 18 months ago.

NOTE Confidence: 0.83119552625

00:39:11.130 --> 00:39:14.898 But Sharif Zaki, who was the chief of

NOTE Confidence: 0.83119552625

00:39:14.898 --> 00:39:18.438 IBD pathology at the NIH and I connected.

NOTE Confidence: 0.83119552625

00:39:18.440 --> 00:39:23.300 Fill with Sharif and Phil got what he needed.

NOTE Confidence: 0.83119552625

00:39:23.300 --> 00:39:25.869 So antibody selection you know I I'll

NOTE Confidence: 0.83119552625

00:39:25.869 --> 00:39:28.344 I'll say like all these examples that

NOTE Confidence: 0.83119552625

00:39:28.344 --> 00:39:31.357 I might get to one or two of your

NOTE Confidence: 0.83119552625

00:39:31.357 --> 00:39:33.674 got a three and your end terminus.

NOTE Confidence: 0.83119552625

00:39:33.680 --> 00:39:36.290 Hey one you know I'm selecting

NOTE Confidence: 0.83119552625

00:39:36.290 --> 00:39:38.991 antibodies I'm I'm trying to invent

NOTE Confidence: 0.83119552625

00:39:38.991 --> 00:39:41.613 new antibodies but but Chuck Frank,

NOTE Confidence: 0.83119552625

00:39:41.620 --> 00:39:43.972 Chuck Town, Frank knows from from you

NOTE Confidence: 0.83119552625

00:39:43.972 --> 00:39:46.636 know going to be going to meetings

NOTE Confidence: 0.83119552625

00:39:46.636 --> 00:39:48.616 listening to listening to lectures

NOTE Confidence: 0.83119552625

00:39:48.616 --> 00:39:51.136 what the you know cutting edge what

NOTE Confidence: 0.83119552625

00:39:51.136 --> 00:39:52.940 the advancing edge of diagnostic.

NOTE Confidence: 0.83119552625

00:39:52.940 --> 00:39:55.090 Pathology is and so that's

NOTE Confidence: 0.83119552625

00:39:55.090 --> 00:39:55.950 antibody selection.

NOTE Confidence: 0.83119552625

00:39:55.950 --> 00:39:57.333 What what immunohistochemical

NOTE Confidence: 0.83119552625

00:39:57.333 --> 00:40:01.500 marker do I want to bring up in my

NOTE Confidence: 0.83119552625

00:40:01.500 --> 00:40:03.645 lab for a diagnostic application

NOTE Confidence: 0.83119552625

00:40:03.645 --> 00:40:05.970 or for research application?

NOTE Confidence: 0.83119552625

00:40:05.970 --> 00:40:08.650 And then this is sort of the sequence

NOTE Confidence: 0.83119552625

00:40:08.650 --> 00:40:11.037 of events from maybe from easy to

NOTE Confidence: 0.83119552625

00:40:11.037 --> 00:40:13.680 hard that I go through and actually.

NOTE Confidence: 0.83119552625

00:40:13.680 --> 00:40:15.792 There's a few tricks of the trade that

NOTE Confidence: 0.83119552625

00:40:15.792 --> 00:40:17.920 I learned from David Rim on this list.

NOTE Confidence: 0.83119552625

00:40:17.920 --> 00:40:20.032 So so the easiest thing is to phone

NOTE Confidence: 0.83119552625

00:40:20.032 --> 00:40:22.060 a friend and you can always phone

NOTE Confidence: 0.83119552625

00:40:22.060 --> 00:40:24.328 you can always phone me phone a

NOTE Confidence: 0.83119552625

00:40:24.328 --> 00:40:26.248 friend works great for esoteric

NOTE Confidence: 0.83119552625

00:40:26.248 --> 00:40:28.040 antibodies so connecting fill the

NOTE Confidence: 0.83119552625

00:40:28.040 --> 00:40:30.280 Sharif was was really that was the

NOTE Confidence: 0.83119552625

00:40:30.280 --> 00:40:32.178 one step solution to that.

NOTE Confidence: 0.83119552625

00:40:32.180 --> 00:40:35.260 The published literature is great is great.

NOTE Confidence: 0.83119552625

00:40:35.260 --> 00:40:39.040 I often go to the public I just go to pubbed.

NOTE Confidence: 0.83119552625

00:40:39.040 --> 00:40:41.833 Has there been a been a paper

NOTE Confidence: 0.83119552625

00:40:41.833 --> 00:40:43.690 published with this marker.

NOTE Confidence: 0.83119552625

00:40:43.690 --> 00:40:45.166 What are the figures look like,

NOTE Confidence: 0.83119552625

00:40:45.170 --> 00:40:45.454 you know,

NOTE Confidence: 0.83119552625

00:40:45.454 --> 00:40:45.880 what are the,

NOTE Confidence: 0.83119552625

00:40:45.880 --> 00:40:47.008 what are the pictures look like?

NOTE Confidence: 0.83119552625

00:40:47.010 --> 00:40:48.322 Does this look good?

NOTE Confidence: 0.83119552625

00:40:48.322 --> 00:40:49.962 Does this look like an

NOTE Confidence: 0.83119552625

00:40:49.962 --> 00:40:51.047 immunohistochemical stain of high

NOTE Confidence: 0.83119552625

00:40:51.047 --> 00:40:52.950 quality that I would want in my lab?

NOTE Confidence: 0.83119552625

00:40:52.950 --> 00:40:56.198 And then Nordic QC is the Scandinavian

NOTE Confidence: 0.83119552625

00:40:56.198 --> 00:40:59.001 equivalent of the CAP Immunohistochemistry

NOTE Confidence: 0.83119552625

00:40:59.001 --> 00:41:02.979 committee and they published their very

NOTE Confidence: 0.83119552625

00:41:02.979 --> 00:41:06.129 transparent and they published very

NOTE Confidence: 0.83119552625

00:41:06.129 --> 00:41:08.015 detailed platform specific protocols

NOTE Confidence: 0.83119552625

00:41:08.015 --> 00:41:11.060 for what I refer to as diagnostic

NOTE Confidence: 0.83119552625

00:41:11.140 --> 00:41:14.068 workhorses so that they've got published.

NOTE Confidence: 0.83119552625

00:41:14.070 --> 00:41:16.572 Protocols and usually 10 different published

NOTE Confidence: 0.83119552625

00:41:16.572 --> 00:41:19.400 protocols that are again platform specific.

NOTE Confidence: 0.83119552625

00:41:19.400 --> 00:41:21.206 So you're running a doco auto

NOTE Confidence: 0.83119552625

00:41:21.206 --> 00:41:23.340 Stainer link 48 or you're running

NOTE Confidence: 0.83119552625

00:41:23.340 --> 00:41:25.056 a VENTANA benchmark ultra,

NOTE Confidence: 0.83119552625

00:41:25.060 --> 00:41:27.814 or you have a or you have a doco

NOTE Confidence: 0.83119552625

00:41:27.814 --> 00:41:30.459 omnis or you have a like a Bond 3.

NOTE Confidence: 0.83119552625

00:41:30.460 --> 00:41:33.844 For for about 150 to 200

NOTE Confidence: 0.83119552625

00:41:33.844 --> 00:41:35.536 different diagnostic antibodies.

NOTE Confidence: 0.83119552625

00:41:35.540 --> 00:41:38.137 So that's where I pointed frank for

NOTE Confidence: 0.83119552625

00:41:38.137 --> 00:41:41.558 packs 8 and socks 10 and erg and then and

NOTE Confidence: 0.83119552625

00:41:41.558 --> 00:41:43.542 then these are more shots in the dark.

NOTE Confidence: 0.83119552625

00:41:43.550 --> 00:41:45.622 So these are these are databases that

NOTE Confidence: 0.83119552625

00:41:45.622 --> 00:41:48.057 you can I usually end up when I'm

NOTE Confidence: 0.83119552625

00:41:48.057 --> 00:41:49.981 bringing up a brand new diagnostic

NOTE Confidence: 0.83119552625

00:41:49.981 --> 00:41:52.627 marker I end up with these databases.

NOTE Confidence: 0.83119552625

00:41:52.630 --> 00:41:54.210 Biocompare is pretty dumb.

NOTE Confidence: 0.83119552625

00:41:54.210 --> 00:41:57.613 It just spits out it just spits out a

NOTE Confidence: 0.83119552625

00:41:57.613 --> 00:42:00.909 list a list of vendors and you can click on.

NOTE Confidence: 0.83119552625

00:42:00.910 --> 00:42:01.284 You know,

NOTE Confidence: 0.83119552625

00:42:01.284 --> 00:42:02.780 you can click on the link and go

NOTE Confidence: 0.83119552625

00:42:02.830 --> 00:42:03.499 to the website,

NOTE Confidence: 0.83119552625

00:42:03.500 --> 00:42:06.370 but these are two that I learned

NOTE Confidence: 0.83119552625

00:42:06.370 --> 00:42:07.600 from David actually,

68

00:42:07.600 --> 00:42:10.995 antibody pedia and bench and bench side.

00:42:11.000 --> 00:42:14.032 And I I think I like benci the

00:42:14.032 --> 00:42:16.000 most because bentsi does for

00:42:16.000 --> 00:42:18.597 me it uses AI and does for

00:42:18.685 --> 00:42:20.539 me what I used to do,

00:42:20.540 --> 00:42:22.592 which is go through every paper

00:42:22.592 --> 00:42:25.167 published and say look at the method

00:42:25.167 --> 00:42:27.067 and is there an immunohistochemical

00:42:27.067 --> 00:42:29.542 method and what's the clone and

00:42:29.542 --> 00:42:31.190 aggregate all this information.

00:42:31.190 --> 00:42:33.829 And bench side does it for you.

00:42:33.830 --> 00:42:36.014 So this is what Nordic QC looks

00:42:36.014 --> 00:42:37.900 like and these are examples,

00:42:37.900 --> 00:42:41.185 so these are examples of these are all the

00:42:41.185 --> 00:42:45.870 different like recommendable her to assays.

00:42:45.870 --> 00:42:47.846 And you know it's not just the clone,

NOTE Confidence: 0.813428826538461

00:42:47.850 --> 00:42:50.554 it's all the conditions of the test and

NOTE Confidence: 0.813428826538461

00:42:50.554 --> 00:42:53.568 you click the link to the PDF and that's

NOTE Confidence: 0.813428826538461

00:42:53.568 --> 00:42:56.130 a starting point for your optimization.

NOTE Confidence: 0.813428826538461

00:42:56.130 --> 00:42:59.270 And then here's biocompare

NOTE Confidence: 0.813428826538461

00:42:59.270 --> 00:43:01.625 antibody pedia ads.

NOTE Confidence: 0.813428826538461

00:43:01.630 --> 00:43:03.156 Biocompare just gives you a list of

NOTE Confidence: 0.813428826538461

00:43:03.156 --> 00:43:05.003 a list of vendors and you can click

NOTE Confidence: 0.813428826538461

00:43:05.003 --> 00:43:06.630 links and go to their websites.

NOTE Confidence: 0.813428826538461

00:43:06.630 --> 00:43:09.138 Antibody Pedia will vouch on and

NOTE Confidence: 0.813428826538461

00:43:09.138 --> 00:43:11.749 you're looking for you're looking for.

NOTE Confidence: 0.813428826538461

00:43:11.750 --> 00:43:15.089 Green Circles will vouch for the quality

NOTE Confidence: 0.813428826538461

00:43:15.089 --> 00:43:18.508 of the experiments that were done to

NOTE Confidence: 0.813428826538461

00:43:18.508 --> 00:43:21.370 validate the specificity of the antibody.

NOTE Confidence: 0.813428826538461

00:43:21.370 --> 00:43:23.434 So all the way back to the beginning

NOTE Confidence: 0.813428826538461

00:43:23.434 --> 00:43:25.487 when I said there's these two

00:43:25.487 --> 00:43:27.322 papers for the basic scientists,

00:43:27.330 --> 00:43:29.808 the one that Angelo de Marzo published,

00:43:29.810 --> 00:43:31.840 this case based, and the Eulen 1.

00:43:31.840 --> 00:43:35.456 That that David collaborated on and so many.

00:43:35.460 --> 00:43:37.116 And then if you do it for a while,

00:43:37.120 --> 00:43:39.787 you know some vendors are more scrupulous

00:43:39.787 --> 00:43:41.759 with their science than others,

00:43:41.760 --> 00:43:43.416 but this gives you a check.

00:43:43.420 --> 00:43:46.210 And so we're looking for a green circle that

00:43:46.210 --> 00:43:49.155 is referring to an enhanced by validation.

00:43:49.160 --> 00:43:49.610 So.

00:43:49.610 --> 00:43:52.310 So they're using some of these

00:43:52.310 --> 00:43:55.110 techniques like like like you know,

00:43:55.110 --> 00:43:57.366 either crisper cast and not to knock it

00:43:57.366 --> 00:43:59.341 out or they're using small interfering

00:43:59.341 --> 00:44:01.980 RNA to knock it down to validate.

NOTE Confidence: 0.813428826538461

00:44:01.980 --> 00:44:04.580 The specificity of the antibody.

NOTE Confidence: 0.813428826538461

00:44:04.580 --> 00:44:06.716 And then here is bench side,

NOTE Confidence: 0.813428826538461

00:44:06.720 --> 00:44:10.016 which gives me which links to the papers

NOTE Confidence: 0.813428826538461

00:44:10.016 --> 00:44:12.420 themselves and not just the papers,

NOTE Confidence: 0.813428826538461

00:44:12.420 --> 00:44:14.844 but links to the figures of the papers.

NOTE Confidence: 0.813428826538461

00:44:14.850 --> 00:44:17.062 So this is I used to use

NOTE Confidence: 0.813428826538461

00:44:17.062 --> 00:44:18.790 biocompare and thank you David.

NOTE Confidence: 0.813428826538461

00:44:18.790 --> 00:44:21.170 Now I go to Bankside 1st and

NOTE Confidence: 0.813428826538461

00:44:21.170 --> 00:44:22.850 antibody pedia and benzite,

NOTE Confidence: 0.813428826538461

00:44:22.850 --> 00:44:24.700 there's they're free for you,

NOTE Confidence: 0.813428826538461

00:44:24.700 --> 00:44:25.920 I think you have.

NOTE Confidence: 0.813428826538461

00:44:25.920 --> 00:44:27.140 They're free to academicians.

NOTE Confidence: 0.813428826538461

00:44:27.140 --> 00:44:29.800 You have to like create a login, but totally,

NOTE Confidence: 0.813428826538461

00:44:29.800 --> 00:44:32.975 totally free, incredibly powerful tools.

NOTE Confidence: 0.813428826538461

00:44:32.980 --> 00:44:34.784 We're doing on time.

00:44:34.784 --> 00:44:36.137 We're doing OK.

00:44:36.140 --> 00:44:38.130 Ethical sourcing of primary antibodies.

00:44:38.130 --> 00:44:39.960 I mentioned this briefly in

00:44:39.960 --> 00:44:41.058 a few conversations.

00:44:41.060 --> 00:44:44.204 I will not source an antibody

00:44:44.204 --> 00:44:48.326 from Santa Cruz in my lab because

00:44:48.326 --> 00:44:51.880 they committed gross animal abuse

00:44:51.880 --> 00:44:56.455 and they actually they they they

00:44:56.455 --> 00:44:59.980 lost their license to sell.

00:44:59.980 --> 00:45:02.385 Animal products derived from animals

00:45:02.385 --> 00:45:05.677 and and the loophole is that mice

00:45:05.677 --> 00:45:08.484 don't qualify as animals so they so

00:45:08.484 --> 00:45:10.336 they can't sell polyclonal's anymore.

00:45:10.336 --> 00:45:11.468 They can't sell rabbit,

00:45:11.470 --> 00:45:13.420 rabbit polyclonal or goat polyclonal

00:45:13.420 --> 00:45:15.370 because those those are considered

NOTE Confidence: 0.813428826538461

00:45:15.433 --> 00:45:17.245 animals by the by the government.

NOTE Confidence: 0.813428826538461

00:45:17.250 --> 00:45:19.035 But mice aren't considered animals

NOTE Confidence: 0.813428826538461

00:45:19.035 --> 00:45:21.580 and so Santa Cruz is still in

NOTE Confidence: 0.813428826538461

00:45:21.580 --> 00:45:23.644 business but I won't source an

NOTE Confidence: 0.813428826538461

00:45:23.644 --> 00:45:25.119 antibody from Santa Cruz.

NOTE Confidence: 0.813428826538461

00:45:25.120 --> 00:45:27.454 Optimization you know I'll I'll sort

NOTE Confidence: 0.813428826538461

00:45:27.454 --> 00:45:30.343 of move along because I want to get

NOTE Confidence: 0.813428826538461

00:45:30.343 --> 00:45:32.233 to at least one specific example.

NOTE Confidence: 0.813428826538461

00:45:32.240 --> 00:45:33.796 Optimization is the series

NOTE Confidence: 0.813428826538461

00:45:33.796 --> 00:45:36.130 of experiments that we do to

NOTE Confidence: 0.89158452875

00:45:36.203 --> 00:45:38.675 optimize the signal to noise ratio.

NOTE Confidence: 0.89158452875

00:45:38.680 --> 00:45:41.848 And the way that I do optimization is

NOTE Confidence: 0.89158452875

00:45:41.848 --> 00:45:44.708 is is very guest check revised and

NOTE Confidence: 0.89158452875

00:45:44.708 --> 00:45:47.689 visually oriented and David has a awesome

NOTE Confidence: 0.89158452875

00:45:47.689 --> 00:45:50.159 scientific way to do optimization.

NOTE Confidence: 0.89158452875

00:45:50.160 --> 00:45:52.308 He optimizes the signal to noise

NOTE Confidence: 0.89158452875

00:45:52.308 --> 00:45:55.010 ratio but he he takes the human.

NOTE Confidence: 0.89158452875

00:45:55.010 --> 00:45:57.380 Right out of the equation.

NOTE Confidence: 0.89158452875

00:45:57.380 --> 00:45:59.010 And this here's an example,

NOTE Confidence: 0.89158452875

00:45:59.010 --> 00:46:01.674 you know these are the the

NOTE Confidence: 0.89158452875

00:46:01.674 --> 00:46:03.450 iterative specific experiments that

NOTE Confidence: 0.89158452875

00:46:03.526 --> 00:46:05.818 I perform to optimize a primary,

NOTE Confidence: 0.89158452875

00:46:05.820 --> 00:46:07.260 new primary antibody.

NOTE Confidence: 0.89158452875

00:46:07.260 --> 00:46:09.660 We mainly attend to the

NOTE Confidence: 0.89158452875

00:46:09.660 --> 00:46:11.400 primary antibody dilution,

NOTE Confidence: 0.89158452875

00:46:11.400 --> 00:46:15.376 the type of antigen retrieval and then the

NOTE Confidence: 0.89158452875

00:46:15.376 --> 00:46:18.398 primary antibody duration of incubation,

NOTE Confidence: 0.89158452875

00:46:18.400 --> 00:46:21.628 the choice of adding amplification to

NOTE Confidence: 0.89158452875

00:46:21.628 --> 00:46:24.413 detection or just straight detection

NOTE Confidence: 0.89158452875

00:46:24.413 --> 00:46:27.659 and then the duration of detection.

NOTE Confidence: 0.89158452875

00:46:27.660 --> 00:46:28.756 And then there's validation.

NOTE Confidence: 0.89158452875

00:46:28.756 --> 00:46:30.126 I talked about validation in

NOTE Confidence: 0.89158452875

00:46:30.126 --> 00:46:31.120 the research space.

NOTE Confidence: 0.89158452875

00:46:31.120 --> 00:46:33.318 This is validation in the clinical space.

NOTE Confidence: 0.89158452875

00:46:33.320 --> 00:46:35.856 So an IHC lab director is going to

NOTE Confidence: 0.89158452875

00:46:35.856 --> 00:46:37.878 pay attention to this White Paper,

NOTE Confidence: 0.89158452875

00:46:37.880 --> 00:46:40.144 principles of analytic validation

NOTE Confidence: 0.89158452875

00:46:40.144 --> 00:46:42.408 of immunohistochemical assays that

NOTE Confidence: 0.89158452875

00:46:42.408 --> 00:46:44.757 specifies the quantity and quality

NOTE Confidence: 0.89158452875

00:46:44.757 --> 00:46:47.417 of the cohorts that one should put

NOTE Confidence: 0.89158452875

00:46:47.487 --> 00:46:50.476 together to to to validate an antibody,

NOTE Confidence: 0.89158452875

00:46:50.480 --> 00:46:53.888 which is necessary to put it

NOTE Confidence: 0.89158452875

00:46:53.888 --> 00:46:55.592 into clinical use.

NOTE Confidence: 0.89158452875

00:46:55.600 --> 00:46:57.898 Here's validation in the research setting.

NOTE Confidence: 0.89158452875

00:46:57.900 --> 00:47:01.407 These are the different types of experiments.

NOTE Confidence: 0.89158452875

00:47:01.410 --> 00:47:04.674 And then let's, let's not do mine, let's do,

NOTE Confidence: 0.89158452875

00:47:04.674 --> 00:47:06.714 let's do annyas, let's do the dry,

NOTE Confidence: 0.89158452875

00:47:06.714 --> 00:47:08.244 let's do the dry challenge.

NOTE Confidence: 0.89158452875

00:47:08.250 --> 00:47:11.825 So Anya wanted proteasome subunit

NOTE Confidence: 0.89158452875

00:47:11.825 --> 00:47:14.542 beta 5T and I said I'm she said

NOTE Confidence: 0.89158452875

00:47:14.542 --> 00:47:17.210 this is not commercially available.

NOTE Confidence: 0.89158452875

00:47:17.210 --> 00:47:19.359 I am so interested in this analyte

NOTE Confidence: 0.89158452875

00:47:19.359 --> 00:47:21.442 and it's not commercially available

NOTE Confidence: 0.89158452875

00:47:21.442 --> 00:47:23.086 and I'm devastated.

NOTE Confidence: 0.89158452875

00:47:23.090 --> 00:47:25.727 And I said I'm sure that I'm sure that

NOTE Confidence: 0.89158452875

00:47:25.727 --> 00:47:28.519 I can make an immunohistochemical test

NOTE Confidence: 0.89158452875

00:47:28.519 --> 00:47:31.310 to proteasome subunit beta 5T and.

NOTE Confidence: 0.89158452875

00:47:31.310 --> 00:47:32.300 And we talked about it.

NOTE Confidence: 0.89158452875

00:47:32.300 --> 00:47:34.276 I was giving I,

NOTE Confidence: 0.89158452875

00:47:34.276 --> 00:47:37.212 I Co direct a week long immunohistochemistry

NOTE Confidence: 0.89158452875

00:47:37.212 --> 00:47:39.716 course and these are three of my

NOTE Confidence: 0.89158452875

00:47:39.716 --> 00:47:41.557 lovely faculty and this is this is

NOTE Confidence: 0.89158452875

00:47:41.557 --> 00:47:43.944 what we talked about at the at the

NOTE Confidence: 0.89158452875

00:47:43.944 --> 00:47:45.810 dinner table in Montreal this summer.

NOTE Confidence: 0.89158452875

00:47:45.810 --> 00:47:48.490 And so here's and then you just have

NOTE Confidence: 0.89158452875

00:47:48.567 --> 00:47:51.855 to trace it and I call this like

NOTE Confidence: 0.89158452875

00:47:51.855 --> 00:47:53.160 immunohistochemistry Sudoku right.

NOTE Confidence: 0.89158452875

00:47:53.160 --> 00:47:55.190 And I want to I want to get to the

NOTE Confidence: 0.89158452875

00:47:55.250 --> 00:47:57.518 solution and as few steps as possible.

NOTE Confidence: 0.89158452875

00:47:57.520 --> 00:48:00.271 So all she told me was proteosome

NOTE Confidence: 0.89158452875

00:48:00.271 --> 00:48:01.450 subunit beta 5T.

NOTE Confidence: 0.89158452875

00:48:01.450 --> 00:48:03.312 And I found this paper that she

NOTE Confidence: 0.89158452875

00:48:03.312 --> 00:48:04.110 was referring to.

NOTE Confidence: 0.89158452875

00:48:04.110 --> 00:48:06.640 So it's a Japanese group

NOTE Confidence: 0.89158452875

00:48:06.640 --> 00:48:09.170 and they created their own,

NOTE Confidence: 0.89158452875

00:48:09.170 --> 00:48:12.836 I believe polyclonal antibody to to

NOTE Confidence: 0.89158452875

00:48:12.836 --> 00:48:15.670 this proteosome subunit beta 5T.

00:48:15.670 --> 00:48:18.234 Fascinatingly, you know proteasomes,

00:48:18.234 --> 00:48:20.988 they're they're cool, they have,

00:48:20.988 --> 00:48:22.230 they have lids,

00:48:22.230 --> 00:48:24.554 they have a cylinder body and they

00:48:24.554 --> 00:48:26.378 have bottoms, they have subunits.

00:48:26.378 --> 00:48:29.990 And the thymus has its a unique proteosome,

00:48:29.990 --> 00:48:31.345 totally different than the proteosome

00:48:31.345 --> 00:48:33.169 and the whole rest of the body.

00:48:33.170 --> 00:48:34.698 Because in the thymus,

00:48:34.698 --> 00:48:36.990 you need to use the proteosome

00:48:37.067 --> 00:48:39.074 to process antigens, to present,

00:48:39.074 --> 00:48:41.140 to grow up, to grow up T cells.

00:48:41.140 --> 00:48:42.184 So that's the,

00:48:42.184 --> 00:48:44.272 that's the science behind this thing.

00:48:44.280 --> 00:48:45.918 And then the first thing that

00:48:45.918 --> 00:48:47.575 I had to solve is, well,

NOTE Confidence: 0.89158452875

00:48:47.575 --> 00:48:50.372 I needed to know what the gene was and

NOTE Confidence: 0.89158452875

00:48:50.372 --> 00:48:52.276 it wasn't clear what the gene was,

NOTE Confidence: 0.89158452875

00:48:52.280 --> 00:48:54.584 but just Googling around I found

NOTE Confidence: 0.89158452875

00:48:54.584 --> 00:48:55.736 a couple different.

NOTE Confidence: 0.833046176071429

00:48:55.740 --> 00:48:57.716 So there's PSMB 5.

NOTE Confidence: 0.833046176071429

00:48:57.716 --> 00:49:01.732 And then I started and then it turned

NOTE Confidence: 0.833046176071429

00:49:01.732 --> 00:49:05.508 out to actually be PSMB 11 was was

NOTE Confidence: 0.833046176071429

00:49:05.620 --> 00:49:09.646 the gene that encodes this proteasome

NOTE Confidence: 0.833046176071429

00:49:09.646 --> 00:49:14.588 subunit beta beta 5T and the PSMB 5 is

NOTE Confidence: 0.833046176071429

00:49:14.588 --> 00:49:18.700 actually the the T stands for thymus,

NOTE Confidence: 0.833046176071429

00:49:18.700 --> 00:49:22.244 thymus specific. So I started with PSMB 5,

NOTE Confidence: 0.833046176071429

00:49:22.250 --> 00:49:24.749 but that's not the thymus specific one.

NOTE Confidence: 0.833046176071429

00:49:24.750 --> 00:49:28.246 So I found this paper and I found just

NOTE Confidence: 0.833046176071429

00:49:28.246 --> 00:49:29.950 that there were only four papers.

NOTE Confidence: 0.833046176071429

00:49:29.950 --> 00:49:33.090 That were published with immunohistochemistry

NOTE Confidence: 0.833046176071429

00:49:33.090 --> 00:49:35.602 with this diagnostic analyte.

NOTE Confidence: 0.833046176071429

00:49:35.610 --> 00:49:38.109 And I would just dig into the,

NOTE Confidence: 0.833046176071429

00:49:38.110 --> 00:49:41.510 dig into the methods and and you have to dig

NOTE Confidence: 0.833046176071429

00:49:41.595 --> 00:49:44.763 and then dig and dig it's detective work.

NOTE Confidence: 0.833046176071429

00:49:44.770 --> 00:49:46.746 So the paper that Anya was referring to

NOTE Confidence: 0.833046176071429

00:49:46.746 --> 00:49:48.736 that was published in AMJ Surge path,

NOTE Confidence: 0.833046176071429

00:49:48.740 --> 00:49:50.080 they said C prior,

NOTE Confidence: 0.833046176071429

00:49:50.080 --> 00:49:53.438 so I kept going back C prior, C prior,

NOTE Confidence: 0.833046176071429

00:49:53.438 --> 00:49:54.974 here's some supplementary material

NOTE Confidence: 0.833046176071429

00:49:54.974 --> 00:49:57.771 and it was a polyclonal that they

NOTE Confidence: 0.833046176071429

00:49:57.771 --> 00:50:00.550 had produced in their lab that wasn't

NOTE Confidence: 0.833046176071429

00:50:00.626 --> 00:50:03.368 commercialized and so was not available.

NOTE Confidence: 0.833046176071429

00:50:03.370 --> 00:50:06.238 But that's OK because I said.

NOTE Confidence: 0.833046176071429

00:50:06.240 --> 00:50:09.960 Basic science is $160 billion

NOTE Confidence: 0.833046176071429

00:50:09.960 --> 00:50:10.858 annual industry,

NOTE Confidence: 0.833046176071429

00:50:10.858 --> 00:50:14.001 and I said there are usually hundreds

NOTE Confidence: 0.833046176071429

00:50:14.001 --> 00:50:16.834 of commercially available antibodies

NOTE Confidence: 0.833046176071429

00:50:16.834 --> 00:50:19.898 to any immunohistochemical target.

NOTE Confidence: 0.833046176071429

00:50:19.900 --> 00:50:22.564 And so I just started this is bio compared,

NOTE Confidence: 0.833046176071429

00:50:22.570 --> 00:50:24.038 this is the dumb,

NOTE Confidence: 0.833046176071429

00:50:24.038 --> 00:50:26.240 this is the dumb database and

NOTE Confidence: 0.833046176071429

00:50:26.323 --> 00:50:28.588 this this antibody that Anya,

NOTE Confidence: 0.833046176071429

00:50:28.590 --> 00:50:30.070 who is an expert,

NOTE Confidence: 0.833046176071429

00:50:30.070 --> 00:50:33.039 she is the IHC lab director at Mayo,

NOTE Confidence: 0.833046176071429

00:50:33.040 --> 00:50:35.476 said this is an antibody that is

NOTE Confidence: 0.833046176071429

00:50:35.476 --> 00:50:36.520 not commercially available.

NOTE Confidence: 0.833046176071429

00:50:36.520 --> 00:50:40.220 There are 63 different commercially

NOTE Confidence: 0.833046176071429

00:50:40.220 --> 00:50:43.920 available antibodies to PSMB 11.

NOTE Confidence: 0.833046176071429

00:50:43.920 --> 00:50:47.054 Now that's a problem because I can't test 63,

NOTE Confidence: 0.833046176071429

00:50:47.054 --> 00:50:48.458 I can only test a few.

NOTE Confidence: 0.842395131111111

00:50:50.500 --> 00:50:52.876 So then I applied it to let's use a,

NOTE Confidence: 0.842395131111111

00:50:52.880 --> 00:50:54.840 let's use a finer screen.

NOTE Confidence: 0.842395131111111

00:50:54.840 --> 00:50:58.179 And then so here's the antibody pedia.

NOTE Confidence: 0.842395131111111

00:50:58.180 --> 00:50:59.636 And. And so again,

NOTE Confidence: 0.842395131111111

00:50:59.636 --> 00:51:02.266 we're looking for the green circles and

NOTE Confidence: 0.842395131111111

00:51:02.266 --> 00:51:04.919 so we've got some more promising targets.

NOTE Confidence: 0.842395131111111

00:51:04.920 --> 00:51:06.798 And then here's the bench side.

NOTE Confidence: 0.842395131111111

00:51:06.800 --> 00:51:09.833 And I ended up going with the bench side.

NOTE Confidence: 0.842395131111111

00:51:09.840 --> 00:51:13.024 And I found from looking at these figures,

NOTE Confidence: 0.842395131111111

00:51:13.030 --> 00:51:14.910 actually this figure here,

NOTE Confidence: 0.842395131111111

00:51:14.910 --> 00:51:17.730 this is a figure that demonstrates

NOTE Confidence: 0.842395131111111

00:51:17.813 --> 00:51:20.589 that I want to see which is nuclear.

NOTE Confidence: 0.842395131111111

00:51:20.590 --> 00:51:22.874 The nuclear staining in

NOTE Confidence: 0.842395131111111

00:51:22.874 --> 00:51:24.587 thymic epithelial cells.

NOTE Confidence: 0.842395131111111

00:51:24.590 --> 00:51:26.270 And so this is the antibody.

NOTE Confidence: 0.842395131111111

00:51:26.270 --> 00:51:28.195 This is the antibody that I that

NOTE Confidence: 0.842395131111111

00:51:28.195 --> 00:51:30.038 I proposed to Anya that she get

NOTE Confidence: 0.842395131111111

00:51:30.038 --> 00:51:32.396 and and work up in her lab for

NOTE Confidence: 0.842395131111111

00:51:32.396 --> 00:51:33.686 this diagnostic application.

NOTE Confidence: 0.842395131111111

00:51:33.690 --> 00:51:35.580 Now the icing on the cake is if in

NOTE Confidence: 0.842395131111111

00:51:35.580 --> 00:51:37.749 the last couple of months we actually

NOTE Confidence: 0.842395131111111

00:51:37.749 --> 00:51:39.569 had had the opportunity to do it.

NOTE Confidence: 0.842395131111111

00:51:39.570 --> 00:51:41.922 I pushed and pushed to do it

NOTE Confidence: 0.842395131111111

00:51:41.922 --> 00:51:44.369 for the uscap deadline and she,

NOTE Confidence: 0.842395131111111

00:51:44.370 --> 00:51:45.693 because she's European,

NOTE Confidence: 0.842395131111111

00:51:45.693 --> 00:51:47.898 was thoughtfully like on vacation

NOTE Confidence: 0.842395131111111

00:51:47.898 --> 00:51:52.150 for six weeks in Germany. So.

NOTE Confidence: 0.842395131111111

00:51:52.150 --> 00:51:53.630 And then actually this is,

NOTE Confidence: 0.842395131111111

00:51:53.630 --> 00:51:54.968 you know, this is a really,

NOTE Confidence: 0.842395131111111

00:51:54.970 --> 00:51:57.880 really good place to stop because

NOTE Confidence: 0.842395131111111

00:51:57.880 --> 00:52:01.470 here's the next step I said you can you

NOTE Confidence: 0.842395131111111

00:52:01.470 --> 00:52:04.490 can do all of the validation in silico,

NOTE Confidence: 0.842395131111111

00:52:04.490 --> 00:52:05.496 in silico.

NOTE Confidence: 0.842395131111111

00:52:05.496 --> 00:52:10.221 And so this is I guess who in the

NOTE Confidence: 0.842395131111111

00:52:10.221 --> 00:52:14.183 room knows what C bio portal is.

NOTE Confidence: 0.842395131111111

00:52:14.190 --> 00:52:14.747 Great.

NOTE Confidence: 0.842395131111111

00:52:14.747 --> 00:52:18.089 So everybody in the room should

NOTE Confidence: 0.842395131111111

00:52:18.089 --> 00:52:21.320 know what C bioportal is.

NOTE Confidence: 0.842395131111111

00:52:21.320 --> 00:52:22.770 It is this for me,

NOTE Confidence: 0.842395131111111

00:52:22.770 --> 00:52:26.934 it is the single most useful and

NOTE Confidence: 0.842395131111111

00:52:26.934 --> 00:52:29.550 user-friendly bioinformatics tool

NOTE Confidence: 0.842395131111111

00:52:29.550 --> 00:52:35.048 that you can use to analyze quickly

NOTE Confidence: 0.842395131111111

00:52:35.048 --> 00:52:38.462 and so easily both molecular genetic

NOTE Confidence: 0.842395131111111

00:52:38.462 --> 00:52:41.286 data and gene expression profiling

NOTE Confidence: 0.842395131111111

00:52:41.286 --> 00:52:45.570 data and the main source of the data.

NOTE Confidence: 0.842395131111111

00:52:45.570 --> 00:52:49.017 Is the TCG a date data sets and so

NOTE Confidence: 0.842395131111111

00:52:49.017 --> 00:52:51.615 there are pan cancer datasets and

NOTE Confidence: 0.842395131111111

00:52:51.615 --> 00:52:55.790 so you you go to the you go to C

NOTE Confidence: 0.842395131111111

00:52:55.790 --> 00:52:58.298 bioportal and you you can click like

NOTE Confidence: 0.842395131111111

00:52:58.298 --> 00:53:00.794 click a button and it says I want to

NOTE Confidence: 0.842395131111111

00:53:00.794 --> 00:53:02.719 analyze all the TCG a tumor types

NOTE Confidence: 0.842395131111111

00:53:02.719 --> 00:53:04.750 and it's like 30 tumor types and

NOTE Confidence: 0.842395131111111

00:53:04.750 --> 00:53:07.720 then at the bottom you just type in the gene.

NOTE Confidence: 0.842395131111111

00:53:07.720 --> 00:53:10.071 So I typed in PS:,

NOTE Confidence: 0.842395131111111

00:53:10.071 --> 00:53:13.075 MB 11 and then you hit a couple buttons like

NOTE Confidence: 0.842395131111111

00:53:13.075 --> 00:53:15.874 it changes a little bit from time to time.

NOTE Confidence: 0.842395131111111

00:53:15.880 --> 00:53:17.287 You have to know where to click.

NOTE Confidence: 0.842395131111111

00:53:17.290 --> 00:53:20.349 You click plots. And then I sorted

NOTE Confidence: 0.842395131111111

00:53:20.349 --> 00:53:23.808 these plots by median gene expression.

NOTE Confidence: 0.842395131111111

00:53:23.810 --> 00:53:27.570 And so in the TCG a data set.

NOTE Confidence: 0.842395131111111

00:53:27.570 --> 00:53:31.188 This is expression of PSMB 11.

NOTE Confidence: 0.842395131111111

00:53:31.190 --> 00:53:32.598 And it's nothing. Nothing.

NOTE Confidence: 0.842395131111111

00:53:32.598 --> 00:53:33.810 Nothing. Nothing. Nothing.

NOTE Confidence: 0.842395131111111

00:53:33.810 --> 00:53:36.715 Nothing. Oh my God. And guess what?

NOTE Confidence: 0.842395131111111

00:53:36.715 --> 00:53:39.085 In the TCG a data set.

NOTE Confidence: 0.842395131111111

00:53:39.090 --> 00:53:41.846 What does THYM mean?

NOTE Confidence: 0.842395131111111

00:53:41.846 --> 00:53:43.310 It means thymoma.

NOTE Confidence: 0.842395131111111

00:53:43.310 --> 00:53:46.768 So before Anya even does this experiment.

NOTE Confidence: 0.842395131111111

00:53:46.770 --> 00:53:47.014 I,

NOTE Confidence: 0.842395131111111

00:53:47.014 --> 00:53:49.210 I know that this is a a winner and

NOTE Confidence: 0.842395131111111

00:53:49.276 --> 00:53:51.488 so a lot of the the diagnostic

NOTE Confidence: 0.842395131111111

00:53:51.488 --> 00:53:53.691 markers that that I you know that I

NOTE Confidence: 0.842395131111111

00:53:53.691 --> 00:53:56.008 ran out of time to share with you.

NOTE Confidence: 0.842395131111111

00:53:56.008 --> 00:53:56.760 I do,

NOTE Confidence: 0.842395131111111

00:53:56.760 --> 00:53:58.848 I do this and I and I do this

NOTE Confidence: 0.842395131111111

00:53:58.848 --> 00:54:01.126 not only to sort of confirm

NOTE Confidence: 0.842395131111111

00:54:01.126 --> 00:54:03.096 specificity but also to identify

NOTE Confidence: 0.842395131111111

00:54:03.173 --> 00:54:05.639 additional diagnostic applications.

NOTE Confidence: 0.842395131111111

00:54:05.640 --> 00:54:07.936 And so the the best example of that

00:54:07.936 --> 00:54:10.598 is IGF 2 where it was published

00:54:10.598 --> 00:54:12.613 in this adrenal cortical carcinoma

00:54:12.689 --> 00:54:14.702 space, adrenal cortical carcinoma

00:54:14.702 --> 00:54:16.838 versus adenoma and Jason?

00:54:16.840 --> 00:54:18.784 My good friend said and I'll sort of

00:54:18.784 --> 00:54:20.818 stop with this story you said what do

00:54:20.818 --> 00:54:22.780 you know about this is this is how

00:54:22.780 --> 00:54:24.668 he interacts with me what do you know

00:54:24.668 --> 00:54:26.740 about IGF two and I said Ohh Sylvia

00:54:26.804 --> 00:54:29.233 and Oscar published it there and you

00:54:29.233 --> 00:54:31.050 know they're endocrine pathologist.

00:54:31.050 --> 00:54:32.766 It works great for this diagnostic

00:54:32.766 --> 00:54:33.910 application that I shared.

00:54:33.910 --> 00:54:35.752 He said I brought this antibody

00:54:35.752 --> 00:54:38.260 up and I'd love it and I want to

NOTE Confidence: 0.863734391904762

00:54:38.260 --> 00:54:40.364 do a project with it and we'll

NOTE Confidence: 0.863734391904762

00:54:40.364 --> 00:54:43.046 we'll what project can we do?

NOTE Confidence: 0.863734391904762

00:54:43.050 --> 00:54:45.138 And and I and I I said well we

NOTE Confidence: 0.863734391904762

00:54:45.138 --> 00:54:47.120 can't do the same project again.

NOTE Confidence: 0.863734391904762

00:54:47.120 --> 00:54:49.446 And so I said, well, let's take a look.

NOTE Confidence: 0.863734391904762

00:54:49.446 --> 00:54:51.380 Let's take a look at this in.

NOTE Confidence: 0.825355993529412

00:54:54.170 --> 00:54:56.195 I'll just pull up the because I want to

NOTE Confidence: 0.825355993529412

00:54:56.195 --> 00:54:58.165 show off see bio portal one more time.

NOTE Confidence: 0.901939468333333

00:55:01.200 --> 00:55:02.598 And these are all the different,

NOTE Confidence: 0.901939468333333

00:55:02.600 --> 00:55:05.561 you know, I I I use other tools to

NOTE Confidence: 0.901939468333333

00:55:05.561 --> 00:55:07.266 visualize gene expression profiling

NOTE Confidence: 0.901939468333333

00:55:07.266 --> 00:55:10.680 as well this GTX alumina and bio GPS.

NOTE Confidence: 0.901939468333333

00:55:10.680 --> 00:55:13.520 I often just use Wikipedia.

NOTE Confidence: 0.901939468333333

00:55:13.520 --> 00:55:16.040 But here's the C bio portal.

NOTE Confidence: 0.901939468333333

00:55:16.040 --> 00:55:19.028 I clicked tcga pan Cancer Atlas

NOTE Confidence: 0.901939468333333

00:55:19.028 --> 00:55:24.989 studies query by Gene, entered IGF 2.

NOTE Confidence: 0.901939468333333

00:55:24.990 --> 00:55:27.110 And here's the plot.

NOTE Confidence: 0.901939468333333

00:55:27.110 --> 00:55:31.510 And actually, so this is high.

NOTE Confidence: 0.901939468333333

00:55:31.510 --> 00:55:34.318 And this is high.

NOTE Confidence: 0.901939468333333

00:55:34.320 --> 00:55:37.848 And this is adrenal cortical carcinoma.

NOTE Confidence: 0.901939468333333

00:55:37.850 --> 00:55:40.800 And this is paraganglioma pheochromocytoma.

NOTE Confidence: 0.901939468333333

00:55:40.800 --> 00:55:43.780 And so by visualizing this,

NOTE Confidence: 0.901939468333333

00:55:43.780 --> 00:55:46.692 I knew that IGF two would be highly

NOTE Confidence: 0.901939468333333

00:55:46.692 --> 00:55:49.850 expressed in paraganglioma pheochromocytoma.

NOTE Confidence: 0.901939468333333

00:55:49.850 --> 00:55:51.762 And then I just have to go do

NOTE Confidence: 0.901939468333333

00:55:51.762 --> 00:55:52.948 the experiment to prove it.

NOTE Confidence: 0.901939468333333

00:55:52.950 --> 00:55:55.902 What's not in the TCG a data set

NOTE Confidence: 0.901939468333333

00:55:55.902 --> 00:55:57.569 next neuroendocrine tumor isn't.

NOTE Confidence: 0.901939468333333

00:55:57.570 --> 00:55:59.970 So I didn't know that.

NOTE Confidence: 0.901939468333333

00:55:59.970 --> 00:56:01.806 I didn't know if this meant

NOTE Confidence: 0.901939468333333

00:56:01.806 --> 00:56:04.693 that IGF two was going to be a

NOTE Confidence: 0.901939468333333

00:56:04.693 --> 00:56:06.281 general neuroendocrine marker or

NOTE Confidence: 0.901939468333333

00:56:06.281 --> 00:56:08.400 perhaps it would be specific.

NOTE Confidence: 0.901939468333333

00:56:08.400 --> 00:56:10.944 In the peripheral versus net differential

NOTE Confidence: 0.901939468333333

00:56:10.944 --> 00:56:14.149 and it was the IT was the latter

NOTE Confidence: 0.901939468333333

00:56:14.149 --> 00:56:16.670 that that I confirmed and IGF two.

NOTE Confidence: 0.901939468333333

00:56:16.670 --> 00:56:18.700 We talked about analytic robustness

NOTE Confidence: 0.901939468333333

00:56:18.700 --> 00:56:21.724 this morning with God at three and

NOTE Confidence: 0.901939468333333

00:56:21.724 --> 00:56:23.104 paraganglioma pheochromocytoma and

NOTE Confidence: 0.901939468333333

00:56:23.104 --> 00:56:25.971 I said TH is incredibly analytically

NOTE Confidence: 0.901939468333333

00:56:25.971 --> 00:56:28.426 robust but it's only expressed

NOTE Confidence: 0.901939468333333

00:56:28.426 --> 00:56:31.790 by sympathetic paragangliomas.

NOTE Confidence: 0.901939468333333

00:56:31.790 --> 00:56:34.240 IGF two is incredibly analytically

NOTE Confidence: 0.901939468333333

00:56:34.240 --> 00:56:36.690 robust that means it's expressed

NOTE Confidence: 0.901939468333333

00:56:36.772 --> 00:56:39.404 even if the sample set on the bench.

NOTE Confidence: 0.901939468333333

00:56:39.410 --> 00:56:42.238 For a month and it's nearly 100%

NOTE Confidence: 0.901939468333333

00:56:42.240 --> 00:56:45.152 sensitive in Paraganglioma pheochromocytoma.

NOTE Confidence: 0.901939468333333

00:56:45.152 --> 00:56:50.078 So again, like simple, simple tools,

NOTE Confidence: 0.901939468333333

00:56:50.080 --> 00:56:51.916 C bio portal, Oh my God,

NOTE Confidence: 0.901939468333333

00:56:51.920 --> 00:56:54.400 you know these databases. Me.

NOTE Confidence: 0.901939468333333

00:56:54.400 --> 00:56:56.628 You know, talk, talk to me, workshop,

NOTE Confidence: 0.901939468333333

00:56:56.628 --> 00:56:58.660 your workshop, your project.

NOTE Confidence: 0.901939468333333

00:56:58.660 --> 00:57:00.770 There are hundreds of commercially

NOTE Confidence: 0.901939468333333

00:57:00.770 --> 00:57:02.880 available antibodies to every analyte

NOTE Confidence: 0.901939468333333

00:57:02.943 --> 00:57:04.815 that you might be interested in.

NOTE Confidence: 0.901939468333333

00:57:04.820 --> 00:57:07.760 You can be a wildly successful

NOTE Confidence: 0.901939468333333

00:57:07.760 --> 00:57:08.882 anatomic pathologist.

NOTE Confidence: 0.901939468333333

00:57:08.882 --> 00:57:11.687 Even if your research budget

NOTE Confidence: 0.901939468333333

00:57:11.687 --> 00:57:13.126 is $300.00 a year,

NOTE Confidence: 0.901939468333333

00:57:13.126 --> 00:57:16.064 and I'll stop and take your and take your

NOTE Confidence: 0.901939468333333

00:57:16.064 --> 00:57:17.690 questions, thank thank you very much.

NOTE Confidence: 0.901939468333333

00:57:17.690 --> 00:57:18.845 I had a I had a blast.

NOTE Confidence: 0.901939468333333

00:57:18.850 --> 00:57:20.010 I always have a blast.

NOTE Confidence: 0.901939468333333

00:57:20.010 --> 00:57:21.140 I always have a blast.

NOTE Confidence: 0.8517446

00:57:28.770 --> 00:57:29.390 Questions.

NOTE Confidence: 0.627831665

00:57:32.180 --> 00:57:33.288 Maybe I start first.

NOTE Confidence: 0.54945062

00:57:34.770 --> 00:57:36.048 Vision of publications.

NOTE Confidence: 0.70763123

00:57:38.580 --> 00:57:38.790 One

NOTE Confidence: 0.70054972

00:57:40.000 --> 00:57:41.912 is that this gene so good

NOTE Confidence: 0.70054972

00:57:41.912 --> 00:57:45.020 for identified this protein.

NOTE Confidence: 0.70054972

00:57:45.020 --> 00:57:47.760 I got all the states, yeah, never,

NOTE Confidence: 0.70054972

00:57:47.760 --> 00:57:52.740 almost never to the original study.

NOTE Confidence: 0.70054972

00:57:52.740 --> 00:57:54.300 All my sins are there. Yeah.

NOTE Confidence: 0.70054972

00:57:54.300 --> 00:57:56.370 So in this situation, OK,

NOTE Confidence: 0.7210180775

00:57:57.120 --> 00:57:59.180 so the basic search research

NOTE Confidence: 0.7210180775

00:57:59.180 --> 00:58:01.348 on my thing doesn't work.

NOTE Confidence: 0.7210180775

00:58:01.348 --> 00:58:03.535 So, you know, I I I will say

NOTE Confidence: 0.7210180775

93

00:58:03.535 --> 00:58:04.990 because I'm very skeptical.

NOTE Confidence: 0.7210180775

00:58:04.990 --> 00:58:08.640 Very skeptical. There are.

NOTE Confidence: 0.7210180775

00:58:08.640 --> 00:58:12.075 I have had multiple instances where

NOTE Confidence: 0.7210180775

00:58:12.075 --> 00:58:14.865 a new biomarker is published in

NOTE Confidence: 0.7210180775

00:58:14.865 --> 00:58:17.508 the diagnostic pathology space,

NOTE Confidence: 0.7210180775

00:58:17.510 --> 00:58:19.166 usually in modern pathology.

NOTE Confidence: 0.7210180775

00:58:19.166 --> 00:58:22.110 And the one that comes to mind,

NOTE Confidence: 0.7210180775

00:58:22.110 --> 00:58:24.130 there was a one.

NOTE Confidence: 0.7210180775

00:58:24.130 --> 00:58:26.150 Like a wonderful appearing

NOTE Confidence: 0.7210180775

00:58:26.150 --> 00:58:27.702 immunohistochemical marker that

NOTE Confidence: 0.7210180775

00:58:27.702 --> 00:58:30.047 was published as the Diagnostic

NOTE Confidence: 0.7210180775

00:58:30.047 --> 00:58:32.500 marker of anaplastic thyroid cancer.

NOTE Confidence: 0.7210180775

00:58:32.500 --> 00:58:34.792 And they discovered it by gene

NOTE Confidence: 0.7210180775

00:58:34.792 --> 00:58:37.281 expression profiling and and I got the

NOTE Confidence: 0.7210180775

00:58:37.281 --> 00:58:40.114 antibody and it didn't and it didn't work.

NOTE Confidence: 0.7210180775

00:58:40.114 --> 00:58:42.169 So so many antibodies don't

NOTE Confidence: 0.7210180775

00:58:42.169 --> 00:58:44.488 work and that's the problem.

NOTE Confidence: 0.7210180775

00:58:44.490 --> 00:58:46.098 And that's the problem.

NOTE Confidence: 0.7210180775

00:58:46.098 --> 00:58:48.108 The problem many antibodies don't

NOTE Confidence: 0.7210180775

00:58:48.108 --> 00:58:50.820 work because foreign antibody to work

NOTE Confidence: 0.7210180775

00:58:50.820 --> 00:58:53.060 in immunohistochemistry is a mirror.

NOTE Confidence: 0.7210180775

00:58:53.060 --> 00:58:55.682 Is a miracle because those antigens

NOTE Confidence: 0.7210180775

00:58:55.682 --> 00:58:59.137 are so so deranged because of formal

NOTE Confidence: 0.7210180775

00:58:59.137 --> 00:59:02.389 and fixation and because of antigenic

NOTE Confidence: 0.7210180775

00:59:02.389 --> 00:59:05.279 degradation with cold ischemia time and.

NOTE Confidence: 0.7210180775

00:59:05.280 --> 00:59:07.070 And so I was disappointed,

NOTE Confidence: 0.7210180775

00:59:07.070 --> 00:59:07.446 like.

NOTE Confidence: 0.7210180775

00:59:07.446 --> 00:59:08.198 I'm skeptical.

NOTE Confidence: 0.7210180775

00:59:08.198 --> 00:59:10.830 I think that some science is that

NOTE Confidence: 0.7210180775

00:59:10.906 --> 00:59:13.146 one of the reasons that it doesn't

NOTE Confidence: 0.7210180775

00:59:13.146 --> 00:59:15.865 work is the science is fate, right?

NOTE Confidence: 0.7210180775

00:59:15.865 --> 00:59:17.560 The the immunohistochemical

NOTE Confidence: 0.7210180775

00:59:17.560 --> 00:59:19.820 results are are fate.

NOTE Confidence: 0.7210180775

00:59:19.820 --> 00:59:22.740 Another reason is you know.

NOTE Confidence: 0.7210180775

00:59:22.740 --> 00:59:23.937 That you know,

NOTE Confidence: 0.7210180775

00:59:23.937 --> 00:59:25.932 it's not necessarily that the

NOTE Confidence: 0.7210180775

00:59:25.932 --> 00:59:27.240 analyte is wrong.

NOTE Confidence: 0.7210180775

00:59:27.240 --> 00:59:30.040 It's maybe that's not the best antibody.

NOTE Confidence: 0.7210180775

00:59:30.040 --> 00:59:32.416 And so, like in that setting,

NOTE Confidence: 0.7210180775

00:59:32.420 --> 00:59:35.660 I would encourage you to not give up.

NOTE Confidence: 0.7210180775

00:59:35.660 --> 00:59:37.851 I would encourage you to at least

NOTE Confidence: 0.7210180775

00:59:37.851 --> 00:59:40.018 try a second and a third time.

NOTE Confidence: 0.7210180775

00:59:40.020 --> 00:59:42.114 And I would encourage you to

NOTE Confidence: 0.7210180775

00:59:42.114 --> 00:59:44.224 try the antibody pedia and the

NOTE Confidence: 0.7210180775

00:59:44.224 --> 00:59:45.834 bench and the bench side.

NOTE Confidence: 0.7210180775

00:59:45.840 --> 00:59:49.522 I trust that more than a single

NOTE Confidence: 0.7210180775

00:59:49.522 --> 00:59:52.788 published paper where the authors are.

NOTE Confidence: 0.7210180775

00:59:52.790 --> 00:59:53.714 Uh, conflicted.

NOTE Confidence: 0.7210180775

00:59:53.714 --> 00:59:55.100 They're incentivized to

NOTE Confidence: 0.7210180775

00:59:55.100 --> 00:59:56.948 have a positive result.

NOTE Confidence: 0.7210180775

00:59:56.950 --> 00:59:57.533 So.

NOTE Confidence: 0.7210180775

00:59:57.533 --> 01:00:00.448 So I trust those databases

NOTE Confidence: 0.7210180775

01:00:00.448 --> 01:00:03.590 more than any single paper.

NOTE Confidence: 0.7210180775

01:00:03.590 --> 01:00:04.534 And then there are,

NOTE Confidence: 0.7210180775

01:00:04.534 --> 01:00:05.006 you know,

NOTE Confidence: 0.7210180775

01:00:05.010 --> 01:00:07.458 there are vendors that I intrinsically

NOTE Confidence: 0.7210180775

01:00:07.458 --> 01:00:09.871 trust more because they do better

NOTE Confidence: 0.7210180775

01:00:09.871 --> 01:00:12.001 science and like 2 great vendors

NOTE Confidence: 0.7210180775

01:00:12.001 --> 01:00:14.376 for primary antibodies, abcam,

NOTE Confidence: 0.7210180775

01:00:14.376 --> 01:00:18.706 wonderful cell signaling, another standout.

NOTE Confidence: 0.7210180775

01:00:18.710 --> 01:00:20.570 There are many other, you know,

NOTE Confidence: 0.7210180775

01:00:20.570 --> 01:00:23.130 again like exceptional, lovely, right.

NOTE Confidence: 0.7210180775

01:00:23.130 --> 01:00:25.142 And these are exceptional.

NOTE Confidence: 0.7210180775

01:00:25.142 --> 01:00:28.160 And then I'll mention one other

NOTE Confidence: 0.7210180775

01:00:28.256 --> 01:00:30.538 thing that that you can try that

NOTE Confidence: 0.7210180775

01:00:30.538 --> 01:00:32.710 you can try that I can't try,

NOTE Confidence: 0.7210180775

01:00:32.710 --> 01:00:34.298 but I mentioned it.

NOTE Confidence: 0.7210180775

01:00:34.298 --> 01:00:37.232 Is Don Pot asked about albumin ish

NOTE Confidence: 0.7210180775

01:00:37.232 --> 01:00:40.515 this morning and albumin ish is only

NOTE Confidence: 0.7210180775

01:00:40.515 --> 01:00:43.356 automate automated on a like a bond three.

NOTE Confidence: 0.7210180775

01:00:43.360 --> 01:00:45.696 I don't have a like a bond 3.

NOTE Confidence: 0.7210180775

01:00:45.700 --> 01:00:49.516 If you have a like of bond three

NOTE Confidence: 0.7210180775

01:00:49.516 --> 01:00:53.695 you can make an RNA scope probe

NOTE Confidence: 0.7210180775

01:00:53.695 --> 01:00:57.282 to any to literally anything and

NOTE Confidence: 0.7210180775

01:00:57.282 --> 01:00:59.236 so and I've been workshopping

NOTE Confidence: 0.7210180775

01:00:59.236 --> 01:01:01.630 this idea with a guy called

NOTE Confidence: 0.7210180775

01:01:01.706 --> 01:01:03.846 Greg Sharvil who's a sarcoma.

NOTE Confidence: 0.7210180775

01:01:03.850 --> 01:01:06.725 Pathologists at Stanford and and

NOTE Confidence: 0.7210180775

01:01:06.725 --> 01:01:09.479 there are some, there are some,

NOTE Confidence: 0.7210180775

01:01:09.479 --> 01:01:11.880 even though the genetics are on point

NOTE Confidence: 0.7210180775

01:01:11.954 --> 01:01:14.285 and the gene expression is on point,

NOTE Confidence: 0.7210180775

01:01:14.290 --> 01:01:16.855 that will never succeed as

NOTE Confidence: 0.7210180775

01:01:16.855 --> 01:01:18.907 immunohistochemical assays because M,

NOTE Confidence: 0.7210180775

01:01:18.910 --> 01:01:21.430 RNA and protein are correlated.

NOTE Confidence: 0.7210180775

01:01:21.430 --> 01:01:24.420 But the R-squared is like

NOTE Confidence: 0.7210180775

01:01:24.420 --> 01:01:28.750 not .9 and so there are some.

NOTE Confidence: 0.7210180775

01:01:28.750 --> 01:01:29.674 You know,

NOTE Confidence: 0.7210180775

01:01:29.674 --> 01:01:32.446 some targets that are incredibly specific,

NOTE Confidence: 0.7210180775

01:01:32.450 --> 01:01:34.650 but there's such low abundance

NOTE Confidence: 0.7210180775

01:01:34.650 --> 01:01:36.410 that you can never,

NOTE Confidence: 0.7210180775

01:01:36.410 --> 01:01:38.942 even though we do signal amplification

NOTE Confidence: 0.7210180775

01:01:38.942 --> 01:01:39.786 and immunohistochemistry,

NOTE Confidence: 0.92976154875

01:01:39.790 --> 01:01:42.290 you can never get the

NOTE Confidence: 0.92976154875

01:01:42.290 --> 01:01:43.790 immunohistochemistry to work.

NOTE Confidence: 0.92976154875

01:01:43.790 --> 01:01:45.606 And for those analytes,

NOTE Confidence: 0.92976154875

01:01:45.606 --> 01:01:48.590 if you really are committed to a,

NOTE Confidence: 0.92976154875

01:01:48.590 --> 01:01:52.070 to a, to a specific target for a

NOTE Confidence: 0.92976154875

01:01:52.070 --> 01:01:54.030 specific diagnostic application,

NOTE Confidence: 0.92976154875

01:01:54.030 --> 01:01:56.564 I would encourage you to, you know,

NOTE Confidence: 0.92976154875

01:01:56.564 --> 01:01:59.180 first try a couple more immunos and try.

NOTE Confidence: 0.92976154875

01:01:59.180 --> 01:02:01.040 Try bench sign antibody pedia.

NOTE Confidence: 0.92976154875

01:02:01.040 --> 01:02:03.371 But but the next thing I would

NOTE Confidence: 0.92976154875

01:02:03.371 --> 01:02:05.201 encourage you to consider is

NOTE Confidence: 0.92976154875

01:02:05.201 --> 01:02:07.847 building an RNA scope assay to that,

NOTE Confidence: 0.92976154875

01:02:07.850 --> 01:02:10.076 to that, to that, to that target.

NOTE Confidence: 0.92976154875

01:02:10.080 --> 01:02:13.490 Because if the you know the M RNA don't lie,

NOTE Confidence: 0.92976154875

01:02:13.490 --> 01:02:15.394 the M RNA might not correlate with the

NOTE Confidence: 0.92976154875

01:02:15.394 --> 01:02:17.894 protein, but the M RNA don't lie so.

NOTE Confidence: 0.699021976666667

01:02:18.810 --> 01:02:19.449 What's your quick?

100

NOTE Confidence: 0.39329159

01:02:21.640 --> 01:02:22.220 The communist.

NOTE Confidence: 0.8703504

01:02:24.890 --> 01:02:25.300 Sure.

NOTE Confidence: 0.70647705

01:02:27.690 --> 01:02:28.220 Sure.

NOTE Confidence: 0.74447984

01:02:31.280 --> 01:02:31.830 Yeah.

NOTE Confidence: 0.6070417

01:02:35.790 --> 01:02:36.130 1.

NOTE Confidence: 0.68153644

01:02:38.520 --> 01:02:41.983 Sure. Yeah, I mean I, you, you,

NOTE Confidence: 0.68153644

01:02:41.983 --> 01:02:44.401 you, you probably would not be

NOTE Confidence: 0.68153644

01:02:44.401 --> 01:02:46.470 surprised that I give like.

NOTE Confidence: 0.68153644

01:02:46.470 --> 01:02:47.934 1st 1st it's really really hard

NOTE Confidence: 0.68153644

01:02:47.934 --> 01:02:49.867 for me to give a 45 minute talk.

NOTE Confidence: 0.68153644

01:02:49.870 --> 01:02:52.866 I usually I usually speak for two

NOTE Confidence: 0.68153644

01:02:52.866 --> 01:02:56.321 or three hours at a time and and of

NOTE Confidence: 0.68153644

01:02:56.321 --> 01:02:59.301 course I have hour and two hour and

NOTE Confidence: 0.68153644

01:02:59.301 --> 01:03:02.585 3 hour PDL 1 lectures and and I I

NOTE Confidence: 0.68153644

01:03:02.585 --> 01:03:04.310 mentioned you know immuno optimist,

NOTE Confidence: 0.68153644

01:03:04.310 --> 01:03:05.378 immuno pessimist,

NOTE Confidence: 0.68153644

01:03:05.378 --> 01:03:09.650 immuno realist and you know I give a

NOTE Confidence: 0.68153644

01:03:09.757 --> 01:03:14.509 PDL 1 lecture that is called PDL 1

NOTE Confidence: 0.68153644

01:03:14.509 --> 01:03:16.689 immunohistochemistry like you know.

NOTE Confidence: 0.68153644

01:03:16.690 --> 01:03:20.827 The Emperor has no clothes so uh

NOTE Confidence: 0.68153644

01:03:20.827 --> 01:03:24.196 Pete and I I gave I gave a biomarker

NOTE Confidence: 0.68153644

01:03:24.196 --> 01:03:27.051 lecture in a global in the global

NOTE Confidence: 0.68153644

01:03:27.051 --> 01:03:29.436 health space this summer and there

NOTE Confidence: 0.68153644

01:03:29.436 --> 01:03:31.770 were lots of questions about PDL

NOTE Confidence: 0.68153644

01:03:31.847 --> 01:03:34.066 one and and and there's a YouTube

NOTE Confidence: 0.68153644

01:03:34.066 --> 01:03:36.791 clip of me saying something like

NOTE Confidence: 0.68153644

01:03:36.791 --> 01:03:39.055 PDL 1 immunohistochemistry sucks.

NOTE Confidence: 0.68153644

01:03:39.060 --> 01:03:42.138 I hate it and it just loops and loops

NOTE Confidence: 0.68153644

01:03:42.138 --> 01:03:46.913 and loops and so and so my my main take on.

NOTE Confidence: 0.68153644

01:03:46.920 --> 01:03:50.128 PDL One immunohistochemistry is.

NOTE Confidence: 0.68153644

01:03:50.128 --> 01:03:54.940 It's PDL one is super important.

NOTE Confidence: 0.68153644

01:03:54.940 --> 01:03:58.774 It was a great, it was a great target,

NOTE Confidence: 0.68153644

01:03:58.780 --> 01:04:02.416 like Nobel Prize, like totally warranted.

NOTE Confidence: 0.68153644

01:04:02.420 --> 01:04:06.722 But it is an entirely unrealistic

NOTE Confidence: 0.68153644

01:04:06.722 --> 01:04:09.756 expectation for, in that space,

NOTE Confidence: 0.68153644

01:04:09.756 --> 01:04:12.948 a single analyte to reflect the

NOTE Confidence: 0.68153644

01:04:12.948 --> 01:04:16.598 entire tumor immune microenvironment.

NOTE Confidence: 0.68153644

01:04:16.600 --> 01:04:19.744 So PD1 immunohistochemistry is

NOTE Confidence: 0.68153644

01:04:19.744 --> 01:04:22.888 an inaccurate diagnostic test.

NOTE Confidence: 0.68153644

01:04:22.890 --> 01:04:26.690 It's about 60% sensitive, 60% specific.

NOTE Confidence: 0.68153644

01:04:26.690 --> 01:04:28.930 It's a coin flip.

NOTE Confidence: 0.68153644

01:04:28.930 --> 01:04:35.253 And they're ohh I I really, really,

NOTE Confidence: 0.68153644

01:04:35.253 --> 01:04:39.168 I really, really hate capitalism.

NOTE Confidence: 0.68153644

01:04:39.170 --> 01:04:42.130 And uh, Pharma really,

NOTE Confidence: 0.68153644

01:04:42.130 --> 01:04:44.350 really loves capitalism.

NOTE Confidence: 0.68153644

01:04:44.350 --> 01:04:46.634 And so, you know,

NOTE Confidence: 0.68153644

103

01:04:46.634 --> 01:04:48.918 the the drug companies,

NOTE Confidence: 0.68153644

01:04:48.920 --> 01:04:50.715 we're going to partner with

NOTE Confidence: 0.68153644

01:04:50.715 --> 01:04:52.968 the device companies and jam a

NOTE Confidence: 0.68153644

01:04:52.968 --> 01:04:54.532 companion diagnostic marker down

NOTE Confidence: 0.68153644

01:04:54.532 --> 01:04:57.004 our throats and they don't really

NOTE Confidence: 0.68153644

01:04:57.004 --> 01:04:59.249 care about the diagnostic accuracy.

NOTE Confidence: 0.68153644

01:04:59.250 --> 01:05:01.194 So PD1 immunohistochemistry sucks.

NOTE Confidence: 0.68153644

01:05:01.194 --> 01:05:03.130 I hate, I hate it.

NOTE Confidence: 0.68153644

01:05:03.130 --> 01:05:04.814 That being said, I spend,

NOTE Confidence: 0.68153644

01:05:04.814 --> 01:05:05.538 you know,

NOTE Confidence: 0.68153644

01:05:05.538 --> 01:05:09.170 hours and hours of my life talking about it.

NOTE Confidence: 0.68153644

01:05:09.170 --> 01:05:12.082 And I read every PDL 1 immunohistochemistry

NOTE Confidence: 0.68153644

01:05:12.082 --> 01:05:14.729 at the University of Iowa and

NOTE Confidence: 0.68153644

01:05:14.729 --> 01:05:16.058 PDL 1 immunohistochemistry.

NOTE Confidence: 0.68153644

01:05:16.060 --> 01:05:17.789 You know this is a good example

NOTE Confidence: 0.68153644

01:05:17.789 --> 01:05:19.580 of a bad of a bad marker.

104

NOTE Confidence: 0.68153644

01:05:19.580 --> 01:05:21.512 There's biochemistry problems

NOTE Confidence: 0.68153644

01:05:21.512 --> 01:05:24.088 and there's readout problems.

NOTE Confidence: 0.68153644

01:05:24.090 --> 01:05:26.206 So like pathologist interpretation

NOTE Confidence: 0.68153644

01:05:26.206 --> 01:05:29.380 problems and they're and they're unsolved.

NOTE Confidence: 0.68153644

01:05:29.380 --> 01:05:31.875 And my like skepticism around

NOTE Confidence: 0.68153644

01:05:31.875 --> 01:05:34.370 capitalism is pharma did not

NOTE Confidence: 0.68153644

01:05:34.460 --> 01:05:37.280 consider the biochemistry or the

NOTE Confidence: 0.68153644

01:05:37.280 --> 01:05:39.536 readout in developing the.

NOTE Confidence: 0.68153644

01:05:39.540 --> 01:05:42.075 The this diagnostic marker because

NOTE Confidence: 0.68153644

01:05:42.075 --> 01:05:44.610 they actually have no technical

NOTE Confidence: 0.68153644

01:05:44.694 --> 01:05:47.310 expertise in immunohistochemistry.

NOTE Confidence: 0.68153644

01:05:47.310 --> 01:05:50.726 So what's better than PDL one not TMB.

NOTE Confidence: 0.68153644

01:05:50.730 --> 01:05:52.950 TMB is just as bad.

NOTE Confidence: 0.68153644

01:05:52.950 --> 01:05:55.510 About 6060 MMR is wonderful

NOTE Confidence: 0.68153644

01:05:55.510 --> 01:05:58.070 if you have an MRI,

NOTE Confidence: 0.68153644

01:05:58.070 --> 01:05:58.778 MRI,

NOTE Confidence: 0.68153644

01:05:58.778 --> 01:06:03.026 immunohistochemistry or MSI is very accurate.

NOTE Confidence: 0.68153644

01:06:03.030 --> 01:06:04.054 Not 100%,

NOTE Confidence: 0.68153644

01:06:04.054 --> 01:06:07.638 but very very very you know high

NOTE Confidence: 0.68153644

01:06:07.638 --> 01:06:09.443 ninety 9899% accurate and.

NOTE Confidence: 0.68153644

01:06:09.443 --> 01:06:10.736 Is very predictive,

NOTE Confidence: 0.68153644

01:06:10.740 --> 01:06:12.044 not 100% percent predictive,

NOTE Confidence: 0.68153644

01:06:12.044 --> 01:06:13.674 but very predictive of response

NOTE Confidence: 0.68153644

01:06:13.674 --> 01:06:15.199 to checkpoint inhibition.

NOTE Confidence: 0.68153644

01:06:15.200 --> 01:06:18.154 And then I've learned so much from

NOTE Confidence: 0.68153644

01:06:18.154 --> 01:06:19.957 my collaboration and interaction

NOTE Confidence: 0.68153644

01:06:19.957 --> 01:06:23.177 with David over the last five years.

NOTE Confidence: 0.68153644

01:06:23.180 --> 01:06:27.576 The answer to the answer to the

NOTE Confidence: 0.68153644

01:06:27.576 --> 01:06:30.160 checkpoint inhibitor predictive marker

NOTE Confidence: 0.68153644

01:06:30.160 --> 01:06:32.800 is Multiplex immunofluorescence act.

NOTE Confidence: 0.68153644

01:06:32.800 --> 01:06:35.074 Actually I said it's unrealistic for

NOTE Confidence: 0.68153644

01:06:35.074 --> 01:06:37.815 a single analyte to integrate the

NOTE Confidence: 0.68153644

01:06:37.815 --> 01:06:40.119 entire tumor immune microenvironment.

NOTE Confidence: 0.68153644

01:06:40.120 --> 01:06:44.356 And there's a lovely meta analysis

NOTE Confidence: 0.68153644

01:06:44.360 --> 01:06:46.940 that was published by Janis Tobb,

NOTE Confidence: 0.82789474

01:06:46.940 --> 01:06:48.480 who's one of David's collaborators.

NOTE Confidence: 0.82789474

01:06:48.480 --> 01:06:51.384 She's a Melanoma doctorate at Hopkins

NOTE Confidence: 0.82789474

01:06:51.384 --> 01:06:55.234 that showed that the area under the

NOTE Confidence: 0.82789474

01:06:55.234 --> 01:06:57.670 curve for Multiplex immunofluorescence

NOTE Confidence: 0.82789474

01:06:57.670 --> 01:07:01.117 for this diagnostic application is

NOTE Confidence: 0.82789474

01:07:01.117 --> 01:07:04.177 vastly superior to immunohistochemistry.

NOTE Confidence: 0.82789474

01:07:04.180 --> 01:07:07.268 And then the problem is that's a huge

NOTE Confidence: 0.82789474

01:07:07.268 --> 01:07:10.620 paradigm shift, like there is no training.

NOTE Confidence: 0.82789474

01:07:10.620 --> 01:07:13.104 In Immunohistochemistry lab directorship,

NOTE Confidence: 0.82789474

01:07:13.104 --> 01:07:15.846 I taught myself. I taught myself.

NOTE Confidence: 0.82789474

01:07:15.846 --> 01:07:18.070 I try, you know, I really,

NOTE Confidence: 0.82789474

01:07:18.070 --> 01:07:20.970 really care to try to teach you.

NOTE Confidence: 0.82789474

01:07:20.970 --> 01:07:23.074 And then to try to teach people to

NOTE Confidence: 0.82789474

01:07:23.074 --> 01:07:24.915 bring up Multiplex immunofluorescence

NOTE Confidence: 0.82789474

01:07:24.915 --> 01:07:27.407 for this diagnostic application.

NOTE Confidence: 0.82789474

01:07:27.410 --> 01:07:30.086 It's a really, really heavy lift.

NOTE Confidence: 0.82789474

01:07:30.090 --> 01:07:33.630 But possibly, you know.

NOTE Confidence: 0.82789474

01:07:33.630 --> 01:07:37.032 And this is perhaps controversial, possibly.

NOTE Confidence: 0.82789474

01:07:37.032 --> 01:07:39.084 And my thoughts on this have

NOTE Confidence: 0.82789474

01:07:39.084 --> 01:07:41.069 changed quite a bit over time.

NOTE Confidence: 0.82789474

01:07:41.070 --> 01:07:44.130 Possibly every lab test should not

NOTE Confidence: 0.82789474

01:07:44.130 --> 01:07:47.308 be offered by every lab and so,

NOTE Confidence: 0.82789474

01:07:47.310 --> 01:07:50.562 so maybe the solution is Multiplex

NOTE Confidence: 0.82789474

01:07:50.562 --> 01:07:52.730 immunofluorescence in 10 or

NOTE Confidence: 0.82789474

01:07:52.817 --> 01:07:55.085 20 labs that have the the,

NOTE Confidence: 0.82789474

01:07:55.090 --> 01:07:55.698 you know,

NOTE Confidence: 0.82789474

01:07:55.698 --> 01:07:58.130 the resources and the expertise to deploy it.

01:07:58.130 --> 01:08:00.517 So thank you for asking me about

01:08:00.517 --> 01:08:02.020 my least favorite stain.

01:08:17.310 --> 01:08:19.700 Yeah, I can and so I can, I can,

01:08:19.700 --> 01:08:22.410 I can talk for half an hour about TRPS,

01:08:22.410 --> 01:08:26.146 1 TRPS. One is classic Gartner hype cycle.

01:08:26.150 --> 01:08:28.292 The study that was the study that

01:08:28.292 --> 01:08:30.129 was designed was highly flawed.

01:08:30.130 --> 01:08:31.438 Highly flawed, yeah.

01:08:31.438 --> 01:08:34.054 And that and that's on the.

01:08:34.060 --> 01:08:36.914 Uh, that's on the authors. You know,

01:08:36.914 --> 01:08:38.713 they should have designed the right study.

01:08:38.720 --> 01:08:40.370 And it's also on the reviewers

01:08:40.370 --> 01:08:41.780 for not identifying the flaw.

01:08:41.780 --> 01:08:43.028 Like, briefly, TRP's like,

01:08:43.028 --> 01:08:45.919 do you want me to talk about TRPS one?

01:08:45.920 --> 01:08:46.490 Yeah.

NOTE Confidence: 0.9616937

01:08:51.150 --> 01:08:51.610 Yeah.

NOTE Confidence: 0.513256115

01:08:56.390 --> 01:08:57.050 That's it.

NOTE Confidence: 0.8959034

01:09:01.240 --> 01:09:01.810 Yeah.

NOTE Confidence: 0.95039

01:09:04.510 --> 01:09:06.940 Yeah, sure.

NOTE Confidence: 0.457451515

01:09:10.940 --> 01:09:14.090 This model and yeah.

NOTE Confidence: 0.832651425

01:09:17.210 --> 01:09:21.246 Ohh yeah, yeah. So. So this is the,

NOTE Confidence: 0.832651425

01:09:21.250 --> 01:09:24.562 I mean I said this is the in silico

NOTE Confidence: 0.832651425

01:09:24.562 --> 01:09:26.850 validation and then the validation

NOTE Confidence: 0.832651425

01:09:26.850 --> 01:09:30.802 is I always do it's this way is

NOTE Confidence: 0.832651425

01:09:30.802 --> 01:09:33.607 actual validation and then I'll say

NOTE Confidence: 0.832651425

01:09:33.610 --> 01:09:36.382 I say floor and then I do much more

NOTE Confidence: 0.832651425

01:09:36.382 --> 01:09:38.939 and then I'll briefly just I'll

NOTE Confidence: 0.832651425

01:09:38.939 --> 01:09:41.656 because it's a good example I'll

NOTE Confidence: 0.832651425

01:09:41.656 --> 01:09:44.446 briefly describe how I validated TRPS

NOTE Confidence: 0.832651425

01:09:44.446 --> 01:09:47.138 one and actually if you want to.

01:09:47.138 --> 01:09:50.188 Know how I validated TRPS 1I tweeted

01:09:50.188 --> 01:09:53.234 how I validated TRP PS1 because I

01:09:53.234 --> 01:09:55.645 because I I thought the my findings

01:09:55.645 --> 01:09:58.459 were sure were significant and so the

01:09:58.459 --> 01:10:01.096 floor to to validate a diagnostic

01:10:01.096 --> 01:10:03.291 marker is 10 expected positives

01:10:03.291 --> 01:10:04.945 and 10 expected negatives.

01:10:04.945 --> 01:10:07.780 And I almost never do the floor

01:10:07.858 --> 01:10:10.483 because if you do the floor then

01:10:10.483 --> 01:10:12.661 there's all kinds of diagnostic

01:10:12.661 --> 01:10:15.583 pitfalls that you will never identify.

01:10:15.590 --> 01:10:17.310 I mainly identify these.

01:10:17.310 --> 01:10:19.460 Potential diagnostic pitfalls by looking

01:10:19.460 --> 01:10:22.240 at this gene expression profiling data,

01:10:22.240 --> 01:10:24.192 mainly using C bioportal.

01:10:24.192 --> 01:10:27.997 So for my validations I use tissue

NOTE Confidence: 0.832651425

01:10:27.997 --> 01:10:30.300 microarray almost you know a combination

NOTE Confidence: 0.832651425

01:10:30.300 --> 01:10:32.460 of whole section and tissue microarray.

NOTE Confidence: 0.832651425

01:10:32.460 --> 01:10:36.296 And for TRPS 1I validated TRPS

NOTE Confidence: 0.832651425

01:10:36.296 --> 01:10:40.556 one in at least 100 breast cancers

NOTE Confidence: 0.832651425

01:10:40.556 --> 01:10:44.980 and at least 100 non breast cancer

NOTE Confidence: 0.832651425

01:10:44.980 --> 01:10:47.320 non breast cancers.

NOTE Confidence: 0.832651425

01:10:47.320 --> 01:10:48.192 Mainly carcinomas,

NOTE Confidence: 0.832651425

01:10:48.192 --> 01:10:50.808 but other tumor types as well.

NOTE Confidence: 0.832651425

01:10:50.810 --> 01:10:53.775 Like it's imperative to validate

NOTE Confidence: 0.832651425

01:10:53.775 --> 01:10:57.852 a new diagnostic marker in a fit

NOTE Confidence: 0.832651425

01:10:57.852 --> 01:11:00.870 for purpose fashion and that means

NOTE Confidence: 0.832651425

01:11:00.870 --> 01:11:03.934 in consideration of differential

NOTE Confidence: 0.832651425

01:11:03.934 --> 01:11:05.466 diagnostic considerations.

NOTE Confidence: 0.832651425

01:11:05.470 --> 01:11:07.054 And I'll tell you what happened

NOTE Confidence: 0.832651425

01:11:07.054 --> 01:11:08.110 with the with the,

NOTE Confidence: 0.832651425

01:11:08.110 --> 01:11:12.009 a couple things with the TRPS one

NOTE Confidence: 0.832651425

01:11:12.010 --> 01:11:13.823 and then another thing that I talk

NOTE Confidence: 0.832651425

01:11:13.823 --> 01:11:16.087 about when I'm doing my straight

NOTE Confidence: 0.832651425

01:11:16.087 --> 01:11:17.515 didactic about immunohistochemistry.

NOTE Confidence: 0.832651425

01:11:17.520 --> 01:11:21.024 Talk about added value of semi

NOTE Confidence: 0.832651425

01:11:21.024 --> 01:11:23.360 quantitative IHC stain assessment.

NOTE Confidence: 0.832651425

01:11:23.360 --> 01:11:25.430 Positive and negative is not enough,

NOTE Confidence: 0.832651425

01:11:25.430 --> 01:11:29.301 you need to at least semi quantitate

NOTE Confidence: 0.832651425

01:11:29.301 --> 01:11:31.202 the signal. In the tier.

NOTE Confidence: 0.832651425

01:11:31.202 --> 01:11:33.050 So when I went to see Bioportal

NOTE Confidence: 0.832651425

01:11:33.116 --> 01:11:35.220 actually I don't know can we go to,

NOTE Confidence: 0.832651425

01:11:35.220 --> 01:11:36.176 can we go to,

NOTE Confidence: 0.832651425

01:11:36.176 --> 01:11:37.891 let's go to see bio portal can

NOTE Confidence: 0.832651425

01:11:37.891 --> 01:11:39.410 I can I back out of here.

NOTE Confidence: 0.832651425

01:11:39.410 --> 01:11:39.580 So

NOTE Confidence: 0.8827970325

01:11:39.590 --> 01:11:41.249 maybe you can discuss it later by

NOTE Confidence: 0.8827970325

01:11:41.249 --> 01:11:42.660 yourself. Yeah, you're going to have

NOTE Confidence: 0.828906456

01:11:42.930 --> 01:11:46.160 do we have more questions?

NOTE Confidence: 0.828906456

01:11:46.160 --> 01:11:47.428 Let's hit another question.

NOTE Confidence: 0.770715745

01:11:49.440 --> 01:11:53.280 Ohh no, I'm screwing everything up.

NOTE Confidence: 0.822935723333333

01:11:51.610 --> 01:11:52.876 I think you know the question.

NOTE Confidence: 0.822935723333333

01:11:52.880 --> 01:11:56.220 Later. Not sure

NOTE Confidence: 0.743419105

01:11:56.220 --> 01:11:58.518 PRPS one, we'll talk about all.

NOTE Confidence: 0.743419105

01:11:58.520 --> 01:11:59.660 We'll talk about all afternoon.

NOTE Confidence: 0.74253033

01:12:00.230 --> 01:12:01.650 Thank you so much Andrew.

NOTE Confidence: 0.824968185

01:12:02.240 --> 01:12:02.996 I think I'm going to eat.