Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.

Welcome to Yale Cancer Answers with your host Doctor Anees Chagpar.

Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it’s a conversation about the role of surgical pathology in certain cancers with Doctor Marie Robert.

Doctor Robert is a professor of pathology and of medicine at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology.

Sure, so I am a surgical pathologist and this is somebody who goes to medical school and does a residency in the specialty of pathology. And that specialty involves looking at diseases in the tissues in biopsy samples and and surgical resection samples from patients. And we look at that very deeply under both with our naked eye and under the microscope,
and then inform the surgeon or the clinician oncologist who's taking care of the patient about what we're seeing and what their disease process might be?

Yeah, you know I often tell patients that there's only two people who can tell you anything for sure. God and the pathologist because we rely so heavily on the diagnosis that's rendered by pathologists.

So you know, tell us a little bit more about what got you interested in pathology and what got you interested in GI and liver pathology in particular.

So that is an easy question to answer and no secret. If you know my family at all, so I am the daughter of a French Canadian. My father Andre Robert, who was a basic scientist studying gastrointestinal diseases so he had both the clinical side MD and the scientific training. And so I grew up visiting his lab and seeing and actually, you know, he would let me do a little help in the lab in participating in his experiments. And so this is when I went to college and Medical school, I thought that medicine
was this the study of disease. And so when I it was, you know, not a far. Challenge for me to decide that pathology was where my heart really lay. And of course, the apple doesn’t fall far from the tree and I was immediately drawn towards all things of the gastrointestinal tract, liver, and pancreas. So tell us a little bit more about kind of what you do. So delighted to talk about this because we are believe it or not, even though we are not meeting your patient first hand, we are constantly mindful of the fact

They have the biopsy done and then we say we need to wait and I always tell patients you know, never rush the pathologist because. You you don’t necessarily want a fast answer. You want the right answer, because everything that we do rests on what you say. So can you give us a little bit more granularity in terms of what happens in terms of that black box while we wait? So delighted to talk about this because we are believe it or not, even though we are not meeting your patient first hand, we are constantly mindful of the fact
that there is a wonderful human being on the other end of this specimen and we are working as fast as we can to provide. As you say the right answer.

So what does this entail? 

So take a biopsy. It is put in a fluid called Formalin, usually that is allowed that sort of hardens the tissues so that we can then put them through an overnight process. And we actually.

This may sound crazy. We actually take the small samples or large samples and put them into paraffin wax. Melted paraffin wax that then hardens in a small little box. If you will, we call it a tissue cassette.

And believe it or not, old fashioned thing like paraffin wax is what holds the tissue in place. While we then apply a very sharp knife, it’s called a microtome to the sample and we’re actually taking small slices of the sample. We take that put it on a microscope slide. Remember from science class.

And that microscope slide is then stained with some very pretty colors. Purples and pinks really. Pathology is like looking at beautiful
art under the microscope and these dyes. If you will are stains adhere to the cells and we during our residency have learned how to recognize cells with these dyes under the microscope so that whole process of just getting to the glass slide takes. At least one day so you know one day gone. Now depending on the type of sample it is, we can then grab it quickly, begin our process of looking under the microscope, and in some situations we are able to give an immediate answer doing nothing else to the sample. Just looking at the microscope for three or four minutes and we’re able to assess everything and give a give the the surgeon, oncologist, whomever gastroenterologist, and then the Patient the answer they need, but in especially in cancer there are often other steps we need to take to get the best possible answer with the greatest amount of detail. And nuance that will really help the person just treating the patient next to know exactly what therapy to apply. So these extra steps include things like we use these terms called special stains,
so if you think of a stain, think of like paint or or these colors I mentioned and there are a variety of very technical and highly honed technologies that we can apply to the tissue. This is getting more and more finessed every day. We can now even do molecular and genetic analysis and put what we call biomarker stains and approaches so we can really get much further now to helping to guide the even the exact medication one might use. But this does take time, so sometimes there’s a first answer. And then there’s another more detailed answer that comes a day or a week later. Sometimes we have to hold up the whole thing for four or five days just to get the right answer from the start, so that’s sort of a long answer to your question, but it is complete. Yeah, yeah, so I mean, This is why I think it’s good information for people who are listening and potential patients to kind of understand why it can take so long, because sometimes we expect these days to to get an answer instantaneously.
And that’s just not practical or feasible. So I want to dig a little bit more into some of the things that you mentioned, Marie. So one is that you know in medical school and in residency, you, as a pathologist got very good at recognizing patterns, understanding what looks benign under a microscope and what looks malignant under a microscope. But can you tell us a little bit more about the secrets that go into that pattern? Recognition? Because that’s another piece that people don’t really understand. How do you make that distinction?

The answer is it all starts with knowing what is normal, what is normal tissue appearance? You know a benign polyp, something that then is perhaps a carcinoma in situ, a precancer. And then something that is truly cancerous that for many people is a nuance that we don’t really understand. How do you make that distinction?

Thank you for these wonderful pathology type questions.
We use the term Histology, it doesn’t matter, but it’s just what you expecting to see. That is normal. So in anything that you look at and in looking at, you know anything around your house or in your workplace. Your desk is something out of place. Were first to understand what is normal tissue, so you want to talk about, say, a colon polyp. We first have to learn, and this is actually, we know, at least a four year training process and residency. We first have to learn, and this is actually, you know, four year training. Training and normal means, how in health are the this our body is organized at the cellular level so that you know you look at your skin and you see your skin. You might. The freckles or some blood vessels underneath under the microscope we learn what all those layers from the outside of the skin to underneath the skin down into even
the muscles and the bone look like.

So once we have that template, sort of that pattern if you will pattern recognition in our mind. Then we begin very slowly to build to learn abnormal and the one of the first things we start with is. Inflammation, you know you get a cut and you notice that there are bee sting and you notice swelling right away. Redness. Well, we learn what that looks like under the microscope with, too much fluid and and inflammatory cells from the immune system being called to that area. The same is true when we start talking about cancer. There's often a process starting from an early, let's say, neoplastic, meaning that the cell is stopped. Just minding its own business and staying put where it should be to maintain the normal but is now dividing and growing and we can see that under the microscope by changes and actually how the cell looks. Over overtime that growth.
Can then. Disrupt the normal to the point that there is disruption of the little little boxes of the the little alleys and lanes that that cells need to stay in and they invade. We talk about invasive cancer. It’s because those cells actually go into a compartment that they have no business being like an epithelial cell which should be on the surface. So if you look at your skin, it’s lined by a certain kind of cell. We call it an epithelial cell, just the lining. Now if it becomes a tumor, it can then go down into the soft tissues, even the muscle and bone, And we can see this all under the microscope. So recognizing cancer or recognizing an abnormal process is recognizing that the normal has been disrupted. And so you know, one of the questions that people often ask is. You know how important is it? Or is it important to get a second opinion with regards to your pathology? So very often you may have your biopsy done at one place if you go to another place to get treatment,
they’ll say, well, we need our pathologist to look at the slides.
So is it that you know a pathologist is a pathologist, and this is a black and white answer and everybody is going to say the same thing, in which case. Why repeat it?
Or is there some nuance there and how important or not important is it to get a second opinion on your pathology slides?
So another great question.
I am a big fan of second opinions and I recommend that when folks are getting impactful diagnosis, that’s going to change their life and start a train in motion of serious therapeutics and operations that a second opinion should always be obtained. And I’m not offended if someone would like to get a second opinion on a pathology diagnosis that I have made it. You know it many times as you sort of allude to probably 90% or more of the time. There will be no disagreement in an original diagnosis. But sometimes there is either a really a complete disagreement, very, very rarely,
a complete disagreement between hey, you know, I actually, I'm not sure this is cancer. I know that. This was thought to be cancer, but actually I’m doing a little more extra work on it and I’m finding that maybe it might be just a precancer, or it may some nuance about that. In addition, in tertiary care centers tend to have specialized pathologists that are only doing one thing. So in my case I’m only doing gastrointestinal pathology, whereas in other centers there’s a group of wonderful general. Pathologists who are looking at all all specimens from all parts of the body, and they are all all outstanding and this is a good system. But if it’s a really impactful diagnosis, it’s not a bad idea to have a very impactful diagnosis reviewed by someone who is a recognized specialist and they exist all over the country and all over the world, perfect, well, we’re going to pick up the story learning more about surgical pathology right after we take a short break.
For a medical minute, please stay tuned to learn more with my guest Doctor Marie Robert. Funding for Yale Cancer answers comes from Smilow Cancer Hospital, where you can view videos from their survivorship team by searching for the smilow survivorship playlist on YouTube. The American Cancer Society estimates that more than 65,000 Americans will be diagnosed with head and neck cancer this year, making up about 4% of all cancers diagnosed when detected early. However, head and neck cancers are easily treated and highly curable. Clinical trials are currently underway at federally designated Comprehensive cancer centers such as Yale Cancer Center and Smilow Cancer Hospital to test innovative new treatments for head and neck squamous cell carcinoma due to resistance to immune DNA damaging and targeted therapy.
More information is available at yalecancercenter.org you’re listening to Connecticut Public Radio.

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We’re talking about the important role pathology plays in cancer and right before the break we were talking about the role that pathology plays in actually making the diagnosis.

Like you go for a biopsy and is this cancer or is this not cancer? That distinction is actually made by a pathologist whom you may never meet, but that your team really relies on. Now Marie, the other thing that pathologists often really provide is some of the genomic information. Whether that comes in the form of special stains like you were telling us about before the break, or whether it comes in. Actually you know doing things like sequencing and telling us about genetic and genomic mutations, can you talk a little bit more about how that’s done and and the importance that that plays in various?

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I’ve been practicing for, you know about 3 decades now and. Over the course of my career there has been really in the past 10 to 15 and I would say even in the past five an explosion of new technologies and new information that help, especially in cancer, help, oncologists and surgeons fine tune and find a very specific therapies for a specific patients tumor. How is this done? And it comes under the general heading of molecular pathology and. This means that so we talked about looking at the microscope, the light microscope and we can determine a lot from there. Now we’re getting inside the cell and specifically the cell nucleus. But the nucleus is where the chromosomes are. The genetic material that are the, you know, the blueprint for what that cell
Tumors tend to occur when those genes or chromas or the chroma, the genes on the chromosomes. The chromosome is divided up into a gazillion genes, each one doing something and tumors happen when what we call mutations occur. Or deletions or other types of fusions and other damage. Overall damage to the genes and the genetic structure on the chromosomes. When this happens, there’s an alteration for the bad. Several things can happen. One is that a cell just recognizes that. You are no longer functioning normally and the body’s going to sort of take you right out of Commission and you’re off the assembly line and actually kills the cell. That’s a good thing. Unfortunately, other times the cell, the mutations or genetic alterations give the cell power. To divide, make more cells with those same problems and that is the beginning of a tumor. We can now detect very smart scientists have created technologies
that allow us to look even from the biopsy that you gave us the same piece of tissue that we made. The diagnosis of a tumor on. We can take the rest of that sample and apply something called next generation sequencing and other. Techniques. Why is this important? This is important because these days there are more and more specific therapies. How do you know when you say this doesn’t apply to every patient and to every tumor? How do you know whether your tumor should have all of those fancy shmancy tests done, or whether simply looking at that pink and purple dyes under the microscope is sufficient? So maybe you had your biopsy done. At a given institution and you were told that this was a particular kind of cancer. Should patients know which particular types of cancer should get advanced kind of diagnostics done that might help their care. How do people figure that out? How do you know which cancers and patients need to have more studies done and which ones don’t? So that is a terrific question. I think that every patient and I hope every patient listening who has a some sort of Tumor or cancer diagnosis and is
beginning down that path of getting treated should ask the question. Does my sample? Will my sample? Will this tumor benefit from genetic testing, molecular testing or whatever phrase you want to use? And it is the oncologist who knows best, so if you’re not talking to an oncologist, talk to an oncologist. The oncologist will know best that, Oh yes, this tumor, if it has this mutation, we have these three drugs that we might want to try, and this is certainly true in many tumors of the. Of the gastrointestinal tract, liver and pancreas. And the oncologist will also know well today. As things stand, we don’t have anything that we’re giving based on genetic analysis, and so they may say at this moment in time we know what to do. This is. This is exactly what we should do, and we don’t need further information. I will also share that at many academic centers there is a philosophy that really we want to sequence. Every tumor and we want to start moving towards a world where every
A diagnosis of malignancy, cancer, type of tumor will automatically have a gene you know. Sequencing of the genetics of that tumor, and this is for two reasons. One is that. We want to continue learning about tumors because we are continuing to develop medicines based on the information we’re finding and the second reason is that sometimes a tumor of 1 type may have a mutation that we weren’t expecting and hey, you know there’s a drug out here. We usually use this drug to treat another tumor, but now that you tell us this tumor surprisingly has this mutation. Well, you know, now we’ve got another thing to put in the toolkit. And so one of the questions people may be asking as they’re thinking about this is, oftentimes, when patients think about genetics, they think about their family history and whether they need to have a blood test or a saliva test to
Look for genetic mutations that may predispose them to certain cancers. So, for example, you know the one that is most often talked about, at least in my sphere is BRC A1 and two, which will increase your risk of breast and ovarian cancer.

How is that different from the work that you’re talking about? Where you’re looking at the genetics of the cancer itself? Yeah, that is super and these things go actually hand in hand so the thing we just discussed was any particular tumor that one might have and that is something that an oncologist and discussion with their patient may may initiate. But in addition, the patient their physician oncologist and sometimes the pathologist will discover that there’s something about the patient as they walk in the door with their first diagnosis of cancer. That, or even they don’t have it yet. But there’s a family history should be analyzed for a specific genetic disorder. Like bracca as you discuss or like in the GI tract, familial polyposis syndrome, or something called Lynch syndrome,
0:25:04.93 –> 0:25:08.008 which are colon cancer syndromes and
0:25:08.008 –> 0:25:10.93 endometrial and other cancer syndromes.
0:25:10.93 –> 0:25:12.63 So in these scenarios,
0:25:12.63 –> 0:25:16.28 there may or may not be a cancer
0:25:16.28 –> 0:25:18.79 diagnosis yet in the patient,
0:25:18.79 –> 0:25:20.68 but they may on their annual visit
0:25:20.68 –> 0:25:22.41 to their you know physician,
0:25:22.41 –> 0:25:24.1 discover that, Oh yeah, well,
0:25:24.1 –> 0:25:25.344 you know my mom,
0:25:25.344 –> 0:25:27.74 dad and three uncles had colon cancer.
0:25:27.74 –> 0:25:29.3 Before the age of 50,
0:25:29.3 –> 0:25:31.498 that person that will be a series
0:25:31.498 –> 0:25:33.906 of things set in motion like early
0:25:33.906 –> 0:25:35.994 screening in the 1st place with
0:25:36.064 –> 0:25:37.869 a colonoscopy and possibly some
0:25:37.869 –> 0:25:40.3 blood tests in it with a genetic
0:25:40.3 –> 0:25:42.16 counselor that might go on where
0:25:42.16 –> 0:25:43.339 a pathologist might be.
0:25:43.34 –> 0:25:45.416 The first one to initiate something
0:25:45.416 –> 0:25:47.758 is that when we get a sample.
0:25:47.76 –> 0:25:50.28 From someone of of the right age group,
0:25:50.28 –> 0:25:51.39 or maybe a young person,
0:25:51.39 –> 0:25:55.094 or that they have for example on colonoscopy,
0:25:55.1 –> 0:25:58.132 have you know 10 or more types of
0:25:58.132 –> 0:26:01.339 polyps that are all precancerous polyps?
0:26:01.34 –> 0:26:03.174 We will raise our hands and say,
0:26:03.18 –> 0:26:04.404 hey, here’s your diagnosis,
0:26:04.404 –> 0:26:05.878 and oh, by the way,
0:26:05.878 –> 0:26:07.594 please sign this patient up for
0:26:07.594 –> 0:26:09.26 some for genetic screening,
0:26:09.26 –> 0:26:10.988 because they have too many
0:26:10.988 → 0:26:13.014 polyps at age 50 that you know
0:26:13.014 → 0:26:14.904 that’s the we want to make sure
0:26:14.968 → 0:26:16.828 it doesn’t mean something more.
0:26:17.55 → 0:26:20.399 Right and but, but there’s a clear
0:26:20.399 → 0:26:22.622 difference in terms of, you know,
0:26:22.622 → 0:26:24.698 in the one instance when we’re
0:26:24.698 → 0:26:26.869 talking about molecular diagnostics,
0:26:26.87 → 0:26:28.442 we’re really talking about
0:26:28.442 → 0:26:30.8 doing these tests to look for
0:26:30.873 → 0:26:33.048 mutations in the cancer itself,
0:26:33.05 → 0:26:36.18 whereas when we’re looking at
0:26:36.18 → 0:26:38.464 predispositions and genetic screening,
0:26:38.69 → 0:26:41.726 for example, we’re really talking about
0:26:41.726 → 0:26:44.94 cells that are baseline that are in
0:26:44.94 → 0:26:47.523 your blood or in your saliva that.
0:26:47.53 → 0:26:49.77 All of your cells carry versus in.
0:26:49.77 → 0:26:50.709 The tumor itself.
0:26:50.709 → 0:26:51.648 Is that right?
0:26:51.92 → 0:26:52.811 That’s absolutely right,
0:26:52.811 → 0:26:55.59 and it’s such a good, nuanced point.
0:26:55.59 → 0:26:58.815 And and so this again,
0:26:58.82 → 0:27:03.634 it’s all good tools that physicians at
0:27:03.634 → 0:27:06.358 all levels of interacting with folks.
0:27:06.36 → 0:27:10.132 So in the in the you know, annual physical
0:27:10.132 → 0:27:13.954 exam at that level by family history,
0:27:13.96 → 0:27:17.548 personal and family history, the physician.
0:27:17.55 → 0:27:19.901 Can can begin the process and say, yeah,
0:27:19.901 → 0:27:22.848 we probably want to check into this.
0:27:22.85 → 0:27:25.37 And at the same time finding finding
0:27:25.37 → 0:27:27.83 early lesions that the pathology level,
0:27:27.83 → 0:27:31.12 in addition to finding a truly already
invasive cancer as they walk in the door. Someone walks in the door at age 45 with colon cancer. They already have it. We’re going to work on that. They’re going to get testing of the tumor itself to see what might work, but because they’re young, this will, with all the clinicians, will say, Oh yes. And by the way, we want to screen your family members now too. We want to just make sure this is not just an isolated thing.

Right, so Marie, in our last kind of 30 seconds here, where do you think the field of pathology is going? Should we be expecting more of these kinds of genetic and genomic tests? Yes, I think it’s going to go further and further and deeper in this direction with hopefully much more useful information down the line. I believe we are also poised to enter the digital era and with artificial intelligence to apply to samples. To improve even further, our ability to glean treatable information.

Doctor Marie Robert is a professor of pathology and of medicine.
If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at yalecancercenter.org.

We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut Public radio. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.