# Pancreatic Cancer Awareness Month

November 14, 2023

**Becca Battisfore:**

Welcome to the latest edition of The College of American Pathologist's CAPcast. I'm Becca Battisfore, Content Specialist with the CAP. In this episode, Dr. Mary Edgerton will be talking with experts in pancreatic cancer research, diagnosis, treatment and patient advocacy.

Pancreatic cancer continues to have one of the highest mortality rates of all major cancers. It's currently the third highest, with a five-year survival rate of less than 12%. It is estimated that over 64,000 Americans will be diagnosed with pancreatic cancer in 2023, with more than 50,000 succumbing to the disease. This month's Cancer Awareness podcast will explore what's on the horizon for pancreatic cancer research, how it will impact patient outcomes, and the role of pathology data in these efforts.

Before we get into the questions, I'll have our guests introduce themselves. Dr. Edgerton, we'll start with you.

**Dr. Mary Edgerton:**

Hi, I'm Dr. Mary Edgerton. I'm a breast pathologist and pathology informatician currently at the University of Nebraska, in Omaha.

**Paula Kim:**

Hi, I am Paula Kim. I am CEO of TRAC, Translating Research Across Communities, and a senior research fellow at George Mason University Center for Health and Risk Communication. And I am the co-founder and former CEO and Chair of Pancreatic Cancer Action Network. Thank you.

**Dr. Ariban Maitra:**

Hi, I'm Ariban Maitra. I'm a professor of pathology and translational molecular pathology and scientific director of the Pancreatic Cancer Research Center at MD Anderson Cancer Center. I'm actually a trained GI and pancreas pathologist. I did my fellowship training at Johns Hopkins, with Dr. Ralph Hruban, who you'll hear about later in the show, and stayed on at Hopkins for about a dozen years before I moved to MD Anderson 10 years ago. And I spend most of my time in the lab doing pancreas cancer research, but I also sign out GI biopsy, so kind of bridge both boats a little bit here as a physician scientist.

**Dr. Nilo Azad:**

Hi, I am Nilo Azad. I'm a medical oncologist here at Johns Hopkins, and I have the honor of serving as the director of our phase one clinical trials program, our developmental therapeutics program. That is really the key program at our cancer center that develops agents that are coming right out of the laboratory and moving into human beings for the first time, when those are being developed in a non-tumor specific fashion, so when they're being developed across different cancer types. I also am a clinician, so I take care of patients with GI cancers including pancreatic cancer as one of my key missions. And I also am co-leader of our cancer genetics and epigenetics program here, which is our research-based program that really focuses on how we can use the genetic and epigenetic abnormalities in cancers to be able to come up with new therapies.

**Dr. Ralph Hruban:**

Hi, I'm Ralph Hruban. I'm the Baxley professor and director of Pathology here at Johns Hopkins, and I direct the Sol Goldman Pancreatic Cancer Research Center here at Hopkins. I'm dedicated to pancreatic pathology and I've had the pleasure of working with many of the people on this podcast. I sincerely believe that tissue is the issue, if you will, that pathology is the foundation for understanding and researching pancreatic cancer. And also, pathology is the foundation for improving patient care. So it's a real pleasure to be here.

**Fatima Zelada-Arenas:**

Hi everyone. My name is Fatima Zelada-Arenas, and I'm the senior director overseeing the research and education initiatives at the Pancreatic Cancer Action Network, where I work closely with patients and caregivers and families and anyone that's impacted by pancreatic cancer through our different programming and services. I've been doing that for over 13 years now, and just love working in that space, supporting patients and families who are going through a pancreatic cancer diagnosis. Thank you so much for having me.

**Becca Battisfore:**

Welcome, and thank you all for joining the podcast, Dr. Edgerton, I'll let you take it from here.

**Dr. Mary Edgerton:**

Okay, well, I'd like to start with Paula Kim, whom I've known, gosh, over 20 years now. Paula, it's great to see you again, even if virtually. Can you share your family's story that led you to form the Pancreatic Cancer Network with your co-founders?

**Paula Kim:**

Thank you, Mary. It's great to be here with everybody. My story was one, back in 1998, when my father was diagnosed but not diagnosed because the biopsy was actually inconclusive. But he ultimately had pancreatic cancer and died within about 75 days of that point in time, which as we know is sometimes not all that uncommon.

But through that journey, I had the privilege and pleasure of meeting one of my favorite people, and happens to be on this call, is Dr. Ralph Hruban. And we met because he responded to an email that I had sent to a chat page that Dr. Hruban had started at Johns Hopkins that had brought together many patients and families and caregivers. On Dr. Hruban's chat page, I met other folks in particular, Pam Acosta, who was one of my co-founders at PanCAN. And there were just a handful of small volunteers. And we, in 1998 had our first Evening with the Stars event, which was our big gala fundraiser that we all worked on. And that led to the development of the first Early Detection Research Laboratory at Johns Hopkins, for Dr. Mike Goggins. It was Pam Acosta, Terry Lierman, who was another, the third co-founder. And Terry had lost his father to pancreatic cancer, Pam lost her mother to pancreatic cancer. And then with the three of us, we had the first event, and then the following year, in 1999, is when we moved forward to establish PanCAN.

**Dr. Mary Edgerton:**

Can I say you took quite a lead because you testified before Congress, you were in Washington, you were meeting with the head of the NIH and then members of Congress again. I was truly amazed by you, and I think I told you last time I saw you, I said to a friend of mine, an oncologist, "I think Paula Kim is the smartest woman I know." And he said, "Oh, she is. Definitely."

**Paula Kim:**

I would say Mary, I would say maybe persistent, maybe so. Right?

**Dr. Mary Edgerton:**

You did a wonderful job.

**Paula Kim:**

Keep this in perspective, and Ariban and Ralph, you guys know this. Back then it was a very small community. It was a very small community of researchers. And Dr. Scott Kern, one of my colleagues at Hopkins, he used to say, when we were talking to NCI, there are less than 10 full-time, fully funded researchers. And Ralph and others, Mary, you and Dr. Berlin, and just all of the wonderful colleagues, Margaret Tempero, Dan Von Hoff, you all helped to inform us what we needed to do to help you in the research community. And so it was one of the greatest partnerships, I think, between a small group of volunteers and a group of very dedicated researchers who were committing their careers to this disease.

But the funding was like teeny, teeny, tiny, right? When we had our first Evening with the Stars event, we worked hard, hard, hard, and we raised something like $120,000, which at that point in time, given we weren't an organization, was actually a reasonably large sum of money.

**Dr. Mary Edgerton:**

Oh, it was.

**Paula Kim:**

I looked at it and I said, "Well, okay, $120,000." And I don't have any scientific background. I don't have policy background. I raised my children. That's my background. But Dr. Hruban and others helped to educate me and our team of volunteers at that time because we were a hundred percent volunteers when we started, they educated me about the public policy process and the difficulty of pancreatic researchers competing for money at NCI/NIH. And then as I further looked into it, I realized that at that time, pancreatic cancer was fifth leading cause of cancer death, but it was only getting about $9.9 million in federal funding to the academic centers. And then if you contrast that with the more highly funded diseases at the time, it didn't take a lot to understand that that was a result of very strong advocacy, at that time, as to what made breast cancer, prostate, lung, and colon have significantly larger budgets.

And so with that in mind, that's what we set our sights on at NCI. And again, like I say, we had a half a dozen volunteers. So growing up in California, and we founded PanCAN in California because Pam and I were both based there. I knew that we had to get to east of the Mississippi and Washington, DC.

And at that time, pancreatic cancer, like I say, was getting pennies on the dollar. And so it created a number of visual charts to basically remind the NCI that pancreatic cancer was this deadly disease, but not getting any attention. And so I focused on Washington, DC and we wrote, along with Terry Lierman and our team, we wrote the very first ever pancreatic cancer report language, which as some of you may understand, is the direction, if you will, from Congress to the NIH with how to allocate and spend research dollars. PanCAN was a new kid on the block at that point in time, and we didn't have a track record. We didn't have a lot of things. We had no money. And so with that, I still had the opportunity to testify twice in Congress and to share with them the important need of why we need to fund more research.

**Dr. Mary Edgerton:**

Very important, indeed. And now let's move on to hearing about some of that research and one of your beneficiaries, Dr. Ariban Maitra, welcome. I know you because we were both at MD Anderson and you serve as the medical director of the Sheikh Ahmed Pancreatic Cancer Research Center. Tell us some about the research that you're currently working on.

**Dr. Ariban Maitra:**

Absolutely, Mary. And thank you for having me on the show. Before I answer that question, I just want to give out a shout-out to the pioneers of this whole area, Ralph and Scott Kern, who Paula mentioned, and then of course, Paula herself.

And I bring this up because we just had this large pancreatic cancer meeting that is organized by the ACR in Boston, and I was one of the core organizers of that. We had over 700 people in the room. And when you think back to the time that Paula just mentioned, 10 people nationally who were funded and these lonely voices trying to say, "Listen to us. Listen to us. We have this terrible disease and nothing's being done." It is just incredible to think back. And so I think the word persistence is really an appropriate description for some of the early pioneers, two of whom are on this call today. And so real salute to them. And where the field is today is really an homage to the early efforts that they all made.

So there's a lot happening. As I said, there's now a meeting just dedicated to pancreas cancer, held by the ACR every year. And we had 700 people attending it. So there's a lot of activity going on. When I think about the major research advances that have been made, a lot of that has happened in the sphere of understanding the molecular genetics of this disease. We now know a lot about what are the key driver genes that are altered in pancreatic cancer. We know a lot about the familial risk that many families with this disease have and some of the germline alterations that caused that risk. Again, work that came out of Johns Hopkins and also the Mayo Clinic, late Gloria Peterson, whom we actually honored at this ACR meeting was one of the pioneers with Ralph and really trying to understand the genetic basis of familial disease. We know a lot about that now.

We know a lot about the molecular alterations outside of the cancer cells, what's happening in terms of the host response, because that's not just a passive bystander as we used to think 20 years ago. We now know that there is a lot of active crosstalk between cancer cells and the host. And some of it, it perturbs the cancer from going and others are co-opted by the cancer in terms of progression and metastasis. And then of course, a lot has happened on the clinical arena, and I'm going to let Dr. Azad speak about that because she's really the expert on that. But it's really almost a renaissance time in this disease in terms of making advances and new therapeutics. So there's a lot to talk about on that front as well.

**Dr. Mary Edgerton:**

So I noticed that you have a gene expression based signature for prognosis in pancreatic adenocarcinoma. Is that being used?

**Dr. Ariban Maitra:**

So there's a lot of work that has been done. Obviously, the early molecular alteration characterization was in the context of mutations, things that are abnormal in the DNA, RAS mutations, P53, SMAD4, et cetera. But we have also come to recognize that there's this whole universe outside of the genome, especially the transcriptome that is also important, in terms of both predictive and prognostic biomarkers in pancreatic cancer. So work that was done by many other groups around the country and as well, as globally groups in Canada and other places, have identified these RNA based signatures that we know now predict responses to first-line therapy. So patients with a certain subtype of RNA signatures that we call basal subtype, for example, very much like the basal subtype in breast and other diseases, are more aggressive and they don't respond to a commonly used first-line therapies. And others that we call classical tend to be more responsive.

So the overarching message from all of this is that there is obviously a universe outside of the genome. The genome is very important, and these are in fact key drivers that are responsible for initiation and progression. But there's also transcription factor driven alterations, epigenetic alterations that, again, Dr. Azad is doing a lot of therapeutic studies in that are also important in terms of disease progression, and in fact are involved in guiding responses to therapy.

So we are seeing now clinical trials being done that are not just dividing patients into strata based on their genomic alterations, but also their RNA subtype, which is kind of a unique way of approaching pancreas cancer. Typically, it used to be one size fits all, but now these trials are happening where we are taking the RNA profile and we are saying, you get this type of therapy and you don't. So that's kind of unique.

**Dr. Mary Edgerton:**

That is very exciting. Well, this is a good time to bring in Dr. Azad. You are the Co-Director of Cancer Genetics and Epigenetics and a professor of oncology at the Johns Hopkins Sidney Kimmel Cancer Center. Can you tell us a little bit about the clinical trials that you were leading in pancreatic cancer and particularly in epigenetics?

**Dr. Nilo Azad:**

Absolutely. I don't think that I'm overstating it to say that after decades of a really small amount of progress in patients with pancreatic cancer, that we are on the precipice of dramatic alteration in the way that patients are going to receive benefit from clinical trials work. And the main area that I'm speaking about is really around KRAS driven therapy. So pancreatic cancer is a cancer that has a mutated KRAS gene in 90% of patients with pancreatic cancer. And this is a mutation that has been considered untargetable for 40 years and is really ubiquitous among many cancers, but there's no tumor type where it is in higher prevalence than what we see in pancreatic cancer.

And in the last four years, what we've seen is, and this is with the advances in technology and medicinal chemistry that have happened, is that we now have drugs that can directly target KRAS mutations, and more importantly, [inaudible 00:17:35] result in benefit in pancreatic cancer. So we've had many times where there have been exciting drugs that seem to work in many other tumor types, but then when we start treating our pancreatic cancer patients, because of so many other histological issues and pathological issues, we don't get that benefit.

But in pancreatic cancer, these KRAS specific mutation inhibitors have been dramatically active and resulting in both tumor shrinkage and disease stabilization in the vast majority of patients that they've been tested in. Now, the biggest area that this has happened is in a particular KRAS mutation, KRAS-G12C, but that's not a very common KRAS mutation in pancreatic cancer. That's only 1 or 2%. We now have in the clinic, G12D inhibitors, that is the most common mutated KRAS mutation that we see. And we have pan-KRAS inhibitors that were literally just reported this weekend at a big international meeting that also has shown significant disease stability in the vast majority of pancreatic cancer patients.

And we've got more and more of these drugs that are coming online, and we're going to learn how to use them better because. Right now, people have benefit, but after a period of time, patients will develop resistance to them. So we're going to start seeing opportunities to combine these agents to make them more powerful and overcome resistance. There has been beautiful preclinical work that has come out, elegant work in high impact journals showing the immune impact of these drugs. And so we're going to start using and seeing these drugs utilized with immunotherapies, which is a second big area where we haven't broken through yet. But we are now starting to some activity of immunotherapy in handfuls of patients that we're using the proper combination therapies for.

So we are really in a very hopeful time in the next few years for our pancreatic cancer patients. And what we really need is investment. We need investment from the research community, we need investment from our government, which has its own challenges right now, and we need investment from philanthropy and private industry. And if we put those pieces together, in five years, we're going to see a completely different life expectancy for patients with pancreatic cancer.

**Dr. Mary Edgerton:**

That is very, very exciting to hear. I'm going to turn a little bit to pathology because, well, we pathologists think that pathology is the center of medicine. Do you use the pathology reports and items in that to help select your patients for clinical trials?

**Dr. Nilo Azad:**

So absolutely. Though, I would say I'd broaden that past just the histological pathology, though that's important as well. And also include the molecular pathology piece, which as I just talked about, is so key in how we take care of patients. We also have about 5% of patients that have mutations in genes that are involved with genetic susceptibility, which both have drugs that we can use to help those patients and then have ramifications for family members as well. So those pieces of the molecular pathology report are very important.

But even our traditional path reports give us a lot of very important information regarding how we can risk stratify patients in the adjuvant setting, for example. And for me, one of the areas I'm really interested in is subsets of pancreatic cancer patients that we don't have good therapies for. So I'm running a clinical trial right now in collaboration with Liz Thompson, who is a pathologist at Johns Hopkins, who has done some really exciting work looking at adenosquamous pancreatic cancer and how different adenosquamous pancreatic cancer is in terms of immune infiltration. And so we're now running a trial and that trial as part of being on that study, there's a path review that has to be undertaken centrally to qualify patients for that as well.

So I think we're really seeing how important tissue is, and I would absolutely agree that tissue is the issue. I want to add one other thing. Pancreatic cancer can be difficult. I think Paula mentioned this as well. Sometimes it's hard to get enough tissue to be able to do the diagnostic work and the sequencing work that we want. And so this is a place where new ctDNA technologies are also extraordinarily important. And so we're starting to use ctDNA as a way to diagnose patients to open up treatment options for them. And I very much believe that in the next few years we'll start using ctDNA to screen patients and detect cancer either early or even in its pre-malignant stage, which again, when we think of 10 years from now, when we think about our children's generation, that's what we want. We want pancreatic cancer to be in the rearview mirror in terms of showing up in the advanced stage the way that it is now.

**Dr. Mary Edgerton:**

So just define CT for our audience.

**Dr. Nilo Azad:**

Oh, CT is circulating tumor DNA, or cell-free CF DNA, which I think is probably even the more accurate terms since we can get cell-free DNA from many different kinds of body specimens and liquids. So that's what I'm referring to.

**Dr. Mary Edgerton:**

So do you use at all, the synoptic reports that come out of the College of American Pathologists, to help organize your pancreatic cancer data?

**Dr. Nilo Azad:**

I would say that at this point, and I think part of this is in treatment of patients, it's a very clean and nice way for us to be able to quickly know how to treat our patients in terms of standard of care. When it comes to clinical trials, the information that's contained in those reports and in that section can be very important to help us qualify patients for clinical trials. But in our cancer, the biggest issue is that we don't have enough clinical trials. If you open up a pancreatic cancer clinical trial, that trial enrolls in the blink of an eye because there is such an unmet need. And so what we really need is more studies.

**Dr. Mary Edgerton:**

That's great to know. I actually know people who would love to be on such studies. So Dr. Hruban, you're also at Johns Hopkins and also have known Paula Kim a very long time. Can you tell us a little bit about what you do as the director of the Sol Goldman Pancreatic Cancer Research Center?

**Dr. Ralph Hruban:**

Sure. Remembering Paula fondly in those early days, and I remember these two women who reached out to us on the internet, Paula was one of them, and said, "Come to Hollywood, California and bring a tuxedo for this fundraiser." And we didn't know if they were real or not. And so Mike Goggins and I rented a tuxedo and I went, and they were of course, wonderful, intelligent, beautiful women who've had such impact on the field. And so that's fondly remembering those days, and it's great to be with everyone on this Zoom.

I just want to echo some of the words of my colleagues. When you think of the pathology of pancreatic cancer, we're in many ways lucky that the genetic drivers of this disease mirror the histology. And so histology is still critically important to the diagnosis and management of patients with pancreatic cancer, and hence, the synoptic reports are so absolutely critical.

But as Nilo and Ariban mentioned, there are other aspects to the disease, then pathologists can help drive an understanding of those. So starting with the germline, as Nilo mentioned, a number of patients with pancreatic cancer actually have inherited a risk factor that caused them to develop it. And the BRCA1, BRCA2, and PALB2, those are not only important for the families, but they're targetable. Probably one of the best targets available is actually based on the patient's germline. So now the standard of care for patients with pancreatic cancer is germline testing to see if they carry one of these.

Then moving to the next step, the somatic mutations. And as Ariban and Nilo hinted, the genes that drive pancreatic cancer are known. They don't influence the classification of the disease as much as they can influence the therapy. So again, the standard for pathologists should be to take not only the germline and send it for sequencing, but the tumor itself and identify whether there's a fusion gene that is targetable or as Nilo mentioned now, unbelievable that KRAS is targetable. So it's an exciting time to be a pathologist in studying pancreatic cancer because when Paula first started where there was no hope, now there is hope for patients, and it's this wonderful partnership between pathologists, clinicians, and patient advocacy groups that's made it happen.

**Dr. Mary Edgerton:**

Oh, thank you. That was very well put. I looked into some of your research and you are working on non-invasive precursor lesions. Can you tell us a little bit about that?

**Dr. Ralph Hruban:**

Yeah. So if you think of colon cancer, when we turn 50, we all go get our colonoscopy. And the hope is not that you're going to find a colon cancer. The hope is that if you're predisposed, you're going to have colon cancer, you find a polyp, a non-invasive lesion that can be removed and the patient never gets cancer. And if you look at the survival rates for colon cancer, the death rates have gone down because of colonoscopy and treating these precursor lesions. We'd love to do the same for pancreatic cancer. They're indeed are well-defined histologic precursors to invasive pancreatic cancer. One's called pancreatic intraepithelial neoplasia, another, intraductal papillary mucinous neoplasms, and another, mucinous cystic neoplasm. The names aren't as important as the opportunities they present for early detection, before there's an incurable invasive cancer and treatment. Of course, the challenge is that it's not like biopsying the skin and taking off a... oh, that wasn't nevus, it wasn't a melanoma, no problem.

The pancreas lies deep in the abdomen, and surgery can be fraught with complications. So the goal now is to identify those precursor lesions, those precancerous that are very likely to progress and leave in place, which you wouldn't do in the skin or colon, those that aren't likely to progress. And I think pathologists will play a critical role in this as we're the ones evaluating the tissues that are resected and determining if there's dysplasia and other features that may suggest progression. So pre-cancerous lesions I think are a real opportunity to make a difference, but they're also a risk for overtreatment.

**Dr. Mary Edgerton:**

Oh, yes, yes. That's fascinating. Of course, in breast, we use the pre-cancerous and then we've pulled back because of the overtreatment issues. So right, knowing which ones are going to progress is very important. Dr. Zelada-Arenas, you are the senior director of patient services and research and education at the Pancreatic Cancer Action Network, PanCAN. So you've picked up the helm from Paula and the co-founders of PanCAN. Can you tell us a little bit about the Know Your Tumor Precision Medicine service and how it helps pancreatic patients better access matched care for their tumor types?

**Fatima Zelada-Arenas:**

Sure, I'm happy to talk about that. And thank you so much for having me. Very happy to be part of PanCAN and the long tradition of supporting families and patients and making progress in pancreatic cancer. So happy to be here. So Know Your Tumor is actually our Precision Medicine service, and we are basically offering and covering the cost of biomarker testing for patients with pancreatic cancer. We've been doing it for almost 10 years. We're celebrating 10 years next year actually, of offering the program. And when we started, we definitely started at a time when this wasn't something that was regularly done, and we wanted to really be able to offer it to patients with pancreatic cancer who weren't having access to it at the time. And so we partner with a company called Tempus who performs the actual testing, the biomarker testing, on the tissue. And once the testing is completed, then there's a report that's delivered to the healthcare team with information on both somatic and germline mutations.

Also things like tumor mutational burden, microsatellite instability, and also provides information on possible treatment options for that patient. And I think as some of my panelists have already shared, provide valuable insight into treatment decisions for that patient. And so it's our way of really providing testing to patients who may not have access to it. Because testing is now part of guidelines and it's something that more patients are getting, we're definitely seeing less patients utilizing Know Your Tumor, but are still continuing to offer the service for patients who might not otherwise have access to it. So in particular, our focus is on patients who maybe are not at higher volume institutions who may not be getting this testing as part of the standard of care that other patients may get. So that's just a little bit about the program.

**Dr. Mary Edgerton:**

Oh, that's fantastic. So does your team at all use synoptic data from the pathology reports?

**Fatima Zelada-Arenas:**

Right now, we don't. So we're not currently accessing or collecting the data from primary source. But it's just overall, the data that it comes out of Know Your Tumor is available for researchers to be able to access and analyze. And right now, we have about 15 ongoing projects with different institutions on the utilization of the KYT data. But for right now, we're not using that as a primary source.

**Dr. Mary Edgerton:**

Well, stay tuned because the CAP is working on synoptic reporting for molecular reports, and the hope is that the pathologist, the poor pathologists, won't have to type it in and copy it from some PDF that was faxed to them with, all those numbers that are hard to read, but it'll actually be sent electronically. And then you can just say, yeah, add that to the report. So I'm excited about that.

I'm going to call on each one of you, and I'd just like you to quickly say, what do you think is going to change in the short term, say three to five years, and what do you think this disease will be like in 10 to 15 years from now? So I'm going to go backwards, so I'm going to start with you Dr. Zelada-Arenas.

**Fatima Zelada-Arenas:**

I think just as all of my fellow panelists have already shared, this is a really exciting time. When I started at PanCAN, it was almost 14 years ago, and there were very few treatment options that we would talk about with patients. And to see all of the progress that's been made, especially in the last few years, has been so wonderful for all of us that have been working in the pancreas space for a long time. So I'm really excited about where we're going.

Our goal, as an organization, is to continue to improve outcomes and improve survival. So we've seen that survival number go up every year, for many years. And so we're hoping to continue to see that progress. We want patients to have access to better treatments, live longer, and to be able to manage the disease. So that's what I'm hopeful for, and I think this is a really exciting time. I'm really looking forward to seeing all the progress that's going to continue to be made in the disease by wonderful researchers and scientists that are working so hard on it every day. And then as an organization, we're going to continue to support patients in the very best way that we can provide resources to them and help guide their conversations with the healthcare team and really support them in whatever they need throughout their journey. So I'm really excited about what's coming.

**Dr. Mary Edgerton:**

Dr. Hruban, what do you think?

**Dr. Ralph Hruban:**

I share excitement. These are extraordinary times as everyone's mentioned. I think for me, early detection, identifying who's at risk and detecting the lesions early is going to be critical. But as a pathologist, one thing we haven't talked about is artificial intelligence and the impact it's going to have. When I started in pancreatic cancer, I remember my colleague, Stan Hamilton, saying, "If you've seen one pancreatic cancer, you've seen them all," implying that they're all deadly and they all look the same. But I think that I'm excited by the opportunity to really start to sub classify tumors perhaps in ways that the human eye can't appreciate. And whether it's the tumor itself or as Ariban mentioned, the stroma or the interaction between the two, integrating in other clinical data. And Mary, you mentioned integrating the molecular into the path report and all that, to come up with a report that helps guide the clinicians to the best treatment for our patients.

**Dr. Mary Edgerton:**

It is a very exciting time, and since the genotype controls the phenotype, I like to think that from imaging we're going to be able to discern some likely molecular findings behind that and be able to streamline that testing and point to it. And Dr. Azad, you're really there at the forefront of the changes as they're happening while running the clinical trials?

**Dr. Nilo Azad:**

Yeah, I mean, I think broadly that in the next three to five years, we're going to start seeing KRAS derived therapies to being a part of the treatment paradigm for every pancreatic cancer patient. I think 10 to 15 years from now, I have real hope that we're going to see meaningful drops in the incidences of this cancer as we start being able to pick it up early and work more in that prevention screening space. And I think that that's what we really need in order to change the amount of suffering that we see from this cancer.

**Dr. Mary Edgerton:**

Yes, I am excited about the circulating tumor DNA as a screening tool. I guess right now it's mainly used for people who have higher stage tumors because that puts it out in higher concentration. Dr. Maitra, how about you?

**Dr. Ariban Maitra:**

Well, I think everyone's focused on the high points already, so I echo those thoughts. A couple of things. One is I'm really hopeful that there'll be greater awareness amongst the primary care physician communities in terms of these early risks signs for pancreas cancer. Many times, unfortunately, patients bounce between physicians and the signs of early pancreatic cancer are not recognized so that when they eventually present with manifest disease, the disease is often spread and is not resectable.

And so things like new onset diabetes, especially when it's combined with features of weight loss, for example, or the diabetes not responding to medications, those are all warning signs that primary care physicians are often the first gatekeepers. Somebody with onset diabetes will not come to Johns Hopkins or MD Anderson. And so organizations like PanCAN are really doing an amazing job at disseminating this knowledge in the lay community amongst primary care physicians. And so we are very hopeful that that will have an impact in terms of earlier detection of the disease.

And then secondly, just coming back to what Ralph said from a pathology perspective, I did my fellowship in 2001, so a long time ago with Ralph. And I think what a pathologist can do for this disease has really changed from just being surgical pathology now to molecular diagnostics, ctDNA, AI and subtyping the disease. And I think pathologists are going to play a huge role. I think the generation of trainees that are coming through, they are going to look at pancreatic cancer very differently from the way I looked at this 22 years ago, or whatever when I was a fellow. And so I think there is just a lot of excitement for them as well to play a part in terms of the management of the disease, not just in the surgical pathology realm, but also in all of these other molecular diagnostic and clinical pathology areas. So I just want to emphasize that.

**Dr. Mary Edgerton:**

Oh, that is exciting. And then that brings us to Paula. And Paula, you must have seen a lot of changes since you started this and the funding, and it's just so exciting to hear. How do you feel about this?

**Paula Kim:**

Well, if you're as good as you say you are, you can make tremendous progress in this disease. And quite frankly, there's less competition, in a sense. But what I think I'm excited about is all the wonderful pathology and clinical advancements that we have heard here today. One of the very first grants that we funded at PanCAN was an AACR Career Development Award to Dr. Tuveson and Dr. Hingorani. And out of that grant, it allowed them to finish the really seminal, genetically engineered animal model, that has still to this day, I believe, one of the most highly cited animal models, I believe.

**Dr. Mary Edgerton:**

Fantastic. Well, thank you all. This has really been a great podcast. It's been fun to be with you. And like I say, it's been very uplifting to hear this news.

**Becca Battisfore:**

Thank you, Dr. Edgerton. And thank you to our guests for sharing your experiences and expertise, especially as this month is Pancreatic Cancer Awareness month and November 16th is World Pancreatic Cancer Day. And I want to thank you all for listening to this CAPcast. You can find links to the CAP's cancer protocols in the episode description. And for more information about the CAP, visit cap.org.