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00:00.000 --> 00:09.400 Support for Yale Cancer Answers comes from AstraZeneca, working to change how cancer is treated with personalized medicine. Learn more at astrazeneca-us.com.

00:09.400 --> 00:49.200 Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. 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 is a conversation about research advances in gastrointestinal cancers with Dr. Nita Ahuja. Dr. Ahuja is the Chair of the Department of Surgery at Yale School of Medicine and Chief of Surgery at Yale New Haven Hospital. Dr. Gore is a Professor of Internal Medicine and Hematology at Yale and Director of Hematologic Malignancies at Smilow Cancer Hospital.

00:49.200 --> 00:56.200 <vGore>I think in the interest of full disclosure, the audience needs to know that I did not just meet you last year when you came here right?

00:56.200 --> 00:59.000 <vAhuja>That's true. We have known each other for a long time.

00:59.000 --> 01:01.200 <vGore> Because we were colleagues at Johns Hopkins.

01:01.200 --> 01:05.300 <vAhuja>Exactly. You know, it is a small world in academic medicine.

01:05.300 --> 01:21.500 <vGore>It is, and I was so delighted to hear that you were the selection for the chair of surgery. How did that come about? I mean, you were pretty well established at Hopkins and everyone loved you there. What brought you up here to New Haven?

01:21.500 --> 01:49.900 <vAhuja>Well, you know all great places are alike with colleagues and good friends. And as you said, you came here and something drew you here. The same thing drew me here. It is the chance to be around good people. Certainly, talking to you and hearing about what was happening here and just thinking about where we are going in healthcare and what I could do in this new position to help our patients. It is an opportunity and this is a great institution and that drew me here.

01:49.900 --> 02:02.800 <vGore>Well, we were so happy that that is the case. But are you still doing your research, is that right? I am sure you have to downsize a little bit because you have got so many administrative responsibilities.

02:02.800 --> 02:36.300 <vAhuja>You know, it takes a while. I think being a surgeon, I always have this very optimistic timetable of my life, but research is what keeps me very grounded about my patients. As you take on these administrative roles, your day to day becomes more big picture and you have to come back to why you became a surgeon or a doctor in the first place and

that for me is the operating room and research, those are the two places that connect me back to why I became a cancer surgeon.

02:36.300 --> 03:04.400 <vGore>Well, I have to say that back in the day, I was always impressed that you could actually have a very high profile laboratory project when you were always wearing scrubs. I mean, you would just come out of the OR and then you are presenting data that was very impressive and as I recall, your interest really was in this wackadoodle field that you and I were both involved with called epigenetics. Isn't that right?

03:04.400 --> 03:21.100 <vAhuja>That's true and I will tell you when I was a surgical resident and in training, I said, what is this thing called epigenetics. We had all learned about genetics, right, that is our DNA code and we all sort of marvelled at it and said if I crack the DNA code, we will have all the answers.

03:21.100 --> 03:21.400 <vGore>They teach it in middle school now.

03:21.400 --> 04:08.800 <vAhuja>Right. But clearly, we knew that it was not enough, and epigenetics is really what I think of as being a surgeon and trying to put connections together, we are all born with the same DNA and yet we have sort of differences and that reflects what we eat, the environment and that gives some of the problems we see later on in life with diseases, which is my case that I study - cancer or other diseases, and that reflects as you know epigenetics. And when I first heard about it, I said aha it makes sense, that's how the environment talks to our DNA and that is how I connected. It is the environment and our other stuff talking to us and giving us what we become as we get older.

04:08.800 --> 04:28.100 <vGore>One of things which I have always found is a really good metaphor or illustration of epigenetics is how the caterpillar has the DNA as the butterfly and yet somehow that same DNA causes 2 very different features right?

04:28.100 --> 05:17.900 <vAhuja>And you know, our body is a marvellous piece of work, and if you think about it, I operate on the GI tract. Well, it is the same DNA as our heart, yet it is very different, it looks very different and has different functions. So, epigenetics has a purpose in how we become human beings. And then of course, we look at the other side of epigenetics, which you and I have studied, what happens in cancer, how does cancer use epigenetics to do all the havoc and damage it does to our patients, and that is what I think you and I have been trying to figure out for the last 2 decades is how to understand what it does in cancer and then how do we then use that knowledge to help our patients.

05:17.900 --> 05:39.000 <vGore> Yeah. Well, it certainly is such a compelling topic and I think the more we learn, the more complicated it gets and sometimes I find it pretty daunting. What is new in GI cancers? I mean, when you operate, you are doing colon as well as pancreas, like all aspects of the GI tract or is there one little area you like the best?

05:39.000 --> 06:12.200 <vAhuja>Well, it is becoming narrower as you go along and as you just said the more you know, the more you realize what you don't know and that becomes a part of our lives, in that you become experts at certain pieces, so I focus a lot on pancreatic cancer partly because recognizing that it is going to become such a big part of what happens to humans, it is going to become the second leading cause of cancer death in a few years.

06:12.200--> 06:15.400 <vGore>Because so many people unfortunately do not survive is what you mean?

06:15.400 --> 06:22.400 <vAhuja> Yup. And it is not that the numbers are increasing, it is because other cancers are making progress and we have not made progress in this.

06:22.400 --> 06:24.900 <vGore> And you just like to knock your head against the wall?

06:24.900 --> 07:21.400 <vAhuja> Kind of. I am stubborn that way as you are, because we want to fix something and you think, well here is this problem and yes we figured out the surgery part, I have spent most of my training, I spent 10 years of training after medical school to become a cancer surgeon and then the last 15 years, I have been perfecting the techniques and you have perfected that but as you just said Steve, we still see that the patients are not living much longer. So, we got to think what we can bring to it by what we know about genetics and epigenetics and how do we make it so our patients are living longer. So, it is a problem and I like problems and the harder they are, the more challenging and we can sort of say, okay, let's tackle this. I think it is one part of why I did this, and then of course, the surgery is technically sort of challenging.

07:21.400 --> 07:29.500 <vGore> Very difficult surgery, pancreas surgery, it takes all day right? I mean it takes several hours at least that is what it used to be.

07:29.500 --> 07:36.400 <vAhuja> I told you we have learned something of the technical part. So, it takes a shorter time, it is not 7 hours, it is maybe now 5 hours.

07:36.400 --> 07:37.800 <vGore> Oh, I was guessing 12, no?

07:37.800 --> 08:09.800 <vAhuja>It is better. But you know, it is still a difficult operation and it is an operation where you really sort of see the human body in all its glory. You have got the blood supplies, you have got this beautiful organ that is really small, the pancreas, it is only about 6 inches big, but it controls a lot, it makes us diabetic if it is not working well and it causes havoc if it gets flared up and then it causes this cancer piece, but yet we need it to live every day.

08:09.800--> 08:15.600 <vGore>Well right, otherwise, we cannot digest our food. And it is stuck there in the middle of all these other important organs.

08:15.600 --> 08:42.900 <vAhuja> Yes, and I say it is all about location, location, location. And I tell my patients that the pancreas sits in prime real estate, surrounded by everything. It is surrounded by the liver and its drainage around all the important blood vessels and around our stomach, so it is wrapped up and it is this marvellous piece that you see in the human anatomy and then you really sort of put the pieces back together after you take the cancer out.

08:42.900 --> 09:04.900 <vGore> But that is one of the reasons why many of the patients who develop pancreas cancer cannot be operated on right? Because often times, as I remember, if it is not in a particular part of the pancreas, you may not find out about it until it has passed the point of surgical benefit.

09:04.900 --> 09:41.200 <vAhuja> If you look at breast cancer or colon cancer, we can pick it up early. We have ways of finding these cancers early. But pancreas, the biggest problem has been finding it really in early stage and that is partly because it can hide in there, unless it is near like the bile duct, which is the liver organ and you get jaundice, but in 70% of the patients, the cancer is found too late and then we are just looking at, how can we use chemotherapy or other things to extend life, but we really cannot take it out because it is already spread.

09:41.200 --> 09:58.300 <vGore> It is so interesting because the people who come in with a bad case of jaundice, they look so sick, but in fact in some ways it is a good sign right, because maybe their pancreas cancer, there are a lots of causes of jaundice obviously, but I mean for those patients who have jaundice where we find out they have pancreas cancer, that is really a good thing.

09:58.300 --> 0:10:33.5 <vAhuja> Well, it is the ultimate glass is half full right? Here we found it early, but it is still pancreas cancer. Yes, you can find it early and then you at least have an opportunity or a chance to go at it surgically. The one thing we do know and this is a lesson you learn again and again in every cancer right, that if you find the cancer early, then you can improve survival and we know that in other diseases. So, that is one of the pieces of why pancreatic cancer because our dream is to find it early, so then we can take it out and hopefully extend life and give people that sort of longer survival.

0:10:33.5 --> 10:34.900 <vGore>So, is there any progress being made at early detection for pancreas cancer?

10:34.900 --> 11:02.200 <vAhuja>Well, as you mentioned, the organ is small in height, so imaging or CAT scans and all those really do not find this cancer, so people are starting to connect, how can science help us? Can we use genetics and epigenetics to find these cancers, and that is what many of the laboratories are now really trying to do, can we find that needle in a hay stack and find those people who are at high risk and find them early?

11:02.200 --> 11:04.200 <vGore>Would that be through a blood test?

11:04.200 --> 11:23.000 <vAhuja>Well, I think hopefully that could be a liquid biopsy, what we call liquid biopsy, these blood tests and this comes back to the

fact that biopsying the pancreas is not something you want to do. If you do have colon cancer, we do a colon biopsy and we tell you age 50, go do your colonoscopy.

11:23.000 --> 11:23.200 <vGore>I have had two.

11:23.200 --> 11:28.200 <vAhuja>Well, good. And we want to remind all your viewers that if they are 50, they should have one.

11:28.200 --> 11:35.800 <vGore> I had my first one at 50 and a week and the next one at 60 and a month or something.

11:35.800 --> 11:35.200 <vAhuja>There you go. That's perfect.

11:35.200--> 11:37.200 <vGore>And I felt so good when everything was okay.

11:37.200 --> 11:56.300 <vAhuja> Right and we should be encouraging all our friends, but unfortunately with the pancreas, there is no scope, it is pretty hard to do those scopes. So, the hope is that a liquid biopsy will allow us to find those people who are at higher risk and then we can come back with these fancy scopes to do the next step.

11:56.300 --> 11:57.900 <vGore> But this is not prime time yet?

11:57.900 --> 12:48.800 <vAhuja> It is not prime time. Many labs are doing this and other labs are trying to find a liquid biopsy solution and certainly we have some interesting targets, but as you know from your own research that it takes a long time from something that seems promising in the lab to then a test on the market. Right now, we have a test for colon cancer and before I got into pancreas cancer, we were trying to develop a test for colon cancer and it took a good 20 years and that is an epigenetic test using your stool DNA. So, that is the hope that in the next decade, we will have a liquid biopsy for patients to sort of figure out who are the ones who are going to be at a higher risk and perhaps find that cancer early or even really the great success would be right before it becomes cancer.

12:48.800 --> 13:08.700 <vGore>Well, the stool test that you mentioned to detect colon cancer early, one of our colleagues did the show with me a little while ago and the take-home I got from that was, it is still preferred to do colonoscopy. Is that your thought as well or is the stool test really pretty good?

13:08.700 --> 13:54.600 <vAhuja> Well, it depends what you are trying to do. As you and I both know 50% of patients still do not get a colonoscopy right. So, yes colonoscopy is preferred because you can not only see the problem, but you could take it out. So, it is not only diagnostic, that means we can diagnose that polyp that will become a cancer, but it is therapeutic because you can remove the polyp. So, that sounds great, one test and you do both. But here is the problem, you have to do the prep and many people do not like doing it and many people do not like taking a day off of work. So, if we can get some more people and everybody to start doing the test, the other 50% will never come to colonoscopy. If they will do the stool test, that is better.

13:54.600 --> 14:09.000 <vGore> Got it. Well, this is a very exciting stuff. Right now, we need to take a short break for a medical minute. Please stay tuned to learn more about advances in gastrointestinal cancers with Dr. Nita Ahuja.

14:09.000 --> 14:23.300 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, working to eliminate cancer as a cause of death. Learn more at astrazeneca-us.com.

14:23.300 --> 15:06.100 This is a medical minute about head and neck cancers. Although the percentage of oral and head and neck cancer patients in the United States is only about 5% of all diagnosed cancers, there are challenging side effects associated with these types of cancer and their treatment. Clinical trials are currently underway to test innovative new treatments for head and neck cancers and in many cases, less radical surgeries are able to preserve nerves, arteries and muscles in the neck, enabling patients to move, speak, breathe and eat normally after surgery. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

14:58.200 --> 16:00.100 <vGore>Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I am joined tonight by my guest, Dr. Nita Ahuja and we have been discussing gastrointestinal cancer and research advances. Nita, we talked a little bit about epigenetics and how it really involves, I guess, translating the DNA code to different kinds of cells and when it goes awry, it can help make a cell cancerous for example, and certainly I know in my field of leukemia, we have a couple of approved drugs that we at least know in the laboratory, they work through epigenetic ways, whether that is truly clinically or not, I think we are still not sure after 20 years of research, so is there any epigenetic kind of drug or treatment proven promising in any of the cancers you treat?

16:00.100 --> 20:17.900 <vAhuja>Your field actually has a few drugs that act epigenetically and have shown some benefit, and then the next part is how do they work? But in sort of more common cancers such as the solid tumors, which colon cancer is, and is very common, these drugs have been tested in the laboratory and of course they seem to work in the laboratory, but then of course, as you and I both know when we take it to clinical trials, that becomes challenging and that is for a multitude of reasons. We come in at very advanced stages of patients and these drugs have to work quickly to show some benefit. These drugs still are very old compounds that we are bringing out and the newer generation drugs are just being tested often in the liquid tumors that you work on. So, clearly, you know I have been working in this big consortium, The Stand Up to Cancer Network for the last 7 or 8 years and trying to see how can we take these epigenetic compounds and use them for the solid cancers like colon cancer, lung cancer, breast cancer. And clearly, we are still learning. We know we can use these drugs in solid tumors and occasionally, you will even see some patients who respond, but it is not a home run. And by using them by themselves, these drugs as I mentioned have a very short window of action in the body, they get rapidly removed from the body, so how long do they last,

we may not know as we use them in stronger doses, they have lots of effects and then you cannot use them. So, there is a little bit of the technology has to catchup and I know many companies are working at it. Hopefully, those better drugs are coming and we will continue on, but in the current time, the other part that has changed is our understanding of how we use these precision targets. If we say that the drugs should become more precise and then the second part is - you still need to combine them with maybe our more traditional drugs we use, like chemotherapy. Colon cancer as you know, Steve, by the time we do clinical trials, these patients have a lot of disease burden, and these epigenetic compounds are acting on a much slower timeline, so then to say, okay use a slower timeline with a disease that is growing really rapidly, our thinking has been that you really need to combine these slower acting drugs with something that could come in and give a one-two-punch. Use your chemotherapeutic drug along with this epigenetic drug. So, The Stand Up to Cancer has just finished a trial in colon cancer, I think we just finished the last patient accrual on chemo resistance, and as we know that in colon cancer, which is a very common cancer, we have got some drugs that have shown really nice responses, but unfortunately, patients develop resistance to these chemotherapeutic drugs and what we are trying to see is, can we make that cancer sensitive again to these compounds. So, using these epigenetic compounds to what we call reprogram the cancer cells to make them sensitive again to these; can we take the drugs we got and use them for a longer time. So, that trial is continuing right now and we will see what that shows. Hopefully, in the next couple of years, we will have an answer. And then, alongside the other exciting pieces there were some nice data on one of our big cancer research meetings recently, can we take solid tumors where the immune system is very cold, you know one of the nicest successes has been is in immunotherapy in lung cancer, where we can now use immune therapies and really show these remarkable responses. But only a few people have those remarkable responses, the majority of the cancers we deal with, the immune drugs do not work. So, we are now trying to see, can we use these epigenetic compounds to wake up the immune system and do a one-two punch there?

20:17.900 --> 20:19.600 <vGore> And you are doing that in some of the GI cancers?

20:19.600 --> 20:29.000 <vAhuja>Some of the GI cancers, more in pancreas cancers and these liver tract cancers, biliary cancers called cholangiocarcinomas.

20:29.000 --> 20:30.100 <vGore> Those are really tough too?

20:30.100 --> 21:01.600 <vAhuja>Those are tough cancers and also do poorly and it seems our data from the lab and from other groups suggest that they may be more sensitive as a group. So, those are some of the more short-term things we are hoping we can take this and learn from them. And it is really back to that bench to the bedside right; you do the clinical trial, you get samples, you learn more and you go to the next trial until you get the home runs like we are seeing now in lung cancer and melanoma.

21:01.600--> 21:30.200 <vGore>Well, I remember back in the day, not so long ago, at our old place in Baltimore, there were a couple of anecdotal cases of lung cancer that got this kind of treatment and then got some immune treatments and it was really a spectacular response. Have you had any on these new trials, something like that to keep you going and motivated for sometime when you see somebody do so well, do you have any of those kind of glimmers coming through?

21:30.200 --> 21:52.100 <vAhuja>There are. The colon trial I mentioned, the chemo resistance trial, we did a first initial trial, which is called the phase-1, which for your audience is where you test a new compound and make sure it is safe, and we had spectacular responses in that initial trial and then have just finished the larger trial to see if what we are seeing is going to hold up.

21:52.100 --> 21:57.300 <vGore>Right. But there was enough that you saw that made you think wow! this could really be a ticket for some patients anyway.

21:57.300 --> 22:44.500 <vAhuja>For some patients. The same in the immune drugs; and as you mentioned, this is what comes out of being in places where all these groups are working together and have an Aha! moment, can this be the real next big deal, and we notice that in our lung cancer patients, they were on immunotherapy and they had these long responses, these what we call durable responses where people are living 5 or 7 years and in April, I was at AECR, which is the big cancer research meeting and they were presenting a trial on melanoma on these durable responses with epigenetic compounds, but not our group but another group that was showing this.

22:44.500 --> 22:48.000 <vGore>That is the formally really bad kind of skin cancer which sometimes is doing very well nowadays.

22:48.000 --> 23:07.500 <vAhuja>Exactly. But now we are seeing that, yes the immune therapy works but if you combine it in this one-two punch, maybe it will work even better and really people can just have these long, long responses. So, again, still too early for us to say this is the next big thing, but certainly these Aha! moments are keeping us all interested in this arena.

23:07.500 --> 23:29.600 <vGore>We have recently done a show about this new immune therapy that uses T-cells, what they call CAR-T and one of our colleagues here was describing research trials where they are using antibodies with these CAR-Ts to even attack things like stomach cancer and breast cancer, anything coming down that way in pancreas or colon that you know of?

23:29.600 --> 23:35.700 <vAhuja>Not in pancreas. As you know, this is probably the toughest, toughest cancer.

23:35.700 --> 23:41.800 <vGore> That is why I am grasping. I am reaching out there.

23:41.800 --> 23:59.900 <vAhuja>I know and as you know, many, many groups have tried to tackle it and I think pancreas cancer almost sits in this immune

privileged area and it is tough, you cannot get the immune cells in. As you know, this has a very strong, what we call a desmoplastic reaction around it.

23:59.900 --> 24:04.600 <vGore» That means like scar tissue?

24:04.600 --> 24:31.500 <vAhuja>Lots of scar tissue. So, I do think it is not where we are seeing, but gastric cancer or stomach cancer is something that we used to kind of say maybe even not so long ago, even 5 years ago, hey stomach cancer is a bad cancer, but now we are starting to learn so much about it. So, it is a good time to be in science and in this area. We are seeing lots of our old assumptions changing.

24:31.500 --> 24:58.100 <vGore> That's great. Here you are clearly ever as enthusiastic about the progress and your surgery and all that, and now you are running a department, so now you have got all these colleagues, how does that feel? I mean, because all of a sudden, I would imagine, sort of anybody's success reflects on you, just like one's kids reflect down on the parents. Is that how it feels to you?

24:58.100 --> 25:54.400 <vAhuja>Oh, it absolutely does, but it is such a special feeling right? Just imagine when your child toddles for the first time and then they run, and that is like watching your faculty in your department, the first time they make something or they figure out a new treatment and they do a robotic valve surgery for heart and you are just so excited for them because at the end of the day, you and I both know that if you are going to do things, it is the teams that put all pieces together and you can only do something in your particular area, but what you want to do is get that enthusiasm around your department about what science has to offer, what our patients can teach us, what are the next big things, and I think that is truly just so powerful and so engaging that I truly love that piece of my life better than my own research.

25:54.400--> 26:35.800 <vGore>You know, I feel the same way. Just from a sort of legacy perspective if you will, I am going to retire one of these days, not any time very soon, but one of these days I think I would like to do that and so, I find that what I develop or hope to imbue into trainees and junior faculty and students, they are going to carry on. I think about our former colleague, yours and mine, Dr. Walsh, who basically invented the modern prostatectomy right down at Hopkins, and that was a long time when he was the only one in the world who could do it the right way, and how many surgeons are doing these wonderful prostatectomies for prostate cancer patients around the world now, huge numbers right?

26:35.800 --> 27:47.700 <vAhuja>And I think you just put your finger on what we do in healthcare. Healthcare touches all of us. We will all need it, and one of the things as you start to get, shall we say more experienced, you start to see retirement, you want to make sure that the next generation has that same desire to figure these big problems you know. Whatever the next problem will be, that someone is going to be excited about tackling it, the surgeons, the physicians, the clinicians are going to not only do what they do every day but think about

the big problems and you want to pass that love for knowledge and connecting on, because most of us wake up with this, it is not like someone says you got to do this, we do it because we worry about this and we do it because someone invested in us and put the spark there and now you are trying to get that spark in your students, in your faculty, in the nurses around you, and your team, and I think this is something we all have seen in our mentors and as you get to that age saying okay, I am seeing that I may need some of this care, you really want to pass it on.

27:47.700 --> 28:00.400 <vGore>So, who was that person or persons for you? Who really made you think Wow! I would like to be like that or I could do something like that or if only I could. Is there one or two people like that for you?

28:00.400 --> 28:06.400 <vAhuja>You know, why did I become a surgeon?

28:06.400 --> 28:06.500 <vGore>Yeah, why did you?

28:06.500 --> 28:15.200 <vAhuja>I went to medical school at Duke University at a time when there were no women surgeons in that department.

28:15.200 --> 28:17.300 <vGore>There were not many women surgeons anywhere right?

28:17.300 --> 29:43.400 <vAhujaThere was no role model. And I was thinking back about this recently and it was the chief of OB/GYN was a surgeon, who just took me under his wing and he was just a big picture thinker and he was kind to me, he thought I could do this and that belief and then confidence really made me believe I could do surgery and then it was a breast cancer surgeon who had a lab at Duke University, an made you do 1 year as part of medical school in the research laboratory, and you know I often pick things with people who are nice and this guy was a nice surgeon. There were still a lot surgeons thinking they have to be mean and we were all afraid of surgery, and my family are not physicians, my mom is a teacher and my dad is an accountant and I did not know anything about medicine, I was this wide-eyed kid at Duke and they said go pick a lab and I am like, well I heard this guy was a nice person, he gave a talk on breast cancer and how vitamin A retinoids, vitamin A can change this. I was just hooked, I was like star struck and I said oh! he is a nice person and he is doing this cool stuff, so I went and worked in this lab and it just kind of connected the pieces.

29:43.400 --> Dr. Nita Ahuja is the Chair of the Department of Surgery at Yale School of Medicine and Chief of Surgery at Yale New Haven Hospital.. 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 will join us next week to learn more about the fight against cancer here on Connecticut Public Radio.