

# Yale CANCER CENTER *answers*

WNPR Connecticut Public Radio



## *Hosts*

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## Hereditary Factors Involved in Cancer

### **Guest Expert: Victor Chang, MD**

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## **Yale Cancer Center Answers**

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*Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and the phone number is 1-888-234-4YCC. This week, Dr. Chagpar welcomes Dr. Victor Chang. Dr. Chang is Assistant Clinical Professor of Medicine at Yale School of Medicine. Here is Anees Chagpar.*

Chagpar Victor, why don't we start off by having you tell us a little bit about yourself and what you do? How long have you been here and what are your day-to-day activities?

Chang I am a medical oncologist, and I work in one of the Cancer Care Centers based in Waterbury and I spend a good part of my day taking care of patients, direct patient contact, and I spend a lot of time interacting with residents and students at Yale.

Chagpar Do you treat a particular kind of cancer or do you treat all kinds of cancer?

Chang I have a personal interest in hematologic malignancies and lymphoma, but because we are based in the community, I do a lot of general oncology and that is really what I enjoy doing.

Chagpar And I understand that you also have an academic bent as well, is that right?

Chang Yes, I direct the hematology oncology curriculum at St. Mary's Hospital, a Yale affiliated internal residency medical program.

Chagpar Before the show we were talking a little bit about hereditary factors and cancer and I think one of the things that a lot of our listeners are thinking about and hearing about and has almost become a buzz word these days, is personalized medicine. Talk a little bit about what exactly that is and is there really a revolution happening in cancer now and what is that?

Chang The field has been transformed by molecular targeted therapy and the root of this type of treatment really came when I was in training in medical school, and this was before microarray was available and we were looking at hereditary factors leading to cancer development, and some of the research led to available targets that we can use to treat cancer. So, if an individual has let's say breast cancer, there are overexpressed molecular protein targets in the cells, these cells can become a target for treatment.

Chagpar Help us to understand, if we take the example of breast cancer, we talk about hereditary factors and I think a lot of us when we think about hereditary factors think about family history and we think about BRCA 1 and 2 gene mutations and things like that, but when we think about targeted

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therapies some of us start thinking about things like estrogen receptors because people that we know may be taking drugs that block estrogen or block this molecule called HER2-neu, are those things the same? How does that play out? Can you talk a little bit about the hereditary factors and these targeted therapies and the connection or lack of connection between the two?

Chang They are somewhat related. Targeted therapy basically looks at molecular protein expression in the cells and these cells can occur in any type of breast cancer, not just hereditary cancer syndromes, and I have a lot of patients who are excited about what is happening with treatment in cancer in general and they come to me and ask about whether these treatments are appropriate for them and I try to explain to them that what is still the most important thing in terms of hereditary factors is personal history and family history, and that these cancer syndromes are very rare, but the study of these syndromes have led to these treatments that are now available, and we are now tailoring treatment for individuals with this area of understanding of the molecular expression in cancer cells. We actually can make a prognosis and select individuals who will respond to treatments that are available. It is quite exciting because now we are tailoring treatment for individuals, as opposed to just pouring chemicals or poison into peoples' veins and hoping that the cancer cells will respond.

Chagpar You talked a little bit about hereditary factors. You talked about personal history and family history. People may be listening to the show tonight and thinking, what is it in a family history that is important? If I am looking at breast cancer, do I only look at my mother's side; do I also have to look at my father's side? Is it only my immediate relatives like my mother and my sister, or do I need to take a broader history? If somebody in my family had colon cancer, does that increase my risk of developing breast cancer? Talk a little bit about all of those things in terms of family history and how it affects people's risk?

Chang The questions you are asking come up a lot in practice. Because whenever I meet someone who has been newly diagnosed with cancer the question eventually comes to, how did I get this? Are my family members going to get this type of cancer as well? I try to explain to them about cancer syndromes, and people are quite savvy these days and are on the internet and they will ask me about specific cancer syndromes, whether they have cancer of the colon or breast, and I tell them, it is your own personal history that is number one that will trump everything and then it is family history, certainly you start with immediate family members and you look through the generations as well as in second cousin, etc. and you see if there is any pattern that arises where you have a rare cancer perhaps that is happening in the family or even common cancers that are happening in clusters among family members.

Chagpar And you would look at this family history and maybe find patterns, some of which may be common patterns like we often think about breast and ovarian going together, but there are also some you might not think, things like thyroid and breast or colon and other things? Do you often refer these patients to genetic counseling, particularly for the rarer syndromes?

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- Chang I try to, and even if I do not suspect a rare cancer syndrome at play, I would like them to go to the counseling, because it gives them some background and helps with their anxiety.
- Chagpar Let's shift then to if you have a genetic mutation, or you have a hereditary factor, it is possible right to have, if your mother had breast cancer, and you went and got tested, and you tested negative for "the gene" which often refers to a BRCA 1 or 2 gene in the sense of breast cancer and I focus a lot on breast cancer, hence the conversation, but that family history still plays into your risk, right?
- Chang Absolutely. I have a lot of people who come with major concerns about their family members, not just their own, because they see the incidence of certain types of cancer in the family and they themselves want to know whether they are at risk or not and it is not always easy to assess that just from the history. For that reason I am happy that there are these genetic counseling clinics available at Yale, for example, where I can refer people to.
- Chagpar Let's suppose somebody comes to you and they say, I had my genetic counseling, I tested negative, can they still get a "targeted therapy?"
- Chang Absolutely, when we are looking at individuals who have been diagnosed with cancer, we are really looking to see whether their cancer will respond to treatment or not and molecular genetics has really transformed oncology treatment because now we can look at individuals, look at their specific cancer cells and see what is expressed on these cancer cells and see if they have the targets that will respond to treatment, and that will minimize a lot of anxiety and potential side effects.
- Chagpar Certainly in terms of breast cancer, tamoxifen, which was a drug that was invented before I was born, that to me is the original targeted therapy. But it sounds like now there are so many more targets and more technology and innovation that is going on to find these targets. You have mentioned molecular profiling and genetics a few times, talk about how that is used in your practice, in treating a variety of cancers?
- Chang For me, as a medical oncologist, I think we are in an exciting time where we actually have drugs that are designed to target cancer cells, but still we are at the infancy of this type of treatment because a lot of these drugs still work better with chemotherapy, but now we have available to us drugs that are homing in on specific targets. To me, this is like infectious disease doctors having penicillin for the first time, where they are not just pouring poison down peoples veins trying to see if they can effect a cure, here we are really trying to target specific cancer cells, the so called guided missile approach, and to use the war analogy, you are trying to minimize collateral damage and that is what we are seeing right now, effective treatments with better quality of life, which is really exciting and it is happening in every aspect of cancer whether it is breast, colon, prostate,

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and the exciting thing is that I am seeing this now in cancers like melanoma and renal cell where we really have not had very effective treatment for many years and now we have drugs that are available that we expect to have good response and we are even treating people with a pill, who would have thought really, a few years ago, that we can effectively manage cancer with a pill, granted tamoxifen has been around for a long time, but we were looking at cancer that traditionally was very difficult to treat.

Chagpar Walk us through how that happens? I mean, presumably with this guided missile approach you take a biopsy and then what? You send that to some special laboratory that tells you what the target is?

Chang And usually it could be immunohistochemical staining or even immunologic techniques they can actually look for expression of the specific molecules it could be on the surface of the cells or inside the cell and these will in some way give us a sense of how aggressive the cancer is. As you know BRCA expression connotes aggressiveness of the cancer, it also tells us that the cancer will respond to drugs like Herceptin.

Chagpar And the thing about this guided missile approach is really that you can now tell the difference between Ms. Jones' cancer and Mr. Smith's cancer, although presumably they are both the same cancer, they may be different and treated with different therapies.

Chang Yes you can and also with genetic profiling now you can also see who is going to be responsive to treatment and who is going to be resistant, and that is very good.

Chagpar Perfect. We are going to take a short break for a medical minute. We are going to come back to this conversation after, so please stay tuned to learn more about hereditary factors in cancer treatment with our guest Dr. Victor Chang.

#### *Medical Minute*

*Breast cancer is the most common cancer in women. In Connecticut alone, approximately 3000 women will be diagnosed with breast cancer this year, but there is new hope. Earlier detection, non-invasive treatments and novel therapies provide more options for patients to fight breast cancer. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection, and a healthy lifestyle breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer center such as Yale Cancer Center to make innovative new treatments available to patients. A potential breakthrough in treating chemotherapy resistant breast cancer is now being studied at Yale combining BSI-101 a PARP inhibitor with the chemotherapy drug irinotecan. This has been a medical minute brought you as a public service by Yale Cancer Center. More information is available at [yalecancercenter.org](http://yalecancercenter.org). You are listening to the WNPR Connecticut Public Radio Station.*

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- Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined today by our guest Dr. Victor Chang. Victor, right before the break, we were discussing targeted therapies and this whole era that we are in now of personalized medicine and targets and how we can use these targets, as you called it a guided missile approach that targets cancers and prevents collateral damage, and I want to pick back up on that concept. Can you talk a little bit about how exactly we do that, what exactly do these targeted therapies do? How do they stop cancers?
- Chang In terms of these therapies, the drugs are really designed to hone in on the molecules that are expressed in the cells or on the cells and these molecules tend to serve different purposes. Often in cell growth signaling and a lot of these drugs will actually interfere with that and cause stoppage of the cell growth or proliferation. There are other types of molecules as well that promote, for example, blood vessel formation, so by cutting the blood supply off to the tumor cells with these drugs you can effect a response or even a cure sometimes. In addition, you can have drugs that are targeted at molecules that promote cell death. They are so-called programmed cell death of molecules that are being looked at actively and drugs are being designed for this purpose, then there are drugs that are used to rev up the immune system to fight cancer and as an extension of that, you have drugs that are laced with toxins that can hone in on these targets and enact a kill.
- Chagpar So it sounds like there has been a lot of activity in terms of finding different ways to target cancer cells and specifically kill off those cancer cells without killing normal cells?
- Chang Correct.
- Chagpar These are certainly exciting times. How do these drugs in these targeted therapies actually get to the point where you can use them in every day practice? How does that happen? Presumably there is some biologist, or geneticist, somebody working in a laboratory, looking at cancer cells and figuring out targets, but then there has to be a process that gets from, this cancer cell has this target to, I have got a drug that can target that target, to this drug really works in mice, to this drug really works in people. Can you talk about that process and how we go from discovery to cure?
- Chang I am not so sure I am the person that can comment on that, but I am happy that there are people out there who actually look at what has been done in the bench-side of research and try to take it to the clinical side. I know that when I was coming up in the training system translational research was sort of a big catch phrase of trying to take what is available at the bench to the bedside and I think certainly in oncology we have done a very good job of doing that. I think we are a sort of model for other disciplines in that we are doing research not just for the sake of learning, but we are also making it applicable for the good of the people.
- Chagpar I think that in reality you actually do participate in that chain because as we were taking about at the break, one of the things that you, like many medical oncologists do, is talk to your patients

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about clinical trials. Can you talk to us about what a clinical trial is? Why are they important, and why should patients think about participating in clinical trials?

Chang Let me give you my perspective because I started out very interested in bench research. I was a lab rat, if you will. In medical school, I spent most of my free time in the lab looking at viral protein expression in cancer cells and when I came to Yale, I came under the influence of Bernard Forget and got a crash course in molecular genetics and I never thought that a lot of the work that was being developed at that time would come into the clinical setting so quickly. When I was in training as a fellow at Yale, microarray technology was just coming into being. Now gene array profiling is common place, you are asked to select these profile studies for your patients and they can tell you their likelihood of recurrence for the given cancer that they have and whether they will respond well, and all these things make being a medical oncologist a really rewarding experience. In terms of the targeted treatments, gene profiling aside, the fact that you can have more confidence in telling your patients that they should select a certain treatment and that it will work for them is wonderful, and my hat is off to the researchers out there, including you for that matter, that are very active in clinical research and I am really excited about being a part of that. As a clinician I can hopefully direct my patients into clinical trials and there are many wonderful trials that are now available in the community through the Smilow Cancer Care Network and I am hoping that we will encourage and get a lot of people interested in participating in clinical studies.

Chagpar One of the things that I think a lot of our listeners and a lot of patients worry about is they think of themselves as a human experiment and they do not want to be a guinea pig and they do not want anything experimental because this is their life that they are dealing with and they have cancer. What do you say to those patients?

Chang I think their fear is well founded. You are going into the unknown, you do not know how the drugs are going to work in your body and you do not know how your body is going to react to these medications. So we sit down and have a nice chat about clinical studies and it takes a lot of time, I cannot really talk to them in the scheduled 15 minute visit, but I think it is so important that I am willing to take time out of my busy day to sit down and talk to them and try to guide them through the whole process of selecting a study to participate in, and at the end of the day, I certainly tell them that if it is not for them for any reason, they should not participate.

Chagpar Certainly one thing that I think is clear is that participation in clinical trials or clinical research of any description is always the patient's choice, and for the most part you can always opt out at any point, but I think the other thing that your kind of intimating is that truthfully there is a lot of benefit to participating in clinical research. In part because we are always comparing standard of care to what we think is better, so the atomic bomb that can wipe out an entire country versus a guided missile that can avoid collateral damage.

Chang You are putting it better than I could have answered. I am in full agreement. It is tough enough to be diagnosed with cancer and then to be faced with the decision about whether to participate in a

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clinical trial or not, it is really difficult. I would never underestimate the amount of information they need to process and that added stress. Sometimes I feel terrible that I am even bringing up that aspect of their treatment, but I do tell my patients that the studies we participate in often involve drugs that we already know work very well and we want to know whether they can work better and it is so critical right now at this juncture in medical oncology with molecular targeted treatment. As I said before, it is like the infectious disease doctors finding penicillin. We really need to know how to use these drugs and the only way to know is to conduct clinical trials.

Chagpar So for people out there who are listening, who are thinking about clinical trials, appreciating all of the stress that they are under, the two things that I often tell patients to think about is one, it is a well known fact that people who participate in clinical trials tend to do better than people who do not simply because they often have the availability of newer targeted drugs that we do not otherwise have off protocol, and the second is, there is a real kind of sense of doing something good for the future of medicine, for future generations and I think that a lot of patients are really drawn to the motivation of helping, as you say, once you have discovered penicillin learning what you can do with that, that was on the backs of many patients who participated in clinical trials and it is the same with cancer care.

Chang I think that when you present it this way to patients most of them will agree to a clinical study and it is really our job to make the whole process less intimidating, and as you know we try very hard to do that, we have clinical research coordinators based in our office just for that purpose to make the whole process easier in terms of information gathering and paperwork that is involved, so I am hopeful that we will get more people on studies.

Chagpar And the other thing that I think is important to note is that it used to be that if you wanted to participate in a clinical trial many people would travel to the big major academic centers to find a clinical trial that they could participate in because they know that is how they can do better and for some people who otherwise have incurable cancers that do not have good treatments, that is the only way they can get treated, but now you have got studies available in the community.

Chang Absolutely, and it is really exciting that now people do not have to travel to New Haven to Smilow to get their treatment. They can participate in a study through our office, through our care center office up in Waterbury and that is very nice, they get to see the nurses and doctors they are used to and they can participate in something meaningful. So, it is wonderful. I also want to make a point that people have certain ideas about clinical trials. Some people think, my cancer is beyond help and that is when clinical trials are offered and that is very far from the case. With these molecular targeted treatments now we have studies that are being conducted in the setting where we are

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trying to prevent cancers from happening again. So I am hoping that patients and family members out there will take a look and speak with their family doctor about opportunities.

Chagpar Can you talk a little bit about some of the exciting clinical trials that you are offering and what do you think is on the horizon? What are the most exciting clinical trials that you are doing?

Chang Personally, for me, I can see the benefit already in terms of effective drugs for people living with cancer, but it is the prevention side that I am very excited about, looking at these drugs and how they are being added to other known effective medications in terms of preventing cancers from happening again, this is prevention. I guess the ultimate goal for me would be to put myself out of business and get to a point where people can live cancer free, that is really what I want to see, so for me personally I would like to focus my efforts more on the prevention side, so patients who have had cancer and perhaps had breast cancer and had their cancer removed, I would like to see that these drugs are been studied to see if we can prevent the cancer from coming back.

*Dr. Victor Chang is Assistant Clinical Professor of Medicine at Yale School of Medicine. If you have questions or would like to add your comments, visit [yalecancercenter.org](http://yalecancercenter.org) where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.*