

Healthline with Yale Cancer Center

Hosts

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WTIC Newstalk 1080

Advances in Ovarian Cancer Research

Guest Expert:

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*Healthline with Yale Cancer Center is a weekly broadcast on WTIC Newstalk 1080
Sunday Mornings at 8:30*

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This is Healthline. A joint venture of WTIC NewsTalk 1080 and Yale Cancer Center. Yale Cancer Center is a resource for cancer programs throughout Connecticut, developing new advances in prevention, screening, diagnosis and treatment. On Healthline you will hear from some of the leading doctors in the country. Healthline is not intended to provide medical advice. Yale Cancer Center urges you to consult with a qualified physician in your community for diagnosis and for answers to your medical questions. And now, our co-hosts oncologists, Ken Miller and Ed Chu.

Miller Good morning and welcome to Healthline. My name is Dr. Ken Miller, and I am the Director of the Survivorship Program at the Yale Cancer Center. Healthline, with the Yale Cancer Center, is our way of providing you with the most up-to-date information on cancer care every Sunday morning at 8:30 am on WTIC NewsTalk 1080. Our Healthline program features some of the nation's leading oncologists and cancer specialists who are in the forefront of the battle to fight cancer, right here in Connecticut. We are joined by a different expert from the Yale Cancer Center each week and together we talk about the myths of cancer, the latest treatment available to people with cancer, and advances in clinical research. Our goal is to give you help by sharing this information, and also to give you hope. If you would like to submit a question about cancer to Healthline, please email us at Healthline@Yale.edu or call 1-888-234-4-YCC. If you are interested in listening to past editions of Healthline, or if you would like to learn more about a specific kind of cancer, all of our shows are now posted in audio and written format on the Yale Cancer Center website, which is www.YaleCancerCenter.org.

Today we are going to talk about progress in ovarian cancer research. My co-host, Dr. Ed Chu, is on vacation so I will be welcoming our guest, Dr. Gil Mor, an Associate Professor of Obstetrics and Gynecology, a lead researcher in a program here at Yale called "Discovery to Cure," and a lead researcher in his field throughout the country.

Miller Gil, thank you so much for being with us.

Mor Thank you, it is a pleasure to be with you.

Miller I would like to start by asking you what the "Discovery to Cure" program is.

Mor The "Discovery to Cure" program is a translational research program that we established almost 4 years ago. The objective of the program is to decrease the time that it usually takes to bring new discoveries from the lab to the benefit of the patient. As you are aware, when we discover something in the lab, it may take 5 to 10 years until someone rediscovers it for the clinic and another 5 years until it goes to a company and clinical trials start.

Miller So in the past it could be up to 15 years from discovery in the laboratory until it benefits someone?

Mor That is correct.

Miller It's a long time.

Mor It is a long, long time. Now, we have been able to accomplish that in 1 year to 16 months. Whatever we discover, we immediately bring it to the clinic, then clinical trials, and then we license our discoveries to pharmaceutical companies who can move these discoveries nationally for use by the patients.

Miller In many ways this is a marriage between academics and industry, using the best skills of both.

Mor That's correct, not only do we work in the academics with our colleagues in the clinic, and in the Gynecologic and Oncology Clinic, but we also work with a lot of pharmaceutical companies. We test new compounds, and we bring whatever we find in the new concepts to clinical trials.

Miller It sounds like one of the goals is to speed up the translation of new discoveries to clinical care. Are there any other major goals of the program?

Mor Yes, let me summarize the two main areas of interest that we have. One area is related to early detection of gynecological cancers. We want to develop tests that can predict, at early stages, when the cancer is appearing. The second major area is to develop new therapeutical approaches to treat those patients that have cancer.

Miller In terms of early detection, men have the PSA screening, which has turned out to be very useful. What is happening in terms of early detection for ovarian cancer?

Mor In early detection for ovarian cancer, there is nothing that can really detect when the disease is at its early stages, stage 1 and 2. CA125, the only marker that we have today has a very low specificity for stage 1 and stage 2 cancers. It is between maybe 20% or 25%. So, the majority of the cases in ovarian cancer are diagnosed when the disease is at stage 3 and stage 4, and treating those stages is very difficult.

Miller In the work that you have been doing in terms of early detection, what are some of your findings, and how are these translating into ways we can improve patient care?

Mor We reported in May 2005, a development of a new blood test that looks for markers in the blood. This test has a specificity and sensitivity of 95%. It is really impressive. This is an example of how we are able to get things moving quickly. We did a first validation with the NCI. We have licensed this product already to a company LabCorp, and we are now in a national clinical trial with validation, and we hope this will be commercially available very soon.

Miller So potentially we might have the equivalent of a PSA for women?

Mor Yes, and I might say even better than PSA.

Miller True, because PSA isn't nearly 95%.

Mor I think it is around 60%.

Miller This is very exciting. Hopefully women that develop this disease can be diagnosed and treated earlier.

Mor The test that we have developed is able to detect stage 1 and stage 2 of the disease. We have several cases where ovarian cancer has been recognized when the ultrasound failed, when C125 failed, when everything was saying that the patient was completely normal, our test found that it was positive and it was confirmed by the pathologist as stage 1A, that is a very early stage of the disease.

Miller How many women develop ovarian cancer?

Mor The statistics indicate that this year it is expected that there will be around 22,600 newly diagnosed ovarian cancer patients. From those 22,600, 16,000 will die of the disease, and the reason is because from those 22,600, about 80% are diagnosed in stage 3 and 4.

Miller If we are diagnosing at stage 1 and 2, it sounds like the chance of survival will be much higher.

Mor That is correct, if it is discovered in stage 1 or 2, and treatment begins subsequently, there is a 90% chance of a 5-year survival, and even maintaining the disease in stable condition. So it is a big, big difference.

Miller Are there any risk factors for developing ovarian cancer, and are there any ways to reduce the risk?

Mor That is a very important question, and after some discussion on this topic I am sure that there will be a lot of people that do not agree with me. The nature of focus when you talk about breast cancer or ovarian cancer is always the genetic risk. Doctors like to study and screen only those who have a genetic risk. My personal opinion is that this should not be the main focus.

Miller Tell us more about why this is.

Mor In the general population, we see that 15% of these cancers are from genetic origin. So you have another 85% of the cancers in which we don't know what genetic component it has. It is critical to screen those women who are at a higher risk from a genetic point of view. However, you have a big population that has a risk that I call environmental risk, or quality of life risk. This means what

they eat, how they exercise, how they behave, if they smoke, when they had children and so on. Those practices may create a higher risk than just having a BRCA-1 or BRCA-2 mutation.

Miller We are going to take a break now for a medical minute. We will be back to talk more with Dr. Gil Mor, an Associate Professor of Obstetrics and Gynecology and an expert on ovarian cancer.

Medical Minute

The American Cancer Society estimates that in 2006 there will be over 62,000 new cases of melanoma in this country. Twenty four hundred patients are diagnosed annually in Connecticut alone. While melanoma accounts for only 4% of skin cancer cases, it causes the more skin cancer deaths. Early detection is the key. When detected early, melanoma is easily treated and highly curable; however, patients with advanced melanoma have more hope than ever before. Each day, patients are surviving the disease due to increased access to advanced therapies and specialized care. New treatment options and surgical techniques are giving melanoma survivors more hope than they have ever had before. Clinical trials are currently underway at Yale Cancer Center, Connecticut's only federally designated comprehensive cancer center to test innovative new treatments for melanoma. Patient's enrolled in these trials are given access to newly available medicines which have not yet been approved by the Food & Drug Administration.

This has been a medical minute brought to you as a public service by Yale Cancer Center. For more information visit our website at www.YaleCancerCenter.org.

Miller Welcome back to Healthline. We would like to remind you to email your questions to us at Healthline@Yale.edu. We would be glad to try to answer them while we are on the air or at a different time. Again, this is Dr. Ken Miller, and I am in the WTIC studios with Dr. Gil Mor who is an Associate Professor of Obstetrics and Gynecology at the Yale School of Medicine.

Miller Gil, right before the break we were talking about the risks for ovarian cancer. Are there any ways that women can reduce their risk?

Mor There are several things that a woman can do in order to reduce her risk. One is, of course, the quality of life, the type of life, a good diet, and exercise. There is another point that is difficult to advise, but we know that pregnancies early in life are a way to decrease the risk of ovarian cancer, as well as breast cancer, because you reduce the amount of ovulation and the amount of stress that you put on those epithelial cells of the ovaries to repair. These factors are very important to take in consideration for reducing your risk.

Miller We talked about how PSA for men may only be 60% to 70% effective, and there has been a lot of work that your lab has done that has increased the ability to detect cancer. From what I understand, you have got a new test. Can you tell us more about that?

Mor Yes. If you want to study the screenings of the general population with a test that has 95% sensitivity, although this is the best that exists today, the false positives, when we start testing large numbers, are a major problem. A perfect test to be used for a general screening has to have a sensitivity of 99.6%. Since we have discovered this test with 95% sensitivity, we have been working very hard to improve the sensitivity. We changed the platform of the system that we used to evaluate the markers, and we added two additional markers to our panel. I am very happy to share with you this recent news that our modification of the original test has now, a sensitivity of 99.67% and a specificity of 98%.

Miller Which is pretty amazing.

Mor It is indeed, and we are very excited about this.

Miller I want to share with you a couple of relevant emails that we have received. One is from Barbara who lives in Haddam. She says,

My mother was diagnosed with ovarian cancer when she was in her 50s. Now that I am approaching 50, is there anything I should be watchful of?

Mor Yes. We know that ovarian cancers, as well as the majority of cancers, start appearing as we age. We are living longer now so there are more cancers. With a history of ovarian cancer in the family, and as we age, it is true, the risk is increasing. What I recommend is a good followup. Our test will be excellent for Barbara. The followup of every 3 months, or maybe every 6 months, with this test is the best way. Our test functions as the mammography for ovarian cancer. It can be used regularly to tell you whether everything is okay or that something may be wrong.

Miller How often do you predict this test will be done?

Mor As we continue learning from this test, things are changing. We know now that it is not just one protein but 6 proteins that we use. It is very difficult to say okay, all the proteins will appear suddenly. What we see is that the proteins start changing their concentration over time. We are advising now between every 3 or 6 months. The more frequent the test, the better picture we can have of what is going on. It is very simple, you need just 5 mL of blood, so it's not an invasive technique, and you aren't required to spend 2 hours in the office to be tested. It takes you exactly 10 minutes.

Miller Is it a blood test?

Mor Yes, it's a blood test.

- Miller The “Discovery to Cure” program has contributed to this new technology, but what makes this model at Yale so successful?
- Mor Everybody talks about translation of research. What makes it successful is the team. We have an incredible team. Everybody plays the role that they have to play; the physicians are taking great care of the patients and we are conducting important scientific research, but that is also what everybody is doing. What makes us different is that we talk. We talk to each other, and what do we talk about? We talk about material from the clinic, clinical information, tissue samples, and blood samples coming to the lab. We perform the studies, we find something new, and immediately a clinical trial is put into action. Our physicians will run the clinical trial, the samples that are collected from the clinical trial come back to us, and again we analyze where we may have failed. Sometimes the failures of our clinical trials have been the success for the next steps.
- Miller This applies to all parts of life; that you learn from your successes and from your failures too. If a woman is interested in having this blood test, or getting more information, who should she contact?
- Mor We have a telephone number women can use to contact us which is, 203-785-6956.
- Miller Thank you, that number again is 203-785-6956, and that will be posted on the website as well. I want to share with you another e-mail from a woman who has had ovarian cancer. I think it reflects on how this test may be useful. Her name is Nancy and she’s from Groton. She writes,
- I was treated for stage 2 ovarian cancer 6 months ago, what monitoring would you recommend?*
- Mor The monitoring that exists today is again, C125 and ultrasounds. C125 is a very good marker, and for recurrence it is even better. It’s between 70%-80% in all recurrence. However, even at the stage of the recurrence, C125 will go up only when the tumor already has grown. What we are trying to do is to detect it before the tumor is big enough to produce these factors and before it can be detected by an image system. We want to detect when the tumor has just a few cells and is not able to secrete enough things in the blood. With our test we are not looking at what the tumor is producing in the majority of cases. We are looking at how the body is responding to the presence of those few cells. In the case of Nancy, we are also evaluating the possibility of using this test for recurrence of the disease and we have several cases where we have been able to detect recurrence in early stages. We are now preparing a national clinical trial, together with the Gynecologic Oncology Group, the GOG, for the use of this test in monitoring recurrent disease. This trial will be opened at the beginning of 2007 and will enroll close to 2000 women nationally.
- Miller So this blood test that you have developed, this platform, will be helpful in early detection before the disease is even diagnosed, and also for women who may have developed a recurrence of ovarian cancer after treatment?

Mor That's correct.

Miller We would like to remind you to please e-mail your questions to us at Healthline@Yale.edu, especially if you have questions for Dr. Gil Mor, a researcher focused on ovarian cancer. We are going to take a short break for a survivorship story.

Survivor Story

A few years ago, the diagnosis of cancer was a death sentence for many patients, but today thanks to advances in clinical research we are turning the corner in the battle against cancer. There are over 10 million cancer survivors now living in the US. They are the true heroes in the war against cancer. Here is the story of a hero from Milford.

My mother passed away last September after a recurrence of breast cancer. Three weeks later the results of an earlier biopsy came back as cancerous. Can you imagine my horror? My Yale based gynecologist Musa Speranza referred me to a wonderful surgeon at the Yale Breast Center, Donald Lannin. Dr. Speranza moved quickly. She gave me the news of the diagnosis on a Thursday and I had an appointment that Friday with Dr. Lannin. Sensing my distress and anxiety over the diagnosis, coupled with the recent death of my mother, Dr. Lannin also moved quickly to alleviate what fear he could and scheduled me for a lumpectomy that Monday. I was then introduced to my oncologist Dr. Kenneth Miller at the Yale Cancer Center and Dr. Joanne Weidhaas who would become my radiation oncologist. I am fortunate. Dr. Miller and the wonderful nursing staff at the Yale Cancer Center got me through the entire ordeal healthy, well, and feeling fabulous.

This survivor story has been brought to you by Yale Cancer Center.

Miller Welcome back to Healthline. This is Dr. Ken Miller, and I am here in the WTIC studios with our guest Dr. Gil Mor, an Associate Professor of Obstetrics and Gynecology at the Yale Cancer Center.

Miller Gil, one of the big advances that I have read about from your work is subclassifying ovarian cancer into different types. Can you share a little bit about that?

Mor One of our major problems is that we classify the patients, using ovarian cancer as model, according to the histology, the pathological diagnosis, they will tell you this is epithelial ovarian cancer, familial, and so on. You take the epithelial ovarian cancer in one box, you give them one treatment, but even with the same type of histologic epithelium not all of them respond the same. Even when new drugs, we will talk a little later about the new treatments that we have developed, are used not all the patients respond, so we have been wracking our brains with the question, why with the same histology that in the lab looks exactly the same, does it responds differently?

- Miller In a sense you have been able to classify ovarian cancer into different groups. How does that then reflect on what you hope to do for women?
- Mor What we did is we took the same epithelial cells and we started studying them. We have new technologies that allow us to study just a single cell from the tumor. That's the beauty of today's technology. What we found is that, although they look the same, they are not the same. Now we have intracellular markers for each tumor that will tell us what the appropriate treatment is. This is the future of the medicine and the future in cancer. We cannot put all the cancers in the same box. There are intracellular markers that will tell us, this patient will respond to paclitaxel or will not respond to paclitaxel, or will be sensitive to this, or resistant to that.
- Miller If a woman has surgery for ovarian cancer at Yale, does the material come to the laboratory to be analyzed, and then the feedback is given to the clinicians, or has it been translated already?
- Mor We have a clinical trial that we are opening now, where each time a patient goes in for surgery, we receive a biopsy of the sample. We use a new technology, Laser Capture Microdissection, where we obtain 500 cells from the tumor. We look up all these sets of markers, and we can define whether this patient will benefit from the treatment of paclitaxel, or if it will help the tumor to grow. We are finding that if you give the patient the same drug it may have the opposite effect. In one patient it will kill the tumor and respond to the treatment, and in another patient the same compound, in the same epithelial ovarian cancer, will induce growth of the tumor.
- Miller So this will impact the drug choices for patients?
- Mor Yes, and that's what we want. We want to be able to help the clinician and the surgeon to determine, according to those markers, what type of specific chemotherapy will be useful for that patient.
- Miller After you get 500 cells from the tumor, how are you analyzing those cells? Is that done under the microscope, or using a different technique?
- Mor We go to the protein level, so we look using technologies like Western blot, Elisa, and so on. These are technologies that allow us to see the expression of specific proteins. Also, using the cells in vivo, that are alive, when we isolate them, we can see how they respond to some of the drugs. The combination of those different tests gives us a better idea of what will be effective for that patient.
- Miller What are the next steps for your research team as you continue working on these projects? Where do you see the field going?

- Mor One of the major problems is that we have found many cancers that are resistant to all the drugs that we know. Another idea that I want to share, is that when we talk about recurrent disease or when we talk about the cancer in advanced stages, it is able to acquire the capacity to use the weapons that we are trying to kill the tumor with, for its own growth. The other area that we are very interested in, and do a lot of work with, is the monological part. The tumor, in advanced stages, uses the immune system to feed its own growth. For example, when we give a vaccination where you have an infiltration of immune cells, we are happy, we are thinking, my goodness we were able to take the immune cells and kill the tumor. It can work the opposite way as well though. Those immune cells that have gone inside the tumor can help the tumor to grow. How do I see the future of research? It is trying to modulate to attack those different aspects of this evolution of the tumor, to stop the inflammatory process, to gain control of the immune system, and to control another area that is called apoptosis.
- Miller What is apoptosis?
- Mor In order to survive, we need to die. Our tissues are dying constantly, and our tissues regenerate tissue and clean it up. Once we become resistant to apoptosis, or normal cell death, that is when it becomes a cancer. Chemotherapy kills those cancer cells by activating apoptosis.
- Miller Two things that may hold a lot of hope are immunology, looking at how we respond to the tumor, and how that may be helping or hurting, and also regulating apoptosis.
- Mor That's correct.
- Miller What kind of clinical trials are available at Yale that may reflect on this research?
- Mor There are several new compounds but, because of time, I will just tell you about one drug that we studied in the lab that we found modulates the apoptotic cascade. The drug is phenoxodiol, and this compound, while regulating the apoptotic cascade, sensitizes the chemo-resistant ovarian cancer cells to the drugs that were previously resistant. We started with a phase I clinical trial and we are now in a phase II clinical trial. There is a company with the compound that is organizing a phase III trial, but we have a phase II clinical trial running now at Yale, combining phenoxodiol and taxotere.
- Miller Does the drug phenoxodiol have a lot of side effects?
- Mor Absolutely not, and this is the advantage in the concept because drugs that are modulators shouldn't be toxic.

Miller This has been a fascinating half hour and I have learned a lot about ovarian cancer. I'm excited about all of these new advances. I would like to thank Dr. Mor for joining us. Are there any final messages that you want to share with the audience?

Mor I would like to thank all of those patients that go to clinic and agree to share a blood sample, or who sign a consent form confirming, it is the tumor or it is my tissue, because, although it may not help them directly, they are helping thousands of women in the future. They are the real ones making the medicine.

Miller I would like to thank Dr. Gil Mor for joining us today. I want to remind you to please tune in to WTIC NewsTalk 1080 every Sunday morning at 8:30 am for Healthline with the Yale Cancer Center. Our next program will focus on the detection and treatment of head and neck cancer, with our guests, Dr. Hari Deshpande and Dr. Clarence Sasaki. Until then, this is Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.