



Cancer Research

Developing New Drugs for the Treatment of Lung Cancer

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Guest: Peter Koo, PhD, Associate Professor of Medicine (Medical Oncology), Yale School of Medicine

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Welcome to a series net casts brought to you by Yale University.

Thank you for joining us for this edition of Yale Cancer Answers where we provide you with up-to-date information on cancer care and research. Our host, Dr. Anees Chagpar, is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital. She interviews some of the nation's leading oncologists and cancer specialists who are on the forefront of the battle to fight cancer. If you are interested in past editions of Yale Cancer Answers, all of the shows are posted on the Yale Cancer Center website at YaleCancerCenter.org. If you would like to join the conversation, you can contact the doctors directly, the address is canceranswers@yale.edu. Here is Dr. Chagpar.

Chagpar Welcome back to another episode of Yale Cancer Answers. I am Dr. Anees Chagpar, and I am joined today by my guest Dr. Peter Koo. Dr. Koo is an Associate Professor of Medicine in Medical Oncology, and he is here with us today to talk about the development of new drugs for the treatment and prevention of cancer. Thank you so much for joining me.

Koo Thanks for having me.

Chagpar Peter, let us start off by talking about lung cancer because that is really as I understand your main focus.

Koo Yes, correct.

Chagpar Tell us about the current therapies for lung cancer. Do we do a pretty good job at the moment treating this disease or is there still a long way to go?

Koo I think we still have a long way to go because each year in the United States, we lose about 600,000 people to cancer.

Chagpar Because it is the #1 cause of cancer-related death, lung cancer.

Koo That's right. It kills about 158,000 men and women, and 1.7 million worldwide. So, there is an urgent and critical unmet clinical need here.

Chagpar But, not everybody with lung cancer dies, right? Because otherwise everybody who is listening to the show thinking about people who have got lung cancer are going to get really scared. There are some treatments, right? Talk a little bit about what the treatments are currently, so if I come in to your clinic today and let us say I have got lung cancer, how would I be treated?

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- Koo As you know, lung cancer also has four different stages and particularly the later advanced stage is very difficult to treat because the lung cancer patients come into the clinic at later stages and we have very limited methods to treat these patients. The 5-year survival rate of lung cancer is about 17% at this stage.
- Chagpar Seventeen? So, a few key points I guess. The first is the need for screening, and my understanding is that there really is not a whole lot of great lung cancer screening out there. It is not like it is breast cancer and you can get a mammogram every year.
- Koo That is correct. There is no good way of screening lung cancer. We use the x-ray, we use the spirometry, the low-dose CT type of thing. However, there is no definitive screening method like with other cancers, and we have a lot of people and physician scientists, working really hard on identifying those biomarkers that can be used for early detection of the lung cancer.
- Chagpar And I know that we have had discussions on Yale Cancer Answers in the past with Dr. Frank Detterbeck talking about how now, especially for people who have a significant smoking history that spiral CT may be used for screening, but lung cancer happens in nonsmokers too, and so, trying to catch those cancers early gets to be difficulty I guess and that is why people present late.
- Koo That is correct. Especially the people who do not have any smoking history, they are still pretty good, like 15% of lung cancer patients are nonsmokers. So, particularly those patients are difficult to identify because there is no prior history in the family or the obvious factors exposed to develop lung cancer. So, the lung cancer is really difficult to treat.
- Chagpar When we talk about later stages especially, I mean in most cancers, later stages are treated with chemotherapy. So, does chemotherapy not work in lung cancer or does it work in some lung cancers but not others?
- Koo Yeah, definitely this is patient to patient cases because some patients respond to chemotherapy; however, the later stages are very difficult to treat with chemotherapy. Now, we are developing new therapy, targeted therapy, and recently immunotherapy.
- Chagpar So, that is a very nice transition into the state of the science now. Now, I understand that you are part of a group of investigators here at Yale, who have gotten a very large grant called a SPORE. You want to tell us what a SPORE is and why that is so important and so prestigious and actually may make a difference in the field?

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- Koo The SPORE is the acronym of specialized program in research excellence, and this program was developed originally by the NIH to support the translation of research that brings the scientific findings in the laboratory to clinic so that the patients can have better opportunities of new clinical effective treatment. And so, explain this SPORE here is maybe too short and we may not have enough time, but let me try to briefly explain this. The Yale Lung SPORE is led by Dr. Roy Herbst and Dr. Lieping Chen, and it is composed of four main projects and three co-projects that supports the main projects. And also, developmental research project and career development program that can identify and nourish the junior scientist and physicians in this research area. So, in this program over 100 scientists and physicians are working really hard together to find new method of lung cancer treatment and prevention.
- Chagpar I want to jump in here just for a brief second to really highlight to our listeners how important that is. Because the key phrase really is translation, and I think that is often a buzz word we throw around and we talk about bench to bedside and back again research, and we talk about physicians and scientists and we banter those terms around as though they really do not mean anything, but putting it into context and I think right now it is particularly meaningful to put that into context when you think about Joe Biden and his son who recently got cancer and now he is moving forth this whole moonshot project and one of the things for our listeners who have heard Joe talk, he really does talk about team science and bringing together scientists who are doing that critical research at the laboratory bench side and making sure that they are communicating and talking with and collaborating with the clinicians seeing the patients at the bedside because it is only when you really bring those two groups of people, those two sets of brain power together that you can really start making significant difference, and so that really is at the crux I think of what SPORE is, is that right?
- Koo Right. The SPORE is really bridging between lab scientists and the physician in the clinic. Because a lot of scientific findings are very difficult to interpret and then translate or move this finding into clinic without the science that supports this transition. So, SPORE is really the tremendous amount of scientific findings that translate into bring drugs and methods of treatment into a clinic so that the patients get benefit out of this.
- Chagpar That is right, and it can start leading to clinical trials, and we have talked so much on this show about the benefit of clinical trials. So, tell me a little bit more about some of the projects that are going on in the SPORE and some of the science that is really being investigated and what promise it holds for new therapies.

Koo Yes. One of the recent therapies in the oncology community is the immunotherapy. And this immunotherapy is specifically targeting the blocking immune surveillance system in humans. What I am saying is, in humans, our immune system is continuously scanning to find bad and malignant cells and get rid of them. However, cancer cells are really smart and evolve, escaping from the immune surveillance system. So, this immunotherapy basically restores the human immune surveillance system so that the immune cells can find the cancer cells and kill them. And this SPORE, one of the projects, is really working toward that immunotherapy because the current limitation with immunotherapy is about 20-30% of cancer patients are responding to this drug. Remaining 70-80% patients are not responding to this miraculous immunotherapy. So, Dr. Roy Herbst and Dr. Lieping Chen and our department are working to identify a new method targeting those patients who are not responding to current immunotherapy or resistant or recurring by the immunotherapy.

Chagpar So, they are trying to figure out, if I understand you correctly, why even with using immunotherapies, which are supposed to take away the invisibility cloak of these cancer cells that makes them hide from the immune system, why that immunotherapy still does not work in fairly substantial number of patients. And so, how far are they on that, have they figured that out because my goodness, if they could figure out what to do with the people who do not respond and why they do not respond and figure out how to make them respond, we might be on the verge of something really great in terms of potentially, dare I say even finding a cure for lung cancer, maybe not?

Koo Yeah. We are really working towards that. I think the best person to answer your question is Dr. Roy Herbst.

Chagpar Yeah, but Roy is not here, he is off in the clinic somewhere treating patients.

Koo Oh, yeah. He is so busy treating these patients because Yale Cancer Center is really the home of immunotherapy because our landmark study for this immunotherapy was originally reported by a group of physicians at Yale, including Dr. Roy Herbst, Dr. Mario Sznol and Dr. Scott Gettinger and Dr. Dan Petrylak. So patients heard about those studies, those landmark studies and saw the outcomes of the response of the therapy. So, the patients come in and we have our physicians really busy taking care of those patients.

Chagpar Yeah. I think that is a good point. I wonder how many of our listeners really know that the landmark studies in immunotherapy, whether it is in the lung cancer or in melanoma, really came out of Yale science and were published by Yale doctors, and it

is really so wonderful to see that moving forward and the fact that we are able to build on our previous strengths and previous publications and now trying to really even hone it further and figure out, well why do some people not respond and other people do. What other therapies or promising treatments are coming out of your research and out of the SPORE?

Koo Specifically speaking, one of the topics that we are currently working is the patients who are not responding to those immunotherapies, and we are identifying new targets, we try to identify new combination therapy so that we can expand the spectrum of patients that we can treat. Another is as basic scientists and translational cancer biologists, we try to identify totally new targets, and recently we identified one of the targets that is not known as the therapeutic target and this is one of E2F transcription effect of family member and this is called E2F8. We reported this finding that this E2F8 is a good therapeutic target in recent journal of National Cancer Institute, and currently we are developing new method and new drugs targeting this transcription effect of E2F8. And this E2F8 is really overexpressed in the majority of human cancers, and we are hoping that we can develop new drugs targeting this E2F8 in the near future.

Chagpar Peter, this is so exciting. I mean, finding new targets, looking at combination targets for people who may not respond to immunotherapy. Are these now in clinical trials or are we still in that translational phase trying to figure out if these combinations will work?

Koo Yes, we are in the currently translational period because the scientific findings to clinic, there is a huge gap even though we say easy, but to translate those scientific findings into clinic takes numerous support and funding and interest and resources. So, we are start seeing these things through the SPORE and through new initiatives such as moonshot program, so we are hoping that all of those resources can support and provide some additional resources for our studies so that we can translate our scientific findings into clinic more rapidly because we know this is very critical target, important for future clinical uses, but to translate this we need more data, more findings and more supportive studies.

Chagpar But a lot of our patients who are listening to this broadcast, they are asking themselves one question, which is when are those targets, when are those therapies going to be in clinical trials so that people can avail themselves of that. Do you think that is going to happen in the next year, 5 years, 10 years, what is your sense?

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Koo Currently, we are talking with the people so that we can move this project forward into clinic. We are expecting 18-24 months, and after finishing those studies that are required for FDA approval, then we can do move on to this in clinical trial, hope in 2 years.

Chagpar It is just amazing to hear what fabulous work is going on at Yale with the lung SPORE and immunotherapies and finding new targets that really will help to get the therapies that will help us to treat these cancers so much better. Thank you so much for joining me, Dr. Koo. It was such a wonderful discussion about your research and the development of new cancer drugs. Until next time, this Dr. Anees Chagpar wishing you all a safe and healthy week.

This has been another edition of Yale Cancer Answers. We hope that you have learned something new and meaningful. If you have questions, go to YaleCancerCenter.org for more information about cancer and the resources available to you. We hope that you will join us again for another discussion on the progress being made here and around the world in the fight against cancer.