

Dr. Thomas Lynch, Jr., Personalized Cancer Care at Yale June 14, 2008
Welcome to Yale Cancer Center Answers with Drs. Ed Chu and Francine Foss, I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and he is an internationally recognized expert on colorectal cancer. Dr. Foss is a Professor of Medical Oncology and Dermatology and she is an expert in the treatment of lymphomas. If you would like to join the discussion, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This evening Ed and Francine welcome Dr. Thomas Lynch. Dr. Lynch is the new Director of the Yale Cancer Center and Physician-in-Chief of Smilow Cancer Hospital. Dr. Lynch is a graduate of Yale University and Yale School of Medicine and has just returned to New Haven after an extended stint at a certain university in the Greater Boston area.

Chu What brought you back here to Yale?
Lynch Ed, it is obviously an incredibly exciting time for cancer at Yale, and there are three key things which made a big difference in my thinking. The first is, as you and Francine well know, we are about to open the Smilow Cancer Hospital in the fall of this year which will be a beautiful state-of-the-art facility for taking care of patients with cancer in a multidisciplinary fashion giving us outstanding facilities to bring new treatments to patients. The second great thing is the opening of the West Campus of Yale University which will enable the establishment of a group of terrific cancer biologists who will be working with other biologists in similar areas to create teams that will be able to focus on cancer biology. Thirdly, I wouldn't have come here if I didn't think that the physicians, nurses, and staff here are the very best. These are the three things, the quality of the people who are here, West Campus, and Smilow, that create a perfect set of conditions to come to Yale.

Foss Tom, could you talk a little bit about what your priorities are coming into Yale Cancer Center, and could you also touch on the fact that Yale Cancer Center is an NCI-designated comprehensive cancer center and what that means and how it fits into the scope of what you are trying to accomplish here?
Lynch The first question, what are the priorities? I think the priorities for the first year are pretty clear. We have a brand new cancer hospital that is going to open in the fall and opening that hospital, and making sure we have it staffed adequately with the right people there to be able to provide services to our patients will be incredibly important. The second big priority this year is beginning to find scientists and scientific leadership for West Campus as we go forward in West Campus. Those are the two biggest priorities for this year. The West Campus opportunity is remarkable because it won't just be cancer biology. It will be cancer biology, a new field called systems biology that will bring investigators who are focused on biologic systems, many of which will be cancer-related I believe, cell biology, chemical biology, and infection will all have a presence in West Campus. I think over the next year, finding the right mix of scientists to bring to West Haven will be important.

The second question about the NCI-designation is that Yale is one of a unique and small group of medical centers in the country that have

the comprehensive cancer center designation. What this indicates is that the National Cancer Institute believes that we have the right combination of resources to be able to look at cancer in a global and comprehensive fashion, meaning we can study and we can investigate new treatments for cancer, understand better what causes cancer, and also bring into play several of the resources of the Cancer Control Group from the Yale School Public Health which we are very excited and happy to be able to work with here in New Haven. What's nice about Yale, and what is great about Yale, is its size, meaning it's not too big or too diverse. We have a size that allows investigators who are working in the laboratory, physicians who are working in the hospital, and epidemiologists who are working in the field to actually get together, work with each other, and bring those resources together to create teams to be able to investigate and improve our outcome against cancer. Chu Tom, you have mentioned the West Campus now a number of times. Could you tell our listeners where is the West Campus in relation to the Main Campus at Yale and the Smilow Cancer Hospital? Lynch The West Campus is right off I-95 in Orange/West Haven. I believe a part of it is in Orange and a part of it is in West Haven. I remember that area well because when I was a college student it was the site of a movie theatre, and I remember going to see Saturday Night Fever out where West Campus is today. But it was a facility that a number of pharmaceutical firms, most recently Bayer, owned and when Bayer was acquired by Schering and merged with Schering AG the need for that facility for them became less important and Yale was able to purchase the facility. It's a beautiful campus. It has several buildings which are dedicated to science and several other buildings that could be great platforms for either clinical care or clinical research infrastructure. It has terrific conferencing facilities and from a patient's perspective, and from a visitor's perspective, it has really great parking, which I think is important in this day and age. Foss You talked about the systems biology approach at the West Campus and I am really intrigued by that concept. Is this going to be the first center in the United States that tries to pull things together in that kind of a context? Lynch It is one of the early ones I would say. There are a number of institutions in the country that are thinking about doing this. But what makes West Campus unique is that compared to any other place in the country right now, it's probably the only place that is bringing in this many6:18 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3 different types of scientists into one group. By bringing in the cancer biologists along with the systems biologists and the chemical biologists, when a cancer biologist generates a lead and they say, "Gosh Ms. Smith's breast cancer might be due to a problem in a certain gene that might encode for a certain type of enzyme within a cell," then the chemical biologist could actually look at that target and think, what kind of drugs could we make in the chemical laboratory to interact with this target? The ability to screen large numbers of chemical compounds to see if we might find a drug that could go in and target that pathway is going to be a unique process and a unique capability of this center. Chu You spent a great part of you career focusing on clinical translational research. Can you

tell our listeners what that means and also how you see your coming to Yale enhancing and building on the clinical translational research efforts at Yale Cancer Center? Lynch Ed, I think that's a really good point. What Yale has always been strong on is that it is a fabulous science institution with terrific depth and background in the laboratory. It's also a terrific cancer care facility with outstanding doctors and nurses at Yale-New Haven Hospital. What a lot of cancer centers are looking for is the ability to bring the two together in a translational research platform and that's something that I really hope we can do here. And what I mean by translational research is research that builds upon findings in the laboratory and brings in patients. I will give you an example of that. There is a trial I was involved in earlier this year before I came here where a group of investigators in Japan had found that there was a new gene abnormality in lung cancer, and the gene abnormality takes together two genes and brings them together that normally aren't close to each other, they normally don't act together, and the genes are called EML4 and the second gene is called ALK. Normally they are not together, but in this abnormality the two genes come together, and when they come together they create an unstable situation for cells and the cell becomes cancerous. These Japanese laboratory doctors found that that was an abnormality they felt was important. What we did in my group was we looked at drugs that might be able to treat patients who have this and we treated a few patients with one of these drugs and found that patients who had this EML4-ALK translocation or abnormality were incredibly sensitive to this one particular drug. What we then began to do was screen all patients who we thought might have this in order to find the patients who might be able to be treated with this particular drug. The difficult thing is we think it's not going to be a high percentage. It is a relatively low percentage of patients who have this abnormality so you have to screen a lot of patients and you've got to create an infrastructure for being able to do that. That is one of the things we want to be able to do at Yale, molecular profiling on a broad group of patients who have lung cancer, breast cancer, colon cancer, lymphoma, and other types of malignancies as we go forward. Interestingly Dr. Foss, being a lymphoma expert, this EML4-ALK target might actually be a target of importance in lymphoma.10:17 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3Foss

Actually I was intrigued when you talked about that because there are a group of lymphomas that over-express this ALK protein as well, and it seems as though we are finding more and more that things we are learning about one kind of cancer actually apply to another one, and genes are showing up in unexpected places. That is certainly the value of having these kinds of screening programs. Can you talk from the patient's point of view and what this all means? If a patient comes in with a tumor, is that tumor going to get put into one of these gene arrays? Is that tumor tissue going to be studied somehow? Lynch One of the things we hope to do, and are in the process of designing and planning for the facility at Smilow Cancer Hospital, will be a facility that will be able to profile a patient's cancer at a genetic level. This will be something that we hope to be able to offer routinely to patients. There

is a lot of planning and construction that needs to go into actually designing this. It's probably still 18 months away in terms of knowing all the hurdles we have to get through, but the goal would be that when the patient comes in and has his/her primary surgery, or has a biopsy taken at Yale-New Haven, a sample of that will go to what we call the molecular profiling lab. In that laboratory, scientists would look for common genetic abnormalities or even rare genetic abnormalities that might be able to guide physicians in terms of helping them with clinical trials and helping them with new types of therapies that might be able to work in a given circumstance. I think that if we don't do that for all cancers, we might miss the opportunity that you just alluded to; it may be that we find a small number of a broad range of cancers share in these genetic abnormalities and it may open up more treatment options for patients. From a patient's perspective, the more information you have the better chance you have to treat the cancer and that's what we hope to be able to do at Smilow.Chu That's terrific. One question Tom, would these type of services be available to our community partners, in that would samples come to Yale-New Haven or Smilow Hospital, be tested, and then we give the information back, or do you see a time when perhaps the same types of resources would be available at the individual hospitals? Or is it to resource intense and labor intense for the community practices, community centers, to offer the same services?Lynch Ed, that's a terrific point. In the beginning of this most of the samples will probably be tested at Yale. But, like with any good test, once it's done reliably you should be able to export this and do this at hospital laboratories and other centers around the state. My hope will be that this is something we could offer throughout other hospitals in Connecticut and throughout the country as we get more experience with it. In November of 2008, I hosted a meeting of hospitals in Boston that were beginning to do this, and there is really only one or two in the country that have started doing broad genetic testing of tumors. Yale will be among the very13:29 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3 first to do this and once we show that it can be done, and it can be done well and can help patients, my strong hope is that this is something you will be able to have done at Bridgeport, Hartford, New London, or any other hospital in the state. However, we are probably a couple of years away from that.Foss I would like to touch a bit more on this after the break, and the whole issue of personalized medicine. At this point we are going to take a break. You are listening to Yale Cancer Center Answers and we are here tonight with Dr. Thomas Lynch, Director of Yale Cancer Center.Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined by my co-host Dr. Ed Chu, and Dr. Thomas Lynch, Director of Yale Cancer Center and Physician-in-Chief of the Smilow Cancer Hospital at Yale-New Haven. Before the break, we were talking a little bit about genetic profiling for patients, and that gets into this whole issue of personalized medicine. Tom, can you define for our listeners what is personalized medicine?Lynch A great question Francine. Personalized medicine, in its most basic form in cancer, is about getting the right drug to the right patient and designing

a treatment based on both the patient's underlying characteristics and the tumor's underlying characteristics. In the past, we gave drugs broadly to patients with cancer, but recently we have learned that if you give drugs more specifically to targeted groups of patients you can improve outcomes. The work that you do, Francine, has been one of the best examples of that in lymphoma patients. We have learned that certain lymphomas express certain molecules on their surface that allow them to be treated effectively with antibodies, and antibody therapy for lymphoma has been one of the best examples of personalized medicine in terms of how we have been able to improve outcomes. For women with breast cancer who over-express the HER2 gene and16:12 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3 have amplified copies of the HER2 gene, the use of drugs that target HER2 have led to improving the cure rate of some women with breast cancer. As we learn more and more about molecular issues within a given patient's cancer, it is going to give us more opportunity to bring new drugs to bear in that circumstance. Chu Tom, in your own disease of lung cancer, there is also this whole issue of individualized medicine that is really becoming a reality in day-to-day clinical practice. Can you tell our listeners a little bit about what's going on in your own field of interest and expertise? Lynch This is actually a very opportune question because on Friday, the European equivalent of the FDA, gave a broad approval for the use of a specific drug called gefitinib for patients who happen to harbor an EGFR mutation. This is a great example of bringing the right drug to the right patient, and reflects some work that I have been involved with. Approximately five years ago now, the group I was doing research work with at Mass General identified that there was a specific gene mutation in a gene called the epidermal growth factor receptor that predicted patients who had dramatic responses from a drug called gefitinib, and in lung cancer this was the first example of being able to tailor a specific drug to a specific patient, but what we didn't know when we found this relationship was how powerful the relationship was or how it compared to traditional therapy. These gene mutations in lung cancer are more common in Asia than they are in the United States, and one of our colleagues from Hong Kong performed a large randomized trial on nearly a thousand patients where half the patients received the drug gefitinib, which is a targeted therapy, and half received chemotherapy. What they found was that the patients who received gefitinib had a better quality of life and did better overall in terms of how long they needed to go before another treatment started. But what else they found that was very important is that the benefit, or lack of benefit, was determined based on what the genetic testing showed, and if you had the mutation you benefited from the treatment, but if you did not have the mutation, you should get chemotherapy. This was the first time in lung cancer that that kind of molecular profiling was shown to improve outcome. That really drove the European FDA to feel the way it did about endorsing this concept of using targeted drugs in targeted populations of lung cancer, and for a long time lung cancer has been a very challenging disease to go after and to treat. This is a nice breakthrough for patients. Chu I'm just curious, in

everyday clinical practice is testing for this EGFR mutation being done? Lynch
What I tend to do is to use some clinical criteria to help decide which patients
to test. What we have learned is that women who have a type of lung cancer
called adenocarcinoma, and most importantly who have a very low or remote
smoking history, so never smokers, remote smokers, people who didn't smoke
a lot, have a higher chance of having this EGFR mutation. 19:51 into mp3
file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3 So,
when I find a patient who has a light smoking history, or is a woman with
adenocarcinoma, or a patient from Asia or Asian background, I will reflexively
test for the EGFR mutation. If I meet a man who is a heavy smoker and
who might have a type of cancer called squamous cell, in that setting, I might
not necessarily test for EGFR mutation. Getting back to Francine's point
about personalized medicine, the patient's characteristics are very important
in helping to decide. This is not just on the molecular basis; the clinical basis
also makes a difference. Foss We are talking about targeted therapies and how
we apply them in the clinic, and often times these therapies will get FDA
approval for a broad range of patients and then it is only after the fact that
we learn the subgroup of patients who benefit. Do you see in general this
whole field of targeted therapy narrowing down as we develop personalized
medicine? Lynch It will be interesting. The difficult issue is that when you
first start developing a drug you often don't know which group of patients
are going to be the ones who benefit. Sometimes you do in advance, but
sometimes you don't. For example, when the drug gefitinib, which I just told
you about, was developed, I was involved in the very first clinical trials. We
had no idea who the people were going to be that would benefit. In fact,
we thought initially that squamous cell patients would benefit the most, and
squamous cell is one type of lung cancer that has a lot of epidermal growth
factor receptors on the surface of the cell, and so we thought that this would
be the group that would have the most benefit. Well, lo and behold, that
wasn't the group that had the most benefit. So, I think the difficult part
is that you would like to be able to develop your drugs as narrowly and
specifically as you can to make sure that they are faster at finding groups
that can benefit. Sometimes it is very hard because, as you pointed out
Francine, we often don't know which groups of patients are going to benefit
until we have time to study that. Foss That is a very good point with respect
to what we are trying to do at the West Campus where we start off with the
basic scientists who develop the therapies, then they move into the clinic and
then the clinicians have to turn back to the basic scientists to start studying
the tissue and trying to understand how these drugs work. That is a really
nice synergy that you are developing here at the West Campus. Lynch Your
point is well taken. I want patients and people to think and to understand
how important it is and how fortunate we are to have patients who volunteer
for biopsy studies, for example, when they are on a treatment. Many of our
clinical trials will ask patients to consider a repeat biopsy to look and see on
a molecular level how their tumor may be responding. Obviously it's not for
everyone, but for many very brave patients that allow physicians to re-biopsy

cancers and look at the molecular profile, this is going to have22:50 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3 enormous benefit for many patients as we go forward. Chu Tom, you have been very actively involved in developing new drugs and new treatment regimens in the setting of clinical trials. Can you tell our listeners why clinical trials and clinical research are so vitally important, because sometimes when people hear the word clinical trial they feel a little uneasy about it? Lynch If we think back to the front page article in the New York Times recently that said if you look at our overall outcome from cancer under president Nixon's declared War on Cancer, compared to president Obama's declared War on Cancer, we have improved very marginally over the past forty years. One of the reasons for this that you can point to is that we are not getting enough patients to be involved in the clinical trials' process. One of the things we need to do is to make clinical trials of new treatments available to patients so that they can consider this as an option and think about whether or not they might want to try a new treatment for their cancer. Far too often patients are willing to participate in a clinical trial, and yet the clinical trial is not offered because it is not available either at their hospital or at a regional cancer center. We need to develop ways in the State of Connecticut, and we are working hard with a number of hospitals in the state to try to develop ways to make clinical trials available closer to patients' homes, and make them available in local practices so that they can get access to trials. And when they are not available in local practices, have them available at the comprehensive cancer centers so that we can get more patients involved in this. Participation in a clinical trial is a voluntary decision and it does not work for every patient, and for many patients it's not the right thing, but as part of good cancer care, being offered participation and being allowed to consider that is an important thing we should look at in terms of what defines the very best cancer care. Foss Another issue that patients often times get bogged down with is this whole concept of research. Some patients think of research as experimental therapy, but oftentimes research and clinical trials involve giving drugs that we already understand, and I think that is the key point in terms of conveying to a patient what a clinical trial is really all about. Lynch You are right. I mean sometimes the clinical trial is about giving a drug that's never been given to a human before and a person has never seen the drug before, and it can be pretty scary. But in other cases, clinical trials involved using drugs that we have used for years and know the safety profile of. One thing that always amazes me is how often a patient will turn to me and say, "Dr. Lynch, you are not going to give me a placebo without telling me?" It's important to note that if placebos are involved in clinical trials it's only after a patient has complete knowledge in advance that this could be part of his/her care. Placebos are never introduced without a patient's complete understanding and knowledge that that is something 26:05 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3 that could happen, and I have always been impressed by how many well-meaning patients get confused on that point. They think if it's a clinical trial, there is a chance that 'I am going to get a placebo.' In the United States, very few

clinical trials actually use placebos. They are much more common in Europe and Asia, but in the United States it's something that we haven't done as often. Patients should understand that there will not be a placebo involved unless their doctor tells them there could be a placebo involved. Chu With respect to cancer clinical trials, if and when there are placebos involved, usually it's added on to standard of care. In most cases patients can feel reassured by the fact that they are receiving standard of care plus either an experimental agent or a placebo, it's a kind of control for that potential placebo effect. Lynch I completely agree with you, and the one thing I try to tell patients is that if you get the arm that has placebo you also get the care you would have gotten from your oncologist's office anyway. Your point is very well made; they are not giving up care. They are getting standard plus something, or standard plus a placebo in most cases, but even those trials are still a minority of what is done in terms of cancer clinical trials. Those will probably be a minority of the trials we do at Smilow and Yale Cancer Center because, I would argue, a lot of our trials will be targeted toward early drug development, and in that setting very few placebo trials are actually done. Chu Tom, tell us a little bit about the new Smilow Cancer Hospital, which is about to open in the fall of this year. Lynch Smilow Cancer Hospital is absolutely a fabulous facility. It will be adjacent and connected to Yale- New Haven Hospital. It will house a number of very interesting facilities. There will be a brand new radiation therapy unit for patients who need radiation to treat diseases like breast cancer or prostate cancer, and that facility will be brand new and will open in October. There also will be new inpatients facilities for patients who had cancer surgery or patients who are getting bone marrow transplants or treatment for lymphoma, and then there will be special multidisciplinary outpatient clinics where patients can see doctors from several disciplines as well as social workers and psychiatry support for cancer. It is going to be a special facility. Chu Tom, we look forward to having you back on a future show to tell us how the opening of Smilow Cancer Hospital has gone. Thanks for being with us on the show. Lynch Ed and Francine, thank you so much. 28:45 into mp3 file http://www.yalecancercenter.org/podcast/Answers_Jun-14-09.mp3 Chu You are listening to Yale Cancer Center Answers and we would like to thank our special guest Dr. Thomas Lynch, Director of Yale Cancer Center and Physician-in-Chief of Smilow Cancer Hospital, for joining us this evening. Until next time, I am Ed Chu from Yale Cancer Center wishing you a safe and healthy week. If you have questions or would like to share your comments, go to yalecancercenter.org where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum from Connecticut Public Radio.