Interview with Dr. Paul Paik
April 5, 2016

Hi, I'm Paul Paik and I'm an assistant attending with Thoracic Oncology Services here at Memorial Sloan Kettering.

Over the past two years, Legwork for Lungs has donated more than $8,000 to lung cancer research, along with a combination of federal grants, other fundraisers, and donations of everyday people that been funneled into cancer research. What is the impact of these contributions and how do you allocate these funds?

That's a good question - I think the most important thing to note is the following statistic. Over the past, let's say at least 10 and approaching 15 years, federal funding for cancer research has been essentially flat - adjusting for inflation - which is a big problem because the pace of research has quickened. The number of new discoveries has accelerated, and I think the other thing is the degree to which we have to rely on our colleagues who research other cancers has increased. What we've discovered is that there are some essentially basic mechanisms that someone who's doing melanoma research may discovered that we're not going to know about, but this is something that's also applicable to lung cancer, and it's something we would not have otherwise understood.

The reason I mention this is because of the role of foundation funding and the role of individual contributions as a result really has become more important as time passes. We've used your particular donation already actually. It was used for a series of in-house experiments to try to figure out why a patient in particular had a very good response to this targeted therapy, and the contribution was used to figure out what the mechanisms of that were. And so when we get these donations, they have real and immediate use in terms of the research that we're doing.

And in terms of the research that you're doing, there's a big stigma about having lung cancer rather than having other cancers. Because of lung cancer's link to smoking, many feel that having cancer is a deserved consequence of their actions. What is your stance on this subject and what could be done to prevent this mentality?

I think there have to be important distinctions that are made. On the one hand we do know that smoking cigarettes substantially increases the risk of not only lung cancer, but the risk of many other types of cancer, and other medical illnesses. For example, heart disease and non cancerous lung disease. So that fact exists. What we need to do is to separate any kind of judgment that exists from that knowledge. Cigarette companies don't make it easy for people to quit, they make it very easy for people to start. That is their essential reason for existence: to make a profit off of selling cigarettes so it's very difficult to quit. Now, the will may be there but it's an addiction, it's a psychological and a physical addiction. And because it's an addiction, judgment should not be there and it cannot be there.

As you mentioned, stigma of this should not exist because patients need to receive treatment. Nowadays, people can undergo screening if they're old enough and if they smoke too many cigarettes, meaning they're at risk. That stigma needs to disappear because it has impeded

patients from getting treatment, and also because it's impeded us from a funding perspective. Patients who feel in some way ashamed of their diagnosis are not going to be advocates for research and for other fellow patients.

Out of all cancers, lung cancer is the most common one worldwide and has been one of the most deadly. Why is this so and why is it so hard to detect its early stages?

In some ways we don't know very well. We just don't know. The idea is that for whatever reason the biology of lung cancer is much more aggressive. And by this I mean its propensity to spread early on is much higher than other cancers. That is why at the end of the day, we have far more difficulty treating lung cancer rather than other cancers. Half of all lung cancer patients are already metastatic which means by definition that's already 50-60% of patients that cannot be cured. For the other 40 to 50% of patients who present early stage disease, we can improve the cure rate. Still, this idea behind the biology means that patients who have a late stage disease that has already metastasized may not be detected yet and the cancer may take a couple years for that to appear.

Colleen: I think that this is a good point to bring in the statistics Nastassja told me about on the MSK website, where it said there is an eight-month survival rate for Stage IV lung cancer. She asked me where that number comes from and I tried to explain the five-year survival rate to her. What are some of your insights about these commonly cited staistics? (Link to in-depth explanation)

Yes. It's hard. The numbers are hard, and they're hard because we're trying to distill from that published number what an individual patient's prognosis is going to be. It's very, very difficult and nearly impossible because the numbers that you'll see published in journals or on websites all come from clinical trial data. These numbers, by and large, are median survival rates, and we know these rates are getting better, but the problem with the median is this you don't know for any individual patient questions what side of the median are they going to be on, the good one or the bad one. And within different patients there are people who do very well even in the context of the median, and there are people who do a lot worse. So it's a number that's there is very useful to compare between studies but for an individual patient there are too many variables.

> When you just meet a patient in particular, there is no way to tell a person what their individual prognosis is going to be. What that means to me on a personal level is that unless they have a reason to *not* be hopeful, even within the context of late-stage diseases that we're not going to be able to get rid of, then we really shouldn't be telling patients, "Things are going to be bad".

If you don't know that, how can you tell people this? You have to say, "We don't know" and then we can have hope that things are going to be on the other side.

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Could you say that because treatment is so targeted today that this number is a lot less useful now than it was in the past?

I think that's exactly right. The reason is that with certain targeted therapies and EGFR or ALK lung cancers (specific types of genetic mutations in lung cancers) we know a patient's chances are substantially better, something like two to three times better than other lung cancer patients. With that information, you can increase the odds of certain cancer patients by a lot, and that number grows to be less important. So while and yes it's reasonable, and we should share that kind of information, sometimes that number doesn't mean a whole lot. But you then you have a bunch of other patients that remain black boxes, and I think it's unfair because they're black boxes to tell them what the average is going to be because the average is not going to apply, by definition it's not going to apply.

They have to balance between having to be realistic and having to be hopeful, but at the end of the day the job of the oncologist is more than just providing treatment, but to guide the patient from point A to point B to point C. And if that's done in a caring fashion, it's going to look a certain way. For a lot of people that means you can't be inaccurately dismal at the beginning of the relationship.

Overall, the odds are better for people with adenocarcinoma lung cancer, and not squamous cell lung cancer, which you specialize in. Why is that so?

That's because most of the gains until very recently have been in targeted treatments and specialized therapies. Almost all targeted therapies have been successful in adenocarcinoma. These changes in adenocarcinoma that have been very effective really don't happen in squamous lung cancer. And that is why there are so few advances within the past 15 years in squamous lung cancer and why the prognosis remains essentially the same. Patients with squamous lung cancer haven't really benefited from these targeted therapies.

Also relating back to treatment, I was thinking about a connected concept in my biology class recently. We were discussing bottleneck effects in regards to evolution, where cancer cells that are not affected by the drugs are the ones that survive to the next generation. So the next time that drug is used, the cancer is immune because the drug-resistant cells have reproduced and they are the only ones that are left. As long as this keeps happening, how is it ever possible to achieve a cure if the cancer continues to evolve using the bottleneck effect?

That's one of the difficulties that we face. That is one great example, another one I like to think of is our treatment of bacterial infections, where bacteria is also constantly dividing and through that process they become resistant to antibiotics, so you get these very resistant bacteria. The bottom line is that it makes it very difficult as cancer continues to divide and mutate and continues to have that chance of developing resistance to any treatment that you're giving. That really at the end of the day impedes our ability to develop treatment.

In some instances clones have been discovered that are from the beginning immune to treatment or develop to be immune to the treatment, in which case we're always one step behind, at the very least. I think compounding that issue is the idea that there is a reservoir of cancer cells that are not really actively dividing. They're just kind of sitting there, these cancer stem cell populations and a lot of treatments requires cells to be actively dividing and this does not apply to these cells. But these are still cells that can spin off cancer cells and that's what makes them so dangerous. So that pool of cells tends to be resistant to our treatment.

Is it possible to get rid of that pool of dormant cells? Or is that the main question that you are trying to work on?

Well, cancers are curable. And in instances where there are curable cancers the idea is that all of the cancer was in the area that we took out or that we radiated and that was it. Or there were instances where there were reservoir populations, but we eradicated them. So it is possible to do that, but depending on the underlying biology of the cancer it may be easier or harder. For lung cancer it is still very difficult to do that.

Is that because of the role that blood vessels play particularly in lung cancer?

It's in part because of this notion of cancer anti-genesis, which is the ability of the cancer to recruit normal elements of the body to feed itself. That overall theme of cancer feeding itself applies in many other ways. One of the newer treatments that I'm sure you're aware of is medication that allow the body to recognize the cancer within itself and fight it. They are called immune checkpoint inhibitors. And what's interesting about this class of medication is the process. This process, anti-genesis, that the cancer has developed is a normal process. It exists in the body. These processes that shut down your immune system after you get a cold, so that you're not always sneezing and developing a fever exist because that inflammatory reaction eventually has to simmer down when the symptoms have been treated.

The cancer has taken that normal process and turned it against the body to promote itself and to hide itself from the immune system.

> One of the issues that we're now facing and that we're now moving towards is what to do with the interaction of the cancer cells and the normal parts of our immune system.

This notion of tumor vs. stroma, these tumor-stroma interactions that we now know about, is very important, but very difficult to target in terms of trying to eradicate cancer.

OK, so some patients do really well with one type of treatment and then others do really poorly with the same exact type even when targeted therapy is being used. What are the driving mechanisms behind this and what treatment options have tried to combat this?

The process of figuring this out involves going back to the drawing board again and again in these patients who have developed resistant diseases that just don't respond to treatment. There are genetic studies that we've done using patient samples to figure out what it is and to try to figure out the differences between responsive and nonresponsive tumors, and that's gotten us a lot of information about additional mutations within that target or changes in other pathways that allow the cancer to escape from inhibition with the targeted therapy. So that's encompassed a fair amount about why, and then there's a whole of the realm of resistance pathways that are literally black boxes and we have no idea what's going on. And that probably has a lot to do with things like tumor-stroma interactions or other complex systems that we still can't get a handle on.

And that I think is very important to mention. Yes, we've made a lot of headway, a lot of smart people have done this research, but in the grand scheme of things we find it very difficult to know because we actually don't have the tools to figure out exactly what changes are happening in the cancer cell in response to treatment in the most detailed ways.

In 2012, you said in an interview that you were now on the cusp opening up a lot of different options in regards to treatment. Four years later, in 2016, what sort of gains have you made despite the fact that there's still a lot you don't know?

Well, in 2012 that was in regards to squamous lung cancer research because at the time there was a great deal of optimism that with next-generation sequencing we were going to be able to find these new alterations. There was a whole bunch of research that was generated testing animal models and their cells testing new treatment options. So we had started a whole bunch of clinical trials, matched patients who had these alterations to these trials, and a number of other investigations were conducted worldwide and what we found was that the problem was much more difficult than we had at first thought. That while these single-target approaches were working, in what we called preclinical models in animals and in cells, they weren't really working in patients. That's in part what your funding is trying to figure out - we don't really know why they weren't working in patients. There's a lot more work that needs to be done to figure out exactly why these strategies have failed. But the bottom line is that these systems are probably much more complicated than they look at first glance.

When I was doing research for this, I stumbled upon the Cancer Genome Atlas. Is this one of the items that is helping you gain more research? Describe this project and your involvement in it.

So it's good that you stumbled upon that because that's one of the most important developments over the past 8 years. It's a big initiative by the NIH, the National Institute of Health and the Cancer Institute. It started because DNA sequencing cost was becoming lower and the turnaround time was becoming faster there was the idea that many cancer clinics across the country were going to coordinate the sequencing of a whole bunch of tumors across all of the cancer types that we have to try to figure out the meaning behind certain alterations to really get a sense in a comprehensive fashion what the underlying biologic issues were. And it's

been wildly successful - TCGA has sequenced lots of different genomes, and the results have been published in lots of great journals. There were papers about squamous lung cancer and about adenocarcinoma, really about all different types of cancer. And that's exactly what provided us with a lot of that insight into what we might be able to target as a starting point.

Okay, so you have all of this research, these brand new sequenced cancer tumors, and a lot of innovative tools at your disposal. But how does that directly relate to your job as a doctor? What do you do with that information?

That's a good question and a very practical question now. At Memorial, and this is going to be increasingly happening at other institutions, and even in community practices, Next-Generation sequencing relates to standard of care.

> So we get back now from our patients, not just limited testing of a couple or a few different genes, but testing of 400 different cancer genes. And this is challenging - looking at all of these alterations and trying to figure out what that means.

There was actually a recent New York Times article about this issue of how to use medicine in this era of next-gen sequencing. The question is that most of the time we don't know what these things are. We know what the genes do in general, but we don't know what the specific alterations are.

You can deal with this issue in a couple of different ways: one is to say, conservatively, "I don't know what this is, so I'm going to sort of ignore it. This is part of someone's cancer, but we don't know what to do about it." The other approach is to take a look at the panel and basically just do a whole bunch of research about what these things might mean and based on what you find, and if there's something that makes sense or seems to make sense, then just go ahead and give it a try. And in fact that's the approach that we took about a year-and-a-half ago with one of my patients, where we received sequencing results back, and I noticed an alteration that was pretty new. It was an old alteration, but it came to light more recently in a gene called MET. So we gave it a shot. We prescribed this patient a new drug for another type of lung cancer, and it worked. That kick-started a whole clinical trial effort because 4% of all adenocarcinoma patients have this alteration.

The bottom line is that this is useful information to have, sometimes it's not very useful but other times it can be. Depending on how much you want to invest on chasing these things, you may end up getting some benefits that you wouldn't have otherwise. I think it should be used with an asterisk, as something to be very cautious about. I think it should be an exercise that is less common in community oncologists, but perhaps more so in an academic setting. More and more people are finding new strategies in developing new treatments.

You just described one strategy to go with, but let's say a brand new patient comes in. How do you decide on a treatment regimen and how do you decide how you want to work with any one patient? What are some factors that you consider when doing that?

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In terms of the normal practice of cancer care, the flow of treatments is pretty much standardized in the United States and across the world based on randomized clinical trials that have been done. So for any given cancer there is a flow that is followed, where you start with the most effective treatment and then you go from there, moving on to less effective treatments this regiment to get tailored according to how fit a person is and what other medical illnesses they might have. So there is some personalization that ends up happening, but by and large the treatment people receive is based off of an algorithmic approach, which is not a bad thing - it's an algorithmic approach because it's based off of all the data that we have. That's essentially how patients are treated most of the time.

One of the options a little bit down the line in terms of treatment is a patient choosing to participate in clinical studies. How do you determine if a person is eligible for these studies?

First we ask them. Out of all of the questions that you asked practically speaking, this is probably the most important one,

> because these advances that are made happen in collaboration with patients, and one of the things that impedes progress is the clinical participation rate, which is very low in general. It's in the single digits across the United States.

The first thing we do is ask patients whether or not they're willing to participate in a clinical trial that generally makes sense for them, that generally they'll be eligible for. Apart from that it's basically looking at the checklist on the protocol based on, again, whether or not the patient is fit enough for the trial, how many treatments they've gotten. More and more though, I feel like this is what your question is getting at, the approach is more personalized than it used to be. With genetic testing and sequencing of tumors we can match patients with clinical trials and newer treatments. Increasingly now, the trial landscape is being changed in terms of treatment. Especially with these inmmune-checkpoint inhibitors, this new class of medications that help a person's immune system to recognize the cancer.

Valentina: Do you use foreign clinical research in your work? I know it's very difficult to test drugs on Americans because they take so many drugs.

We do. A lot of these studies are worldwide, out of necessity in some ways because of the lack of of patients. There just aren't enough willing patients in the United States, for instance. A lot of them are done with our collaborators in Asia and in Europe as well.

You've mentioned repeatedly the low clinical trial participation rate and that directly segues into my next question. Why do patients not want to enter into them and how do patients usually feel about clinical trials?

The fact that the participation rate is low is not surprising. Even though I mentioned it, it's not surprising. There is a stigma against clinical trials, that these are experiments that are being

done on people. And from a certain perspective, that's not inaccurate. We don't know what the outcome is going to be, so in many ways these are experiments about what the effects are going to be on a patient, and whether these effects are going to be good or bad. So that stigma is out there to begin with.

I think the other thing is that traditionally we have not being very good at explaining clinical trials to patients. There are informal consent forms that guide patients through what a trial is about, but at the end of the day, it's your role as their doctor to guide the patient and tell them what the study is about, whether or not it makes sense for them to participate, what is the chance that there will be some benefit, and what's the real deal behind the study. When you put all this together, there is a big reluctant to participate in trials.

Now, I think we're getting better at this sort of thing, and I think that's because the applicability of the study to the patient is getting more real. I talked about these targeted therapy studies before, and individualization of the clinical trial to a patient makes it much more easier for someone to participate because this is something that directly targets your cancer. It's much easier for someone to conceptualize that. It's much easier to say this [to the patient] than to say, "This is some random drug, we're going to test it out on you because it worked on some cells in a petri dish." It's much more easier to participate in these new kinds of studies rather than the old ones. Trials have been traditionally been done in patients that have gone through many, many treatments and [their cancer] has progressed, so they do not have any other options.

Again, that's a patient population that is very different from the patient population that has just been diagnosed, but there are trials for the newly diagnosed that make plenty of sense. There's a lot more optimism in that case than in a setting at the end of a treatment course, where there's a great deal of discouragement.

When you put all of these things together, it makes sense that the trial participation rate is so low. And I'm not saying that that's necessarily on patients, I think it's a reflection of the fact that in the past our clinical trials have not been very good. Most Phase 1 studies, where were trying to find the right dose, do not later go on to Phase II studies, where we're looking for an effectiveness signal, and many also don't move on to a randomized Phase 3 study. A lot of it is our blame also, in terms of the oncology community because a lot of things that we try just don't work.

Valentina: How long is the typical clinical study?

It depends on what kind of study it is. Early phase studies where we're looking for the safe dose to give patient, or studies we were looking for an initial signal about how effective it is, these studies finish accruing patients generally within 1 to 2 years. You get the results pretty soon after that because because the endpoints that we're looking for we get very quickly. How many patients respond, for instance. Then there are these larger studies, these randomized Phase 3 studies, which are looking for overall survival, take much longer to analyse because we have to

follow patients for years to figure out how long they're living and then figure out why they passed away. So, those studies take years to get the data to a point where it's mature for analysis.

In your opinion, is the stigma behind clinical trials justified? For example, is it mostly because people don't want to feel like they're animals that are being experimented on, or is it because the trials are honestly more for the scientific community to get more research, rather than for the benefit of the patient?

It's justified. If the rate is that low, there's got to be some justification that seems to make sense on the side of the patient. Otherwise, the participation rate would be much higher. So, it's justified. The medical community has done bad things in terms of experimenting on people. There's the Tuskegee syphilis experiment, for instance, so we've done bad things in the name of science. We've tried to move things forward in unethical ways, so there's that shadow that hangs over us which makes the stigma justified. We haven't really gotten over that, and I don't think we ever should because it's the reality check for us in terms of how we perform research.

> In addition to that, again, it's not inaccurate to say a lot of the times that we are doing trials **ON** patients, rather than **WITH** patients. There's got to be that distinction that has to be made.

There has to be a shift in mentality, but for that shift to happen there's got to be a greater collaborative sense, and that's only going to happen with greater trust. That trust can only be engendered when people and patients and their families see that there is some kind of good that can result. The components to that are a little bit complicated, but it has to do a lot with the relationship between the doctor and the patient and their families. That trust has to be there, otherwise comma it's going to be very difficult to explain certain things. In addition, on a larger scale, patients have to see that there are fruits to these endeavors because if nothing is happening, then it's not entirely inaccurate for them to say, "There really is no point for me to participate. Nothing is happening anyway."

And that's why more recently, we've gained more ground, and it's become easier to talk to patients and collaborate with them. And advocacy groups, like your website, how found it easier to tell people that yes, you should participate in clinical trials. This is the way forward. Patients themselves have heard from past patients that have participated in clinical trials are now deciding to participate also.

This seems to be a really basic question, but how do you start a clinical trial? Who do you go to, and what has to happen first?

A lot of clinical trials start by a pharmaceutical companies already having a drug and having some original experiments that test whether or not the drug is effective in models of that cancer. And then they say, "Okay we've done this work, and it's been effective in these models. Now, we want to test it on real patients." So, they start that process. They'll need to find investigative

sites, they have to find funding, and clinical trials can be really expensive. That's one way to do it.

There are a few other different ways. One is for an investigator, a medical oncologist, to say, "I've done some work, myself or in collaboration with someone, and there are some interesting results." Then, you go to the drug company and say, "Hey, you've got this drug. This is some work we've done and we think it would be interesting to see the results in a study." that's something called an investigator-initiated trial. These are the trials that I like the best. I find them the most interesting, and the ones I can trust because it is based upon work that we've done. There's some real hope that it can translate for something effective on patients. That's another way that things are done. Those are the two main ways that clinical trials are run these days.

Do these drug companies benefit from having these clinical trials?

Yes, they do. It depends on how you view the world. There's a tendency to demonize drug companies, and that's a lot of the talk that's out there. In fact, a lot of the most recent immediate attention has been on an individual, for example, that has increased the price of a drug that used to be cheap, and that doesn't really help matters. This is by and large because in medicine, things should be altruistic because it's a basic human right to receive Health Care. That sort of butts heads with the notion that you have a company that's going to make profit. Since the reason for their existence is to make a profit, otherwise they wouldn't be in business.

These things, in some ways, they collide, and they don't necessarily need to. It's a larger issue of our brand of capitalism in the world, but they don't need to. A lot of the times they actually don't. We need to think of this as a larger-scale endeavor to figure out how to treat cancer. There are lots of people who are involved in this process, and some of these people are part of drug companies, and it's important to work with them in order to work things forward.

I think that's how a lot of people view the situation, and that is how most of the successes end up happening. People in drug companies also want to be able to help cancer patients, they genuinely want this to happen, and they're not going to do anything that's not going to work out. If they don't think something is going to work, they are not going to pursue that. On the other hand, if something is working out they're going to want to move it forward as well. There is a lot of complexity here, probably too much complexity to get in here, and there are a lot of personal views. At the end of the day, they benefit because they make profits. But I wanted to explain that that is not necessarily a bad thing.

Once you collect data from clinical studies, how does that impact how patients are treated? Or does it not have that much of an effect, and you just tell your patient, "Now we're done with this clinical study, and we're going to move on to something else?"

That's a good question. Most of the time, the patient has derived all the benefit that they were going to during the duration of that study. Sometimes that's a great thing because their cancer responded and now they're feeling better, or sometimes they haven't responded and you now

have to move on to the next thing. In some instances, insights from the trial as to why they became resistant can help you to figure out what their next treatment is going to be, and that is in part what happened to your family friend. So there can be some benefits that we can discover these patients are participating in clinical trials.

If a patient responds really well to a clinical trial, is there any way to keep them on the medication?

Yes, there are mechanisms in place that will help you do that as much as possible. And there are some risks that this could not happen, for example, if there weren't a lot of people who responded to this drug and the patient was a minority in that sense, they may not have been able to stay on that drug because the drug company is shutting down the trial. But a lot of the time, the patient is able to make that case, and the drug company knows that someone has responded and they keep on providing the drug for patients to continue to receive them.

This is more of a question regarding your personal optimism, but do you think that it is possible to achieve a cure, or at least significant advances in lung cancer in your lifetime?

So, the answer is yes but maybe not in the way that you might have envisioned it. I should start by saying that the most insight I have in cancer is regarding lung cancer. The fastest way, the most durable way, and the way that we'll have the biggest impact in curing lung cancer is in banning cigarette smoking, but that is very difficult to do. However, it's important to mention that because it's the cheapest, most effective way to end up with a cure for lung cancer.

> The other part of the curability equation has to do with research on early-stage patients. Nearly all of the research that we do is on patients who already have a metastatic disease, in whom we know that in all likelihood, a cure is not going to happen. We have early-stage patients who are not the focus of these new advancements, and that's for a lot of different reasons. But the bottom line is, that's a lot of patients who can benefit from newer treatment options. .

As an example, a patient has a Stage 2 may have caused by surgery alone, a 50% chance for being cured. If we're able to boost that number, for example to 75%, that's a whole lot of patients that we can now cure. But that requires research studies to be done in that patient population. So, for me shifts in terms of trial work towards early-stage patients will be a big part of improving the cure rate for lung cancer.

I think your question is more focused towards patients who have incurable cancers and whether or not we're going to be able to cure them, whether or not there's going to be a paradigm shift, and there is some hope that with these newer treatments that we have such as immune checkpoint inhibition that we're going to be able to have patients immune system to basically deal with the cancer. This will happen either with the cancer remaining as a chronic low-level issue the patient doesn't have to worry about , or the immune system will fully do its job and

simply eradicate the cancer by itself. Some people are very optimistic about this, but I think it's going to require a lot of follow-up to see whether or not this gets born out. I think there's a lot of optimism, the optimism is certainly there, and there's more optimism now because our understanding is greater.

> Most of my optimism comes from the fact that we know so little still. And so when you know so little that means in some ways that the sky's the limit because you don't know where the sky ends. So for me, that's the way that I conceptualize hope in a setting where there doesn't appear to be a lot of hope because again, we don't know a lot. We know that we don't understand the complexity of the system, which means that there is potentially a great deal of optimism in trying to figure this out.

The problem with catching early-stage cancers is that there are not usually a lot of symptoms. What is a way to combat this?

Screening is one way. We have recently started annual CT scan screening in people who are at the highest risk of developing lung cancer, patients who are greater than 55 years of age who have a very heavy smoking history, either former or current. And we have shown in a recent study, that there have been improvements in survival that come from screening this patient population. But, screening is difficult. Screening is not just having a good test, screening is a balance of what happens after that test is done in terms of the procedures and the side effects of the procedures, and whether or not on a societal level the cost of screening is justified. Right now, the consensus is that screening is justified for CT scans in high-risk populations, but that leaves a whole bunch of patients who are not as high risk who will develop lung cancer and who we are not screening.

So, the onus is on us to figure out how to make the screening better, more accurate in particular. This is not just in lung cancer, this is an all cancers, and we are developing the tools to be able to do this. I think that we can have the expectation that screening is going to get better. It's going to take some time because again, this patient population is hard to study. These are people who don't have cancer, and you are trying to figure out if they do have cancer. It takes a lot of patience to do this, it takes a lot of time to follow them, so it's not something that's going to happen very quickly. But again, the tools and technology that are needed are now there to be able to improve our diagnostic accuracy.

What can outside forces do to help how well we diagnose patients? For example, if you were in Washington, and had the ability to make a law, for example a cigarette tax or something similar to that; what would you do to promote lung cancer research and treatment in general?

So the first thing is advocacy for NIH (National Institute of Health) funding from the government. That's one of the first things. The second thing I would do as you mentioned is to try to make better headway in the battle against big tobacco. That probably is the number one priority for me in trying do this. It's also one of the most difficult things the try to accomplish and to try to enact.

I think it's those two things, from a governmental perspective that make sense. It's sort of getting rid of the thing that we know causes lung cancer and then it's also trying to get as much money as possible to do research.

Part of the problem with the flat and NIH funding, is that you never know where the next great discovery is going to come from. Research tells us that this is the case. We don't know how interrelated the research is going to be. For example, this notion of immune checkpoint inhibition, this new way of therapy, the underpinning for this was research in Hepatitis C, a viral illness. So it stands to reason to make funding as broad as possible because you don't know where the next discovery is going to be, and so to limit funding to a very small pool shoot ourselves in the foot and really hampers our ability to make advances.

Extras

Those are all the questions I had planned for you. However, seeing that you have some time, I'd like to clarify a couple of last things. You said that you already used the $8,000 Legwork for Lungs has given to you, but how significant is that really?

I'm going to tell you how. This series of experiments I was talking about in the first question was largely funded by your donations. It's safe to say we would not have been able to conduct a series of experiments with the anti-tumor corefacility, which performs xenograft modeling.

Valentina: But you have to understand, this is not just us, it's not just our money. It's the entire community coming together.

Yes, I do understand. This is what I mean - the way things work now, particularly for investigators at cancer centers, the thought is that you need hundreds of thousands of dollars, but you don't. Increasingly what we're looking for is initial information to be made based on observations that may lead to something else. You need funding to be able to do that.

The reason why contributions are important for funding because the NIH and

> any larger advocacy group that is looking to fund something will be looking to put money towards a trial that has an immediate impact in terms of patient care.

What that means is that the initial observations for funding get left by the curb side, and that's what I mean by flat funding being an issue:

> there's not enough money to do these high risk, high-reward types of experiments. That's where philanthropic contribution plays a very big role - they increase our ability to do these kinds of experiments.

Do you know of any countries where they are more eager to fund these high risk and reward experiments or is flat funding a problem across the world?

Interview with Dr. Paul Paik
April 5, 2016

I don't know the data for funding rates in Europe or in Asia, but I imagine the United States being the United States and the percentage of money out of the GDP that we spend on Healthcare that we are very high on the list up there in terms of absolute dollars that is being put towards our research. We also tend to be, as the United States a unified country - the EU as a group of separate countries is still politically problematic in terms of the efforts that they can spearhead. And, on the international level, all countries are smaller than the United States in relation to funding. So, I would suspect the United States leads in terms of funding despite the fact that it's been flat.