

Transcript Details

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Personalized Diagnostics & Targeted Therapies

Announcer:

Welcome to Medical Breakthroughs from Penn Medicine, advancing medicine through precision diagnostics and novel therapies. Your host is Dr. Lee Freedman.

Dr. Lee Freedman (Host):

The Philadelphia Chromosome provided the first evidence that genetic abnormalities were linked to cancer. The discovery at Penn Medicine more than 50 years ago ushered in the modern period of cytogenetics. Now, the Center for Personalized Diagnostics or CPD builds on this legacy and is set to pave the way for a new era of genomic and therapeutic pathology. To discuss this unique center and its offerings for patients is Dr. David Roth, Chair of the Department of Pathology and Laboratory Medicine and the Simon Flexner Professor of Pathology and Laboratory Medicine at Penn Medicine. Dr. Roth, welcome to the program.

Dr. David Roth (Guest expert):

Hi. Thank you very much for having me.

Dr. Lee Freedman:

Well, I'm excited to hear about what you are doing. Maybe we should start off with what your role is at the Center for Personalized Diagnostics.

Dr. David Roth:

Well, right now I am the Acting Director as we search for a director who has broad competencies in genomic diagnostics and molecular pathology testing. So, that search is on going, meanwhile, I'm devoting a considerable portion of my time to trying to help keep things together.

Dr. Lee Freedman:

And how long has the Center been around? What is its history?

Dr. David Roth:

We got started shortly after I arrived in the summer of 2011 and the Center actually grew out of Peter Nowell's old cytogenetics lab which I think is poetic since he co-discovered the Philadelphia Chromosome. We've matured out of that space and we inhabit brand new space a short walk from the Penn campus on Market Street.

Dr. Lee Freedman:

And is the Center now focusing predominantly on oncology and malignancies or are there other things that are under its purview?

Dr. David Roth:

We decided to start with oncology because we thought we could make an impact there most quickly, but the long range plan is to branch out into other areas. Right now, it is strictly on oncology.

Dr. Lee Freedman:

I get it. I get it. And I know that you develop diagnostic profiles for patients with cancer. Can you tell us a little bit about these diagnostic profiles and how you approach the cancer patient?

Dr. David Roth:

Well, when we were starting in 2011 it wasn't completely clear what kind of genomic test to offer and coincidentally at the time we were

just making initial decisions on which way to go, a sequencing instrument from Illumina came out called the MiSeq and that turns out to be really great for doing what we call gene panels. So, panels of target genes that are commonly hid in various kind of cancer.

So, we developed a custom hematologic malignancy panel particularly focused on a particular type of leukemia called acute myeloid leukemia or AML and we also offer a solid tumor panel that is more broadly focused at solid tumors like melanoma, non-small cell lung cancer and various what we call solid malignancies as opposed to the leukemia.

Dr. Lee Freedman:

And so, you look at particular gene sequences that have been shown to contain mutations in these cancers and try to identify them?

Dr. David Roth:

That's correct. In some cases we look at the entire gene, in other cases we look at so called hot spots in the gene that are known to be highly likely to be mutated. This is a very practical effort aimed at identifying mutations that can refine the prognosis or change the therapy for a patient. So, it's not a comprehensive research discovery test. It's more focused on areas that we think are likely to have impact for a particular patient.

Dr. Lee Freedman:

So, you kind of know where to look to answer the questions about which therapies might be most efficacious and which might be best tolerated. That type of thing?

Dr. David Roth:

Yes and that's building on several years of work by a large number of laboratories generally funded by the NIH where we're doing what I would call discovery sequencing in cancers to try to find the commonly mutated genes, commonly mutated sites, and so building off of that knowledge, we are looking at the likely suspects. I won't say the usual suspects but the likely suspects.

Dr. Lee Freedman:

I understand. And how often would you say in a group of patients with a given malignancy will findings like this be able to impact their clinical treatment?

Dr. David Roth:

It really depends on the malignancy. In non-small cell lung cancer, we find what we call actionable mutation a pretty high fraction of the time. Also in melanoma and in AML we find useful mutations not always drug targets but information that helps us decide whether the patient is high risk or low risk. For example, we find that kind of information a high fraction of the time.

I would say overall, we've done over a thousand patients, now. We've done right about a thousand patients after our first year and in that cohort we find what we call disease associated mutations that is _____ (04:58) mutations that have been _____ (05:00) a genetic alterations that are known to have significance in the particular tumor. We find that about 70 to 75 percent of the time, so that's a pretty good hit rate.

Dr. Lee Freedman:

Absolutely.

Dr. David Roth:

I have to add, that doesn't mean 75 percent of the time that we change a patient's therapy. I did a rough calculation a few months ago and it works out to about ten percent overall of all the patients we look at. We come up with something that really is a fundamental ah-ha moment that changes therapy. So, that's ten percent out of a thousand. That's not an insignificant number if you're thinking the individual patient level. We would of course like to get that number higher. We're about to deploy larger panels in the belief that looking more broadly will help us increase that hit rate.

Dr. Lee Freedman:

If you're just tuning in, you're listening to ReachMD, the channel for medical professionals. I'm your host, Dr. Lee Freedman and joining me today is Dr. David Roth talking about the Center for Personalized Diagnostics at Penn Medicine. Dr. Roth, the information that you gained is strictly information about efficacy of chemotherapeutic agents or can you comment on susceptibility to radio therapy or other therapies?

Dr. David Roth:

Well, in some cases we are helping to stratify the patient's risk level based upon the mutations. So like, are you a candidate for say standard therapy or are you a candidate for more aggressive therapy and that's particularly the case in the AML panel. In the solid tumor panel, one thing we're certainly looking for are mutations that create a particular target for a targeted therapy like a tyrosine-kinase inhibitor or some of the new molecularly targeted therapies. There are examples say in melanoma, a gene called BRAF. If you

get a particular mutation in BRAF, you can be a candidate for a targeted agent and the response rates from those targeted agents can be quite high. So, we're very happy when we find one of those.

Dr. Lee Freedman:

In terms of the practicality of something like this from time to diagnosis until the time you can garner some of this information, what is the turn around time? What is the cost? Is insurance helping with any of this?

Dr. David Roth:

Those are very good questions. I'll start with turnaround time. In the usual molecular pathology world, we would normally test for these mutations one at a time. Sometimes it would take several to many weeks before you actually found a mutation that is informative. So, you're sort of going one gene at a time. One of the nice things about this multiplex testing paradigm is that we're testing it all at the same time. Our typical turnaround is five to ten days from receipt of a suitable sample in the laboratory and then we can have the whole panel tested and we'll get the results back and so that's only going to speed things up.

Dr. Lee Freedman:

That's very impressive. I'd imagine that depends on the specific panels you've been able to develop at Penn?

Dr. David Roth:

No. It's just a matter of getting the workflow right.

Dr. Lee Freedman:

I see.

Dr. David Roth:

Very grateful that we have very smart people in the lab who figured out how to optimize the workflow. One of the very nice things about doing the panel is you can design, validate, and deploy 50, 100 or even more genes simultaneously which would be a much slower process if you're doing it one at a time. So, that's really one of the advantages of the panel technology is the time for developing a new test is shorter. So, your next question was about, was it cost? Cost and insurance, right?

Dr. Lee Freedman:

Right. Right.

Dr. David Roth:

We're getting some reimbursements from commercial insurance. We did an analysis of the first six hundred and some odd patient bills and of those, I think, 96 percent of the patient got bills of a hundred dollars or less. The rest was covered by insurance. This is not counting Medicare because Medicare has not developed an official position on whether or how to reimburse these tests so we're still working with Medicare to get that clarified. But I'm sure that will get worked out in the reasonably near future.

Dr. Lee Freedman:

To me that is an incredibly impressive, the low cost for this high technology and very valuable information. Is it wrong of me to think that if you look at the big picture, this is very cost effective in terms of not using therapies that maybe less efficacious and deciding who is a candidate for more aggressive therapy that may engender side effects and costs related to that?

Dr. David Roth:

Absolutely. I mean, I'd say the real cost of the test, the list price, is a few times what it will cost to do one of the single gene tests and obviously we're doing 35 to 50 something genes and so in that sense, that's very cost efficient. The cost of getting the right treatment on the first time, that's obviously a great thing for medical care _____ (09:48) including the side effect profile that you brought up and it is also obviously a much more cost efficient way to go about giving therapy if you have molecular guidance before you start trying different therapies. But I have to caution, I'm not a practicing oncologist so really to get into those details you would need to talk to a card carrying oncologist.

Dr. Lee Freedman:

I hear what you're saying. I hear what you're saying. Now, this is available at Penn Medicine for those of us who are not practicing at Penn, when should we be thinking about referral and how is that process handled?

Dr. David Roth:

We have a website. You can Google Penn Center for Personalized Diagnostics and we show on the website, you can download a requisition form. You can fill out, it's one page. It's the simple _____ (10:33) requisition form. We could _____ (10:34) and we will take all comers so I've actually done a decent number of non-Penn patients although by far the majority of our work is of Penn patients and obviously you get the advantages of being in the system and having the consultations with our wonderful oncologists if you are working

within our system but we're happy to do testing outside of the system.

Dr. Lee Freedman:

Will this typically be initiated by a treating oncologist or could a primary care doctor even initiate something like this?

Dr. David Roth:

In my experience of traveling around and talking to people, it is virtually all oncologists that are ordering the tests and interpretation of these tests, we provide as much help as we can but it's a fast moving field and I think it's something that you probably want to talk with a specialist about. We don't release the reports directly to the patients. We release them to the oncologist and the oncologist has to discuss with the patient what the implications are. So, I think it probably would work best through oncologists.

Dr. Lee Freedman:

Very good. And in the minute we have left, Dr. Roth, as you look to the future, what kind of things do you see coming out of the Center for Personalized Diagnostics?

Dr. David Roth:

Well, we're interested in exploring other areas beside cancer. Some constitutional disorders, for example. We are also interested in going beyond the DNA at some point looking at the protein products, looking at RNA and anything else we can measure so we're very committed to providing really good diagnostic tools to help doctors make decisions on a case by case basis.

Dr. Lee Freedman:

Very nice. Well, Dr. Roth, thank you so much for being with us today and sharing your insights on the exciting work being done by the Center for Personalized Diagnostics at Penn Medicine. And we thank all of our listeners for being with us today on Medical Breakthroughs from Penn Medicine.

Dr. David Roth:

Thank you for having me.

Dr. Lee Freedman:

Our pleasure.

Announcer:

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