EPISODE ONE:

New Challenges for the Pathologist in the Era of Precision Medicine

Dr. Tony Magliocco, H. Lee Moffit Cancer Center | November 26, 2018

Welcome to The Precision Medicine Podcast, where experts come to discuss the problems oncologists, reference labs, and payers face as precision medicine grows, and consider solutions for advancing the quality of patient-centered cancer care.

Jerome Madison: Hello, I'm Jerome Madison Vice President of Provider Relations at Trapelo™ and one of the hosts of the Precision Medicine Podcast.

Jerome Madison: Today, I have with me Dr. Tony Magliocco, Chair of its Anatomic Pathology at the H. Lee Moffitt Cancer Center, and we'll be discussing new challenges for the pathologists in the Era of Precision Medicine.

Jerome Madison: Dr. Magliocco's research focuses on finding the molecular mechanisms of cancer progression, and the development of drug resistance. In addition, he works on the development of clinical markers of radio therapy resistance. Using cervical cancer, as a model system, as GYN and breasts pathology is his specialty.

Jerome Madison: Please help me welcome to the Precision Medicine Podcast, Dr. Tony Magliocco. Thank you for being on the show.

Dr. Tony Magliocco: Thank you Jerome, it's my pleasure to be here.

Jerome Madison: When predictive markers like ER, and PR, Her2 emerged, Dr. Magliocco, hospital labs found a way to bring that in house and turn it into a revenue source. But today, we have a lot of specialty reference labs who are only focused on genomics. So, what impact does this have on the community pathologists' ability to keep up with emerging biomarkers and the data in order to effectively advise cancer treating physicians?

Dr. Tony Magliocco: Yes, thank you for bringing up this topic. It's very timely, and very important. Over the last 10 years, there's really been an explosion in technologies, particularly in molecular genomics that are being implemented into cancer care.

Dr. Tony Magliocco: These technologies are really revolutionizing the way that we understand how cancer behaves. But they're also essential for oncologists to select the right therapies for their patients. Most notably, we've seen the greatest advances in lung cancer, where now, there are multiple targeted therapies, along as immune therapies for patients with lung cancer. Selecting the right targeted therapy requires extensive testing of the specimen.

Dr. Tony Magliocco: Now, as you point out, doing this type of testing is very challenging. Often, it's beyond the scope of a community hospital lab. That means that our community

hospital lab is faced with trying to find a reference lab that can provide this type of test. This can be a problematic activity, as there are many different reference labs available and the ability to select the right one can be a challenge for community pathologists.

Jerome Madison: Yeah. What has been the history? I mean, I get into conversations with pathologists who, when, ER and PR came out, there was a debate on whether or not they were necessary to test for every patient. What has been the conversation amongst your peers about bringing these different molecular tests into the laboratory and routinely testing it for cancer patients?

Dr. Tony Magliocco: Right. Well, I work at a cancer center, a very large one. The Moffitt Cancer Center is actually the third largest by patient volume in the United States. It's currently ranked number six by US News and World Report in terms of rankings. So, at this institution the oncologists are very forward thinking, which means that they're writing the guidelines, they're running the pivotal clinical trials, and they're the ones who are actually driving the lab, in many instances, in terms of demanding that the internal hospital lab produces advanced testing technologies for them to deploy for their patients to enroll them on trials, and to better understand the disease.

Dr. Tony Magliocco: So, at a place like Moffitt, there's a lot of enthusiasm for bringing in this new type of testing. Bringing estrogen receptor and progesterone receptor in for breast cancer, it took time. It happened over a period of many years. But, it was based on technology called immunohistochemistry in the second generation that most hospitals had. So, pathologists were comfortable with that technology.

Dr. Tony Magliocco: Now, looking at molecular technologies, there's only a subset of pathologists that have expertise and specific training in molecular diagnostic technology. Many pathologists feel somewhat uncomfortable with these technologies because they are very recent, they're complicated, it's hard to understand how the data will be used and analyzed. So, there is this variation in how pathologists approach this. In large academic centers, generally, pathologists embrace the technology. They view it as being cutting edge, and giving us new insight into tumor biology.

Dr. Tony Magliocco: In community practice, it's different. I've had the opportunity to visit many community centers and speak with pathologists there. One of the challenges in community centers are that pathologists have to do a lot of multi-tasking. So, they have limited time. Many of the pathologists have been trained some time ago. So, these new technologies are foreign to them. They feel challenged by them. They're not quite sure how to access them, and sometimes they feel pressured by the oncologists to use them. There are many community pathologists that feel uncomfortable about deploying these technologies, and they're looking for, sometimes, help and guidance in how to do this. I can say that there is still a lot of debate between pathologists and oncologists when the technology should be used.

Dr. Tony Magliocco: You mentioned in breast cancer that, now, it's standard. Every breast cancer should have an ER, PR, and Her2 test. It's also becoming standard now, that maybe, every breast cancer should also have the BRCA1 and 2 sequencing, particularly if they're triple negative breast cancers. So, there are new tests coming in that even impact breast cancer too.

Dr. Tony Magliocco: The challenge is how to implement these tests. The technologies are costly, and insurers don't reliably pay for them. So, this has led to a lot of debate at the current time.

Jerome Madison: Speaking of the biggest challenges, one of the biggest challenges with implementing precision medicine as we know, are many of these genomicists, are not reimbursed, and are only paid for by insurance through submitting either prior-auth, or after appeal, by some of those laboratories.

Jerome Madison: But, in your opinion, what needs to happen in order to gain greater access to precision medicine tools and have insurance pay for them?

Dr. Tony Magliocco: Yes. Insurance needs to pay for things that are medically necessary. So, I think the medical community needs to make a strong case that these tests are not research tests, that these tests are medically necessary, they're essential for proper diagnosis, and for proper treatment of our cancer patients.

Dr. Tony Magliocco: If the medical voice is insufficient, I think we also have to look to patient advocates and have them speak out on behalf of patients as well, that these technologies, in the overall scheme of things, aren't really that expensive. I've seen some analysts say the cost of testing and laboratory services are less than 3% of the medical budget, yet they contribute almost 90% of the actionable information.

Dr. Tony Magliocco: So, it is extremely cost effective to perform testing, and I think it's a gap in terms of knowledge, in terms of the value of these particular tests. Perhaps it's a reflection that the technologies have advanced very quickly, and that there's a lag between the payers' understanding how they should be ideally used, and that they have truly transitioned from research into routine clinical care.

Dr. Tony Magliocco: This is a very, very important area, and I think it is an area that is impeding the development and availability of molecular tests, and it's an area that we need to address.

Jerome Madison: At H. Lee Moffitt, you guys are very unique because you've built your own molecular diagnostics lab. What was the vision for creating the lab, and what impact has that made on the institution?

Dr. Tony Magliocco: The Moffitt Cancer Center is actually one of the youngest comprehensive cancer centers in the United States. You might not believe something that is 35 years as being that young, but it is in terms of institutional terms. When Moffitt was created, it was created on a unique model that was very patient centered and team orientated.

Dr. Tony Magliocco: Moffitt has always been forward thinking. In fact, it fully engaged something called total cancer care, which was the foundation for personalized oncology as early as 2006. Back then, Moffitt partnered with Merck and others to create something called the Total Cancer Care Program, where now, over 150,000 patients have been enrolled. They give their tissues and their tissues are molecularly profiled. They

volunteer their medical information so that we can really understand the molecular basis of cancer, and how we can better classify cancer to better select therapies.

Dr. Tony Magliocco: I think Moffitt was always very fully invested in this. When there became real clinical demands for next generation sequencing for advanced genomics, there was a big push from Moffitt leadership and Moffitt oncologists to make this technology available right on site, right in house within Moffitt.

Dr. Tony Magliocco: There are reasons for that. The first is to understand the technology so that we could have it in our own hands and really understand how it works. The second is to support research so that we could learn new things and how to improve the technology. The third is to support clinical trials so that we'd always have the latest technology available for our patients. So, that's what really drove it. This commitment to early access and to patient care.

Dr. Tony Magliocco: It was really our leaders and our oncologists that really drove this, and really led the foundations to Moffitt's commitment to personalized oncology. You really can't have personalized oncology without having a full molecular service. That enables you to do the most advanced testing, the most efficient costing, and the fastest turn-around time possible.

Jerome Madison: You mentioned the early adopters, and I've been in what we now know as the Precision Medicine industry, for nearly 16 years, and back then, there were ... few oncologists who really believed in biomarket-directed therapy. And even fewer pathologists who really had it.

Jerome Madison: One of your colleagues, Dr. Jose Lopez wrote an article in *The Pathologist* that was titled “The Invisible Doctor.” What he suggested is that the role of the pathologist will be diminished as precision medicine evolves.

Jerome Madison: Now, do you see an opportunity for pathologists to be the resident expert in genomic biomarkers as they have been for prognostic and predictive markers in the past?

Dr. Tony Magliocco: Yes, absolutely. So, pathologists are more than just microscopists. They are physicians, first and foremost, but they are lab experts.

Dr. Tony Magliocco: Pathologists understand every type of testing, they understand how it's to be used, and how to be implemented. They understand how to interact with the medical team. So, I think it's completely natural for pathologists to take ownership of the molecular genetic testing, and incorporate it into pathology practice.

Dr. Tony Magliocco: So, currently in a hospital like Moffitt, we offer over 2,000 different tests. Pathologists preside over these, and we're continuously introducing new ones. So, pathologists are really at the very center of the information that drives medicine. It's incumbent on the pathologists to maintain their expertise, to remain engaged on the clinical side, and to remember that they are physicians, and that they're not just, as I said, microscopists, and it's really their duty to manage this data, and to contribute to it, and to learn how to understand how to utilize it better for patient care.

Jerome Madison: Yeah, I think one of the remarkable things that Dr. Lopez mentioned, is he suggested that pathologists are similar to the genetic counselor. There's an opportunity for the pathologist to be the genomic counselor, to have even office hours to counsel a patient on their genomic expression. What do you think about that?

Dr. Tony Magliocco: I think it's a very interesting idea as he pointed out, that often patients don't even know their pathologists exist. In popular media, on television, sometimes you see surgeons and internists appear to being doing the work of pathologists, and pathologists are not featured.

Dr. Tony Magliocco: So, once patients become aware of pathologists, sometimes they become curious about them. In my practice, I've had the occasion to interact with patients on numerous occasions. They've come to my office to review their slides, we've discussed their case, we've discussed what other tests might be available to them. And, in most cases, the patients seem to be very interested in pathology practice, and were very keen to learn more.

Dr. Tony Magliocco: So, I think about the idea of pathologists interacting more directly with patients is an interesting one. But, pathologists aren't always fully trained, or experienced in doing that. There probably will have to be a transition period, or identification of pathologists that are more interested in doing that compared to others that may not want to be involved so much with direct patient care.

Jerome Madison: Mm-hmm (affirmative).

Jerome Madison: For those of you out there on Linked In or on social media, please follow Dr. Magliocco. You can find him on Linked In. Do you have any other social media tags or platforms that people can follow you?

Dr. Tony Magliocco: Yes, definitely. You can follow me on Twitter @MagliоccoTony, I'm on Linked In. I have a website called Lifeline Diagnostics that I write blogs on, and so, I'm quite available, and happy to engage in discussion. I like to write about current trends, and one of the most exciting things is almost every day there's a new breakthrough in terms of discovery about the biology of cancer, and about new potential therapies. There are so many new immuno-oncology therapies coming, there's so many new ways to combine them with other therapies. One of the really cool things that's happening at Moffitt is something called Evolutionary Biology, and Evolutionary Biology of Cancer, where we're really understanding how to manage cancer better, so that we don't force it into developing drug resistance.

Dr. Tony Magliocco: These are very exciting times for personalized medicine. It's transitioning very, very fast, almost on a weekly basis. There are new developments, liquid biopsies, more expanded genomic analysis. Micro R and A, it goes on and on, and that's not even getting into artificial intelligence and digital pathology. So, there's plenty of areas for people to get interested in, and get involved. Particularly scientists, and high technology people. The more they know about opportunities in pathology, the better, as well, as we can work in teams to develop some convincing new diagnostic services.

Jerome Madison: Awesome. You're one of the very few pathologists – that's the reason why I bring up social media for those of you out there, please follow him – because you're one of the very few pathologists who speaks and writes articles on precision medicine.

Jerome Madison: My question is two part. What makes the voice of the pathologist unique in this era of precision medicine, and is CAP and CLIA, adopting a similar message to become the go-to experts on genomics?

Dr. Tony Magliocco: Yes, thank you for the plugs, I really appreciate that, and thanks for following me.

Dr. Tony Magliocco: I think pathology is one of the more misunderstood specialties. To become a pathologist, you know, a typical course, like myself, you've got to do undergraduate. I did my undergraduate in Lethbridge, and then I did Medical School in Edmonton, in Canada. I wasn't quite sure what I wanted to do, and pathology looked interesting. So, I spent four years doing pathology, and then I did two more years after that doing research in molecular genomics. I actually went back to a practice that was in Saskatoon, it was a very broad practice, and did everything from forensics to subtle pathology to molecular. I think that many pathologists have quite a broad background. But, first and foremost, they are physicians. So, they do understand medical disease. Often, it's been said that pathologists are the doctor's doctor, that we always see the most interesting cases – that other specialists come to us with their most challenging cases, and we have the tools that enable them to answer those cases.

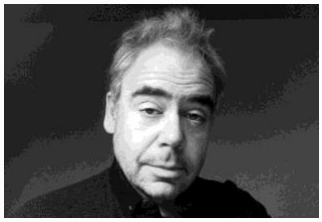
Dr. Tony Magliocco: So, I think that pathology is uniquely positioned in that we see the interesting cases, we see the technology. We have them right in our very own lab, and we can access them. We work in teams with oncologists, particularly at large cancer centers the multi-disciplinary team always has a pathologist. Now, routine tumor boards are typically led by a pathologist. So, the value of pathology is apparent to oncologists. I think that pathology is, really, ideally placed to help move this field forward.

Jerome Madison: Yeah, absolutely. Dr. Magliocco, I really appreciate you coming on and discussing the new challenges for pathology in the area of precision medicine, because as you mentioned, as a pathologist, you cannot execute precision pathology without excellent diagnosis, and that lies in the hands of the pathologist. So, we appreciate that.

Dr. Tony Magliocco: Well, thank you very much, and thank you for inviting me on. I think this is a revolutionary time in pathology and genomics. I hope pathologists stay central to it. As I said, they are experts in the lab, they have a singular focus on lab quality, and patient service. So, I think the future is very bright for pathology, and I really look forward to what new developments are coming down the road.

Jerome Madison: We do, and I know our listeners do. So, I want to thank Dr. Tony Magliocco, and all of our listeners for joining us today. I hope you'll tune in for the next episode of The Precision Medicine Podcast, and don't forget, you can download full transcripts of today's episode at PrecisionMedicinePodcast.com.

Jerome Madison: If you enjoyed this episode, you probably know someone else who would, so please tell them. They'll thank you, and so will we.



About Our Guest: Anthony Magliocco, M.D.

Dr. Magliocco has over 25 years or experience as a Professor, Researcher, Pathologist, Laboratory Director, Consultant, Tissue Banker, and public speaker. He is Board Certified in Anatomic Pathology and has extensive experience and sub-specialty expertise in Breast, Gyn, and Molecular Pathology. He has held continuous peer reviewed funding in translational research and his laboratory is currently investigating the mechanisms of ovarian cancer metastasis and treatment evasion.

He has founded numerous molecular diagnostic laboratories in the USA and Canada, has published over 200 manuscripts in oncology, and holds numerous diagnostic technology patents.
He is currently Executive Director of Esoteric Laboratory Services at the Moffitt Cancer, as well as Scientific Director for Moffitt Tissue Core, one of the largest bio banking programs in the world. He also directs the newly formed Moffitt Morsani Advanced Diagnostics Laboratories which is focused on accelerating development of new CLIA laboratory diagnostics. Dr. Magliocco also directs fellowship programs in Molecular Diagnostics and Digital Pathology.

He has held numerous national and international roles including Chair of Pathology for the Radiation Therapy and Oncology Clinical Trials group, member of the NCI GU steering committee, and member of the Canadian Cancer Clinical Trials Network Steering committee, as well as previous editorial position with the Journal of Surgical Oncology and is frequent reviewer for numerous other Oncology and Pathology Journals.

Most recently Dr. Magliocco has founded a new biotechnology Company, Protean BioDiagnostics

Protean BioDiagnostics is a Tampa-based Biotechnology company committed to creating and deploying innovative cancer laboratory diagnostic products supporting the delivery of precision cancer treatments. www.proteanbiodx.com

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