“The BostonGene Tumor Portrait Report and How to Access It" (Michael Hensley and Michelle Lanman) [#72]

Brad Power and Russ Hollyer
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“The novel thing about BostonGene is being able to portray the tumor microenvironment.” – Michael Hensley

“What we do is show what the tumor microenvironment is composed of, and whether it's immune hot or immune cold.” – Michael Hensley

Meeting Summary

Advanced cancer patients want as much high quality data about their disease as they can get to inform their treatment decisions. Beyond the increasingly common DNA sequencing, there are emerging tests which can look at the transcription of your DNA to proteins (RNA sequencing and proteomics) and your tumor microenvironment. These tests can uncover the unique features of your tumor, identify new personalized, targeted treatment options, and tell you whether you will be a likely responder to a therapy.

Michael Hensley is uniquely qualified to describe some of the newer tests that you can consider. He is a Senior Strategic Account Manager at BostonGene, and has sixteen years of diversified and comprehensive pharmaceutical, cancer diagnostics, and medical sales experience, and thirteen years of hospital experience in pharmaceutical and diagnostic sales. Michelle Lanman is National Sales Director at BostonGene. BostonGene provides comprehensive molecular and immune profiling to assist in treatment selection. In a recent discussion Dr. Sumit Subudhi of MD Anderson described how he used BostonGene as a leading provider of immune system profiling.

What are some of the tests and reports you should consider getting?

- **Tumor analysis** includes genomic profiling of tumors, including whole exome DNA sequencing and whole transcriptome RNA sequencing. DNA sequencing has become common, while RNA sequencing is less common. RNA sequencing can identify biomarkers and fusions that can lead to targeted treatment options. Using both DNA and RNA sequencing can paint a more complete picture of your cancer. BostonGene's Tumor Portrait Report provides actionable insights into a patient's cancer, including potential drug targets, prognosis, and clinical trial matching.
- **Spatial analysis** can identify immune-rich (“hot”) and suppressive (“cold”) tumor microenvironments, indicating whether you will be likely to respond to immunotherapy. Spatial analysis can create a three-dimensional picture of the tumor microenvironment and identify subclones, which can lead to new biomarker targets and improved cancer treatment.
- **Liquid biopsies** (blood draws) can provide valuable DNA information and immune system profiling. Blood is easier to access, and usually more current than tissue samples, but harder to analyze, and there may be differences between reports from

different companies due to differences in sensitivity and sequencing depth. BostonGene's liquid biopsy test is going to be available soon.

- A **tumor evolution report** repeats DNA and RNA tests at different times to let you see how your cancer is evolving.
- **Immune system profiling** can tell you whether you will likely respond to immunotherapies. If your tumor microenvironment is immune-enriched, and tumor mutational burden high, you have an exceptional opportunity to have a durable benefit of immunotherapy in excess of 70 to 80% in some cancers. If you have a suppressive tumor microenvironment with a low tumor mutational burden, you have less than a 7% chance of a durable response to immunotherapy. BostonGene's multiplex immunofluorescence platform enables three-dimensional pictures (“spatial imaging”) of the tumor microenvironment, providing a more detailed understanding of how the tumor is interacting with its environment.

How are your test results translated into treatment options and strategies?

- Your primary diagnosis, medical history, and genetic profile from the test results, especially biomarkers, are fed into a matching algorithm linked to the approved evidence-based treatments (the National Comprehensive Cancer Network guidelines) to provide personalized treatment recommendations.
- Algorithms matching biomarkers and treatments and clinical trials are constantly updated with new information from patients and the literature.

How can you access these tests?

- You need to request tissue samples from pathology for DNA and RNA sequencing and get a blood draw for liquid biopsy tests.
- Your physician will order the tests through a requisition form.
- You give a saliva or blood sample for the normal DNA collection.
- Once these inputs are in the lab, they will usually have results in 10 to 12 calendar days.

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Meeting Notes

SUMMARY KEYWORDS

tumor microenvironment, report, gene, tumor, boston, md anderson, biomarker, immunotherapy, sequencing, tests, information, clinical trial, therapy, liquid biopsy, tissue

SPEAKERS

Michael Hensley (62%), Michelle Lanman (15%), Rick Stanton (9%), Robert Gurmankin (9%), Amit Gattani (3%), Richard Anders (3%)

OUTLINE

SUMMARY

- **Personalized cancer treatment with BostonGene.** 0:02
    - Michael Hensley from BostonGene discusses personalized cancer diagnostic testing.
- **Genomic sequencing and cancer diagnosis.** 2:30
    - In a future session, BostonGene's Katerina Postovalova will describe BostonGene’s genomic profiling capabilities, highlighting rapid industry advancements.
    - BostonGene provides comprehensive genomic profiling for various cancers, including prostate cancer, through their RNA sequencing and deconvolution tool, Cassandra.
    - Their reports include a biomarker database based on the patient's primary diagnosis, and they collaborate with the NCCN guidelines to provide personalized treatment recommendations based on the patient's clinical history and genetic profile.
- **Cancer diagnosis and treatment options using DNA and RNA sequencing.** 6:55
    - The benefits of using both types of sequencing and the importance of comparing normal DNA to tumor DNA.
    - The potential of RNA sequencing for identifying fusions and other biomarkers, and the importance of quantitative analysis versus observer variability in pathology labs.

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    - Researchers identify immune-rich and suppressive tumor microenvironments in cancer, with high TMB associated with improved response to immunotherapy.
    - Example of a prostate cancer report at MD Anderson, highlighting key information such as patient details, tissue tested, tumor content, and treatment options.
    - The importance of understanding the tumor microenvironment and immune enrichment for prostate cancer treatment.
    - How BostonGene’s collaboration with NCCN can provide personalized recommendations for patients.
- **Cancer genetic testing and clinical trial matching.** 14:25
    - The process of creating a BostonGene Tumor Portrait involves requesting tissue samples from pathology and marrying them with DNA collection for analysis.
    - MD Anderson prioritizes clinical trial matches based on patient history and institution.
    - BostonGene has a financial assistance program for eligible patients.
- **Immunotherapy and tumor microenvironment analysis.** 18:00
    - Understanding the tumor microenvironment and how it responds to therapy.
    - Doctors usually address information learned about the tumor microenvironment through medication and radiation. This information can be used to change treatment approaches for prostate cancer patients.
    - Researchers aim to validate the potential of changing tumor microenvironments to improve immunotherapy responses.
- **Cancer biomarkers and imaging technology.** 24:45
    - Rick Stanton discusses commercial availability of CODEX technology, which is expensive and not reimbursed for all patients.
    - Michelle Lanman explains CODEX is a spatial imaging platform used by BostonGene, allowing for precise location of gene expression levels in tumors.
    - The potential of using gene expression analysis to better understand cancer.
    - While the technology is expensive, it could be offered as a fee-for-service.
    - MD Anderson has customized two platforms for bladder cancer and prostate cancer.
    - BostonGene is able to portray the tumor microenvironment and identify subclones, which can lead to new biomarker targets and improved cancer treatment.
    - BostonGene is working to escalate clinical trial matches at MD Anderson by providing valuable insights and advocating for their trials.
- **Using RNA sequencing for cancer treatment insights.** 31:41
    - Rick Stanton discusses using immunohistochemistry to identify specific proteins in tumors.
    - Rick Stanton shares how he uses RNA sequencing data to inform his cancer treatment decisions.
- **Liquid biopsy and tissue biopsy differences.** 35:25
    - Michelle Lanman provides valuable insights on spatial imaging and immuno-profiling, highlighting the importance of understanding the tumor microenvironment.
    - Amit Gattani asks about calibration issues between liquid biopsy reports from different companies
    - Michelle Lanman cites differences in sensitivity and sequencing depth.
    - Blood is harder to analyze than tissue for cancer cells.
    - Marketing efforts may vary between companies.
- **Liquid biopsy accuracy and variability.** 41:05

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    - Differences in liquid biopsy tests, including gene panels and technology used, can result in variations in reported findings.
    - Challenges with liquid biopsies, including true negatives and false positives. BostonGene addresses these issues through chip filtration.
    - Robert Gurmankin asks about the outcomes of liquid biopsy reports and their impact on treatment decisions.
    - Richard Anders asks about following patients for clinical outcomes in dozens of cancer types, with some cases being formal partnerships and others being informal case reports.
    - Following metastatic castrate resistant prostate cancer patients with high TMB and high MSI, treating them with immunotherapy and monitoring outcomes.
- **Cancer diagnostics and patient access to information.** 48:52
    - Integrates emerging biomarkers and clinical outcomes into reports for patients and physicians.
    - Richard Anders: Asks about the number of tests done per month, interested in stratifying the universe for statistical significance.
    - BostonGene gets in about 400 tests a month, mostly from MD Anderson.
- **Cancer biomarkers and treatment strategies.** 53:44
    - BostonGene's internal databases, including biomarker and clinical trial databases, are constantly updated with new information from patients and literature.
    - Tumor microenvironment in primary tumors can be positive, but changes to fibrotic in bone or other tissues over time.
    - Challenges and opportunities in understanding and treating cancer, with a focus on tumor microenvironment and evolution.

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Meeting Transcript

Robert Gurmankin
Welcome to this Cancer Patient Lab meeting with Michael Hensley from BostonGene.

As advanced cancer patients, we always want to have the best data about our disease as possible to help inform treatment decisions. BostonGene provides AI-based molecular and immune profiling. Their tests uncover unique features of our tumor, enabling doctors to design the best treatment for our cancers.

In a recent discussion we had with Dr. Subhudi from MD Anderson, Dr. Subhudi described how he used BostonGene as a leading provider of immune profiling. He's the one who got us in touch with BostonGene.

Today, our speaker is Michael Hensley, senior strategic account manager at BostonGene, with 16 years of diversified comprehensive pharmaceutical cancer diagnostic medical experience. He'll be presenting a BostonGene report and explain how patients can get access to their services.

I want to thank Michael and also Dr. Subhudi for helping me and Brian McCloskey get some testing. We have to find out what's happened with my samples. We also have a meeting coming up with Katerina Postovalova of BostonGene for an inside look at how it's being done.

Michael Hensley 2:29
Yes. Katerina’s going to be presenting all the BostonGene capabilities outside of our commercial Tumor Portrait Test.

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Michael Hensley 3:20
Thank you all so much for having me today. This has been a very exciting adventure, starting to work with Cancer Patient Lab.

I'll lead with this: I'll never forget when BostonGene was recruiting me. I had just celebrated my one-year anniversary, and one of my great mentors, the chair of breast oncology at MD Anderson, was telling me about how this industry, next gen sequencing or comprehensive genomic profiling, whatever you want to call it, is advancing so rapidly. It's like computers were in the 1990s. By the time you brought a new computer home, it was already out-of-date. There was already faster RAM, better video cards, and so forth. That's how this industry is progressing. I came to BostonGene because I truly believe that we are leading that revolution.

When you think about it, everybody does sequencing to a certain aspect. The question is: what can you do with the sequencing besides just providing biomarker targets with therapies or biomarker targets that have a matched prognosis?

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At BostonGene, we do all that and more. We now have four different tests. Today, I'm going to focus on our tissue Tumor Portrait Report test because it is our most comprehensive. We do whole exome sequencing, where we look at all of the 21,000 genes in the DNA. We do the whole transcriptome, so we're looking at all of the RNA. There are no limited panels here. If you look at all of our research collaborations, if we want to go back and mine all the sarcoma patients at MD Anderson for an emerging biomarker, we can do that because it was in our sequencing. The biggest thing at BostonGene that is the most exciting for prostate cancer is we use our RNA sequencing through a deconvolution tool that we've named Cassandra to portray the tumor microenvironment. Everybody investigates that tumor biopsy or that metastatic lesion as the seed, but we go and investigate all of the normal tissues surrounding that. What we do is show what the tumor microenvironment is composed of, and whether it's immune hot or immune cold. We also do companion IHCs.

In our reports, we've mined it through a biomarker database that's based on that primary diagnosis. All the reports will be different based on the patient's primary diagnosis. We also have a formal collaboration with the NCCN guidelines. When we do a BostonGene Tumor Portrait along with getting the tumor tissue, we also get a patient's normal DNA through saliva or blood. We also get the patient's progress notes, and we build out our report based on the patient's clinical history: treatments they've been on, response, progression, so forth, and then we provide that in the report.

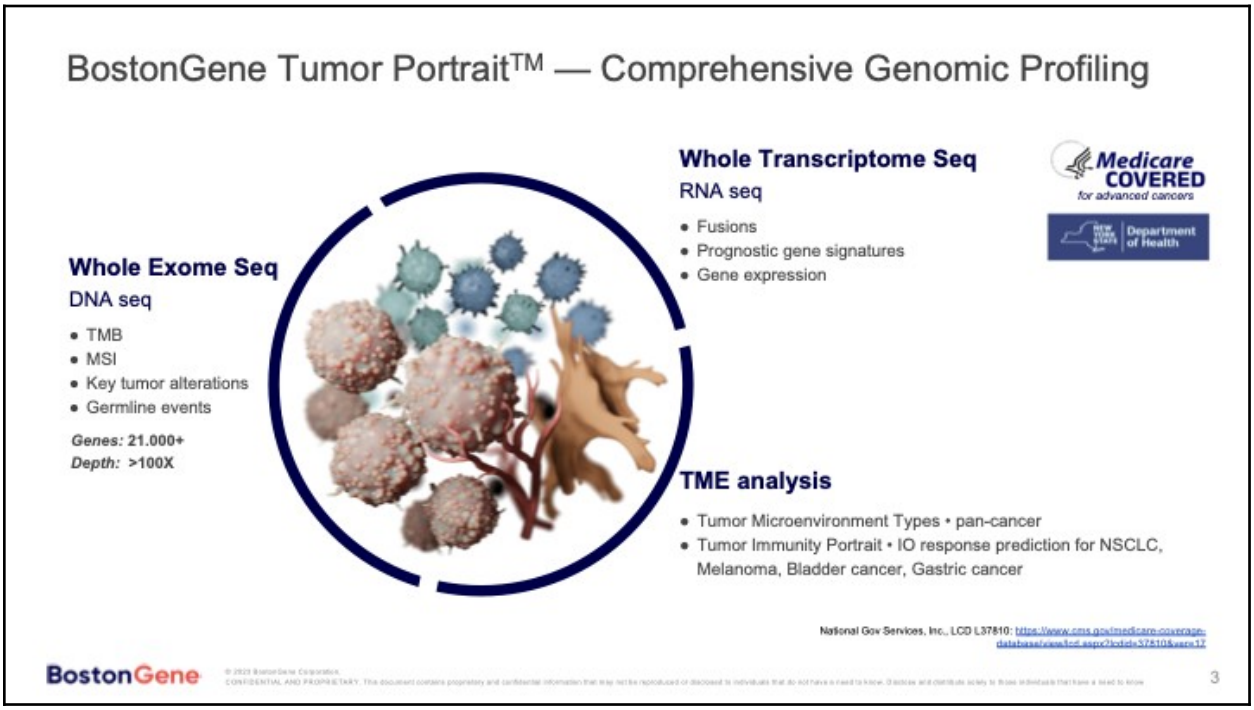
But we also have an algorithm we built with the NCCN guidelines, and we run that through an algorithm and we present the next preferred therapies for that patient based on the NCCN decision tree. For community oncologists this is huge because all the NCCN guidelines are

changing so rapidly. They used to change once every two years but now they change every three to six months.

We also have a “CUP test” for patients where there's a “cancer of unknown primary”. We use DNA and RNA sequencing to make a primary diagnosis call. It's a very exciting test.

We just got our CAP and CLIA certifications. We attach that to the BostonGene Tumor Portrait.

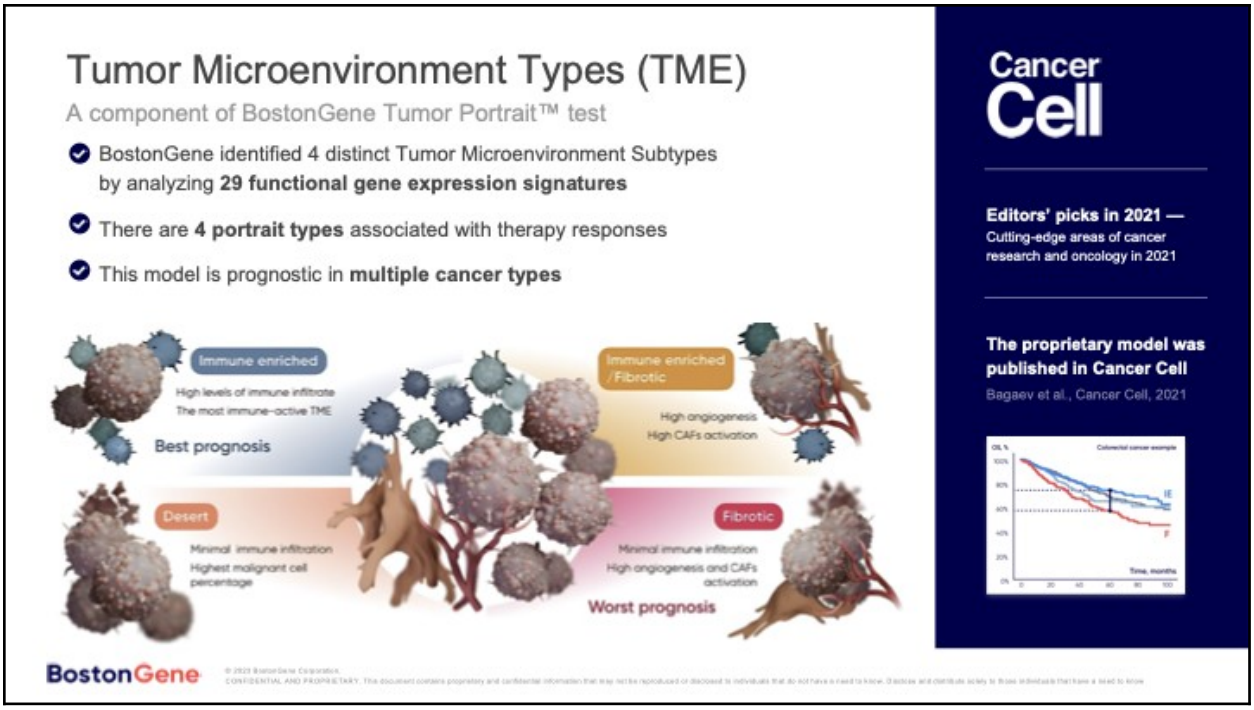
As for our liquid biopsy test, we are going to be launching this in early 2024. This will be launched as a reflex from our Tumor Portrait. In the case that all the tumor tissue that's available is exhausted, we can reflex to liquid biopsy, which provides great results, but much more limited than tissue.



The BostonGene Tumor Portrait handles some of this, but we do whole exome sequencing. We do tumor mutational burden, MSI. We look for key tumor alterations, as well as when we get the normal DNA sample, we also learn to look for germline mutations, and we'll report that, but we also use the normal DNA to compare to the tumor DNA. If you don't do this, you can get a lot of noise. But when you sequence the normal DNA, then match it against the tumor DNA, it greatly enhances your accuracy. That really helps, and it allows us to provide more accurate results.

RNA sequencing is very exciting. There are a lot of fusions that are of high interest. We also use RNA sequencing so we'll have PD-L1 and other biomarkers and the concordance between PD-L1 testing, MSI, tumor mutational burden via IHC, and RNA sequencing. The concordance is very high. But there are quite a few cases because of the variability in IHC reads that we've actually shown something like a PD-L1 high, and then they went back and ran the PD-L1 IHC,

and found it to be different from the original one. It's quantitative through RNA sequencing versus observer variability in a pathology lab.



Then finally, the tumor microenvironment profiling. We put this in our reports.

The way that it works is we have an algorithm built through RNA sequencing. We have 29 molecular functional signatures that look at different elements in the tumor microenvironment, and based on how they're represented, we will have a call of one of four profiles. On one side, you have this immune-enriched tumor microenvironment. This has a lot of really exciting immune cells that can be targeted with immunotherapy, immune checkpoint inhibitors. These patients want to have a better prognosis, but to have a much greater chance and sensitivity to respond to immunotherapy because there's a lot of exciting immune cells to turn on. Maybe even more important is that we can identify the immune-suppressed tumor microenvironment. We call it a “desert” or “fibrotic”. These patients have a very cold tumor microenvironment. It probably has a greater chance of responding to chemotherapy. But it's really interesting to see this because what you'll see through all of these is you'll see high tumor mutational burden in these fibrotic or deserts. You can also see high tumor mutational burden in the immune-enriched, but you see a variability of the classical biomarkers that we use present day to determine whether patients are going to get immunotherapy or not, which is mainly MSI, tumor mutational burden, or PD-L1.

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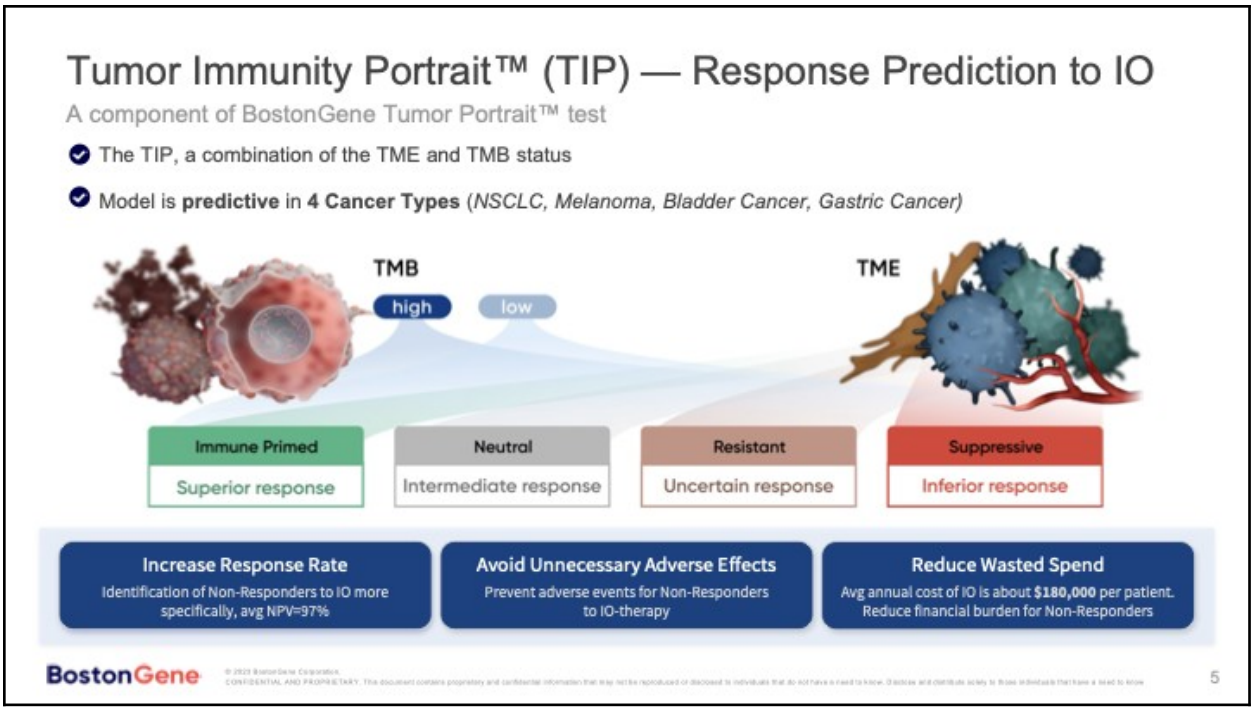

We are prognostic in 34 different solid tumor types now. The first paper in *Cancer Cell* that was published, the first validation, was focused on lung cancer, melanoma, bladder, and gastric cancer. We were able to show that when you have this immune-primed response, that is immune-enriched, and tumor mutational burden high, these patients have an exceptional opportunity to have a durable benefit of immunotherapy in excess of 70 to 80% in some of the different cancers. On the other side of that is this suppressive tumor microenvironment. If this is long with a low TMB, these patients can have less than a 7% chance of a durable response to immunotherapy. So the point is to look at all these factors together, obviously,to get BostonGene tumor microenvironment profiling into the standard of whether or not you'd go on immunotherapy, like ipi (ipilimumab) or nivo (nivolumab) or Keytruda (pembrolizumab). It takes prospective validation. It takes a lot of money. It takes a lot of time. This is one of the focuses of our research alliance with MD Anderson.

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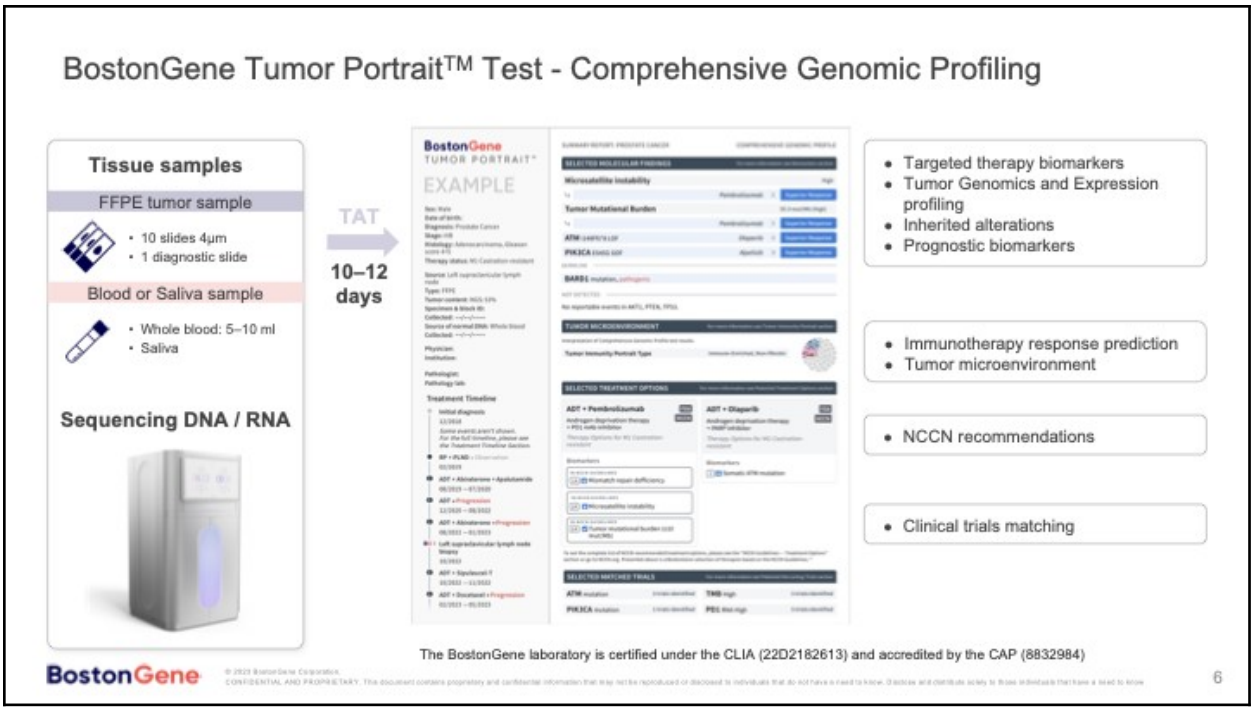

Michael Hensley 12:06
This is the report. I can’t remember who said that this report was hard to read. This is the first page of the report. This is the summary page. We've developed this because this has all of the key information that a physician would want to make a decision. This is a prostate report here. I don't know if you can see it well. It's small. On the left side, we have all the patient's information: the tissue that was tested, where pathology was, the tumor content. You can see the first glimpse of the treatment timeline. It's a nice Cliff Notes (summary) for the physician, as well as others looking at where the patient's been as far as therapy and response versus progression.

One of the places where people get confused that's easy to fix is there are two different areas of therapy options, and they can be remarkably different. At the top, you see this patient has MSI (microsatellite instability) high, TMB (tumor mutational burden) high, an ATM mutation, a PIKC3A mutation, as well as a germline mutation. This is based on our sequencing. If there is a targeted therapy, it would be to the right of it. If it's a prognostic biomarker, it would not have a targeted therapy. It would just have a blue or red, which you see, the blue is a superior response. The middle section is the first glimpse at the tumor microenvironment. This patient had an immune-enriched non-fibrotic, which is the hottest.

The second section can be completely different because this is what I'll talk about – our collaboration with the NCCN, where we're running the patient's clinical history through an algorithm that we built with the NCCN. Depending on if they have biomarkers, this can change because if there was nothing significant in the sequencing, then this would be completely different. For this patient with MSI high, TMB high, immune-enriched tumor microenvironment, this is the holy grail for prostate cancer for a patient to really have a great opportunity for response to ADT (androgen deprivation therapy) plus pembro (Keytruda). But as you go into the

reports, it gets much more granular. We go much more in detail to the biomarkers. We go much more in detail to the therapy selections. We'll put the cohort analysis, the progression free survival, overall response rates. We prioritize into the level of evidence. We can get really deep and granular into the results.

But as far as how this all happens, when a physician orders a BostonGene Tumor Portrait, it's ordered like any of the industry tests through a requisition form. We go and request that with the pathology report and the progress notes, and then have the patient do a saliva or blood sample for the normal DNA collection. At the same time we will request from pathology the tumor biopsy that the physician wants to order. Once we marry those in our lab, we will usually have results in 10 to 12 calendar days. We operate very efficiently.

Tissue is the elephant in the room, so to speak, because viable tissue is key. It's not so much the size of the tissue, but it's the actual tumor content that is what we look for.

Another thing that I thought that would be of interest to you guys, based on the mission of the Cancer Patient Lab, is whenever we spend a lot of time doing research for clinical trial matching, most of the industry tests, they will have an algorithm built that's connected to clinical trials.gov. You can be in Houston and get a clinical trial that's open in Sacramento. There are certain times when we would travel for a clinical trial. We customize our clinical trial match to two things: one, based on the sequencing, based on the patient's clinical history, but also based on the institution. So if you go to MD Anderson, you're going to get – this as an example of MD Anderson – you're going to get all the MD Anderson trials, and we prioritize them to probably the ones that are the biggest bang for the buck, so to speak, for where you're at in your cancer journey.

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This is a summary slide of everything that we do. The one thing I want to note is that we have a robust financial assistance program. It's weighted two ways. It's not for just the indigent population. It's weighted on financial. You have to put your household income and your number of dependents. We don't require any supporting documentation to do that. But the other side of it, which I think is really unique to us, because in my career I've never had this, is there are other situational factors. At MD Anderson, I get a lot of patients with excessive medical bills, travel costs for medical care, but there's also like, fixed income, retired, forth. At MD Anderson, more than 90% of our patients get qualified at 100%, which means that regardless of insurance determination, you might have had inferior testing, but in the MD Anderson BostonGene Tumor Portrait, we will work through the claim and through the appeals process. But in the instance that they deny or partially pay, we don't pass on those costs to our patients. That's a great testament to BostonGene.

The other thing that we can do is we can do multiple tests for patients, before and after therapy, or later on in their journey, and then we can add a tumor evolution report, which is really cool because it shows the changes in key biomarkers. It also shows changes in the tumor microenvironment composition and the profile. This can be really interesting with how therapy changes things, whether you make a cold tumor go hot, or vice versa. Then how do you treat it after that therapy? I know Katerina is going to come on in a couple of weeks to present all the other things that we do. The BostonGene Tumor Portrait test is really a great example of how we're taking this industry to the next level. I know you had Dr. Subhudi on a few weeks ago. He's a great mentor of mine. We're doing some incredibly exciting work with him and the prostate cancer team, in which we're looking at this tumor microenvironment and the variability of classical factors like PD-L1, MSI, and so forth, and seeing these patients that respond or don't respond to immunotherapy. It's going to be really interesting. It will be treatment-changing for prostate cancer patients.

Robert Gurmankin 19:45
There were a couple of questions in the chat:
How do doctors usually address information learned about the tumor microenvironment? Medication? Radiation? Where do you usually see docs going?

Michael Hensley 20:22
We're still pursuing the ability for that to make the call for immunotherapy or not. Obviously, right now in the labels of most of the immunotherapy agents, you're looking at TPS scores or CTS scores, PD-L1, looking at MSI, tumor mutational burden. We're highly confident that the tumor microenvironment profile is going to tell a much bigger story there. One, based on it's coming from RNA sequencing, which is highly accurate, which is compared to the variability of various IHC tests. Right now, you still have physicians that will give patients immunotherapy because it is the standard of care. It is the greatest opportunity for global benefit. But they go into that therapy with a much clearer picture of expectations. Because in the world of science, there are no absolutes. We never see a zero or 100%. Right now, that's the big story that we're trying to push forward. It takes a lot of research to do that. There are a lot of different solid tumor types.

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Everyone is different in their responses or lack thereof to immunotherapy. That's where we're at now.

As far as medication or supplements: I don't know. I've never heard of anything like that trying to change the tumor microenvironment. The most prominent thing that changes the tumor microenvironment is various chemotherapies or monoclonal antibodies. But that's still hypothetical, and it's still not the standard of care. Because if we knew how to change a cold tumor microenvironment into a hot tumor microenvironment, and then give the patient immunotherapy, that would be a total game changer. It's very difficult. It is definitely BostonGene’s highest area of interest, but as with a lot of our collaborations, we continue the pursuit of validating this.

Rick Stanton 22:47
The excitement of BostonGene, and the promise that you hold for our group, and hopefully for Brian, is the combination of genomics, RNA seq, and your CODEX implementation. So without the CODEX, you're just the same as other shops to me. I know how to do immune deconvolution. Other shops know it. We came up with our signatures, that's great. That's fairly cutting edge. That's wonderful. But I've been trying to push on Gary Nolan's lab to get the CODEX system that would hopefully provide insights that would be complementary and beyond RNA seq and genomic interpretations. The last time we talked, I really tried to help facilitate Brian who has tissue. We’ve got our guy Brian. He actually has three sets of tissues from three glimpses of his progression. I had hoped that we could use BostonGene as our first access to the CODEX high dimensional immunofluorescent analysis in that emerging world.

Michael Hensley 24:47
Brian and I talked about it. I can start off. Then Michelle Lanman, who is one of our BostonGene brilliant team members, can comment. The point of my presentation today was to present what we have commercially. The MxIF (multiplex immunofluorescence) technology is extremely expensive. There is no reimbursement for it. So it's not available to all patients. Katerina is our wizard in this area of research. We're pursuing this within a research setting with various institutions throughout the United States. Because our MxIF platform is outstanding. We've been able to pioneer some different breakthroughs in that area. But, right now, we do that through research collaborations. Either they're done through investigators’ funding, or under a pharma agreement, or a cash pay agreement, but there's no reimbursement for it right now. It's very expensive. Today I was presenting about what we have commercially available, that's available to all patients. But if you come back for Katerina's presentation, I guarantee she's going to blow you away. You'll be holding on to your seat. We're able to identify different cells in the tumor outside of the tumor. We're able to look at all of them. Michelle, I don't know if you had anything to add.

Robert Gurmankin 26:27
Could you also very briefly explain what CODEX is for the rest of us?

Michelle Lanman 26:35

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CODEX is a type of spatial imaging platform that BostonGene uses. It's a very advanced version of what is typically used in clinic IHC (immunohistochemistry). It would be a replacement of IHC imaging, but it allows us to see exactly in the tumor and the tumor microenvironment, where all of the different expression level data are and where it is located. We can specifically see if certain genes or certain biomarkers are invading the tumor, if they're outside of the tumor. That can play an important role in understanding if something is not actually invading the tumor, then we might not want to target it, because it might not actually make any impact on the cancer cells themselves. It gives us a much deeper picture and a much deeper look at imaging.

BostonGene does offer this, but as Michael mentioned, it is extremely expensive. That's the main reason why we haven't been utilizing it more clinically. We can offer it, and I believe we can do it as a fee for service, so we can get that information for you. We've really been utilizing it as a research platform typically in institutional systems. But most people don't want it yet. It's just a bit beyond what they're asking for. really, that's the only reason. But we can definitely look at what we can offer to you, Rick, and see if there's a way that we can help your patients. We can find out some more information for you and follow up with you on that.

Michael Hensley 28:09
Brian and I have discussed the opportunity to do his as well. We're still talking about it. But the other thing, it looks like if you ever looked at Google Earth, or you look at a GPS, and look at the night skies, or like big cities that are all lit up. It looks like that. It looks like a Christmas tree. At MD Anderson, we customized it on two different platforms. We have an MxIF platform for bladder cancer, and we have an MxIF platform for prostate cancer, looking at different important markers, because we can do 40 to 60 markers on a single slide versus cutting 25 slides to do different various single markers. It is very exciting. It's definitely one of our core pillars in our platform. The market has got to get there. It's got to move through research to show any clinical actionability. The big thing is for reimbursement.

In my prior role, I was doing unlimited DNA panels. I used to always say, “NGS testing is a commodity. Who can do it the fastest?” Because my old company could do it very fast. There's a lot of talent in the depth and the ability to make your calls on DNA. I think that RNA is still an art form. Some of our guys in our lab are the equivalent of Van Gogh. But the deal is everybody in the market is looking at the tumor, and they give you what that tumor is saying. The novel thing about BostonGene is being able to portray the tumor microenvironment. The other thing that we're able to do, which is really exciting, is we can identify in that tumor tissue the main clone, and then we can also identify subclones, or how the cancer is escaping or getting smarter. We can also look in to see what's driving the subclones. Maybe there's a new biomarker target. It allows you to fight the war from various angles.

At MD Anderson, for example, and probably mostly towards other academic institutions, we are really escalating their clinical trial matching. If you go to the breast department, they have like 125 clinical trials open. It's really hard to place patients, unless your primary investigator is a great salesman, for lack of better words, and really advocating for their trial. So we've really

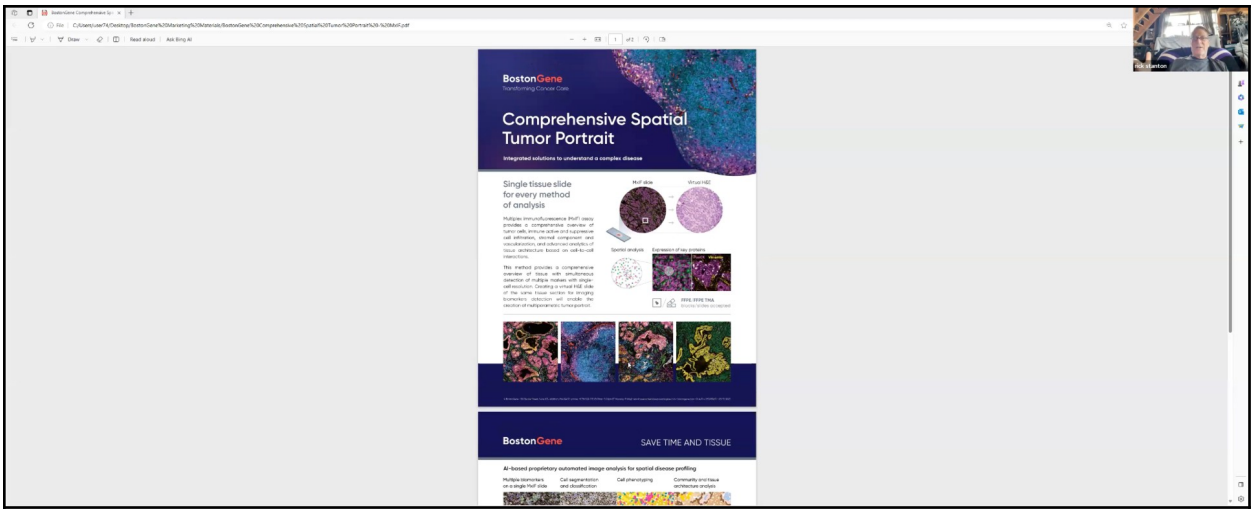
helped MD Anderson escalate their clinical trial matching. So that's another exciting part of BostonGene as well.

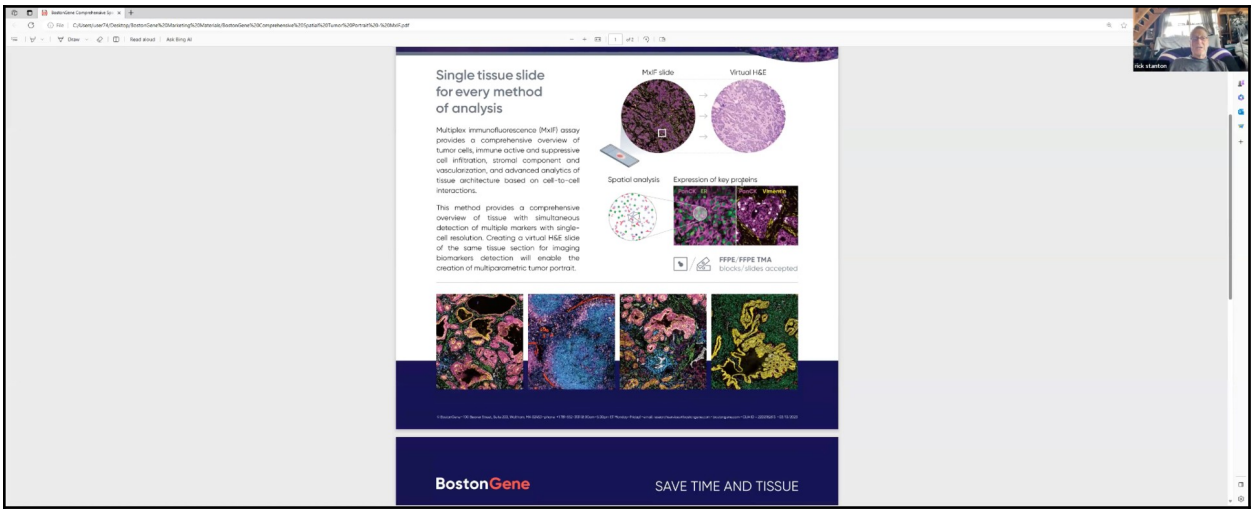
But I do understand on face value that to make a clinical decision you find the biomarkers that have the targets, and you treat the patients based on his targets. With BostonGene, we just keep on peeling back layers of the onion, to decode the cancer. That's where a lot of the value comes. But you're correct. A lot of this is thought provoking, it's confidence building. But, it takes a lot of time, money, and research to get it to be the standard of care. That's what we're working on at BostonGene.

Rick Stanton 31:41
Very expensive. What does that mean? It was like $6,000 or $8,000 out of Gary Nolan's lab for a 40-plex. They have a little 40-plex panel. To explain what this is to other folks, it's like immunohistochemistry of a slice of your tumor, and then use a stain on it or you wash over. And this will be my interpretation. Michelle, please correct me if I'm living in the past of two years ago, whatever. But this is where I was really pushing to try and get spatial for me and our group. You wash over antibodies with fluorescent tags, let's say red. These antibodies are specific to a certain checkpoint or an immune modulator or even a cell surface marker, that would be indicative of a certain cell types, such as CD-4, CD-8, or immunosuppressive cells. You wash it over and it sticks from the antibodies. You do it typically, three plaques, like three colors. You take an image, and you get those three colors. You go, “Okay, now I know where these genes are, or these proteins that are expressed. And then I wash those off, and I do it again.”

What I'm hoping for is more insight. We're all advanced patients, and there's a lot of clinical trials, that's true, but when I go see my oncologist, he goes, “Rick, what do you want to do?” He may push out seven options. Same with Rana McKay at UC San Diego. “What are you comfortable with? Do you want to do chemo? Do you want to try this clinical trial?” So we go to see our oncologist armed with our RNA seq data or genomic data. We normalize, at least I've normalized to the Cancer Genome Atlas. To say, “Okay. Right now, I know I have a high relative expression of B7-H3. So I pushed. I'm on a clinical trial of B7-H3 right now. An antibody drug conjugate. So this understanding directly led to my current therapy.

“The BostonGene Tumor Portrait Report and How to Access It" (Michael Hensley and Michelle Lanman) [#72]





Michael Hensley 34:56
I was trying to show this image. This is the marketing piece, but it gives you an idea. We have a lot of projects that are utilizing this, and it is incredibly informative. If you have the resources to do it, it's great. From the cost, it's a lot different. We're doing 100 patient studies versus a one-off. But, Michelle, I don't know the approximate cash pay.

Michelle Lanman 35:35
I don't want to give wrong information. I'd rather follow up and provide that to you. I have a couple of slides that I could share just a little bit more detail, similar to what Michael was showing.

Michael Hensley 35:53
We have another exciting product that's blood tests that is immune-profiling, like immune fitness tests that basically does what we do with the tissue from the tumor microenvironment, and a bunch of other things, that's an emerging product for us. But when Katerina presents to everyone, she's going to present both of these different technologies in a few weeks.

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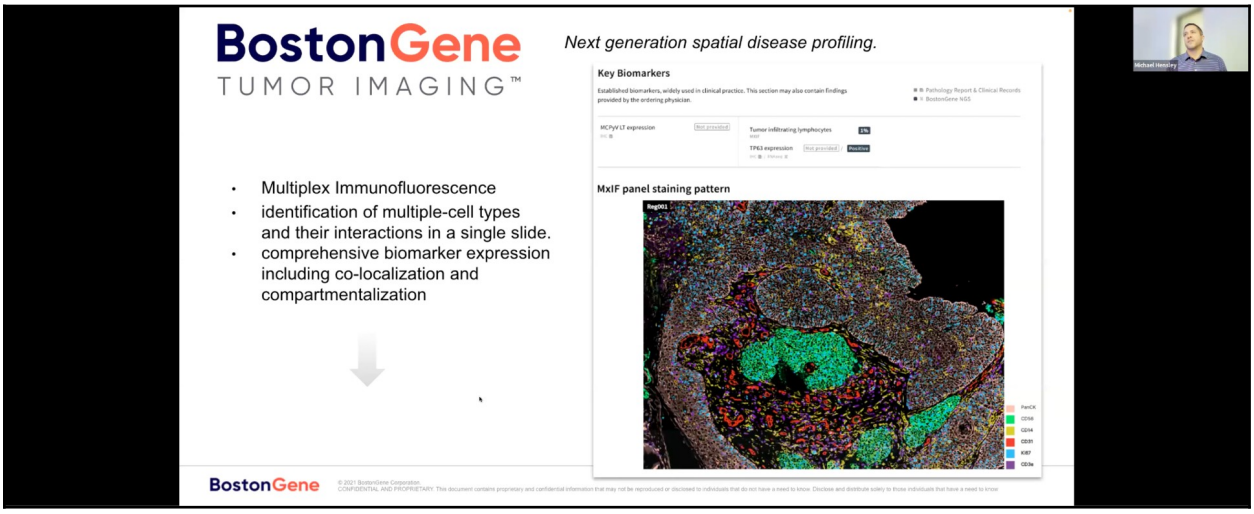
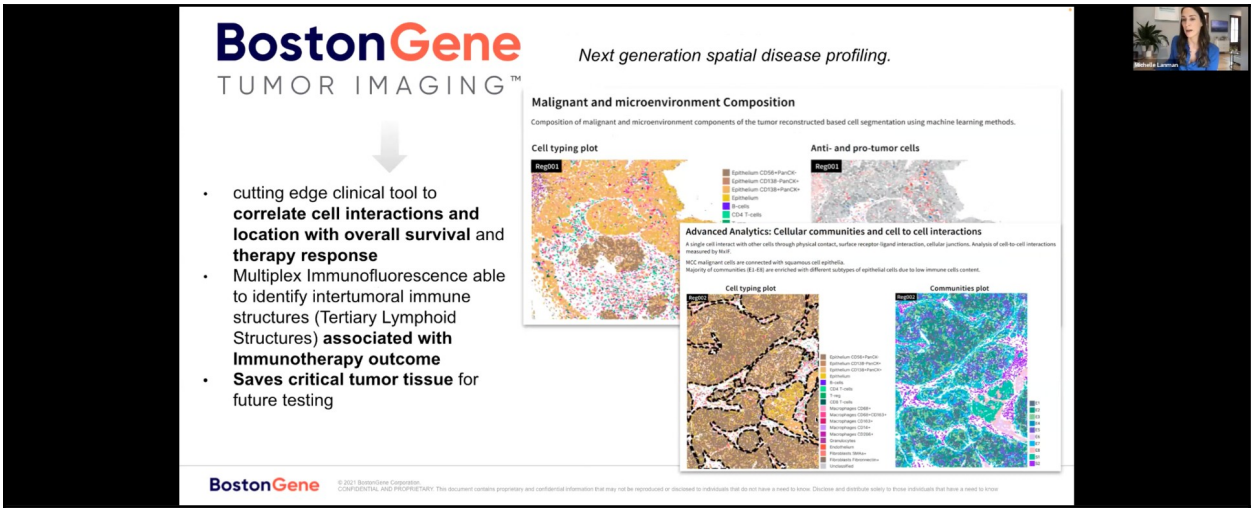
Rick Stanton 36:19
What is her background?

Rheanna Carter, BostonGene in the chat 36:25
Katerina has her PhD in cell/cellular biology and histology.

Michelle Lanman 36:30
She's one of our pathologists. She leads our pathology team and is one of our program managers and project managers.



This gives you a better picture of our spatial imaging. Looking at some of the specific stains, it highlights exactly where those individual biomarkers are located. If I can click through these, we can plot out just exactly where everything that we find lives in and around the tumor.



It gives us a much better picture in terms of the plotting of these different biomarkers.

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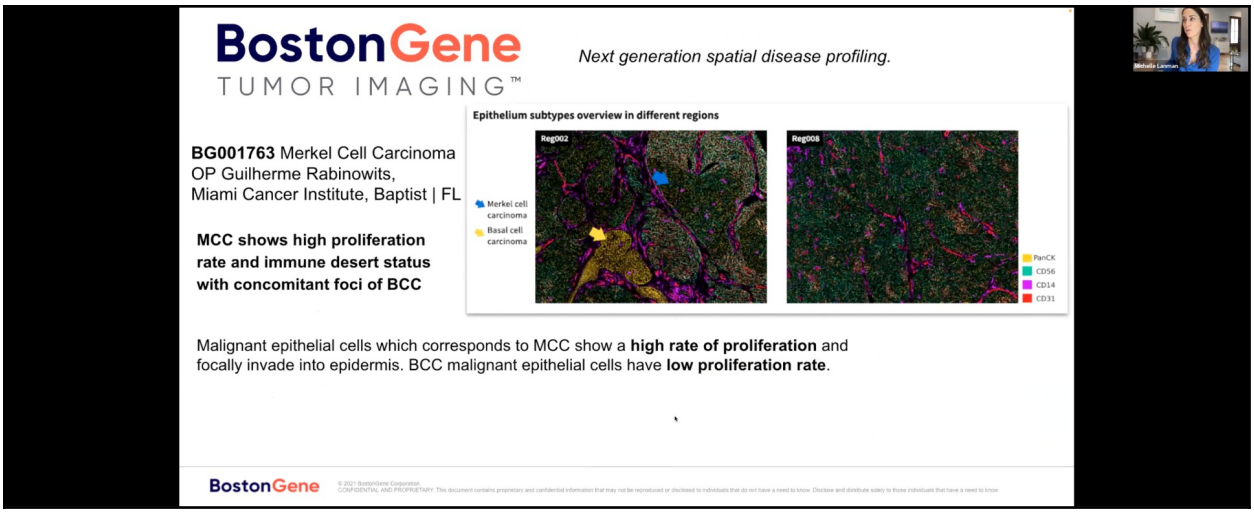
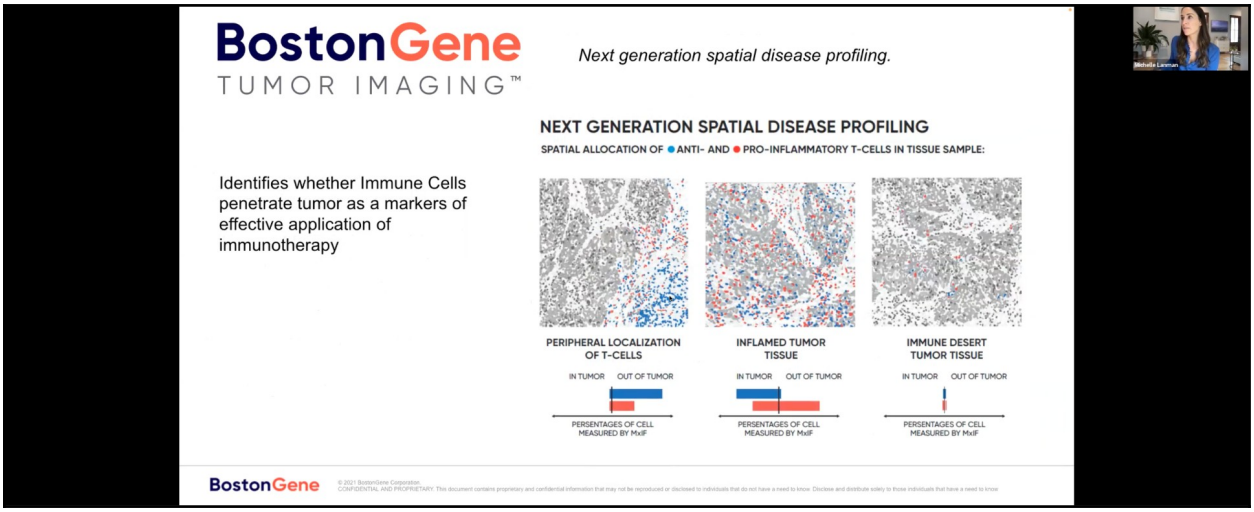


These are just some examples of some of the reports that we're able to provide.



This is why it's helpful to us. We can look at what is inside of the tumor or outside of the tumor and compare that to our tumor microenvironment. We can see the differences in terms of how much are not actually activating in the tumor, and how that translates with our tumor microenvironment profile versus those that are more active in the tumor. This is what we offer. But, Rick, we will definitely let us find more information out for you and get back to you on that. I don't want to give you incorrect information.

Amit Gattani 38:01
I haven't used BostonGene, but I've had liquid biopsies and tissue biopsies done through Guardant, Tempus, and Strata. I see calibration issues between the reports that we get. There are a few dominant things everybody reports the same, but not stuff that is at the next level. I did one of my last liquid biopsies with Tempus and Guardant at the same time, and I got a very different report. I want to understand what the calibration issues are? Why do they exist? How do you trust what you're getting? Because different companies are giving you different things.

“The BostonGene Tumor Portrait Report and How to Access It" (Michael Hensley and Michelle Lanman) [#72]

Michael Hensley 38:54
The first thing is the difference between tissue and blood. It's a lot harder to find circulating tumor cells or DNA fragments in the blood. A lot of times if you get a negative test, you might not have found it. Sensitivity is getting much greater in liquid biopsy testing. Blood is a lot easier than a biopsy. That could be the difference between them.

On the tissue test, one thing BostonGene has not been great at is marketing because our competitors, our marketing peers, have 150 reps, and we have 12 reps. We did it backwards where we develop all this validation and build up this body of scientific evidence. Now we're in a commercial launch. A lot of people have never heard of BostonGene. I always ask, “What was a patient that you didn't find anything great that you got Tempus testing that nothing was remarkable?” Once a patient keeps you up at night, let me do that as a pilot. Let me do a test for free for you. It's remarkable how many times we will find stuff that was missed. It depends on your depth of sequencing. A lot of these tests say that they are looking at everything, especially on the RNA side, but they're not. They have a limited RNA panel. There's just a lot of different talents in the sequencing of doing this. It is very, very difficult to do this technology, and especially on a commercial level, because you have to size for growing volume.

But Michelle, I don't know if you or Rheanna (Carter), if you had anything to add to that. It's a common question. Because you do see the same big results, but then you see differences in other things.

Michelle Lanman 40:57
On your question on why there are differences between two different liquid biopsy reports: There are a couple of different reasons for it. Number one is that all of the liquid biopsies that are on the market today are designed a little differently; meaning, they look at a lot of the same genes and biomarkers, but there are some differences. Each of them are different sizes (number of genes), so you might get the same genes, one set of genes from one company and one from another. For example, our liquid biopsy panel has about 216 genes, Guardant’s FDA-approved panel has 55, I think they have a 74-gene panel. Tempus is around 105. All of them vary in terms of what they're looking at. That's one of the differences.

But also, in terms of the technology itself: while all of the labs could use the same exact equipment, it's how they actually tailor that equipment and design it for their own sequencing purposes, in terms of setting up the probes, the depth of coverage, like how deep they're reading into the DNA information, that will determine what can be recorded and what cannot be recorded. There are differences among reports in liquid biopsy, and that's one of the challenges. It's a great product.

One of the challenges is that there are going to be differences between different tests, but also in liquid versus tissue.

I can't speak a lot to the other labs, but we have validated our product to make sure that what we report is high sensitivity and high specificity. True negatives are something that is difficult. You cannot you cannot truly write off a biomarker finding if it is not found in liquid biopsy because there is a chance that it may not have been picked up. There's also a concern about false positives with liquid biopsies. For BostonGene, we have something that we built into our assay called “chip filtration”, which essentially helps us to filter out all of the noise. There are a lot of mutations in the blood that look like they might be a somatic mutation, but they're not. We analyze white blood cells, which helps us determine which of those are true mutations and which ones are not. But for all of those reasons, and I know that was a long-winded answer, there are differences among each assay, because they're all designed a little differently.

I hope that gives you a better idea as to why you might see different results.

Amit Gattani 43:40
How do you make decisions when you get different results? To give you a specific example: I did a liquid biopsy with two companies at the same time, one reports an mTOR of 55% allele frequency, the other one reports mTOR not detected. As a clinician or as a patient, where do you go with that data?

Michelle Lanman 44:04
You said that the blood draws were taken at the exact same time for those two tests?

Amit Gattani 44:08
Well, not the exact same time, in the same week. My body environment stayed the same, but it wasn't the exact same time.

Michelle Lanman 44:18
I asked because that is actually important. Circulating tumor DNA can change, and it does change over time. The timing of the blood draw can make a big difference in terms of the information that we are detecting. If you are having blood draws done at different points in time, we are definitely expecting to see that the results are going to vary. That's part of why we're now using this to look at disease monitoring because we know that if we see some mutations drop off then that might show response to some treatments. If you're not having them done at the exact same time, there will be a difference. My best recommendation would be going back to your oncologist to determine what information is the best to act on. Because while it reports a lot of good information, not all of it might be the most actionable or might not be the most relevant to you immediately. That would be something that would be a decision for your oncologist to make and potentially to follow back up with the liquid biopsy company for them to explain a bit more as well.

Michael Hensley 45:27
I love David Plunkett's quote in the chat: “Segal's law: A man with one watch knows what time it is. A man with two is never sure.”

“The BostonGene Tumor Portrait Report and How to Access It" (Michael Hensley and Michelle Lanman) [#72]

Dr. Subhudi warned me about you guys. I had to “phone a friend” and have Michelle join me because he told me your guys were at the top of the IQs.

Richard Anders (via the chat) 45:49
Since you're doing a lot with MD Anderson, are you looking at the outcomes that are happening based on your reports and the treatment that's occurring and creating that feedback loop?

Michael Hensley 46:11
That's one of the weaknesses in diagnostic labs.

A lot of the weaknesses with these companies is you have these archived tissue banks, and you can go and mine like 200 prostate cancer patients and find biomarkers, but many of these patients are lost to follow up with. One of our big collaborations with MD Anderson is called the “bigger study”. Some of them are very formal IRB arrangements. Some of them are more like when we find a unique report, we make a case out of it, and then our research team will reach out to the patient. They agreed to let us call the patient. We will reach out to him every three to six months to understand the patient, how they're doing on their current therapy, whatnot. Some of these patients we will test multiple times as they go through their journey.

The biggest thing, especially with their tumor microbiome profiling, is following these patients, not only short term. Some of these studies are seeing huge PSA drops to these immune-rich tumor microenvironments. That's great for a time, but how does that look six months down the road? We just started our commercial test in 2021. We're on this pursuit, but yes, we are absolutely following patients for clinical outcomes in dozens of different cancer types. Many of them are very formal as part of a biopharma partnership. Some of them are more informal, finding a unique case in a cancer where it doesn't normally happen and whatnot. We follow them together, and then we write a case report, or in essence with Dr. Subhudi, and Dutch Siddiqui. We're looking at all metastatic castrate resistant prostate cancer patients, looking at patients that have high TMB and high MSI, but they have different tumor marker environments. You're taking a homogeneous population, and making it heterogeneous now. They're treating them with immunotherapy. Now we're following them to see outcomes. Yes, in multiple ways, we are following patients.

Richard Anders 48:46
This is obviously not like an iteration of an operating system where you throw out the next revision. As you get this data, I assume you can't just throw it into your report, an anecdotal report is now sort of built into the next version of your report. But it's really useful information, particularly for patients who probably are very eager for anything that they can get that would be helpful. Do you have a way to get the case reports? Can patients see the case reports? Can the doctor see the case reports? How do you integrate it into the report? What's your strategy for that?

Michael Hensley 49:31

If there's a case report that we work with a physician on, then we will usually publish that together. One thing at BostonGene, which we talked about internally, is to develop patient cases, outcomes for external marketing purposes or just education purposes. We don't have an avenue right now for patients to look at that, besides if it's one we've published in medical journals. If there's a biomarker that either is emerging, or it now is a companion diagnostic, it's put into our report. It's extremely fast. We have teams that look like an army of ants at all the different conferences. When we come back, we mine everything from small studies to the pivotal phase three studies that are presented that are up on stage, and we adopt those into the report. In our report, we also prioritize information by level of evidence. For example, sarcoma mirrors breast cancer a lot. You'll see a lot of off label therapies in sarcoma because they have great efficacy in breast cancer for a PIK3CA mutation. You work up the prioritization of therapy recommendations based on the level of evidence, and then also on clinical outcomes. Just because we have an exciting little pilot with castrate resistant prostate cancer patients, that doesn't go into the report. This has to be published in a conference and validated. Those are exciting case studies, but they don't get adopted into the report. The report goes through a lot of clinical validation.

Richard Anders 51:43
Can you give some idea of how many diagnostics you run a month say?

Michael Hensley 51:52
I'd say, at MD Anderson alone, we're probably doing about, for all tumor types, 300 to 400 tests a month. Not nationally. I'm just not sure that we are really good allies at many of the large academic centers because they get it, and they'd like to go deep into the weeds with what we provide. But if you remember what I presented to you on our new summary page, that was our solution for our community oncologist because they don't have the time to go deep. They need to make clinical treatment decisions. Everything's up on that front page. Now we're getting an incredible amount of growth in the community. Also, as patients go, like to MD Anderson, they go back to San Diego with their report, and the San Diego oncologist is calling me, “Hey, what is this? I want this.” Then I call Rana McKay.

Richard Anders 52:58
The reason I was asking is because maybe MD Anderson is a major partner. Maybe you're doing a few thousand a month. If you start to stratify the universe into a reasonable number of markers, you're very quickly going to be into very small numbers of markers. You're not going to have any statistical significance. But nevertheless, you might have some useful data, but it's not a discussion to get lost in the weeds about. I just was curious if there are ways to take that information and let patients get access to it, because I think some of it would be, at least anecdotally, very interesting to them.

Michelle Lanman 53:37
We get about 400 tests a month right now. 400 to 450 is what we're receiving at BostonGene overall. That includes MD Anderson, but that is across the nation.

Michael Hensley 53:54
We have a huge biomarker database that we use. It is not based on only BostonGene samples tested.

Michelle Lanman 54:08
We have built a lot of our own internal databases. We have a biomarker database, clinical trial database, and treatment database. We have those built internally, where they are constantly scouring the literature and information out there. That way any new FDA-approved therapies, any new biomarker discoveries are fed into our databases. We also have AI learning that is built into them as well. To what you were saying, Richard, as we continue to aggregate the data from the patients, we are building up those internal cohorts and our databases. As we are building those out, we are learning more information from the patients we're testing and then using that to make smarter decisions and help with the biomarker selection, the treatment selection. We definitely do use that data. In terms of case reports, though, we haven't made those publicly available yet. But I know that we've discussed that with our marketing team. We want to be able to share that. We have a couple of patient stories on our website. We want to share more stories about how we've been able to help patients, what the findings were, how those were helpful. That is something that we want to do more of in the future.

Robert Gurmankin 55:32
You talked about doing multiple tests in the tumor microenvironment. In doing testing over time, have you seen a tumor microenvironment in the primary tumor that is very positive?

When you test, say, in bone, or somewhere else, that the tumor microenvironment is going fibrotic, what changes? Have you seen any determinations as to what happens with that over time?

Michael Hensley 56:11
The bone tumor microenvironment is always going to be different from soft tissue. There are complexities of bone and being decalcified in a non-acidic solution. Being able to pull DNA and RNA is very difficult.

When you talk about the tumor microenvironment changing between treatments, whether it's cytotoxic, chemotherapy versus immunotherapy, even among the experts like Dr. Subhudi, the jury's still out on this. It's mostly anecdotal case examples, but we do see it because we do our tumor evolution report a lot. It really depends. We see drastically different changes in key biomarkers as well as the tumor microenvironment.

I don't know how to answer the question of what can cause hot to cold, or cold to hot. There are no absolutes. It is a high area of interest. We have a project in bladder cancer and mesothelioma because we're trying to understand that more. We want to turn it off. How do we do that? That's an area of research discussion.

“The BostonGene Tumor Portrait Report and How to Access It" (Michael Hensley and Michelle Lanman) [#72]

I've enjoyed every minute of visiting with all of you. I love the website. I've been looking through the forums and past presentations. What you're doing is remarkable. I'm very excited that you're moving to other solid tumor types. I've definitely celebrated you and your mission within BostonGene, and we would love to collaborate further with you. I'm thankful for the future opportunities as well.