**“Testing Your RNA with Liquid Biopsies” (Alex Rolland)** [#116]

Brad Power
October 16, 2024

*“You may have heard about the exciting new world of exosomes. Exosomes are membrane-bound vesicles (small sacs filled with fluid). They're excreted by cells, and all cells use them to communicate. More importantly, they're used by cancer cells. Cancer cells will spread their mutations and their altered DNA and their transcribed RNA and all of their different molecular mechanisms are found in cancer-causing exosomes.”* – Alex Rolland

*“It's really important to use as many different tests as possible. Education is power. Knowledge is power. The more different platforms we have to look at, the better. Each one of these platforms is slightly different.”* – Alex Rolland

**Meeting Summary**

Time pressures and money constraints can cause you and your medical team to miss out on the latest advancements in new, effective diagnostic tests. For example, the use of RNA testing is increasingly being considered as a useful diagnostic test (beyond scans and DNA testing). Scans (ultrasounds, X-rays, MRIs, and CT scans) can only spot tumors that are larger than 0.8 cm. Sometimes these scans find areas that seem "suspicious" or "high risk," but they can’t tell for sure if they are cancer tumors. In these cases, doctors often use a “watch and wait” approach, tracking whether the area grows. But focusing only on the size and density of the tumor can mean missing early chances to detect and treat cancer.

Alex Rolland, Chief Research Director and co-founder of Cancer Treatment Options and Management is uniquely qualified to talk about a new test that offers additional capabilities: RNA testing using liquid biopsies. He is passionate about ensuring that anyone who receives a cancer diagnosis has access to the most effective and least invasive forms of testing and treatment possible. Alex holds a BSc in Molecular/Cell Biology from the University of Victoria, and studied Medical Genetics at the Terry Fox Laboratory in Vancouver (BC Cancer Agency). With over a decade of experience researching, consulting, and advocating for cancer patients, Alex also works directly with the medical system to explore the newest optimal treatments for his clients. He’s an expert in discovering how to optimize your cancer treatment, and making this a reality for you.

***Why might you want to learn about liquid biopsies that look at RNA in exosomes?***

Ideally cancer can be detected early, before it forms a visible tumor.

Liquid biopsy (blood or other liquid) tests that look at tumor exosomes (small, membrane-bound sacs filled with fluid) can find cancer activity early, leading to faster detection and better treatment outcomes. An exosome is a tiny bubble-like structure that cells release. These bubbles carry various molecules, such as proteins, DNA, and RNA, from one cell to another. Exosomes play an important role in cell communication and can be found in body fluids like

blood, urine, and saliva. Scientists can use exosomes to study what's happening inside the body without needing a traditional tissue biopsy.

Exosomes are produced by the cancer cell as soon as it is transformed. The process of metastasis starts well before a tumor is even detectable. By the time a tumor is 1 cm, it has a billion cells, and there are tumor cells all over the body.

When cancers are detected at an early stage, you have fewer different kinds of cancer cells (“heterogeneity”), and they will not have spread as widely throughout your body. Your test should also ideally identify your specific molecular drivers in real time and understand how your genes are being turned on and off (“epigenetic regulation”).

***What are the benefits of exosome-based liquid biopsies?***

- Detect if there is cancer activity happening before there's a visible tumor.
- Detect if you are responding to therapy in real time.
- Determine what RNA molecules are highly overexpressed that are involved in driving the cancer at that given moment (possibly pointing to a targeted therapy).
- Determine drug response very quickly – by seeing if there are a lot of exosomes or not.
- Detect “pseudo-progression” – if you are on an immunotherapy, the immune cells can enter your tumor and make your tumor look bigger, but they're actually eating them from the inside out. It’s hard to detect with imaging, but there will be a low amount of exosomes in the body if you are responding to immunotherapy.
- Detect emerging treatment resistance over expressed oncogenes for targeted therapies.

***How does this liquid biopsy exosome test differ from other liquid biopsy tests?***

Most liquid biopsy tests use circulating tumor DNA. They are designed for detecting emerging DNA mutations. They're not designed for detecting the level of the actual mutation in the blood, because they are not looking at the exosomes. The exosomes are a cancer-specific mechanism, and by isolating the exosomes, you're looking at exactly what the cancer is doing, and you're getting the relative amount of that mutation in the blood.

Some other companies are looking at genes expressed through RNA. Some of them are doing it from exosomes. But the problem is the panel that they're using is designed for detecting mutations, and it's not accurate for detecting expression.

RNA gets degraded significantly once you take it out of the body. Therefore, you can't always tell what was actually produced by the tumor there if you're not looking specifically at the exosomes and looking at a gene panel or an expression panel designed specifically for expression.

***Is this exosome test a good fit for you?***

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Exosomes are only typically released in high numbers if your cancer is metastatic. If you are responding to therapy, or are in remission, you won't see a lot of these exosomes.

***How can you get these exosome tests?***

You can order this test yourself. (You don't need a doctor to order this for you.) The cost is about $1500.

There are a couple of websites for access:

- The Cancer Treatment Options and Management site offers a research and analysis team and a patient navigation program. It includes experts like Alex who analyze the test data and make sure it's utilized to your best advantage. There are navigators who help with access. They coach you on the language to use with your oncologist to get better uptake, and on the back end with all the programs and the paperwork.
- At Liquid Biopsy Labs you can order the specific test, if you don’t want the other services.

***How can you learn more about RNA testing and other key elements of personalized treatment?***

- Book a one-on-one cancer care consultation on testing and treatment options
- Join the free precision cancer medicine education and advocacy program: “Cancer – Just The Facts” with video lessons, downloadable .pdfs and live question and answer video sessions
- Join the Facebook community Cancer Treatment Options and Management
- Visit Alex’s YouTube channel, “The Cancer Guy”; subscribe to stay informed (new videos every week)
- Review sample reports of the liquid biopsy test
- Review formal research on the liquid biopsy test once the commercialization process is complete
- Contact Alex at contact@ctoam.com

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**Meeting Notes**

## KEYWORDS

liquid RNA, cancer diagnosis, exosomes detection, precision oncology, tumor suppressors, oncogenes, epigenetic regulation, molecular drivers, pseudoprogression, hyper progression, liquid biopsies, RNA expression, tumor cells, pathology reports, direct-to-consumer

## SPEAKERS

Alex Rolland (63%), Brad Power (18%), Michelle Morand (15%), Brian McCloskey (4%)

## CHAT

Allen Morris, Stratis Telloglou, Roger Royse, Ari Akerstein, Rick Davis, Ryan Ramanujam, Jane Wilkinson, Brian McCloskey, Chris Apfel, Eric Dishman

## SUMMARY

Alex Rolland discussed the potential of liquid RNA as a diagnostic tool for cancer, emphasizing its role in detecting early-stage cancer and real-time molecular drivers. He explained the mechanisms of “oncogenes”, “tumor suppressors”, and “transcribed RNA”, and highlighted the benefits of exosome-based liquid biopsies, including rapid drug response detection and identifying pseudo-progression. He noted the limitations of current tests, such as circulating tumor DNA (ctDNA) and RNA panels, which often lack specificity and accuracy. He also discussed the importance of pathology and the use of laser capture microdissection to isolate tumor cells for precise analysis. The test costs $1,500 and is available directly to consumers.

## OUTLINE

### Introductions

- Alex Rolland was recommended to the Cancer Patient Lab by Roger Royse, who found Alex's advice helpful in his cancer journey.
- Alex introduced his partner, Michelle Morand, who is the operational leader in their company, Cancer Treatment Options and Management.

### Cancer Basics and Personalizing Cancer Care

- Alex introduced the basic mechanisms of cancer and the importance of targeting these mechanisms in personalized cancer care.
- “Oncogenes” (a mutated gene that can cause cancer by causing cells to grow and divide uncontrollably), “tumor suppressors” (also known as anti-oncogenes, genes that regulate cell growth and division to prevent cancer; when they are mutated, they can no longer control cell growth, which can lead to cancer.), and “transcribed RNA” (or the RNA transcript, the RNA strand produced when a gene is copied from DNA into RNA) have roles in cancer development.

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- There are many challenges in cancer detection, including late-stage detection and identifying molecular drivers in real-time.
- “Epigenetics” describes how genes turn on and off to create different cell types. Environmental and behavioral factors can impact how genes function without changing the DNA sequence. Epigenetic changes can be reversible and can be passed on from one generation to the next.
- Epigenetic changes can lead to cancer and the potential of detecting cancer at an early stage through epigenetic analysis.
- Ideally cancer can be detected before it forms a visible tumor.

## Exosomes and Liquid Biopsies

- Exosomes are small, membrane-bound sacs with fluids (vesicles) that are released from cells and carry proteins, lipids, nucleic acids, and metabolites.
- Exosomes have a role in cancer cell communication and the spread of cancer.
- Exosomes can convert normal cells into tumor cells.
- Exosomes offer the potential to detect real-time molecular drivers in cancer.
- The benefits of exosome-based liquid biopsies include determining drug response quickly and detecting pseudoprogression in immunotherapy.
- Exosomes can be isolated from blood and analyze the RNA inside for diagnostic purposes.

## Development and Validation of the Test

- Their panel was developed in collaboration with Norgen Biotek to isolate cancer-specific exosomes from blood.
- The process of isolating RNA from these exosomes and analyzing it uses a panel of nearly 21,000 genes.
- A healthy tissue database was created for comparison and the use of statistics (Stat-1 and Stat-2) to assess RNA expression.
- The diagnostic and predictive capabilities of the test uniquely enable detecting cancer activity before a visible tumor and real-time response to therapy.

## Challenges and Limitations

- Exosome-based liquid biopsies have limitations, such as the need for high exosome numbers in metastatic patients.
- Verifying cancer activity before a visible tumor is difficult; test results must be compared with clinical data to validate the test.
- There is an ongoing collaboration with an AI group to detect specific signals and identify unique molecular features of certain cancers.
- An example was a test run with breast cancer, demonstrating the test's ability to differentiate between breast and lung cancer.

## Q&A: Diagnostic Challenges and Market Positioning

- Brad Power asked about the challenges of getting a diagnostic tool to market and the regulatory pathway in Canada.
- Alex and Michelle Morand explained their approach of heavily stratifying patients and using extensive tumor DNA sequencing and RNA expression testing.

- They discussed the importance of working with public healthcare oncologists and using a CLIA CAP-approved lab in the US for validation and commercialization.
- Alex and Michelle emphasized the unique aspects of their test, including the use of exosomes and a specialized RNA expression panel.

## Q&A: Prostate Cancer and Interpreting Results

- Brian McCloskey asks about the sensitivity threshold for prostate cancer and the interpretation of results into treatment options.
- Alex explained the limitations of PSA monitoring and the importance of using CtDNA and PSMA from PET scans.
- He discussed the test's ability to detect neuroendocrine differentiation in prostate cancer and the importance of using multiple approaches for diagnosis.
- Alex and Michelle highlighted the test's role in validating tumor DNA sequencing results and providing actionable insights for treatment.

## Q&A: Business Model and Scaling

- Brad Power and participants in the chat asked about the business model, reimbursement pathway, and scaling the test.
- Michelle Morand outlined the four steps for scaling the test: equipment, training, analysis, and delivery of results.
- She emphasized the importance of direct-to-consumer tests and the preparation for scaling, including a partner lab in Orlando.
- Alex and Michelle discussed the distinction between thorough RNA testing and fusion gene testing, highlighting the unique aspects of their test.

## Q&A: Pathologist Collaboration and Final Thoughts

- Brad Power asked about the collaboration with pathologists and the process of working with biopsy samples.
- Alex explained the use of laser dissection to isolate tumor cells and the importance of working with highly purified samples.
- Michelle Morand adds that their lab uses a 550-gene DNA panel and a 21,000 RNA panel, with samples sent to a specialty pathology lab for laser dissection.
- Alex and Michelle provided final thoughts on the importance of accurate RNA testing and the potential for future publications and commercialization.

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## TRANSCRIPT

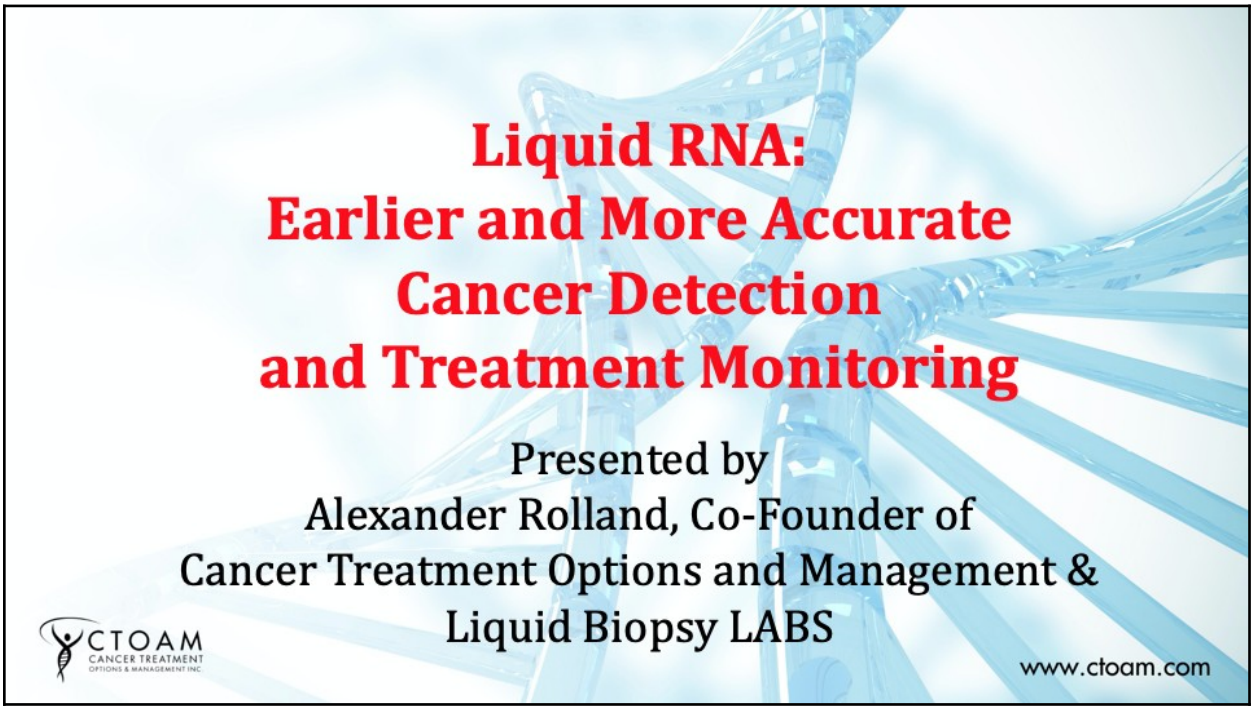
Brad Power
This is the Cancer Patient Lab.

We are honored to have Alex Rolland with us. He’s beaming to us from a hotel somewhere in British Columbia. He's going to talk to us today about liquid RNA and some of the things he's been seeing and its use as a potential diagnostic tool for us.

This is for information purposes only. This is not medical advice. We try to arm our patients and caregivers with information they can take to their medical team, giving them ideas that might help in navigating their care.

We are a nonprofit, and welcome all donations, which you can do by going to cancerpatientlab.org, and finding the donate button.

Roger Royce introduced us, even though maybe Alex doesn't remember him. Roger, early in his journey, was looking for resources to help him, and found Alex and got some advice from him and recommended that we learn from Alex today.




Alex Rolland 2:05
Thank you very much for having me today. I'm very excited to share some of our latest data and latest research. Today I'm going to talk about using liquid RNA. “Liquid” means blood, but really, “liquid” can be any sort of fluid.

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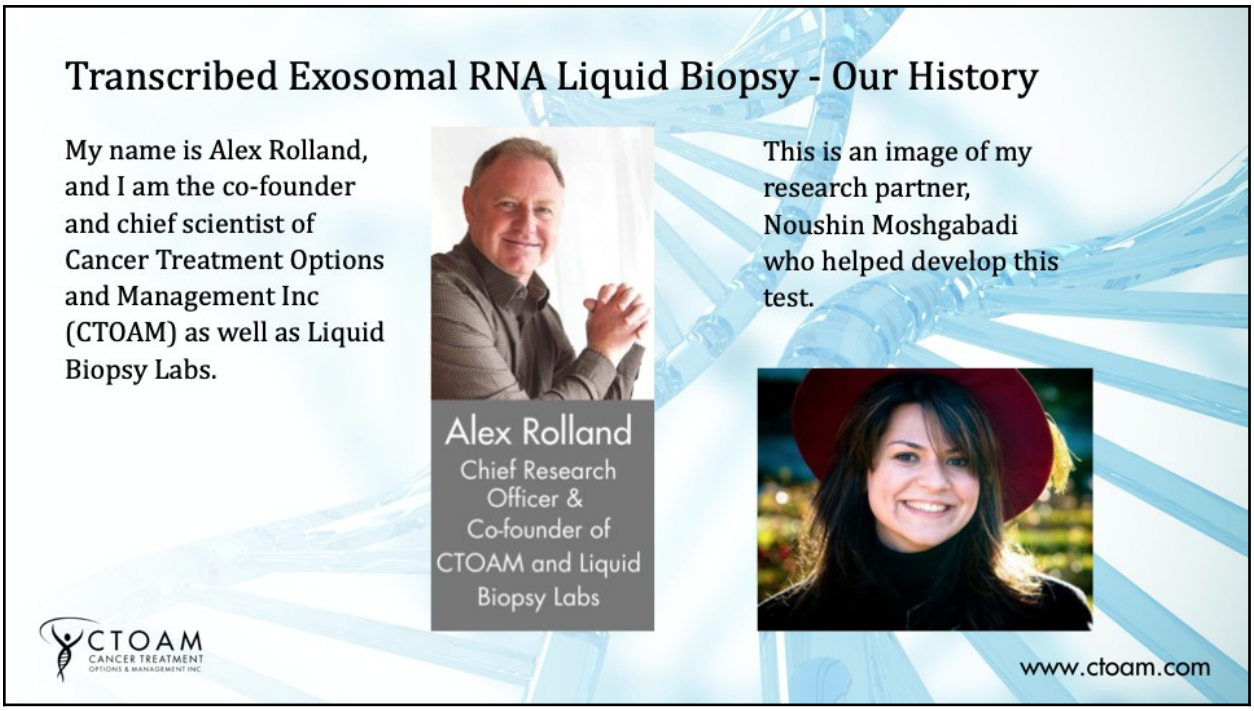
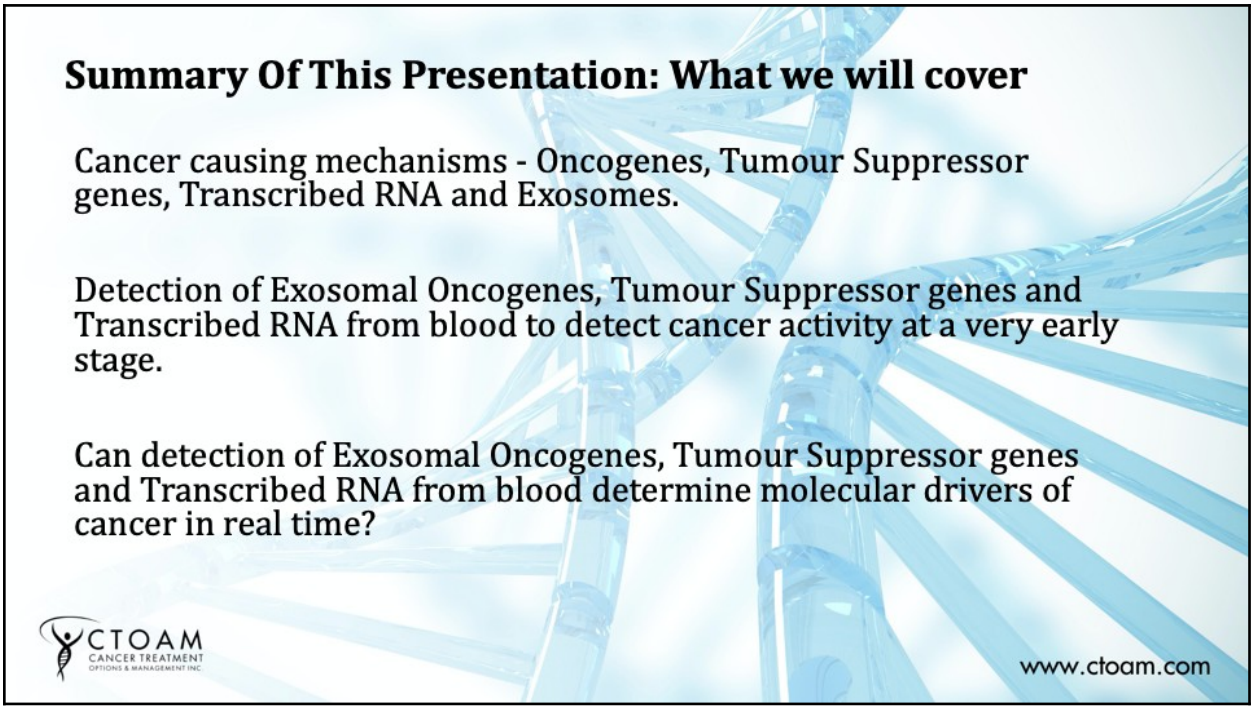



This is my partner, Noushin Moshgabadi, on the bottom right. She can't attend today, but she's been active in our company from day one, as well as helping me develop everything.




A quick summary. What I'd like to start out talking about is some of the basic mechanisms of cancer, and really how targeting the mechanisms of cancer is really the base point of precision oncology. We'd like to talk about first some oncogenes, tumor suppressors, what transcribed

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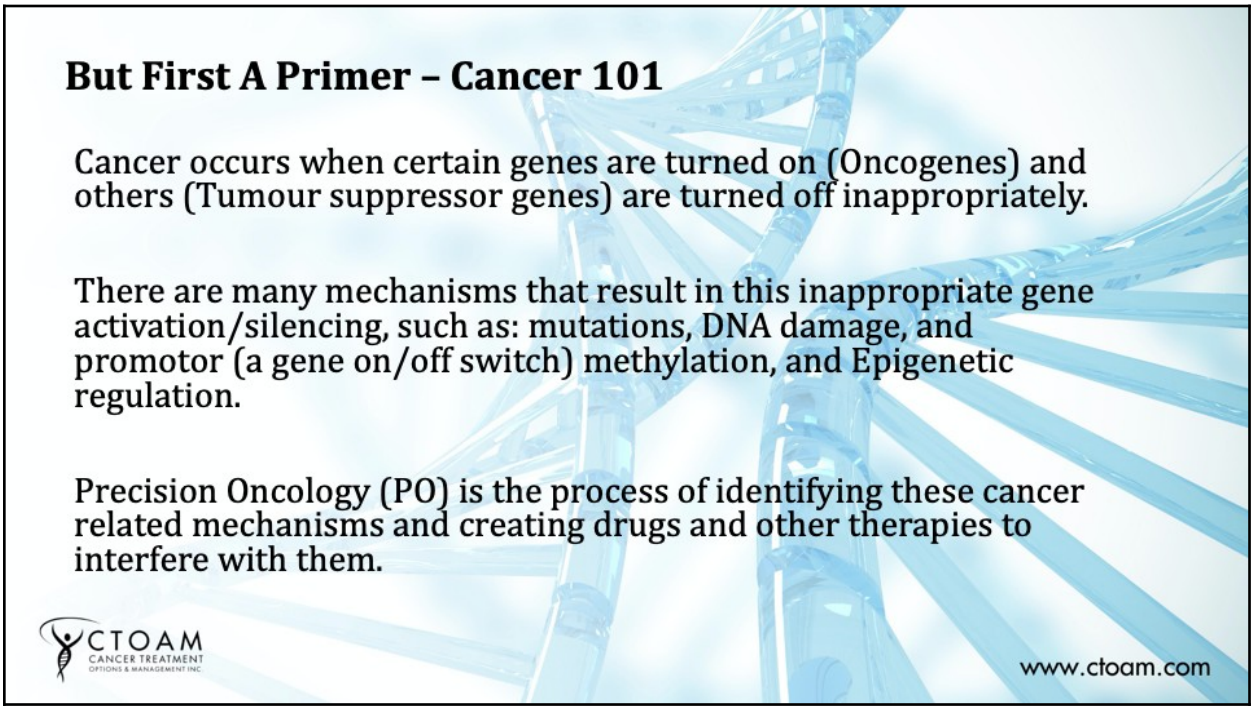
RNA is, and exosomes, and then also the detection of exosomes, oncogenic exosomes, specifically, and how all of these elements can be found inside of exosomes. Then using exosomes as detectors of real-time molecular drivers in cancer.




A bit of a primer. As everyone knows, cancer occurs when certain genes are turned on inappropriately and tumor suppressor genes are turned off. There are also many different mechanisms involved in this inappropriate gene activation and silencing, such as DNA mutations that cause a gene to stay stuck on or prevent it from working properly; promoter methylation, which is really the turning off and on of a gene, and then epigenetic regulation.

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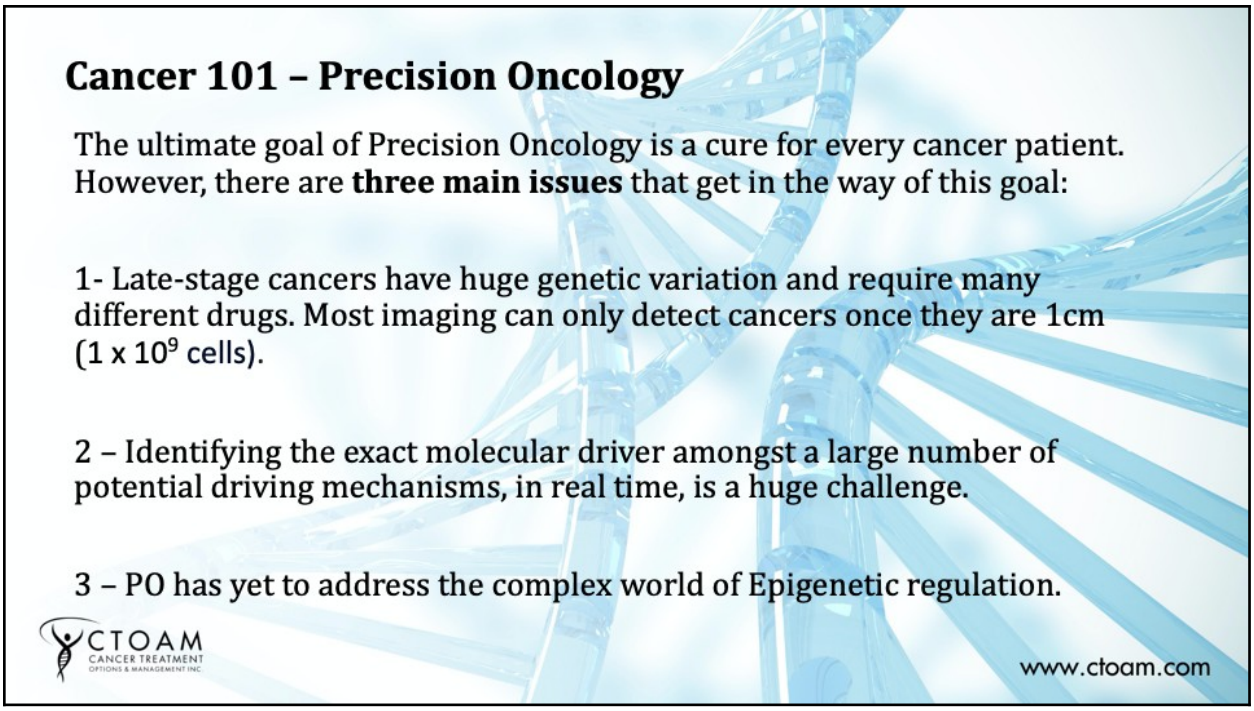
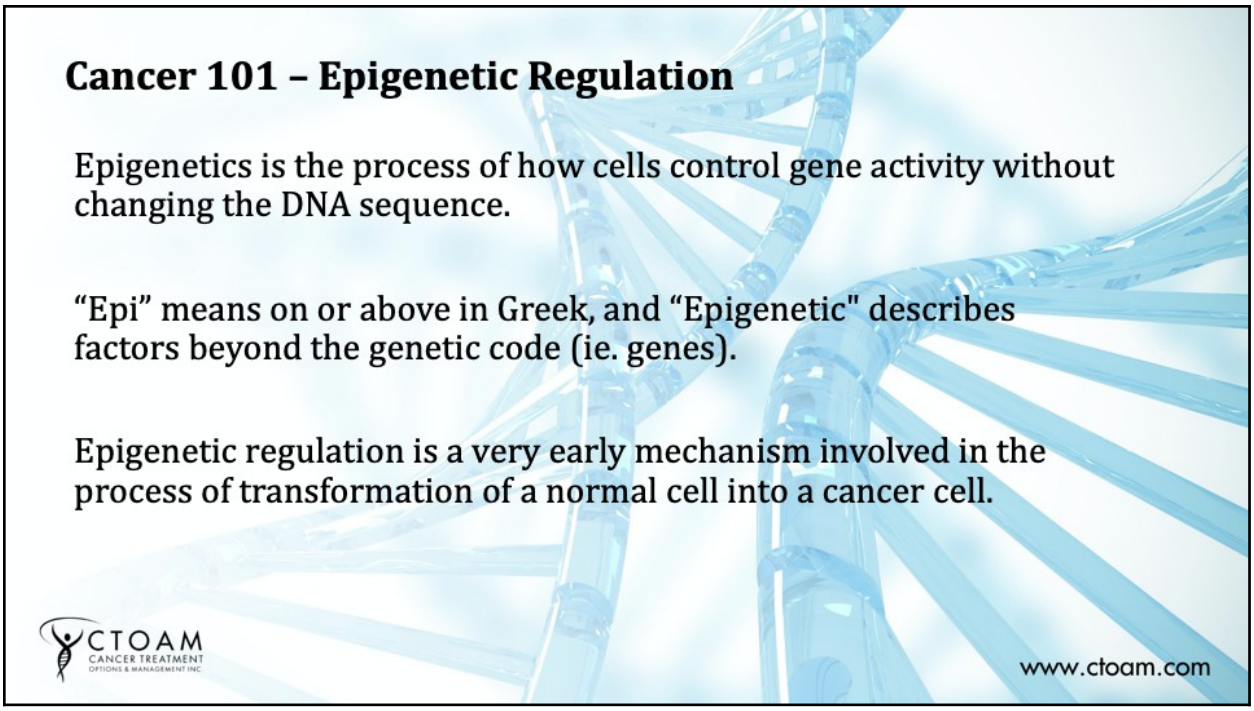



Precision oncology is a process of identifying what those mechanisms are and designing a drug for them specifically. The ultimate goal, obviously, for everyone is a cure.

But the three main issues that are getting in our way right now is that most cancers are detected at a late stage. And believe it or not, when you detect a cancer at even one centimeter size of a tumor, you have a lot of cells there. I put a little quote there, one by 10 by the power of nine. It's a lot of different cells, and they could probably spread throughout the body. Now we know that it's the stem cells that typically are the ones that can metastasize, and they're at a much lower number, but even having a one centimeter tumor means that there's probably some disseminated cancer cells throughout the body.

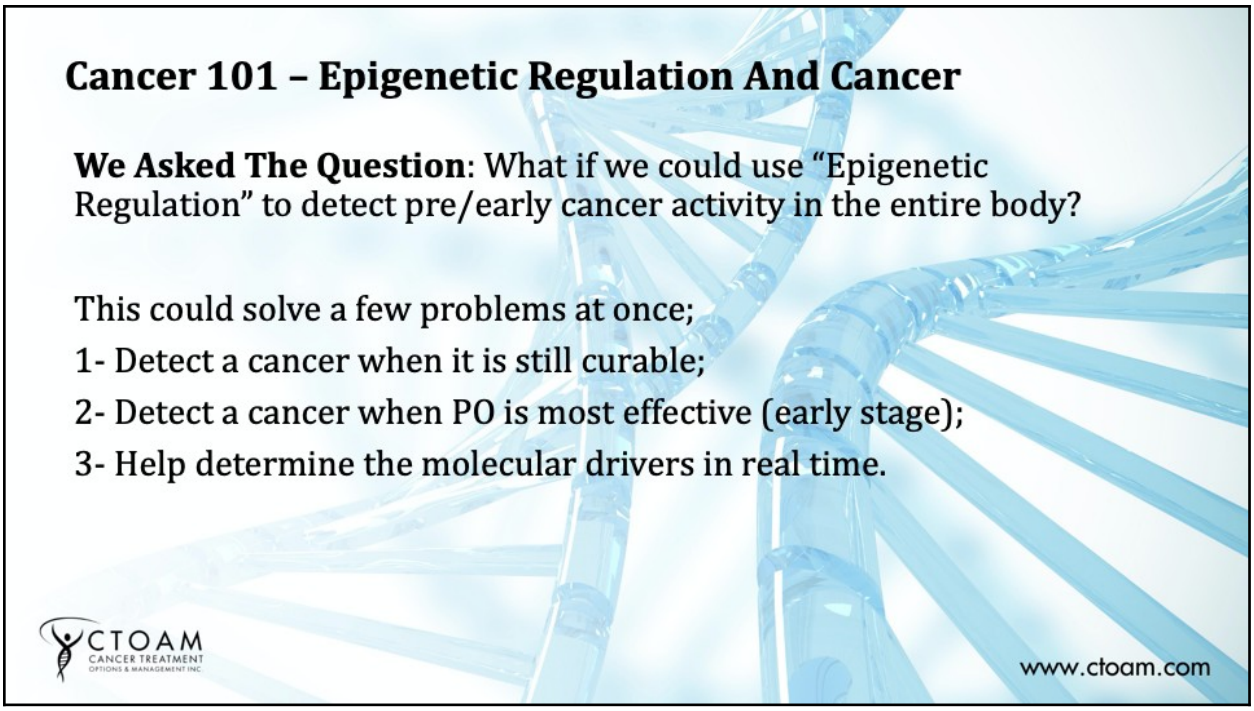
The other thing is identifying the exact molecular driver amongst a large number of potential drivers in real time. And when I say real time, I mean, what's going on today? What molecular features are the tumors using to drive the cancer today?

And then, of course, this ever changing and exciting world of epigenetic regulation.



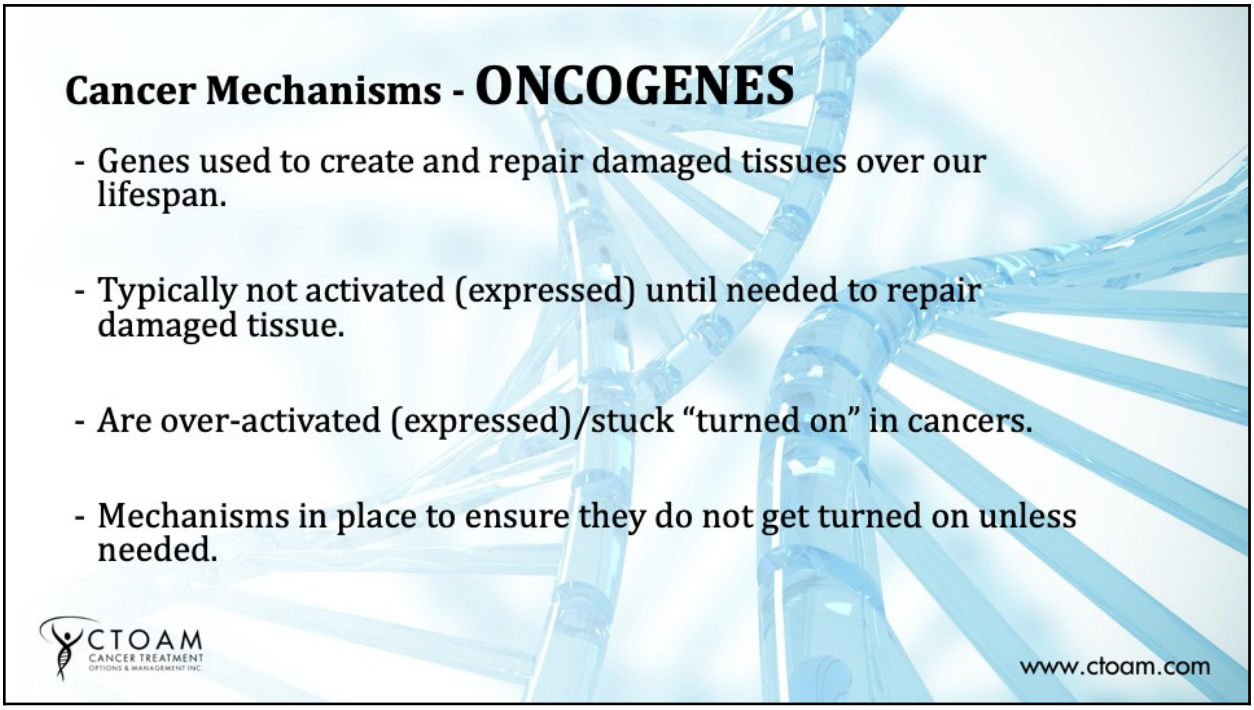

Epigenetics is the process of turning on many genes and turning off many genes. It's basically how our bodies use the same DNA. In our cells, we have literally the same DNA, the same genome, except we have an abundance of different types of cells and tissues. The way our bodies do that is through “epigenetics”. In other words, they turn certain genes on and certain genes off to create muscle tissue, and then certain genes on and certain genes off to create bone tissue. It's the turning off and on through epigenetics that really defines what a cell does.

Importantly, epigenetics is one of the first things that turn on and off certain genes in the development of transformation of a normal cell into a cancerous cell. That's called transformation.

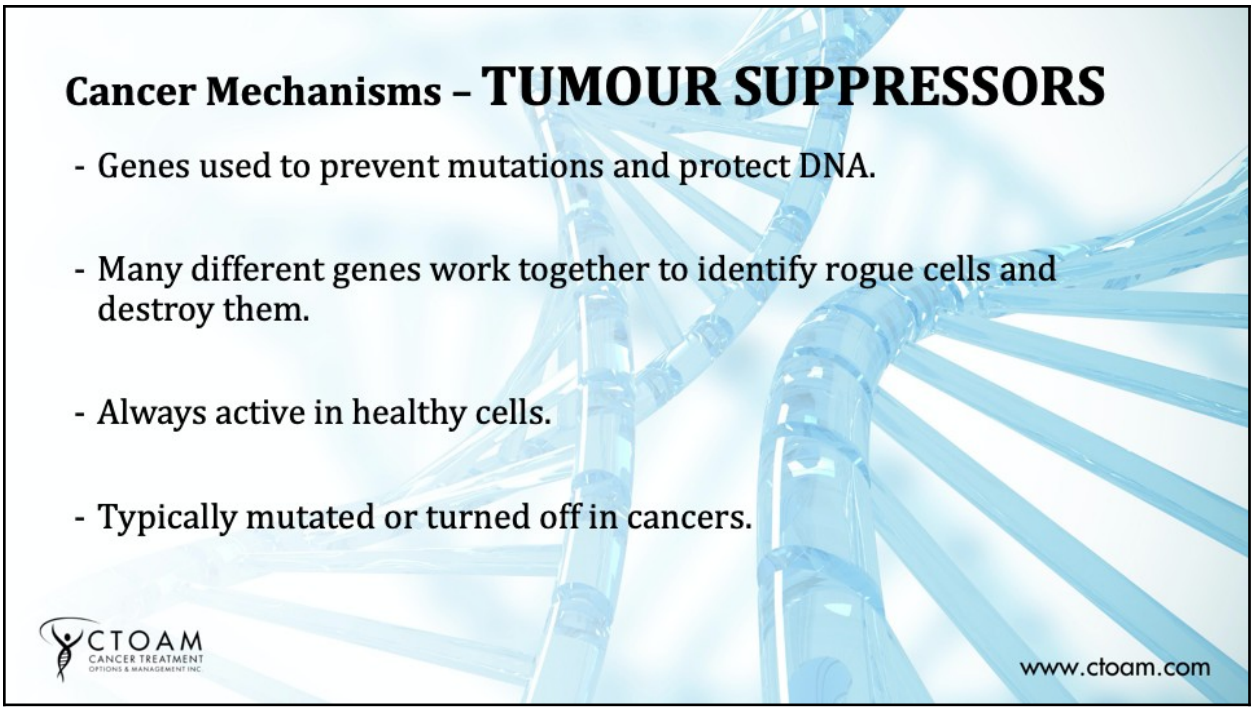



If we could discover how to detect epigenetics properly, then we could solve a lot of problems. We could detect cancer at a very early stage before it forms a visible tumor. We could detect cancer when precision oncology is most effective because there's a lack of heterogeneity. In other words, the cancer hasn't broken off into subpopulations. We could help determine molecular drivers in real time.

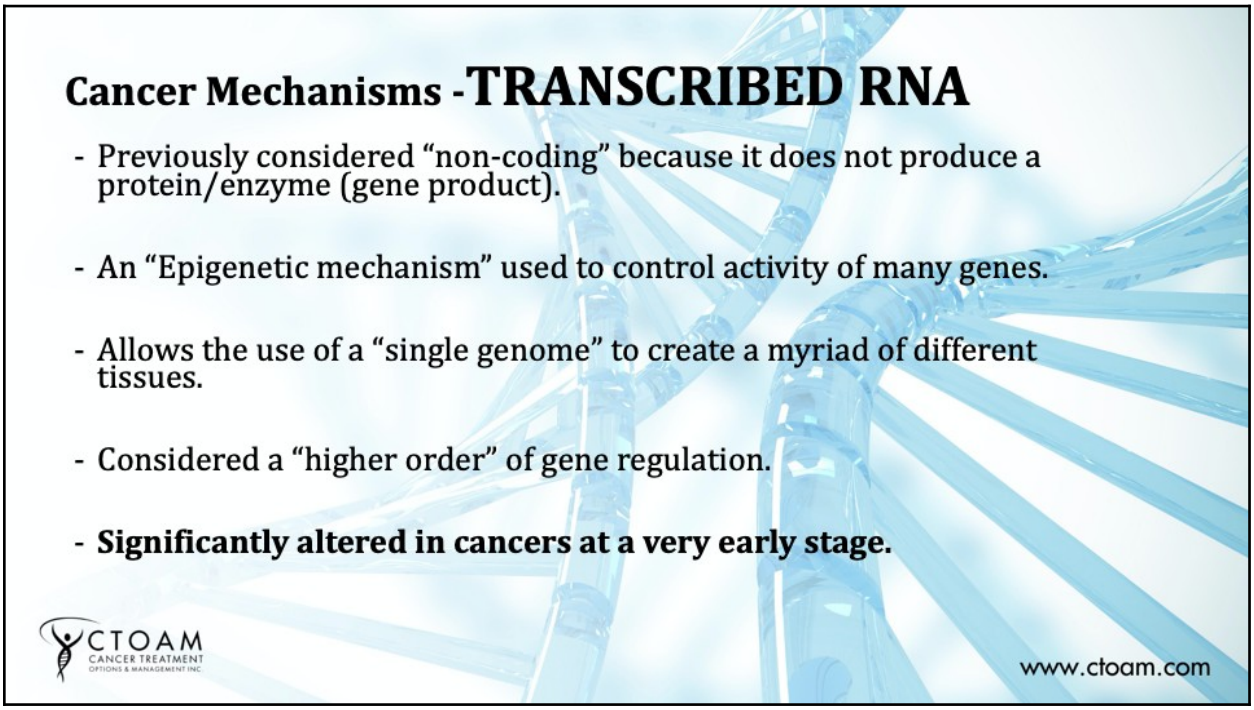
This is a really exciting approach to dealing with cancers.


You may know what oncogenes are. They're typically turned on inappropriately. They're part of the wound repair process that gets turned on to replace damaged tissue, but it gets stuck.

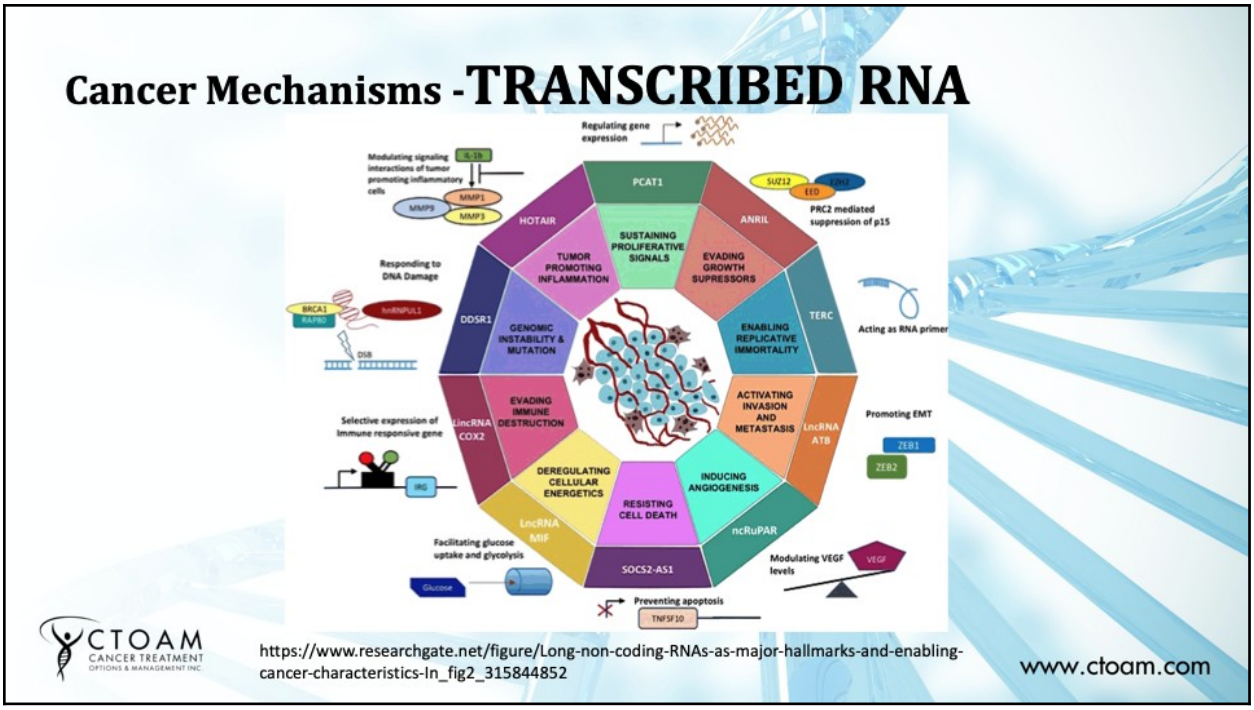



Tumor suppressors detect DNA mutations and fix DNA alterations so they don't develop into mutations. They're always turned on. They're always working 24 hours a day. They're very vigilant, and they typically get turned off and damaged during cancer.




Transcribed RNA is an exciting thing. Only a small part of our genome encodes for proteins. I think it's between 5 and 3%. It changes all the time, but the rest of it was considered “junk

DNA”. What was interesting about this so-called “junk DNA" is that it's all transcribed. In other words, it's all turned into RNA, but we didn't know what it was doing. We found that this “transcribed RNA” is a new way of regulating gene control. It's one of the most common early mechanisms in cancer. All cancers have epigenetic alterations, but it is really something that we need to be addressing in precision oncology.




Here are some of the mechanisms of transcribed RNA involved in cancer. As you can see, there are many different mechanisms. These are just examples. “LNC” means long, non-coding RNA. They're not even genes. They're just pieces of DNA that get turned into RNA, and this RNA floats around in the cell and has a variety of different mechanisms and functions.

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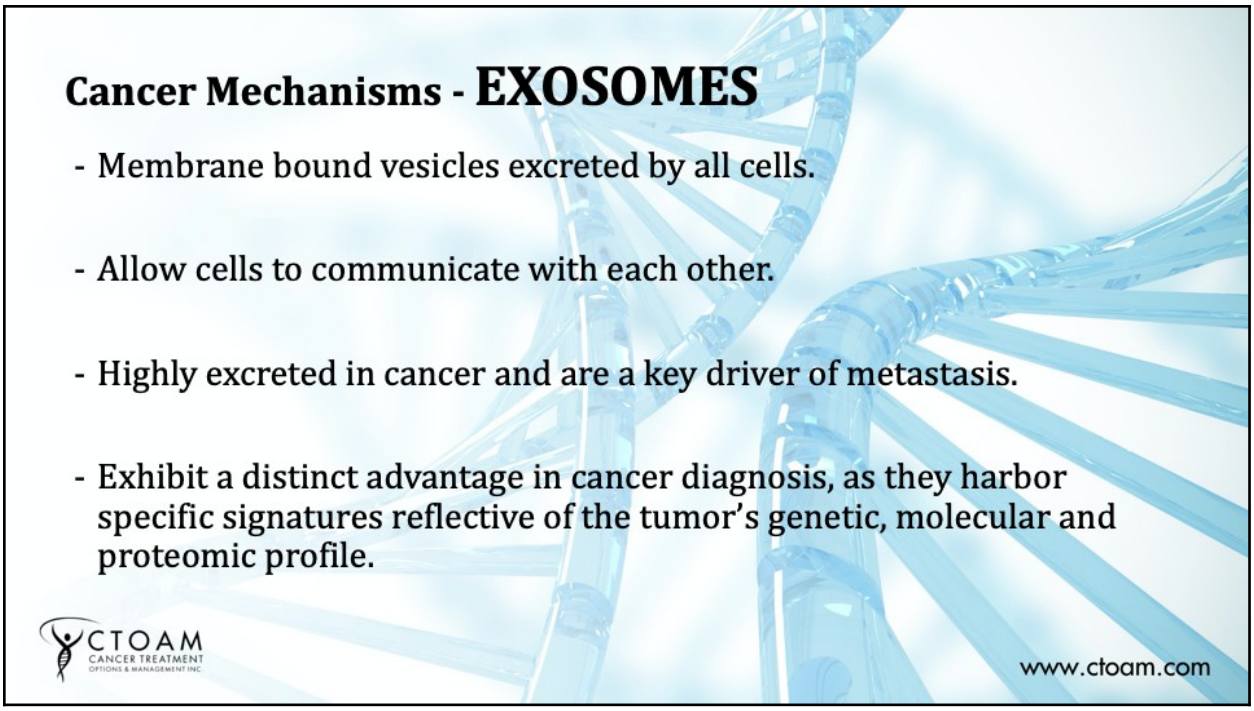


You may have heard about the exciting new world of exosomes. Exosomes are membrane-bound vesicles (small sacs filled with fluid). They're excreted by cells, and all cells use them to communicate. More importantly, they're used by cancer cells. Cancer cells will spread their mutations and their altered DNA and their transcribed RNA and all of their different molecular mechanisms are found in cancer-causing exosomes. We believe that these exosomes can convert normal cells into tumor cells. This is typically what we see when a person is having metastatic cancer. We'll see that their cancer is excreting these exosomes. We can capture these exosomes now and look at them and see what they are excreting in order to determine what the molecular drivers are of the cancer.

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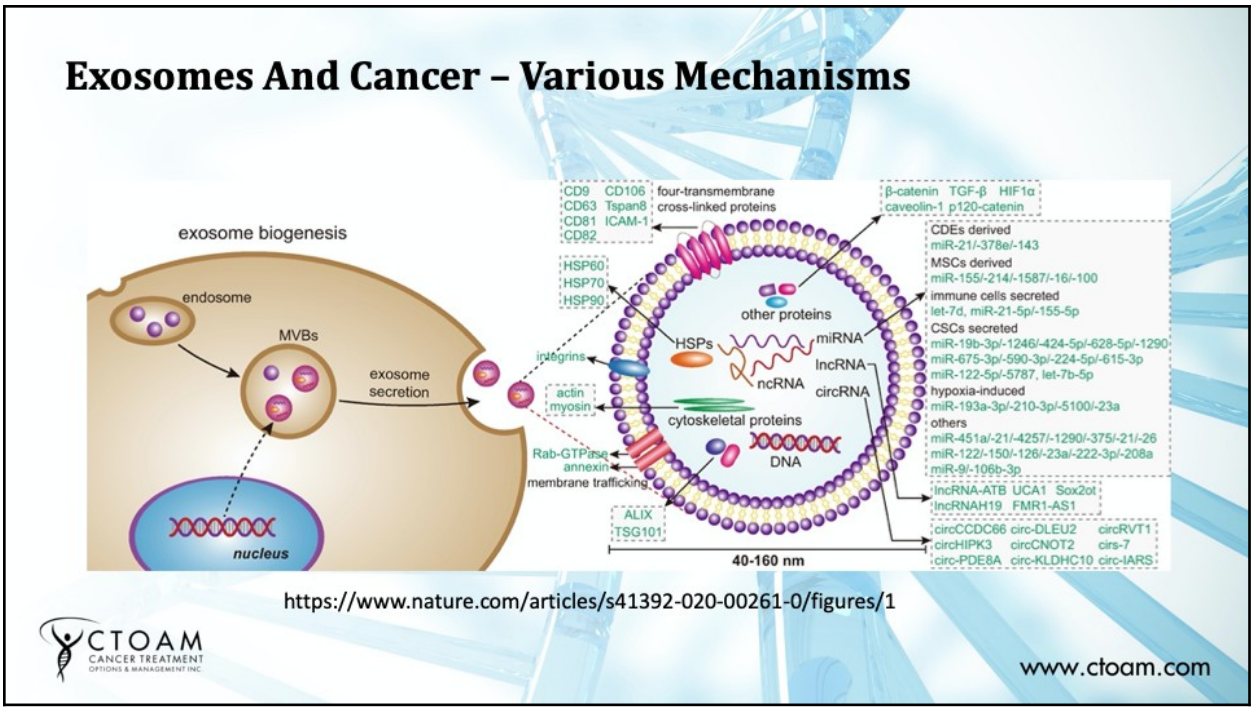
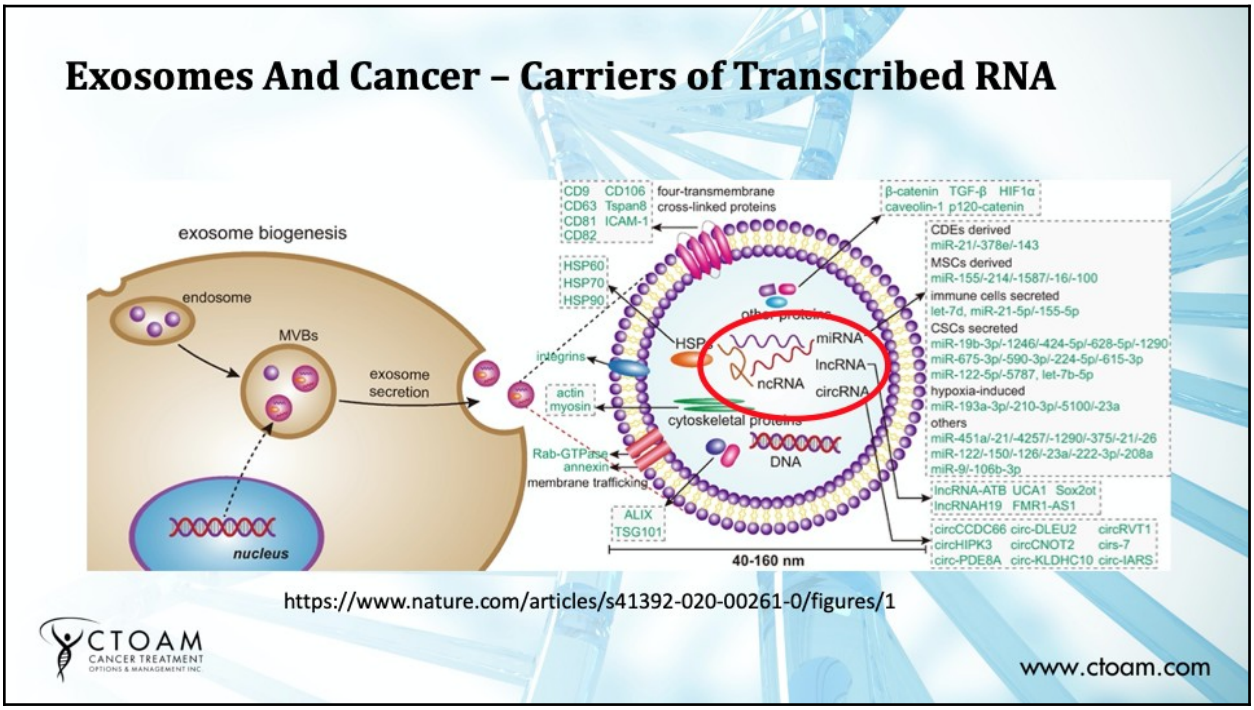



This is a brief overview of exosomes. They contain many different things. They contain proteins. They contain circulating DNA. It contains a variety of different molecular driving mechanisms. They contain non-coding RNA.




We're going to be focusing on transcribed non-coding RNA.

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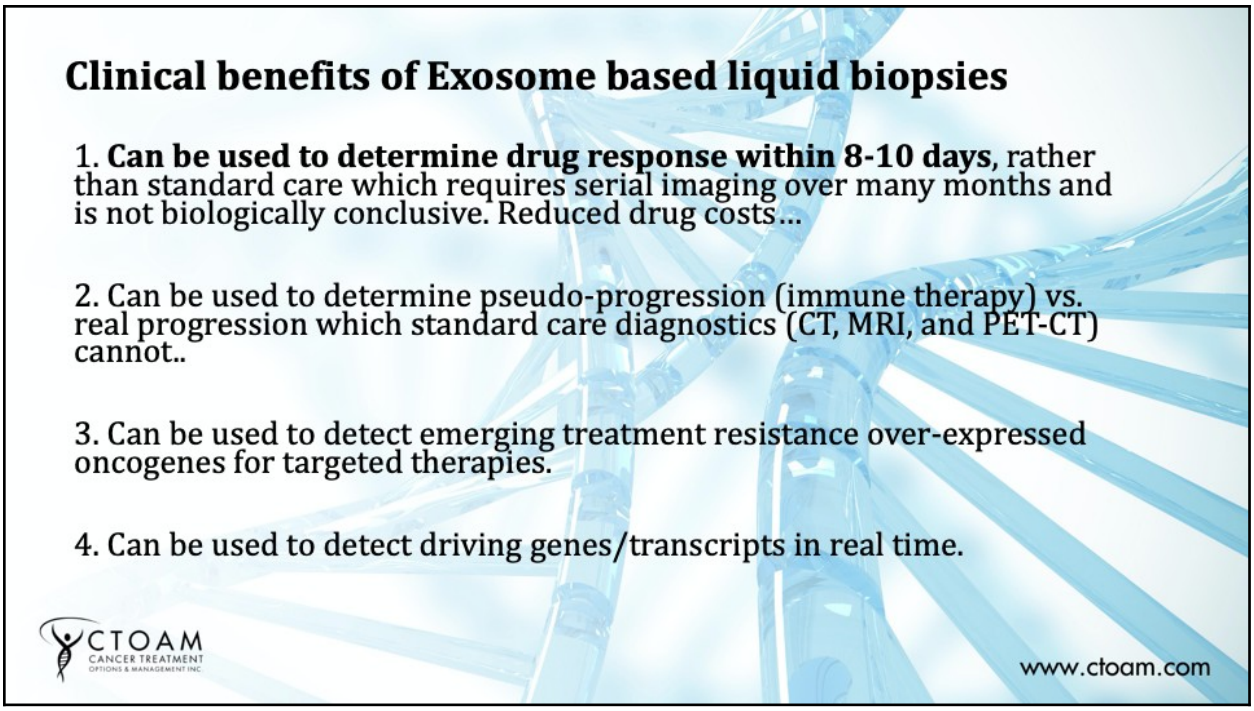


A summary on the benefits of exosome-based liquid biopsies:

1. They can be used to determine drug response very quickly. Instead of having to go through a process of having to wait months and months to see if a tumor is grown or not, you can determine very quickly with exosomes, just by seeing if there are a lot of them or not.
2. They can also be used to detect “pseudo-progression”. When somebody is on an immunotherapy, one of the common problems is something called pseudo-progression, where the immune cells enter the tumor, and they make the tumors look bigger, but they're actually eating them from the inside out. Pseudo-progression is a form of response that often doesn't get recognized as such, and it's very hard to detect. In fact, I'm not sure any imaging can do that. PET CT is not able to detect that. These exosome-based liquid biopsies are very good at detecting that, because there'll be a low amount of exosomes in the body if a person is responding to immunotherapy.
3. They can also be used to detect emerging treatment resistance over expressed oncogenes for targeted therapies.
4. These exosomes contain all of the genes that are currently being used in the metastatic process, and importantly, they can be used to detect things in real time.

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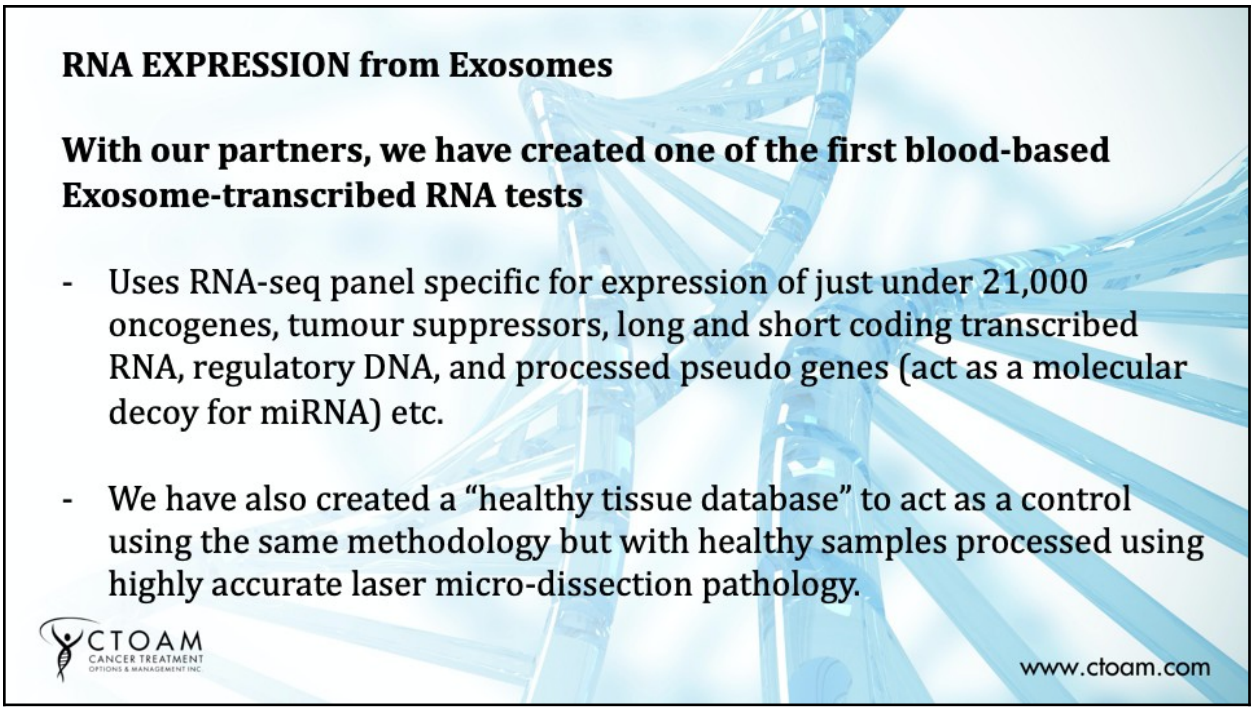


We've developed a panel where we've worked with another company called Norgen Biotek. They've helped us isolate exosomes from blood cancer-specific exosomes. It is a series of filtration processes that identify these cancer-specific exosomes. We isolate the RNA from these exosomes, and we use a panel of just under 21,000 genes. This panel is a very special panel. It's designed for RNA expression. It's not designed for detecting mutations, like a lot of the RNA panels are. This one is just designed for counting the amount of RNA molecules of a specific gene. It does that in a reads per million basis.

We've also created a “healthy tissue database” of probably close to 40 tissues that we then compare the expression of the tumor RNA that we get from blood, and we compare that to this database of different tissues to find out what their normal levels are.

We use the same methodology for this.

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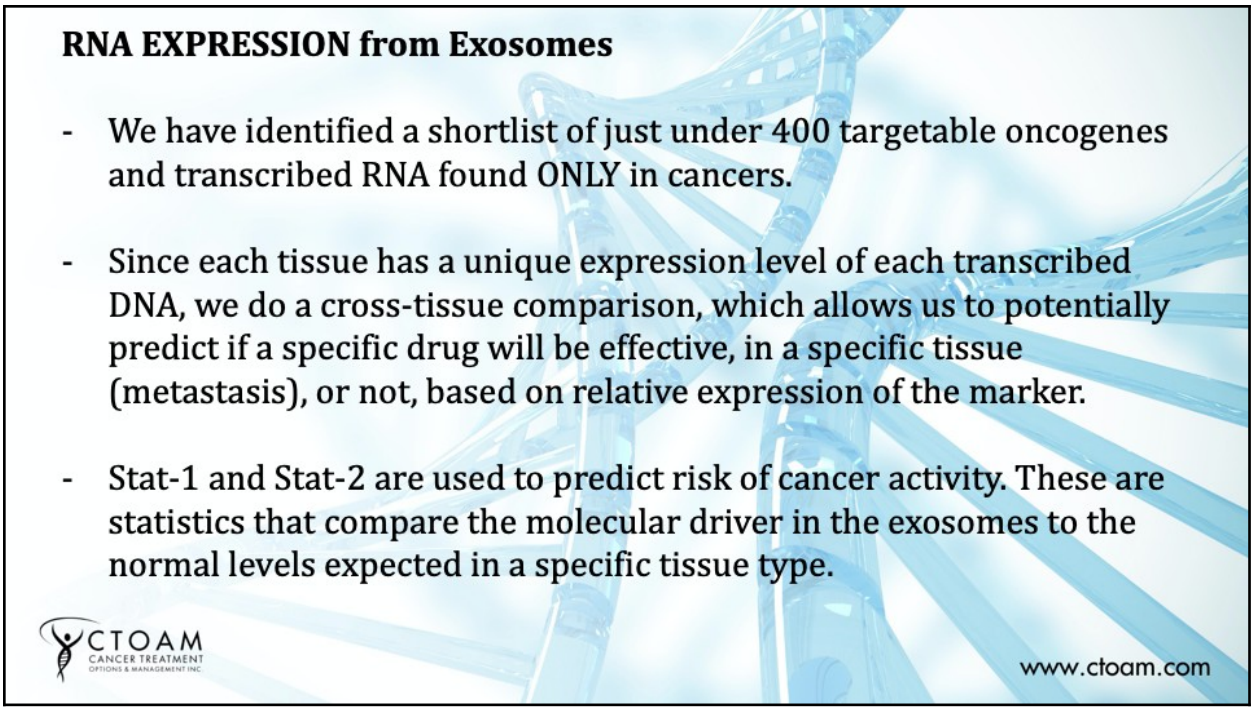
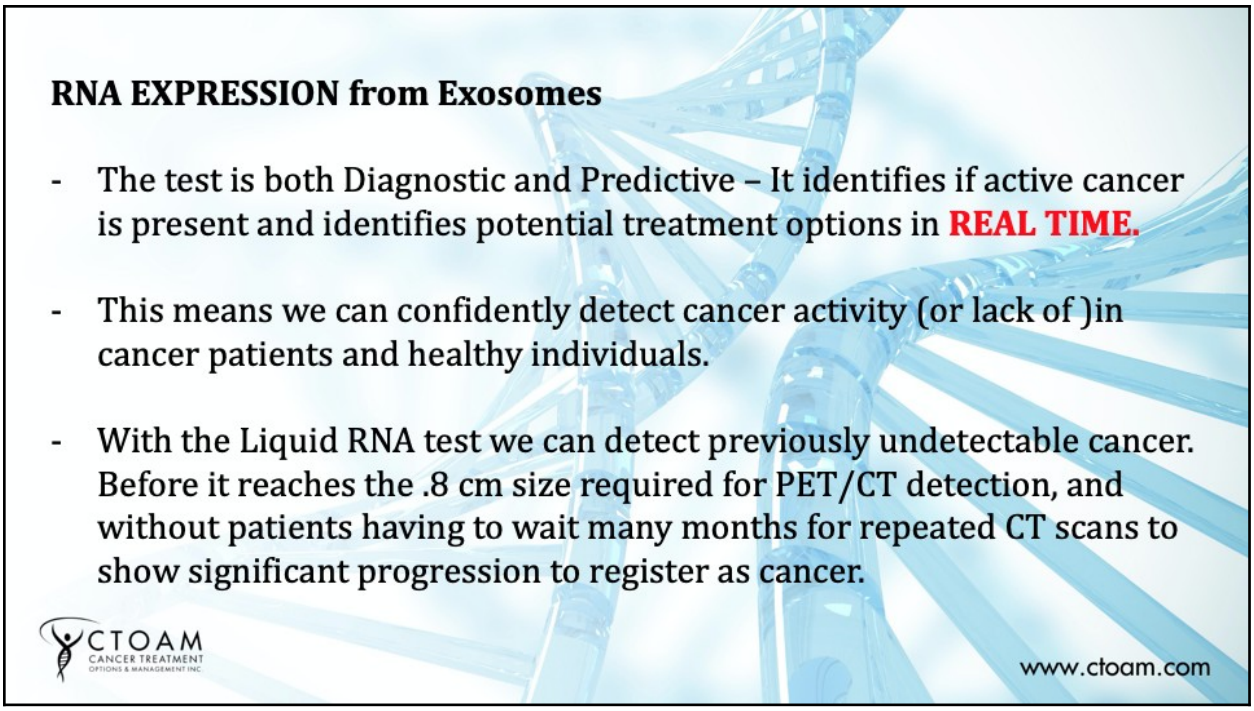
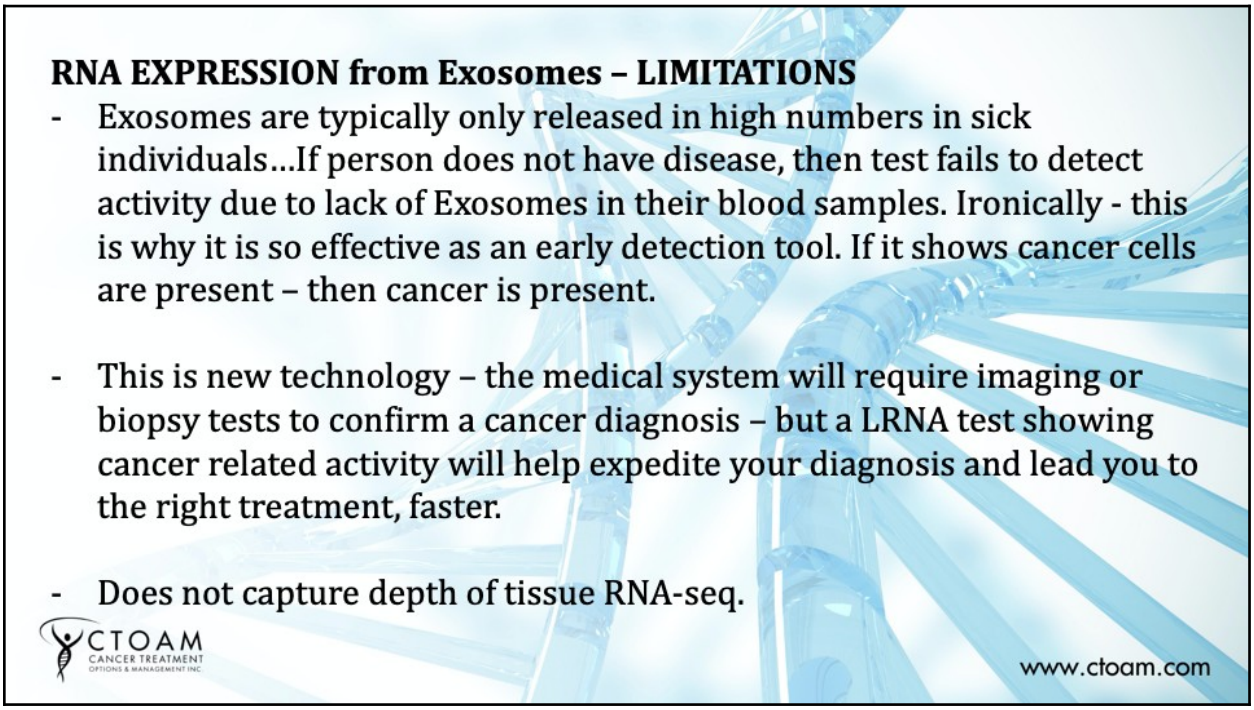



We have a short list of just 400 targetable oncogenes and transcribed RNAs that are only found in early cancer development. Since each tissue has its own unique expression level of each transcribed RNA or DNA, we do this cross-comparison tissue, and this cross-comparison tissue so far is allowing us to determine what specific tissues a drug will work in and what tissues it won't work in. It's quite an exciting development.

We use these two statistics commonly used in RNA, called Stat-1 and Stat-2. They are a way of looking at whether the expressed piece of RNA that you're looking at is higher than all of the tissues in the body, or if it's higher than the average of all of the tissues in the body. So there are two different statistics. We use both of those to make sure we have a fairly accurate assessment of it.




The beauty of this test is that it's both diagnostic and predictive. In other words, it can tell if there is cancer activity happening before there's a visible tumor. It could tell if somebody is responding to therapy in real time. It can tell us what genes are highly overexpressed, or what RNA molecules are highly overexpressed that are involved in driving the cancer at that given moment. We can use a targeted therapy that's useful at that particular time. It's important for detecting cancers at a very early stage.

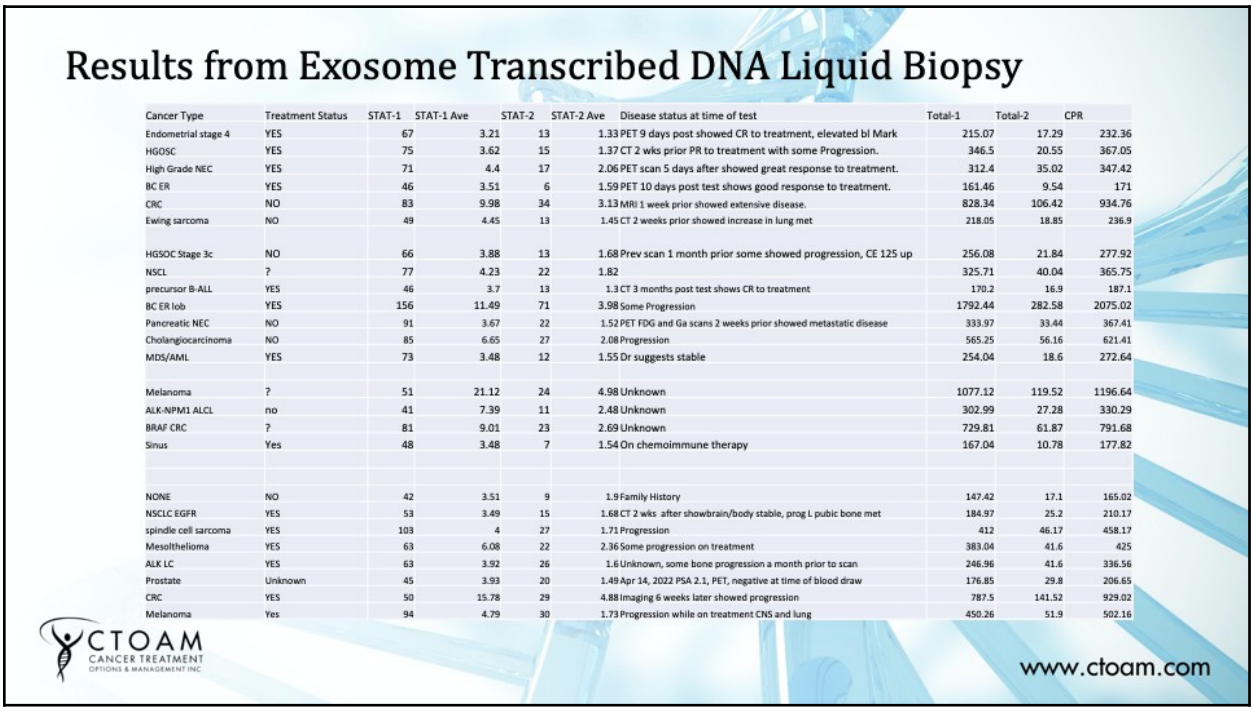


Some limitations: exosomes are only typically released in high numbers that we could use for analysis in individuals that have metastasis. If a cancer patient is responding to therapy, we won't really see a lot of these exosomes. That is one of the limitations of this process.

But it's also a great early detection tool, because if there are a lot of exosomes, then we know that there's some cancer activity coming along.

Also, because we're detecting cancer activity before there is a visible tumor, it's a little hard to verify exactly what's going on and to confirm things. We've had this series of tests that we've done, and we've compared that to the clinical data, PET CTs, blood tests, and so on. We do that surrounding the time, and we found that this test is able to detect cancers in patients that don't know that they have cancer yet. These patients end up developing cancer.

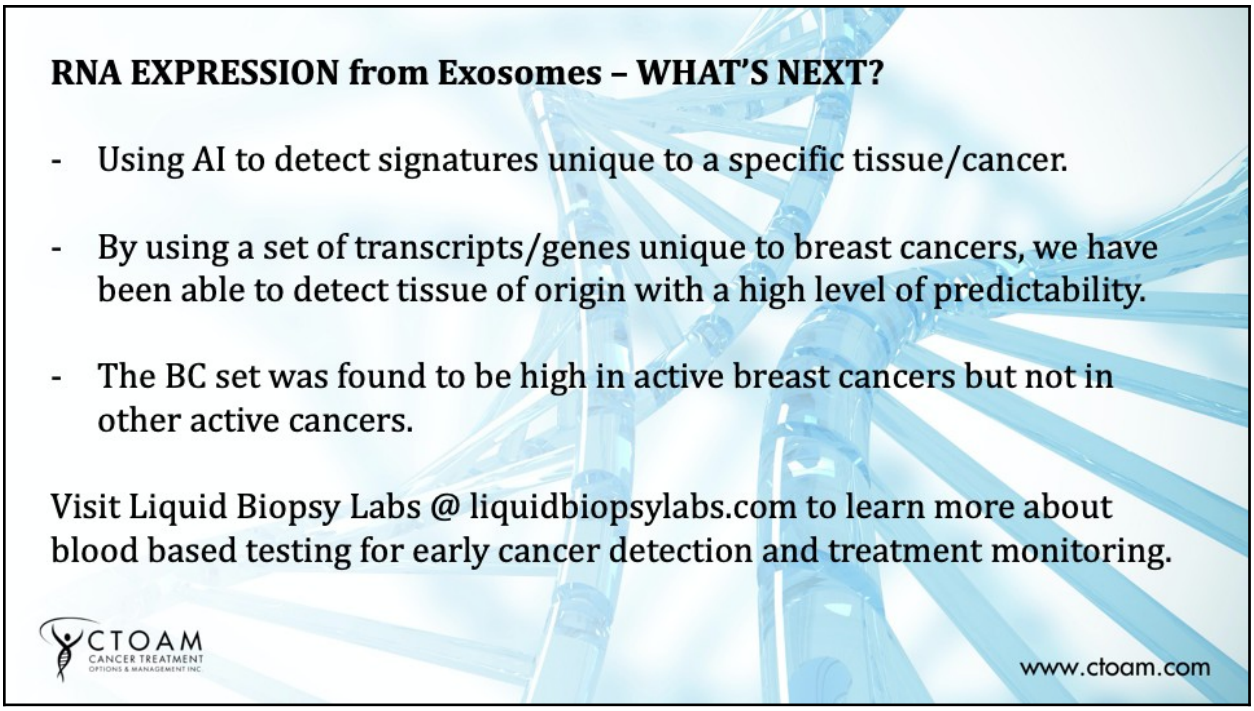
The only problem is that it doesn't capture the depth of the tissue RNA. The tissue RNA really is a solid source of RNA.



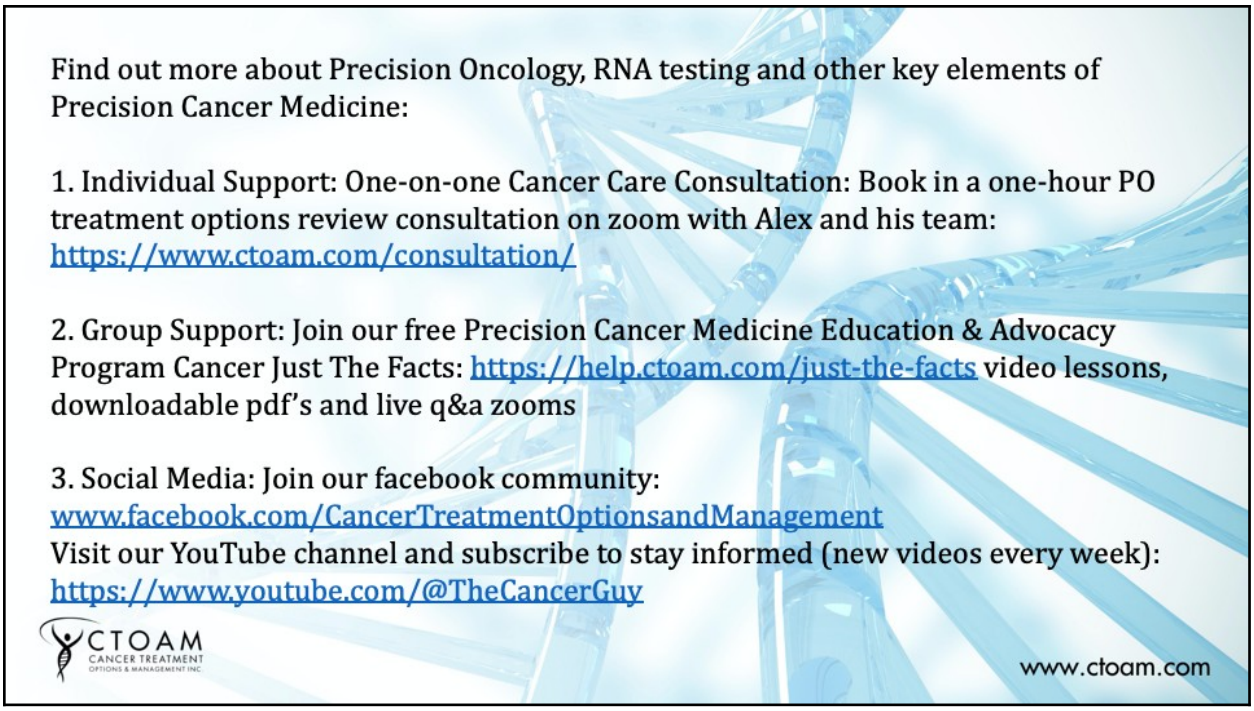

| Cancer Type | Treatment Status | STAT-1 | STAT-1 Ave | STAT-2 | STAT-2 Ave | Disease status at time of test | Total-1 | Total-2 | CPR |
|---|---|---|---|---|---|---|---|---|---|
| Endometrial stage 4 | YES | 67 | 3.21 | 13 | 1.33 | PET 9 days post showed CR to treatment, elevated bl Mark | 215.07 | 17.29 | 232.36 |
| HGOSC | YES | 75 | 3.62 | 15 | 1.37 | CT 2 wks prior PR to treatment with some Progression. | 346.5 | 20.55 | 367.05 |
| High Grade NEC | YES | 71 | 4.4 | 17 | 2.06 | PET scan 5 days after showed great response to treatment. | 312.4 | 35.02 | 347.42 |
| BC ER | YES | 46 | 3.51 | 6 | 1.59 | PET 10 days post test shows good response to treatment. | 161.46 | 9.54 | 171 |
| CRC | NO | 83 | 9.98 | 34 | 3.13 | MRI 1 week prior showed extensive disease. | 828.34 | 106.42 | 934.76 |
| Ewing sarcoma | NO | 49 | 4.45 | 13 | 1.45 | CT 2 weeks prior showed increase in lung met | 218.05 | 18.85 | 236.9 |
| | | | | | | | | | |
| HGSOC Stage 3c | NO | 66 | 3.88 | 13 | 1.68 | Prev scan 1 month prior some showed progression, CE 125 up | 256.08 | 21.84 | 277.92 |
| NSCL | ? | 77 | 4.23 | 22 | 1.82 | | 325.71 | 40.04 | 365.75 |
| precursor B-ALL | YES | 46 | 3.7 | 13 | 1.3 | CT 3 months post test shows CR to treatment | 170.2 | 16.9 | 187.1 |
| BC ER lob | YES | 156 | 11.49 | 71 | 3.98 | Some Progression | 1792.44 | 282.58 | 2075.02 |
| Pancreatic NEC | NO | 91 | 3.67 | 22 | 1.52 | PET FDG and Ga scans 2 weeks prior showed metastatic disease | 333.97 | 33.44 | 367.41 |
| Cholangiocarcinoma | NO | 85 | 6.65 | 27 | 2.08 | Progression | 565.25 | 56.16 | 621.41 |
| MDS/AML | YES | 73 | 3.48 | 12 | 1.55 | Dr suggests stable | 254.04 | 18.6 | 272.64 |
| | | | | | | | | | |
| Melanoma | ? | 51 | 21.12 | 24 | 4.98 | Unknown | 1077.12 | 119.52 | 1196.64 |
| ALK-NPM1 ALCL | no | 41 | 7.39 | 11 | 2.48 | Unknown | 302.99 | 27.28 | 330.29 |
| BRAF CRC | ? | 81 | 9.01 | 23 | 2.69 | Unknown | 729.81 | 61.87 | 791.68 |
| Sinus | Yes | 48 | 3.48 | 7 | 1.54 | On chemoimmune therapy | 167.04 | 10.78 | 177.82 |
| | | | | | | | | | |
| | | | | | | | | | |
| NONE | NO | 42 | 3.51 | 9 | 1.9 | Family History | 147.42 | 17.1 | 165.02 |
| NSCLC EGFR | YES | 53 | 3.49 | 15 | 1.68 | CT 2 wks after showbrain/body stable, prog L pubic bone met | 184.97 | 25.2 | 210.17 |
| spindle cell sarcoma | YES | 103 | 4 | 27 | 1.71 | Progression | 412 | 46.17 | 458.17 |
| Mesolthelioma | YES | 63 | 6.08 | 22 | 2.36 | Some progression on treatment | 383.04 | 41.6 | 425 |
| ALK LC | YES | 63 | 3.92 | 26 | 1.6 | Unknown, some bone progression a month prior to scan | 246.96 | 41.6 | 336.56 |
| Prostate | Unknown | 45 | 3.93 | 20 | 1.49 | Apr 14, 2022 PSA 2.1, PET, negative at time of blood draw | 176.85 | 29.8 | 206.65 |
| CRC | YES | 50 | 15.78 | 29 | 4.88 | Imaging 6 weeks later showed progression | 787.5 | 141.52 | 929.02 |
| Melanoma | Yes | 94 | 4.79 | 30 | 1.73 | Progression while on treatment CNS and lung | 450.26 | 51.9 | 502.16 |

This is one of our initial studies. The way we calculate everything here is “the combined positive score”, or “combined positive result”, “CPR”. We use the Stat-1 statistic and the Stat-2. We look at the average expression of these genes, the level of the expression of these genes. We've looked across a variety of different cancers. We found that it can detect whether a person's responding or not based on their other standard care identifiers and so on.

**“Testing Your RNA with Liquid Biopsies” (Alex Rolland)** [#116]




What's next? We're currently working with an AI group to detect specific signals. So we can say, “While we can't see that you have a visible tumor, yet you do have high exosome activity. We're seeing the markers of this cancer, and we believe it's potentially breast cancer.” At this time, we can't do that. We could just say we have cancer activity, but we're working on that to identify the unique molecular features of certain cancers. We've done a test run already with a breast cancer summary, and we found that the breast cancer summary was able to detect which patients had breast cancer versus patients with lung cancer or other tumors.




Brad Power 16:24
We have a CancerHacker Lab accelerator, which has startups that like yours, are offering diagnostic services. We're learning about the challenge a diagnostic company faces in getting their diagnostic tool to market, basically gathering evidence that can persuade everyone that what you're seeing is signal and not noise. Can you speak to – and I don't know what the regulatory regime is in Canada – the journey or pathway you face as you have what looks like a very interesting theory, and a very interesting model.

But how do you get data, and how do you then get that as evidence you can then share and persuade, whether it's investors or the next patient who comes along? You've got something that looks like something that's really useful.

Alex Rolland 17:49
That's a great question, and I feel it has a few different levels.

As far as in Canada, there's not a lot going on in the deep research levels. There are some great companies, but there's not a lot of funding in Canada on the private level, as we have a public medical system, and so most things are done at universities at a very early level.

How we gain the data is we heavily stratify our patients. In other words, all these patients that I showed you and that we've gone over, that we've done these tests for, they've all had extensive tumor DNA sequencing; they've had RNA expression testing. They've had all of the standard pathological markers established. We know what we're looking for with these patients before we actually look for them. In other words, when we do see these genes, if we know that this patient has a driving gene, then we are pretty well looking to identify what's driving it, but we know in

advance. Having a heavily stratified population that you work with really helps provide credibility, because you have many different molecular levels of clarifying what you're seeing.

Michelle Morand 19:18
We've done many hundreds of these tests, for starters, and the joy of the way that we work is that we're working in tandem with the patient's public healthcare oncologist, or whatever country they're in, their main oncologist. These test results through the years that we've been validating this assay have been backed up by public health care, PET, PET CT, CT, MRI, biopsy surgeries, and various things like that. We've got that.

For validation and commercialization we're using a lab in the US – a CLIA CAP approved lab, of course – and they're going to help us commercialize this test in the next few months.

Brad Power 20:07
Do you have some kind of observational registry where you track all the patients that have gone through your tests? Do you have a place where you can say, “We've got hundreds of people in our database.”

Michelle Morand 20:19
Yes, exactly. Then spreadsheets, as Alex was saying, to start to not just look at the overall data of the 21,000 genes that we're testing for each person, but what are we seeing in terms of a subset? Once we know this person has a validated cancer of a certain type in a certain place, as Alex says, they're now able to say, “Okay. There's a subset of genes that keep showing up associated with the person then getting this diagnosis.” We have the big assay of the whole genome, and then smaller assays specific to different cancer types that are in development right now.

Brad Power 20:58
How would you position yourself relative to other diagnostic companies in this space? Liquid biopsies are fairly new, and fairly interesting. There are a number of companies that are pursuing them. I have gotten a test from Signatera several times. There's Guardant, Grail. There are a number of these biopsies, and not to mention that Tempus has theirs, or Foundation Medicine has theirs, etc. How would you distinguish your services and your tests from those others in the liquid biopsy space?

Alex Rolland 21:40
Most of these companies are using circulating tumor DNA. Unfortunately, the issue there is that they are designed for detecting emerging mutations, DNA mutations. They're not designed for detecting the level of the actual mutation in the blood, and that's because they are not looking at the exosomes. The exosomes are a cancer-specific mechanism, and by isolating the exosomes, first, you know you're looking at exactly what the cancer is doing, and you're getting a relative amount of that mutation in the blood. While these are all great tests that you mentioned, they only specifically are designed for detection of emerging mutations, and you can't trust the percentage, because they have to heavily amplify the material that they're accessing. We use

exosomes. We use CtDNA from exosomes, and we found that that is much more effective at determining whether someone is responding or not. We use a digital PCR platform, which is the most accurate platform for detecting CtDNA. That's a different test that we do. Our test could detect one piece out of 20,000 pieces of normal DNA, one mutated DNA. The exosome process is really the key here.

Additionally, other companies are using RNA, and they're trying to look at genes expressed through RNA. Some of them are doing it from exosomes. But the problem is the panel that they're using is designed for detecting mutations, and it's not accurate for detecting expression. This expression panel is very new. It uses a mechanism that is very unique in the sense that it only has one amplicon per gene, whereas other detection methods require a series of amplicons, and if not all of the amplicons are there, then it's not going to score as a positive finding.

RNA gets degraded significantly once you take it out of the body. Therefore, you can't always tell what was actually produced by the tumor there, if you're not looking specifically at the exosomes number one, and then number two, looking at a gene panel or an expression panel designed for expression specifically.

Brad Power 24:15
We are a community of advanced cancer patients, highly engaged, highly educated. I'm totally floored and persuaded by your argument. I want your service. How do I access it? Can you speak for a moment about how patients and caregivers can access your test?

Michelle Morand 24:57
We have a couple of websites you can access us through. There's ctoam.com where we have our full research and analysis team, and we have a very unique patient navigation program as well.

Somebody was saying earlier about getting a huge report and then, what to do with it? Obviously having experts like Alex analyze that data and make sure it's utilized to your best advantage is important. But then having somebody help you navigate, just even coach you on the language to use with your oncologist to get better uptake, but also to have somebody working on the back ends with all the programs and the paperwork is something that we do.

Then there's liquidbiopsylabs.com, where you can go and order a test specifically, if you just like the test.

Alex's email will be posted. You can certainly reach out to him directly.

Brad Power 26:07
We love direct-to-consumer marketing, and it sounds like as a consumer, I can do that. Do I need to get approval from my doctor before I can order it? What is the price if I'm going to pay for this out of pocket? What would be my retail price?

Michelle Morand 26:26
You don't need a doctor to order this for you, so you can just decide that you would like to know what's happening in your body precisely. The cost is about $1500 for the test at this time. Obviously that changes as time goes by, but that's where we're at right now.

Brian McCloskey 26:51
I have two questions.

The first is specific to prostate cancer. For many CtDNA tests, there's usually a sensitivity threshold where the PSA has to be. It's been a while. I think it's like 0.5 or 0.1. I think I haven't been successful at 0.75. But anyway, is there a sensitivity threshold for your test in prostate cancer?

The second question is, do you help with interpreting the results into treatment options, and are you constantly going back to validate that those treatment options you suggest are evolving and improving in accuracy as you get data?

Alex Rolland 27:41
On PSA monitoring for prostate cancer: PSA is a molecule that's produced by prostate cells. It has a role in aiding the traveling of sperm. It liquefies part of the cervix, the mucous membrane of the cervix, and allows the sperm to travel. It's not specific to cancer. When you get a prostate cell that's constantly reproducing, the consequences often increase PSA, but not always. Also in very advanced prostate cancers, they tend to take on a more of a neuroendocrine subtype over time. You've probably heard of that. It's called neuroendocrine differentiation, where they occupy a lot of the different genes. I'm not a huge fan of looking at PSA as a sole guide. I like to use CtDNA. I like to use PSMA from a PSMA PET scan. PSMA is a different molecule. This is Prostate Specific Membrane Antigen. An antigen is a molecule on the outside of a cell that tells the immune system and the rest of the body what's in that cell – kind of like a street address. I like to use as many different approaches, not just PSA. Now the obvious bottom line is, if your cancer is following the PSA spectrum, then typically, if you have a very low PSA, we're probably not going to see a lot of these exosomes in the blood because you're probably not progressing at that time. However, we have seen, and we have seen this in people with nonexistent PSA. We have seen higher exosome loads, and that could mean that part of their cancer is actually differentiating. We had a recent case where a patient had one lymph node tumor that was going into neuroendocrine differentiation, and our test was able to pick that up.

Brian McCloskey 29:45
I think you said this before, and you might have just said it just now, but I want to be 100% clear: if someone's cancer is responding, and we're just going to use PSA as a product. We can look at the radiographic component of this as well. But if it is responding, then your test is not going to be as good.

Alex Rolland 30:12

That's one of the limitations of it.

Brian McCloskey 30:20
Sometimes it's difficult for doctors to interpret the results into treatment, into clinical decision-making. This is where we would be dependent upon your expertise in pairing results to treatment options. Does your report provide that? That's a dynamic environment. You've got new treatments coming out all the time, as well as new information about what's working and what's not working. Just curious about how you look at that relationship,

Alex Rolland 30:52
We're totally on board to help in any way we can. We want to see the analysis component of this test get used and applied. We cast such a wide net, just under 21,000 genes, that often what we get is we'll get a doctor saying, “Hey. This patient originally had an EGFR positive lung cancer, and we're just not sure if it's transforming into a small cell lung cancer, because this is one of the consequences that can happen with that type of cancer, or if it's still driven by EGFR. We'll do this blood test, and we'll say, “Well, actually, the EGFR is quite high, so the EGFR inhibitor that you've been using is not effective anymore.” And so we have many simple case scenarios like that.

We've also had cases where we've done the test to see if the patient was responding or not, and then we got a call from the doctor and said, “By the way, his test showed high levels of CDK4, and we're thinking of using the CDK4/6 inhibitor like abemaciclib (a medication for the treatment of advanced or metastatic breast cancers, which acts as a CDK inhibitor selective for CDK4 and CDK6) or palbociclib (a medication developed for the treatment of HR-positive and HER2-negative breast cancer, a selective inhibitor of the cyclin-dependent kinases CDK4 and CDK6.). Copy number variation that we see is supposed to result in an increased expression, but it doesn't always. Sometimes we'll see increased copies of the CDK4 gene, for example, which is an oncogene. We'll see copies of it, but we don't see increased expression. This test is really good for validating what you see on your tumor DNA sequencing. If you're seeing increased copy numbers of certain genes, but you're not seeing increased expression, then it's a moot point, because it's not a driver. That's another classic example that we get a lot of questions on: “is this gene copy that we're seeing producing increased expression or not?”

Brian McCloskey 32:45
Because there is this synergy between tissue-based testing and your liquid biopsy, would you partner with, for example, a Tempus, BostonGene, or Foundation Medicine, who might be already be doing tissue-based biopsies, so that you get the patient and the doctor gets a complementary view of what's actually happening with the patient's cancer?

Alex Rolland 33:16
It's really important to use as many different tests as possible. Education is power. Knowledge is power. The more different platforms we have to look at, the better. Each one of these platforms is slightly different. For example, Signatera uses standard PCR (polymerase chain reaction test, a laboratory procedure that analyzes a sample for genetic material to identify certain diseases,

cancers, and genetic changes), so it can't tell you the amount of that molecule, but it just tells you whether it's present or not, and it uses that as a score for minimal residual disease, which is very different from the NGS platforms, such as Foundation One or Guardant that use a liquid approach, that are looking at actual circulating tumor DNA. Looking at the mechanism of the test and understanding what niche and understanding it is going to fill is really important when you're pairing tests.

Brad Power 34:07
Allen Morris, our friend and pathologist in Northern California, asked about “hyper-progression” and “pseudo-progression” and the definitions of each.

Alex Rolland 34:40
Pseudo-progression is an interesting phenomenon. We know about it because we're one of the first to ever use pembrolizumab, one of the first PD -1 inhibitors in Canada, and we used ipilimumab (Yervoy, a drug used to treat several types of cancer by activating the immune system to attack and destroy cancer cells). This patient's still alive today, and so after that, we started seeing cases of pseudo-progression. You have your tumor cells. In the case of the pembrolizumab, for example, or nivolumab, one of the PD-1 inhibitors, they have this protein called “programmed death one”. This programmed death one protein is like an access card that allows you to enter a building. If you have that programmed death one on the outside of your cells, then the immune system will not attack you. But if you don't have it, then the immune system will attack you. What happens in cancers is they tend to upregulate or use this PD-1 to shut off the immune system. They target these cells called TILs, tumor infiltrating lymphocytes. These are usually classified as a CD4, and then you have Tregs, which are called regulatory T cells. They both work together. What happens in pseudo-progression is the TILs get turned off, and they can be inside of the tumor. They enter the tumor, and they go in there to destroy it, and they get turned off by this PD-1 pathway. When you take this pembrolizumab or one of the PD-1 inhibitors, it acts like a molecular sponge and soaks up that free floating PD-1. I'm generalizing here, but it allows these tumor infiltrating lymphocytes to recognize their surroundings and say, “Hey, we're in the middle of a tumor. Now let's start attacking it.” They multiply their numbers, and there's a series of immune cells that are involved in that, and as they multiply their numbers, they do it very quickly, and they rapidly expand the tumor, so the tumor gets bigger immediately. Now normally, if a tumor gets bigger, you can look at PET CT to look at, to look at biological activity. A PET CT is very great for determining whether a lump is alive or dead and how aggressive it is or how fast it's growing. The problem is that when you do a PET CT on a pseudo-progression lump, these rapidly reproducing immune cells that are eating the tumor from the inside out, tend to set off the PET because they are PET avid as well. They're using a lot of sugars, and so you can't tell the difference. So a PET CT is not very useful at detecting pseudo-progression. We started seeing pseudo-progression quite a bit where the doctors took the patients off the immune therapy, and then years later, the patients are still alive and completely cancer free, and doctors are like, wait a minute, you are progressing.

The other thing that pseudo-progression can do is if you have a tumor that is below the resolution of imaging, which is typically about half a centimeter, four to five millimeters.

Depending on how aggressive that lump is, it can be really small, and then if the immune system comes in and attacks it and makes it bigger, now all of a sudden you can see it on a scan. One of the things that we can tell about a pseudo-progression is immediately the tumors get bigger, and then you see a bunch of new tumors, and it's at a progressive rate that is not in keeping with how the cancer has progressed. Let's say the cancer is metastasizing here and there, and then the patient goes on immunotherapy, and all of a sudden, all these new tumors show up within the first couple months. Then you can have a pretty good idea that that is pseudo-progression, and because it mimics hyper-progression.

Hyper-progression is where you get a mass amount of tumor cells growing very quickly. That is often caused in response to some sort of immune repression, or often we see hyper-progression more in patients and people that don't get a lot of movement, or when they become bed bound and have to go on high morphine levels. They're the opposite processes, but they're both very important to detect. With hyper-progression, you'll also see a positive PET, but we believe the secret to this is really using liquid biopsies, both circulating tumor DNA, and RNA. If the person does not have, let's say, a BRAF, e6, 100 e mutation that we can track on a CtDNA test, this is where the RNA comes in. We could say, “We're seeing increased expression of the genes we know, the driving genes of your cancer, and now we're seeing increased expression of those.” So we said, “We feel that this is probably hyper-progression versus pseudo-progression.”

Brad Power 39:37
I'm going to connect some dots between what Brian was talking about, how you get other tests to give you a more complete picture of what your testing is coming up with, with the exosomes. I'm looking at a comment in the chat here from Stratis Telloglou, who said that he recently got two liquid biopsies, and they also wanted to look at his tumor issue from a block from his original biopsy, and they needed that to detect disease. I know that from my Natera test, they wanted those same results to identify the biomarkers that they should be looking for in the liquid biopsies.

Can you talk a little bit about how you use your test and complement it with other tests to get a more complete picture of what's going on with a cancer in an individual patient?

Alex Rolland 40:30
In a perfect world, we would start with the primary tumor. We would get a nice tumor DNA panel, 300 to 600 genes, determine all of the potential drivers and all of the passengers, all of the mutations that are present. Most cancers, when they're first detected, have all of the mutations they need. They have a driver, and then that driver gets exchanged through some of the passenger mutations, so that is one of the processes that happens early on. Determining what all the players are up front is pretty important, and then also getting a tumor RNA liquid or a tissue tumor RNA panel is really good. We like to use the same panel that we use for the tissue for the liquid, and then we know exactly what we're looking for. If we want to see if the person is responding or are not responding, or if we want to know what sort of drugs to use for that person, then we can use both of those and say, “Okay, now we use the liquid, so we know

who all the players are. Let's use the liquid test, such as a CtDNA test, like the Foundation One liquid or the Guardant, to see which ones are being used here. You know what the players are there. And use the RNA test to look at the expression of the genes. That way we can come up with the real time drivers that are driving the cancer today, not yesterday, not tomorrow, but the ones driving it today. Having a good solid tissue-based analysis of both RNA and DNA is a really important starting point, because then you know what you're looking for and you're not looking for. You are not looking for a needle in a haystack, so to speak.

Brad Power 42:25
There are a couple of questions again in the chat, one from Ari and one from Eric, that are really getting at your business model as a new diagnostic company offering this service, and how you can scale.

Ari asks, “How do you assume you get over the reimbursement pathway in the US, which is a big issue, presumably in Canada as well. Is your idea to keep it direct-to-consumer?

How do you grow your market?

Would you then also be selling to providers?

Eric makes the same or a similar point: how do you get adoption?

There's a classic, I think it's apocryphal, but it says, “If you have a great new solution, a new treatment or therapy in the US market, it takes 17 years to get widespread adoption, because you have to retrain all the doctors to use it.”

Can you speak a little bit to that?

Alex Rolland 43:29
I can speak to technology.

Brad Power 43:30
What does the scale up ramp look like? How do you overcome those obstacles?

Alex Rolland 43:36
I'm going to pass this question over to Michelle, because she's the expert here in business. I do want to say I'm a big fan of direct-to-consumer tests. Many of the tests that are now being standard of care, like Foundation One, when we first started using them, were direct-to-consumer. This was many, many years ago, and I've seen many different companies start as direct-to-consumer and then develop the technology. I'm a big fan of direct-to-consumer tests, plus it gives people the options to use a variety of different applications.

Michelle, would you like to respond to this?

Michelle Morand 44:14
I've got a list of things to respond to. I'll start with this and work back.

We definitely have a team in place. We've been envisioning this growth for quite some time. There are four steps for this test:

- There's the equipment that you need to run the test.
- There's the training that people need in order to prepare the samples for the testing.
- There's the analysis of the results.
- There's the delivery of these results in a way that makes sense to the patient and that helps their doctor act on this information.

We've got teammates ready to go with all of these things. We are definitely prepared for scaling. We also have our partner lab in Orlando that is better equipped than we are. They've been doing this longer than us, and they can put through about a few 1000 samples every week right now, without adding any new technology or staff. We definitely have been preparing for this for some time.

I want to come back to a couple of things that Alex was saying. One of the things about the Foundation One CDx (companion diagnostic), for example, that is now, as you probably all know, owned by Roche and many other tests of its nature, is that a lot of tests are saying that they do RNA testing. And sadly, patients are confused and they believe that they've had their RNA tested. In reality, what's happening is a couple of fusion genes are being tested as well as their DNA. You guys might all be so educated that you know that already, but I just wanted to make that point, and maybe Alex can speak further to that. But if you have a test like a Tempus or a Foundation One CDx, and they say that they did RNA testing, or some of the smaller panels that some governments are using now, it is important to understand the distinction between thorough RNA testing, which requires a special type of sample preparation in order to get a good quality sample, because RNA is delicate and degrades very quickly, from the type of a few fusion genes that are tested in these standard tests. Alex, maybe you want to speak to that, but it feels like an important distinction, especially for this crew.

Alex Rolland 46:39
There is a big difference between using RNA to detect a fusion protein along with DNA, which is what a lot of these tests do, and actually looking at an expression panel. The difference is, one is using it to detect alterations in the splicing sites of the gene, in other words, actual mutations or alterations or changes in the gene, and it uses the RNA molecule for that, because RNA molecules can be different from the DNA template as they get processed, and an actual expression panel which counts the amount of RNA molecules for a specific gene, regardless of if it's mutated or not, it just counts some molecules for that gene. They're two different things, apples and oranges, and they're not the same. When you do see RNA, you need to know, is this an expression test that is counting the amount of RNA molecules for a gene, or are they just using RNA to detect a fusion gene or some other molecular feature?

Michelle Morand 47:42
There was a question about whether we're working to partner with some of these companies, and we absolutely are. We're the only company on the planet that we know of now who's created their own normal tissue RNA comparison library. So that makes our RNA data that much more accurate, because we know exactly how our comparison tissues were created. And they were all created equal. They were all used by the same pathologist with the same tools, so that when you're comparing, you know relative expression, you want to make sure that the thing you're comparing it to is stable and confirmed. We have that. We're in the process of licensing our library to these types of companies, including CureMatch, which you've probably heard of as well.

Brad Power 48:29
CureMatch is one of our partners. We love their drug combinations.

Michelle Morand 48:38
They've done a great job with the DNA, and now we're going to help them add the RNA, because, as we're talking about today, it really is where things are going. So many new treatments are being developed based on RNA, so we need to make sure your tumors can be properly assessed for that.

Brad Power 48:55
What patient is best, and what do they need? You said it'd be great to have your DNA from your tissue biopsy. It would be great to have some CTC. What level of CTC is needed, and what would be the ideal profile of the best patient for your test?

Alex Rolland 49:30
On a CTC note, circulating tumor cells. I'm not crazy about circulating tumor cell tests. The technology has come a long way. I was a huge fan of it, you know, 10 or 15 years ago. I thought this is the way to go. But most of the tests that use circulating tumor cells use markers that are not specific to tumors, and it's really hard to tell the difference between a tumor. I'm sure any pathologist will tell you here is a circulating tumor cell, or it could be a tumor cell that is partially halfway through differentiation. It's not quite a tumor cell. It's got some of the molecular features of it. There's a whole range from a normal cell to a transformed cell. When you're speaking of a circulating tumor cell, what type of circulating tumor cell is it? Also we know that only the stem cells are the ones that can metastasize, and they're typically one in 6 million tumor cells. A test that determines or detects circulating tumor stem cells would be very interesting to me, but most of these CTC tests are not as accurate as I would like them to be. That’s a limitation there. I don't like to go with a minimal CTC. I also don't like going with a minimal residual disease based on molecular features alone. I think you need to look at a variety of different factors there.

Brad Power 50:59
One more question from Allen Morris: how do you work with pathologists in this process? I imagine they're used to looking at stained slides, and now you're coming with a liquid biopsy.

**“Testing Your RNA with Liquid Biopsies” (Alex Rolland)** [#116]

How do pathologists work with you?

Alex Rolland 51:17
I'm sure Michelle's just chomping at the bit to answer this, because she's an expert in this side of things. I'll just give you a summary, and I'll let her talk about this. Pathologists are bread and butter. We love them. They're very important to us. We use standard care pathology reports. One of the first things we look at is the pathology reports. We look at the different stains. We look at how the sample is processed with RNA. One of the fundamental things you have to do when you're looking at tissue RNA, for example, is you have to isolate the tumor cells. You have to do expression on the tumor cells alone. A biopsy sample is going to be anywhere from 10 to 20, 30, 40, 50% tumor cells. It's going to have all other cells in their fibroblasts. It's going to have every kind of cell you can imagine. When we do our RNA, we will want to isolate those tumor cells. We have a specialty pathology lab in the states that we work with. We've been working with this pathologist for quite a while that does something called Laser dissection. And laser dissection, basically, they are able to isolate just the tumor cells, pull them out of the biopsy and put them in a vial for us, and that's what we work with.

Michelle, would you like to talk more about laser technology here?

Michelle Morand 52:40
Oh, not necessarily. I'm sure you folks can look it up: laser capture, micro dissection. The main point there is that when we are working with a sample in our lab, it is highly purified tumor cells only that we're testing with. We use a 550-gene DNA panel, and then the 21,000 RNA panel, and our samples go to this lab in the US, where the pathologist uses this laser in this high powered microscope to give us a purified sample of the tumor DNA and the tumor RNA. As far as I know, there's no nobody else that does this. I can guarantee you, CDx, Caris, etc., do not do this. That is why, statistically, 40% of the time, those tests fail to produce viable data. That's the statistic right now, and it is because of the degraded samples that they're working with. We often have labs say, “We don't even want to send you the sample. There's not enough tissue in it.” And we say, “Send it.” We get more than enough because of the preparation we use.

At our sister partner lab in Orlando, there's an excellent pathologist there by the name of Tony Magliocco. I'm sure you've heard of him; wonderful fellow. If we need a second opinion on pathology, or a patient would like a second opinion from a pathologist, specifically, it would be him that we would refer them to where we would help coordinate a consultation for you there.

Brad Power 54:15
Tony Magliocco and Protean BioDiagnostics, is also a friend of the Cancer Patient Lab. He's also in the CancerHacker Lab, our accelerator. Good friend. Highly recommended. I personally use his services and endorse them. He gave me concierge advice on what tests I should get.

There was a question in the chat about more information that we might get from your website or other studies you might be able to point us to that would reinforce the findings you have; anything like that.

Michelle Morand 55:03
Two things.

There is a question about outsourcing the laser dissection. Is everything else we do in our own next generation sequencing lab? Unless patients are financially tied, or their budget is a little too low to allow for the large panels and the LCM process, then we will help coordinate other tests like CDx, which are more economical, but everything else is done in house, from start to finish, aside from the LCM process.

Someone asked about a sample report. Excellent question. I can certainly make sure that you get a couple of sample reports.

Brad Power 55:49
And literature citations.

Michelle Morand 55:55
I've been pushing Alex to do this for about a decade, but Alex is a little, understandably, from a business perspective, reluctant to share the process until we've got the commercialization. And so that's where we're at. Every patient that we do a report for is an individual research study, essentially. We have sample reports we can share. We have yet to publish anything formally, but that will be coming once we have a formal patent and commercialization.

**“Testing Your RNA with Liquid Biopsies” (Alex Rolland)** [#116]

## CHAT DISCUSSION

00:23:50 allen morris: Can your technology differentiate between pseudoprogression and hyperprogression - in the context of immuno-therapy?
00:24:31 allen morris: Which begs the question - Do you believe hyperprogression is well defined?
00:31:47 Stratis Telloglou: recently i did 2 blood liquid biopsies in US and Germany. Besides Blood one of the companies asked part ot the tumor block of the surgery in order to check which of the mutations were present. The company that did not have the tumor did not detect any disease.. Is this part of the process?
00:39:49 Roger Royse: liquidbiopsy.com?
00:40:53 ari akerstein: Related to Brad’s q: is there an estimated timeline to a reimbursement pathway (e.g., ordered by oncologist), or is the idea to keep it d2c with decreasing costs over time as you scale (or both).
00:43:13 Rick Davis, AnCan Foundation: What level of CTC is needed?
00:44:41 Eric Dishman: If we assume all the proof and payment steps happen, how ready is the laboratory workforce to scale this? Are all the equipment and materials already existent or is new infrastructure needed? And how hard is the scale up of training/education?
00:47:16 allen morris: Natera reports molecular signature per ml
00:55:39 Ryan Ramanujam: Are there any published articles on your methods I can read further?
00:57:34 ari akerstein: Liking d2c = a Contrarian take!
00:58:14 Brian McCloskey: Reacted to "Liking d2c = a Contr..." with 👍
01:01:53 allen morris: Who is the pathologist who reads your tissue?
01:04:52 Jane Wilkinson: Thank you everyone! See you all next time. Jane
01:06:37 allen morris: so you outsource laser dissection. What other processes do you outsource?
01:08:17 Brian McCloskey: It would be nice to have sample report
01:08:30 Dr. Chris Apfel: Great presentation. Have to leave right now. Looking forward learning more about what you do.
capfel@sagemedic.com
01:08:49 Eric Dishman: Great session. Learned a ton.
01:09:00 ari akerstein: Reacted to "Great session. Learn..." with 👍
01:09:45 ari akerstein: Same here. Need to drop in a minute. Alex and Michelle 👏great and important work you’re doing. Thanks for sharing with us.