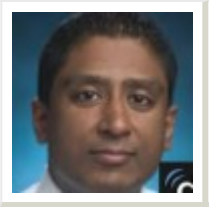
Improving Outcomes for Ewing Sarcoma Patients

In Ewing Sarcoma patients, exosomes in the blood may be an early detector of relapse. Partnering with the University of Kansas, Glenson Samuel, MD created a chip that could detect and analyze these exosomes and their proteins with minimum blood. Now, he is using that knowledge to find, and reverse, chemo-therapy-related resistance in tumor cells, making patients more responsive to therapy.

Join Glenson Samuel, MD as he discusses his studies and his work with the genome center.



Featured Speaker:

Glenson Samuel, MD

Glenson Samuel, MD is a pediatric hematologist-oncologist and hospitalist at Children's Mercy and Assistant Professor of Pediatrics at the University of Missouri Kansas City School of Medicine. Dr. Samuel has a strong research focus and has won the Midwest Cancer Alliance Grant and the Alex's Lemonade Stand Young Investigator Award for his work.

Transcription:

Dr. Michael Smith (Host): So, our topic today is "Improving Outcomes for Ewing Sarcoma Patients". My guest is Dr. Glen Samuel. He's a pediatric hematologist/oncologist and a hospitalist at Children's Mercy, and Assistant Professor of Pediatrics at the University of Missouri Kansas City School of Medicine. Dr. Samuel, welcome to the show.

Dr. Glen Samuel (Guest): Thanks for having me.

Dr. Mike: So, let's do this. Let's start off--there's a lot of excitement right now in oncology because of the exosome, right? Tell us a little bit about the exosome and how it is being associated with invasive cancers, and even relapse of certain cancers.

Dr. Samuel: So, exosomes is a field of research that's pretty much up and coming within the past decade or so, more in adult oncology than in pediatric oncology. Just recently, in the past few years, pediatric oncology has started to uptake in terms of their interest in exosome, as well. So, exosomes are basically nano-sized vesicles that are released from many cells in our body into the extracellular space. They contain lipids, proteins, and various other nucleic acids. They're contained within the exosomes and they float within the blood or other biological fluid such as urine and serum. They've been found in ascites and even pleural fluid. So, it's a non-invasive, or a less-invasive, manner of use for potential markers of disease in various cancers. A lot more has been done in adults comparatively to pediatrics, unfortunately, and that's just the way research is currently with the state that we're in.

Dr. Mike: Right. Right. So, I mean, essentially, the exosome is a packet of information that can help you to analyze how chemotherapy is working for somebody, if there's relapse. I mean, that's the basic gist of it, correct?

Dr. Samuel: Well, that's the hope that we have for our research, specifically. And that's what several researchers have shown with adult oncology ranging from brain tumors to pancreatic cancer to breast cancer, prostate cancer. Like I mentioned before, very little has been done in pediatrics comparatively.

Dr. Mike: So, let's talk about what you're doing then. So, bringing it into the pediatric practice--the oncology practice. First, correct me if I'm wrong, you developed a technique for identifying the exosome, correct? So, tell us a little bit about that.

Dr. Samuel: So, in Ewing Sarcoma, specifically, which is a disease that we're focusing heavily on and the other pediatric sarcomas just as much, the first was to determine whether these cancers were exosomes to begin with because there was no research done on this cancer and the presence of exosomes being released from these tumor cells. So, that was the first step. We did discover that we found specific markers that are typically found in a tumor cells and the tumor tissues that are also found in the tumor-derived exosomes that we're studying. And so, that's of particular interest because in our patients, we don't really have the ability to have a marker of any sort besides just regular scans to see if their tumor is getting better or worse.

Dr. Mike: So, that was your first step, correct? So, first of all the question was, with Ewing Sarcoma, for instance, is it releasing these exosomes? So, that was the first question. You found that out and then you found a way to actually identify those exosomes. So, now what do you do with that information? So, now you've identified an Ewing Sarcoma exosome. What's the next step and what's the hope in the research? What's really the end game, here?

Dr. Samuel: So, my end game, big picture, for this is for multiple avenues for this to be used. One is more for a diagnostic and prognostic marker. So, tumors, when releasing these exosomes, they're viable, they're alive, and they're releasing these exosomes for multiple reasons for them to survive. With chemotherapy, when we're killing these cells, the tumor cells, therefore, there should be less exosome production. And so, my hope is that as a prognostic marker, that we can be able to follow the amount of exosomes that person has in their blood over a period of time to show that those exosomes are being decreased with therapy. Or if, unfortunately, some patients don't respond to therapy, we can be able to pick them up early and say that they're not responding to therapy and then, obviously, change our therapy accordingly. The other part is we're also, at times, identifying markers that shows that there's specific resistance to certain chemotherapy agents, and that would alleviate the fact of using drugs that would potentially cause them heavy like, toxicity and side effects that we can avoid. So, that's the end game is basically decrease morbidity and mortality, to be able to pick up early recurrence in patients, to basically be almost like personalized medicine to treat patients according to them specifically and how they're reacting to what we're doing to them.

Dr. Mike: So, how do you test for the exosomes?

Dr. Samuel: So, in our lab, we have proven that in less than 250ml of blood, which is a tenth of a teaspoon of blood, we're able to identify these exosomes. We've been able to make almost like a magnet with specific proteins that were interested antibodies on them to basically pick up the exosomes that we're interested in. That technique, we're hoping to push forward into further into the microfluidic chip, which one of our collaborators who works at the University of Kansas Lawrence, has developed a microfluidic chip where it uses less than 100mls of blood and it can pick up specific exosomes. Ewing

Sarcoma has a very specific abnormality, or genetic abnormality, where they have a translocation. And we've been able to show that that translocation is also present in these exosomes, too. The hope is that this microfluidic chip not only will be able to detect exosome quantity, but it will also be able to show you that the presence of the translocation and the abundance of the translocation with therapy as you're getting treatment. So, that's a big step to be able to do that.

Dr. Mike: Well, Dr. Samuel, how far away are we from using exosomes in prognosis and in testing for resistance? I mean, I know you're at that research level. When do you see this really coming into oncology clinical practice?

Dr. Samuel: Well, unfortunately, with the state of how things, I mean, just the science in general, we're kind of at the baby step, we're just on the ground floor of where this needs to be. My hope is that we can prove it in the patients that we have here at Children's Mercy and then go on to Children's Oncology Group and show them that there's something that we've seen in our small population that we do see here and that whether it can be used institutionally in various different institutions and then gain enough evidence to show that it's beneficial to all Ewing Sarcoma patients. And then, it can be used potentially as a marker regularly, whether that's going to happen any time soon, that's probably unlikely. But, sometime in the future, that's what I hope.

Dr. Mike: Yea. So, it's a numbers game. You start with a small sample that you're doing at Children's Mercy, then we spread that out to other institutions where we just keep increasing the data, right? We're increasing the database, the number of patients that have seemed to, have shown to have these exosomes, then we can start drawing some conclusions. Unfortunately, it is sometimes, a painfully long process, right?

Dr. Samuel: Yes, it is, unfortunately. I mean, and I think in pediatric oncology, I think our patients and our parents, they want to do as much as they can for their children, obviously, but they also see the big game, and they want to do more for other kids, too. So, I've been fortunate, I mean, I've already accrued 16 Ewing Sarcoma patients, 6 rhabdomyosarcoma patients, and 9 osteosarcoma patients on my study.

Dr. Mike: Okay.

Dr. Samuel: And these are all patients and their children that have volunteered to, basically, whenever they come into the clinic, or when they're diagnosed, they give us the sample of blood, which is purely voluntary, that they're doing this out of their own kindness. So, we have that abundance of samples, which, from other researchers that I've talked to, they've said that this is a very good sample collection that we have because we've collected prior to every single cycle of therapy. So, we have almost close to 200, 300--almost 250 samples of blood.

Dr. Mike: So, let me ask you one more question then about the exosomes themselves. So, we've talked about the potential, right, in prognosis and identifying relapse and resistance, but what about in early detection? Does an exosome come from a tumor that's simply just well-matured and advanced, or is there potential in these being used in the diagnostic workup?

Dr. Samuel: Theoretically, I would see that it could be as a diagnostic workup as well because all the

samples that I've run so far to date, are all prior to any patient starting therapy and we've been able to show those exosomes are prevalent. Every single patient is different, so we have patients who have metastatic disease, we have patients with localized disease, we have patients with a large amount of localized disease, and a small amount of localized disease. So, regardless of size, or shape of tumor, or age of the patient, we've been able to show that. So, potentially as a diagnostic marker. Definitely, hopefully, as a prognostic marker, too, as well.

Dr. Mike: Okay. Well, Dr. Samuel, I want to thank you for the work that you're doing with Children's Mercy and want to wish you the best of luck in the research and I'm pretty confident this is going to work out for you. Also, thank you for coming on the show today. You're listening to Transformational Pediatrics with Children's Mercy Kansas City. For more information, you can go to www.childrensmercy.org. That's www.childrensmercy.org. I'm Dr. Mike Smith. Thanks for listening.