

Bob Barrett: This is the podcast from '*Clinical Chemistry*.' I'm Bob Barrett. Circulating tumor cells can be used both as a diagnostic tool, as the circulating tumor cell count can follow disease progression, and as a treatment tool, since circulating tumor cells can be used to develop personalized therapeutic strategies. To be effective however, circulating tumor cells must be isolated with high purity, yet, without inflicting cellular damage.

In the May 2012 issue of '*Clinical Chemistry*,' Dr. Michael King, an associate professor in the Department of Biomedical Engineering at Cornell University, and his colleagues designed a Microscale flow device that achieves the desired isolation of circulating tumor cells in blood samples, opening the door for personalized cancer treatment.

Dr. King is our guest in this podcast. Doctor, why should we care about circulating tumor cells?

Dr. Michael King: Well, there's currently a great interest in circulating tumor cells as you can see in the literature and in various conferences that have sprung up. Basically, it's accepted now that circulating tumor cell count is a good predictor of patient's survival in many metastatic cancers, in particular, Prostate Cancer and Breast Cancer. By just taking a blood sample, you have access to the primary tumor cells, so this can facilitate a lot of hypothesis-driven research and a personalized medicine.

Bob Barrett: Personalized medicine, we hear a lot about that. Explain what do you mean by that?

Dr. Michael King: Yeah, so there's a little of this going on now. If you can isolate viable, intact CTCs, then you could do things like screen drug response on a patient's own cells to kind of figure out the best treatment regimens on ex-vivo instead of experimenting on the patient. That's the idea.

Bob Barrett: How does your approach differ from previous methods developed to isolate CTCs from blood?

Dr. Michael King: Well, most of the existing methods are based on either using magnetic microparticles, or microfluidic chips that are coated with antibodies against surface markers such as Abcam, and they worked fairly well at isolating Abcam positive cells. What our approach does is a little different in that, you can think of it as a biomimetic approach, because what we're trying to do is re-create the environment in the microcirculation, and basically we get CTCs to stick and roll on selectin proteins, which is via the interaction that occurs in vivo.

- Bob Barrett: Selectins, now those are important in inflammation, right?
- Dr. Michael King: That's right. Selectins, E-selectin, P-selectin are important, they are expressed on inflamed endothelial and they rapidly recruit leukocytes from circulation, and as it turns out, many CTCs express Selectin Ligands as well. And it's believed, as mounting evidence that CTCs actually mimic this interaction of leukocytes and that's how they can get out of the circulation and into a tissue.
- Bob Barrett: Doctor, is there a general consensus about what constitutes a circulating tumor cell?
- Dr. Michael King: Yeah, so this is a highly discussed question and part of the -
- I wouldn't say controversy, but part of the discussion centers around the fact that there is no universal biomarker for circulating tumor cells. Now, probably the most popular marker is Abcam or Epithelial cell adhesion molecule, which is expressed on most, but not all CTCs. People also look at in terms of identification of CTCs to see that the cell is DAPI-positive, has an intact nucleus. Morphology is sometimes considered CTCs, basically, the size of leukocytes and larger other labs look at things like cytokeratin expression, which is expected and another approach is to label for CD45 which is leukocyte marker to exclude those cells from counting, if you will.
- Bob Barrett: What is the role of the nanotubes?
- Dr. Michael King: Yeah, so we've been experimenting with creating thin coatings of nanoparticles or nanotubes and studying cell adhesion to that nanoscale roughness of the surface. So what we found is that when we create a monolayer of hellosite nanotubes and then functionalize that surface with our adhesion proteins, basically we caught the same, roughly the same number of CTCs, but that leukocytes are essentially repelled by that nanostructured surface.
- Bob Barrett: That's interesting. What you mean by repelled?
- Dr. Michael King: Right! So leukocytes can adhere and spread onto smooth surfaces, but the nano particle coatings we've studied and that we used in this particular study, basically there's very weak adhesion and zero spreading of the leukocytes, and so by creating a difference, basically the same amount of CTCs adhesion, but far less leukocyte adhesion, this significantly improved the purity of the CTCs we captured.
- Bob Barrett: Would it be easy for other labs to adopt your technique or would that require a significant investment in time and resources?

Dr. Michael King: Correct! I think that's kind of a beautiful thing about this study is that it basically is completely based on off-the-shelf materials, doesn't require any expensive or specialized equipment, and so this is a technique that research in clinical labs could adopt right away. They basically describe everything in our methodology, and so I think that laboratory technicians for instance, could have this up and running very quickly and so laboratories can do this type of CTC isolation itself to enable their own studies.

Bob Barrett: Well finally doctor, let's look ahead, what would be the next frontiers for this type of research on circulating tumor cells.

Dr. Michael King: Okay, what we see nowadays is labs that are interested in CTCs are using methodologies to identify them. We're now starting to see the emergence of larger scale studies where CTC count or some immunofluorescence characterization, it's not just a novelty, but it's becoming an integral part of new clinical trials. So that's something on horizon, and that's happening now.

The research in my own laboratory, another thing that we have been working on is to actually take it a step further and try to therapeutically target circulating tumor cells in blood stream. And so, we have some very effective technique for this in vitro and we're starting to get really intriguing data from mouse models for the test assistive as well.

Bob Barrett: Dr. Michael King is an associate professor in the Department of Biomedical Engineering at Cornell University. He's been our guest in this broadcast from '*Clinical Chemistry*.'

I'm Bob Barrett, thanks for listening!

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