Clinical Chemistry

Discerning Trends in Multiplex Immunoassay Technology with Potential for Resource-Limited Settings

Bob Barrett: This is the podcast from *'Clinical Chemistry'*. I am Bob Barrett. Innovation and new assay technologies have fueled the growth of the medical diagnostics industry and have provided laboratorians with cutting-edge tools, allowing them to provide state-of-the-art diagnostic information.

However, the transition from the early conceptual stages of technological development to the assay's implementation in a clinical setting may be difficult and lengthy, particularly for those laboratories that do not have the resources to acquire the latest developments.

In a review published in the April 2012 issue of *'Clinical Chemistry,'* Dr. Julian Gordon, a researcher from the Foundation for Innovative New Diagnostics group in Geneva, Switzerland analyzed technology trends that could have applicability to high sensitivity multiplexed immunoassays in resource-limited settings. His findings reveal a stark difference between the potential of new immunoassays and the reality of implementing these techniques in underfunded laboratories.

Dr. Gordon is our guest in this podcast. Doctor, let's talk about your group first: FIND, the Foundation for Innovative New Diagnostics group. What is FIND and how does this kind of review fit in with their interests?

Dr. Julian Gordon: FIND is a foundation in Geneva in Switzerland and they apply diagnostics technology in resource-limited settings so what they do is validating technology and then putting it into clinical trials to show that it really works in the environment that it's meant to go in. They are typically funded by organizations like the Gates Foundation.

Bob Barrett: And doctor, how do you fit in with this organization?

Dr. Julian Gordon: I am a consultant and it's a long distance relationship so I am located in the Chicago area in the US and as I said they are in Geneva in Switzerland. So as a consultant, what I do is if any technology comes up that they might be interested, they draw my attention to it and I provide them with the review and I also help them keep abreast of emerging technologies and try to identify something that might be relevant.

As part of this job, I maintain a database so everything I do is accessible to them and recoverable

and the database will have a checklist of items that I need to consider to see how it fits in with their needs and this is something that is just available for them internally, but it is of value to them if periodically, parts of these gets turned into review article, which is then subject to a refereeing process. So that helps reassure them that it is a useful activity.

Bob Barrett: And how can people in the world of '*Clinical Chemistry'* benefit from this type of review?

Dr. Julian Gordon: Well, it gives you a snapshot of the current state of the art in the area that I've covered and by the way I do it, I try to find publications in areas that may be related to technology or physics areas or technical papers which may not normally come to the attention of people in '*Clinical Chemistry'* area and then when I find them I can try to indicate what the shortcomings might be, since I think when people are publishing work, they get carried away with enthusiasm for their own work, often without even meaning to, they may minimize what might be pitfalls or shortcomings, so I try to explore or understand the area sufficiently well so I can see the bad sides as well as the good sides.

Bob Barrett: Now what is special about the way you have gone about collecting publications to review?

Dr. Julian Gordon: First of all, the sweep is so broad, but it's not realistic to be comprehensive so this is nothing like an annual review. So I start out with known companies in the area or known technologies and typically use the Web of Science database for identifying publications or books or meetings' abstracts and then when I have identified relevant ones, I then see from reading them which papers they cite or who are they cited by.

So I try to pick out highly cited papers and then that X is a catalyst in a way so it's like a human web crawling through branches of networks and I do a lot of judgment calls that something is totally irrelevant from the titles so I won't bother to read it. There is always some fear by doing that, I can be missing something important and the other thing is it's a moving target because it takes a finite time to go through this kind of work and as time progresses, more and more stuff comes out.

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So there was an interesting example in the review article, there is one publication by Petoskey and co-workers and when I had finalized writing the review, that had been cited 344 times. By the time it had been through the editorial process at *'Clinical Chemistry,'* the editor who went through it was very diligent and he was able to update that number.

So between September the 26th last year and January the 3rd this year, the number of citations of that particular article increased from 344 to 432. So that's what I mean by I am looking at a moving target.

Bob Barrette: So doctor, you have already said this can't be a comprehensive review of everything. How do you go about selecting the articles, selecting exactly what you are going to review?

Dr. Julian Gordon: Okay, well, I am trying to look for some unique set of features for any technology and then to see from those features whether there is some pathway for applicability to resource-poor setting. So that it may be stated in the paper itself that that's where they think it can go or I can see from the technology features that that's where it might be suitable.

There was an earlier '*Clinical Chemistry'* paper in this field where they had the acronym ASSURED, that was the technology should be affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, and deliverable, and then added on to that was additional criteria from FIND in Geneva that it should be stable to extremes of temperature and humidity, should be low weight, low waste, and also look at the possibility of being manufactured in a resource-poor setting and the other criteria applies, it has to be potentially run as a multiplex assay.

Bob Barrette: Okay, so doctor, what's the overall conclusion from this work?

Dr. Julian Gordon: Okay well, there wasn't any well-defined conclusion. As I indicated, it's a snapshot and individual conclusions which can be kind of reality checks on certain kinds of work when you look at a prominent publication and trying not to be vindictive, but this highly cited Petoskey paper was in the Proceedings of the National Academy of Science and it looks really incredible. They were able to detect single viruses and looked like fairly simple setup, simple electronics to detect it, but you look at the method section interactive, see how they manufacture it, that they

have not been very diligent and so we try to go back to past publications that there isn't anything that describes in detail, how they manufacture and this involved nanowires, so how they made their nanowires?

Now going forward in a later publication and in a patent, there are descriptions in more details so you can kind of figure it out and the manufacturing is so complex. There are seven separate steps involving some transfer from liquid to solid phase and it's just not obvious how those kinds of steps could be scaled up for large scale manufacturing process.

It took a lot of work to tease that out. So I guess the bottom line is there is no overall conclusion, but I provide pros and cons of separate technologies.

Bob Berrette: Are there any technologies that stand out to you?

Dr. Julian Gordon: Well, first of all, I have no commercial axe to grind. I am not favoring or disfavoring any commercial organization. I am kind of proud that I was one of the original founders of lateral flow immunoassay technology, but I see all the shortcomings of it as well and it's often described as a dipstick, but it's not really a dipstick.

You have to add a sample to the sample well and let it run and wait. So even that, it's somehow not optimal for a totally user-friendly assay, so even if it's referred to as a dipstick sometimes, it's not a true dipstick, and what I am always looking for is a dipstick and the closest you can come to that is an optical technology which uses optical interference.

So if same optical effects is the coatings on sun glasses or interference filters used for cameras so it just has a thin layer of coating which is about the same thickness as the wavelength of the light so you get an interference between the internally reflected light and the incident light which can give color effect.

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So this gives rise to something called White Light Reflectance Spectroscopy and so you see a shift in the spectrum of the white light when the incident and reflected light interfere.

So then when there is a coating on that surface it changes the optical thickness, then it gives a shift in

the spectrum and this can be done without any label and you can directly look at the binding reaction in real time and the company ForteBio has a system called Octet, where they have done this on the tips of optical fibers. So they themselves don't put this out as something that is a low-cost technology for resource-poor settings, but for me, I like it because it is a true dipstick technology.

The limits of sensitivity may be a problem. I think that, I haven't seen anything that really explores the limits of that sensitivity. So that's one that I can say it's my personal favorite.

Bob Barrett: Dr. Julian Gordon is a researcher from the Foundation for Innovative New Diagnostics group in Geneva, Switzerland. He has been our guest in this podcast from *'Clinical Chemistry'*. I'm Bob Barrett, thanks for listening!

Total Duration: 11 Minutes.