Clinical Chemistry

MicroRNA Signature Helps Distinguish Early from Late Biochemical Failure in Prostate Cancer

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Guest:
Dr. George Yousef is from St. Michael's Hospital in Toronto and from the Department of Laboratory Medicine & Pathology at the University of Toronto.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

The elevation in the concentrations of prostate-specific antigen, or PSA, in blood after prostatectomy is the only available marker from monitoring relapse after surgery. This increase in PSA is sometimes called biochemical failure or biochemical relapse. PSA monitoring, however, cannot predict relapse at the time of surgery.

Moreover, it's been shown that biochemical failure does not always correspond with clinical relapse. There is currently no biomarker that can accurately determine the risk of relapse at the time of prostatectomy.

However, a paper in the November 2013 issue of *Clinical Chemistry,* by researchers from Toronto, has shown that measurement of certain MicroRNAs can help to predict biochemical failure risk at the time of prostatectomy. The senior author of that paper is Dr. George Yousef from St. Michael's Hospital in Toronto and from the Department of Laboratory Medicine & Pathology at the University of Toronto. He is our guest in this podcast.

Dr. Yousef, in your paper, you described a MicroRNA signature that can distinguish between early and late biochemical failure in prostate cancer. Can you give us more details on this?

Dr. George Yousef: Well, MicroRNAs are short single-stranded RNA molecules that actually does not code for a protein but rather function by regulating the expression of their target genes. And this manuscript will report for the first item the identification of a number of MicroRNAs that can predict with high accuracy, the chances of biochemical failure after surgery, that's the rising of PSA level in blood after prostatectomy. So by measuring the level of these particular MicroRNAs at the

time of surgery, you will be able to tell the patient the likelihood of disease recurrence within the first three years after removal of prostate. We also show that MicroRNAs are involved in the acquisition of an aggresive behavior in prostate cancer.

Bob Barrett: Doctor, currently physicians rely on serial measurements of PSA in blood at regular intervals after surgery to detect biochemical failure. How different is your discovery and how can this improve patient management?

Dr. George Yousef: Well, our discovery, validated in a larger cohort of patients, can lead to a significant improvement in patient management because in the current system as you correctly said we rely on monitoring PSA levels in the blood at regular intervals after surgery to be able to detect tumor recurrence, but after it happens. But now with this new MicroRNA testing, we should be able to predict with high accuracy the chances of recurrence at the time of removal of the prostate and before the disease recurrence manifests itself as a rising in the PSA level.

Now this can lead us or help us to take some extra measures, for example, adding new adjunct therapy, or providing a closer followup for those patients who are at risk of recurrence and obviously an early action would significantly improve the outcome.

Bob Barrett: Now that's impressive, but wouldn't it be better if you could perform this test before surgery, so that those patients who do not have an aggressive disease, will have a much better chance to avoid unnecessary removal of their prostate?

Dr. George Yousef: Well, that's an excellent question because you hit the right problem. Let me tell you, after introduction of PSA testing years ago, we ran into the problem of over-treatment of prostate cancer, simply many of those patients with prostate cancer have a very tiny tumor with a non-aggressive behavior and this tumor will not kill them in the next 20 or 30 years.

These patients will benefit more from a more conservative line of treatment. For example watchful waiting or active surveillance as compared to surgery which can result in complications and a poor quality of life.

And that's exactly our plan. So in the next phase of this research we will test these MicroRNAs, as a preoperative test before removal of the prostate, in the blood and urine of patients to be able to identify those patients with less aggressive disease who do not really need surgery.

Bob Barrett: Well, that is something to look forward to. Everyone would

like to save many men from unnecessary removal of their prostates. It is clear from recent papers in *Clinical Chemistry* and podcasts that we have done, that a lot of attention is being paid now to MicroRNA research. In your opinion, do you think that MicroRNAs can also be of therapeutic potential?

Dr. George Yousef: Absolutely! The field of MicroRNA-based therapy is recently gaining a lot of attention, for a number of reasons. First, these MicroRNAs are small molecules; that means that they can be easily delivered into different body organs and tissues with minimal toxicity and minimal complications as compared to other larger molecules.

Another interesting advantage, that by altering the level of a single MicroRNA, you can actually simultaneously target multiple biological pathways, thus ensure a much more efficient therapy, and that's why there are now a number of clinical trials that are ongoing for the use of MicroRNAs in therapy, and actually the preliminary results of these trials are very encouraging.

Bob Barrett: Well, that is interesting. We hear about new discoveries everyday, but very few of them are translated into a meaningful clinical application. What's your take on that?

Dr. George Yousef: I totally understand your disappointment, but what people do not realize is that the transition from a research bench into a bedside or clinical application is a long multistep process, that can take up to almost ten years in certain situations, because after the exciting initial discovery, we need to do validation and then we need to do a prospective analysis. And then there are a number of technical issues that have to be taken care of, including, for example, the standardization, quality assurance, setting a normal range, and many other factors that has to be considered before the test is released.

But I still believe that we are moving forward in the right direction and with some patience, we will eventually reap the fruits of these discoveries still slowly, slowly, and one step at a time.

Bob Barrett: Well, finally doctor, can you give us a glimpse of where your research in this field is going in the future?

Dr. George Yousef: Actually, we are now in the new era of amazing advancement in high throughput technology, and we are taking our research into a whole new dimension of what we call integrated genomics.

Now we have the tools and technical abilities to focus on biological processes rather than individual molecules and we

have the ability to also explore the interaction between the different level of genomic and pro-genomic changes. So now we can get the full picture, and I think down the road this would revolutionize our tumor marker discovery and also our therapeutic strategies for prostate and other cancers.

Bob Barrett: Dr. George Yousef is from St. Michael's Hospital in Toronto and from the Department of Laboratory Medicine & Pathology at the University of Toronto. He has been our guest in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening!