Advances in Breast Cancer Diagnostics: Examining Microscaled Proteogenomic Analysis

Announcer:

You're listening to ReachMD, and this episode of *Project Oncology* is sponsored by Lilly. On today's program, we're joined by Dr. Matthew Ellis, who's the Director of the Lester and Sue Smith Breast Center at Baylor College of Medicine. Dr. Ellis is here to share a brief overview of the Microscaled Proteogenomic Analysis method, which is a new tool in breast cancer diagnosis. Here's Dr. Ellis now.

Dr. Ellis:

So, the first thing I want to talk about is the methodology for microscale proteogenomics and really the inspiration for pursuing this type of technology. As someone who's treated breast cancer for long periods of time and anyone in the field would recognize is that breast cancer is enormously heterogeneous collection of malignancies. In other words, it's not one disease. And the struggle that we've always had is to work out essentially what the diagnosis is for each patient, what are the driving molecular features of each cancer, and how can we individually drug those abnormalities.

So, proteogenomics is an approach to this problem. So although in the last decade or so, there's been increasing emphasis on genomics, that is to say DNA-based diagnostics, as well as RNA-based diagnostics in breast cancer with some success. The real question we struggle with is how does each individual corrupted genome encode the driving biology in an individual cancer when that driving biology is not dependent on DNA, that's the hard-wiring, if you'd like in the tumor, it's dependent on protein function and all the complexities of how protein function in modulated through, for example, phosphorylation. And so in a proteogenomics approach, we are able to now extract DNA, RNA, and protein from very small core-needle biopsies and run each anilide through a different pipeline, that is to say standard omics using next generation sequencing, transcriptomics to achieve RNA sequencing, but then for the proteins using mass spectrometry and for both protein quantification, but also for protein phosphorylation. And we're beginning to apply this proteogenomic approach to samples from patients treated in various ways to get new insights into the nature of drug sensitivity and resistance, as well as to identify new therapeutic targets.

So in terms of the future and how we would apply proteogenomic technologies, our current approach is to place proteogenomic technologies into various treatment settings in breast cancer where we can contrast different patient outcomes. And so a very fruitful approach where we definitely need diagnostic advances for, for example triple negative breast cancer. Triple negative breast cancer, as its name implies, is a disease we don't understand very well. It's defined by what it isn't, not what it is. And the second thing about triple negative breast cancer is these are often very aggressive tumors that are only partially effectively treated with chemotherapy and often occur in young women and people with African ancestry. So we really need to understand this disease better.

So the application of microscale proteogenomics that we're working on right now is the take biopsies from patients before they receive neoadjuvant chemotherapy, that is to say, chemotherapy before surgery and then patients either have complete responses to the course of chemotherapy or they don't, and then we're comparing the proteogenomic information between those two groups. And I think that that will lead to some very, very important results into the nature of chemotherapy-resistance or sensitivity. Afterall, if you can diagnosis a triple-negative breast cancer as not being responsive to chemotherapy, you've effectively defined and orphan disease for which there is no adequate therapy and investigational agents in that setting would be the first things you would want to look at, not the sort of last thing which is typically what happens to these patients; they fail lots of drugs and then finally get the experimental drug. Wouldn't it be better to use logical experimental drugs up front? But that requires you to identify the chemotherapy-resistant cases.

And then finally, and in our recent publication in communications, we focus on the issue of HER2 positive breast cancer and how heterogeneous it is and the fact that proteogenomics can pick up cases that are mis-assigned HER2 positive and in fact they are HER2

negative and that can have lots of implications clinically as obviously if the targeted, in fact, is not present, then the patient shouldn't be treated with anti-HER2 drugs.

So I think the future is very promising for proteogenomics and there will be many more studies in the future not just in breast cancer, but also in many other diseases and if you go to the Clinical Proteomic Tumor Analysis Consortium website of the NCI, you will be able to see how many different disease have already been studied with this approach.

Announcer:

This episode of *Project Oncology* was sponsored by Lilly. To revisit any part of this discussion and to access other episodes in this series, visit ReachMD.com/ProjectOncology, where you can Be Part of the Knowledge. Thanks for listening.