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

Traditional methods of prenatal diagnosis of genetic disorders require samples obtained by amniocentesis, or chorionic villus sampling, both invasive procedures that carry a small but clear risk of miscarriage.

The discovery of cell-free fetal nucleic acids in the plasma of pregnant mothers has led to the development of several non-invasive prenatal diagnostic techniques over the past decade. An article published in the August issue of *Clinical Chemistry* reported that the rapid advances in sequencing and related technologies, including size, selection techniques, may enable many novel tools for the study of cell-free nucleic acids, not only for prenatal diagnosis, but also for early cancer diagnosis.

Dr. Stephen Quake is the author of the paper. The Lee Otterson Professor and co-Chair in the Department of Bioengineering at Stanford University, and a Howard Hughes Medical Institute Investigator. He is our guest in this podcast.

Dr. Quake, could you tell us, how you and your team were able to determine the size distribution of fetal DNA?

Dr. Stephen Quake: We used some of the latest next-generation DNA sequencing technology, and in effect what we did was sequenced both ends of each molecule, and then by mapping those, m-sequences back to the reference human genome, we could further distance in between them, and so that gave us a distance measuring for each molecule that we sequenced.

Host: How did you go about determining the balance between enriching the fetal DNA and read loss?

Dr. Stephen Quake: We used the scheme to calibrate the sequencer, so we used lambda phage of the control and we cut it up with the restriction enzyme. So we knew exactly what the size distributions were and by looking at the measured distribution that we got on the output as opposed to the known distribution of size put in the input we were able to work out how much the sequencing process affected the results by biasing for smaller sizes and affecting other properties of the reads.

Host: Part of the expected clinical application of this methodology is to become the first-line test for detection of fetal aneuploidy. How adaptable is this for other applications?

Dr. Stephen Quake: Oh, I think it will be useful for things beyond aneuploidy for sure, looking at deletions, point mutations, perhaps even methylation states so there will be quite a number of other prenatal questions one can ask.

Host: What do you see is the future benefits for this technique or technology, and do you anticipate that it might move into other clinical applications?

Dr. Stephen Quake: Oh, I definitely think we will move in another clinical applications, and we feel that fetal DNA covers more than just pre-natal and more than just aneuploidy detection. People all have used it in area like cancer and organ transplants, and the other work we have done here I think will also apply to those other areas. And I think there will be tremendous diagnostic benefits for patients with questions about all these things: pregnancy, transplant rejection, cancer. It's going to be sort of a new wave of non-invasive diagnostics.

Host: Well, finally what areas of research do you see yourself moving towards over the coming years?

Dr. Stephen Quake: My group's research is going to continue in genomics and exploring applications of the genome and next-generation sequencing technologies in areas as diverse as cancer, immunology, and diagnostics.

Host: Dr. Stephen Quake is the Lee Otterson Professor and co-Chair in the Department of Bioengineering at Stanford University, and a Howard Hughes Medical Institute Investigator.

He has been our guest in this podcast from *Clinical Chemistry*. I am Bob Barrett. Thanks for listening.

Total Duration: 3 Minutes