

## Identifying risks for early onset pre-eclampsia

“Now we are seeing a shift toward prediction and prevention of issues during pregnancy, including early onset pre-eclampsia. As we move forward with increased research in the field, early prediction and prevention will be key factors.”

**Morey Kraus** has served as Chief Scientific Officer of the Diagnostics division of PerkinElmer, Inc. since 2007. He is the scientific founder of ViaCord, PerkinElmer's family cord blood and tissue preservation business. Prior to his work at ViaCord, he was the founder, chairman and chief executive officer of t. Breeders, a cellular therapy company focused on stem cell expansion technologies for clinical transplantation. Morey was a PhD candidate at Worcester Polytechnic Institute in an interdisciplinary Bioprocess Engineering Program combining Chemical Engineering and Biotechnology. Morey has published numerous articles in various peer-reviewed journals on topics ranging from the expansion of umbilical cord blood stem cells for clinical use to the *in vivo* homing of uncultured and selectively amplified cord blood stem cells. In addition, he is the inventor or co-inventor on numerous issued patents.

**Kypros Nicolaides** is Professor of Fetal Medicine, King's College, London, UK. He was born in Cyprus and studied Medicine at Kings. He trained in Obstetrics and Gynecology and specialized in Fetal Medicine. He has carried out extensive research in many aspects of fetal diagnosis and therapy leading to the publication of more than 1200 peer-review papers in scientific journals. He provided training in Fetal Medicine to more than 500 doctors from 50 countries and has supervised more than 50 doctors to undertake research leading to PhDs and MDs. In 1995 he founded the charity Fetal Medicine Foundation, which has donated more than GBP£15 million to promote research and training in Fetal Medicine throughout the world.

**Q** What is your interest in this specific field?

**Morey Kraus:** I am a stem cell biologist by training. My work with newborn stem cells has given me great appreciation for the processes of development from conception, to fetal development, to birth and to newborn health. The health of the pregnancy, mother and baby are often dependent on key factors at each stage of these dynamic processes. Screening mothers early in the pregnancy using biochemical and molecular techniques offers an opportunity for medical professionals to identify problems and apply actionable solutions in an effort to prevent potentially serious adverse outcomes for the mother or baby.

**Q** Nicolaides, as a Professor of Fetal Medicine, and indeed, a world expert in this field, what would you identify as being the main challenges with respect to therapeutic development in this field?

**Kypros Nicolaides:** There are a lot of moving parts that all funnel into preventing, diagnosing and treating pre-eclampsia. The main challenge is accurately identifying the group of individuals that are at high risk of suffering from the disorder and determining how they would benefit from therapeutic intervention. We are also looking to determine what are the most effective time and dose for intervention.



**Morey Kraus**

Author for correspondence:  
PerkinElmer, 940 Winter Street,  
Waltham, MA 02451, USA  
Tel.: +1 781 663 6125  
[morey.kraus@perkinelmer.com](mailto:morey.kraus@perkinelmer.com)



**Kypros Nicolaides**

Fetal Medicine Foundation,  
137 Harley Street, London,  
W1G 6BG, UK

**Q Why is prevention or early diagnosis of pre-eclampsia so important?**

**Kraus:** Early screening and detection of early onset pre-eclampsia provides an expectant mother with options, such as increased monitoring, modified activity, bed rest and medication that can help reduce or avoid complications.

**Nicolaides:** By preventing and diagnosing pre-eclampsia early on in pregnancy, the chances of the baby or the mother being in danger from adverse effects of the condition are greatly reduced. Currently, women are diagnosed late in the pregnancy and doctors are forced to manage the condition without having the ability to modify the course of the disease. In order to move beyond strictly managing the disease, early prediction and prevention are critical.

“We are looking to reduce the rate of pre-eclampsia for all pregnant women and provide insights into key identifiers of early onset pre-eclampsia in women prior to a diagnosis.”

**Q What are the main objectives of the 3-year multinational ASPRE study?**

**Nicolaides:** Overall, the main objectives of the ASPRE study are to screen approximately 35,000 women across Europe to more accurately identify the group of individuals that are at high risk for pre-eclampsia and study the effects of aspirin therapy on those individuals found to be diagnosed with or more susceptible to pre-eclampsia. We are looking to reduce the rate of pre-eclampsia for all pregnant women and provide insights into key identifiers of early onset pre-eclampsia in women prior to a diagnosis. Our hope is that within 2 years, we will have a positive result that will provide us with the support needed for widespread implementation of best practices in prevention and early diagnosis.

**Q How does the study differ from previous studies into the use of low-dose aspirin during pregnancy?**

**Nicolaides:** There are three key differences to keep in mind about the ASPRE study:

- Our method of identifying high-risk individuals is a more effective algorithm that takes into account blood pressure, blood flow from the placenta, the individual’s medical characteristics and other components. Previously, researchers referred to previous instances of pre-eclampsia or high blood pressure to determine the probability of pre-eclampsia in patients. The ASPRE study will employ a much more effective method of screening;

- The dosage of aspirin will be increased to 150 mg while in other studies around the world a more frequently used dosage level is nearly half that level;
- The study will focus on treatment of pre-eclampsia earlier in the pregnancy – at approximately 12 weeks, the stage in which the placenta is developing. Previous studies have routinely begun treatment around 16 weeks which we believe is already too late.

**Q How did PerkinElmer become involved in this study? Can you tell us about the screening kit that they are supplying?**

**Kraus:** We are a global leader in prenatal screening. As the first company to offer a lab service based screen to identify women at risk for severe early onset pre-eclampsia (<34 weeks) during the first trimester in 2013 (the Preeclamp-siaScreen™ | T1 serum screening test), we have been collaborating with key researchers for several years to study this condition – and we hope these efforts will lead to better outcomes. Perkin-Elmer’s PIGF 1–2–3™ screening kit combines first trimester blood test results with ultrasound and blood pressure measurements.

**Q The US FDA has not formally assigned aspirin to its ‘pregnancy category’ but the Gynaecological Association of Europe advocates for its use – can you explain why this is the case?**

**Nicolaides:** Many strategies in obstetrics have been tested in vigorous ways in various parts of the world, leading to the adoption of different treatments in a wide range of countries. Data that we acquire from the ASPRE study will be something that the FDA will hopefully be unable to ignore.

“We hope with the introduction and widespread use of PerkinElmer’s test ... clinicians will be in a better position to avert the devastating consequences of this disease.”

**Q What changes do you hope to see regarding the management of pre-eclampsia as a result of this study?**

**Nicolaides:** What we really want to see happen is have pregnant women around the world see the value in first trimester screening for pre-eclampsia. That way, we will be better suited to identify the high-risk group of individuals and treat them with the most effective dosage of aspirin therapy. Overall, we want to see pre-eclampsia elevated to the level of other conditions that can occur amid pregnancy and provide those affected with an easy and effective treatment.

Q In general, how do you both see the field of fetal medicine & in particular, research in pre-eclampsia, progressing the next 5–10 years?

**Kraus:** We hope with the introduction and widespread use of PerkinElmer's test, which identifies mothers at risk of developing early onset pre-eclampsia, clinicians will be in a better position to avert the devastating consequences of this disease.

**Nicolaides:** As it is today, the field of fetal medicine will continue to evolve. In its early existence, much of the work revolved around ultrasounds and intrauterine interventions for specific medical conditions. Now we are seeing a shift toward prediction and prevention of issues during pregnancy, including early onset pre-eclampsia. As we move forward with increased

research in the field, early prediction and prevention will be key factors.

#### Disclaimer

The opinions expressed in this interview are those of the interviewees and do not necessarily reflect the views of Future Medicine Ltd.

#### Financial & competing interests disclosure

M Kraus is employed by, owns stock in and receives options from PerkinElmer, Inc. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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