Screening marker for early-onset preeclampsia

Hudson researchers have identified a novel biomarker for early-onset preeclampsia that is expressed before other symptoms are visible.

Our team of world-leaders in placental biology and disease have found that expression levels of the cytokine IL11 is higher in women who go on to develop preeclampsia. IL11 has strong potential for incorporation into a novel, early-onset preeclampsia screening test with greatly improved predictive value to those currently available.

Summary

Preeclampsia is the most common medical complication of pregnancy, affecting 5-8% of pregnancies. It is a major cause of fetal and maternal morbidity and mortality.

Preeclampsia can have severe outcomes for mother and baby, and failure to manage or diagnose the disease can be life-threatening. Preeclampsia and associated complications are responsible for approximately 15% of maternal deaths, and up to 20% of the 13 million preterm births worldwide each year.

Characterised by high blood pressure and proteinuria, other symptoms include headaches, abdominal pain, shortness of breath and nausea. Early-onset preeclampsia (before 32 weeks' gestation) is the most severe and difficult to treat form of the disease, affecting 4 per 1000 pregnancies and associated with poor outcomes. As the only current treatment for preeclampsia is delivery of the baby and placenta, either by labour induction or Caesarean section, early-onset preeclampsia can result in very or extremely premature birth.

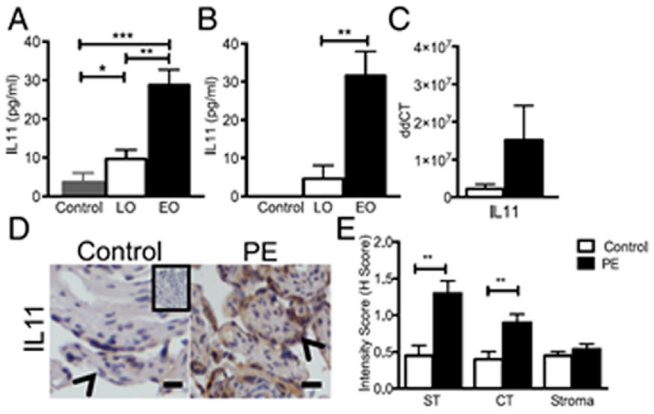
Preeclampsia is challenging to diagnose, yet early detection will help identify pregnancies in which more intensive monitoring or management strategies can be utilised to prevent or reduce the risk of severe disease.

Despite years of research, we still do not have a clear understanding of the underlying causes of preeclampsia. This has hindered the development of better diagnostic or screening tools, and the development of potential therapeutics. Researchers at Hudson Institute have found that the cytokine interleukin-11 (IL11) plays a role in the development of preeclampsia. They have also found that levels of IL11 are elevated in the sera of women before onset of preeclampsia symptoms, and have identified IL11 as a biomarker for disease.

Applications

As well as being one of the most serious complications of pregnancy, early-onset preeclampsia is amongst the most difficult to detect. Currently, diagnosis of preeclampsia relies on the development of hypertension and proteinuria, along with other non-specific symptoms. However, the same combination of symptoms may be common side effects in a healthy pregnancy; they may also be masked by other conditions such as pre-existing high blood pressure or diabetes. Clinical presentation of preeclampsia is highly variable, and may progress suddenly or may progress slowly over weeks. The use of improved biomarkers for early detection of this disease will help identify women at elevated preeclampsia risk, a crucial step in improving outcomes for both mother and baby.

Key data



IL11 was significantly increased in sera from women with early-onset preeclampsia (OE) compared with late-onset preeclampsia (LO) or normal pregnant gestation-matched controls, in samples taken both before (A) and after (B) diagnosis of disease, *p<0.05, ** p<0.01, *** p<0.001. By two other measures, IL11 mRNA levels trended higher in preeclamptic placenta compared to preterm matched control (C), and immunohistological staining revealed a significant increase in IL11 protein levels in preeclamptic placenta samples compared to preterm matched control (D,E), **p<0.01.

Publication

Winship et al. (2015) Interleukin 11 alters placentation and causes preeclampsia features in mice. Proc Natl Acad Sci USA. 112(52):15928-33.

Unmet market need

Preeclampsia is estimated to cost the US healthcare system more than USD2 billion per year in short-term costs, with the incidence of disease increasing in the population over the last three decades. Pre-eclampsia is estimated to affect more than 8 million women worldwide every year, with 70 000 maternal deaths.

Management of preeclampsia is associated with significant healthcare costs, including from the unnecessary admission of women with suspected preeclampsia. In the UK, 38 000 women suffer preeclampsia each year, however, a further 40 000 are admitted to hospital for up to 48 hours' monitoring - but do not suffer the condition. The non-specific symptoms of preeclampsia, and lack of an effective screening test, creates an increased burden on healthcare systems. Improved screening will allow for better patient management, so that low-risk patients can be managed in an outpatient setting while higher-risk patients receive more intensive monitoring and interventions to mitigate complications.

The value of currently available diagnostic tests for preeclampsia is limited by their low positive predictive value, and improved biomarkers are needed to improve their utility. Indeed, currently marketed commercial tests are presently not recommended by the American College of Obstetricians and Gynecologists (Committee Opinion 638, 2015; reaffirmed 2017) due to their modest predictive value. Despite the low positive predictive value, these tests are currently used in other markets as an adjunct to current diagnostic testing as there are no other viable alternatives available. Our team offers a novel and simple biomarker that could improve detection of preeclampsia and improve the cost effectiveness of early-onset preeclampsia screening.

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IP position

PCT/AU2016/050883 filed September 2016 – 'A method of treatment and prophylaxis'.

Development pathway

To date we have demonstrated efficacy in in vitro models, including with human patient samples, and an in vivo murine model. The next stage is to further validate IL11 as a biomarker for preeclampsia screening. Our team have also identified IL11 as a novel therapeutic target for disease, and developed a novel in vivo preeclampsia model for testing potential therapeutics (see separate fact sheets).

They welcome opportunities for co-investment, licensing or collaboration to further develop an IL11-based screening tool or therapeutics for preeclampsia.

Hudson Institute of Medical Research

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- Cancer
- Endocrinology and metabolism
- Fetal, infant and child health
- Immunology and infectious diseases
- Reproductive health and biology
- Women's health

Opportunities for collaboration and partnership

Partnership opportunities include:

- Therapeutics, including oncology and gene therapy
- Reproductive, women's and children's health
- Regenerative medicine
- Infectious disease, inflammation and immunology
- Diagnostics and biomarkers

Hudson can facilitate access to:

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- Platform technologies and clinical trials centre
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Key Indicators

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