A preclinical murine *Phd2* knockout model of early-onset preeclampsia that exhibits clinical signs of the disease

Sinai Health | Lunenfeld-Tanenbaum Research Institute

Quick Facts

Sector
Women's & Infant's Health (Research Tools)

Product
Mouse model of preeclampsia

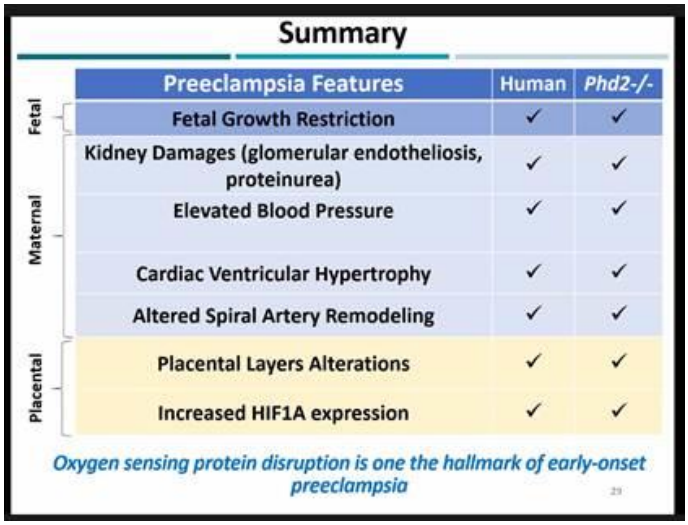
Institution
Sinai Health System and its Lunenfeld-Tanenbaum Research Institute (Toronto, Ontario, Canada)

Principal Investigator/ Developer
Dr. Isabella Caniggia

Contact
Michael Hanna
Sr. Business Development Officer
C. 647.869.9455
hanna@lunenfeld.ca

Opportunity Profile

Researchers at Sinai Health System have developed a murine model of early-onset severe preeclampsia that exhibits all the clinical features of the disease in pregnant mothers: hypertension, renal and myocardial pathology, and proteinuria. Early-onset preeclampsia (E-PE) is more debilitating to the mother and fetus than late-onset preeclampsia (L-PE). E-PE and L-PE are thought to be two distinct disease entities, with E-PE having more severe maternal and fetal outcomes.



To date, there have not been reliable animal models to study preeclampsia due to the different underlying pathophysiological pathways involved in the disease, and the limitations of established animal models. One of the key mechanisms involved in preeclampsia is placental dysfunction and maternal vascular dysfunction. Hypoxia-Inducible Factor (HIF1) is a master regulator of oxygen homeostasis and is essential for placental development.

Several other mouse models have attempted to replicate human E-PE by excess HIF1A (the alpha subunit of HIF) due to the placental hypoxia. While these models recapitulate the pathological aspects of preeclampsia, such as incomplete remodeling of maternal spiral arteries, fetal growth restriction, hypertension, and proteinuria, their limitation is excess of HIF1A throughout the body and in organs other than the placenta.

The mouse model created by removal of *Phd2* in the junctional zone of pregnant mice, results in localized placental excess of HIF1A and exhibits similar placental changes seen in E-PE mice.

Application(s):

- Useful preclinical model of early-onset preeclampsia for preventive and therapeutic studies
- Studies to better understand the pathophysiology and management of preeclampsia

Advantages:

- Excess HIF1A is primarily localized to the placenta resulting in better representation and symptoms of disease
- Reproduces all the clinical features of human early-onset preeclampsia including a return to normal blood pressure postnatally

Commercial Opportunity

- Available for non-exclusive licensing