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Current opinion

The Human Placenta Project: Placental structure, development, and function in real time

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ABSTRACT

Despite its crucial role in the health of both the fetus and the pregnant woman, the placenta is the least understood human organ. Since a growing body of evidence also underscores the importance of placental development in the lifelong health of both mother and offspring, this lack of knowledge about placental structure and function is particularly concerning. Given modern approaches and technologies and the ability to develop new methods, we propose a coordinated “Human Placenta Project”, with the ultimate goal of understanding human placental structure, development, and function in real time.

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The placenta is the least understood human organ and arguably one of the more important, not only for the health of a woman and her fetus during pregnancy but also for the lifelong health of both. Throughout fetal development, the placenta functions both as a unique agent of human symbiosis and as the fetal renal, respiratory, hepatic, gastrointestinal, endocrine, and immune systems. Yet, our understanding of the human placenta is woefully limited.

Placental structure and function affect the health of the mother, as seen in the development of insulin resistance [1] and of pre-eclampsia, gestational hypertension, and eclampsia [2–5]. Placental dysfunction affects the fetus, causing prematurity [6] and fetal growth and neurodevelopmental abnormalities [7]. The concept of “placental origins of adult disease” stem from studies where variations in placental development affect the supply of nutrients to the fetus and the development of systems linked to adult diseases [8,9]. In addition, placental size and shape have been linked to maternal nutrition and the lifespan of men [10,11]. Pregnancy is a “stress test” for lifelong maternal health; placental function may be both a marker and cause of future cardiovascular disease [12–15]. The maternal–fetal–placental unit’s unique ability for tolerance and immunologic acceptance [16–19], coupled with the aggressive invasive growth of the placenta into the decidua, parallels that of cancer cells.

Current significant knowledge gaps in placental biology and medicine reflect inadequate molecular and cellular definitions of placental phenotypes and lack of delineation of the mechanisms by which such phenotypes are associated with fetoplacental disorders, maternal health complications, neonatal diseases, and adult-onset

diseases. This paucity of information is primarily due to limitations in current non-invasive “interrogation” of the placenta. Existing techniques essentially rely on post-delivery examination of the placenta, and typically focus only on molecular and histological investigation. This is akin to relying on postmortem histology alone to understand how the human body functions, and malfunctions, throughout life. That the placenta is the human organ for which animal models have proven least adequate further constrains research [20,21].

Lack of knowledge is the problem. A problem for which we believe a concerted effort, The Human Placenta Project, would make substantial inroads.

It is time to harness modern approaches and technologies – and to develop new ones – to understand human placental structure, development, and function in real time, which would be an ultimate goal of the Human Placenta Project. An early step will be to gather experts who study the placenta – and other creative thinkers who have never previously applied their approaches to the placenta – along with potential funders, to help define the scientific opportunities and approaches, long-term goals, intermediate metrics and deliverables, and timetable of the Project. The *Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health* is currently organizing such a meeting for 2014 and looks forward to partnering with others to support the science that emerges.

Understanding the human placenta would lead to both preventive and therapeutic interventions with lifelong impact. For example, creating new understanding of placental function and novel techniques for monitoring function in vivo could lower rates of preeclampsia and, may lower mothers’ lifelong risks for cardiovascular disease. New understanding and monitoring of placental function could also help to identify pregnancies at increased risk for

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preterm delivery and even lead to decreased rates of prematurity, an important public health need. Placenta-based approaches to prevention of low birthweight could reduce rates of stroke, hypertension, and myocardial infarction when the infants become adults. Recent data indicate that the placenta may play a role in at least promulgating transgenerational effects, which suggests that using better knowledge of the placenta and placenta-based interventions to improve the course of pregnancy might someday even improve the health of multiple generations [22,23].

A growing body of data indicates that placental structural and functional abnormalities can cause numerous adverse pregnancy outcomes. Recent evidence also underscores the importance of placental development in long term health and disease for both mother and offspring. Yet, limited understanding of in vivo human placental development hinders our ability to identify abnormal placental structure or function, predict their impact on maternal and fetal health, or improve clinical decision making. By increasing the understanding of the placenta and the ability to prevent and treat placental abnormalities, we could improve not only pregnancy outcome but also the lifelong health of the child and the mother. The Human Placenta Project should have a historic impact on research and on the health of all who ever have been or will be attached to a human placenta.

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