Clues to ancestral origin of placenta emerge in Stanford study

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Researchers at the Stanford University School of Medicine have uncovered the first clues about the ancient origins of a mother's intricate lifeline to her unborn baby, the placenta, which delivers oxygen and nutrients critical to the baby's health.

The evidence suggests the placenta of humans and other mammals evolved from the much simpler tissue that attached to the inside of eggshells and enabled the embryos of our distant ancestors, the birds and reptiles, to get oxygen.

"The placenta is this amazing, complex structure and it's unique to mammals, but we've had no idea what its evolutionary origins are," said Julie Baker, PhD, assistant professor of genetics. Baker is senior author of the study, which will be published in the May issue of *Genome Research*.

The placenta grows inside the mother's uterus and serves as a way of exchanging gas and nutrients between mother and fetus; it is expelled from the mother's body after the birth of a baby. It is the only organ to develop in adulthood and is the only one with a defined end date, Baker said, making the placenta of interest to people curious about how tissues and organs develop.

Beyond being a biological curiosity, the placenta also plays a role in the health of both the mother and the baby. Some recent research also suggests that the placenta could be a key barrier in preventing or

allowing molecules to pass to the unborn baby that influence the baby's disease risk well into adulthood.

"The placenta seems to be critical for fetal health and maternal heath," Baker said. Despite its major impact, almost nothing was known about how the placenta evolved or how it functions.

Baker and Kirstin Knox, graduate student and the study's first author, began addressing the question of the placenta's evolution by determining which genes are active in cells of the placenta throughout pregnancy in mice.

They found that the placenta develops in two distinct stages. In the first stage, which runs from the beginning of pregnancy through mid-gestation, the placental cells primarily activate genes that mammals have in common with birds and reptiles. This suggests that the placenta initially evolved through repurposing genes the early mammals inherited from their immediate ancestors when they arose more than 120 million years ago.

In the second stage, cells of the mammalian placenta switch to a new wave of species-specific genes. Mice activate newly evolved mouse genes and humans activate human genes.

It makes sense that each animal would need a different set of genes, Baker said. "A pregnant orca has different needs than a mouse and so they had to come up with different hormonal solutions to solve their problems," she said. For example, an elephant's placenta nourishes a single animal for 660 days. A pregnant mouse gestates an average of 12 offspring for 20 days. Clearly, those two pregnancies would require very different placentas.

Baker said these findings are particularly interesting given that cloned

mice are at high risk of dying soon after the placenta's genetic transition takes place. "There's obviously a huge regulatory change that takes place," she said. What's surprising is that despite the dramatic shift taking place in the placenta, the tissue doesn't change in appearance.

Understanding the placenta's origins and function could prove useful. Previous studies suggest the placenta may contribute to triggering the onset of maternal labor, and is suspected to be involved in a maternal condition called pre-eclampsia, which is a leading cause of premature births.

Baker intends to follow up on this work by collaborating with Theo Palmer, PhD, associate professor of neurosurgery; Gill Bejerano, PhD, assistant professor of developmental biology, and Anna Penn, MD, PhD, assistant professor of pediatrics. Together, the group hopes to learn how the placenta protects the growing brain of the unborn baby, a protection that seems to extend into adulthood.

Source: Stanford University