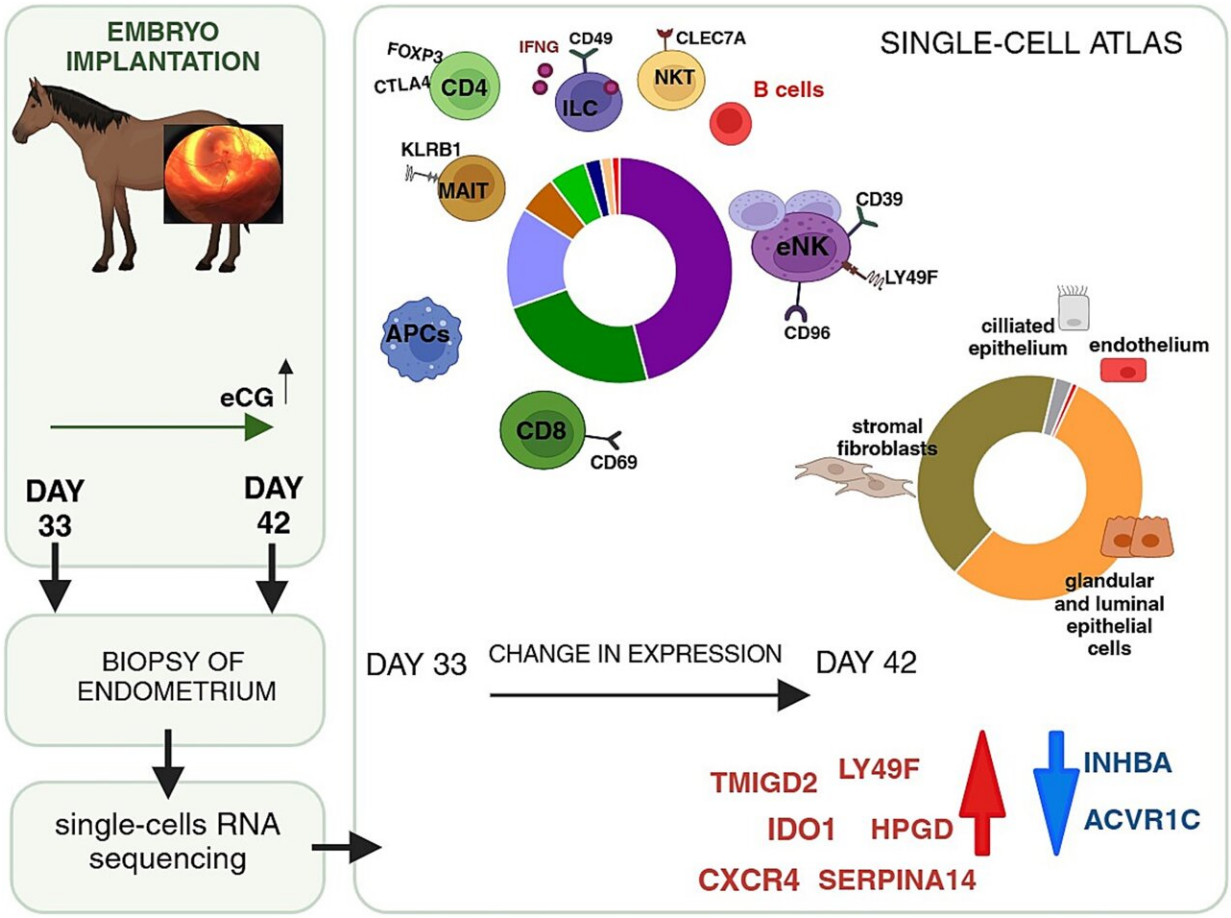
# Cell atlas reveals parallels between horse and human pregnancies

February 17 2025, by Lauren Cahoon Roberts




Graphical Abstract. Credit: *Biology of Reproduction* (2025). DOI: 10.1093/biolre/ioaf004

New research has resulted in the first high-resolution molecular picture

of the equine endometrium—the inner lining of the uterus—before and after embryo implantation. This picture, or cell atlas, highlights key similarities in immune cells between early human and horse pregnancy, a surprise given the vastly different placentas.

Unlike most mammals, implantation of the equine embryo is delayed, occurring roughly 40 days after the egg is fertilized.

"The factors that regulate this late implantation in the mare, and whether they are unique to horses, remain poorly understood," said Mandi de Mestre, the Dorothy Havemeyer McConville Professor in Equine Medicine at the Cornell College of Veterinary Medicine and director of the Baker Institute for Animal Health.

De Mestre is senior author of "Single-cell Atlas of the Pregnant Equine Endometrium Before and After Implantation," which was published in the journal *Biology of Reproduction*. Joanna Jaworska, assistant professor at the Polish Academy of Sciences in Olsztyn, is the first author; among the co-authors is Shebl Salem, a postdoctoral researcher in de Mestre's lab.

To better understand the molecular pathways activated during equine pregnancy, the team used single-cell RNA sequencing to characterize the transcriptome (the library of RNA molecules expressed) of nearly 97,000 individual endometrial cells before and after implantation. This high-tech approach allowed them to identify 40 distinct groups of cells, creating an atlas of what genes are or are not expressed within each individual cell.

This revealed multiple new immune subpopulations active at implantation and allowed them to directly compare each cell type with those present during early human pregnancy.

"Implantation comes with remodeling and complex cellular interactions involving epithelial, stromal and immune cells, as well as glands and blood vessels," de Mestre said. "The molecules regulating this process have been undefined, and we had a unique opportunity to understand the critical events in early equine pregnancy."

The data from the study has been compiled into a detailed atlas of equine pregnancy, enabling future studies to examine which genes may or may not go awry during miscarriage or other fertility issues.

The atlas revealed some unexpected results, including the abundance of cells known as endometrial natural killers (eNK) throughout implantation.

"This was surprising to us, as eNK cells are traditionally associated with highly invasive placentae and had only been described in small numbers in the mare," de Mestre said. "Application of these highly sensitive techniques allowed us to show they actually represent nearly half of all the immune cells in the uterus."

Based on the genes they expressed, the researchers believe these cells may be involved in key adaptions required for a successful pregnancy, such as regulating maternal immune responses to the fetus, facilitating remodeling of the endometrium and protection against viral pathogens.

"We know that these cells are the predominant immune cell present in many other species," de Mestre said, "which means these cells have been evolutionarily conserved and adapted for the pregnant state across all mammals."

With these newly understood similarities between horses and humans, the atlas promises to yield insights into fertility for both species. "The data provides a comprehensive transcriptomic resource for researchers

who are interested in investigating early pregnancy in horses, as well as performing comparative studies in other mammals, including humans," de Mestre said.

High-resolution methods have changed how scientists think about species-specific differences in maternal immunity to the implanting embryo, de Mestre said, and such methods show promise in identifying novel targets that could impact fertility in both horses and humans.

**More information:** Joanna Jaworska et al, Single-cell atlas of the pregnant equine endometrium before and after implantation, *Biology of Reproduction* (2025). DOI: 10.1093/biolre/ioaf004

Provided by Cornell University