Comparative analysis of mouse and human placentae across gestation reveals species-specific regulators of placental development.

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Public Summary:
Mouse and human placenta are very different structurally; in addition, mice do not develop placenta-based diseases as humans do. In order to learn more about what makes the human placenta unique, we did a comparative study of the placenta in the two species, focusing on gene expression changes across gestation. The results showed that the mouse placenta resembles the human placenta during the first half of pregnancy. More significantly, we found that a key gene (called Eomes) that regulates early mouse development is absent in human; instead, we identified a key gene (VGLL1) unique to the human placenta and propose that it likely plays a regulatory role during early placental development.

Scientific Abstract:
An increasing body of evidence points to significant spatio-temporal differences in early placental development between mouse and human, but a detailed comparison of placentae in these two species is missing. We set out to compare placentae from both species across gestation, with a focus on trophoblast progenitor markers. We found that CDX2 and ELF5, but not EOMES, are expressed in early post-implantation trophoblast subpopulations in both species. Genome-wide expression profiling of mouse and human placentae revealed clusters of genes with distinct co-expression patterns across gestation. Overall, there was a closer fit between patterns observed in the placentae when the inter-species comparison was restricted to human placentae through gestational week 16 (thus, excluding full-term samples), suggesting that the developmental timeline in mouse runs parallel to the first half of human placental development. In addition, we identified VGLL1 as a human-specific marker of proliferative cytotrophoblast, where it is co-expressed with the transcription factor TEAD4. As TEAD4 is involved in trophectoderm specification in the mouse, we posit a regulatory role for VGLL1 in early events during human placental development.