

What deer mice can tell us about high-elevation pregnancies and fetal growth

June 14 2023, by Anne Manning



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Biologist Kate Wilsterman is amazed by pregnancy. This essential mammalian life process is both complicated and dynamic: In addition to creating the next generation, pregnancy requires changes in nearly every

organ of the gestational parent; dramatic changes in physiology; and perhaps most impressively, the growth of an entire organ (the placenta) using cells from two different individuals.

That's why Wilsterman, assistant professor in the Department of Biology at Colorado State University, wants to understand how the physiology of pregnancy has evolved and diversified across mammals. In particular, she's interested in species' adaptive strategies for dealing with the effects of [high elevations](#), where oxygen is less abundant. For mammals, including humans that gestate at high elevations, a fetus may be deprived of an adequate supply of oxygen, which is called gestational [hypoxia](#). Gestational hypoxia in humans is linked to low birth weight and birth defects.

In new research published in *Proceedings of the National Academy of Sciences*, Wilsterman and colleagues show that mammals' ability to support [fetal growth](#) is significantly affected by decreased oxygen at high elevations. At the same time, species that have adapted to living at high elevations have differences in their genes that protect against the effects of hypoxia. This adaptation has been observed among some [human populations](#), such as people of Tibetan or Andean ancestry, in which mothers carry added placental protections against the effects of hypoxia on their fetuses.

According to this new research, it turns out humans' distant mammalian cousins, deer [mice](#), are a good model for studying [evolutionary adaptations](#) that offset the effects of hypoxia on fetal and placental development across all mammal species, including humans.

Wilsterman's experiments were conducted in collaboration with Zachary Cheviron and Jeff Good at the University of Montana, while Wilsterman was a postdoctoral researcher at their institution. She joined the CSU faculty in 2022.

Highland and lowland mice

The researchers studied different populations of field mice that live at both high and low elevations. They found that lowland mice suffered stunted fetal growth when exposed to hypoxia, but highland mice were able to prevent the effects of hypoxia on fetal growth by altering their placentas. The study by Wilsterman and co-authors also uncovered genetic changes that were associated with this adaptive strategy.

Evolutionary adaptation to high elevations is well studied in both humans and deer mice, but historically that work has been largely focused on cardiovascular effects, i.e., things related to exercise, Wilsterman explained. The *PNAS* study is a first insight into gestational adaptations in mice.

"Our results suggest that these reproductive changes are an important part of how mammals must adapt to high elevations over evolutionary timescales," she said. "These findings thus highlight an underappreciated set of physiological processes that are involved."

According to Wilsterman, there are deeply conserved processes that contribute to placental development across mammals, and the deer mice they used in their study share some of these gene networks and developmental processes with humans.

"We hope that by understanding placental responses to hypoxia and the developmental effects on fetal growth in deer mice, we can also improve our understanding of human biology," she said. "Specifically, if we can understand how [deer mice](#) have 'solved' the problem of hypoxia for fetal growth, we may eventually be able to identify targets for treatment development in humans or be in a better position to identify where things are going wrong in gestational diseases that involve hypoxia."

Wilsterman's team at CSU will continue their line of inquiry into hypoxia adaptations by drilling down into the cell types that are driving the tissue-level changes they saw. They also hope to identify the genetic variants that contribute to how specific placental [cell types](#) respond to hypoxia.

More information: Kathryn Wilsterman et al, Adaptive structural and functional evolution of the placenta protects fetal growth in high-elevation deer mice, *Proceedings of the National Academy of Sciences* (2023). [DOI: 10.1073/pnas.2218049120](https://doi.org/10.1073/pnas.2218049120)

Provided by Colorado State University

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