Highlight: Our Reptilian Brethren: Mammals and Live-Bearing Lizards Show Similar Pregnancy Mechanisms

Danielle Venton

Corresponding Author: E-mail: danielle.venton@gmail.com.

Accepted: 12 February 2012

It is easy to think that, as mammals, we have cornered the market on innovative parenting. Our name as a group of animals is even taken from the glands that mothers use to feed their young. But while mammals represent the best-known example of vivipary, many other animals have made the same leap. Reptiles have, it seems, a prolific ability to jump from egg laying to live birth. They hold the record for the vertebrate lineage—more than 100 unique transitions—a fact that encourages wonder and, indeed, some humility.

One particular branch of reptiles is the star of the live-birth reptile show. About 20% of the squamate group, which includes about 8,000 species of lizards and snakes, participate in the “miracle of birth” in a range of predelivery styles. Some essentially hang onto eggs till the offspring are ready to hatch. Some squamates develop elaborate placentas to nourish their embryos.

Similarities between the function and shape of mammal and squamate placentas indicate convergent evolution. Until recently, however, researchers have not examined the genetics at play in the background. A study published in Genome Biology and Evolution, conducted by Brandley and colleagues at Yale University (Brandley et al. 2012), throws a spotlight on the prominent genes expressed in the viviparous eyed skink Chalcides ocellatus, giving us a glimpse of what genes were important in the evolution of live birth.

“Live birth is an integral part of what makes us mammals,” Brandley said. “But I knew it was going on in this other group of lizards, and the fact that it was [genetically] unexplored territory was really attractive.”

Using next-generation sequencing, Brandley and colleagues obtained a read out of nearly all expressed messenger RNA in the uterus of a pregnant and the uterus of a nonpregnant lizard. (Brandley chose C. ocellatus because it is one of the few live-bearing lizards available commercially in the United States.) The analysis was relatively simple. They compared the two readouts, also called “transcriptomes,” tallied the mRNAs for all the genes they could identify and determined which genes were expressed at statistically significant levels.

Part of the motivation for the study, says Brandley, was to use this type of sequencing to prove such a study could be done. “We wanted to know if you could ask, ‘When one of these lizards becomes pregnant, what happens?’ This would have taken ages with traditional sequencing and been such a boring process.”

As the placenta develops, the tissue is remodeled to prepare for the babies, in a way similar to mammals. Old tissue is broken down. New growth is promoted. The building up and tearing down expands the uterus and increases the surface area through which the embryo and mother can connect. In this paper, Brandley and colleagues focus on the up-regulation or down-regulation of a few suites of salient genes: remodelers, transporters, immune system influencers, and those affecting estrogen and progesterone. They found many similar patterns to mammals, showing that the outwardly apparent convergent evolution between the groups is reflected genomically. Proteases, for example, enzymes that break down proteins were massively up regulated, or “turned on,” in a similar pattern to mammals. Also, previous studies of physiology have shown that live-bearing lizards can exchange water, ions, and nutrients across the placenta. Their results confirmed the up-regulation of genes involved in those processes. Mammals also up-regulate genes that increase blood flow to the uterus, for example, ensuring the fetus gets enough oxygen.

They found the maternal immune system is down regulated. Part of this immune system tweaking includes dialing down inflammatory promoters. Uterine inflammation is bad for pregnancy. In humans, for example, Intra Uterine Devices prevent pregnancy by keeping the uterus slightly inflamed.

“This is fascinating,” Brandley writes, “because this is the exact same thing that happens in mammals.” Since the fetus expresses a mixture of paternal and maternal genes, there is always a threat that the mom’s immune system will see the fetus as foreign and try to attack it.

In one interesting twist, some genes in mammals are turned off completely depending on whether the animal is pregnant. In lizards, that does not seem to happen. Low levels of all genes seem to be around all the time. This
may reflect a difference between the way mammals and reptiles physiologically recognize pregnancy.

The study has its limits, as Brandley points out. This is a snapshot of just one lizard, not a wide survey. And, in the absence of experimental manipulation, they are making lists and looking for correlations basically. “It’s assumed we’re looking at patterns. I can’t prove that the genes that are up-regulated have a very specific function,” he says. As an added difficulty, the team was able to recognize only 60 percent of the genes they found, because they were using a distant relative as a comparison point. Only one lizard genome, the Carolina anole (Anolis carolinensis) has been sequenced. It and C. ocellatus last shared a common ancestor 175 million years ago. Making it “like using the genome of a platypus to study the gene expression of a human.”

But it is a first look, he says, and it looks very similar to the genetics of mammal pregnancy.

“It’s an open question how convergent phenotypes evolve, and it’s been hard to get at that [genetically],” says Vincent Lynch, an evolutionary biologist, also at Yale, studying the evolution of pregnancies in mammals. “I can’t think of a paper that’s been done in a same way.”

It is not clear if this work will form the basis of applied science, shedding light on genetic causes for human infertility, for example. But similar studies are likely to speak to basic science, illuminating the evolutionary path to pregnancy. “If we were to find many of the same gene transitions across viviparous reptiles,” Brandley says, “then we could say that this is a pretty old pattern, and something similar was probably going in mammals.” And, as animals ever fascinated by our selves and our history, that—at least—would be interesting.

**Literature Cited**

Brandley MC, Young RL, Warren DL, Thompson MB, Wagner GP. 2012. Uterine gene expression in the live-bearing lizard, Chalcides ocellatus, reveals convergence of squamate and mammalian pregnancy mechanisms. Genome Biol Evol. Advance Access published February 14, 2012, doi:10.1093/gbe/evs013.

**Associate editor:** George Zhang