Loss of egg yolk genes in mammals and the origin of lactation and placentation

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The emergence of alternative nourishment resources (lactation and placentation) during mammalian evolution set the stage for mammals' progressive loss of egg yolk nourishment (as a consequence of the loss of egg yolk genes). Credit: Image: Rasmus Kaessmann

If you are reading this, you did not start your life by hatching from an egg. This is one of the many traits that you share with our mammalian relatives. A new paper in this week's *PLoS Biology* explores the genetic changes that led mammals to feed their young via the placenta and with milk, rather then via the egg, and finds that these changes occurred fairly gradually in our evolutionary history. The paper shows that milk-protein

genes arose in a common ancestor of all existing mammalian lineages and preceded the loss of the genes that encoded egg proteins.

There are three living types of mammals: placental mammals (you, me, dogs, sheep, tigers, etc.), marsupial mammals (found in Australasia and South America, including kangaroos and possums), and monotremes (the duck-billed platypus and two species of Echidna).

The reproductive strategies of these three groups are very different. Placental mammals have long pregnancies and complicated placentas that provide nourishment to the embryo, followed by a relatively short period of lactation. Marsupials have a simpler form of placenta and much shorter pregnancies, followed by an extended period where the offspring is fed milk that changes in composition to meet the baby's altering nutritional needs.

Monotremes—once a diverse group, but now restricted both in species number and distribution—have a much more reptilian beginning, as they lay eggs filled with yolk. While they do feed their young with milk, it is secreted onto a patch of skin rather then from a teat. How did these different strategies arise from our reptilian ancestors"

A new paper by David Brawand, Walter Wahli, and Henrik Kaessmann investigates the transition in offspring nutrition by comparing the genes of representatives of these three different mammalian lineages with those of the chicken—an egg-laying, milkless control. The authors found that there are similar genetic regions in all three mammalian lineages, suggesting that the genes for casein (a protein found in milk) arose in the mammalian common ancestor between 200 and 310 million years ago, prior to the evolution of the placenta.

Eggs contain a protein called vitellogenin as a major nutrient source. The authors looked for the genes associated with the production of

vitellogenin, of which there are three in the chicken. They found that while monotremes still have one functional vitellogenin gene, in placental and marsupial mammals, all three have become pseudogenes (regions of the DNA that still closely resemble the functional gene, but which contain a few differences that have effectively turned the gene off). The gene-to-pseudogene transitions happened sequentially for the three genes, with the last one losing functionality 30-70 million years ago.

Therefore, mammals already had milk before they stopped laying eggs. Lactation reduced dependency on the egg as a source of nutrition for developing offspring, and the egg was abandoned completely in the marsupial and placental mammals in favor of the placenta. This meant that the genes associated with egg production gradually mutated, becoming pseudogenes, without affecting the fitness of the mammalian lineages.

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