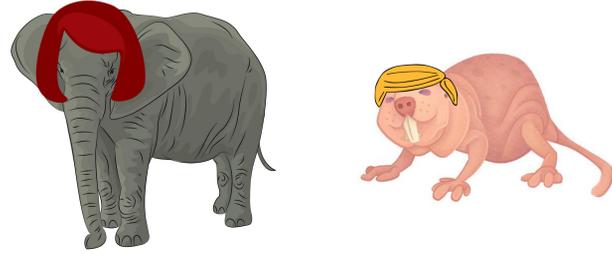




Reduced hair quantity is accompanied by convergent evolutionary rate acceleration in relevant genes and conserved noncoding elements across the mammalian phylogeny

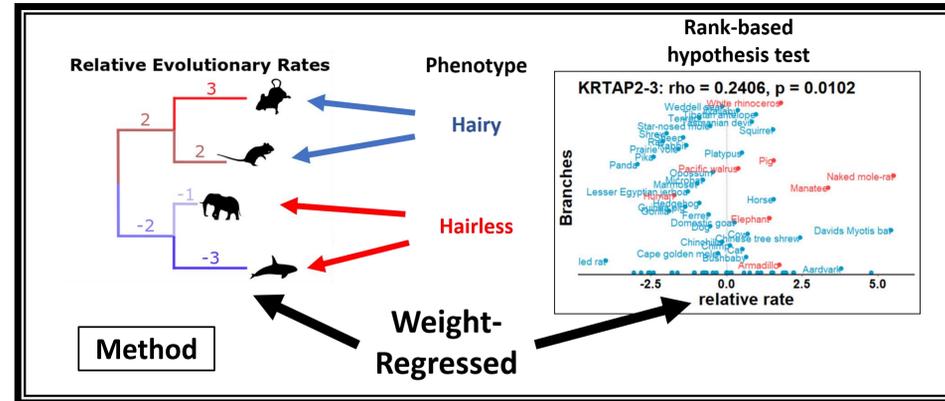


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Body hair is a defining characteristic of mammals, and as such, all mammal species have some hair during at least one stage of development. However, several mammal species, including elephants, rhinos, naked mole-rats, and whales, have notably lower body hair density and coverage than traditional “furry” mammals. Despite lacking fur, such mammals tend to retain thick vibrissae, or sensory hairs, which implies that the species have the genetic capability to grow some hair. Further complicating the study of reduced hair quantity are complementary skin changes that accompany hair loss, many of which are controlled by the same pleiotropic genes.

Here, we investigate the genetic basis of hairlessness in mammals using **RERconverge**, an evolutionary rates-based method to find genetic elements evolving at significantly different rates in hairless mammals compared to non-hairless mammals. We regress out species weight to remove body size as a confounding factor, and additionally we perform Bayes factor analyses to investigate the contribution of the marine phenotype versus the hairlessness phenotype to signals in the data as important methodological improvements.

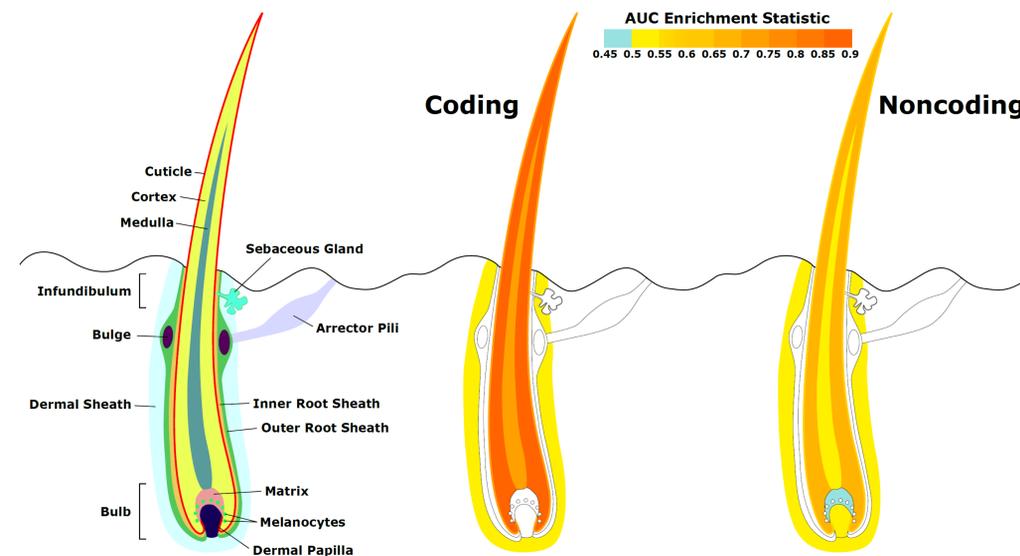
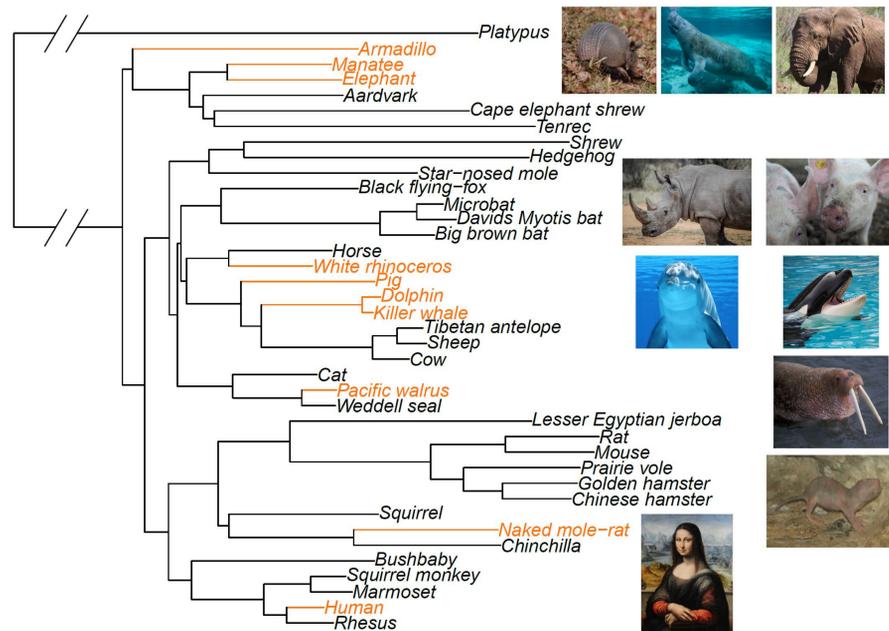


In **coding sequence**, we find that pathways related to hair **texture** evolve faster in hairless species. Signal-driving genes include **HR, FOXN1, KRTs, and KRTAPs** known to be associated with hair and skin. We also successfully detected that for some genes (such as HR and FOXN1) the hairlessness phenotype more significantly contributes to rate shifts than the marine phenotype, thus disentangling the two heavily-confounded traits. Our top-ranked gene after multi-faceted filtering is **FGF11**, a gene with unknown function that is a strong candidate for hair growth-related functionality.

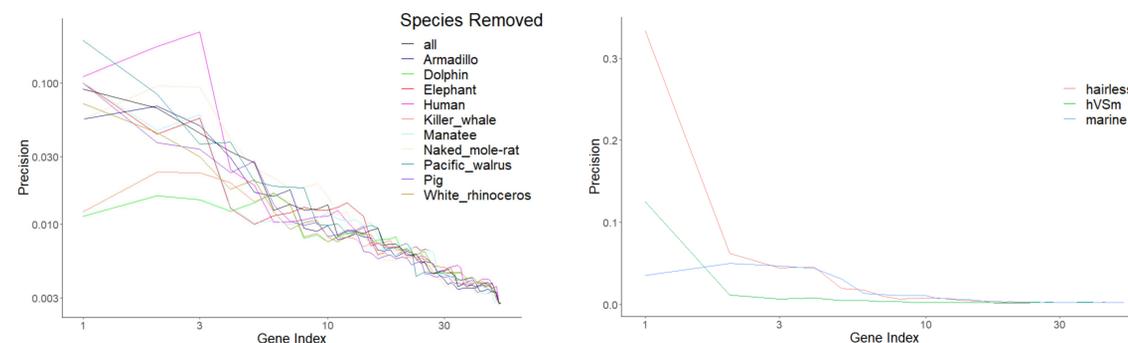
In **noncoding sequence**, we find enrichment for quickly-evolving noncoding regions near **MIR205**, a microRNA known to be associated with hair growth and skin development. Interestingly, MIR205HG sequence itself does not show significant rate shifts, which supports the assumption that evolution of hairless proceeds through changes in coding and noncoding sequence working in tandem. Additionally, noncoding regions near genes associated with the dermal papilla and the hair matrix experience evolutionary rate shifts, indicating potentially altered functionality of those essential hair growth regions.

Our Dataset:

- Mammalian phylogeny (modified from Meredith *et al.* 2011) with 62 species
- 19,149 protein-coding genes
- 343,598 PhastCons conserved non-coding regions



Noncoding regions near dermal papilla and hair matrix genes experience evolutionary rate shifts in hairless species, but their related genes do not.



Coding genes related to hair texture evolve faster in hairless species (left), an enrichment that is robust to single-species removal. Bayes Factor analyses reveal that signal is driven more strongly by the hairless phenotype than by the marine phenotype (right).

MicroRNAs with nearby noncoding regions that evolve quickly in hairless mammals.

Top-Ranked MicroRNAs		
Name	Statistic	q-value
MIR205	0.238	8.58e-10
MIR1305	0.162	1.09e-6
MIR924	0.178	6.80e-6
MIR124-1	0.218	2.44e-5
MIR346	0.283	2.44e-5
MIR759	0.152	8.29e-5

Conclusions

Complementary changes to coding and noncoding sequence allow for the evolution of hairlessness

- **Coding sequence:** changes to hair-specific texture-related genes and pathways
- **Noncoding sequence:** changes near microRNAs and genes related to hair proliferation

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A subset of the phylogeny used for analysis. Names of mammals classified as “hairless” are listed in orange.