Genetic basis for the evolution of hair discovered in the clawed frog

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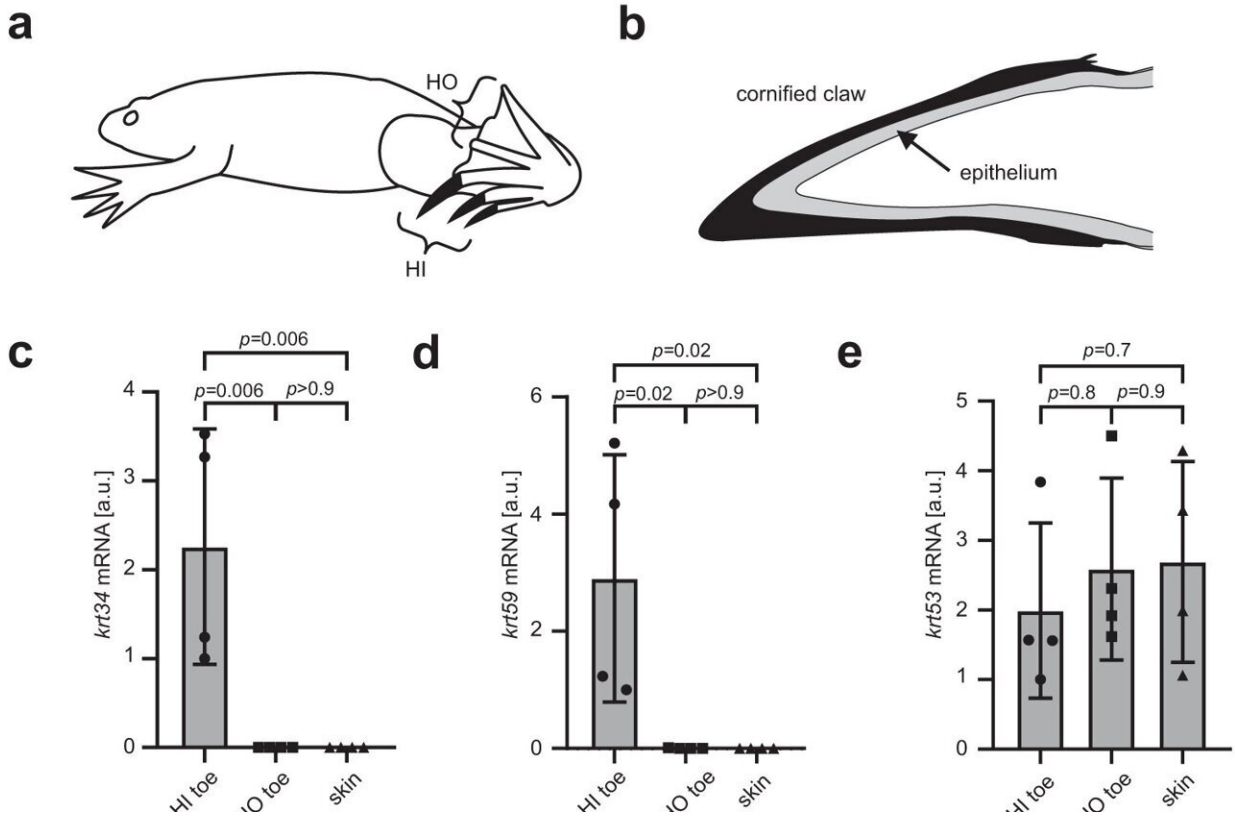

Expression of hair keratin homologs of Xenopus tropicalis is associated with cornified claws. **a** Schematic depiction of a clawed frog (*X. tropicalis*) bearing cornified claws on the hindlimb inner (HI) toes (toes I, II, III) and no claws on the hindlimb outer (HO) toes (toes IV, V) and on toes of the forelimbs. **b** Schematic of a frog clawed toe tip. The term "claw" refers to the cornified claw that is formed by the differentiation of the epithelium on the tip of the toe. **c–e** Quantitative RT-PCR analysis of mRNA expression of *krt34* (**c**), *krt59* (**d**), *krt53* (**e**) relative to the housekeeping gene, *eef1a1*. Mass-spectrometric quantification

of Krt34 (**f**), Krt59 (**g**) and Krt53 (**h**). a.u., arbitrary units. RNA and protein were sampled at an age of 7 months. Statistics was calculated by one-way ANOVA for $n = 4$ (**c**–**e**) and three (**f**–**h**) biological replicates, respectively, in each of 3 groups. Bars and error bars indicate means and standard deviations, respectively. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-46373-x

The development of hair was of central importance for the evolution of mammals and, thus, also of humans. However, the evolutionary origin of the genetic program of hair was previously unknown. An international research team led by Leopold Eckhart from MedUni Vienna has now been able to show that important hair components and their genetic control have already evolved in amphibians.

Human hair, therefore, shows unexpected similarities to the claws of clawed frogs. The results were published in *Nature Communications*.

In order to investigate the evolution of skin appendages, which include human hair and nails, the MedUni Vienna research team, in collaboration with the University of Ghent (Belgium), used the tropical clawed frog (Xenopus tropicalis) as an experimental model.

The study revealed that the cornified claws of Xenopus frogs consist of special proteins (keratins) that are very similar to the main components of mammalian hair and nails. The formation of these keratins was found to be controlled by a specific gene, Hoxc13, in both humans and frogs.

"It is known that patients with mutations in the Hoxc13 gene have defects in the growth of hair and nails. In our study, we were able to block the formation of claws in the clawed frog by switching off this gene," reports Leopold Eckhart from MedUni Vienna's Department of

Dermatology. These results indicate that the genetic program for the development of keratinized claws originated in a common ancestor of humans and frogs.

"During the evolution of mammals, the program of claw formation was modified for the development of hair," says Eckhart.

Important research question clarified

The evolution of terrestrial vertebrates is characterized by the appearance of an effective skin barrier against water loss in a dry environment and by the development of hard, keratinized skin appendages such as claws, scales, feathers, and hair, which are crucial for catching prey, protection, supporting special types of locomotion and thermal insulation.

The evolution of skin appendages is, therefore, an important research question. The findings from the project contribute to clarifying the evolutionary origin of keratinized skin appendages and also help to understand the regulation of hair in humans better. "Our publication will stimulate further exciting studies in basic and preclinical research," concludes Eckhart.

More information: Marjolein Carron et al, Evolutionary origin of Hoxc13-dependent skin appendages in amphibians, *Nature Communications* (2024). DOI: 10.1038/s41467-024-46373-x

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