UNIVERSITÉ DE GENÈVE

PRESS RELEASE

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How mammary glands appeared in the course of evolution

A joint team of geneticists from the University of Geneva (UNIGE) and the Swiss Federal Institute of Technology in Lausanne (EPFL), Switzerland, demonstrated that the emergence of mammary glands in placental mammals and marsupials results from recycling certain 'architect' genes. The latter, known as *Hox* genes, are responsible for coordinating the formation of the organs and limbs during the embryonic stage. Such genes are controlled by complex regulatory networks. In the course of evolution, parts of these networks were reused to produce different functions. Architect genes were thus requisitioned to form the mammary bud and, later, for gestation. This team's work has been published in the journal *PNAS*.

Giant ant-eater © Malene Thyssen

Giant kangaroo © Fir0002/Flagstaffotos

Platypus © Stefan Kraft

The DNA sequence called MBRE is present in placentals (upper) and in marsupials (middle), but is not present in those mammals that lay eggs (lower).

An ubiquitous regulatory module

The group led by Denis Duboule, a geneticist at UNIGE and EPFL, is interested in the mechanisms involved in the appearance of mammary glands. As the professor notes, 'We observed that certain architect genes are at work during the development of the mammary bud in mice, and we wanted to understand how and why'.

The research team had previously identified a section of DNA adjacent to the *HoxD* gene cluster, which formed a particular 3D structure in order to interact with and activate certain *Hox* genes. 'We established that this particular DNA sequence adopts the same three-dimensional structure in tissues as diverse as those destined to become arms, intestines or mammary glands', says Leonardo Beccari, a member of the Geneva team and the project leader.

This does not concern the platypus

The three-dimensional conformation of this DNA is identical to that of other organs but we still had to understand what characterised the regulatory mechanism for the *Hox* genes in the mammary bud, which appeared later in the evolutionary cycle. 'We discovered the existence of a short DNA sequence capable of activating a specific *Hox* gene, and which is present only in placental mammals and marsupials', explains Ruben Schep, the first author of the article. Indeed, mammals that lay eggs, such as the platypus, do not have this sequence.

This short DNA sequence, called MBRE, was only able to carry out its function because it appeared in a region of this three-dimensional DNA where there was already a contact with genes from the *HoxD* group. Control of these genes' expression in the mammary bud has thus evolved thanks to the hijacking of this pre-existing regulatory module, thereby explaining the later arrival of such a structure, and thus of the placental mammals and the marsupials .

contact

Denis Duboule
+41 22 379 67 71/ +41 21 693 83 38
Denis.Duboule@unige.ch
Denis.Duboule@epfl.ch

UNIVERSITÉ DE GENÈVE
Service de communication
24 rue du Général-Dufour
CH-1211 Genève 4

Tél. 022 379 77 17

media@unige.ch
www.unige.ch