Press release

To the media

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Our body plan contains instructions in filigree

Prof. Denis Duboule's team discovers that architect genes are modulated by epigenetic mechanisms, in Switzerland

Architect genes are essential for coordinating body patterning during embryonic development. Research projects led by Denis Duboule during the last twenty years have shed light on how these tiny conductors direct construction operations. Until now, the processes modulating these genes themselves remained an enigma. The professor and his collaborator Natalia Soshnikova provide now key answers in the 5th June 2009 edition of *Science* magazine. Their study demonstrates that architect gene expression is influences by epigenetic mechanisms that modify DNA without affecting its sequence. These processes are reversed as these genes become successively mobilised.

How can genes spread over different chromosomes coordinate the formation of our limbs during embryonic life, assigning to each of them a precise location in the body? This question has been driving for two decades the research of Denis Duboule, geneticist at the University of Geneva and the School of Life Sciences, Federal Institute of Technology, in Switzerland. The professor's team has namely discovered in mammals the existence of a family of "architect genes", named *Hox*.

The 39 *Hox* genes ensure the smooth progress of construction operations, each of them giving a precise instruction at a given time during our development. The scientist has shown that architect genes are aligned on our chromosomes in the order of appearance of the structures: first the elements of the shoulder, followed by those of the arm, the forearm and then the fingers.

Reversible modifications...

Laid-out in small groups of ten, architect genes are placed in the order in which they are expressed. "However, not much was known about the mechanisms involved in the sequential activation of these genes, in order to ensure a perfect synchronisation of the operations", points out Natalia Soshnikova, member of his group and of the National Centre of Competence in Research *Frontiers in Genetics*. A thorough and lengthy work done by the scientist provides now key answers: "*Hox* genes are blocked by biochemical modifications named methylations very early during mouse development".

... that constitute a metronome
These modifications are termed “epigenetic” because they do not induce a change in DNA sequence *per se*. The inhibitory molecules act more like a signal, a kind of molecular switch. Their function is to ensure that all of the architect genes do not become activated at the same time, in a chaotic way. “Our study also demonstrates that this suppression is reversible. The tiny obstacles will be removed progressively, from one end of the group of genes to the other, with a precise timing”, the researcher explains. *Hox* genes will thus be ready for their activation in a successive fashion, ensuring a harmonious development of the body structures.

The project done by the two biologists emphasizes the importance of epigenetic mechanisms in the precise control of the modulation of certain genes. These processes, unveiled only a few years ago, are recognized as being more important with time. “Moreover, our results suggest that, in certain cases, the linearity of this big DNA molecule that constitutes our chromosomes could by used, somehow, as a measure of the time necessary for the smooth progress of our genetic program”, concludes Denis Duboule

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