First sex determining genes appeared in mammals 180 million years ago

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The Y chromosome, which distinguishes males from females at the genetic level, appeared some 180 million years ago. It originated twice independently in all mammals. The team of professor Henrik Kaessmann at the Center for Integrative Genomics and the SIB Swiss Institute of Bioinformatics managed to date these events that are crucial for both mammalian evolution and our lives, because the Y chromosome determines whether we are born as a boy or girl. The results of this research have just been published in *Nature*.

Man or woman? Male or female? In humans and other mammals, the difference between sexes depends on one single element of the genome: the Y chromosome. It is present only in males, where the two sexual chromosomes are X and Y, whereas women have two X chromosomes. Thus, the Y is ultimately responsible for all the morphological and physiological differences between males and females.

But this has not always been the case. A very long time ago, the X and Y were identical, until the Y started to differentiate from the X in males. It then progressively shrank to such an extent that, nowadays, it only contains about 20 genes (the X carries more than one thousand genes). When did the Y originate and which genes have been kept? The answer has just been brought to light by the team of Henrik Kaessmann, Associate Professor at the CIG (UNIL) and group leader at the SIB Swiss Institute of Bioinformatics, and their collaborators in Australia. They have established that the first "sex genes" appeared concomitantly in mammals around 180 million years ago.

4,3 billion genetic sequences

By studying samples from several male tissues – in particular testicles – from different species, the researchers recovered the Y chromosome genes from the three major mammalian lineages: placentals (which include humans, apes, rodents and elephants), marsupials (such as opossums and kangaroos) and monotremes (egg-laying mammals, such as the platypus and the echidna, a kind of Australian porcupine). In total, the researchers worked with samples from 15 different mammals, representing these three lineages, as well as the chicken, which they included for comparison.

Instead of sequencing all Y chromosomes, which would have been a "colossal task" according to Diego Cortez, researcher at CIG and SIB and main author of the study, the scientists "opted for a shortcut". By comparing genetic sequences from male and female tissues, they eliminated all sequences common to both sexes in order to keep only those sequences corresponding to the Y chromosome. By doing so, they established the largest gene atlas of this " male " chromosome to date.

This study required more than 29,500 computing hours! A gigantic task, which could not have been performed without important technical means: the high-throughput DNA sequencers of the genomics platform at the Center for Integrative Genomics, for the generation of the genetic sequences, and the calculation means of Vital-IT, SIB's high-performance computing centre, for the biological analyses.

Two independent sex-determining genes

The study shows that the same sex-determining gene, named SRY, in placentals and marsupials had formed in the common ancestor of both lineages around 180 million years ago. Another gene, AMHY, is

responsible for the emergence of Y chromosomes in monotremes and appeared some 175 million years ago. Both genes, which according to Henrik Kaessmann are "involved in testicular development", have thus emerged "nearly at the same time but in a totally independent way."

The nature of the sex-determination system present in the common ancestor of all mammals remains unclear, given that mammalian Y chromosomes did not yet exist at that time - at least not those discovered in this study. So what triggered back then that an individual was born male or female? Was this determination linked to other sex chromosomes, or even environmental factors such as the temperature? The latter is not an unreasonable scenario, given that temperature determines sex in present-day crocodiles. As far as mammals are concerned, "the question remains open," concludes Diego Cortez.

More information: Origins and functional evolution of Y chromosomes across mammals, *Nature*, dx.doi.org/10.1038/nature13151

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