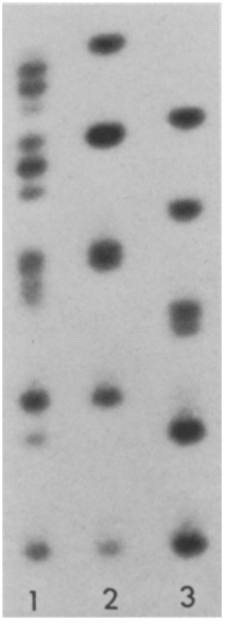
des mâles F1 n'a abouti. De même, nous n'avons jamais obtenu d'hybride de F2, ceci suggérant la possibilité d'une stérilité mâle chez les hybrides F1. Nous n'avons pas essayé de croiser les femelles F1 avec des mâles *M. spretus*.

Analyse des hybrides. Nous avons vérifié par électrophorèse que les hybrides de F1 étaient hétérozygotes aux locus différemment fixés dans les 2 espèces parentales, soit: *Ldh-B, Alb-1, Es-1, Adh-1* (figure).



Zymogrammes de la lactate-deshydrogénase (LDH) d'un hybride (1), de *Mus musculus* (2) et de *Mus spretus* (3).

Conclusion. En laboratoire, *Mus musculus* et *Mus spretus* donnent des hybrides de F1 parfaitement viables. De tels hybrides n'ont jamais été trouvés dans la nature, même dans les habitats où les 2 espèces cohabitent de façon permanente. Mais comme au moins les femelles de F1 sont pleinement fertiles, il y a une possibilité théorique d'introgression. Cependant les 2 espèces ont fixé à plusieurs locus des allèles différents, montrant par là que cette introgression ne se fait pas dans la nature, et laissant supposer l'existence de puissants mécanismes précopulatoires d'isolement reproductif basés sur des différences éthologiques ou physiologiques qu'il reste à étudier. La facilité avec laquelle les femelles hybrides de F1 ont été croisées par retour avec *Mus musculus* nous donne la possibilité d'introduire artificiellement dans des souches de laboratoire des allèles propres à *Mus spretus*. Ces nouveaux marqueurs peuvent être précieux pour certains travaux expérimentaux.

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Satellite DNAs in eukaryotes: a non-adaptive mechanism of speciation which originated with sexual reproduction?[1]

G. Corneo

Centro di Studi di Patologia Molecolare, Via Pace 15, I-20122 Milano (Italy), 20 January 1978

Summary. Satellite DNAs may have originated during evolution at the same time as sexual reproduction in order to suppress crossingover between the 2 heterogametic sex chromosomes, and may have acquired a function of sterility barriers in hybrid species during evolution. This origin of satellite DNAs appears to be reflected in different stages of speciation: partial and total heterogametic sex hybrid sterility and full hybrid sterility might correspond to subspecies, semispecies and full species.

The function of satellite DNAs and other repeated DNAs in eukaryotic genomes is puzzling. It has been suggested that they may have an evolutionary role[2-4]. The highly repeated satellite DNAs constitute long blocks of DNA clustered in restricted, mainly heterochromatic regions of the chromosomes, while other middle repeated nucleotide sequences are interspersed along the genome. Satellite DNAs are not transcribed 'in vivo', while the other repeated sequences might be transcribed but not translated into proteins. One of their main characteristics is to accumulate mutations: the single repeated units of which a satellite DNA is made up are similar, but not exactly identical. Since mutations occur randomly in any section of the genome, satellite DNAs accumulate mutations because they are not, or are less submitted to pressure by natural selection than the non-repeated sequences of the genome. Most mutations which occur within structural genes are eliminated by natural selection, while those occurring in satellite DNAs are neutral with regard to natural selection and therefore are accumulated.

Another observation which might throw some light on the function of satellite DNAs is the moment of the appearance of repeated nucleotide sequences during evolution. They are absent in prokaryotes and appear in the simplest eukaryotes at the same time as chromosomes and sexual reproduction. In a previous publication[5], it has been proposed that satellite DNAs function as sterility barriers in hybrid species. Therefore they could be responsible for hybrid sterility, hindering the pairing of homologous chromosomes in meiosis. According to this hypothesis, satellite DNAs constitute a mechanism of reproductive isolation, and therefore of speciation, independent of natural selection.

Another noteworthy point is the relationship between satellite DNAs and chromosomal structure and organization[2]. The distribution of repeated sequences along the chromosomes and the interaction between repeated DNAs with a specific molecular conformation and chromosomal proteins might be important factors in determining chromosome conformation. This latter has a relevant function in homol-

ogous chromosome pairing in meiosis. For this reason satellite DNAs might be conserved within a species as important hereditary factors. Satellite DNAs are conserved in the amount typical of a given species in the germ cells. In other actively replicating tissues, satellite DNAs may be underreplicated compared with the remaining sectors of the genome. This occurs in the giant chromosomes of the salivary glands of some Diptera[6]. An important mechanism to conserve satellite DNAs within a species might be that individuals with too widely different satellite sequences from the average give rise to sterile progeny. In meiosis of such progeny, homologous chromosome pairing would be hindered by the too wide difference between the satellite sequences of the parents. This mechanism could explain some cases of genetic sterility in the human species[5].

With regard to the contemporary appearance of satellite DNAs and sexual reproduction during evolution, a causal relation between them could be proposed. There are a few elements in favour of this hypothesis. In fact the chromosomal determination of sex depends on the presence of different genes on each sex chromosome. The crossingover between the 2 heterogametic sex chromosomes had to be suppressed during meiosis, to keep the different genes of the 2 sex chromosomes separate. This is an essential condition for the gradual differentiation of the 2 sexes[7]. This might have happened through the appearance of different satellite sequences making up the heterochromatic portions of the 2 sex chromosomes. In particular the heterogametic sex chromosome, that is the W chromosome in bird and reptile females and the Y chromosome in males of other animal orders, might contain an additional or more satellite DNA, not contained in the DNA of the other sex. This has been confirmed in a reptile species[7]. Furthermore, repeated nucleotide sequences specific to the male and absent in the female have been demonstrated in the human genome[8,9]. From this primitive function of satellite DNAs in sex chromosomes, a function of hindering the meiotic pairing of non-sexual chromosomes in the meiosis of hybrids of 2 different species might have evolved subsequently by translocation of satellite sequences from sex chromosomes to autosomes. When satellite DNAs in 2 distinct populations of a species have become so different that the pairing of the homologous chromosomes is hindered, the hybrid species obtained is sterile. The lack of chromosome pairing leads to a meiotic non-disjunction of chromosome pairs and then to hybrid sterility, and the non-pairing of homologous chromosomes and the subsequent meiotic non-disjunction may occur at the level of sex chromosomes or of autosomes. It appears likely that in the initial phases of speciation the most conspicuous differences in satellite sequences in individuals of opposite sex of the 2 distinct populations are in the sex chromosomes. In this case the function of sterility barriers of satellite DNAs would be in a very initial phase. The satellite DNAs located on the autosomes of the 2 populations from which the hybrid was born would not yet be sufficiently differentiated to constitute an efficient sterility barrier. On the other hand, the satellite DNA present on the heterogametic sex chromosome could, due to its initial diversity, have become sufficiently different from the satellite DNA of the other sex chromosome to constitute a more or less efficient sterility barrier. This happens, for example, in the hybrids between different subspecies of *Drosophila*[10] in which the heterogametic male hybrids are more or less sterile, while the non-heterogametic female hybrids are fertile. This example could be an indication that the satellite DNA function of differentiation between sexes could develop into a function of differentiation between new species.

As shown in the table, the evolution of satellite DNAs in local populations might give rise to different and consecutive stages of speciation, by a different extent of interspecific hybrid sterility. The first 2 stages would depend respectively on partial and total differences in satellite sequences in the 2 different sex chromosomes of the heterogametic hybrid, and would result in partial or total heterogametic sex hybrid sterility, while homogametic sex hybrids are fertile. These 2 stages could correspond respectively to subspecies and semispecies[10]. In these 1st and 2nd stages of speciation during evolution, the more conspicuous difference between satellite sequences in the 2 different sex chromosomes of the heterogametic hybrid than in the autosomes would be due to the initial difference between satellite DNAs of the 2 different sex chromosomes of the same species. The 3rd stage of speciation with differences of satellite sequences in the autosomes and complete hybrid sterility would correspond to full species. This mechanism of speciation depending on hybrid sterility is post-gametic. Obviously other pregametic mechanisms of speciation might develop independently of this mechanism and give rise to sexual isolation.

Vestiges of the above-mentioned genetic mechanisms of speciation might appear in pathological conditions in the human species. Differences in the satellite sequences in sex chromosomes could determine unpairing and consequent meiotic non-disjunction of sex chromosomes in human male meiosis. Individuals with this anomaly could generate a Klinefelter syndrome (XXY) or a Turner syndrome (XO) due to non-disjunction in the 1st meiotic division. In cases of satellite sequence differences in the autosomes of the 2 parents, there could be cases of trisomy, such as trisomy 21, or sterility.

Satellite DNAs, sterility barriers and speciation

Stage of speciation	Hybrid sterility	Satellite DNAs
1st stage: subspecies	Partial heterogametic sex hybrid sterility (i.e. in different percentage of cases)	Partial difference in satellite sequences of heterogametic sex chromosome
2nd stage: semispecies	Total (100%) heterogametic sex hybrid sterility	Complete difference in satellite sequences of heterogametic sex chromosome
3rd stage: full species	Homogametic sex hybrid sterility	Differences in satellite sequences of homogametic sex chromosome and autosomes

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