DECODING ROBERTSONIAN TRANSLOCATIONS

Robertsonian translocations, present in about 1 in 800 humans, are fusions between two acrocentric chromosomes. These can cause infertility, miscarriages and aneuploidies. The origin of Robertsonian translocations has remained unclear for over a century.

In 2023, a study in Nature (1) showed that the short arms of human acrocentric chromosomes (13, 14, 15, 21 and 22) share large pseudo-homologous regions, including the macrosatellite SST1, and undergo continuous recombination. This discovery provided the first strong evidence that sequence homology between different acrocentrics could facilitate chromosomal exchanges.

Now, in a follow-up study conducted by essentially the same team , Nature (2) reports the first complete assemblies of three acrocentric chromosomes. They uncovered a common breakpoint within the SST1 arrays on chromosomes 13, 14 and 21. An inversion on chromosome 14 brings these repeats into the correct orientation to allow a meiotic crossover, fusing the long arms of two chromosomes and eliminating the ribosomal DNA arrays.

The resulting chromosomes carry two centromeric arrays, but usually one is epigenetically inactivated, ensuring stable segregation during cell division. This combination of sequence homology, structural inversion and epigenetic adaptation explains the formation and persistence of Robertsonian translocations.

Taken together, these studies not only resolve a long-standing puzzle in human cytogenetics, but also provide a framework for understanding how structural variants arise and shape genome evolution.

1- https://www.nature.com/articles/s41586-023-05976-y

2. https://www.nature.com/articles/s41586-025-09540-8