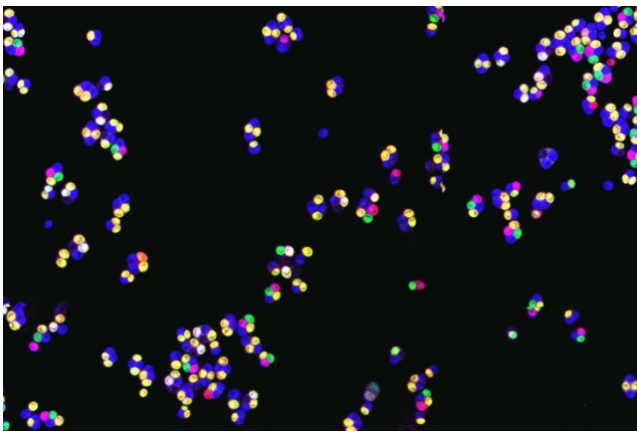


Meiosis and crossing over: pairing and separating

Meiosis separates “homologous” chromosomes (of maternal or paternal origin) to form gametes. This meiotic division uses a highly sophisticated process which is found in many living organisms from yeast to humans, in which homologous chromosomes pair up along their entire length using a “synaptonemal” (“zip” -like structure) protein complex. Then they exchange DNA regions, which temporarily links them and allows genetic mixing (homologous recombination). At Institut Curie, the “Chromosome Dynamics and Recombination” team headed by Valérie Borde, CNRS research director, identified the molecular bases of this mechanism – during meiosis - involving pairing and recombination of homologous chromosomes, using the *Saccharomyces cerevisiae* yeast model. This study is published in the journal *Genes and Development*.



S. cerevisiae yeast tetrads produced after meiosis. Each tetrad contains 4 spores (the equivalent of gametes) that have recombined their genome, which produces different spore colorations due to different combinations of fluorescent markers inserted along the chromosomes.

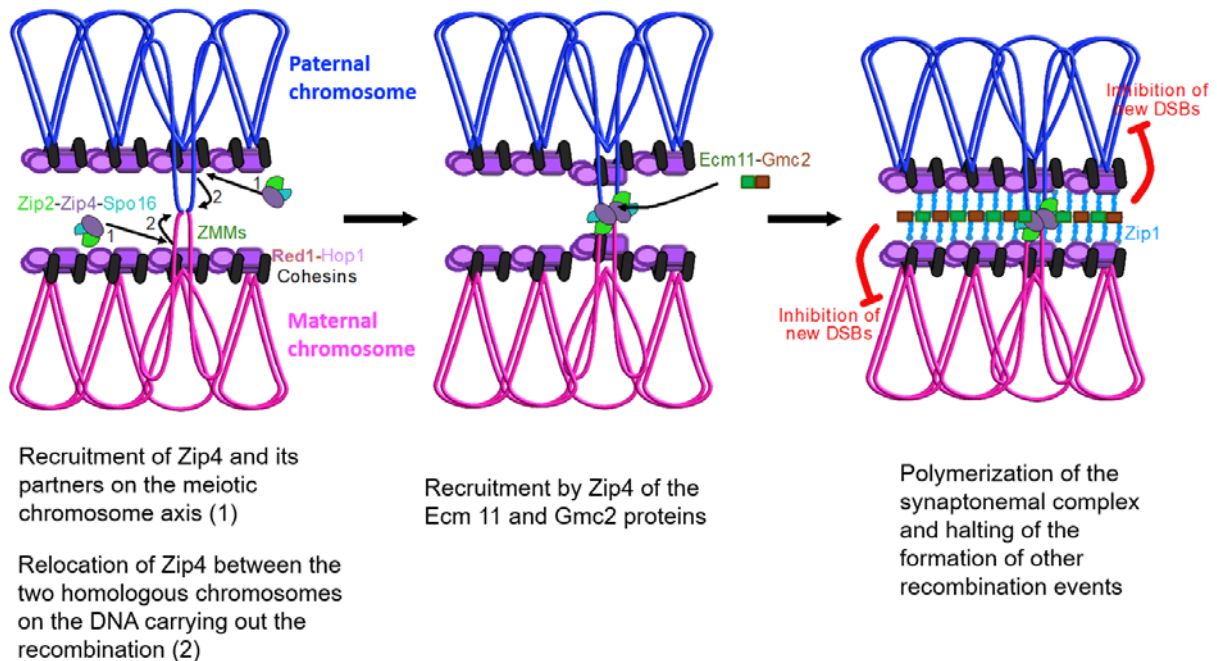
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During meiosis, the homologous chromosomes of the germ line cells (the cells that produce oocytes or sperm) separate, and each gamete inherits only one maternal or paternal copy of each chromosome. To do this, the homologous chromosomes have to meet, then pair along their entire length, before being separated and distributed into each daughter cell. The precise separation of these chromosome pairs is essential to ensure that gametes are generated with the proper chromosome content, thus avoiding problems of sterility and/or anomalies of chromosome segregation (as with Down Syndrome or Turner Syndrome). During this process, the genetic material is also rearranged between the homologous chromosomes. This type of “recombination” can only take place via fine-tuned programmed breakage mechanisms and subsequent repair of DNA molecules. These mechanisms are highly conserved in eukaryotes, from yeast to humans. “Nodes” (Holliday junctions) form between the homologous chromosomes to make them exchange their arms, during crossing over. At the same time, the homologous chromosomes are paired along their entire length within a “zip” -like structure, namely the synaptonemal complex. This complex exerts control over the number and distribution of recombination events along the chromosomes.

While the functional links between these two essential aspects of meiosis - recombination and the synaptonemal complex - were known, their molecular nature was not known.

Using genetics, proteomics and *in silico* modeling of protein interaction fields, the Chromosome Dynamics and Recombination team (Institut Curie, CNRS, Sorbonne University), led by Valérie Borde, in collaboration with CEA/12BC researchers, identified a protein, Zip4 (TEX11 in humans), which makes a direct connection between the recombination machinery and the central elements of the synaptonemal complex (Ecm11-Gmc2). When this link is broken following Zip4 mutations, the “zip” between the homologous chromosomes is no longer present, and the meiotic recombination is deregulated.

These phenomena observed in *Saccharomyces cerevisiae* are highly conserved in eukaryotes, thus rendering yeast, which is easy to use, an essential model organism. Researchers identified and studied functional and structural pairs of recombination proteins and of the synaptonemal complex in humans. In particular, one of the proteins studied, TEX12, normally restricted to meiotic cells, has just been found to be abnormally expressed in many cancers and contributes to the growth of cancer cells.



Model of functional interactions between recombination and synaptonemal complex.

The “ZZS” complex containing Zip4 is loaded on the chromosome axis, via the interaction between Zip4 and Red1 (1). Then, the ZZS complex is relocated on the recombination intermediaries, between the two homologous chromosomes (2). This allows the Ecm11 and Gmc2 proteins to be recruited, triggering polymerization of the synaptonemal complex. In return, this shuts down the formation of new recombination intermediaries.

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Reference:

[The Zip4 protein directly couples meiotic crossover formation to synaptonemal complex assembly.](#) Alexandra Pyatnitskaya, Jessica Andreani, Raphaël Guérois, Arnaud De Muyt et Valérie Borde. *Genes and Development*. 30 décembre 2021, doi:10.1101/gad.348973.121