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Meiotic recombination mechanisms

Mécanismes de la recombinaison méiotique

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ABSTRACT

Meiosis is a specialized cell division at the origin of the haploid cells that eventually develop into the gametes. It therefore lies at the heart of Mendelian heredity. Recombination and redistribution of the homologous chromosomes arising during meiosis constitute an important source of genetic diversity, conferring to meiosis a particularly important place in the evolution and the diversification of the species. Our understanding of the molecular mechanisms governing meiotic recombination has considerably progressed these last decades, benefiting from complementary approaches led on various model species. An overview of these mechanisms will be provided as well as a discussion on the implications of these recent discoveries.

Mots clés :
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RÉSUMÉ

La méiose assure la réduction de moitié du niveau de ploïdie des cellules à l'origine des gamètes, compensant ainsi le doublement de l'information génétique survenant au moment de la fécondation. Elle est donc à la base de la génétique mendélienne. La recombinaison et la redistribution des chromosomes homologues parentaux survenant au cours de la méiose constituent une importante source de diversité génétique, lui conférant une place particulièrement importante dans l'évolution et la diversification des espèces. La compréhension des mécanismes en jeu lors de la méiose a considérablement progressé au cours de ces dernières décennies, bénéficiant d'approches complémentaires menées sur une gamme variée d'espèces modèles. Cette revue présente une vue générale de ces mécanismes et propose une discussion sur les implications de ces découvertes récentes.

1. Meiosis and recombination: a general overview

Meiosis is essential for the fertility of most sexually reproducing eukaryotes. This peculiar cell division halves the number of chromosome sets, compensating the chromosome doubling occurring during fertilization. Meiosis is thus a key step in the sexual life cycle. It consists in two rounds of chromosome segregation that follow a single round of DNA replication (Fig. 1). In a vast majority of species, the first round of chromosome segregation separates the homologous chromosomes – and is at the origin of the ploidy reduction – while the second round of chromosome segregation separates

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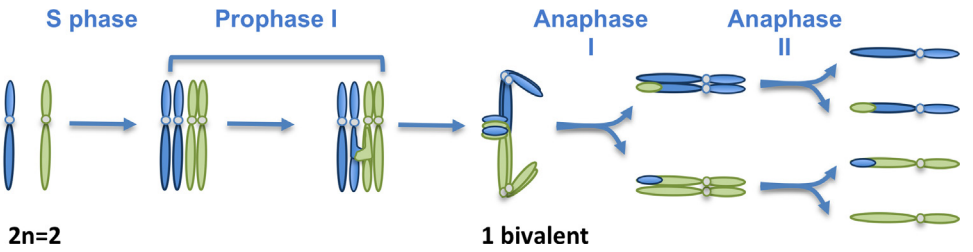

Fig. 1. Schematic representation of a meiotic division. In meiocytes, as in any sporophytic cell, a set of chromosomes of maternal origin (blue) coexists with a set of chromosomes of paternal origin (green). They correspond to pairs of homologous chromosomes (or homologs). Here, a hypothetical organism with a diploid number of chromosomes of 2 has been chosen. Replication (S phase) duplicates each chromosome into two sister chromatids that are kept together by the action of cohesins (not shown). Meiosis consists in the succession of two rounds of chromosome segregation (Anaphases I and II) after a single S phase. During prophase I, homologous chromosomes recombine and associate into bivalents. Meiosis I separates the homologous chromosomes, while meiosis II separates the sister chromatids.

the sister chromatids – as during a mitotic division (Fig. 1).

The success of ploidy reduction that occurs during the first meiotic division depends on the preliminary association of the homologous chromosomes into pairs forming a structure called bivalent. In most species, bivalent formation relies on meiotic recombination, and more precisely on the occurrence of crossovers (COs). COs correspond to large reciprocal exchange of two non-sister chromatids that connect physically the two homologous chromosomes (Fig. 2). In these species, the presence of at least one CO per bivalent is an absolute requirement for the proper segregation of the homologous chromosomes and thus to obtain fully viable gametes.

Meiosis is a very important source of genetic variability. First because COs reorganise allelic combination within chromosomes and second because anaphase I reshuffles parental chromosomes into daughter cells. Over the last twenty years, considerable progresses have been made in deciphering the mechanisms that govern meiotic recombination. The aim of this review is not to get into the details of such mechanisms (for which a number of recent reviews will be provided), but more to discuss the implication of these discoveries.

2. Meiotic recombination specificities

Recombination corresponds to one of the molecular processes available to repair the DNA lesions that affect the two strands of a DNA molecule – the double strand breaks (DSBs). It is encountered in all three branches of life – bacteria, archaea and eukaryotes – and relies on the selection of a similar or identical DNA matrix as a template to repair the compromised one. It is therefore described as a conservative DNA repair process in opposition to the mechanisms such as non-homologous end joining (NHEJ) where the repaired DNA duplex looses genetic information [1]. Homologous recombination generates two types of products: the COs that correspond to reciprocal exchanges of large chromosomal fragments between homologous chromosomes and the non-crossovers (NCOs) that correspond to a local repair of the DNA with a short and non-reciprocal replacement of one DNA sequence with a homologous one (Fig. 2). The different steps and overall mechanisms that govern meiotic and somatic recombination are very similar, but meiotic recombination shows some interesting specificities in regards to its somatic counterpart.

2.1. The initiation of meiotic recombination

Contrary to somatic recombination, the DNA lesions that initiate meiotic recombination are not fortuitous but genetically programmed [2]. Besides, an intriguing feature of meiotic recombination is that in most organisms, the number of DSBs induced at meiosis is surprisingly high, estimated in many species to several hundreds [2,3]. Meiotic recombination therefore starts by submitting the gamete mother cells to an outstanding level of DNA damage. This is particularly unexpected for cells on which relies the transmission of the genetic heritage. As expected, multiple layers of controls that regulate DSB localization, rate and fate have been characterised [4].

A number of meiotic proteins required for meiotic DSB formation have been identified, mostly in *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Arabidopsis thaliana* and *Mus musculus* [2]. SPO11 is one of the few of these "DSB proteins" to be widely conserved among species. In the late 1990s, it was found that SPO11 shows similarity with the catalytic domain of a topoisomerase form Archaea – the topoisomerase VI or TopoVI – and that it could be purified covalently linked to the 5′ extremities of the meiotic DNA DSBs [5,6]. Since then, it is assumed that SPO11 carries the catalytic activity responsible for DSB formation. However, no evidence of such biochemical activity could be obtained, and hardly any progress in the understanding of the function of the other DSB proteins has been done. However, the recent characterisation in *A. thaliana* of the long-sought partner of SPO11, corresponding to the complementary part of the topoisomerase from Archaea [7], as well as the identification of distantly related homologues in vertebrates, insects and ascomycetes [8] now makes us revisit the nature, structure and functions of the meiotic DSB forming complex [9].

2.2. The choice of the template for DSB repair

Homologous recombination requires the search, the recognition and the use of a "similar" DNA molecule as a matrix for DNA repair. In a diploid cell after replication

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