Ending up with the right partner

Titia de Lange

How do the correct maternal and paternal chromosomes find one another during sexual reproduction? New data from fission yeast indicate that the search for the right partner is simplified by pre-alignment of the chromosomes through clustering of their ends.

Arguably the most intimate event in sexual reproduction is the tight embrace of paternal and maternal chromosomes that occurs during the formation of gametes (in humans, the eggs or sperm). In a process known as meiosis, the two copies of each chromosome (called homologues) snuggle up to form precisely aligned pairs and exchange genetic information (recombination). The pairing and recombination of homologues permits their faithful separation, such that each gamete is haploid — that is, endowed with just one copy of each chromosome. But how do homologous chromosomes meet? On pages 825 and 828 of this issue, Nimmo *et al.*[1] and Cooper *et al.*[2] pinpoint the ends of chromosomes (telomeres) as major movers in homologous pairing in the fission yeast *Schizosaccharomyces pombe*.

The problem of homologue pairing is one of staggering complexity. During meiosis in the human germ line, for instance, the search for homology takes place amongst the more than 6 million kilobase-pairs of DNA organized on 23 chromosome pairs. Early cytologists noted that, in a phase of meiosis called prophase, chromosomes tend to be positioned with their telomeres clustered at one pole of the nucleus and the chromosomal arms looping out in the other direction. Known as the bouquet stage (see Fig. 1, and ref. 3 for review), this configuration might promote chromosome pairing. However, it has been hard to progress from this descriptive work to testing experimentally how telomeres are involved in meiosis.

Fission yeast has emerged as an invaluable tool to address this question. Unlike most eukaryotes, this organism prefers a haploid lifestyle, opting for meiosis as soon as the joining of two haploid cells has generated the diploid zygote. The formation of a zygote in fission yeast involves a specialized kind of nuclear fusion (karyogamy) that unites the two haploid nuclei of the parental cells (Fig. 1). Subsequent meiotic events include DNA replication, a prolonged prophase and, finally, the two meiotic divisions that segregate the homologues and give rise to four haploid spores.

An unusual feature of *S. pombe* meiosis is that its newly formed zygotic nucleus is highly mobile in prophase I, moving back and forth through the cell during the exact period in which homologues pair and recombine[4]. These striking nuclear oscillations have been captured by video microscopy, and they could explain the elongated 'horsetail' shape of prophase I nuclei that had previously been noted in fixed zygotic cells[4]. The horsetail movement is driven by a structure called the spindle pole body (SPB), which is embedded in the nuclear envelope and connects to dynamic microtubules.

Where do the telomeres come in? Normally, the SPB is associated with a specialized region of the chromosome known as the centromere. But, at the horsetail stage, telomeres cluster at this position[4,5]. This centromere–telomere switch occurs in haploid cells when they are exposed to mating pheromone[5]. Thus, telomeres end up at the leading edge of the elongated nucleus, with the rest of the chromosomes trailing behind as the SPB moves the nucleus back and forth through the cell. This curious mechanism seems particularly well-suited to orientate the chromosomes and position homologous sequences close together. In effect, it is similar to grabbing a bunch of ropes by their ends and giving them a good shake — the ropes will align according to their lengths. Because the *S. pombe* genome is organized on just three chromosomes of different sizes, it has been proposed that the search for homology in meiosis is facilitated considerably by arranging the chromosomes as loops held together by their ends.

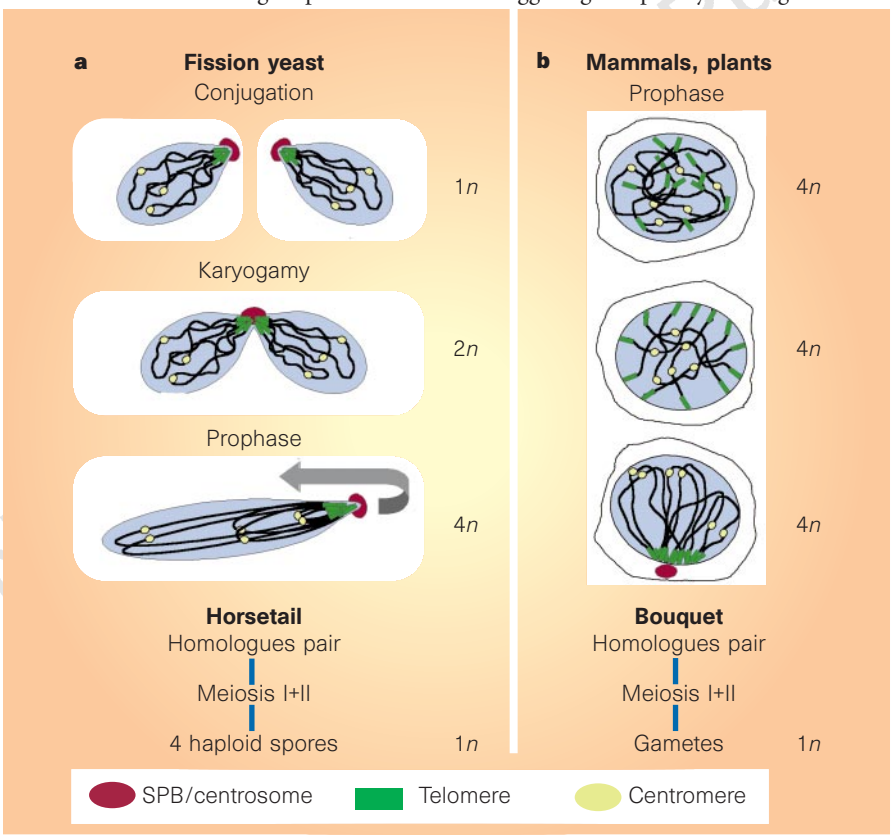

Figure 1 **Chromosome movements that occur before pairing of maternal and paternal (homologous) chromosomes during sexual reproduction in fission yeast, mammals and plants.** a, **Fission yeast. After cellular joining (conjugation) and nuclear fusion (karyogamy) between two haploid (1*n*) cells with opposite mating type, a zygote (2*n*) is formed. Meiosis (the formation of gametes) is initiated immediately and, in a stage of meiosis I known as prophase, nuclei undergo rapid movements back and forth through the cell, led by the spindle pole body (SPB). The ends of the chromosomes (telomeres) are connected to the SPB, and the telomere-led movement of the so-called 'horsetail' nucleus facilitates alignment of homologous chromosomes. Nimmo *et al.*[1] and Cooper *et al.*[2] have shown that loss of the telomere–SPB connection results in reduced exchange of genetic information and diminished spore viability.** b, **Mammals and plants. Telomeres similarly cluster at one pole of the nucleus (in mammals, at a structure called the centrosome, which is analogous to the SPB) in prophase of meiosis I. The resulting configuration of the chromosome is known as the bouquet stage.**

Nimmo *et al.*[1] and Cooper *et al.*[2] now show that this view is likely to be correct, and that telomeres are important in the pairing and recombination of homologues. Their findings arose from an interest in the proteins that form a complex at the telomere. The product of the *taz1* gene, Taz1p, was identified[6] in Tom Cech's lab from a one-hybrid screen for factors that bind telomeric DNA. It was shown to affect telomeric silencing and the maintenance of telomere length. The findings also hinted at a meiotic function for Taz1p, because the spore viability was greatly reduced in the mutant strain[6].

Nimmo *et al.*[1] carried out a genetic hunt for genes involved in telomere function, using telomeric silencing as a screening tool. They identified the *lot2* gene (as well as *taz1*), and showed that a mutation in *lot2* (like *taz1*) results in inappropriate telomere elongation and a marked reduction of viable spores.

The nature of the meiotic defect in *taz1* and *lot2* mutants became clear when the positioning of telomeres at the SPB was examined — rather than showing the normal clustering of all chromosome ends at the SPB, both Nimmo *et al.* and Cooper *et al.* found that most of the telomeres were scattered in the mutants.

Nimmo *et al.* recorded the behaviour of defective telomeres, and their effect on the horsetail stage, by video microscopy. They had previously found that a protein known as Swi6p localizes to both centromeres and telomeres, where it is involved in controlling transcriptional repression[7]. They now use a fusion protein between Swi6p and green fluorescent protein to label telomeres and centromeres as bright fluorescent dots in living cells. The authors produced a movie[8] documenting the vigorous swinging back and forth of the wild-type horsetail nucleus, with telomeric Swi6p dots in the lead and centromeric dots lagging behind. In the *lot2* mutant, however, the telomeric dots fail to cluster at the SPB, and are dispersed throughout the nucleus. The SPB still seems to try and move the nucleus through the cell but, because there is no connection to the chromosomes, it merely manages to drag a small bit of nuclear material back and forth.

Loss of the connection between telomeres and the SPB — and the resulting defect in movements at the horsetail stage — has severe consequences for recombination between homologous chromosomes. The *taz1* and *lot2* mutants showed[1,2] a marked reduction (3–10-fold) in the rate of recombination both within and between genes. This defect could be even more extreme than these figures imply, because over 90% of the mutant spores were not viable — probably because the chromosomes had failed to segregate normally in meiosis I. These data indicate that telomere clustering at the SPB is required for the recombination and segregation of homologous chromosomes, in keeping with the idea that the telomere-led horsetail movement facilitates chromosome pairing.

What is the significance of these findings with regard to meiosis in other organisms? It is now clear that meiotic strategies can be quite diverse[9], and a horsetail stage in strictest sense has not been seen in budding yeast, fruit flies or humans. But the meiotic tango of fission-yeast chromosomes is likely to be more than a cell-biological curiosity. After all, mammalian and plant chromosomes also move — when their telomeres adhere to the nuclear envelope in prophase and then gather at one pole of the nucleus to form the bouquet stage[10,11]. Moreover, the timing of the bouquet stage is compatible with its role in the pairing of homologous chromosomes, because telomeric clustering precedes alignment of the homologues and formation of the synaptonemal complex, an elaborate structure that holds the homologues together until recombination has been completed[11].

A further hint for a telomere-mediated pairing mechanism in mammals is the functional and structural similarity of Taz1p to the mammalian telomeric protein TRF1 (refs 6, 12, 13). TRF1 can promote parallel pairing of telomeric tracts *in vitro*[14], an activity that is potentially significant to meiosis. Mice lacking TRF1 should reveal the function of this protein in the formation of mammalian gametes. Human telomeres have been implicated in cellular ageing and in cancer — sex may be next. □

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Planetary science

Comet leaves a trail in the air

Laura Garwin

The inner Solar System is a dusty place. As the Earth makes its way around the Sun, it travels through a tenuous cloud of dust, the 'zodiacal cloud', thought to be produced mainly by colliding asteroids and active comets, with a small contribution of dust from outside the Solar System. About 10,000 tonnes of this dust hits the Earth each year, and a tiny fraction finds its way — with human aid — into laboratories, under microscopes and through mass spectrometers. The compositions of these interplanetary dust particles (IDPs) show that they are extraterrestrial, but a more detailed understanding of their origin, such as whether a given particle has come from an asteroid or comet, has been elusive. Now some of these particles have been coaxed into giving up a bit more of their life story, according to a talk given last month*. Scott Messenger (Natl Inst. Standards Technol., Gaithersburg) suggested that a population of the fluffy, fragile aggregates known as 'cluster IDPs' collected in the stratosphere in the summer of 1991 come not just from a comet, but specifically from the periodic Earth-crossing comet Schwassmann–Wachmann 3 (Fig. 1). If Messenger is right, dust from this comet, and perhaps from several others, can be sampled repeatedly using nothing more sophisticated than a high-altitude aircraft.

The large interplanetary dust particles known as cosmic spherules can be collected from the sea floor and from polar ice. But melting on atmospheric entry and subsequent alteration on Earth lead to changes in composition that limit their usefulness as samples of extraterrestrial material. The place to find nearly pristine IDPs is the stratosphere. Since 1974, NASA has flown decommissioned U-2 spy planes at about 20 km altitude, with simple impact collectors mounted under the wings. These planes are usually 'ships of opportunity', collecting dust while performing other research, so it can take months for a collector to accumulate the 30–40 hours of exposure required to harvest a useful crop of a few hundred IDPs, ranging from about 5 to 50 μm across. IDPs are identified as extraterrestrial by the presence of solar-flare particle tracks, implanted noble-gas atoms from the solar wind, and by non-terrestrial isotope ratios of hydrogen, nitrogen and oxygen. Most IDPs also have major-element compositions that are similar to those of the primitive meteorites known as carbonaceous chondrites, consistent with an origin in comets or certain types of asteroid. Specifically, the more porous IDPs are thought to come from comets[1]. But without

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