next chapter in our understanding of mammalian development unfolds, it seems that marsupials are long overdue their place at center stage.

DECLARATION OF INTERESTS

The author declares no competing interests.

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Cell biology: Selfish B chromosomes unleashed by a dysfunctional chromosome segregation system

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A study in the fruit fly *Drosophila melanogaster* shows that a defective chromosome segregation system allows non-essential B chromosomes to transmit at higher-than-Mendelian frequencies.

Higher eukaryotes harbor a range of different selfish genetic elements (SGEs). One type of SGE — B chromosomes — has gained strong research interest over the past few decades. B chromosomes are typified by several key characteristics: they are pervasive in nature, having been observed in thousands of plants and animals; they arise as extra copies from whole regions of chromosomes that make up the organism's core genome; they are usually diminutive and heterochromatic, expressing few or no functional genes; and, as a result, they provide no benefit to the organism[1,2]. Because B chromosomes are nonessential, they are prone to loss during cell division. To counter this tendency, many B chromosomes drive, or transmit themselves, from parent to offspring at frequencies higher than are predicted by Mendelian rules. The different ways that B chromosomes drive mirrors the diversity of their resident organisms. For example, a B chromosome in maize undergoes improper sister chromatid separation during the mitotic division that produces pollen (i.e., sperm), resulting in one cell with two B chromosome copies and another with no B chromosomes — the pollen cell with two B chromosomes

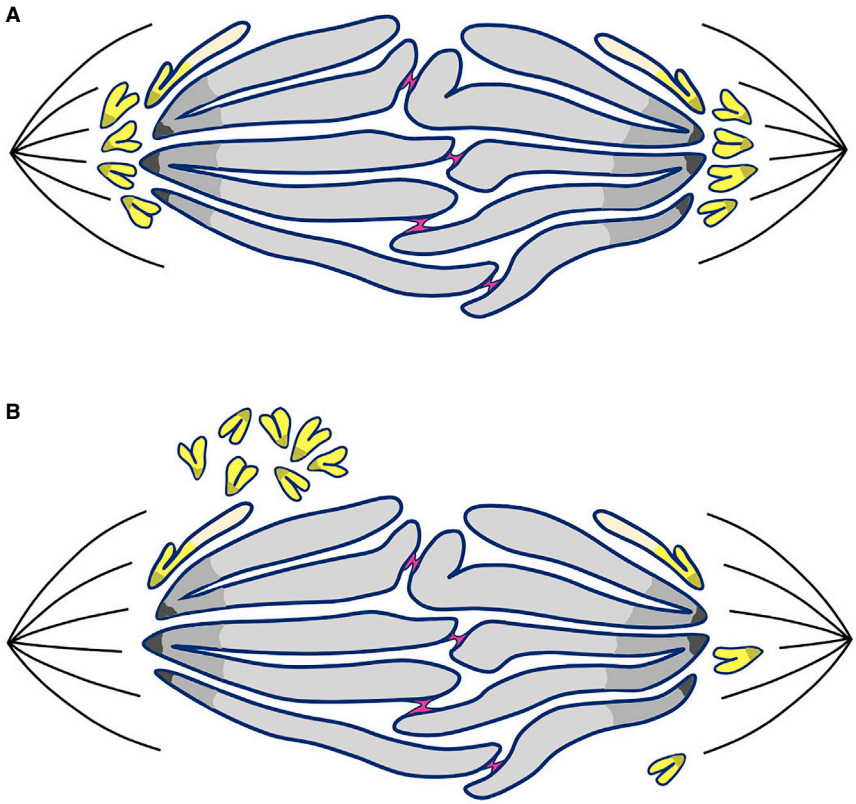

Figure 1. Matrimony genotype determines the distribution of *Dmel*-B copies on the first meiotic spindle.
(A) In the wild-type (*mtrm*$^{+}$) genotype, *Dmel*-B copies (small yellow chromosomes) exhibit an even, symmetrical distribution on either side of the spindle. Only eight *Dmel*-B copies are shown here for simplicity. The 4th chromosomes, the likely precursors of *Dmel*-B, are also shown in yellow. The chiasmata holding together euchromatin of the other chromosomes are shown in magenta. Certain details, like sister chromatids, are not shown for simplicity. (B) In the matrimony mutant (*mtrm*^{126}) genotype, the *Dmel*-B copies become irregularly distributed across the spindle. This effect may somehow underlie *Dmel*-B drive.

preferentially fertilizes the egg[3]. In contrast, B chromosomes in the grasshopper, *Myrmeleotettix maculatus*, and the lily, *Lillum callosum*, utilize an asymmetry in the spindle apparatus of the female's first meiotic division[4,5]. This spindle has a longer side that points toward the future egg and a shorter side that terminates at a non-gametic product. In each case, the B chromosome finds itself more frequently on the spindle's longer side, thereby segregating preferentially into the egg.

A long-standing puzzle is: under what genetic conditions do B chromosomes arise and propagate? A new study by Hanlon and Hawley appearing in this issue of *Current Biology* addresses this question[6]. The authors investigated a B chromosome that was previously identified in a mutant laboratory stock of the fruit fly, *Drosophila melanogaster*. That initial reporting[7] and another subsequent study[8] revealed some clues about this B chromosome (referred to henceforth as *Dmel*-B). Like most other B chromosomes, *Dmel*-B was found to be heterochromatic, with no detectable gene expression. It contained an abundance of two different simple satellite DNA repeats — AATAT and AAGAT — both of which are found almost exclusively on the fruit fly's heterochromatic 4th position chromosome (4th), suggesting that *Dmel*-B originated from this chromosome. *Dmel*-B is found in both sexes, and it is present in multiple, identical copies averaging 10 per somatic cell, with a range of 3–14. This variation indicates uneven segregation during mitotic division. Nevertheless, the *Dmel*-B copy load remains steady within the mutant stock over time. Interestingly, when outcrossed repeatedly to wild-type flies, the *Dmel*-B copies were eventually lost. These results hinted that *Dmel*-B may drive, but only in the mutant stock. In this study, Hanlon and Hawley investigated this possibility, uncovering several aspects of female meiosis that may influence the formation and transmission of B chromosomes. Their main findings are highlighted here, with implications.

Certain genotypes promote the formation and drive of B chromosomes

It was previously suspected that the genotype of the mutant stock played a role in the formation of *Dmel*-B. This stock contains a nonfunctional copy of a gene called matrimony, *mtrm*^{126}. The wild-type, or functional, version of *matrimony*, *mtrm*$^{+}$, encodes a protein that interacts with polo kinase, a major regulator of cell division[9]. Earlier work showed that the *mtrm*^{126} mutation causes heightened chromosome fragmentation[10]. It was therefore posited that the *mtrm*^{126} mutant effect may have caused a 4th fragmentation event that produced *Dmel*-B[7], which then expanded in copy number. This possibility is supported by the discovery of another, smaller B chromosome also derived from the 4th in a different *matrimony* mutant stock[8].

Following formation, any persisting B chromosome must be successfully transmitted from parent to offspring, perhaps through drive. Hanlon and Hawley examined whether *Dmel*-B is capable of drive in the *mtrm*^{126} mutant stock by counting the number of *Dmel*-B copies transmitted by an individual *mtrm*^{126} parent to its progeny. Because, in this experiment, a *Dmel*-B-carrying parent was crossed with a B chromosome-less individual, the average frequency of *Dmel*-B copies in progeny should be 50% if transmission were Mendelian. Remarkably, when *Dmel*-B was transmitted from the female parent, the copy frequency in progeny was 63%, a significant increase from the null expectation. No such increase in transmission was seen from *Dmel*-B-carrying fathers (in fact, transmission from males resulted in an unexplained

transmission decrease). Importantly, when the same transmission measurements were taken on progeny from wild-type females or *mtrm*^{126} females carrying a transgenic copy of *mtrm*$^{+}$, *Dmel*-B transmission frequency fell to ~50%. This work showed that *Dmel*-B can drive, but the effect is restricted to *mtrm*^{126} females. Broadly, these findings suggest that certain mutant genotypes such as *mtrm*^{126}, which enhance genome instability, may facilitate not just B chromosome formation but also their drive. This conclusion may be especially true for heterochromatic B chromosomes, which, carrying few genes at their inception, would be spared of negative selection due to inappropriate contribution to gene dose.

B chromosome drive hints at unforeseen meiotic or post-meiotic asymmetries

Does *Dmel*-B behave unusually in *mtrm*^{126} females in a way that would explain its drive? In principle, female meiosis is a fruitful platform for SGE drive because it produces four meiotic products, only one of which becomes a functional egg — the other three become non-gametic polar bodies. An SGE that can preferentially segregate into the future egg will enjoy an increase in transmission. This alone would be sufficient motivation for Hanlon and Hawley to visually examine *Dmel*-B behavior during the first meiotic division in *mtrm*^{126} females. However, an additional incentive was the fact that *matrimony* plays a chief role in the distributive segregation system. During the first meiotic division, each pair of homologous chromosomes must align on the spindle before separating to opposite sides of the cell. At this time, the homologous chromosome pairs are held together by crossover points known as chiasmata. Although they are byproducts of meiotic recombination, these connections play a crucial role in counterbalancing the pulling force that microtubules exert on the chromosomes toward each spindle pole. Certain chromosomes occasionally fail to form chiasmata, while others that are largely heterochromatic, such as the *D. melanogaster* 4th, never form them. The role of the distributive segregation system is to ensure that achiasmatic chromosomes segregate properly[11]. In *matrimony* mutants, this system is defective, resulting in a high level of 4th mis-segregation[12]. Such mis-segregation could also happen to *Dmel*-B, which, if true, may somehow underlie its drive.

Microscopic inspection of eggs from *mtrm*^{126} females revealed a range of abnormal *Dmel*-B configurations on the first meiotic spindle. In many eggs, the *Dmel*-B copies clustered irregularly on the spindle, sometimes being separated from the other chromosomes (Figure 1). This finding suggests that disruption of the distributive segregation system leads to improper *Dmel*-B segregation, which could facilitate drive. An important remaining question is: how? Hypothetically, a tendency of *Dmel*-B copies to cluster on the egg-destined side of the spindle could lead to enhanced transmission. However, unlike in other organisms[4,5], the fruit fly's first meiotic spindle is thought to be structurally symmetrical and parallel to the plasma membrane, with no known bias for either of the two spindle poles toward the future egg. One far-reaching, but intriguing, possibility is that random clustering of *Dmel*-B copies may induce subtle molecular differences across the spindle's microtubules, such as those detected in mice[13], which in turn polarize the spindle, thereby leading to a directional gamete bias. This idea is not outlandish — at least one other B chromosome is known to actively manipulate the organism's cell division machinery for enhanced transmission[14]. Alternatively, *Dmel*-B drive may depend on some feature of the second meiotic division or subsequent chromosomal events leading up to the union of sperm and egg nuclei. Microscopic examination of B chromosome behavior during this period will likely be telling.

The distributive segregation system may be a safeguard against selfish B chromosomes

Hanlon and Hawley propose that the distributive segregation system may have evolved as a defense against B chromosomes. Under this model, an ancestral genome was more prone to chromosome fragmentation events, leading to newly formed B chromosomes that drive. Upon the advent of genes like *matrimony*, such events would be suppressed. Alternatively, suppression of B chromosome drive by the distributive segregation system may instead be a fortuitous side effect of a more ancestral, basic function in genome stability. Testing these and other ideas will benefit from the many experimental tools available in the well-established model organism that is *D. melanogaster*.

DECLARATION OF INTERESTS

The author declares no competing interests.

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Stem cells: The cell that does it all

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How do animals replace all their worn-out cells to maintain their tissues? A new study shows that, in the cnidarian *Hydractinia symbiolongicarpus*, a single adult stem cell is sufficient to generate the entire repertoire of somatic and germ line cells.

Animals are composed of cells that differ vastly in their molecular fingerprint, morphology, and physiology. Producing these different cells at the right time and in the right place is a formidable task during embryonic development, but also in adult organisms in which specific cells or tissues need to be replaced following insults or the wear-and-tear of everyday life. Stem cells are typically the source of differentiated cells, but the range of cell types that they can generate differs between species and between stem cells within a species. In adult vertebrates, for example, stem cells are typically limited to the production of cell types within one organ or tissue. In a new study, published recently in *Current Biology*, using the cnidarian *Hydractinia symbiolongicarpus* as a model organism, Varley *et al.*[1] characterized a true stem cell champion.

Cnidarians are a group of animals that includes corals, sea anemones and jellyfish and they have long been known to have an astonishing capacity to regenerate missing body parts after encounters with predators or with the scalpels of developmental biologists. In hydrozoans, a species-rich subgroup of cnidarians, this capacity for regeneration is mostly based on a population of interstitial stem cells (i-cells) that are embedded among the cells of the epidermis, the outer of the only two layers of epithelial cells present in cnidarians[2]. In elegant and minimally invasive experiments, Varley *et al.*[1] showed that a single adult i-cell can generate all cells of an animal. To achieve this, they generated double transgenic animals in which the i-cells specifically express a green fluorescent protein, while their differentiated progeny switch towards expressing a red fluorescent protein, thus allowing a real-time follow-up of cell-fate transitions. These authors then exploited the colonial organization of *Hydractinia*, in which functionally and morphologically distinct polyps are connected by a network of epithelial tubes called stolons (Figure 1). If genetically compatible, the stolons of two *Hydractinia* colonies can fuse and i-cells can migrate from one colony to the other. Varley *et al.*[1] fused colonies carrying a few transgene-labeled i-cells with unlabeled colonies and waited until a single green i-cell had migrated into the host stolon. Once this had occurred, they excised the small stolon piece and observed what the GFP-labeled i-cell would do while the stolon regenerates into a new colony. In all successful fusion experiments, the labeled i-cell showed no regrets and gave rise to epithelial cells, neurons, stinging cells and even gametes, leading in some parts of the new colony to polyps that consisted exclusively of the red transgenic cells derived from the single green i-cell. This demonstration of the pluripotency of individual i-cells is particularly beautiful as it occurred within the regular tissue environment of the animals, i.e. without depleting the stem cells of the host to facilitate integration of the donor i-cell.

Pluripotency of individual adult stem cells (here meaning the ability of one stem cell to generate all cell types of an animal, including germ cells) has previously been demonstrated only for a subset of neoblasts in planarians[3,4], with acoels and sponges as additional candidates for the presence of such adult pluripotent stem cells (aPSCs)[5,6]. From a mammalian perspective, these cells might seem an anomaly restricted to a collection of weird aquatic creatures, yet these species are actually positioned very distantly from each other in the animal tree of life, suggesting an evolutionary value. But do aPSCs have a shared evolutionary origin (derived from a single common ancestor) or did they evolve independently in unrelated organisms? Are the molecular mechanisms involved in adult pluripotency maintenance similar between species? Is there more than one mechanism to maintain pluripotency in