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EVOLUTIONARY BIOLOGY

Infection elevates diversity

Chromosomal shuffling in parental eggs or sperm can create new characteristics in the next generation. In fruit flies, it seems that mothers with a parasitic infection produce more such recombinant offspring than uninfected mothers.

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In most plants and animals, offspring are genetically distinct from their parents. Through the process of recombination, which occurs as sperm and egg cells (gametes) are produced, a parent can mix the two copies of a given chromosome received from its own parents, thus transmitting unique chromosomes to its offspring. Writing in *Science*, Singh *et al.*¹ show that fruit flies produce a higher frequency of offspring with recombinant chromosomes when the mother is infected with a parasite than when it is uninfected. This intriguing observation may be an important piece in the long-standing puzzle of why recombination is so common.

Why should organisms shuffle their genomes through sex and recombination? Natural selection should create an excess of good gene combinations, so ‘undoing’ the work of past selection by rearranging these genotypes seems counterproductive. One possible explanation is that what constitutes a good combination of alleles (gene variants) changes over time. In that case, undoing the work of past selection is beneficial because selection in the future demands something different. This idea requires that selection on gene combinations changes regularly².

Coevolving natural enemies — particularly parasites — might provide just the right type of selection pressures for this scenario. This is the basis for the ‘Red Queen’ hypothesis, which proposes that sexual reproduction and recombination are favoured because they help hosts to adapt to the ever-shifting selection imposed on their gene combinations by the parasites^{3,4}. However, even rapidly evolving parasites do not always induce selection for recombination; there are times in the coevolutionary cycle when hosts are well adapted and non-recombinant offspring will be more resistant to infection than recombinant ones^{5,6}. Intuitively, it might seem that the ideal solution is to

increase recombination when infected because being infected indicates that your current gene combination is not working.

To test this, Singh *et al.* performed hundreds of test crosses using female *Drosophila melanogaster* fruit flies that carried mutations at each of two genes on one chromosome, but that had normal versions of the genes on their other copy of the chromosome. The presence of either mutation leads to visible physical characteristics that allow determination of whether one or both mutations are present in their offspring — because the genes are in close physical proximity, the normal or mutated versions will be inherited together unless there has been recombination (Fig. 1).

The females were injected with one of two bacterial pathogens (*Serratia marcescens* or *Providencia rettgeri*) or given a sham injection. By examining tens of thousands of the flies’ progeny, the authors found that infected mothers produced a higher fraction of recombinant offspring than non-infected mothers. This effect was seen in four fly strains. Infection with a parasitoid wasp (*Leptopilina clavipes*) also induced an increase in recombinant progeny. Unlike the bacterial experiments, in which reproductive adults were infected, the parasitoid wasp infects fruit-fly larvae and the parasites must be killed for the larva to survive to adulthood. Thus, in this situation, the infection is cleared long before meiosis (the cell division necessary to produce gametes and during which recombination occurs).

An increase in the observed frequency of recombinant progeny from infected mothers could be due to an increase in the recombination rate or to transmission distortion (for example, if recombinant chromosomes are more likely than non-recombinant chromosomes to end up in successful gametes). To tease these possibilities apart, Singh *et al.* made use of the fact that exchange of chromosomal material (crossover events) occurs 4–5 days before eggs are laid. In their bacterial-infection experiments, the authors found an increase in recombinant progeny even in the first 4 days after the mothers were infected. This rapid response points to transmission distortion. A remaining challenge will be to understand how this distortion occurs. Are recombinant chromosomes less likely than non-recombinant ones to end up in polar bodies, the small

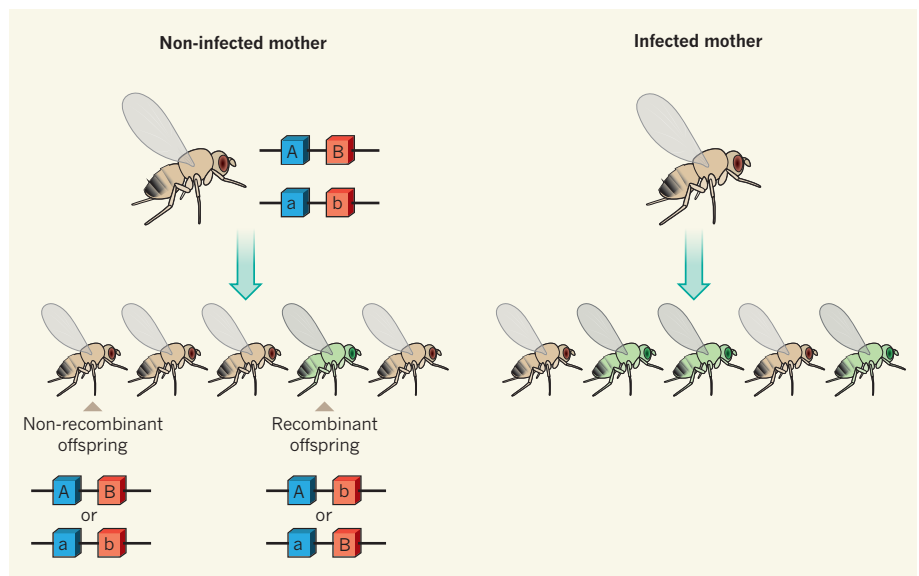


Figure 1 | Frequency of recombinant offspring altered by infection. Diploid organisms, such as fruit flies and humans, have two copies of each chromosome, which can vary in DNA sequence (represented by A versus a and B versus b) in every cell except gametes (sperm and egg cells). Gametes contain only one copy of each chromosome, such that fertilization results in two copies again in the offspring. The sequence in the offspring can be the same as the parental chromosome, or an exchange of genetic material between the two chromosomes during gamete production — recombination — can result in different sequences. Singh *et al.*¹ show that fruit-fly mothers that are infected with parasites produce more recombinant offspring than uninfected mothers.

cells that are formed during meiosis but do not transmit genes to future generations? Are gametes bearing recombinant chromosomes more viable, or do they somehow outcompete gametes that have non-recombinant chromosomes? What mechanism might mediate such a bias? Furthermore, Singh and colleagues' study focuses on a single genomic region — it will be of interest to assess whether similar responses occur elsewhere in the genome, and if not, why this region is particularly responsive.

Previous work has demonstrated that pathogens increase recombination in plants during meiotic and somatic (non-gamete) division^{7–9}. That the few existing examples of this phenomenon span plants and animals suggests that pathogen-induced increases in the recombinant fraction could be widespread, although perhaps achieved through different means, for example transmission distortion in flies but higher recombination in plants. If so, does this intriguing connection between pathogens and natural variation in recombination constitute convincing evidence to support the Red Queen hypothesis?

Changes in the proportion of recombinant

offspring in flies and other organisms have been reported in response to various types of environmental stress (such as temperature, nutrition and social stress; reviewed in ref. 10), although rarely with the rigour of Singh and colleagues' work. Is selection by parasites a driver of the evolution of plasticity in the recombinant fraction, perhaps one that spills over to other types of stress? Or is the observed response to pathogens a by-product of whatever causes plasticity in response to these other stresses? A crucial first step towards answering these questions would be to obtain evidence — so far lacking — that recombinant offspring are less likely to become infected than non-recombinant offspring.

Although plasticity in the recombinant fraction has been known for around 100 years, it is still poorly studied. We have only the crudest picture of what conditions alter the recombinant fraction, by how much and in which genomic regions. Moreover, theoretical models¹⁰ suggest that the evolution of recombination plasticity is not easily explained for 'normal' stresses in diploid organisms (those that have two copies of each chromosome,

including flies). Even the seemingly intuitive Red Queen interpretation of Singh and colleagues' results is questionable because offspring will always receive half the alleles carried by their mother, regardless of whether they are recombinant or not. Although studies such as this shed light on variation in recombination, there is a long way to go in terms of fully describing this variation and understanding it from both a mechanistic and an evolutionary perspective. ■

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COMPUTATIONAL ASTROPHYSICS

Monstrous galaxies unmasked

The enigma of how the most luminous galaxies arise is closer to being solved. New simulations show that these are long-lived massive galaxies powered by prodigious gas infall and the recycling of supernova-driven outflows. SEE LETTER P.496

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Three billion years after the Big Bang, the Universe was a different place from today. During that epoch, known as cosmic noon, the average star-formation rate across the cosmos was 100 times higher than it is at present, and individual galaxies were growing commensurately rapidly. This was illustrated by the surprising discovery¹, more than a decade ago, of galaxies whose star-formation rates during that era were 1,000 times the Milky Way's current output — no such galaxies are seen in the present-day Universe. On page 496 of this issue, Narayanan *et al.*² present numerical simulations that offer unprecedented clarity in understanding the origins of such deep-space monsters.

These galaxies have extreme properties and are the most luminous in the Universe. However, despite their enormous total energy output, they are faint at optical wavelengths: most of the radiation emitted by their stars is absorbed by a 'mask' of interstellar

dust and re-emitted at longer wavelengths. Consequently, they remained undiscovered until the advent of surveys at submillimetre and radio wavelengths¹. The very existence of these submillimetre galaxies (SMGs) presented a challenge to models of galaxy formation in a cosmological framework, and has since sparked a vigorous debate in the field of galaxy-formation theory.

Two schools of thought emerged, centred around the 'merger-starburst' and the 'smooth-accretion' hypotheses, respectively^{3–6}. The former proposes that a given SMG is the product of a collision between two gas-rich disk galaxies — this process drives a short-lived (about 10⁸ years) but spectacular burst of star formation during the galaxies' coalescence. The latter argues that SMGs represent the most massive members of the entire galaxy population, being long-lived phenomena that are continuously fed by gas accretion over periods of about 10⁹ years.

The merger-starburst hypothesis stems from a scaled-up analogy of the observation

that the most luminous galaxies in the present-day Universe are almost always involved in spectacular collisions⁷. The smooth-accretion hypothesis is founded on the prediction³ that, at early cosmic epochs, galaxies were accreting gas at extremely high rates — they could thus potentially sustain their excessive star-formation activity.

Neither scenario has been successful in fully replicating the observed properties of SMGs. Researchers have been unable to reproduce the number of systems required to match the observations under the merger-starburst hypothesis⁶, because collisions between sufficiently large galaxies were rare at those early times. An influential study⁴ has argued that collisions between more-numerous low-mass galaxies could lead to the formation of SMGs, but only under the assumption that the star-formation process stimulated by the mergers was heavily weighted towards the production of massive stars. However, this assumption was subsequently disfavoured by observational results⁸.

Similarly, the smooth-accretion scenario has been tested in cosmological simulations that generated SMGs matching those observed, but they did not reproduce the high luminosities of these systems^{5,6}. Given that SMGs are thought to be the progenitors of the well-studied elliptical galaxies found in the present-day Universe, the inability to fit these sources straightforwardly into a cosmological galaxy-formation context has been worrying.

In the current study, Narayanan *et al.* present a hydrodynamic simulation in a cosmological framework that yields the first SMG with a luminosity that is a good match to the