100 YEARS AGO

On the shore of the island of Hadod, latitude 68° 40′ about, in Vesteraalin, north of Lofoten, there was found, probably in the autumn of 1897, a wooden ball, 4½ centimetres in diameter, covered by a thin layer of gum. The ball is of fine workmanship, and just able to float in the water. Circles are engraved upon four parts, and form small rhumbs over the whole surface; and on two places there is engraved with Latin Majuscles the name *Melfort*. Perhaps some of your readers can say from whence this ball has come. I am writing to the man who has the ball now, to ask him to send it to me.

From *Nature* 9 November 1899.

50 YEARS AGO

The speed of the meteors is so great that as they rush into the atmosphere of the earth they burn away at heights of about sixty miles. Until recently, the streaks of light produced by the burning meteors provided the only method by which astronomers could study this phenomenon. Such observations are hindered or prevented by cloud and moonlight, and are impossible in daylight. On the other hand, the burning meteor leaves behind it a dense trail of electrons which can reflect radio waves … An important consequence of the radio observations has been the discovery of great meteoric activity in summer day-time. The well-known visual meteor showers ... usually last for a few nights. The summer daytime showers detected by the radio method are far more extensive and attain higher rates. The daylight activity, which in May comes from the direction of Pisces, develops rapidly, extending over a wide belt stretching towards the sun, and continues as a great succession of meteor showers until late August. The origin of the streams of meteoric debris is a most important problem of meteor astronomy. It is almost certain that most of them move in orbits around the sun. A few are associated with comets; but it is unlikely that this is the case with all of them. There is difference of opinion as to whether the meteoric debris is all localized in the solar system or whether some comes from interstellar space. The radio observations now being made will help answer these questions. The accurate determination of speeds will resolve the problem as to whether any meteors originate from outside the solar system.

From *Nature* 12 November 1949.

Genetics

Distorting sex ratios

Keith R. Willison

During sperm production in mammals, the process of meiosis generates spermatozoa that are genetically different but functionally equivalent. So, with respect to the sex chromosomes, for example, equal numbers of sperm are produced carrying either an X or a Y chromosome. Because X and Y sperm are equally capable of fertilizing an egg, equal numbers of male and female embryos are produced, and the mammalian sex ratio at birth is 50%.

All other pairs of chromosomes show this 50% transmission ratio, but there are rare exceptions. For example, some mice contain naturally occurring variants of chromosome 17 — the so-called *t*-haplotypes — that do not obey this rule. Remarkably, sperm carrying these unusual chromosomes can propagate themselves with transmission ratios as great as 99% in their own favour. It was not known how this process, known as transmission ratio distortion (TRD), is achieved at a molecular level. But on page 141 of this issue, Herrmann and colleagues[1] describe a unique protein kinase encoded by the *t*-haplotype. This kinase affects a signal-transduction cascade that probably controls the speed and directionality of sperm as they make their long journey up the female reproductive tract.

Within a mouse *t*-haplotype, several hundred functionally unrelated genes have been locked together by a series of chromosomal inversions that prevent recombination with wild-type chromosomes[2]. All *t*-haplotypes derive from a single common ancestor, and wild mice carrying these chromosomes can be found all over the world. The *t*-haplotype variants (known as t^{w12}, t^{w32} and so on) differ in the functionally unrelated genes, but not in the TRD system. Presumably, it is the common TRD system that allowed the successful propagation of *t*-haplotypes.

Over 40 years ago, Mary Lyon began a genetic study of TRD in the t^6 haplotype of laboratory mice. She eventually developed a model for TRD, involving interactions between three or more genetic loci[3–5]. According to this model, several loci — the *t*-complex distorters, *Tcd* — act on the single *t*-complex responder locus, *Tcr*, to distort transmission ratios (Fig. 1a). Normally, of course, all the component genes of the TRD system are encoded in the *t*-region of chromosome 17, and are locked together by the chromosomal inversions. But experiments have shown that the distorters (*Tcd*s) can act in *trans* on the *cis*-acting *Tcr* responder[3]. Put more simply, this means that the

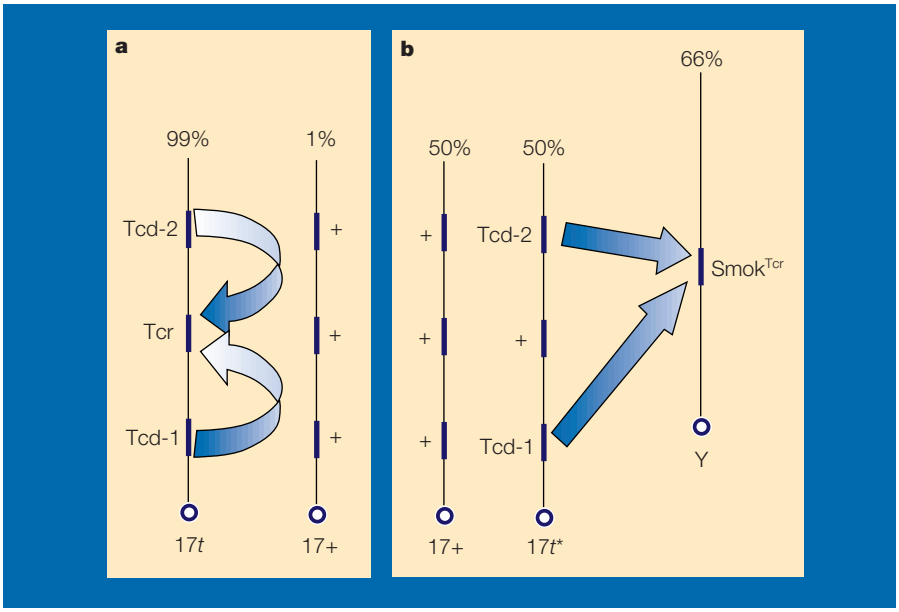

Figure 1 **Genetic models of transmission ratio distortion.** a, **Naturally occurring configuration of genetic elements required for 99% transmission of a *t*-haplotype chromosome (17*t*) compared with a wild-type chromosome (17+). Two or more distorters (Tcd-1 and Tcd-2) act on the responder (Tcr) (simplified model from refs 3,4).** b, **Experimental configuration of genetic elements created by Herrmann and colleagues[1], which produce twice as many male mice as females. The natural distorters are carried by a modified *t*-haplotype lacking Tcr (17*t**), and they act in *trans* on a transgenic Tcr DNA construct carried on the mouse Y chromosome.**

Box 1 : Sperm sexing and selection

There are obvious advantages to being able to pre-select the gender of farm animals — in breeding cattle for milk production, for example[10]. Current techniques use sperm sorting followed by artificial insemination, based on the difference in DNA content between the X and Y chromosomes. In mammals, sperm bearing X chromosomes have 2.8–7.5% more DNA than those with Y chromosomes. Although this process works (it can produce sex ratios of 85–90% in either direction), it is inefficient and not generally applicable.

Assuming the Smok-kinase system is evolutionarily conserved in mammalian sperm production, it may be possible to use the *Tcr* responder to manipulate the transmission ratio of sex chromosomes genetically. Male cattle carrying *Tcr* on the Y chromosome might be expected to transmit the X chromosome preferentially. The *Tcr* responder could also be useful in mouse genetics. In genetic crosses where many construct genes are being segregated, tagging constructs or chromosomes with *Tcr* cassettes could give better segregation in subsequent manipulations. **K. R. W.**

chromosome carrying *Tcr* is transmitted at a high ratio. It is the identification[1] of this *cis*-acting element, *Tcr*, that is now so exciting.

The location of *Tcr* had previously been restricted to a 155-kilobase region of the *t*-haplotype[6]. Within this region, Herrmann and colleagues[1] found a protein kinase gene spanning 80 kilobases. This *Tcr* kinase gene is a fusion of two kinases — a ribosome S6 kinase 3 (Rsk3), and a hitherto unknown kinase related to the microtubule-associated protein (MAP)/microtubule affinity-regulating kinase (MARK) family[7]. This family of serine/threonine kinases is known to phosphorylate MAPs and cause them to detach from microtubules. Several members of the new, MARK-related family are found on the *t*-haplotype chromosome, and also on wild-type chromosome 17. They have been designated 'sperm-motility kinases' (gene symbol *Smok*).

The *Tcr* gene probably derived initially from a rearrangement between a *Smok* gene and the neighbouring *Rsk3* gene. Presumably, during evolution of the *t*-haplotype, mutation and selection generated the dominant genetic factor, $Smok^{Tcr}$, or *Tcr* for short. Although there are many *Smok* genes in this region of chromosome 17, there is only one *Tcr* kinase. Because the generation and subsequent selection of *Tcr* seems so unlikely, it is not surprising that TRD only evolved once, and that all *t*-haplotypes are so similar.

To show that the *Tcr* kinase corresponds to the genetic element defined by Lyon, Herrmann *et al.*[1] constructed *Tcr* transgenic mice in which *Tcr* has randomly incorporated into various mouse chromosomes. The authors found that *Tcr* behaves exactly as predicted by Lyon's model[3,4], giving high transmission of the *Tcr*-containing chromosome in the presence of *Tcd*s, yet less than 50% transmission in their absence. One *Tcr* transgenic strain has *Tcr* incorporated on the Y chromosome, and this produces twice as many males as females (Fig. 1b and Box 1).

But what do these results mean physiologically? The *t*-haplotypes are known to compromise the flagella that power sperm swimming[8], rather than sperm production *per se*. The flagellum, found in the sperm tail, is composed mainly of microtubules (made from a protein called tubulin) and other components that regulate their activity, such as dyneins. Dyneins allow special paired microtubules to slide against each other, then cross-linking proteins help to convert this sliding to a bending motion that allows the sperm tail to beat.

Herrmann *et al.*[1] speculate that the *Tcr* system targets the dyneins. During sperm formation, cells containing a normal copy of chromosome 17 are thought to be damaged by distorter proteins produced by cells that contain the *t*-haplotype chromosome 17. This is possible because developing sperm grow together in a syncytium, in which groups of cells remain connected to each other through large junctions, allowing macromolecules to diffuse freely[9]. The action of *Tcr*, on the other hand, could be to protect those sperm cells that contain the *t*-haplotype from the harmful action of its own distorters — that is, *t*-haplotypes encode both the poison and the antidote. But it is not clear how the antidote might function in only half the cells in the syncytium, even with the knowledge that *Tcr* is a protein kinase and that it is expressed in the right cells at the right time. It is to be hoped that cell-biological analysis of the system will tell us how *Tcr* can act in *cis*, and how it interacts with the newly discovered kinase cascade that regulates the sperm flagellar apparatus. ■

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Condensed matter

Through a glass, lightly

A. Lindsay Greer

Glass formation arises when a liquid is cooled below its freezing point without crystallization. It has been shown that the glass transition is kinetic rather than thermodynamic in origin, but how atomic motion becomes stifled below the glass transition temperature (T_g) is a long-standing problem. On page 160 of this issue[1], Tang *et al.* demonstrate with particular clarity that atomic motion below T_g involves single-atom hopping, whereas motion above T_g is more collective. The idea of such changes in mechanism around T_g is far from new, but this paper helps remove speculation about the exact mechanism. Tang and colleagues' contribution may be compared with the first view of Earth from space — not surprising to see that it is round, but very nice to have the picture.

The new work concerns the diffusion of atoms in bulk metallic glass, but has implications for glass-forming systems in general. Although metallic glasses have been around for some 40 years[2], they are still parvenus. But with the discovery of more stable examples (that is, with greater resistance to crystallization) a broader range of experimental studies is now possible. The more stable metallic glasses are alloys, such as $Zr_{41.2}Ti_{13.8}Cu_{12.5}Ni_{10}Be_{22.5}$ (the composition is in atomic %) studied by Tang *et al.*[1]; they permit glass formation at a slower cooling rate and therefore in greater bulk. When heated through the glass transition, the new metallic glasses yield a supercooled liquid state of unusual stability for metals, permitting reliable measurements of atomic motion in this state for the first time.

The essence of the new study is the comparison of hopping rates for beryllium atoms (Be), as measured by nuclear magnetic resonance (NMR), with diffusive transport rates of Be measured by composition profiling. The problem with NMR measurements in