

## Genetics

## Sex is simple

from Peter Goodfellow

In mammals, chromosomal determination of sex is relatively homogeneous: females are homogametic (XX) and males are heterogametic (XY). Consideration of individuals with abnormal sex chromosome contributions has proved that the Y chromosome is male-determining as XO individuals are phenotypically female and XXY individuals are male, although XO and XXY individuals are usually sterile<sup>1,2</sup>. In other orders of animals different chromosomal sex-determining mechanisms exist (reviewed in ref. 3). Females may be heterogametic as in birds (in female heterogamety the sex chromosomes are known as Z and W, females and ZW and males are ZZ) and sex determination may depend, as in *Drosophila*, on chromosomal dosage rather than the presence of a single sex-determining chromosome. In the latter case XO individuals are male rather than female; in an extreme form of this type of determination the Y chromosome is lost altogether, giving XO males and XX females (O meaning that no second sex chromosome is present in males). The wide variation in chromosomal sex-determining mechanisms, often with differences between members of the same order or even family, poses a problem for the evolution of sex. Assuming that the basic sex-determining mechanism has not evolved independently on several different occasions, how do you progress from one chromosomal sex-determining mechanism to another?

The first part of the answer was provided by Fisher in his classic text, *The Genetical Theory of Natural Selection*<sup>4</sup>. He suggested, for mammals, that a single Y-linked gene controlled the expression of a series of sex-limited autosomal genes. Thus, the complicated male and female phenotypes would be under the control of a single gene. This hypothesis has the advantage that any phenotype could easily fall under sex-control and could explain the wide variations found in sexual dimorphism.

The second part of the answer comes from studying sex in *Caenorhabditis elegans*, a nematode. The male *C. elegans* has an XO constitution, XX animals are

hermaphrodites. In this issue of *Nature*<sup>5</sup>, J. Hodgkin in an elegant series of genetic experiments has created a variant of *C. elegans* which has a ZZ (male), ZW (female) sex-determining mechanism. Remarkably this transformation requires only two mutations, both of which are at the same autosomal locus<sup>5</sup>.

As discussed by Hodgkin, mutations at several loci can affect sex determination; however, the most profound changes are caused by mutations at the *tra-1* locus. Recessive null mutants at the *tra-1* locus convert XX hermaphrodites to phenotypic males which are often fertile<sup>6</sup>. The null mutants have no effect on male XO animals. Several dominant mutants at the *tra-1* locus convert XX and XO animals into fertile females<sup>7</sup>. Mating null *tra-1* (male) homozygotes with dominant *tra-1*/null *tra-1* (female) heterozygotes produces offspring the same as the parental types in a 1:1 ratio<sup>5</sup>. Thus, the experimental nematode has been converted from an

XX-XO dosage system to as ZW-ZZ female heterogametic system.

The important conclusion is that sex is simple: the whole sexual phenotype, both somatic and gonadal, is under the control of the apparently single *tra-1* locus. A similar conclusion could be drawn from recent experiments in mice in which a Y-linked controlling locus, defined by *sxr*<sup>8</sup>, and a series of autosomal modifiers have been described (reviewed in ref. 9). To take the analogy as far as homology it would be interesting to see if the *tra-1* locus is associated with the Bkm sequences known to be linked to the *sxr* locus<sup>10</sup>. Of course, the final answer on homology will be obtained from cloning the *tra-1* gene; it can be safely predicted that this sequence will be used to search many mammalian gene banks and will be injected into the zygotes of mice. □

Peter Goodfellow is at the Human Molecular Genetics Laboratory, Imperial Cancer Research Fund, London WC2A 3PX.

## Galactic emission lines

## Spectra that defy explanation

from C. Martin Gaskell

In this issue of *Nature* (p.241), A. P. Fairall reports observations which, if valid, challenge the basis for our understanding of an entire category of galaxies. What he has reported are 30-minute variations in the 'forbidden' lines of a southern active galaxy (number 427 in a list of galaxies whose activity has been discovered by Fairall). These variations are about six orders of magnitude too fast to be explained within the framework of our present theories on how the variations are generated, for reasons I shall explain in this article, in which I also want to offer an unspectacular explanation for the findings.

A Seyfert galaxy is a very low-luminosity quasar. Such galaxies are recognized by strong emission lines from photoionized gas clouds in the nucleus of the galaxy. They show two types of line emission: 'narrow' lines whose small Doppler widths imply velocities of a few hundred kilometres per second, and 'broad' lines with Doppler widths of many thousands of kilometres per second. A galaxy is called a Seyfert 1 galaxy if the strong hydrogen lines are dominated by the broad-line component and a Seyfert 2 galaxy if the broad-line component is absent. Fairall 427 is a Seyfert 2 galaxy. Intermediate cases are known as Seyfert 1.5, 1.6, 1.7 and so on. The two components of line emission come from physically distinct regions: the broad-line region and the narrow-line region.

The narrow-line region is dominated by what is called 'forbidden'-line emission. A forbidden line arises when an electron makes a transition that has an extremely low probability (typically  $10^8$  times lower than a 'permitted' transition), giving rise to

a visible photon. Because the probability of the transition is so low the electron spends a long time in the upper level before spontaneously making the downward radiation transition. If the density of the gas is relatively high it is more likely that the electron will be knocked out of the level to some other level by a passing electron before it has got round to making the forbidden transition that would give rise to a photon. At high gas densities the transition is thus prevented, or 'forbidden'. Whenever we see forbidden lines, therefore, we know that the gas density is lower than some critical value.

This is the case for the narrow-emission-line regions in Seyfert galaxies and quasars which typically have densities of about  $10^4$  particles per cubic centimetre. The broad-line region, on the other hand, does not show forbidden-line emission so we know that the density is high (in fact about  $10^{10}$  particles  $\text{cm}^{-3}$ ). The emissivity of a gas (number of photons created per unit volume per unit time) is proportional to the square of the density so a much larger volume of gas is needed to produce the narrow lines than is needed to produce broad lines of the same strength. These arguments tell us that the narrow forbidden lines typically come from a region at least 100–1,000 light yr across, while the broad lines come from a region < 1 light yr across.

These size scales are among the best established physical parameters of quasars and quasar-like objects. Photoionization-based estimates of the size of the broad-line region are supported by observations of its variability. Ten years ago A. M. Cherepashchuk and V. M. Lyutyi (*Astrophys.*

- Ohno, S. *Sex Chromosomes and Sex-linked Genes* (Springer, Berlin, 1967).
- Davis, R. J. *med. Genet.* **18**, 161 (1981).
- Austin, C.R., et al. in *Mechanisms of Sex Determination in Animals and Man* (eds Austin, C.R. & Edwards, R.G.) 1 (Academic, London, 1981).
- Fisher, R.A. *The Genetical Theory of Natural Selection* (Clarendon, Oxford, 1930).
- Hodgkin, J. *Nature* **304**, 267 (1981).
- Hodgkin, J.A. & Brenner, S. *Genetics* **86**, 275 (1977).
- Hodgkin, J. *Genetics* **96**, 649 (1980).
- Cattanach, B.M., Pollard, C.E. & Hawkes, S.G. *Cytogenet. Cell Genet.* **10**, 318 (1971).
- Eicher, E.M. in *Prospects for Sexing Mammalian Sperm* (eds Amann, R.P. & Seidal, G.E.) 121 (University Press, Boulder, 1982).
- Singh, I. & Jones, K.W. *Cell* **28**, 205 (1982).