right techniques with the right recipient cells and a suitable DNA delivery system may still keep us waiting a little while longer. We must remember too, that for agriculture, the ability efficiently to insert genes into one monocot crop species is not enough. We must learn how to manipulate all the major crop species. □

1. Herrera-Estrella L. *et al EMBO J.* **2**, 987 (1983).
2. Herrera-Estrella, L., Depider, A., Van Montague, M. & Schell, J. *Nature* **303** 209 (1983).
3. Fraley, R.T. *et al. Proc. natn. Acad. Sci. U.S.A.* **80**, 4803 (1983).
4. Bevan, M., Flavell, R.B. & Chilton, M.D. *Nature* **304**, 184 (1983).
5. Bevan, M.W. & Chilton, M.D. *A. Rev. Genet.* **16**, 357 (1982).
6. Ledoux, L. & Huart, R. *J. molec. Biol.* **43**, 243 (1969).
7. Soyfer, V.N. *et al. Mutat. Res.* **36**, 303 (1976).
8. Korohoda, J. & Strzalka, K. *Z. Pflanzenphysiol.* **94**, 95 (1979).
9. Potrykus, I. *Advances in Protoplast Research* (eds Ferenxzy, L., Farkas, G.L. & Lazar, G.) (Akademiari Kiado, Budapest, 1980).
10. Potrykus, I., Harms, C.T. & Lorz, H. *Theor. appl. Genet.* **54**, 209 (1979).
11. Chourey, P.S., Zurawski, D.B. *Theor. appl. Genet.* **59**, 341 (1981).
12. Green, C.E., Armstrong, C.L. & Anderson, P.C. *Miami Winter Symp.* **20**, (1983).
13. Vasil, V. & Vasil, I.K. *Theor. appl. Genet.* **56**, 97 (1980).
14. Vasil, I.K. in *Plant Improvement and Somatic Cell Genetics* (eds Vasil, I.K., Scowcroft, W.R. & Frey, W.J.) 179–204 (Academic Press, 1982).
15. Raman, K., Walden, D.B. & Greyson, R.I. J. *Heredity* **71**, 311 (1980).
16. Wigler, M. *et al. Cell* **16**, 777 (1979).
17. Spradling, A.C. & Rubin, G.M. *Science* **218**, 341 (1982).
18. Rubin, G.M. & Spradling, A.C. *Science* **218**, 348 (1982).
19. Spradling, A.C. & Rubin, G.M. *Cell* **34**, 47 (1983).
20. McClinlock, B. *Cold Spring Harb. Symp. quant. Biol.* **16**, 13 (1951).
21. Federoff, N., Wessler, S. & Shure, M. *Cell* (in the press).
22. Döring, H.P., Tillmann, E. & Starlinger, P. *Nature* **307**, 127–130 (1983).
23. Peacock, W.J. *et al. Miami Winter Symp.* **20**, (1983).
24. Shimamoto, K. & King, P.J. *Molec. gen. Genet.* **191**, 271 (1983).
25. Freeling, M. *Genetics* **83**, 70 (1976).

Genetics

The origins of men with two X chromosomes

from Paul Burgoyne

APPROXIMATELY one in 20,000 men have a female (XX) sex-chromosome constitution. The occurrence of XX males is of great interest because it raises the question of whether testes can develop in the absence of the testis-determining locus located on the Y chromosome. Recent work has done much to support the view that XX males have a testis-determining fragment of the Y chromosome attached to one X chromosome, but a group of three related XX men do not fit this explanation. As is often the case, these exceptions are potentially the most informative.

In 1966 Ferguson-Smith[1] suggested that the paternally derived X of XX males may harbour a testis-determining fragment of the Y. He envisaged that the fragment might have been transferred to the X by 'accidental crossing-over' between the X and the Y in the father and referred to the event as an X–Y interchange. Originally the idea of X–Y interchange was founded on the observation that some XX men fail to inherit their father's allele for the X-linked red cell antigen Xg^a. The interchange model explains this by assuming that the *Xg* locus, which is located at the tip of the short arm of the X chromosome, is lost from the paternal X when it acquires part of the Y short arm containing the testis-determining locus.

In 1979 another dimension was added to the X–Y interchange model when Evans *et al.*[2] showed a difference in length between the short arms of the two X chromosomes of some but (as others have emphasized[3]) not all XX men. This was taken as evidence for the addition of Y-chromosomal material to the short arm of the paternal X, and in terms of the interchange model this implied that the accidental crossing-over could be unequal with more Y-chromosomal material being gained than X-chromosomal material lost. Polani[4] considers that the organization of the X and Y pairing segments may predispose them to unequal exchanges.

Two recent reports provide further genetic evidence of X–Y interchange. The first[5] indicates that the steroid sulphatase locus (*STS*), which, like *Xg*, is near the tip of the X short arm and escapes X-inactivation, can likewise be missing from the paternal X in some XX males. While most XX men have high levels of STS activity befitting their XX status, in the case described not only was STS activity low but one of the Xs failed to express STS when incorporated in a human–mouse somatic cell hybrid line. The second report[6], published in this issue of *Nature*, describes an XX male who failed to inherit his father's *Xg* allele but did inherit his father's Y-linked 12E7 ('*Yg*')[7] allele. This is the first genetic demonstration of both the loss and gain of material by the paternally derived X of an XX male.

In view of the weight of evidence for X–Y interchange in the aetiology of XX maleness, it was reassuring to hear a report by Bishop, Fellous and Weisenbach at a recent meeting in Oxford that by using Y-specific probes[8] they have identified Y-specific sequences in the DNA from all three XX males they have examined (and see this issue of *Nature*)[9].

The case for X–Y interchange thus seems to be proven, but is this the whole story? Albert de la Chapelle[3] has long argued for a heterogeneous aetiology for XX males, and when the extremely rare familial cases are considered there is certainly food for thought. Let us consider two pedigrees; that described by Kasdan and colleagues[10] where there is an autosomal dominant pattern of inheritance, and that of de la Chapelle[3] in which transmission through females formally rules out dominance. The autosomal dominant pedigree has a direct counterpart in the XX sex-reversal mutation *Sxr* in the mouse. Although inherited in autosomal fashion *Sxr* has turned out to be a fragment of the Y which is regularly transferred to the X during meiosis in carrier males[11, 12]. This intriguing finding was discussed in an earlier article[13]. The important point in the present context is that an apparently autosomal pattern of inheritance can be produced if crossing-over is obligatory in the pairing segment of the X and Y[14]. Thus the Kasdan pedigree may, like *Sxr*, be explained by X–Y interchange.

The de la Chapelle pedigree cannot be dismissed so easily. First, the recessive inheritance in my view argues strongly against the involvement of the Y-borne testis-determining locus. More important, in one of the three XX males in this pedigree both X chromosomes appear to be maternal, since he does not express the paternal alleles for *Xg* (located at the tip of the X short arm) or *Xm* (located near the end of the X long arm). I believe this unlikely anomaly of X inheritance suggests that this XX male has received from his mother two X chromosomes bearing a recessive 'testis-determining' mutant. Wolf[15] has put forward a model for testis determination in which testis differentiation is prevented in XX individuals by an X-borne repressor locus. When a Y chromosome is present this repressor locus is in some way neutralized so allowing testes to develop. This model allows for the development of testes in XX individuals if both copies of the X-borne repressor locus are inoperative through mutation or deletion. Such an X-borne recessive effect is consistent with the de la Chapelle pedigree, provided that the X-borne repressor locus is inherited in a pseudoautosomal fashion (like *Sxr*). I have previously suggested pseudoautosomal inheritance of this repressor locus in order to explain recessive XX sex reversal in goats[14].

The XX males from these two pedigrees are a must for investigation using Y-specific probes. The XX males from the Kasdan pedigree may well reveal Y-chromosomal sequences, but I for one shall be very surprised if this is also true of de la Chapelle's XX males. □

Paul Burgoyne is at the MRC Mammalian Development Unit, 4 Stephenson Way, London NW1 2HE.

1. Ferguson-Smith, M.A. *Lancet* 27 August, 475 (1966).
2. Evans, H.J. *et al. Hum. Genet.* **49**, 11 (1979).
3. de la Chapelle, A. *Hum. Genet.* **58**, 105 (1981).
4. Polani, P.E. *Hum. Genet.* **60**, 207 (1982).
5. Wieacker, P. *et al. Cytogenet. Cell Genet.* **35**, 71 (1983).
6. de la Chapelle, A. *et al. Nature* **307**, 170–171 (1983).
7. Goodfellow, P.N. & Tippett, P. *Nature* **289**, 404 (1981).
8. Bishop, C.E. *et al. Nature* **303**, 831 (1983).
9. Guettaen, G. *et al. Nature* **307**, 172–173 (1983).
10. Kasdan, R. *et al. New Engl. J. Med.* **288**, 539 (1973).
11. Singh, L. & Jones, K. W. *Cell* **28**, 205 (1982).
12. Evans, E. P. Burtenshaw, M. & Cattanach, B.M. *Nature* **300**, 443 (1982).
13. Simpson, E. *Nature* **300**, 404 (1982).
14. Burgoyne, P.S. *Hum. Genet.* **61**, 85 (1982).
15. Wolf, U. in *Development and Function of Reproductive Organs*, 260 (Excerpta Medica, Amsterdam).

0028-0836/84/020109-01$01.00