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CHAIRPERSON'S INTRODUCTION

Other genes of the Y chromosome

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From the moment that the major part of the mammalian Y chromosome ceased to recombine with the X, the action of Muller's ratchet began to whittle away at it to remove all but the essential genes. Consequently, by comparison with their respective X homologues, both human and mouse Y chromosomes are relatively small and probably contain very few genes in a fabric of accumulated junk. Nevertheless, molecular biologists have not been deterred from searching for Y-linked genes and in recent years this has become an increasingly popular pastime. Although hard to find, any Y-linked genes are likely to play important roles in either sex determination or male fertility, a fact which has spurred the search.

How many genes are likely to be present on the chromosome? If we accept the hypothesis that most genes are preceded by an *Hpa*II tiny fragment (HTF) island, we can place an upper limit on the number of genes by considering the frequency with which such islands occur on the chromosome. We have screened sixty randomly chosen Y-derived cosmid clones for clusters of *Hpa*II sites in my laboratory and have found four (V. Shortle, unpublished results). In one of these cases, the sites are not cleavable in genomic DNA and are probably methylated, the other cases have not yet been investigated. This suggests an upper limit of one HTF island per 800 kb or about 40 HTF islands in total. The real number may be much less than this and indeed less than ten genes have been identified so far from genetic evidence. Contributions to this section of the symposium address many of them.

The first gene to be cloned from the human Y chromosome was *MIC2*. This gene is interesting in a number of respects. It is located in the pseudoautosomal region of the X- and Y-chromosome short arms and is the nearest distal marker to *TDF*, it is not subject to X inactivation and the genetics of its interaction with *XG* (to which it is closely linked on the X chromosome) have led to the hypothesis of a second pseudoautosomal gene *XGR*. The contribution of Goodfellow *et al.* reviews all these aspects of *MIC2*. In the mouse, steroid sulphatase, *STS*, is pseudoautosomal (see Bishop *et al.*) but in humans *STS*, although tightly linked to the pseudoautosomal region on the X chromosome, is present on Yq only as a pseudogene (see Fraser *et al.*), which suggests the occurrence of a recent pericentric inversion of the Y chromosome. This is consistent with the relative positions of *TDF* and *H-Y* on man and mouse Y chromosomes as discussed more fully by Craig *et al.* in their summary of the symposium.

Apart from the sex-determining gene (and that hoary chestnut *hairy ears*) the most widely known Y-linked gene is *H-Y* which codes for a male-specific transplantation antigen. Until recently the dominant (though controversial) theory of sex determination was that *H-Y* and the sex-determining gene were synonymous. In this symposium, Simpson *et al.* present compelling evidence which proves that not only can *Tdy* and *H-Y* (as defined by cytotoxic T cell assays) be separated by mutation in the mouse but also that in the human *TDF* and *H-Y* can be mapped to very different regions of the Y chromosome.

Much of the controversy surrounding the hypothesis that *H-Y* was the sex-determining gene centred on the interpretation of experiments performed using low titre antibodies to define the H-Y antigen. Now agreement seems to have been reached that in mammals there are two male-specific antigens. The antigen recognized by cytotoxic T cells is H-Y and is different to that identified by antisera and known variously as *Sdm* (serologically detectable male antigen) or *Sxs* (serologically sex-specific antigen). Wiberg and Scherer in this symposium demonstrate by using a new, high titre antiserum that *Sxs* is expressed in XX true hermaphrodites in whom no Y DNA can be detected. This suggests that in humans *Sxs* is not Y linked and is therefore part of male sexual differentiation downstream of the primary sex-determining event.

Apart from its role in sex determination (where it may act primarily in the Sertoli cells, see Singh *et al.*) the Y chromosome is important for spermatogenesis. Burgoyne demonstrates that in the mouse at least two Y-linked genes are involved one of which may be *H-Y*. Page suggests that, in man, a Y-linked gene, *GBY*, which probably has a function in spermatogenesis, may predispose dysgenic gonads to gonadoblastoma. He tentatively places *GBY* in the same deletion interval as *H-Y*. None of these genes has yet been cloned but an attempt by Leroy *et al.* to do so has thrown up two Y-chromosome pseudogenes homologous to abundant testis-specific transcripts.

Finally, Bishop *et al.* reported the isolation of a single-copy genomic probe derived from the *Sxr* region of the mouse Y chromosome and homologous to a mRNA found in testis but not liver. Whether or not this is *H-Y* or *Tdy*, it is certain to be interesting. With the rapid increase in the number of probes coming from the Y chromosomes of both man and mouse, there is little doubt that we shall soon know a great deal more about the role of this chromosome.