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CHAIRPERSON'S INTRODUCTION

Mapping the Y chromosome

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DNA probes isolated from the human Y chromosome have been used to resolve two fundamental problems concerning the biology of sex determination in man. Coincidentally, resolution of these problems has generated genetic maps of the short arm of the human Y chromosome and has allowed the regional localization of *TDF*.

The first problem to be solved was the origin of XX males (de la Chapelle, this symposium): the majority of XX males are caused by a telomeric exchange between the X and Y chromosomes that results in *TDF* and a variable amount of Y-derived material being transferred to the X chromosome. The differing amounts of Y-derived material present in XX males has been used as the basis of a 'deletion' map of the Y chromosome (Müller; Ferguson-Smith & Affara; this symposium). In construction of these maps, it has been assumed that there is a unique order of sequences on the Y chromosome; that sequences proximal to *TDF* will be present in only some XX males and that sequences distal to *TDF* will be present in all XX males. Although these assumptions seem to be generally correct, occasional XX males appear to have been caused by complex translocations or have been derived from Y chromosomes with rearranged sequence orders (Ferguson-Smith & Affara; Müller; this symposium). These caveats notwithstanding the *TDF* locus maps to a distal position on the short arm of the Y chromosome.

The second problem was the nature of the pairing region responsible for the correct meiotic association and segregation of the X and Y chromosomes in mammals. 50 years ago, Koller & Darlington suggested that pairing is due to homologous sequences shared by the sex chromosomes and that recombination can occur between these sequences. Recently, Burgoyne coined the adjective pseudoautosomal to describe the predicted genetic behaviour of the shared sequences. Molecular analysis of the human Y chromosome has confirmed Koller & Darlington's hypothesis. Several sequences, isolated at random from the human Y chromosome, have been shown to recombine between the sex chromosomes with a high frequency in male meiosis (Weissenbach *et al.* this symposium). The results are consistent with a single obligate recombination in male meiosis; the position of the recombination event within the pseudoautosomal region is variable and this allows the construction of a meiotic map of the pseudoautosomal region (Weissenbach *et al.* this symposium). *MIC2*, the only gene known to be shared by the human sex chromosomes, is the most proximal pseudoautosomal marker known (Goodfellow *et al.* this symposium). Obviously, *TDF* must be located outside the pseudoautosomal region and the consensus map position for *TDF* is, therefore, on the distal part of the Y chromosome short arm proximal to *MIC2* and the pseudoautosomal region (Ferguson-Smith & Affara; Müller, this symposium).

In an attempt to refine the map position of *TDF*, Pritchard & Goodfellow (this symposium) attempted to use chromosome-mediated gene transfer to generate hybrid cells containing subchromosomal fragments from the Y chromosome. Unfortunately, these studies were confounded by the frequent occurrence of interstitial deletions; however, the hybrid cell lines produced proved to be a useful source of new DNA probes for the *TDF* region (Pritchard & Goodfellow, this symposium).

Further progress will require the construction of long-range restriction maps to locate precisely the *TDF* gene; this will be rapidly followed by chromosome walking to clone this region of the genome.

The following papers summarize a remarkably rapid advance in our understanding of the genetics of the human Y chromosome and presage the imminent cloning of *TDF*.