Editorial

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Gene mapping and medical genetics

The mapping of the human genome has a respectable, even venerable, history in the development of human genetics. The first autosomal linkage (the Lutheran and Lewis blood groups) dates back to more than 30 years ago,¹ while linkage on the X chromosome between haemophilia and colour blindness was recognised by Bell and Haldane in 1937.² Since these early discoveries a devoted group of workers has steadily increased our knowledge of the human gene map, as can be seen from the reports issued by the international workshops on human gene mapping held regularly since 1968.³

During the past four years this field has been totally changed by the advent of a new group of polymorphisms based on inherited variation detectable by direct DNA analysis. These restriction fragment length polymorphisms (RFLPs) have proved to be so abundant that the main previous brake on mapping of human genes, the small number of suitable marker loci, has now been removed, at least in principle. It has now become a matter of resources, time, and knowing where to look, rather than a high probability of any study ending in a negative or inconclusive result from lack of markers.

This potential abundance of polymorphisms also has important practical implications for prediction. If the polymorphism is related to a specific gene probe for a disorder, the chance of recombination will be negligible and accuracy of prediction will be limited only by family structure and by degree of polymorphism of the locus. The haemoglobinopathies and haemophilias are already providing examples of the practical use of this approach. Where the marker loci are linked, rather than causally related, the potential for error from recombination is greater and less easy to quantify, but some practical use is already foreseeable, especially when markers exist that 'flank' or 'bridge' the disease locus, as is the case for the X linked muscular dystrophies.

This new situation means that gene mapping is now of immediate importance to all workers in medical genetics, not just to the small number directly involved in gene mapping research. Those intending to use DNA polymorphisms in prediction must know not only the current state of the human gene map, but also be aware of the limitations and potential pitfalls that exist.

The *Journal of Medical Genetics* has for many years published a number of major advances in genetic linkage in man, most based on the use of classical genetic markers, but more recently discoveries using DNA polymorphisms. Readers and potential authors may like to know that the Journal intends to develop this emphasis further, with rapid publication possible for brief or particularly important reports.

This issue also publishes the first of a regular series of gene mapping reviews, starting appropriately with the X chromosome. Subsequent reviews on the Y chromosome and individual autosomes will follow systematically and will stress the clinical and practical aspects of the mapping. A further contribution that the Journal intends to make regularly is an informal listing of new DNA polymorphisms, as a means of communication with those who may find them useful in their own research.

The Eighth International Gene Mapping Workshop will be held this month in Helsinki, and will undoubtedly show how much ground has been covered since the previous meeting two years ago in Los Angeles. New sources of genetic variation, including the use of highly variable 'mini-satellite' DNA sequences⁴ and polymorphisms identified by DNA melting techniques,⁵ are already promising to take their place alongside RFLPs. A moderately detailed gene map for

every human chromosome now seems a possibility for the immediate future, while the existence of a complete map of the human genome no longer seems an unrealistic dream.

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References

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