Recent Research on Human DNA-polymorphism

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The recent developments in recombinant DNA technology have opened up entirely new possibilities in the study of genetic variation and inheritance. Thousands of fragments from the human genome have been amplified by bacterial cloning and used as probes to detect polymorphisms in the restriction enzyme cleaving pattern of the homologous sequences in the genome. Many laboratories, including our own, have mapped and characterized a number of such restriction fragment length polymorphisms (RFLPs). Approximately 1000 such chromosomally localized RFLP markers have now been described and more are coming.

The RFLP analysis is presently done by digestion of extracted DNA from a cell sample from different individuals with suitable restriction enzymes followed by electrophoretic separation of the generated fragments according to size and visualization of the relevant fragments by hybridization with radioactively labelled probes and autoradiography.

Since the analysis can be performed on relatively small quantities of DNA and even on DNA from blood and semen stains, this opens up the theoretical possibility of identification and paternity testing with next to unlimited precision. However, the analysis involves the use of a great number of different probes and will thus be time consuming and expensive even if the methodology is being simplified by automatization and non-radioactive labelling.

Of particular interest in this connection are some RFLP markers that consist of tandemly repeated sequences. Especially the so called α-repeats that are clustered in the centromere regions of the chromosomes and are organized as a number of basic units (approximately 170 base pairs long) that form a block that in turn is reiterated manyfold. Recently probes have been developed that selectively hybridizes to chromosome specific variants of the basic repeat. If the DNA is cleaved with a restriction enzyme that does not cleave in the basic repeat and then analyzed with such a probe most of the homologous DNA is in very long fragments but due to individual variation in rare basic repeats a ladder of small fragments is also generated. It has been claimed that every X chromosomal centromere can be recognized by its unique pattern of fragments with this type of analysis. Such highly informative polymorphisms of course obviates the need for multi marker analyses. Though mendelian inheritance of these markers have been demonstrated, it is not yet completely clear whether they are stable enough to permit practical use even in paternity testing.

Another possibility is to use a probe that is homologous to repetitive, highly polymorphic sequences spread throughout the genome. With this technique one can obtain a complex pattern of fragments that is more or less unique to the individual. It is presently unclear if this analysis is reproducible enough to be clearly interpreted and practically managable in forensic medicine.

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