Better markers for genetic diseases

Some years back, geneticists could pinpoint inherited diseases (chromosomal abnormalities and genetic disorders) only by studying family pedigrees. This was classical Mendelian genetics (predicting defects on the basis of mathematical probability). Then scientists got so they could visualize certain chromosomal abnormalities by karyotyping—photographing chromosomes in dividing cells and examining the silhouettes of the chromosomes. Only a few of the chromosomes showed up clearly, however. Then two years ago investigators learned how to visualize all human chromosomes with certainty by analyzing chromosomes with a fluorescent microscope or by staining different regions of chromosomes (SN: 9/25/71, p. 200).

Now scientists at the University of California, Livermore, and the University of Pennsylvania have devised techniques to determine the amount of DNA (genetic material) in human chromosomes with a precision that has not been possible before. These techniques also promise to provide markers for human chromosomal abnormalities and perhaps also for genetic disorders.

Mortimer L. Mendelsohn, Brian H. Mayall, Elliot Bogart and Dan H. Moore II of California and Benson H. Perry of Pennsylvania report their findings in the March 16 SCIENCE.

First they identified chromosomes in six cells from two men by means of the fluorescent microscope. Then they stained the chromosomes with a dye specific for DNA, so that any DNA on the chromosomes would become visible. The stained chromosomes were then scanned by a digital computer by the process known as quantitative image analysis. The computer displayed on a screen the relative DNA content of each chromosome, showing up differences as small as two percent (5×10^{-15} grams). Not only did homologous (genetically comparable) chromosomes from the two men differ significantly in DNA content; several homologous chromosomes from one man also differed markedly in DNA content.

The researchers now intend to examine the DNA content on chromosomes from males and females of various ages and from various segments of the population to get a better idea of what the normal chromosomal contents of DNA are. Then they intend to look for possible abnormalities in DNA content and try to see whether the abnormalities might be related to certain genetic diseases. For example, they might find that there is an unusual amount of DNA on the X chromosome of women who carry the X-linked gene for hemophilia. If this should be the case, then an abnormal amount of DNA might be used to help diagnose carriers of hemophilia. Singular amounts of DNA might also be found on chromosomes in cancer cells, and tell scientists something about cancer development. The California scientists hope to explore these possibilities.

The amounts of DNA they can detect sound incredibly small, but Mayall says they are not nearly as small as individual genes that are responsible for various genetic disorders. He doubts whether genes responsible for such disorders will ever be detected by optical techniques; instead they will probably have to be diagnosed biochemically. . . .

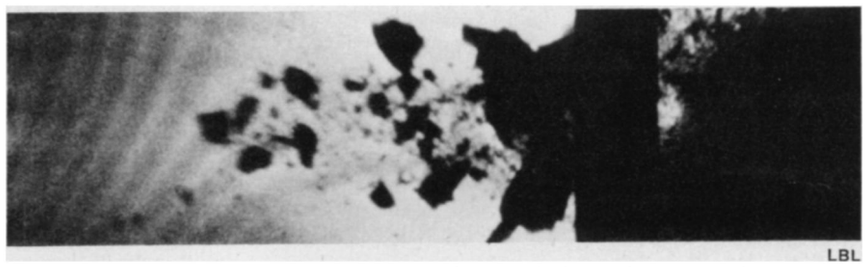
* * * *

. . . Scientists are making progress in this direction too. Some of the latest findings are reported in another paper in the March 16 SCIENCE.

F. A. McMorris of the Massachusetts Institute of Technology and colleagues at Yale University and the M. D. Anderson Hospital and Tumor Institute in Houston crossed human and mouse cells, by a technique known as cell hybridization. During hybridization certain human chromosomes are retained or lost. If certain human chromosomes are retained and certain human enzymes also continue to be manufactured, then the genes for those enzymes can be assigned to those chromosomes. Concomitantly if certain human chromosomes are lost and certain human enzymes are no longer made, then the genes that make the enzymes can be assigned to those chromosomes. Using these deductions the biologists found that glucosephosphate isomerase, a crucial energy-metabolizing enzyme, is made by a gene on human chromosome F-19, and that mannosephosphate isomerase, a minor energy-metabolizing enzyme, is made by a gene on human chromosome C-17.

Thanks to cell hybridization, human gene mapping has seen "a tremendous advance," McMorris says. Two years ago only four or five genes had been mapped. Now some 20 have been assigned to a number of human chromosomes. The more genes that can be mapped, the better will scientists understand human genetics, particularly gene regulation, about which little is known. Also, as more genes are pinned to specific chromosomes and perhaps linked with each other, geneticists should also be better able to predict whether a couple is likely to bear a child with a particular genetic disease. □

The promise of tunneling by electron beam



A 50-nanosecond burst of electrons blows a hole in 0.4 inch of granite.

Tunneling through rock is a slow procedure. For each advance, holes must be drilled and explosive charges set. Then people are cleared from the area and the charges are detonated. The debris is removed and the cycle starts again.

Experiments in progress at the Lawrence Berkeley Laboratory in California show promise of speeding up rock tunneling by using intense beams of electrons to cut through the rock.

The work is being done by Robert T. Avery and Denis Keefe of LBL and Tor L. Brekke and Iain Finnie of the University of California at Berkeley. It is supported by the National Science Foundation as part of its Research Applied to National Needs program (RANN). The electrons come from accelerators that are quite low-energy by today's standards—about one million electron-volts (one MeV). These machines produce bursts of electrons many times more intense than those used in particle-physics experiments. The bursts, which last only 50 nanoseconds (one twenty-millionth of a second), deliver intense pulses of heat to the rock. This sets up a thermal expansion wave in the rock. Says Avery, "The rock wants to expand. If it expands rapidly enough, the expansion exceeds the tensile strength of the material and material spalls off." A single burst does not flake off very much, only a few centimeters, but repetition rates of hundreds of times a second are possible. For a working model Avery envisions an apparatus about the size of the mole machines that now do earth tunneling. This would scan a four- or five-MeV beam across the rock face. At several hundred bursts a second it could chip off a sizable quantity of rock in a time that is short by human standards. "This may provide the breakthrough in tunneling speed," says Avery. □

Science Service, Inc. is collaborating with JSTOR to digitize, preserve, and extend access to *Science News*. www.jstor.org