Biology

New landmarks on human chromosomes

Diagnosis and prenatal determination of the thousands of genetic diseases require a detailed map of the human chromosomes. The number of one type of known landmark on this map has just doubled, according to scientists at Collaborative Research, Inc., of Lexington, Mass. At the recent Human Gene Mapping Workshop in Helsinki, Finland, they reported 500 newly discovered markers, 29 of which they expect to be exceptionally useful for mapping human genes.

Each landmark is a pattern of DNA pieces resulting from the cutting of the chromosomes by specific enzymes called restriction enzymes. The 500 new markers represent regions of the chromosomes where different people show different patterns. These regions are said to be "polymorphic" and the landmarks are known as RFLPs (restriction fragment length polymorphisms). The most useful markers will be those for which the most patterns occur in different individuals, so that they are most likely to distinguish between chromosomes, for instance one inherited from the father and one inherited from the mother. The cut DNA pieces are identified by their binding to short segments of DNA called probes (SN: 8/18/84, p. 104).

"Twenty-nine of these 500 [probes] are among the most polymorphic human markers known and will significantly facilitate tracing the inheritance of certain chromosomes in families," says Thomas O. Oesterling of Collaborative Research. Previously, only one such "highly informative" probe had been identified.

Collaborative Research recently filed a patent application for the first commercial use of RFLPs. A set of highly informative probes is described for paternity testing and for determining after bone marrow transplantations which cells are derived from the patient and which from the donor.

"The test," Oesterling says, "will give doctors a method that can tell with 99 percent accuracy whether bone marrow transplantations have been successful."

Who will judge gene-therapy research?

With medical scientists nearing the moment when they will request permission to attempt gene therapy on human patients (SN: 8/24/85, p. 117), federal agencies are still debating which agency will have the power to grant consent. A recent skirmish has focused attention on the Food and Drug Administration (FDA), the National Institutes of Health (NIH) and a recently proposed Biotechnology Science Board, intended to coordinate federal actions on biotechnology.

The NIH Recombinant DNA Advisory Committee (RAC) has been the main review body for gene-splicing experiments since the technology's early days (SN: 2/23/85, p. 122). A RAC working group has prepared over the last two years guidelines called "points to consider" in evaluating gene-therapy proposals. A draft of this document was published in January and a revised version was to be published this summer.

Although historically, the FDA has not become involved in the regulation of certain early clinical experiments, including NIH-funded work with only a few patients, that agency now appears eager to take on gene therapy as part of its authority over drugs, medical products and devices. The FDA objected that the RAC's "points to consider" should not be published until they are reviewed by the Biotechnology Science Board, although that proposed committee has not yet been officially chartered.

A compromise between FDA and NIH was reached. The "points to consider" are again scheduled for publication in the Federal Register, but that document will state that they apply only to NIH-funded researchers. This early skirmish indicates that researchers probably will not be able to seek permission only from the now-familiar RAC. They must prepare to contend with the FDA and perhaps a new coordinating board.

Computers

Assessing a RISCy business

Albert Einstein once remarked that things should be made as simple as possible, but no simpler. Computer architects are beginning to learn a similar lesson when deciding how a computer should translate commands written in a language like FORTRAN into electrical signals that ripple through an integrated-circuit chip. Instead of packing microprocessors with circuits for more, increasingly complex instructions, some designers are "wiring in" only those for a few, frequently used commands. The result is a new class of streamlined computers called "reduced instruction set computers" or RISC machines.

A simple analogy illustrates the idea. The instructions that tell a computer chip how to shift "bits" (electrical pulses) while doing elementary operations such as LOAD, STORE, COMPARE and ADD are somewhat like the keys on a calculator keyboard. Some calculators feature dozens of keys, many of which perform special functions like taking square roots or calculating standard deviations. These calculators tend to be expensive, many keys are rarely used, and users face a bewildering array of choices when trying to solve a problem. In contrast, simple calculators stick to the basics: addition, subtraction, multiplication, division and little more. For many calculations, this is enough.

In a RISC machine, a small set of built-in instructions allows plenty of extra room on a chip for temporarily storing data close at hand rather than on separate memory chips. Compilers, which translate a computer program's high-level commands into elementary chip-based instructions, face an easier task because they have fewer choices to reconcile. Now, several companies are gambling that this type of architecture, an academic curiosity only a few years ago, will lead to faster, cheaper computers. Some commercial products with RISClike features are already available (SN: 3/12/83, p. 169).

The Hewlett-Packard Co. of Palo Alto, Calif., is making one of the largest corporate commitments to RISC architectures. In its Spectrum project, company researchers carefully measured the behavior of a wide range of computer programs to find which instructions came up most often and which functions were most useful. These studies led to a design for a family of computers that share a simple core and can easily be extended for particular applications. The company now has about 100 working prototypes and plans to introduce its first products next year.

Taking a slightly different approach, MIPS Computers Inc. in Mountain View, Calif., is designing a computer processor that allows several instructions to be executed at the same time without clogging the system. Based on research originally done at Stanford University, this RISC processor requires special compiler software to speed it up. The firm intends to sell processor "boards" that can be built into computers produced by other manufacturers.

Meanwhile, David A. Patterson, one of the earliest advocates of a simple approach to computer architecture, and his group at the University of California at Berkeley have in the last three years designed and fabricated three experimental RISC chips that, according to a variety of tests, really do run faster than more sophisticated computers. The first, RISC I, had only 31 instructions compared with the 304 instructions embedded in a VAX-11/780 superminicomputer. Their latest effort involves a RISC chip tailored for a programming language called Smalltalk. Initial results show that Smalltalk programs would run faster with this chip than on the best computer now available for running the software.

Despite these successes, some computer engineers are not convinced that running RISCs is the way to go. Such computers often require larger programs for a particular application. Manufacturers are also more familiar with the kinds of microprocessors now available and are resistant to change. Detailed, critical examinations of RISC concepts appear in this month's IEEE SPECTRUM and next month's IEEE COMPUTER.