

Genetic susceptibility to disease

In 1962, shortly after a party held on board the *USS Little Rock*, 602 members of the crew developed bacterial dysentery. Most recovered without incident, but 10 went on to develop a form of arthritis called Reiter's syndrome. Some 15 years later, acting on a hunch that susceptibility to Reiter's disease is genetically determined, Stanford University immunogeneticists Andrei Calin and James Fries battled against military bureaucracy to track down the 10 sailors involved. The results of their research were summarized at the CASW meeting by Hugh O. McDevitt, another Stanford immunogeneticist.

Calin and Fries have located eight of the 10 original Reiter's victims and found that seven of them have a rare type of white blood cell, labeled B27. White blood cells can be distinguished by surface chemicals called "antigens" — markers that are genetically determined. About 70 of these antigen types are known, with B27 occurring in about four percent of the Caucasian population. Establishing this connection between the occurrence of dysentery, Reiter's syndrome and white blood cell type B27 has provided a vital clue toward understanding the inheritance of susceptibility to disease.

Forty diseases — ranging from several kinds of arthritis to multiple sclerosis, schizophrenia, psoriasis and various cancers — have now been linked to specific types of white blood cell antigen. The frequency of each antigen varies widely among different populations. For example, 25 percent of European Caucasians have antigen type B8, which occurs in only eight percent of African blacks and not at all among Japanese. Presumably the B8 type white blood cells evolved among Caucasians in order to bestow immunity to bacteria commonly encountered in Europe. But as a result, Caucasians with B8 type cells are *more* susceptible to some kinds of arthritis, myasthenia gravis, Addison's disease, Hodgkin's disease, acute lymphatic leukemia and other diseases.

In some cases a "triggering event" — such as a bout of dysentery — appears to disrupt a person's immune system, thus leading to development of the chronic disease to which the individual is susceptible. Once a more complete catalog can be established to link these diseases with the appropriate blood antigens and triggering events, people can be warned more systematically about their inherited susceptibilities. McDevitt said, for example, that he plans to warn his young son (a B27) to take extra precautions to avoid bacterial dysentery, since there would be about one chance in five that it would be followed by Reiter's disease.

In the more distant future, McDevitt says, people may be immunized according to antigen type at birth against the diseases to which they are susceptible. Also, this whole line of research appears promising as a way eventually to develop injections that could effectively suppress specific cancer tumors.

Gene "families": Key to diversity

Accounting for the extreme diversity of nature has always been one of the great problems facing biologists. A simple one-gene-to-one-trait theory of inheritance works well for explaining diversity in simple systems, like eye color. But how could one account for the evolution of thousands of single genes that this theory would require for the production of complex systems like the cells that produce antibodies?

A recent discovery — that strands of genetic material can split and recombine in various sequences — is having a profound impact on the understanding of diversity and evolution (SN: 7/7/79, p. 12), as Lee Hood of the California Institute of Technology explained. Different traits in a complex system can be un-

derstood as resulting from different *combinations* of genes, and a system's evolution is seen as the development of its multi-gene "family."

For example, the structure of one portion of an antibody involved in recognizing some virus as "foreign" is determined by a combination of genes from two separate groups. Any gene from the "V" group can combine with any gene from the "J" group to produce a wide variety of virus-detecting molecules.

The discovery of such multi-gene families may also have significant implications for embryology. Biologists have long wondered how related cells in a developing embryo group together to form bones, the brain and various organs. One possibility, Hood says, is that the cell surfaces contain "recognition molecules" similar to those on antibodies. Presumably the structure of these diverse molecules could also be controlled by various combinations of genes in another multi-gene family.

Toward the 'information economy'

In one of a series of talks sponsored by the Stanford Research Institute as an auxiliary to the CASW meeting, Richard T. Knock discussed the outlook for the electronics industry in the 1980s. The recent proliferation of extremely low-cost computing devices, he said, will be followed by an explosion of low-cost electronic storage units. The result will be an "information economy" in which power will depend more on the ability to control information than to control things.

Within five years, he predicted, it will be possible to buy an electronic device small enough to sit on a desk, costing perhaps \$150,000, that can store perhaps 2.5×10^{14} bytes (8-bit computerized "words"). That's about equal to the storage capacity of the human brain. The secret: replacing magnetic disks with those that store information optically.

The development of new "natural languages" by which non-professionals can communicate with computers will help to make the next generation of devices more useful. At present the cost of programming computers is roughly nine times as expensive as buying them. One new language, called PASCAL, is cutting that cost ratio down to 3:2 for some applications.

A 'clock' for evolution?

The announcement that a distinctly human line apparently diverged from the related australopithecine line much more recently than many paleontologists (particularly the Leakeys) had expected (SN: 6/2/79, p. 362) came as no surprise to Vincent Sarich, a molecular anthropologist at the University of California at Berkeley. Since 1967, he and his colleagues have been predicting a recent divergence based on molecular studies, and he told the CASW audience that the recent fossil discoveries make him feel "reasonably vindicated."

The basic tenet of molecular anthropology — only grudgingly being accepted by traditional paleontologists — is that mutation at the molecular level takes place at a fairly constant rate. It can serve as an evolutionary "clock." Thus, no matter how much the fossils of extinct species may resemble each other, just how closely they are actually related may perhaps be best determined by examining the genetic differences among their present descendants.

To take a case in point, paleontologists emphasizing the structural differences between humans and apes have sometimes concluded that they diverged from a common ancestor 20 or 25 million years ago. Yet the protein structure of humans and apes is as similar as that between grizzly bears and polar bears — indicating a common ancestor as recently as four to six million years ago.

In particular, this evidence puts pressure on paleontologists who still insist that *Ramapithecus* (10 to 15 million years ago) belonged to a distinctly hominid line. Molecular anthropology would insist that it be a common ancestor of *both* apes and humans. Says Sarich: "*Ramapithecus* cannot be a hominid, no matter what it looks like."