Biomedicine

Carol Ezzell reports from Bar Harbor, Maine, at the Short Course in Medical and Experimental Mammalian Genetics

Geneticists uncover heart disease gene

Geneticists have discovered a gene they say could account for roughly half of all cases of the blood vessel-clogging disorder atherosclerosis, the major cause of heart attacks.

Patsy M. Nishina and Jürgen K. Naggert of the Jackson Laboratory in Bar Harbor report that a gene called atherosclerosis susceptibility, or ATHS, causes a set of characteristics that trebles an individual's risk of myocardial infarction. These characteristics include upper-body obesity, low concentrations of high-density lipoprotein (HDL) in the blood, high blood concentrations of fatty compounds, and a preponderance of the small, dense form of low-density lipoprotein (LDL) in the blood. Together they are called an atherogenic lipoprotein profile. An estimated 30 percent of the U.S. population has this profile.

Nishina and Naggert – together with researchers at the Children's Hospital Oakland (Calif.) Research Institute and the Lawrence Berkeley (Calif.) Laboratory – studied the incidence of the atherogenic lipoprotein profile among 72 members of 11 different families. By analyzing the pattern of how the profile passed down from generation to generation in these families, they determined it is caused by a single, dominant gene.

The researchers reported in the Jan. 15 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES that this inheritance pattern suggests that the ATHS gene lies on chromosome 19, near the gene for the LDL receptor. Body cells use this receptor to remove LDL cholesterol from the blood.

Beverly J. Paigen, the Jackson Laboratory scientist who directs Nishina and Naggert's research, says a genetic phenomenon called incomplete penetrance could account for the fact that myocardial infarctions strike mostly men and postmenopausal women. Sex hormones and diet probably also influence the effects of the gene, she adds.

Artificial chromosomes: Just add genes

Geneticists working on the Human Genome Project – the worldwide effort to map and decipher all of the genes that make up a human being – are well on their way to constructing an artificial mammalian chromosome, a technical advance that could speed and simplify the herculean endeavor.

Peter N. Goodfellow of the Imperial Cancer Research Fund in London, England, and his colleagues have successfully moved a telomere – the specialized structure that keeps the tips of chromosomes from unraveling – up toward the center of the long arm of a mammalian X chromosome. As a result, they have created a chromosome whose long arm consists only of a centromere – the pinched region that holds the two halves of a chromosome together – and a telomere, with no intervening genes.

"This is the first step for creating mammalian artificial chromosomes," asserts Goodfellow, who recently accepted a new post at the University of Cambridge. He says the artificial chromosome will be complete once his team moves a second telomere up the short arm of the chromosome. The artificial chromosome will consist of only two telomeres joined by a centromere, forming a blank "cassette" into which researchers can insert single human genes for study.

Currently, geneticists must use artificial bacterial and yeast chromosomes to copy and manipulate inserted human genes. But these chromosomes are sometimes too small to contain entire human genes, which often consist of millions of units of DNA.

Artificial mammalian chromosomes would enable geneticists to manipulate human DNA in a way more nearly resembling the action of genes in the body, Goodfellow says. He suggests they might also serve as vehicles for inserting foreign genes into patients during gene therapy for genetic diseases.

Physics

A single-crystal route to tunneling

A Josephson junction generally consists of a thin layer of an electrical insulator sandwiched between two slabs of superconducting material. Extraordinarily sensitive to changes in electromagnetic fields, such junctions lie at the heart of SQUIDs, superconducting quantum interference devices used for mapping tiny variations in magnetic fields, whether in geological formations or in the human brain.

Now researchers have found that a single crystal of a copper-oxide superconductor can by itself act as a set of Josephson junctions. R. Kleiner and co-workers at the Walther Meissner Institute in Garching, Germany, observed this effect in a high-temperature superconductor made up of bismuth, strontium, calcium, copper, and oxygen.

"Although our results are strongly influenced by crystal imperfections, they show the possibility of using small . . . single crystals as naturally grown series arrays of Josephson junctions," the researchers say.

One can picture this particular superconductor as stacked layers of strontium and bismuth atoms (together with oxygen) separating sheets of copper and oxygen atoms. The bismuth and strontium layers act as insulators between the superconducting copper oxide sheets, creating conditions under which pairs of electrons can "tunnel" through the barriers separating superconducting layers. A crystal only 3 microns tall would contain approximately 2,000 Josephson junctions arranged in a stack.

"This is a significant demonstration of true Josephson behavior, which few other types of high-temperature junctions have shown," physicist Colin Pegrum of the University of Strathclyde in Glasgow, Scotland, comments in the July 16 NATURE. "Whilst their findings do not form the basis of a direct method to engineer true junctions for device applications, they give some insight into the mechanism of interlayer superconductivity in the material."

Such insights may also suggest ways of improving current methods of fabricating Josephson junctions, which normally involve the establishment of tunneling between adjacent superconducting grains or crystals (SN: 1/11/92, p. 30). Kleiner's group described their experiments in the April 13 PHYSICAL REVIEW LETTERS.

Pushing quarks to the limit

So far, physicists have experimentally identified five types of quarks: up, down, strange, charm, and bottom. And they expect to find a sixth, called the top quark. But are there any additional quarks? New calculations by a team of physicists at the University of Tsukuba in Japan provide a glimpse of what would happen to interactions between quarks if their number were larger than six. The results suggest that the strong force responsible for keeping quarks under wraps would no longer confine them, meaning that one would be able to detect single, isolated quarks. This finding contradicts accumulated experimental evidence that quarks can't be found in isolation. Y. Iwasaki and colleagues report their results in the July 6 PHYSICAL REVIEW LETTERS.

In the June 8 issue, a large group of physicists working with data from the Collider Detector at Fermilab in Batavia, Ill., reported success in detecting significant numbers of B-particles, which result from the production and fragmentation of bottom quarks in high-energy collisions between protons and their oppositely charged counterparts, antiprotons. Because such collisions typically create a tremendous amount of subatomic debris, physicists weren't sure they could sift out B-particles from among the fragments. With this new source of B-particles, researchers may yet find an explanation for the universe's apparent imbalance between matter and antimatter.