Biomedicine

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

Hot on the heels of a ball-court killer

Researchers appear tantalizingly close to identifying the genetic and biochemical basis of Marfan's syndrome, an inherited disorder that leaves one in 10,000 Americans with progressively faulty skeletons, hearts, eyes and lungs. Those inheriting this mysterious syndrome generally grow unusually tall, lanky and long-fingered. Many die before age 40.

The puzzling disorder gained recent attention when it took the lives of Olympic volleyball star Flo Hyman and University of Maryland basketball player Chris Patton. Both died suddenly from exertion-induced bursting of the major blood vessel leading from the heart — the result of a gradual, hereditary weakening in that vessel's wall. Discovering the gene responsible for Marfan's would help researchers develop prenatal tests for the disorder, and might point the way toward novel therapies, says Reed Pyeritz of the Johns Hopkins University School of Medicine in Baltimore.

Three new studies provide important clues about Marfan's underpinnings.

People with Marfan's syndrome lack sufficient amounts of a widely distributed body protein called fibrillin, according to Pyeritz, David W. Hollister (now at the University of Nebraska Medical Center in Omaha) and their colleagues at Hopkins, who collaborated with researchers at the Shriners Hospital for Crippled Children in Portland, Ore. Without fibrillin, the body's billions of cells cannot surround themselves with microfibrils — tiny filaments of connective tissue that provide structural support in the spaces between cells. The finding, reported in the July 19 New England Journal of Medicine, means that in Marfan's, "there's something wrong with the scaffolding, or glue, that holds you together," Pyeritz says.

Physicians have long theorized that Marfan's is a connective-tissue disease. But until now, they weren't sure which of the many connective-tissue components held the defect. In recent years, scientists have ruled out onetime candidates elastin and collagen. Now, with good evidence that the syndrome results from a disabled fibrillin gene, the race is on to pinpoint the location of that gene.

But where to start? With no knowledge of the fibrillin connection, chromosomal cartographers for years have sought the Marfan's gene by tracking the syndrome's inheritance pattern in affected families. Six months ago the search narrowed to two of the 23 chromosome pairs present within human cells. Now, Pyeritz says, Finnish researchers appear to have pegged the gene to chromosome-15. If the finding proves correct, researchers will focus their search for the fibrillin gene on that chromosome.

The unpublished Finnish study involved about 20 patients in three families, but has yet to be repeated in the United States, Pyeritz says. "Obviously, many of us are now scrambling around with our markers for chromosome-15 and looking at our Marfan's families," he says.

Additional unpublished research led by Shriners Hospital geneticist Lynn Y. Sakai has scientists closing in on the killer gene from yet another front. After more than a year of genetic screening tests performed on Marfan's patients' cells, the team has now found and cloned a stretch of DNA that appears to be part of the fibrillin gene. The newfound DNA sequence "spells out" directions that a cell would need to make a fibrillin fragment. But while the researchers have found the sequence in cells, they still don't know which chromosome carries this sequence. If, as scientists hope, the fibrillin gene and Marfan's gene both reside on chromosome-15, researchers may at last confirm that the Marfan's gene is but a mutated form of the fibrillin gene.

Though, the Marfan's gene today remains unmapped, Pyeritz says, "Check back in a couple of weeks."

Materials Science

High-tech metalmakers throttle up R&D

The 30 or 40 U.S. makers of specialty metals have been looking over their shoulders lately. Right now, they maintain an edge over their European and Pacific Rim competitors entering this market, observes Robert J. Torcolini, a vice-president of Carpenter Technology Corp. in Reading, Pa. But during the 1980s, U.S. metalmakers reduced their research and development efforts because their production capacity outpaced demand for their wares. Their products include such materials as the lithium-aluminum alloys that can lighten airplanes, making them more energy efficient, and the nickel, chromium or cobalt-based "superalloys" that perform reliably under a jet engine's high stresses and temperatures.

To rekindle basic research into metallic materials in the United States, 10 companies (including Torcolini's) signed an agreement July 18 with the Department of Energy's Sandia National Laboratories in Albuquerque, N.M. It establishes the Specialty Metals Processing Consortium, a collaborative research group to develop new, high-tech metals that are lighter, more corrosion resistant, stronger and more fatigue resistant than existing materials. The consortium will also focus on advancing the processing techniques for producing these metals.

Member companies will each pay $50,000 per year. Sandia will share its facilities and technical know-how. The Energy Department will provide additional funds until 1995, when members expect the program to pay for itself.

Synthetic membranes smell and taste

Thousands of molecules evoke smell and taste sensations in humans, but the mechanisms underlying their action remain unknown. Although many researchers suspect protein receptors in cell membranes within the taste buds and olfactory tissue play key roles, scientists have not isolated such receptors, nor can they explain how a limited cast of receptors could each respond to thousands of structurally different bitter and odorous chemicals.

Yoshio Okahata and his colleagues at the Tokyo Institute of Technology are testing an alternative hypothesis: that bitter and odorous substances trigger sensory cells in the tongue and nose by adhering to the cells' lipid membranes, and not by latching onto protein receptors. This adsorption presumably changes the electrical potential across the membranes, which in turn triggers specific neural-activity patterns corresponding to bitterness or specific smells.

To test this, the chemists made multilayer membranes out of synthetic lipids, measured how much of a particular bitter or odorous substance adsorbed onto their surfaces, and monitored changes in the membranes' electrical potential and resistance in response to the different chemicals.

"Such simple membrane systems may provide useful models of chemoreceptors in biological membranes," the scientists suggest in the July 15 Analytical Chemistry. Sweet compounds, such as sucrose, and chemicals associated with other nonbitter tastes did not adsorb onto the membrane, they say, leaving open the possibility that receptors play a role in sensing them (SN: 5/19/90, p.315).

Indeed, the more intensely bitter or odorous a compound, the greater its tendency to adsorb onto the membrane. Strychnine and nearly all other bitter substances tested make the membrane's electrical potential more positive; odorous compounds such as camphor make it more negative. Bitter compounds have virtually no effect on a membrane's electrical resistance, whereas odorants decrease it. Many of these differences may reflect the adsorbed odorants' comparatively smaller and slinkier structures compared with bitter compounds, and their easier penetration into lipid membranes.