Personality linked to immunity

In the last several years, an increasing number of reports have linked particular psychological states, such as depression, to immunological changes that can contribute to ill health (SN: 6/2/84, p.341). There is now evidence that an individual's overall personality is related to immune function and vulnerability to disease.

J. Stephen Heisel of Charles River Hospital in Wellesley, Mass., and his colleagues compared natural killer (NK) cell activity with scores on the MMPI – a 566-item personality inventory with 12 "psychopathology" scales – obtained from 111 healthy college students. Moderate but statistically significant correlations were found between a laboratory measure of NK cell activity and 10 of the 12 MMPI scales. Students with the highest NK cell activity, they found, had a "healthier" MMPI profile than those with the lowest immune activity.

NK cell activity was not substantially affected by the regular use of medications, alcohol or marijuana; it also did not differ significantly for students who had received medical treatment in the previous year.

There is strong evidence that the NK cell, one of many important elements in the immune system, plays a key regulatory role in protecting against malignancy and infection, the researchers note in the November AMERICAN JOURNAL OF PSYCHIATRY.

While correlations between depression scores and NK cell activity were expected, the investigators point to similarly strong associations – both negative and positive – across a wide range of personality scales. For example, high scores on the MMPI depression scale, which imply unhappiness, social withdrawal, guilt, fatigue, low self-esteem and pessimism, are associated with low immune scores, but the link is about as strong as that between the other nine personality scales and NK cell activity.

The strongest association was between lowered immune activity and high scores on the MMPI's maladjustment scale, which is concerned with an individual's "fit" or adaptation to his or her environment. Conversely, high scores on the ego strength scale, often used as an index of general psychological health, coincided with more robust NK cell activity.

Although scores on the hysteria scale, which measures denial of anxiety and depression and conversion of emotional problems into physical symptoms, showed the lowest correlation with the measure of immune function, the six subjects with markedly elevated hysteria scores had very low NK cell activity, according to the researchers.

The findings support theories of an interaction between mental state and immune function, they conclude, but the underlying nature of the interaction remains largely unexplored. Some scientists, for instance, argue that depressed people tend to find depressed mates and transfer genes for psychopathology and low immunity to their descendants; others contend that phobias and social avoidance may be evolutionary adaptations for individuals with lowered immune function. *– B. Bower*

One-cell origin for atherosclerosis?

Atherosclerotic plaque cells contain genes that cause uncontrolled growth, and these genetic elements, when transferred into other cells, cause them to become cancer-like, New York University researchers have found.

Despite the high prevalence of atherosclerosis, the cause of the condition is one of the great mysteries of cardiology. Two major theories have been developed by different researchers at the University of Washington in Seattle. One is the response-to-injury hypothesis, which holds that atherosclerotic plaques appear where the blood vessel has been injured (SN: 3/16/85, p.170). The other is the monoclonal hypothesis, in which plaques are essentially benign tumors that arise from single smooth-muscle cells.

The NYU report, which appears in the October PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol. 83, No. 20), supplies a mechanism for the monoclonal hypothesis. Arthur Penn, Bruce Mindich and their colleagues looked at the proliferating smooth-muscle cells of atherosclerosis by applying techniques developed for the study of genes that are believed to make single cells grow into cancer.

They started by isolating DNA from human atherosclerotic tissue and normal tissue, and transferring both sets into mouse cell lines. The cells exposed to atherosclerotic DNA lost their normal growth control in the same way they would if exposed to cancer genes, though testing for three known cancer genes indicated they were not present. The normal DNA had no effect on the growth of the mouse cells.

The researchers then injected the atherosclerosis-transformed cells into mice. The mice developed tumors at the site of injection, indicating that the transformed cells were viable.

"We've demonstrated that human atherosclerotic plaque DNA contains a genetic element capable of transforming cells in culture, and these cells can give rise to tumors," says Penn. "The results indicate that one or more as-yet-unidentified transforming genes play a role in plaque cells comparable to the role oncogenes play in cancer cells.

"To my knowledge, this represents the first direct experimental support for the monoclonal hypothesis," he says.

Thomas Pearson of Johns Hopkins Medical Institutions in Baltimore, who confirmed some of the early monoclonal work, says of the NYU study, "I think it's intriguing evidence and the best evidence yet that at least some atherosclerosis is marked by error in the genetic material, and that would suggest it may be a neoplastic [cancer-like] event." A monoclonal origin for atherosclerosis doesn't necessarily rule out the response-to-injury hypothesis, he says.

If the monoclonal hypothesis is borne out, the next step is to discover what activates or mutates the responsible gene. Among the possible initiating events, Penn suggests, are viruses or chemical carcinogens. As for the role of of high serum cholesterol in plaque development, Penn says that while it is unquestionably a factor, its role in these particular events is unknown. *– J. Silberner*

Salting away guest molecules

Preserving perishables by mixing them with salt has a long history. Now a group of chemists has come up with a modern, microscopic version of this ancient practice. They have prepared tiny salt crystals that incorporate neutral molecules to create a new kind of composite material.

The idea is to store volatile or otherwise unstable molecules within, say, an alkali halide such as common salt, says Josef Michl, now at the University of Texas at Austin. Chemists can then study these "guest" molecules under controlled conditions. In the past, they had to use frozen gases like solid nitrogen or argon as hosts, which vaporized too easily for high-temperature experiments. Michl and his colleagues report their findings in the Oct. 29 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

The researchers prepare their samples by condensing alkali halide vapor along with molecules of the chosen guest compound on a surface at 77 kelvins. When the resulting crystals are brought up to room temperature, the molecules are now trapped in their salt "storage boxes." Guest molecules make up as much as a few percent of the final product.

"The permanency of the incorporation is astonishing," the chemists say. They found, for example, that naphthalene stays trapped within cesium iodide crystals even after two hours at 450°C. By itself, naphthalene, a common mothball ingredient, vaporizes easily and melts at 80.5°C.

In most cases, the guest molecules

seem to form small clusters within the host crystals. Michl and his group are now looking for ways to keep guest molecules isolated from one another. "If we can get the molecules singly isolated," says Michl, "it creates a very unusual environment for these molecules." Benzene, for instance, surely doesn't want to be in the middle of a highly polar, ionic environment like that, he says. The researchers want to study the photochemical properties of molecules under these conditions.

Michl, who already has a patent on this technique, is also considering possible applications. Using salt as a way of storing organic compounds, he says, could be a convenient way of getting drugs to cows, which like licking salt but often dislike medicinal preparations.

This method could also be used to generate "molecular imprints" on surfaces. Any guest molecules that evaporate from a surface may leave behind a hollow. "If this footprint is stable," says Michl, "you'll have a shape that will presumably accept the same sort of molecule that left and not others that are bigger." This could lead to useful detectors for specific compounds. *– I. Peterson*

Firefly gene sets tobacco plants aglow

Live tobacco plants that glow before they're lit may sound like a promotion for a cigarette company, but they actually are a demonstration of a powerful new tool in the field of genetics. Using the gene responsible for the firefly's glow, scientists from the University of California at San Diego (UCSD) have developed a glowing genetic tag.

Until now, the standard procedure for marking and monitoring gene activity has involved radioactivity, which, aside from posing the danger of accidental exposure, can be costly and time consuming. The new procedure not only solves all these problems, says UCSD plant biologist Stephen H. Howell, but also is "100 to 1,000 times more sensitive" in detecting gene expression.

The key to the process is luciferase, a firefly enzyme that catalyzes a chemical reaction between luciferin, a small organic molecule, and adenosine triphosphate (ATP), the cell's energy storage molecule. When all three are present, luciferin reacts with ATP and emits light.

Last year, the UCSD team isolated the gene that codes for luciferase and transplanted it into bacteria. This year, in the Nov. 14 SCIENCE, they report success in growing luciferase-producing plants by inserting the luciferase gene into the plants' DNA.

What makes this gene such an attractive tool is the ease of detecting the luciferase; and it is just as easy to detect in a whole plant as it is in a single cell. On the single-cell level, Howell and his colleagues inserted the luciferase gene into cultured carrot cells. After 24 hours they ground up the cells and added luciferin and ATP. A flash of light announced the presence of luciferase, which meant that the cells had been producing the firefly enzyme.

The researchers also grew whole tobacco plants containing the firefly gene. To test for luciferase production, they "watered" the plants with a luciferin solution. Several hours later they had glowing plants – proof that the plants were expressing the luciferase gene.

Many applications await this gene, especially in the study of gene expression. Biologists have long been puzzled by differential gene expression: Why, for example, don't liver cells produce kidney cells, when every cell within a single organism contains the same genetic material? To study such phenomena, scientists can physically link a "reporter" gene, in this case the luciferase gene, to a "target" gene. Testing for luciferase will then reveal which cells are expressing the target gene and whether this gene is turning on and off in response to environmental cues.

Presently the standard reporter gene codes for chloramphenicol acetyltransferase (CAT). However, to assay the CAT gene, scientists must grind up – and consequently destroy – the sample. This aspect, coupled with the radioactivity involved in the CAT assay, taints the CAT gene's usefulness as a reporter gene, says Keith V. Wood, another member of the UCSD team, which also included Marlene DeLuca, Donald R. Helinski, David W. Ow and Jeffrey R. de Wet, who is now at Stanford University.

Howell told SCIENCE NEWS that at the outset of the experiment, "we thought what we were going to have to do was grind up parts of the plant. . . . But it was a real bonus when we found out that we could actually observe this [glowing] in the plant itself."

The luciferase assay also shows promise as a quick, cheap and nondestructive test for inherited plant traits, says DeLuca. One such application would be in the development of disease-resistant crops. "If you had a gene coding for the disease-resistant trait and you linked that to the luciferase gene, then it would be possible to determine whether the resistance had been maintained by successive generations, or whether it had been lost by segments of the population," says DeLuca. She adds that scientists could perform this test by simply dunking young seedlings into a luciferin solution. They could weed out those that don't light up and plant those that do.

Helinski, DeLuca, de Wet, Wood and Suresh Subramani have also induced monkey cells to produce luciferase; a report on their work should appear next year. Wood says that, as in plants, the luciferase gene will be a powerful new reporter gene for multicelled animal systems. However, don't expect to see any glowing Marlboro men.

– R. Monastersky

Photos: Wood

Researchers created a glow-in-the-dark tobacco plant (right) by inserting a firefly gene into the plant DNA. At left is the same plant in ordinary light.

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