A disease caused by body's defenses

A handful of human diseases has been dubbed "autoimmune" in nature—notably multiple sclerosis, rheumatoid arthritis, myasthenia gravis, lupus erythematosus and postvaccinal encephalomyelitis. Autoimmunity means that the body's immune system turns against the body's own tissues or organs, rather than against antigens (foreign organisms or materials). But are these diseases really triggered by autoimmunity? Many investigators are skeptical until scientific evidence becomes more compelling.

Now research reported in the July 10 NATURE by a team of Israeli investigators provides some of the best evidence to date that at least one of these diseases—myasthenia gravis—truly stems from an autoimmune phenomenon. Specifically, Rebeca Tarrab-Hazdai and her colleagues have produced autoimmune myasthenia gravis in primates, and the neurophysiological, immunological and tissue effects in the monkeys closely parallel those of human patients suffering from myasthenia gravis. Myasthenia, which usually strikes young adult women, leads to fatigue, muscular weakness and sometimes death due to respiratory failure.

During the past several years Tarrab-Hazdai and her colleagues at the Weizmann Institute of Science and at Hadassah University Hospital, as well as several other investigative teams, have amassed ample evidence that myasthenia gravis is caused by the body's immune system attacking acetylcholine receptors. Acetylcholine is the chemical messenger between nerves and muscles. Receptors for the compound lie on the membranes of muscle cells.

First they found a reduced number of acetylcholine receptors on myasthenia muscles, suggesting that the primary defect in the disease concerns the receptors. When major cells of the immune system of myasthenia patients were placed in a test tube with acetylcholine receptors, these cells vigorously attacked the receptors. And when rabbits were injected with purified acetylcholine receptors, the rabbits' immune systems reacted against the receptors just as they did against foreign antigens, and the rabbits came down with some of the symptoms of myasthenia gravis—fatigue, muscle weakness and death from respiratory distress. In other words, what appeared to happen in this experiment was that introduction of foreign acetylcholine receptors into the rabbits broke down the rabbits' immune tolerance to their own acetylcholine receptors. As a result, the receptors couldn't function normally—inhibiting normal nerve and muscle action and leading to fatigue, muscle paralysis and death.

Consequently, Tarrab-Hazdai and her team felt the time was ripe to attempt to induce autoimmune myasthenia gravis in primates—animals closest to humans on the evolutionary scale, whose physiological reactions parallel those of humans.

They isolated and purified acetylcholine receptors and injected them into two female Rhesus monkeys four separate times over a nine-week period. Two control monkeys received placebo injections. The monkeys receiving receptor injections showed fatigue, appetite and weight loss. A week after they received their fourth receptor injection, muscles in their jaws, legs and back deteriorated to the point of paralysis. They had trouble holding their heads up and breathing. Meanwhile, the control monkeys remained in good health.

Throughout the experiment, the monkeys were given neurophysiological, immunological and tissue examinations. Monkeys receiving receptor injections showed a decreased response to nerve stimulation; control monkeys showed a normal response. Major components of the immune system taken from the monkeys receiving receptor injections reacted vigorously in the test tube against acetylcholine receptors; the immune systems from the control monkeys did not. Components of the immune system were found in the muscles of monkeys receiving the receptor injections, but not in the muscles of control monkeys.

Most likely, the immune systems of these monkeys receiving receptor injections were stimulated to react against the receptors and, in turn, against the monkeys' own acetylcholine receptors. When the monkeys' own receptors became blockaded by the immune system, nerve and muscle actions deteriorated, triggering symptoms of myasthenia gravis—fatigue, muscular weakness, etc.

"These findings," Tarrab-Hazdai and her co-workers conclude, "thus provide supporting evidence that myasthenia gravis is an autoimmune disease, and that acetylcholine receptor is the auto-antigen. . . . The acetylcholine receptor-induced myasthenia in monkeys, so similar to the human disease, provides a valuable experimental model for studying both the mechanism and therapy of myasthenia gravis." □

Microbes in maize: Extraleguminous fix

It seems so logical. Nitrogen-fixing bacteria can live happily with legumes. Why can't they get along with cereals, like corn, too? If these helpful little microbes would just cooperate and move in with some staple cereal roots, the food and fuel crises would let up considerably. The bacteria would fix atmospheric nitrogen into ammonia, the plants would turn the ammonia into amino acids and proteins and the farmer would put less petroleum-based fertilizer into his fields. Logical.

Well, some nitrogen-fixing bacteria are, apparently, being bio-logical. *Spirillum lipoferum*, a Brazilian team now reports, can inhabit the roots of corn growing in the fields and fix nitrogen almost as well as *Azotobacter* does in soybeans. Joachim F.W. Von Bülow and Johanna Döbereiner of the Federal Rural University of Rio de Janeiro report their field experiments in the June PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

Nitrogen fixation in tropical grasses is not new. Döbereiner reported last summer finding *Spirillum* fixing nitrogen efficiently in the roots of the forage grass *Digitaria decumbens*. Also, *Spirillum* has been found in corn roots grown under high light intensity in the laboratory. But this latest report, for the first time, measures *Spirillum* nitrogen fixation in corn under field conditions and at an activity higher than any yet reported for a grass-bacteria association. The team tested various corn strains and measured nitrogen fixation with a special acetylene (C_2H_2) reduction technique that allows plants to continue growing and producing seeds. A maize strain called S_1 showed the highest nitrogen fixing rates, approaching that of soybeans. Activity is measured in nanomoles of acetylene fixed per gram of dry plant roots. Some S_1 maize exhibited 7,124 nanomoles, compared to 9,137, 12,544 and 9,792 nanomoles of acetylene fixed for soybeans.

There are some hang-ups to the wholesale infection of world corn crops with *Spirillum*, though, the team states. The main one is temperature. *Spirillum* functions best at soil temperatures between 31 and 40 degrees C. and fixes very little nitrogen below 25 degrees C. Soils in temperate regions, such as the U.S. cornbelt, are cooler than this. One Wisconsin researcher, Robert Burris of the University of Wisconsin, is trying now to infect corn grown in temperate soils with *Spirillum*, SCIENCE (Aug. 1) reports.

Another problem is the wide variation displayed in nitrogen fixation rates. While some S_1 plants showed mean values of 7,124 nanomoles of acetylene fixed per gram of dry roots, others showed values as low as 15 nanomoles fixed.

More research must be done to determine the most suitable corn strains, to provide definitive proof that *Spirillum* is the major nitrogen fixing strain involved, to outline the most favorable growth stages and soil and climatic conditions and to search for *Spirillum* associations in other staple cereal crops, such as wheat. In the meantime, though, Von Bülow and Döbereiner state, it appears that in the majority of tropical regions around the world, plant breeding may make possible efficient nitrogen fixing partnerships between maize and bacteria. □