A parasite with the guts of a burglar

A lot of unfriendly parasites would like nothing better than to take up residence inside some of the body's cells, where they can ensure their existence by feeding happily on their host. There are even some cells in the body that encourage such visitors. The cells, called macrophages, act like janitors, sweeping up bacteria and dead tissue. But these cells are probably the last place an unfriendly invader wants to be – once attached to the cell, the parasites are usually doomed, as a macrophage respiratory burst generates toxic oxygen molecules to destroy the attacker.

But two scientists now believe they may have uncovered the way in which one parasite not only gets into a macrophage, but also avoids death once inside. David M. Mosser and Paul J. Edelson of Cornell University Medical College in New York City have found that *Leishmania major*, which causes parasitic diseases common to the tropics, uses one of the body's nine components of complement – proteins that help destroy foreign invaders – to stay alive. Leishmania, which first live in an insect before changing form and transferring to a warm-blooded host, often affect children and are responsible for mild to fatal lesions and ulcers on the body. The diseases caused by leishmania have been cited by the World Health Organization and others as one of the five major health parasitic scourges worldwide.

Since macrophages try to make mincemeat out of microorganisms upon binding, the trick for a parasite is to get past the cell's defense mechanism and into its new home. "Leishmania have to have a way of ringing the doorbell without triggering the burglar alarm," Edelson says. Although it has been known that leishmania and other organisms, such as *Toxoplasma gondii*, have learned how to enter a macrophage without triggering a burst, Edelson believes this is the first time scientists have shown how leishmania achieve that feat. "Leishmania have figured out," Edelson says, that a specific receptor on a specific complement can be "the doorbell."

Edelson speculates leishmania are successful perhaps because not all receptors trigger the respiratory burst, and leishmania have figured out which one bypasses the deadly process. Edelson believes the third component of complement (C3) is responsible for getting leishmania into the cell and decreasing the effects of respiratory burst once there. By binding to a specific receptor, leishmania are able to trigger the unlocking of the door. Complement normally works, in part, by coating an invader for ingestion by a macrophage. In this case, the parasites have learned to change complement from adversary to ally. And if successful in disarming the cell, leishmania multiply to the point where they burst their host.

The study, published in the May 28 NATURE, looked at the number of surviving intracellular organisms at 24 and 48 hours following ingestion of leishmania into about a million mouse macrophages. In the absence of the serum complement, more than 95 percent of the parasites were killed once ingested by the macrophages. Those exposed to serum complement, however, increased their chances of survival 10-fold.

Mosser and Edelson believe it could be common practice for leishmania and perhaps other intracellular parasites to activate C3 and gain entrance into cells.

The findings might be used to help researchers discover ways to prevent invading organisms from picking up the complement they need to penetrate the cell or to help program cells to initiate a respiratory burst against any invader.

– K. Hartley

Gene search narrows

Joseph Merrick, the 19th-century Londoner better known as the "Elephant Man," may be remembered by medical historians and theatergoers as the unlucky victim of an unusual deformity. But the disease from which he suffered – von Recklinghausen neurofibromatosis (NF) – remains one of the world's most common genetic disorders, afflicting roughly one in 3,000 people, including an estimated 100,000 in the United States. Although few victims develop the severe disfigurement that Merrick did, a variety of bone and central nervous system complications are commonly associated with the ailment, and until recently, scientists knew little about its etiology.

Now, two teams of scientists have identified the approximate location of the gene apparently responsible for NF, spurring hope that early detection and treatment of the disease may be possible in coming years. Moreover, their research suggests that although it can manifest itself in a number of ways – ranging from minor skin discoloration to solid tumor malignancy – the disease is probably the result of a defect or defects in a single gene. That finding, along with the fact that about half of all NF cases are the result of new mutations found in offspring of genetically normal parents, has led some of the scientists to theorize that the gene may be unusually large, and therefore susceptible to more mutations.

Research teams from the University of Utah in Salt Lake City and Massachusetts General Hospital and Harvard Medical School in Boston report in the May 29 SCIENCE and the June 5 CELL, respectively, that they have narrowed the location of the NF gene to a region close to the central constriction of chromosome 17. Working independently, the two groups traced previously mapped genetic markers that are typically inherited along with the disease – a technique that has been used to pinpoint the genes responsible for cystic fibrosis and muscular dystrophy, making possible the development of prenatal tests for such defects. *– R. Weiss*

Parkinson's protection?

Low doses of a chemical known as MPTP cause brain damage and movement disorders that closely match Parkinson's disease in both humans and monkeys (SN: 3/1/86, p.132). Robert J. D'Amato of Johns Hopkins University in Baltimore and his colleagues now report that conventional doses of the antimalarial drug chloroquine partially protect monkeys from MPTP-induced symptoms.

"Conceivably, chloroquine or a similar drug could be used to retard the progression of Parkinson's disease in human patients," they conclude in the May 28 NATURE.

The investigators propose that chloroquine interferes with the binding of a poisonous MPTP by-product – MPP+ – to cells that produce the neurotransmitter dopamine in a small area of the brain known as the substantia nigra. In a previous report, D'Amato and his coworkers suggested that MPP+ sticks only to dopamine cells containing the pigment neuromelanin. Nerve terminals that channel MPP+ out of neuromelanin-bearing dopamine cells in other brain structures are scarce around the substantia nigra.

The proposed neuromelanin connection, while not endorsed by all MPTP researchers, is supported by the new data. Three monkeys were injected with MPTP on four consecutive days, three monkeys received chloroquine for 12 days before and 10 days after MPTP injections, and three monkeys received chloroquine for 24 days before and 10 days after the injections. MPTP alone produced tremors, muscle rigidity, hunched posture and decreased movement within five days. But five of the six chloroquine-treated monkeys displayed significantly fewer parkinsonian symptoms. The five "protected" animals, particularly those given the longer pretreatment, retained more neuromelanin-containing cells in the substantia nigra and showed a much smaller dopamine reduction in two other brain areas implicated in Parkinson's disease, say the researchers.

– B. Bower