Slipping past the immune centurions

The cells of the immune system, like gallant warriors, protect the body from foreign invaders. Yet these cells appear to grant a special privilege to some tissues. Testes, eyes, and even the brain appear to slip quietly past the body's guardians.

These immune-privileged tissues can be transplanted from one individual to another without rejection, even among unrelated donors and recipients. Conversely, the immune system permits other tissues to be transplanted into these privileged sites.

Now, a study indicates that privileged tissues may not have been granted free rein by the immune system's lymphocytes after all. Instead, the tissues appear to produce a molecule, known as Fas ligand, that kills immune cells approaching with destructive intent. This finding could someday improve transplantation outcomes and mediate self-destructive autoimmune diseases.

"This is a highly specific immune suppression," says study author Richard C. Duke of the University of Colorado School of Medicine in Denver. "And if the cells [of a transplanted organ] express Fas ligand, it is protected from the immune system."

When lymphocytes become activated during an immune response, whether to a virus, bacterium, or transplanted organ, they manufacture a large number of molecules known as Fas and imbed them into their cell surfaces. When these Fas molecules encounter a Fas ligand on another lymphocyte, it triggers a process called apoptosis, which leads the Fas-carrying lymphocytes to commit suicide. Presumably, the interaction helps the immune system regulate itself, though scientists don't know how.

As it turns out, however, lymphocytes aren't the only tissues that produce Fas ligand. The Colorado group reports in the Oct. 19 NATURE that the Sertoli cells found in the testes also produce large amounts of Fas ligand.

The researchers transplanted rat testes into the kidney capsule of unrelated rats and found that the transplants were not rejected. In order to demonstrate that the Fas ligand produced by Sertoli cells lends immune privilege to the testes, they transplanted the testes of a strain of mice that can't produce any Fas ligand into a normal rat. Without Fas ligand, the transplanted testes were aggressively rejected.

"We know now that Fas ligand is necessary to confer immune privilege," says Duke. "But we don't know yet that it is sufficient."

Nevertheless, Thomas A. Ferguson of the Washington University School of Medicine in St. Louis says that Duke's work "is really a nice story, and it explains a lot." Ferguson plans to publish similar results soon explaining immune privilege in the eye.

Duke has begun work on creating rats with pancreatic Fas ligands in order to see whether the organ will become immune-privileged when transplanted. The Fas ligands could also help combat autoimmune disorders such as rheumatoid arthritis, he suggests. — *L. Seachrist*

Living free of photosynthesis

Microorganisms that could survive on Mars live in the Columbia River's basalt aquifers near Richland, Wash., researchers assert.

For the first time, scientists have found a community of bacteria that requires only carbon dioxide, basalt, and water—substances that lie below the surface of the Red Planet, Todd O. Stevens and James P. McKinley of Pacific Northwest Laboratory in Richland report in the Oct. 20 SCIENCE. None of the bacteria relies directly or indirectly on photosynthesis.

"We think these ecosystems in the basalt aquifer are actually the first ones [ever found] that are completely independent [of] photosynthesis," says Stevens. Although some organisms living in hydrothermal vents at midocean ridges and in other, less exotic environments do not depend on plants for energy, they live alongside organisms that do.

"It's fairly convincing evidence that they've put forward," says R. John Parkes of the University of Bristol in England. The several approaches they employed to investigate the organisms "are all in agreement."

The bacteria get the energy they need to fix dissolved carbon dioxide from the hydrogen produced when water interacts with basalt, Stevens and McKinley report. They also produce the carbon that feeds other bacteria, performing the function of green plants, Stevens says. "Only instead of using sunlight, they are using the energy in hydrogen," he explains.

"This may be an example of how life could have existed [on Earth] before photosynthesis"—or nowadays on Mars, he says.

The finding is "very exciting, because it suggests that it's possible that there could be life in the subsurface of Mars, and this is how it could get its energy," says Christopher P. McKay of NASA's Ames Research Center in Mountain View, Calif. NASA hopes to look for signs of bacterial life on Mars. — *T. Adler*

Ferreting out cancer risk with novel mice

Two types of genetically altered mice appear capable of screening chemicals for carcinogenicity more cheaply and effectively than current assays can.

Using fewer than half as many animals as 2-year rodent tests—the current gold standard for carcinogen identification—and taking only one-quarter as long, "we were able to get unambiguous data," explains Raymond W. Tennant of the National Institute of Environmental Health Sciences in Research Triangle Park, N.C.

His team administered known carcinogens and noncarcinogens to the novel mice. One strain, known as knockout mice, possesses a single functioning *p53* tumor-suppressor gene in each cell; normal cells have two. The other strain, so-called TG.AC mice, carries a cancer-causing gene. When activated by a carcinogen, this gene triggers the development of benign skin tumors known as papillomas.

Most carcinogens alter, or mutate, one or more genes in their host. In the October ENVIRONMENTAL HEALTH PERSPECTIVES, the NIEHS researchers report that *p53* knockout mice exposed to such mutagenic carcinogens develop the same tumors within 6 months that normal rodents develop during the standard, 2-year bioassays. However, carcinogens that do not induce mutations, as well as chemicals that induce mutations but do not cause cancer, failed to initiate tumors in these animals.

The TG.AC mice, in contrast, proved susceptible to both mutagenic and nonmutagenic carcinogens painted onto their backs. Tumor promoters—incomplete carcinogens that cannot initiate a malignancy by themselves—also initiated papillomas.

One big advantage of the 6-month tests, says Tennant, is that they're completed well before naturally occurring tumors usually develop. As a result, he points out, "you don't have to sort through a lot of spontaneously occurring tumors to determine which were chemically induced."

"It's impossible today to say whether these [mouse strains] will ever be universally applicable," but Tennant's group "is definitely going in the right direction," says Lawrence A. Donehower of the Baylor College of Medicine in Houston. Tennant agrees, noting that for now, transgenic mouse assays should be validated with the 2-year bioassays. But insights gleaned from the shorter assays could make the longer, follow-up ones more useful, he says—by suggesting, for example, how low an exposure can be and still trigger the development of cancers. — *J. Raloff*