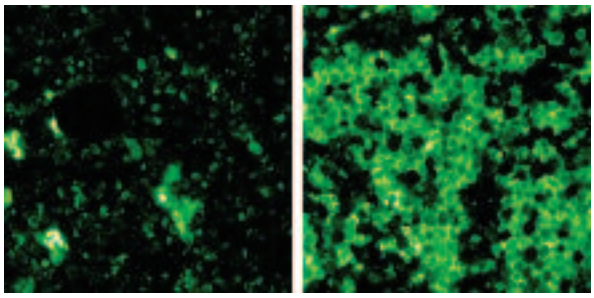
Prescreening Patients for Use of Anti-Cancer Drug

Researchers at Penn Medicine and Penn Vet have determined a way to pre-screen cancer patients to see if they are suitable candidates for proteasome inhibitors, a promising class of anti-cancer drugs. They propose to test for p53, a well-known tumor-suppressor protein that is broken down by cellular machinery called proteasomes. This study appears in the June 2007 issue of *Blood*.



Green staining depicts tumor cells dying after treatment with proteasome inhibitors. In the left panel, the tumor lacks p53, and only a fraction of the cells are killed. In the right panel, the tumor produces p53, resulting in massive cell death.

Image Credit: Andrei Thomas-Tikhonenko, PhD, University of Pennsylvania School of Medicine; *Blood*.

In cancer patients whose tumors do not produce p53, proteasome inhibitors might be ineffective. This patient group could be spared unnecessary treatment with possible harmful side effects. On the other hand, proteasome inhibitors are highly effective against lymphomas that do have the ability to produce p53.

"These findings have important implications for clinical practice," Dr. Thomas-Tikhonenko said. "The proteosome inhibitor bortezomib is approved by the FDA for the treatment of multiple myeloma, another cancer of lymphoid cells. Yet, only a fraction of multiple myeloma patients respond to the drug."

Gene Therapy Can Restore Vision

Gus Aguirre, V'68, professor of ophthalmology and medical genetics, was part of a multi-institutional study whose results demonstrated that gene therapy used to restore retinal activity to the blind also restores function to the brain's visual center, a critical component of seeing. The study, led by Geoffrey Aguirre, assistant professor of neurology at Penn Medicine, shows that gene therapy can improve retinal, visual-pathway and visual-cortex responses in animals born blind and has the potential to do the same in humans.

Findings of the study were reported in the journal *PLoS Medicine*.

Skin Secretion Linked to Parasite

Strongyloides stercoralis. Courtesy of Smittskyddsinstitutet, the Swedish Institute for Infectious Disease Control.

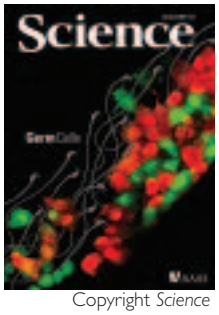
Researchers from Penn Medicine and Penn Vet have found a link between some of the most common parasites that cause infection and disease throughout the developing world and their attraction to a chemical secreted from human and animal skin.

These skin-penetrating parasites infect more than 600 million people worldwide and contribute to anemia, ill health and poor physical and cognitive development among children of developing nations.

Urocanic acid, a common histidine metabolite abundant in mammalian skin, attracts the parasitic nematode *Strongyloides stercoralis*. But, according to researchers, the attraction can be suppressed by metal ions, suggesting a potential new strategy for preventing infection.

The findings were reported in the *Proceedings of the National Academy of Sciences*. **Drs. Gerhard Schad**, professor of parasitology; **Mario Brenes**, research specialist; and **Seth Dunipace**—all from the Department of Pathobiology at Penn Vet.

Reversing Infertility in Cancer Patients



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In the April 20 issue of *Science*, **Ralph Brinster, V'60**, Richard King Mellon Professor of Reproductive Physiology, reports methods for the recovery, culture and transplantation of spermatogonial stem cells. Recovering stem cells and freezing them at very low temperatures (cryopreservation) can be a way to preserve the male germ line of valuable livestock animals, companion animals and endangered species. Perhaps the most potentially valuable medical application of spermatagonial stem cell (SSC) research is for prepubertal boys undergoing chemotherapy or irradiation for cancer. In many cases, the SSCs are destroyed as a side effect of treatment, and the patient is left infertile. It is possible to obtain a testicular biopsy and cryopreserve a cell suspension produced from the biopsy. This cell suspension containing SSCs could then be transplanted back into the patient's testes at any age after treatment, potentially resulting in reversal of infertility through renewed sperm production.