$1 million study renews HIV/transplant research

By any immunology standards, scientists at the University of California San Francisco (UCSF) are embarking on a complicated research project—a $1 million study of organ transplants in HIV-infected patients. "Since the advent of highly active anti-retroviral therapy (HAART) for HIV infection about three years ago, patients' life expectancy has increased, leaving them susceptible to death from non-HIV-related causes, including end stage organ disease," says project leader Peter Stock, explaining why transplants for such patients have become more feasible.

The study marks a resurgence of interest in organ transplants for HIV-infected patients, which were attempted in the 1980s but were discontinued after it became clear that patients with HIV had poorer chances of survival than did non-infected persons. Although it remains to be demonstrated conclusively, this no longer seems to be the case. Stock says that UCSF plans five transplants over the next six months, and adds that his program is moving faster than expected because of a strong response from the patient community.

Six HIV-infected patients have already received kidney transplants since 1997 at the Starzl Center in Pittsburgh, according to chief of transplantation surgery John Fung, and other centers that have expressed interest in resuming organ transplants for this population group include Mount Sinai in New York and the University of Maryland.

The immunological complexity of the experimental situation is clear in the different views held by specialists involved. John Fung notes that drugs like tacrolimus and cyclosporine, used to prevent graft rejection, will also affect the immune systems of HIV-positive patients, as they inhibit T-cell activation, the process that drives cells from a resting to a mitotic state, when they are susceptible to virus-mediated killing. "The idea that some of these drugs may help the immune system, even though they suppress it, sounds contradictory, but at a theoretical level there might be a benefit," Fung says.

However, Mike McCune, who will examine the immunological data from the UCSF study, admits that ideas like this are controversial. Although he does expect that "the transplanted organs will confer benefit," he has no expectation that the immunosuppression will ameliorate the HIV-related disease.

The study plans to examine new drug interactions in light of the altered pharmacological environment in which today's HIV patients live. Patients in the UCSF study will be on cyclosporine augmented by steroids to suppress graft rejection, plus stable HAART regimens to keep their HIV in check. These drugs interact with both the cytochrome p450 system and the P-glycoprotein multidrug efflux pump, located in the liver and gut. "We expect that the immunosuppressant will affect plasma concentrations of the anti-retrovirals, but it is also likely that the protease inhibitor and non-nucleoside anti-retrovirals will affect metabolizing enzymes and transport proteins in such a way as to increase the levels of cyclosporine as well," says Leslie Floren, who is in charge of pharmacology for the study.

The National Institutes of Health has taken an active interest in the trials. According to Bill Duncan, associate director of the National Institute of Allergic and Infectious Disease (NIAID), who has organized meetings on the topic over the last six months, "a feeling of consensus has grown up that the various transplant centers can share data [and work together]".

The investigators hope that by establishing proof of the principle that liver and kidney transplantation is appropriate for HIV-positive patients, they will be able to persuade insurers to pay for the procedures. "HIV is a contraindication for transplantation in most Medicare and Medicaid programs. But that's based on very old literature, and we are trying to show that you can get a transplant and be on antiviral programs and still have a pretty good outcome," says Fung.

In other clinical trials news…

The National Institutes of Health has launched a new clinical trials database aimed at the general public carrying information on over 4,000 federal and private medical studies at more than 47,000 locations nationwide. ClinicalTrials.gov provides information on the location of trials, their design and purpose, criteria for participation, and some disease and treatment information. The data-base is available at http://clinicaltrials.gov/.

Potter Wickware, San Francisco

Survey shows secrecy among scientists

Those who feel that research is not as open a business as it once was may have their suspicions confirmed by a new survey conducted by the Institute for Health Policy at Harvard University. Nearly 13% of more than 2,000 biomedical researchers questioned reported that they have been refused when they asked a colleague to share data.

Scientists with commercial ties—such as those who hold patents on potential products—seem to get the door slammed in their face most often. Among researchers who hold patents, 30% reported that a colleague had denied them access to data. And more than 20% of those with start-up companies reported getting turned away.

The data confirm the feelings of researchers at the Fox Chase Cancer Center in Philadelphia who work with Patricia Harsche, vice president for business, development and regulatory affairs. The word on her campus is that industry-sponsored scientists both give and get less data. "That's the impression that investigators here have given me," she says. Harshe, however, says she is not sure that impression is based on actual events or simply anxiety about the possible effect of industry sponsorship.

"A logical explanation is that some scientists are reluctant to share research results with commercially active investigators for fear that their shared data will be used for commercial rather than academic purposes," the authors write in the journal *Research Policy*. Or they may want to use it themselves, says Mark Frankel, the director of the Scientific Freedom, Responsibility and Law Program of the American Association for the Advancement of Science. "[These days there is a] tendency to play things closer to the chest because of some expectation of economic reward down the road," he said. This suggestion is backed up by data from a similar 1997 survey in which 20% of medical researchers admitted delaying publishing results for up to six months to protect a scientific lead or patent filing.

Tinker Ready, Boston