NATIONAL INSTITUTES OF HEALTH

Gene Therapists Jump Ship...

They worked together as residents at the Massachusetts General Hospital, and then came to the National Institutes of Health (NIH) on the same day in 1971. Now, 22 years later, Ronald G. Crystal and Arthur W. Nienhuis will leave NIH on the same day, 1 April 1993. And with the departing duo will go a big chunk of NIH's talent in the arena of gene therapy research. The departure of Crystal and Nienhuis—who are moving separately to top academic jobs—reflects intense competition among research centers to snare top-flight gene therapists. Their plans, coming on the heels of the departure of several other key NIH gene therapy pioneers, raise questions about NIH's future in a field it helped create.

Crystal, chief of the pulmonary branch in the National Heart, Lung, and Blood Institute, will become chairman of the pulmonary and critical care divisions at the Cornell University Medical Center-The New York Hospital, with a joint appointment at Rockefeller University. Nienhuis, chief of clinical hematology in the National Heart, Lung, and Blood Institute, will become director of St. Jude Children's Research Hospital in Memphis, Tennessee.

Just last month, Crystal received NIH approval to begin treating cystic fibrosis patients with gene therapy. Crystal intends to start that study before leaving NIH, but he will be taking much of his gene therapy program with him. Nienhuis, who has launched several gene therapy studies, primarily aimed at inserting genes into bone marrow, could help turn St. Jude's into a gene therapy powerhouse. Although he will be the hospital's top administrator, he intends to continue his gene therapy research. He will join Malcolm Brenner, who has used gene marking techniques to show that autologous bone marrow transplants in cancer patients harbor tumor cells that cause the disease to recur. Brenner has permission from NIH to use experimental forms of gene therapy to treat neuroblastoma, a type of brain cancer.

These are just the latest institutions to make major commitments to gene therapy programs. In what is fast becoming the hottest new trend in academic medicine, the University of Michigan in Ann Arbor and the University of Pittsburgh have set up programs. More recently, the University of Pennsylvania recruited James Wilson from Ann Arbor to head a new gene therapy center in Philadelphia.

NIH's capacity to conduct gene therapy research is dwindling, even as the field rapidly expands. The erosion began last summer when W. French Anderson, a gene therapy pioneer in whose NIH lab Crystal and Nienhuis started, moved to the University of Southern California to begin setting up a gene therapy institute. Anderson, along with National Cancer Institute (NCI) collaborators R. Michael Blaese and Kenneth Culver, launched the first effort to use gene therapy in 1990 by treating two girls with an inherited immune deficiency.

Culver, who in addition to his work with Anderson developed a genetic treatment for brain cancer, also has left government service. For now, he remains on the NIH campus, where he works for Genetic Therapy Inc. of Gaithersburg, Maryland, but he expects to set up a private gene therapy research foundation at Iowa Methodist Medical Center later this year.

Although gene therapy researchers Blaese and Steven A. Rosenberg, also at NCI, apparently plan to remain at NIH, the recent brain drain presents a problem for NIH Director Bernadine Healy. Healy recently said she hopes that hiring University of Michigan geneticist Francis Collins, the codiscoverer of the cystic fibrosis gene, to head the Human Genome Project will help stem the flow of talent. The genome program will include a therapy component on the NIH campus. "He will be a magnet for other recruitment to NIH," she said. Still, Healy faces an uphill battle. Collins is the first senior scientist recruited to NIH for a full-time post in years, and many old NIH hands are chafing as a result of poor morale on campus and low government salaries. Indeed, both Crystal and Nienhuis say salary considerations contributed to their decisions, but neither of them is leaving lightly. "I have agonized over this," Crystal said. "I love NIH. I have been here for 22 years. NIH made my career."

–Larry Thompson

Larry Thompson is a science writer living in Bethesda, Maryland.

...Top AIDS Official to Leave

After 5 frequently stormy years at the head of the flagship AIDS unit at the National Institutes of Health (NIH), Daniel Hoth has announced plans to resign. Hoth told his staff and superiors at the Division of AIDS (DAIDS), a branch of the National Institute of Allergy and Infectious Diseases (NIAID), that he feels he's accomplished what he came to NIH to do. "This was not a hot decision," says Hoth. "I've had one of the most extraordinary opportunities in biomedical research anywhere. But life goes on and careers go on."

Hoth, an oncologist, moved to DAIDS from the National Cancer Institute in 1987. His tenure has been a growth phase for the program, which funds research around the country on everything from HIV pathogenesis to clinical trials of drugs and vaccines. Since Hoth came, the DAIDS staff has grown from 24 to 135 and the budget has tripled to $325 million. In fact, Hoth's unit oversees more than 35% of the entire NIH AIDS budget. "When I took over this place, we had to fight a war at the same time we had to build the warship," he says of the growth spurt.

Many researchers compliment Hoth for building up the AIDS Clinical Trials Group (ACTG), a nationwide network of researchers who test new treatments. "Hoth was very important in helping to organize and get the ACTG on track when it was foundering," says AIDS researcher Douglas Richman of the University of California, San Diego. Hoth also has been a prime mover behind the decision to beef up the NIH's AIDS vaccine effort, both in the United States and abroad. "He's done a very good job," said Hoth's boss, NIAID chief Anthony Fauci, "and I didn't want to see him go."

But Hoth does have critics, many in the community of AIDS activists, who claimed that he allowed the ACTG to focus too much attention on AZT while ignoring other promising treatments. Activists have also assailed DAIDS for footdragging, for not including women and children in trials, and for ignoring the regions hardest hit by the epidemic. Tempers got so hot in 1990 that activists "occupied" Hoth's office, and NIH felt compelled to assign him bodyguards at that year's international AIDS conference in San Francisco. "Hoth presided over a tremendous and very painful growth period in DAIDS," says Derek Hodel of the D.C.-based AIDS Action Council. "Now we have the chance to solidify and address the problems with the organization we've identified."

The 46-year-old Hoth isn't leaving immediately. He's still hunting for a new job, he says, and he doesn't intend to pack his bags until he finds one, which may take several months. He says the reason he revealed now that he plans to leave is that "I couldn't do any serious looking without everybody talking about it."

As for Hoth's replacement, Fauci says NIAID will conduct a wide search both inside and outside NIH. The ideal candidate, says Fauci, would be a person with "a solid scientific background, administrative and people skills who could handle a very, very high-pressure job." Resumes are now being accepted.

–Jon Cohen