That would not have been the last time that proto-North America served as the core of a larger assemblage. Gerard Bond, Peter Nickeson, and Michelle Kominz of Lamont-Doherty Geological Observatory have pinned down the breakup of another supercontinent having North America at its core, this time in the late Proterozoic. By determining the cooling rate of continental margins formed during the rifting of the supercontinent, they estimate that the breakup occurred between 625 and 555 million years ago, a far narrower range than previously available. The apparent coincidence of this breakup, which created and then dispersed 18,500 kilometers of new continental margin, and the explosion of new life forms at the end of the Proterozoic suggests some causal link.

If Anderson is right about supercontinents inevitably breaking up and eventually reforming from the dispersed fragments, over and over again, then this late Proterozoic and the possible early Proterozoic breakups would simply be two in a series of such episodes that most recently included the breakup of the patchwork continent Pangaea supercontinent 180 million years ago. Hoffman and Bowring have another to propose. They suggest that the Archean Superior craton is itself a composite of two continental fragments sutured by a continent-continent collision. They appear to have caught the usual island arc debris between them about 2.7 billion years ago, just as in the case of younger orogens. Instead of being the ultimate building blocks of continents, Archean cratons could be just more fragments of larger assemblages that suffered disruption and dispersal.

This would explain why many Archean cratons now found around the world were assembled at about that same time, during an orogeny called the Kenoran. In fact, the 1.9-billion-year Trans-Hudson orogen not only binds the cratons of North America together but is found in southeast Asia, Siberia, Australia, South America, and Scandinavia. Instead of some deep-seated mechanism in the mantle triggering a burst of mountain building around the globe, as previously suggested, "global orogenies" would result from motion of the shallow parts of Earth, like ice floes drifting together and freezing into a single mass, only to be broken apart, perhaps in new combinations, and shuffled once again.

The North America finally assembled during the Proterozoic has stabilized enough to resist a billion years of jostling, and rifting. In fact, it has continued to grow through the plastering of bits and pieces of continents and arcs to its edges. Using the present as a key to the ever more distant past, geologists want to find just how long Earth has been behaving this way.—**RICHARD A. KERR**

Additional Reading

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Burst of Publicity Follows Cancer Report

The results are still preliminary, but suggest that the patients' own immune cells can be bolstered to fight a wide variety of solid cancers

A preliminary clinical trial of an experimental cancer therapy suggests that the treatment may limit the growth of a broad spectrum of cancers. The therapy, which is being developed by Steven Rosenberg and his colleagues at the National Cancer Institute, seeks to destroy cancerous tumors by mobilizing an immune attack on them. Although the results of the first tests of the treatment in patients with a variety of advanced cancers appear promising, Rosenberg sounds a note of caution. "This is just the first step," he points out. "It is not a cure for cancer in 1985."

The treatment being studied at NCI is part of a growing effort aimed at exploiting the tumor-fighting capabilities of naturally occurring, biologically active substances, especially those that act through the immune system. The Rosenberg group uses interleukin-2, a protein that is produced by the T cells of the immune system and is required for normal immune responses, to stimulate tumor-killing by the patients' own cells.

The investigators first withdraw lymphocytes from the patients' blood and activate the cells by growing them in culture with interleukin-2. The cells are then injected back into the patients, who are also given large doses of interleukin-2 to maintain the killer activity of the lymphocytes. Rosenberg and his colleagues had previously shown that this treatment could produce the regression of several different types of cancerous tumors in mice.

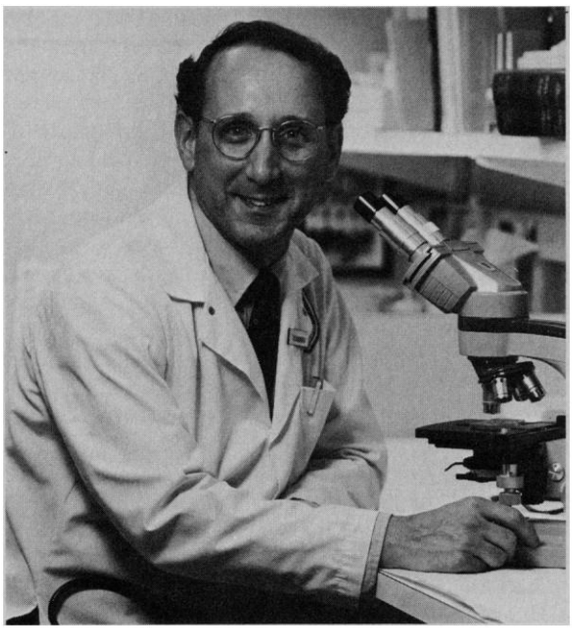
The results of the first clinical trial of this therapy in human patients, which have been published in the 5 December issue of the *New England Journal of Medicine*, showed that 10 of 25 patients experienced partial tumor shrinkages of at least 50 percent. An 11th patient, who had melanoma, had a complete remission that has now lasted 1 year. All of the individuals had very advanced disease that had not responded to previous treatments. "Given the clinical state of the patients he has treated, getting responses in that fraction is very encouraging," says NCI's Daniel Longo.

The treatment can have serious side effects, however. In particular, the patients may experience fluid retention that causes them to gain 10 percent or more of their body weight and may result in fluid accumulation in the lungs. One patient, who was treated after the original group of 25, apparently died as a result of the therapy, although the individual had widely disseminated melanoma.

The death was not mentioned either in the *New England Journal* report or in a press "update" sent out by NCI's Office of Cancer Communications. According to Rosenberg, this was because he did not wish to discuss unpublished results, although he did mention the death on the CBS News program "Face the Nation." An occasional treatment-related death is not unusual in the very ill patients who participate in the early trials of cancer therapies.

Other side effects of the interleukin-2 treatment include malaise, fever and chills, nausea, diarrhea, and anemia, although these resemble the effects of many chemotherapeutic drugs. The fluid retention and other side effects were reversible when the treatment was stopped.

In earlier studies the NCI workers had



Steven Rosenberg

Developer of an immunotherapy for cancer

found that neither interleukin-2 nor the activated lymphocytes would work by themselves. According to Rosenberg, the doses of interleukin-2 that can be given are limited by its toxicity and it was not possible to administer enough of the agent to trigger lymphocyte activity in the patients. Work with mice had demonstrated, however, that if the cells are activated in culture they continue to divide and function in the body provided that interleukin-2 is also administered to the animals.

Rosenberg and his colleagues have been concentrating their efforts on attempts to treat the solid cancers that have all too often proved refractory to chemical and radiation therapies. Among the human tumors that responded to their new treatment are multiple myeloma, and kidney, lung, colon, and rectal cancers. Lung and colorectal cancers are the two leading causes of cancer deaths in the United States today.

Attempts to treat lung and colon cancers with other biological agents have so far shown little effect, although for the most part these studies are in the very early stages. The best-studied biological agent, interferon, induces remissions of some tumors, but primarily leukemias and lymphomas, which are cancers of the blood and lymphoid systems. Even Jordan Gutterman of M. D. Anderson Hospital and Tumor Institute in Houston, who is a leader in interferon research, says, "There is clearly a disappointment with alpha-interferon," when it comes to solid tumor therapy.

Although a new weapon against the solid tumors is highly desired, a great deal more work will be required to confirm and extend the current NCI results. Questions still remain about how long the anticancer effects of the therapy will be maintained in the patients, for example. "It may be 5 years down the road before we are anywhere approaching community hospital application," estimates Frank Rauscher of the American Cancer Society, who otherwise has very positive views of the research.

The therapy is expensive—it costs tens of thousands of dollars per patient, Rosenberg estimates—and cumbersome. The patients must be hooked up to the machine that collects their lymphocytes for 4 hours a day for 5 days running. Growing the cells requires from 10 to 30 or 40 liters of culture fluid per patient. When the lymphocytes and interleukin-2 are being infused, the patients must remain in intensive care.

Rosenberg concedes that the therapy will not be widely applicable in its present form, but he says, "My philosophy is to develop a treatment that mediates the regression of solid tumors without worrying about the practical problems." If something can be found to work, then it may be possible to modify it to make it more practical.

The NCI workers plan to determine, for example, whether it might be feasible to use lymphocytes grown and maintained in culture, rather than having to collect cells from the patients. In addition, Rosenberg suggests, the therapy may find its greatest potential as an adjuvant to surgery, chemotherapy, or other treatments that reduce tumor size. In mice at least it works best when the tumor burden is low.

When Rosenberg was asked whether he was concerned about the reports of this work raising overly optimistic expectations in the public mind, he replied that he is. At present the treatment is available only through NCI, which is not able to accept any more patients. A multicenter trial is scheduled to begin in a month or so, however.

Meanwhile, Judith Stein of the NCI's Cancer Information Service says that on each of the 2 days after the *New England Journal* report became public, the service logged more than 1000 calls about the treatment, mainly from cancer patients or relatives of patients. The last time the service logged that many calls devoted to a single topic was the day after President Reagan's cancer surgery, when 1000 people telephoned with inquiries about colon cancer. Reports of potential new cancer therapies generally bring about increased numbers of calls, Stein says.

Rosenberg's work received widespread publicity that may have been partly engendered by the November cover story of *Fortune* magazine, which trumpeted "Cancer Breakthrough" and described the interleukin-2 research in glowing terms. In addition, Rosenberg had already achieved some visibility as a member of, and spokesman for, the President's surgical team, a situation which probably did not diminish interest in his latest work. Although NCI officials sent out a press update on the research, they decided against having a press conference, partly out of concerns about raising unrealistic hopes.

Interleukin-2 was discovered in the mid-1970's by Robert Gallo and his colleagues at NCI, who then called it T-cell growth factor. The development that has made clinical trials possible is the cloning of the interleukin-2 gene, which allows the production of large quantities of what would otherwise be a very scarce material. In fact, Rosenberg has been awarded the 1985 Armand Hammer award for cancer research with Tadatsugu Taniguchi of the Japanese Foundation for Cancer Research in Tokyo, who was the leader of the group that originally cloned the human interleukin-2 gene. Genes for other potentially valuable therapeutic agents, including the interferons, interleukin-1, and tumor necrosis factor, have also been cloned, thus permitting the testing of these substances against cancer and other diseases.

The heralding of breakthroughs is clearly premature, but the work with interleukin-2 and the interferons hints that the biological agents may provide additional weapons against cancer. "We are beginning to develop an armentarium of biologicals that may one day approach the diversity of chemotherapy," Gutterman predicts.—**JEAN L. MARX**