who studies the fungal infection candidiasis, observed that IL-12 treatment in mice that normally have self-limited candida infections unexpectedly provoked disseminated disease. Robert Modlin of the University of California, Los Angeles, has argued that IL-12 can, in certain circumstances, set off an inflammatory pathway that promotes the formation of atherosclerotic plaques. "Does IL-12 have a role in atherosclerosis?" asked Joseph A. Kovacs of the NIH's Clinical Center. "That would concern me."

Side effects aside, there are clearly many promising avenues for clinical research, and the round-table discussion at the end of the meeting was pitched to identify two or three diseases meriting clinical trials. The discussion featured representatives of G.I. and Hoffman-LaRoche, the two companies that have filed for IL-12 patents and cross-licensed its development to one another. As one organizer, Lee Hall of NIAID, framed the final session's question, "You've heard 20 different models. How do you choose one?"

The answers could not have pleased the basic research community: Executives from the two companies chose none—for reasons ranging from possible side effects to the economic downside of trying to treat Third World diseases at this stage of IL-12's development.

John Ryan, who recently left Merck to become director of clinical development at G.I., warned that the success of IL-12 against, say, leishmaniasis at this point would be a "disaster" for the company: G.I. would be committed to scale up manufacturing costing millions of dollars and would probably wind up distributing the drug through the World Health Organization, which would in essence give it away, leaving the company with huge costs and little or no revenues. This prompted one scientist to ask: "So what the scientists should be finding are economically viable infectious diseases for you?"

At the end of the day, infectious-disease experts were left with an immensely powerful molecule and perhaps nowhere to go clinically until IL-12 proves its mettle against cancer or AIDS. What recourse do basic researchers have? "What's valuable to a company," said Stan Wolf, who cloned the gene at G.I., "is dose, schedule, and how to use a drug. . . . How could people in academia help? Think from a pragmatic point of view, and supply that information back to the companies." That may sound like asking basic investigators to do product-oriented research, but in today's high-stakes drug development, the alternative may be no IL-12 to test.

–Stephen S. Hall

Stephen S. Hall is a science writer in New York.

LOW-TEMPERATURE PHYSICS

Helium-3 Crystals Captured on Video

AMSTERDAM—How can you get a good look at processes that only take place at temperatures just above absolute zero, when the very act of observing them creates heat? Raymond Wagner and Giorgio Frossati at the Kamerlingh Onnes Laboratory at the University of Leiden in the Netherlands have just solved the problem with some ingenious technology, obtaining the first video pictures of the growth of helium-3 crystals at temperatures below 0.001 kelvin. "It is obviously a technical tour de force to observe things at those temperatures," says low-temperature physicist David O. Edwards of Ohio State University.

This feat is more than just a record-setting achievement. At these temperatures, helium has some unusual properties: It becomes a superfluid—a substance with a viscosity of zero that can spontaneously form vortices and flow up and over the rim of a glass. Low-temperature physicists have long wondered how these properties affect the formation of crystals, because atoms in a superfluid can move easily to the place where the crystal is forming and crystallization is speeded up because the heat shed by atoms as they slot into place in the crystal is carried away instantaneously.

A couple of decades ago, they got their first look at crystals in superfluid helium-4, which has two protons and two neutrons in its nucleus and becomes superfluid at a relatively balmy 1.8 K. But helium-3, which has one less neutron, has been more elusive because it only becomes superfluid at 0.002 K. Researchers have been particularly keen to study the formation of helium-3 crystals because the atoms have different magnetic properties from those of helium-4.

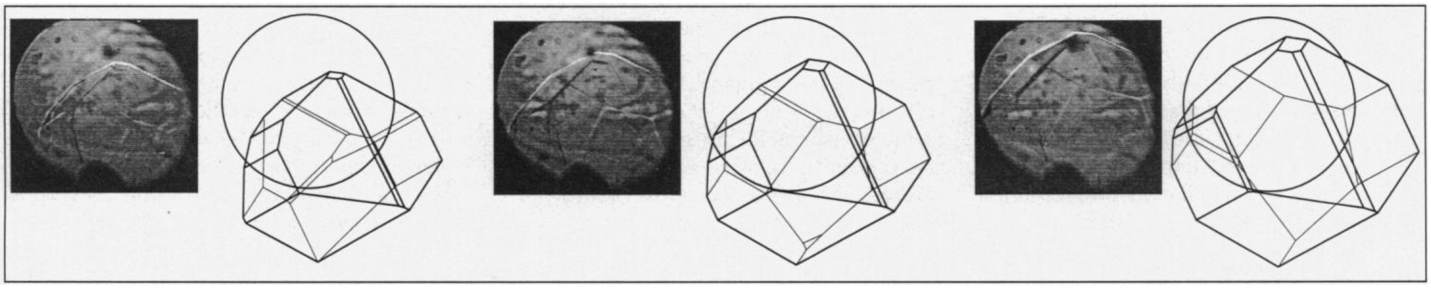
Jukke Pekola, Alexei Babkin, and Pertti Hakonen at Helsinki University of Technology in Finland managed to get the first single images of superfluid helium-3 in 1992. Now the Leiden team has gone one step further by obtaining video images of the growth of helium-3 crystals. "It's very difficult work," says Hakonen. "Before their work and ours, the minimum temperature at which pictures have been obtained was a factor of 40 higher."

To get pictures, the Leiden researchers had to prevent any radiation leaking in from the outside world. Pointing a camera in through a window was out of the question, so the researchers decided to mount a charge-coupled device (CCD) camera inside the cryostat. CCDs only work above 60 K, so the camera had to be cocooned inside a small, shielded, copper box inside the cryostat and heated up slightly. "The big difficulty was to combine the helium-3 at a temperature of 1 millikelvin and a camera that operated at a much higher temperature," says Wagner. Illuminating the crystal enough to take a picture also posed a problem, because of the heat from the light. The researchers used a tiny glass fiber to direct light pulses from an LED, specially shaped to reduce the light-emitting region, onto the crystal.

The sharp point of a needle inside the cryostat served as the nucleation site, and the group was able to observe different stages of the formation of the crystal. They observed three different facets of the crystal, two of them for the first time. (One first facet was observed by Sébastien Balibar at the Ecole Normale Supérieure in Paris at 0.07 K, a temperature at which helium-3 is not superfluid.) For Balibar, the observation of the other two facets confirms theory and is a key to understanding the crystal: "Helium crystals are real prototype crystals that allow us to study the general properties of all crystals."

–Alexander Hellemans

Alexander Hellemans is a writer in Amsterdam.



RAYMOND WAGNER

Cool pictures. Images of the growth sequence of helium-3 crystals at 0.002 K and associated 3D reconstructions.