to be addressed. Until recently, the regulatory procedure was geared to drugs, usually relatively simple chemicals, that could be mass-produced and given to anyone suffering from a given condition. But some of the new immunotherapies need to be individually designed. That can be the case, for example, for the gene therapies, in which each patient's own, appropriately modified, tumor cells have to be used.

Still, David Glover, vice president of medical development at Cambridge Antibody Technology, believes the general attitude of the regulatory authorities is becoming more helpful in the development of antibodies and other biological therapies. "Everybody is interested in the new technologies, and getting agreement on new medicines is not so difficult as it was 4 to 5 years ago," he says. The fact that some of the therapies need to be individually tailored may also make them less appealing to drug companies, who tend to shy away from products for which demand is likely to be small.

And even after a clinical trial has received regulatory approval, frustrations can arise. One cited by Vitetta is difficulty in changing course. An example comes from her own team, which wanted to change the antibody used in one of their trials to one that is more "humanized" and therefore less likely to generate an immune attack on the therapeutic molecules themselves. But that, Vitetta says, "would mean the start of a whole new trial"—and a whole new round of regulatory approvals.

But despite the formidable difficulties, the advances in understanding how the immune system works and the resulting new armory of experimental immunotherapies are enough to keep many researchers optimistic. "I'm sure cancer vaccines are ultimately going to be an exciting example of the translation of laboratory success into human treatments," says Kwak. If he's right, even Jenner might be impressed by the vigor of his legacy 200 years later.

–**Nigel Williams**

Additional Reading

J. P. Allison and M. F. Krummel, "The Yin and Yang of T Cell Costimulation," *Science* **270**, p. 932 (1995).

A. Van Pel *et al.*, "Genes Coding for Tumor Antigens Recognized by Cytolytic T Lymphocytes," *Immunological Reviews*, No. 14, p. 229 (1995).

C. B. Kobrin and L. W. Kwak, "The Current Status of Cancer Vaccines," *Expert Opinion in Investigational Drugs* **3**, p. 1241 (1994).

MATERIALS SCIENCE

Ceramic Shrinks When the Heat Goes On

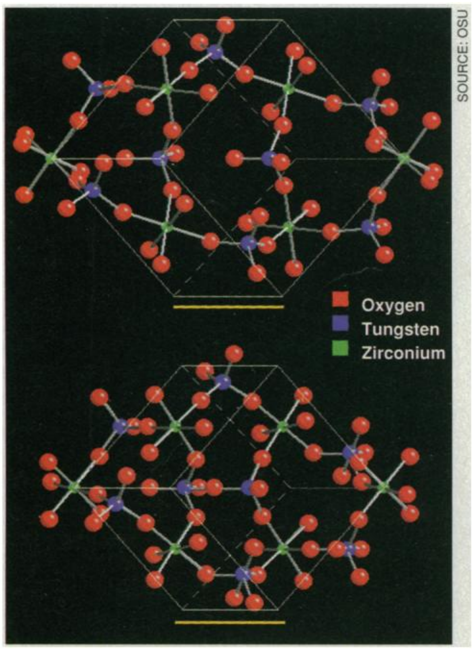
It's hard to break the laws of physics, but sometimes one can bend the rules. Take the well-founded principle that more heat means more size: Added energy—heat—usually causes atoms to swing around more violently, taking up more space and causing materials to expand. But on page 90 of this issue, researchers at Oregon State University in Corvallis and at Brookhaven National Laboratory in Upton, New York, describe a ceramic that's found a huge loophole in the rule: It steadily shrinks as the temperature rises over 1000 degrees.

The shrinking ceramic is a blend of tungsten, oxygen, and zirconium atoms known as zirconium tungstate. Its slimming secret, the researchers have found, is the behavior of its oxygens, which vibrate in a restricted manner that actually pulls the lattice closer together as the heat goes on. "This is really a very unusual material," says Mas Subramanian, a solid-state chemist at DuPont Central Research and Development in Wilmington, Delaware.

A few other materials also slim slightly as they warm; cordierite, for instance, shrinks as its temperature rises from roughly 20 to 500 degrees Celsius. But this ceramic shrinks in just one direction, while it still expands in the other two. The zirconium tungstate's performance is much more dramatic, and it contracts on all sides. That might make the ceramic useful in the construction of electronic circuit boards, where it could counter the heat-driven swelling that can break apart components.

The ceramic's own construction—its atomic lattice—is a complex web of oxygen atoms with tungsten and zirconium atoms scattered among them. Each tungsten atom binds to four surrounding oxygens, while each zirconium atom binds to six oxygens. The many bonds, pulling in different directions, make it difficult for a tungsten or zirconium atom to move around when excited by heat.

Most of the oxygens, on the other hand, bind just two other atoms, hanging between a tungsten and a zirconium like a flag on a rope used in a tug of war. The oxygen can't move much toward either side, all forces being equal, but it can shake up and down or side to side. When heat is added to the crystal, this is exactly what the oxygens do. And the result mirrors what would happen if someone pushed the center of a tug-of-war rope in a direction perpendicular to the tugs. The two people—or in this case, atoms—on either end would be drawn closer together. "The distance between the zirconium or tungsten and oxygen doesn't change," says chemist Art Sleight of Oregon State, who led the research effort. "But the distance between the tungsten and zirconium decreases" as the material warms from 0 to 1050 kelvin, says Sleight.



Getting small. This ceramic's lattice is relatively roomy at low temperatures *(top)*, but heat causes oxygen atoms to shake, tugging their zirconium and tungsten partners closer *(bottom)* and contracting the material.

Because these "ropes" extend in all directions, the decrease causes the overall material to shrink evenly by 0.75%, an effect the group measured with an atom position tracking technique known as neutron diffraction. The vibrating oxygens don't force the material to bulge, either, because the lattice has large enough voids for them to move without forcing neighboring atoms outward. The overall effect is so strong, Sleight says, that the shrinking stops only when the temperature climbs high enough to destroy the zirconium tungstate material itself.

By blending such shrinking ceramics with the polymers now used in circuit boards, engineers might be able to compensate for the polymers' tendency to expand as they are heated, disrupting circuits. But the effort could run into some minor resistance. Circuit boards must allow electric currents to flow freely through the embedded wires, and polymers, although not as robust as engineers might like, perform this task quite well. The zirconium tungstate, on the other hand, is slightly more electron hungry and would swipe electrons from embedded circuits. Still, Subramanian believes that researchers "may be able to work a compromise" by tailoring the composition of a polymer-ceramic blend so that the final material isn't too electron hungry. If so, shrinking ceramics could be in growing demand.

–**Robert F. Service**