further potentiate the patients' immune responses. Cyclophosphamide is generally considered to be immunosuppressive, but in this case it may repress the activity of the suppressor cells that normally serve to keep immune responses in check.

Other researchers, including Marc Wallack of Mount Sinai Medical Center in Miami, Florida, and Volker Schirrmacher of the German Cancer Research Center in Heidelberg are exploring still another approach to boosting the activity of tumor cell vaccines. They make the tumor cells more immunogenic by infecting them with viruses.

In a preliminary trial in human cancer patients, Schirrmacher has found that nearly 80% of the patients treated with his vaccine subsequently develop an immune response to their tumor cells. "But whether this response is sufficient to have the desired effect against the tumor we do not yet know," Schirrmacher says. The result is nonetheless encouraging in view of the other reports of a correlation between vaccine-stimulated immune response and tumor suppression.

The generally promising results being obtained with tumor cell vaccines do not mean that all the problems have been solved. Mitchell, for example, has noted a troubling development in his melanoma patients. Melanomas often spread to the brain, although the patients' other metastases usually kill them before the more slowly growing brain tumors become apparent.

Mitchell is now finding that patients who have had remissions are relapsing because they are developing brain metastases. This has happened to the woman who had the complete remission, although she had only a single, operable brain tumor, and is still living more or less normally. Apparently, the tumor cell–killing immune cells cannot get into the brain to control metastases there. "No matter how successful we are with this immune therapy, we are still going to be backed up against the blood-brain barrier," Mitchell says. Learning how to crack that barrier will be one of the future directions for his work.

In addition, the cloning of the interferon and interleukin genes has made these natural immune stimulators available in large quantities. So the researchers are also beginning to investigate whether these agents can improve the efficacy of their vaccines.

Although everyone is optimistic about the vaccine results, no one would want to claim a cure for cancer at this stage of the work. "Let's be realistic," Bystryn says. "People have been trying to develop cancer immunotherapy for 20 or 30 years without success. The odds are fairly long, but I think that this approach has as good a chance of working out as any other." ■ JEAN L. MARX

Math Team Vaults Over Prime Record

No, this isn't yet another story about how high-speed computers have allowed number theorists to set a new record for the largest known prime number. This is about a prime that is not only larger but of a different kind from all those that have reigned in recent years. And the techniques used to verify it actually have real-world applications.

The new king of the mountain is $391581 \times 2^{216193} - 1$. The mathematical pole vaulters who achieved it were six computer scientists at the Amdahl Corporation in Sunnyvale, California.* The Amdahl team sifted through hundreds of thousands of possible primes before settling on several thousand meganumbers for final testing. The computations ran quietly in the background for a year and a half. On 6 August, the Amdahl team had achieved new heights— a number they officially announced only after an independent check, run by Jeff Young at Cray Research Inc. in Mendota Heights, Minnesota, had verified (see box) the number as prime.

Until the Amdahl group's claim, recent record large primes have belonged to a class known as Mersenne primes: numbers that are one less than a power of 2. The largest known Mersenne prime is $2^{216091} - 1$, which was proved to be prime by David Slowinski at Cray Research Inc. in 1985. Written out in full, Slowinski's Mersenne prime has 65,050 digits. (Decimal digits, however, are not the best way to write out Mersenne primes; binary, base 2 digits, which the computer prefers anyway, are better: Slowinski's prime appears in base 2 as a string of 216,091 1's.)

The Amdahl prime tops Slowinski's number by 37 decimal digits—the mathematical equivalent of adding an eighth of an inch to the current world mark in the pole vault.

Of course, some will say that finding a new largest known prime has about the same intrinsic value as setting a new pole vault record. Indeed, any such record is made to be broken, for mathematicians proved a long time ago that the list of prime numbers is infinite. But finding a new prime represents more than an entry in the record books. Bodo Parady of the Amdahl group calls it "a clear level of accomplishment," comparable to going to the moon. Even if he's exaggerating, the fact is that the underlying number theory has implications for computer science. "In the future you're going to see number theory playing an increasing role in the development of new computer architectures," Parady predicts.

Actually, there have already been useful spinoffs. In the course of their prime number search, the Amdahl group developed a new algorithm for high-speed convolution (a key ingredient for multiprecision multiplication) tailored to the Amdahl computer architecture. That algorithm has possible applications in seismic research, weather prediction, and aeronautical simulation, Parady notes. And it has already been sent to the University of Manchester for use in a pulsar search system; the search for astronomical prime numbers may have applications in astronomy itself.

■ BARRY A. CIPRA

Is It Prime?

How is primality verified for such large numbers? The obvious method of trial division is out of the question: even a modest hundred-digit prime can't be verified that way.

The test for Mersenne numbers works as follows: Starting with the number 4, square it and subtract 2. Do this again (square and subtract 2) on the resulting number, repeating the procedure a total of $m - 2$ times. If the Mersenne number $2^m - 1$ divides the final result, then $2^m - 1$ is a prime (and if it doesn't, then it isn't). For example, the first three numbers that are produced are 14, 194, and 37,634, and these are enough to prove that $2^5 - 1 = 31$ is prime, since 31 divides 37634. A modified version of this test works on numbers of the form $k \times 2^m - 1$, in which the starting number 4 is replaced by a number related to the square root of k.

For numbers with tens of thousands of digits the amount of computation becomes daunting, especially since most of the time the test succeeds only in verifying that the large number is *not* prime. Indeed, one reason the Amdahl group decided not to look for a Mersenne prime is that the next Mersenne prime is expected to occur at around the 500,000th power of 2, and the computational loads start to get fearsome by then. ■ B.A.C.

*John Brown, Landon Curt Noll, Bodo Parady, Gene Smith, Joel Smith, and Sergio Zarantonello.

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