ing the gene in the bacterium *Escherichia coli*, they found they could get good crystals but had trouble getting enough FtsZ to work with because the bacteria degraded the protein rapidly. By heating up the *E. coli*, Löwe and Amos caused the enzymes that degrade FtsZ to break down, while the FtsZ, which had evolved to tolerate heat, remained stable. As a result, they could produce crystals in sufficient quantity for x-ray studies and have now solved the protein's structure to a resolution of 2.8 angstroms. This revealed that FtsZ, which is just a single protein, looks most like β-tubulin, especially in the GTP-binding region. In both cases, the nucleotide binds to the tip of the proteins, rather than deep within an interior fold as in most other GTP-binding proteins.

Other aspects of the two proteins' structures are also similar, even though their amino acid sequences show only minimal homology. But there is one notable difference: FtsZ lacks two helices found on one end of tubulin. These helices make up the outer surface of the microtubule; there they could provide points of contact for a range of other molecules, such as the motor proteins that transport molecules along the microtubules. "My guess is that [the helices] have been added so that the special motor proteins could interact [with the microtubule]," says Amos.

With both structures in hand, Löwe hopes to be able to apply what's known about the polymerization of tubulin to learn about polymerization by FtsZ, which is much less well understood. "We can try to predict what the FtsZ polymer would look like," he explains. That should lead to a better understanding of the exact role FtsZ plays in bacterial cell division.

Other researchers will use the structures to make sense of work they have already done on microtubule structure and function. They want to know, for example, what causes microtubules to grow in certain directions and how transport along them can be unidirectional. "An awful lot of people have been working on tubulin for 20 years," Downing points out. "This really provides the framework for understanding their results."

–Elizabeth Pennisi

CELL BIOLOGY

Immortality Gene Discovered

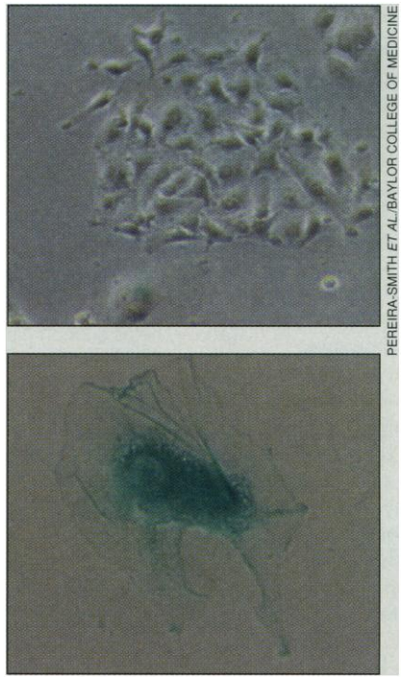
For cells, aging and cancer are often opposite sides of a genetic coin: With "heads," cells will eventually stop dividing, reaching a permanently quiescent stage called senescence, as do normal human cells in lab cultures. With "tails," the cells with genetic defects can become immortal and never stop dividing—a common characteristic of cultured cancer cells. Now, a group at Baylor College of Medicine in Houston has found a gene that may help determine which side the coin lands on.

Last month, at the annual meeting of the American Society for Cell Biology,* Michael Bertram reported that his group at Baylor, led by Olivia Pereira-Smith and James Smith, had cloned a gene that, when mutated, helps make some types of cells immortal. Although researchers have identified many genes in which mutations lead to loss of normal growth control, at least for a number of generations, this is the first one specifically linked to immortality. The finding "is going to give us insights into the whole process of [cellular] immortality," predicts Harvey Ozer, a molecular and cell biologist at the New Jersey Medical School in Newark.

The Baylor team doesn't know exactly how the new gene works. But the structure of the gene, called *MORF4* (for *MORtality Factor from chromosome 4*), suggests that it makes a transcription factor, a protein that controls the activity of other genes. The hope is that it will be possible to track down those genes, shedding light on both the cellular causes of immortality and its opposite number, senescence and aging. In addition, the work could also help provide a better understanding of cancer, because *MORF4* may act as a tumor-suppressor gene—one whose loss or inactivation contributes to cancer development.

The discovery of *MORF4* is an outgrowth of previous work, in which the Baylor group and others showed that mutations in any one of four different sets of genes can cause cultured cells to become immortal. They did this by fusing various kinds of immortal cells with either normal senescent cells or with one another. These experiments showed that the gene defects causing immortality are recessive: They could be corrected by the presence of the normal gene. The researchers also found that all of the 40 lines of immortal cells they examined fell into four distinct groups, each apparently having different gene mutations, because the hybrids between members of different groups showed normal senescence.

By fusing immortal cells with "microcells" containing only single chromosomes, the Baylor team and others identified chromosomes carrying the mutations, but the amount of DNA on each chromosome stymied their efforts to identify the genes themselves. They succeeded in identifying only *MORF4*—one of perhaps a number of genes responsible for immortality in the group designated B, which includes brain and cervical cancer cells—through "pure serendipity," Pereira-Smith says.



PEREIRA-SMITH *ET AL.*/BAYLOR COLLEGE OF MEDICINE

Becoming mortal. *MORF4* caused immortal cervical cancer cells *(top)* to enlarge and stop dividing permanently.

Two years ago, when a graduate student tried to introduce chromosome 4 into a cell line for unrelated experiments, only a small piece of it was properly incorporated. "Just for the heck of it," recalls Pereira-Smith, the student decided to check if that small piece contained the critical senescence gene. To the group's surprise, putting the DNA chunk into group B cells made them senescent, an indication that the segment carried the normal version of a gene whose mutation was critical to those cells' immortality.

The Baylor team found that the piece contained five genes. Of these, only one—*MORF4*—caused group B cells to become senescent, while having no effect on other immortal cells. They also found that the gene was up-regulated in senescent and quiescent cells, but down-regulated in actively dividing cells. The researchers still do not know exactly what *MORF4* does, although they suspect it encodes a transcription factor, because its protein product contains two "motifs"—a helix-loop-helix and leucine zipper—found in known transcription factors.

The Baylor team now hopes to find the genes this protein might regulate and to understand their functions. That might put them on the way to learning how cells can live forever—and how normal cells age.

–David Ehrenstein

*The meeting was held in Washington, D.C., from 13 to 17 December 1997.