blocks must be cleared away. Written by the Labor and Health and Human Services subcommittee chaired by Senator Arlen Specter (R–PA), the Senate bill proposes to spend more money on jobs and education programs than was allocated to the subcommittee by budget chiefs. The bill gets around this problem by deferring costs and recalculating accounts in ways that leave even seasoned congressional hands befuddled.

One academic lobbyist who attended the bill's markup on 3 September says that Senator Pete Domenici (R–NM), chair of the budget committee, seemed ready to go along with a "rescoring" process that would make available about one-third of the money needed to float this bill. But it's not clear how Specter and the subcommittee's top Democrat, Tom Harkin (IA), will find the remainder.

The political roadblocks could be formidable, too. Mainly because conservatives and moderates differ so sharply, the House has not yet acted on an NIH funding bill drafted by a subcommittee chaired by Representative John Porter (R–IL). This proposal would give NIH a $1.2 billion increase (9.1%). But other parts of the bill would end funding for popular summer jobs and home heat subsidy programs. Even moderate Republicans have refused to support these cuts, and President Clinton has said he would veto the bill. This problem must be solved before the House and Senate can agree.

Congress has only a couple of weeks left to resolve these issues before the fiscal year ends on 1 October. Already, Republicans are talking about the need to pass "one or two" stopgap funding resolutions to keep the government afloat as they wheel and deal.

–ELIOT MARSHALL

BIOLOGY

RNA-Splicing Machinery Revealed

For proteins in human cells, teamwork often beats working alone. Many proteins gather in complexes that contain up to dozens of components and help cells replicate DNA, turn on genes, and perform other key tasks. It can take years of work to isolate and identify the proteins in these complexes, then track down their genes. But teaming up pays off in the biology lab, too. By pairing a new high-speed technique for analyzing proteins with a database of partial gene sequences, a European group fingered nearly all of the parts of a critical piece of protein machinery in one fell swoop.

In the September issue of *Nature Genetics*, Matthias Mann of Odense University in Denmark, Angus Lamond of Dundee University in Scotland, and their colleagues report that they have identified 44 components of the human spliceosome, a multiprotein machine that splices the noncoding sequences out of newly minted RNAs to produce messenger RNAs, the cell's templates for protein production. Having an almost complete parts list for the spliceosome should help researchers figure out how it works. The feat, achieved while Mann and Lamond were both at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, also proved the worth of the database of human gene fragments called "expressed sequence tags" (ESTs), which some genome experts once dismissed as a poor substitute for the complete gene sequences to come from the Human Genome Project. "They have leapfrogged over what would have been years of work," says Francis Collins, director of the National Human Genome Research Institute. "The significance goes beyond spliceosomes, although that's significant enough."

Although researchers had been working on the human spliceosome for 2 decades, they had only identified about half of its proteins, Lamond says. To find the remaining ones, the team fished out intact spliceosomes from cultured human cells and separated them into what appeared to be 69 individual proteins. With a protein-splitting enzyme, they digested each protein component into shorter pieces. They then analyzed each piece by a technique called nanoelectrospray mass spectrometry, pioneered by Mann's group, which rapidly and accurately identifies amino acid sequences by shattering the protein fragments and comparing the mass of the resulting pieces.

Next, the EMBL team compared the amino acid se-

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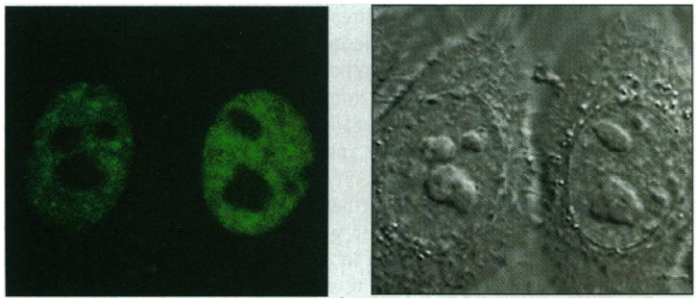


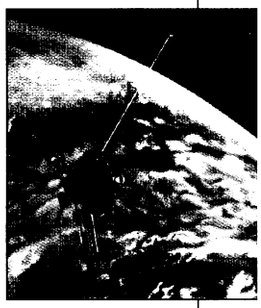
Positive identification. A newly identified component of the cell's RNA splicing machinery, fused to green fluorescent protein, shows up right where it should: in the cell nucleus but not in the nucleoli, the islandlike structures seen in the micrograph at right.

ScienceScope

SPACECRAFT MOTIONS PUZZLE ASTRONOMERS

Could the trajectories of three space probes force scientists to revise the laws of physics? Experts are debating that provocative question, raised in a paper to appear in *Physical Review Letters* later this year.

NASA



Accelerating? Pioneer 10.

From measurements made with radio signals, John Anderson of NASA's Jet Propulsion Laboratory in Pasadena, California, and colleagues have concluded that three spacecraft—the Jupiter explorers Pioneer 10 and 11 and the sun probe Ulysses—are apparently encountering an extra gravitational tug as they leave the solar system. The subtle pull—about 10 billion times less than the acceleration of an apple falling on Earth—can't be explained by current theories. "There's a small probability that we've found something important," says Anderson.

But theorist Irwin Shapiro of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts, believes further scrutiny of the radio data will reveal nothing unusual. "The devil is often in the details," he says.

OUTSIDERS VET KOREAN LABS

South Korean science officials have enlisted outside help in a campaign to reform the country's inefficient national laboratories.

The Ministry of Science and Technology (MOST) has hired a U.S. consulting firm, McKinsey Inc., to tell it something it already knows: that cronyism, a lack of standards, and petty corruption are reducing the size of an expected payoff from the country's R&D investment (*Science*, 10 July, p. 163). The ministry even has a plan to fix things by consolidating labs and subjecting research projects to more rigorous review.

What MOST doesn't have is the clout to convince politicians to go along. So officials are hoping that McKinsey will write a highly critical report that will bolster their case. The firm plans to inspect 11 institutes, including Korea's flagship Institute of Science and Technology, during a 10-week study that ends next month.

Contributors: Govert Schilling and Michael Baker

quences with the growing public EST database, known as dbEST, searching for gene fragments that might code for them. They managed to find matches for 65 of the 69 potential spliceosome components. They then sequenced the full lengths of DNA represented by the ESTs to get the complete genes, which yielded insights into the nature and function of the proteins. Some of the 65 proved to be variants of the same protein, so in the end the team was left with 25 known spliceosome proteins and 19 new ones. To confirm that all the new proteins were really part of the spliceosome, the researchers linked the gene for each one to the gene for a fluorescent protein. They showed that the hybrid genes produced proteins that glowed in parts of the nucleus where spliceosomes were expected.

The spliceosome analysis "is a technical tour de force," says spliceosome researcher Thoru Pederson of University of Massachusetts Medical School in Worcester. Although it took 3 years, the researchers say they could perform it in a matter of months now that they have proven the techniques. Their success shows, for example, that the dbEST database now contains fragments of almost all the genes for the spliceosome—and, most likely, for many other multiprotein complexes, says molecular biophysicist Charles Cantor, of Sequenom Inc., a genomics company in San Diego. That had been in doubt because no one knew exactly how many of the more than 50,000 human genes were represented by the database.

The spliceosome work is also a pioneering example of "proteomics"—the effort to get from genome sequence data to protein function by analyzing many proteins at once. "We've all been excited by the genomics project," Pederson says. "This is the beginning of the proteomics project." **–DAN FERBER**

Dan Ferber is a science writer in Urbana, Illinois.

CELL BIOLOGY

Leptin Sparks Blood Vessel Growth

You can hardly find two hotter biomedical research areas these days than angiogenesis, the growth of new blood vessels, which has emerged as an exciting new target for anticancer drugs, and obesity, a field that was energized 4 years ago by the discovery of leptin, an appetite-suppressing hormone made by fat cells. Now, in a curious twist, biochemist M. Rocío Sierra-Honigmann of Yale University and her colleagues have forged a direct link between those two fields. They report on page 1683 that leptin triggers angiogenesis in experimental animals.

"No one would have thought that leptin has anything to do with angiogenesis. This is a paper that is going to change people's thinking," says angiogenesis pioneer Judah Folkman of Harvard Medical School in Boston. Just what leptin's double duty means for the workings of the body isn't clear yet. But findings by Sierra-Honigmann's team and others suggest several intriguing possibilities. One is that leptin contributes to the formation of the new blood vessels needed when fat increases in volume. Leptin may also spur blood vessel growth in the maturing egg and early embryo and in healing wounds as well.

M. R. SIERRA-HONIGMANN

Circle dance. Endothelial cells treated with leptin draw together to begin to form tubes.

Sierra-Honigmann decided to see whether leptin promotes angiogenesis because of a chance discovery she made a year and a half ago while helping out her husband, Jaime Flores-Riveros, who was then at the Bayer Research Center in West Haven, Connecticut. He had engineered cultured cells to make the cell surface receptor through which leptin exerts its effects—a receptor then known to be found mainly in the brain. Sierra-Honigmann was using antibodies to confirm that the cells actually contained the receptor. As a negative control for the antibody test, she used endothelial cells—the type of cells that form blood vessels. To her surprise, those cells scored positive, indicating that they naturally contain the leptin receptor. "It kept me awake at night," says Sierra-Honigmann. "If I were an endothelial cell, why would I want leptin receptors?"

To find out, Sierra-Honigmann enlisted the help of two postdocs from a nearby lab, Guillermo García-Cardeña and Andreas Papapetropoulos, who study angiogenesis. They found that leptin causes cultured endothelial cells to aggregate, forming tubes that resemble the early stages of blood vessels. Then with the help of Peter Polverini of the University of Michigan School of Dentistry in Ann Arbor, the team tested whether leptin would cause new blood vessels to form in the corneas of rats, the "gold standard" for an angiogenic molecule. Leptin passed the test.

Apparently, says Folkman, "nature used one molecule for two functions." In addition to its well-known role of controlling appetite and metabolism, leptin may, he suggests, "drive the blood vessels to match the fat." It does not appear to be essential for that second job, however, because the copious fat tissue in mutant mice that completely lack leptin manages to recruit an adequate blood supply.

But embryologist Jonathan Van Blerkom and his co-workers at the University of Colorado, Boulder, found a hint of another role for leptin-induced angiogenesis last year. They discovered that leptin is made in human ovarian follicles, which is where eggs mature until they are ready to be released and fertilized. What's more, Van Blerkom's team found that the protein is packaged with two known angiogenic factors in the follicle and in parts of the egg that develop into the cells responsible for forming the placenta. These findings led Van Blerkom to wonder if leptin is angiogenic. The discovery that it is, he says, suggests that it could help the follicles generate the many new blood vessels they produce as they mature and help the young embryo itself induce the mesh of blood vessels in the placenta.

Wound healing also depends on blood-vessel growth, and researchers had noted that healing is slow in leptin-deficient mice. In preliminary experiments, Sierra-Honigmann and her colleagues have now shown that extra leptin can speed healing. "A normal wound in a mouse heals in 5 to 7 days," she says, but with leptin treatment "it is completely healed by day 3 or 4." In addition, she says, the slow-healing wounds of leptin-mutant mice "heal like normal wounds" when treated topically with leptin.

The leptin-angiogenesis connection raises another possibility as well: that, like all other known angiogenic factors, leptin may be deployed by some cancers to recruit blood vessels. Folkman's team is checking to see if any tumors make leptin, which could then serve as a target for controlling cancer growth. Leptin made by tumors could in some cases also contribute to the appetite and weight loss that are common in cancer, he says. With all these new potential roles for leptin, this already famous protein is poised for even wider stardom.

–MARCIA BARINAGA