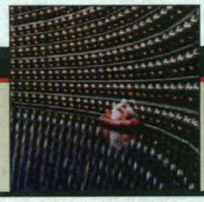
1584
Young investigators: "Feelings of disappointment, frustration, and even despair are palpable."

LEAD STORY 1588
How the cerebellum fine-tunes movement



1594
Neutrinos weigh heavy in physics theory

and Cornell University offers findings that support a novel explanation for the increased numbers and virulence of *E. coli* outbreaks over the past decades. The problem, they say, may stem in part from diet changes among beef cattle.

The digestive tracts of cattle nurture some of the most virulent strains of *E. coli*, which can later find their way into beef and also into other foods that come in contact with infected manure. Since the Second World War, cattle diets have shifted from hay to starchy grain feed. And the Cornell team, including USDA microbiologist James Russell, postdoc Francisco Diez-Gonzalez, graduate student Todd Callaway, and undergraduate Menas Kizoulis, now shows that the digestive systems of cows fed hay generate less than 1% of the *E. coli* found in the feces of grain-fed animals. What's more, bacteria from the grain-fed animals were much more resistant to acid, making them more likely to survive in the human stomach and cause infection.

BILL BEATTY/VISUALS UNLIMITED

Healthy diet? Feeding cows hay may help prevent the spread of *E. coli* in beef.

"This [research] is in a class by itself," raves Gary Schoolnik, chief of the infectious disease division at Stanford University Medical School. "[It] opens the door to a whole field of research that needs to be done." Schoolnik suggests deliberately infecting cows with the O157 strain, so that researchers can directly compare its incidence in animals fed hay and grain diets rather than focusing broadly on the bacteria as Russell's team did. More work will also be needed to test a practical implication of the new finding: that switching cattle to hay a few days before they are slaughtered could limit the frequency of dangerous *E. coli* outbreaks.

The researchers began by surveying 61 Cornell-owned cows that were consuming different types of feed. One group was eating hay or grass, which is naturally rich in fiber, while the other two received either 60% or 80% corn diets. After at least 3 weeks on the diets, the three students tackled the not-so-pleasant task of removing fecal samples from the cows' rectums and determining their *E. coli* counts.

They found that *E. coli* flooded the digesta of the high- and midlevel grain groups, with more than 6 million cells in every gram. But among animals fed hay, researchers logged a mere 20,000 cells per gram. When the samples sat for an hour in acid similar to that in the human stomach, virtually all *E. coli* in the hay-group digesta were destroyed; in the 80% grain division, 250,000 per gram survived—more than enough to sicken an individual if the O157 strain is present. "We were absolutely shocked by the difference," says Russell. "We never found an animal that didn't agree with the trend."

Russell attributes this dramatic variance to the digestive tract of cattle, which has a hard time breaking down starch. Consequently, large amounts of grain can pass into a cow's intestines undigested. This triggers a fermentation process that provides more nutrients for the bacteria to grow on, as well as releasing acid, thus exposing the *E. coli* to an environment that selects in favor of acid-resistant strains. This theory got a boost when Russell's team found that the colonic contents of grain-fed cattle were up to 100 times more acidic than those of animals given hay.

Not all microbiologists were convinced by the data in the paper, however. Michael Doyle, who directs the Center for Food Safety and Quality Enhancement at the University of Georgia, Griffin, argues that lauryl sulfate broth, used to determine the numbers of *E. coli* by dilution, is no more selective for *E. coli* than other bacteria and would not reveal an accurate count. "The methods as they're written" don't make sense, he says. Russell counters that although lauryl sulfate isn't a foolproof selection method for *E. coli*, "the results were confirmed by other tests." For example, the researchers showed that, as expected for *E. coli*, the bacteria could grow in a medium containing lactose, releasing carbon dioxide gas as an end product.

If further work confirms the connection between diet and bacterial growth, the cattle industry might help keep *E. coli* O157:H7 out of the food supply by switching cattle off grain before slaughter. Russell says their work showed that "in 5 days on hay, you can eliminate all acid-resistant *E. coli*."

It may not be easy to persuade the cattle industry, however. "I think people in feed lots are going to be hesitant to institute a change" in cattle diet, says Fred Owens, a ruminant researcher at Optimum Quality Grains in Des Moines, Iowa. Owens cites logistical problems, such as having to transport and store large quantities of hay, as well as a potential drop in market value should the cows' weight fall while on hay.

But many microbiologists believe the costs might be worth it. "I think whatever steps we think make sense we ought to consider doing," says John La Montagne, deputy director of the National Institute of Allergy and Infectious Diseases. He adds, "*E. coli* O157 is a big problem, potentially a very big problem." —JENNIFER COUZIN

BIOMEDICAL RESEARCH

Senate Committee Votes Boost for NIH

Biomedical researchers can chalk up another big advance on Capitol Hill: The Senate Appropriations Committee last week approved a bill that would raise the National Institutes of Health (NIH) budget by almost $2 billion, to $15.6 billion, a massive increase of 14.7%. This is much more than Congress has offered other research agencies, and $800 million more than the NIH increase proposed by the White House. If the bill is approved as written, it would put NIH on track for doubling its budget within 5 years, an ambitious goal set by health research advocates and congressional leaders early this year (*Science*, 10 April, p. 196). The bill would also establish a new earmark: At the behest of Appropriations Committee Chair Ted Stevens (R–AK), it includes a $175 million set-aside in NIH's budget for prostate cancer research. This year, NIH is spending about $114 million.

But before any of these plans come to fruition, congressional aides say, a few road-

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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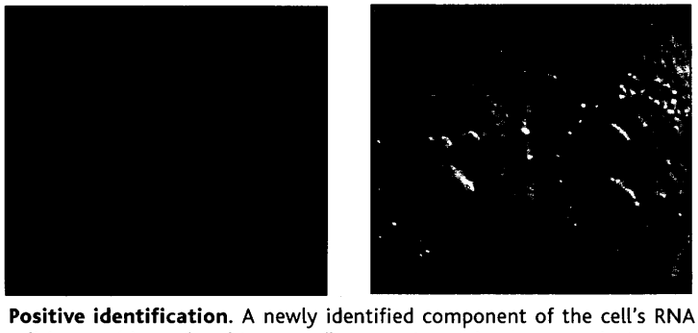

Positive identification. A newly identified component of the cell's RNA splicing machinery, fused to green fluorescent protein, shows up right where it should: in the cell nucleus but not in the nucleoli, the islandlike structures seen in the micrograph at right.

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