opment. He points out that the details of human embryo development after implantation are essentially unstudied. Animal models haven't been useful, he says: "For example, the placenta and all the extraembryonic membranes differ fundamentally between humans and mice." Now, scientists may be able to produce cells specific to stages of human development that have been inaccessible to research. By manipulating gene expression in these cells, they might be able to probe how development can go wrong.

Another payoff, one that could be lucrative for Geron in the not-too-distant future, according to Geron Vice President Thomas Okarma, will be drug screening. Okarma says, "The potential to supply unlimited quantities of normal human cells of virtually any tissue type could have a major impact on pharmaceutical research and development." Cell lines used for drug screening are currently derived from animals or "abnormal" human tissue, such as tumor cells.

"Home run." Geron VP Thomas Okarma sees potential for tissue repair.

The real "home run" of this technology, Okarma says, is the "enormous" possibility that researchers might be able to tailor stem cells genetically so that they would avoid attack by a patient's immune system, then direct them to specialize into a particular kind of tissue and transplant them into diseased organs. Geron suggests it might be possible to repair damaged heart muscle by injecting new cardiomyocytes, for example. Okarma points out that researchers have already used mouse stem cells to produce cardiomyocytes that were successfully transplanted into a mouse heart.

But that possibility also remains the most distant. "Right now," says Thomson, "we don't know how to direct [stem cells] to become any specific cells." And developing cells that can be immunologically suitable for transplantation will take even more work. Still, Thomson says, "it's no longer in the realm of science fiction; I really believe that within my lifetime I will see diseases treated by these therapies."

For some researchers, however, the complicated legal issues associated with the cell lines may prove discouraging. Federal law governing this topic was updated most recently in the 4000-page appropriation bill Congress passed on 20 October. It says U.S. funds may not be used for "the creation of a human embryo" for research purposes, or for "research in which a human embryo or embryos are destroyed, discarded or knowingly subjected to risk of injury or death. ..." The embryo is defined as any organism not protected as a human subject under other laws (such as those applying to fetal tissue) "that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or diploid cells."

When NIH officials learned of Thomson's work, their initial reaction was that federal funds could not be used for research using his cell lines. But director Harold Varmus sought legal counsel, and a top aide told *Science* that the cells may be exempt from the law because they could not grow into embryos. NIH was scrambling to come up with a final ruling by the time Thomson's paper was published. The cell line Gearhart is developing may not have the same legal complications because it was derived from fetal, not embryonic, cells.

The law clearly prohibits the use of federal funds for the initial development of an embryonic stem cell line, however. Okarma says Geron carefully considered the ethical implications before proceeding. "We recognize and affirm that there is moral authority associated with this tissue," he says. Geron has established a panel of ethical advisers, chaired by Karen Lebacqz of the Pacific School of Religion in Berkeley, California, representing "five different religious traditions," Okarma says. The panel approved the stem cell project, he says, on the basis that Geron was making beneficial use of fetal tissue and IVF embryos that would have been discarded or frozen indefinitely.

Researchers are hoping that the legal uncertainties hanging over Thomson's cell lines can be cleared up quickly. "People have been a little scared off by the controversy" already, says Smith, and "it would be a tragedy if [legal barriers] exclude the best people" from the field.

–ELIOT MARSHALL

U.K. RESEARCH FUNDING

Life Sciences Win Bulk Of Cash Bonanza

LONDON—When the British government announced in July that it would pump an additional $1.1 billion into science spending over the next 3 years, researchers whose budgets had been squeezed hard for more than a decade greeted the news with delight. Last week, the government released the details of how this new largess will be distributed, and life scientists were left cheering the loudest.

Among Britain's six research councils, which provide most of the government's funding for basic research, the biggest increase—6.8% above inflation—will go to the Medical Research Council (MRC). "I'm enormously pleased," MRC chief executive George Radda told a press conference in London when the allocations were announced last week. The MRC subsequently said it would spend part of its increase on three major new initiatives: in mouse genetics, cancer research, and the study of the human form of mad cow disease. Not everyone is celebrating, however. The council responsible for particle physics and astronomy is slated to get no significant increase in real terms.

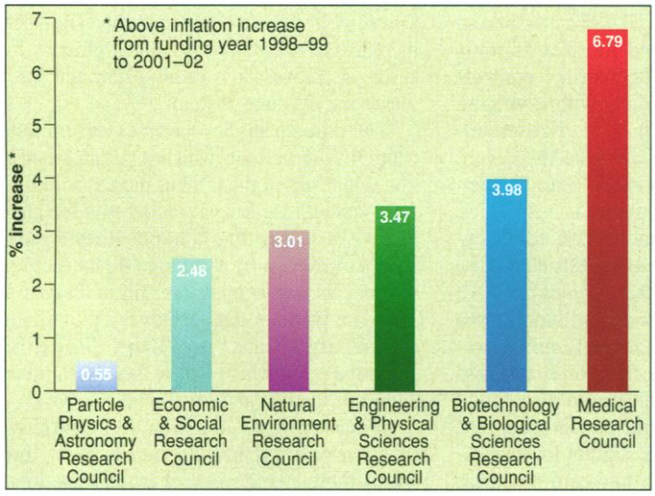
These increases are the fruits of a yearlong comprehensive review of government spending launched by the Labour government soon after it was elected in May last year. The first results of the review, announced in July, put science among the most favored areas of spending (*Science*, 17 July, p. 314). When he announced the allocation of the promised money last week, trade and industry secretary Peter Mandelson, the Cabinet minister responsible for research, said he wanted the increases to tackle the "post-genomic challenge": helping British scientists exploit advances in genetic research in which they have been key players.

All smiles. John Collinge will head new CJD center.

This is reflected in the allocations: Alongside the MRC's 6.8% boost, the other two councils involved in life sciences—the

Natural Environment Research Council (NERC) and the Biotechnology and Biological Sciences Research Council (BBSRC)—will get increases of more than 3% above inflation. BBSRC says it plans to back more projects that attempt to exploit novel gene products as therapeutics and other high-value chemicals, while NERC is planning a program of research on genomes and the environment, such as looking at how the genomes of different populations of plants may affect their response to climate change. The smaller Economic and Social Research Council, which has also won an increase, is expected to step up funding on the social and ethical implications of genetic research.

The MRC's budget increase—a total of $144 million over the next 3 years—will allow it to expand existing work in three priority areas. The council will devote an as-yet-undecided sum to boost research on mouse genetics, including sequencing more of the mouse genome and developing mutant mouse strains. "With genome sequence data and the ability to develop new mutant strains, the mouse is a powerful way to get models for human diseases," says geneticist Nick Hastie of the MRC Centre for Human Genetics in Edinburgh, part of the mouse genetics effort.



Biology boost. Life sciences get the biggest rises in Britain's 3-year budget allocation.

The MRC is also putting $13 million over the next 3 years into a new center aimed at converting advances in the molecular analysis of cancer into improved patient treatment. The new center, which will be established in collaboration with Cambridge University and a medical charity, the Cancer Research Campaign, will be headed by cancer biologist Ron Lasky of the Wellcome Centre for Cancer and Molecular Biology in Cambridge. It will be up and running by early 2001. Among the initial goals will be the development of tests for early diagnosis of common cancers, including cervix, lung, breast, and colon. Longer term goals include better diagnostic analysis of tissue samples to determine how far the disease has progressed and tracking down genes that predispose people to cancer.

The third MRC initiative will focus on the study of so-called new variant Creutzfeldt-Jakob disease (CJD), the fatal brain disorder linked to mad cow disease that has so far killed 29 people. The MRC will set up a new center in London based around the unit headed by molecular biologist John Collinge at the Imperial College School of Medicine at St. Mary's Hospital. "We hope to develop a critical mass of around 60 people," says Collinge. He will be joined next year by another leading specialist in the field, molecular biologist Charles Weissman of the University of Zurich. The MRC plans to provide $2.4 million a year in addition to funds Collinge will receive as a principal fellow of the research charity the Wellcome Trust. A high priority for the new center will be the development of simple new tests for the hallmark "prion" protein that has been linked to the disease. A screening test is urgently needed for blood samples to ensure that the disease is not spread through transfusions and to detect the protein in tissues such as tonsils.

Physical scientists have feared that the government's enthusiasm for biology would leave them out in the cold. But they can take some comfort from the new allocations. The Engineering and Physical Sciences Research Council won a respectable 3.4% increase in real terms. And even the hard-pressed Particle Physics and Astronomy Research Council (PPARC), with an increase of just 0.55%, won added security through a new contingency fund designed to absorb currency fluctuations that can increase subscriptions to bodies such as the CERN particle physics center near Geneva. "Our domestic budget has now been assured, and the problems created by currency fluctuations for our overseas commitments have also been addressed to help plan our future," a spokesperson says. But Astronomer Royal Martin Rees of the University of Cambridge says that the budget outcome is very disappointing. "It's a pity PPARC did not make a better case for addi-

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ScienceScope

FAST TRACK FOR SEQUENCES?

For scientists interested in the human genome, the wait for sequence data can be painfully long. But the National Institutes of Health (NIH) is taking steps to speed up the process for the most biologically interesting regions.

The new procedure will make use of an international peer-review panel, Francis Collins, director of NIH's National Human Genome Research Institute, told researchers last week at a Denver meeting of the American Society for Human Genetics. The panel will review requests from teams hoping to have a particular region of the genome sequenced sooner rather than later. If the panel decides the arguments are compelling, "then that sequence moves to the top of the list for the center that's working on that chromosome," says Collins. He hopes to have the system in place by early next year.

A NEW HAUL OF GENOME PROJECTS

Add social amoebas—once known as slime molds—and the zebrafish to the growing menagerie of organisms having their genes mapped or sequenced. Amoeba researchers hope to discover the basic genes that make multicelled organisms possible, while zebrafish geneticists are fishing for clues to human diseases and development.

The zebrafish project, begun in September, has wide appeal: Thirteen of the National Institutes of Health (NIH) have pledged a total of $4.7 million to fund five 3-year grants to map 10,000 *Danio rerio* genome markers. Biologists hope the map will help them connect hundreds of known fish mutations to human genes and diseases (*Science*, 14 February 1997, p. 923). Two reports in the November *Nature Genetics* of the first examples of zebrafish models for human disease—porphyria and a type of genetic anemia—are just "the tip of the iceberg," says Leonard Zon of Children's Hospital in Boston.

This week, the European Union joined the NIH and the Deutsche Forschungsgemeinshaft in a $2.7-million-a-year effort to sequence the amoeba *Dictyostelium*'s 34 million base pairs. Three labs are working on the 3- to 5-year project.

tional investment," he says.

As part of the budget allocation, the government also announced a raft of measures to help improve career prospects for university researchers. This year it increased the minimum annual grant for Ph.D. students by $1600 to $10,500—the first increase above inflation for 30 years. And now the number of fellowships awarded by the Royal Society will be increased from 265 to more than 300. The increased research council budgets will also mean that university-based researchers on council grants will be able to hire more graduate and postdoctoral staff, and the councils' own labs will also be able to create new positions.

Even the lobby group Save British Science, a longtime critic of government funding policy set up during the previous Conservative government, could find little to complain about. Says lobby chair Richard Joyner, dean of research at Nottingham Trent University: "I'm very pleased to see that everybody has got something." —NIGEL WILLIAMS

AGING RESEARCH

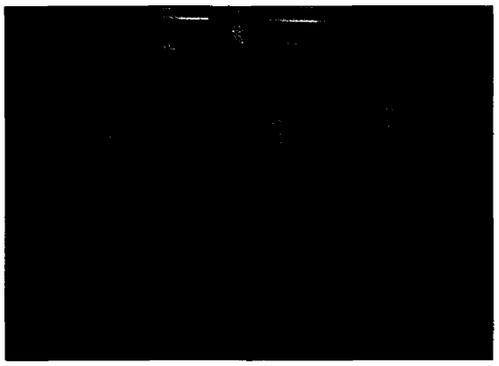
Low-Calorie Diets May Slow Monkeys' Aging

Scientists are edging closer to proving in primates what's been demonstrated dozens of times in rodents since the 1930s: Sharply reducing caloric intake can slow the process of aging to a crawl.

At a Society of Toxicology meeting 2 weeks ago in Reston, Virginia, three groups presented data showing that rhesus monkeys fed severely calorie-restricted diets show fewer signs of diseases associated with advancing age, including diabetes, heart disease, and cancer, than their comfortably full—and in some cases comparably lean—counterparts. Because most of the hungry monkeys are only now entering middle age, it's too early to tell whether the low-calorie diets will significantly extend their life-spans. But one of the studies provided a tantalizing hint: Mortality due to disease among the calorie-restricted monkeys was slightly lower than among the controls.

Even if monkeys do live longer on low-calorie diets, it doesn't necessarily follow that humans would experience similar benefits—or that they would find such diets acceptable. But researchers hope that these animals might provide clues to why calorie restriction is beneficial—information that could point to strategies and medications for delaying aging in humans.

The three groups reporting their results at the meeting—which were led by Mark Lane at the National Institute on Aging (NIA), Richard Weindruch at the University of Wisconsin, Madison, and Barbara Hansen at the University of Maryland, Baltimore—kept the animals on tight rations but well above starvation levels. The Wisconsin and the NIA teams provided the test animals with 30% fewer calories than the controls (while enhancing their diets with a vitamin and mineral supplement), while Hansen tailored the monkeys' food intake to prevent them from putting on more pounds than they carried in young adulthood.



Hungry but healthy. Monkeys eating sharply restricted diets (right) may live longer than well-fed controls.

All three groups found that in nearly every system tested, the calorie-restricted (CR) animals were better off than the controls. All recorded lower blood lipids and blood pressure, enhanced insulin sensitivity, and a lower incidence of diabetes in calorie-restricted monkeys. The Wisconsin group also found less spinal arthritis, while Lane's team saw fewer cancer cases and a slightly lower mortality rate due to diabetes and cardiovascular disease. One of the 120 animals on the diet died, compared to five among the 120 controls. "[The] major message from the monkeys is that 99.9% of those markers that we have examined in the monkeys behave exactly as they do in rodents," says Lane.

What's more, the severe calorie reduction seems to produce few adverse effects. Lane's group, which began caloric restriction in young animals, saw the only potential problem: delayed sexual and skeletal maturity. None of the primates have been bred, however, so no one knows whether their reproductive capabilities are affected. And although all three groups acknowledged that their animals were regularly hungry—wolfing down food more quickly than controls, or becoming excited if accidentally given excessive food—none found that the added stress affected behavior. Controls and CR monkeys were equally energetic, social, and nonaggressive, and a weeklong videotape of Lane's animals showed no measurable differences between the two groups.

Why caloric restriction so dramatically improves the functioning of organ systems remains under debate. Certain changes, like the reduced incidence of diabetes, might simply be a benefit of leanness, as obesity predisposes to the disease in nonhuman primates as well as in most humans. Others are more puzzling, however.

One possibility, Weindruch says, is that restricting food consumption reduces the production of tissue-damaging oxygen free radicals that are a byproduct of food metabolism. He has shown in mice that such oxidative damage leads to muscle atrophy, producing the frailty common in old age.

But reducing oxidative damage is only one way calorie restriction might work. "The problem with [caloric restriction] is that it fits any of the theories of aging," says Roy Walford, a professor of pathology at the University of California, Los Angeles, and a pioneer in the field. "[It] increases DNA repair, regulates glucose insulin, decreases free radical damage, preserves the immune system."

The primate studies haven't gone on long enough to determine whether caloric restriction will result in the kind of increases in life-span seen in near-starving rodents, which live up to 40% longer than controls. Rhesus monkeys can live up to about age 40 in the lab, whereas the test animals are still in their mid-20s. The primate data are "very tantalizing preliminary results," says Lane. "But [I'm] not at the point where I'm willing to stand up and wave the flag and say it works."

If further work confirms that caloric restriction pays off in extended primate life-spans, though, and researchers can pin down the reasons why, aging experts hope to tap into something that, until now, has been restricted to the realm of fiction—controlling the process of aging. —JENNIFER COUZIN

NEUROBIOLOGY

New Leads to Brain Neuron Regeneration

Neurobiologists have long considered the neurons in the adult brain to be like a precious nest egg: a legacy that dwindles with time and illness and is difficult if not impossible to rebuild. Two sets of findings published this week raise hopes that this principle could one day be overturned. In one, research teams at Harvard and the National Institute of Neurological Disorders and Stroke (NINDS) independently isolated what appear to be the first human cells that can differentiate into all the cell types found in the brain—so-called neural stem cells. In the other, a team based in California and Sweden found a small area of the human brain that produces new neurons into old age.

The discoveries aren't biologically surprising, because both neural stem cells and

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