Science units spared in shuffle

The Office of Science and Technology Policy (OSTP) and the Council on Environmental Quality (CEQ) have survived President Carter's White House reorganization virtually unscathed. Speculation had run high recently concerning the probable demise of CEQ, and Frank Press, director of OSTP, told reporters this week that the reorganization team had originally been "disbelievers" in the value of his office. Now, he says, the few changes that have been proposed will probably further "integrate us into the daily life of the President."

Under the reorganization act, Congress has permitted the President to shift management responsibilities within the executive branch of government at will, so long as legislatively mandated functions are preserved and unless Congress specifically objects to some change. Carter's proposed modifications in the Executive Office of the President, announced last week, will thus become official in 60 days if Congress does not object. Reorganization of the rest of the federal bureaucracy will come in subsequent stages, over the next three or more years.

Changes proposed for the science-advising apparatus generally affect the panels of outside experts appointed to investigate specific issues, rather than the daily function of OSTP itself. The President's Committee on Science and Technology, for example, will be abolished and its duties reassigned by the reorganization team. The Federal Coordinating Council on Science and Technology will be moved out of OSTP and reestablished as a working group attached to the cabinet. Preparation of the congressionally mandated reports on the state of science will now be reassigned to the National Science Foundation.

Similarly, some of CEQ's routine review duties will be passed to operating agencies. The Environmental Protection Agency, for example, will take over CEQ's evaluation responsibility under the Federal Nonnuclear Energy Research Development Act. The Council will, however, continue to publish its annual report on environmental quality.

Press used the occasion of the reorganization announcements to tell reporters about some of the projects his office has become involved in and to introduce some new assistant directors.

The OSTP is now helping conduct eight or so policy-making reviews on national security affairs, including staff work for studying the comprehensive test-ban treaty and antisatellite weapons agreement. In other areas, the office is leading a review of uranium resources and is involved in studies of dam safety, world hunger, recombinant DNA research, climate, patent policy, technology for development, ocean policy, storage of radioactive wastes, a review of the defense R&D budget and other projects.

Press announced appointment of three new assistant directors, two senior consultants and several policy analysts including: Benjamin Huberman, assistant director for National Security, International and Space Affairs; Gilbert S. Omenn, assistant director for Human Resources and Social and Economic Services; and Philip M. Smith, assistant director for Natural Resources and Commercial Services.

"I feel in a very upbeat mood," Press said in describing his job now that he has had time to adjust to Washington. Of OSTP itself: "I am pleased with the way the office has evolved." Press says he can see the President "when I want to" but usually writes memoranda, about twice a week. These, he says, almost always prompt a handwritten reply from Carter.

Clearly, Press has established a rapport with the President and clout in the White House unparalleled by any other science adviser in recent times. □

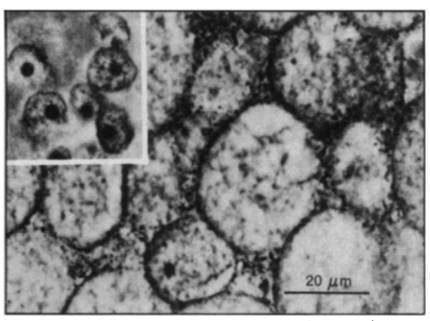
Gene control: Frog DNA in newt eggs

Each cell in a complex organism consults a small fraction of the information coded in DNA in its nucleus. A liver cell never reads the parts of its DNA instructions that describe proteins peculiar to a nerve cell. And adult cells, under normal conditions, never revert to making the proteins specific to immature cells. Yet under experimental conditions, closed chapters of the DNA manual can be reopened. For example, the nucleus from the skin cell of an adult frog can, if transplanted into an egg, still direct tadpole development. How genes switch on and off during development is one of the most intriguing mysteries of biology.

A strange combination of cell parts, resembling the contents of the witches' cauldron in *Macbeth*, now promises to illuminate that question. Instead of "Eye of newt and toe of frog," Eddy M. DeRobertis and J.B. Gurdon combined immature egg cells (called oocytes) of newts with nuclei, containing DNA, from African clawed frogs. In the remodeled cells, each containing about 200 frog nuclei, the frog DNA directs production of frog proteins, which are clearly distinguishable from newt proteins.

The cue as to what part of the frog DNA should be read comes from the newt part of the cell. The hybrid cells make at least three proteins that are normally found only in immature frog eggs. The hybrid cells also produce several proteins typical of both oocytes and the adult frog cells (in this case, laboratory-grown descendants of kidney cells). The cells make no protein of types not found in oocytes. Thus, the researchers state, molecules in the newt oocyte "reprogram" the gene expression of the frog nuclei.

These experiments differ from previous work in which nuclei were transplanted between cells, because formerly the new proteins were detected only after many cell divisions. Researchers proposed that cell division is necessary for major changes in gene activity. The recent experiments rule out that hypothesis because although they have not divided, frog nuclei, after they are injected into the newt oocytes, express a different set of genes. "This shows that oocytes contain *specific* gene-controlling substances," DeRobertis and Gurdon write in the June PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.



PNAS

Frog nuclei swell from original size (inset) after injection into immature newt eggs.

Not all the proteins made by normal frog oocytes were detectable in the hybrid eggs. The investigators point out that the newt they used (*Pleurodeles*) is only distantly related to the frog *(Xenopus)* and might be able to recognize some, but not all, of the signals that regulate frog gene expression.

Purified DNA molecules, as well as whole nuclei, have been injected into amphibian oocytes to pose other questions about cell operations. One paradox that Gurdon, Andrew H. Wyllie and Jenny Price examined is how cells containing enzymes that degrade DNA avoid destroying their own genetic material. Some investigators propose that the membrane of the nucleus keeps those enzymes from the essential DNA. In further work at the Medical Research Council in Cambridge, England, the biologists found evidence that, instead of relying only on physical separation, the nucleus contains a component that makes DNA invincible to the enzymes. When DNA from SV40, a virus that infects monkey cells, is injected into the cytoplasm of oocytes, it is always degraded, Gurdon and co-workers found. When the DNA is injected into the oocyte nucleus, it is conserved in its circular, supercoiled form. However, if the injection ruptures the nuclear membrane, so that the viral DNA first enters the nucleus but then leaks out, the DNA remains intact in the cytoplasm. Such a shield, the researchers suggest in the July 14 NATURE, is important to protect DNA during cell division, when the nuclear membrane breaks down.

Gurdon and colleagues also consider

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the amphibian oocyte as "a living test tube" for studying gene expression. In experiments with purified cell parts in normal glass test tubes, expression of animal DNA is inefficient and much less accurate than in an intact cell. However when purified DNA from a variety of sources is injected into frog oocyte nuclei, it is reliably copied into messenger RNA, the intermediary between DNA and protein synthesis. Janet E. Mertz and Gurdon demonstrated such gene action for several days after cells were injected with DNA from animal and bacterial viruses, bacterial plasmids and fruit fly genes, they reported in the April PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. When the amount of SV40 DNA injected is 1,000 times the amount of frog oocyte DNA, most of the new messenger RNA produced is specific to the virus. These viral messenger molecules seem to be the same as those that predominate when the virus infects monkey cells. Therefore, the oocyte closely mimics normal selection of DNA regions and normal processing of messenger RNA. Furthermore, the SV40 and fruitfly DNA can direct production of protein in oocytes, the researchers indicate.

Oocytes may be more suitable "living test tubes" for studying gene control in plants and animals than are bacterial cells because the oocytes are more likely to respond to relevant control signals. Unlike the naked bacterial DNA, genetic material of higher organisms is assembled with proteins into a complex called chromatin. Gurdon and co-workers observe that purified SV40 DNA injected into an oocyte nucleus is also assembled into such a complex. Therefore, the foreign genes may be sufficiently disguised to direct the cell action. The exact role of the nuclear proteins may be revealed by further studies in this system. □

Malaria, herpes vaccines: Progress

In spite of eradication of smallpox and other infectious diseases throughout the world, malaria persists as an enormous problem. One of the difficulties is that the mosquitoes that carry malaria parasites have become resistant to DDT, and biological controls for such mosquitoes have not yet become effective (SN: 8/2/75, p. 73).

However, last year saw a major advance toward a human malaria vaccine. For the first time, human malaria parasites could be continuously propagated in the test tube, thus providing a ready source of vaccine material (SN: 6/5-12/76, p. 361). Now another landmark achievement brings a human malaria vaccine still closer to reality—nonhuman primates have been successfully immunized against a human malaria parasite.

Wasim A. Siddiqui of the University of Hawaii School of Medicine first maintained *Plasmodium falciparum,* a human malaria parasite, in the lab by serial passages of blood-induced infections in owl monkeys. He then cultivated the parasites in the test tube, harvested them for vaccine purposes and used five owl monkeys in a pilot experiment. Two of the monkeys served as controls, three were vaccinated with a parasite solution twice three weeks apart.

As Siddiqui hoped, the vaccine was weak enough in parasite content that it did not produce any malaria in the monkeys. He then injected all five monkeys with enough of the parasite to trigger malaria. Both control monkeys died two-weeks later. In contrast, the three vaccinated monkeys survived, with one completely malaria-free, and the two others showing only minor infection.

Although the number of monkeys used in this experiment was small, the difference between the course of infection in immunized and nonimmunized animals was impressive, considering how lethal *P. falciparum* usually is for owl monkeys. Indeed, this is the first report of a study in which 100 percent survival has been achieved in owl monkeys following a dose of the human malaria parasite *P. falciparum.* In fact, the only comparable malaria immunity ever achieved in monkeys before was against a nonhuman malaria parasite.

These results, coupled with those of last year, suggest that a human malaria vaccine may become a reality in the not-too-distant future.

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Significant progress is also being made in the development of a human herpesvirus vaccine. Herpes viruses are known to cause cold sores and genital infections in people. Evidence strongly suggests that herpes viruses also trigger human cervical cancer and some other kinds of human malignancies.

A herpes virus vaccine that is effective in primates has already been developed (SN: 6/29/74, p. 413). The problem with using such a vaccine in humans, however, is that even though it has been inactivated, it contains viral genetic material that might possibly cause infection rather than prevent it. Gary R. Pearson and Robert E. Scott of the Mayo Clinic/Foundation in Rochester, Minn., have conducted experiments to see whether a herpes vaccine might be developed using material obtained from herpes virus-infected cells, not from the viruses themselves. Not containing viral genetic material, such a vaccine would have to be safe. The question is, would it be effective as well?

Using a newly developed method for isolating plasma membrane vesicles from cells, the researchers managed to extract plasma membrane vesicles from herpes-infected cells that were virus-free yet containing virus-induced membrane antigens. The vesicles were then injected into four monkeys and, as the researchers hoped, the vesicles raised antibodies to herpes virus in the animals.

The results of this pilot experiment, the investigators conclude in the June PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, strongly suggest that a herpes vaccine prepared from herpes-infected cell vesicles would be both effective and safe in humans. □

Test detects liver damage in alcoholics

A New York doctor says he has developed the "first reliable blood test" enabling the early detection of liver disease among alcoholics. Detection at that stage renders many liver problems "fully reversible," heading off more serious ailments, such as cirrhosis of the liver, says Charles Lieber, chief of the Section and Laboratory of Liver Diseases, Nutrition and Alcoholism at the Bronx Veterans Administration Hospital.

The new technique represents a considerable improvement over previous blood tests, which were not specific enough to accurately detect liver damage due to alcohol, Lieber says. Those tests attempted to identify liver problems by measuring transaminase, an enzyme released into the serum by injured body tissues. But the detection of transaminase could indicate problems in any number of tissues, including the liver, he notes. And, he adds, the enzyme is more suited to identifying viral hepatitis than alcohol-related liver complications.

Lieber's test hinges on the activities of the mitochondria, the rod-shaped "power plants" of liver cells, where the cells' energy is produced. Mitochondria exist in every cell but, according to Lieber, play a specific, critical role when liver damage occurs. In such cases, the diseased liver releases glutamate dehydrogenase (GDH), an exclusively mitochondrial substance, into the bloodstream.

In a study of 100 alcoholics versus 100 control patients, Lieber and his colleagues recently measured GDH levels in the blood and compared them to the presence of lesions that develop in the liver. He says the team found an excellent correlation between blood levels of GDH and the degree of liver necrosis in alcoholics.

Researchers still have no sure way of predicting which alcoholic patients with early liver disease would go on to develop cirrhosis, notes Lieber, who is also professor of medicine and pathology at Mount Sinai School of Medicine in New York. But he says the new blood test for liver disease may be a step toward developing "a blood test to predict cirrhosis."

In his search for such a test, Lieber believes that his experiments with baboons have provided some clues. He found that some "alcoholic" animals had pericentral sclerosis in the liver, a condition not present in normal ba-

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