Cell membranes: Critical in diseases

For all their pedestrian appearance—through a microscope they look like little plastic bags punched through with holes—cell membranes are crucial to the human body. They pass nutrients, hormones and electric current in and out of cells; they are the gatekeepers of life (SN: 7/1/72, p. 14; 7/8/72, p. 28).

There is now growing evidence that cell membranes are intimately involved in disease susceptibility and resistance. Much of this evidence was highlighted last week at the 9th Annual Basic Science Research Symposium of the American Society of Clinical Pathologists in Washington. "There is no human disease," declared William O. Russell, a pathologist with the M.D. Anderson Hospital and Tumor Institute, "that is not concerned with the cell membrane in some respect."

Malfunctioning cell membranes participate in obesity, C. Ronald Kahn, an endocrinologist with the National Institute of Arthritis, Metabolism and Digestive Diseases, reported. Kahn and his colleagues have found that insulin binds to the membranes of target cells only half as well in fat persons as in nonobese persons. This decreased binding is due to a deficiency in the number of insulin receptors on the membranes of target cells. Thus obese persons require higher levels of insulin than thin people require to achieve the same effects on glucose metabolism. When fat people fast, the insulin receptor sites on their target membranes revert to their normal number.

A family of lipids called gangliosides are highly concentrated in the membranes of cells. If cells become cancerous, most of the gangliosides disappear from their membranes, Roscoe O. Brady, a neurochemist with the National Institute of Neurological Diseases and Stroke, and his colleagues have found. And this near disappearance of gangliosides is due to the blocking of one of two particular membrane enzymes that help make gangliosides. Brady and his co-workers have also determined that tumor virus genes have to be inserted into the chromosome of a host cell in order to block the strategic enzymes. So it looks as if cancer virus genes interfere with the transcription of the genes that code for the enzymes, resulting in the production of inactive or only partially active enzymes.

Brady and other colleagues at the University of Maryland Medical School encountered a strange clinical case four months ago that dramatically underscores the role of membrane gangliosides in disease. A baby was born with severe mental retardation and physical malformation. Brady and the Maryland investigators were perplexed because the newborn's problems did not resemble any of the usual lipid-storage diseases.

The newborn died, and they performed an autopsy on him. They found that his brain cell membranes did not contain the usual large ganglioside molecules and lacked an enzyme required for the synthesis of the large gangliosides. This defect was identical to that in the cancer cells, yet intriguingly, the infant did not have any tumors. Brady speculates that the infant's retardation and physical deformity may have been triggered by a cancer virus incorporated into the sex chromosome of the child's mother because a male relative of the infant on the mother's side had died from a similar disease.

In 1971 Colorado investigators reported that cancer cells' rapid and uncontrollable growth appeared to be linked to a deficiency in the intracellular messenger cyclic AMP, and to a deficiency in the membrane enzyme adenyl cyclase. Adenyl cyclase helps cells make cyclic AMP. These findings were rapidly confirmed by Ira Pastan and his molecular biology team at the National Cancer Institute (SN: 2/23/74, p. 118). Last week Pastan amplified these findings. He suggested that one way a cancer virus might turn a normal cell into a cancer cell would be to alter its adenyl cyclase, and hence its cyclic AMP production. He and his coworkers are now trying to incriminate a cancer virus in such activities.

Cell membranes are as crucial in disease defense as they are in disease participation. F. Carl Grumet, an immunohematologist with the Stanford University Medical School, reported research conducted by both himself and others that testifies to this fact. Certain immune response genes have been mapped on certain chromosomes. Some of the functions of these genes, such as antibody recognition of antigens, have been identified. Markers on T cells, one of the major kinds of cells in the immune system, have been found to be coded by genes that are located almost exactly in the spot where immune response genes are located. So it is possible. Grumet suggests, that immune response genes code for these markers, and the markers serve as receptors for foreign antigens.

If the membrane markers indeed turn out to be coded by immune response genes, and to be receptors for foreign antigens, they would be the first identifiable products of immune response genes. □

Energy research agency replaces AEC

Within about four months, the Atomic Energy Commission will cease to exist, its research and development capabilities taken over by a new Energy Research and Development Administration (ERDA) and its regulatory duties passed to the Nuclear Regulatory Commission (NRC). President Ford signed the enabling legislation last week, which also sets up an Energy Resources Council (ERC) to coordinate energy policy. Secretary of the Interior Rogers C. B. Morton will head ERC; chairmen for the other new agencies have not yet been named.

Breaking up the AEC follows several years of argument over whether such a regulatory agency should also be responsible for encouraging development of the industry it is supposed to regulate. Environmentalists have insisted the existing arrangement constitutes a conflict of interest, inevitably creating a cozy relationship between Federal regulators and nuclear executives. Industry representatives, for their part, continually complain about a lack of direction and coordination among various governmental agencies regarding regulations and environmental restrictions.

The new agency will face a stiff challenge in trying to solve these difficulties, for the United States is already falling behind other nations in some areas of developing nuclear power and environmental safeguards (SN: 10/5/74, p. 217). The new legislation strengthens regulatory control over the nuclear industry by authorizing personal penalties for responsible officers in companies that fail to obey regulations and requiring public disclosure of all safety-related "abnormal occurrences" at facilities, within 15 days. To achieve political balance the NRC will not be allowed to have more than three of its five members drawn from either political party (all current AEC members are Republicans). By bringing together the energy research activities of several different departments and agencies, ERDA is designed to encourage development of many diverse energy sources without the nuclear bias of AEC's programs.

Ultimately, the Administration wants to create a cabinet-level Department of Energy and National Resources to completely integrate energy research programs. It would absorb the present Interior Department. Legislation to this effect is expected early next year. In the meantime, ERDA has a planned five-year budget of $10 billion that will be distributed among various energy and environmental projects. □