Hepatitis Agents Defined, Cultured

A mysterious particle that piggybacks onto the hepatitis B virus has been characterized, and the hepatitis B virus itself has now been grown in the laboratory. These two advances, reported last week, promise to accelerate greatly the speed of hepatitis research, scientists say.

The discoveries relate to the bloodborne hepatitis B virus, which infects as many as a million people in the United States and hundreds of millions worldwide. While some people, though infectious, carry the virus with no ill effects to themselves, others are chronically ill and may also develop liver cancer. Hepatitis B infection, for which there is no treatment, can be complicated by something called the delta agent — a "defective" virus that exists only in conjunction with the hepatitis B virus. Delta infection, believed to be on the rise worldwide, can make chronic hepatitis B infection lethal.

Myron Essex and his colleagues at the Harvard School of Public Health have grown the hepatitis B virus in the test tube. They inserted hepatitis B genetic material into cells from human liver cancer and were able to isolate cells that produced particles immunologically and structurally identical to the hepatitis B virus.

With the virus in hand, researchers will be able to screen a wide variety of drugs against the virus in an *in vitro* setup, says Camille Sureau, one of the investigators. The same group previously had inserted the virus's genetic material into bone marrow cells, but the production of virus particles was transient. The newly reported cell line has been producing viruses for a year, Sureau told SCIENCE NEWS.

Researchers have been racing to develop a hepatitis B culturing procedure. Several other laboratories along with Essex's reported at an August meeting that they had produced the virus in culture. Essex's lab was the first to get its results in print; the work is described in the Oct. 10 CELL.

The ability to culture hepatitis B virus is also expected to speed research on the delta agent. Knowledge of the "satellite" virus, as researchers call it, was boosted last week when two laboratories described its structure, sequence and function in the Oct. 9 NATURE.

In papers from the Netherlands and a consortium of researchers from Chiron Corp. in Emeryville, Calif., the University of California at San Francisco and a Georgetown University laboratory in Rockville, Md., delta's genetic material was described as a single-stranded circle of RNA similar in size and shape to certain agents that infect plants. In addition, the U.S. group determined the agent's genetic sequence and discovered antibodies to a protein encoded by the RNA in the blood of patients with delta infections.

These new findings, says Michael Houghton of Chiron Corp., will someday enable researchers to develop a blood test for diagnosing delta infection — which currently must be diagnosed through liver biopsy — and will allow researchers to conduct experimental vaccine research.

John Taylor of the Fox Chase Cancer Center in Philadelphia, whose own description of the delta infectious agent is scheduled for publication in the PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, says the similarities with the plant infectious agents, about which a good deal is known, may shed some light on the delta agent. In addition, he says, using what is now known of delta and the hepatitis B culturing system, researchers should be able to determine how the two interact.

— J. Silberner

Collaborators Cohen, Levi-Montalcini win medical Nobel

This year's Nobel Prize in Physiology or Medicine goes to Rita Levi-Montalcini and Stanley Cohen, the Karolinska Institute announced this week. The two researchers, who collaborated on their early work, were honored for discoveries that are "of fundamental importance for our understanding of the mechanisms which regulate cell and organ growth." Cohen and Levi-Montalcini will share the prize's approximately $290,000.

Levi-Montalcini began her research in her native Italy in the late 1930s. Forced to work out of a makeshift bedroom laboratory because of anti-Semitic laws that resulted in her dismissal from the University of Turin, she studied chicken eggs smuggled to her by friends. After the war and time spent treating refugees in Italy, she emigrated in 1947 to Washington University in St. Louis to join a laboratory run by Viktor Hamburger.

There, she showed that mouse tumors transplanted into chick embryos induced nerve growth, even without direct contact with the embryos' developing nerve tissue. The tumors' nerve growth factor (NGF) was so potent that minute quantities — one-billionth of a gram per milliliter of culture solution — induced nerve growth within 30 seconds.

After Cohen joined Hamburger's laboratory in 1952, he purified the factor, a protein, and determined the sequence of its amino acids. Cohen continued his work with a second growth factor he accidentally encountered while using crude extracts of NGF-containing mouse salivary glands. This factor, later termed epidermal growth factor (EGF), stimulates many different processes in the body, including proliferation of cells in the skin, cornea, immune system, liver, blood cells, thyroid, ovaries and pituitary gland. Several National Institutes of Health researchers recently showed that EGF's presence is necessary for sperm production in mice (SN: 8/30/86, p.135).

Following their seminal work, Levi-Montalcini returned to Rome to join the Institute of Cell Biology, where she now teaches; Cohen moved to Vanderbilt University in Nashville, where he is studying the mechanism by which EGF interacts with its receptor and stimulates cells. He has found that the receptor also acts as an enzyme. What intracellular proteins the enzyme acts on is something "everybody's trying to discover," he says.

The two growth factors hold great clinical promise, the Nobel committee notes. EGF has already proved its ability to enhance wound healing in animals, and clinical trials in humans have begun with recombinantly produced EGF. NGF, the committee suggests, may prove useful in enhancing repair of damaged nerves, and studying its function will add to the knowledge of errors of development, senile dementia, wound healing, muscular dystrophy and certain tumors.

Since the discovery of EGF and NGF, several other growth factors have been discovered. Levi-Montalcini and Cohen, the Nobel committee notes, "have created a scientific school with an increasing number of followers."

The two researchers recently shared the Albert Lasker Basic Medical Research Award (SN: 9/27/86, p.197). This marks the third year in a row in which recipients of one of the two prestigious medical awards also won the other.

— J. Silberner