

# NEWSRELEASE



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CORPORATION

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## CHIRON CLONES HEPATITIS NON-A, NON-B VIRUS WHICH MAY ALLOW SCREENING FOR PREVIOUSLY UNDETECTABLE DISEASE

WASHINGTON, D.C., May 10, 1988 -- Scientists at Chiron Corporation (NASDAQ:CHIR) have identified, cloned and expressed proteins from a long-sought blood-borne hepatitis non-A, non-B virus, and have developed a prototype immunoassay that may lead to a screening test for hepatitis non-A, non-B antibodies, the company announced here today.

The research was carried out in part under the auspices of The Biocine Company™, a joint venture of Chiron and Ciba-Geigy, which is responsible for researching, developing, manufacturing and marketing any vaccine, and with support from its partner Ortho Diagnostic Systems, a subsidiary of Johnson & Johnson, which will market any immuno-diagnostic products which result.

Despite widespread, intensive research efforts dating back more than 15 years, neither the virus nor the antibodies from the virus have been identified, and thus this serious disease has been transmitted partially through blood transfusions. Now that the virus has been discovered, work on a vaccine can begin.

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Blood-borne hepatitis non-A, non-B is another major type of hepatitis, different from hepatitis A and hepatitis B, the viruses of which have previously been identified. Blood-borne hepatitis non-A, non-B is transmitted through contaminated blood or blood products, via blood transfusions or other close personal contact.

In the acute form, from which patients may fully recover, symptoms can range from mild to severe jaundice, fever, nausea, loss of appetite and fatigue. In the chronic form, infected patients at high frequency develop chronic liver disease, including cirrhosis.

Prior to 1986, according to National Institutes of Health estimates, up to 10 percent of the three million patients receiving transfusions annually in the U.S. were infected by blood-borne hepatitis non-A, non-B. Some 50 percent of those infected developed chronic hepatitis, and 20 percent of those, or 30,000 people each year, eventually developed cirrhosis of the liver.

Blood banks in the U.S. currently screen for hepatitis B with a specific immunoassay. In 1987, blood banks began screening to eliminate a portion of non-A, non-B infected blood using two tests that substitute for actual identification of the virus. The first test screens for hepatitis B anticore antibodies to identify people at high risk; the second, called ALT, indicates liver damage.

This surrogate testing has reduced the incidence of post-transfusion hepatitis non-A, non-B by 40 to 60 percent. Still, 90 to 95 percent of transfusion-related hepatitis is caused by the blood-borne non-A, non-B virus and almost 1,500 people each week receiving transfusions in the U.S. contract chronic hepatitis non-A, non-B.

"Solving blood-borne hepatitis non-A, non-B has been one of the toughest challenges in the world of infectious disease," said Edward E. Penhoet, president and chief executive officer at Chiron. "Our discovery and subsequent work is a significant first step that we expect will have major impact for the millions of people receiving transfusions each year. Longer term, we believe our discovery will lead to a vaccine and therapeutics for this serious disease."

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Chiron estimates that the hepatitis non-A, non-B testing market in the U.S. is approximately \$85 million annually. Pre-clinical trials of an antibody test are underway. The company expects an Investigative New Drug (IND) application for its immunoassay kit to be filed with the U.S. Food and Drug Administration later this year.

Chiron has begun manufacturing scale-up of the viral protein through yeast fermentation in its manufacturing facility in Emeryville, California, where the company is headquartered.

When approved and available, blood banks will be able to apply a relatively simple assay procedure, using a plate coated with the virus protein, to screen for blood infected with hepatitis non-A, non-B virus. Antibodies from the infected blood bind to the plate, which is then rinsed -- if the antibodies are present, a second coating of indicator antibodies will signal a color. The immunoassay kit will be marketed by Ortho Diagnostic Systems, Chiron's partner in immuno-diagnostic products.

A team of scientists consisting of Michael Houghton, Ph.D., Qui-Lim Choo, Ph.D., George Kuo, Ph.D. and Amy Weiner, Ph.D., cloned the virus in 1987. They collaborated with Daniel Bradley, Ph.D., of the Center for Disease Control in Atlanta, who supplied non-A, non-B infected materials. Later in 1987, the team expressed the virus protein and confirmed that antibodies for the virus are present in the blood of individuals with blood-borne hepatitis non-A, non-B. The extremely small numbers of the virus present in infected patients prolonged the discovery process, particularly compared to other hepatitis viruses and the AIDS virus, all of which are present in larger numbers and were discovered relatively faster.

Houghton, the project leader, presented the research results at a scientific seminar May 9 at the University of California at San Francisco. The process of discovery involved screening millions of clones to find a single viral clone.

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"The discovery of the blood-borne hepatitis non-A, non-B virus reinforces Chiron's leadership in the overall field of hepatitis," said Penhoet. "It follows similar breakthroughs in hepatitis A, hepatitis B and hepatitis D or delta, and demonstrates our scientific prominence in a critical area of infectious disease."

In July 1986, the FDA approved marketing of a vaccine for hepatitis B that uses recombinant DNA technology developed by Chiron. Chiron licensed the basic technology to Merck & Co., Inc., which manufactures and markets the product as Recombivax HB®.

Chiron scientists have also cloned and expressed the proteins that form the hepatitis A virus shell, and research is underway to develop a vaccine. Houghton's team previously discovered the structure of the hepatitis D virus, a type of hepatitis virus occurring as a satellite to hepatitis B which increases the severity of the disease.

The discovery of the blood-borne hepatitis non-A, non-B virus was part of a major research effort in virology underway at Chiron and its joint venture, The Biocine Company, to research, develop, manufacture and market a new generation of synthetic vaccines. Subsequent vaccines will be marketed by The Biocine Company, which combines the recombinant DNA technology of Chiron with Ciba-Geigy's proprietary technology in adjuvants, which enhance the immune response to vaccines.

Additional applications of the research may include: confirmed clinical diagnosis of patients with symptoms of blood-borne hepatitis non-A, non-B and monitoring during therapy; investigation of vaccines; and investigation of therapeutics to control chronic carriers.

Currently, cases of blood-borne hepatitis non-A, non-B are diagnosed by exclusion -- that is, people who have hepatitis symptoms but who do not test positively for other viruses such as hepatitis A or B are assumed to have hepatitis non-A, non-B. Also, the virus can be present in people who have never had transfusions -- for example, of the blood donors carrying the virus, an estimated 90 percent have never been transfused. Thus the virus can be transmitted efficiently other than via transfusion, presumably through blood transmission or close personal contact.

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"The discovery and cloning of a blood-borne hepatitis non-A, non-B virus is clearly a scientific achievement of great importance," said William J. Rutter, Ph.D., chairman of Chiron. "It affirms again the promise of recombinant DNA technology in developing solutions to the world's major health problems. We intend to complete and publish the research results in the near future and share the knowledge with our scientific colleagues."

Chiron Corporation develops therapeutic and diagnostic products for the health care market using recombinant DNA and other techniques of modern biology. The company emphasizes four areas of product development: vaccines, therapeutic hormones and growth factors, therapeutic enzymes and related diagnostics. Ciba-Geigy is a major international pharmaceutical company. Johnson & Johnson is a major international pharmaceutical and health care products company.

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