Scientists shed light on mystery surrounding hepatitis B virus: Discovery is decades in the making

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(Medical Xpress)—Scientists from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), part of the National Institutes of Health, and the University of Oxford, U.K., have shed light on a long-standing enigma about the structure of a protein related to the Hepatitis B virus. Their findings, reported in *Structure*, could lead to new therapeutic strategies for chronic liver disease.

World-wide, some 350 million people are chronically infected with Hepatitis B Virus (HBV), of whom 620,000 die each year from HBV-related liver disease. Like any other pathogen, HBV expresses protein antigens that trigger the body's immune system to defend itself. A relatively small and simple virus, HBV has three major clinical antigens that elicit an immune response: the surface antigen (which is also used safely and effectively to vaccinate individuals against HBV), the core antigen (HBcAg), and the e-antigen (HBeAg).

The HBV core antigen and the e-antigen are basically two versions of the same protein, but the core antigen is important for virus production, while the e-antigen is not. The e-antigen plays a role in establishing immune tolerance and chronic HBV infection. In addition, the core antigen assembles into the shell (capsid) that houses the genetic material of the virus, while the e-antigen is secreted into the bloodstream in an unassembled form. The relationship between the e-antigen and the core antigen has been a mystery for the past three decades.

In the new study, the NIH scientists developed a unique antibody that binds to and forms a stable complex with e-antigen. This complex was found to form well-diffracting crystals whose analysis allowed the structure of the complex to be determined. They discovered that the e-antigen subunit has essentially the same fold as the core antigen subunit, but that it pairs into dimers (two associated subunits) in an entirely different way, with a relative rotation of 140 degrees between the subunits. The rotation obviates the protein's ability to assemble and transforms its antigenic character. This switch represents a novel mechanism for regulating a protein's structure and function.

Understanding the e-antigen structure provides a framework upon which future studies can build to fully elucidate its role in HBV persistence and possibly a way to prevent the establishment of chronic liver infections. For more information, visit www.niams.nih.gov/News_and_Eve … 2013/hepatitis_b.asp.

Provided by National Institutes of Health

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