Researchers uncover structure of new protein implicated in diabetes

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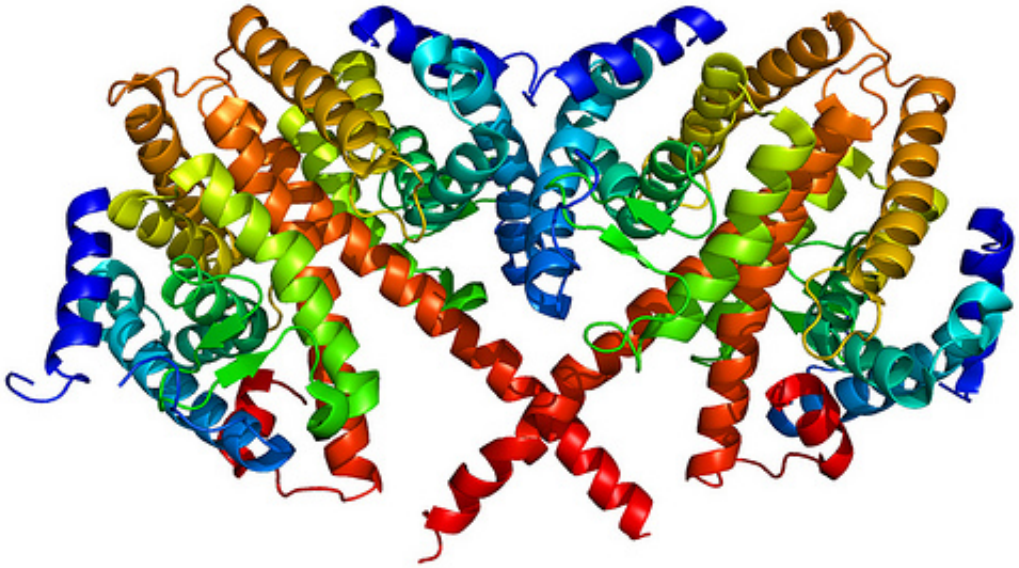

A look at the structure of the HNF-4A protein, which plays a critical role by binding to specific DNA sequences and regulating the production of a number of key proteins for normal cellular processes.

(Phys.org) —Scientists at the U.S. Department of Energy's Argonne National Laboratory, in collaboration with researchers from the Sanford-Burnham Medical Research Institute in Orlando, Fla., recently determined and analyzed the three-dimensional structure of a protein found in the nuclei of liver and pancreatic cells. The protein, called hepatocyte nuclear factor 4α (HNF-4α), plays a critical role by binding

to specific DNA sequences and regulating the production of a number of key proteins for normal cellular processes. Some of its mutations have been linked to maturity-onset diabetes, kidney failure and metabolic syndrome.

Structural biologist Youngchang Kim of Argonne's Structural Biology Center (SBC) used the high-intensity synchrotron X-rays provided by the laboratory's Advanced Photon Source (APS) to investigate the three-dimensional structure of this nuclear receptor protein in the multi-component complex.

The researchers discovered that some of the most common mutations that cause this diabetes are the ones interfering with DNA binding, and they occur in domains associated with the receptor's ability to bind different molecules. To make this discovery, they needed to rely on X-ray diffraction data obtained at the SBC beamline at the APS, which creates some of the most brilliant X-rays in the world.

While a cure for this diabetes is likely many years off, studies of the basic cellular and molecular mechanisms adopted by diseases to ravage the body are the first step to producing new therapies.

"The goal of structural biology is to work from the ground up – enhancing our understanding of the most intricate processes will, we hope, one day lead to much better answers to the problem of diabetes," Kim said.

Provided by Argonne National Laboratory