Cornell University
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Researchers reveal key human protein's structure, promising new discoveries for leukemia, AIDS and cellular calcium release

By Krishna Ramanujan

ITHACA, N.Y. -- Cornell University researchers have discovered the 3-D crystal structure of a protein, human CD38, which may lead to important discoveries about how cells release calcium -- a mineral used in almost every cellular process. The findings also may offer insights into mechanisms involved in certain diseases, ranging from leukemia to diabetes and HIV-AIDS.

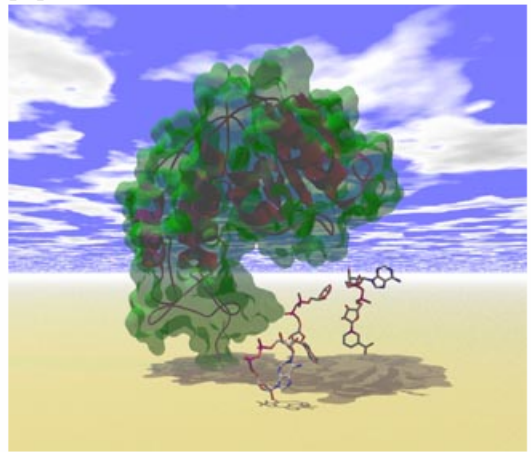
Levels of the protein climb, for reasons unknown, when people fall ill, making human CD38 a marker for these diseases.

As one example, researchers have shown that CD38 interrupts an interaction between the AIDS virus and its point of entry into cells -- a protein receptor called CD4. By looking at CD38's 3-D structure, the Cornell researchers identified a peptide, an organic compound composed of amino acids, that they believe may play a role in interrupting the interface between CD4 and HIV-AIDS.

The findings, published in the journal Structure (Vol. 13, Sept. 2005), mark a major step toward designing drugs that could inhibit processes related to certain diseases. Knowing the protein's structure also opens the door to understanding CD38's many functions related to key biological processes about which researchers know very little.

"For example, the mechanism of how a cell mediates calcium release is largely unknown," said the paper's senior author, Quan Hao, director of the Macromolecular Diffraction Facility (MacCHESS), the biomedical research arm of the Cornell High Energy Synchrotron Source (CHESS). "So this is a very fundamental question for biologists."

It turns out that CD38 helps produce at least two calcium messenger molecules, each of which then opens channels for the release of calcium from specific stores, or reservoirs, within cell organelles.



Qun Liu and Quan Hao. Copyright Elsevier Ltd.

This artistic rendering of the molecular structure of human CD38 appears on the cover of this month's issue of the journal Structure.

High intensity X-rays made it possible to pass photons through a protein crystal to reveal its structure. Cornell's synchrotron produces beams of X-rays millions of times more intense than conventional X-ray generators allow. The very intense beams were necessary to determine the atomic structure of CD38. The research group, which includes researchers from the University of Minnesota, also developed new calculations that allowed them to extract the protein's entire structure from the X-ray images.

By revealing CD38's detailed structure, scientists can now begin to examine how the protein's form influences its molecular functions.

"People have been struggling with this for a long time, and we have finally solved it," said Hao.

The National Institutes of Health, which supports MacCHESS, also funded this research. The paper's other lead authors include MacCHESS graduate student Qun Liu and researcher support specialist Irina Kriksunov.