

Vaccines for HIV: A new design strategy

San Diego, Calif. – HIV has eluded vaccine-makers for thirty years, in part due to the virus' extreme ability to mutate. Physical scientists and clinical virologists from the Massachusetts Institute of Technology (MIT) and the Ragon Institute in Cambridge, Mass., have identified a promising strategy for vaccine design using a mathematical technique that has also been used in problems related to quantum physics, as well as in analyses of stock market price fluctuations and studies of enzyme sequences. The team, led by Arup Chakraborty of MIT and Bruce Walker of the Ragon Institute, gave an update on its work at the Biophysical Society 56th Annual Meeting, held Feb. 25-29 in San Diego, Calif.

Vaccines prime the immune system to target molecular signatures associated with a particular pathogen. But HIV's ability to mutate has made it difficult to identify reliable vaccine targets. In their search for a new type of target, the team from the Ragon Institute did not focus on individual amino acids. Instead, the researchers sought to identify independently evolving groups of amino acids where, within each group, amino acids mutate in tandem (meaning that they rely on one another to maintain the viability of the virus). In particular, they looked for groups of amino acids within which combinations of mutations would have a greater chance of making the virus unviable. By staging a multi-pronged attack against these regions of HIV, the researchers reasoned, they might be able to trap the virus between two bad choices: be destroyed by the immune system, or mutate and destroy itself.

With a mathematical tool called random matrix theory, the team searched for high-order evolutionary constraints in the so-called Gag region of HIV. The researchers were looking for collectively co-evolving groups of amino acids with a high number of negative correlations (meaning multiple mutations would destroy the virus) and a low number of positive correlations (meaning the virus could survive multiple mutations). They found this combination in a region, which they call Gag sector 3, that is involved in stabilizing the protein shell of the virus: too many mutations here, and the virus' structure would collapse.

Interestingly, when the team studied HIV-infected individuals whose bodies are naturally able to fend off the virus' attacks – so-called “elite controllers” – they found that these individuals' immune systems preferentially targeted Gag sector 3 over other proteins.

At the moment, the study authors are working to extend their methods to HIV proteins beyond Gag. The team is also developing elements of the active components of a vaccine that would prime the immune system to selectively target Gag sector 3 proteins. They expect to begin testing in animal models soon.

The presentation, “Analysis of collective coevolution in HIV proteins suggests strategies for rational vaccine design,” was presented by Dr. Chakraborty's graduate student Karthik Shekhar.

ABSTRACT: <http://tinyurl.com/6sz7kuf>

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This news release was prepared for the Biophysical Society (BPS) by the American Institute of Physics (AIP).

ABOUT THE 2012 ANNUAL MEETING

Each year, the Biophysical Society Annual Meeting brings together over 6,000 research scientists in the multidisciplinary fields representing biophysics. With more than 4,000 poster presentations, over 200 exhibits, and more than 20 symposia, the BPS Annual Meeting is the largest meeting of biophysicists in the world. Despite its size, the meeting retains its small-meeting flavor through its subgroup meetings, platform sessions, social activities, and committee programs.

The 56th Annual Meeting will be held at the San Diego Convention Center (111 W. Harbor Drive, San Diego, CA 92101), located three miles from the San Diego International Airport and less than one mile from the Amtrak station. The San Diego Trolley has two stops directly in front of the Center at Harbor Drive/First Avenue and Harbor Drive/Fifth Avenue.

QUICK LINKS

Meeting Home Page:

<http://www.biophysics.org/2012meeting/Main/tabid/2386/Default.aspx>

Program Abstracts and Itinerary Planner:

<http://www.abstractsonline.com/plan/start.aspx?mkey=%7B5B4BAD87%2D5B6D%2D4994%2D84CE%2DB3B13E2AEAA3%7D>

ABOUT BPS

The Biophysical Society (BPS), founded in 1956, is a professional scientific society established to encourage development and dissemination of knowledge in biophysics. The Society promotes growth in this expanding field through its annual meeting, monthly journal, and committee and outreach activities. Its 9000 members are located throughout the U.S. and the world, where they teach and conduct research in colleges, universities, laboratories, government agencies, and industry. For more information on the Society or the 2012 Annual Meeting, visit www.biophysics.org.

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