

Newsletter

College of Physical and Mathematical Sciences

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BYU-Johns Hopkins Team Gets Inside a Long-suspected HIV Hideout in Humans

Scientists have broken inside a cell long suspected of harboring HIV during drug treatment and determined it is indeed a reservoir of the virus in humans, where it remains highly infectious.

Researchers at Brigham Young University and Johns Hopkins School of Medicine have discovered the genetic nature of HIV trapped by follicular dendritic cells, also called FDCs, which are located throughout the body in specialized sites known as lymphoid tissues.

Even during drug treatment, HIV trapped on the surface of FDCs remains highly infectious and genetically diverse. The study, funded by the National Institutes of Health and the American Foundation for AIDS Research, will appear in the June issue of the *Journal of Virology*.

“One of the biggest obstacles in treating patients with HIV is the establishment of these reservoirs that resist treatment,” said Greg Burton, a BYU biochemistry professor and principal investigator on the study. “The ability to understand the virus in these reservoirs, and to characterize the reservoir itself, provides information with which we can begin to try to devise strategies that target the virus in these reservoirs.”

Two other types of cells, macrophages and the latently infected CD4+ T cell, have previously been shown to be reservoirs of HIV. With the BYU-Johns Hopkins study, FDCs conclusively join the list.

FDCs act as bank vaults storing material necessary to maintain the immune system’s armies of antibodies. If the ranks of a particular antibody dwindle, FDCs release proteins that trigger an immune response boosting levels of specific antibodies.

The FDCs’ vault mechanism works so well that trapped HIV particles remain out of reach of drugs flowing through the blood stream, contributing to persistent infection. Medical researchers also found it challenging to break inside to investigate whether FDCs harbor infectious forms of the virus.

“This is a rare cell, and its long arms tend to grab onto the tissues in which it is found,” Burton said. “So when you try to get them to release those arms so we can separate the different cells, they don’t like to do that and the cell can get destroyed in the process.”

Researchers at Johns Hopkins teamed up with Burton to plot a way to open the vault from samples of HIV patients. Suzanne Gartner, an HIV virologist at Hopkins, says she and Burton “hit it off” instantly in 1995 based on their shared interest in FDCs’ possible role.

Their method of getting inside involves gently digesting tissue with enzymes, then separating FDCs with a cell sorter and specific antibodies that react with FDCs. As predicted, the team found infectious HIV trapped on the surface of FDCs. The next step was figuring out whether FDCs were stocked with the virus upon infection and if they continued to acquire samples of the virus over time.

The genetic makeup of HIV changes as it multiplies inside the body, which is evident when comparing blood samples of a patient receiving treatment and one who is not. Untreated, the virus is free to roam and sees more genetic variations. When treated, the virus does not replicate as often and fewer mutations occur.

Important Dates & Events in the College

January 2009

Annual Awards Banquet
January 30th 2009, 6:00 PM
BYU Wilkinson Center Ballroom

Mentored Research Opportunities Double in the BYU Computer Science Department

In the last several years, donations from outside sources, comprising generous friends, alumni, and industrial partners, have allowed the BYU Computer Science Department to experience unprecedented growth in mentored research. From the 2006-2007 academic year to the 2007-2008 academic year alone, the number of mentored research positions made possible by outside sources doubled from 30 to 61. The expansion of mentored learning reflects the department's goal to fulfill former-LDS Church President Gordon B. Hinckley's hope that "very soon every student will have a unique BYU mentoring opportunity that will increase both the rate and depth of their learning."

The opportunities to participate in mentored research in the Computer Science Department have opened up a variety of possibilities for students, undergraduates and graduates alike. The funds provided allow students to work in flexible, on-campus jobs, earning money to provide for themselves and their growing families, while still remaining focused on their education. Furthermore, research experiences deepen the students' educations by allowing them to forge meaningful relationships with faculty mentors and familiarize themselves with the latest research methods and cutting-edge technology. Through mentored research, even undergraduate students have had the opportunity to publish and present papers in major journals and conferences.

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Using a pair of supercomputer clusters at BYU, biologist Keith Crandall constructed the viruses' family tree for three patients from Johns Hopkins. Blood samples taken at different points in time gave reference points to establish a time frame for different versions of the virus recovered from FDCs.

"It turned out the data matched the hypothesis that one, the FDC is a reservoir, and two, it's actually acquiring genetic variance throughout the course of mutation," Crandall said. "We saw the accumulation of drug-resistant mutation, and saw exceptionally high genetic variation. This makes treatment extremely difficult."

BYU graduate Trever Burgon worked on this part of the study, sequencing individual HIV genomes from FDCs to compare with samples from other tissues. Burgon, now seeking a Ph.D. in microbiology and immunology at Stanford School of Medicine, said his research experience as a BYU undergraduate yielded acceptances to every graduate program he applied.

The BYU-Johns Hopkins team is currently seeking another NIH grant to explore how to attack the viral reservoir in FDCs.

"As we learn about what this virus is doing with FDCs and our immune system, it opens up the door to understanding what happens with a lot of other diseases," Burton said.

Students Pass ASQ Certified Quality Process Analyst Exam

American Society for Quality is the leading authority on career-boosting certifications for quality professionals, with more than 60 years of experience. An ASQ certification demonstrates an individual's dedication to quality. This fall semester in the Statistics 462 class (Quality Control and Industrial Statistics), nine senior students prepared for the ASQ Certified Quality Process Analyst exam. This is one of the only two ASQ certifications that does not require job experience; it does require a college degree. All nine students passed the exam and will be awarded their certificate at the time of graduation later this year. This certificate will give the graduates a definite advantage in the job market. The students passing the exam this year were: Mindy Browning, Michael Hammer, Lindsay Hunt, Johnny Ma, Scott Merrell, Hanna Westover, Cameron Willden, Phillip Witt and Roman Zakharov.



“Statistics Professor Shane Reese Co-Authors NSF Report: *Test and Evaluation of Biological Standoff Detection Systems*”

A biological warfare agent (BWA) is a microorganism, or a toxin derived from a living organism, that causes disease in humans, plants, or animals or that causes the deterioration of material. The effectiveness of a BWA is greatly reduced if the attack is detected in time for the target population to take appropriate defensive measures. Therefore, the ability to detect a BWA, in particular to detect it before the target population is exposed, will be a valuable asset to defense against biological attacks. The ideal detection system will have quick response and be able to detect a threat plume at a distance from the target population. The development of reliable biological standoff detection systems, therefore, is a key goal.

However, testing biological standoff detection systems is difficult because open-air field tests with BWAs are not permitted under international conventions and because the wide variety of environments in which detectors might be used may affect their performance. This book explores the question of how to determine whether or not a biological standoff detection system fulfills its mission reliably if we cannot conduct open-air field tests with live BWA.



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