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Information Science and Technology Seminar Series

Bette Korber
Los Alamos National Laboratory

"Transforming Under Pressure: A Evolutionary Tale of Two Pathogens, HIV and M. tuberculosis"

Wednesday, March 7, 2012
3:00 - 4:00 PM
TA-3, Bldg. 1690, Room 102 (CNLS Conference Room)

Abstract: The first half of this talk will describe a strategy for vaccine design in the context of a highly variable pathogen. HIV evolves rapidly, and mutations that have repeatedly arisen in the circulating population are likely to reflect common patterns of immune evasion during natural infections, selected to escape the assault by the human immune response while retaining fitness. An effective vaccine response should be able to block HIV infection by most of the circulating forms of the virus. The goal of our new design is to maximize the cross-reactive potential of antibody vaccine responses at the population level. We build on principles we previously worked out for a T cell vaccine design, but we have adapted the methods to antibody vaccines by optimizing population diversity coverage relative to a 3-dimensional folded protein. To enable this, we based our vaccine design on a newly resolved structural model of the HIV Envelope trimer, provided by Dr. Joe Sodroski at Harvard. We have developed a vaccine design that may have the potential to address HIV diversity at a global level.

The second part of the talk will describe the evolution of a drug resistant form of *M. tuberculosis*. In the wake of encouraging reductions in TB deaths and incidence resulting from the WHO-coordinated global effort to treat TB, comes a disturbing increase in the incidence drug resistant TB. Rifampicin (Rif) is one of the most effective frontline TB therapies, and TB that acquires Rif resistance is generally less fit, and so thought to be less transmissible. Working with teams in S. Korea and at the NIH, lead by Dr. Clif Barry, we have helped to uncover patterns of compensatory mutations that can restore fitness to Rifampicin resistance strains. We found that Rif resistant forms accompanied by compensatory mutations are actively being transmitted. Using structural modeling we have identified a potential mechanism for this compensatory action.

Biography: Bette Korber is a Laboratory Fellow at Los Alamos National Laboratory and an external professor at the Santa Fe Institute. She obtained a Ph.D. in Immunology from Caltech in 1988, and was a postdoctoral fellow in retrovirology at Harvard before joining the Theoretical Biology group at Los Alamos in 1990. She has received an E. O. Lawrence award from the DOE in 2004, was an Elizabeth Glaser Scientist of the Pediatric AIDS Foundation. She has been the PI on the HIV sequence and immunology database project since 1996. She studies the impact of the human immune response on HIV evolution and HIV transmission and the biology of acute infection, with the motivating purpose of developing rational vaccine designs for variable pathogens. She works with an interdisciplinary team providing bioinformatics, theoretical, and statistical support, in collaborative efforts with researchers from around the globe. She has co-authored over 215 scientific papers.

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