The Center for Theoretical Biological Physics

PRESENTS
Seminar Speaker

Dr. Shenshen Wang

Massachusetts Institute of Technology

"Guiding Affinity Maturation to Generate Broadly Neutralizing Antibodies"

Tuesday, March 25, 2014

12:30 - 1:30 PM

BRC, 10th Floor, Room 1060 A/B

Abstract:

The immune system comprises an intricate collection of cells and molecules that enables defense against pathogenic agents. Its workings present a rich source of physical problems that impact human health. One intriguing example is the process of affinity maturation (AM) through which an antibody (Ab)—a component of the host immune system—evolves to more efficiently bind an antigen (Ag)—a unique part of a foreign pathogen such as a virus. Sufficiently strong binding to the Ag enables recognition and neutralization. I will focus on HIV-1, the causative agent of AIDS. The high mutability of this virus and its ability to evade immune recognition pose major barriers to the quest for a vaccine. In recent years, researchers have isolated from patients families of broadly neutralizing Abs (bNAbs) that can bind many Ag variants. But the problem is upon natural infection these bNAbs arise very late and in very low concentrations. So our query is, can we induce bNAbs efficiently through vaccination strategies? This requires a thorough understanding of AM against mutating Ags and multiple Ags administered in different order and combination. During AM, Ab-encoding cells undergo cycles of mutation and selection, a process reminiscent of Darwinian evolution yet occurring in a short time (weeks to months). We develop an agent-based computational model of AM against multiple varying Ags. This dynamic model not only reveals significant stochastic effects associated with the relatively small and highly dynamic population size, it also uncovers the markedly distinct maturation outcomes if designed Ag variants are presented in different temporal procedures. We propose candidate vaccination protocols that could lead to efficient induction of bNAbs.