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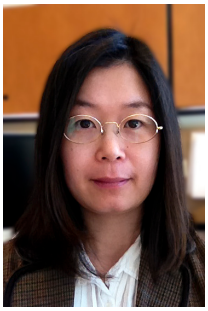
BIOMATH

Department of Biomathematics Seminar Series:
Frontiers in Systems and Integrative Biology

Theoretical Approaches towards HIV Vaccine Designs and Incidence Assessment



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13-105 Center for the Health Sciences (CHS)

ABSTRACT:

The world is facing a serious global pandemic of HIV/AIDS, with more than 35 million people infected. Controlling and eventually eradicating this unprecedented pandemic will require a better surveillance tool and improved vaccine design. An effective HIV vaccine must induce immune responses that recognize as many HIV strains as possible in order to better protect against the rapidly-mutating virus. The surface morphology of peptide-MHC (pMHC) complexes is one of the key factors controlling the breadth of reactive T cell population. Here we present our computational design for predicting pMHC surface morphology, which assembles homology-based models and all-atom molecular dynamics simulations. Our method shows high precision, with root mean square deviation=1.58 Å over a 17 pMHC test set. A blind test is performed on three peptides with undetermined structure, and high resolution X-ray crystallography data has corroborated our predictions. Once a functional HIV vaccine is implemented, monitoring HIV incidence, the number of newly infected people, is necessary to evaluate its efficacy. There is no universal standard for assays measuring HIV incidence since conventional approaches rely on variable and inaccurate HIV-specific antibody responses. Our group has focused on developing HIV genomic incidence assays utilizing signatures embedded in an individual's HIV sequence population. Since HIV sequences are evolving throughout the course of infection, we can quantify the amount of evolution as a fingerprint of infection duration. We have produced over 18,000 HIV envelope gene segments by combining high-throughput next-generation sequencing and a signal-masking bioinformatics pipeline. Two biomarkers we created successfully related sequence similarity to the infection stage, distinguishing between recent and chronic infections with over 95% accuracy. Furthermore, mathematical modeling has allowed us to extend our accuracy in determining infection duration for recently infected individuals. Taken together, analytical approaches are becoming indispensable components to medical research.

Host: Tom Chou, Ph.D.

To receive e-mail seminar notices, contact David Tomita (dtomita@biomath.ucla.edu)