



IGEM Seminar



DR. CHIRAG KRISHNA

Wednesday, August 14th at Noon, SERC 604

Molecular evolution of the HLA system and its influence on disease risk

ABSTRACT

Antigen presentation by the human leukocyte antigen class I (HLA-I) and II (HLA-II) loci and subsequent recognition by the T cell receptor comprise the foundation of the adaptive immune response. Overdominant selection has led to the evolution of thousands of HLA allotypes with variable peptide binding specificities, protecting individuals against a wide range of parasites. This 'heterozygote advantage' has been demonstrated against infections in mice and humans, though its influence on cancer risk—mediated in part by HLA presentation of smoking-induced neoantigens—has been less explored.

In the first part of this seminar, I will present recent work from our group demonstrating that heterozygosity at the HLA-II loci is associated with reduced risk of lung cancer. We combine epidemiological studies of HLA heterozygosity in population-scale biobanks with genomic studies of antigen presentation and the lung tumor microenvironment to show that genetic variation in immunosurveillance is a hallmark of cancer susceptibility.

In the second part of this seminar, I will present new ideas from our group focused on understanding the evolution of the HLA system over millions of years. Specifically, we aim to connect phylogenetic analysis of HLA alleles to their molecular properties and associated disease risk. These analyses may address long-standing questions in HLA evolution and help interpret associations between HLA alleles and various diseases.

ABOUT

Dr. Krishna is a Senior Computational Geneticist with Pfizer Systems Immunology in Cambridge, MA.



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