

**You are cordially invited to a Computational Genomics
Seminar**

Dr. Tzachi Hagai

School of Molecular Cell Biology & Biotechnology, Life Sciences, TAU

*"Trapped between pathogens and autoimmunity:
The evolution of the mammalian immune system"*

Wednesday December 18 at 11:15

**Check Point building, room 420, School of Computer Science,
TAU**

Abstract: The immune system is under constant pressure from pathogens to evolve and mount a sufficiently strong response. At the same time, an overresponsive immune system can lead to tissue damage and autoimmunity. How these conflicting demands have shaped human immunity is not well understood. Here, we focus on the innate immune response – a cell-intrinsic expression program that acts as the first line of defence against pathogens. We characterise this program's transcriptional divergence between species and expression variability across cells. Using bulk and single-cell transcriptomics in fibroblasts and mononuclear phagocytes from different mammalian species, challenged with viral and bacterial stimuli, we reveal a striking architecture of the innate immune response. Genes involved in response regulation, such as transcription factors and kinases, are conserved between species and display low variability in gene expression across cells. Furthermore, the proteins products of these genes are targeted by viruses, suggesting that regulatory constraints imposed on conserved host genes are exploited by viruses to subvert the host. In contrast, rapidly diverging genes, including cytokines and chemokines, vary across cells, have distinct promoter structures, and tend to be depleted of interactions with viral proteins during infection. We suggest that the distinct expression patterns in different classes of immune genes, observed across species and conditions, have evolved as a mechanism for fine-tuned regulation, to achieve an effective but balanced immune response.

**Host: Prof. Ron Shamir (rshamir@tau.ac.il), School of
Computer Science**