

# SgN Immunology Seminar

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### The unique role of non-catalytic tyrosine phosphorylated receptors in immune recognition

My group studies the mechanism by which leukocytes such as T cells use cell surface receptors to recognise infected or otherwise abnormal cells. The T cell antigen receptor (TCR) plays a major role in this process by probing the surfaces of cells for the presence of 'foreign' peptides presented on MHC molecules in a peptide-MHC (pMHC) complex. A major focus of our work is understanding how the binding of TCRs to foreign pMHC leads to T cell activation. The first step in TCR signal transduction following ligand engagement is tyrosine phosphorylation of the TCR/CD3 complex, which we term triggering. We have proposed a novel mechanism of TCR triggering, termed the kinetic-segregation model. It postulates that TCR binding to pMHC segregates the TCR, and the tyrosine kinases that phosphorylate it, from tyrosine phosphatases with large extracellular domains such as CD45 and CD148.

A large number of leucocyte cell-surface receptors share key similarities with the TCR, suggesting that they signal by the same kinetic-segregation mechanism. These proteins, which comprise the largest group of leukocyte surface molecules, are termed non-catalytic tyrosine phosphorylated receptors (NTRs) or immunoreceptors. Over 100 NTRs have been described in at least 15 families. One focus of our work is to investigate whether other NTRs trigger by the kinetic-segregation mechanism.

Leukocytes express multiple NTRs, some of which are activatory, like the TCR, and some of which are inhibitory. We are investigating the mechanism by which activatory and inhibitory NTRs integrate their signals when they engage ligands. We have proposed that close-colocalizing at the cell-cell interface is critical for this signal integration, and that NTR/ligand complexes need to span similar intermembrane distances in order to colocalize.

*Host*  
Prof Laurent Renia  
Singapore  
Immunology  
Network, A\*Star

*Date*  
**Monday**  
**29 September**  
**2014**

*Time*  
11am – 12pm

*Venue*  
SgN Seminar  
Room  
Immunos Building  
Level 4  
Biopolis