NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

Talin1 sets the stage for TLR-mediated activation of dendritic cells

Date: **2 October 2020, Friday**

Time: **4pm**

Venue: **Classroom 1, SBS**

Talin critically controls integrin-dependent cell migration, but its regulatory role in skin dendritic cells (DCs) during inflammatory responses has not been investigated. Here we found that talin1 not only regulated integrin-dependent Langerhans cells (LCs) migration, but also MyD88-dependent toll-like receptor (TLR) stimulated DC activation. Talin1-deficient LCs failed to exit epidermis, resulting in reduced LC migration to skin-draining lymph nodes (sdLNs) and defective skin tolerance induction, whereas talin1-deficient dermal DCs were unexpectedly accumulated in the dermis albeit their actomyosin-dependent migratory capabilities. Talin1-deficient DCs exhibited compromised chemotaxis, NFκB activation and pro-inflammatory cytokine production. Mechanistically, talin1 was required for the formation of a TLR pre-complex with TIRAP and MyD88 via interacting with MyD88/PIP5K, and the subsequent assembly of TLR signalosome upon stimulation but was dispensable for the MyD88-independent, TLR3-induced assembly of TRIF-complex. Collectively, our data demonstrate that talin1 plays an essential role in dendritic cell (DC) maturation and activation by promoting the formation of a pre-assembled TLR–Myddosome signaling complex in steady-state DCs but not macrophages. This may also explain why DCs respond faster and more vigorously to TLR ligand binding than their closely related macrophages.

Speaker:

Su I-Hsin
Associate Professor
School of Biological Sciences
Nanyang Technological University