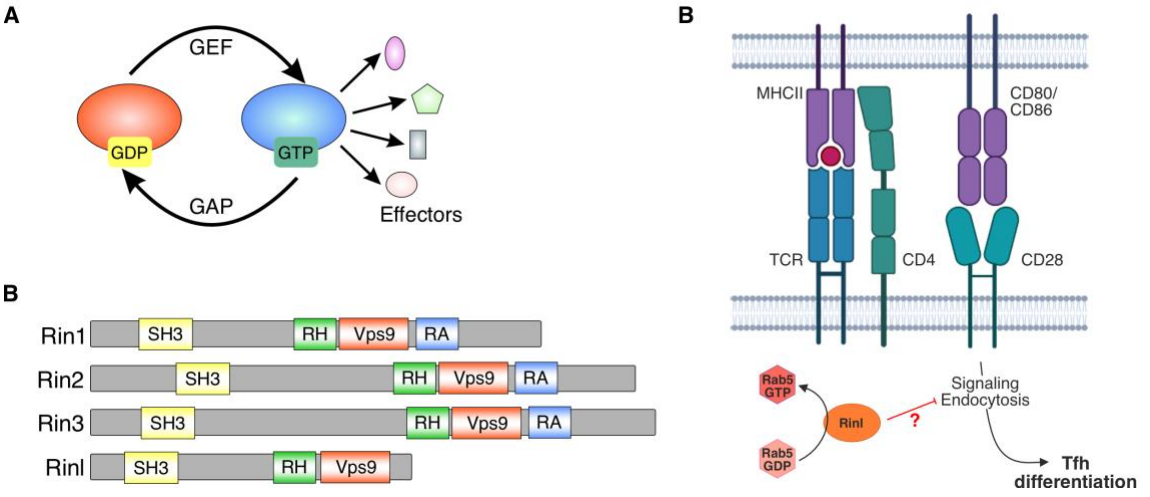
The role of Rin-like during T cell development

T helper (Th) cells are crucial for adaptive immunity, as they orchestrate tailored immune responses to invading pathogens. Th subsets differentiate from naive CD4+ T cells, some giving support to B cells for antibody production such as T follicular helper (Tfh) cells and some migrating to the site of infection to manage immune responses. Th cell differentiation is tightly linked to the initial T cell activation via the TCR and CD28 co-stimulation. In particular, the strength and quality of TCR and CD28 signaling were shown to fate naive CD4+ T cells into a particular subset. Therefore, regulators of T cell activation might affect and shape Th differentiation.
Ras and Rab interactor (Rin) proteins are a family of guanidine exchange factors (GEFs) reported as regulators of endocytotic events that show high-affinity binding properties for Rab5 family members. The Rab GTPase subfamily, with more than 70 different members, predominantly regulates membrane trafficking including endocytosis and exocytosis/secretion. Moreover, they control signaling events associated with membrane traffic and cytoskeletal regulation. Rin-like (Rinl) is the fourth member of the Rin family and was identified as an interaction partner of the muscle-specific tyrosine kinase MuSK, a mediator in neuromuscular junction formation. Rinl co-localized with Rab5a or Rab22 in actin abundant membrane reserves suggest a regulatory role in the recruitment of GTPases to the cytoskeleton. Higher fluid-phase uptake and increased EGFR endocytosis upon Rinl overexpression also foreshadow the contribution of Rinl in Rab5-mediated membrane trafficking.



Rinl a gatekeeper for Tfh differentiation

We have recently discovered that Rinl acts as negative regulator of Tfh cell differentiation. Rinl KO mice display increased numbers of Tfh cells alongside with an increase in GC B cells. In the absence of Rinl CD28 endocytosis and signal transduction in naive CD4+ T cells are affected. This suggests that Rinl controls Tfh cell differentiation by affecting signaling pathways within CD4+ T cells. Based on these findings, we aim to decipher the Rinl-dependent molecular mechanisms that control Tfh differentiation by identifying and characterizing interaction partners of Rinl.

Publications

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