Psoriasis is a chronic inflammatory skin disease and represents a significant cause of long-term morbidity and premature death. The disease affects more than 125 million people worldwide, including approximately 50,000 Singaporeans. Despite advances in the characterization of disease mechanisms, there is no curative therapy for psoriasis; hence, an effective and safe therapeutic strategy is still an unmet need.

The immunopathogenic features of psoriasis result from a complex interplay between immune cells, keratinocytes and inflammatory mediators in the lesional skin. In particular, the secretion of IL-23 and IL-12 by myeloid dendritic cells activates IL-17-producing T-cells, Th22 and Th1 cells, leading to the production of inflammatory cytokines such as IL-17, IFNγ, TNFα and IL-22. While specific involvement of the above cytokines in mediating the inflammation loop in psoriasis is recognized, molecular basis associated with abnormal accumulation of T-cells to the skin and their functional consequences in skin autoimmunity are not fully understood. The goal of this project is to characterize molecular processes involved in T-cell tissue infiltration and their functional relevance in immune response regulation in psoriasis. Specifically, the student will address the following three specific aims:-

Aim1: Analyse changes in genes/proteins/microRNAs/signalling pathways in peripheral/skin-localized T-cells associated with moderate-to-severe psoriasis. We will also perform CYTOF analysis to characterize phenotypic and functional diversity of psoriatic T-cells.

Aim2: Validate psoriasis-specific molecular signature(s) in T-cells and elucidate relevant mechanism(s) using an in vivo model system (e.g. imiquimod-induced psoriatic mice). We will knockdown selected genes identified in Aim1 and characterize their functional role(s).

Aim3: Determine T-cell tissue infiltration using the imiquimod-induced psoriasis mouse model through adoptive transfer/homing-to-the-skin-lesion versus homing-to-normal-skin experiments.
We believe, this project will provide new molecular information about the T-cells associated with psoriasis, suggest a safer therapeutic approach that will have broader implications beyond skin inflammation. The student will gain specialized training in cell culture, *in vivo* model systems, flow cytometry, high content analysis, cellular, molecular, biochemical and imaging assays. He/she will write scientific papers that will form the basis of his/her PhD thesis.

**Contact Us**

If you have questions regarding this project, please email the Principal Investigator.

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