## Table of Contents

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## Single-cell RNA sequencing analysis of irAE skin rash

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## Abstract

Immune checkpoint inhibitor (ICI) therapies, such as anti-PD1 and anti-CTLA4, have proved to be clinically effective in numerous malignant diseases due to their ability to maintain immune surveillance of tumors by overriding the mechanisms in which lymphocytes establish peripheral tolerance. However, these therapies act in a systematic manner and thus may lead to autoimmune-like side effects termed immune-related adverse events (irAEs) in many organ systems that can ultimately halt treatment or lead to death. Therefore, understanding the underlying drivers of these irAEs is imperative in ensuring the quality of life and safety of our patients on ICI. Over the last decade, single-cell RNA sequencing (scRNA-seq) technologies have been widely expanded to allow for the investigation of gene expression and surface-level protein at a single-cell level. Through scRNA-seq, we can pinpoint the cellular subtypes that may be the culprit causing these irAEs. We profile matched irAE rash, normal skin, and blood from a patient on ICI at the time of rash onset, and again at the time of rash resolution. By doing this, we hope to capture the temporal difference (rash onset vs. post-resolution) in cellular behavior and also the interplay between circulating (blood) and tissue-resident (skin) lymphocytes. In addition, we utilize a Th2/Th17 transcriptional web interface (RashX) to compare our irAE rash scRNA-seq-derived data. Using RashX, we plan to categorize the irAE rashes into these canonical skin disease categories based on their shared signatures.