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scRNA-seq transcriptomic profiling of irradiated mouse skin reveals altered cell types, pathways, and cell-cell interactions

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ABSTRACT

Objective: To investigate the substantial changes in cell types, pathways, and cell-cell interactions occurring in the irradiation-induced alopecia and dermatitis (IRIAD) mouse model and to identify potential targets for patients experiencing skin adverse reactions to radiotherapy.
Methods: Mice were irradiated at 15 Gy, targeting the head and neck region. After a 14-day interval, living cells were extracted from both wild-type (WT) mice and irradiated mice for single-cell RNA sequencing (scRNA-seq). The scRNA-seq data, retrieved from the GEO database (GSE201447), underwent stringent quality control using the Seurat (v4.3.0) R package. Cell type annotation relied on previously reported typical markers and CellMarker 2.0. Differentially expressed genes were calculated to perform gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses. Cell-cell interactions were evaluated using the Cellchat R package.
Results: The application of single-cell RNA sequencing (scRNA-seq) enabled a comprehensive characterization of the intricate cellular composition of both wild-type (WT) and irradiated mice skin. Remarkably, cells within irradiated mice skin exhibited a significant alteration in the intensity of cell-cell interactions compared to their wild-type counterparts. This change in interaction intensity was observed across various cell types, including fibroblast cells, endothelial cells, and dendritic cells. Importantly, these "interacting cells" shared common signaling pathways, notably the upregulation of the IL-17 pathway following irradiation.
Conclusions: The modification of intercellular communication induced by irradiation primarily involves fibroblast cells, endothelial cells, and various types of immune cells. This investigation provides a novel perspective on potential targets and holds promise for enhancing the clinical management of IRIAD.

1. Introduction

Irradiation-induced alopecia and dermatitis present significant challenges for cancer patients undergoing radiation therapy, leading to distressing experiences during hospitalization and a decline in overall quality of life.[1] Despite numerous clinical trials and recommendations from international experts, such as interventions like photobiomodulation therapy and the use of Mepitel film in individuals with breast cancer proposed for clinical use to prevent and manage Irradiation-Induced Alopecia and Dermatitis (IRIAD),[2] these approaches primarily offer symptomatic relief for patients. The focus of these interventions is predominantly on addressing ulcers and fibrosis[3] consequences of fractionated radiotherapy that limits the time-frame for cellular tissue repair.[4] Importantly, the specific mechanisms and potent targets for IRIAD remain elusive.

The skin, constituting the body's largest organ and accounting for approximately 16% of body weight, consists of three layers—the epidermis, dermis, and subcutaneous tissue—encompassing the entire body surface. However, the intricate nature of the skin complicates a comprehensive understanding of its specific mechanisms. Single-cell

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