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TCR-agnostic identification of tumor-specific T cells for cancer diagnostics and therapy

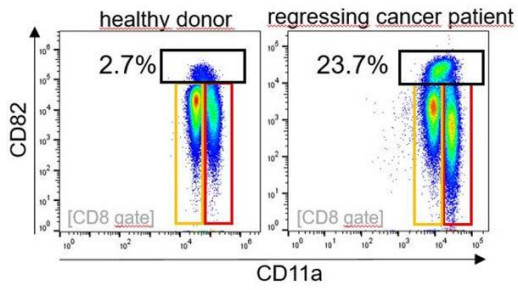
Keywords: T cells, tumor specificity, CD8+, CD82, CD11a, CD244, FACS, PBMC, adoptive cell transfer

INVENTION NOVELTY

Innovative cancer treatments utilizing immune checkpoint inhibitors demonstrated a remarkable potency of tumor eradication by tumor-specific CD8 T cells. Due to the pharmaceutical abrogation of the immune tolerance of the cancerous tissue, the immune system regains the capability to target the abnormal cells and to activate cytotoxic T cells. However, with state-of-the-art methods cell therapy by adoptive transfer of polyclonal and unmodified tumor-specific T cells is not clinically feasible. The introduced T-Lymphocyte marker proteins enable the rapid identification of T cells with specificity towards mutation- and/or tumor-related cell abnormalities according to the identified phenotype. The TCR-independent identification of cancer-targeting T cells does not require any prior knowledge about the TCR sequence, antigen composition or tumor entity. Thus, the method has great potential to be used for isolating the entire pool of mutation related T cells of an individual for diagnostic and therapeutic purposes.

VALUE PROPOSITION

The TCR-independent identification of mutation- and/or tumor specific T cell offers the possibility to selectively monitor the immune response of a patient against malignant tissue alterations. The marker combinations can be utilized in a companion diagnostics approach to determine the efficacy of a cancer treatment after a therapeutic intervention. Furthermore, the invention has the advantage to isolate mutation- and/or tumor specific T cells from peripheral blood mononuclear cells (PBMCs) just within hours. Subsequently, they can be expanded ex-vivo and retransferred in large number by adoptive transfer to the patient to specifically target cancer cells.



three occurring CD8 T cell populations:

- $CD11a^{lo}$ $CD82^{lo}$ naive T cells
- $CD11a^{hi}$ $CD82^{lo}$ pathogen-specific
- $CD11a^{int}$ $CD82^{hi}$ tumor-specific T cells

TECHNOLOGY DESCRIPTION

Activated Lymphocytes recognize mutation- and/or tumor specific antigens and can be differentiated from the T cell population responsive to pathogen induced cell alterations based on surface protein markers. Importantly, the analysis can be performed on PBMC preparations allowing minimal invasive sample acquisition and efficient marker analysis using flow cytometry or comparable techniques. Viable cells can be isolated for further analysis or ex vivo expanded and retransferred. The TCR-independent approach to identify mutation- and/or tumor specific $CD8^+$ T cells uses the biomarkers $CD82^+$, $CD194^+$, $CD244^-$, $CD28^+$, $CD62L^+$ and $CD55^+$. Additionally, $CD11a^+$, $CD18^+$ and $CD43^+$ can be included in the analysis in order to further increase the reliability and resolution of T cell characterization.

COMMERCIAL OPPORTUNITY

In-licensing or collaboration for further development is possible.

DEVELOPMENT STATUS

The identified marker proteins have been validated.

PATENT SITUATION

Patent applications based on WO2021074291A1 with priority of 16.10.2019 are pending in Europe and US.

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