Identification of CCR8 as a specific marker of tumor tissue-infiltrating regulatory T cells and its possibility as a therapeutic target in renal cell carcinoma

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Abstract

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Introduction

• Immunotherapy targeting immunocheckpoint molecules for renal cell carcinoma (RCC) has a certain clinical effect but it is still important to identify therapeutic targets with the higher response and fewer side effects.

• We have reported that tumor grade correlated with high expression of regulatory T cells (Tregs) and the efficacy of Nivolumab treatment in RCC patients.

• Tregs could serve as target cells for cancer immunotherapy and it is important to identify surface molecules specific to Treg within tumour microenvironments in order to maximize its therapeutic effect and overcome conventional drug resistance.

Objectives

• To identify surface molecules specific to Tregs within tumour microenvironment of RCC patients.

• To explore the possibility of novel cancer immunotherapy targeting tumour tissue infiltrating Tregs by antibody therapy

Material and Methods

Exploring surface molecules specific to Tregs within tumour microenvironment of RCC patients

Confirmation of the expression of the above molecule on Tregs using flowcytometry

Evaluation of therapeutic potential of antibody targeting specific molecules to Tregs

Evaluation of therapeutic effect and safety of anti-mouse CCR8 antibody in mouse model

• Examination of tumour reduction effect and safety by anti-mouse CCR8 antibody administration against colon cancer cell line (CT26) xenografts.

• Examination of removal tumour specific Tregs by anti-mouse CCR8 antibody.

• Examination of reactivation of intra-tumoral CD8 T cells by anti-mouse CCR8 antibody.

Conclusions

• We identified CCR8 as a specific molecule to tumour tissue-infiltrating Tregs of RCC patients.

• Anti-CCR8 antibody has been promising cancer immunotherapy with few side effects and high response.