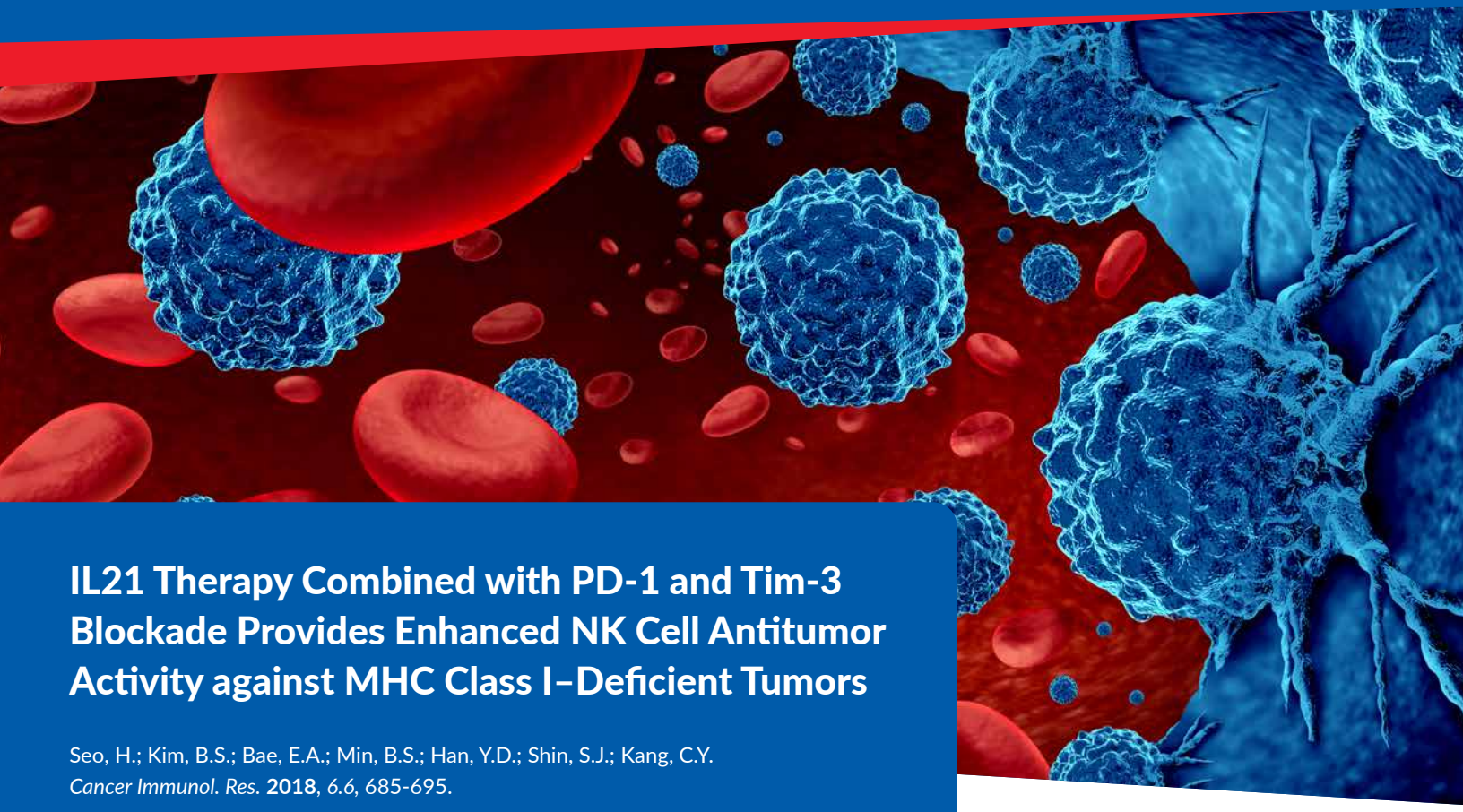
Tumor Cells

CASE STUDY



IL21 Therapy Combined with PD-1 and Tim-3 Blockade Provides Enhanced NK Cell Antitumor Activity against MHC Class I–Deficient Tumors

Seo, H.; Kim, B.S.; Bae, E.A.; Min, B.S.; Han, Y.D.; Shin, S.J.; Kang, C.Y.
Cancer Immunol. Res. **2018**, *6.6*, 685-695.

INTRODUCTION

Checkpoint inhibitors have shown some promise as cancer immunotherapies, but antitumor effects of checkpoint blockade on NK cells have not been clearly elucidated. Therefore, it is necessary to understand how anti–PD-1/anti–Tim-3 and rIL21 treatment suppresses tumor progression. Mouse models with MHC class I-deficient tumors were employed to assess the efficacy of checkpoint blockade through a combination of treatments. Lymphocyte Separation Medium (LSM™) from MP Bio was utilized in these experiments to separate tumor-infiltrating lymphocytes from tumor samples.

OVERVIEW

KEYWORDS: Lymphocyte preparation, human and mouse MHC class I-deficient tumor cell, tumor infiltrating NK cells, recombinant IL21 (rIL21)

AIM OF THE STUDY: Antitumor effects of checkpoint blockade on NK cells

APPLICATION:
FACS staining tumor-infiltrating NK cell

SAMPLE NAME: Human and mouse MHC class I-deficient tumor cells

MATERIAL: Lymphocyte Separation Medium *(LSM™, Cat. No. 0850494)* from MP Bio

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CASE STUDY: IL21 Therapy Combined with PD-1 and Tim-3 Blockade Provides Enhanced NK Cell Antitumor Activity against MHC Class I–Deficient Tumors

PROTOCOL AND PARAMETERS

1. Dissociated mouse and human tumors were incubated at 37 °C for 30 minutes and washed in PBS.
2. Lymphocytes were separated using Lymphocyte Separation Medium (LSM™) and filtered in a 70-µm nylon mesh.
3. Lymphocytes were counted and used for FACS staining.

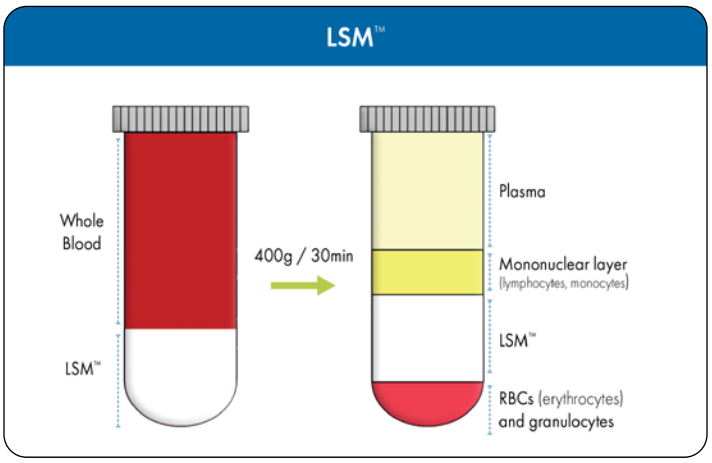

Figure 1. Isolation of mononuclear cells from whole blood using LSM™ density separation medium.

CONCLUSION

The isolated lymphocytes were utilized to determine the percentage of tumor infiltrating NK cells within these tumors after recombinant interleukin 21 (rIL21) was administered.

The researchers were able to show that intratumoral delivery of rIL21 attracted NK cells to the tumor site.

This study demonstrated that anti-PD-1/anti-Tim-3 treatment suppressed tumor progression in mice bearing MHC class I-deficient tumors. The suppression was further enhanced by recombinant IL21 (rIL21) treatments through an NK-cell-dependent mechanism.

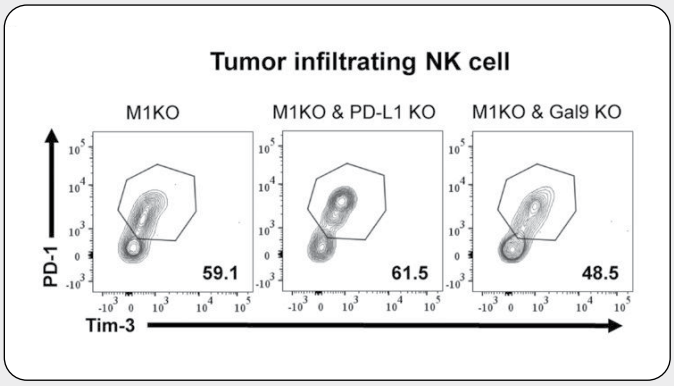

Figure 2. Flow cytometry analysis of PD-1 and Tim-3 expression on intratumoral NK cells in mice bearing MHC class I knockout (M1 KO), MHC class I and PD-L1 knockout (M1 and PD-L1 KO), and MHC class I and galectin-9 knockout (M1 and Gal9 KO) MC38 tumors.

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