

Abstract: PB2692

Title: A NOVEL AND PERSONALIZED PRECISION-PDX MODEL FOR ELIMINATION OF MINIMAL RESIDUAL DISEASE(MRD) FOR PATIENTS WITH MULTIPLE MYELOMA (MM) BY MAGNETIC-INDUCED NK CELLS—MAGIC-NK

Abstract Type: Publication Only

Topic: Myeloma and other monoclonal gammopathies - Biology & translational research

Background:

Advances in the management of patients with multiple myeloma (MM) have led to significant improvements in clinical outcomes. However, minimal residual disease (MRD) persists in most patients, and recurrence and subsequent resistance to conventional chemotherapy develops. The development of a patient-derived xenografts (PDX) model offers a promising tool for personalized treatment yet conventional PDX models are limited by low success rates and protracted development times. We have developed an innovative PDX model by exploiting magnetic-induced (MagIC) NK cell.

Aims:

A novel and personalized Precision-PDX model for patients with MM was established to explore the potential of magnetic-induced NK cells (MagIC-NK) of MRD eliminatio.

Methods:

1. Modeling: On d0, primary myeloma cells and the microenvironment supporting cells were isolated from the bone marrow of drug-resistant patients, labeled by recombinant lentiviral vectors carrying luciferase and GFP. On d1, the cells were loaded with “magnetic nanorobots” before injection into the right femur of 8-12w NSG female MagIC group mice under the guidance of a precise magnetic field. Traditional IV PDX models were set as controls through tail vein injection. The general conditions of the mice (survival, blood routine test, weight), tumor formation and metastases were monitored at different time points.

\2. MagIC NK cells treatment: Stable tumor signals were formed in both groups respectively. Bioluminescence, flow cytometry, and pathology techniques were applied to monitor the infiltration of NK cells into MM, the proliferation of NK cells, and the expression of immune-killing-related cytokines.

Results:

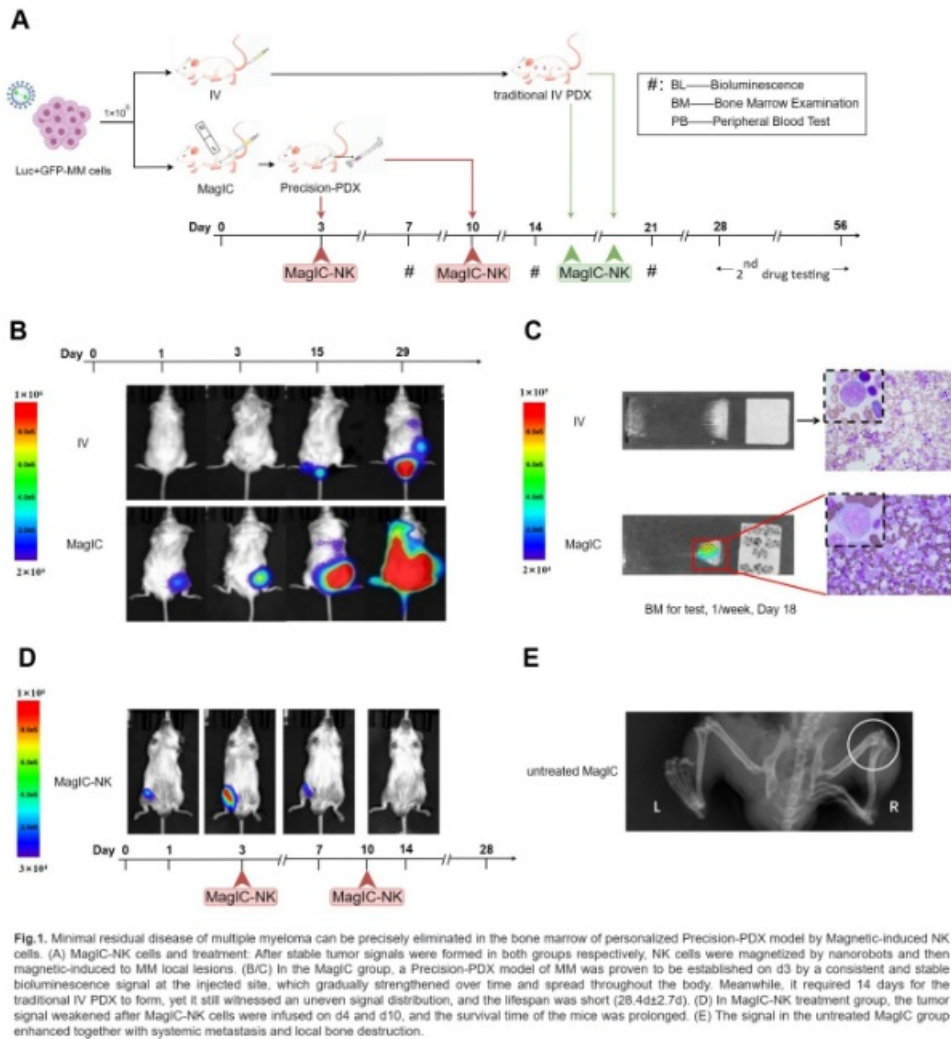
\1. Modeling: In the MagIC group, we were able to establish a Precision-PDX model of MM on d3, as shown by a consistent and stable bioluminescence signal at the injection site that expanded over time, as well as by metastases (Fig1B/C). In contrast, the traditional IV PDX required 14d to become detectable, with uneven signal distribution, and the lifespan of the animals was short ($28.4d \pm 2.7d$ vs $62.4d \pm 4.8d$ in MagIC group). In the MagIC group, the tumor microenvironment leads to higher rates and more persistent tumor formation within a significantly shorter period, the experimental window is prolonged to $59.4d \pm 4.8d$, instead of $14.4d \pm 2.7d$ in conventional IV PDX model.

In MagIC-NK treatment group, the tumor signal weakened after MagIC-NK cells were infused on d3 and d10 (Fig1D), and the survival time of the mice was prolonged. This indicated that MagIC-NK cells displayed an effective killing on tumor lesions by precise targeting and penetrating, and the effector-target ratio was significantly increased. Meanwhile, the signal in the untreated group enhanced with systemic metastasis and local bone destruction (Fig1E). As for the traditional IV PDX group, the fluorescence signal weakened after two doses MagIC-NK treatments yet without the prolongation of survival.

Summary/Conclusion:

This study has established an innovative Precision-PDX model that outperforms traditional IV PDX in simulating

clinical MM. MagIC-NK cells can precisely target and eradicate MRD. Our model will facilitate the development of personalized medicine for MM as well as other malignant diseases.



Keywords: MRD, Multiple myeloma, NK cell