NLRP3 inhibitor treatment reverses melanoma-induced vitiligo in mice

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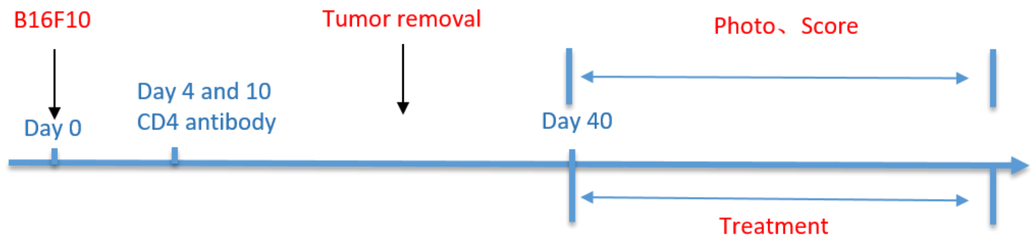
Introduction

Vitiligo is an autoimmune disorder characterized by the progressive destruction of melanocytes in the skin. This condition is driven by the infiltration of endogenous autoreactive $CD8^+$ T cells, which target and destroy melanocytes, resulting in the clinical manifestation of skin depigmentation. As a common acquired skin disease with no highly effective treatments, vitiligo has a global incidence of approximately 1%, significantly impacting both the physical and psychological well-being of patients. Thus, there is a critical need for the development of more effective therapies. Recent studies have shown that several NLRP3 inhibitors can reduce $CD8^+$ T cell activity, highlighting NLRP3 as a promising therapeutic target for vitiligo.

Method

Female C57BL/6 mice were randomly assigned to two groups: the Sham group and the Model group. On the day of the experiment, mice in the Model group received an intracutaneous injection of B16F10 cells. CD4 depletion antibodies were administered intraperitoneally to the Model group on Days 4 and 10. Tumor size was measured on Days 4 and 12, and mice with tumors of the requisite size were further divided into the Vehicle group and the NLRP3 treatment group. After re-grouping, tumors were surgically excised. NLRP3 treatment began on Day 28. The ImageJ software was used to analyze the pigmented area on the tails. The pigmented area on the tail was quantified weekly from Week 6 until the study's endpoint using photographic image analysis. Tail skin samples were collected and fixed for pathological staining.



Results

Starting from Week 6, the pigmented area progressively increased in the Vehicle group, confirming the successful establishment of the vitiligo model. In contrast, the NLRP3 inhibitor reduced the pigmented area compared to the Vehicle group. Histological analysis revealed that the NLRP3 inhibitor reversed the melanocyte depletion observed in the Vehicle group.

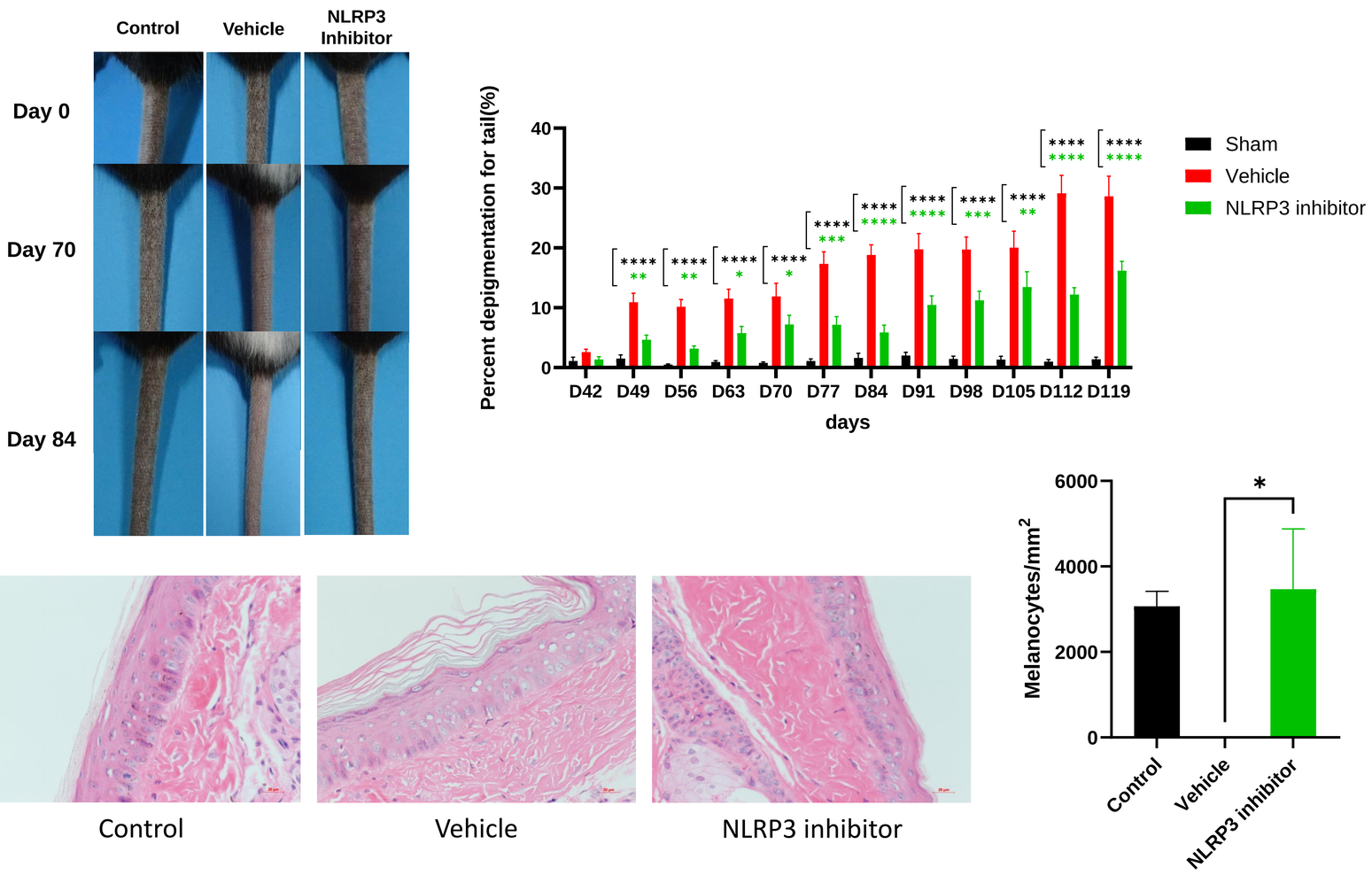


Figure 1. Image of depigmentation on the tails of mice. The skin of the tails in the Vehicle group exhibited significant depigmentation. In contrast, the NLRP3 inhibitor reduced the depigmented area compared to the Vehicle group.

Figure 2. Histopathological analysis of melanocytes. The skin of the tails in the Vehicle group exhibited a complete absence of melanocytes. In contrast, NLRP3 inhibitor treatment increased the number of melanocytes in the tail skin.

Conclusion

In this study, we successfully established a murine model of melanoma-induced vitiligo, characterized by a significantly increased depigmented area on the tail and a decrease in melanocytes in the tail skin. Treatment with the NLRP3 inhibitor effectively reversed the symptoms of melanoma-induced vitiligo in mice, as evidenced by an improved pigmented area on the tails and an increase in melanocytes in the tail skin.

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