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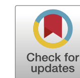
Letter to Editor

Astragaloside IV-enhanced anti-hepatocarcinoma immunity of dendritic cells



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To the editor,

A large body of research has shown that strengthening the function of DCs, such as by improving the recognition of tumor antigens or upregulating the expression of co-stimulation molecules, can regulate the body's anti-tumor immune response. For this reason, DC-based immunotherapy could be used to control tumor progression. Among the various Chinese medicines that can regulate immune function, certain single-drug components are worthy of research and discussion as potential additions to existing tumor treatments.[1–3] The present study observed the modulation of astragaloside IV (ASI), an important monomeric component of astragaloside, on the immune effect of DCs on liver cancer and explored the feasibility of ASI as a new immunopotentiator for DC-related tumor immunotherapy.

Mononuclear cells from the peripheral blood of healthy donors were isolated, and DCs were induced by cytokine combination of rhGM-CSF, rhIL-4, and TNF-α. ASI was added during the process. Cell morphology was observed by light and electron microscopy, the DC phenotype was detected by flow cytometry, and the level of IL-12 in the culture supernatant was determined. The effect of ASI on the proliferation of T lymphocytes stimulated by sensitized DCs was observed, and the specific killing effect of induced cytotoxic T lymphocyte cells (CTL) on the hepatoma cell line SMMC-7721 was evaluated.

The growth status and morphological characteristics of DCs under ASI were not significantly different from those of conventionally induced DCs (Fig. 1a). Except for CD1a, the surface markers CD14, CD40, CD80, CD83, CD86, and HLA-DR were significantly upregulated compared with conventionally induced DCs (Table 1). ASI promoted the maturation of DC phenotypes. The positive expression of the CD83 phenotype under different concentrations of ASI was a concentration-dependent trend (Figure 1b). In addition, the IL-12 level (pg/mL) in the culture supernatant of the ASI-regulated induction was significantly higher than the conventional induction group (632.65 ± 14.26 vs. 442.85 ± 38.96, $P = 0.000$) (Fig. 1c), and lymphocyte proliferation in the ASI-added group was significantly enhanced (Fig. 1d). Compared with DCs without ASI in the conventional induction group, DCs under the effect of ASI in the traditional Chinese medicine regulation-induction group significantly increased the killing rate of SMMC-7721 by inducing effector T lymphocytes (59.98 ± 5.23 vs. 46.50 ± 2.31, $P = 0.002$) (Fig. 1e).

In summary, ASI can enhance DC-induced specific CTL cytotoxicity against liver cancer cell SMMC-7721 by promoting DC maturation and antigen presentation function and increasing the release of the functional cytokine IL-12, which is considered a natural immunity enhancer used in DC-mediated anti-liver cancer treatment. However, additional experiments are needed to further analyze the effects of ASI in clinical trials.

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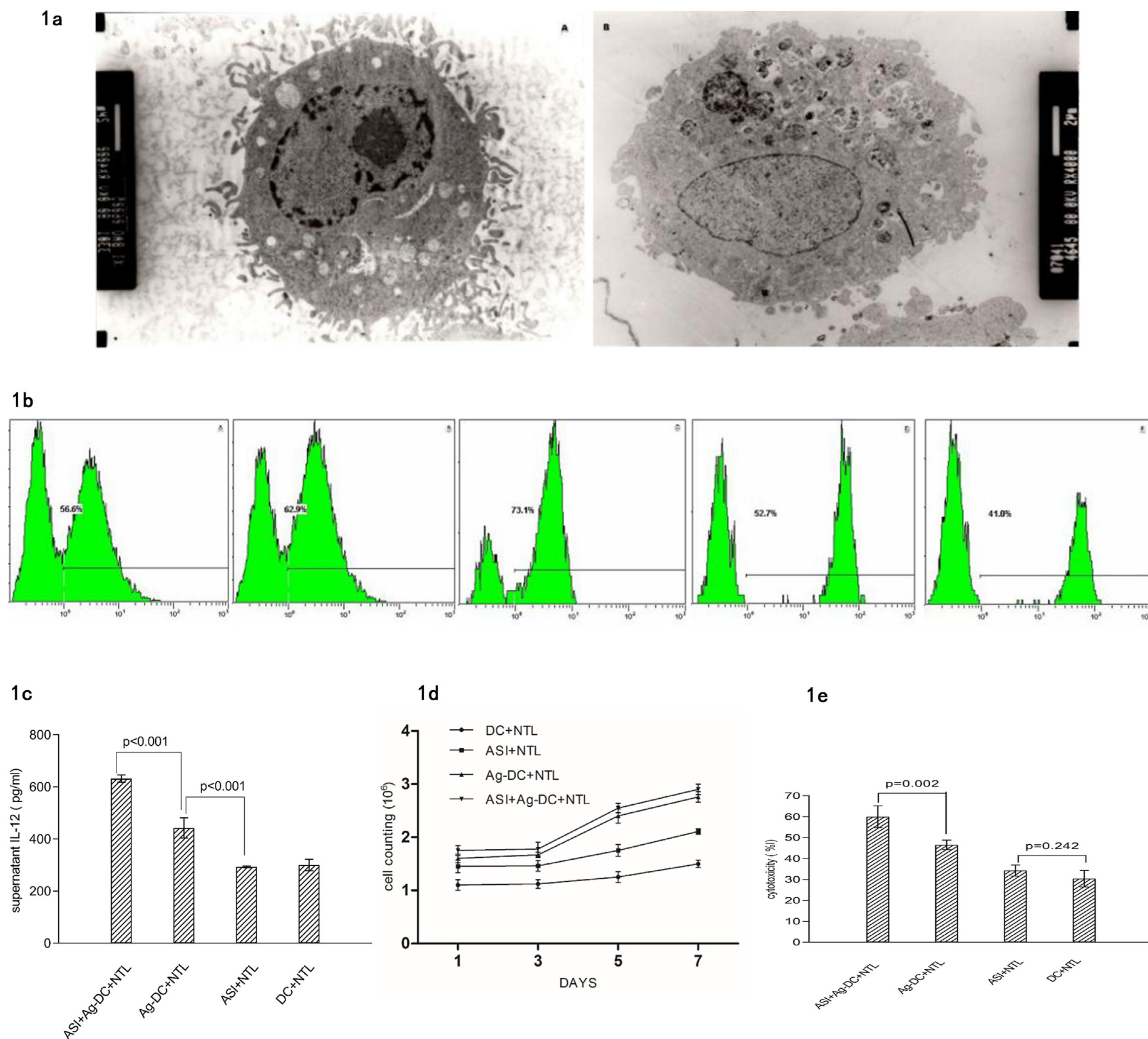

Fig. 1. a DC under electron microscope A) DC (5 d × 4000) with ASI-added induction. B) DC (5 d × 4000) without induction
b The expression of CD83 in each group of DCs under the action of different concentrations of ASI. A) ASI 25 μg/mL, B) ASI 50 μg/mL, C) ASI 100 μg/mL, D) ASI 200 μg/mL, and E) regular cytokine induction
c IL-2 levels of supernatant in groups with different induction methods. The ASI concentration in the groups was 100 ug/ml.
d Proliferation of naïve T lymphocytes cocultured with sensitized DCs or non-sensitized DCs. The ratio of DC:NTL was 1:20.
e Killing effects of AMC-regulated DC and Dex-induced SMMC 7721 at a ratio of 20:1.

Table 1
Comparison of DC surface-marker expression in each group.

Cell surface marker	Chinese medicine combined induction group (ASI100μg/mL) %	Conventional induction group %	Pure Chinese medicine group (ASI100μg/mL) %	Unprocessed group %
CD 14	14.82 ± 0.64*△	26.40 ± 0.79*	41.43 ± 0.68	64.13 ± 4.22
CD 1a	41.51 ± 1.34*	38.30 ± 12.30*	1.35 ± 1.03	3.90 ± 0.50
CD 40	89.30 ± 5.21*△	54.65 ± 0.07*	5.27 ± 0.65	1.50 ± 0.52
CD 83	72.96 ± 1.37*△	47.28 ± 3.32*	4.77 ± 1.29	5.63 ± 2.40
CD 86	89.23 ± 2.39*△	53.27 ± 3.13*	1.97 ± 0.53	13.03 ± 1.72
HLA-DR	92.63 ± 0.25*△	60.39 ± 2.26*	15.87 ± 6.79	17.03 ± 4.31

Note:* There was a significant difference compared with the latter two groups.
△There was a significant difference compared with the conventional induction group.

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Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.asjsur.2022.01.074.

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Hongxing Guo
Tianjin Third Central Hospital Affiliated to Nankai University, Tianjin, 300170, China

Institute of Hepatobiliary Disease, Tianjin Key Laboratory of Extracorporeal Life Support for Critical Diseases, Tianjin, 300170, China

Tianjin Zibo High-tech Co.Ltd, Tianjin, 300170, China

Jian Zhao
Department of Oncology, Tianjin Third Central Hospital Affiliated to Nankai University, Tianjin, 300170, China

Chenxuan Wu*
Department of Oncology, Tianjin Third Central Hospital Affiliated to Nankai University, Tianjin, 300170, China

* Corresponding author. Department of Oncology, Tianjin Third Central Hospital affiliated to Nankai University. No. 83, Jintang Road, Hedong District, Tianjin, 300170, China.
E-mail address: wu_chxuan@163.com (C. Wu).

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