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Analysis of the High-Salt Intake Effect on Immune System

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Summary

Excessive salt intake is known to lead to hypertension and cardiovascular diseases, but it has not been fully elucidated how excessive salt intake affects the immune system. It has been reported that mice fed a high-salt diet promote differentiation into Th17 cells and exacerbate brain dysfunction and autoimmune diseases. Ingestion of a high-salt diet can exert an anti-tumor effect that suppresses the growth of tumors such as malignant melanoma transplanted into mice by activating NK cells. On the other hand, human cohort epidemiological studies have revealed that men with high salt intake have an increased risk of developing gastric cancer.

In recent years, immune checkpoints have attracted attention as a new immune control mechanism, which functions as a brake to suppress excessive immune reactions. On the other hand, cancer cells use this immune checkpoint to escape immune surveillance. Immune cells express the receptor PD-1 on the cell surface, and binding of the ligand PD-L1 causes immunosuppression. Many cancer cells express PD-L1 to avoid attacks from immune cells and enable survival. Antibodies that inhibit the binding of PD-1 and PD-L1 are approved as anti-cancer agents. In this study, we examined whether immune checkpoint factors are regulated by high salt intake and analyzed the effects on the immune system.

When leukemic cell K562 was cultured in a medium supplemented with NaCl at the concentration used in the Th17 cell differentiation, it was found that the expression of PD-1 and PD-L1 was attenuated. When the effect on cell proliferation under these culture conditions was investigated, it was found that the number of dead cells and the cell cycle was hardly changed. We analyzed regulators of PD-L1 expression and found that RUNX1, which is involved in blood cell differentiation and immune function, increased PD-L1 expression at the transcriptional level. Culturing in high NaCl medium attenuated the expression of RUNX1. We also found that high NaCl medium decreased the expression of the antitumor cytokine TRAIL, which we found to be a target of RUNX1. The mice were then fed a high-salt diet and analyzed. Mice fed a high-salt diet for 7 days showed a decrease in white blood cell count and an increase in platelet count, but this was not significant. When we examined the effects on the expression of PD-1 and PD-L1 on the surface of blood cells, we found that PD-1 expression in the spleen was slightly increased in high-salt-fed mice, whereas PD-L1 was not change. It would be necessary to analyze the effects of a high-salt diet for a longer period and the expression of immune checkpoint factors by dividing blood cell components.