Dietary alterations in gut microbiota impact anti-tumor immunity: towards novel strategies to boost cancer immunotherapy 2267281

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Abstract

Introduction Dietary factors could profoundly shape host immunity and gut microbiota and disease. High salt intake has been shown to be detrimental in autoimmune conditions by directly affecting the immune cell balance or indirectly altering gut microbiota and metabolites. We have recently demonstrated that a high salt diet (HSD), could be beneficial in cancer by promoting enhanced antitumor immunity through modulation of myeloid-derived suppressor cell (MDSC) function.

Methods We investigated different tumor transplantation models in mice by using various microbial, immunological, bioinformatics and molecular biology state-of-the-art techniques.

Results Here we show that HSD can further boost the efficacy of checkpoint inhibitors and the gene expression analysis of MDSCs from tumor bearing mice revealed that HSD disrupts key immunosuppressive signaling pathways in vivo. Interestingly, the effect of HSD on tumor growth is highly dependent on the gut microbiota. The inhibitory effect of salt intake on tumor growth was absent in germ-free mice and profiling of the gut microbiota revealed significant changes upon HSD. The salt mediated inhibitory effect on tumor growth could be transmitted by fecal microbiome transplantation to animals receiving a regular diet and metagenomic analysis revealed specific microbial signatures contributing to this effect. Importantly, the administration of a single identified microbial taxa alone results in delayed tumor growth by reducing MDSC-mediated immunosuppression in tumor-bearing mice.

Conclusion Overall, our data suggest that salt-sensitive changes in the gut microbiota could potentially be explored to inhibit tumor growth and boost checkpoint inhibitors. Thus, our findings may have critical relevance for cancer immunotherapy.

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