ENHANCING CANCER IMMUNOTHERAPY WITH DEINOCOCCUS GEOTHERMALIS IN COMBINATION WITH PD-1 INHIBITORS: A NOVEL STRATEGY FOR NON-SMALL CELL LUNG CANCER TREATMENT

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Background Cancer immunotherapy has emerged as a promising approach for cancer treatment. However, the efficacy of current immunotherapies is limited by the immunosuppressive tumor microenvironment, novel strategies to further enhance anti-tumor activity of immunotherapy are still required. Recent studies reveal the profound impact of microbiomes on host immunity, influencing anti-tumor responses. Efforts to enhance immunotherapy involve microbial preparations with immunostimulatory properties, but these approaches remain in early stages.

Methods In this pre-clinical research, we analyzed the metagenomic profiles of 24 non-small cell lung cancer (NSCLC) patients who had been treated with PD-1 inhibitors (11 responders and 13 non-responders) and identified an enrichment of the bacterium Deinococcus geothermalis (D. geothermalis) in responder’s tumor tissues. To further investigate the effects of D. geothermalis on immunotherapy for NSCLC, we established patient-derived organoid (PDO) models from surgical samples of primary NSCLC tissues and assessed the activation of cytotoxic T cells in vitro. We evaluated the expression of TNF-α and IFN-γ using enzyme-linked immunosorbent assay (ELISA) and assessed cell viability in different treatment groups. Immunofluorescence staining was performed to detect the expression of Granzyme B (GZMB) and CD3, allowing us to evaluate the activation of cytotoxic T cells by calculating the ratio of GZMB-positive to CD3-positive cells.

Results Our results showed that the combination therapy with D. geothermalis and PD-1 inhibitors significantly increased the expression of TNF-α (approximately 100-fold) and IFN-γ (50–60 fold) in the NSCLC PDO models and also led to 20–30% reduction in tumor cell viability compared to control group. Immunofluorescence staining revealed significant increase in the proportion of GZMB-positive cells in lung cancer PDOS treated with the combination therapy, indicating enhanced activation of cytotoxic T cells. These findings suggest that the combination of D. geothermalis and PD-1 inhibitors could increase the activation of cytotoxic T cells in the tumor microenvironment, leading to significant tumor growth inhibition.

Conclusions Our study demonstrates the potential of combining D. geothermalis with immune checkpoint inhibitors as a novel strategy for cancer immunotherapy. This combination therapy has the potential to overcome the limitations of current immunotherapies and improve the clinical outcomes of cancer patients. Further studies are warranted to evaluate the safety and efficacy of this combination therapy in clinical trials.

Acknowledgements This study was supported by the Science Foundation of Peking University Cancer Hospital (18–02), the General Program of National Natural Science Foundation of China (82073247), Beijing Municipal Administration of Hospitals Incubating Program (PX2019038), and Beijing Youth Program for Outstanding Talents (2018000021469G262).

REFERENCES

Abstracts