| | | |
|---|---|---|
| ID No. | K2012 | |
| Project Title | Study on gene regulation and histone lactating in cancer | |
| Principal Investigator | Xiao-dong He | (Lecturer, Shandong Univ.) |
| Project Members<br>IMSUT Host | Makoto Nakanishi | (Prof., IMSUT) |
| Researcher Members | Hai Yu<br>Jia-Yi Zeng | (Postgraduate, Shandong Univ.)<br>(Postgraduate, Shandong Univ.) |

Report

In tumor tissues, due to the presence of the Warburg effect, a large amount of lactic acid is often produced and accumulated, which is an important characteristic of tumor, we can distinguish it from normal tissues. As an energy substance and metabolite, lactic acid has been known for a long time, but its metabolic function in physiological and pathological conditions is still unclear.

Over the past year, we stimulated mouse macrophages with the construction of the lactylation of tumor microenvironment and performed transcriptome analysis to determine the possible mechanisms of tumor cell interaction with mouse macrophages. Methods: Peritoneal macrophages were extracted from 8-week-old female C57/6N mice and successfully cultured to construct 8 simulated tumor microenvironments including pH6.2, pH7.4, LA and Hela cell culture medium of LPS (+/-). Transcriptome sequencing and differential analysis were performed after incubation. GO functional enrichment analysis and KEGG pathway enrichment analysis were performed for differential gene sets. Results: Transcriptome analysis showed that there were multiple enrichment pathways. LPS stimulation could induce the differentiation of mouse peritoneal macrophages into M1-type macrophages, and promote the regulation of immune and defense responses. Lactic acid stimulation can promote the anti-inflammatory effect of macrophages, which may inhibit inflammation through NLRs signaling pathway and MAPK signaling pathway. Conclusion: Studying the mechanism of interaction between macrophages and tumor microenvironment may promote the identification of new targets or signaling pathways for tumor-related therapy.

The results were presented at the 8th National Conference on Computational Biology and Bioinformatics (NCCBB) and The Biomedical Big Data and Artificial Intelligence. At the same time, we published a review paper. Both of these are written: "This study was

partly supported by a Grant from the International Joint Usage/Research Center, The Institute of Medical Science, the University of Tokyo."

In addition, with the support of IMSUT, we have a certain foundation to work on, So I successfully applied for the Interstellar Initiative project of Japan Agency for Medical Research and Development (AMED) in 2021. We also attended two international conferences (In-Person & Virtual) In Berlin and New York.

At the same time, we have also obtained the project support from the National Natural Science Foundation of China and the Outstanding Innovation Fund of Shandong University, and trained two postgraduate students and one doctoral student.