

No.	K22-2056	
研究課題名	Functional polarization of tumour-associated macrophages by tumor microenvironment	
研究代表者	何 曉東 (山東大学・講師)	
研究組織	受入教員	中西 真 (東京大学医科学研究所・教授)
	分担者	Xiao-dong He (Shandong University・Lecturer)
	分担者	Hai Yu (Shandong University・Graduate student)
	分担者	Tian-shu Liu (Shandong University・Graduate student)
	分担者	Makoto Nakanishi (Cancer Cell Biology, Institute of Medical Science, University of Tokyo・Professor)

IMSUT International Joint Usage/Research Center Project <International>

Joint Research Report (Annual/Project Completion)

Annual Report
Report
<p>In 2022, 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.</p> <p>At the same time, we constructed a co-culture system of HGC-27 and Raw264.7 cells, successfully isolated exosomes from the supernatant of cell culture medium, and analyzed microRNA-seq of exosomes. We use the CSHL research to develop a small program (https://github.com/wososa/PSI-Sigma), RNA splicing, RNA m6A methylation, DNA methylation and Gene expression analysis were combined for comprehensive analysis, mainly focusing on RNA splicing. We found some interesting biomarkers and validated them by cellular molecular biology methods.</p> <p>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 and a research paper. 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."</p> <p>In addition, with the support of IMSUT, we have a certain foundation to work on, 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.</p>

Journal of Nutritional Biochemistry 2023, 104
 https://doi.org/10.1016/j.jnbi.2023.101602

RESEARCH Open Access

Chondroitin sulfate alleviates osteoporosis caused by calcium deficiency by regulating lipid metabolism

Tianshu Liu^{a,*}, Hai Yu^{a,*}, Shuai Wang^a, Huimin Li^a, Xinyiran Du^a and Xiaodong He^a

Abstract
 The role of chondroitin sulfate in alleviating osteoporosis has attracted attention in recent years. Although calcium and vitamin D are essential for bone health, the underlying mechanism of osteoporosis is still unclear. The regulation of lipid metabolism by chondroitin sulfate and calcium to alleviate osteoporosis has been proposed. In this study, we investigated the effect of chondroitin sulfate on lipid metabolism and bone health in a mouse model of osteoporosis. The results showed that chondroitin sulfate treatment significantly increased the levels of HDL-C and LDL-C, and decreased the levels of TG and TC. Chondroitin sulfate also significantly increased the levels of bone mineral density (BMD) and bone mineral content (BMC). These results suggest that chondroitin sulfate may alleviate osteoporosis by regulating lipid metabolism. Further studies are needed to confirm this hypothesis.

Keywords: Chondroitin sulfate, osteoporosis, lipid metabolism

Additional file 1: Table S1 MiRNA analysis showed significant differences in microbial community structure between group N and group C, and between group C and group Ca.

Additional file 2: Table S2 The differential metabolites of fecal metabolites between the N group and the C group. The differential metabolites of fecal metabolites between the C group and the Ca group. The differential metabolites of fecal metabolites between the C group and the C3 group.

Additional file 3: Table S3 The differential metabolites of plasma metabolites between the N group and the C group. The differential metabolites of plasma metabolites between the C group and the Ca group. The differential metabolites of plasma metabolites between the C group and the C3 group.

Acknowledgements
 The authors want to thank Translational Medicine Core Facility of Shandong University for consultation and instrument availability that supported this work. This study was supported by a Grant from International Joint Usage/Research Center of the Institute of Medical Science, the University of Tokyo.

第八届全国计算生物学与生物信息学学术会议
 暨生物医学大数据与人工智能大会
 2022年7月22-25日 中国·广州 Paper ID: 928354

小鼠腹股原代巨噬细胞模拟肿瘤微环境的转录组学分析

曹露露, 王浩, 王一帆, 李瑞

摘要: 巨噬细胞在肿瘤微环境中扮演着重要的角色, 其转录组学特征对于理解肿瘤的发生和发展至关重要。本研究通过模拟小鼠腹股原代巨噬细胞的转录组学特征, 揭示了其在肿瘤微环境中的转录组学变化。我们使用单细胞RNA测序技术, 对小鼠腹股原代巨噬细胞进行了转录组学分析, 并比较了其在正常生理状态和模拟肿瘤微环境下的转录组学特征。结果显示, 在模拟肿瘤微环境下, 巨噬细胞的转录组学特征发生了显著变化, 包括炎症反应相关基因的表达上调, 以及免疫抑制相关基因的表达下调。这些结果提示, 巨噬细胞在肿瘤微环境中可能通过调节其转录组学特征来促进肿瘤的生长和转移。本研究为理解巨噬细胞在肿瘤微环境中的作用提供了新的见解, 并为开发针对巨噬细胞的靶向治疗策略提供了理论依据。

关键词: 巨噬细胞, 转录组学, 肿瘤微环境, 单细胞RNA测序

cancers MDPI

Pathogenic Roles of RNA-Binding Proteins in Sarcomas

Yu Hai¹, Arika Kawachi¹, Xinghai He¹ and Akihide Yoshimi^{1*}

Simple Summary: RNA metabolism can be regulated via miRNA. This process is called transcription and protein can be subsequently synthesized using the information in mRNA as a template (called translation). Approximately 4000 RNA-binding proteins (RBPs) in the cells covalently regulate these multiple processes between transcription and translation. It has been recently recognized that some of the RBPs have abnormal expression and/or function, leading to the initiation or maintenance of malignant diseases including sarcomas, which is the greatest cause for a broad group of malignancies that begin in the bone and soft tissue. Unfortunately, there are currently very few effective treatments in many types of sarcoma at advanced stage. Therefore, we need to understand more deeply how sarcoma develops in our body and how they are efficiently regulated by therapeutic interventions. Studies on the disease mechanism in terms of RBPs will provide us with the opportunity to have a better understanding of the sarcoma pathogenesis.

Author Contributions: A.K. and A.Y. designed the manuscript. Y.H., A.K., X.H. and A.Y. wrote the manuscript. A.K. and A.Y. prepared all the figures and table. All authors have read and agreed to the published version of the manuscript.

Funding: This study was partly supported by the following grants awarded to A.Y.: Science and Technology Platform Program for Advanced Biological Medicine (grant number JP24000007), the Japan-Canada joint call for Strategic International Collaborative Research Program (SCORP; grant number JP220220085) from the Japan Agency for Medical Research and Development (AMED), Grant-in-Aid for Scientific Research (A) (grant number 21040420), the Home-Returning Researcher Development Research (grant number 19C20491) from the Japan Society for the Promotion of Science (JSPS), Fusion Oriented Research for Innovative Science and Technology from the Japan Science and Technology Agency (JST) (grant number 22-2210M126), the National Cancer Center Research and Development Funds (grant number 250-1-A-2), the ASH Clinical Research Award from the American Society of Hematology (ASH), the CDP Special Fellow Achievement Award from Leukemia and Lymphoma Society (LLS), and grants from the Shimadzu Science Foundation, the Yasuda Medical Foundation, the Chemo-Sero-Therapeutic Research Institute, the Sumitomo Foundation, the Uehara Memorial Foundation, the Prince Takamatsu Cancer Research Fund, the Takeda Science Foundation, the Mochida Memorial Foundation for Medical and Pharmaceutical Research, and the Astellas Foundation for Research on Metabolic Disorders. This study was also partly supported by the MEXT Joint Grant (grant number New-3033-K20105) awarded to A.K.

Research Results from the Project during FY2022

<Publications>

Hai Y., Kawachi A., He X., Yoshimi A. (2022) Pathogenic Roles of RNA-Binding Proteins in Sarcomas. *Cancers* (Basel). 14(15):3812.

Tianshu Liu; Hai Yu; Shuai Wang; Huimin Li; Xinyiran Du; Xiaodong He. (2023) Chondroitin sulfate alleviates osteoporosis caused by calcium deficiency by regulating lipid metabolism, *NUTRITION & METABOLISM*, 2023, 20(6)

<Patent Applications>