The role of intracellular and extracellular GRP78/Bip in the activity and progression of rheumatoid arthritis

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Abstract

Objective: This study aimed to examine the expression of GRP78/Bip (glucose regulated protein-78 / binding immunoglobulin protein) in both intracellular space (synovial tissue) and extracellular space (articular fluid and blood) in patients with rheumatoid arthritis (RA). Additionally, the study sought to investigate the role of intracellular and extracellular GRP78/Bip in the activity and progression of RA.

Methods: 96 patients with different activity and progression of RA were selected from January 2020 to June 2021. According to the DAS28 score, the patients were divided into the remission stage and active stage, and divided into early stage, middle stage and late stage by progression of RA, namely RA. R.E group, RA. R.M group, RA. R.L group, RA. A.E group, RA. A.M group, RA. A.L group, and 16 patients in each group. The expression of GRP78/Bip in serum was detected by Elisa. 6 typical RA patients with different stages were selected from 96 outpatients as the RA experimental group by the results of serum GRP78/Bip, clinical symptoms, and laboratory tests. 1 patient admitted for arthroscopic surgery due to discoid meniscus was a healthy control group and 1 patient admitted for joint replacement due to osteoarthritis (OA) was a control group.1 patient admitted for arthroscopic surgery due to discoid meniscus was a healthy control group and 1 patient admitted for joint replacement due to osteoarthritis (OA) was a control group.The Elisa was used to assess the expressions of TNF-α, IL-10 and GRP78/Bip in serum, synovial tissue and articular fluid. The western blot (WB) was used to assess the expressions of GRP78/Bip and Caspase-3 in synovial tissue

Results: In terms of overall comparison among the 8 groups, the expression of

GRP78/Bip in RA serum and synovial tissue was ranked in descending order: active stage > remission stage, late stage> middle stage> early stage, and the RA articular fluid: remission stage > active stage, early stage> middle stage> late stage, with statistically significant overall difference in all the groups ($P<0.05$). The expression of Caspase-3 in RA synovial tissue was ranked in descending order: active stage > remission stage, late stage or middle stage> early stage, with statistically significant overall difference in all the groups ($P<0.05$). The expression of TNF-α in serum, synovial tissue and articular fluid was ranked in descending order: active stage > remission stage, late stage> middle stage> early stage, with statistically significant overall difference in all the groups ($P<0.05$). The expression of IL-10 in serum and synovial tissue was ranked in descending order: active stage > remission stage, late stage> middle stage> early stage, and the RA articular fluid: remission stage > active stage, late stage> middle stage> early stage, with statistically significant overall difference in all the groups ($P<0.05$).

Conclusion: The intracellular and extracellular GRP78/Bip was involved in the activity and progression of rheumatoid arthritis, and could be used as a new therapeutic target to provide new ideas and methods for clinical remission or treatment of RA.

Key words: GRP78/Bip (glucose regulated protein-78 / binding immunoglobulin protein); Rheumatoid arthritis (RA); Activity; Progression; Serum; Synovial tissue; Articular fluid.

Biography

Guoyin Liu has completed his Master's degree from Medical School of Nanjing University, and is currently a PhD candidate in Nanjing Medical University. He is the doctor-in-charge and associate professor at the Department of Orthopaedics, Jinling Hospital of Nanjing Medical University. He worked mainly on the role of intracellular and extracellular GRP78/Bip in particles-induced periprosthetic osteolysis and rheumatoid arthritis; the clinical application of extracorporeal shock wave therapy, corticosteroid injection, and needle-knife therapy in the treatment of chronic plantar fasciitis; and the application of lamina osteotomy and replantation with miniplate fixation (restorative laminoplasty) in intraspinal occupying lesions. He had been invited

as a speaker to the "World Congress on Virology & Infectious Diseases" during November 20-22, 2017 in Miami, FL, USA, and as a speaker to the International Conference on Biomarker Research in Clinical Medicine scheduled for February 19-21, 2018 in Paris, France (BRCM 2018). He was a member of the Standing Committee of the China Medicine Education Association (CMEA), and a managing director of National Association of Health Industry and Enterprise Management (NAHIEM). He was an editorial board member for Journal of《Orthopaedic Surgery and Research》, 《Innate Immunity》, 《Frontiers in Bioscience-Landmark》, 《Current Molecular Medicine》and《Current Pharmaceutical Design》. He was also an editorial board member for Tianjin Medical Journal, Chinese General Practice , China Medical Herald，New Medicine, Drugs & Clinic, Chinese Traditional and Herbal Drugs, Anhui Medical and Pharmaceutical Journal, Anhui Medical Journal, Translational Medicine Journal, Journal of Medical Research, Health Medicine Research and Practice, Hebei Medicine, Hainan Medical Journal, Zhejiang Clinical Medical Journal, China Modern Medicine, China Modern Doctor, and Henan Medical Research. He have obtained several project: The National Natural Science Foundation of China (NSFC)(82102547), The Natural Science Foundation of Jiangsu Province (BK20181113), The Science and Technology Foundation of Nanjing City (201803059), Youth Science Foundation Project of Jingdu Hospital (20170302), Technological Innovation Foundation of Nanjing Military Region (15ZD020), The Science and Technology Foundation of Nanjing City (201503007) ,Clinical Scientific Project of Wu Jieping Medical Foundation (320-2745-16-115), Technological Innovation Foundation of Nanjing Military Region (14MS046).

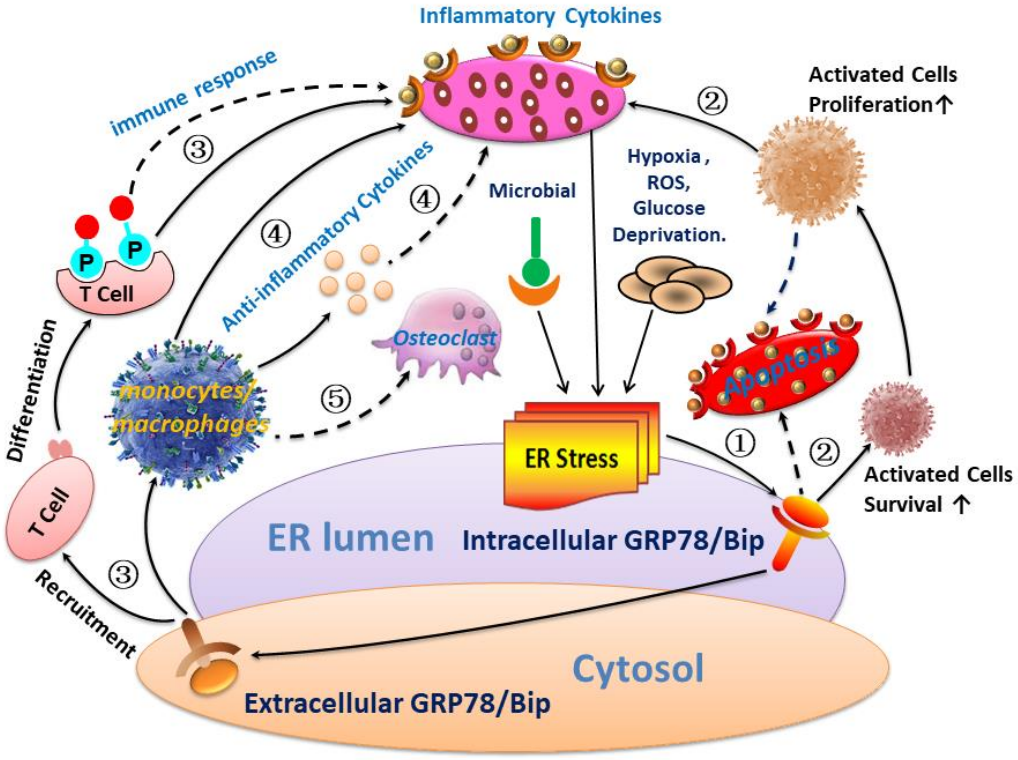
About Research Topic

The role of intracellular and extracellular GRP78/Bip in the activity and progression of rheumatoid arthritis has been extensively studied. GRP78/Bip, a chaperone protein, has been found to be upregulated in the synovial tissue of patients with rheumatoid arthritis. It is involved in the regulation of inflammation and apoptosis, and has been shown to play a role in the pathogenesis of rheumatoid arthritis. Additionally, extracellular GRP78/Bip has been found to be involved in the activation of immune cells, suggesting a potential role in the development of autoimmune diseases such as rheumatoid arthritis.

The effects of intracellular and extracellular GRP78/Bip are as follows:

GRP78/Bip is involved in most stress responses in vivo, and can be transferred from nucleus (intracellular protein) into cell surface (extracellular protein). Currently, the research of GRP78/Bip in rheumatoid arthritis (RA) is controversial, and the role and regulatory mechanism of intracellular and extracellular GRP78/Bip in the activity and progression of RA has not been reported yet. The results of our experiments showed that GRP78/Bip can be continuously highly expressed in and out of RA cells at the same time, and its change trend is closely related to RA activity and progression; the roles GRP78/Bip played in and out of cells in the process of RA activity and progression are different. Therefore, we put forward the hypothesis of the mechanism of GRP78/Bip in and out of RA cells, which explains the reason why GRP78/Bip has different action mechanisms under different stresses, and even plays different roles under the same

stress; besides, it explains the expression differences of GRP78/Bip in and out of RA cells, and also the differences of the targeted therapy in RA activity and progression. Based on this hypothesis, this research elucidates the effects and mechanism of intracellular and extracellular GRP78/Bip in the activity and progression of RA, so as to solve the current controversial and unknown problems.



About Institution:

Jinling Hospital of Nanjing Medical University, also named as General Hospital of Eastern Theater Command, located in Nanjing, China, is a tertiary hospital.

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