

Discussion and Conclusions: Short-term treatment with microgravity caused significantly changed of inflammatory cytolines production. The differential effects of simulated microgravity on TNF- α , IL-6, IL-1 β , TLR-4 expression suggested the different sensitivity to microgravity of signaling pathways regulating different inflammatory cytokines in macrophages. Furthermore, microgravity impaired the function of macrophage. The decreased inflammatory response of macrophages and the damaged function caused by microgravity may contribute to the increased susceptibility to infections of astronauts. LPS stimulates immune responses by interacting with the membrane receptor TLR-4 to induce the generation of cytokines. In the future work, the LPS-induced activation of signaling pathways downstream of TLR4, such as NF- κ B and MAPK pathways will be tested.

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Session: Disease & Treatment – Tumors

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Mfn2 INHIBITS THE PROLIFERATION OF OSTEOSARCOMA VIA DOWNREGULATION OF plk1

Qingsong Tian ^a, Zhaoxia Hu ^a, Heng Zhang ^a, Huadong Pei ^b, Xinhzhi Li ^a

^aRenhe Hospital of Three Gorges University, China

^bState Key Laboratory of Proteomics, Beijing Proteome Research Center, China

Objective: The tumor suppressor role of mitochondrial fusion gene 2 (Mfn2) have been confirmed in many tumors. However, there are few reports about the mechanism of mfn2 on the development and progression of tumor. We will study the osteosarcoma in this research to reveal the correlation of Mfn2 and osteosarcoma. A further demonstration of the potential mechanism between them will be included.

Methods: We collect the pathological specimens of osteosarcoma patients, and then analysis the expression of mfn2 and its effect on the survival of patients with osteosarcoma. A construction of lentiviral which overexpress the mfn2 is needed. We would infect the osteosarcoma cell lines MG63 and U2OS with the lentiviral and then selected the positive cells with puromycin to obtain the stable line. The exploration of the overexpression of mfn2 on the proliferation and the apoptosis will be carried out. The purification of flag-mfn2 and a mass spectrometry analysis are necessary to detect the interaction protein of mfn2. What's more, the interaction will be further identified through the immunoprecipitation (IP). The knock out or knock down of mfn2 in the osteosarcoma cell through the CRISPR/cas9 are vital important to our mechanism analysis. After the above clinical research and cell based experiments, we would like to construct an mfn2 knock in mouse model and induce the development of osteosarcoma. We will study the effect of mfn2 on the development and the progression of osteosarcoma and the potential mechanism, to provide a research foundation for precision treatment.

Results: (1) The expression of mfn2 is lower in osteosarcoma tissue than the adjacent non tumor tissue both in mRNA and protein level. And the low expression of mfn2 is corrected with the poor prognosis. (2) We are the first time identified the plk1 has an interaction with mfn2 through mass spectrometry analysis. The interaction between mfn2 and plk1 has been further confirmed through the IP. (3) The stable line U2OS in which the mfn2 is knocked down has been obtained by the CRISPR-cas9 technique. (4) There has a negative relationship between the expression level of mfn2 and plk1.

Conclusion: mfn2 is a novel tumors pressor for osteosarcoma. And it functions its tumor inhibition roles through the negative regulation of the expression level of plk1.

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Session: Others

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RESVERATROL ATTENUATES OXIDATIVE STRESS INDUCED UP-REGULATION OF P-SELECTIN, PSGL-1, vWF AND TM VIA SIRT1 PATHWAY IN HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS

Zhenkai Lou

First Affiliated Hospital of Kunming Medical University, China

Objective: To investigate the effects and underlying mechanisms of resveratrol on pro-thrombosis factors in human umbilical vein endothelial cells under oxidative stress injury.

Methods: Construct H₂O₂ induced HUVEC cells injury model *in vitro*, inspecting PI3-K/Akt/GSK3 β , MAPKs, NF- κ B and Nfr2/ARE signaling pathway in OSI mediated endothelial cells injury and apoptosis, exploring effects and molecular mechanism of resveratrol protecting venous endothelial cells from oxidative injury and apoptosis. By overexpression and inhibition of SIRT1, explore regulation effects of resveratrol on the secretions of pro-thrombotic molecular—P-Selectin, P-selectin glycoprotein ligand-1 (PSGL-1), thrombomodulin (TM) and von Willebrand factor (vWF) in HUVECs and downstream key signaling pathways.

Results: PI3-K/Akt/GSK3 β , MAPKs (c-Jun, ERK1/2, p38), NF- κ B, Nfr2/ARE signaling pathway are involved in venous endothelial cells apoptosis induced by oxidative stress. Resveratrol could inhibit pro-apoptotic pathway (MAPKs), inhibit inflammatory response pathway (NF kappaB), up-regulate anti-apoptotic pathway (PI3-K/Akt/GSK3 β), protecting endothelial cells from oxidative stress induced apoptosis and injury. Resveratrol could inhibit P-Selectin, PSGL-1, vWF and mRNA TM and protein expression in oxidative induced endothelial cells via SIRT1 pathway.

Conclusion: Resveratrol could protect endothelial cells from oxidative induced apoptosis and injury, inhibit pro-thrombosis molecules secretion, suggesting a new target for drug prevention and treatment of deep venous thrombosis.

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Session: Traumatology – Fixation

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SINGLE LOCKING PLATE CONSTRUCTS ARE LESS SENSITIVE TO SCREW REMOVAL THAN DUAL LOCKING PLATE CONSTRUCTS FOR MID-DIAPHYSEAL FRACTURE FIXATION

Arvind Nana ^a, Victor Kosmopoulos ^a, Keith Fishbeck ^b

^aUniversity of North Texas Health Science Center, Fort Worth, Texas, USA

^bUniversity of North Texas, Denton, Texas, USA

Background: Single large-fragment plate constructs are currently the norm for internal fixation of mid-diaphyseal humerus fractures. In cases where anatomy limits the size of the humerus available for fixation however, recent studies support the use of a dual small fragment locking plate construct. This study aims to compare the simulated performance of both a single locking plate and a dual-locking plate construct with decreasing number of locking screws and with changes in screw fixation location.

Subjects and Methods: Mid-diaphyseal humeral fracture fixation using a single (Model S) and a dual (Model D) locking plate construct were simulated using the finite element method, a numerical technique commonly used to computationally approximate solutions for complex structural mechanics problems. Different configurations were tested by removal of either one or two screws from the superior half of the fixation construct and compared to a control having no screws removed. Models are labelled based on the location of the screw removed with 1 denoting the most superior screw and 4 denoting the inferior screw adjacent to the fracture (e.g., S1 denotes removal of the most superior screw from the single plate model). Results: Model D4 was the only construct to show an increase in stiffness as compared to the original dual plate construct without any screws removed. For the single-plate constructs, models S1-S3 all resulted in less than 2.5% stiffness reductions as compared to the control. Noteworthy, three of the single plate constructs, having two screws removed (models S12, S13, and S23), showed less than a 6% reduction in construct stiffness. In contrast, all of the dual-plate constructs with 2 screws removed showed high stiffness reductions (greater than 55%).

Discussion and Conclusion: Results support that screw number and/or location and construct type (single vs dual) are important factors to consider in achieving successful fixation. Based on the simulations performed, the single plate models were found to be less sensitive to screw removal. A balance must be achieved between hardware (i.e., screws and plate) stresses and construct stiffness. Increased hardware stress can lead to early failure while changes in construct stiffness may affect the ability for bone to heal. Future experimental and clinical studies are needed for surgical recommendations especially with regards to the relationship between our outcome measures and healing based on interfragmentary motion.

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Session: Biomaterials and Implants – Bioinert/Bioactive Materials

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IN VITRO AND IN VIVO EVALUATION OF MACRO-PORE BIOGLASS BONE BLOCKS AND THE APPLICATION IN LOAD-BEARING DEFECTIVE BONE

Xiaojie Li, Tenglong Hu, Liu Yang, Qiang Jie

Xijing Hospital, The Fourth Military Medical University, China

Seeking for a kind of suitable bone biomaterials to repair the heavy defective bone of load-bearing region is an essential mission and effort direction of materials experts and Orthopaedics Surgeons. Current biomaterials used in load-bearing region are limited because of poor bioactivity. Therefore the generation of bioactive bone substitute with improved mechanical features is a possible way to dissolve these clinical problems. We develop a new bioactive bone substitute, Macro-Pore Bone Block (MPBB), which presents good biomechanical strength and persisting bioactivity. We implanted it into the femoral condyles of rabbits and also, cultured osteoblasts on the surface of the material *in vitro*. The MPBB presents better mechanical strength and shows a good bioactivity and appropriate degradation rate in the *in vivo* study. MPBB is also proved to promote osteoblast adhesion, proliferation and differentiation *in vitro*. Furthermore, even a clinical