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Characterizing miRNA profiling of skin wound: the case of increased expression of miR-21 during wound healing

Tao Wang[1]*, Yimei Feng[1,2]*, Huiqin Sun[1], Lei Hao[2], Xinghua Chen[2], Yongping Su[1] and Zhongmin Zou[1]

[1]Institute of Combined Injury, State Key Laboratory of Trauma, Burn and Combined Injury, China
[2]Department of Hematology of Xinqiao Hospital, 3Department of Chemical Defense and Toxicology, School of Preventive Medicine, The Third Military Medical University, China

Aims During wound healing, wound repair cells and growth factors, such as TGF-_, work collaboratively and co-ordinately to promote a satisfying wound healing, but the mechanisms that control the behaviour of factors and cells have not been understood yet. The concept of miRNA reveals a new regulatory dimension of gene expression and in present study the featuring miRNA profile of wound healing was explored.

Methods: RNA extracted from normal mouse skin and wound tissue at 7 days after skin incisional injury was subjected to micro RNA microarray analysis. The expression of miR-21 was verified by Northern blot on wound tissue in vivo, and TGF-_ (2.5 ng/ml) treated multi potent mesenchymal cells C3H10T1/2 in vitro. The proliferation and differentiation of C3H 10T1/2 cells stimulated by TGF-_ or in combination with synthesized locked nucleic acid modified anti-miR-21(LNA-antimiR-21) were examined by CCK-8 and immune fluorescence staining against SMA and NG2. The expression of PTEN, TPM1 (both are putative miR-21 target genes), and Bcl-2 (closelyinvolved in miR-21-mediated effects), was detected by RT-PCR. Synthesized LAN-anti-miR-21 oligos were directly delivered to wound and its effect on healing progress was observed

Results : Among 198 mi RNAs analyzed, 27 mi RNAs were up-regulated and 21 mi RNAs down-regulated for more than 2-fold in wound tissue 7 d after the injury. These mi RNAs are mainly involved in cell proliferation, differentiation and epithelial to mesenchymal transition (EMT), and more often expressed in cancer cells and stem cells. The elevated miR-21 expression was confirmed by Northern blot. TGF-_ treatment increased cell proliferation, miR-21 expression, and protein level of _-SMA and NG2 in C3H10T1/2 cells, which were inhibited by knock down miR-21. TGF-_ stimulation led to up-regulated Bcl-2 and down-regulated PTEN and TPM1 in C3H10T1/2 cells. LAN-anti-mi R- 21 oligos-treated wounds showed significant inhibition of wound healing at as early as 3 days after the intervention, and lasted for the next 10 days.

Conclusion: The featuring miRNA profile of skin wound is depicted. For the first time, we demonstrate that the elevated miR-21 expression promotes skin wound healing possibly by mediating the proliferation and differentiation of wound repair cells, suggesting that miR-21 may be a new target in wound manipulation. Keywords: micro RNA; miR-21; MSCs; TGF-_; skin incisional wound.

Biography

ZHONGMIN ZOU, M.D., Ph.D. He received his medical degree at the Forth Military Medical University, and doctorate degree Ph.D. in Radiation Medicine at the Third Military Medical University (TMMU). He served as an lecturer, associate professor at Department of Radiation Medicine, School of Preventive Medicine, TMMU. He worked at the Burnham Institute and the Scripps Research Institute in San Diego as a visiting scholar from 2001 to 2005. In late 2005, Dr. Zou returned to TMMU as a Professor in the Department of Radiation Medicine and Vice director of Institute of Combined Injury (ICI). He is currently Professor and Director of Department of Chemical Defence and Toxicology, School of Preventive Medicine, TMMU.