TRAFFICKING OF ENDOGENOUS STEM CELLS FOR TISSUE REPAIR

Hyun Sook Hong Ph.D[1,2]. and Youngsook Son Ph.D. KHU fellow[1,2]*

[1]Department of Genetic Engineering and Graduate School of Biotechnology, Kyung Hee University & [2]Institute of Regenerative Medicine, Kyung Hee University Hospital, Seoul, Korea *ysson@khu.ac.kr

Background: Tissue injury may create a specific microenvironment, which brings up the systemic participation of reparative stem cells in the repair process. Previously, we identified a new role of substance-P (SP) as an injury-inducible messenger to mobilize bone marrow stromal cells, namely mesenchymal stem cells (BMSC or MSC) from the marrow to the blood, home to the injured tissue, and be engaged in the tissue repair in the alkali-burn corneal injury model (*Nature Medicine, 2009 April*). This elucidates endogenous healing mechanism recalling BMSC to the wound site.

Principle Findings: In addition to SP's BMSC mobilizer function, SP also mobilize endothelial precursor cells (EPC) from the bone marrow to the peripheral blood. We explored SP's dual positive roles in the orchestration of the tissue repair in a variety of the animal models such as the spinal cord injury, acute myocardiac infarction, stroke, radiation-induced BM injury and gastrointestinal injury. At the early stage of wound healing, SP directly exerts anti-inflammatory role by mobilizing monocytes from the bone marrow to the blood as well as inducing M2 type macrophages and stimulating their infiltration to the injured tissue, which in turn suppresses the injury-induced tissue inflammation and clean up dead cells for tissue repair. This unique role of SP comes much earlier than its action on BMSC and EPC mobilization and seems to play positive roles in the reduction of inflammation-induced secondary cell death and the creation of favorable microenvironment for the engraftment of incoming stem cells. At later stage, endogenous stem cells such as BMSC and EPC mobilized by SP finally participate in the tissue repair as reparative stem cells.

Conclusion and Significance: SP may orchestrate tissue repair by reducing inflammation-provoked tissue damages at early stage and ameliorate chronic inflammation-related disease and then by recruiting endogenous stem cells from bone marrow to the injured tissue for the tissue repair. These multiple roles of SP may stimulate its development as a potential stem cell stimulating agent.

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