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Prevention of stress-induced MSC premature senescence by 5-methoxytryptophan

Kenneth K Wu
National Health Research Institutes and CMU, Taiwan

Premature senescence of Mesenchymal Stem Cells (MSCs) contributes to MSC growth arrest and secretory phenotype. It hampers MSC expansion in culture and MSC cell therapy. To develop strategies to prevent MSC senescence, we assessed 5-methoxytryptophan (5-MTP). We previously reported that human fibroblasts and endothelial cells produce and release 5-MTP into the extracellular milieu including circulating blood. Serum 5-MTP concentrations in healthy human subjects were 0.5-1.2 μM. 5-MTP inhibits stress-induced cyclooxygenase-2 (COX-2) and cytokine expressions in macrophages and protects endothelial barrier function and integrity. To determine whether 5-MTP controls MSC senescence, we pretreated bone marrow-derived MSC (BM-MSC) with chemosynthetic pure L-5-MTP followed by high glucose (HG) or H2O2. HG metabolic stress or H2O2 oxidant stress induces typical premature senescence such as growth arrest, increased p16 and p21, SA-βgal and senescence-associated secretory phenotype (SASP). 5-MTP prevented all the senescence phenotypes induced by HG or H2O2. Our preliminary data suggest that 5-MTP exerted the anti-senescence effect by upregulating Foxo3a expression. We conclude that 5-MTP is a valuable lead compound to develop new agents to prevent MSC senescence and improve MSC cell therapy.

Biography

Kenneth K Wu, MD, PhD was the Professor and Director of Hematology and Vascular Biology Research Center at University of Texas Health Science Center at Houston, Texas, USA and served as the President of National Health Research Institutes of Taiwan. He is currently Chaired Professor at China Medical University (CMU) Taichung, Taiwan and National Tsing-Hua University Hsin-Chu, Taiwan. He has published more than 350 papers and served as Editorial Board Member or Associate Editor of several journals.

kkgo@nhri.org.tw

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