ICoLA 2019
The 8th International Congress on Lipid &Atherosclerosis(ICoLA)
The 58th Conference of the Korean Society of Lipid & Atherosclerosis
September 5(Thu.) ~ 7(Sat.), 2019, Conrad Hotel Seoul, Republic of Korea

DEVELOPMENT OF A NOVEL ANGIOGENESIS ASSAY FOR VASCULAR DISEASES

Sajita SHAH[1,2], Hyunsook LEE[1,2], Kyu-Tae KANG[1,2]*

[1] *College of Pharmacy, Duksung Women's University, Seoul, Republic of Korea*
[2] *Duksung Innovative Drug Center, Duksung Women's University, Seoul, Republic of Korea*

ktkang@duksung.ac.kr

Abstract

Angiogenesis have been an aggressively-growing research field in the last few decades with the recognition that angiogenesis is a hallmark of more than 50 different pathological conditions, such as rheumatoid arthritis, oculopathy, cardiovascular diseases, and tumor metastasis. During angiogenesis modulator development, it is crucial to use *in vitro* assay systems with appropriate cell types and proper conditions to reflect the physiologic angiogenesis process. To overcome limitations of current *in vitro* angiogenesis assay systems using mainly endothelial cells, we developed a 3-dimensional (3D) co-culture spheroid sprouting assay system. Co-culture spheroids were produced by two human vascular cell precursors, endothelial colony forming cells (ECFCs) and mesenchymal stem cells (MSCs). ECFCs+MSCs spheroids were embedded into type I collagen matrix to mimic the *in vivo* extracellular environment. A real-time cell recorder was utilized to continuously monitor the progression of angiogenic sprouting from spheroids for 24 hours. Live cell fluorescent labeling technique was also applied to tract the localization of each cell type during sprout formation. Angiogenic potential was quantified by counting the number of sprouts and measuring the cumulative length of sprouts generated from the individual spheroids. Comparison experiments demonstrated that ECFCs+MSCs spheroids showed greater sprout number and cumulative sprout length compared with ECFCs-only spheroids. Bevacizumab, an FDA-approved angiogenesis inhibitor, was tested with the newly-developed co-culture spheroid assay system to verify its potential to screen anti-angiogenic drugs. The IC_{50} value for ECFCs+MSCs spheroids compared to the ECFCs-only spheroids was closer to the effective plasma concentration of bevacizumab obtained from the xenograft tumor mouse model. The present study suggests that 3D ECFCs+MSCs spheroid angiogenesis assay system is relevant to physiological angiogenesis, and can predict an effective plasma concentration of drug candidates in advance of animal experiments.

Keywords

angiogenesis, co-culture spheroid, endothelial colony forming cells, mesenchymal stem cells, type I collagen gel, bevacizumab