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Development of novel antiangiogenic agents for the treatment of retinal neovascularization

Hypoxia is a special feature occurring in vascular diseases and induces the transcriptional genes involved in glycolysis, hematopoiesis, invasion and angiogenesis. Hypoxia-inducible factor-1 α (HIF-1 α), which is a key mediator of angiogenesis is overexpressed under hypoxic condition and transcribes various genes. Our initial studies confirmed that deguelin, a rotenoid disrupts ATP binding to hsp90 and consequently induces destabilization of HIF-1 α . We have identified novel hsp90 inhibitors through the SAR studies including structure truncation of deguelin. The new hsp90 inhibitors exhibited excellent antiproliferative and antiangiogenic activities, which are applicable for treatment of the angiogenesis-related ocular diseases. In particular, two representative hsp90 inhibitors exhibited suppression of hypoxia-mediated retinal neovascularization and vascular leakage in diabetic retina. They effectively suppressed expression of target genes of HIF-1 α including VEGFA in the retina of oxygen-induced retinopathy (OIR) mice but do not induce definite toxicity. We will report our recent progress on the development of antiangiogenic agent with detailed discussions.

Biography

Young-Ger Suh is a Professor of College of Pharmacy, Seoul National University, South Korea. He was graduated from Seoul National University with BS degree in Pharmacy in 1975 and received PhD degree from University of Pittsburgh in 1987. Currently, he is a President of Korean Society of Organic Synthesis, a full Member of The Korean Academy of Science and Technology, a Fellow of Asian Federation for Medicinal Chemistry and Vice President of The Korean Federation of Science and Technology Societies. He has published more than 150 papers in reputed journals and presented more than 200 papers at scientific meetings.

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