IMS-IL-2 **Development of Novel Antiangiogenic Agents for the Treatment of Retinal Neovascularization**

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Hypoxia is a special feature occurring in vascular diseases and induces the transcriptional genes involved in glycolysis, haematopoiesis, invasion and angiogenesis. Hypoxia-inducible factor-1α (HIF-1α), which is a key mediator of angiogenesis, is overexpressed under hypoxic condition and transcripts various genes. Our initial studies confirmed that deguelin, a rotenoid, disrupts ATP binding to hsp90 and consequently induces destabilization of HIF-1α. 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-1α 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.