Perturbing Angiogenesis Using Small Molecules

Ho Jeong Kwon

Chemical Genomics National Research Laboratory, Department of Biotechnology, Translational Research Center for Protein Function Control, College of Life Science and Biotechnology, Yonsei University, Seoul 120-752, Korea

Small molecules have been successfully utilized as molecular probes to decipher molecular and cellular functions of their binding proteins in a given biological phenotype of interest. This ligand and receptor information further facilitates structure based better drug design and development. My laboratory has developed and applied this powerful potential of small molecules to explore the complicated and multi-components involved biological system such as angiogenesis. From our continuing efforts to discover new small molecules perturbing angiogenesis, a number of structurally distinct small molecules such as terpestacin, curcumin, HBC, HNHA, OMe-Syn, and NHOBTD have been identified from our synthetic and natural products library on the basis of their phenotype suppressing activity toward the endothelial cells. Direct binding proteins of these small molecules were identified using phage display biopanning consisting of human whole cDNA expressing T7 phage library. As the results, UQCRB, aminopeptidase N, calmodulin, and histone deacetylase were discovered as the target proteins of these small molecules. New insights from these small molecules and target proteins in respect to angiogenesis have enabled us to uncover new molecular and signaling mechanisms underlying angiogenesis and to translate into the development of new therapeutics towards angiogenesis related diseases. In this presentation, our activities on systemic investigations toward angiogenesis using small molecules will be provided by introducing our terpestacin and its target protein, UQCRB, as one of case studies.

Ho Jeong Kwon Professor, Department of Biotechnology, Yonsei University; B.S. 1984, Seoul National University; Ph.D. 1995, Tokyo University (advisor: Teruhiko Beppu and Sueharu Horinouchi); Postdoctoral Training, 1995-1998, Harvard University. (advisor: Stuart L. Schreiber); *Chemical biology, genomics, proteomics*; *Discovery of bioactive small molecules and their targets, and application towards understanding of biological systems*; Tel: 82-2-2123-5883, Fax: 82-2-362-7265, E-mail: kwonhj@yonsei.ac.kr