

WORLD CONGRESS ON RECENT ADVANCES IN OPHTHALMOLOGY & VISION RESEARCH

April 28-29, 2025 | VIENNA, AUSTRIA



Yanzhong Hu, Dan-Dan Chen, Yuxuan Wang

Henan University School of Medicine; Eye Institute of
Henan Academy, Zhengzhou, China

The Regulation of Heat Shock Protein 90 on Visual Cycle Homeostasis

Abstract:

The visual cycle in RPE cells is stepwisely regulated by a cascade-enzymes including LART1, RPE65, RDH5 and regulatory protein RLBPI. Dysregulation of those enzymes result in congenital retinitis pigmentosa or AMD. Heat shock protein90 (HSP90) is a small family of cellular ATP-dependent chaperones that protect the proteostasis in both physiological and pathological conditions. Here we find that HSP90 regulates the expression of RLBPI and RDH5 in a distinct mechanism. In APRE-19 cells, deletion either HSP90a and HSP90b by using the CRISPR-cas9 results in the downregulation of the expression of RLBPI mRNA and RDH5 protein. HSP90 regulates RLBPI transcriptional expression by interacting with and stabilizing the transcriptional factor SP1. The latter can bind to and drive RLBPI mRNA expression. For RDH5, deletion of HSP90 results in RDH5 degradation via the autophagy-lysosomal pathway. HSP90, RDH5 and Calnexin form a complex through intermolecular interactions. Deficiency of HSP90a or HSP90b dissociates RDH5 from Calnexin, and increases RDH5 translocation from the endoplasmic reticulum (ER) to the cytosol, binding to P62 and undergoing degradation in macroautophagy-lysosomes. In C57BL6J mice, administration of HSP90 inhibitor IPI504 can downregulate RLBPI and RDH5 in RPE tissues and attenuate the amplitude of a and b-waves in scotopic adaption in ERG. Taken together, HSP90 is a critical chaperone in the regulation of visual cycle homeostasis. Downregulation of RLBPI and RDH5 may be responsible for the nyctalopia side effect in the tumotherapy of HSP90 inhibitors.

Keywords: heat shock protein 90, RDH5, RLBPI and visual cycle, autophagy and SP1

Biography: B.S. Henan Medical University, Zhengzhou, China 1983

Ph.D. Peking Union Medical College, Beijing, China 1996.

Postdoctor fellowship: Karolinska Insitute, Stockholm, Sweeden 1996-2000

Research Scientist, Augusta University, Georgia, USA. 2000-2011

Distinguished Professor, Henan University School of Medicine, China, 2011- present