Metabolic control of plasma cell longevity

Yeonseok Chung

Seoul National University, Seoul, Republic of Korea. Email: yeonseok@snu.ac.kr

Plasma cells are the cornerstone of long-term humoral immunity, requiring an extraordinary capacity for continuous antibody secretion. This high secretory output imposes chronic endoplasmic reticulum (ER) stress, yet the mechanisms that allow plasma cells to preserve ER integrity and bypass stress-induced apoptosis remain poorly understood. In this study, we identify Liver X Receptor (LXR) as a critical metabolic regulator of plasma cell survival. Our findings reveal that plasma cell differentiation is accompanied by significant lipidome remodeling and induction of LXR. Utilizing both in vivo and in vitro models, we demonstrate that LXR deficiency leads to profound defects in ER morphology and a marked reduction in plasma cell longevity. We characterize a novel metabolic-to-stress signaling circuit where LXR tunes the sensitivity of the Unfolded Protein Response (UPR) through specific lipid saturation pathways. These results reveal a fundamental link between lipid metabolism and organelle homeostasis, providing new insights into how plasma cells sustain their specialized function under proteostatic pressure.