

## **Defining the Molecular Mechanism of the UBA6-USE1 pathway in lung cancer**

Peter Chang-Whan Lee

Department of Biomedical Sciences, University of Ulsan College of Medicine, ASAN

Medical Center, Seoul, Korea

The UBA6-USE1 ubiquitin enzyme cascade is a poorly characterized arm of the ubiquitin-proteasome system. We found that USE1 proteins are frequently overexpressed in lung cancer patients (92.45%, n = 106). Stable overexpression of USE1 significantly increased cell proliferation, migration, and invasiveness in lung cancer cells and xenograft models, whereas their knockdown significantly reduced cell proliferation, migration, and invasion. USE1 has a conserved D-box domain and the level of the protein was regulated by the anaphase-promoting complex (APC/C) through its interaction with CDC20 and CDH1. Furthermore, five missense mutations in USE1 identified in patients prolong the half-life and stability of the protein. These data reveal an unexpected role for USE1 in lung cancer promotion, migration, and invasion.