화학과 세미나

박종민 교수님
강원대학교 화학과

Exploration of New Chemical Space for Tissue-Specific Protein Degradation

Current PROTAC development relies on two E3 ligases, cereblon (CRBN) and von Hippel-Lindau (VHL), for targeted protein degradation (TPD). However, this reliance presents several challenges. First, the expression levels of CRBN and VHL vary depending on tissue types, making it difficult for current PROTACs to effectively degrade the desired target proteins in all cases. Additionally, unintended protein degradation in non-target tissues by PROTACs may lead to side effects. Another recently reported issue is the development of drug resistance during disease treatment with PROTACs. To overcome this drug resistance, the discovery of various E3 ligase ligands is necessary. Beyond the known CRBN and VHL ligands, more than 600 E3 ligases exist in cells, with expression patterns that vary depending on human cells, tissues, and diseases. Therefore, identifying E3 ligase ligands specific to certain tissues or pathological cells can facilitate the development of tissue-, cell-, and disease-specific targeted protein degradation (TPD). The discovery of such novel E3 ligase ligands will serve as an important foundation for the development of next-generation therapeutics for intractable diseases using PROTAC technology.

For this purpose, we explored new chemical space to identify ligands for tissue-specific E3 ligases through virtual and AI-based screening. Subsequent development of PROTACs using those ligands successfully demonstrated tissue-specific protein degradation. Muscle-specific protein degraders will be highlighted as the first example of tissue-specific PROTACs. The preclinical application of muscle-specific protein degradation for muscle related disease treatment will be described to demonstrate the therapeutic potential of tissue-specific protein degradation. In addition, discovery of ligands for other tissue-specific E3 ligases will be presented to provide future directions for tissue-specific protein degradation.

Date : 2026년 11월 26일 (목) 오후 5시
Location : 과학관 B133호
Host : 연세대학교 화학과