Investigating THBS1 for Overcoming Radioresistance in Head and Neck Squamous Cell Carcinoma (HNSCC) : Transcriptomic Insights and Drug Prediction

Minji An[1], Changhoon Choi[2], and Wankyu Kim[1*]

[1]*Department of Life Science, Ewha Womans University, Seoul, South Korea.*
[2]*Department of Radiation Oncology, Samsung Medical Center, Seoul, South Korea.*

Radiation therapy plays a essential role in the management of Head and Neck Squamous Cell Carcinoma (HNSCC); however, the emergence of radioresistance often leads to unfavorable outcomes. In this study, we aimed to explore THBS1 as a potential therapeutic target to overcome radioresistance in HNSCC by delving into the underlying mechanisms and drug prediction aspects.

We select THBS1 as a potential candidate for endogenous radioresistance by analyzing data from Cancer Cell Line Encyclopedia (CCLE). To validate its role, we conducted knockdown experiment in radioresistant HNSCC cell lines, cal27 and detroit562. It showed the suppression of tumor growth and an increase in sensitivity to proton irradiation, demonstrating the functional significance of THBS1 in overcoming radioresistance.

To uncover the underlying mechanisms of THBS1 inhibition-induced radiosensitivity, we conducted transcriptomic analysis. This analysis explored pathways related to radioresistance affected by THBS1 inhibition and assessed its clinical relevance by integrating data from the Cancer Genome Atlas (TCGA). In our pursuit of radiosensitizing strategies for HNSCC, this study compares the THBS1 signature with drug-induced signatures from the Connectivity Map (CMap), utilizing public datasets from the Gene Expression Omnibus (GEO) to identify potential radiosensitizing drugs.

This study not only highlights THBS1 as a promising target for radiosensitization in HNSCC but also offers a comprehensive approach to understanding the transcriptomic mechanisms and drug prediction.