Small-molecule Em360 suppresses TKIs-resistant Non-Small Cell Lung Cancer (NSCLC) growth by degradation of EGFR protein

Speaker: Chun-Sheng Fang (4th year)/ Supervisors: Dr. Ching-Shih Chen

Lung cancer is one of the most common cancer types in terms of both incidence and mortality in the United States, and it is predicted to cause more than 100,000 predicted deaths in 2016\(^1\). Malignant lung cancer is associated with EGFR mutations (30%) and overexpression of EGFR protein\(^2\), which makes EGFR an important target in small molecule target therapy. Various group have designed tyrosine kinase inhibitors (TKIs) that compete with ATP for the ATP-binding site of EGFR in order to block the downstream signaling cascade\(^3\). However, once tumors acquired the secondary mutation T790M, the tumor cells are 50% less sensitive to TKIs treatment\(^4\) and become resistant.

In our lab, we found that the small molecule Em360 demonstrated great potency against the cell viability of lung cancer cells, with an IC50 range below the micromolar (\(\mu M\)) level. Em360 can also induce the EGFR protein degradation through the post-transcriptional regulation, including the proteasome and lysosome degradative pathways. Most importantly, Em360 was nontoxic to the animal model and significantly suppressed tumorigenicity in the H1975 lung cancer xenograft model. We expect this compound to provide the TKI-resistant patients with another option to cure cancer.

References