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### Dichloroacetophenone derivatives as pyruvate dehydrogenase kinase inhibitor in non-small cell lung cancer models

Kin Tam

*University of Macau, Macau*

Pyruvate dehydrogenase kinase 1 (PDK1) is a key enzyme involved in glucose metabolism and is often overexpressed in cancers exhibiting glycolytic phenotypes, such as non-small-cell lung cancers (NSCLC). Targeting PDK1 appears to be an attractive anticancer strategy. Based on a previously reported moderate potent anticancer PDK1 inhibitor, **64**, we developed some dichloroacetophenone biphenylsulfone ethers, which exhibited good inhibitory effects on PDK1. The anticancer effects of these novel dichloroacetophenone derivatives were evaluated in NSCLC cell lines, namely NCI-H1299 and NCI-H1975. It was found that one of the derivatives, **31**, exhibited sub-micromolar cancer cell IC<sub>50</sub>s and significantly suppressed the tumor growth in NCI-H1975 mouse xenograft model, outperforming the anticancer effects of **64**. Our results suggested that **31** strongly inhibited PDK1 leading to effective modulations of the aberrant glucose metabolism in cancer cells, which could be an alternative anticancer strategy.