Project title: Comprehensive Cancer Center of Taipei Medical University Program title: Investigation of HMGA2 role in the pathogenesis, prevention, diagnostic biomarkers and novel therapeutic drugs

Identification of Novel Therapeutic Compounds for Colorectal Cancer

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Colorectal cancer (CRC) is one of the main causes of cancer death in the world. CRC treatment is often limited by the development of drug resistance. Our team previously found that HMGA2 is highly expressed in CRC patients and is associated with drug resistance and poor clinical outcome. In this project, we established a HMGA2-mediated interaction network and identified novel inhibitors for proteins in the network. In addition, we identified highly overexpressed proteins in CRC as new therapeutic targets. Structure-based virtual screening was performed to identify potential inhibitors for each protein. In total, we discovered 14 novel compounds that inhibited the growth of CRC cell lines with IC50 values of <10μM. Enzyme-based assays showed that the compounds inhibited proteins associated with HMGA2 or proteins overexpressed in CRC, such as PDGFRB, MKNK2, ABL1, PDGFRA, RSK2, and AURKB. These inhibitors have the potential to be developed as therapeutic drugs for CRC.