OXA-resistance in *colorectal cancer cells mediated by* NF-κB and *IGF-1R/PI3K/Akt signaling pathway.*

Yi-Jiun lin[1],Wei-Wen Kuo[4], Chih-Yang Huang[1,2,3]

[1]Graduate Institute of Basic Medical Science, China Medical University, Taichung, Taiwan

[2]Graduate Institute of Chinese Medical Science, China Medical University, Taichung, Taiwan

[3]Department of Health and Nutrition Biotechnology, Asia University, Taichung, Taiwan

[4]Department of Biological Science and Technology, China Medical University, Taichung, Taiwan

Abstract

Colorectal cancer (CRC) is one of the most commonly diagnosed cancers in both males and females all over the world; however, its incidence is rising in Asian during the past few decades. Oxaliplatin (OXA), a *first-line* chemotherapy in CRC, is a *platinum*-containing agents by forming inter- and intra-strand DNA crosslinks to *inhibit* DNA *replication* and transcription. **Nevertheless,** drug resistance remains a major clinical challenge for cancer treatment. The mechanisms involved in *oxaliplatin resistance* are *still* poorly understood. LoVo CRC cell line were treated in a gradually increasing concentration of Oxaliplatin. Firstly, we found that the survival rate of OXA-R cells is higher compared to parental cell by MTT assay. OXA-R cells promote pro-survival capability via IGF-1R/PI3K/Akt and *NF-κB* signaling pathway. The expression of cell cycle proteins, cyclinD and cyclinB, is higher than parental LoVo cells. *NF-κB* has been shown to regulate cell survival, migration and metastasis in colon cancer cells. To understand whether *NF-κB* determined chemoresistance in OXA-R cells, we estimate the survival rate after quinazoline (QNZ) treatment, an *inhibitor* of *NF-κB*. Compare to parental LoVo cells, the cell viability is decreased. Moreover, chemoresistance is one of critical factors that facilitate migration and metastesis. We observed that migration ability is decreased in OXA-R cells compare to parental cells by wound-healing assay. Taken together, the resistance of LoVo to OXA is regulated through IGF-1R/PI3K/Akt and *NF-κB* signaling pathway.