NF-κB-mediated Prosurvival Network in Low Dose Radiation-induced Radioadaptive Response in Human Skin Keratinocytes

Authors: Danupon Nantajit, Cuihong Jin, Demet Candas, Nadire Duru, Rui Liu, Claire Wang, Ming Fan, and Jian Jian Li

Institution: Department of Radiation Oncology, University of California Davis, CA 95817

This collaborative research project aims to elucidate the molecular mechanism through which exposure to a low dose radiation (LDR) induces radioadaptive response. Data from these studies may generate significant information in inventing potential therapeutic approaches to improve normal tissue protection in caner radiation therapy. We found that ATM, a DNA damage sensor, is induced by LDR and responsible for activation of transcription factor NF-κB. Our results indicate a cooperative function of ATM, ERK, and NF-κB in the induction of clonogenic survival advantage in radioadaptive response as a result of LDR treatment (10-cGy x-ray). By using human skin keratinocytes, we show that phosphorylation of ATM, MEK and ERK are enhanced along with the two-fold induction in NF-κB luciferase activity at 24 h post-LDR. Protein-protein interaction between ATM and NF-κB subunit p65 is detected in the resting keratinocytes, and their interaction is significantly increased in cells after LDR treatment. We are currently investigating protein-protein interaction between LDR-induced ATM, MKP1 and other mitochondrial influx elements including cyclins and 14-3-3s. The results obtained as far suggest a pro-survival network can be induced by LDR via activation of NF-κB-regulated pathways. Since mitochondrial protein influx seems to play a role in the NF-κB-mediated radioprotection, we are currently studying the LDR-induced protein influx with mitochondrial function and apoptosis (supported by DE-SC0001271, JJL).