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## **Analysis of DNA damage responses and repair mechanisms after boric acid-mediated boron neutron capture therapy in hepatocellular carcinoma**

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**Background:** Boron neutron capture therapy (BNCT) is a two-step radiation treatment modality, which kills tumor cells and leaves normal cells undamaged. In previous studies, boric acid (BA)-mediated BNCT has demonstrated its therapeutic efficacy in treating hepatocellular carcinoma (HCC) in rat and rabbit models. However, the DNA damage responses and repair mechanisms induced by BA-BNCT in HCC remain unclear.

**Aim:** This study thus aims to investigate whether the BA-BNCT induced DNA double-strand break (DSB) and to explore which DSB repair pathways, homologous recombination (HR) and non-homologous end joining (NHEJ), would be the primary pathway.

**Methods:** Huh7 (human HCC cell line) was pre-treated with BA 30 minutes before exposing to neutron irradiation at Tsing Hua open pool reactor in National Tsing Hua University, Taiwan. Afterwards, cells were harvested for immunocytochemistry and immunoblotting analysis.

**Results:** The expression of  $\gamma$ H2AX, a marker of DSB damages, was observed to peak at 4 h and diminished by 24h after BA-BNCT. The protein expression of BRCA1 and Rad51, both involving the HR pathway, were activated at 4 h. Surprisingly, BRCA1 sustained its activation to 48 h, while NHEJ-related proteins Ku70/Ku80 did not show significant changes after BA-BNCT.

**Conclusion:** These results suggested that DSB damages induced by BA-BNCT were primarily repaired through the HR pathway in HCC. Our findings could enable the identification of radio-sensitizer or adjuvant treatment by targeting the HR pathway, which could help to address treatment resistance and potentiate the efficacy of BA-BNCT for HCC.

### **Recent Publications**

1. Bai Y C, Hsia Y C, Lin Y T, Chen K H, Chou F I, Yang C M and Chuang Y J (2017) Effect of tumor microenvironment on selective uptake of boric acid in HepG2 human hepatoma cells. *Anticancer research*, 37(11):6347-6353.

### **Biography**

Kuan-Hao Chen is pursuing his Master's degree. He worked as an Intern at Academia Sinica for two months, where he studied heme oxygenase 2 protein-protein interactions with cytochrome P450 reductase. He was awarded for poster competition at 2018 Taiwan Zebrafish Symposium. He is now investigating the BNCT-induced biological effects in hepatocellular carcinoma (HCC), especially the DNA damage responses.

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