

## B-8

# Autophagy Inhibition on In Vitro and In Vivo PanNET Models

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**BACKGROUND:** Autophagy is a “self-eating” degenerative pathway through which cells digest foreign proteins or organelles to supply amino acids. Autophagy inhibition has been shown inhibitory effect on cancer cells, inducing apoptosis on them, and clinical trials using autophagy inhibitor chloroquine (CQ) or hydroxychloroquine (HCQ) are ongoing in several cancers. The aim of this study is to investigate whether HCQ shows inhibitory effect on PanNET models in vitro and in vivo.

**METHODS:** MIN6 cells and QGP-1 cell were used as in vitro PanNET models. Men1 heterozygous null (Men1+/-) mouse were bred for 18 months and then HCQ 10 mg/kg or saline was intraperitoneally administered for 21 consecutive days. On day 22, mice were sacrificed and whole pancreases were sectioned and histopathologically analyzed.

**RESULTS:** CQ showed inhibitory effect on both PanNET cell lines. Apoptosis was induced and ki-67 labeling index declined. CQ treated cells showed dilated ER and ER stress-mediated proapoptotic protein CHOP was upregulated. In the spontaneous PanNET mouse model, all 18-month-old Men1+/- mice had pancreatic tumors, and HCQ administration decreased mean tumor size. Histological analyses showed more TUNEL positive apoptotic cells in HCQ group than in control group.

**CONCLUSION:** Autophagy inhibition induced apoptosis on PanNET cell lines and mouse model. Inhibitory effect of HCQ might be beneficial on PanNET patients.

