CELL AND MOLECULAR BIOLOGY

Hepatitis C virus entry inhibitor Aryloxazole modulates Autophagy. JAZMIN M. ESCAMILLA1,2, ZONGYI HU2 and JAKE LIANG 2 Department of Biology, Berea College, Berea, KY 404041  Liver Disease Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Health, Bethesda, MD 208142

 Autophagy degrades and recycles cytosolic components and plays a role in the pathogenesis of various diseases including Hepatitis C virus (HCV) infection. HCV can activate the autophagic process which is involved in the replication of HCV. Using high throughput screening, a novel small molecule with aryloxazole moiety (designated as chemotype 6, CT6) was identified as a potent HCV inhibitor. Functional studies demonstrated that CT6 targets HCV at late entry stage (trafficking) of the viral life cycle. We hypothesized that CT6 may interfere with viral trafficking and thus block HCV entry by the modulation of cellular autophagic process. HCV permissive Huh7 cells in culture were used for the study of autophagy modulation. Transfection of autophagy protein plasmids, fluorescent confocal microscopy, and western blot for detecting autophagy marker protein LC3 were used to study the autophagy modulation properties of CT6. Huh7 cells transfected with LC3-RFP and treated with green fluorescent dye bodipy-labelled CT6 showed colocalization of CT6 with LC3. CT6 treatment significantly increased the level of LC3-II in a dose dependent manner. CT6 treatment also appeared to block LC3-II degradation. CT6 appears to modulate autophagy in Huh7 cells through blocking autophagosome fusion with the lysosome. Future studies will characterize the inhibition mechanism of HCV entry by aryloxazole.