Hepatitis C virus (HCV) affects 3% of the world’s population. Natural clearance of HCV is dependent on a broad and strong anti-HCV specific T-cell response. Insulin resistance and abnormal metabolic profiles is associated with impaired HCV specific T-cell responses (Palmer et al., Hepatology 2008). Since the mTOR corporates with PI3K/Akt signaling and participates in glucose metabolism and T-cell effector functions, we hypothesize that the mTOR/PI3K/Akt junction is impaired in HCV infected patients and could negatively impact disease progression. In this study we aimed to: 1), evaluate the distribution of selected components of the mTOR/PI3K/Akt machinery in T-cells and 2), determine if the Akt signaling is impaired in the major T-cell subsets during HCV infection. PMA/Ionomycin activated PBMCs caused a 6.5 and 3 fold increase in the pAkt-S473+CD4+ T-cell population in healthy donors and HCV infected patients, respectively. Similarly, there was a 6.5 fold increase in the pAkt-S473+CD8+ populations in the healthy controls but only a 2 fold increase in the HCV infected patient. Conclusion: Akt signaling in response to mitogenic activation is impaired in CD4 and CD8+ T-cells during chronic HCV infection. We are currently evaluating the integrity of the mTOR/PI3K/Akt signaling in T-cell from HCV infected patients in response to HCV antigenic stimulation and to evaluate its significance on antiviral outcomes.