

Autophagy Contributing to Tumor Recurrence after Radiofrequency Ablation in a Clinically Relevant Murine Model of HCC

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Hepatocellular carcinoma (HCC) is the second leading cause of cancer death worldwide and continues to increase in United States. Radiofrequency ablation (RFA) is a minimally invasive treatment and emerging as the first therapeutic option for primary and metastatic liver cancer when the patients are not suitable for surgical resection. Unfortunately, local recurrence and distant metastasis after RFA has been an issue, especially with larger tumors. The underlying mechanism of tumor recurrence after RFA is not entirely clear. An increasing number of studies have demonstrated that heat stress-induced the generation of heat shock proteins (HSPs), facilitates recovery of tumor cells from heat damage by acting autophagy signaling. Hsp90, member of HSPs superfamily, has been reported to play a critical role in cellular autophagy via regulating the stability and activity of autophagy-related protein. Further studies to explore how RFA affects autophagy and impact HCC tumor relapse might provide significant targets which could be used to improve RFA in the treatment of HCC. In the study, mice with similar tumor size were selected and divided into two groups: one without treatment, one receiving RFA. With optimized parameters of 75°C for 60s, RFA were performed in the mice. Seven days after RFA, all mice were terminated, tumor tissue were collected and used for IHC and electron microscope imaging following the instruction of EMC in University of Missouri-Columbia. Imaging with JEOL JEM-1400 Transmission Electron Microscope was used to detect the alteration and autophagy of different cell types in tissue. Antibodies-mediated IHC staining (Figure 1a) indicated RFA treatment induced dramatic upregulation of HSP90 in tumors. Electro-microscopy is able to detect typical autophagy structures which present in mice from control and experiment groups. But more autophagy cells were observed in in RFA-treated mice (Figure 1b). These preliminary results suggest that effective RFA drives abundance of Hsp90 in tumors which is companied with the occurrence of more autophagy tumor cells. Hsp90 or autophagy might be a useful targets which could be modulated to improve RFA in the treatment of HCC.

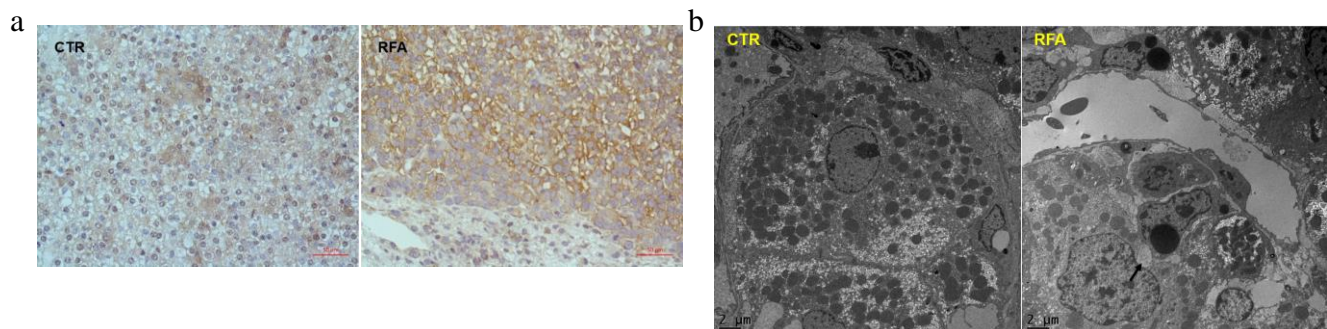


Figure 1. RFA upregulates autophagy through Hsp90 in HCC tumor microenvironment. a. dramatically increased Hsp90 expression is shown by IHC staining with Hsp90 antibody (CST. #4877). b. autophagy structure (black arrow) under electron-microscopy, scale on the images: 2 μM.