Extracellular matrix remodeling and immune reprogramming drive residual tumor progression of liver cancer after incomplete microwave ablation

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Abstract

Although microwave ablation (MWA) constitutes an effective targeted treatment for liver cancer, the mechanisms driving high recurrence rates remain poorly understood. To elucidate these processes, we established an incomplete MWA (iMWA) model in rabbit VX2 tumors and conducted proteomic profiling of residual tumors at Days 3 (D3) and 14 (D14) postablation. By integrating genomic profiles from mouse radiofrequency ablation (RFA) models, we identified 81 and 92 upregulated proteins at D3 and D14, respectively. Functional enrichment analysis (STRING and Enrichr) revealed acute injury response and extracellular matrix (ECM) remodeling predominating at D3, then markedly declining by D14. Conversely, pathways associated with signal transduction, tumorigenesis, and immune pathways were substantially upregulated at D14. Specifically, protein–protein interaction (PPI) analysis revealed that macrophage remodeling and immune checkpoint networks are functionally coupled at D14 to orchestrate an immunosuppressive microenvironment. Stouffer analysis confirmed the shift from matrix remodeling at an early stage to late-stage oncogenic signal transduction and immune suppression at progression. Overall, these findings characterize the dynamic mechanisms of postablation residual tumor growth and highlight potential therapeutic targets to inhibit protumorigenic pathways while enhancing antitumor immunity.