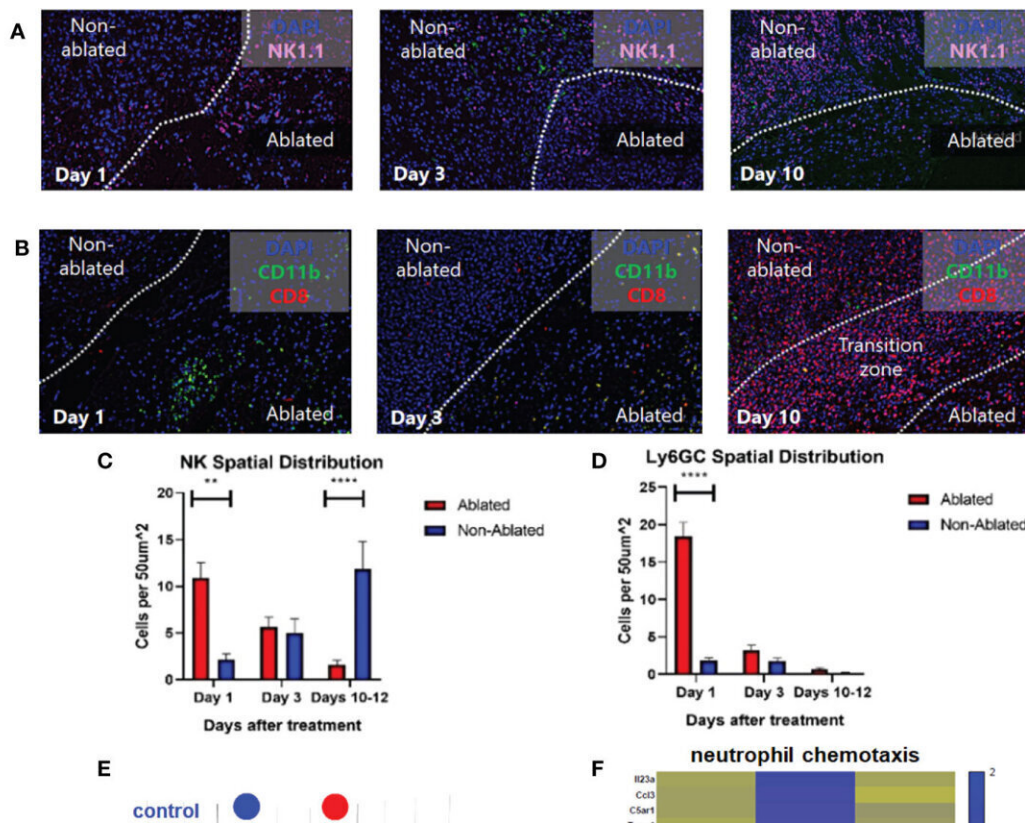


How sound waves trigger immune responses to cancer in mice

January 31 2023



Histotripsy ablation is followed by infiltration of innate and adaptive immune cell populations. Mice bearing bilateral B16F10 tumors were treated with unilateral sham (control) or partial histotripsy ablation on day 10. Multicolor immunofluorescence performed 1, 3 and 10 days after sham or histotripsy partial histotripsy ablation revealed (A) early infiltration of NK1.1+ cells initially localized within the histotripsy ablated zone that gradually migrated outward toward peripheral, non-ablated zones on days 3 and 10, and (B) early and transient infiltration of CD11b+ cells within the histotripsy ablated zone on day 1

and delayed infiltration of CD8+ T cells within the non-ablated zone on day 10. (C) Quantitation of NK1.1+ cells within ablated zones (red) and non-ablated zones (blue) of histotripsy-treated tumors at various time points revealed gradual migration of NK cells away from ablated zones toward non-ablated zones. (D) Quantitation of Ly6GC+ cells at various time points after histotripsy confirmed immediate but short-lived infiltration strictly localized to the ablated zone. (E) RNASeq of CD45+ immune cells performed 3 days after unilateral partial histotripsy ablation revealed marked differences in transcriptional activity between control tumors (blue) and histotripsy-treated ("HT-Tx") tumors (red) as evidenced by principal component analysis. (F) Upregulated transcription of genes associated with neutrophil chemotaxis was observed in histotripsy-treated but not histotripsy-abscopal ("HT-Abs") tumors. (G) Mice bearing bilateral Hepa1-6 tumors were treated with unilateral partial histotripsy ablation on day 10. Flow cytometric analysis of tumor-draining lymph nodes of control (blue), histotripsy-treated (green) and histotripsy-abscopal (red) tumors performed on day 13 revealed significant increases in cDC1 and cDC2 populations within lymph nodes draining histotripsy-treated tumors. (H) Similarly, flow cytometric analysis revealed significant increases in activated CD8+ T cells within lymph nodes draining histotripsy-treated tumors. (n=3-6 mice per group; *=p

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