Hydrogel-assisted mechanical histotripsy for synergistic immune priming strategy

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Recent trials coupling drug delivery systems with ultrasound treatment are actively performed in cancer immunotherapy. One of the nonlinear ultrasonic techniques, histotripsy, is a minimally invasive mechanical approach to the fragmentation of abnormal cancer tissue[1,2]. Although several reports demonstrate that monotherapy of histotripsy enhances antitumor effects in animal models by presenting tumor-specific antigens, danger-associated pattern molecules, or facilitating the release of cytokines, the development of proper drug delivery systems for posing synergistic potential with histotripsy technique is not fully ongoing until nowadays. The development of innovative and effective drug delivery systems for immune priming with histotripsy is therefore highly desirable in immunotherapy field. As a pilot proof-of-concept study, we report a synergistic drug delivery system characterized by hydrogel-assisted histotripsy. The hydrogel is designed by possing thermosensitive properties and loading with immune adjuvant (i.e., Resiquimod, R848) that is one of the typical Toll-like receptor 7/8 agonists for polarizing the innate immune cells[3,4]. Although exact phase of hydrogels' residue in ablated region is not clearly confirmed, our pilot results show that this hydrogels-assisted histotripsy produces abundant region of tumor-related molecules with the coexistence of hydrogels' debris. This priming strategy also induces superior suppressive effects on melanoma tumor as compariosn with monotherapy with either hydrogels or histotripsy. We expect that this priming approach provides a personalized cancer vaccination platform in actual clinical stiuations without anticancer drugs. In the near future, the proposed approach will be combined with blockade therapy using anti-PD-1 to maximize therapeutic potential, as well as validating exact actuation mechanism.

References:

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