1. **No.**

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2. **Title**

   The mechanism for fumor regression by immune adjuvant

3. **Period**

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4. **Summary**

Radiotherapy induces anti-tumor immunity by induction of tumor antigens and damage-associated molecular patterns (DAMP). However, the immune response does not always parallel the inflammation associated with radiotherapy. This lack of correspondence may, in part, explain the radiation-resistance of tumors. Additive immunotherapy is expected to revive tumor-specific CTL facilitating radiation-resistant tumor shrinkage. Herein pre-administration of the double-stranded RNA, polyinosinic-polycytidylic acid (polyI:C), in conjunction with radiotherapy, was shown to foster tumor suppression in mice bearing radio-resistant, ovalbumin-expressing Lewis lung carcinoma (LLC). Extrinsic injection of tumor antigen was not required for tumor suppression. No STING- and CTL-response was induced by radiation in the implant tumor. PolyI:C targeted Toll-like receptor 3 with minimal effect on the mitochondrial antiviral signaling protein pathway. Likewise, the STING pathway barely contributed to LLC tumor suppression. By combination therapy, CTL efficiently infiltrated into tumors with upregulation of relevant chemokine transcripts. Furthermore, polyI:C was shown to stimulate tumor-associated macrophages and release tumor necrosis factor alpha, which acted on tumor cells and increased sensitivity to radiation. Hence, polyI:C treatment prior to radiotherapy potentially induces tumor suppression by boosting CTL-dependent and macrophage-mediated anti-tumor responses. We have created a non-inflammatory dsRNA-based adjuvant ARNAX. Eventually, ARNAX and radiotherapy in combination would be a promising therapeutic strategy for radiation-resistant tumors.