Biomaterials to boost robust cancer immunotherapy to inhibit tumor metastasis and recurrence after local radioisotope therapy

With the support by the National Natural Science Foundation of China, the research team led by Prof. Liu Zhuang (刘庄) from the Institute of Functional Nano & Soft Materials (FUNSOM), in collaboration with Prof. Yang Kai (杨凯) from the School of Radiation Medicine and Protection, both at Soochow University, developed a biomaterial-based radio-immunotherapy strategy to effectively inhibit tumor metastasis and recurrence after local tumor treatment. This work was recently published in *Nature Biomedical Engineering* (2018, 2: 611—621).

Radiotherapy including external beam radiotherapy and internal radioisotope therapy has been extensively used for cancer treatment in clinics. Unfortunately, the clinically used cancer radiation therapy has many limitations including damages to normal tissues, resistance by hypoxic solid tumors, and incapability of treating distant metastases. In order to overcome these changllenges, Catalase (Cat), an enzyme that converts tumor endogenous H_2O_2 into oxygen, is labeled with a therapeutic radioisotope ^{131}Iodine, and then mixed with sodium alginate (ALG), a soluble polysaccharide that can be rapidly transformed into a hydrogel in the presence of Ca^{2+}. After injection into tumors, the *in-situ* gelation of ALG would fix ^{131}I-Cat locally within tumors, resulting in long-term relief of tumor hypoxia and 100% tumor elimination under rather low radioactivity doses, as demonstrated in mouse, patient-derived xenograft, and rabbit tumor models. By further introducing an immunostimulatory CpG oligonucleotide, local treatment with ^{131}I-Cat/CpG/ALG hybrid fluid after eliminating local tumors could trigger systemic antitumor immunities, which in combination with checkpoint-blockade would attack distant tumors for metastasis inhibition. Afterwards, a strong vaccine-like immune-memory effect to protect mice against tumor re-challenging is further realized.

This work presents a simple *in-situ* gelation-based radioisotope-immunotherapy strategy using all-biocompatible components to achieve highly effective local tumor treatment, as well as systemic therapeutic outcomes in inhibiting tumor metastasis and preventing tumor recurrence. This method may have potential for tumor interventional therapy to treat many types of solid tumors, and would be particularly meaningful for those late-stage cancer patients who are not curable by conventional surgery or radiotherapy strategies. One important note is that all the components used in this strategy are biocompatible, promising for clinical translation.

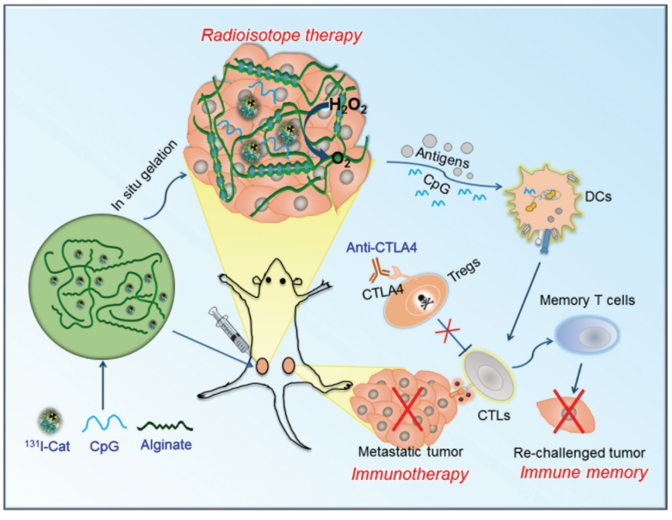

Figure Mechanism of ^{131}I-Cat/CpG/ALG-based radio-immunotherapy in combination with checkpoint blockade to inhibit tumor metastasis and recurrence.