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Enhancing Cancer Response to Immune Checkpoint Inhibitors and Radiation Therapy

Inventors

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Patent status:
Patent for Flagrp170 issued: U.S. rights are available.

Patent for anti-SRA antibody pending: U.S. and foreign rights are available.

License status:
These technologies are available for licensing to industry for further development and commercialization.

Category:
Cancer Treatment

VCU Tech #:
WAN-12-007F, WAN-18-113, WAN-19-014, and WAN-19-032F

***In vitro* and *in vivo* data available**

Overview

Xiang-Yang (Shawn) Wang, PhD, Professor, Department of Genetics, Immunology, and Radiation Oncology, Virginia Commonwealth University, a recognized expert in the study of cancer immunology, has developed a unique immunotherapeutic agent and a novel antibody that improve the benefits of immunotherapy and radiotherapy to a wider population of cancer patients.

Immunotherapy is a fourth treatment modality for advanced cancers and immune checkpoint inhibitors (ICIs) have significantly improved the prognosis of patients; however, only a small subset of 20-30% of patients responds to such a treatment. The overall response rate is extremely poor in other less immunogenic cancers, including prostate cancer, breast cancer, and pancreatic cancer.

The novel immunostimulatory agent, Flagrp170, created by Dr. Wang, possesses distinct features that are essential for effectively mounting a cytotoxic T lymphocyte response by promoting cross-presentation of weakly immunogenic tumor antigens and concurrent activation of dendritic cells *via* co-stimulation. ***In situ* immune reprogramming with the Flagrp170 can re-shape the tumor environment and transform immunologically *'cold'* tumors to *'hot'* ones, which become highly responsive to ICIs.**

In addition to Flagrp170, unique anti-SRA (scavenger receptor A or CD204) antibodies have been developed, which not only highly sensitize the immunologically *'cold'* cancer to ICI therapy through the blockade of SRA function on myeloid cells, but also improves tumor response to radiotherapy and reduces cancer recurrence following radiotherapy.

Radiation therapy is used to treat 50% of cancer patients and achieving loco-regional tumor control is the primary goal of radiation therapy. However, recurrence within the radiation treatment field remains a serious problem for several cancers. The VCU-developed anti-SRA antibodies can combat this problem.

Key features

Immunostimulatory agent, Flagrp170

- Reprograms the tumor immune environment to induce expansion and recruitment of tumor-reactive T-cells; highly sensitizing the immunologically *'cold'* cancer
- Improves the responsiveness of cancers that are otherwise resistant to ICIs
- Can be used as an immunotherapeutic agent on its own
- Prevents patient relapse when used in conjunction with other treatment modalities
- Can be administered to tumor sites to induce systemic antitumor immunity

Anti-SRA antibody

- Reprograms and creates an immune-inflamed tumor environment
- Improves the low response rate in cancer patients undergoing ICI therapy
- Can promote antitumor immune response and inhibits cancer recurrence
- Can block tumor revascularization and enhance radio-sensitization
- Improves treatment outcomes in patients undergoing radiation therapy

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Patent estate

The immunostimulatory agent, Flagrp170, is protected by an extensive international patent estate. Issued patents and patent applications ensure patent protection until 2034 at a minimum with the potential for additional protection. The patent estate claims cover both compositions of matter and methods of use.

A patent for the utilization of a short-hairpin RNA (shRNA) to downregulate/silence SRA in dendritic cells for enhancing an immune response to antigen targets is patent protected until 2028 at a minimum.

Additional information about the patent estate is available upon request.

Data, additional info

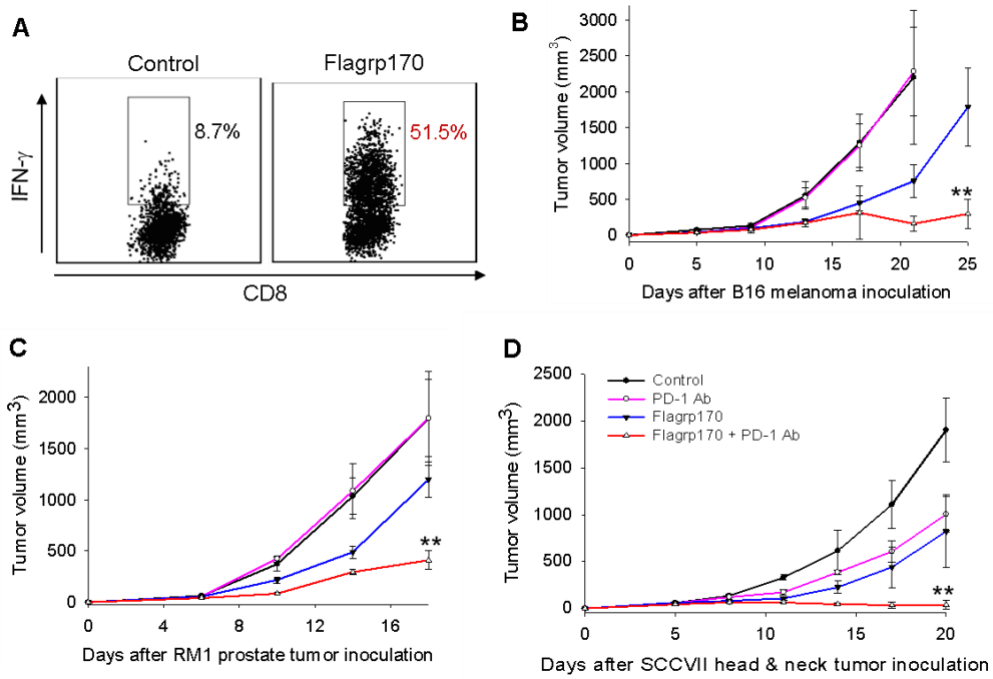

Figure 1. In situ Flagrp170 therapy creates a CD8⁺ T cell-inflamed tumor environment (A) and highly sensitizes tumor response to the PD-1 inhibitors (B-D), as indicated by profound inhibition of melanoma (B), prostate cancer (C), head and neck cancer (D). **, combination *vs* anti-PD-1 treatment, $p < 0.01$

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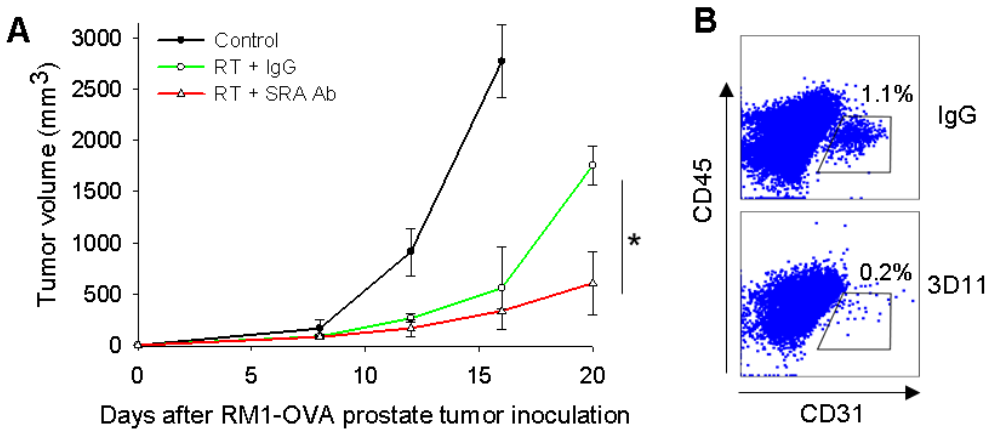

Figure 2. Antibody blockade of SRA enhances treatment outcome of radiation therapy (RT, A) by inhibiting tumor revascularization, indicated by impaired recruitment of CD31$^+$ endothelial cells following RT (B).

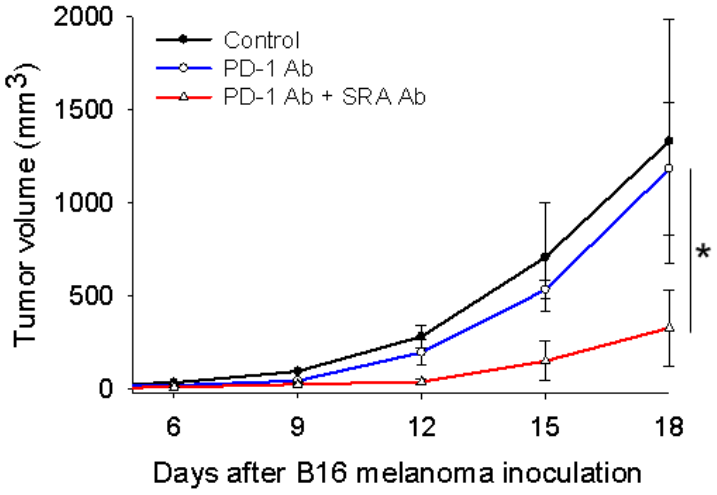

Figure 3. Antibody blockade of SRA enhances melanoma responsiveness to the PD-1 inhibitor, indicated by potent tumor suppression upon combined treatment with anti-SRA antibodies and anti-PD-1 antibodies.

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Selected Publications

- Wang XY & Subjeck JR. High molecular weight stress proteins: Identification, cloning and utilisation in cancer immunotherapy. *International Journal of Hyperthermia* 2013; 29(5): 364-375.

- Yu X, Subjeck JR and Wang XY. Integrating a "danger" signal into cross-priming chaperone Grp170 to achieve therapeutic vaccination. *Expert Reviews on Vaccines* 2013, 12(6):581-583

- Yu X, Guo C, Yi H, Qian J, Fisher PB, Subjeck JR, and Wang XY. A multifunctional chimeric chaperone serves as a novel immune modulator inducing therapeutic antitumor immunity. *Cancer Research* 2013, 73(7): 2093-2103

- Wang H, Pezeshki AM, Yu X, Guo C, Subjeck JR, Wang X-Y. The endoplasmic reticulum chaperone GRP170: from immunobiology to cancer therapeutics. *Front. Oncol.*2014; 4:377.

- Wang XY, Facciponte JG, Chen X, Subjeck JR and Repasky EA. Scavenger receptor-A negatively regulates tumor immunity. *Cancer Research* 2007, 67(10):4996-5002.

- Yi H, Guo CQ, Yu X, Gao P, Qian J, Zuo D, Manjili MH, Fisher PB, Subjeck JR and Wang XY. Targeting the immunoregulator SRA/CD204 potentiates specific dendritic cell vaccine-induced T cell responses and antitumor immunity. *Cancer Research* 2011, 71(21):6611-6620.

- Yu X and Wang XY. Antagonizing the innate pattern recognition receptor CD204 to improve dendritic cell-targeted cancer immunotherapy. *OncoImmunology* 2012, 1(2): 771-773.

- Zheng Y, Li X, Pagare PP, Yuan Y, Wang XY, Zhang Y. Design, synthesis, and characterization of rhein analogs as novel inhibitors of scavenger receptor A. *Bioorganic & Medicinal Chemistry Letters* 2017; 27(1):72-76.

- Pagare PP, Zaidi SA, Zhang X, Li X, Wang XY, Zhang Y. Understanding molecular interactions between scavenger receptor A and its natural inhibitors through molecular modeling studies. *J Mol Graph Model* 2017; 77: 189-199.

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