

POSTER PRESENTATION

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# Activation of innate and adaptive immunity as an effective combined strategy for cancer immunotherapy

Alexander Rakhmilevich<sup>1\*</sup>, Mildred Felder<sup>1</sup>, Lauren Lever<sup>1</sup>, Tyler Van De Voort<sup>1</sup>, Alan J Korman<sup>2</sup>, Stephen D Gillies<sup>3</sup>, Paul M Sondel<sup>4</sup>

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Immunotherapeutic approaches can demonstrate some antitumor benefit, but their efficacy is limited when they are used as a single modality. We asked if a combinatory approach activating both innate and adaptive immunity would improve cancer immunotherapy. We have previously shown that an agonistic anti-CD40 monoclonal antibody (anti-CD40) in combination with a toll-like receptor 9 agonist, CpG, can activate macrophages in mice, leading to tumor cell killing. Separately, we have shown that a direct intratumoral injection of an immunocytokine (IC) consisting of anti-GD2 antibody linked to interleukin-2 can activate NK and T cells, resulting in antitumor effects. We hypothesize that activation of macrophages (with anti-CD40/CpG) and NK cells (with IC) will increase tumor destruction and presentation of tumor antigens, leading to T cell activation, which in turn could be further augmented by anti-CTLA-4 antibody, resulting in tumor eradication and prevention of tumor recurrence. Using the mouse GD2<sup>+</sup> B78 melanoma model, we show that anti-CD40/CpG and IC/anti-CTLA-4 synergistically induced regression of established subcutaneous tumors, resulting in the cure of 50% of mice and development of immunological memory against B78 as well as wild type B16 tumors. While the antitumor effect of anti-CD40/CpG was T cell independent, the antitumor effect of IC/anti-CTLA-4 required T cells. Anti-CD40/CpG treatment led to upregulation of T cell activation markers in draining lymph nodes. Finally, the combined treatment with anti-CD40/CpG and IC/anti-CTLA-4 was effective against B16 lung

metastases. We suggest that a combination of anti-CD40/CpG and IC/anti-CTLA-4 should be tested as a clinically relevant novel treatment strategy.

#### Authors' details

<sup>1</sup>UW-Madison, Madison, WI, USA. <sup>2</sup>Bristol-Myers Squibb Company, Redwood City, CA, USA. <sup>3</sup>Provenance Biopharmaceuticals, Carlisle, MA, USA.

<sup>4</sup>Department of Human Oncology, Department of Pediatrics, University of Wisconsin-Madison, Madison, WI, USA.

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<sup>1</sup>UW-Madison, Madison, WI, USA

Full list of author information is available at the end of the article



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