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Dual-targeting nanoparticles for reprogrammed T cell responses in the tumor microenvironment

Alyssa K Kosmides[1*], Jonathan Schneck[2]

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One of the largest obstacles in cancer immunotherapy involves overcoming the immunosuppressive tumor microenvironment [1]. While many therapies are focused primarily on activating antigen-specific CD8+ T cells, the tumor microenvironment often expresses immunosuppressive cytokines and other immunoregulatory proteins such as checkpoint blockade molecules that diminish their effects [2]. Programmed death ligand 1 (PD-L1) is an inhibitory checkpoint molecule upregulated on many cancers, including melanoma, ovarian cancer, and renal cancer [3]. This can shield a tumor from immune attack by binding to its receptor, PD-1, on T cells. We have developed a nanoparticle platform that combines blockade of PD-L1 with the T cell co-stimulatory signal, anti-4-1BB. This dual targeting system redirects effector cells to recognize target cells while simultaneously blocking checkpoint inhibitors. Antagonistic anti-PD-L1 antibodies and agonistic anti-4-1BB antibodies are conjugated to the surface of biocompatible 50-100 nm iron dextran nanoparticles. The nanoparticles cause a 6-fold increase in IFN-γ production by CD8+ T cells with an exhausted phenotype in the presence of tumor cells *in vitro*. Additionally, we have shown tumor suppression and a 30% decrease of PD-1 expression in tumor infiltrating lymphocytes in an *in vivo* B16 mouse melanoma model. This approach may not only reprogram local signaling within the tumor microenvironment, but also promote polyclonal cytotoxic T cell responses in the absence of defining the antigenic specificity of the infiltrating T cells.

Authors' details
[1]Johns Hopkins University, Baltimore, MD, USA. [2]Johns Hopkins School of Medicine, Department of Pathology, Institute for Cell Engineering, Baltimore, MD, USA.

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References

1. Rabinovich GA, Gabrilovich D, Sotomayor EM: **Immunosuppressive strategies that are mediated by tumor cells.** *Annu Rev Immunol* 2007, **25**:267-96.
2. Freeman GJ, Sharpe AH, Kuchroo VK: **Protect the killer: CTLs need defenses against the tumor.** *Nat Med* 2002, **8**:787-9.
3. Kamphorst AO, Ahmed R: **Manipulating the PD-1 pathway to improve immunity.** *Curr Opin Immunol* 2013, 1-8.

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[1]Johns Hopkins University, Baltimore, MD, USA
Full list of author information is available at the end of the article