

POSTER PRESENTATION

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Blockade of surface bound TGF- β abrogates Treg suppression of effector T cell function within the tumor microenvironment

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Regulatory T cells (Treg) play a role in suppression of anti-melanoma immunity; however, the exact mechanism is poorly understood. Through intravital two photon microscopy, we found that tumor-specific Pmel-1 effectors engage in cell-cell interactions with tumor resident Tregs. To determine if contact between Tregs and Teff hinders killing of tumor cells *in vivo*, we utilized *ex-vivo* three-dimensional collagen-fibrin gel cultures of B16 melanoma cells. Collagen-fibrin gel cultures recapitulated the *in vivo* suppression, rendering the dissociated tumor resistant to killing by *in vitro* activated antigen specific T cells. *In vivo* depletion of Tregs in Foxp3-DTR mice prior to tumor excision reversed the suppression. *In vivo* modulation of Tregs by GITR ligation had a similar effect, reducing the number of intra-tumor Tregs leading to ex-vivo tumor killing. Using neutralizing antibodies, we found that blocking TGF- β reversed the suppression. In addition, soluble factors from collagen-fibrin gel tumors do not inhibit killing suggesting that suppression is contact or proximity dependent. The CD8 T cells recovered from these gels exhibit a decrease in Granzyme B expression and an increase in expression of T cell exhaustion marker PD-1. These findings support the conclusion that intra-tumor contact with Tregs during the effector phase of the immune response is responsible for inhibiting anti-melanoma immunity in a TGF- β dependent manner shedding light into novel ways to inhibit intratumoral Tregs.

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