

Intra-tumoral IL-12 promotes CD8+ T Effector/Memory Cell-mediated, IFN-gamma and FASL dependent elimination of CD4+CD25+Foxp3+ T-suppressor cells from tumors.

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Immunology and Microbiology

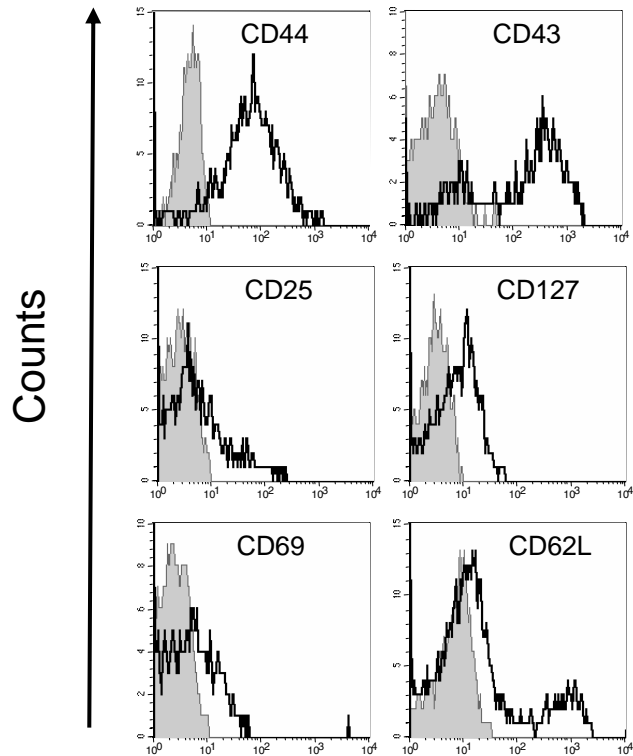
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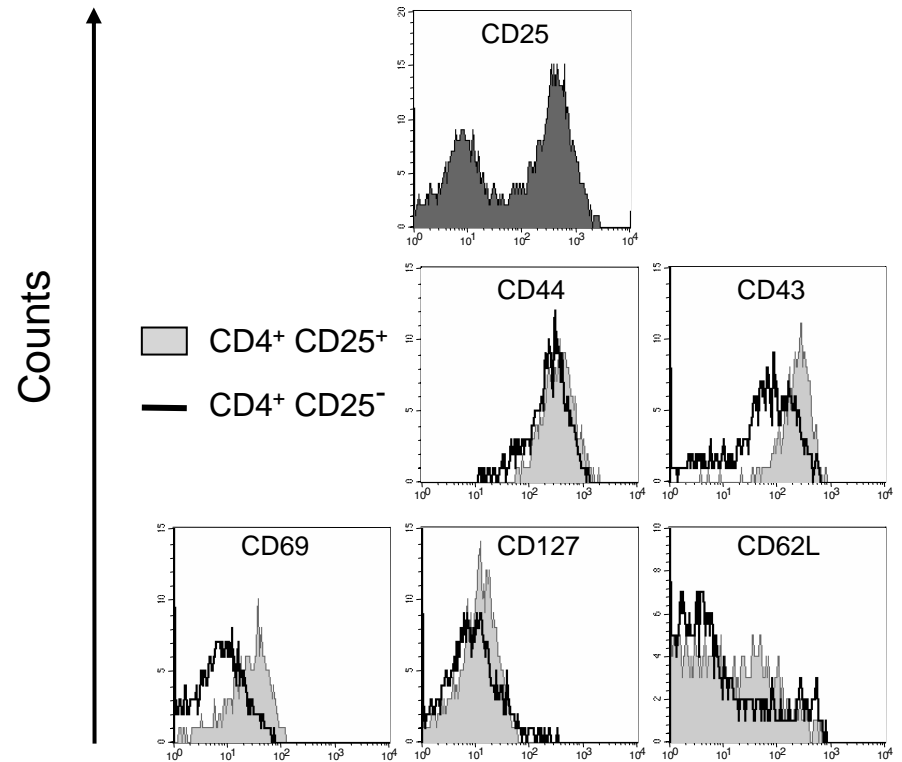
University at Buffalo
The State University of New York

Tumors are Infiltrated by CD8+/CD4+ CD25- Tem and CD4+CD25+ T-effector/suppressor Cells

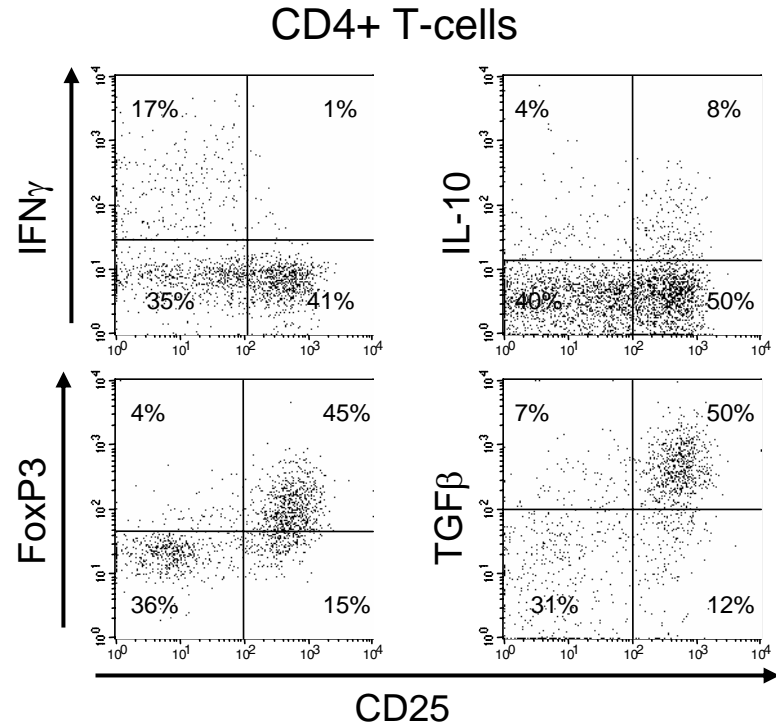
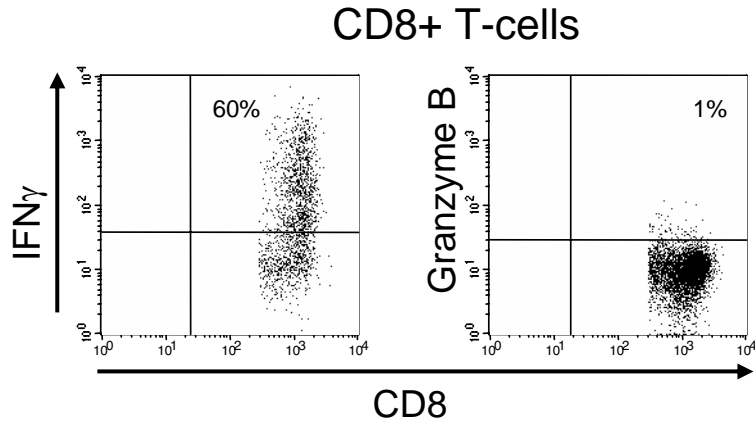
CD8+ T cells



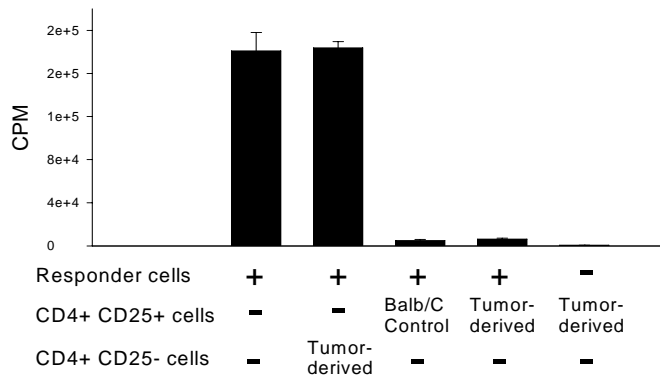
CD4+ T cells



CD8+/CD4+ Tem are Functionally Impaired Whereas CD4+ CD25+ T-cells Demonstrate Suppressive Activity



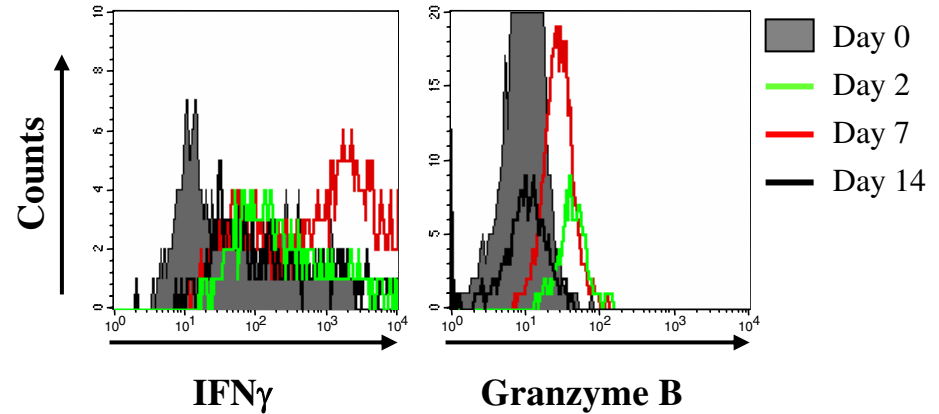
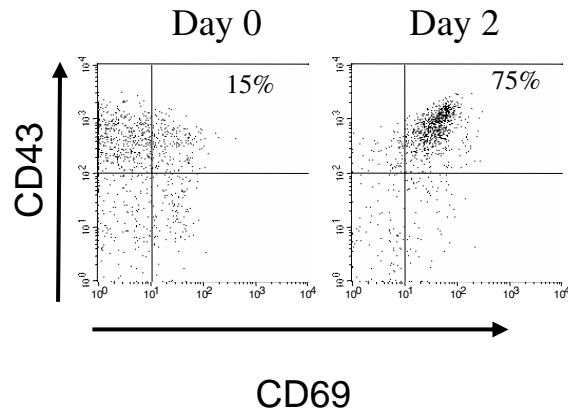
CD4+ CD25+ Suppression assay



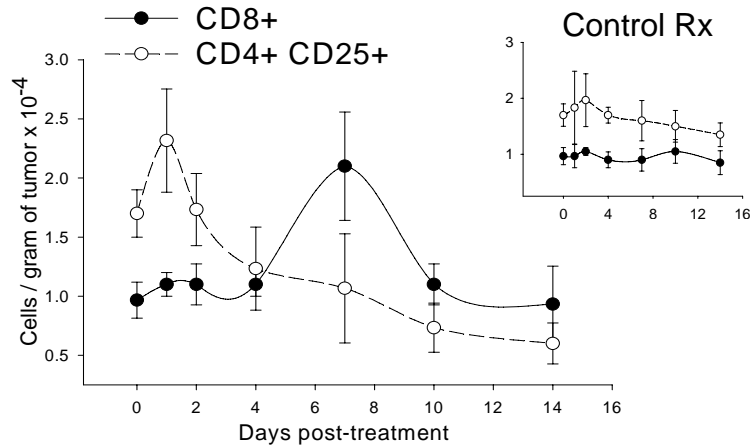
| | | | | | |
|------------------|---|---------------|----------------|---------------|---------------|
| Responder cells | + | + | + | + | - |
| CD4+ CD25+ cells | - | - | Balb/C Control | Tumor-derived | Tumor-derived |
| CD4+ CD25- cells | - | Tumor-derived | - | - | - |

Intra-tumoral IL-12 Induces CD8+ T-cell Activation and Tsuppressor Cell Elimination

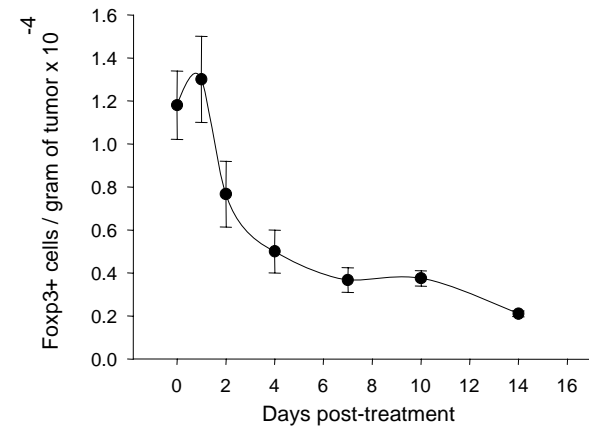
Post-Rx CD8+ T-cell Activation



Post-Rx T-cell kinetics

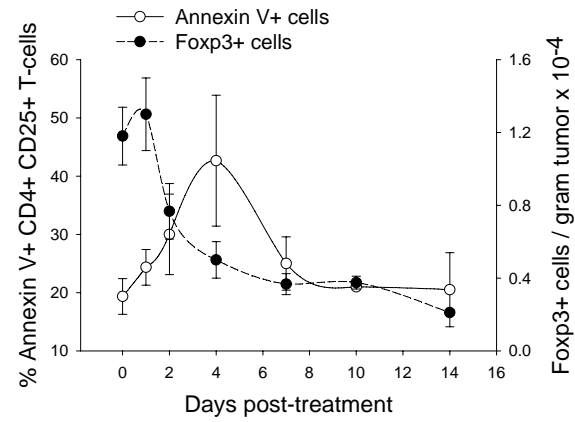


Post-Rx Foxp3+ Tsuppressor kinetics



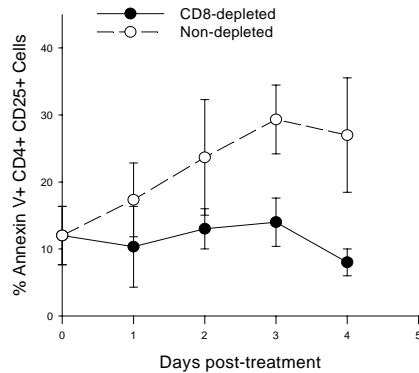
Tsupp Loss is Associated with Apoptotic Cell Death

Annexin V binding to Tsupp

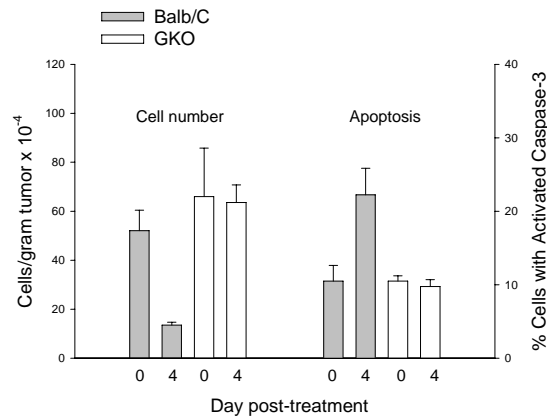


IL-12-induced T-suppressor Cell Apoptosis is CD8+ T-cell, IFN γ and FasL-dependent

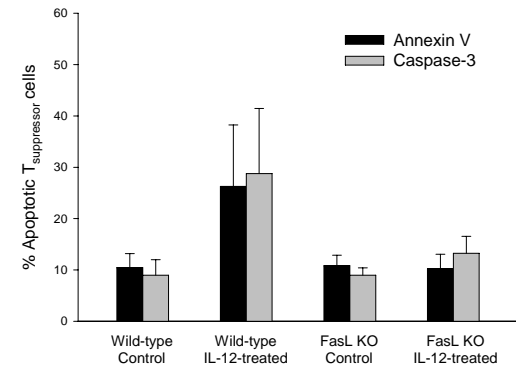
CD8+ T-cells



IFN γ



FasL



Summary

- Tumors are infiltrated by functionally-impaired CD8/CD4 Tem and fully-active Tsupp.
- Intra-tumoral IL-12 induces the activation of pre-existing Tem, elimination of Tsupp and infiltration of CD8+ Teff.
- Elimination of Tsupp is due to apoptotic death and is dependent on pre-existing CD8+ Tem, IFN γ and FasL.



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