

Presenter Disclosure Information

Amir A. Al-Khami, PhD

The following relationships exist related to this presentation:

No relationships to disclose



Metabolic Inhibition of Cancer-Associated Myeloid-Derived Suppressor Cells

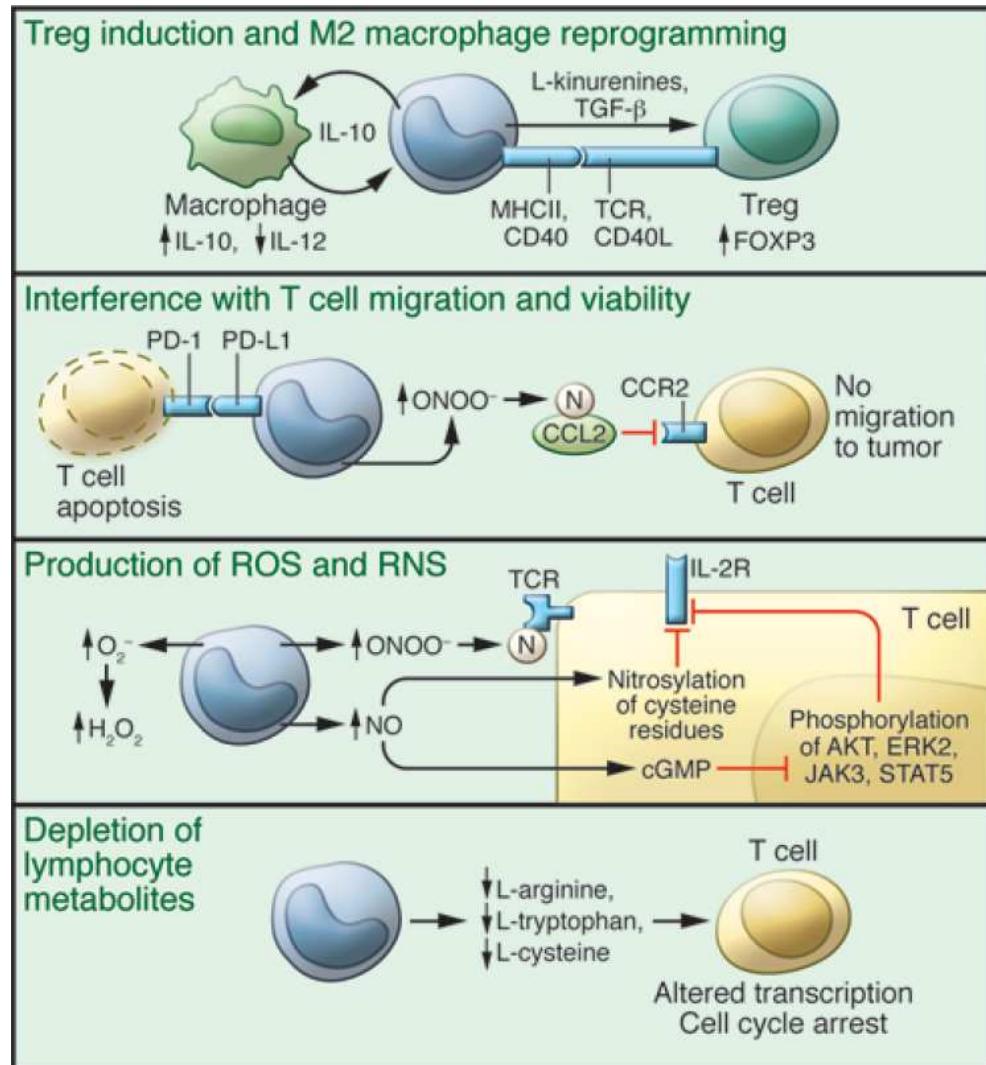
Poster #411

Amir A. Al-Khami, PhD

Stanley S. Scott Cancer Center
LSU Health Sciences Center - New Orleans

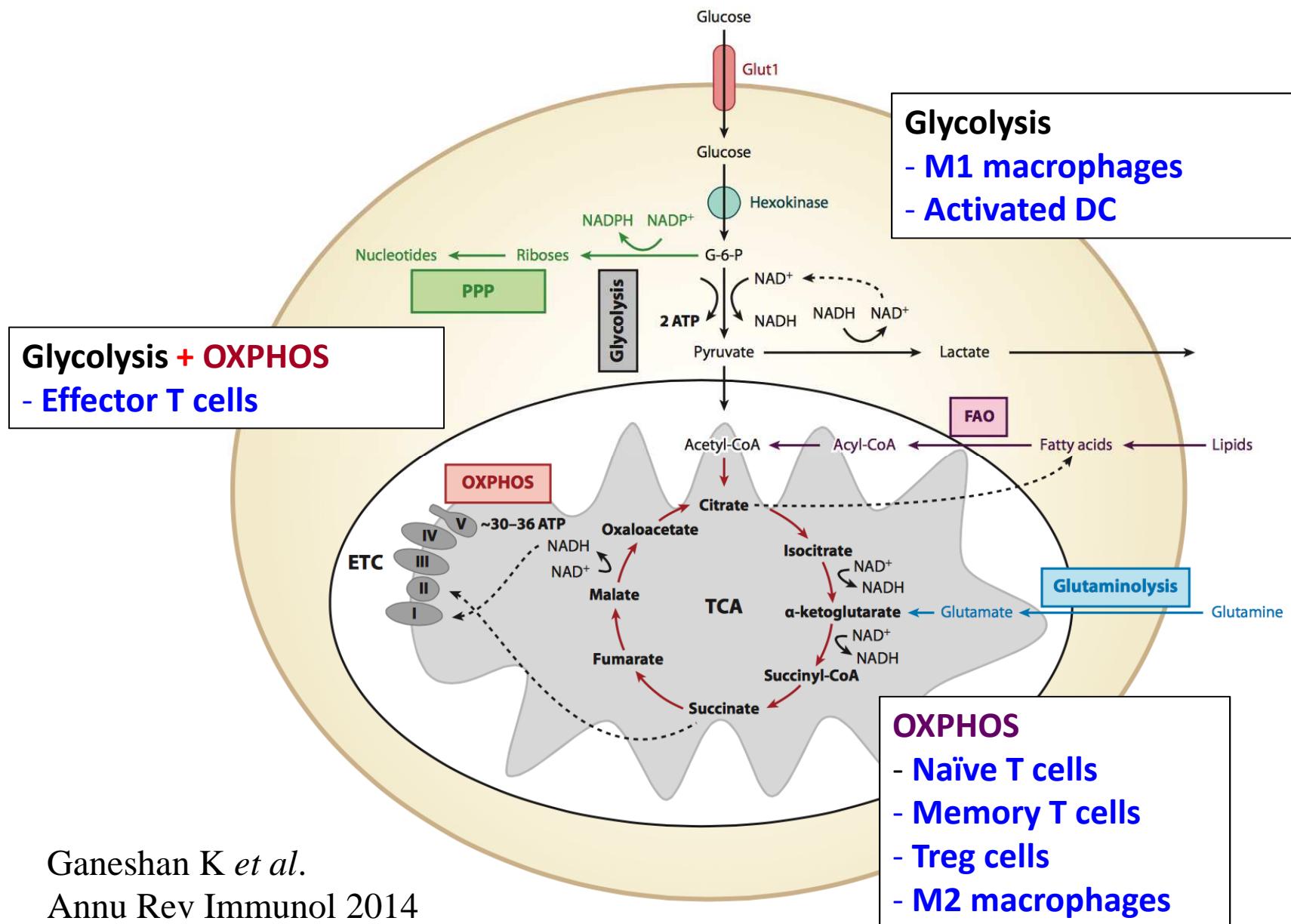
Myeloid-derived suppressor cells (MDSC)

- Represent a heterogeneous population of myeloid progenitor cells that accumulate in inflammation, infection, and cancer.
- Consist of granulocytic MDSC and monocytic MDSC.
- Possess a remarkable ability to block T cell antitumor immunity using multiple mechanisms.
- Approaches to blocking MDSC are limited and not completely effective.



Ugel S *et al.* J Clin Invest 2015

Metabolism drives the differentiation and function of immune cells



Ganeshan K *et al.*
Annu Rev Immunol 2014

Gap of knowledge:

The metabolic characteristics of MDSC remain unknown?

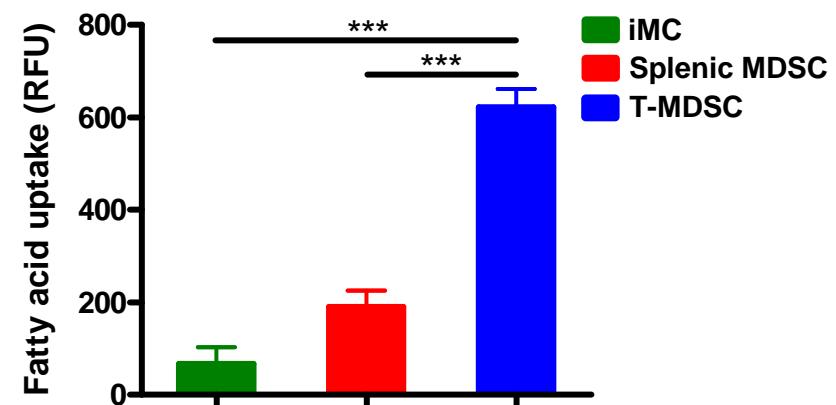
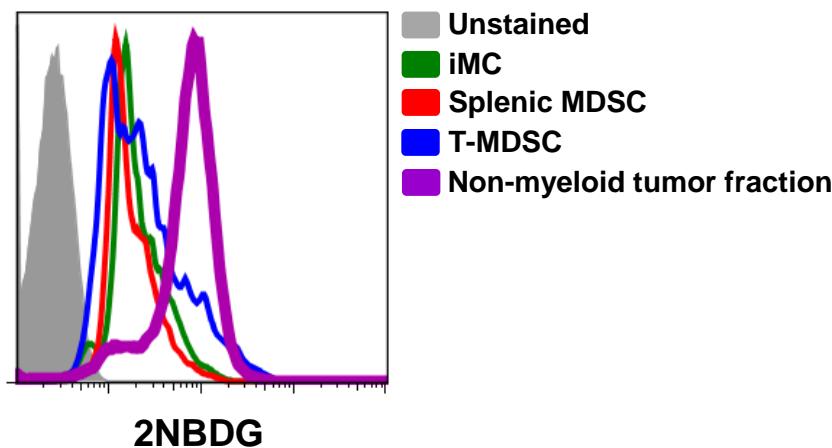
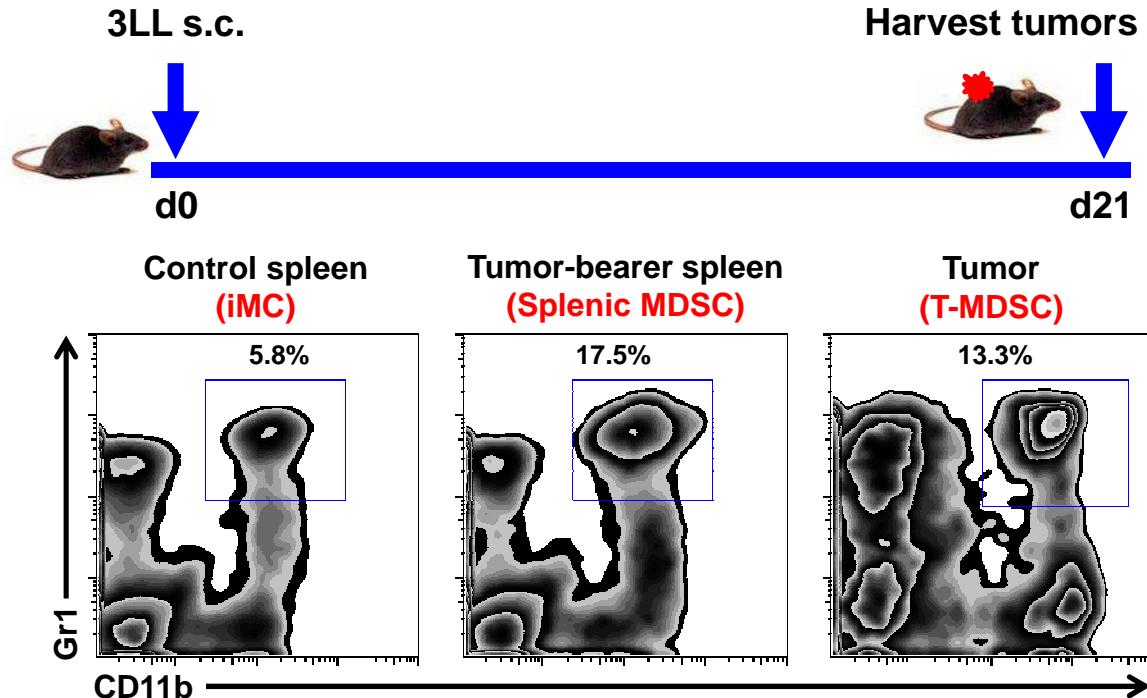
Study questions

- ? Characterize the major energy metabolic pathway used by tumor-associated MDSC (T-MDSC)**
- ? Determine whether inhibition of this pathway blocks the immunosuppressive function of T-MDSC**
- ? Test whether inhibition of this pathway enhances anti-tumor therapies**

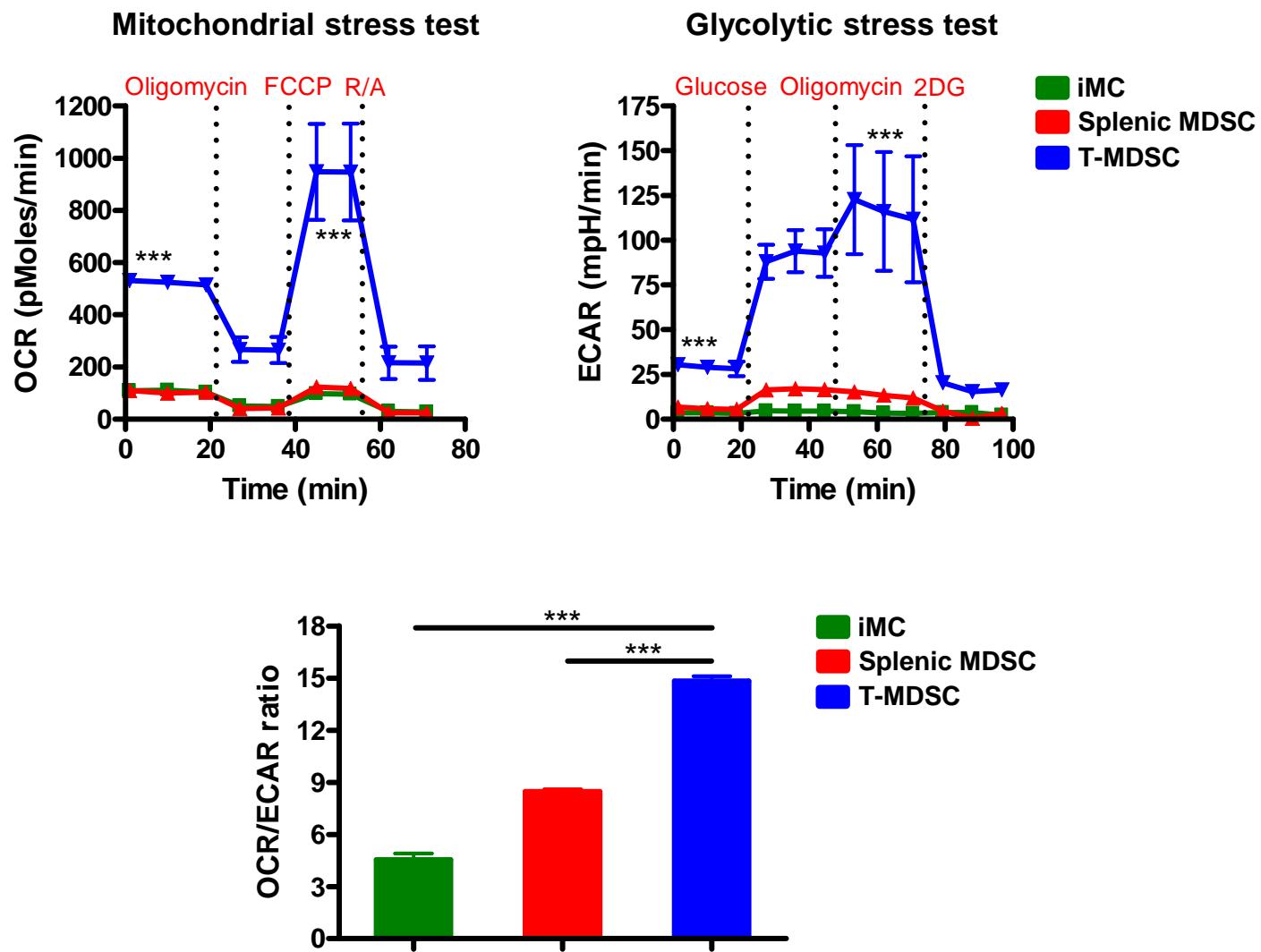
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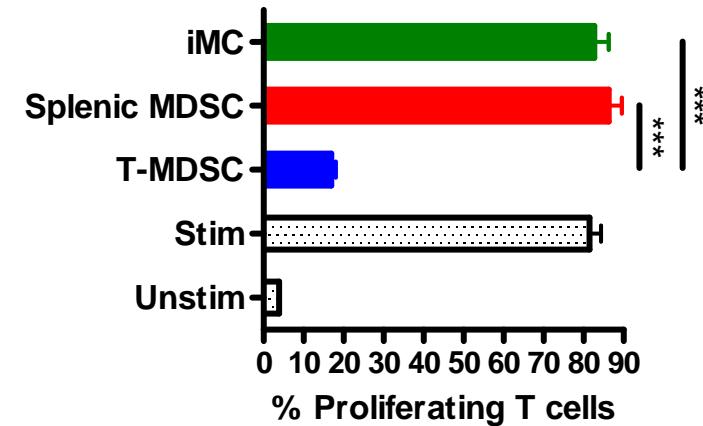
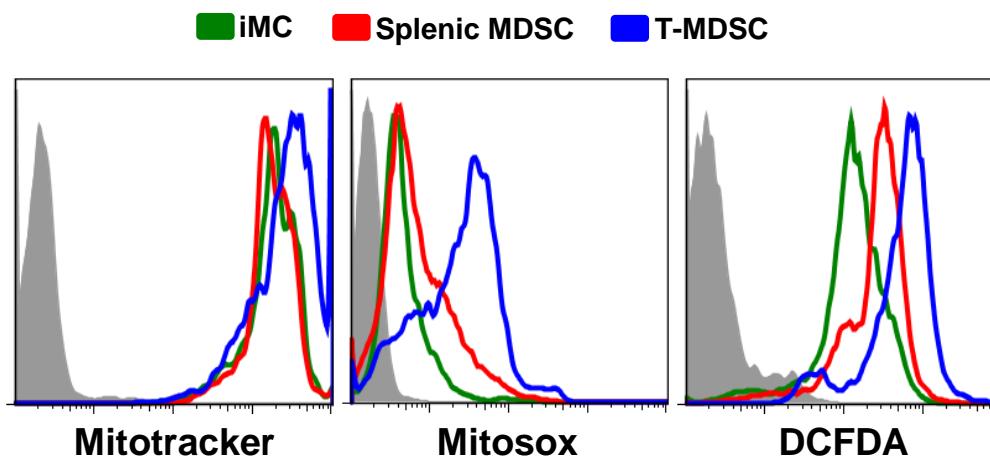
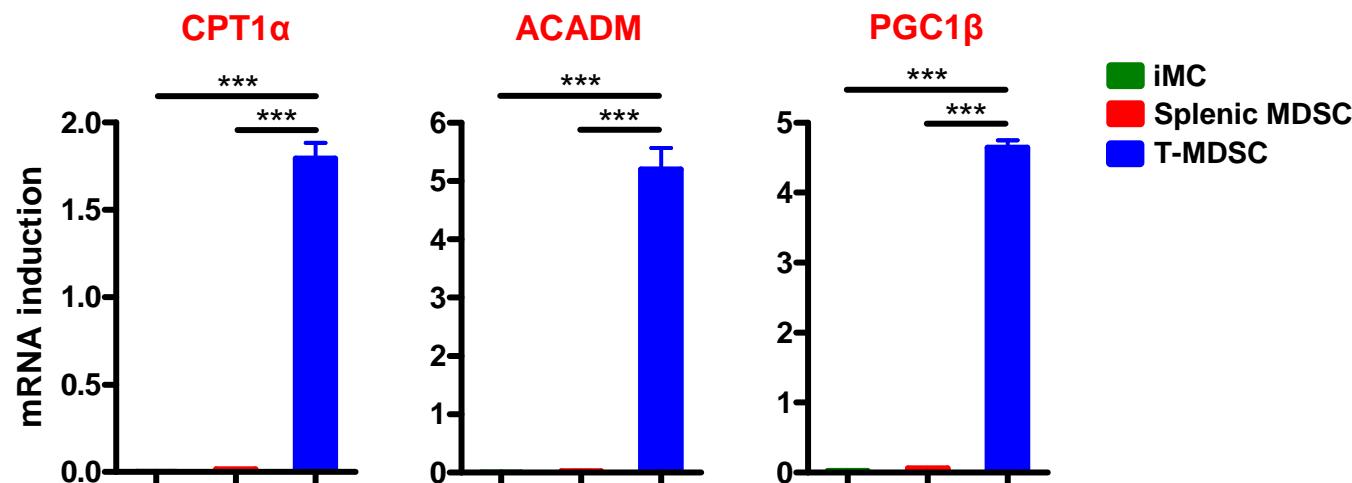
T-MDSC display an increased fatty acid uptake and fatty acid oxidation (FAO)



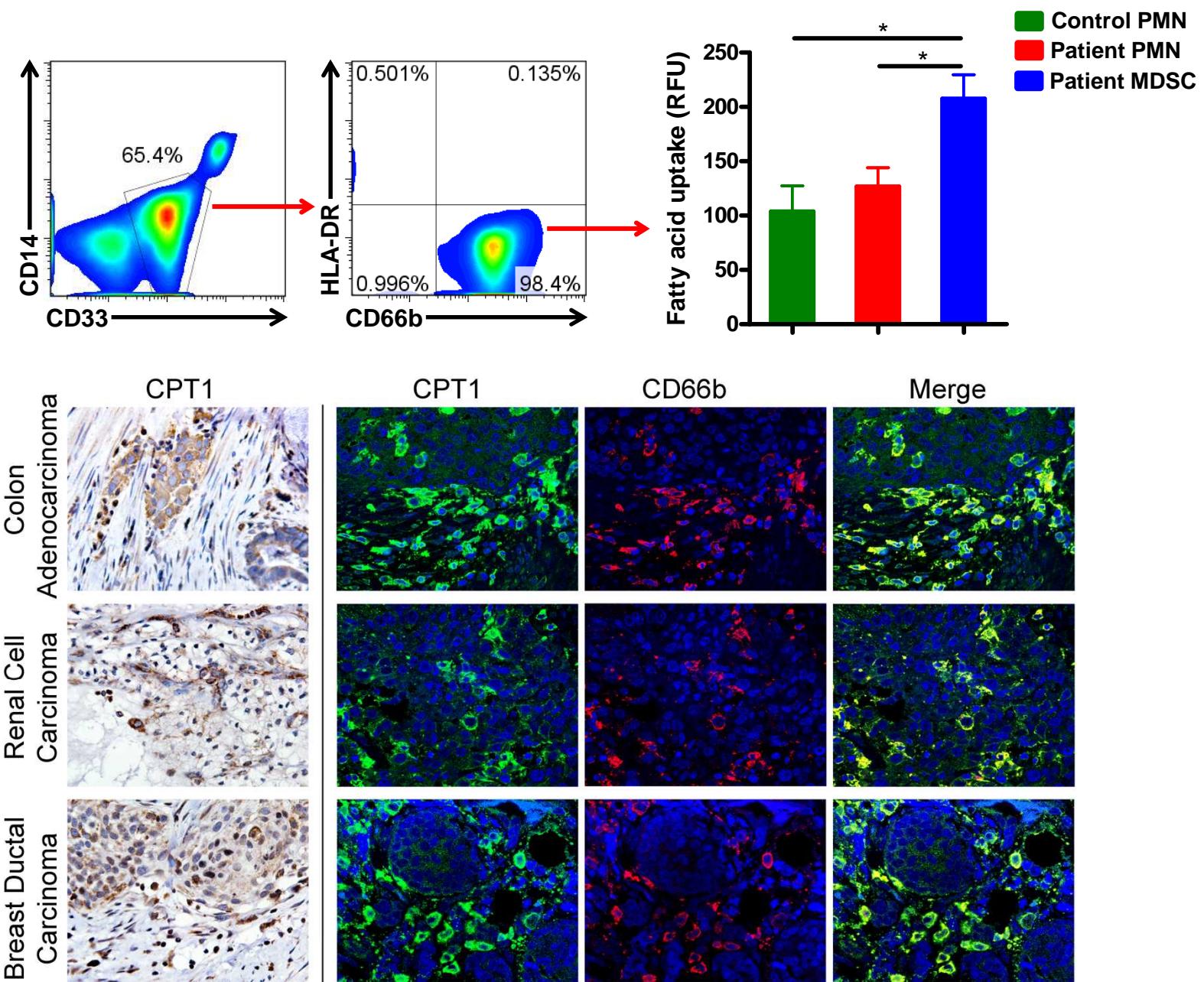
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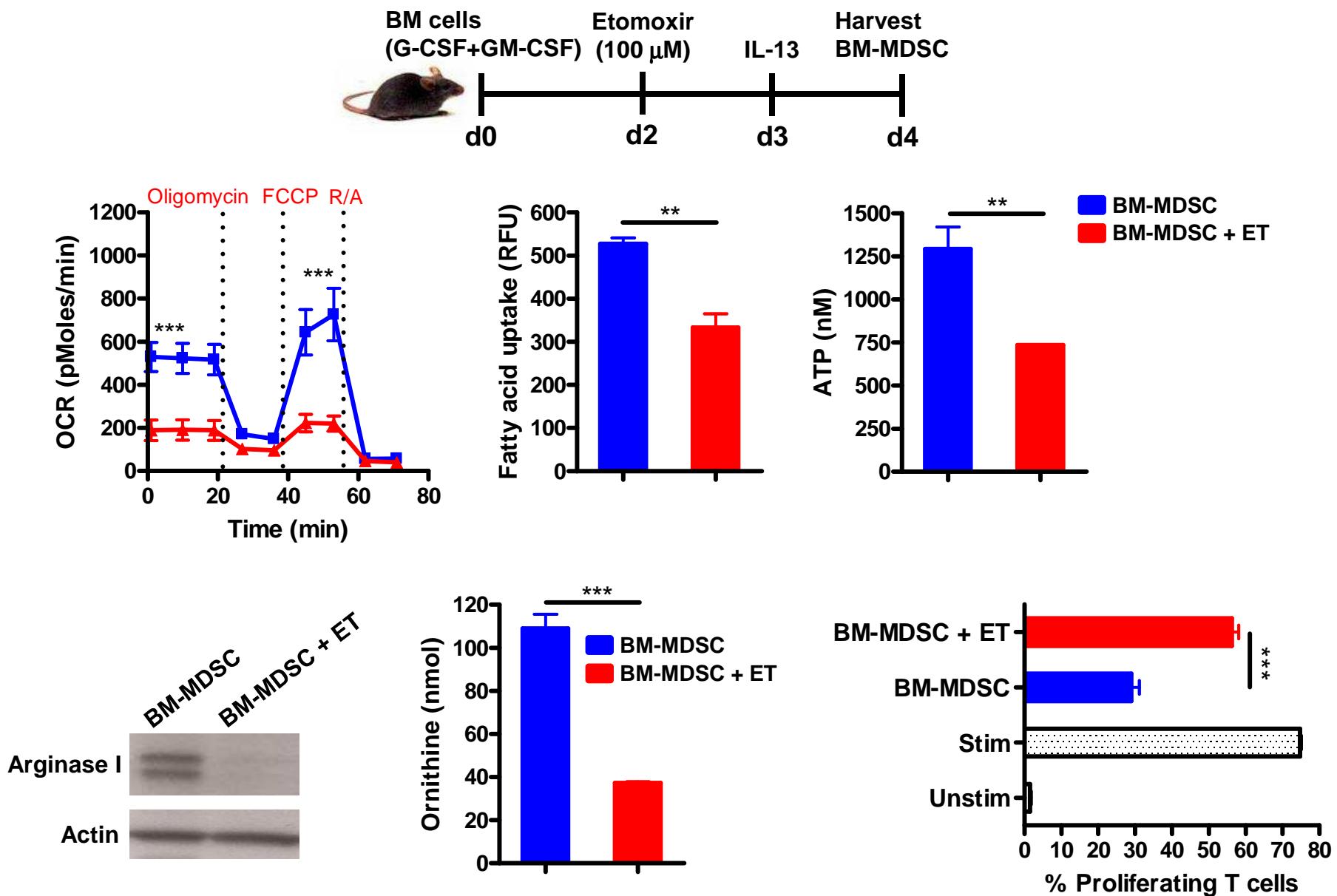
Human MDSC increase fatty acid uptake and FAO enzyme expression



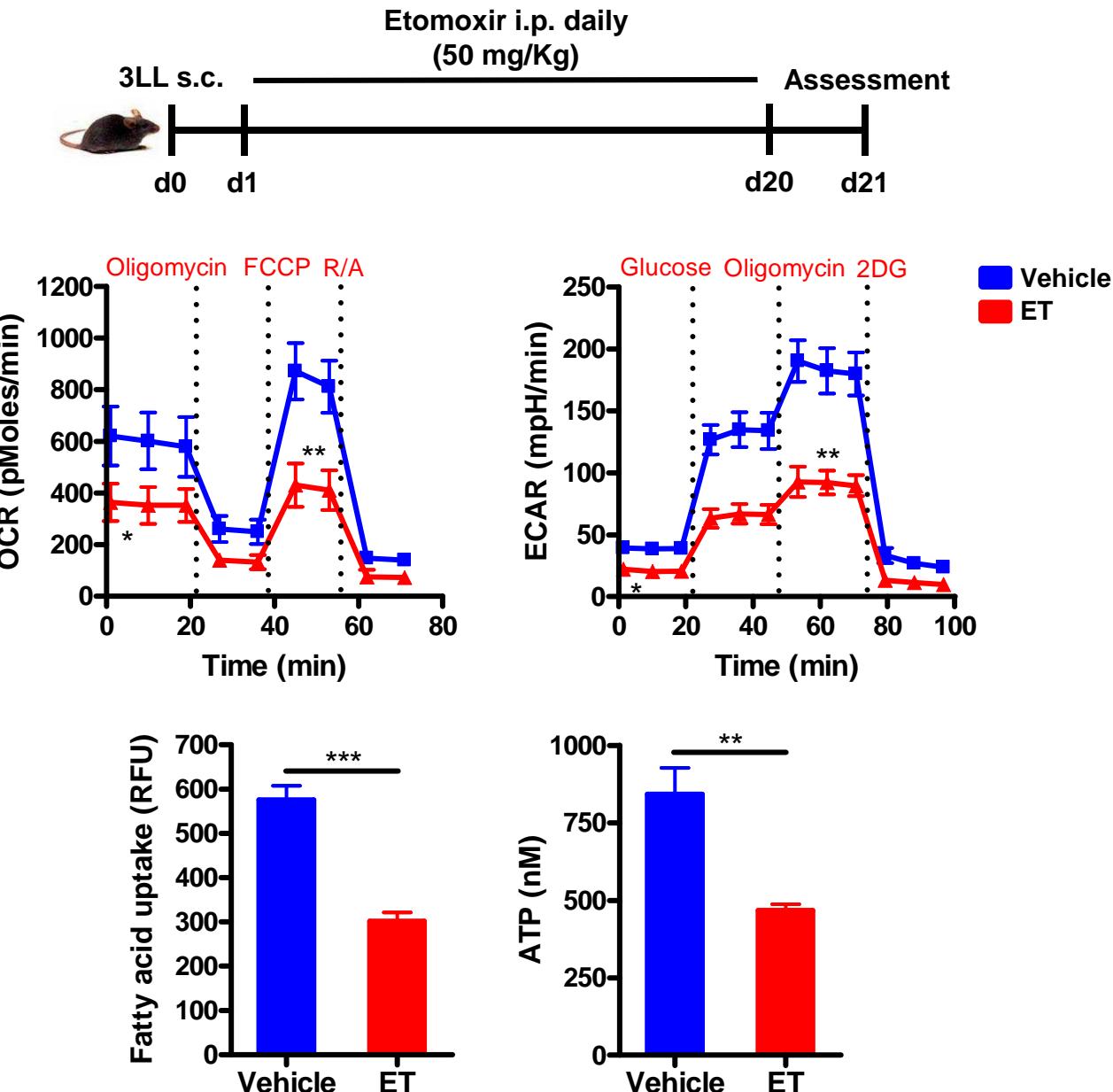
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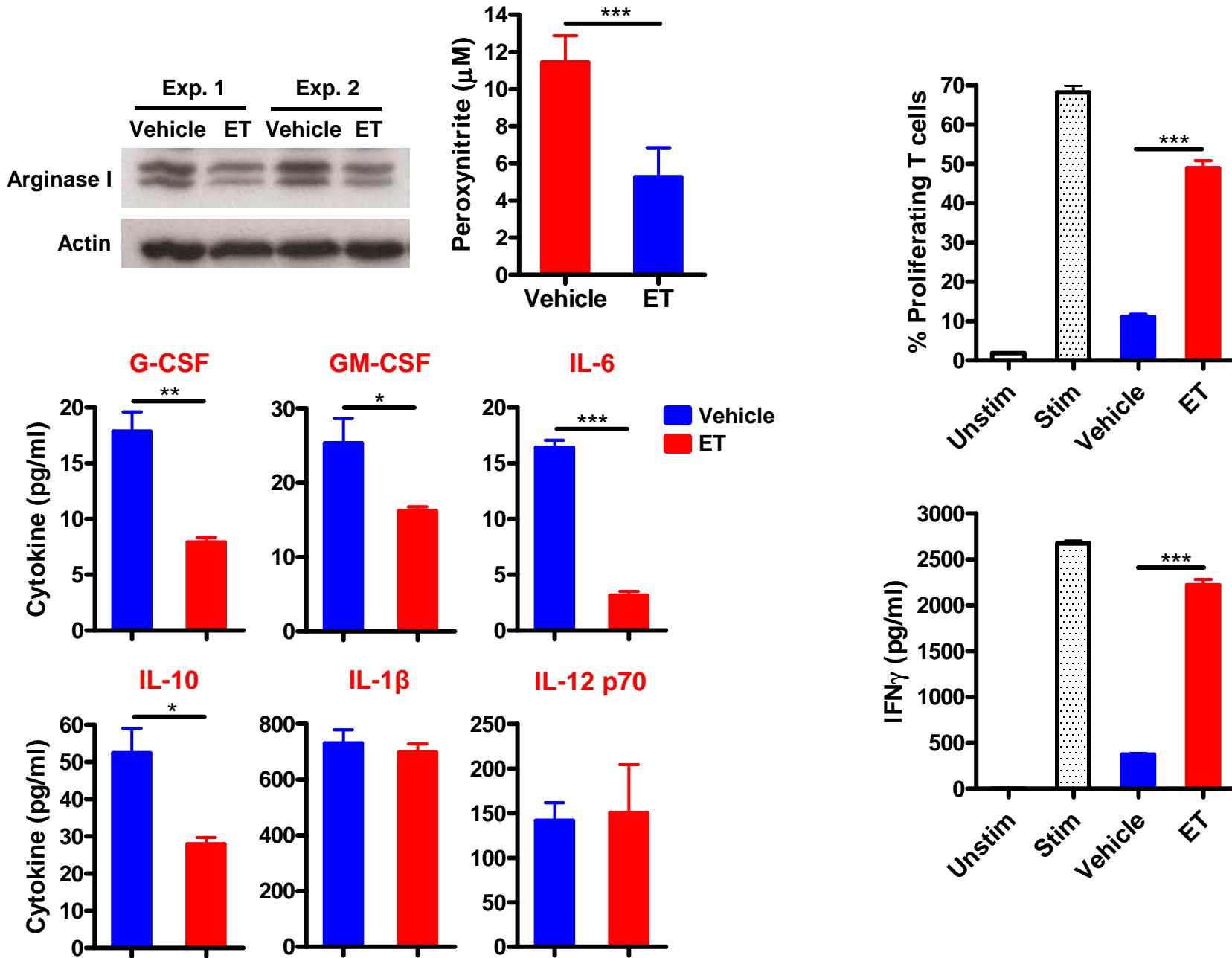
FAO inhibition impairs the function of BM-MDSC



FAO inhibition impairs the function of T-MDSC



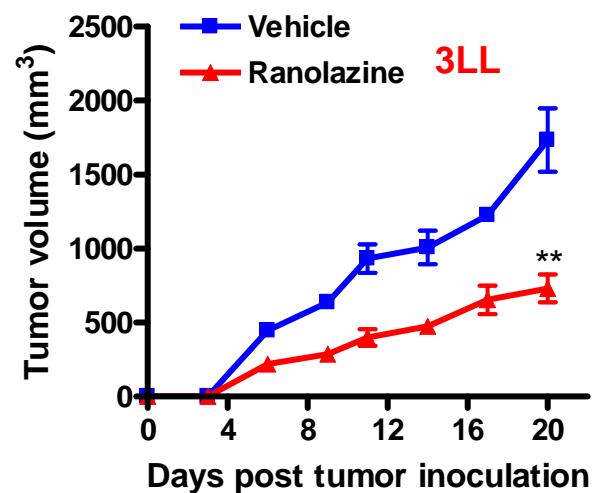
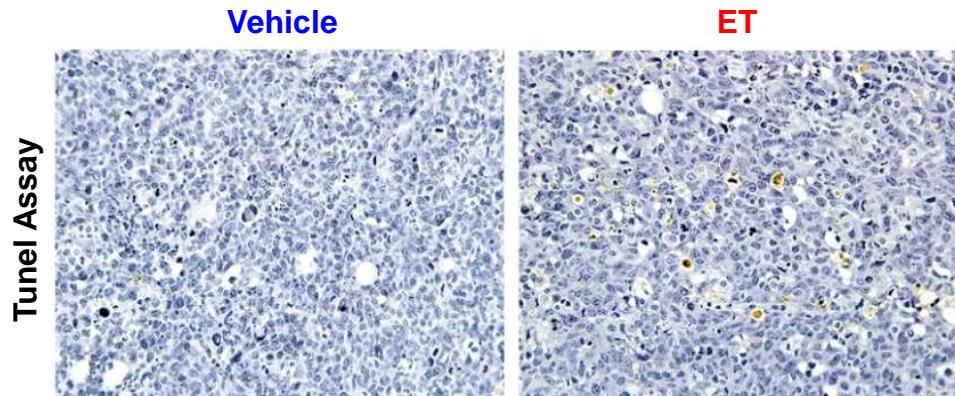
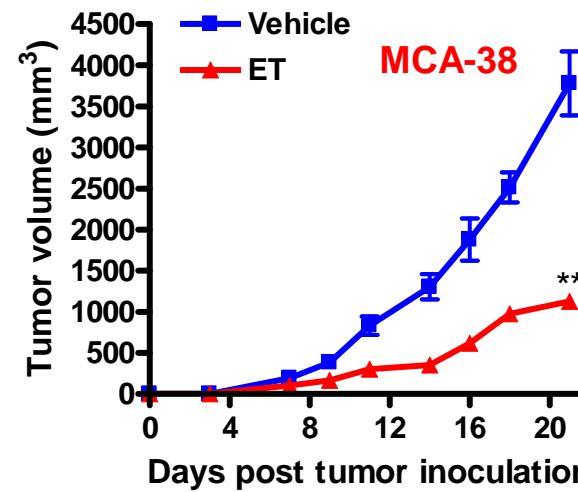
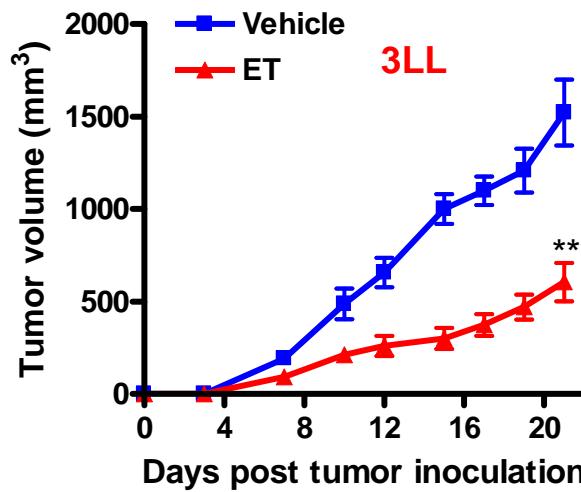
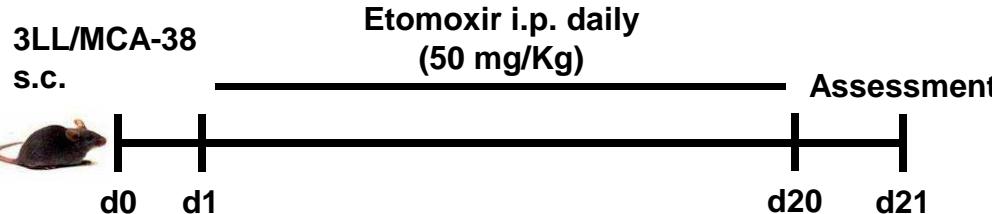
FAO inhibition impairs the function of T-MDSC



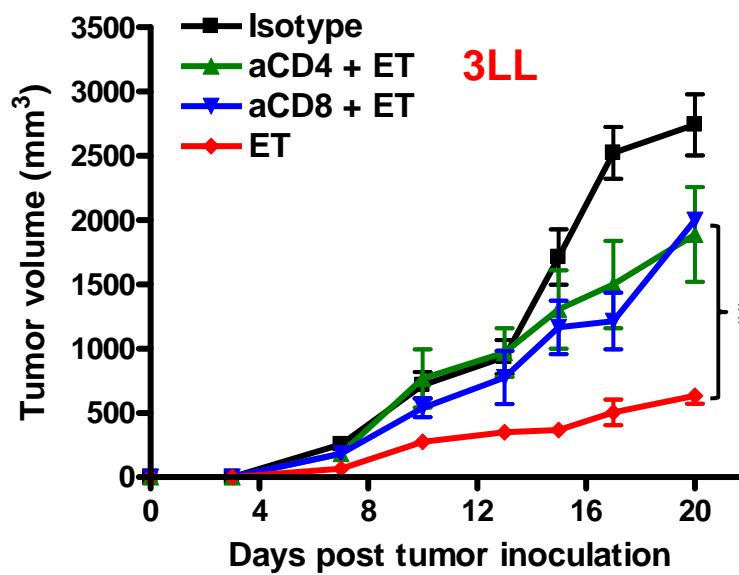
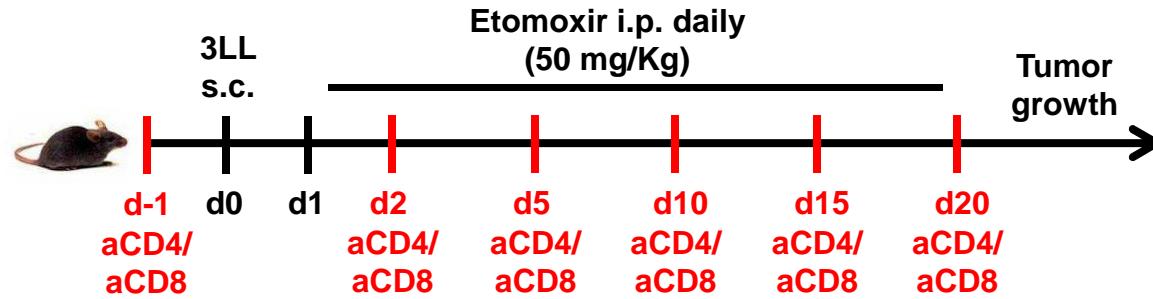
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FAO inhibition delays tumor growth

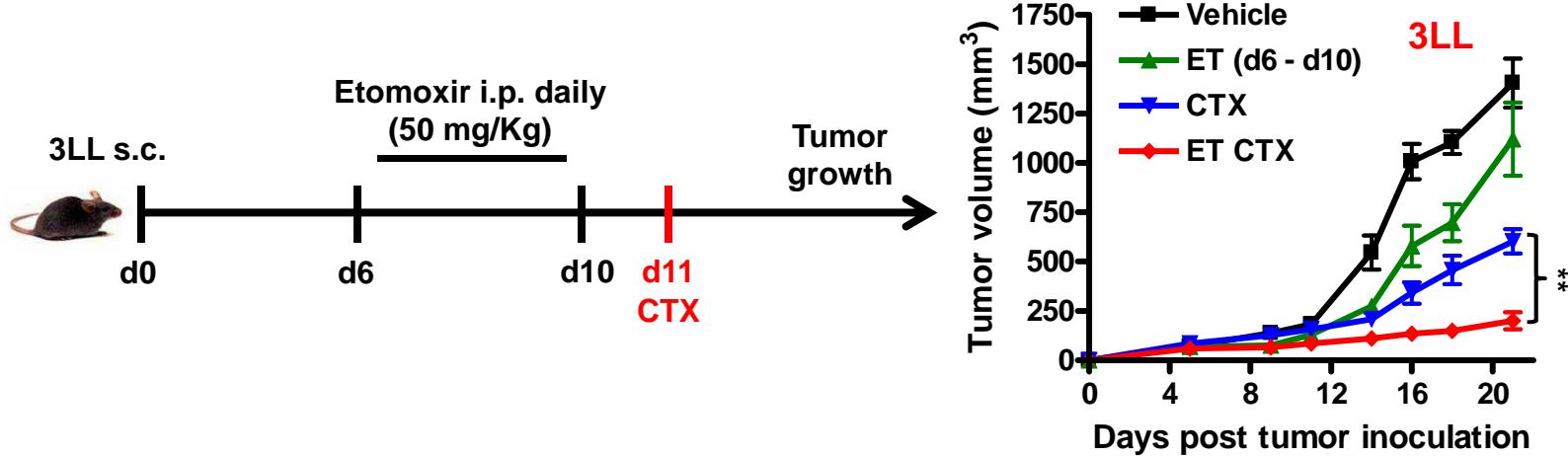
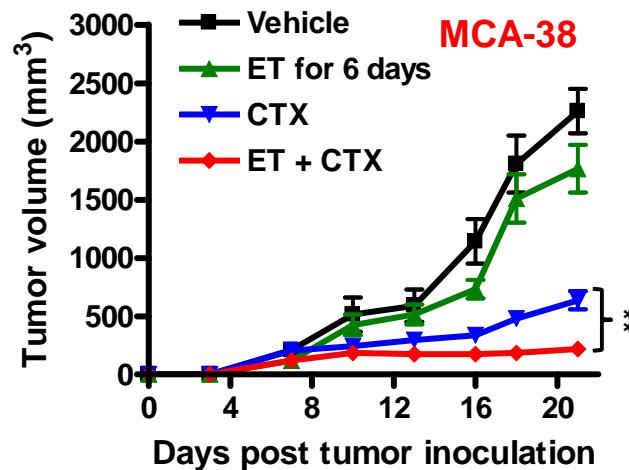
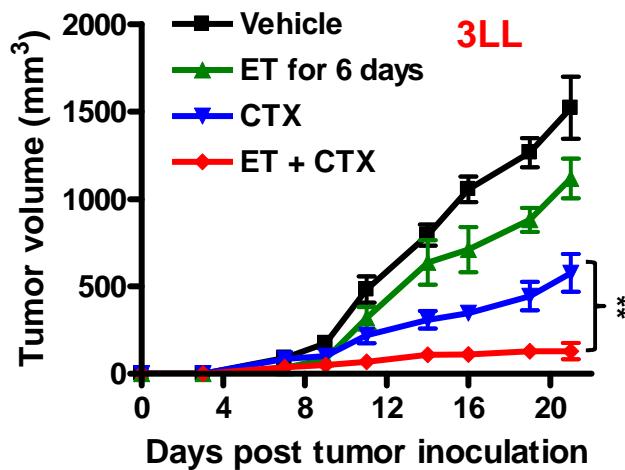
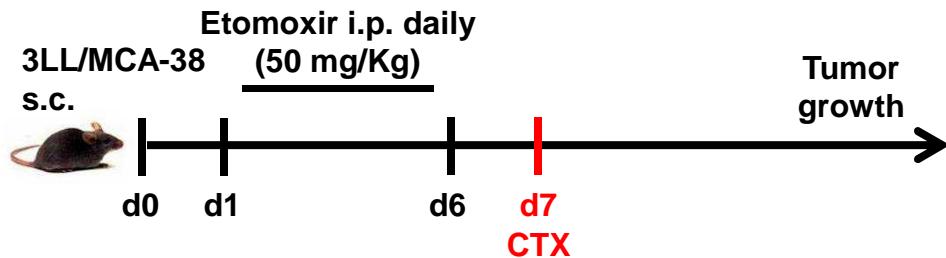


FAO inhibition delays tumor growth in a T cell-dependent manner

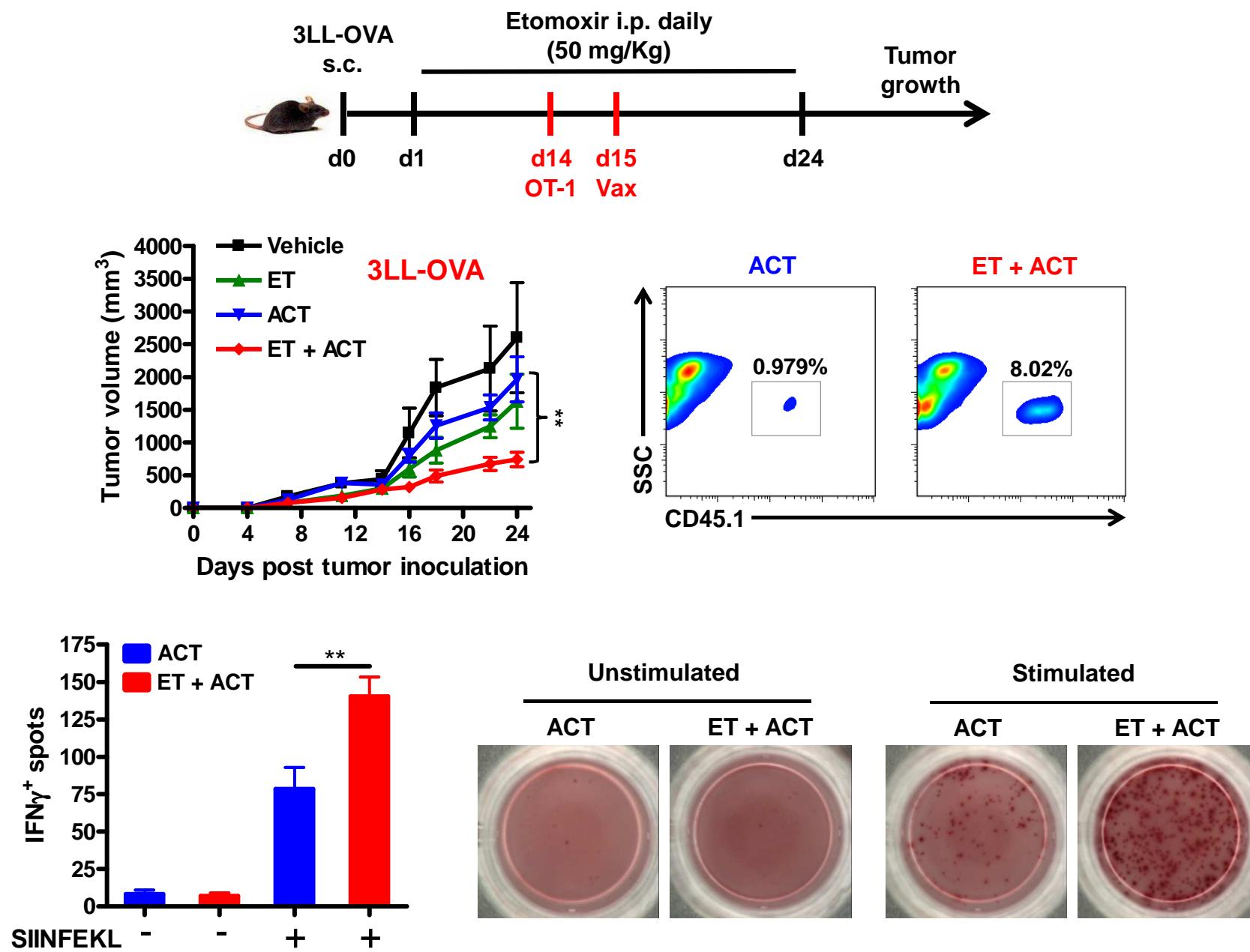


Anti-Cancer therapy: Which combination works better?

FAO inhibition synergizes with chemotherapy



FAO inhibition synergizes with adoptive T Cell therapy



Summary

- T-MDSC are associated with an increased incorporation of fatty acids and fatty acid oxidation.
- Inhibition of FAO blocks the immunosuppressive mechanisms and function of T-MDSC and results in a T cell-dependent inhibition of tumor growth.
- FAO inhibition has a synergistic effect with low-dose chemotherapy and adoptive cellular therapy.

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