Presenter Disclosure Information

Amir Al-Khami, PhD

No relationships to disclose

Metabolic Inhibition of Cancer-Associated Myeloid-Derived Suppressor Cells

Poster #411

Amir Al-Khami, PhD

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

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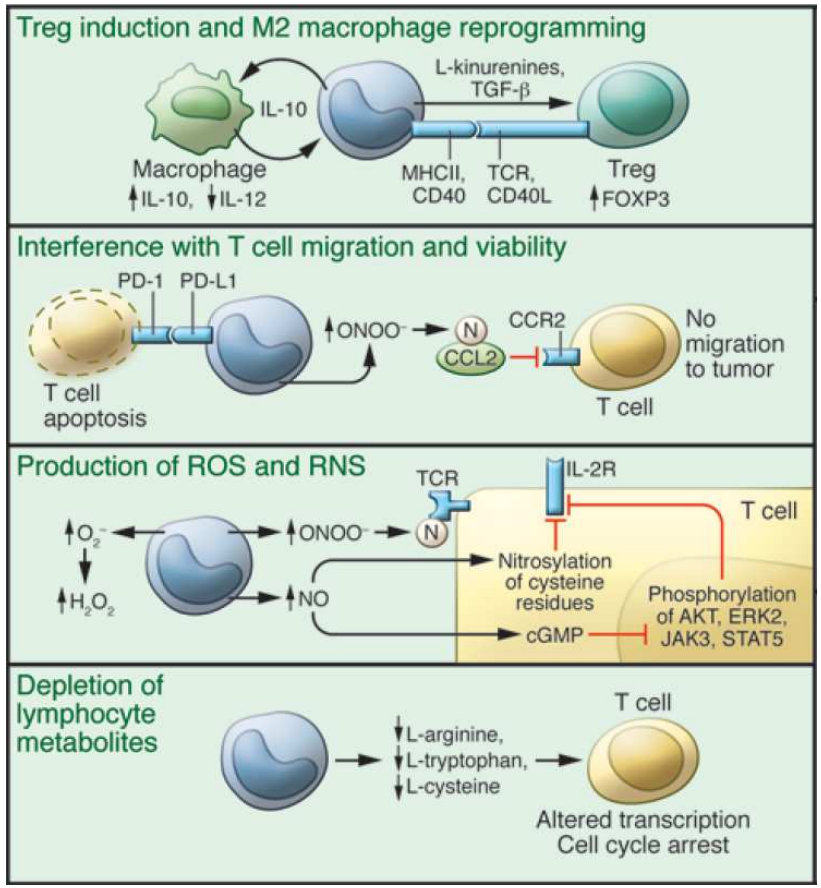
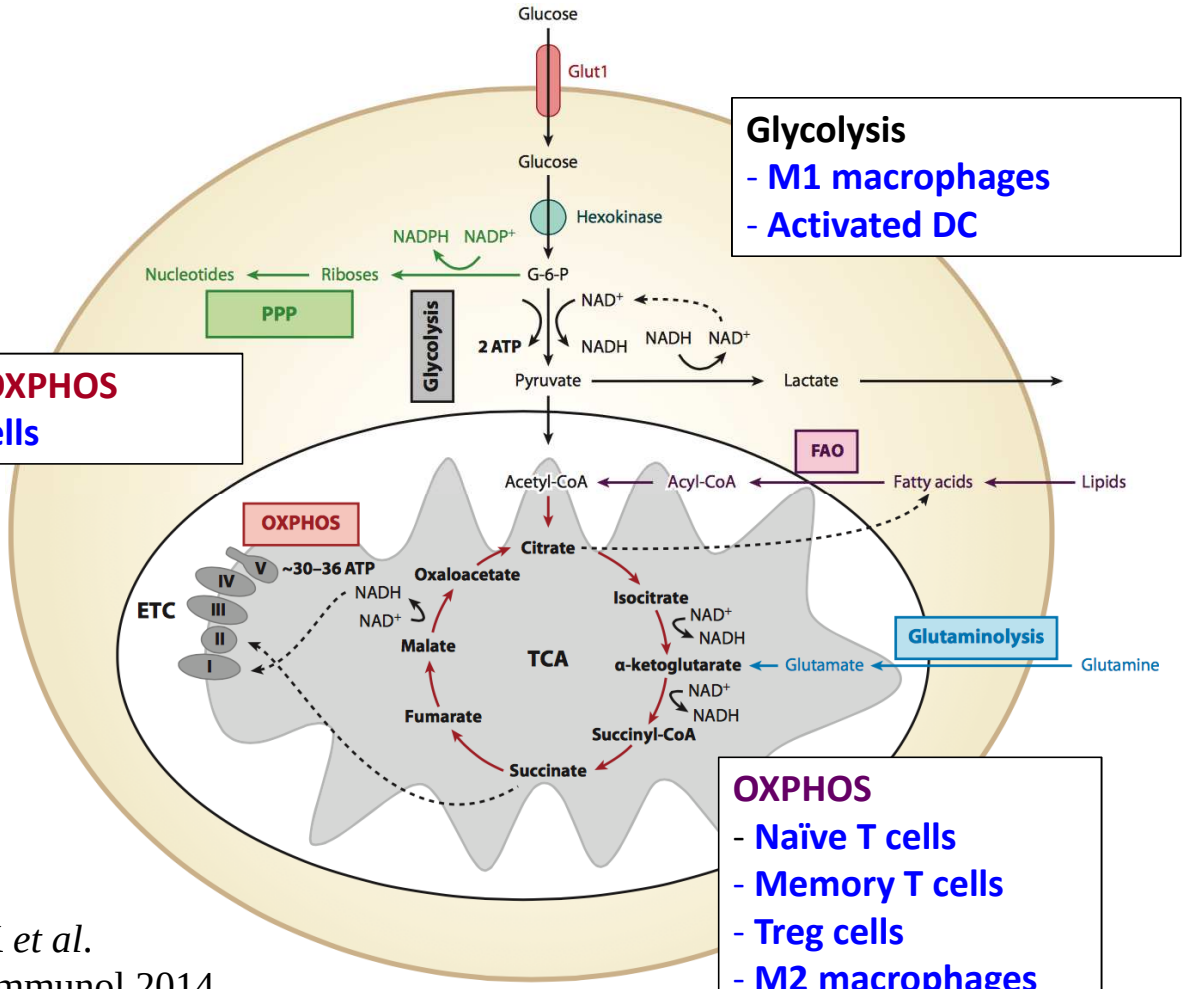
Myeloid-derived suppressor cells (MDSC)

- 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



Glycolysis
- **M1 macrophages**
- **Activated DC**

Glycolysis + OXPHOS
- **Effector T cells**

OXPHOS
- **Naïve T cells**
- **Memory T cells**
- **Treg cells**
- **M2 macrophages**

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

Study questions

? **Characterize the major energy metabolic pathway used by tumor-associated MDSC (T-MDSC)**

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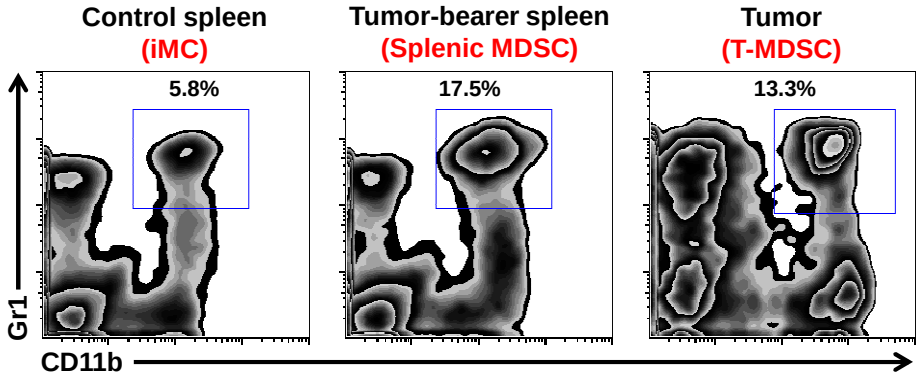
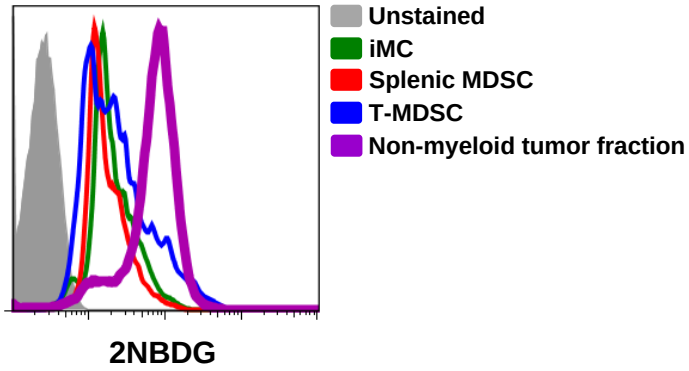
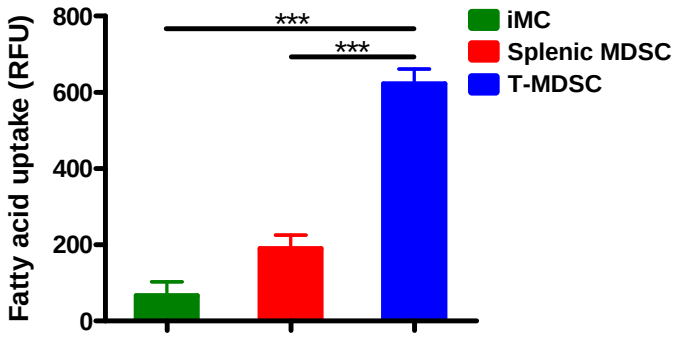
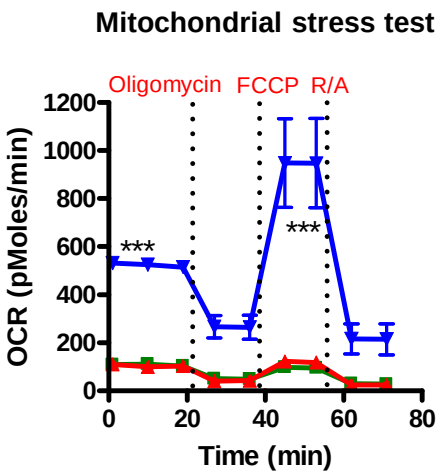
T-MDSC display an increased fatty acid uptake and fatty acid oxidation (FAO)

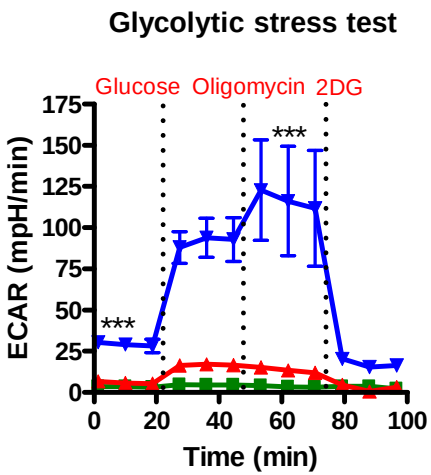


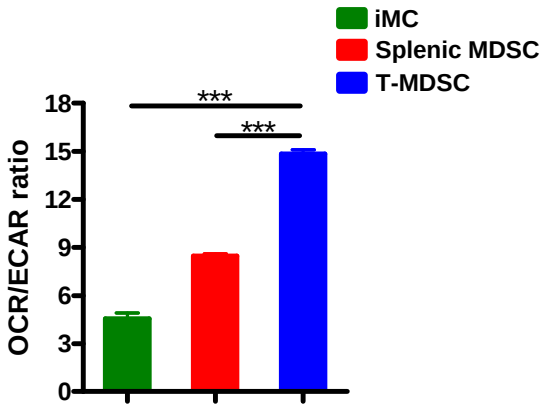


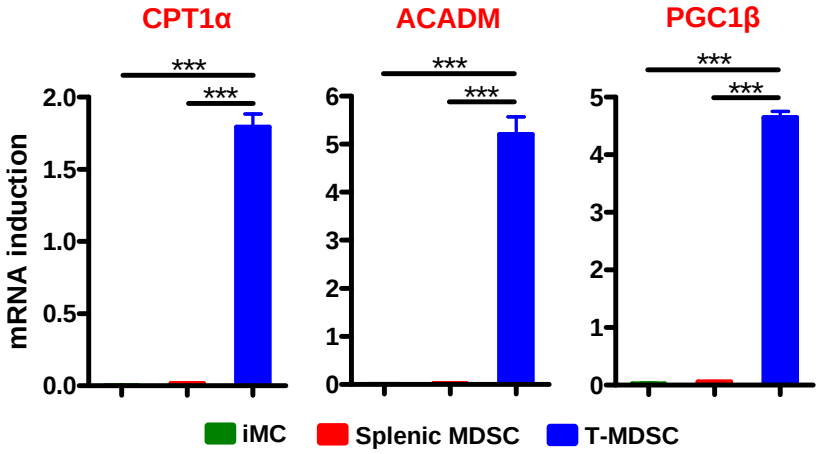


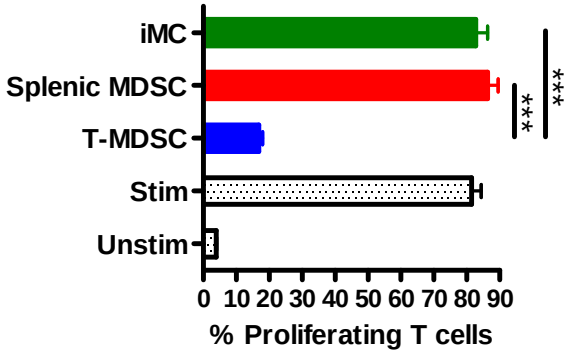
T-MDSC display an increased fatty acid uptake and FAO



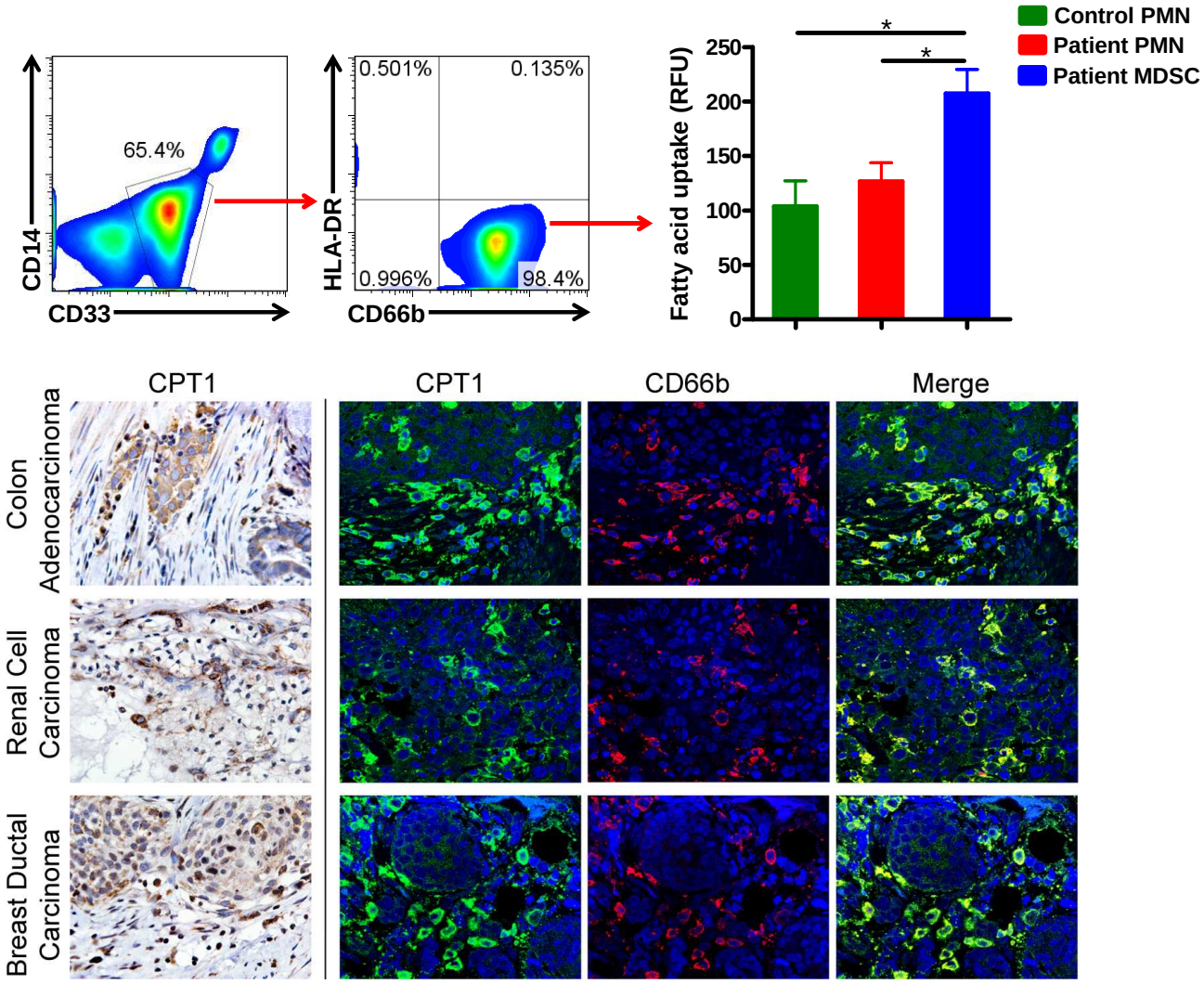








Human MDSC increase fatty acid uptake and FAO enzyme expression



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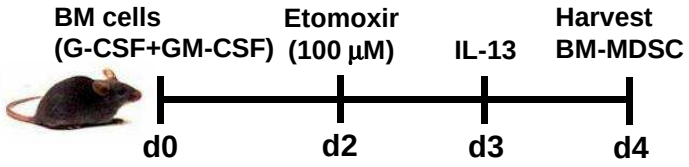
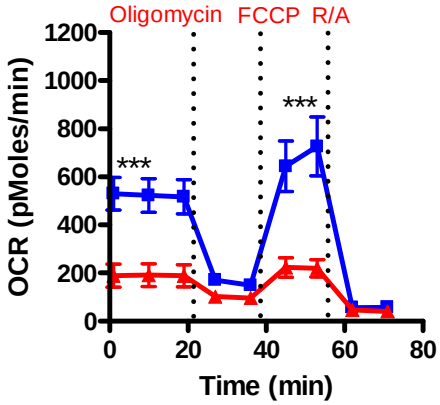
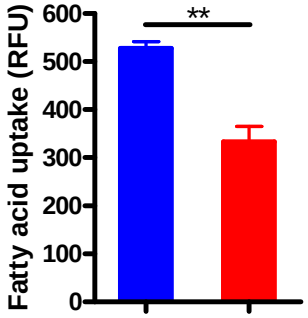
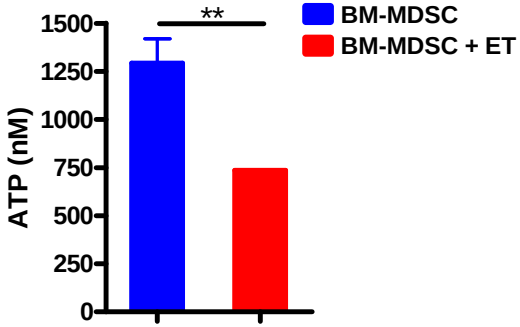
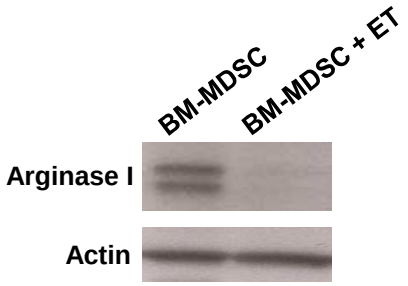
FAO inhibition impairs the function of BM-MDSC

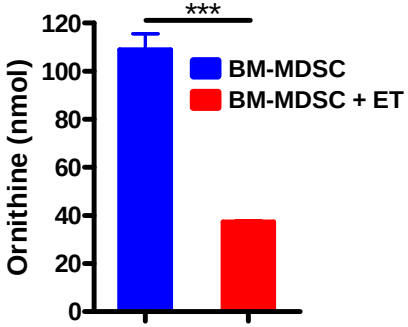


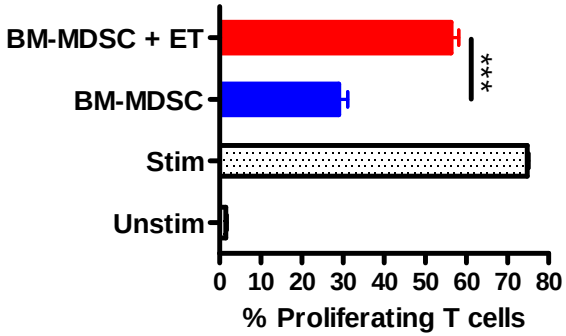




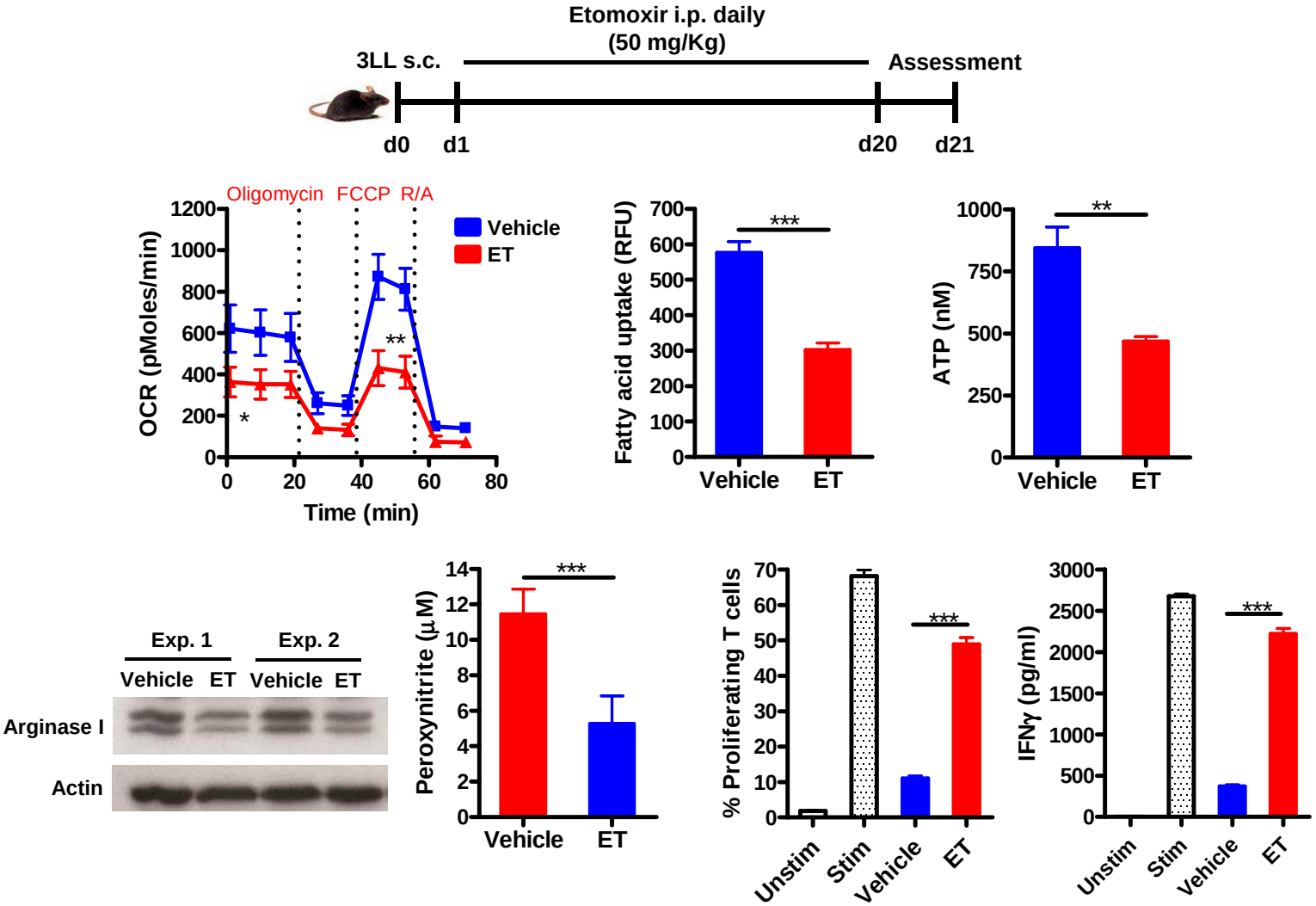








FAO inhibition impairs the function of T-MDSC



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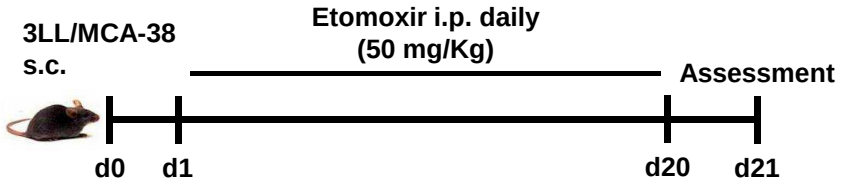
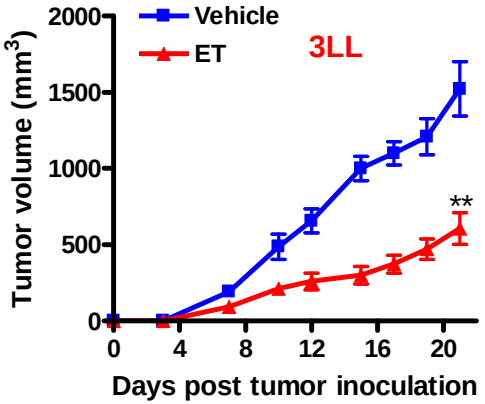
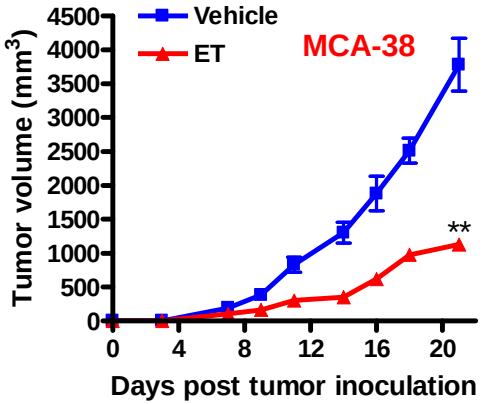
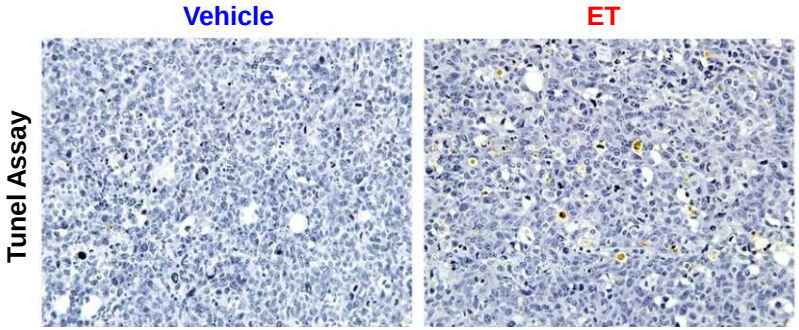
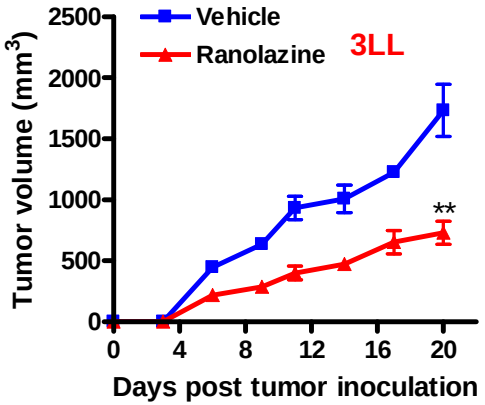
FAO inhibition delays tumor growth



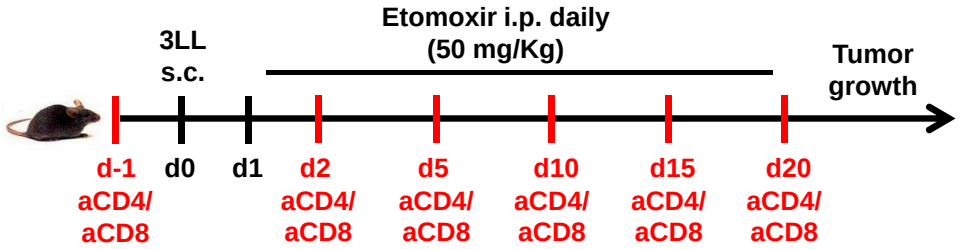


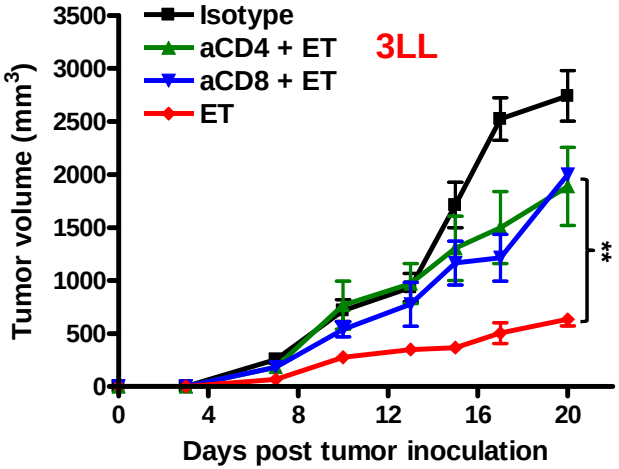






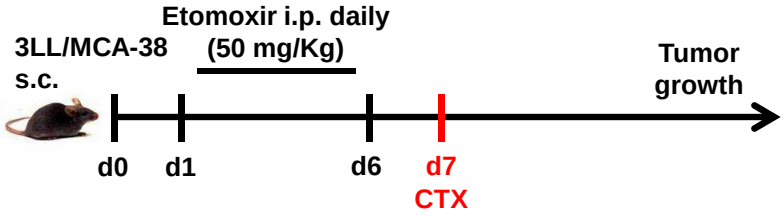
FAO inhibition delays tumor growth in a T cell-dependent manner

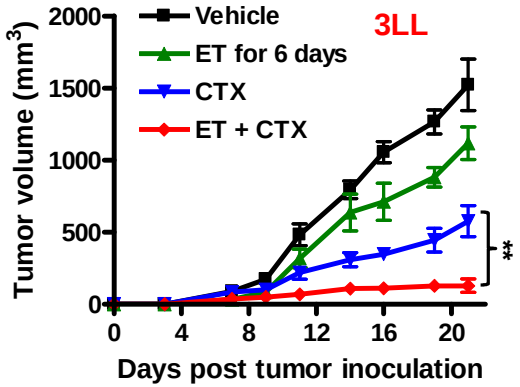


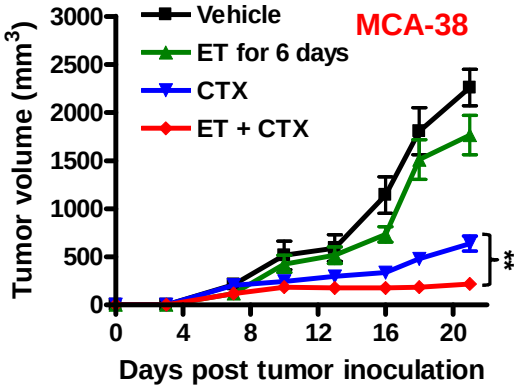


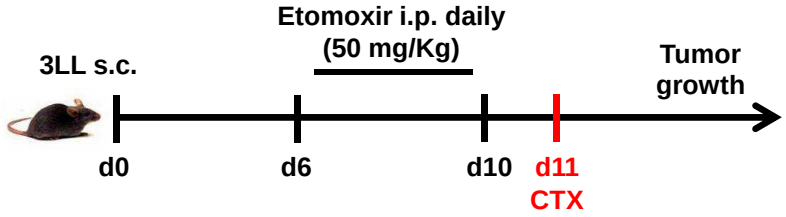
Which combination therapy works better?

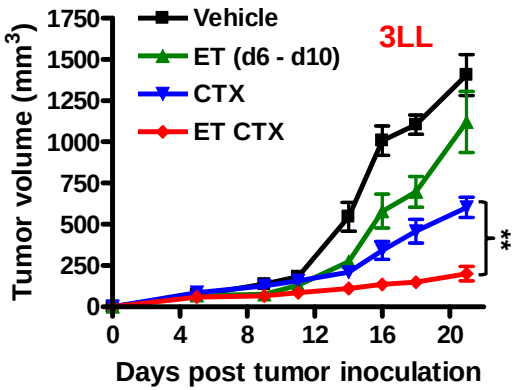
FAO inhibition synergizes with chemotherapy



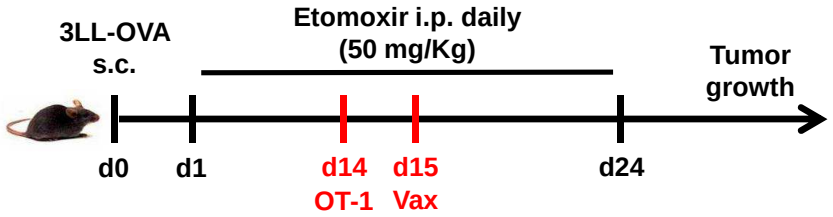


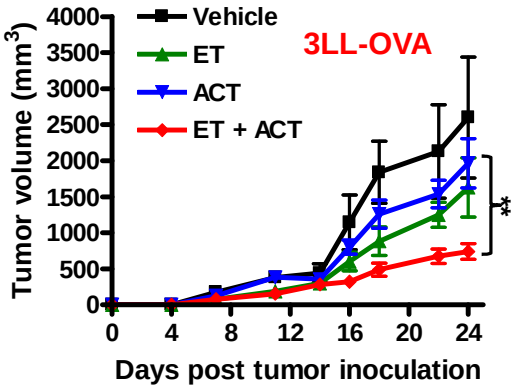


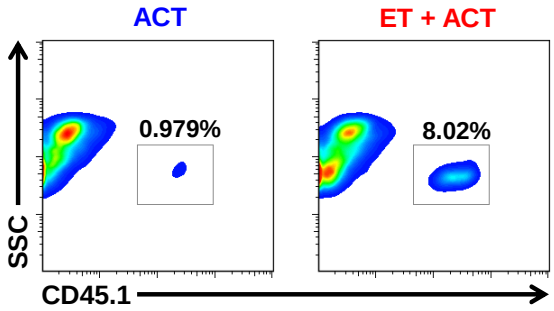


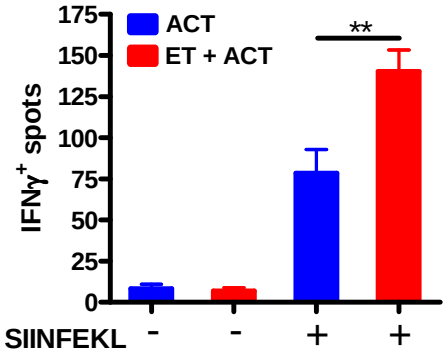


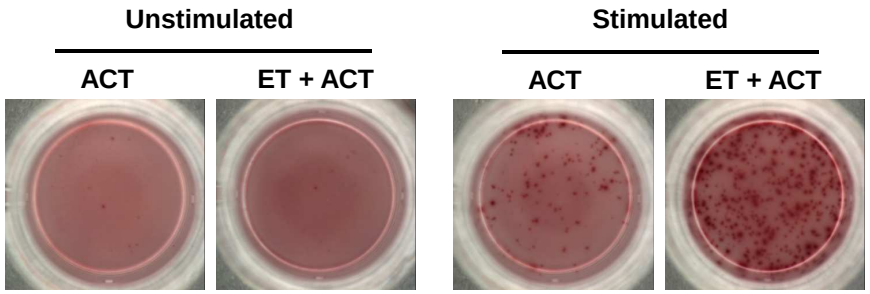
FAO inhibition synergizes with adoptive T Cell therapy











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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