

Re-educating macrophage through metabolism-mediated metabolic and epigenetic reprogramming

Ping-Chih Ho

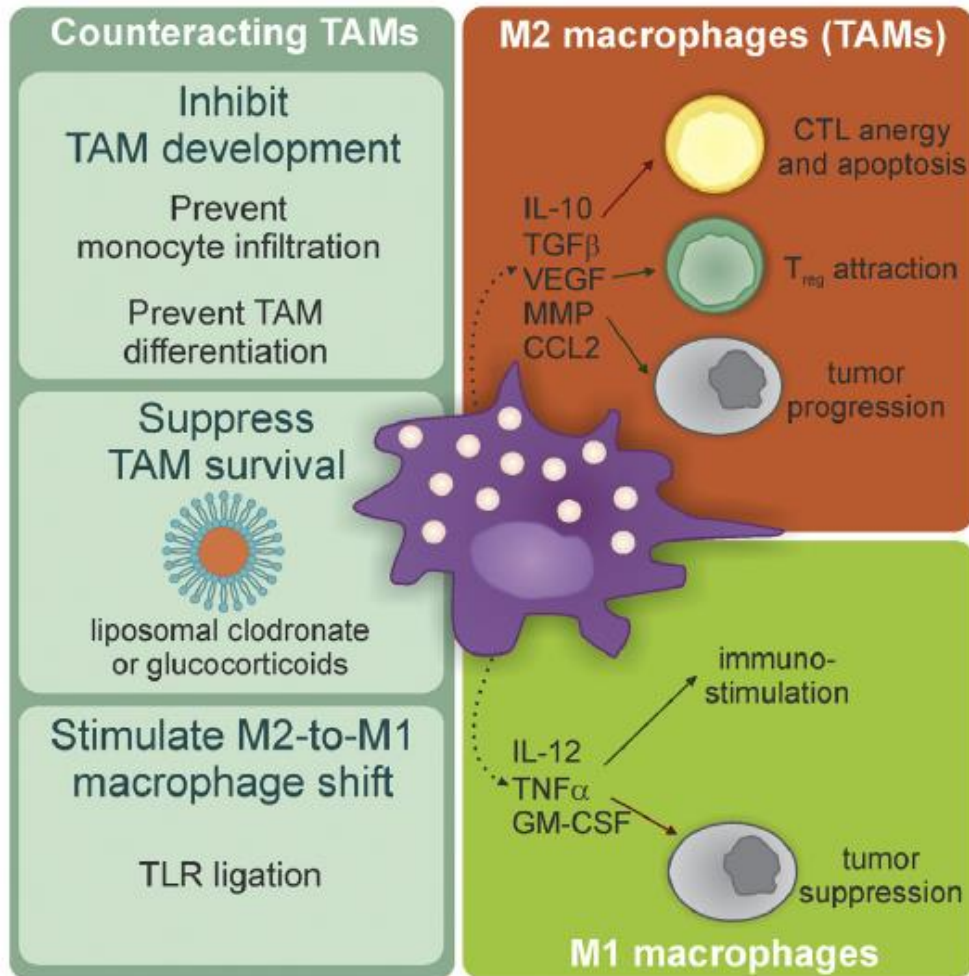
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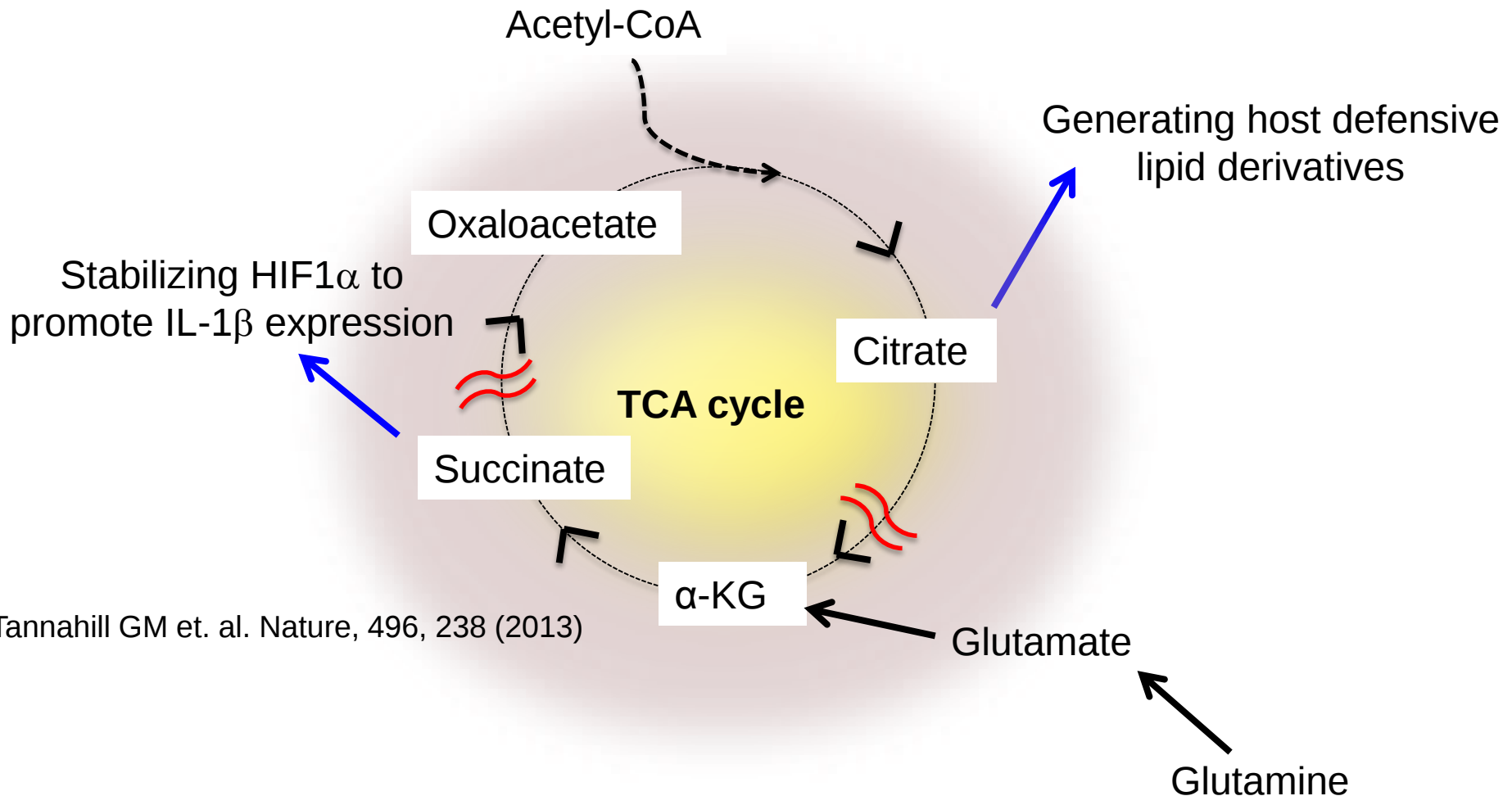
Tumor-associated macrophages: the corrupted police in the crime village



1. How does the TME promote generation of M2-like tumor-associated macrophages?

2. Can we re-educate TAMs to boost efficacy of cancer immunotherapies?

TCA Cycle controls macrophage polarization

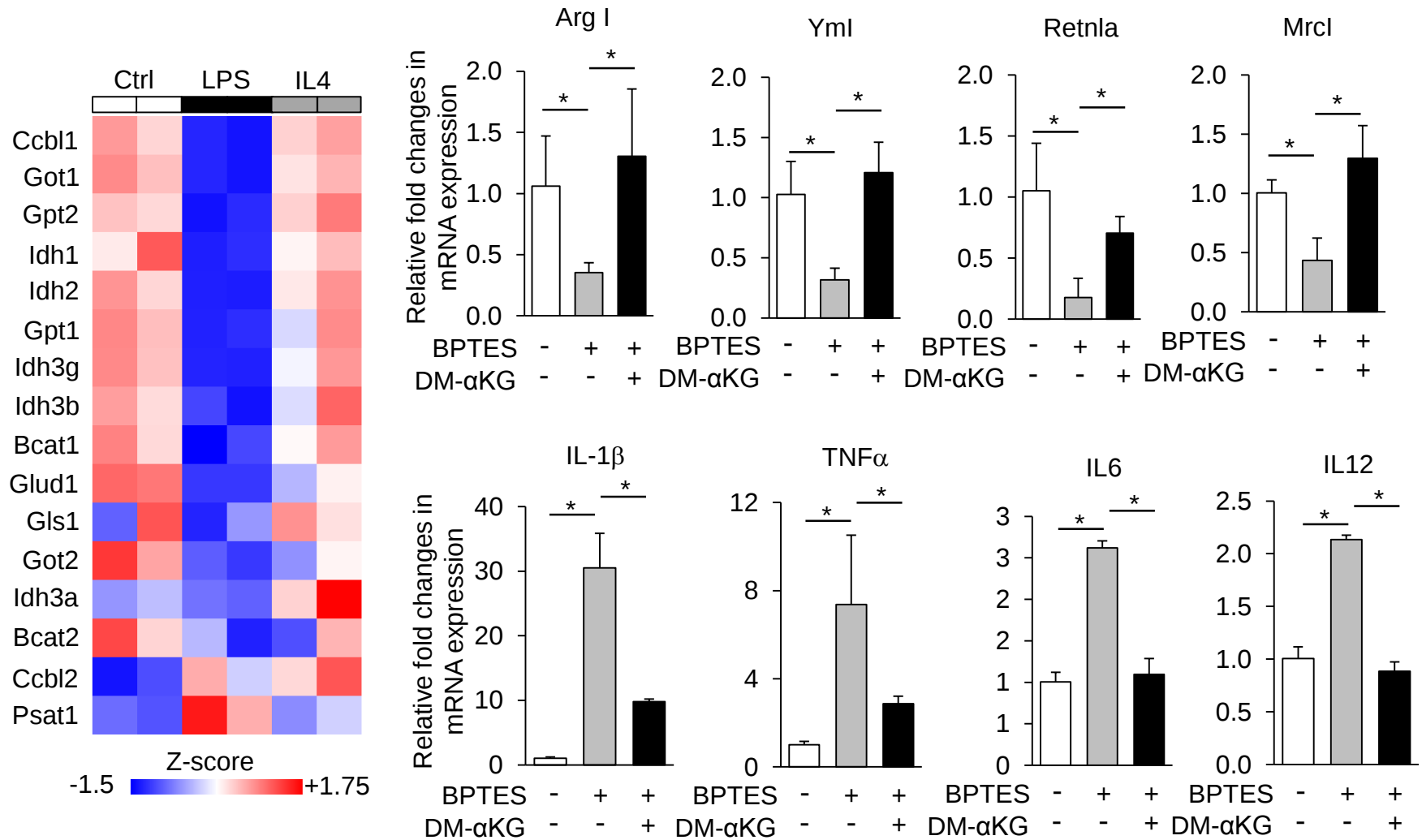


Tannahill GM et. al. Nature, 496, 238 (2013)

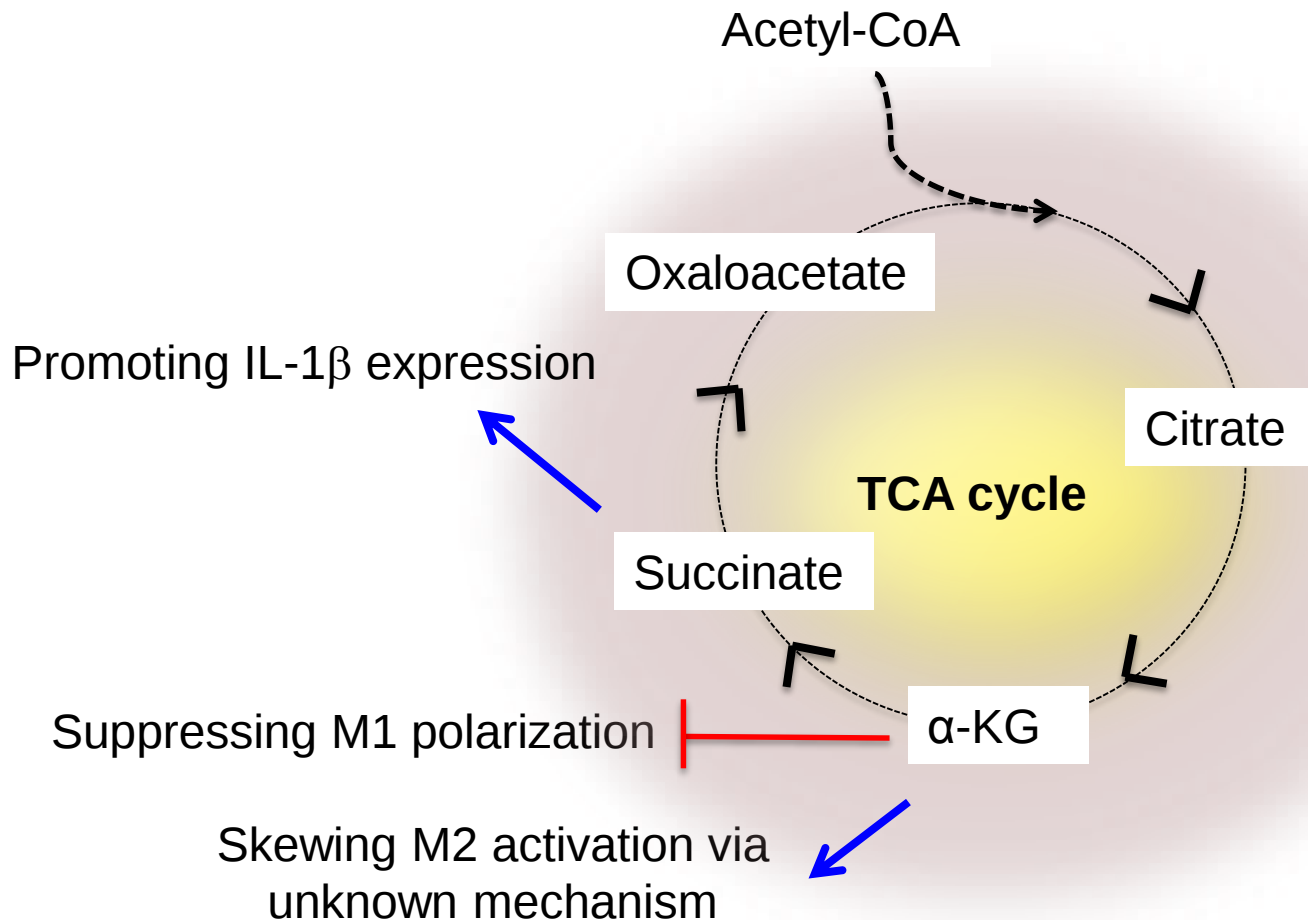
However, glutaminolysis supports M2 activation without detailed mechanism

Jha AK et. al. Immunity, 42, 419 (2015)

M2 macrophages express higher level of a gene set contributing to α -ketoglutarate production

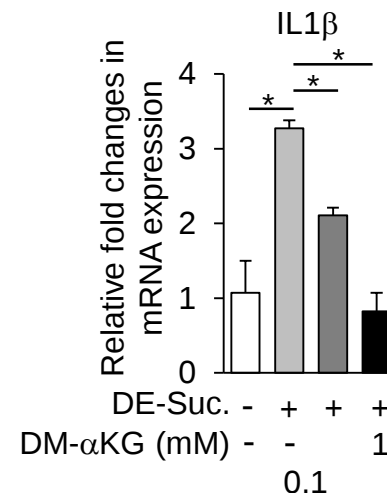
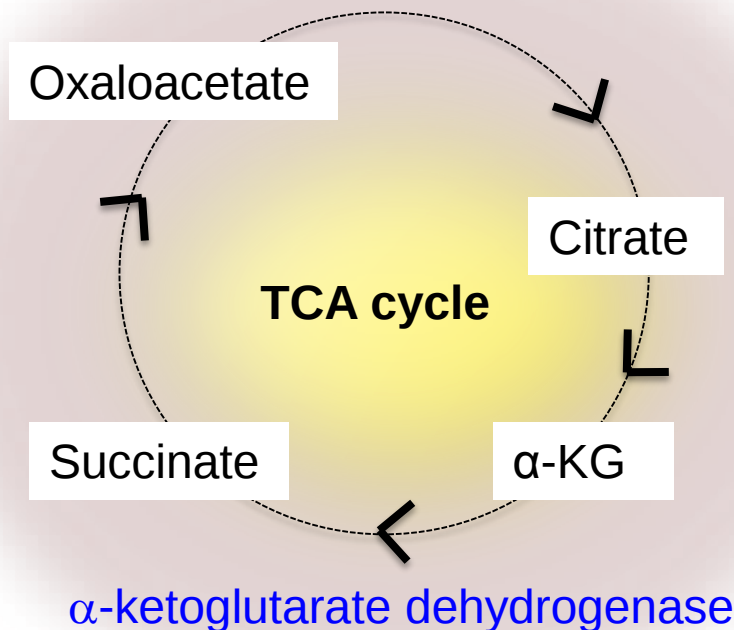
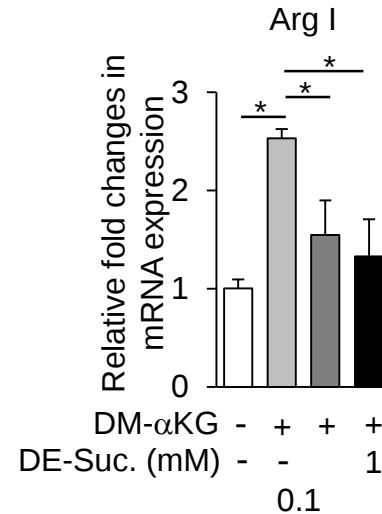
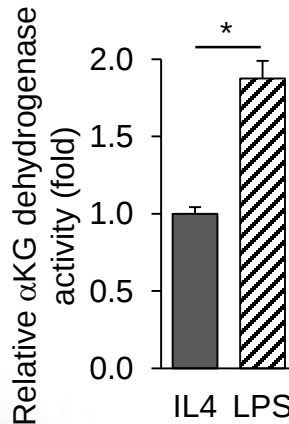
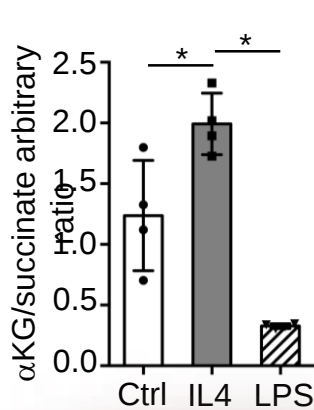


Metabolic balance between succinate and α -ketoglutarate fine-tunes M2 activation

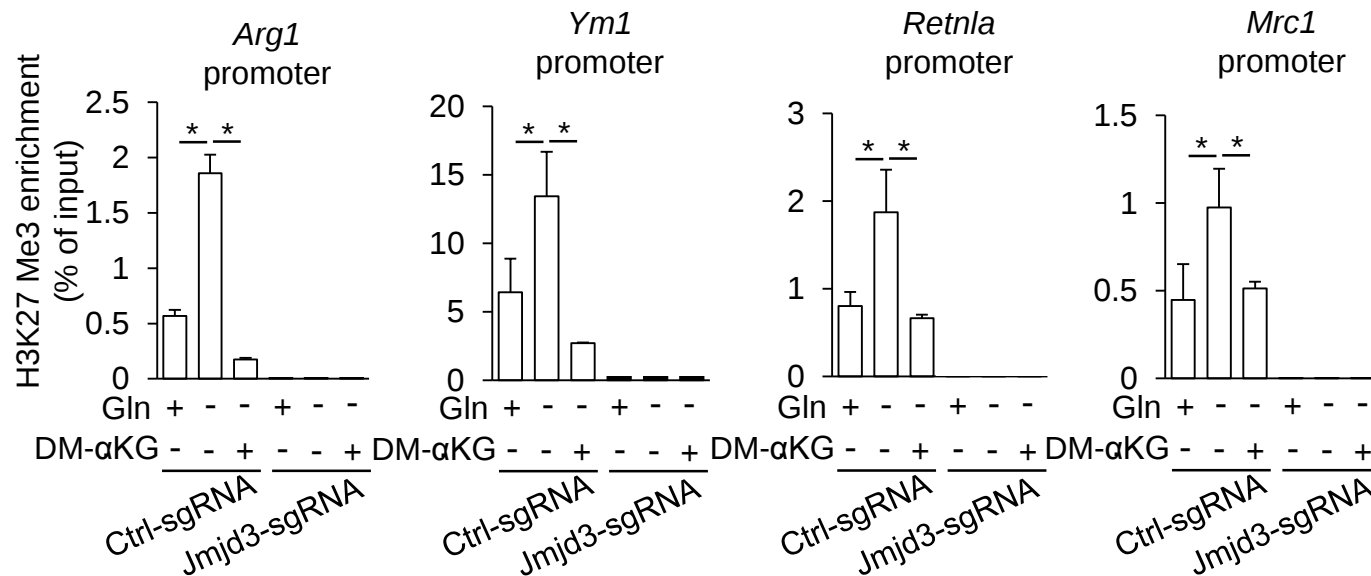
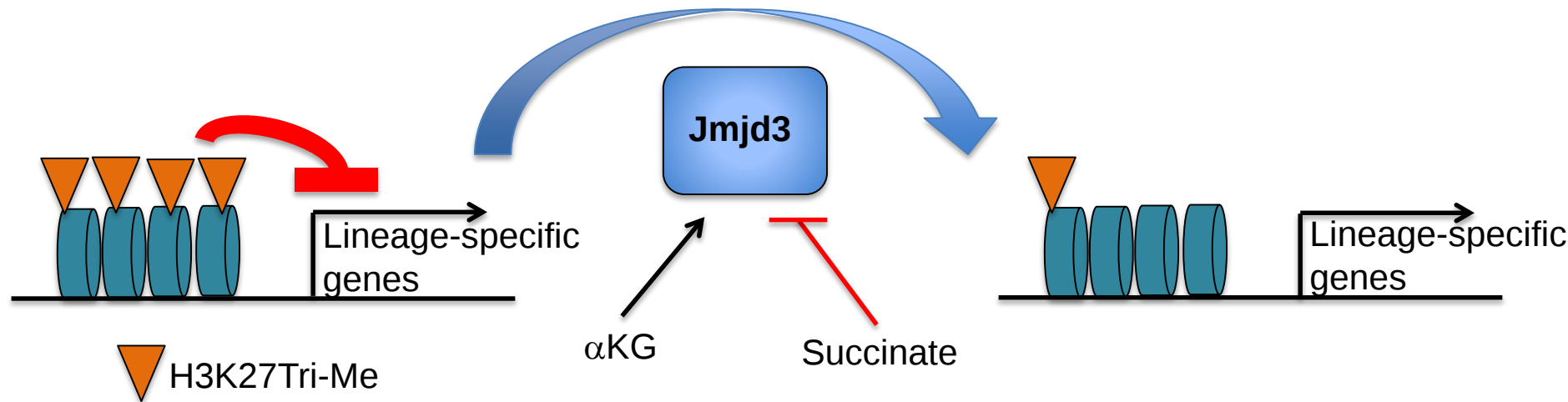


Can M1 and M2 polarization lead to different levels of α -ketoglutarate and succinate?

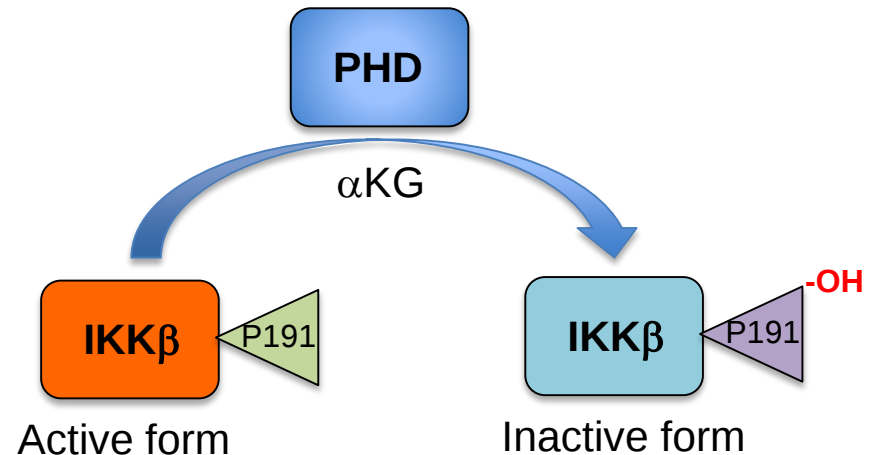
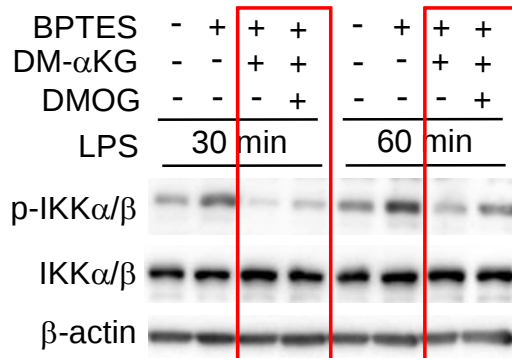
Metabolic balance between succinate and α -ketoglutarate fine-tunes macrophage activation



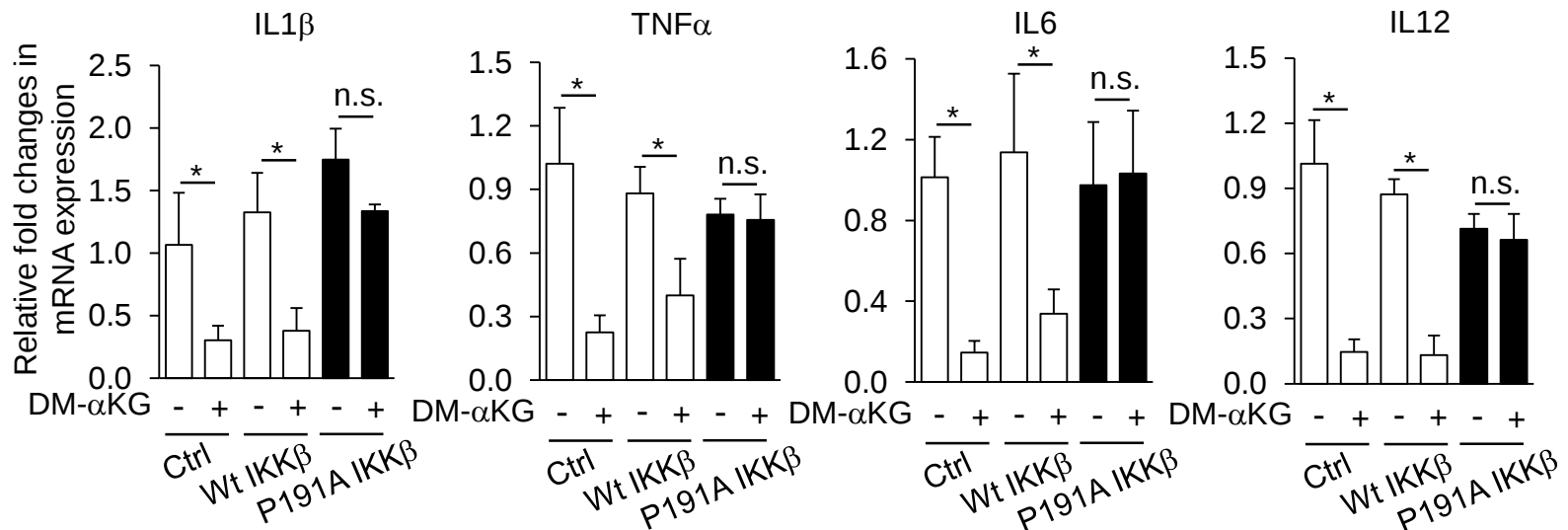
α -ketoglutarate promotes M2 activation through a Jmjd3-dependent mechanism



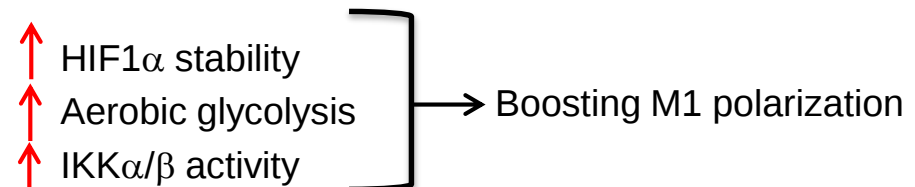
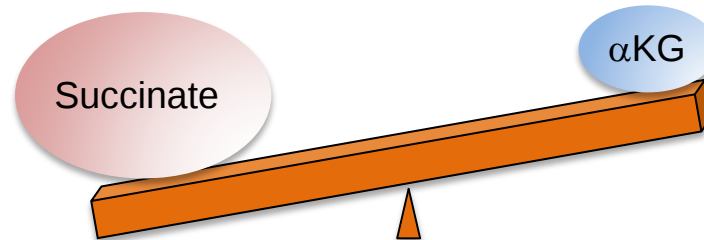
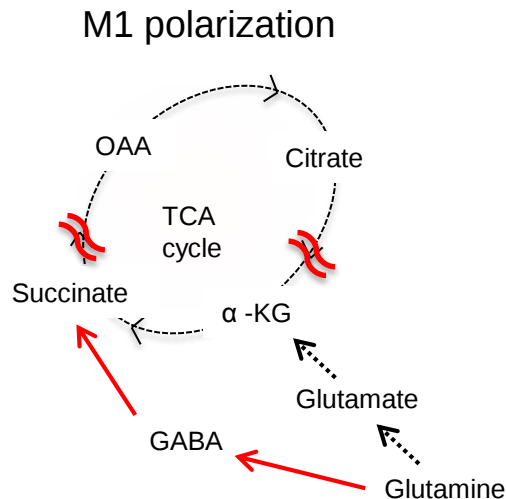
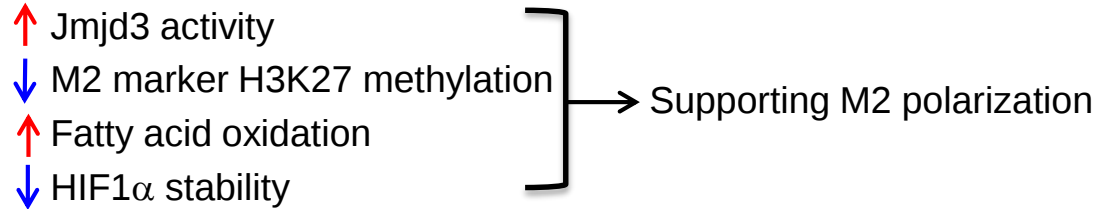
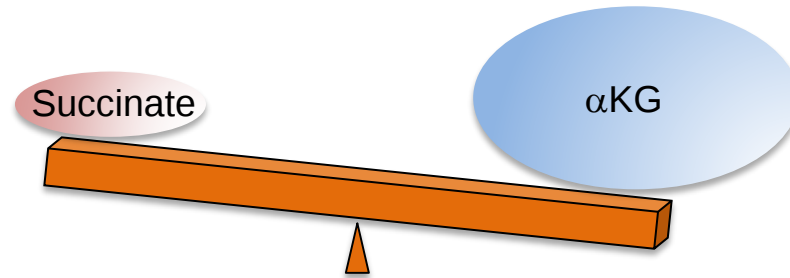
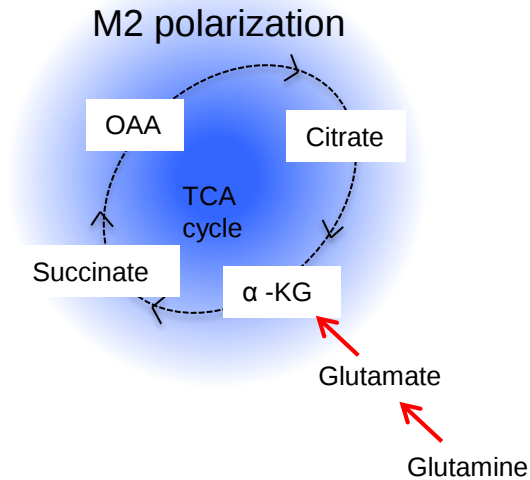
Metabolic balance between succinate and α -ketoglutarate fine-tunes M1 activation



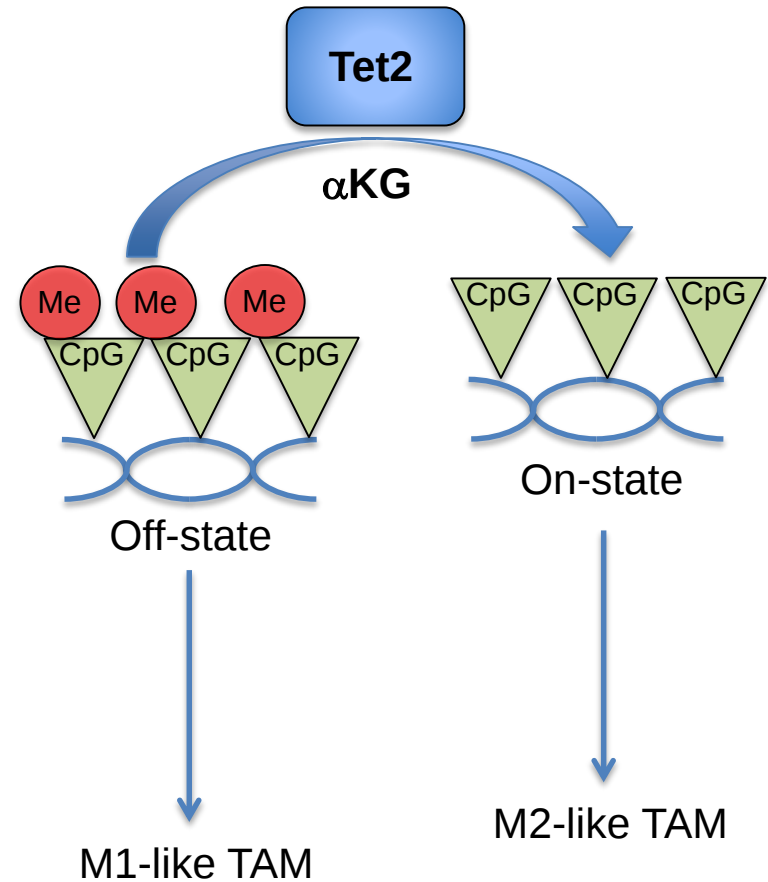
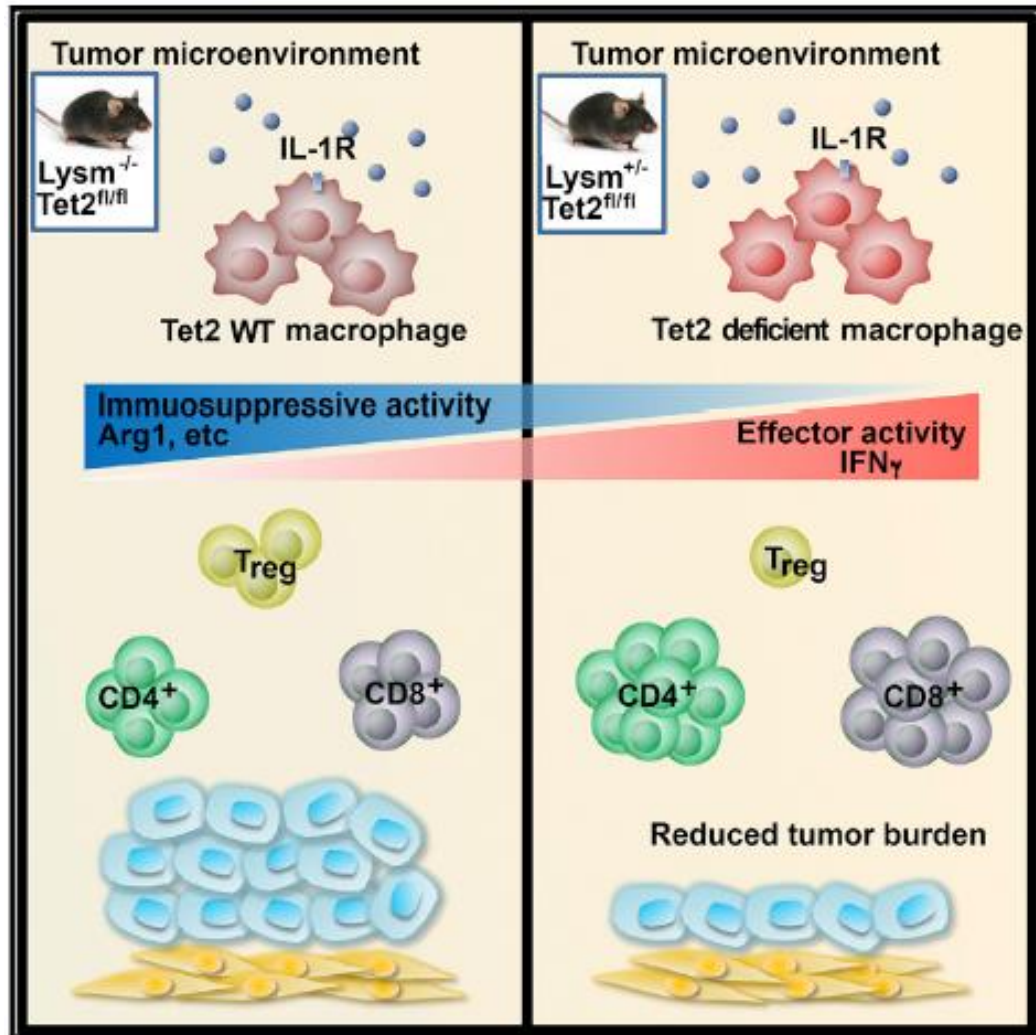
Cummins EP et. al, PNAS (2006)



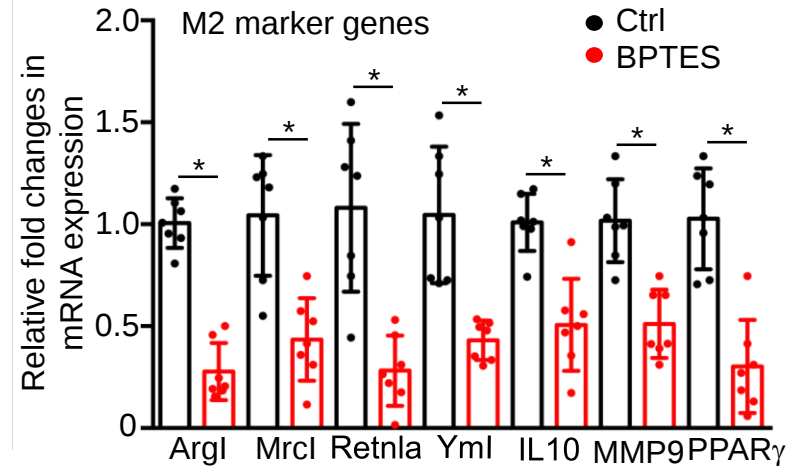
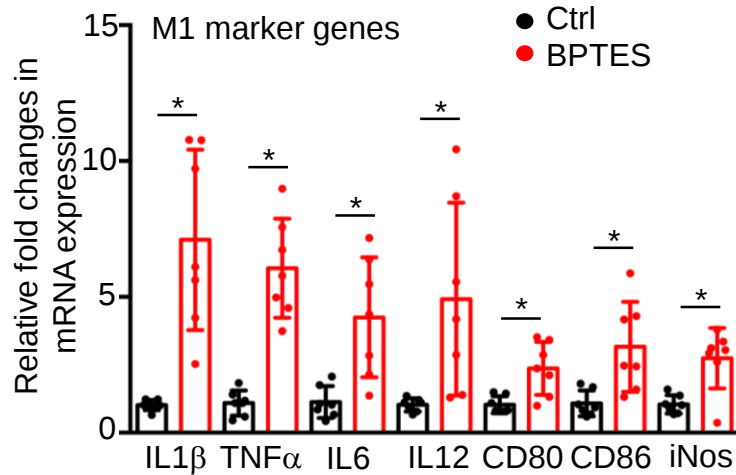
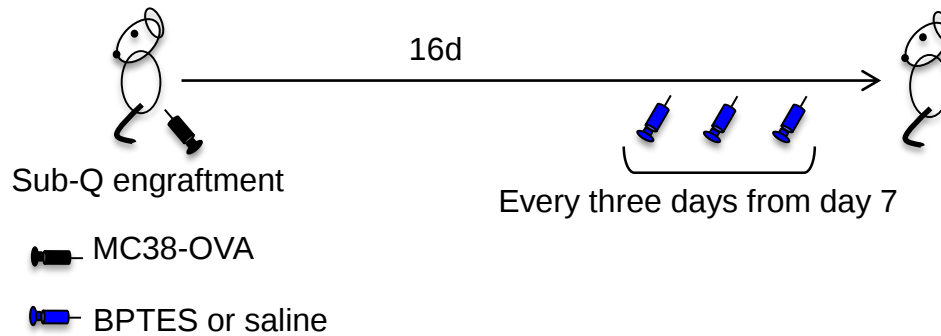
Metabolic relay determines macrophage polarization: a new opportunity to harness macrophages



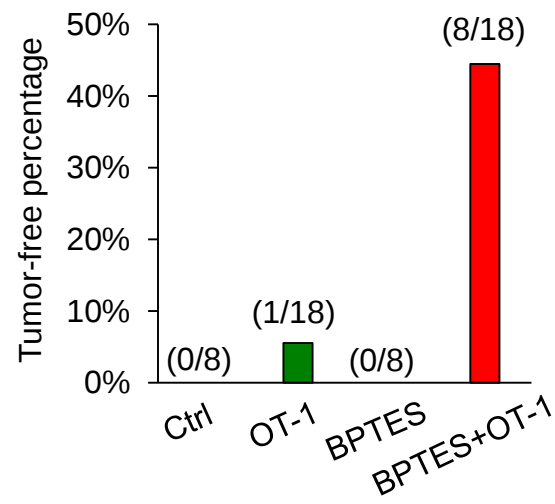
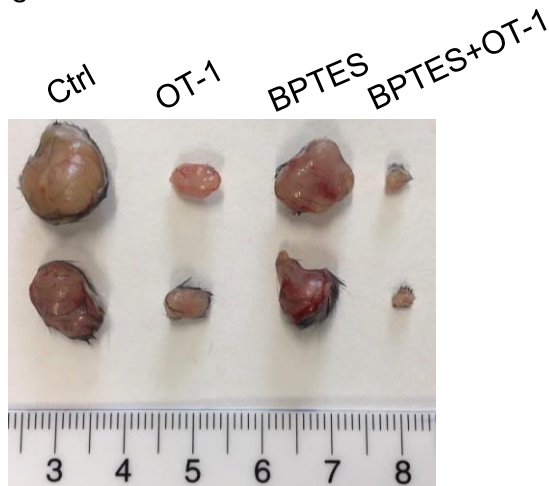
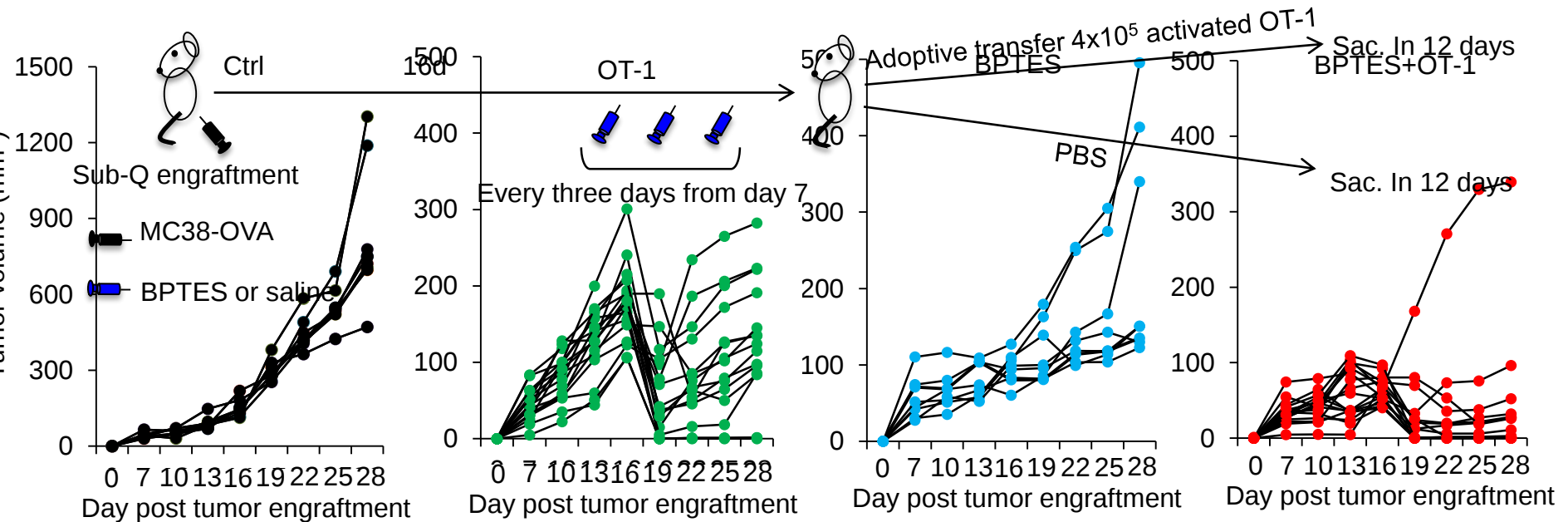
Epigenetic controls in tumor-associated macrophages



BPTES treatment reprograms TAMs into M1-like phenotype



BPTES treatment synergizes with T cell therapy to induce tumor regression



Acknowledgements

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