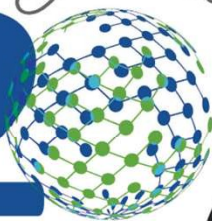




Reimagined
2020 
NOVEMBER 9-14 



Society for Immunotherapy of Cancer



Sexual dimorphism in myeloid-derived suppressor cells promote GBM progression in females via IL-1 β

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Society for Immunotherapy of Cancer

#SITC2020



Disclosure

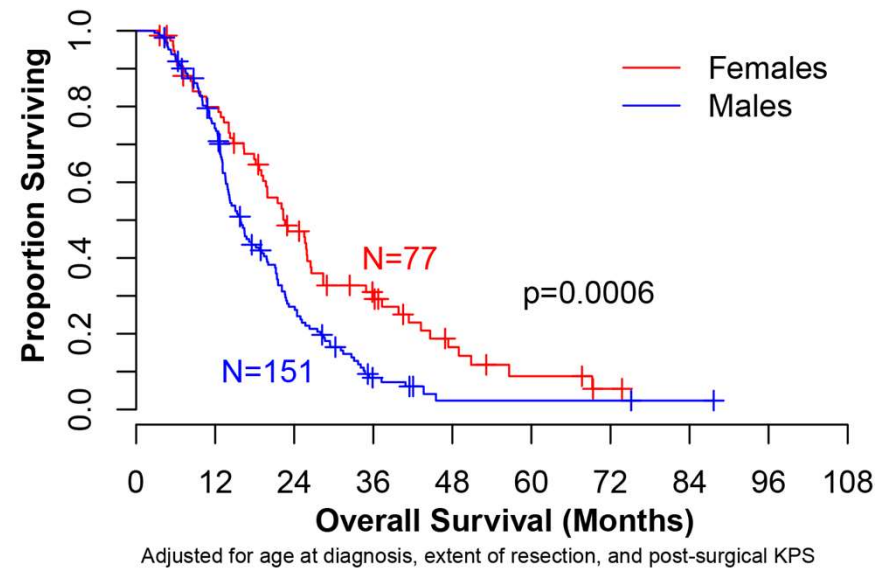
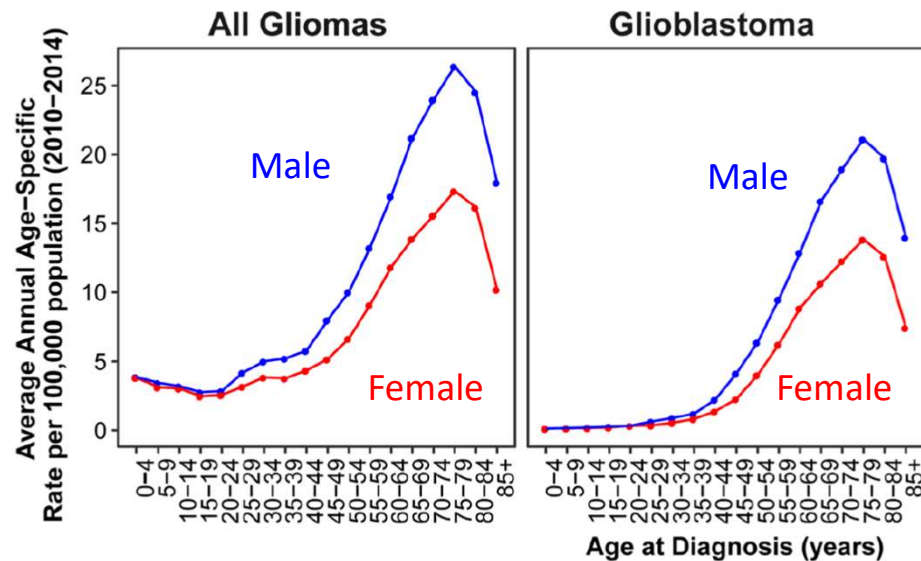
I have no actual or potential conflict of interest in relation to this program/presentation.



Society for Immunotherapy of Cancer

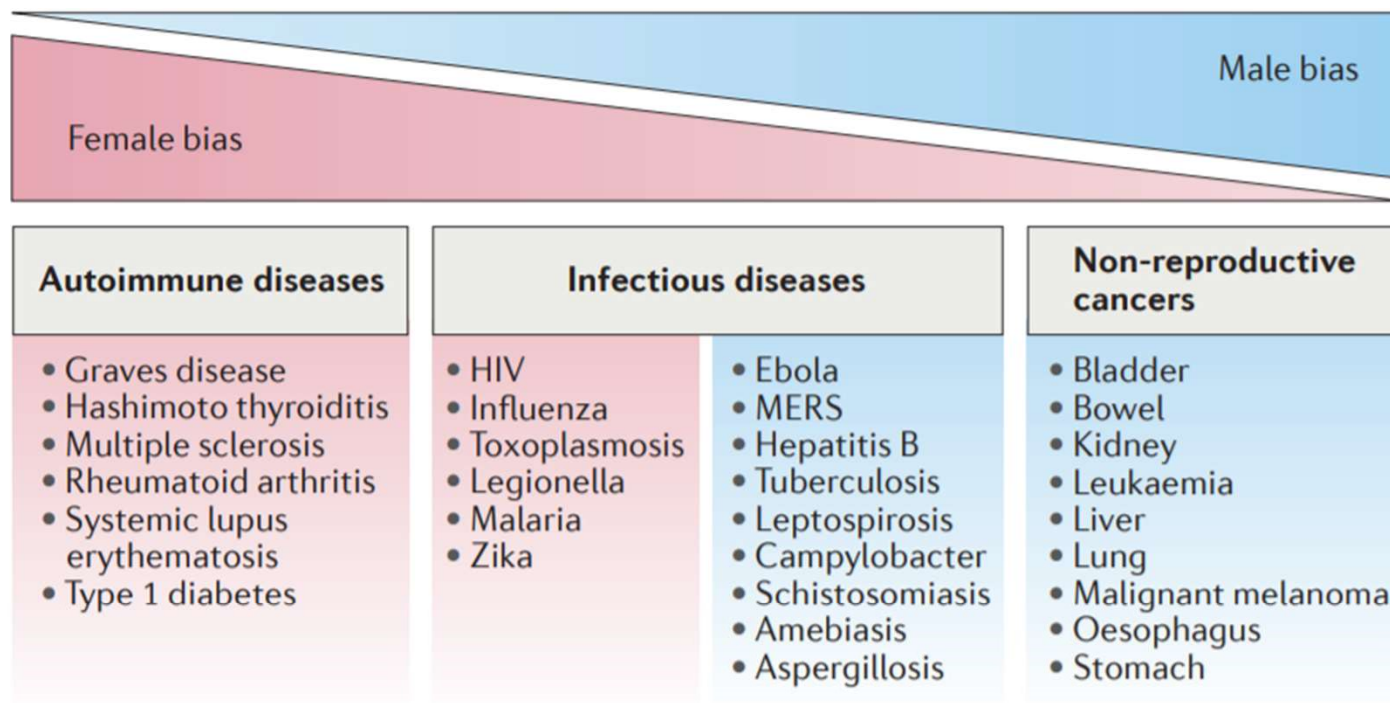
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Males have higher glioblastoma (GBM) incidence rates and worse outcome



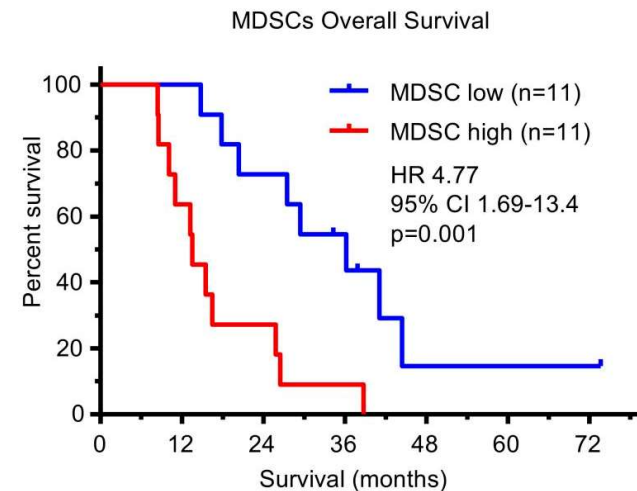
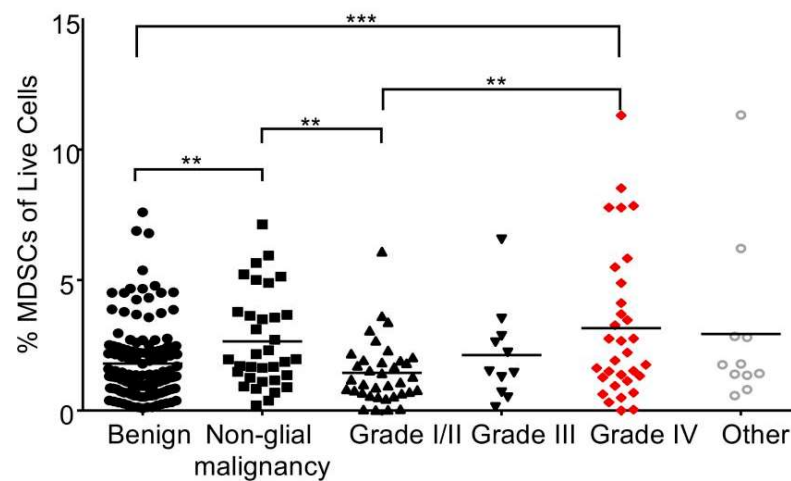
(Ostrom *et al.*, *Scientific Reports*, 2018)

Sex differences in immune response associate with disease prevalence



(Klein and Flanagan, *Nat Rev Immunol*, 2016)

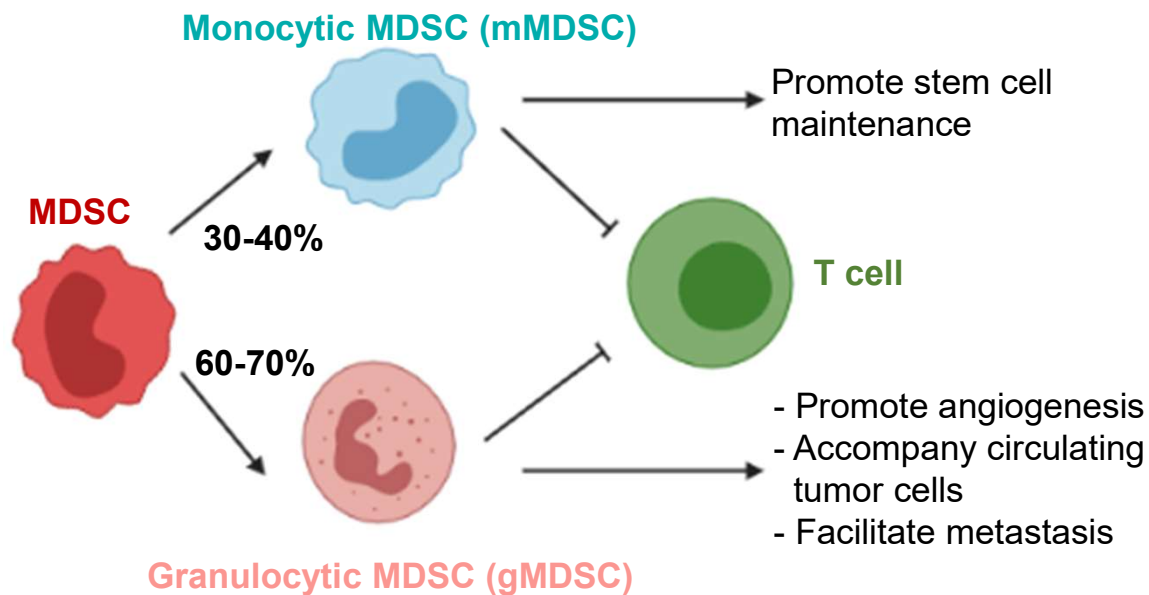
Myeloid-derived suppressor cells (MDSCs) correlate with poor GBM outcome



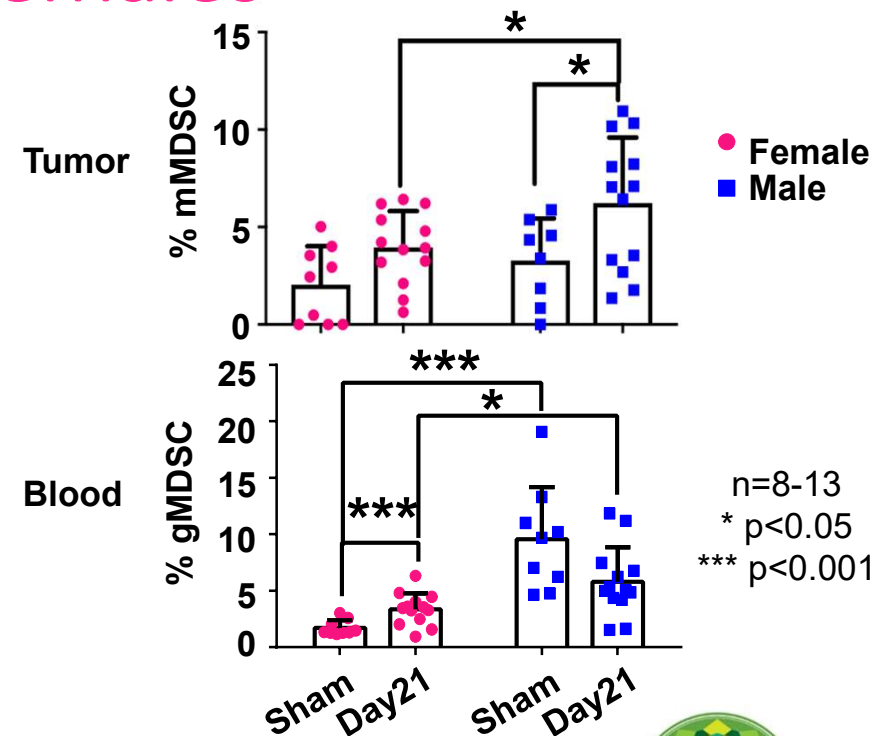
(Alban et al., *JCI Insight*, 2018)

Outstanding Question: What is the impact of biological sex on MDSC-driven GBM immunosuppression?

MDSC subsets differentially accumulate in males versus females



(adapted from Gabrilovich et al., *Nature Rev Immunol.*, 2009)

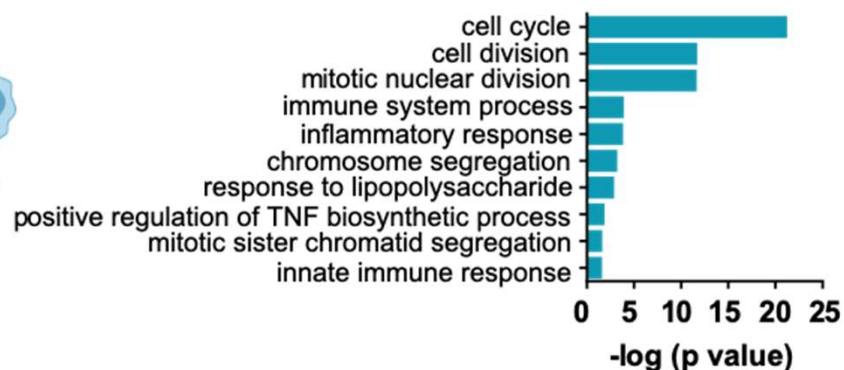


(Bayik et al., *Cancer Discovery*, 2020)

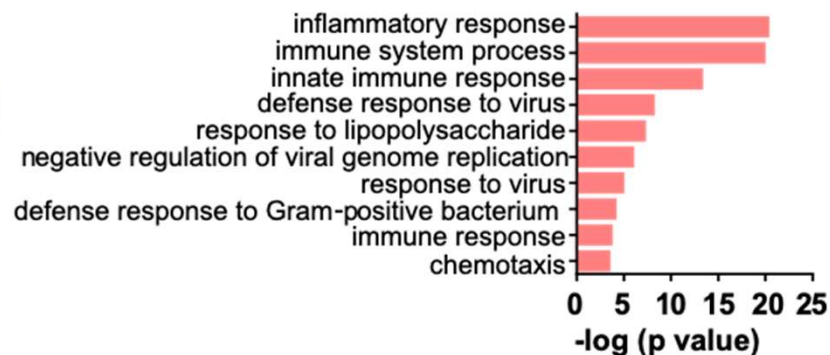
Differential expression profile of MDSCs identify therapeutic vulnerabilities



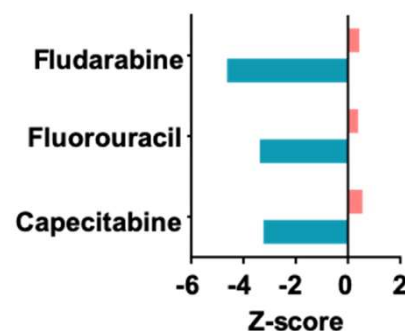
mMDSC



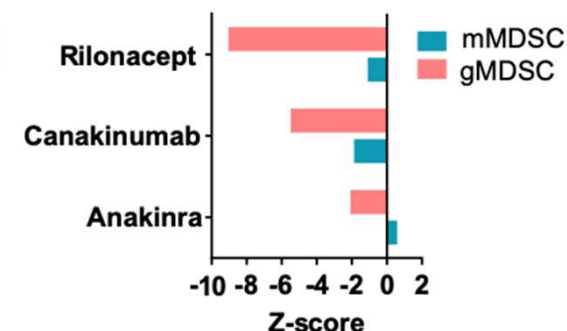
gMDSC



Chemotherapies

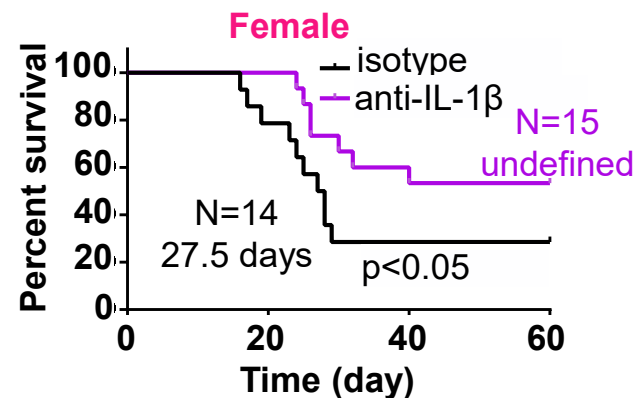
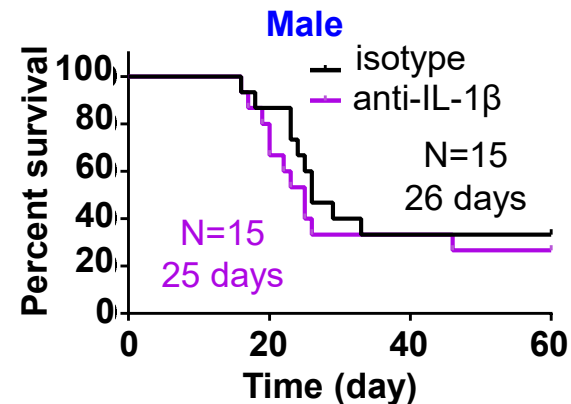
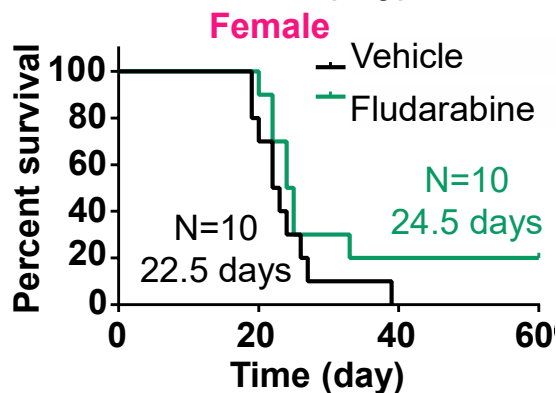
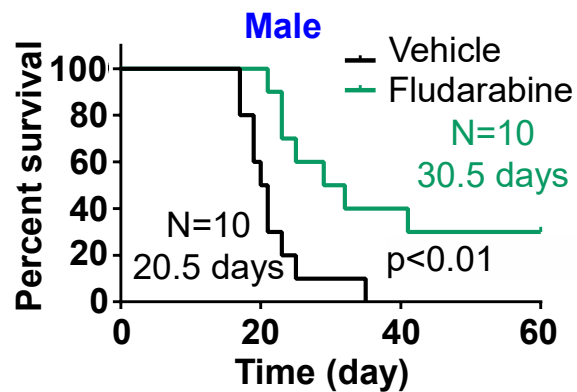


IL-1 inhibitors



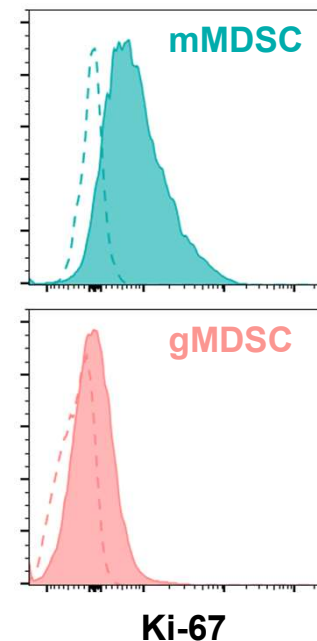
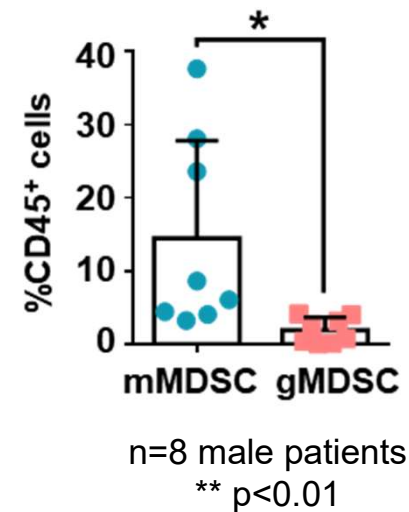
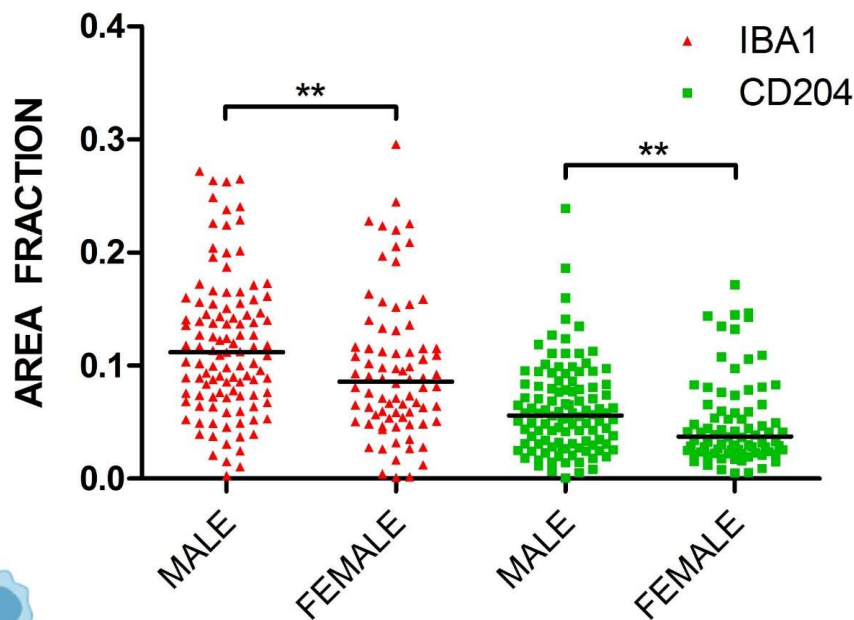
(Bayik et al., *Cancer Discovery*, 2020)

MDSC subsets are susceptible to different drugs



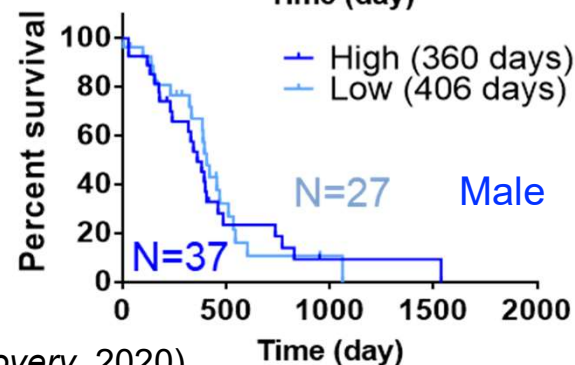
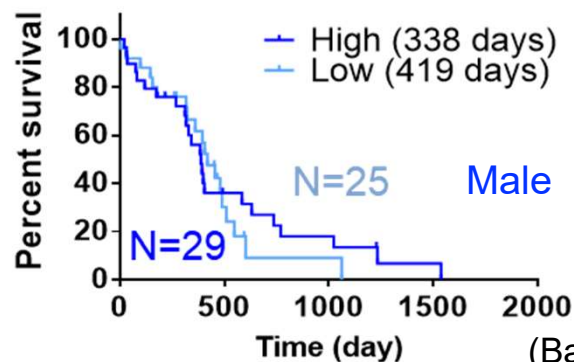
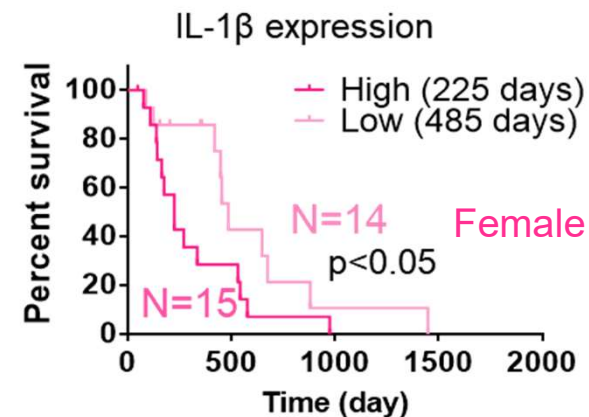
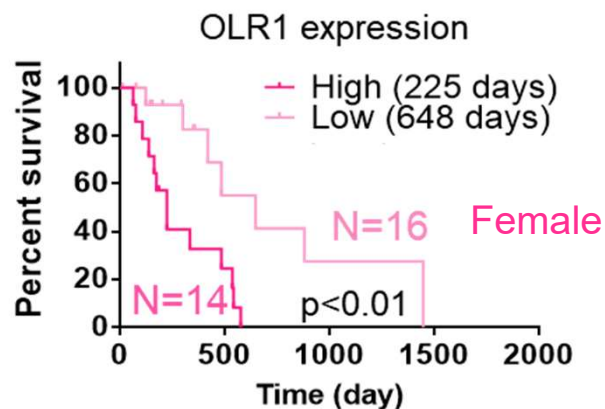
(Bayik et al., *Cancer Discovery*, 2020)

Male patients have more tumor-infiltrating immunosuppressive myeloid cells



(Bayik et al., *Cancer Discovery*, 2020)

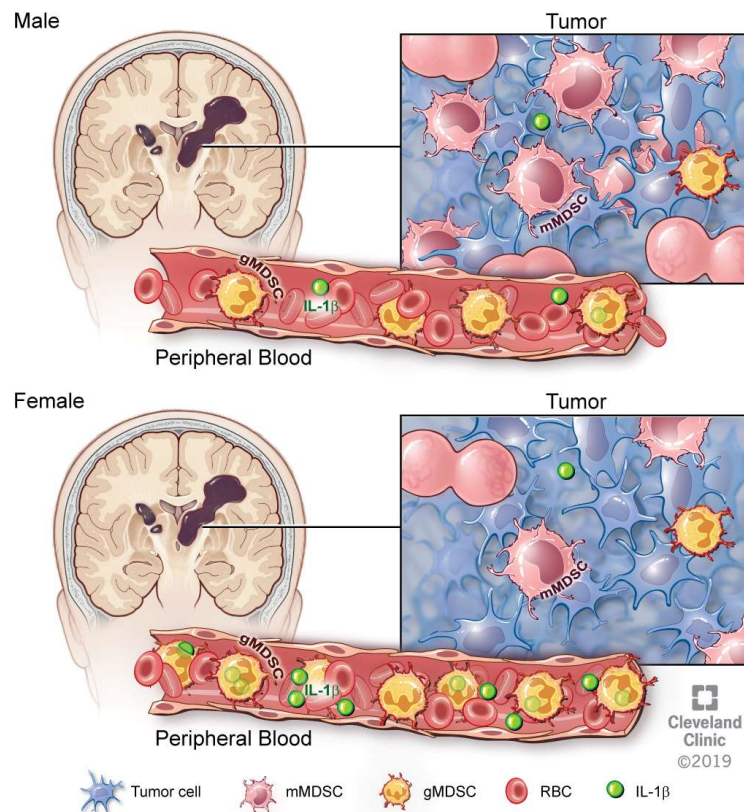
gMDSC signature correlate with prognosis of female GBM patients



(Bayik et al., *Cancer Discovery*, 2020)



Interim Conclusions

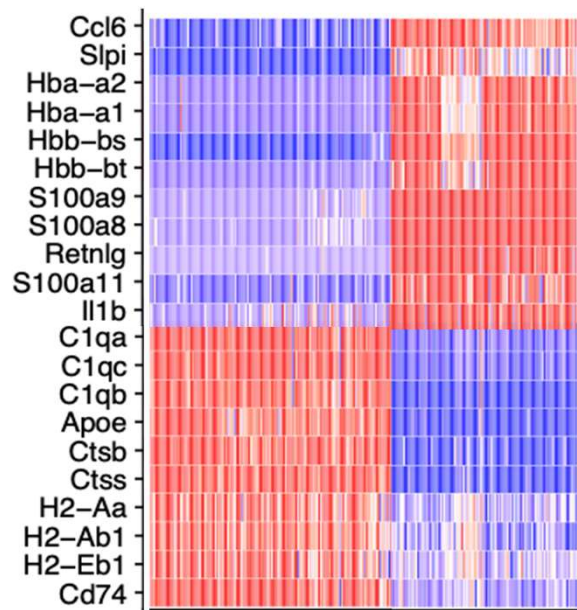


- **mMDSCs** infiltrate the tumor microenvironment, where they actively proliferate.
- IL-1 β secretion by **gMDSCs** comprise a therapeutic target for **females** (*clinical trial pending in 2021*).

(Bayik et al., *Cancer Discovery*, 2020)

Outstanding Question: How does systemic gMDSC accumulation drive GBM and what biological pathways regulate gMDSC activity?

Potential for systemic-local immunity communication



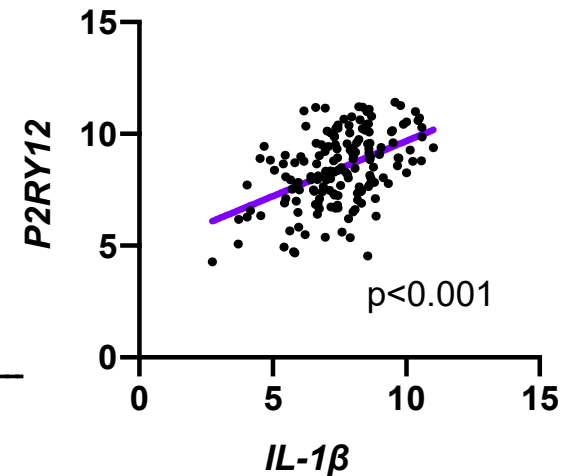
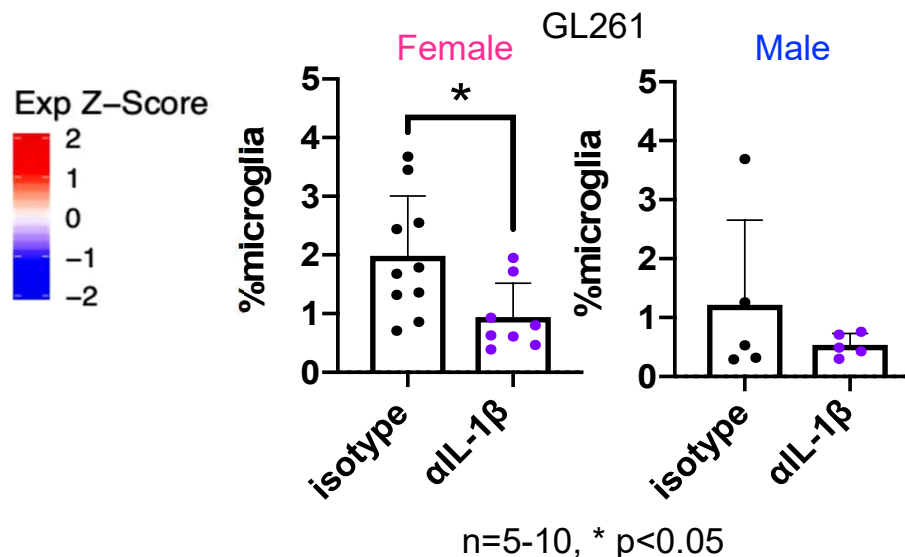
tumor
gMDSC

blood
gMDSC

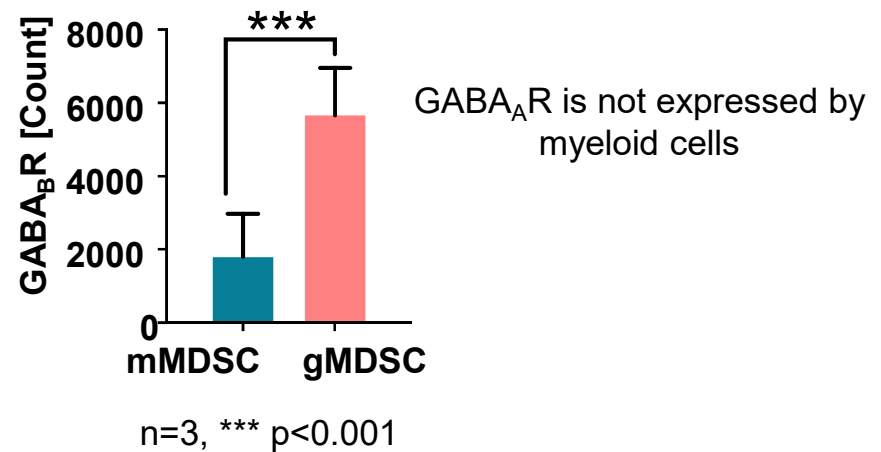
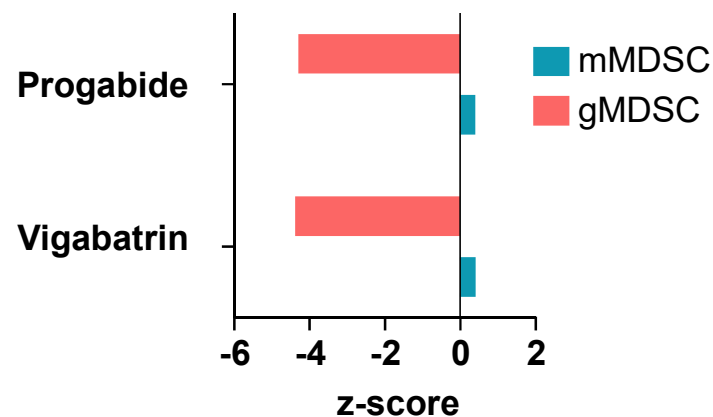


gMDSC

(unpublished)



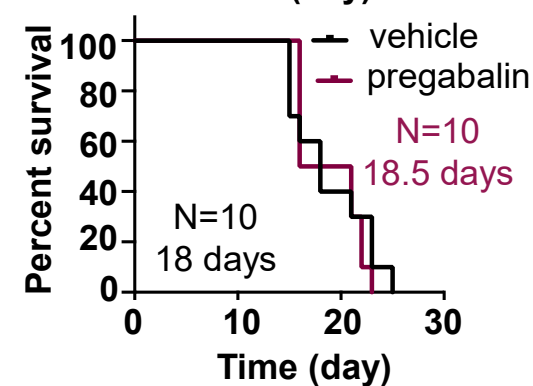
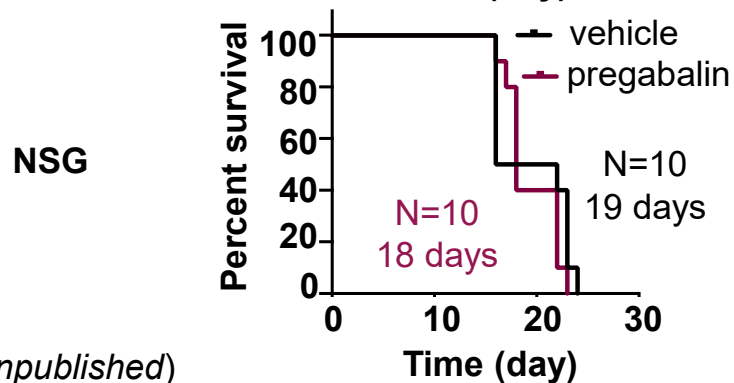
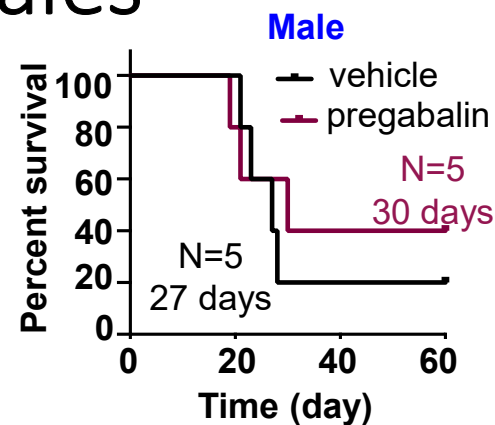
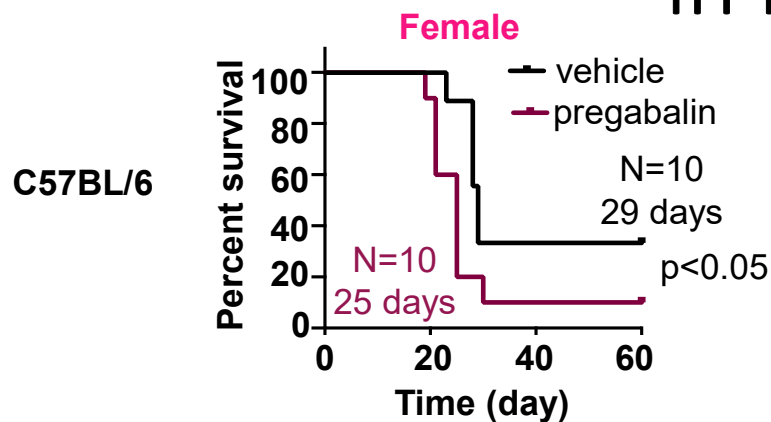
gamma-Aminobutyric acid (GABA) signaling as a potential regulator of gMDSCs



gMDSC

(unpublished)

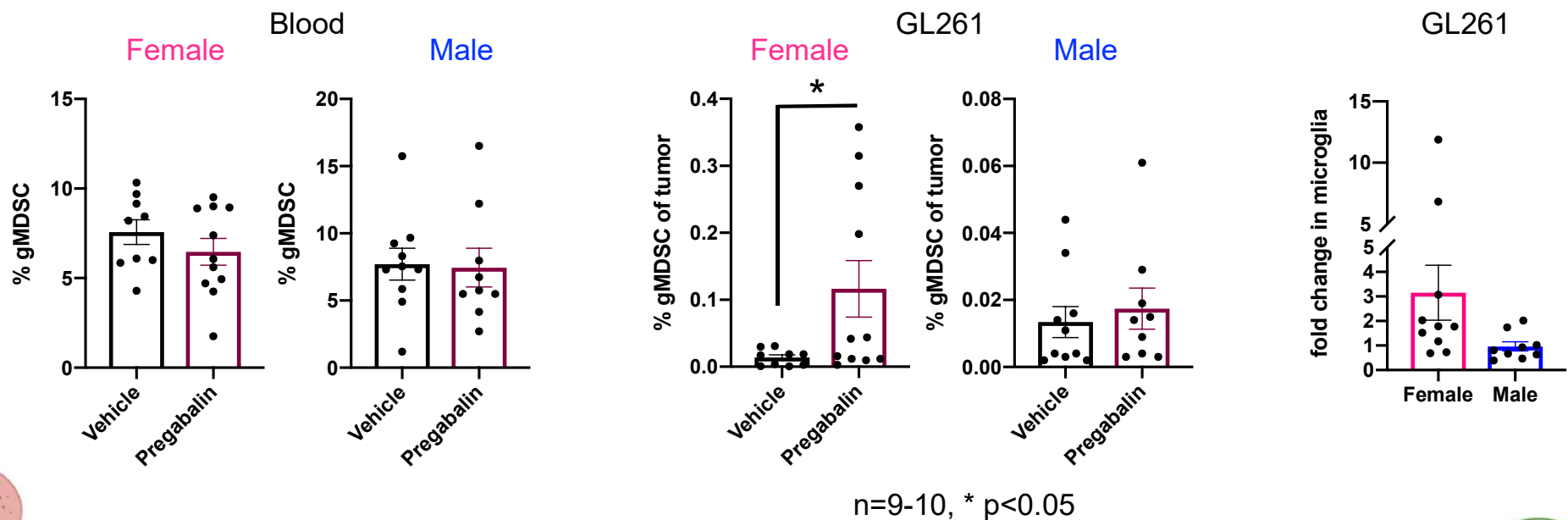
GABA analogue accelerates GBM progression in females



gMDSC

(unpublished)

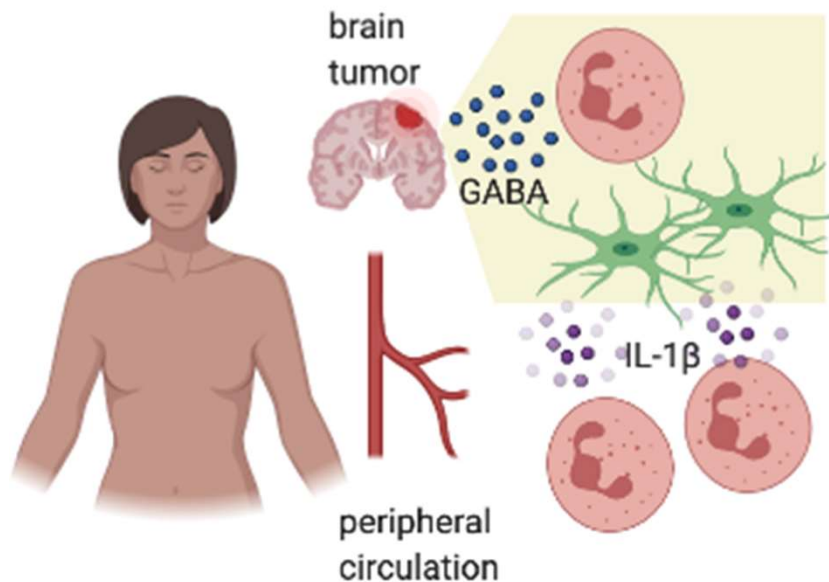
GABA analogue increases tumor infiltration of gMDSCs in females



gMDSC

(unpublished)

Conclusions & Future Perspective



- Systemic **gMDSC** accumulation drives microglia infiltration of GBM via IL-1 β signaling
- Altered GABA signaling serves as a potential regulator of local **gMDSC** activity.
- Investigation of the effect of IL-1 β on microglia polarization
- Analysis of the effect of GABA on **gMDSC** behavior



CASE
COMPREHENSIVE
CANCER CENTER



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