

Antibody targeting of TAMs in pancreatic cancer and melanoma

- Remodel the tumor microenvironment to revives immune targeting of tumor cells**

Dhifaf Sarhan, Assistant Professor

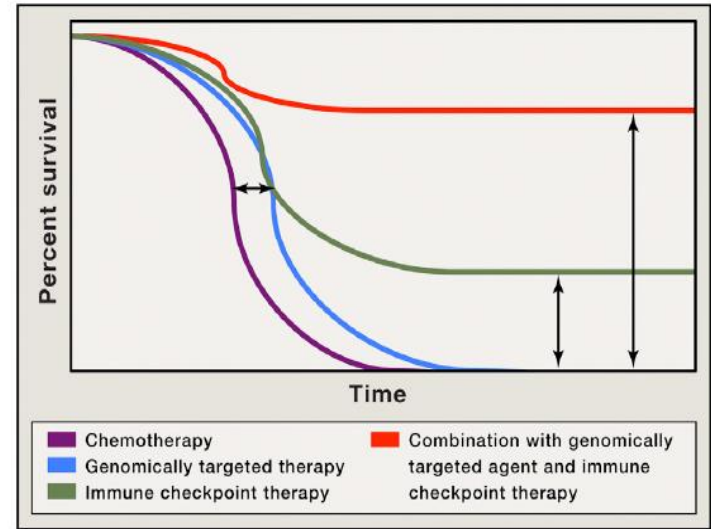
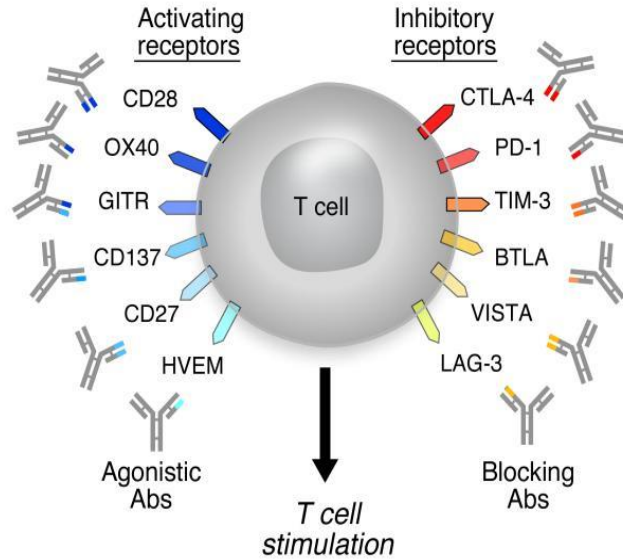
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No financial relationship to disclose

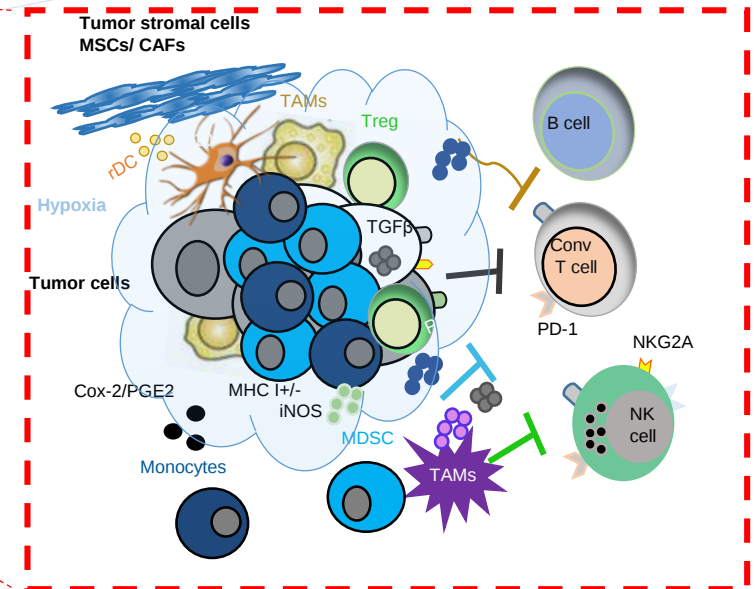
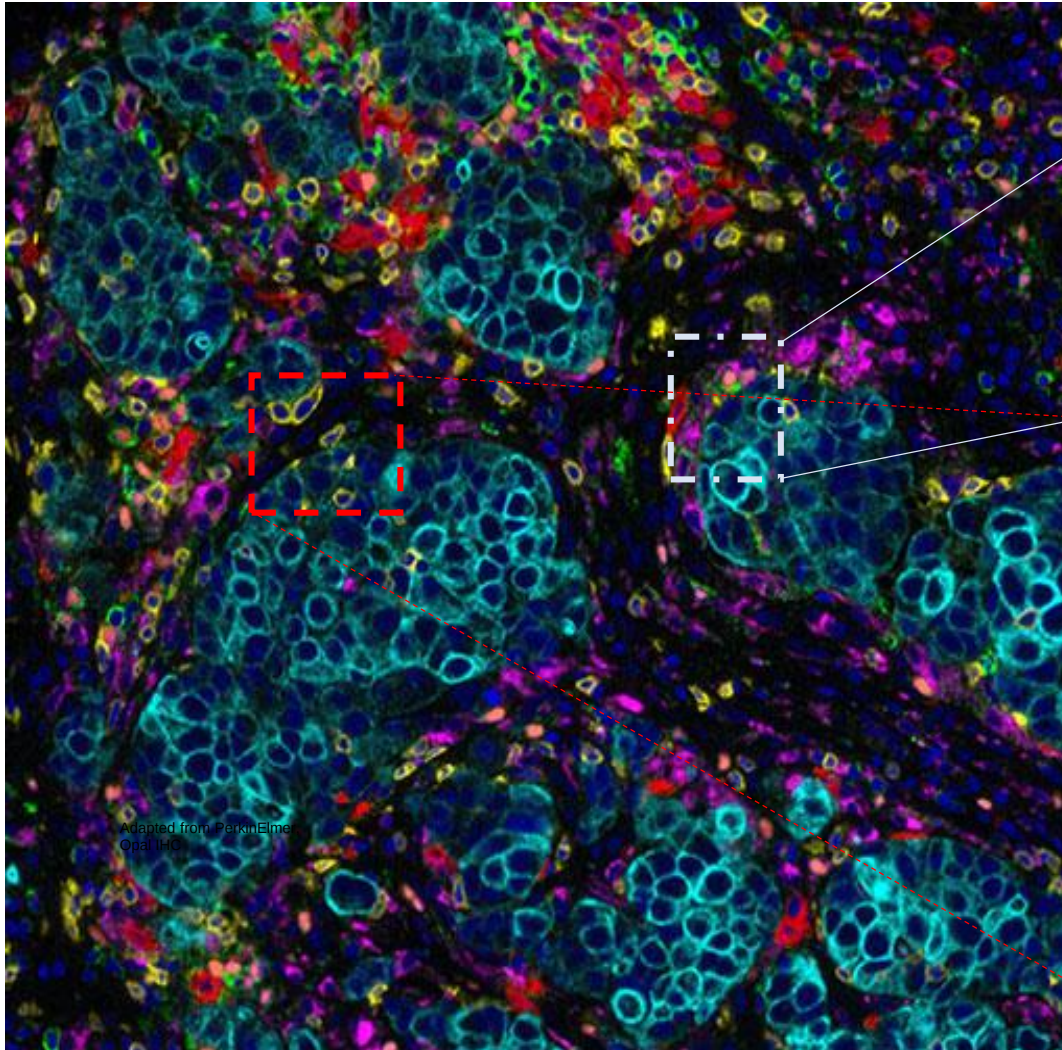
Immunotherapy for Cancer



Sharma and Allison: Cell 2015

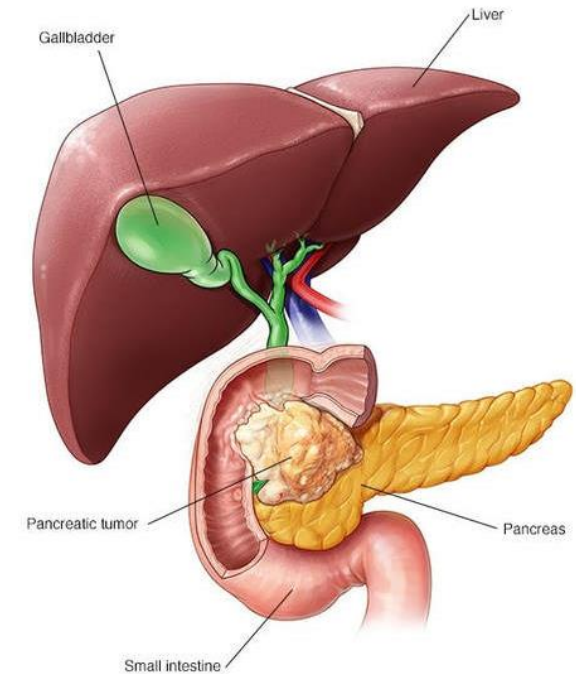
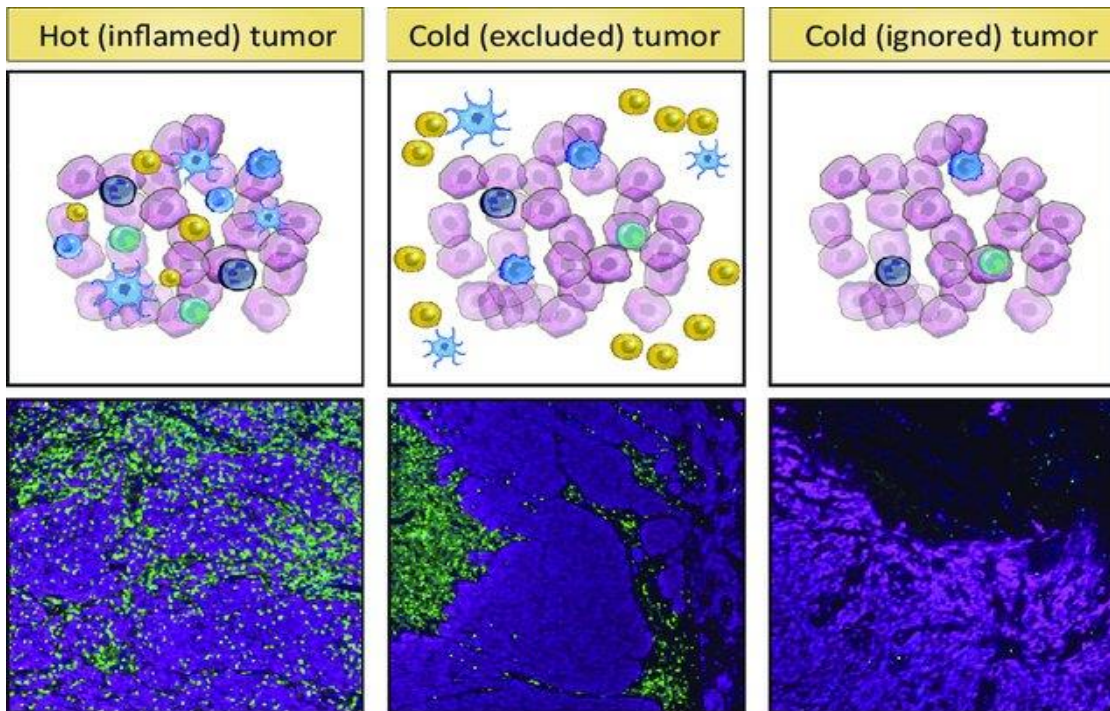
≥ 50% expected to respond
TME?

The tumor microenvironment

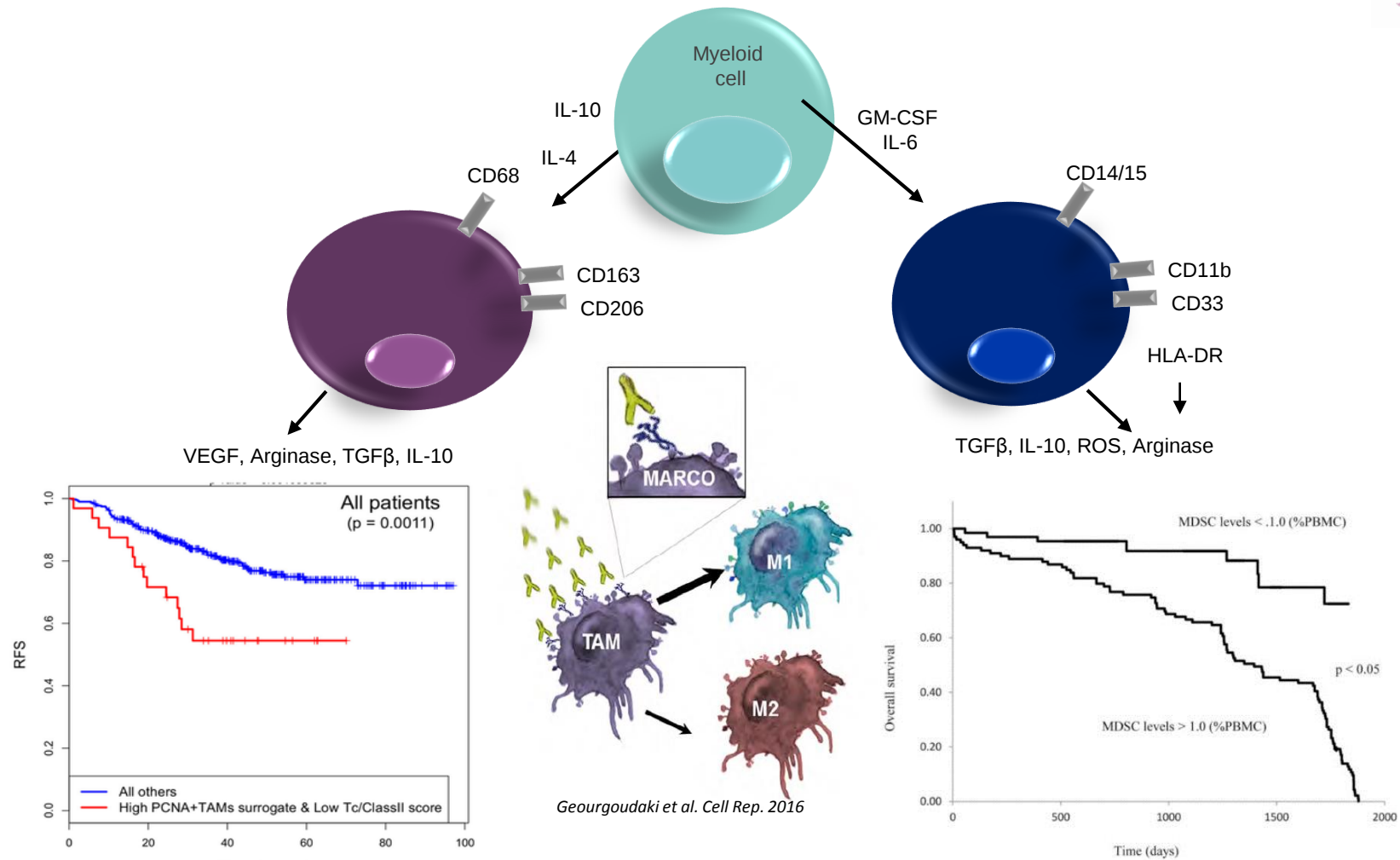


Pancreatic cancer

- *Tumor characteristics, cold tumor, immune-excluded, hot tumor, low immunogenicity*
- 80% of stromal tissue (tumor microenvironment, TME) composed of lymphoid structures, suppressive immune cells including MDSC and TAMs
- Macrophages, shift to M1 and M2 in TME depending on stimuli



TAMs vs. MDSCs

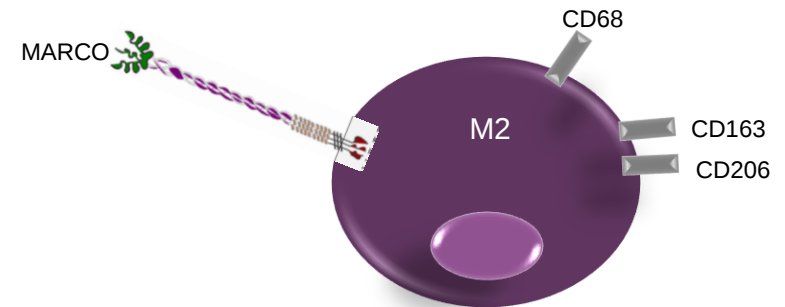


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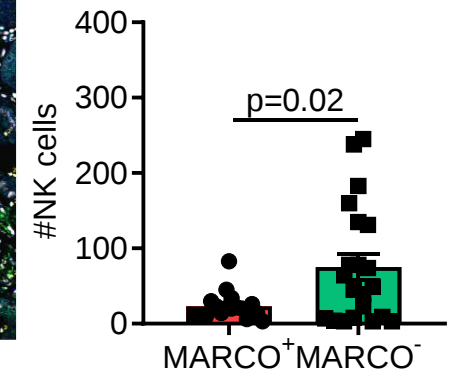
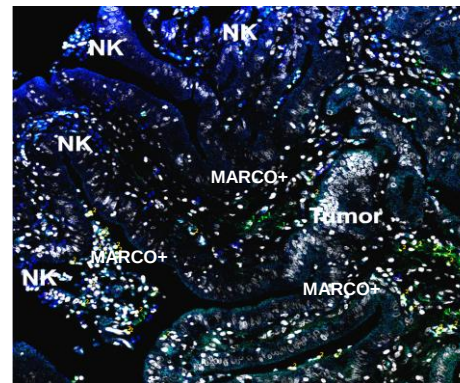
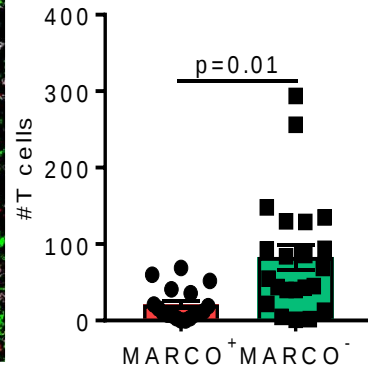
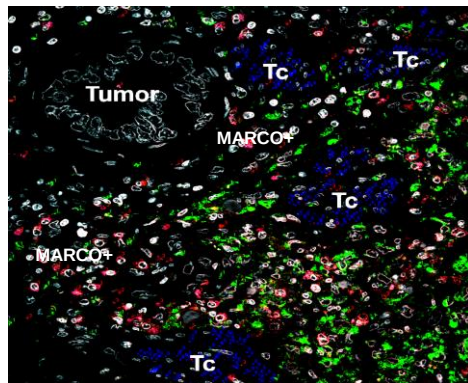
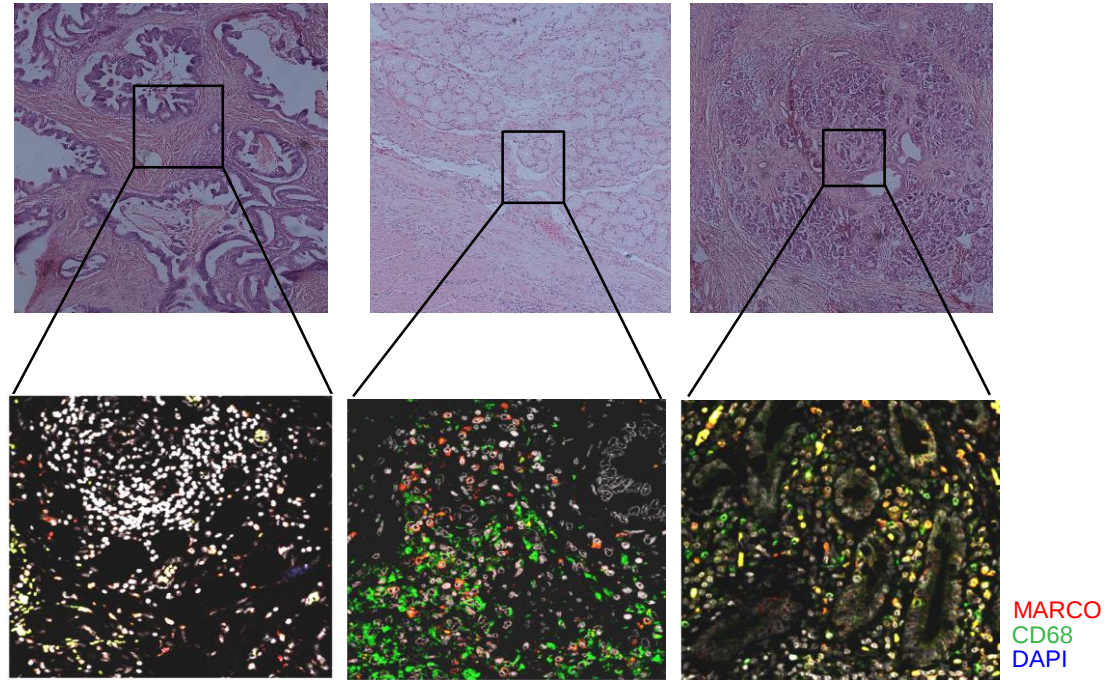
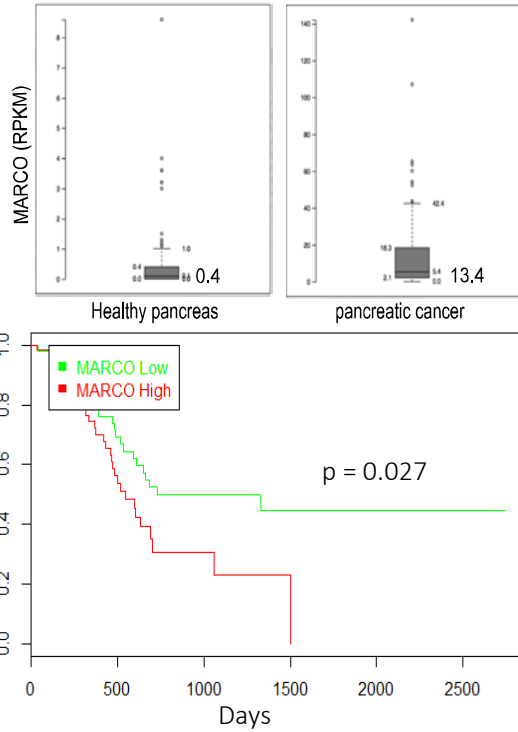
<https://doi.org/10.3892/ol.2017.6305>

Scavenger receptor MARCO

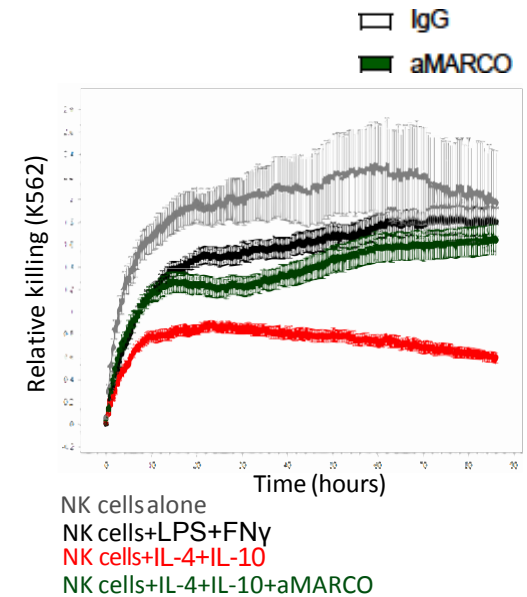
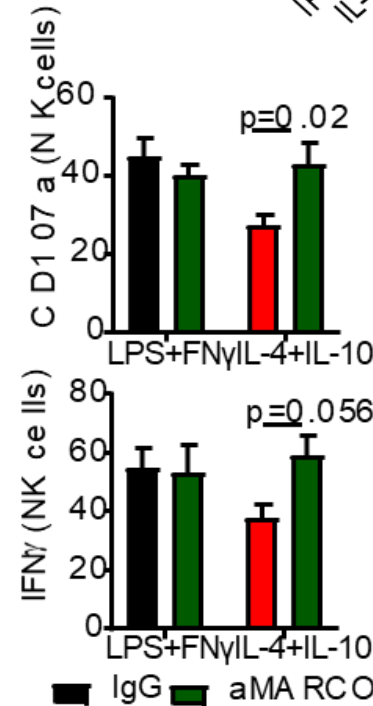
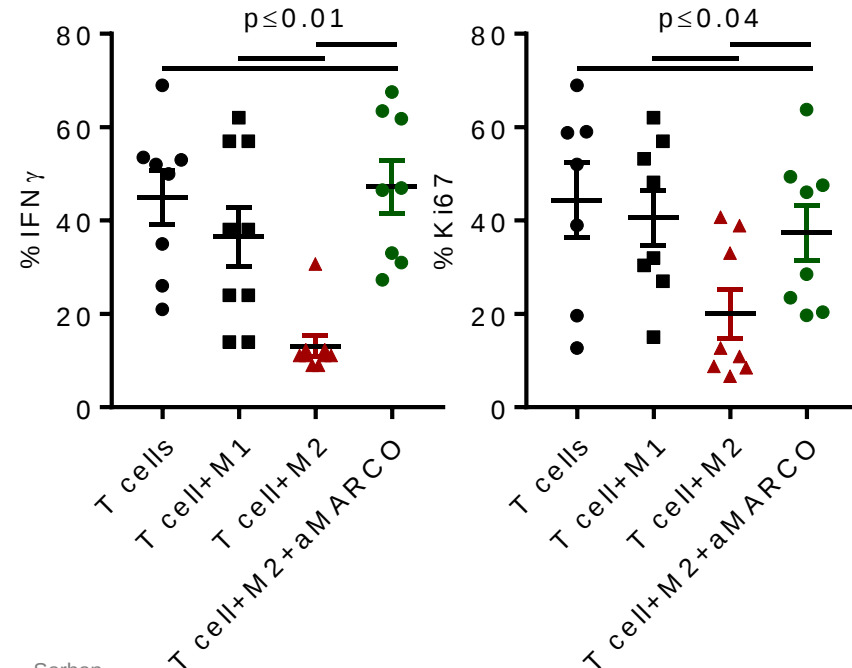
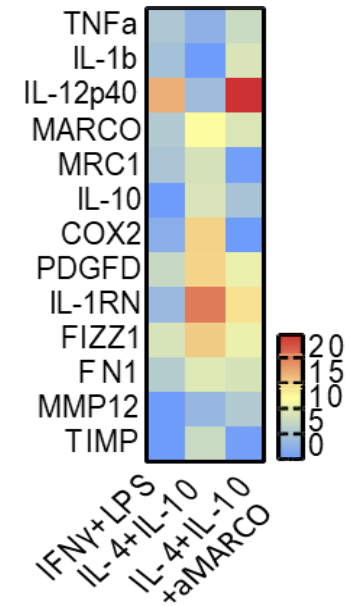
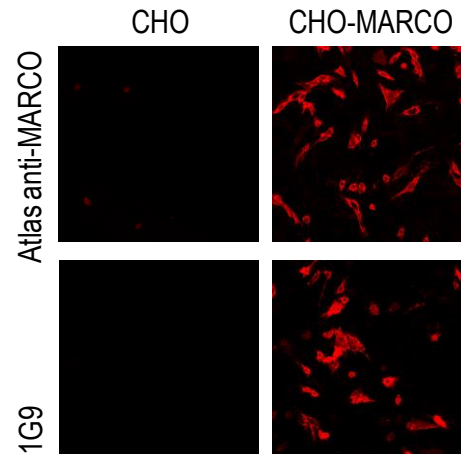
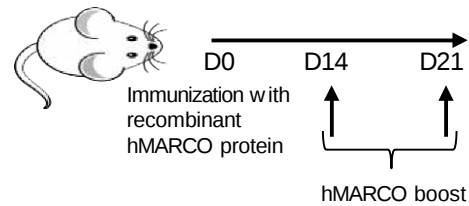
- Janitorial function, uptake & clearance
 - foreign ligands: pathogens
 - self ligands: apoptotic cells, oxLDL
- Restricted normal expression:
 - subpopulation in the spleen, peritoneum and LN
- **Overexpressed in the tumor microenvironment**



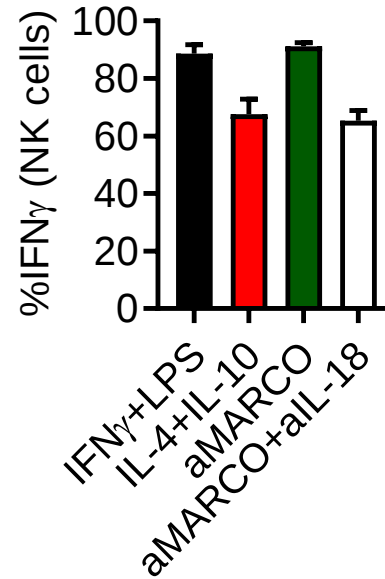
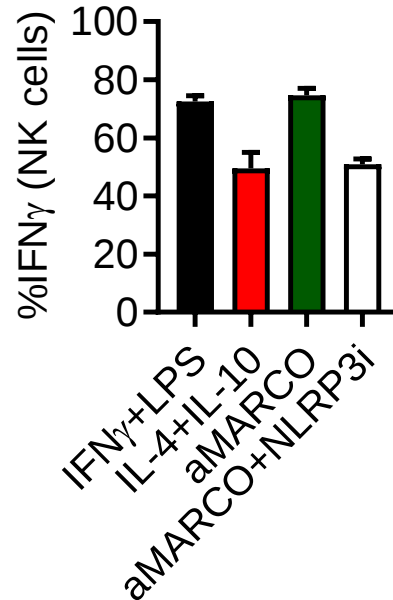
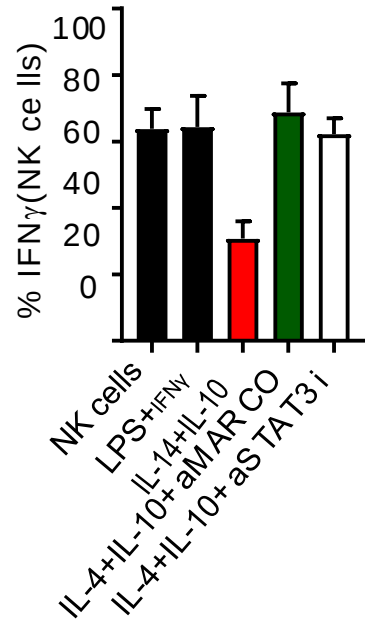
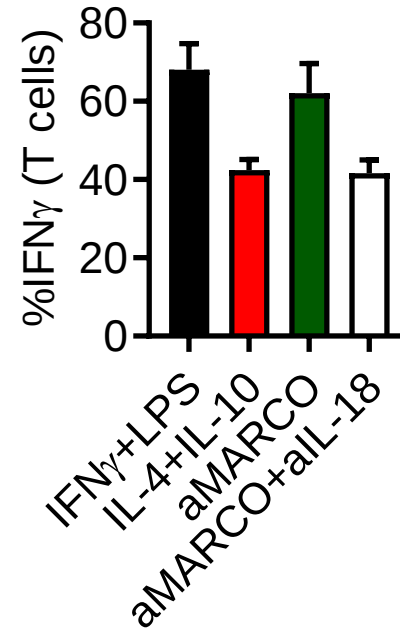
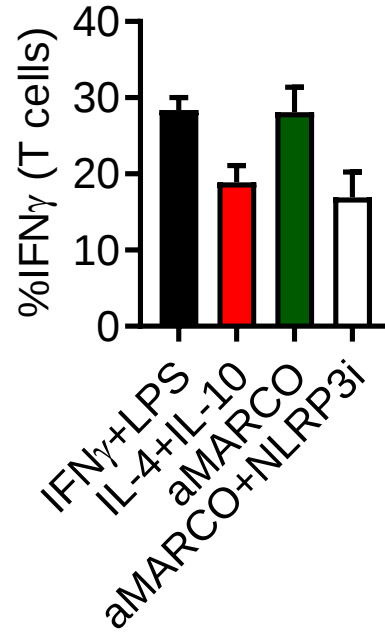
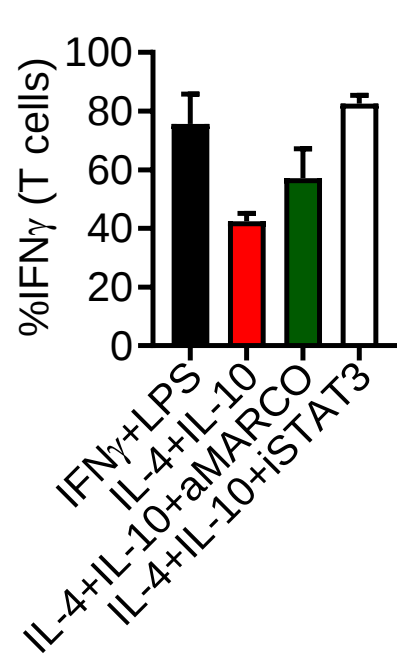
MARCO is involved in tumor microenvironment modulation



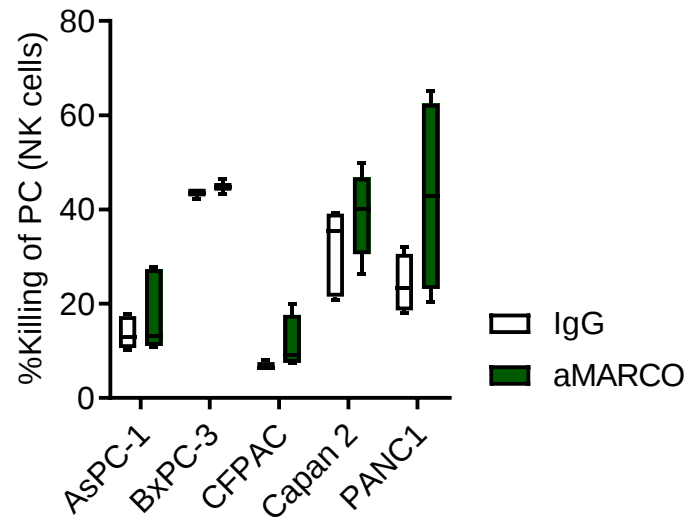
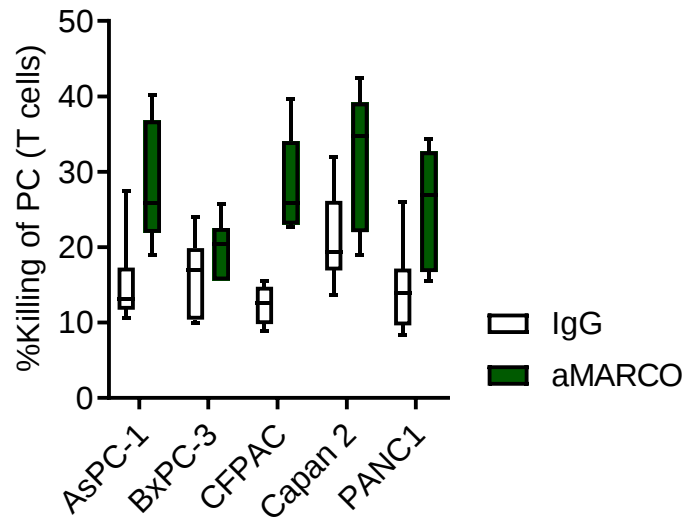
Anti-MARCO antibody treatment



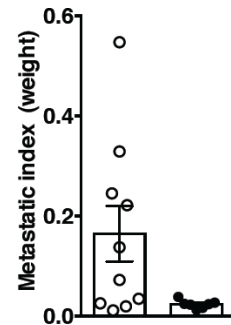
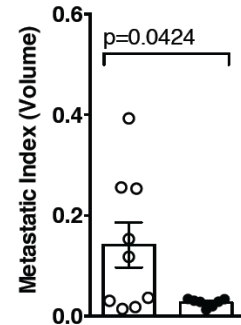
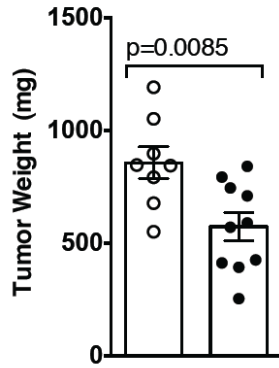
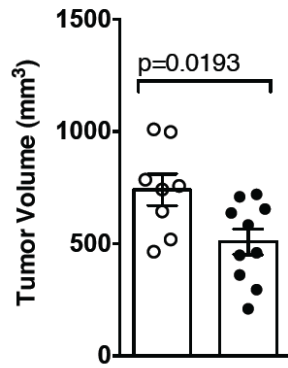
Mechanism of aMARCO treatment



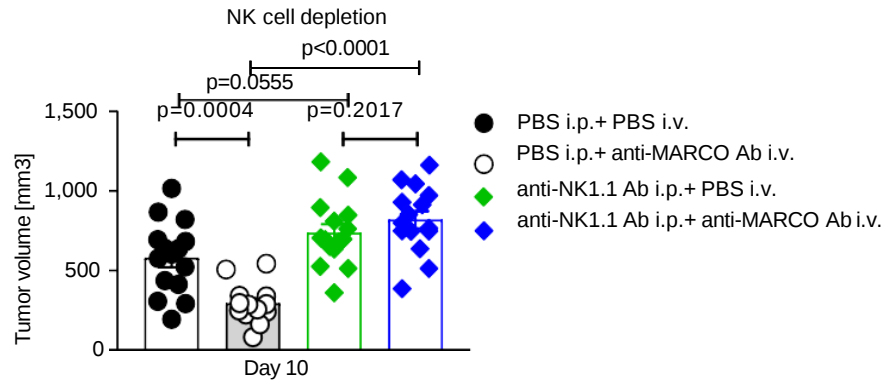
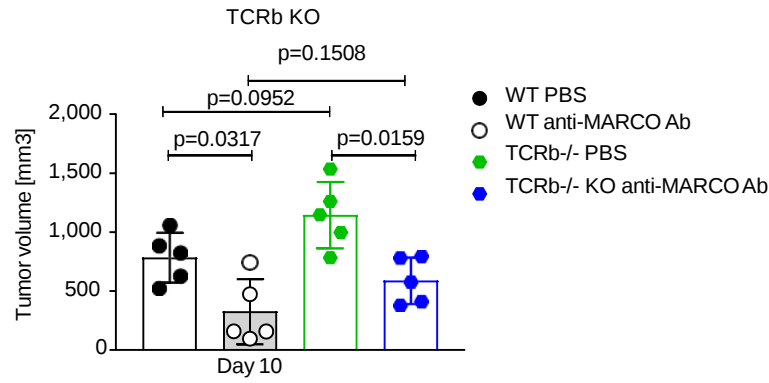
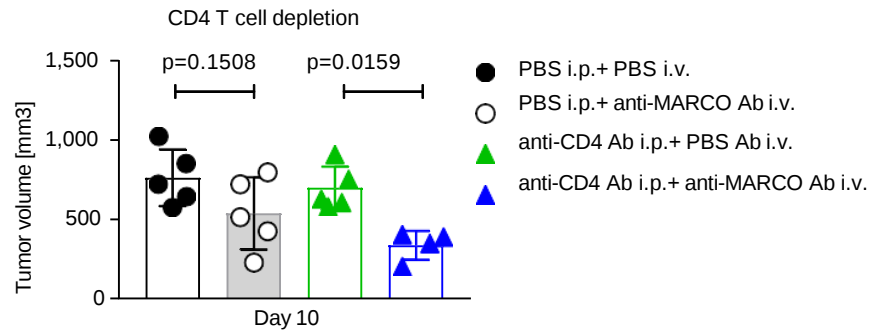
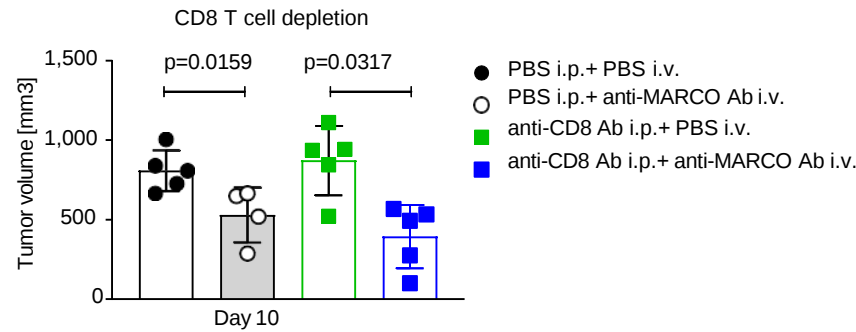
aMARCO treatment in PC



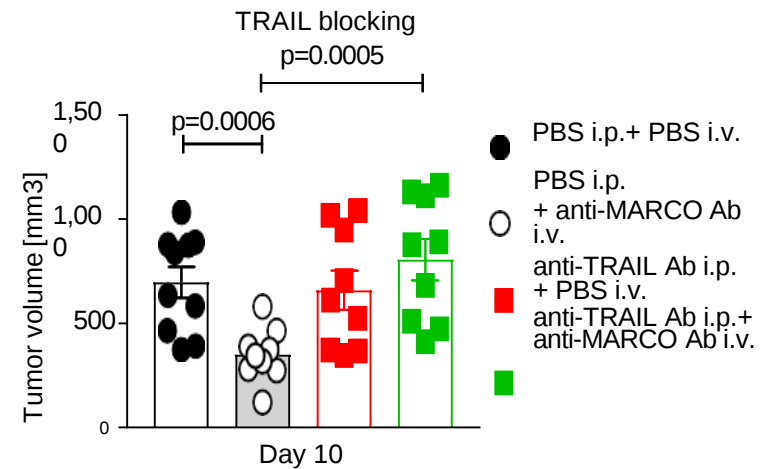
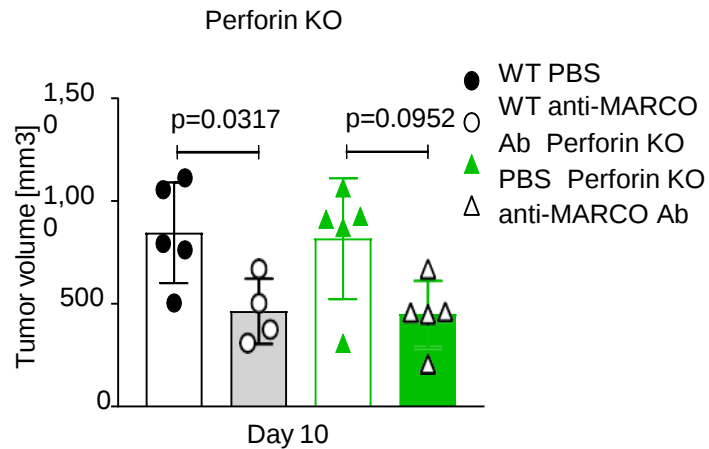
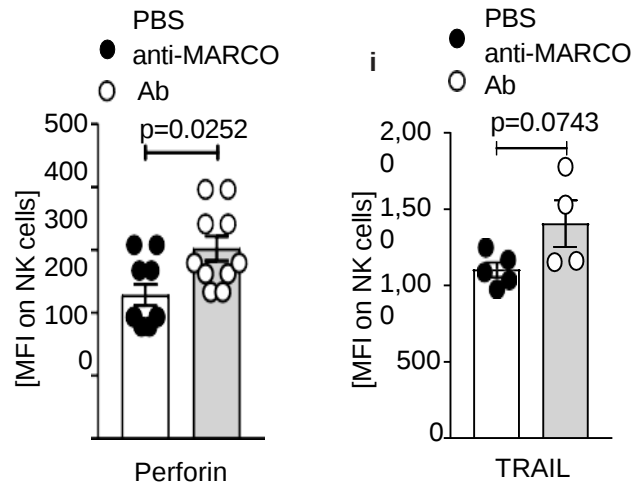
aMARCO treatment Melanoma *In vivo*



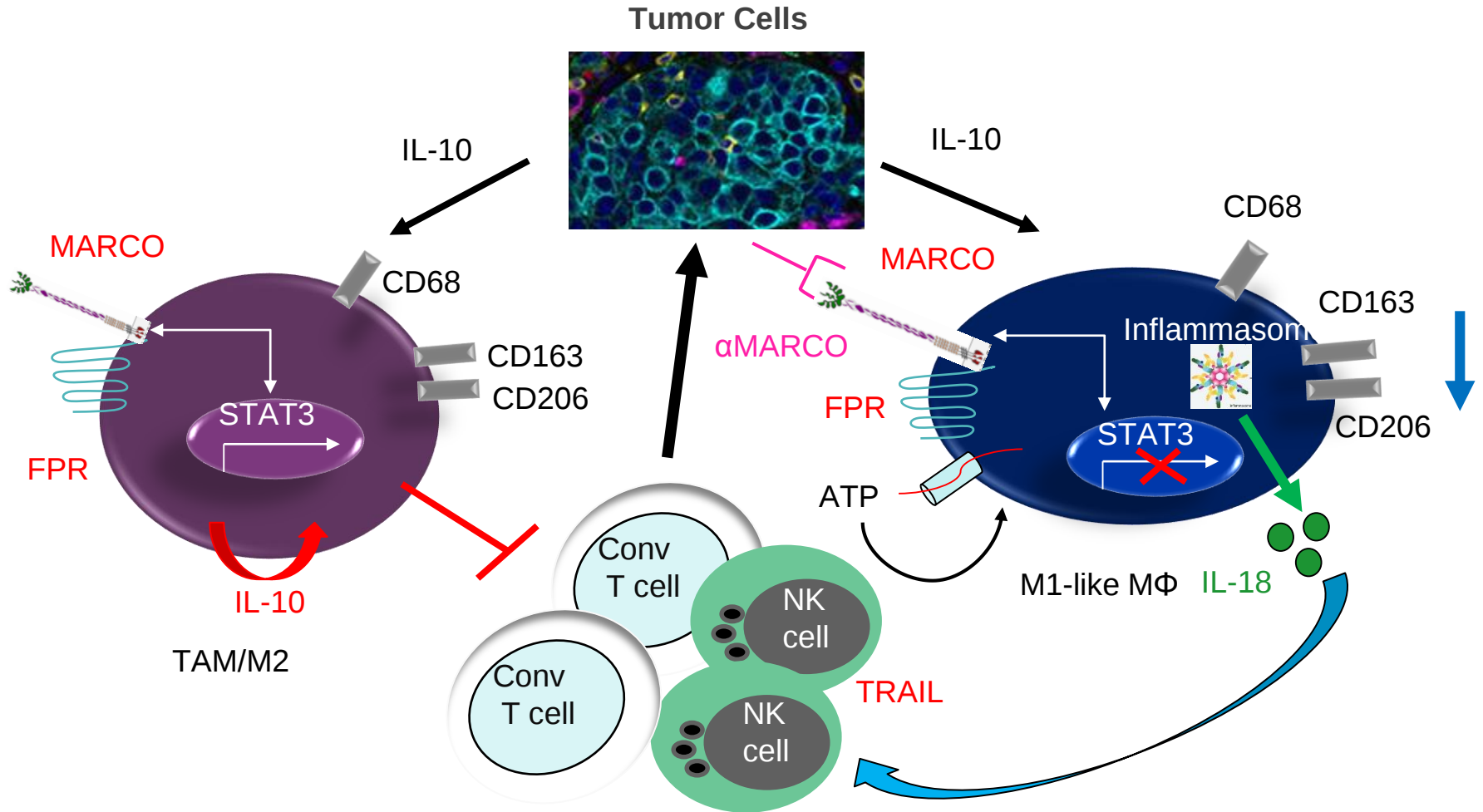
Geourgoudaki et al. Cell Rep. 2016



aMARCO treatment Melanoma *In vivo*



Summary



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