Outcompeting Cancer's "Don't Eat Me" Signal to Promote Immune Clearance

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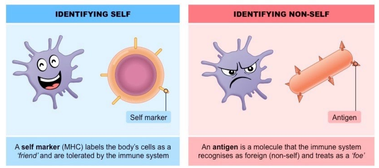
InterLACE 2023

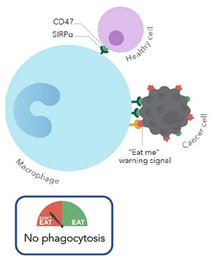
Introduction

The Immune System can effectively differentiate self from non-self to mount an immune response.

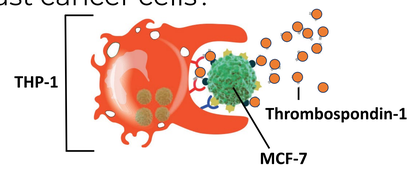


Cancer cells exploit "self" recognition by:

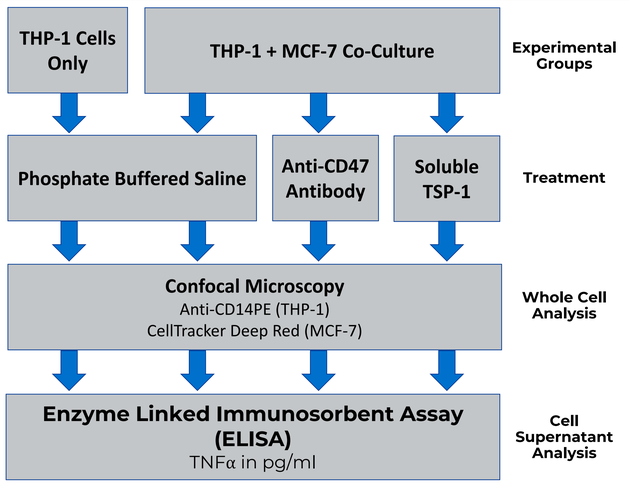
- Being of human origin
- Hijacking cells: produce more self-cell surface marker CD47
- Mimicking healthy self cells through CD47-SIRPα interaction



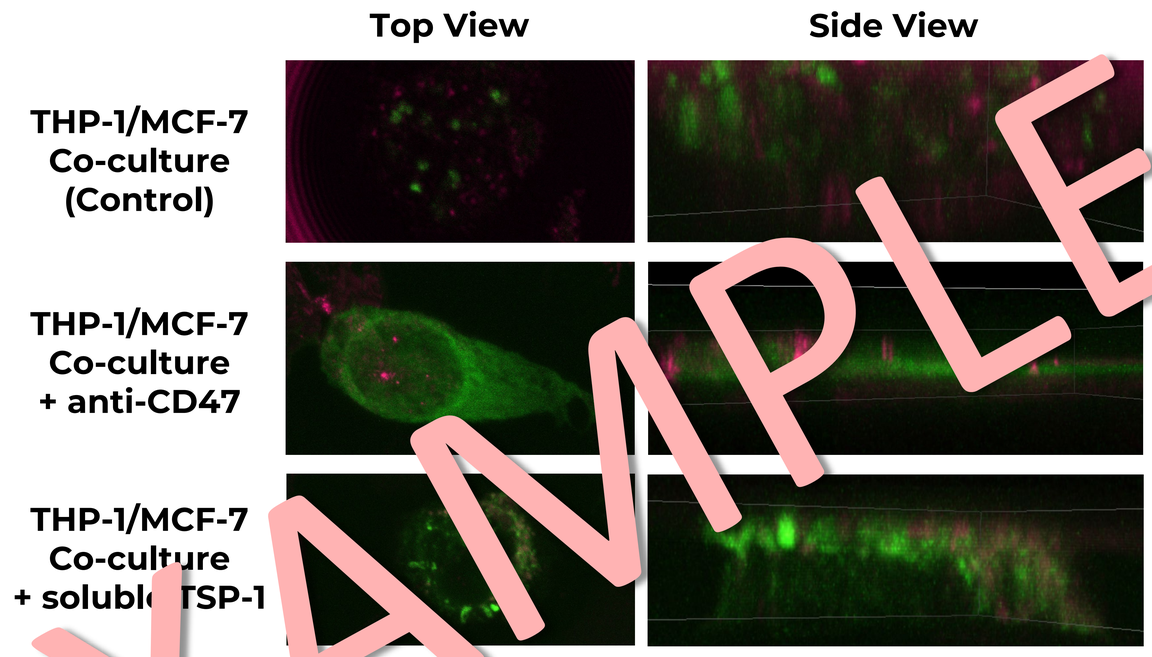
Research Question: Will the known high affinity CD47 ligand, Thrombospondin-1, outcompete the CD47-SIRPα interaction and allow THP-1 macrophage to phagocytose MCF-7 breast cancer cells?



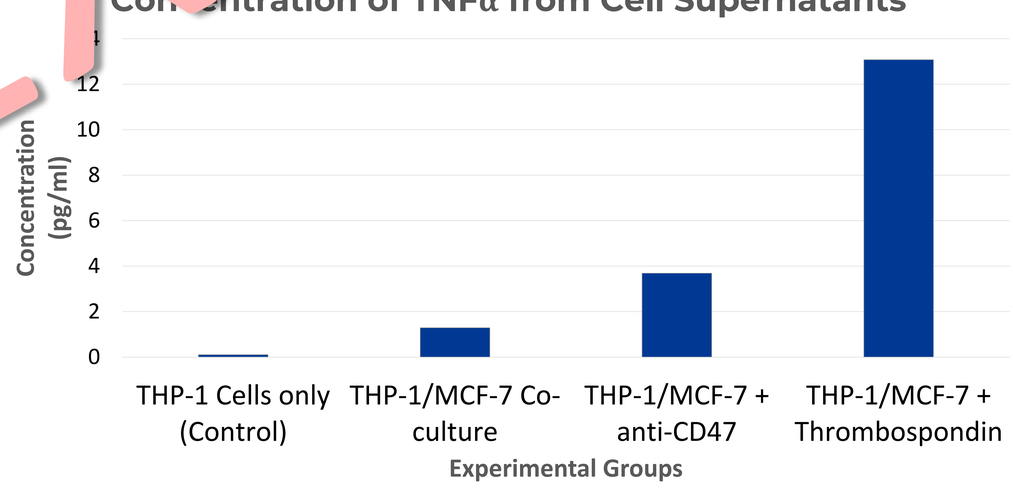
Methods



Results



THP-1: Anti-CD14PE (Green); MCF-7: CellTracker Deep Red (Red)



TNFα	Concentration (pg/m	Absorbance (OD
THP-1 Cells only (Control)	0.10465	0.0951
THP-1/MCF-7 Co-culture	1.289645	0.1152
THP-1/MCF-7 + anti-CD47	3.687839	0.1440
THP-1/MCF-7 + Thrombospondin	13.07613	0.2835

Conclusion

THP-1/MCF-7 co-culture	THP-1/MCF-7 co-culture + anti-CD47	THP-1/MCF-7 co-culture + Thrombospondin-1
• MCF-7 cells not clearly inside-outside THP-1 macrophage • Slight increase in TNFα production	• MCF-7 cells appear to be internalized by THP-1 macrophage • Moderate increase in TNFα production	• MCF-7 cells not clearly inside-outside THP-1 macrophage • Large increase in TNFα production

Improvements:

- Optimize co-incubation time
- Utilize whole cell label for THP-1

Future Studies:

- Try other known CD47 ligands
- Use activated THP-1 cells (M1 vs M2)

Research Team

The interdisciplinary and interprofessional team included a diverse set of experts (students, lab techs, clinicians, and research scientists) from multiple departments in the College of Science and Medicine, with skills in biochemistry, medicine, biology, and morphology.

References

1. Overview of the Immune System. (2013). National Institute of Allergy and Infectious Diseases. https://www.niaid.nih.gov/research/immune-system-overview
2. [Self vs Non-Self]. BioNinja. https://ib.bioninja.com.au/higher-level/topic-11-animal-physiology/111-antibody-production-and/self-versus-non-self.html
3. Chao, M.P., Takimoto, C.H., Feng, D.D., McKenna, K., Gip, P., Liu, J., Volkmer, J., Weissman, I.L., Majeti, R. (2020). Therapeutic Targeting of the Macrophage Immune Checkpoint CD47 in Myeloid Malignancies. *Frontiers in Oncology. 22*(January 2020). https://doi.org/10.3389/fonc.2019.01380
4. Takimoto, C.H., Chao, M.P., Gibbs, C., McCamish, M.A., Liu, J., Chen, J.Y., Majeti, R., Weissman, I.L. (2019). The Macrophage "Do not eat me" Signal, CD47, is a Clinically Validated Cancer Immunotherapy Target. *Annals of Oncology. 30*(3). 486-489. https://doi.org/10.1093/annonc/mdz006

EXAMPLE