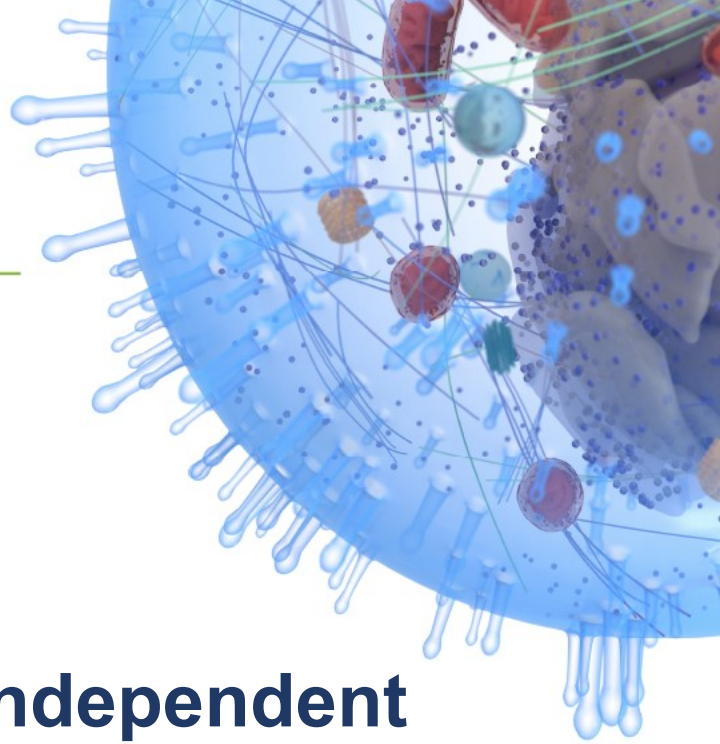


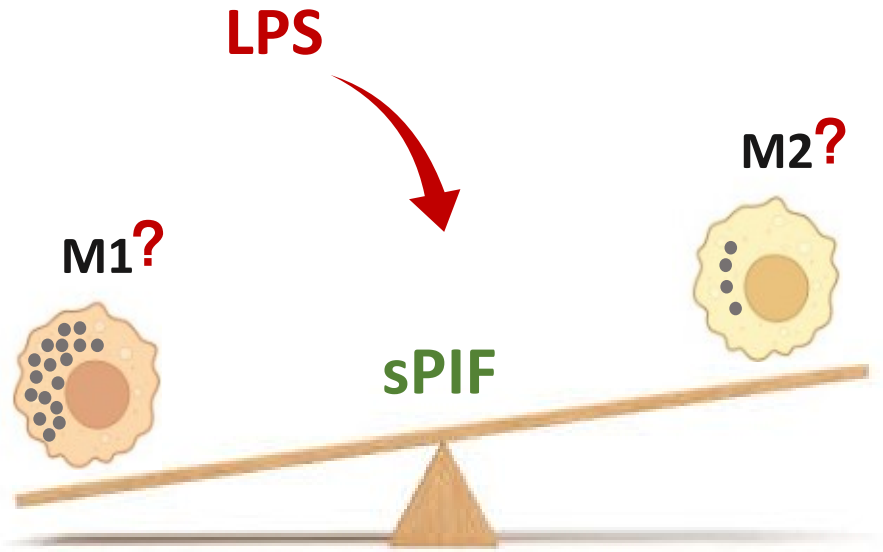
Preimplantation factor (PIF) modulates opsonin-independent phagocytosis of cultured human macrophages

Chen Li
Julian Schneider
Christian Scheiber
Prof. Dr. Marion Schneider

Division of Experimental Anesthesiology, University Hospital Ulm, Germany

Background:

- Opsonin-independent phagocytosis describes the ubiquitous engulfment of non-opsonized particles by macrophages[1].
- CD163 is a marker of anti-inflammatory M2 macrophages and is linked to high, CD47-independent phagocytic activities [2].
- LPS activates NF-κB and drives M1-directed polarization [3].
- Preimplantation Factor (PIF) is an embryo-derived anti-inflammatory peptide characterized by downmodulating LPS-driven miRNA let-7 [4].

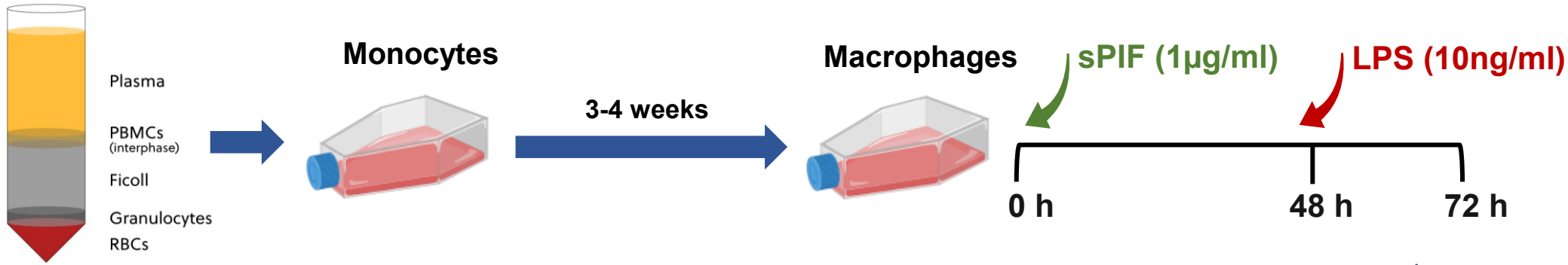


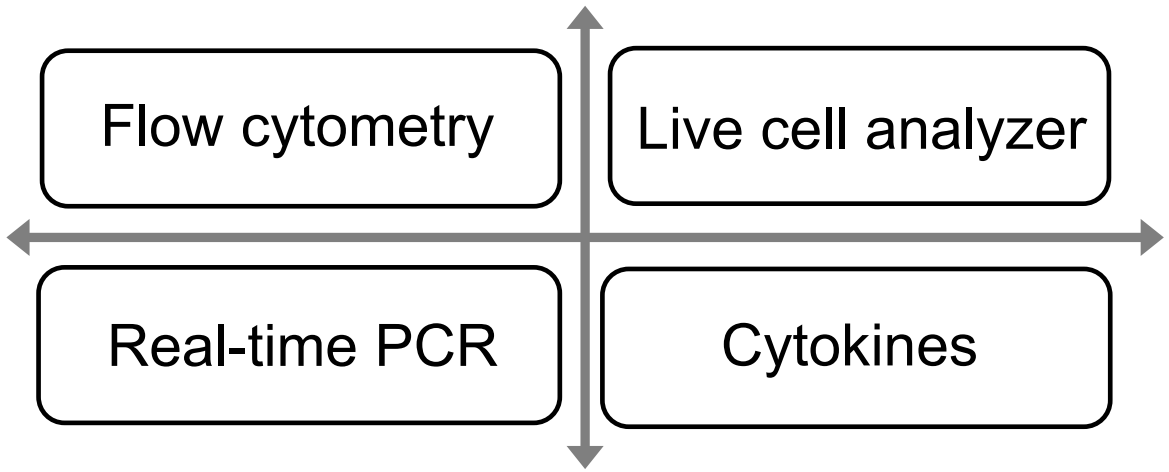
Aim:

- To study the modulation of synthetic PIF (sPIF) on opsonin-independent phagocytosis of M2 macrophages.

Patients and methods:

Macrophages were derived from peripheral blood of healthy controls (HCs, n=4), patients with brain tumors (n=5) and acute infections (n=5).

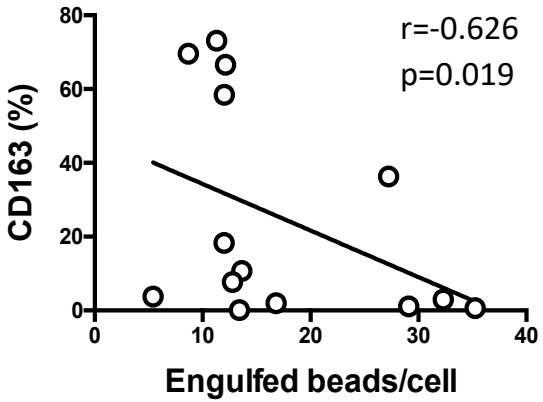




Results (unpublished):

CD163 expression negatively correlated with opsonin-independent phagocytosis of macrophages

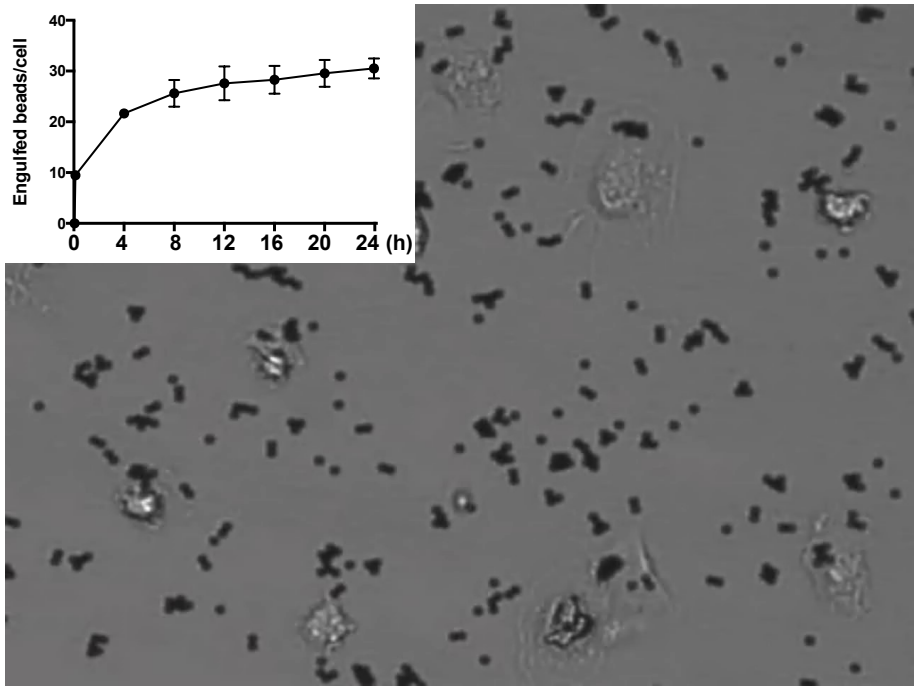
A



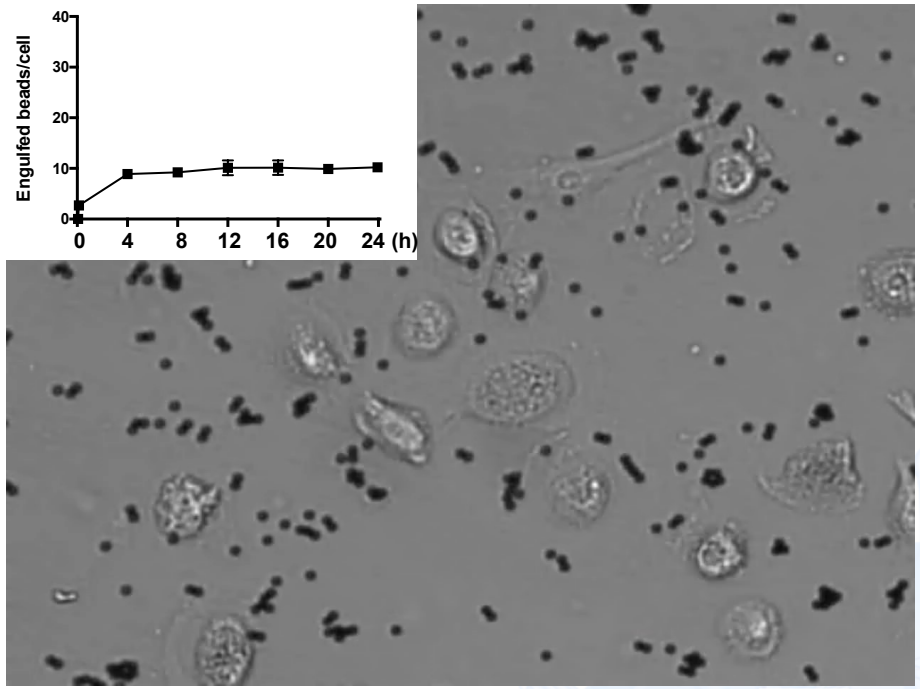
A. Spearman rank correlation. ($p<0.05$: statistically significant.)

B. Kinetics of non-opsonized epoxy Dynabeads® M-450 engulfed by $CD163^{lo}$ Mφs and $CD163^{hi}$ Mφs in 24h.

B



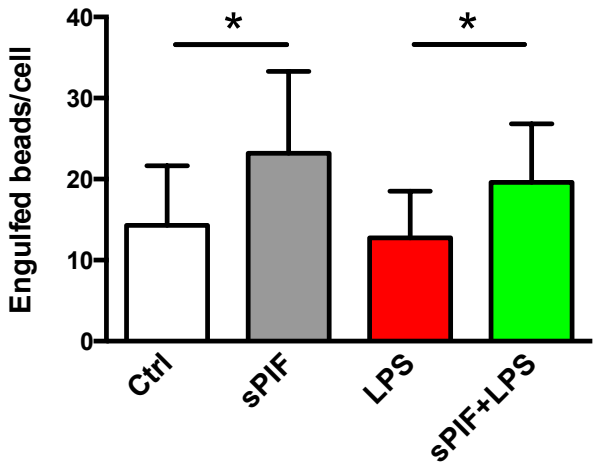
$CD163^{lo}$ Mφs (<30% CD163)

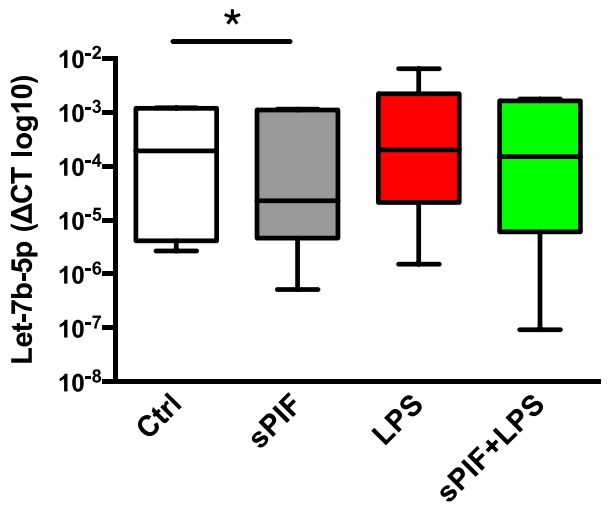


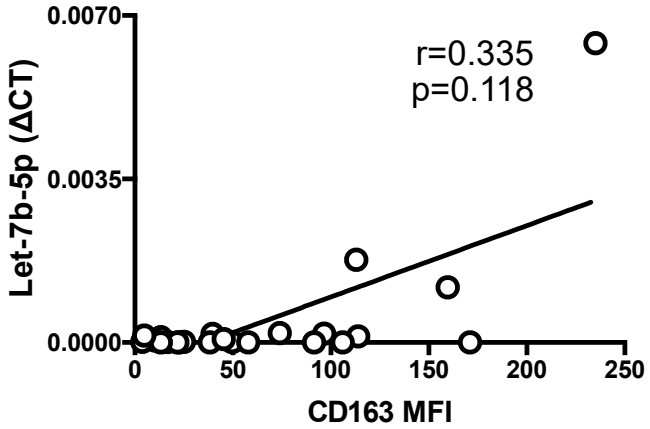
$CD163^{hi}$ Mφs (>30% CD163)

Results (unpublished):

sPIF ↑ opsonin-independent phagocytosis and ↓ Let-7b miRNA in CD163^{hi} Mφs

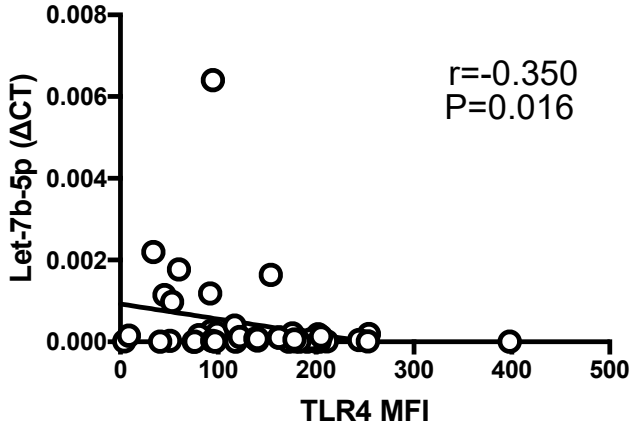


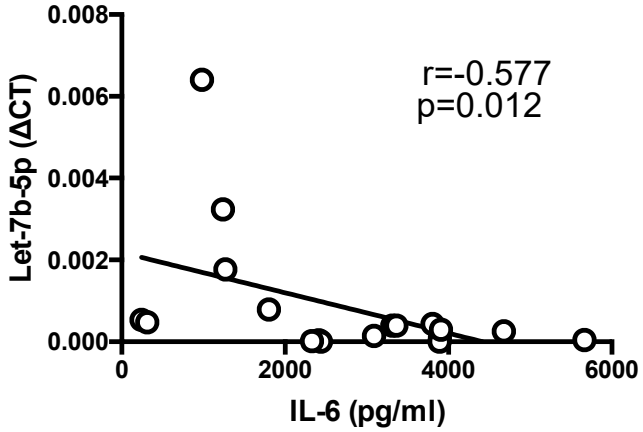


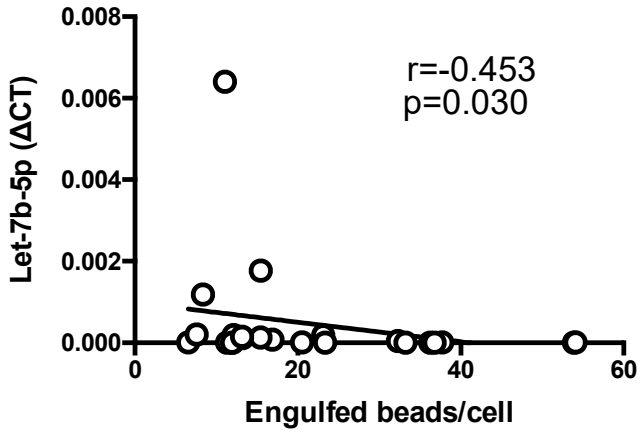


Results (unpublished):

Let7b negatively correlates with TLR-4, IL-6, and opsonin-independent phagocytosis







Conclusion:

- CD163^{hi} correlates with low opsonin-independent phagocytosis of macrophages.
- CD163^{hi} Mφs were largely refractory to LPS-induced M1 polarization potentially related to high dose glucocorticoid-treatment [2] in brain tumor patients.
- Let-7b-5p negatively correlated with the pro-inflammatory TLR4 pathway but positively correlated with the anti-inflammatory marker CD163.
- sPIF increased opsonin-independent phagocytosis of CD163^{hi} Mφs by downregulating the let-7b-5p level which negatively correlated to the phagocytic capacity of macrophages.

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1. Palecanda A, Kobzik L. Receptors for unopsonized particles: the role of alveolar macrophage scavenger receptors. Curr Mol Med 2001; 1(5):589-595.
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3. Yunna C, Mengru H, Lei W, Weidong C. Macrophage M1/M2 polarization. Eur J Pharmacol 2020; 877:173090.
4. Mueller M, Zhou J, Yang L, Gao Y, Wu F, et al. PreImplantation factor promotes neuroprotection by targeting microRNA let-7. Proc Natl Acad Sci U S A 2014; 111(38):13882-13887.

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Thanks for your attention !