

In vitro Pharmacology: Human Primary Leukocyte Assays

Primary Leukocyte Activation

Leukocytes play an important role in the development and progression of various inflammatory diseases. Primary leukocytes are blood cells that patrol the body and possess a potent arsenal of bactericidal agents and chemical messengers that regulate inflammation, immune responses, blood vessel formation and wound healing.

Fidelta's Pharmacology group has developed a variety of assays on primary leukocytes as a first step of an *in vitro* cascade for the characterization of potential anti-inflammatory effects of new drugs.

Our portfolio for leukocyte activation covers various types of immune responses with multiple readouts and endpoints. Most of the assays are highly flexible in terms of set up and adaptable. Applying experience and expertise, Fidelta offers customized assay development as need.

Primary cells

- Whole blood
- Isolated PBMCs
- Isolated granulocytes
- Isolated monocytes
- Isolated T-cells

Activation

- Various pro-inflammatory stimuli:
 - LPS, fMLP,
 - TNF α , IFN γ , IL-8,
 - PMA, PHA, etc.
- Antibodies: aCD3/aCD28

Available read-outs

- ³H-thymidine incorporation
- ELISA
- Flow cytometry
- Multiplex cytokine/chemokine assays
- RT-qPCR

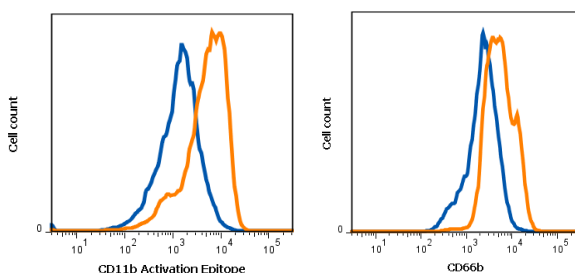
Whole Blood

Flow cytometric measurement of activation (CD11b Activation Epitope expression) and degranulation (CD66b expression) on CD45⁺CD16^{high} human peripheral blood neutrophils stimulated by chemoattractant.

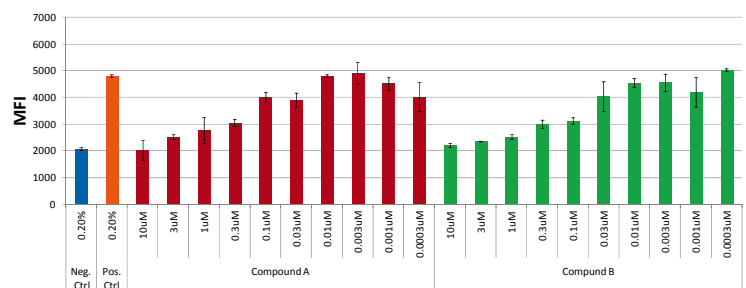
Cmpd A and Cmpd B dose-dependently inhibited the activated neutrophil immunophenotype.

Neg. Ctrl

Pos. Ctrl

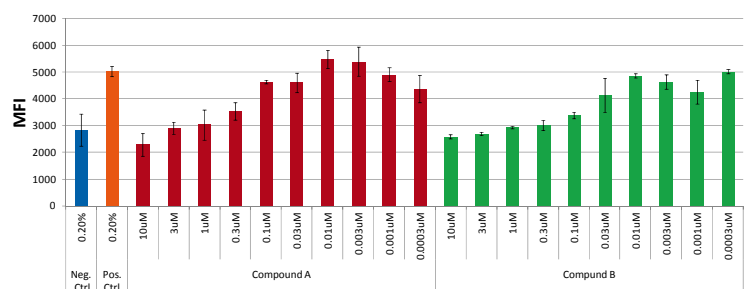


CD11b Activation Epitope



Error bars: SDEV from triplicates

CD66b



Error bars: SDEV from triplicates

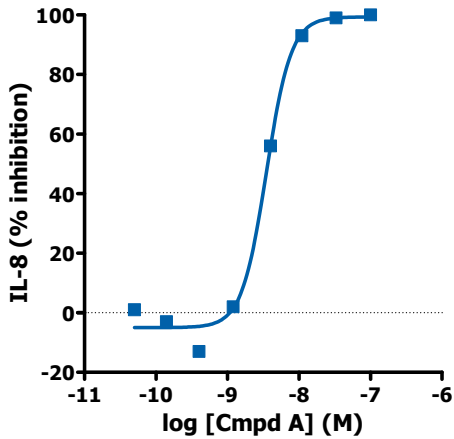
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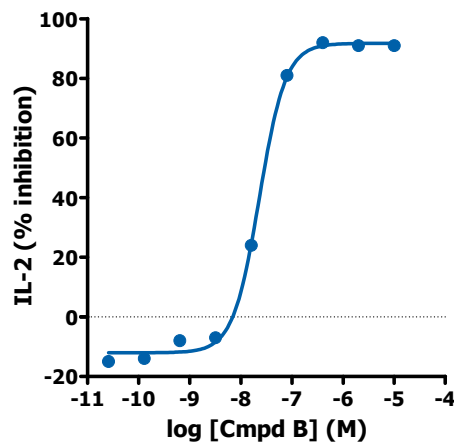
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PBMCs

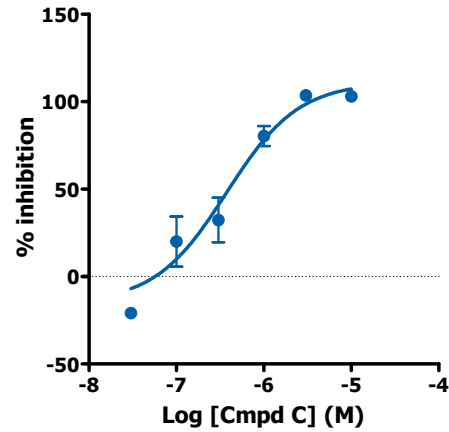


LPS-stimulated
IL-8 production (ELISA)



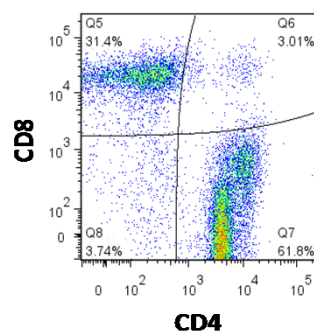
aCD3/aCD28-stimulated
IL-2 production (ELISA)

T-cells

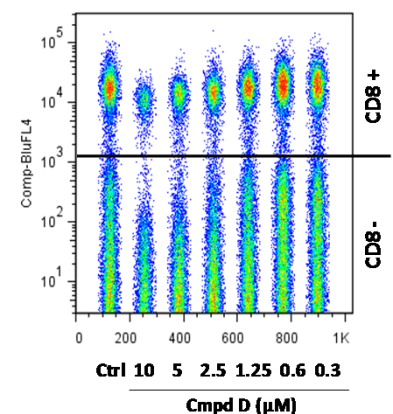
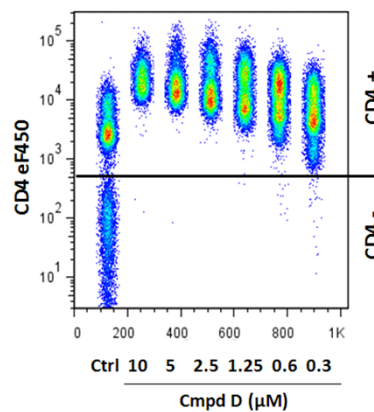
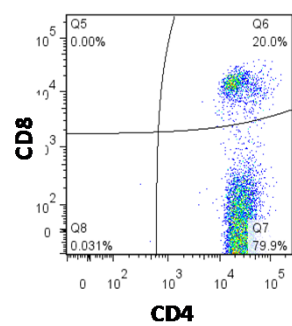


Dose-dependent inhibition of T-lymphocyte proliferation stimulated with aCD3/aCD28 (³H-thymidine incorporation)

CD3/CD28+ DMSO



CD3/CD28+ Cmpd (5 μM)



Dose-dependent influence on immunophenotype of proliferating human T-cells (flow cytometry)

References

1. Ory et al. 2007, J Leukoc Biol, 82(5), 1115;
2. Coutinho et al. 2005, Curr Top Microbiol Immunol, 293, 43 ;
3. Riddell et al. 1990. J Immunol Meth, 128(2),189.