

In Vitro Pharmacology - Functional *In vitro* Assays

Human Leukocyte Activation and Function

Leukocyte Activation and Function

White blood cells (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.

Once exposed to cell to a specific antigen or nonspecific mitogens leukocytes respond with changes in morphology and behaviour. Leukocyte activation come up with production and release of inflammatory mediators, overexpression of cell surface adhesion molecules, and an increase in migration and infiltration, phagocytosis, and degranulation, as well as receptor phosphorylation and signal transduction.

Our portfolio of in vitro assays cover various types of functional responses related to the leukocyte activation with multiple readouts and endpoints. Most of the assays are highly flexible in terms of set up and adaptable to customer needs. Applying our experience and expertise, we offer customized assay development as needed.

Primary cells

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

Differentiated cells

- Monocyte-derived macrophages
- Monocyte-derived dendritic cells

Cell lines

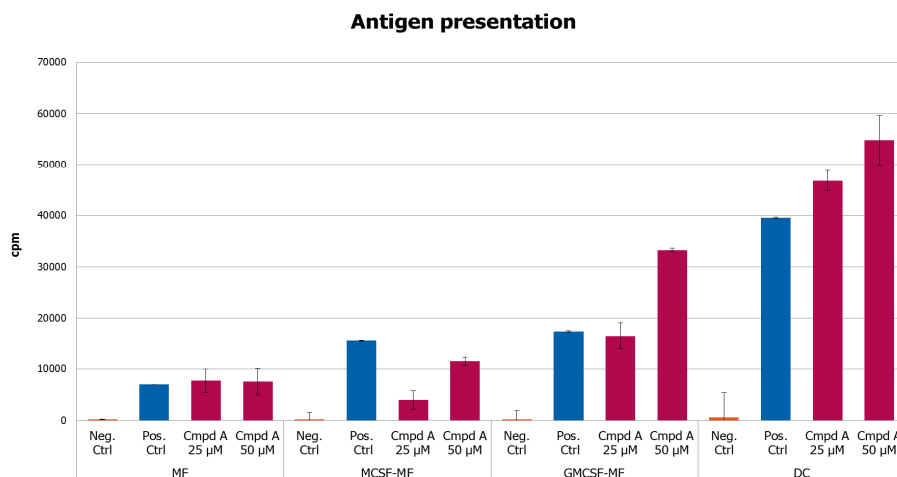
- Jurkat cell line
- Epithelial cell lines

Available read-outs

- Flow cytometry
- Chemiluminescence
- ³H-thymidine incorporation

Antigen Presentation

When present during the differentiation process Cmpd A significantly augmented antigen presentation (AP) of monocyte-derived macrophages and dendritic cells obtained by GM-CSF- and GM-CSF/IL-4-induced differentiation, respectively. AP was reduced in monocyte-derived macrophages obtained by stimulation with M-CSF. No influence was noticed on spontaneous differentiation of monocytes into macrophages by simple plating.



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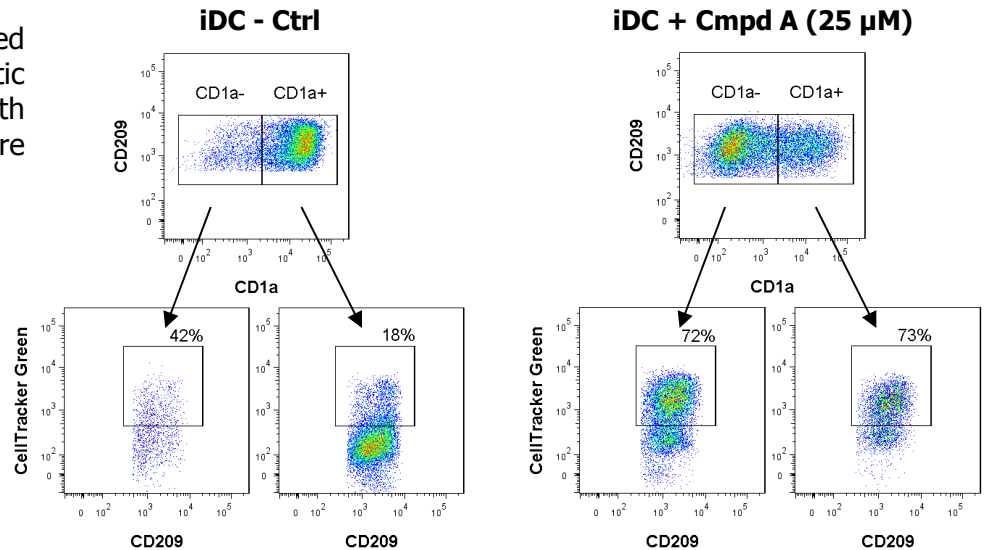
Phagocytosis of Apoptotic Cells

Cmpd A significantly augmented phagocytosis of apoptotic lymphocytes in both immunophenotypes of immature monocyte-derived dendritic cells:

classical iDCs
(CD209+CD1a)

tolerogenic-like iDCs
(CD209+CD1a-)

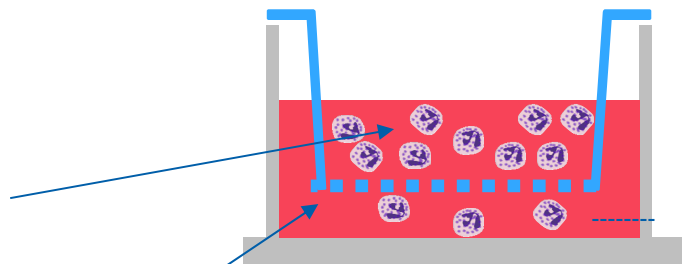
Stupin Polancec et al. 2012.



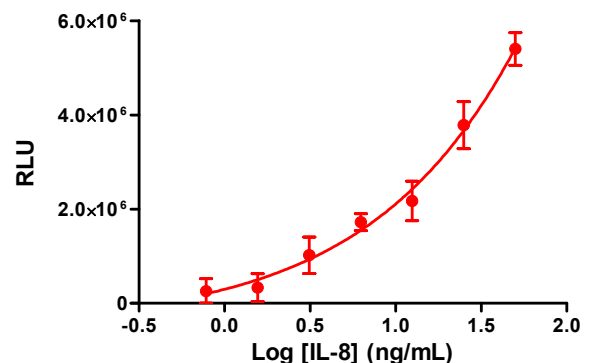
Neutrophil Chemotaxis

IL-8 –induced neutrophil chemotaxis

- Upper compartment:
freshly isolated human neutrophils
(preincubated with compound)
- Lower compartment:
Chemoattractant (+ compound)
- After incubation migratory cells are lysed and cell migration to the lower compartment is determined by measuring ATP level (luminiscence)



IL-8 –induced neutrophil chemotaxis



References

- Stupin Polancec et al. 2012, J Leuk Biol 91, 229.
- Hammond et al. 1995, J Immunol 155, 1428.
- Henkels et al. 2011, FEBS Letters, 585 (1), 159.
- Kiama et al. 2001, J Aerosol Med, 14(3), 289.
- Majai et al. 2010, J Leukoc Biol, 88(5),981.

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