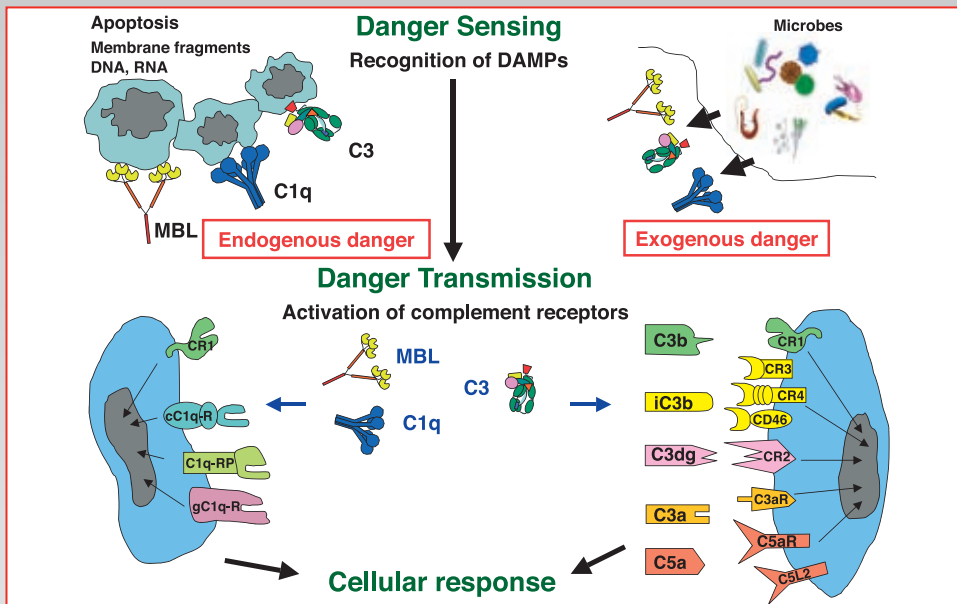


Hycult Scope

Complement and endogenous danger



Immunity has evolved from recognition of tissue damage rather than foreignness. Therefore, also endogenous danger signals (such as apoptosis, membrane fragments etc) are capable of stimulating the complement system. The complement components with clear afferent functions C1q, mannan binding lectin (MBL) and C3, are the essential soluble danger sensing proteins, which are activated by both endogenous and exogenous stimuli. This afferent arm of the complement system is critical for tissue homeostasis under steady-state conditions as well as in response to infection and cell injury. It translates the danger information into specific efferent cellular responses by interaction with specific receptors on distinct cells. Recent findings provide evidence that complement regulates not only innate immune responses but is also a dominant player in adaptive immune responses. Therefore, endogenous cell injury-mediated complement regulation of the adapted immune-response may play a more than hitherto recognized role in auto-immune diseases and diseases as atherosclerosis.

J. Köhl, *Immunol Res* 2006, 34: 157

Hot new products

Complement assays for functional lectin activity

The new Hbt MASP-2 ELISA allows sensitive and accurate quantification of MASP-2 in plasma and other body fluids, allowing studies on MASP-2 deficiency in patients. As MBL has been found to be involved in a wide range of pathologies, MASP-2 quantification will be of importance for studies on bacterial infection, autoimmune diseases, cancer, HIV, transplantation, atherosclerosis, cystic fibrosis and many other diseases.

ASSAYS	CAT. #
Human MASP-2	<i>Unique</i> HK326
Human MBL (Lectin activity)	HK323
Functional Human MBL/MASP-2 (C4 deposition)	<i>Unique</i> HK327
Human TCC (MAC/sC5b-9)	HK328
Mouse MBL-A	<i>Unique</i> HK208
Mouse MBL-C	<i>Unique</i> HK209

Complement and Apoptosis

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Important facts on MBL and MASP-2 in clinical research

The Mannan Binding Lectin (MBL) pathway has recently been shown to be a major regulator of the complement system. MBL is a serum protein important in innate immunity and is protective against various infective organisms. The MBL/MASP complex recognizes exogenous (microbial) as well as endogenous ligands (including apoptotic cells). The MBL/MASP complex can directly activate C3 and is as such a key player in translating endogenous and exogenous danger into cellular responses. Some major facts supporting the importance of MBL and MASP-2 research in the clinical field are:

Immunodeficiency

- MBL-deficiency is the most common congenital immunodeficiency occurring in 10% of the population¹.
- MBL-deficiency is a risk factor for infection in combination with an immunocompromised condition².
- MBL-deficiency is a risk factor for the occurrence of autoimmune diseases³.
- MBL-deficiency is associated with increased susceptibility to sepsis⁴.

Cardiovascular diseases

- MBL serum levels may predict decreased likelihood of myocardial infarction, particularly in diabetic patients⁵.
- MBL serum levels indicate risk of future coronary artery disease in apparently healthy men but not in women⁶.
- MBL serum levels are associated with vascular complications in type I diabetes⁷.

Transplantation

- MBL levels are associated with graft survival in kidney and heart transplantation^{8,9}.

Cancer

- MASP-2 expression is increased in oesophageal squamous cell carcinoma and associated with aggressive tumour behaviour¹⁰.
- Elevated MASP-2 serum levels are correlated to poor survival and recurrence in colorectal cancer patients¹¹.
- MBL-deficiency is associated with severe infections after chemotherapy¹².

Apoptosis

- MBL binds DNA fragments present in apoptotic cells initiating a cellular response¹³.

Aging

- MBL-bound MASP-2 activity declines in aging¹⁴.

Selected articles on MBL/MASP-2:

1. Thiel, S et al; Mol Immunol 2006, 43: 86
2. Boniotti, M et al; J Mol Med 2005, 83: 308
3. Tsutsumi, A et al; Autoimmun Rev 2005, 4: 364
4. Gordon, A et al; Shock 2006, 25: 88
5. Saevarsdottir, S et al; J Exp Med 2005, 201: 117
6. Keller, T et al; Arterioscler Thromb Vasc Biol 2006, 26: 2345
7. Hansen, T et al; Diabetes 2004, 53: 1570
8. Fiane, A et al; Eur Heart J 2005, 26: 1660
9. Berger, S et al; Am J Transplant 2005, 5: 1361
10. Verma, A et al; Int J Cancer 2006, 118: 2930
11. Ytting, H et al; Clin Cancer Res 2005, 11: 1441
12. Mullighan, C et al; Leuk Lymphoma 2004, 45: 247
13. Palaniyar, N et al; J Biol Chem 2004, 279: 32728
14. Mayilyan, K et al; Int J Immunopathol Pharmacol 2006, 19: 567

Hot news in complement research:

CR1g:

a new conserved complement receptor that is important in phagocytic clearance of circulating pathogens.

Helmy, K et al; Cell 2006, 124: 915

SIGN-R1

activates C1q pathway without immunoglobulin.

Kang, Y et al; Cell 2006, 125: 47

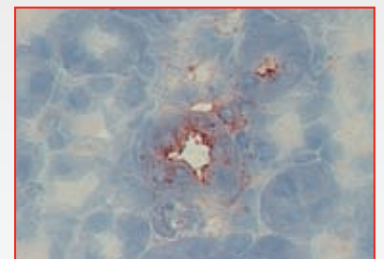
Good news for congress travelers!

Findings do not support the hypothesis that hypobaric hypoxia, of the degree that might be encountered during long-haul air travel, is associated with prothrombotic alterations in the hemostatic system in healthy individuals at low risk of venous thromboembolism.

Toff, W et al; JAMA. 2006, 295: 2251

Unique panel of antibodies for lectin pathway studies

ANTIBODIES:	CAT. #
MBL-A, Mouse	Unique HM1035, HM1036
MBL-C, Mouse	Unique HM1037, HM1038
MBL, Human	HM2061, HM2081
H-Ficolin (Hakata), Human	Unique HM2089
L-Ficolin, Human	Unique HM2090, HM2091
M-Ficolin, Human	Unique HP9039
MAASP-1/3, Human	HM2092, HM2093
MAASP-2, Human	Unique HM2190
MAASP-2/MAp19, Human	Unique HM2191
TCC, C9 neoantigen, Human	HM2167

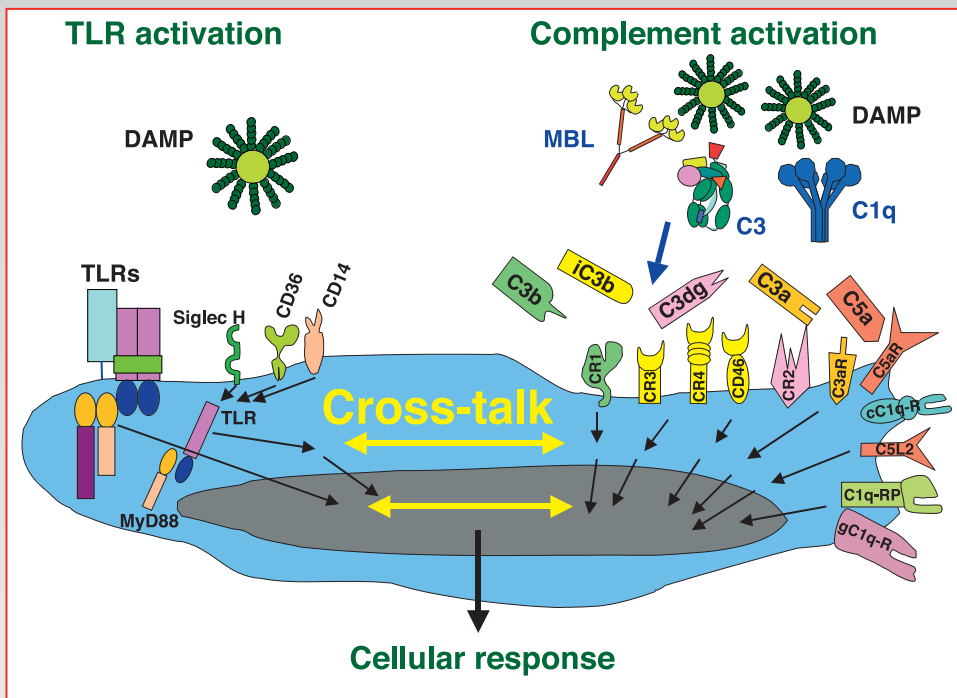


Tubular MBL-C deposition in mouse kidney subjected to ischemia and reperfusion. Immunohistochemical staining on frozen section with monoclonal antibody to MBL-C (Cat. # HM1038).

Cross-talk between TLR and complement signaling pathway

TLRs as well as the complement system are capable of recognizing danger signals, such as danger-associated molecular patterns (DAMPs), which initiate cellular responses. Since many cells of the myeloid lineage co-express TLRs and receptors for DAMP induced cleavage products of C3, (i.e. C3a, C3b/iC3b), and C5, (i.e. C5a), DAMP initiated signal transduction is not so straightforward as has been hypothesized. Recent data suggest substantial cross-talk between the signalling pathways downstream of complement receptors and other receptors of the innate immune system that function as sensors and/or transmitters (i.e. the TLRs). Sensing the importance of complement in innate and adaptive immune responses, a complement-related view at the immune system will lead to a better understanding in the field of autoimmunity, allergy, cancer as well as transplantation.

J. Köhl, *Immunol Res* 2006, 34: 157



COMPLEMENT RECEPTOR ANTIBODIES

Specificity	Cat. #
C3aR, Human	<i>Unique</i> HM2195
C3aR, Rat	HM3028
CD88 (C5aR), Human	HM2094
CD88 (C5aR), Mouse	<i>Unique</i> HM1076
CD88 (C5aR), Rat	<i>Unique</i> HM3017
CD11b, Human	HM2125
CD21 (CR2), Human	HM2139
CD35 (CR1), Human	HM2107
CD46, Human	HM2103
CD55 (DAF), Human	HM2105
C5L2, Human	HP9036
C5L2, Mouse	<i>Unique</i> HP8015
C5L2, Rat	<i>Unique</i> HP8018

And many more antibodies to human, mouse and rat complement proteins. Please visit our website www.hbt.nl for more information.

TLR & RELATED ANTIBODIES

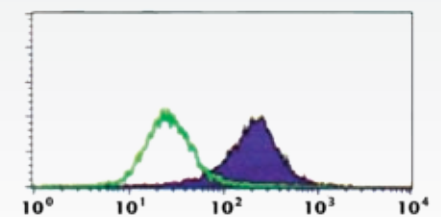
Specificity	Cat. #
TLR1 (CD281), Human	HM2085
TLR2 (CD282), Human	HM2064
TLR2 (CD282), Mouse	HM1054
TLR3 (CD283), Human	HM2096
TLR4 (CD284), Human	HM2068
TLR4/MD2, Mouse	HM1029
TLR9 (CD289), Human	HM2087
TLR9 (CD289), Mouse	HM1042
MD-1, Mouse	HM1040
RP105 (CD180), Human	HM2083
RP105 (CD180), Mouse	HM1031
Siglec-H, Mouse	<i>Unique</i> HM1075
SIGN-R1, Mouse	HM1080
CD14, Human	HM2040
CD14, Mouse	<i>Unique</i> HM1060
CD36, Human	HM2122
CD36, Mouse	HM1074
CD36, Rat	<i>Unique</i> HM3019

Hot in research

Effective agonists for Toll-like receptor 9

The innate immune systems has developed particular receptors to bind various types of structures expressed by pathogens, which are in principal absent in vertebrates. One of the best characterized receptors is the Toll-like receptor 9 (TLR9), that recognizes CpG motifs in bacterial and viral DNA. Short synthetic CpG oligodeoxynucleotides are powerful agonists for TLR9. Therefore, CpG DNAs are useful tools to study the downstream effect of TLR9 activation, which is of great importance in fields of infectious disease, cancer and asthma/allergy.

CPG-DNA	CAT. #
CpG-A DNA, Human, Mouse, ODN 2216	HC4037
CpG-B DNA, Human, Mouse, ODN 2006	HC4039
CpG-C DNA, Human, Mouse, ODN 2395	HC4041
Non-CpG DNA, Human, Mouse	HC4034
CpG-B DNA, Rat	HC4040
CpG DNA, Rabbit, ODN 2007	HC4038
Non-CpG DNA, Rabbit, ODN 2041	HC4042



Flow cytometry on dendritic mouse cells stained with anti-TLR2-FITC (Cat. # HM1058F) versus isotypte control.



Early apoptosis detection

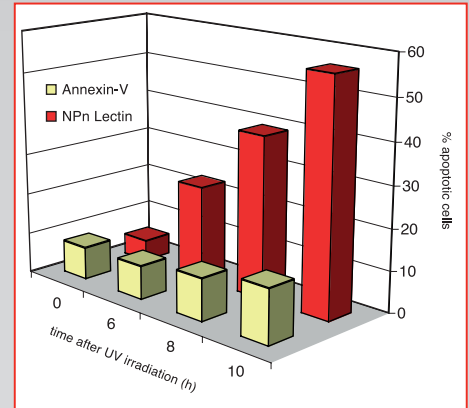
Lectin *Narcissus pseudonarcissus* (NPn) assay for early apoptosis detection.

Cat. # HIT303

Special features of the assay:

- Highly reproducible and sensitive detection of very early phases of apoptosis.
- Detection of apoptosis induced by several stimuli with high sensitivity.
- NPn lectin staining detects apoptotic events earlier than annexin V (see figure; induction of apoptosis in human peripheral blood lymphocytes by UV-B irradiation).
- Staining is stable for at least 12 hours, facilitating everyday laboratory use.
- Reliable tool for cell death research.

Early apoptosis detection by NPn Lectin versus Annexin-V staining of PBLs



Unique reagents for endothelial cell research

Antibodies to VAP-1: new tools for liver-specific immunosuppression.

In experimental models, blockage of vascular adhesion protein-1 (VAP-1) adhesion leads to significant decrease of T-lymphocyte infiltration and alleviation of histological changes of acute rejection in liver allografts.

Martelius, T et al; Am J Pathol 2004, 165: 1993

Now available:

- ▶ Unique panel of antibodies to human, mouse and rat VAP-1.
- ▶ Antibodies to human endothelial markers PLVAP (PAL-E, PV1, FELS) and CD73.

Visit our website www.hycultbiotech.com for more information.

Granzyme B and apoptosis

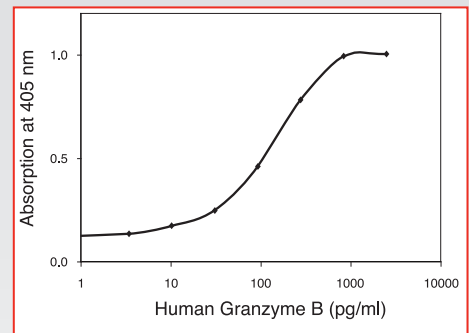
Human Granzyme B activity assay for apoptosis and immune response studies.

Cat. # HK332

Special features of the assay:

- Quantifies Granzyme B protease activity.
- Useful for quantitative measurement of natural functional human Granzyme B in cell culture medium, plasma, tissue homogenates and wound fluid.
- Standard curve: 3.4 to 2,500 pg/ml.

Human Granzyme B protease activity assay



FURTHER APOPTOSIS PRODUCTS:

Cat. #	Product Name	Feature
HIT304	Annexin V-FITC	
HM2154	mAb to human apoptotic neutrophils	Unique

Hycult Biotech is distributed by:



P.O. Box 30
5400 AA Uden
The Netherlands

T +31 413 25 23 35
F +31 413 24 83 53
E info@hycultbiotech.com