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.


**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.

<table>
<thead>
<tr>
<th>ASSAYS</th>
<th>CAT. #</th>
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</thead>
<tbody>
<tr>
<td>Human MASP-2 (Lectin activity)</td>
<td>HK328</td>
</tr>
<tr>
<td>Functional Human MBL/MASP-2 (C4 deposition)</td>
<td>HK327</td>
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<tr>
<td>Human TCC (MAC/c5b-9)</td>
<td>HK328</td>
</tr>
<tr>
<td>Mouse MBL-A</td>
<td>HK208</td>
</tr>
<tr>
<td>Mouse MBL-C</td>
<td>HK209</td>
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</table>
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/MA complex recognizes exogenous (microbial) as well as endogenous ligands (including apoptotic cells). The MBL/MA complex can directly activate C3 and is 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 population.1
- 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 transplantation8,9

**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

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**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 travellers!**
- Findings do not support the hypothesis that hypobaric hypoxia, of the degree that might be encountered during long-haul air travel, is associated with pro-thrombotic alterations in the hemostatic system in healthy individuals at low risk of venous thromboembolism.
  Toff, W et al; JAMA. 2006, 295: 2251

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**Unique panel of antibodies for lectin pathway studies**

**ANTIBODIES:**

<table>
<thead>
<tr>
<th>SPECIFICITY</th>
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<tbody>
<tr>
<td>MBL-A, Mouse</td>
<td>Unique HM1035, HM1036</td>
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<tr>
<td>MBL-C, Mouse</td>
<td>Unique HM1037, HM1038</td>
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<tr>
<td>MBL, Human</td>
<td>HM2061, HM2081</td>
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<tr>
<td>H-Ficolin (Hakata), Human</td>
<td>Unique HM2089</td>
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<td>L-Ficolin, Human</td>
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<td>MASP-1/3, Human</td>
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<td>MASP-2, Human</td>
<td>HM2190</td>
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<td>MASP-2/MAP19, Human</td>
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<tr>
<td>TCC, C9-neantigen, Human</td>
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</tbody>
</table>

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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 signalling 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/C3b), 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.


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**

<table>
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<td>CpG-A DNA, Human, Mouse, ODN 2216</td>
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<td>CpG-B DNA, Human, Mouse, ODN 2096</td>
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<td>CpG-C DNA, Human, Mouse, ODN 2395</td>
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<tr>
<td>Non-CpG DNA, Human, Mouse</td>
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<td>CpG-B DNA, Rat</td>
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<td>CpG DNA, Rabbit, ODN 2007</td>
<td>HC4038</td>
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<tr>
<td>Non-CpG DNA, Rabbit, ODN 2041</td>
<td>HC4042</td>
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</tbody>
</table>

**Flow cytometry on dendritic mouse cells stained with anti-TLR9-PE (Cat. # HM1058P) versus isotype control.**
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.


Now available:
- Unique panel of antibodies to human, mouse and rat VAP-1.
- Antibodies to human endothelial markers PL/VAP (PAL-E, PV1, FELS) and CD73.

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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.

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.

Further apoptosis products:

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