Name:	**C3c**
Catalog Number:	**A116C**
Sizes Available:	250 µg/vial
Concentration:	1.0 mg/mL (see Certificate of Analysis for actual concentration)
Form:	Frozen liquid
Purity:	>90% by SDS-PAGE
Buffer:	10 mM Sodium phosphate, 145 mM NaCl, pH 7.2
Extinction Coeff.	$A_{280\ nm}$ = 1.10 at 1.0 mg/mL
Molecular Weight:	139,000 Da (3 chains)
Preservative:	None, 0.22 µm filtered
Storage:	-70°C or below. Avoid freeze/thaw.
Source:	Normal human serum (shown by certified tests to be negative for HBsAg and for antibodies to HCV, HIV-1 and HIV-II).
Precautions:	Use normal precautions for handling human blood products.
Origin:	Manufactured in the USA.

General Description

C3c is derived from iC3b (inactivated C3b) by proteolytic cleavage (Law, S.K.A. and Reid, K.B.M. (1995)). iC3b is created by cleavage of C3b by factor I in the presence of factor H, CR1 or MCP. C3c can be produced by an additional cleavage by factor I if the iC3b is bound to CR1. Factor H cannot serve as a cofactor for this cleavage. C3c can also be produced by the action of trypsin-like proteases on iC3b. If the C3b precursor was attached to a surface, then the iC3b will remain attached to that surface and when iC3b is cleaved the C3c is released into the surrounding solution while the C3dg/C3d fragment remains on that surface. The breakdown of fluid phase C3b is similar, but in this case both C3c and C3dg/C3d are soluble fragments.

Physical Characteristics & Structure

Molecular weight: 139,000 daltons composed of three disulfide linked chains (75,000 Da, 39,000 Da and 25,000 Da). C3c is glycosylated. There can be considerable heterogeneity in the structure of C3c due the fact that it is formed by the action of proteases and it is extremely sensitive to additional proteolytic digestion. The initial stage of digestion of iC3b (75,000, 63,000, and 39,000 Da) produces C3c (75,000, 25,000, and 39,000 Da) and C3dg (38,900 Da). The 25,000 Da fragment is from the N-terminal and the 39,000 Da fragment is from the C-terminal of the alpha chain of C3b. An additional cleavage of C3dg produces C3d (33,800 Da). The two smaller fragments of C3c (25,000, and 39,000 Da) are linked to each other by a disulfide bond and the smaller fragment (25,000 Da) is linked to the beta chain (75,000 Da) by a disulfide bond (Morley, B.J. and Walport, M.J. (2000); Law, S.K.A. and Reid, K.B.M. (1995); Dodds, A.W. and Sim, R.B. editors (1997); Morgan, B.P. ed. (2000)). Some of the chains have a C-terminal arginine residue which may be partially cleaved by serum carboxypeptidases leading to additional heterogeneity.

Function

There are no known biological functions of C3c. It is released from complement-activating particles by the action of factor I with CR1 as the cofactor or by the action of trypsin-like proteases (Lambris, J.D. (1988)). It is rapidly cleared from circulation.

Assays

There are no functional assays for C3c. ELISA and nephelometry are used to quantitate C3c in plasma, however C3, C3b and iC3b may interfere with some tests. Western blots of SDS gels may be used to identify and quantitate the protein and to determine the chain structure.

In vivo

During complement activation C3b arises from the proteolytic cleavage of C3. During aggressive complement activation (in sepsis and at sites of infection) high concentrations of C3b may be formed, but most of it is fluid phase C3b. In blood, factors H and I rapidly cleave C3b forming iC3b. Although iC3b is very sensitive to trypsin-like enzymes it is very long lived in plasma or serum (half-life many hours). Because of the excess of protease inhibitors in plasma there is very little free thrombin, plasmin or other active proteases and iC3b remains as iC3b. In blood, however, the CR1 receptor on human erythrocytes induces a third cleavage by factor I and this releases C3c from C3dg (Dodds, A.W. and Sim, R.B. editors (1997)).

Regulation

C3c is cleared from circulation rapidly. It has no known functional activities nor any known specific regulatory mechanisms.

Genetics

Human chromosome location of the C3 gene is 19p13.3. The mouse chromosome location is chromosome 17 and the rat chromosome 9. Accession numbers K02765 (human) and K02782 (mouse). Human C3 genomic structure: the gene spans 41 kb with 41 exons

Precautions/Toxicity/Hazards

The source of this protein is human serum, therefore precautions appropriate for handling any blood-derived product must be used even though the source was shown by certified tests to be negative for HBsAg, HTLV-I/II, STS, and for antibodies to HCV, HIV-1 and HIV-II. MSDS sheet is available upon request.

References

Dodds, A.W. and Sim, R.B. editors (1997) Complement. A Practical Approach (ISBN 019963539) Oxford University Press, Oxford.

Lambris, J.D. (1988) The multifunctional role of C3, the third component of complement. Immunol Today. 9:387-93.

Law, S.K.A. and Reid, K.B.M. (1995) Complement 2nd Edition (ISBN 0199633568) Oxford University Press, Oxford.

Morgan, B.P. ed. (2000) Complement Methods and Protocols. (ISBN 0-89603-654-5) Humana Press, Inc., Totowa, New Jersey.

Morley, B.J. and Walport, M.J. (2000) The Complement Facts Book (ISBN 0127333606) Academic Press, London.