Name:	**C4b Binding Protein**
Catalog Number:	**A109C**
Sizes Available:	250 µg
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.	$A_{280\ nm}$ = 0.93 at 1.0 mg/mL
Molecular Weight:	540,000 Da (8 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, HTLV-I/II, STS, 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

C4b binding protein (C4BP) regulates complement activation of the classical and lectin pathways. It binds to C4b and accelerates the dissociation of C2a from the C3/C5 convertase C4b,C2a. This inactivates the central enzyme of both pathways. It also functions as a cofactor allowing factor I to cleave and permanently inactivate C4b. C4BP has a flower shaped structure with each alpha chain radiating out from a central core. The arms are linked by disulfide bonds in the center and the ends of each arm bind C4b. Studies have shown that on surfaces densely coated with C4b, C4BP can bind up to four C4b molecules simultaneously (Rawal, N. et al. (2009)).

Physical Characteristics & Structure

C4BP (540,000 daltons) is composed of six or seven alpha chains (72,000 daltons each) and one beta chain (46,000 daltons). While this form is the most common, a small proportion of C4BP in most plasma samples has no beta chain and some have only six alpha chains. The six or seven arms are attached by disulfide bonds at their C-terminal ends as is the beta chain. Each alpha chain arm is composed of eight CCP repeat domains similar to those in factor H, CR1 and many other complement proteins. The pI of the intact C4BP depends on the allelic type of C4BP, but all are in the range between pH 6.6 and 6.8.

Functions

C4BP has two functions. It accelerates the decay of the unstable C3/C5 convertase (C4b,C2a) causing the release and permanent inactivation of C2a. It also possesses factor I cofactor activity. Factor I binds to the complex of C4BP and C4b. Factor I is a serine protease that cleaves the C4b alpha chain yielding the soluble C4c fragment (147,000 Da) and C4d (45,000 Da). If the C4b was attached to a surface, then the cell-bound C4d fragment remains bound to that surface and can act as a ligand for the CR1 complement receptor.

Assays

C4BP may be most conveniently assayed by following the cleavage of the alpha chain of C4b by factor I with SDS-PAGE (Morgan B.P., 2000)). This reaction is completely dependent on the presence of C4BP. It is also possible to measure the decay accelerating activity using EAC42 cells (Dodds A.W. and Sim, R.B. (1997); Morgan, B.P. ed. (2000)).

In vivo

Plasma contains approximately 225 µg/mL of C4BP with a normal range 150 to 300 µg/mL. The primary site of biosynthesis of C4 is the liver.

Regulation

C4BP is an acute phase protein meaning that its concentration in blood is elevated during inflammation. Biosynthesis of C4BP is upregulated by INF alpha and gamma and by a variety of inflammatory cytokines.

Genetics

The gene for C4BP resides on the first chromosome at 1q32. The alpha chain gene contains 12 exon while the beta chain contains 8 exons. Gene accession numbers: Human (M31452 and M29964), Mouse (M17122 and Z21944).

Deficiencies

A complete deficiency of C4BP is very rare. It is associated with Behcet's disease and angioedema.

References

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

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.

Rawal, N., Rajagopalan, R., Salvi, V.P. (2009) Stringent regulation of complement lectin pathway C3/C5 convertase by C4b-binding protein (C4BP). Mol Immunol. 46:2902-10.