

Name:	Factor Ba (fragment of factor B)
Catalog Number:	A154
Sizes Available:	100 µg/vial
Concentration:	1.0 mg/mL (see Certificate of Analysis for actual concentration)
Form:	Frozen liquid
Purity:	>95% by SDS-PAGE
Buffer:	Phosphate-buffered saline, pH 7.3
Molecular weight:	33,000 Da (single chain)
Extinction Coeff.:	$A_{280\text{ nm}} = 1.27$ at 1.0 mg/mL
Preservative:	None, 0.22 µm filtered
Storage:	-70°C or below. Avoid repeated 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

Factor Ba is the fragment of complement factor B that results from activation of the alternative pathway. CompTech prepares the factor Ba fragment from factor B which was purified from normal human serum. Complement factor B is a glycosylated protein composed of a single 93,000 Da polypeptide chain. Factor B is an essential component of the alternative pathway of complement activation and is found in plasma at approximately 200 µg/mL. In the presence of Mg^{++} factor B binds to C3b and the C3b,B complex can be activated by factor D, a serine protease that circulates as an active trypsin-like serine protease. Cleavage of factor B by factor D causes the release of the Ba fragment (33,000 Da) and leaves the 60,000 Bb fragment bound to C3b. This Ba fragment comes from the N-terminal of factor B and it contains three CCP domains which interact with C3b (Morley, B.J. and Walport, M.J. (2000)). The isolated fragment Ba has been reported to have a weak affinity for C3b and to inhibit the interaction of factor B with C3b thus inhibiting the activation of the alternative pathway (Pryzdial, E.L. and Isenman, D.E., (1987)).

The fragments of factor B (Ba and Bb) have been proposed to elicit several biological responses. See the section titled Function below and in the product description for the Bb fragment.

Physical Characteristics & Structure

Molecular weight: 33,000 daltons, single chain protein containing carbohydrate (Rother, K. et al. (1998); Morley, B.J. and Walport, M.J. (2000)). The protein is negatively charged at serum pH. The Ba fragment contains the three CCP domains of factor B while the Bb fragment, contains the active serine protease site of C3b,Bb. Crystal structures for the serine protease domain at 2.1 angstrom resolution (Jing, H. et al. (2000)), the Ba domain (Milder, F.J. et al. (2007)) and the whole protein (Bhattacharya, A.A. et al. (2004)) at 2.3 angstrom resolution have been published.

Function

The fragments of factor B (Ba and Bb) have been proposed to elicit numerous biological responses; however, many of these activities have proved to be controversial

with an inconsistent record of reproducibility. It is not yet clear whether these failures are due to different experimental conditions, more highly purified Ba and Bb than available in the early days or the need to test fresh, *in situ*-prepared fragments, as has been suggested.

Both fragments Ba and Bb have been reported to bind to B lymphocyte receptors and modulate proliferation (Kolb, W.P., et al. (1989)). Ba, but not Bb, was shown to exhibit growth-supporting activity for activated murine B lymphocytes (Praz, F. and Ruuth, E. (1986)). On the other hand, Ba has been reported to inhibit human B cell proliferation (Ambrus, J.L. et al. (1990)). The small fragment Ba has been reported to show chemotactic activity with neutrophils and macrophages, but this effect is so much lower than that of C5a or even C5adesArg that its effect *in vivo* may be negligible (Morgan, B.P., (1990)). In a study of smooth muscle contractile activity, neither Ba nor Bb caused contraction of guinea pig ileum (a sensitive test for C5a) or histamine release from rat mast cells, but Ba caused guinea pig PMN to increase chemotactic activity (Hamuro, J., et al. (1978)).

Assays

There are no convenient assays for the biological activity of Ba. Several companies produce ELISA kits for measuring Ba levels in blood samples (Dodds, A.W. and Sim, R.B. (1997)).

Applications

Split products of factor B in plasma are indicative of activation of the alternative pathway *in vivo*. ELISA kits for measurement of Ba and Bb are commercially available. These have been used in numerous human and animal studies (Lynch, A.M., et al. (2008)). See *In vivo* section below.

In vivo

The average concentration of factor B in blood is 200 µg/mL (range 170-258 µg/mL) in human plasma. Factor B is an acute phase protein whose plasma levels increases during inflammation. The fragments Ba and Bb are released upon activation of the alternative pathway and circulate in blood until cleared (Lynch, A.M., et al. (2008)). Baseline levels in normals have been reported to be 29 ng Ba/mL (0.015% of the factor B concentration). The concentration of fragment Ba in patients with tubular proteinuria was found to be elevated more than 100-fold (4800 ng/mL)(Oppermann, M. et al. (1991)). There was a minimal increase in the plasma concentration of fragment Bb in these patients.

Genetics

The gene for factor B is located on human chromosome 6p21.3 within the MHC class III region between the class I and class II regions. The factor B gene lies between the larger gene for C2 (to which it is highly homologous) and genes for C4A and C4B. The gene is composed of 18 exons and spans 6 kb.

Deficiencies

No natural deficiencies of factor B have been identified in humans or animals. Mice deficient in factor B (B^{-/-} mice), compared to wild-type, exhibit much lower or no

pathology in a wide variety of diseases where alternative pathway activation is the cause of or exacerbates the pathology of these diseases. See Diseases section below. Acquired and secondary deficiencies do occur in humans. Human factor I deficiencies exhibit very low factor B levels due to the fact that C3b is not inactivated in the absence of factor I and C3b accumulates in blood. This results in binding of factor B, cleavage by factor D and rapid release of fragments Ba and Bb. Transfusions with normal plasma or reconstitution with factor I temporarily stop or slow production of these fragments.

Diseases

While mice with complete deficiencies of factor B exhibit increased susceptibility to infections, they also show reduced or the complete absence of pathology in many inflammatory diseases including SLE (systemic lupus erythematosus), rheumatoid arthritis, intestinal and renal ischemia/reperfusion injury, immune-mediated spontaneous fetal loss and asthma (Holers, V.M. (2000); Kolb, W.P. et al. (1989); Thurman and Holers, (2006); Morgan, B.P. (1990)).

Measurement of Ba fragment levels have been used to monitor complement activation in disease such as in renal failure (Oppermann, M. et al. (1991)).

Precautions/Toxicity/Hazards

This protein is purified from human serum and 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.

Hazard Code: B

MSDS available upon request.

References

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