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## C1q Protein from Normal human serum

### C409490

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**Storage temperature:** Store at -80°C long term.

#### Introduction:

C1q separated from C1r and C1s and from other stabilizing proteins tends to aggregate easily. Because it was isolated and studied in numerous research laboratories, many buffers have been used to stabilize concentrated C1q and prevent aggregation. About half of the scientists prefer high salt and the other prefer 40% glycerol in the storage buffer.

C1q is purified from pooled normal human plasma. C1q is part of the C1 complex and this complex is the first complement component in the cascade referred to as the classical pathway of complement. C1 is actually a non-covalent assembly of three different proteins (C1q, C1r, and C1s) bound together in a calcium-dependent complex. C1q has six extended arms with domains at the end of each arm that bind to the Fc domains of immunoglobulins. When antibodies bind to antigens forming immune complexes they cluster allowing two or more of its six arms of C1q to bind to the Fc domains of antibodies such as IgG or IgM. The binding of multiple arms to immune complexes causes the two C1r proteins in the complex (protease zymogens) to auto-activate producing two C1r proteases that cleave and activate the two C1s protease zymogens in the complex. Activated C1s cleaves complement component C4 releasing C4a and initiating covalent attachment of C4b to the activating surface. Activated C1s also cleaves C2 and the larger fragment of C2 binds to the surface-attached C4b forming C4b,C2a which is the C3/C5 convertase of the classical pathway.

Extinction Coeff.  $A_{280 \text{ nm}} = 0.68$  at 1.0 mg/ml for pure C1q

Molecular weight: 410,000 Da (18 chains)

Preservative: None, 0.22  $\mu\text{m}$  filtered.

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).

#### Physical Characteristics & Structure

C1q is a high molecular weight complex of 18 polypeptide chains. Each of the six arms of C1q contains three chains, an A chain (26,000 daltons), a B chain (25,000 daltons) and a C chain (24,000 daltons). The three chains are coiled into a collagen-like triple helix over approximately half their length. Half of this collagen region forms a central core where all 18 chains come together. The chains are joined in this core by disulfides in the pattern A-B and C-C. There is a bend in the center of the collagen region allowing the arms to extend away from each other. Globular heads at the far ends of the collagen arms possess binding sites for Fc domains of immunoglobulins. C1 complex is composed of one C1q molecule (410,000 daltons), two C1r molecules (92,000 daltons) and two C1s molecules (86,000 daltons). The complex is stable in the presence of calcium, but easily dissociates if calcium is removed.

When C1 is activated the C1r and C1s subunits are each cleaved into two chain molecules due to proteolytic activation. Thus, the SDS gel pattern of C1 is very complex.

## Function

The biological functions of C1q are described above in the General Description and Physical Characteristics sections. C1q functional activity may be assayed using C1q-depleted serum and EA cells. These assays are extremely sensitive to C1q typically yielding 50% lysis with less than 2 ng C1q in assays measuring the lysis of EA cells.

## Assays

The unit of classical pathway activity is the CH50. A similar unit, the C1qH50, is used to quantitate the activity of C1q. A C1qH50 unit is the amount of functional C1q needed to lyse 50% of  $3 \times 10^7$  EA cells (antibody-sensitized sheep erythrocytes) when that amount of C1q is incubated with 5-20  $\mu\text{L}$  of C1q-Dpl in GVB++ in a total volume of 500  $\mu\text{L}$  for 30 min at 37°C. This amount of C1q indicates the sensitivity of the assay for C1q which is typically about 1 ng C1q with 10  $\mu\text{L}$  C1q-Dpl. See the Certificate of Analysis for lot specific values.

## Applications

C1q is used to coat ELISA plates to capture and quantitate immune complexes in clinical samples. A number of commercial companies sell diagnostic kits for immune complex detection and quantitation. These kits are based on the ability of C1q to bind well to immune complexes, but to not bind significantly to monomeric immunoglobulins. GeneticsThe EMBL/Genbank cDNA accession numbers are: C1q A chain (P02745), C1q B chain (P02746), and C1q C chain (P02747). The genes for C1q chains A, B and C are all located on chromosome 1p in the order A-C-B.

## Deficiencies

Deficiencies of each of the three components of C1 have been found. Patients lacking C1q generally have immune-complex-mediated renal disease and skin lesions. Like all patients lacking early classical pathway components C1q deficient individuals are prone to systemic lupus erythematosus (SLE) and recurrent pyogenic infections. They lack classical pathway function and may or may not exhibit C1q antigen in blood.

## Diseases

See section titled Deficiencies above.

## 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.