

# Complement receptor 1 in autoimmune disorders

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**Complement receptor 1 (CR1) has gained much attention in recent years. The reason is manifold. Growing understanding on this protein has facilitated insight into the pathophysiology of autoimmune disorders. CR1, a polymorphic protein, is important as a complement regulatory protein, as well as a vehicle for immune complex clearance. Functional and clinical significance of CR1 polymorphism is a continuously revealing area in complement research. The levels of CR1 are altered in autoimmune disorders like rheumatoid arthritis, glomerulonephritis and systemic lupus erythematosus. This envisages CR1 as a potential prognostic marker for such diseases. Lower levels of erythrocyte CR1 are observed in patients suffering from the above diseases. This partially explains the tissue injury and inflammatory manifestations in patients suffering from these disorders. The benevolent role of CR1 in autoimmune and inflammatory disorders and propagation of disease manifestations due to its deficiency are further established with the therapeutic success of recombinant soluble CR1 in inflammatory and autoimmune disorders. This review is a brief and update account of CR1 and its importance in autoimmune disorders.**

COMPLEMENT receptor 1 (CR1) has gained much attention in recent years due to the following reasons. With growing understanding of this protein, greater insight into the pathophysiology of autoimmune disorders has now been achieved. Tissue injury in these disorders, primarily is a consequence of deficient regulation of complement cascade as well as diminished clearance of immune complexes. The integrity of both these functions is determined by the status of CR1 levels to a great extent. Variation in CR1 levels and its expression has been reported in a number of autoimmune disorders like glomerulonephritis (GN) and rheumatoid arthritis (RA)<sup>1,2</sup>. This endows CR1 with a potential role as a diagnostic and prognostic marker for such diseases.

CR1 is a polymorphic protein. Significance of its genomic and structural diversity is under extensive investigation. Association of CR1 polymorphism with disease is envisaged and hence CR1 genotyping and/or phenotyping may emerge as a useful tool in the risk assessment of a related disease. Most importantly, solu-

ble CR1 (sCR1) has been found to be highly effective as a therapeutic agent in the treatment of inflammatory diseases in animal models. These include myocardial infarction, myasthenia gravis and experimental allergic encephalomyelitis<sup>3-5</sup>. This may hold true for different autoimmune disorders as well<sup>6,7</sup>. This review puts forth a composite account of CR1 and its role in the pathophysiology, diagnosis/prognosis, risk assessment and therapy of autoimmune disorders.

## Biological functions of CR1

### *Regulation of complement cascade*

Activation of complement cascade induces production of potent effector molecules. Protein fragments like C3a, C4a and C5a, having anaphylactic and chemotactic activities with the ability to enhance elimination of foreign particles, are generated. Activation of complement cascade therefore results in inflammatory responses. Complement regulatory proteins like soluble Factor H, C1-inhibitor, C4-binding proteins, Factor I, S-protein and membrane-bound CR1/CD35, decay accelerating factor (DAF/CD55), membrane cofactor protein (MCP/CD46) and homologous restriction factor (HRF/CD59) are involved in the containment of inflammation. Table 1 lists the diverse activities of these regulatory proteins<sup>8</sup>. CR1 prevents the formation of alternative pathway convertase, since the binding site for CR1 on C3b is close to that for Factor B (Figure 1a). By binding to CR1, it inhibits the formation of classical pathway convertase in a similar fashion<sup>9</sup>. CR1 also serves as a cofactor for irreversible cleavage of C3b into iC3b and C3dg and C4b into C4c and C4d by Factor I (Figure 1b). This complement inhibitory activity of CR1 occurs both when CR1 is bound and also when CR1 is present in the soluble form.

### *Immune complex clearance*

CR1 on erythrocytes acts as a vehicle for clearance of C3b-coated immune complexes (Figure 1c). The immune complexes altered in this way become less pathogenic<sup>10</sup>. The liver is the main site for removal of C3b-bearing immune complexes (ICs)<sup>11</sup>. Kupffer cells trap immune complexes after cleavage of C3b into iC3b or

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**Table 1.** Regulators of complement system

| Protein                                     | Type of protein | Pathway affected       | Immunologic function   |
|---|-----------------|------------------------|--|
| C1 inhibitor                                | Soluble         | Classical              | Serine protease inhibitor: causes $\text{Clr}_2\text{s}_2$ to dissociate from $\text{Clq}$               |
| C4b-binding protein (C4bBP)                 | Soluble         | Classical              | Blocks formation of C3 convertase by binding C4b, cofactor for cleavage of C4b by Factor I               |
| Factor H                                    | Soluble         | Alternative            | Acts by blocking formation of C3 convertase by binding C3b, cofactor for cleavage of C3b by Factor I     |
| Complement receptor 1 (CR1)                 | Membrane-bound  | Classical, alternative | Blocks formation of C3 convertase by binding C3b, C4b, cofactor for cleavage of C3b or C4b by Factor I   |
| Membrane cofactor protein (MCP)             | Membrane-bound  | Classical, alternative | Blocks formation of C3 convertase by binding C3b, C4b, cofactor for cleavage of C3b or C4b by Factor I   |
| Decay accelerating factor (DAF)             | Membrane-bound  | Classical, alternative | Accelerates dissociation of $\text{C4b2a}$ and $\text{C3bBb}$ (classical and alternative C3 convertases) |
| Factor I                                    | Soluble         | Classical, alternative | Serine protease, cleaves C4b or C3b using C4bBP, CR1, Factor H, DAF or MCP as cofactor                   |
| S-protein                                   | Soluble         | Terminal               | Binds soluble C5b67 and prevents its insertion into cell membrane  |
| Homologous restriction factor (HRF)         | Membrane-bound  | Terminal               | Binds on autologous cells, blocking binding of C9  |
| Membrane inhibitor of reactive lysis (MIRL) | Membrane-bound  | Terminal               | Binds on autologous cells, blocking binding of C9  |

C3dg. CR1 does not have affinity for iC3b. However, CR3 and CR4 present in high density on Kupffer cells, bind iC3b. ICs that contain C3dg or C3d may also be trapped by B cells, which express CR2 receptor<sup>12</sup>. In addition, follicular dendritic cells can trap complexes bearing iC3b and C3dg.

*Phagocytosis*

The CR1 expressed on the surface of phagocytic cells may bind soluble polymeric C3b, which is covalently fixed to ICs or particles and enhances their phagocytosis<sup>13</sup> (Figure 1 d). The CR1 and Fc gamma receptors cooperate for phagocytosis of targets that have been coated with sub-optimal amounts of IgG. The cross-linking of these receptors elicits a number of secondary responses in phagocytic cells. These include neosynthesis and release of arachidonic acid metabolites, stimulation of oxidative burst, release of toxic oxygen derivatives and lysosomal enzymes<sup>14</sup>.

*Regulation of immune responses*

The stimulation of human monocytes with C3b induces the intracellular production and extracellular release of interleukin 1 (IL-1) in serum-free conditions. It en-

hances the differentiation of B cells, but does not have any effect on memory responses.

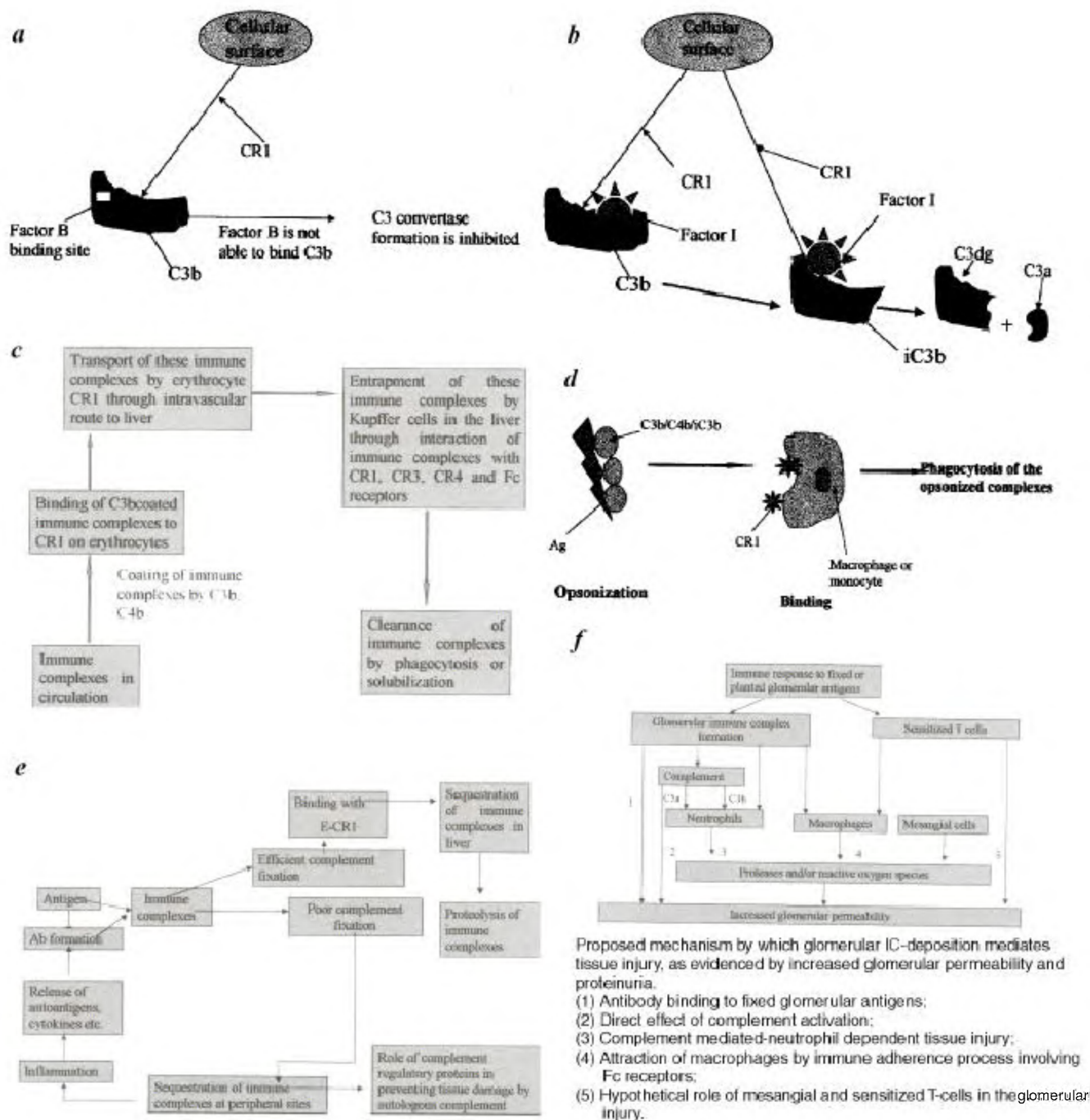
*Speculated role on renal podocytes*

CR1 antigenic determinants have been found to be present on the surface of podocytes. Fischer *et al.*<sup>15</sup> have demonstrated that podocyte CR1 shares the functional, antigenic and biochemical properties of erythrocyte CR1 (E-CR1). It has been speculated that the presence of CR1 on podocytes might be necessary for the inactivation of C3b in a compartment, which is otherwise devoid of complement inhibitors.

**Expression of CR1**

*Cell surface bound expression*

CR1 or C3b/C4b receptor is a single-chain integral membrane glycoprotein, differentially expressed as membrane-bound protein on erythrocytes, eosinophils, monocytes, B-lymphocytes, some T-lymphocytes, dendritic cells and kidney podocytes<sup>16</sup>. Distribution and function of CR1 on the surface of these cells are given in Table 2 (refs 17 and 18).



**Figure 1.** Function of CR1. *a*, Inhibition of alternative pathway convertase formation; *b*, Cofactor activity of CR1; *c*, Immune complex clearance by CR1; *d*, Opsonization and phagocytosis by CR1; *e*, Possible fate of immune complexes in autoimmune disorders; *f*, Proposed mechanism for tissue injury in kidney disorders manifested by immune complexes.

### Soluble CR1

CR1 is also present in the plasma in a soluble form as sCR1, which is indistinguishable in size and antigenicity from E-CR1. sCR1 has been shown to be secreted by leukocytes<sup>18</sup>. CR1 also occurs in urine as urinary CR1 (u-CR1), which arises by shedding from the surface of glomerular podocytes<sup>19</sup>.

### CR1 polymorphism

Human complement receptor is a single-chain glycoprotein, with complex tri- and tetra-N-linked oligosaccharides in its mature form<sup>20,21</sup>. It is a member of the regulators of complement activation (RCA) gene cluster that also includes members such as DAF and MCP. This RCA gene cluster is located on the q32 band of chromo-

some 1. Minor differences of 6 kDa in apparent molecular weights have been observed between CR1 isolated from erythrocytes and those isolated from neutrophils or T cells of the same individual. This might be due to differential glycosylation<sup>20</sup>. A second polymorphism of CR1 is also known, which arises due to variation in molecular weight from 160 to 250 kDa. Four polymorphic forms have been identified with relative molecular weights (under non-reducing conditions) on SDS-PAGE of 160,000 (C), 190,000 (A), 220,000 (B) and 250,000 (D). The nature of CR1 allotypes and their corresponding molecular weights are shown in Table 3 (ref. 22). This polymorphism is regulated by four autosomal co-dominant alleles<sup>23</sup>. A and B are the most common alleles of CR1, having gene frequencies of 0.8 and 0.2. The A allotype is comprised of a 41 amino acid signal peptide, 30 short consensus repeats (SCRs) region and a 42 amino acid cytoplasmic domain<sup>24</sup>. Each SCR contains 11 to 14 conserved cysteine residues, including four highly conserved cysteine residues and several hydrophobic residues<sup>25</sup>. Cysteine 1 and 3 as well as 2 and 4 are disulphide-linked. This results in a triple loop structure for the SCR, which is connected in tandem by a short stretch of 4 to 5 amino acids. Twenty-eight SCRs at the 5' end are organized into four tandem long homologous repeats (LHRs) termed as A, B, C, D (Figure 2). Each contains seven SCRs encoding 405 amino acids and the sequence homology among the corresponding SCRs in each LHR ranges from 60 to 90% (refs 20, 23). Erythrocytes, which bear alleles B or D,

are more efficient than allele A in binding immune complexes (ICSs), due to the presence of more binding sites<sup>26</sup>. A third polymorphism determining the quantitative low (L) and high (H) expressions of CR1 on erythrocytes, has also been found to occur<sup>27</sup>. A *Hind*III restriction fragment length polymorphism (RFLP) has been found to have an association with low and high expression of CR1. *Hind*III digestion of DNA amplified with primers specific for *CR1* gene yields three fragments of 1.8, 1.3 and 0.5 kb for individuals heterozygous for CR1 high-density allele, whereas 1.8 kb band indicates homozygous CR1 high-density allele<sup>28</sup>. The pattern of fragments obtained after *Hind*III digestion of PCR-amplified *CR1* gene is shown in Figure 3. These polymorphisms have been found to be present at different frequencies in different individuals.

CR1 polymorphism and disease association

An overall account of CR1 polymorphism and its association with the disease is given in Table 4. A series of investigations has provided some evidence linking the polymorphism of CR1 with the pattern of disease observed in patients. One of the early studies by Van Dyne *et al.*<sup>29</sup> indicated an association between C allele of CR1 and systemic lupus erythematosus (SLE). In this study, C allele was found to occur at a frequency of 61.4% of the total CR1 in SLE patients, compared with 21.7% of the total CR1 among normal individuals. This observation indicates a possibility that a linked gene is respon-

Table 2. Relative distribution and function of cellular CR1

| Location of CR1       | Average number of CR1/cell | Function on the surface of the cells                  |
|-----------------------|----------------------------|---|
| Erythrocytes          | 500–600                    | Processing and transport of immune complexes          |
| Neutrophils           | 5000                       | Phagocytosis, endocytosis of soluble immune complexes |
| Monocytes/macrophages | 5000                       | Phagocytosis  |
| B-Lymphocytes         | 20,000–40,000              | Cell activation                                       |
| T-Lymphocytes         | Not known                  | Not known   |
| Glomerular podocytes  | 200,000                    | Trapping immune complexes                             |

Table 3. CR1: Different structural forms

| Allotype | Molecular weight reduced/non-reduced (kDa) |
|----------|--|
| D        | 320/250                                    |
| B/S      | 290/220                                    |
| A/F      | 250/190                                    |
| C/F'     | 210/160                                    |

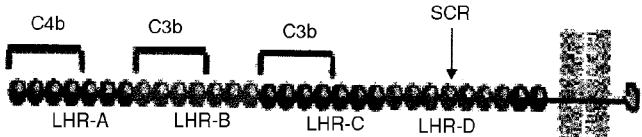


Figure 2. Molecular structure for CR1.

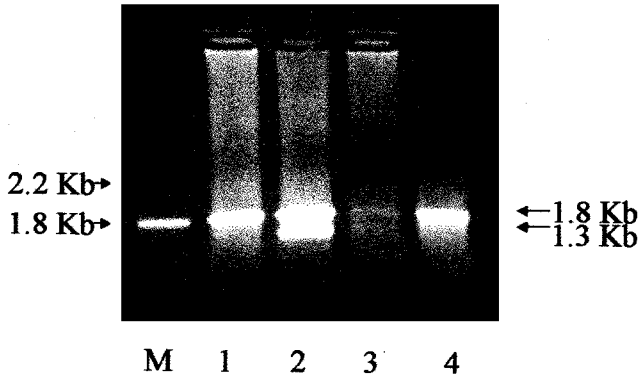


Figure 3. Genomic polymorphism for *CR1* gene. Representative photograph of the PCR-RFLP for the *CR1* gene. M, Marker; 1 and 2, Samples with intermediate expression pattern; 3, Sample with high expression of CR1.

**Table 4.** CR1 polymorphism and disease association

| References | Disease system for investigation | Predominant allele | Percentage in normal individuals      | Percentage in patients    |
|------------|----------------------------------|--------------------|---------------------------------------|---------------------------|
| 29         | SLE                              | C allele           | Relative expression of C allele–21.7% | Relative expression–61.4% |
| 30         | SLE                              | None               | –                                     | –                         |
| 31         | AGN                              | None               | –                                     | –                         |
| 32         | SLE                              | B allele           | Relative expression of B allele–26%   | Relative expression–51%   |
| 33         | Hydralazine (Hz)-induced SLE     | None               | –                                     | –                         |
| 34         | RA                               | None               | –                                     | –                         |

SLE, Systemic lupus erythematosus; AGN, Acute glomerulonephritis; RA, Rheumatoid arthritis; None, None of the alleles showed higher frequency. Frequencies for the expression of all the alleles in patients as well as normal individuals were similar.

sible for the association between the C allele and SLE. Association between CR1 genomic polymorphism and susceptibility to SLE was disproved in a study conducted by Moulds *et al.*<sup>30</sup>. They found that CR1-C is not a genetic risk factor for SLE and the frequencies of the CR1 structural alleles do not differ from race-matched healthy controls. Studies by Panchamoorthy *et al.*<sup>31</sup> on acute glomerulonephritis (AGN) patients indicated similar gene frequencies for CR1 alleles in normal individuals and patients.

*HindIII* RFLP studies carried out in patient group also to some extent, have indicated a link between the CR1 genomic polymorphism and susceptibility to autoimmune disorders. Some other studies have indicated that differences in the number of CR1 expressed on erythrocyte surface do not predispose an individual to autoimmune disorders. A study by Cornillet *et al.*<sup>32</sup> in 1992 using *HindIII* polymorphism indicated that B allele is present at a higher frequency of 51% among SLE patients, compared to a frequency of 26% among controls. Mitchell *et al.*<sup>33</sup> on the other hand, found that individuals who are genotypically low expressors of E-CR1 (with homozygous expression of 6.9 kb allele) do not have increased susceptibility to hydralazine-induced SLE. Kumar *et al.*<sup>34</sup> have indicated through *HindIII* polymorphism that low levels of CR1 on erythrocytes in patients with RA are not inherited, rather they are acquired during the disease process.

### CR1 levels: Diagnostic and prognostic implications

The complement system is a double-edged sword. It is benevolent against the autoimmune disorders by promoting phagocytosis and clearance of immune complexes from circulation. However, excessive and persistent IC load may cause unabated activation, which leads to tissue injury. Patients suffering from RA

tend to have excessive load of immune complexes, the IgG component of which is unglycosylated. This renders them incapable of binding to Fc receptors. Subsequently, abnormal complexes persist and lead to tissue injury, persistent activation of complement, chemotaxis and generation of inflammatory peptides. Under such a situation, CR1-mediated immune complex clearance is essential to control the disease manifestations.

In GN patients, tissue injury is mainly caused by the deposition of immune complexes. This triggers generation of leukochromatic factors, attraction of neutrophils and inflammation followed by onset of proteinuria, hematuria and other clinical manifestations of GN. Possible fate of glomerular immune complex deposition and the proposed mechanism for tissue injury manifested by these immune complexes is shown in Figure 1 *e* and *f*.

The principle mechanisms for tissue injury in SLE appear to be the deposition of circulating immune complexes, *in situ* immune complex formation and production of anti-tissue antibody. Regulatory proteins like CR1 prevent excessive activation of complement cascade due to immune complex load. A reduction of CR1 in SLE, RA, kidney disorders<sup>1,2</sup> on the surface of erythrocytes has been found to be responsible for ineffectiveness of the protective role of the complement system (see Table 5). Decrease in CR1 levels hampers immune complex clearance from the circulation, enhancing deposition of immune complexes in different tissues and thereby contributing to the development of autoimmune disorders. Levels of CR1 expression have been found to be very low in several disease systems, including SLE and AGN along with RA patients (Table 5). Mitchell *et al.*<sup>33</sup> found that individuals with SLE had lower mean levels of CR1 compared to normal controls. In AGN patients too, CR1 expression on erythrocytes showed a decreasing trend<sup>28</sup>. Arora *et al.*<sup>1</sup> have shown that CR1 expression on the capillary walls in glomeru-

**Table 5.** Relative CR1 expression in different disease systems

| References | Disease system | Relative CR1 expression  | Level in normal individuals  | Level in patients  |
|------------|----------------|--|--|--|
| 33         | SLE            | Low number of CR1 on erythrocytes  | Hz SLE normal relatives $774 \pm 46$<br>Hz control- $756 \pm 80$<br>Hz healthy control relatives- $825 \pm 65$                                 | $564 \pm 65$   |
| 1          | DPGN           | Low mean fluorescence intensity of CR1 in erythrocytes                         | Absolute value not given   | Mean fluorescence of CR1-20.6% of mean fluorescence in normal erythrocytes |
| 2          | RA             | Low number of CR1 on erythrocytes  | Genotypically low expressors- $256 \pm 73$<br>Genotypically moderate expressors- $576 \pm 132$<br>Genotypically high expressors- $839 \pm 171$ | $277 \pm 65$<br>$323 \pm 110$<br>$427 \pm 144$                             |
| 35         | FSGS           | Low mean fluorescence intensity of CR1 in RBCs                                 | 83.93 on normal erythrocytes   | 47.26  |
| 36         | MCNS           | No expression of CR1 on biopsies taken from infants compared to adult patients | Not done   | No expression  |
| 37         | Nephropathy    | High soluble CR1   | $44.68 \pm 12.5$ ng/ml   | $106.40 \pm 24.34$ ng/ml   |

SLE, Systemic lupus erythematosus; DPGN, Diffuse proliferative glomerulonephritis, RA, Rheumatoid arthritis; FSGS, Focal segmental glomerulosclerosis; MCNS, Paediatric minimal change nephrotic syndrome.

lus of lupus nephritis was reduced. In RA patients also, CR1 expression was found to be lowered<sup>2</sup>. In addition, quantitation of CR1 levels on the erythrocytes of focal segmental glomerulosclerosis (FSGS) patients showed reduced expression of CR1<sup>35</sup>. Anand *et al.*<sup>36</sup> established an absence of CR1 expression in children suffering from minimal change nephrotic syndrome (MCNS), in contrast to normal CR1 expression on the capillary walls of adults suffering from the same disorder. Our studies on sCR1 showed increased levels of this protein in the plasma of GN patients<sup>37</sup> compared to the normals. The source of increased sCR1 may be because of increased synthesis due to complement activation in the patients, increased leukocytosis or shedding off from erythrocytes. This observation gives a fair chance to use sCR1 as a prognostic marker to assess the disease activity in these patients. Our observations also indicated a significant reduction in E-CR1 of patients suffering from different categories of lupus nephritis compared to controls. Glomerular CR1 also showed clear differences between immune complex and non-immune complex mediated diseases. Glomerular CR1 was virtually found to be absent in lupus kidneys (*Asian Pacific J. Allergy Immunol.*, in press). Follow-up studies of E-CR1 levels were also conducted in normal controls, non-IC disor-

ders and lupus nephritis patients. E-CR1 expression at the onset and at different times of treatment was monitored. It was observed that there is a dramatic increase in E-CR1 expression once the patients were kept on steroids and anti-inflammatory drugs. CR1 is present in the urine as u-CR1 and the source of this under normal conditions is renal podocytes. Podocytes are the only cells which express CR1 on their surface in the kidney. It is well-documented that the glomerulus is damaged in most renal diseases and as a consequence of this, CR1 from podocytes is shed off and comes in the urine. Quantitation of CR1 in normal conditions and in renal patients and its correlation with kidney biopsy results may help in follow-up of the patients, without the need to repeat painful invasive biopsy. u-CR1 therefore has a prognostic potential, which needs to be explored.

### Soluble CR1 as a therapeutic agent

A knowledge of the molecular reactions elicited by CR1 and its role in the pathogenesis of many autoimmune and inflammatory diseases, has given rise to two major thrusts in complement research. The common goal for both has been the development of a means for interrupt-

**Table 6.** Inhibitory activity of the regulators of complement activation protein family

| Protein  | Dissociation of C3 and C5 convertases |           | Factor I-cofactors |     | Restriction by alternative pathway activation |
|----------|---------------------------------------|-----------|--------------------|-----|---|
|          | Alternative                           | Classical | C3b                | C4b |   |
| Factor H | Yes                                   | No        | Yes                | No  | Yes   |
| C4-bp    | No                                    | Yes       | No                 | Yes | Not applicable                                |
| DAF      | Yes                                   | Yes       | No                 | No  | Not known                                     |
| MCP      | No                                    | No        | Yes                | Yes | Not known                                     |
| CR1      | Yes                                   | Yes       | Yes                | Yes | No  |

C4-bp, C4-binding protein; DAF, Decay accelerating factor; MCP, Membrane cofactor protein; CR1, Complement receptor 1.

ing tissue injury in these diseases. Such an inhibitor might be found among the endogeneous regulatory proteins of complement, that block the enzymes that activate C3 and C5. An overview of the inhibitory activities of the RCA members is given in Table 6 (ref. 3). Among the regulators of complement activation (RCA) members, CR1 has the greatest potential for this role. It has specificity for C3b and C4b, with distinct binding sites for both proteins. CR1 also possesses a capacity for displacement of the catalytic subunits from the C3 or C5 convertases of both activating pathways, and co-factor function for the degradation of C3b and C4b by Factor I. In addition, the proteolysis of C3b and C4b releases CR1 and allows it to recycle in the inactivation process. Finally, and perhaps of critical importance, these functions of CR1 are not restricted by alternative activating surfaces, as are the inhibitory effects of Factor H<sup>38</sup>. This makes the receptor especially suitable for blocking complement activation by non immunologic stimuli. CR1, however, is restricted to a few cell types and has a low plasma concentration of 0.01% of the total soluble regulatory protein. This limits its function *in vivo*. Interest in this field has been renewed with demonstration of the effectiveness of recombinant complement inhibitor protein in diverse animal models. So the limitation of CR1 discussed above is overcome by preparing a truncated, recombinant soluble form, lacking the transmembrane and cytoplasmic domains<sup>3</sup>. sCR1 retains the C3b- and C4b-binding function and Factor I-cofactor activities of membrane-associated CR1. In addition, CR1 inhibits activities of the classical and alternate pathways *in vitro*, at concentrations that are 100 times less than those of serum RCA protein.

### sCR1 in glomerulonephritis

Glomerulonephritis is a major cause of end-stage renal disease (ESRD) and is characterized by glomerular deposition of immunoglobulin with activation of the complement system. Anti thy-1 models of mice analogous to human diseases were taken. These animal

models resembled human diseases like IgA nephropathies, lupus nephritis and membranoproliferative GN, in which mesangial cell proliferation occurs. This proliferation has been found to occur in association with immunoglobulin and complement deposition. In animal models, sCR1 therapy showed significant reduction in mesangiolysis, platelet and macrophage infiltration and proteinuria. The con A-treated animal models of GN is similar to human lesions such as diffuse proliferative lupus nephritis and type I membranoproliferative GN. sCR1 treatment in this animal model abolished the early platelet infiltrate and neutrophil infiltration in the glomerulus. It is noteworthy that the beneficial effects have been observed at sCR1 concentrations as low as 3 mg/kg. With PHN model (membranous nephropathy in humans), sCR1 treatment significantly reduced proteinuria<sup>6</sup>. Promising results were seen in animal models of RA when administered with sCR1, as local complement inhibition is of greater therapeutic benefit than decompensation<sup>7,39</sup>. sCR1 therapy in animal models of experimental autoimmune myasthenia gravis (EAMG) significantly reduced weight loss and severity of clinical symptoms and retained normal muscle function<sup>4</sup>. Administration of recombinant sCR1 to rats subjected to transient myocardial ischaemia with subsequent reperfusion, reduced the size of myocardial infarction. The suppression of tissue damage by sCR1 was by complement inhibition and it was found that sCR1 did not interfere with the healing process<sup>3</sup>. In addition, sCR1 has shown promising results in animal models of antibody-mediated demyelinating experimental allergic encephalomyelitis<sup>5</sup>.

### Conclusion

To summarize, CR1 is a polymorphic complement regulatory protein of immense importance in the containment of immune complex and complement-mediated autoimmune injury. It has potential to serve as a marker in the diagnosis, prognosis and risk assessment of autoimmune disorders. Further, CR1 can act as a prospec-

tive candidate in the treatment of autoimmune and inflammatory disorders.

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