Appendix S2. Supplementary information on T1000N variant in C3

In the T1000N CR3–mutant, a threonine residue has become changed to an asparagine in the lower leg part of the α-chain of the protein. The threonine residue is susceptible to posttranslational modification, such as *O*-linked glycosylation, whereas an asparagine residue can accept an N-linked oligosaccharide only if the residue is part of a consensus sequence (Asn-X-Ser or Asn-X-Thr), which is not present in the CR3 T1000N variant. Thus, it is possible that this variant lacks any sugar moiety in this position. O-linked sugars may play a role in blocking the access to protease-sensitive site. Thus, the lack of protective sugar-moieties may predispose the integrin to degradation. Furthermore, the CR3 T1000N mutation is located in the lectin domain, which allows CR3 to bind polysaccharides on yeast and bacteria and facilitate the cytotoxic functions of the receptor. In addition, the perturbation of the extracellular membrane-proximal region of CD11b leads to enhanced adhesive activity and influences the ability of CR3 to respond to inside-out signaling[1], suggesting that mutation in this region would affect the signaling of the receptor.

Outcomes of CR3 signaling include a decreased ability of dendritic cells to produce inflammatory cytokines and dendritic cell-mediated suppression of T cell activation, which both negatively regulate the activation of adaptive immunity[2–5]. A study in mice has identified strong expression of CD11b and CD18 in the feto-maternal interface, suggesting a regulatory role for iC3b in the placenta during late pregnancy by a CR3-driven anti-inflammatory cytokine response[6].

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