**The complement system**

The complement system is a part of the innate immune system that consists of a large number of plasma proteins. Initially, its major function was thought to be the elimination of pathogens in the innate immune system. However, complements were found to be involved in the pathogenesis of autoimmune diseases. The complement system is activated via three pathways, the classical, alternative and lectin pathways. In the classical pathway, the complement activation depends on IgG or IgM immune complexes. C1q binds to the IgG or IgM of immune complexes through the Fc portion. This is the initial trigger for the classical pathway. These three pathways lead to the activation of C3 convertase, and then this enzyme cleaves C3 into anaphylactic peptide C3a and opsonin C3b. The C3b finally generates C5 convertase, and then C5 cleaves into C5a and C5b. The C5b finally forms membrane attack complex (MAC) C5b-9, which can cause cell lysis. Both anaphylactic C3a and C5a can induce inflammation via the recruitment of neutrophils or macrophages, and C5a is a more powerful anaphylactic peptide than C3a *in vivo*.

Supplementary reference

S1 Ballanti E, Perricone C, Greco E *et al.* Complement and autoimmunity. Immunol Res 2013: 56: 477–91.

S2 Mackay I R, Rosen F S, Walport M J. Complement. Second of two parts. N Engl J Med 2001: 344: 1140–1144.

S3 Stegert M, Bock M, Trendelenburg M. Clinical presentation of human C1q deficiency: How much of a lupus? Mol Immunol 2015: 67: 3–11.

S4 Thurman J M, Holers V M. The central role of the alternative complement pathway in human disease. J Immunol 2006: 176: 1305–10.

S5 Tsao P Y, Arora V, Ji M Q *et al.* KRN/I-Ag7 Mouse Arthritis Is Independent of Complement C3. J Clin Immunol 2011: 31: 857–863.

S6 Solomon S, Kolb C, Mohanty S *et al.* Transmission of antibody-induced arthritis is independent of complement component 4 (C4) and the complement receptors 1 and 2 (CD21/35). Eur J Immunol 2002: 32: 644–51.

S7 Sitaru C. Experimental models of epidermolysis bullosa acquisita. Exp Dermatol 2007: **16**: 520–31.

S8 Bieber K, Sun S, Ishii N *et al.* Animal models for autoimmune bullous dermatoses. Exp Dermatol 2010: 19: 2–11.

S9 Sitaru C, Mihai S, Otto C *et al.* Induction of dermal-epidermal separation in mice by passive transfer of antibodies specific to type VII collagen. 2005: 115

S10 Woof J M, Russell M W. Structure and function relationships in IgA. Mucosal Immunol 2011: **4**: 590–597.