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The complement system is also important in immunogenic cell death

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We recently came across a Review (*Nat. Rev. Immunol.* doi: 10.1038/nri.2016.107 (2016))[1] published in your distinguished journal. We completely agree with the authors' statement that immunogenic cell death (ICD), whether occurring in cancer cells or pathogen infection, requires the two key factors antigenicity and adjuvanticity. However, this Review neglects the important role of the complement system in ICD. Complement-mediated opsonization has a pivotal role in the uptake of apoptotic cells, a process that is aberrantly handled under complement-deficient conditions[2].

The interaction of C1q and its receptor, calreticulin, is involved in immune tolerance by recognition and uptake of apoptotic cells and modulation of cytokine release[3]. In the autoimmune disease systemic lupus erythematosus, intracellular self-antigens are targeted by a mechanism related to the classical complement system, the early components of which lack inheritably[4]. Factor H is a cofactor for factor I-mediated inactivation of the alternative pathway C3 and C5 convertases that drive alternative pathway amplification of the cascade.

Anti-inflammatory cytokines produced by apoptotic cells coated with factor H decrease the immunogenicity of autoantigens and their ability to elicit inflammation[5]. Furthermore, reduced expression of membrane-bound complement inhibitors, including CD59, CD46 and CD55, may be linked to antibody-mediated complement-dependent killing of tumour cells and to passive immunotherapy[6]. Therefore, in summary, the complement system also has a role in ICD in the context of cancer and inflammation.

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Competing interests statement
The authors declare no competing interests.