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PREFACE

Complement activation and innate immunity

This special issue stems from presentations made at the Sixth International Workshop, on the First Component of Complement C1 and Collectins, which was held in Seeheim, in June 2006 amid the friendly and festive context of the world soccer competition. Specialists of complement, biologists and clinicians, met together and clearly demonstrated that there is a continuing interest in the study of the early components of the complement cascade. This cascade (Fig. 1), involving a large number of proteins, is initiated and proceeds via three main distinct pathways, through which initially inactive proteins acquire biological activities.

The Collectins, which are involved in the three activation pathways (classical, lectin, and alternative pathway), are oligomeric molecules composed of C-type lectin domains attached to collagen-like sequences through α-coiled neck regions. C1q, which also contains collagen-like sequences but which has C-terminal globular domains related to the TNF-protein superfamily, rather than carbohydrate recognition domains, contributes with the collectins to form a link between innate and acquired immunity.

Recent evidence was presented at the meeting, which indicated that there was direct activation of the alternative pathway by the human mannan-binding lectin (MBL) in C2- and C4-deficient sera, based on a novel test using specific oligosaccharides from Salmonella O bound to a solid phase. In this study, cleavage of C3 was observed at high concentrations of serum, but without clear evidence for the protease(s) involved in this cleavage. The description of this pathway bypass of C2 and C4 (Selander et al., 2006), which was highlighted by an editorial commentary (Atkinson and Frank, 2006), was sadly the last contribution of Anders Sjöholm, who passed away a few days before the workshop.

The roles of collectins and C1q were also further documented in a variety of situations, involving, for example, the therapeutic use of synthetic peptides, purified molecules or fragments of C1q and surfactant protein D (SP-D) in pulmonary allergies and infections.

The characterisation of the structures and function of ficolins (consisting of a short N-terminal cysteine-rich domain followed by a collagen-like and a C-terminal fibrinogen-like domain) was presented at the Workshop. The ficolins, when viewed in the electron microscope, have an overall structural similarity to C1q and the collectins, and several of these ficolins have been shown to be able to contribute to complement activation (utilising the Lectin Pathway – as per Fig. 1), and probably all of them play a role in defence at the cellular level.

There is also clearly a role of C1q, ficolins and MBL in the handling of apoptotic material, either directly or via their receptors, and since they are involved in apoptosis, they may also be involved in antigen handling and antigen presentation and hence subsequently in autoimmunity.

Other contributions underlined new multifaceted links between complement and other systems. For example, it was shown that C1-inhibitor (C1-INH), a highly glycosylated serine protease inhibitor (SERPIN) circulating in blood, interacts not only with the complement system but also with other proteolytic cascades such as blood clotting, the kinins and fibrinolysis. Other roles of C1-INH were reviewed, distinct from the serpin activity: interaction with the alternative pathway at the level of Factor B; interaction with extracellular matrix compounds; interaction with E and P Selectins; and interaction with Gram negative bacterial endotoxin.

Advances in understanding the roles of the early components of the complement, either in the activation steps of the cascade, or more individually at the cellular level, appears likely to be a very fruitful area of research in the future, especially with the contributions made using the ever-increasingly powerful tools of structural and molecular biology – and it is hoped that this will lead to the development of new therapeutics which will be a focus of future workshops.

Abbreviations: C1q, the collagen-like first component of the classical complement activation pathway; C1r and C1s, the serine proteases that associate with C1q in the C1 complex and activate C4 and C2 by cleavage; MBL, a collagen-like mannan-binding lectin; MASP, MBL-associated serine protease; Factor D, the serine protease of the alternative pathway that cleaves factor B when it is bound to the major cleavage product (C3b) of the third complement component C3

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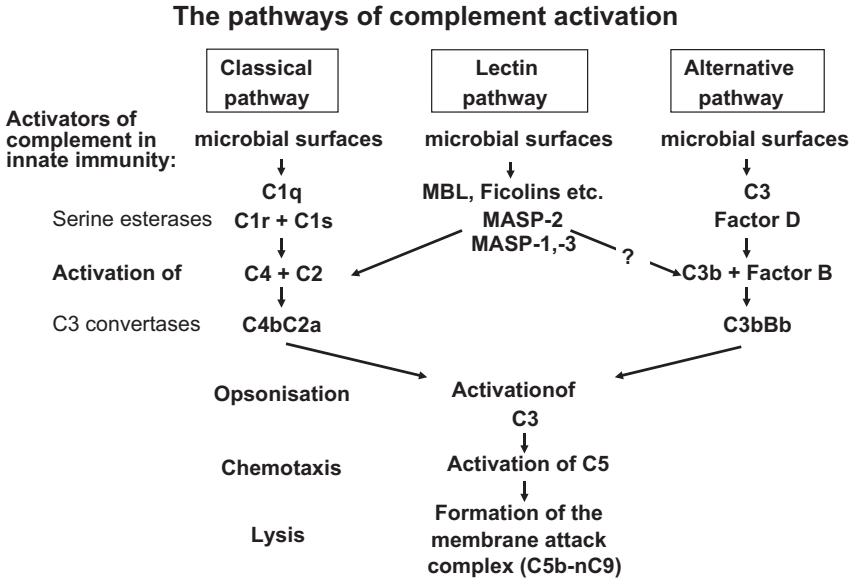

Fig. 1. The classical, lectin and the alternative pathway of complement activation.

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The organizers of the workshop are grateful to the Editor in Chief, Prof. Wilhelm Schwaeble, and the Editorial Coordinator, Dr. Brent W. Kiernan, for their support in publishing this special issue of Immunobiology. The issue presents the principal topics discussed at the meeting covered in review-like articles by participants who had been invited to do so. It provides a comprehensive, updated view of the ongoing research in the field of C1 and the collectins.

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