Unexpected and Novel Functions of Complement Proteins

Complement activation was probably one of the first observations in humoral innate immunity and this field of research would not have been evolved without the pioneering work of Jules Bordet (1870–1961) [1]. Bordet, who started his scientific career in Metchnikoff's lab at the Pasteur Institute, discovered that, apart from a cellular immune response (phagocytosis), serum also has the ability to kill bacteria. In recognition of these findings, Bordet was awarded the Nobel Prize in Physiology or Medicine 'for his discoveries relating to immunity' as early as 1919. Today, our knowledge about the complement system has advanced enormously and, with the discovery of the lectin pathway [2], it was thought that its role in innate immunity was completely unraveled. However, as with many other areas in life science, recent discoveries point to additional roles for the complement system in various pathophysiological processes, including rheumatic diseases and organ transplantation [3, 4], making the complement system an interesting therapeutic target in drug discovery [5, 6]. Thus, within the last couple of years, *Journal of Innate Immunity* has published several articles dealing with different functions of the complement system, such as its role in inflammation [7], age-related macular degeneration [8], chronic renal failure [9] and the lectin pathway [10], as well as its interactions with eukaryotic cells [11–14] and microbial pathogens [15–17].

In this issue of *Journal of Innate Immunity*, Uday Kishore, Kenneth B.M. Ried and Robert B. Sim have edited a thematic focus section entitled 'Unexpected and Novel Functions of Complement Proteins'. The section

consists of three articles published by outstanding researchers in the field. The review by Alex Langford-Smith and his colleagues [8] presents a timely overview on the role of complement in macular degeneration. The article summarizes the recent findings on the role of complement factor H on eye inflammation which show that polymorphism in protein factor H has a significant impact on the development of age-related macular degeneration. The reader will learn that this affects the interaction of factor H with heparin sulfate, which in turn contributes to chronic eye inflammation. The other two contributions are original research articles. Mélanie Verneret and coworkers [18] show that complement factor C1q interacts with surface-exposed calreticulin on early apoptotic cells. The authors describe that this leads to an important role of C1q in regulating the inflammatory responses of dying cells. Joseph O'Flynn and collaborators [14] are also working with phagocytes. In their article it was found that several neutrophil-derived proteins, including myeloperoxidase, elastase, lysozyme and cathepsin G, interact with properdin, a member of the alternative part of the complement system. Interestingly, only the interaction with myeloperoxidase leads to a subsequent activation of the complement system as measured by C5b-9 deposition. Together, these articles show that the complement system still bears many unknown sides that need to be discovered and will enhance our knowledge of one of the first-reported humoral parts of the innate immune system.

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