The Ficolins

The ficolins are oligomeric proteins that share sequence homology and have similar topology. They may sense pathogens as well as host-derived danger signals. The clinical importance of the ficolins is still poorly defined, but recent observation of ficolin deficiency in patients with infections suggests that the ficolins may also be of importance for clinical medicine.

The first ficolin to be discovered was the Hakata antigen, now known as ficolin-3 or H-ficolin. In 1978, Inaba and Okuchi [1] reported some preliminary characteristics of a thermolabile serum protein they named the Hakata antigen, which reacted with an autoantibody from patients with systemic lupus erythematosus (SLE). However, already in 1973 autoantibodies present in some SLE sera had been shown to react with a thermolabile macroprotein present in all normal human sera [2]. This antigen disappeared from SLE patients' sera when the autoantibody appeared, and the phenomenon was associated with hypocomplementemia and marked disease activity. These seminal findings were probably the first indications of the presence of the ficolin family of proteins. However, it was not until 1998 that ficolin-3 was fully characterized and cloned [3]. Nevertheless, the first biochemical characterisation of a ficolin was made by Ichijo et al. [4, 5], who purified a transforming growth factor β -1 binding protein from porcine uterus membranes. Subsequently, a human protein, which we today designate as ficolin-2 or L-ficolin was purified from plasma by Matsushita et al. [6]. The third human ficolin (ficolin-1 or M-ficolin) was subsequently identified by genomic DNA and cDNA cloning and was actually a by-product of the characterisation of ficolin-2 [7, 8]. All ficolins show a similar overall structure that contains collagen-like and fi-

brinogen-like domains. Although the fibrinogen-like recognition domains are different, the structure resembles C1q and MBL from the complement system. Thus, the possible role of ficolins in the complement system was an obvious line of investigation. Because of the groundbreaking work of Matsushita, Fujita and colleagues it has now been established that the ficolins indeed act as recognition molecules in the lectin pathway of complement using the same set of serine proteases as mannose-binding lectin [9–11].

We have dedicated this issue of the *Journal of Innate Immunity* to the ficolins primarily because we believe that they are an important component of the molecules involved in first-line host defence. Moreover, the ficolin field is currently expanding and developing rapidly, thus a comprehensive view on the different angles of ficolin research is urgently needed.

Evolutionary and genetic aspects are discussed by Garred et al. [12], while structural and functional aspects are discussed by Garlatti et al. [13] and Matsushita, respectively [14]. In addition, Endo et al. [15] demonstrate that ficolins and mannose-binding lectin can interact with both fibrinogen and fibrin and that this interaction augments the lectin pathway of complement activation. This important observation supports the notion that a direct cross talk between the lectin complement pathway and the coagulation system may exist.

We hope that this thematic issue on ficolins will inspire you to further explore the biology of this blooming field.

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