The role of lectin-saccharide interactions in the evolution of cytokines

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Based on the assumption that invertebrates, like vertebrates, possess factors regulating responses to infection or wounding, studies dealing with the evolution of immunity have focused on the isolation and characterization of putative cytokine-related molecules from invertebrates. Until recently, most of our knowledge of cytokine- and cytokine receptor-like molecules in invertebrates relies on functional assays and similarities at the physico-chemical level. As such, a phylogenetic relationship between invertebrate cytokine-like molecules and vertebrate counterparts could not be convincingly demonstrated. Recent genomic sequence analyses of cytokine-related molecules suggest that invertebrate cytokine-like molecules and vertebrate factors do not have the same evolutionary origin. We propose instead that the convergence of function of invertebrate cytokine-like molecules and vertebrate counterparts involved in innate immune defenses may be based on similar lectin-like activities. Indeed, many cytokines possess lectin-like activity that may be essential for the expression of their full biological activities.

The invertebrate pattern-recognition protein named coelomic cytolytic factor (CCF) and the mammalian cytokine tumor necrosis factor (TNF) share functional analogies that are based on similar saccharide recognition specificity. In particular, CCF and TNF have been shown to interact with ion channels on the surface of vertebrate cells via *N*,*N*'-diacetylchitobioselectin-like activity. In the present study, we show that CCF-induced membrane depolarization results in the release of TNF, IL-6 and nitric oxide (NO) by macrophages via nuclear factor-κB signaling. Interestingly, our data suggest that TNF contributes, through lectin-saccharide interaction, to the secretion of IL-6 and NO induced by CCF. This experimental non-physiological setting based on the interaction of an invertebrate defense lectin with vertebrate cells involved in the innate immune response may have highlighted an evolutionarily ancient mechanism of macrophage activation in vertebrates.