Editors' Choice

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Macrophages: Past, Present and Future

In the last issue of the *Journal of Innate Immunity* for 2013, four papers appear that focus on macrophages, addressing different aspects of the roles of these cells in innate immunity. In the article by Grayfer and Robert [1], the importance of bone marrow-derived macrophages in *Xenopus laevis* is demonstrated. Previously, the subcapsular region of the liver was thought to be the major source of macrophages in this species. Geiser et al. [2] study the effect of γ-tocopherol on human airway macrophages, showing that this agent suppresses inflammatory responses in airway-derived macrophages from allergic asthmatics. The other two articles cover aspects of macrophage responses to stimulation with bacteria or viral products. To this end, the work by Braian et al. [3] with *Mycobacterium tuberculosis* shows that neutrophil-derived NETs evoke proinflammatory responses in macrophages. Khan et al. [4] show that the Nef protein of HIV-1 interacts with the core protein from hepatitis C virus (HCV) in the context of HIV/HCV co-infection. Both of these proteins signal through TRAFs that activate NF-kB and favour replication of HIV-1 in monocytes/macrophages. These articles offer the reader a glimpse of the enormous repertoire of one of the most important cell types involved our early defense against an invading pathogen.

Macrophages have always attracted a great deal of attention because of their key role in both health and disease [5]. The ubiquitous presence of macrophages in many biological tissues and fluids [6–11] infers a wide range of efficacy. The origin and differentiation cues for the subsets of monocytes, tissue macrophages and dendritic cells in mice, and the corresponding cell populations in humans, remain to a large extent unknown [12]. On the other hand, much information is available on other aspects such as the regulation of apoptotic processes by macrophages [13], their role in lymph nodes [9], chronic obstructive pulmonary disease [14] and other pulmonary inflammatory conditions [15] that have been studied extensively. There are also many other mechanisms that we are just beginning to understand. These include, for instance, the role of macrophages in iron homeostasis [16] and metabolic disease [17]. Though our knowledge has increased dramatically over the last decades, the question remains as to whether the findings can be translated into novel therapeutic approaches. New studies are promising. Moghimi et al. [18], for instance, propose an important role for macrophages in nanomedicine as a target for drug-release processes. There are also other potential implications, such as for tumor angiogenesis and atherosclerosis which are currently the subject of intense discussion [19, 20]. These reports are promising and they show that although macrophages were described for the first time by Élie Metchnikoff as long ago as the beginning of the 20th century [21], these cells are still far from being completely understood and have great potential as targets for novel therapeutic applications.

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