Monocytes and macrophages in chronic sarcoidosis pathology

To the Editor:

Kaiser *et al.* [1] make a compelling case for T-lymphocytes in the pathogenesis of sarcoidosis, particularly when considering the initiation of granulomatous inflammation and patients with acute, self-resolving sarcoidosis (Lofgren's syndrome). However, in some situations it seems that T-cells are less important. For example, SCID (severe combined immunodeficient) mice, which have no lymphocytes, develop macrophage-rich granulomas when infected with mycobacteria [2]. In clinical practice, powerful suppression of T-lymphocytes with anti-rejection medication cannot prevent recurrence of granulomas in one third of patients who have undergone lung transplantation for pulmonary sarcoidosis [3].

Visually, chronic sarcoid granulomas have a well-defined macrophage-rich core and a sparse peripheral ring of lymphocytes. Indeed, pathologists use the term "naked granulomas" to contrast macrophage-dominant sarcoid pathology with the lymphocyte-rich lesions of tuberculosis. Recently, animal models and studies in patients have highlighted the importance of macrophages and their bone-marrow derived precursors, blood monocytes, in chronic sarcoidosis pathology. Mice genetically engineered with overactive mTORC1 specifically in their myeloid cells spontaneously developed granulomas in the lungs and skin reminiscent of sarcoidosis, and mTORC1 activation in biopsies correlated with disease progression in sarcoidosis patients [4]. Several clinical studies have demonstrated heightened inflammatory responses in circulating blood monocytes from sarcoidosis patients [5–7].

In sarcoidosis it is likely that there is a complex interplay between adaptive and innate immunity, represented by T-lymphocytes and monocyte-derived macrophages. An important research focus going forward will be to identify the drivers of non-resolving and progressive sarcoidosis that lead to considerable morbidity, loss of quality of life, and economic hardship.

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