Background Sarcoïdosis is characterised by release of pro-inflammatory cytokines in affected tissues. Lung macrophages, derived from blood monocytes, are potent producers of tumour necrosis factor (TNF) and interleukin-6 (IL-6) which contribute to the formation of sarcoïd granulomata. Abnormalities of regulatory pathways that normally act to dampen inflammation could explain the hyper-active immunological state seen in sarcoïdosis. The aim of the study was to assess the role of regulatory receptors in modulating monocyte cytokine production in sarcoïdosis.

Methods Patients with sarcoïdosis and healthy controls were recruited. Whole blood cytokine release in response to stimuli was measured by ELISA. Expression of the regulatory molecules IL-10R, SIRP-α/β, CD47, CD200R, and CD200L was measured by flow cytometry, and functional activity was determined using blocking antibodies.

Results Patients with sarcoïdosis had less than half the number of T-lymphocytes in blood compared with healthy controls (p < 0.0001). Despite this, patients with sarcoïdosis produced higher concentrations of TNF and IL-6 from whole blood in response to stimulation with phytohaemagglutinin. Kinetic analysis of TNF was consistent with release from monocytes. Expression of the monocyte regulatory receptor CD200R in patients with sarcoïdosis showed a bimodal distribution (Figure 1), with 52.9% of patients having a CD200Rlow phenotype compared with 11.7% of healthy control subjects (p < 0.0001). CD200Rlow subjects produced more IL-6 in whole blood assays compared with CD200Rhigh subjects (p < 0.05). Experimental blockade of the CD200R axis increased pro-inflammatory cytokine responses, recapitulating the hyperactive monocyte phenotype seen in sarcoïdosis.

Conclusions Reduced expression of CD200R on monocytes may be a mechanism contributing to monocyte and macrophage hyper-activation in sarcoïdosis.