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CCL2 and CR2 are essential for the formation of osteclasts and foreign body giant cells

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Osteoclasts are multinucleated cells responsible for bone resorption. They are derived from the fusion of cells in the monocyte/macrophage lineage. Monocytes and macrophages can also fuse to form foreign body giant cells (FBGC). Foreign body giant cells are observed at the interface between a host and a foreign body such as implants during a foreign body reaction. Macrophages are attracted to the site of bone resorption and foreign body reactions by different cytokines. Chemokine (C-C) ligand-2 (CCL2) is an important chemotactic factor and binds to a receptor CCR2. In this study we investigated the importance of CCL2 and the receptor CCR2 in the formation of osteoclasts and FBGC. CCL2 mRNA was more highly expressed in giant cell culture than macrophages, being 9-fold and 16-fold more abundant in osteoclasts and FBGC respectively. Significantly fewer osteoclasts and FBGC were cultured from the bone marrow of CCL2 and CCR2 knockout mice, when compared to wild-type. Not only were the number of giant cells reduced but there was a significant reduction in the number of nuclei and the size of these cells in the cultures of CCL2 and CCR2 knockout mice. Formation of osteoclasts and FBGC were recovered in cultures by addition of exogenous CCL2 to the media containing marrow cells from CCL2-/- mice. We conclude that CCL2 and its receptor CCR2 are important for the formation of osteoclasts and FBGC and absence of these genes causes inhibition of osteoclast and FBGC formation.