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Macrophage Fusion into Multinucleated Giant Cells In Vitro

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Macrophage Fusion into Multinucleated Giant Cells *In Vitro*

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Multinucleated giant cells (MGC) have been observed in a variety of granulomatous conditions, including microbial infections (e.g., tuberculosis), foreign body reactions to implants (e.g., medical devices), foreign body reactions to inhaled particles (e.g., engineered nanomaterials), and disorders of unknown etiology (e.g., sarcoidosis). Generally, MGC are morphologically classified based on the number and arrangement of nuclei. The two major types of MGC are foreign body giant cells and Langhans giant cells. These MGC are formed by the fusion of macrophages, often in response to persistent, foreign microorganisms or materials. Although MGC are known to be associated with granulomas, their involvement in the development of these conditions has not been well described. This is in part due to a lack of well-characterized models of MGC populations. The objective of this study is to develop an *in vitro* model of macrophage fusion in order to study MGC function. Previous reports have shown that MGC formation is induced by interleukin-4 (IL-4). Therefore, we investigated a model of IL-4-induced fusion in murine bone marrow-derived macrophages (BMdM). As expected, IL-4 treatment resulted in increased percent fusion of BMdM. The formation of MGC was optimized by modification of culture conditions, including alteration of the growth surface and treatment with either macrophage colony-stimulating factor (M-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF). Ongoing studies involve identification of molecules that regulate MGC formation. An increased understanding of this mechanism will provide additional targets to control fusion. Further development of this controlled *in vitro* model will facilitate future investigation of MGC inflammatory activity and contribution to pathogenesis of granulomas.