1.08 High levels of human Macrophage migration inhibitory factor (MIF) potentiate Mesenchymal stromal cell (MSC) efficacy in a murine model of allergic asthma

Ian Hawthorne[1], Hazel Dunbar[1], Seamas Donnelly[2], Karen English[1]

[1]Kathleen Lonsdale Institute for Human Health Research, Department of Biology, Maynooth University, Co. Kildare, Ireland. [2]Department of Medicine, Trinity College Dublin and Tallaght Hospital, Co. Dublin, Ireland.

Human mesenchymal stromal cells (MSCs) rely on specific inflammatory disease microenvironments in order to carry out their anti-inflammatory actions *in vivo*. One of the barriers to the success of MSC therapy is the inability to identify potential responders. Macrophage migration inhibitory factor (MIF) has been identified to play a pivotal role in the pathogenesis of several inflammatory disorders including asthma. Our previous work has demonstrated a dominant role of MIF allelic variants through the use of humanised mice with either high- ($CATT_7$) or low- ($CATT_5$) expressing MIF promoter polymorphisms with the high expressing $CATT_7$ mice exhibiting a more severe asthma phenotype. In this study we sought to investigate the efficacy of MSCs in high vs low hMIF environments using humanised mice in a house dust mite (HDM) model of allergic asthma. Intravenously infused human bone marrow-derived MSCs significantly attenuated airway inflammation in high MIF expressing $CATT_7$ mice by reducing the number of eosinophils and levels of IL-4, IL-5, and IL-13 in the bronchoalveolar lavage (BAL) fluid. MSCs also had a significant effect on airway remodelling in the $CATT_7$ mice with reduced subepithelial collagen deposition and goblet cell hyperplasia. Little to no effects of MSC administration were observed in the low MIF expressing mice or wildtype controls. Differences in efficacy correlated with retention as MSCs appear to be retained longer in the lungs of $CATT_7$ mice compared to $CATT_5$ or wildtypes. These data contributes to a broader understanding on how disease microenvironments can affect MSC therapeutic efficacy and identifies MIF as a potential biomarker for MSC success.

Conflict of Interest: The authors declare that they have no conflict of interest.