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Effects of cytokines on the function of monocytes/macrophages in a model of graft versus host disease

cute graft versus host disease (aGVHD) is a severe complication of hematopoietic stem cell transplantation, and the most common cause of mortality and morbidity post-transplant. The studies of aGVHD often rely on humanized mouse models, which provide limited insight into the pathology mechanisms. This highlights the need for developing the in vitro model of aGVHD based on using human cells and whole blood to study functional potential of human monocytes/macrophages in allogeneic reaction. It is widely accepted that monocytes differentiate into macrophages based on the microenvironment cytokine such as interferon-gamma (IFN-y) activate classical M1 macrophages type that promotes inflammatory functions, whereas interleukin-4 (IL-4) activate the alternative M2 macrophages with tissue repair functions. This study proposes to generate inflammatory setting, which mimics patient's condition after total body irradiation, then to add mismatched blood cells to trigger immunological response similar to aGVHD. The cytokines IFN-y and IL-4 were used to allow monocytes to differentiate towards M1 or M2 macrophages. This study assessed the variation in CD86 and HLA-DR expression on the surface of responder/donor monocytes and T cells proliferation by flow cytometer. Furthermore, pro-inflammatory cytokines were measured by ELISA. The results show that both IFN- γ and IL-4 up-regulate the expression of CD86 and HLA-DR on the surface of classical CD14+ monocytes, and both cytokines allow T cells proliferation. Indeed, this indicates that in aGVHD environment monocytes/macrophages might be able to up-regulate co-stimulatory molecules and activate T cells in the presence of IL-4 cytokine despite its reported role in resolving inflammation.

Biography

Deema Kamal Sabir has completed her MSc degree in Hematology with distinction from the University of Westminster in 2016 and currently, is pursuing her Mphil/PhD at the same University.

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