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Effects of GM-CSF, IFN-γ and IL-4 on the function of monocytes/macrophages in a model of graft versus host disease

Deema K Sabir
University of Westminster, UK

Acute graft versus host disease (aGVHD) is a lethal complication which limited the success of Haematopoietic Stem Cell Transplantation (HSCT). This study develops 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 monocyte differentiate into macrophages based on the differential microenvironment the growth factor granulocyte monocyte colony stimulating factor (GM-CSF) and cytokine such as Interferon-gamma (IFN-γ) will polarise monocytes into classical M1 type that promotes inflammation, whereas Interleukin-4 (IL-4) will polarise monocytes towards 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 allogenic response similar to aGVHD. GM-CSF and cytokines IFN-γ and IL-4 were used to allow monocytes to differentiate towards M1 or M2 macrophages.This study assessed the variation in Co-stimulatory molecules (CD80, 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 enzyme-linked immunosorbent assay (ELISA). The results show that GM-CSF, IFN-γ and IL-4 up-regulate the expression of CD86 on the surface of classical CD14+ monocytes in similar level. However, HLA-DR expression varied based on the stimulus. Unexpectedly, the effects GM-CSF and IFN-γ expression of co-stimulatory molecule CD86 on CD14+ monocytes are particularly weak comparing to the allogenic reaction untreated control. Indeed, T cell response in GVHD setting is confirmed by T cells proliferation measurements using crystal field stabilisation energy (CFSE) method, which shows the same level of response in the presence of IL-4, as that seen with the high dose of GM-CSF and IFN-γ. This implies that generally accepted views on distinct roles of M1 and M2 macrophages in inflammation need to be re-evaluated in the complex setting of aGVHD pathology.

Biography

Deema was awarded MSc in heamatology with distinction from the University of Westminster in 2016 and currently studies for Mphil/PhD at the same University. Princess Nourah bint Abdulrahman University, Riyadh Sasudi Arabia University of Westminster, London, UK

Deema_sabir@hotmail.com

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