The role of pattern-recognition receptors in graft-versus-host disease and graft-versus-leukemia after allogeneic stem cell transplantation.

Abstract:
Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only treatment with curative potential for certain aggressive hematopoietic malignancies. Its success is limited by acute graft-versus-host disease (GVHD), a life-threatening complication that occurs when allo-reactive donor T cells attack recipient organs. There is growing evidence that microbes and innate pattern-recognition receptors (PRRs) such as toll-like receptors (TLR) and nod-like receptors (NLR) are critically involved in the pathogenesis of acute GVHD. Currently, a widely accepted model postulates that intensive chemotherapy and/or total-body irradiation during pre-transplant conditioning results in tissue damage and a loss of epithelial barrier function. Subsequent translocation of bacterial components as well as release of endogenous danger molecules stimulate PRRs of host antigen-presenting cells to trigger the production of pro-inflammatory cytokines (cytokine storm) that modulate T cell allo-reactivity against host tissues, but eventually also the beneficial graft-versus-leukemia (GVL) effect. Given the limitations of existing immunosuppressive therapies, a better understanding of the molecular mechanisms that govern GVHD versus GVL is urgently needed. This may ultimately allow to design modulators, which protect from GvHD but preserve donor T-cell attack on
hematologic malignancies. Here, we will briefly summarize current knowledge about the role of innate immunity in the pathogenesis of GVHD and GVL following allo-HSCT.

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