World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:9, No:09, 2015

The Involvement of the Homing Receptors CCR7 and CD62L in the Pathogenesis of Graft-Versus-Host Disease

Authors : Federico Herrera, Valle Gomez García de Soria, Itxaso Portero Sainz, Carlos Fernández Arandojo, Mercedes Royg, Ana Marcos Jimenez, Anna Kreutzman, Cecilia MuñozCalleja

Abstract : Introduction: Graft-versus-host disease (GVHD) still remains the major complication associated with allogeneic stem cell transplantation (SCT). The pathogenesis involves migration of donor naïve T-cells into recipient secondary lymphoid organs. Two molecules are important in this process: CD62L and CCR7, which are characteristically expressed in naïve/central memory T-cells. With this background, we aimed to study the influence of CCR7 and CD62L on donor lymphocytes in the development and severity of GVHD. Material and methods: This single center study included 98 donor-recipient pairs. Samples were collected prospectively from the apheresis product and phenotyped by flow cytometry. CCR7 and CD62L expression in CD4+ and CD8+ T-cells were compared between patients who developed acute (n=40) or chronic GVHD (n=33) and those who did not (n=38). Results: The patients who developed acute GVHD were transplanted with a higher percentage of CCR7+CD4+ T-cells (p = 0.05) compared to the no GVHD group. These results were confirmed when these patients were divided in degrees according to the severity of the disease; the more severe disease, the higher percentage of CCR7+CD4+ T-cells. Conversely, chronic GVHD patients received a higher percentage of CCR7+CD8+ T-cells (p=0.02) in comparison to those who did not develop the complication. These data were also confirmed when patients were subdivided in degrees of the disease severity. A multivariable analysis confirmed that percentage of CCR7+CD4+ T-cells is a predictive factor of acute GVHD whereas the percentage of CCR7+CD8+ T-cells is a predictive factor of chronic GVHD. In vitro functional assays (migration and activation assays) supported the idea of CCR7+ T-cells were involved in the development of GVHD. As low levels of CD62L expression were detected in all apheresis products, we tested the hypothesis that CD62L was shed during apheresis procedure. Comparing CD62L surface levels in T-cells from the same donor immediately before collecting the apheresis product, and the final apheresis product we found that this process down-regulated CD62L in both CD4+ and CD8+ T cells (p=0.008). Interestingly, when CD62L levels were analysed in days 30 or 60 after engraftment, they recovered to baseline (p=0.008). However, to investigate the relation between CD62L expression and the development of GVHD in the recipient samples after the engraftment, no differences were observed comparing patients with GVHD to those who did not develop the disease. Discussion: Our prospective study indicates that the CCR7+ T-cells from the donor, which include naïve and central memory T-cells, contain the alloreactive cells with a high ability to mediate GVHD (in the case of both migration and activation). Therefore we suggest that the proportion and functional properties of CCR7+CD4+ and CCR7+CD8+ T-cells in the apheresis could act as a predictive biomarker to both acute and chronic GVHD respectively. Importantly, our study precludes that CD62L is lost in the apheresis and therefore it is not a reliable biomarker for the development of GVHD.

Keywords : CCR7, CD62L, GVHD, SCT
Conference Title : ICI 2015 : International Conference on Immunology
Conference Location : London, United Kingdom
Conference Dates : September 25-26, 2015