ImmunoTools *special* Award 2015

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Study of B cell subsets in lung transplant recipients and involvement in humoral rejection

Patients on waiting list for lung transplantation have a chronic failure of lung function. Among them, the patients with chronic obstructive pulmonary disease have a high incidence of moderate hypogammaglobulinemia (serum IgG <700 mg/dL). However, after lung transplantation this situation worsens dramatically due mainly to immunosuppressive therapy with glucocorticoids, mycophenolic acid and calcineurin inhibitors (1,2). The immunodeficiency secondary to immunosuppressants causes an increased risk of infections by opportunistic pathogens and has been shown as an independent risk factor for rejection of acute and chronic lung graft graft loss after the development of bronchiolitis obliterans (BOS) (1,2). Therefore, the pretransplant immune status seems critical to lung graft survival in the long-term.

In addition, regardless of the underlying lung disease, our group has found a link between increased immature B lymphocyte subpopulations before lung transplantation and subsequent development of infections (3), confirming that there might be a deficiency in the maturation of B cells in these patients associated with low levels of IgG. The study of B cell subpopulations before lung transplantation could identify patients with risk of infection but also at risk of humoral acute rejection and subsequent graft failure. Moreover, the monitoring of B cell subpopulations early after lung transplantation could be useful to detect ongoing humoral alloresponses. We use CD19 and CD20 markers to identify B-lymphocytes, CD5, CD10 CD24 for immature B cells, CD25 and CD27 for memory B cells, CD38 and CD138 for plasma cells. Some of these markers could be quantified using proper isotype-controls. Nevertheless, currently no detailed studies of B cell subpopulations (LB) in lung transplant patients have been performed.

Thus, flow cytometry is basic to assess a detailed B cell subpopulations study, and the reason why ImmunoTools antibodies would be very helpful to carry out our project.

On the other hand, not only immunophenotyping but also the study of survival factors involved in proliferation and differentiation of B cells could be useful to define their role in humoral alloresponses. The most studied is B-cell activating factor (BAFF), and we can perform functional studies adding BAFF to previously isolated B cells from the patients and measure how they respond to the survival factor by means of Carboxyfluorescein succinimidyl ester (CFSE) staining and measurement of proliferation rates and cell death after anexin-V staining.

The diagnosis of humoral rejection in lung transplant recipients is based in immunopathological (C4d deposition on biopsy), histopathological (presence of capillaritis) and serological (donor-specific anti-HLA antibodies development) criteria (4-6). Although not all of these criteria are present in biopsies hindering their diagnosis (7,8) and such criteria are present in the context of another type of rejection (9), demonstrating the complexity of the mechanism of humoral rejection. Our work is expected to increase the knowledge of the humoral rejection entity and indentify patients at risk of humoral rejection after lung transplantation.

References

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