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TNF- α and Its Importance in Transplantation

Humberto Bohorquez¹, and Ari J Cohen^{1,2*}

¹Laboratory of Transplant Research, Institute of Translational Research, USA

²Multi-Organ Transplant Center, Ochsner Health System, 1514 Jefferson Highway, New Orleans, LA 70121, USA

Dear Editor

Orthotopic liver transplantation (OLT) is the treatment for end stage liver disease with 1-year and 5-year national patient survival rates of 89% and 80%, respectively. The number of potential recipients on the national waiting list far surpasses the number of healthy organs available per year for transplantation. The options for increasing the donor pool includes live donors, split livers, and marginal livers. Examples of marginal liver donors are livers from older donors, donors with significant macrosteatosis and donors with anticipated long cold ischemia times. Transplantation of marginal livers is a known risk factor for the development of primary non-function after liver transplantation. Primary non-function is a common cause for re-transplantation and death early after OLT. Optimization of marginal liver grafts would expand their utilization without increasing the perioperative morbidity and mortality. Although the precise cause of primary non-function is not known, ischemia/reperfusion (I/R) injury has been strongly implicated.

Hepatic I/R injury is a multifactorial event involving immunological responses such as cytokine and chemokine cascades, the complement system, and inflammation as well as other physiological pathways. The cytokine tumor necrosis factor- α (TNF- α) plays a critical role in both the physiologic defensive response and the pathogenesis of ischemia/reperfusion (I/R) injury in liver tissue. TNF- α , a potent mediator of inflammation, is a soluble cytokine primarily produced by activated monocytes, macrophages, and T-lymphocytes. During ischemia, TNF- α levels peak during the early phase at 30 minutes to 2 hours after reperfusion due to increased production of reactive oxygen species. The subsequent infiltration of innate immune cells to the liver results in additional TNF- α production, 6-48 hours after reperfusion. Data from experimental models of I/R injury in which TNF- α is blocked or decreased suggest a potential clinical benefit. Thus, we observed TNF- α plays major role in Orthotopic liver transplantation.

***Corresponding author:** Ari J. Cohen, Laboratory of Transplant Research, Institute of Translational Research, Ochsner Health System, 1514 Jefferson Highway, New Orleans, LA 70121, USA, E-mail: aricohenj@yahoo.com

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