Role of CD44 in Immune Functions and Endothelial Cell Injury

By

Asimah Rafi-Janajreh

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APPROVED:

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Prakash S. Nagarkatti, Chairman

_____	_____
Mitzi Nagarkatti	Gerhardt Schurig
_____	_____
G. William Claus	D.P. Sponenberg

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Asimah Rafi-Janajreh

Dr. Prakash S. Nagarkatti, Chairman

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(Abstract)

In addition to the antigen-specific receptors, the T and B cells also express a variety of adhesion molecules, which are known to participate in cell-cell interaction, migration, homing and signal transduction. CD44 is a widely distributed cell surface glycoprotein whose principal ligand has been identified as hyaluronic acid (HA), a major component of the extracellular matrix. In the current study, we investigated whether HA or mAbs against CD44 would induce a proliferative response in mouse lymphocytes. Spleen cells from normal and nude but not severe combined immunodeficient mice, exhibited strong proliferative responsiveness to stimulation with soluble HA or anti-CD44 mAbs. Furthermore, purified B cells but not T cells were found to respond to HA. These data demonstrated that interaction between HA and CD44 can regulate murine B cell effector functions and that such interactions may play a critical role during normal or autoimmune responsiveness of B cells.

Endothelial cell injury resulting in vascular leak syndrome (VLS) is one of the most widely noted phenomenons in a variety of clinical diseases, however, the underlying reason for which remains unclear. We used interleukin-2 induced VLS as a model to investigate the role of cytolytic lymphocytes in the direct cytotoxicity of endothelial cells. BL/6 wild-type mice developed significant VLS in the lungs, liver and spleen following IL-2 administration. Interestingly, perforin-knockout mice exhibited marked decrease in VLS in all three organs tested. Also, FasL-defective (*gld*) mice and Fas-deficient (*lpr*) mice exhibited

decreased VLS in the liver and spleen, but not in the lungs. These results demonstrated for the first time that perforin and FasL may actively participate in endothelial cell injury and induction of VLS in a variety of organs.

Inasmuch as, CD44 also plays a major role in the lymphocyte adhesion to the endothelial cells, we used CD44-knockout mice and observed that such mice exhibited markedly diminished VLS following IL-2-treatment. Our data also suggested that blocking CD44 helps in reducing the IL-2-induced VLS and therefore such an approach may serve as a useful tool to prevent endothelial cell damage seen in a variety of clinical disorders.