Differential gene expression in the thymus to establish low toxicity chemotherapeutic agents

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Thymic recovery can be a rate limiting process in full immunological recovery following chemotherapy. Emerging literature suggests that thymic insufficiency may have significant clinical consequences, exacerbating graft-versus-host disease and compromising the graft-versus-leukemia effect. Data have demonstrated that the thymus is damaged following current transplant preparative regimen, with a disproportionate depletion of UEA+ thymic epithelial cells (TEC). Very little is known about the effects of the individual components of such preparative agents. We have established an array of 25 murine genes expressed throughout the thymus, including UEA+ TEC, Ly51+ TEC and all thymocytes. Using quantitative PCR, we were able to use expression levels from this panel of genes to monitor the effects of chemotherapeutic agents on the thymus. To establish feasibility of this model, we first studied the effect of cyclophosphamide, a common agent in many chemotherapeutic regimens. Using a dose of 120 mg/kg x 2, we found significant changes (p<0.05) in 11 of 23 genes in the TEC populations (2 up and 9 down), as well as, 11 genes in the thymocyte population (11 down). Our data suggests that our current panel of thymic expression genes is capable of detecting changes after treatment with potential thymus altering agents.

Biography

Philip J Lucas received his PhD from The George Washington University, Washington, DC in 1991 in Immunology and Molecular Biology and completed his Postdoctoral studies with the Howard Hughes Medical Institute at Washington University School of Medicine in St. Louis, MO. He is currently a Staff Scientist in the Experimental Immunology and Transplantation Branch, NCI, NIH where he studies the effects of stem cell transplantation on thymus.

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