The graft versus host reaction in mice was used to test the hypothesis that chronic stimulation of lymphocytes can lead to the development of malignant lymphoma. Long-term survivors of the reaction developed lymphomas that appeared to arise from lymphocytes of the recipients. [The SCF indicates that this paper has been cited in over 255 publications since 1965.]

Robert S. Schwartz
Division of Hematology-Oncology
New England Medical Center Hospital
Tufts University School of Medicine
Boston, MA 02111

December 8, 1982

"My interest in immunological diseases began in 1953 when, as a New York University medical student working in Bellevue Hospital, I witnessed the dramatic response to cortisone of a woman with lupus erythematosus. Long-term survivors of the disease caused by systemic lupus erythematosus Four years later, while a medical resident at the Yale-New Haven Hospital, I heard a remarkable lecture on autoimmunity by William Dameshek. That experience made up my mind about future training, and in 1957 I went to Boston to study hematology under his direction at the New England Medical Center. The idea that autoimmunity even existed was at that time hotly contested by numerous 'authorities.' Dameshek's conviction was based principally on his own clinical observations, especially in cases of lupus erythematosus. He maintained that the immune system into a normal animal. This hypothesis was tested in mice by injecting parental strain spleen cells into F1 hybrid animals. The recipients of the spleen cells developed not only immunohemolytic anemia, but also thrombocytopenia. The graft versus host reaction in mice was used to test this hypothesis because it provided a means to induce chronic in vivo stimulation of lymphocytes. The injection of C57B1/6 splenocytes into (C57B1/6 x DBA/2)F1 mice caused malignant lymphomas in about 50 percent of the recipients, whereas none appeared in control mice. An interesting aspect of the results was that the lymphomas arose from lymphocytes of the recipients, and not from those of the donor. Thus, the mechanism really seemed to involve the proliferation of autologous lymphocytes."

"I think this work on the mouse has been highly cited because it explains some important aspects of the pathogenesis of human lymphomas. In Burkitt's lymphoma, for example, the Epstein-Barr virus seems to instigate a polyclonal proliferation of lymphocytes that terminates as a monoclonal neoplasm. Moreover, recent experiments suggest that retroviruses may act either by providing a sustained antigenic stimulus or by causing the production of mitogenic factors by the T lymphocytes they infect. Finally, a gratifying aspect of this work has been its innovative extension by my former postdoctoral fellow, Ernst Gleichmann."

6. van Rappard-van der Veen F M, Rolink A G & Gleichmann E. Diseases caused by reactions of T lymphocytes towards incompatible structures of the major histocompatibility complex. VI. Autoantibodies characteristic of systemic lupus erythematosus induced by abnormal T-B cell cooperation across I-E.