

CALIFORNIA STATE SCIENCE FAIR 2003 PROJECT SUMMARY

Name(s)

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Project Number

S1417

Project Title

Comparing Effects of 3 Non-Myeloablative Conditioning Regimens for Bone Marrow Transplantation on Mice w/ Bcell Lymphoma

Objectives/Goals

Abstract

Allogeneic bone marrow transplantation (BMT) can cure patients with hematological diseases who are not curable by other treatments. Non-myeloablative conditioning before allogeneic BMT aims to decrease toxicity for the recipient and leads to the coexistence of host and donor blood cells. Non-myeloablative BMT is generally performed with additional cellular treatment (adoptive immunotransfer). Because little is known about the effects of non-myeloablative BMT on tumor reduction, we investigated three conditioning regimens in mice with BCL1 lymphoma. This study was designed to determine which conditioning regimen would be most suitable for use in future adoptive immunotransfer experiments.

Methods/Materials

Balb/c mice were inoculated with BCL1-gfp/luc tumor cells one week prior to conditioning. Three non-myeloablative conditioning regimens were used (aCD40L/TBI, TLI/ATS, Flu/TBI/Cy), followed by allogeneic BMT from C57BL/6 donor mice. Experiments determined the effects these regimens had on weight loss, tumor reduction, chimerism and survival. Tumor burden was assessed by bioluminescence (quantifying light emission from luciferase transfected tumor cells). Chimerism was measured by FACS.

Results

All conditioning regimens were able to achieve mixed chimerism. While in the Flu/TBI/Cy and TLI/ATS groups achieved 30% mixed chimerism 2 weeks after BMT, the animals treated with aCD40L/TBI regimen needed 4 weeks to achieve similar levels of mixed chimerism. Engraftment with mixed chimerism was stable in the TLI/ATS and aCD40L/TBI groups (> 180 days), while mixed chimerism was lost in the Flu/TBI/Cy group after 7 weeks. The Flu/TBI/Cy regimen was most effective in inducing a long lasting remission. Animals treated with TLI/ATS relapsed immediately after BMT. aCD40L/TBI treated animals experienced no disease relief. All mice treated with Flu/TBI/Cy survived throughout the observation period while BCL1 controls did not.

Conclusions/Discussion

Non-myeloablative conditioning regimens are expected to induce low toxicity with regard to weight loss, achieve mixed chimerism and have little impact on tumor reduction. The three non-myeloablative conditioning regimens yielded surprisingly different effects on weight loss, tumor reduction, chimerism and survival. Because of these differences, further studies will be performed with each of these regimens to see if they also affect the outcome of additional cellular treatment.

Summary Statement

This study compared the effects of three different kinds of a special low-toxicity preparatory procedure for allogeneic bone marrow transplantation in a murine tumor model using bioluminescence imaging.

Help Received

used lab equipment at Stanford University under the supervision of Dr. Schimmelpfennig