Tumor Cell Biology Laboratory

Shantaram S. Joshi, Ph.D.

Functional Genomics of Leukemia
Dendritic Cell Based Therapy for Cancer

Dept. of Genetics, Cell Biology and Anatomy
University of Nebraska Medical Center
Omaha, Nebraska 68198-6395
Phone: 402-559-4165/4560, Fax: 402-559-7328, Email:ssjoshi@unmc.edu
Research Summary

Overall Goals: The long-term goal of this laboratory is to improve therapy for human B lymphocyte malignancies. Where feasible, to apply the same approach to other malignancies, such as breast cancer and also cancers of the nervous system. This is a translational research laboratory as described below.

Project I: Improved Therapy for Chronic Lymphocytic Leukemia (CLL): Gene Targeting Approach using Functional Genomics

CLL is a common leukemia of the older population in Western countries. Resistance to therapy due to alterations in apoptosis is a major problem in clinical management of CLL. Using DNA microarray analysis, the differentially expressed genes in therapy resistant CLL cells from patients, are being identified. Selected differentially expressed genes were targeted to revert their altered expression which resulted in making resistant CLL cells significantly more susceptible to therapy.

Collaborators: Collaborators in this study are Drs. Phillip Bierman, M.D. Greg Bociek, M.D. John (Wing) Chan, M.D., Steve Pavletic, M.D.; and James Lynch, Ph.D.

Potential Impact: This is truly a translational research project where patient cells are analyzed to improve the therapy for CLL. One of the differentially expressed genes, Bcl-2, identified by us and others is being targeted in a multi center Phase II Clinical trial including UNMC sponsored by Genta Inc and NCI. Several candidate genes for targeting are being reviewed.
Project II: Use of Umbilical Cord Blood (UCBC) for Cellular Therapy Against Cancer:

We have shown that human umbilical cord blood contain precursors of both antigen non-specific and antigen specific cytotoxic effector cells against leukemia/lymphoma and breast cancer. IL-2 activated killer cells and Her2/neu specific CTLs showed a significant antitumor cytotoxicity in vitro and in vivo against human leukemia/lymphoma and breast cancer.

Collaborators: Drs. Anne Kessinger, M.D., Charles Kuszunski, Ph.D., Samuel Pirruccello, M.D., and Stefano Tarantolo, M.D.

Potential Impact: This is another translational research project in which the laboratory results have lead to patient treatment. Both in animal models and in patient we have shown the therapeutic effects of UCBC. A Phase I/II clinical trial is being planned by Drs. Tarantolo and Haupke.

Legend: A: Cord Blood Derived DC Ultrastructure; B: Antigen presentation by DC to T Lymphocytes

Project III: Dendritic Cell Based Therapy for Mantle Cell Lymphoma and Other Cancers.

The main objective of this project is to stimulate DCs to initiate antitumor response using two different approaches. In one approach DCs derived from human peripheral blood or umbilical cord blood mononuclear cells will be primed with tumor specific antigens such as Her2/neu and N-Myc. Such antigen primed DCs are being used to generate CTLs against specific tumor cells. In the second approach, which is being done for mantle cell lymphoma (MCL), DCs will be generated from mononuclear cells from MCL patients and fused with autologous lymphoma cells. Such DC-MCL hybrids will then be used as vaccine against Mantle Cell Lymphoma.

Collaborators: Drs. Anne Kessinger, M.D., Stefano Tarantolo, M.D.; and Julie Vose, M.D.

Potential Impact: If successful in preclinical studies, this translational research will be used in a clinical setting to treat mantle cell lymphoma patients.
Funding Sources

1) Elsa U. Pardee Foundation, Midland MI; 2) I Berlex Laboratories, Richmond, CA ; 3) Susan G. Komen Foundation, Dallas, TX; 4) Nebraska State Department of Health, LB506 Funds, Lincoln, NE and 5) National Institutes of Health, Bethesda, MD.

Publications from


Joshi SS, Kuszynski CA, Benner EJ, Bagchi M, Bagchi D. Chemopreventive effects of grape seed proanthocyanidin extract on Chang liver cells. Toxicology 155: 83-90, 2000


Cluster analysis of CLL DNA Microarray Results