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November 14, 1996

Philip Migliore, M.D.
Research Director
Moran Foundation
Department of Paholgy

Dear Dr. Migliore

I wish to take this opportunity to thank the Moran Foundation for the funding provided for my research entitled "Molecular detection of Breast Cancer Cell In Stem Cell Isolates of Breast Cancer Patients". Please find enclosed a copy of the progress report of the above research.

Sincerely

Sri Rajagopalan, Ph.D.
Dept.of Pathology

KAJA GOPALAN
BAYLOR COLL OF MED
HOUSTON TX

## 2nd Annual Scientific Meeting of the American Society for Blood and Marrow Transplantation

### Joint Special Conference with the American Association for Cancer Research

# *Novel Approaches in Blood and Marrow Transplantation*

*Jointly Sponsored by the College of Physicians & Surgeons of Columbia University*

*ASBMT and AACR gratefully acknowledge Sandoz Oncology and SyStemix, Inc., who have provided generous unrestricted educational grants for this meeting.*

Hotel del Coronado • San Diego, CA • October 2-6, 1996

MOLECULAR DETECTION OF BREAST CANCER CELLS IN STEM CELL HARVESTS OF BREAST CANCER PATIENTS. S. Rajagopalan, P. Li, D. Witte, R. Iyer, P.L. McCarthy, Jr., C.O. Freytes, D.H. Yawn, R.E. Champlin, G.R. Lynch and C.M. Leveque. Baylor College of Medicine and The Methodist Hospital, UT M.D. Anderson Cancer Center, Houston, Texas and A.L. Murphy Memorial Veterans Administration Hospital, San Antonio, Texas.

The frequency and the clinical significance of the presence of breast cancer cells in hematopoietic stem cells of breast cancer patients remains unknown. By employing polymerase chain reaction (PCR) technique to detect kerain-19 mRNA as a marker for breast cancer cells, samples of peripheral blood stem cell (PBSC) harvests of patients undergoing high dose chemotherapy and autologous stem cell support for breast cancer at three different centers were screened. Allele specific oligonucleotide (ASO) hybridization of the PCR product with digoxygenin-11 UTP labeled probe specific for keratin-19 functional gene sequences yielded sensitivity of detection of one breast cancer cell admixed with $10^6$ lymphocytes. Eighteen out of eighty (18/80, 22%) patient's stem cell isolates were found to contain breast cancer cells. This finding combined with the fact that most patients who are treated with high dose chemotherapy and autologous stem cell support have advanced metastatic breast cancer with involvement of bone marrow indicates the possibility of frequent occurrence of malignant cell reinfusion post chemotherapy.

**Progress Report on the project entitled " Molecular Detection of Breast Cancer Cells in Hematopoietic Progenitor Cell Isolates of Breast Cancer Patients: Implications on Therapy " :**

Utilising the funds provided by the Moran Foundation for supply and reagents a robust molecular assay for the detection of breast cancer cells in stem cell isolates of breast cancer patients has been developed. This assay is capable of detecting breast cancer cell with the sensitivity of detection of one cancer cell present in a population of ten million leukocytes. When this assay is used for routine screening of stem cells of breast cancer patients, it is anticipated that the information would aid in answering an important question of whether such cancer cells lead to disease relapse in patients undergoing high dose chemotherapy with hematopoietic salvage by stem cell autotransplantation.

By employing this test nearly 100 stem cell preparations of breast cancer patients undergoing therapy at The Methodist Hospital, Houston, M.D.Anderson Cancer Center, Houston and Audie L. Murphy Veterans Hospital, San Antonio have been screened. Efforts are underway to determine the clinical significance of the presence of cancer cells in some of the stem cell preparations analysed. Part of the information was presented at the American Society for Blood and Bone Marrow Transplantation held at San Diego on Oct 5-9, 1996( Copy of the abstract enclosed). A manuscript for submission to a peer reviewed journal is in preparation. We have also obtained $ 45,000 from the Methodist Hospital Foundation to continue this research through June 1997.