



**SARCOMA FOUNDATION OF AMERICA
FINAL REPORT**

Project Title: Sarcoma cell line resource with molecular
and kinase annotation

Project Number: SFA04-Q

1. Date project was initiated: 4/1/2004
2. Period covered by this report: From 4/1/04 To 6/30/06
3. Publications, Abstracts, and Presentations:
 - a. List all manuscripts submitted for publication during the period covered by this report resulting from this project. Include those in the categories of lay press, peer-reviewed scientific journals, invited articles, and abstracts. Each entry must include the author(s), article title, journal [book, editors(s), publisher, volume number, page number(s), and date.]
 - (1) Lay Press: N/A
 - (2) Peer-Reviewed Scientific Journals: van de Rijn M and Fletcher JA. Genetics of Soft tissue Tumors, Annu Rev Pathol 2006; 1: 435-66.
 - (3) Invited Articles: N/A
 - (4) Abstracts: N/A
 - b. List presentations made during the last year (international, national, local societies, etc.). Use an asterisk (*) if presentation produced a manuscript.

This work was presented at the Annual Sarcoma Foundation of America Educational Conference, New York City, NY, May, 2008
4. Provide a brief list of keywords: (limit to 20 words): sarcoma, cell lines, microarray

5. Summarize the progress during the period of this report and its impact on your plans for the remainder of the project. Include a summary of the progress toward the achievement of the originally stated aims and list the significant results:

The aim of the research was to create a molecular cytogenetic profile for each of 30 sarcoma cell lines, and to validate that the lines were faithful biologically to the sarcomas from which they were originally established. This was accomplished for cell lines relating to liposarcoma and GIST.

Next genomic profiles were determined that indicated that liposarcoma exhibited massive MDM2 signal amplification. Importantly, subsequent MDM2 inhibition lead to a large decrease in sarcoma cell proliferation. Profiles of GIST showed KIT activation and signaling, and that the HSP90 inhibitor 17-AAG caused GIST apoptosis (cell death) via KIT oncoprotein degradation.

6. In layperson's terms, summarize the progress during the period of this report. Explain any medical significance or implications of your results to date:

We managed to produce sarcoma cell lines that mimicked the human disease. To date focus has been on liposarcoma as well as GIST. Using these cell lines, we have found targets of opportunity that might be sensitive to various drugs. These "druggable" targets and in vitro data on sensitivity of the lines to potential therapeutic compounds have been communicated to the medical community. This information will hopefully be met with a response by pharmaceutical companies who have similar drugs under development that attack these targets.

Principal Investigator (signature)

Date

Department Chair (signature)

Date