



SARCOMA FOUNDATION OF AMERICA
FINAL REPORT

Project Title: Cancer stem cells and sarcoma

Project Number: SFA06-BY

1. Date project was initiated: June 2006
2. Period covered by this report: From 6-1-6 To 5-31-08
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:

(2) Peer-Reviewed Scientific Journals:

Kuscuoglu U, Tataria M, Akhavan B, Fuerer C, Ailles L, Weissman I, Nusse R, Sylvester KG. Canonical Wnt signaling identifies a subset of sarcoma initiating cells from a mixed mesenchymal population. (in preparation)

(3) Invited Articles:

(4) Abstracts:

Tataria M, Quarto N, **Sylvester KG**. Mesenchymal stem cells from two distinct compartments have enhanced osteogenesis in response to a p53 tumor suppressor mutation. American Pediatric Surgical Association- 37th Annual Meeting. Hilton Head, SC., May 21-24, 2006

Tataria M, Kuscuoglu U, Ailles L, Cheshier S, Nusse R, Weissman I, **Sylvester KG**. Highly Enriched Mesenchymal Stem Cells (MSC) can initiate Sarcoma Formation *in vivo*. American College of Surgeons – Surgical Forum, Chicago, IL., October 9, 2006

- b. List presentations made during the last year (international, national, local societies, etc.). Use an asterisk (*) if presentation produced a manuscript.
4. Provide a brief list of keywords: (limit to 20 words) **mesenchymal cell, osteosarcoma, Wnt signaling, β -catenin, stem cell, tumor initiation**
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: We have found that mixed populations of primary culture mouse mesenchymal cells could be fractionated based upon a functional response to exogenous Wnt protein. A lentiviral reporter was used to enrich for Wnt responsive these cells (GFP+) by FACS and then to sub-cultivate them. A consistent pattern of GFP+ cell transformation was observed. These cells could then be used to initiate tumors in a mouse upon heteropic transplantation. These cells could also be inhibited in responsiveness by a dominant negative TCF4 construct that blocks nuclear Wnt/ β -catenin signal transduction. In the transformed cell population widely disparate and erratic karyotypes were observed without a consistent pattern of transformation. While the GFP+ population easily transformed and initiated tumors, the GFP- population was also capable of transforming in a much delayed manner.
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: Although a subset of highly proliferative and malignant cells could be identified based upon our unique functional reporter assay for canonical Wnt signaling, it does not appear that this method identifies tumor initiating cells exclusively. Also, since no consistent pattern or mechanism, (*i.e.* a specific chromosomal translocation), of transformation was identified we believe that cell isolation based upon Wnt signal transduction may not be a discriminatory means by which to study sarcoma tumor initiating cells (stem cell, mesenchymal stem cell).



Principal Investigator (signature)

August 26, 2008

Date

Department Chair (signature)

Date