



**SARCOMA FOUNDATION OF AMERICA
FINAL REPORT**

Project Title: Identifying the sources of synovial sarcoma

Project Number: SFA07-01

1. Date project was initiated: 12/1/2006
2. Period covered by this report: From 6/1/2007 To 5/31/2008
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: N/A (Manuscript in preparation)
 - (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.
4. Provide a brief list of keywords: (limit to 20 words)

Synovial Sarcoma, Mouse Model, SYT-SSX, CreER, Conditional System.

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:

This project was based on our recently established mouse model of synovial sarcoma, a rare and aggressive cancer mostly affecting young adults. In our previous model, we demonstrated that myoblasts of skeletal muscle lineage may give rise to this enigmatic tumor. However, there may be other potential sources of this tumor. More importantly, the histology and the clinical behavior of the tumor may be influenced by its source.

The aim of this project was to attempt at identifying all potential sources of synovial sarcoma using our recently established conditional mouse model as a tool. Using the technique of conditional gene expression in our mouse model, we have induced expression of the synovial sarcoma-associated chimerical oncogene SYT-SSX2 in various tissue types. We have discovered that this unique oncogene is toxic to most cells leading to lethality when expressed ubiquitously in most tissue types. This suggested that in order to generate synovial sarcomas we have to express SYT-SSX2 far more discreetly in fewer cells within a particular tissue. Therefore, we adopted a strategy of random sporadic induction. This tamoxifen-dependent CreER dual-control genetic strategy allows us to express SYT-SSX2 within a small subset of any cell type. Using this strategy we discovered that random and sporadic expression of SYT-SSX2 within multiple cell types leads to tumor formation.

We are currently analyzing the nature of the tumors generated. However, we do believe that such a system recapitulates the human disease more closely since the genetic re-arrangement leading to expression of SYT-SSX2 within humans are also random in nature occurring sporadically in somatic tissue.

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:

The results of this project suggest that synovial sarcomas may have multiple cell of origin. We are currently investing if the cell of origin may influence clinical behavior of the tumor and if the origin could be traced by transcriptional signature of the tumor. If origin does influence tumor behavior, then it may be clinically relevant to attempt at identifying the source using techniques such as microarray to guide the most effective therapy.

Malay Haldar
Principal Investigator (signature)

6/10/08
Date

Mario Capecchi
Department Chair (signature)

6/13/08
Date