



SARCOMA FOUNDATION OF AMERICA  
FINAL REPORT

Project Title: Discovery of small molecule inhibitors  
of the MDM2-ubch5 interaction

Project Number: SFA06-A

1. Date project was initiated: June 1, 2006
2. Period covered by this report: From 6/1/06 To 5/31/07
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:
    - (3) Invited Articles:
    - (4) Abstracts:
  - b. List presentations made during the last year (international, national, local societies, etc.). Use an asterisk (\*) if presentation produced a manuscript.

**Ariel G. Herman and Brent R. Stockwell. Disrupting MDM2 E3 Ligase Activity with Small Molecules. Columbia University Biophysics Retreat. March 23, 2007.**
4. Provide a brief list of keywords: (limit to 20 words)  
**MDM2, E3 ligase, cancer, sarcoma, cell death, p53, DNA damage, proteasome, ubiquitin, screen, high-throughput, drug, small molecule**

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 were able to screen ~40,000 compounds for their ability to inhibit MDM2 E3 ligase activity in a cell-based assay, including ~2500 compounds we selected from an in silico screen targeting the MDM2-E2 interface. We have identified several candidate hits that have been verified in several additional assays. Our focus is now on confirming the mechanism of action of these compounds, and subsequently optimizing their selectivity and potency.**

6. In layperson's terms, summarize the progress during the period of this report.

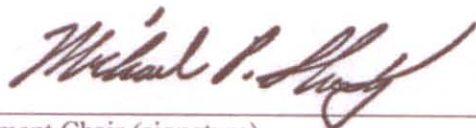
Explain any medical significance or implications of your results to date:

**We have discovered several drug candidates that may be suitable for further development. These compounds have the potential to reveal a new strategy for eliminating sarcomas containing the MDM2 oncogene, and may serve as a proof of concept for a new class of anti-sarcoma agents.**



Principal Investigator (signature)

6/4/07  
Date



Department Chair (signature)

6/4/07  
Date