



FINAL REPORT

Project Title: Functional analysis of Mirk/Dyrk
1B in osteosarcoma

Project Number: SFA10-01

1. Date project was initiated: _____ 5/1/2008 _____
2. Period covered by this report: From ____ 6/1/2010 _____
To ____ 5/31/2011 _____
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:

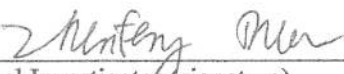
- 1: Duan Z, Choy E, Harmon D, Liu X, Susa M, Mankin H, Hornicek FJ. MicroRNA-199a-3p is Down Regulated in Human Osteosarcoma and Regulates Cell Proliferation and Migration. Mol Cancer Ther. 2011 Jun 10. [Epub ahead of print] PubMed PMID: 21666078.
- 2: Liu X, Choy E, Harmon D, Yang S, Yang C, Mankin H, Hornicek FJ, Duan Z. Inhibition of polo-like kinase 1 leads to the suppression of osteosarcoma cell growth in vitro and in vivo. Anticancer Drugs. 2011 Jun;22(5):444-53. PubMed PMID: 21399492.
- 3: Liu X, Choy E, Hornicek FJ, Yang S, Yang C, Harmon D, Mankin H, Duan Z. ROCK1 as a potential therapeutic target in osteosarcoma. J Orthop Res. 2011 Aug;29(8):1259-66. doi: 10.1002/jor.21403. Epub 2011 Mar 8. PubMed PMID: 21387396.
- 4: Susa M, Choy E, Liu X, Schwab J, Hornicek FJ, Mankin H, Duan Z. Cyclin G-associated kinase is necessary for osteosarcoma cell proliferation and receptor trafficking. Mol Cancer Ther. 2010 Dec;9(12):3342-50. Epub 2010 Sep 29. PubMed PMID: 20881269.

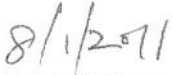
- b. List presentations made during the last year (international, national, local societies, etc.). Use an asterisk (*) if presentation produced a manuscript.
4. Provide a brief list of keywords: (limit to 20 words)
osteosarcoma, kinase, multidrug resistance, MDR1, Stat3, Mirk, PLK1
 5. Summarize the 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:

Our research funded by the SFA involved determine the impact of overexpression of Mirk in human osteoblast cell lines on cell differentiation, proliferation and neoplastic transformation; and analyze the molecular consequences of inhibiting Mirk in osteosarcoma cell lines. Our long term goal is to elucidate the regulatory mechanisms controlling expression of Mirk and ultimately develop therapeutic strategies that can be used to improve the treatment of patients with osteosarcoma. We have constructed Mirk expression vector and have confirmed Mirk open reading fram (ORF) by sequence analysis. We also generated or purchased several human osteoblast cell lines that will be used for testing the impact of overexpression of Mirk.

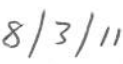
6. In layperson's terms, summarize the progress during the period of this report. Explain any medical significance or implications of your results to date:

The human genome contains at least 600-protein kinases that play critical roles in human diseases. A functional understanding of the role of the kinases in osteosarcoma is not well understood, and a study of these proteins and their functions will contribute to the discovery and development of new therapeutics. We found osteosarcoma cells display high levels of Mirk kinase expression and high level of Mirk are associated with more aggressive clinical behavior. Mirk expression knocked down inhibits cell growth in osteosarcoma cells. We believe that this study provides a new insight to the potential role of Mirk in the osteosarcoma pathogenesis, which suggests that Mirk could be novel candidates for targeted therapy in the treatment of osteosarcoma.


Principal Investigator (signature)


Date


Department Chair (signature)


Date