AMERICAN ACADEMY OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY FOUNDATION

ATTN: Stephanie Jones
Assistant Director, Research and Quality Improvement
1650 Diagonal Road
Alexandria, VA 22314-2857
sljones@entnet.org
PH: 703-535-3747

COVER SHEET FOR FINAL PROGRESS REPORT

Type of Grant:

- AAFPRS Leslie Bernstein Grant
- AAFPRS Leslie Bernstein Resident Research Grant
- AAFPRS Leslie Bernstein Investigator Development Grant
- AAOA Foundation/AAO-HNSF Combined Research Grant
- AAO-HNSF Resident Research Award
- AAO-HNSF Maureen Hannley Research Training Award
- AAO-HNSF Percy Memorial Research Award
- AAO-HNSF Health Services Research Grant
- AAO-HNSF Rande H. Lazar Health Services Research Grant
- AHNS Pilot Grant
- X AHNS Alando J. Ballantyne Resident Research Pilot Grant
- AHNS/AAO-HNSF Young Investigator Combined Award
- AHNS/AAO-HNSF Surgeon Scientist Combined Award
- AHRF Wiley H. Harrison Memorial Research Award
- ALA/ALVRE Award
- ANS/AAO-HNSF Herbert Silverstein Otology and Neurotology Research Award
- ARS New Investigator Award
- ARS Resident Research Grants
- ASPO Research Grant
- ASPO Daiichi Innovative Technology Grant
- PSEF/AAO-HNSF Combined Grant
- The Triological Career Development Award
- XORAN Resident Research Grant

Start date: 7/1/2010   Stop date: 7/1/2011

Principal Investigator: Vlad C. Sandulache

Institution: Baylor College of Medicine

Title of Project: Targeting glycolysis in head and neck squamous cell carcinoma.
Abstract:
Background: The management of head and neck squamous cell carcinoma (HNSCC) often requires multimodality therapy, including chemotherapy. When used alone, conventional chemotherapeutic agents provide only a marginal survival benefit, and many tumors are resistant to this type of treatment. Alternative approaches are therefore required in order to improve the effectiveness of existing strategies. Recently, anti-metabolic strategies have been explored and appear to be a promising new field in adjuvant therapy. We hypothesize that a subset of HNSCC tumor cells exhibit elevated glycolytic activity making them particularly susceptible to chemotherapeutic strategies which include anti-glycolytic agents. To test this hypothesis we propose the following aims: 1) to evaluate the metabolic profile of a panel of HNSCC cell lines using biochemical analysis and determine the proportion of primarily glycolytic cell lines; 2) to evaluate the cytostatic/cytotoxic effects of four previously described anti-glycolytic agents in vitro both alone and in combination with cisplatin; 3) to evaluate the anti-tumorigenic and anti-metastatic effects of anti-glycolytic agents, alone and in combination with cisplatin, using an orthotopic mouse model of HNSCC.

Methods: HNSCC cell lines will be analyzed for dependence on glycolysis for survival and energy production. Four anti-glycolytic agents will be screened against the subset of HNSCC cells with increased glycolytic activity for in vitro cytotoxicity alone and in combination with cisplatin. In vitro cytotoxicity data will be confirmed using an established orthotopic mouse model.

Conclusion: We will identify the subset of HNSCC cell lines which are particularly susceptible to anti-glycolytic strategies. We will evaluate potential synergy of novel anti-glycolytic compounds with existing chemotherapeutic agents and provide pre-clinical data to help define a role for anti-glycolytic strategies in the treatment of HNSCC.

Briefly describe progress in completing the project:
To date we have completed a metabolic analysis of 15 HNSCC cell lines and evaluated their relative sensitivity to anti-metabolic agents. In addition, we have identified wild type p53 function as an important regulator of HNSCC metabolism. We have evaluated the cytotoxic profiles of several anti-metabolic agents in combination with conventional chemotherapeutic agents under in vitro and in vivo conditions.

What work was completed?
All proposed work was completed.

What work was not completed?
All proposed work was completed.

Were all of the funds spent?
All funds were expended.

Have the results been presented? Poster? Oral? What meeting? What publication?
The results from this project were presented in poster fashion at the 2011 Combined Otolaryngology Spring Meetings, Chicago, IL. In addition, the data have been published in the following 2 manuscripts.


Clinical Applications, Either Immediate or Potential, of This Research:
We have identified mutant p53 status as contributory to altered HNSCC metabolism, potentially making tumors which express mutant p53 more susceptible to targeted anti-metabolic agents. We are currently in the planning stages of additional pre-clinical studies to validate this finding prior to proposing initiation of clinical investigation.

Other Pertinent Information:
None.