RECEIVED
AUG 28 2000
OSTI

Final Technical Report for Grant DE FG02 96ER62239 for Granting Period 7/14/96 to 7/13/98

The grant was initially funded in May 1994 to St. Mary's Hospital and Medical Center located in Grand Junction, CO (Agreement No. DE-FG03-94-ER61842). When the Principal Investigator, Marshall Anderson, relocated to the University of Cincinnati, a continuation of the initial grant was awarded to this institution with Dr. Anderson as Principal Investigator for one year and a no cost extension for another year. This report summarizes the research results obtained with this grant.

Lung cancer is one of the leading causes of death in the United States and in Western Europe. The incidence of lung cancer in developing countries is rising as their cigarette smoking habits increase. The objectives of this grant were to analyze genetic alterations associated with the development and progression of non-small cell lung carcinoma (NSCLC). Endpoints that may be realized from the research accomplished are: 1) detection of early genetic and/or cellular alterations which ultimately could lead to diagnostic modalities for the early detection of lung cancer; and 2) detection of a novel tumor suppressor gene(s) on chromosome 9p. This proposal analyzed both tumor specimens and sputum samples.

A major focus of the research was to examine lung tumors for the presence of tumor suppressor genes (TSG) on 9p. The p16/CDKN2 gene, a cyclin dependent kinase inhibitor, is a well-known TSG on 9p21. Our data strongly suggest the existence of at least one additional TSG on 9p (Wiest et al, Cancer Research 57, pp 1-6, 1997; and Wiest et al, Journal of Cellular Biochemistry Supplement 28, pp64-73, 1997). This was the major accomplishment of this grant. We have subsequently narrowed the chromosomal region of this putative TSG and presently are examining this region for candidates. Based on our results and published reports by other investigators, a high frequency loss of heterozygosity is observed in each major histologies subtypes of human lung cancer. We will continue to attempt to identify a novel TSG(s) on 9p.

Mutations in the p53 TSG gene are detected in approximately 50% of human lung non-small cell carcinomas (NSCLC). This gene is also overexpressed in preinvasive lesions of the bronchial epithelium. p53 overexpression may serve as a biomarker for high-risk assessment of lung cancer. A study was conducted to analyze p53 overexpression in cells from sputum samples collected prior to histological tumor diagnosis. The rationale was based on the observation that preinvasive cells of the bronchial epithelium can be exfoliated into the airways and detected in sputa based on morphology. Our data suggested that sputa cells which overexpress p53 and/or cytokerastion in conjunction with morphological criteria may define a new class of atypical cells which are predisposed to cancer development (Anderson et al, Journal of Cellular Biochemistry 64 pp185-190, 1996). We will continue to explore this new potential class of atypical cells to be utilized in early detection of lung cancer by analysis of sputum samples (Anderson et al, Analysis of Sputum Specimens for the Presence of Atypical Cyanophilic Epithelial Cells, submitted for publication).

We have no objection from a patent standpoint to the publication or dissemination of this material.

Mark P. Dvorscak 8/22/00

Office of Intellectual Property Counsel
DOE Field Office, Chicago

Date

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor any of their employees, make any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

We also conducted an extensive study to examine a new procedure to prepare slides of sputum specimens. These new types of slides are referred to as "Megafunnel slides" and the procedure is outlined in our published manuscript (Michels et al, Acta Cytologica, 41, pp1774-1780, 1997). The objective of this study was to compare Megafunnel slides to Saccomanno smear slides of sputum samples. We demonstrated that Megafunnel slides compared favorable to Saccomanno smear slides in the quality of specimen. The Megafunnel slides are more expensive and labor intensive to prepare. However, the reduction in screening time by cytotechnologists may be advantageous. Moreover, their potential for immunocytochemical analyzing, FISH, and other special clinical and research analyses is enormous since they exhibit better cell adhesion, a more uniform monolayer of cells and decreased background staining.