CIGARETTE RESTITUTION FUND PROGRAM

A Joint Report On Intellectual Properties And Discoveries Under The Statewide Academic Health Centers Grants

by the

Maryland Department of Health and Mental Hygiene
Maryland Technology Development Corporation
Maryland Department of Business and Economic Development

and the

University of Maryland Medical Group and
Johns Hopkins Institutions

January 2006

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CIGARETTE RESTITUTION FUND PROGRAM
REPORT ON INTELLECTUAL PROPERTIES AND DISCOVERIES UNDER THE STATEWIDE ACADEMIC HEALTH CENTER GRANTS

Table of Contents

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REPORT ON INTELLECTUAL PROPERTIES AND DISCOVERIES UNDER THE STATEWIDE ACADEMIC HEALTH CENTER GRANTS

I. Introduction and Background

Tobacco use has had a devastating affect on the health of Maryland's citizens and is the leading cause of premature deaths in the state. Maryland was among the top 10 states leading the nation in cancer mortality in the 1990s. These dismal facts prompted the Governor and the Maryland General Assembly to commit a significant portion of the monies from the Master Settlement Agreement with the tobacco manufacturers to create the Cigarette Restitution Fund Program (CRFP). The CRFP, designed to focus on reducing cancer mortality and mitigating the impact of tobacco use on the health of Maryland's citizens, was codified in legislation in 2000. The Maryland General Assembly committed to the concept of long term funding of the CRFP, which is united by an integrated public health model encompassing research, prevention and community health care.

Maryland was one of 46 states, five territories, and the District of Columbia to benefit from the 1999 multi-state lawsuit against the cigarette manufacturers. Subsequently, the Governor and the Maryland General Assembly established the multi-million dollar Cigarette Restitution Fund (CRF) to distribute funds throughout the state for tobacco use prevention and cessation programs, cancer research, prevention, education, screening and treatment programs, tobacco crop conservation assistance, and other health-related activities.

A major component of the Cancer Prevention, Education, Screening and Treatment Program under the CRFP was the creation of the Statewide Academic Health Center grants, through which cancer research funds for the University of Maryland and Johns Hopkins Institutions were appropriated. Grant funds to the academic health centers support translational cancer research and are aimed at reducing cancer morbidity and mortality in Maryland.

The purpose of this report is to identify all results, discoveries and potential commercialization of inventions under the CRFP research grants after the first six years of funding under the CRF.

II. Role of State Agencies in the Intellectual Property Discoveries of the Statewide Academic Health Centers under the CRFP

The CRFP statute requires each academic health center to enter into a Memorandum of Understanding with three state agencies to:

- Establish a plan for expediting the translation of cancer research activities into treatment protocols and clinical trials;

- ❖ Establish the scope of the state's ownership or other financial interest in the commercialization and other benefits of the results, products, inventions and discoveries of cancer research activities funded by a statewide academic health center cancer research grant under the CRFP; and

- ❖ Reflect the intellectual property policies of the statewide academic health center.

The three state agencies include the Maryland Department of Health and Mental Hygiene (DHMH), the Maryland Technology Development Corporation (TEDCO) and the Maryland Department of Business and Economic Development (DBED). The three state agencies entered into Memoranda of Understanding for this purpose with the University of Maryland Medical Group on March 28, 2001 and with the Johns Hopkins Institutions on May 21, 2001. A copy of the Memorandum of Understanding with each academic health center is found in Appendices A and B, respectively.

Some of the provisions in the Memoranda of Understanding are as follows:

- The University* shall encourage faculty to publish and otherwise disseminate all knowledge and information derived from the research supported by the CRFP.

- The University shall screen faculty disclosures of inventions made with support from the CRFP to identify Intellectual Property. It shall inform the state agencies of the Intellectual Properties within 60 days of disclosure, the invention title or other description of the Intellectual Property, and a brief explanation of the Intellectual Property.

- The University shall review the Intellectual Property, determine whether the University will elect to take title to the invention, and require inventors to assign their interests in the invention to the University subject to the University's Patent Policy.

- For each invention assigned to the University, the University shall make best efforts to commercialize each invention through a license of similar arrangement with an entity in Maryland. The University shall consult with DBED and TEDCO to identify potential licensees.

- If the University decides not to take title to the invention, the University shall give written notice to the other parties of the MOU within 30 days of making the decision and shall include a summary of the efforts undertaken to commercialize within Maryland.

- Any license agreements made by any of the parties of the MOU for commercialization shall include provisions intended to promote treatment protocols and clinical trials being conducted in Maryland so that the results of the cancer research grants can be available to Maryland citizens at the earliest practicable opportunity.

* The term "University " unilaterally refers to both University of Maryland and Johns Hopkins Institutions

- In the event the University licenses or commercializes an invention, after out-of-pocket expenses have been paid by the University, 25 percent of the remaining revenue from a CRFP-funded invention available for distribution by the University shall be used to support cancer-related translational research and commercialization.

After entering into the Memorandum of Understanding with each statewide academic health center, the three state agencies set up routine advisory group meetings with each university that met two to three times a year to discuss the intellectual property policies and procedures at each institution and to monitor progress in intellectual property discoveries at the academic health centers under the CRFP.

III. Summary of the Funds Awarded to the Statewide Academic Health Centers

University of Maryland Medical Group (UMMG)

Under the CRFP, DHMH awards funds to the University of Maryland Medical Group for two different research grants each year: a Cancer Research grant and a Tobacco-Related Diseases Research grant. DHMH has awarded UMMG a total of $53,120,400 for research grants under the CRFP from fiscal year 2001 to 2005 (See Table 1).

Table 1
Funds Awarded to University of Maryland Medical Group
for All Research Grants under the CRFP

Fiscal Year	Cancer Research Grant	Tobacco Related Diseases Research Grant	Total Amount Awarded
2001	$7,125,000	$0	**$7,125,000**
2002	$9,530,000	$3,000,000	**$12,530,000**
2003	$9,530,000	$3,000,000	**$12,530,000**
2004	$8,628,000	$2,288,000	**$10,916,000**
2005	$8,029,400	$1,990,000	**$10,019,000**
Total	**$42,842,400**	**$10,278,000**	**$53,120,400**

The UMMG has used funds under the cancer research grant to support faculty and other staff to conduct research in hematologic malignancies, gastrointestinal, liver, lung, breast and prostate cancers, pharmacology, and new drug development. Funds were also used for behavioral studies of minority cancer patients, biostatistical support, preclinical modeling and clinical trials support. In addition, funds were allocated to support and maintain the following six shared services facilities in the core service areas: proteomics, biomarker/gene discovery, tissue collecting and banking, flow cytometry, biostatistics, and clinical trial protocol management. Lastly, funds were used for renovations of clinical and laboratory space and to pay for major medical equipment.

The UMMG has used funds under the Other Tobacco-Related Diseases Research Grant (OTRD) to support faculty to conduct health services research, translational research, and clinical research.

Johns Hopkins Institutions (JHI)

Under the CRFP, DHMH awards funds to the Johns Hopkins Institutions (JHI) for a cancer research grant each year. DHMH has awarded JHI a total of $14,749,000 under the CRFP for cancer research grants from fiscal year 2001 to 2005 (See Table 2).

Table 2
Funds Awarded to the Johns Hopkins Institutions
for Cancer Research Grants under the CRFP

Fiscal Year	Amount Awarded
2001	$3,750,000
2002	$3,000,000
2003	$3,000,000
2004	$2,590,000
2005	$2,409,000
Total	**$14,749,000**

According to Section 6 of the CRFP statute, funds under the cancer research grant at Johns Hopkins in fiscal years 2001, 2002, and 2003 were used to:

1) recruit high-quality faculty in the behavioral research, genetic epidemiology, cancer epidemiology, molecular genetics of cancer, and viral vaccine development fields;

2) retain high-quality faculty, including clinicians and researchers, who contribute to a community-focused cancer research program; and

3) cancer surveillance and epidemiology, including the development of a comprehensive list of cancer causing agents, compilation and mapping of sources of exposure, a focus on the unique cultural and other factors related to delays in treatment and lack of success in care and treatment in underserved urban and rural communities, and improved understanding of cancer risk factors and how they impact on the state's unique cancer statistics.

Johns Hopkins awards its cancer research funds under a competitive grant process to its faculty each year. A total of 85 research grants have been funded by JHI under the CRFP from fiscal year 2001 to fiscal year 2005 (See Table 3).

Table 3
Number of Faculty Research Grants Funded
at Johns Hopkins Institutions under the CRFP

Fiscal Year	Number of Faculty Recruitment Grants Awarded	Number of Faculty Retention Grants Awarded	Number of Translational Research Grants Awarded	Total Number of Research Grants Awarded
2001	5	5	9	19
2002	6	4	6	16
2003	10	2	9	21
2004	5	5	8	18
2005	6	1	4	11
Total	**32**	**17**	**36**	**85**

The JHI has leveraged CRF awards in dollars from external funders. In 2001, Mr. Sidney Kimmel made a gift to the JHI Cancer Center because of the partnerships with the state of Maryland. Since this gift, CRF investigators have earned more than $50 million dollars to sustain their research efforts and momentum achieved under CRF.

IV. Intellectual Property Results of CRFP-Funded Research

This section discusses the intellectual properties and discoveries that have resulted from the funding to the statewide academic health centers under the CRFP from fiscal year 2001 through fiscal year 2005. These results can be reflected in the number of articles that have been published in peer-reviewed scientific journals and by the number of inventions or discoveries that have been made.

University of Maryland Medical Group

The University of Maryland Medical Group has produced the following intellectual property results with funding under the CRFP from fiscal year 2001 through fiscal year 2005.

Publications

Ninety-four faculty (94) supported by the CRFP have published one hundred and seventy-six (176) scientific articles in peer-reviewed scientific journals (See Appendix C). Scientific publications are the primary mode of releasing new findings and discoveries.

Inventions and Discoveries

As of November 2005, the Office of Research and Development (ORD) at the University of Maryland, Baltimore (UMB) has received two invention reports wherein the inventors attributed part of their supporting research funds to the Cancer Research grant or the Other Tobacco

Related Diseases Research grant under the CRFP. Information regarding the two inventions is summarized in Table 4 and described below.

Table 4
Inventions and Discoveries at the University of Maryland Medical Group Associated with Funding Under the CRFP

Disclosure Date	Inventor(s)	Relevant Affiliation(s)	Invention Title	Patent Status	Licensing Status
02/17/2004	Paul Shapiro	UMB School of Pharmacy, Pharmaceutical Sciences Department; University of Maryland Greenebaum Cancer Center	Inhibition of Mixed Lineage Kinases and Uses	3/16/04: provisional application filed. 3/16/04: PCT and U.S. applications filed.	Licensed to Cephalon Corporation effective 10/22/04
10/07/2004	UMB:Steven Kitner, Braxton Mitchell, John Cole, Colin Stine. Morehouse College: Quing Song, Gary Gibbons, Patrick Thomas	UMB School of Medicine, Departments of Neurology; Endocrinology, Diabetes and Nutrition; Epidemiology; and Preventive Medicine	Single Nucleotide Polymorphism (SNP) Associated with Stroke	12/22/04: original provisional application filed. 10/28/05 and 11/03/05: subsequent provisional applications for new SNP filed.	None; in early marketing phase

Invention #1: "Inhibition of Mixed Lineage Kinases and Uses," *invented by Dr. Paul Shapiro.*

Dr. Shapiro is a faculty member with the UMB's School of Pharmacy and a member of the UMB's Greenebaum Cancer Center staff. Dr. Shapiro's invention would block the action of a specific enzyme, Mixed-Lineage Kinase (MLK). MLK in a cancer cell has been identified as an important drug target for cancer therapy. In this invention, the MLK is inhibited selectively to inhibit proliferation of a cancer cell (including lung cancer). The invention also includes methods of treating cancer by co-administering the MLK inhibitor with a conventional cancer drug therapy (example of cancer drug therapy: taxol). In the co-administration methods, the MLK inhibitor reduces the dosage of the conventional cancer drug needed to achieve the same effect.

The invention was disclosed to ORD on February 17, 2004 and was reviewed internally by the Technology Commercialization Group. Dr. Shapiro presented the invention to UMB's Scientific Review Committee on July 14, 2005. ORD determined at that time to retain title to this invention.

UMB filed a provisional patent application for this invention on March 16, 2004. Subsequently, UMB concurrently filed PCT and U.S. applications on March 16, 2004.

Dr. Shapiro's research involved the use of resources purchased under a Cancer Grant. The specific MLK inhibitor used by Dr. Shapiro was acquired from a colleague at another institution. This material was originally acquired from Cephalon, Inc. under an Academic Materials Transfer Agreement, made effective November 14, 2002 between Cephalon and the other institution. Under that agreement, Cephalon retained certain rights to inventions and discoveries made using its material. As a result, UMB negotiated a Materials Transfer Agreement, effective October 22, 2004, wherein Cephalon, Inc. is granted a worldwide, paid-up and royalty-free, exclusive license to develop and commercialize the invention. The agreement allows UMB to continue to seek patent protection for the invention and permits Dr. Shapiro to continue research related to his invention.

Invention #2: "Single Nucleotide Polymorphism Associated with Stroke," *invented by Drs. Steven Kittner, Braxton Mitchell, John Cole and Colin Stine of UMB; co-invented with collaborators Quing Song, Gary Gibbons and Patrick Thomas at Morehouse College.*

Dr. Cole is a member of the faculty in UMB's School of Medicine and the Department of Neurology. A portion of the funds used in the research that led to this invention was derived from the Other Tobacco-Related Diseases Research grant through the Maryland CRFP.

This invention identifies a Single Nucleotide Polymorphism (SNP) associated with Stroke susceptibility, particularly in young adult smoking populations. A "SNP" is a single base change in the DNA coding sequence of a gene. The single base change usually affects the protein structure and/or function encoded by the gene that possesses the SNP. The inventors identified a novel SNP in the PDE4D gene that strongly correlates to early onset of stroke in persons of multi-cultural, ethnic and gender backgrounds. The strongest correlation appeared in the African-American segment of the test population.

The invention was disclosed to ORD on October 7, 2004 and was reviewed internally by the Technology Commercialization Group. The inventors presented their invention to UMB's Scientific Review Committee on September 14, 2005. ORD determined at that time to retain title to this invention.

UMB filed a provisional patent application based on the initial invention disclosure on December 22, 2004. Subsequently, as additional data became available to the researchers, they identified a new SNP that was more strongly associated with members of the smoking population than the original SNP identified in the first provisional patent application. Therefore, UMB filed another provisional patent application incorporating this new data on October 28, 2005. UMB filed yet another provisional patent application on November 3, 2005 to include new figures provided by the inventors subsequent to the October 28 filing. UMB plans to file additional patent applications on or before the expiration of the second provisional patent application (October 28, 2006).

UMB has contacted 12 potential licensees with general information about this invention. Until such time that the provisional patent applications have been converted to U.S. and/or PCT applications, specific information will only be shared with prospective licensees under confidentiality agreements. UMB will continue to present the technology to companies active in markets for cancer diagnostics and therapeutics.

Case Study

Dr. Angela Brodie is the first woman scientist to receive the prestigious Charles F. Kettering Prize. She is a Professor of Pharmacology and Experimental Therapeutics in the University of Maryland School of Medicine and a member of the Hormone Responsive Cancers research program of the University of Maryland Marlene and Stewart Greenebaum Cancer Center. Dr. Brodie received the Kettering Prize in recognition of her pioneering work in developing aromatase inhibitors, a new class of drugs widely used today to treat breast cancer.

Dr. Brodie and her co-workers developed compounds that successfully inhibited the synthesis of aromatase in animal models. These compounds, known as aromatase inhibitors, lower the amount of estrogen made in the body after menopause. Without estrogen, the growth of cancer slows or stops. Three of these compounds are now FDA approved for use in women with estrogen receptor positive metastatic breast cancer.

As Dr. Brodie can attest, bringing a new discovery from the laboratory into the clinic is a long, involved process. Initially, doctors were reluctant to try an experimental drug when drugs like tamoxifen were already working in their patients. Brodie's animal models clearly showed that aromatase inhibitors worked well. She and her co-workers experimented with animal models to test combinations of tamoxifen and aromatase inhibitors, but the results showed that this wasn't an improvement. In fact, the subjects were better off using only the aromatase inhibitors. Subsequent clinical trials completed in later years proved this to be the case

In the beginning, Dr. Brodie found the scientific community convinced that her idea couldn't work – that anti-estrogens were the only way to go. She tried to interest a number of drug companies in manufacturing these new compounds, but new drug development is a risky business and, consequently, they were not interested. It wasn't until her colleagues in London began conducting clinical trials with her compound formestane and showing positive results that she was able to interest the pharmaceutical companies in developing this class of drugs

Formestane was the first selective aromatase inhibitor to be used clinically and, at that time, was the first and only new drug specifically designed for the treatment of breast cancer in the last 10 years. It was released for worldwide use in 1994.

It is important to note that Dr. Brodie began her initial research with aromatase inhibitors in the 1970's. The time required for the overall development of her idea – from bench top to clinical use – spanned over 20 years and required millions of dollars in research funding. This is not an uncommon scenario for the development of new cancer therapeutics. Although Dr. Brodie's initial discovery occurred prior to federal legislation that now allows UMB to protect

and seek licenses for its intellectual property, her work serves as a relevant example of the potential successes that may result from the Cancer and Tobacco Related Disease Grants.

Johns Hopkins Institutions

Moving scientific discoveries forward is recognized as necessary and imperative in order to improve patient care and maximize findings from university-based studies funded primarily with public dollars. This is an infrastructure task that is well supported and part of the everyday work of every school at the Johns Hopkins Institutions. As a condition of the CRFP cancer research grant, the JHI has followed a Plan to Expedite Research Discoveries to the marketplace since 2000. Tracking these activities is the responsibility of Dr. Ted Poehler, Vice Provost for Research, Johns Hopkins University.

The JHI have produced the following intellectual property results with funding under the CRFP from fiscal year 2001 to fiscal year 2005.

Publications

Forty-nine (49) researchers supported by the CRFP at the JHI have published one hundred and twenty (120) scientific articles in peer-reviewed scientific journals (See Appendix D). Scientific publications are the primary mode of releasing new findings and applications. These publications are a sampling of investigator output most relevant to the CRF and are not intended to be comprehensive.

Inventions and Discoveries

To date, seven inventions initiated under the CRFP have been disclosed and moved toward development into products useful to consumers. This process is time consuming and requires significant amounts of investment until the point of cash return on a license or a product. The process from discovery to commercialization may take years and millions of dollars, depending on the discovery. Drug development tends to take the longest and is the most costly. Thus, there is considerable collaboration between the University's research offices and investigators to assure that prospects are assessed well, patents obtained, licenses sold, and other steps in the process of commercialization are taken. Table 5 below describes briefly these seven inventions and the status of each discovery.

Table 5
Inventions and Discoveries at the Johns Hopkins Institutions
Associated with Funding Under the CRFP

Disclosure Date	Inventor	Description	Status
04/1/03	Feinberg	Screening: Epigenetic Test for Colorectal Cancer Risk	Licensed to Epigenomics
10/29/04	Park	Biologic Investigational Tool: P21 Knock-Out Human Mammary Epithelial Cell Lines	Discussion with faculty for depositing in JHSC and ATCC.*
08/12/04	Wang	Genomic Cancer Risk Profiling: Cancer Mutational Analysis of the Tyrosine Phosphatame in Prostate Cancer	60/571,436 provisional patent application; TEDCO market study done for JHU-$1420, Ambit reviewing the technology
07/19/04	Biswal	Drug Target Identified: Novel Approach for Tackling Cancer Chemotherapy	60/571,329 provisional patent application
	Gibbons	Field-Based Palm PC for Data Collection: Hand-held Patient Tracking, Education and Decision Support Tool	Questionnaire is copyrighted; discussion with vendor about licensing
10/28/04	Eshleman	Ultrasensitive Test for Detection of Mutations: LigAmp: Sensitive Point Mutation Detection	Provisional patent filed
07/21/05	Biswal	Clinical Target Identified: Nrf2, an Intervention Target for Pulmonary and Systemic Inflammation	Provisional patent filed; possible interest in applying for UTDF for technology**

*JHSC (Johns Hopkins Special Collection) provides cells at cost to investigators from any institution. To help Principal Investigators (PIs) provide these materials to other investigators, Johns Hopkins University (JHU) has entered into a collaboration with the American Type Culture Collection (ATCC) to develop this service. Through this collaboration, PIs will be able to easily share their biological materials with the scientific community and at the same time better preserve any intellectual property rights associated with these materials. The material must be published, used for research, i.e. not clinical samples, and have been sent out at least five times in the last calendar year. JHU has demonstrated its commitment to helping PIs with this sharing responsibility by establishing the Biological Distribution and Resource Center (BDRC) in the Office of Licensing and Technology Development to implement the ATCC collaboration and to provide assistance on additional issues such as improving the Material Transfer Agreement process. *http://cellcenter.grcf.jhmi.edu.celltocell.shtm*

**The goal of the Maryland Technology Development Corporation (TEDCO) University Technology Development Fund (UTDF) is to provide resources to Maryland universities to support pre-commercial research on university

intellectual property to increase the likelihood of commercializing that intellectual property. The program helps universities to license early stage technologies more effectively and serves as a source of technology development projects for Maryland companies that are eligible for additional TEDCO and other State financing programs. *http://www.marylandtedco.org/programs/UTDF.html*

Case Study #1: Community Service to Cancer Control: Connie Trimble, M.D.

Dr. Connie Trimble, with assistance from the Cigarette Restitution Fund Program at Johns Hopkins, has been able to build a research program, establish multidisciplinary collaborations and serve the community. From her CRF award, she established a Center for Cervical Health at Johns Hopkins (Bayview) where she primarily serves Baltimore area women.

The center is actively following women with Human Papillma Virus (HPV) infections and cervical abnormalities. Building upon the success of the CRF project seed dollars, her current research support includes a Flight Attendants Medical Research Institute (FAMRI) grant, a National Cancer Institute (NCI) Specialized Program of Research Excellence (SPORE) project, and NCI investigator-initiated support (R-01). The center has the accumulated experience to effectively care for women in Baltimore who are at greater risk of cervical cancer. Her work has shown that women entering Johns Hopkins Hospital for any condition are likely to not have a current Pap smear. Her center assures that these women are offered, and if desired, given a Pap smear before discharge from the hospital.

Her collaborations include working with labs crafting new vaccine and immunologic strategies for addressing cancer (Pardoll); partnering with epidemiologists to identify populations at risk for no Pap smear or at risk for the disease (Gravitt, Klassen, Alberg); and forging public-private partnerships with biotech in combining the Hopkins vaccines with needle-free vaccination delivery systems that magnify the vaccine effect while using less sera. She is the Principal Investigator of two Hopkins Cervical Cancer SPORE projects. Taken together, these interactions have moved Dr. Trimble's science forward at a rapid pace over the first five years of CRF funding at JHI.

Case Study #2: Generalizing Knowledge About One Cancer Site to Others: Biswal, Kensler, Nelson, Rudin, and Visvanathan

Building upon two decades of work with a compound isolated from broccoli sprouts, CRF investigators are documenting the molecular effects of sulforaphane on cancer risk biomarkers and ultimately cancer. Investigations began with prevention of liver cancer, uncovering the genes influenced by the drug and the biologic mechanisms of action. Currently there is evidence that sulforaphane will reduce risk for other cancers. Studies are underway to examine effects in lung, breast, prostate, and liver tissue from healthy individuals or those undergoing cancer surgery. While broccoli sprouts are already patented, there is room for other inventions that may provide a culturally appropriate and cost-efficient intervention for cancer prophylaxis. For example, in an area of China where liver cancer occurrence is very high, broccoli sprout tea is the mode of delivery for a daily dose of prevention. CRF investigators are instrumental in guiding these studies through the planning and implementation phases.

Case Study #3: Tools for Analysis: Velculescu, Califano, Park and Others

To conduct their scientific investigations, many JHI scientists are developing the tools necessary to measure, monitor and evaluate the science. Several investigators are engaged in these efforts. Dr. Victor Velculescu's laboratory (Wang, et al) has developed a method called digital karyotyping that provides quantitative analysis of DNA copy number at high resolution. This approach involves the isolation and enumeration of short sequence tags from specific genomic loci. Analysis of human cancer cells using this method identifies gross chromosomal changes, as well as amplifications and deletions, including regions not previously known to be altered. Foreign DNA sequences not present in the normal human genome could also be readily identified. Digital karyotyping provides a broadly applicable means for systematic detection of DNA copy number changes on a genomic scale. Using this tool, Dr. Velculescu was able to identify genes implicated in colon cancer and opened a new venue of research around tyrosine kinase's role in cancer.

Dr. Joseph Califano, has developed a selected set of modified genes that can profile risk of recurrence for patients with oral cancer. This test can be done on tissue adjacent to the cancer while the patient is under anesthesia, and informs the physician if a molecularly clean margin has been achieved; thus obviating the need for subsequent surgeries due to recurrence. In the future, efforts like this may lead to an "oral Pap smear" to noninvasively detect precancerous conditions. Dr. Ben Ho Park has developed a cell line that does not have a particular protective gene. The cells will be useful tools for researchers of human breast cancer. Facilitated access to these cells at cost will assure that this tool will be available to further science.

V. Summary

This report shows that the statewide academic health centers have produced tangible, scientific results with funding under the CRFP during the first five years of this program. The first step in intellectual discovery is the publication of articles in peer-reviewed scientific journals. Both universities have published a long list of approximately 300 articles in a multitude of scientific journals. In addition, nine inventions have been discovered between the two universities in these first few years. These inventions are moving in the long process from discovery to commercialization – a process that can take over 20 years. Sustained funding is needed for these inventions to move to the marketplace and for additional discoveries to be made under the CRFP.

APPENDIX A

Memorandum of Understanding with the University of Maryland Medical Group

3/28/01

MEMORANDUM OF UNDERSTANDING REGARDING RESULTS OF RESEARCH SUPPORTED WITH GRANTS FROM THE TOBACCO FUND

This Memorandum of Understanding ("MOU") is entered into by the University of Maryland, Baltimore ("the University"), an agency of the State of Maryland acting on behalf of the University of Maryland Medical Group (as defined by Section 13-1101(ii)), Health General Article) ("UMMG") and by the Maryland Department of Health and Mental Hygiene ("DHMH"), an executive agency of the State of Maryland, and by the Maryland Department of Business and Economic Development ("DBED"), an executive agency of the State of Maryland, and by the Maryland Technology Development Corporation ("TEDCO"), a corporation and public instrumentality of the State of Maryland, to fulfill the requirements of Section 13-1116(b)(2) and 13-1117(c)(2) of the Health General Article, Annotated Code of Maryland.

Recitals. In accordance with Maryland Law, Section 13-1116, Health General Article, Annotated Code of Maryland, the University, directly or through another member of the UMMG will apply for, and anticipates receiving, a Statewide Academic Health Center Cancer Research Grant ("Cancer Research Grant") from DHMH. The Cancer Research Grant will be made from the Maryland Cigarette Restitution Fund ("the Fund") for the purpose of conducting cancer research. More specifically, the Cancer Research Grant will be for the purpose of enhancing cancer research activities that may lead to a cure for a targeted cancer and increasing the rate at which cancer research activities are translated into treatment protocols in Maryland. As a condition of receiving a Cancer Research Grant, the University (representing the UMMG), enters into this MOU with DBED, TEDCO, and DHMH (the State Agencies) concerning issues specified in Section 13-1116(b)(2). Furthermore, the University (representing the University of Maryland Medical Group) enters into this MOU to satisfy the requirements of Section 13-1117(c)(2) Health General Article, Annotated Code of Maryland, which requires an MOU concerning the issues prior to receiving a grant for tobacco-related diseases research ("Tobacco Related Diseases Research Grant") when funds are appropriated for the purpose of enhancing research activities that may lead to a reduction in morbidity or mortality rates for tobacco-related diseases in Maryland.

Agreements.

1. **Research Plan** A Cancer Research Grant or a Tobacco-Related Research Grant will

3. **Invention Disclosures** The University shall screen faculty disclosures of inventions

support activities to conduct tobacco related diseases research and cancer research under a research plan ("Research Plan") submitted to DHMH as required by law. Activities under a Research Plan may have results, products, inventions, and discoveries ("Intellectual Property") useful in the prevention, treatment and cure of cancer and/or tobacco related diseases. Such Intellectual Property will be owned by the University and managed in accordance with its institutional policies concerning intellectual property, especially the University System of Maryland Policy on Patents as approved May 31, 1990 and issued as Policy IV-3.00 in the Policies and Procedures of the Board of Regents ("Patent Policy") . In accordance with State law, this MOU is not intended to require any modification in the Patent Policy or any departures from the Patent Policy.

2. **Publication and Dissemination of Research Results** The University shall encourage faculty to publish and otherwise disseminate all knowledge and information derived from research supported by the Fund, and shall inform faculty that it is a condition of research support from the Fund that they acknowledge the support from the Fund in any publication resulting from the research. The University shall work in conjunction with the Cancer Council in order to communicate results of the research supported by the Fund to the other Statewide Academic Health Center, to general practitioners, to Maryland legislators, and to the general public. The University shall work with the DHMH Chronic Disease Division in order to communicate results of the research supported by the Tobacco Related Disease Grant to the other Statewide Academic Health Center, to general practitioners, to Maryland legislators, and to the general public.

3. **Invention Disclosures** The University shall screen faculty disclosures of inventions

made with support from Cancer Research Grants and Tobacco Related Diseases Research Grants (collectively, "Grants") to identify Intellectual Property. As the University identifies Intellectual Property, it shall inform the State Agencies of the Intellectual Property, providing the date of disclosure, the invention title or other description of the Intellectual Property, and a brief explanation of the Intellectual Property. To expedite actions to carry out research needed to translate the results of Grants-supported work to treatment protocols and clinical trials ("translational research"), the Intellectual Property, including but not limited to any invention within the Intellectual Property (a "Tobacco Fund Invention"), shall be reviewed quarterly, by an appropriate group of scientists and technology development personnel in the University's Office of Research and Development ("ORD"). ORD shall determine, for each Tobacco Fund Invention, whether the University will elect to take title to the invention. Following a decision to take title, the University shall require inventors subject to the Patent Policy to assign their interests in the invention to the University.

4. **University Commercialization**

(a) As to each Tobacco Fund Invention assigned to the University, it shall explore potential translational research, sources of funding for translational research, costs of clinical trials, and costs of treatment under clinical protocols.

(b) The University shall make best efforts to commercialize expeditiously each Tobacco Fund Invention being managed by the University. Due consideration shall be given to commercialization through a license or similar arrangement with an entity organized under the laws of Maryland and having its principal place of business in Maryland, or an entity which

would use the Tobacco Fund Invention in manufacturing in Maryland.

(c) At the outset of commercialization efforts for a Tobacco Fund Invention accepted by the University for management and commercialization, the University shall consult with DBED and TEDCO to identify potential licensees as described in the preceding sentence. Upon abandoning efforts to commercialize a Tobacco Fund Invention within Maryland as described above, the University shall notify DBED and TEDCO and provide a summary of efforts undertaken to commercialize within Maryland.

5. **Due Diligence and Reassignment**

(a) If the University decides not to take title to a Tobacco Fund Invention, or having taken title, elects to abandon all pending patent applications and/or marketing efforts for the Tobacco Fund Invention, the University shall give written notice to the other parties to this MOU within 30 days of making the decision.

(b) If at any time a party to this MOU finds that the University is not making best efforts to commercialize a Tobacco Fund Invention as required by this MOU, that party may give written notice to the University and the other parties. Within 30 days of that notice, the University shall either agree to abandon the invention and give notice pursuant to (a), or meet with the other parties to review commercialization activities and the University plans for further activities. If the explanation and/or plan is not acceptable to the State Agencies, or the State Agencies decide that the University has not implemented the plan after reasonable opportunity, the University shall be given final notice by the State Agencies of their intent to take title.

(c) Following notice by the University given under part (a), or following final notice by

the State Agencies under part (b), the State Agencies within 60 days may elect that the Tobacco Fund Invention be assigned or licensed upon reasonable terms to TEDCO or any entity identified by the State Agencies. The terms of the assignment or license under this subparagraph shall include: (i) a reserved right on the part of the University to use the Tobacco Fund Invention for academic purposes and to permit other academic and research institutions that are nonprofit in nature to use the Tobacco Fund Invention for academic purposes; (ii) an obligation on the assignee's or licensee's part to make best efforts to seek from any eventual commercial licensee of the Tobacco Fund Invention a payment to the University sufficient to reimburse the University for out of pocket expenses associated with patenting and marketing the Tobacco Fund Invention, the payment to be due upon execution of the license; (iii) recognition that the University will have no financial responsibility for expenses associated with patenting and marketing the Tobacco Fund Invention which expenses are incurred after notice under subparagraph (a) or final notice under subparagraph (b) of this paragraph.

(d) The State Agencies shall pay to the University 25 percent of any income (net of out of pocket expenses incurred by the State agencies or deducted by a private assignee or licensee from revenues due the State agencies for patenting and commercialization) through licensing of the Tobacco Fund Invention.

6. **Licensing** Any license or assignment of a Tobacco Fund Invention made by any party to this MOU shall be subject to a continuing, non-exclusive, royalty-free right of UMMG to use the Tobacco Fund Invention to conduct research and clinical care using the Tobacco Fund Invention and also shall be subject to a right on the University's part to permit other nonprofit

academic or research institutions to use the Tobacco Fund Invention to conduct research. Also, any license made by any of the parties for commercialization shall include provisions intended to promote treatment protocols and clinical trials being conducted in Maryland (if permitted by the federal rules then in effect) so that the results of the Cancer Research Grants and the Tobacco Related Diseases Research Grants can be available to Maryland citizens at the earliest practicable opportunity.

7. **Revenue** The University revenue from a Tobacco Fund Invention shall be managed and distributed in accordance with the Patent Policy, subject to the requirement that income distributed for research support will be used for research relating to cancer and tobacco related diseases. Further, the University agrees that no less than 50 percent of the income available to the University (i.e., not distributed to inventors in accordance with the Patent Policy) shall be used to support translational research relating to cancer and tobacco related diseases.

8. **Reporting** No less than 30 days prior to each scheduled meeting of the committee defined in section 10, the University shall report to the State Agencies plans and activities of the University to develop, license and commercialize the Intellectual Property and any involvement of Maryland businesses in development of the Intellectual Property. If any report includes information of the University or third parties which, pursuant to Section 10-617(d), Section 10-618(d), or Section 10-618(h) of the Maryland Public Information Act, is not required to be disclosed in response to a request under the Maryland Public Information Act, the University, and the State Agencies shall enter into an appropriate confidentiality agreement regarding that part of the report before the report is provided by the University.

9. **Priority of Interest**

(a) If, under federal law, there is a federal interest in a Tobacco Fund Invention due to federal funding of the research leading to the Tobacco Fund Invention, the federal interest shall take priority over the interests of any party to this MOU.

(b) If, under the terms of any grants from non-governmental parties, there is an interest by the grantor in a Tobacco Fund Invention due to the grantor's funding of the research leading to the Tobacco Fund Invention, the grantor's interest shall take priority over the interest of any party to this MOU.

(c) Before entering into any agreement for the acquisition of the University's rights in a Tobacco Fund Invention by a non-governmental entity, the University shall require that the non-governmental entity provide as part of the agreement an affidavit to the State of Maryland that the non-governmental entity is not (a) a business entity that manufactures or distributes tobacco products; (b) a subsidiary of such a business entity; or (c) an entity that owns or controls as a subsidiary or otherwise, such a business entity.

10. **Committee**

(a) Each signatory to this MOU shall appoint one representative to a committee that shall recommend to the parties: (i) any policies needed by the University for reporting commercialization activities related to Tobacco Fund Inventions; (ii) any changes needed in this MOU; (iii) any policies needed by the University for use of the revenues from Tobacco Fund Inventions that are reserved for translational research; and, (iv) with advice from the parties' legal counsel, what confidentiality agreements are needed among or between the parties so that

disclosure of information about Tobacco Fund Inventions by the University to TEDCO or the other signatories does not prejudice patent rights or commercialization activities related to Tobacco Fund Inventions.

(b) The committee shall be appointed on or before June 1, 2001. The University shall provide to the committee, on or before June 30, 2001, a plan satisfactory to DHMH for expediting translational research . The committee shall meet quarterly for the first year following the award of research funds. Thereafter the committee shall meet semi-annually or as determined necessary by the committee members. The first meeting shall take place on or before June 30, 2001 to advise UMMG on the proposed plan for translational research.

11. **Notices** Notices to be provided to parties shall be mailed to the following addresses, or to an alternative address designated in writing by the recipient party:

To University of Maryland Baltimore:
Vice President for Academic Affairs
University of Maryland, Baltimore
515 West Lombard Street, 4th Floor
Baltimore, MD 21201

To DHMH:
Director, MD Cigarette Restitution Fund
Dept. of Health & Mental Hygiene
201 West Preston Street, Room 500
Baltimore, MD 21201

To TEDCO:
Director, Technology Transfer
Maryland Technology Development Corp.
5575 Sterrett Place, Suite 240
Columbia, MD 21044

To DBED:
State Technology Coordinator
Dept. of Business & Economic Development
217 East Redwood Street, 20th Floor
Baltimore, MD 21202

12. **Entire Agreement** This MOU and its Exhibit(s)contain the entire agreement among

the parties with respect to the Intellectual Property. No amendments or changes to this MOU shall be effective unless made in writing and signed by authorized representatives of all parties who have executed this MOU.

13. **No Third Party Rights Created** This MOU is not intended to create and does not create legal rights on the part of any individual or business that is not a party to this MOU.

SIGNATURES/DATE:

University of Maryland, Baltimore
by David J. Ramsay, President

Department of Health and Mental Hygiene
by Georges C. Benjamin, MD, Secretary

Department of Business and Economic Development
by David S. Iannucci, Secretary

Phillip A. Singerman 4/20/01
Maryland Technology Development Corporation
by Phillip A. Singerman, Executive Director

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APPENDIX B

Memorandum of Understanding with the Johns Hopkins Institutions

MEMORANDUM OF UNDERSTANDING
REGARDING RESULTS OF RESEARCH
SUPPORTED WITH GRANTS FROM THE TOBACCO FUND

This Memorandum of Understanding ("MOU") is entered into by the Johns Hopkins University ("the University"), acting on behalf of the Johns Hopkins Institutions (as defined by Section 13- 1101(k)), Health General Article) ("JHI"), and by the Maryland Department of Health and Mental Hygiene ("DHMH"), an executive agency of the State of Maryland, and by the Maryland Department of Business and Economic Development ("DBED"), an executive agency of the State of Maryland, and by the Maryland Technology Development Corporation ("TEDCO"), a corporation and public instrumentality of the State of Maryland, to fulfill the requirements of Section 13-1116(b)(2) of the Health General Article, Annotated Code of Maryland.

Recitals. In accordance with Maryland Law, Section 13-1116, Health General Article, Annotated Code of Maryland, the University, directly or through another member of the Johns Hopkins Institutions will apply for, and anticipates receiving, a Statewide Academic Health Center Cancer Research Grant ("Cancer Research Grant") from DHMH. The Cancer Research Grant will be made from the Maryland Cigarette Restitution Fund ("the Fund") for the purpose of conducting cancer research. More specifically, the Cancer Research Grant will be for the purpose of enhancing cancer research activities that may lead to a cure for a targeted cancer and increasing the rate at which cancer research activities are translated into treatment protocols in Maryland. As a condition of receiving a Cancer Research Grant, the University (representing the Johns Hopkins Institutions), enters into this MOU with DBED, TEDCO, and DHMH (the State Agencies) concerning issues specified in Section 13-1116(b)(2).

Agreements.

1. **Research Plan** A Cancer Research Grant will support activities to conduct cancer research under a research plan ("Research Plan") submitted to DHMH as required by law. Activities under a Research Plan may have results, products, inventions, and discoveries ("Intellectual Property") useful in the prevention, treatment and cure of cancer. Such Intellectual

Property will be owned by the University and managed in accordance with its institutional policies concerning intellectual property, especially the Johns Hopkins University Intellectual Property Policy as approved October 27, 1992, and amended March 27, 2001, ("Patent Policy"). In accordance with State law, this MOU is not intended to require any modification in the Patent Policy or any departures from the Patent Policy.

2. **Publication and Dissemination of Research Results** The University shall encourage faculty to publish and otherwise disseminate all knowledge and information derived from research supported by the Fund, and shall require faculty conducting research supported by the Fund to acknowledge the support from the Fund in any publication resulting from the research. The University shall work in conjunction with the Cancer Council in order to communicate results of the research supported by the Fund to the other Statewide Academic Health Centers, to general practitioners, to Maryland legislators, and to the general public.

3. **Invention Disclosures** Subject to the provisions in Section 8, the University shall screen faculty disclosures of inventions made with support from Cancer Research Grants (collectively, "Grants") to identify Intellectual Property. As the University identifies Intellectual Property, it shall inform the State Agencies of the Intellectual Property within 60 days of disclosure to the School of Medicine Office of Technology Licensing (OTL) or the University Office of Technology Transfer (OTT), as appropriate, the invention title or other description of the Intellectual Property, and a brief explanation of the Intellectual Property. To expedite actions to carry out research needed to translate the results of Grants-supported work to treatment protocols, clinical trials, commercialization of Tobacco Fund Inventions, and population research ("translational research"), the Intellectual Property, including but not limited to any invention

within the Intellectual Property (a "Tobacco Fund Invention"), shall be reviewed quarterly, by an appropriate group of scientists and technology development personnel in the University's Office of Technology Licensing (OTL) or Office of Technology Transfer (OTT), as determined by the University, which shall determine, after appropriate review, for each Tobacco Fund Invention, whether the University will elect to take title to the invention. Following a decision to take title, the University shall require inventors subject to the Patent Policy to assign their interests in the invention to the University.

4. **University Commercialization**

(a) As to each Tobacco Fund Invention assigned to the University, it shall explore potential translational research, sources of funding for translational research, costs of clinical trials, and costs of treatment under clinical protocols.

(b) The University shall make best efforts to commercialize each Tobacco Fund Invention being managed by the University through a license or similar arrangement with an entity organized under the laws of Maryland and having its principal place of business in Maryland or an entity which would use the Tobacco Fund Invention in manufacturing in Maryland.

(c) At the outset of commercialization efforts for a Tobacco Fund Invention accepted by the University for management and commercialization, the University shall consult with DBED and TEDCO to identify potential licensees as described in the preceding sentence.

(d) In any event, the final decision regarding with whom to license a Tobacco Fund Invention rests with the University.

5. **Due Diligence and Reassignment**

(a) If the University decides not to take title to a Tobacco Fund Invention, or having taken title, elects to abandon all pending patent applications and/or marketing efforts for the Tobacco Fund Invention, the University shall give written notice to the other parties to this MOU within 30 days of making the decision and shall include a summary of efforts undertaken to commercialize within Maryland.

(b) The State Agencies and the University will work together to identify potential opportunities to commercialize a Tobacco Fund Invention. If at any time a party to this MOU finds that the University is not making best efforts to commercialize a Tobacco Fund Invention, the University and the State Agencies shall work together to improve such efforts. If after fifteen months from an invention disclosure a party to this MOU finds that the University has not made best efforts to commercialize a Tobacco Fund Invention as required by this MOU, that party may give written notice to the University. Within 60 days of that notice, the University shall either agree to abandon the invention and give notice pursuant to (a), or meet with the other parties to review commercialization activities and the University's plans for further activities. If the explanation and/or plan is not acceptable to the State Agencies, or the State Agencies decide that the University has not implemented the plan after reasonable opportunity, the University shall be given final written notice by the State Agencies of their intent to take title. Within 30 days the University may request a referral to an advisory panel whose membership shall be mutually agreed to by the University and the State Agencies. The advisory panel shall within 30 days meet with representatives of both the University and the State Agencies to collect information. Within 30 days of the meeting, the advisory panel shall issue a decision that shall be binding on

all parties. In the event that both the University and the State Agencies decline to take title to a Tobacco Fund Invention, then the Tobacco Fund Invention shall revert to the inventor, as provided for in the University's Patent Policy.

(c) Following notice by the University given under part (a), or following a decision by the advisory panel to assign title to the State Agencies under part (b), the State Agencies within 60 days may elect that the Tobacco Fund Invention be assigned or licensed upon reasonable terms to TEDCO or any entity identified by the State Agencies. The terms of the assignment or license under this subparagraph shall include: (i) a reserved right on the part of the University to use the Tobacco Fund Invention for academic purposes and to permit other academic and research institutions that are nonprofit in nature to use the Tobacco Fund Invention for academic purposes; (ii) an obligation on the assignee's or licensee's part to make best efforts to seek from any eventual commercial licensee of the Tobacco Fund Invention a payment to the University sufficient to reimburse the University for out of pocket expenses associated with patenting and marketing the Tobacco Fund Invention, the payment to be due upon execution of the license; (iii) recognition that the University will have no financial responsibility for expenses associated with patenting and marketing the Tobacco Fund Invention which expenses are incurred after notice under part (a) or a decision by the advisory panel assigning title to the State Agencies under part (b) of this paragraph.

(d) In the event the State Agencies take title to the Tobacco Fund Invention as provided in part (c) above, after out-of-pocket expenses have been paid by the University, twenty-five percent of the remaining revenue from a Tobacco Fund Invention available for distribution by the University shall be managed and distributed in accordance with the Johns Hopkins

University Intellectual Property Policy. After out-of-pocket expenses have been paid by the University, seventy-five percent of the remaining revenue from a Tobacco Fund Invention available for distribution by the University shall be used to support cancer-related translational research/commercialization ("Translational Research Fund"), which includes 10% Total Direct Costs to be used for the management of the Translational Research Fund.

6. **Licensing** Any license or assignment of a Tobacco Fund Invention made by any party to this MOU shall be subject to a continuing, non-exclusive, royalty-free right of JHI to use the Tobacco Fund Invention to conduct research and clinical care using the Tobacco Fund Invention and also shall be subject to a right on the University's part to permit other nonprofit academic or research institutions to use the Tobacco Fund Invention to conduct research. Also, any license made by any of the parties for commercialization shall include provisions intended to promote treatment protocols and clinical trials being conducted in Maryland (if permitted by the federal rules then in effect) so that the results of the Cancer Research Grants can be available to Maryland citizens at the earliest practicable opportunity.

7. **Revenue** In the event the University licenses or commercializes a Tobacco Fund Invention (a) after out-of-pocket expenses have been paid by the University, seventy-five percent of the remaining revenue from a Tobacco Fund Invention available for distribution by the University shall be managed and distributed in accordance with the Johns Hopkins University Intellectual Property Policy.

(b) After out-of-pocket expenses have been paid by the University, twenty-five percent of the remaining revenue from a Tobacco Fund Invention available for distribution by the University shall be used to support cancer-related translational research/commercialization ("Translational

Research Fund"), which includes 10% Total Direct Costs to be used for the management of the Translational Research Fund.

8. **Reporting** No less than 30 days prior to each scheduled meeting of the committee defined in section 10, the University shall report to the State Agencies plans and activities of the University to develop, license and commercialize the Intellectual Property and any involvement of Maryland businesses in development of the Intellectual Property. If any report required pursuant to this Section or Section 3 includes information of the University or third parties which, pursuant to Section 10-617(d) or Section 10-618(d) of the Maryland Public Information Act, is not required to be disclosed in response to a request under the Maryland Public Information Act, the University shall mark such portions of the report "Confidential". The parties agree that invention disclosures and activity reports submitted in accordance with this MOU will in all likelihood contain some or all confidential commercial information, confidential financial information and/or trade secrets as described in Section 10-617(d) and shall be handled accordingly. In the event that there is a request for release of this information, the State Agencies shall make every effort to protect this information and agrees to provide prior written notice reasonably in advance to provide the University the opportunity to respond or intervene.

9. **Priority of Interest**

(a) If, under federal law, there is a federal interest in a Tobacco Fund Invention due to federal funding of the research leading to the Tobacco Fund Invention, the federal interest shall take priority over the interests of any party to this MOU.

(b) If, under the terms of any grants from or contracts involving research with non-governmental parties, there is an interest by the grantor in a Tobacco Fund Invention due to the

grantor's funding of the research leading to the Tobacco Fund Invention, the grantor's interest shall take priority over the interest of any party to this MOU.

(c) The University agrees it will not enter into a license with a non-governmental entity that (a) manufactures or distributes tobacco products; (b) is a subsidiary of such a business entity; or (c) is an entity that owns or controls as a subsidiary or otherwise, such a business entity. Before entering into any agreement for the acquisition of the University's rights in a Tobacco Fund Invention by a non-governmental entity, the University shall require that the non-governmental entity provide as part of the agreement an affidavit to the State of Maryland that the non-governmental entity is not (a) a business entity that manufactures or distributes tobacco products; (b) a subsidiary of such a business entity; or (c) an entity that owns or controls as a subsidiary or otherwise, such a business entity.

10. **Committee** Each signatory to this MOU shall appoint one representative to an advisory committee. Other ad hoc participants may attend on an as needed basis. The Committee shall reach decisions by consensus. The Committee shall recommend to the parties: (a) any suggested actions which should be taken with respect to the commercialization activities related to the Tobacco Fund Invention; (b) any issues related to this MOU; (c) any suggested actions which should be taken with respect to the University's use of the revenues from Tobacco Fund Inventions that are reserved for translational research; and, (d) with advice from the parties' legal counsel, what confidentiality agreements are needed among or between the parties so that disclosure of information about Tobacco Fund Inventions by the University to TEDCO or the other signatories does not prejudice patent rights or commercialization activities related to Tobacco Fund Inventions. This committee will function as an advisory committee only. The

committee shall be appointed on or before June 1, 2001. The Committee will receive on or before June 30, 2001, a plan satisfactory to DHMH for expediting translational research . The committee shall meet quarterly for the first year following the award of research funds. Thereafter, the committee shall meet semi-annually or as determined necessary by the mutual agreement of the committee members. The first meeting shall take place on or before June 30, 2001 to advise JHI on the proposed plan for translational research.

11. **Notices** Notices to be provided to parties shall be mailed to the following addresses, or to an alternative address designated in writing by the recipient party:

To: Johns Hopkins University:
Vice President for Research
The Office of the Provost
The Johns Hopkins University
276 Garland Hall, 34th and Charles Streets
Baltimore, MD 21218

To: DHMH:
Director, MD Cigarette Restitution Fund
Dept. of Health & Mental Hygiene
201 West Preston Street, Room 500
Baltimore, MD 21201

To: TEDCO:
Director, Technology Transfer
Maryland Technology Development Corp
5575 Sterrett Place, Suite 240
Columbia, MD 21044

To: DBED:
State Technology Coordinator
Dept. of Business & Economic Development
217 East Redwood Street, 20th Floor
Baltimore, MD 21202

12. **Entire Agreement** This MOU and its Exhibit(s) contain the entire agreement among the parties with respect to the Intellectual Property. No amendments or changes to this MOU shall be effective unless made in writing and signed by authorized representatives of all parties who have executed this MOU.

13. **No Third Party Rights Created** This MOU is not intended to create and does not create legal rights on the part of any individual or business that is not a party to this MOU.

14. **Term of Agreement** This MOU shall be effective upon signature of all parties and will terminate on May 31, 2016, unless terminated earlier by mutual agreement. However, the provisions of Section 7 shall survive the termination of this agreement.

SIGNATURES:

Johns Hopkins University
by William R. Brody, President — Date 5/21/01

Department of Health and Mental Hygiene
by Georges C. Benjamin, MD, Secretary — Date 5/21/01

Department of Business and Economic Development
by David S. Iannucci, Secretary — Date 5/21/01

Maryland Technology Development Corporation
by Phillip A. Singerman, PhD, Executive Director — Date 5/24/01

APPENDIX C
Publications from the University of Maryland Medical Group under the CRFP

1. Ali, T.Z., et al., *Splenic hamartoma: immunohistochemical and ultrastructural profile of two cases.* Int J Surg Pathol, 2005. **13**(1): p. 103-11.
2. Bachman, K.E., et al., *p21(WAF1/CIP1) mediates the growth response to TGF-beta in human epithelial cells.* Cancer Biol Ther, 2004. **3**(2): p. 221-5.
3. Bachman, K.E. and B.H. Park, *Duel nature of TGF-beta signaling: tumor suppressor vs. tumor promoter.* Curr Opin Oncol, 2005. **17**(1): p. 49-54.
4. Badros, A.Z., *Case 38-2004: a large tumor of the skull.* N Engl J Med, 2005. **352**(15): p. 1610; author reply 1610.
5. Badros, A.Z., et al., *Phase II study of G3139, a Bcl-2 antisense oligonucleotide, in combination with dexamethasone and thalidomide in relapsed multiple myeloma patients.* J Clin Oncol, 2005. **23**(18): p. 4089-99.
6. Bauer, K.S., et al., *A phase I and pharmacologic study of idarubicin, cytarabine, etoposide, and the multidrug resistance protein (MDR1/Pgp) inhibitor PSC-833 in patients with refractory leukemia.* Leuk Res, 2005. **29**(3): p. 263-71.
7. Bedor, M., C. Alexander, and M.J. Edelman, *Management of common symptoms of advanced lung cancer.* Curr Treat Options Oncol, 2005. **6**(1): p. 61-8.
8. Berlin, A.A., et al., *Inhibition of stem cell factor reduces pulmonary cytokine levels during allergic airway responses.* Clin Exp Immunol, 2004. **136**(1): p. 15-20.
9. Bolanos-Meade, J., et al., *A phase II study of timed sequential therapy of acute myelogenous leukemia (AML) for patients over the age of 60: two cycle timed sequential therapy with topotecan, ara-C and mitoxantrone in adults with poor-risk AML.* Leuk Res, 2004. **28**(6): p. 571-7.
10. Bolanos-Meade, J., et al., *Lymphocytic pneumonitis as the manifestation of acute graft-versus-host disease of the lung.* Am J Hematol, 2005. **79**(2): p. 132-5.
11. Bolanos-Meade, J., et al., *Timed sequential therapy of acute myelogenous leukemia in adults: a phase II study of retinoids in combination with the sequential administration of cytosine arabinoside, idarubicin and etoposide.* Leuk Res, 2003. **27**(4): p. 313-21.
12. Bolanos-Meade, J., G.L. Phillips, 2nd, and A. Badros, *Tandem transplantation in multiple myeloma.* Oncology (Williston Park), 2003. **17**(3): p. 389-98; discussion 398-400, 405-7.
13. Brodie, A., et al., *Therapeutic observations in MCF-7 aromatase xenografts.* Clin Cancer Res, 2005. **11**(2 Pt 2): p. 884s-8s.
14. Brodie, A., et al., *Model systems: mechanisms involved in the loss of sensitivity to letrozole.* J Steroid Biochem Mol Biol, 2005. **95**(1-5): p. 41-8.
15. Brooks, S.E., et al., *Resource utilization for patients undergoing hysterectomy with or without lymph node dissection for endometrial cancer.* Gynecol Oncol, 2002. **85**(2): p. 242-9.
16. Carter, W.B., *HER2 signaling--induced microvessel dismantling.* Surgery, 2001. **130**(2): p. 382-7.
17. Carter, W.B. and M.D. Ward, *Parathyroid-produced angiopoietin-2 modulates angiogenic response.* Surgery, 2001. **130**(6): p. 1019-27.

18. Costello, L.C., et al., *Role of zinc in the pathogenesis and treatment of prostate cancer: critical issues to resolve.* Prostate Cancer Prostatic Dis, 2004. **7**(2): p. 111-7.
19. Costello, L.C., et al., *Re: Zinc supplement use and risk of prostate cancer.* J Natl Cancer Inst, 2004. **96**(3): p. 239-40; author reply 240-1.
20. Costello, L.C., et al., *Zinc and prostate cancer: a critical scientific, medical, and public interest issue (United States).* Cancer Causes Control, 2005. **16**(8): p. 901-15.
21. Cui, Y., et al., *Body mass and stage of breast cancer at diagnosis.* Int J Cancer, 2002. **98**(2): p. 279-83.
22. Cui, Y., et al., *Can obesity explain the racial difference in stage of breast cancer at diagnosis between black and white women?* J Womens Health Gend Based Med, 2002. **11**(6): p. 527-36.
23. Cunningham, S.C., et al., *Neoadjuvant chemoradiation to convert locally advanced pancreatic body adenocarcinoma to resectable disease.* Clin Adv Hematol Oncol, 2003. **1**(12): p. 741-2.
24. Cunningham, S.C., D. Shibata, and C. Volpe, *Isolated abdominal wound metastasis from a gastrointestinal stromal tumor.* Int J Gastrointest Cancer, 2003. **33**(2-3): p. 129-32.
25. Cusnir, M. and Y.Z. Patt, *Novel systemic therapy options for hepatocellular carcinoma.* Cancer J, 2004. **10**(2): p. 97-103.
26. Dawson, N.A., *Bisphosphonates: their evolving role in the management of prostate cancer-related bone disease.* Curr Opin Urol, 2002. **12**(5): p. 413-28.
27. Dawson, N.A., *Therapeutic benefit of bisphosphonates in the management of prostate cancer-related bone disease.* Expert Opin Pharmacother, 2003. **4**(5): p. 705-16.
28. Dawson, N.A., *Point: It's never too soon.* Can J Urol, 2003. **10**(6): p. 2036-7.
29. Dawson, N.A., R.O. Fourcade, and D. Newling, *The management of localized prostate cancer.* Prostate Cancer Prostatic Dis, 2002. **5 Suppl 2**: p. S3-7.
30. Dawson, N.A., et al., *A phase II trial of gefitinib (Iressa, ZD1839) in stage IV and recurrent renal cell carcinoma.* Clin Cancer Res, 2004. **10**(23): p. 7812-9.
31. Dawson, N.A. and S.F. Slovin, *Novel approaches to treat asymptomatic, hormone-naive patients with rising prostate-specific antigen after primary treatment for prostate cancer.* Urology, 2003. **62 Suppl 1**: p. 102-18.
32. Deacu, E., et al., *Activin type II receptor restoration in ACVR2-deficient colon cancer cells induces transforming growth factor-beta response pathway genes.* Cancer Res, 2004. **64**(21): p. 7690-6.
33. DiBiase, S.J., et al., *Outcome analysis for stage IE and IIE thyroid lymphoma.* Am J Clin Oncol, 2004. **27**(2): p. 178-84.
34. Doyle, L.A. and D.D. Ross, *Multidrug resistance mediated by the breast cancer resistance protein BCRP (ABCG2).* Oncogene, 2003. **22**(47): p. 7340-58.
35. Edelman, M.J., *New directions in the treatment of non-small cell lung cancer: an overview.* Oncologist, 2001. **6 Suppl 1**: p. 1-3.
36. Edelman, M.J., *Neoadjuvant chemotherapy in early-stage non-small cell lung cancer.* Expert Rev Anticancer Ther, 2001. **1**(2): p. 229-35.
37. Edelman, M.J., *Past, present, and future of gemcitabine and carboplatin regimens in advanced non-small cell lung cancer.* Lung Cancer, 2002. **38 Suppl 2**: p. S37-43.
38. Edelman, M.J., *Taking stock of targeted therapy in cancer: rational expectations or irrational exuberance?* Expert Rev Anticancer Ther, 2003. **3**(2): p. 127-9.

39. Edelman, M.J., *Neoadjuvant chemotherapy and chemoradiotherapy for non-small cell lung cancer: current status and future prospects.* Expert Opin Pharmacother, 2003. **4**(6): p. 843-52.
40. Edelman, M.J., *Gemcitabine and carboplatin regimens in advanced non-small-cell lung cancer: focus on randomized phase III trials.* Clin Lung Cancer, 2003. **4 Suppl 2**: p. S40-4.
41. Edelman, M.J., *Evidence-based approaches to overcoming barriers to clinical trial accrual.* Cancer J, 2004. **10**(5): p. 288-9.
42. Edelman, M.J., *Lung cancer - Second Annual Winter Conference.* IDrugs, 2005. **8**(5): p. 366-9.
43. Edelman, M.J., *Second-line chemotherapy and beyond for non-small-cell lung cancer.* Clin Adv Hematol Oncol, 2004. **2**(6): p. 373-8.
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APPENDIX D

Publications from the Johns Hopkins Institutions under the CRFP

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Publications from the Johns Hopkins Institutions under the CRFP

Anthony Alberg, Ph.D.

1. Zheng, Y. L., Loffredo, C. A., Yu, Z., Jones, R. T., Krasna, M. J., **Alberg, A. J.** et al. (2003). Bleomycin-induced chromosome breaks as a risk marker for lung cancer: a case-control study with population and hospital controls. *Carcinogenesis, 24,* 269-274.

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Mary Armanios, Ph.D.

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Yin Yao, Ph.D.

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***CRF funded project or CRF funded investigator activity**