

# Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is “None”, please specify “None” as your response. “Not applicable” is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution: Institute for Hepatitis and Virus Research**
2. **Reporting Period (start and end date of grant award period): 1/1/2011-12/31/2011**
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees): Chari Cohen, MPH, DrPH(c)**
4. **Grant Contact Person’s Telephone Number: 215-489-4930**
5. **Grant SAP Number: 4100054853**
6. **Project Number and Title of Research Project: Project 1, Selective and Therapeutic Elimination of Cells that Produce Hepatitis B Virus**
7. **Start and End Date of Research Project: 1/1/2011-12/31/2011**
8. **Name of Principal Investigator for the Research Project: Timothy Block, PhD**
9. **Research Project Expenses.**

9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

\$ 16,012.67

9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project	Cost
None			

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

Last Name	Position Title	% of Effort on Project
Timothy Block	PI	5%
Ju-Tao Guo	Co-PI	5%
Pamela Norton	Director of Student Interns	2%
Andrea Cuconati	Co-PI	5%
Hai-Tao Guo	Co-PI	5%
John Rogowosky	Student Intern	100%
Mathew Campagna	Student Intern	100%
Laura Dipaulohave	Student Intern	100%

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

Type of Scientific Equipment	Value Derived	Cost
None		

**10. Co-funding of Research Project during Health Research Grant Award Period.** Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes \_\_\_\_\_ No  \_\_\_\_\_

If yes, please indicate the source and amount of other funds:

**11. Leveraging of Additional Funds**

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes \_\_\_\_\_ No  \_\_\_\_\_

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert “not funded” in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

A. Title of research project on grant application	B. Funding agency (check those that apply)	C. Month and Year Submitted	D. Amount of funds requested:	E. Amount of funds to be awarded:
	<input type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify: _____)		\$	\$
	<input type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify: _____)		\$	\$
	<input type="checkbox"/> NIH <input type="checkbox"/> Other federal (specify: _____) <input type="checkbox"/> Nonfederal source (specify: _____)		\$	\$

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes  No

If yes, please describe your plans: We are in the process of writing additional grants to federal and private funding sources

**12. Future of Research Project.** What are the future plans for this research project?

While will continue to study Oubain to confirm and understand this property, and we will be screening additional compounds that may exert a similar effect. As we identify drugs which have this selective effect, the correlation of the drugs' known mechanism and the selective targeting of HBV-producing cells may reveal previously unknown information about the biology of HBV infection. In addition, it may result in the discovery of a novel drug property that may eventually lead to a new use in hepatitis B.

**13. New Investigator Training and Development.** Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes  No

If yes, how many students? Please specify in the tables below:

	Undergraduate	Masters	Pre-doc	Post-doc
Male	2			
Female	1			
Unknown				
<b>Total</b>	<b>3</b>			

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic				
Unknown	3			
<b>Total</b>	<b>3</b>			

	Undergraduate	Masters	Pre-doc	Post-doc
White	3			
Black				
Asian				
Other				
Unknown				
<b>Total</b>	<b>3</b>			

**14. Recruitment of Out-of-State Researchers.** Did you bring researchers into Pennsylvania to carry out this research project?

Yes  No

If yes, please list the name and degree of each researcher and his/her previous affiliation:

**15. Impact on Research Capacity and Quality.** Did the health research project enhance the quality and/or capacity of research at your institution?

Yes  No

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

The continued training of undergraduate students allows our researchers to strengthen their teaching skills, offers diversity and renewed energy to our research center, and helps to train the next generation of scientific researchers in Pennsylvania.

**16. Collaboration, business and community involvement.**

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes  No

If yes, please describe the collaborations:

16(B) Did the research project result in commercial development of any research products?

Yes  No

If yes, please describe commercial development activities that resulted from the research project:

16(C) Did the research lead to new involvement with the community?

Yes  No

If yes, please describe involvement with community groups that resulted from the research project:

This research project allowed us to widen and strengthen our relationships with Pennsylvania-based colleges and universities. As we recruit our student interns from colleges and universities throughout Pennsylvania, we have begun to develop relationships with faculty members from a number of institutions. Individual faculty members were contacted to promote the summer internship program to promising science majors, and in the process, were made aware of the multi-faceted and renowned research taking place at the Institute for Hepatitis and Virus Research. These budding relationships have been strengthened over the past few years as the summer intern program has progressed and faculty members have seen the impressive final projects of their students.

It is our expectation that these new relationships will be expanded and solidified over the next few years to include new potential partnerships for both science education and research.

### **17. Progress in Achieving Research Goals, Objectives and Aims.**

List the project goals, objectives and specific aims (as contained in the grant application's strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the period that the project was funded (i.e., from project start date through end date). Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

**There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha ( $\alpha$ ) and beta ( $\beta$ ) should not print as boxes ( $\square$ ) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.**

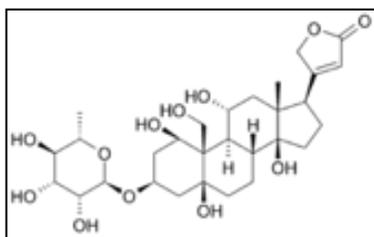
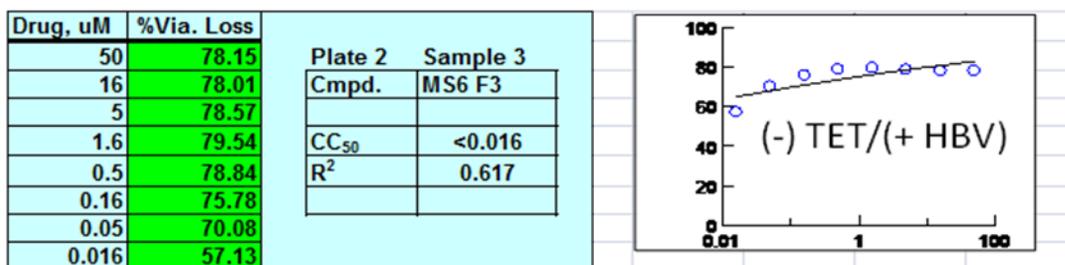
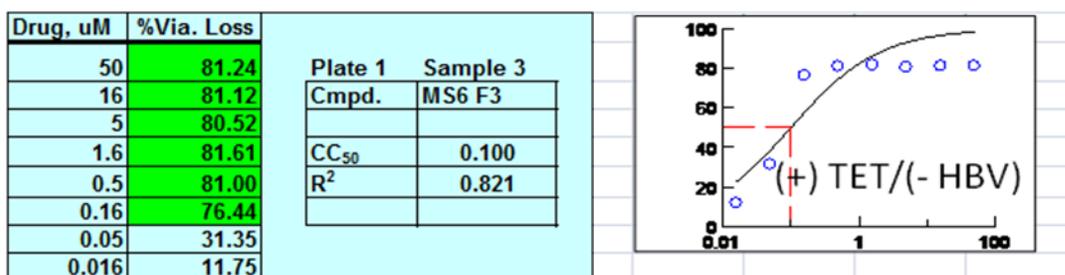
HBV producing cells, in culture, are consistently approximately 2-3 times more growth sensitive to NaK ATPase ion channel inhibitors, Oubain and Oleandrin, than are congenic cells that do not produce HBV. This is an interesting lead, since although the difference in sensitivity is small, it is reproducible, and suggests that HBV producing cells may require a level of NaK ATPase activity greater than do uninfected cells. It also validates the approach. Another possibility is that the effects of Oubain and Oleandrin are due to "off target" effects. Two strategies will be taken, from here. The first will be to determine if other NaK ATPase inhibitors or other structurally related compounds have similar or, hopefully, enhanced, selective HBV cell

producer killing affects against the cell systems used, to date, and other cell systems. If so, the mechanism of action and specific viral gene products associated with the selective cell killing will be pursued. The second strategy will be to screen a larger library compounds of selective HBV killing.

In any event, the results could also suggest that people who are chronic carriers of HBV might have selective sensitivity to drugs that are otherwise well tolerated by uninfected individuals.

Figure 1: Oubain appears to be selectively toxic to HBV producing cells. The liver tissue cancer cell derived line Huh7, was engineered such that it produces HBV when tetracycline is removed from the culture medium. In this way, the effect upon cell growth of various drugs, such as Oubain (shown here, in Figure 1A.) can be evaluated under conditions where the only apparent difference between the cells is tetracycline and the production of HBV. At 0.16 uM, Oubain has little effect upon the growth of these cells when HBV is not produced (tet on, less than 20% cytotoxicity).

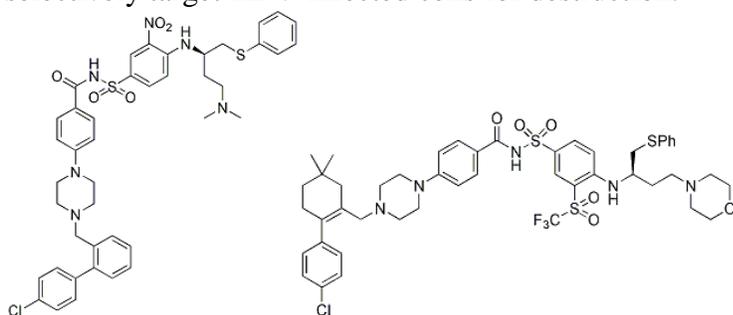
Figure 1A. Chemical structure of Oubain.



However, in the presence of even 0.016uM Oubain, as much as 60% of the cells are killed, when HBV is produced.

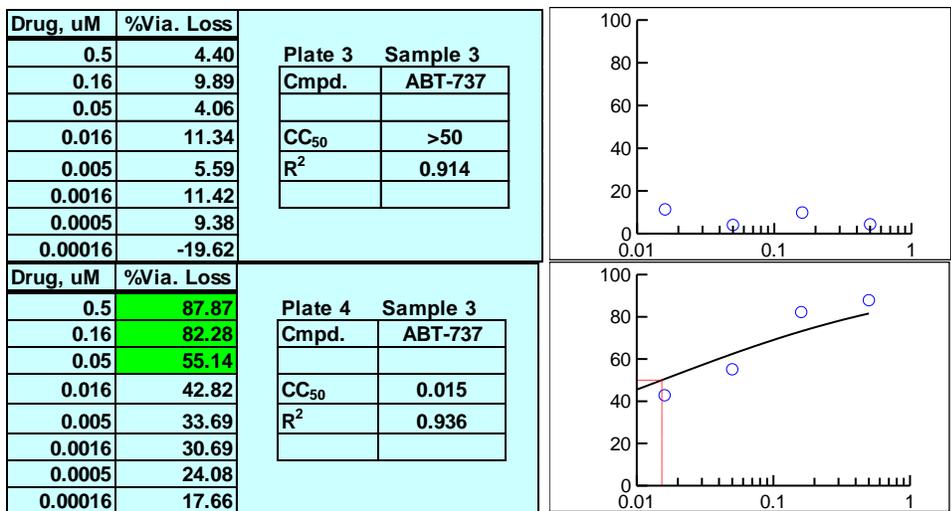
Our results indicate that this FDA-approved drug which is normally used to treat cardiac problems such as arrhythmia, displayed the ability to selectively kill hepatitis B virus (HBV)-producing cells in cell culture. This property is interesting because it suggests that it may be possible to completely cure hepatitis B by destroying the minority of cells in the chronically infected liver that are actively replicating and producing the virus.

We have also begun to study a class of compounds that are currently being studied at a major pharmaceutical company as potential treatment for acute myeloid leukemia and other cancers. These are termed BH3 domain mimetics, and they function by inhibiting a family of proteins called Bcl2 pro-survival factors. In cancer cells, the presence of these proteins prevents the process of apoptosis, or programmed cell death, thereby promoting cancer growth. We have observed that HBV-producing cells also undergo a weak level of apoptosis induction, possible due to metabolic stress on the cells from the process of viral replication. We reasoned that inhibition of Bcl-2 proteins in these cells may lead to greater levels of apoptosis, and therefore selectively target HBV-infected cells for destruction.



**Figure 1. Chemical structures of BH3 domain mimetics. Left: ABT-737. Right: ABT-263 (navitoclax).**

Indeed we have observed that ABT-737 and -263 both appear to induce apoptosis in HBV producing cells. Using a cell line that harbors a copy of the HBV genome that can be switched on or off (*i.e.*, induced), we found that treatment with ABT-737 resulted in lower levels of viable cells after incubation, but only when HBV expression had been turned on. With no expression and production of the virus, the cells are comparatively resistant (Figure 2). Similar results have been obtained with ABT-263. The effect is much more selective than that of Oubain; the CC<sub>50</sub> value for ABT-737 may be as low as 0.015 micromolar in HBV producing cells, with no effect on HBV negative cells. Although these observations are preliminary, we will be working on confirming and extending the result in the near future.



**Figure 2. ABT-737 selectively reduces viability of HBV expressing liver cancer cells.** % Viability loss indicates increase in cell death or growth arrest, compared to controls without drug. In graphs, Y axis=% viability loss, X axis= compound concentration in micromolar.

**18. Extent of Clinical Activities Initiated and Completed.** Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be “No.”

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?  
 Yes  
 No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?  
 Yes  
 No

**If “Yes” to either 18(A) or 18(B), items 18(C) – (F) must also be completed.** (Do NOT complete 18(C-F) if 18(A) and 18(B) are both “No.”)

18(C) How many hospital and health care professionals were involved in the research project?

\_\_\_\_\_Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

\_\_\_\_\_Number of subjects originally targeted to be included in the study  
\_\_\_\_\_Number of subjects enrolled in the study

**Note:** Studies that fall dramatically short on recruitment are encouraged to provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:

\_\_\_\_\_Males  
\_\_\_\_\_Females  
\_\_\_\_\_Unknown

Ethnicity:

\_\_\_\_\_Latinos or Hispanics  
\_\_\_\_\_Not Latinos or Hispanics  
\_\_\_\_\_Unknown

Race:

\_\_\_\_\_American Indian or Alaska Native  
\_\_\_\_\_Asian  
\_\_\_\_\_Blacks or African American  
\_\_\_\_\_Native Hawaiian or Other Pacific Islander  
\_\_\_\_\_White  
\_\_\_\_\_Other, specify: \_\_\_\_\_  
\_\_\_\_\_Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

**19. Human Embryonic Stem Cell Research.** Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?

Yes  
 No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?

Yes  
 No

19(C) Please describe how this project involved human embryonic stem cells:

**20. Articles Submitted to Peer-Reviewed Publications.**

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication or paper submitted for publication, listed in the table, in a PDF version 5.0.5 (or greater) format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the “Cognition and MRI in Older Adults” research project (Project 1), and two publications for PI Zhang for the “Lung Cancer” research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI

Project 1 – Smith – Publication 2 – Cognition and MRI

Project 3 – Zhang – Publication 1 – Lung Cancer

Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

**Note:** The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

Title of Journal Article:	Authors:	Name of Peer-reviewed Publication:	Month and Year Submitted:	Publication Status (check appropriate box below):
1. None				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published
2.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published
3.				<input type="checkbox"/> Submitted <input type="checkbox"/> Accepted <input type="checkbox"/> Published

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes  No

If yes, please describe your plans: We are currently writing up our preliminary year 1 results for publication, and presentation at professional conferences.

**21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project.**

Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None

**22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment.**

Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert “None”; do not use “Not applicable.” Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

Current treatment for chronic hepatitis B relies on a class of therapeutics that have high resistance profiles. We seek to find new therapeutic avenues that will result in improved patient outcomes and lower resistance in patients with chronic hepatitis B. This research project is an important step in the potential discovery of a novel drug property that may eventually lead to a new use in hepatitis B.

**23. Inventions, Patents and Commercial Development Opportunities.**

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes \_\_\_\_\_ No x\_\_\_\_\_

If “Yes” to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is “No.”)

- a. Title of Invention:
- b. Name of Inventor(s):
- c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):
- d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?  
Yes \_\_\_\_\_ No \_\_\_\_\_

If yes, indicate date patent was filed:

- e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?  
Yes \_\_\_\_\_ No \_\_\_\_\_  
If yes, indicate number of patent, title and date issued:  
Patent number:  
Title of patent:  
Date issued:

- f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes \_\_\_\_\_ No \_\_\_\_\_

If yes, how many licenses were granted? \_\_\_\_\_

- g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes \_\_\_ No \_\_\_\_\_

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes \_\_\_\_\_ No x\_\_\_\_\_

If yes, please describe your plans:

**24. Key Investigator Qualifications.** Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages. *For Nonformula grants only – include information for only those key investigators whose biosketches were not included in the original grant application.*

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**BIOGRAPHICAL SKETCH**

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NAME	POSITION TITLE
Block, Timothy M.	Professor

eRA COMMONS USER NAME			
TBLOCK			
EDUCATION/TRAINING ( <i>Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
State University of New York, Buffalo, NY	B.A.	1975	Biophysics
SUNY-Buffalo, Roswell Park Mem. Inst., NY	Ph.D.	1979	Mol. Virology
Princeton University, Princeton, NJ	Post Doc	1982	Biochemistry

## Positions and Honors

### Positions and Employment

2011-Present Adjunct Professor, The Commonwealth Medical College

2006-Present Founder and President, Pennsylvania Biotechnology Center

2004-Present Founder and President, Institute for Hepatitis and Virus Research

2004-Present Director, Drexel Institute for Biotechnology and Virology Research  
 Professor, Department of Microbiology and Immunology  
 Drexel University College of Medicine

2004-Present Professor, Institute for Hepatitis and Virus Research

1998-2004 Director, Jefferson Center for Biomedical Research  
 Professor, Department of Biochemistry and Molecular  
 Pharmacology  
 Jefferson Medical College of Thomas Jefferson University

1991-Present Co-Founder and President, Hepatitis B Foundation

1991-2004 Associate Professor, Department of Microbiology and Immunology  
 Jefferson Medical College of Thomas Jefferson University

1991-2004 Associate Professor, Department of Biochemistry and Molecular  
 Pharmacology  
 Jefferson Medical College of Thomas Jefferson University

1989-Present Adjunct Professor, The Wistar Institute of University of Pennsylvania

### Other Experience and Professional Memberships

*Editorial Board:* Disease Markers, J of Neurovirology, DNA & Cell Biology, Antiviral Research, Cancer Biomarkers, Emerging Microbes and Infections

*Ad Hoc Reviewer:* Antiviral Therapy, Ann Internal Med, Antiviral Research, Cancer Epidem Biomar, Cancer Research, CRC Reviews, Future Virology, Genes Immun, Hepatology, Int J Clin Lab Res, J Biol Chem, J Gen Virology, J Neurovirol, J Proteome Res, J Virology, Lab Invest, Nature, PLoS Path, PNAS, Science, Viral Hepatitis, Virology

*Consulting Scientist:* Council of Expert Consultants, ABC News, NY NY; Hoffmann-La Roche, Inc.

*Study Sections and National Committees:* US Naval Research Command (1995), NIH NIAD (1999-2000), NIH Oral Biology (1999-2001), NIH Consensus Development Conference on Management of Hepatitis B, NIDDK, NIH (2007-2008), EDRN Internal Review (2007-2010), Alliance of Glycobiologists for Detection of Cancer and Cancer Risk NCI (2007-Present), Consortium for Functional Glycomics, NIGMS, NIH (2008-Present), AASLD SIG for Hepatitis

(2009-Present), NIAID Biological & Emerging Infections Resources Repository Program  
Scientific Working Group (2011-Present)

### **Member of Scientific Advisory Boards**

Hepatitis B Foundation  
Institute for Hepatitis and Virus Research  
Immunotope, Inc.  
BioLeap, LLC  
Pennsylvania Center for Drug Discovery  
Novira Therapeutics

### **Selected Honors and Special Presentations**

1991 Member, Glycobiology Institute of Oxford University, England  
1992-93 EMBO Sabbatical Fellow, Balliol College, Oxford University, England  
1993 Elected Fellow, International Union Against Cancer  
1998 Honorary degree (with Raymond Dwek and Edward Southern) Romania  
Academy of Sciences  
1998 Special Citation, Researcher of the Year, American Liver Foundation  
1998 Visiting Professor, Dygook University, Kyoonyu, Korea  
2000 100 Most Important People of the Century in Bucks County, Intelligencer News  
2000 Heritage Professor, University of Edmonton, Alberta, Canada  
2001 Hepatitis B Foundation, Founder's Award  
2003 Featured Speaker, American Association Cancer Researchers (Phoenix, AZ)  
2003 Elected to the Bulgarian National Academy of Medicine (Honorary Medical  
Doctor)  
2004 Representative, 40<sup>th</sup> Anniversary US/Japan Cooperative Medical Science Program  
2004 Temple University Distinguished Lecturer in Neurovirology and Viral Oncology  
2005 Meeting Chair, International Hepatitis Meeting, Heidelberg, Germany  
2007 Lifetime Achievement Award, Central Bucks, PA  
2007 Distinguished Service Recognition, NCI EDRN  
2007 Visiting Professor of Gastroenterology, University of Michigan  
2007 Special citation from US House of Representatives in recognition of outstanding  
achievements  
2008 Elected AAAS Fellow (American Association for the Advancement of Science)  
2009 Emory Eminent Scholar Seminar  
2010 Judge's Choice CEO of the Year, Phila. Business Journal's Inaugural Life Science  
Award  
2011 Named one of 100 Most Inspiring People in the Life-Sciences Industry in 2011  
(PharmaVoice 100, PharmaVoice Magazine)

### **C. Selected Peer-reviewed Publications (Selected from 135+ peer-reviewed publications)**

#### **Most relevant to the current application**

1. Mehta, A.S, and Block, T.M. (2012). Fucosylated Biomarkers for liver fibrosis, cirrhosis and cancer. *Glycobiology*, In press. PMID: PMC Journal - In Process
2. Comunale, M.A., Wang, M., Rodemich-Betesh, L., Hafner, J., Lamontagne, A., Klein, A., Marrero, J., Di Bisceglie, A., Gish, R., Block, T.M. and Mehta, A. (2011). Novel changes in

glycosylation of serum Apo-J in patients with hepatocellular carcinoma. Cancer Epidemiology, Biomarkers & Prevention, 20(6): 1222-9. PMID: PMC3111882

3. Kawamoto, S., Moriwaki, K., Nakagawa, T., Terao, M., Shinzaki, S., Yamane-Ohnuki, N., Satoh, M., Mehta, A.S., Block, T.M. and Miyoshi, E. (2011). Overexpression of alpha1,6-fucosyltransferase in hepatoma enhances expression of Golgi phosphoprotein 2 in fucosylation-independent manner. International Journal of Oncology, 39(1): 203-8. PMID: PMC3095700

Romano P.R., Mackay A., Vong M., DeSa J., Lamontagne A., Comunale M.A., Hafner J., Block T.M., Lec R. and Mehta A. (2011). Development of recombinant Aleuria aurantia lectins with altered binding specificities to fucosylated glycans. Biochemical & Biophysical Research Communications, 414(1): 84-9. PMID: PMC3202172

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### **BIOGRAPHICAL SKETCH**

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NAME	POSITION TITLE
Ju-Tao Guo, M.D.	Associate Professor

eRA COMMONS USER NAME			
JUTAOGUO1			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Lanzhou University, College of Medicine, Gansu, China	M.D.	07/1985	Medicine
Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China	M.S.	07/1988	Virology
Fox Chase Cancer Center	Postdoctoral	04/1994	Molecular Virology

### **Positions and Employment**

- 1988-1990 Research assistant, Institute of Medicinal Biotechnology (IMB), Chinese Academy of Medical Sciences (CAMS) & Peking Union Medical College (PUMC), Beijing, China
- 1991-1994 Assistant/associate professor, IMB, CAMS & PUMC
- 1994-1997 Postdoctoral associate, Fox Chase Cancer Center
- 1997-1998 Visiting associate professor, IMB, CAMS & PUMC, Beijing, China
- 1998-2004 Research associate/Staff Scientist, Fox Chase Cancer Center
- 2004-2008 Assistant professor, Department of Microbiology and Immunology, Drexel University College of Medicine
- 2008-present Associate professor, Drexel Institute for Biotechnology and Virology Research, Department of Microbiology and Immunology, Drexel University College of Medicine

### **Honors and Professional Memberships**

- 1988 Scientific Research Merit Award, Ministry of Health, China
- 1990 Dr. Satoshi Omura Award, Kitasato Institute & Kitasato University, Japan
- 1990 Outstanding Thesis Award from Beijing Association for Science and Technology.
- 1991 Scientific Research Merit Award, Ministry of Health, China
- 2007 Bruce Witte Scholar, Hepatitis B Foundation, USA

### **Selected peer-reviewed publications (selected from over 50 peer-reviewed publications)**

1. Dong Jiang, Jessica M. Weidner, Min Qing, Haitao Guo, Chunxiao Xu, Xianchao Zhang, Alex Birk, Jinhong Chang, Pei-Yong Shi, Timothy M. Block and **Ju-Tao Guo** (2010) Identification of five interferon-induced cellular proteins that inhibits West Nile virus and dengue virus infection. *J. Virol.* 84(16):8332-8341 (*Covered by JVI Spotlight*)
2. Jiang D., Guo H., Xu C., Wang L., Gu B., Block T. M. and **Guo J.-T.** (2008) Identification of three interferon-inducible cellular enzymes that inhibit the replication of hepatitis C virus. *Journal of Virology*, 82(4):1665-78.
3. Jessica M. Weidner, Dong Jiang, Xiao-Ben Pan, Jinhong Chang, Timothy M. Block and **Ju-Tao Guo** (2010) Interferon-induced cell membrane proteins, IFITM3 and tetherin, inhibit vesicular stomatitis virus infection via distinct mechanisms. *J. Virol.* 84(24):12646-57

4. Guo H., Jiang D., Ma D., Chang J., Dougherty AM., Cuconati A., Block T. M. and **Guo J.-T.** (2009) Activation of pattern recognition receptor-mediated innate immunity inhibits the replication of hepatitis B virus in human hepatocyte-derived cells. *Journal of Virology*. 83(2):847-58.
5. **Guo J.-T.**, Hayashi J. and Seeger C. (2005) West Nile virus inhibits signal transduction pathway of interferon-alpha. *Journal of Virology*. 79(3):1343-1350
6. Xiaowang Qu, Xiao-Ben Pan, Jessica Weidner, Wenquan Yu, Dominic Alonzi, Xiaodong Xu Terry Butters, Timothy Block, **Ju-Tao Guo** and Jinhong Chang. (2011) Inhibitors of endoplasmic reticulum alpha-glucosidases potently suppress hepatitis C virus virion assembly and release. *Antimicrob Agents Chemother*. 55(3):1036-44
7. Chunxiao Xu, Haitao Guo, Xiao-Ben Pan, Richeng Mao, Wenquan Yu, Xiaodong Xu, Lai Wei, Jinhong Chang, Timothy M. Block and **Ju-Tao Guo** (2010) Interferons accelerate the decay of replication-competent nucleocapsids of hepatitis B virus. *J. Virol*. 84(18):9332-9340
8. Haitao Guo, Richeng Mao. Timothy M. Block and **Ju-Tao Guo** (2010). Production and function of the cytoplasmic deproteinized relaxed circular DNA of hepadnaviruses. *J Virol*. 84(1):387-96
9. Dongling Ma, Dong Jiang, Min Qing, Jessica M. Weidner, Xiaowang Qu, Haitao Guo, Jinhong Chang, Baohua Gu, Pei-Yong Shi, Timothy M. Block and **Ju-Tao Guo**. (2009) Antiviral Effect of Interferon lambda against West Nile Virus. *Antiviral Research*, 83(1):53-60
10. Jinhong Chang\*, **Ju-Tao Guo\***, Dong Jiang, Haitao Guo, John M. Taylor and Timothy M. Block. (2008) Liver Specific microRNA, miR-122, Enhances the Replication of Hepatitis C Virus in Non-hepatic Cells. *Journal of Virology*. 82(16):8215-23. \*Equal contribution
11. Guo H., Zhou T., Jiang D., Cuconati A. Xiao G.-H., Block T. M. and **Guo J.-T.** (2007) Regulation of Hepatitis B Virus Replication by Phosphatidylinositol 3-kinase-Akt Signal Transduction Pathway. *Journal of Virology*, 81(18):10072-80
12. Guo H., Jiang D., Zhou T., Cuconati A., Block T. M. and **Guo J.-T.** (2007) Characterization of the Intracellular Deproteinized Relaxed Circular DNA of Hepatitis B Virus: An Intermediate of Covalently Closed Circular DNA Formation. *Journal of Virology*, 81(22):12472-84
13. Zhou T., Guo H., **Guo J.-T\***. Cuconati A, Metha, A and Block T\*. (2006) Hepatitis B Virus e Antigen Production is Dependent upon Covalently Closed Circular (ccc) DNA in HepAD38 Cell Cultures and May Serve as a cccDNA Surrogate in Antiviral Screening Assays. *Antiviral Research*, 72(2):116-24 (\* Co-corresponding authors)
14. **Guo J.-T.**, Zhu Q. and Seeger C. (2003) Cytopathic and noncytopathic interferon responses in cells expressing hepatitis C virus subgenomic replicons. *Journal of Virology*. 77(20):10769-10779
15. **Guo J.-T.**, Bichko V.V. and Seeger C. (2001) Effect of alpha interferon on the hepatitis C virus replicon. *Journal of Virology*. 75(18): 8516-23.

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### BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Haitao Guo, Ph.D	Associate Professor

eRA COMMONS USER NAME HAITAOGUO1			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Wuhan University, Wuhan, P.R. China	B.S.	1992-1996	Virology
Wuhan University, Wuhan, P.R. China	Ph.D.	1996-2001	Molecular Virology
Fox Chase Cancer Center, Philadelphia, PA	Post Doc	2002-2004	Viral Pathogenesis

### **Positions and Employment**

2002.1 - 2004.10	Post-Doctoral Fellow, Fox Chase Cancer Center, Philadelphia, PA
2004.11- 2006.8	Research Associate II, Drexel University College of Medicine. Doylestown, PA
2006.9 - 2008.9	Instructor, Drexel University College of Medicine. Doylestown, PA
2008.10- 2011.8	Assistant Professor, Drexel University College of Medicine. Doylestown, PA
2011.9 - date	Associate Professor, Department of Microbiology and Immunology, Drexel University College of Medicine. Doylestown, PA

### **Honors, Professional Memberships, and other experience**

2000	First award of the 3 <sup>rd</sup> Conference of Young Microbiology Investigators, Wuxi, China
2002	First Award of Outstanding Popular Science Literature, Hubei, China
2006	First Prize Poster Award for the Young Investigator, 19th International Conference on Antiviral Research. San Juan, Puerto Rico.
2008-	Bruce Witte Fellow of Hepatitis B Foundation, USA
2005-	American Society for Virology (Full Member)
2006-	International Society for Antiviral Research (Member)
2010-	American Society for Microbiology (Member)
2010	Convener, Workshop "Hepatitis Viruses", Annual Conference of American Society for Virology
2011	Moderator, Session "Reverse transcription/assembly, morphogenesis", Annual Meeting for Molecular Biology of Hepatitis B Virus

### **C. SELECTED PEER-REVIEWED PUBLICATIONS**

1. **Guo, H.**, T. Zhou, D. Jiang, A. Cuconati, G. H. Xiao, T. M. Block, J. T. Guo. Regulation of Hepatitis B Virus Replication by Phosphatidylinositol 3-kinase-Akt Signal Transduction Pathway. **Journal of Virology**. 2007, 81: 10072-80.
2. Jiang, D., **H. Guo**, C. Xu, J. Chang, B. Gu, L. Wang, T. M. Block, J.T. Guo. Identification of Three Interferon-Inducible Cellular Enzymes That Inhibit the Replication of Hepatitis C Virus. **Journal of Virology**. 2008, 82: 1665-78.

3. **Guo, H.**, D. Jiang, D. Ma, J. Chang, A. M. Dougherty, A. Cuconati, T. M. Block, J. T. Guo. Activation of Pattern Recognition Receptor-Mediated Innate Immunity Inhibits the Replication of Hepatitis B Virus in Human Hepatocyte-Derived Cells. **Journal of Virology**. 2009, 83: 847-858.
4. Xu, C., **H. Guo**, X. B. Pan, R. Mao, W. Yu, X. Xu, L. Wei, J. Chang, T. M. Block, J. T. Guo. Interferons Accelerate the Decay of Replication-competent Nucleocapsids of Hepatitis B Virus. **Journal of Virology**. 2010, 84: 9332-40
5. Mao, R., J. Zhang, D. Jiang, D. Cai, J. Levy, A. Cuconati, T. M. Block, J. T. Guo, **H. Guo**. Indoleamine 2, 3-dioxygenase Mediates the Antiviral Effect of Gamma Interferon Against Hepatitis B Virus in Human Hepatocyte-derived Cells. **Journal of Virology**. 2011, 85: 1048-57.

**Additional relevant publications of importance to the field**

6. **Guo, H.**, W. S. Mason, C. E. Aldrich, J. R. Saputelli, D. Miller, A. R. Jilbert, J. E. Newbold. Identification and characterization of avihepadnaviruses isolated from exotic anseriformes maintained in captivity. **Journal of Virology**. 2005, 79: 2729-42
7. **Guo, H.**, C. E. Aldrich, J. R. Saputelli, C. Xu, W. S. Mason. The Insertion Domain of the Duck Hepatitis B Virus Core Protein Plays a Role in Nucleocapsid Assembly. **Virology** 2006, 353: 443-50.
8. Zhou, T.\*, **H. Guo**\*, J. T. Guo, T. M. Block. Hepatitis B Virus e Antigen Production is Dependent upon Covalently Closed Circular (ccc) DNA in HepAD38 Cell Cultures and May Serve as a cccDNA Surrogate in Antiviral Screening Assays. (\*equal contribution) **Antiviral Research**. 2006, 72: 116-24.
9. **Guo, H.**, D. Jiang, T. Zhou, A. Cuconati, T. M. Block, J. T. Guo. Characterization of the Intracellular Deproteinized Relaxed Circular DNA of Hepatitis B Virus: An Intermediate of Covalently Closed Circular DNA Formation. **Journal of Virology**. 2007, 81: 12472-84.
10. J. T. Guo, T. Zhou, **H. Guo**, T. M. Block. Alpha interferon-induced antiviral response non-cytolytically reduces replication defective adenovirus DNA in MDBK cells. **Antiviral Research**. 2007, 76: 232-40.
11. Dougherty A. M.\*, **H. Guo**\*, G. Westby, Y. Liu, E. Simsek, J. T. Guo, A. Mehta, P. Norton, B. Gu, T. M. Block, A. Cuconati. A Substituted Tetrahydro-Tetrazolo-Pyrimidine is a Specific and Novel Inhibitor of Hepatitis B Virus Surface Antigen Secretion. (\*equal contribution) **Antimicrobial Agents and Chemotherapy**. 2007, 51: 4427-37.
12. Chang, J, JT. Guo, D. Jiang, **H. Guo**, J. M. Taylor, T. M. Block. Liver Specific microRNA, miR-122, Enhances the Replication of Hepatitis C Virus in Non-hepatic Cells. **Journal of Virology**. 2008, 82: 8215-23.
13. Ma, D., D. Jiang, X. Qu, J. Kennedy, **H. Guo**, J. Chang, B. Gu, P. Y. Shi, T. M. Block, J. T. Guo. West Nile Virus Differentially Inhibits the Signal Transduction Pathways of Type I and III Interferons. **Antiviral Research**. 2009, 83: 53-60.

**BIOGRAPHICAL SKETCH**

NAME	POSITION TITLE
Cuconati, Andrea	Project Leader

eRA COMMONS USER NAME			
acuconati			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
The Richard Stockton College of New Jersey, Pomona, New Jersey	B.S.	1991	Biology
Stony Brook University School of Medicine, Stony Brook, New York	Ph.D.	1997	Molecular Genetics and Microbiology
Howard Hughes Medical Institute and Rutgers University, Piscataway, New Jersey	Post- Doctoral	2002	Molecular Cell Biology and Virology

### **Positions and Employment**

1990	Intern, National Science Foundation Center for Microbial Ecology, Michigan State University, East Lansing, MI
1990-1991	Laboratory Technician, NJ Dept. of Environmental Protection, Leeds, NJ Teaching Assistant, The Richard Stockton College of New Jersey, Pomona, NJ
1991-1992	Graduate Teaching Assistant, State University of New York at Stony Brook, Stony Brook, NY
1992-1997	Graduate Research Assistant, State University of New York at Stony Brook, Stony Brook, NY
1997-1998	Post-Doctoral Associate, Rutgers University, Piscataway, NJ
1998-2002	Research Associate, Howard Hughes Medical Institute, Piscataway, NJ
2002-2004	Senior Scientist, ViroPharma Incorporated, Exton, PA
2004-Present	Project Leader, Institute for Hepatitis and Virus Research, Doylestown, PA
2007-Present	Adjunct Assistant Professor, Drexel University College of Medicine, Philadelphia, PA
2008-Present	Vice President of Biology, Pharmabridge Inc.

### **Honors, Professional Memberships and Invited Service**

1990	Richard Stockton Research Foundation Grant award, December
1990	National Science Foundation Internship in Microbial Ecology, June
1992-1997	National Institutes of Health Graduate Trainee (selected)
2003	Ben Franklin Technology Partners grant awards, February and December
2003	Innovation Philadelphia grant award
2004-present	International Society for Antiviral Research, member
2005-present	American Society for Microbiology, member
2005-present	Bruce Witte Fellow of the Hepatitis B Foundation (selected)
2007	Member of Special NIH Study Sections ZMH1-ERB-Y(06) and ZMH1-ERB-Y(07) (HTS Assay development)
2009, 2010	Member of Special NIH Study Sections ZRG1 BST-J (51) R (HTS Assay development)
2010	Travel Award recipient, Molecular Biology of Hepatitis B Virus Meeting, Taiwan

### **B. Selected Peer-Reviewed Publications (in chronological order)**

1. Rohit Duggal, **Andrea Cuconati**, Matthias Gromeier and Eckard Wimmer. Genetic Recombination of Poliovirus in a Cell-Free System. *Proceedings of the National Academy of Sciences*, Vol. 94: 13786-13791(1997).
2. **Andrea Cuconati**, Wenkai Xiang, Frederick C. Lahser, Thomas Pfister and Eckard Wimmer. A Protein Linkage Map of the P2 Non-Structural Region of the Poliovirus Polyprotein. *Journal of Virology*, Vol. 72, No. 2: 1297-1307 (1998).
3. **Andrea Cuconati**, Akhteruzzaman Molla, and Eckard Wimmer. Brefeldin A Inhibits Cell-Free, *De Novo* Synthesis of Poliovirus. *Journal of Virology*, Vol. 72, No. 8: 6456-6464 (1998).
4. Wenkai Xiang, **Andrea Cuconati**, Debra Hope, Karla Kirkegaard, and Eckard Wimmer. A Protein Linkage Map of the Poliovirus P3 Proteins. *Journal of Virology*, Vol. 72, No. 8: 6732-6741 (1998)
5. Yvan Verlinden, **Andrea Cuconati**, Eckard Wimmer, and Bart Rombaut. The Antiviral Compound 5-(3,4-Dichlorophenyl) Methylhydantoin Inhibits the Post-Synthetic Cleavages and the Assembly of Poliovirus in a Cell-Free System. *Antiviral Research*, Vol. 48, No. 1: 61-69 (2000).
6. **Andrea Cuconati**, Kurt Degenhardt, Ramya Sundararajan, Alan Ansel, and Eileen White. Bak And Bax Function to Limit Adenovirus Replication Through Apoptosis Induction. *Journal of Virology*. Vol. 76, No. 9: 4547-4558 (2002).
7. Yvan Verlinden, **Andrea Cuconati**, Eckard Wimmer, and Bart Rombaut. The Viral Protein 3CD Induces an Equilibrium Between the Viral Protein and RNA Synthesis in a Cell-Free System for Poliovirus Replication. *Archives of Virology*. Vol. 147, No. 4: 731-744 (2002).
8. **Andrea Cuconati** and Eileen White. Viral Homologs of BCL-2: Role of Apoptosis in the Regulation of Virus Infection. *Genes and Development*. Vol. 16, No.19: 2465-2478 (2002).
9. **Andrea Cuconati**, Chandreyee Mukherjee, Denise Perez, and Eileen White. DNA Damage Response and MCL-1 Destruction Initiate Apoptosis in Adenovirus-Infected Cells. *Genes and Development*. Vol. 17, No. 23: 2922-2932 (2003).
10. Baohua Gu, Serguey Ouzunov, Liguang Wang, Peter Mason, Nigel Bourne, **Andrea Cuconati**, and Timothy M. Block. Discovery of Small Molecule Inhibitors of West Nile Virus Using a High-Throughput Sub-Genomic Replicon Screen. *Antiviral Research*. Vol. 70, No. 2: 39-50 (2006)
11. Tianlun Zhou, Haitao Guo, Ju-Tao Guo, **Andrea Cuconati**, Anand Mehta, and Timothy M. Block. Hepatitis B Virus e antigen production is dependent upon covalently closed circular (ccc) DNA in HepAD38 cell cultures and may serve as a cccDNA surrogate in antiviral screening assays. *Antiviral Research*. 2006 72: 116-124.

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### BIOGRAPHICAL SKETCH

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NAME Norton, Pamela	POSITION TITLE Associate Professor, Microbiology and Immunology
eRA COMMONS USER NAME nan101	

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Cornell University	B.A.	1977	Biology
Tufts University	Ph.D.	1986	Molecular Biology
Massachusetts Institute of Technology	Post Doc	1990	Molecular Biology

**Training and Experience:**

1976-1977 Cornell University, Undergraduate research  
 1977-1978 Wesleyan University, Graduate research  
 1978-1980 Sidney Farber Cancer Institute, Research assistant  
 1981-1986 Tufts University, dissertation research  
 1986-1990 Massachusetts Institute of Technology, Postdoctoral fellow  
 1990-1993 Brown University, Assistant Professor of Medicine (Research)  
 1990-1993 Roger Williams Hospital, Staff Scientist, Gastroenterology Division  
 1991-1993 Roger Williams Cancer Center Transgenic Mouse Facility, Director  
 1993-1996 Thomas Jefferson University, Research Assistant Professor of Medicine  
 1996-2000 Thomas Jefferson University, Research Associate Professor of Medicine  
 2000-2004 Thomas Jefferson University, Research Associate Professor of Biochemistry and Molecular Pharmacology  
 2004-2011 Drexel University College of Medicine, Associate Professor of Microbiology and Immunology  
 2004-2011 Associate Director, Drexel Institute for Biotechnology and Virology Research  
 2008-2011 Director, Masters Program in Molecular Medicine

**Honors and Advisory Committees:**

1986-1989 National Research Service Award (F32 CA08027)  
 1991 Rhode Island Foundation Grant for Medical Research  
 1991-1996 FIRST Award (R29 GM46402)  
 1996 NIAMS Special Grants Review Committee Member  
 1998 NIH Fellowship Application Review Committee, ZRG3 BIO Member  
 1998 NIH Special Emphasis Panel, ZRG3 BIO Member  
 2000 NIH Ad Hoc Mail Reviewer (2000)  
 2001-2002 NSF reviewer  
 2009 Hungarian Scientific Research Fund/ERA-Chemistry consortium ad hoc reviewer  
 2009 Maryland Industrial Partnerships Ad Hoc Reviewer  
 2010-11 Indo-US Science and Technology Forum, Ad Hoc Reviewer

**PUBLICATIONS** (in chronological order, selected from 47)

1. Gorski, G.K., M.C. Aros and P.A. Norton. (1996) Characterization of mouse fibronectin alternative mRNAs reveals an unusual isoform present transiently during liver development. *Gene Expression* **6**:139-149.

2. Mirza, A., S.-L. Liu, E. Frizell, J. Zhu, S. Maddukuri, J. Martinez, P.J.A. Davies, R. Schwarting, P.A. Norton and M.A. Zern. (1997) A role for tissue transglutaminase in hepatic injury and fibrogenesis, and its regulation by nuclear factor- $\kappa$ B (NF- $\kappa$ B). *Am. J. Physiol.* **35**:G281-G288.
  3. Zhu, J., J. Wu, E. Frizell, S.-L. Liu, R. Bashey, R. Rubin, P. Norton and M.A. Zern. (1999) Rapamycin inhibits stellate cell proliferation in vitro and limits fibrogenesis in an in vivo model of liver fibrosis. *Gastroenterol.* **117**:1198-1204.
  4. Wu, J., S.-L. Liu, J.-L. Zhu, P.A. Norton, S. Nojiri, J.B. Hoek and M.A. Zern. (2000) Roles of tissue transglutaminase in ethanol-induced inhibition of hepatocyte proliferation and  $\kappa$ 1-adrenergic signal transduction. *J. Biol. Chem.* **275**:22213-22219.
  5. Norton, P.A. (2000) Introduction of DNA into cultured mammalian cells. In "Gene Transfer Methods: Introducing DNA into Living Cells and Organisms", P.A. Norton and L.C. Steel, eds. BioTechniques Press, Eaton Publishing, Natick, MA.
  6. Norton, P.A., Q. Gong, A.S. Mehta, X. Lu and T.M. Block. (2003) Hepatitis B virus-mediated changes in apolipoprotein mRNA abundance in cultured hepatoma cells. *J. Virol.* **77**:5503-5506.
  7. Norton, P.A., H.M.G.P.V. Reis, S. Prince, J. Larkin, J. Pan, J. Liu, Q. Gong, M. Zhu and M.A. Feitelson. (2004) Activation of fibronectin gene expression by Hepatitis B virus X antigen. *J. Viral Hepatitis* **11**:332-341.
  8. Norton, P.A., B. Conyers, Q. Gong, L.F. Steel, T.M. Block and A.S. Mehta. (2005) Assays for the anti-viral activity of glucosidase inhibitors: secreted alkaline phosphatase as a surrogate marker. *J. Virol. Methods.* **124**:167-172.
  9. Gu, B., P. Mason, L. Wang, P. Norton, N. Bourne, R. Moriarty, A. Mehta and M. Despande, R. Shah, and T. Block. (2007) Improved antiviral profiles of deoxynojirimycins with conformation-locking and hydroxylated side chains against Bovine Viral Diarrhea virus, West Nile virus, Dengue virus and Hepatitis B virus. *Antiviral Chem. Chemother.* **18**:49-59.
  10. Liu, Y., E. Simsek, P. Norton, G. Sinnathamby, R. Philip, T.M. Block, T. Zhou, A.S. Mehta. (2007) The role of the downstream signal sequences in the maturation of the HBV Middle Surface glycoprotein: development of a novel therapeutic vaccine candidate. *Virology*, **365**:10-19.
  11. Norton, P.A., B. Gu and T.M. Block. (2007) Imino sugars as antiviral agents. In "Iminosugars: From Synthesis to Therapeutic Applications", P. Compain and O.R. Martin, eds., John Wiley & Sons, Ltd., London, 209-224.
  12. Norton, P.A., M.A. Comunale, J. Krakover, L. Rodemich, N. Pirog, A. D'Amelio, R. Philip, A.S. Mehta and T.M. Block, (2008) N-linked glycosylation of the liver cancer biomarker GP73. *J. Cell. Biochem.*, **104**:136-149.
- Simsek, E, G. Sinnathamby, T.M. Block, Y. Liu, R. Philip, A.S. Mehta, and P.A. Norton. (2009) Inhibition of cellular glucosidases results in increased presentation of hepatitis B virus glycoprotein-derived peptides by MHC class I. *Virology* **384**:12-15.