

# 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:** Duquesne University
2. **Reporting Period (start and end date of grant award period):** 1/1/2010 - 12/31/2013
3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Julie H. Christy, BS
4. **Grant Contact Person’s Telephone Number:** (412) 396-1886
5. **Grant SAP Number:** SAP # 4100050894
6. **Project Number and Title of Research Project:** Project # 02 *Engineering A $\beta$ -selective Enzymes for Treatment of Alzheimer's Disease*
7. **Start and End Date of Research Project:** 1/1/2010 - 12/31/2013
8. **Name of Principal Investigator for the Research Project:** Michael Cascio
9. **Research Project Expenses.**

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

\$ 54,072.72

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, First Name	Position Title	% of Effort on Project	Cost
Pope, Darrick	Graduate Student (Master's)	50%	\$3,362.00
Divito, Erin	Clerical-Part Time, Pre-doctoral Student	10%	\$2,128.00
Nacarelli, Tim	Clerical-Part Time, Summer Undergraduate Student	16.7%	\$4,621.20

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, First Name	Position Title	% of Effort on Project
Ayuk, Kareen	Undergraduate	10%
Cascio, Michael	Principal Investigator	10%

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
Tabletop centrifuge	Provide ease of temperature controlled centrifugation of routine laboratory samples.	\$10,950

**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 X \_\_\_\_\_

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 X \_\_\_\_\_

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: _____ )		
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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: I plan to apply for extramural funding from the NIH and/or the Alzheimer's Association to continue the work initiated by this project.

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

As stated above, I hope to solicit extramural funding from the NIH and/or the Alzheimer's Association to continue the work initiated by this project.

**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		1		
Female	1			
Unknown				
<b>Total</b>	<b>1</b>	<b>1</b>		

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic	1	1		
Unknown				
<b>Total</b>	<b>1</b>	<b>1</b>		

	Undergraduate	Masters	Pre-doc	Post-doc
White		1		
Black	1			
Asian				

Other				
Unknown				
<b>Total</b>	<b>1</b>	<b>1</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.

Funding if this project allowed me to expand my research program and also provided funding for supplies for 1 Masters student (Darrick Pope) and one undergraduate student (Karen Ayuk, an under-represented female minority student).

**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:

The funds allowed me to continue collaborative studies with Dr. Marc Glucksman at Rosalind Franklin medical School in Chicago, IL.

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:

I initiated a new collaboration with Dr. Jeffrey Madura, a computational biophysicist in my department at Duquesne University.

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

List the project goals, objectives and specific aims (as contained in the grant agreement). 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.**

## **Project Overview**

Protein engineering offers the opportunity to design proteins with altered functions, via site-directed mutagenesis of regions targeted towards catalytic and/or substrate-binding sites as determined by atomic resolution structural studies. We propose two specific aims in order to engineer A $\beta$ -selective enzymes for treatment of Alzheimer's Disease (AD):

Aim 1: Utilize peptidomic methods to profile substrates of neprilysin, neprilysin-2 and insulin degrading enzyme. These mass spectrometric methods will also be used in Aim 2 to similarly profile substrates of mutagenized enzymes, and identify cleavage sites in A $\beta$ .

Aim 2: Engineer a more selective form of these metalloendoproteases with increased specificity solely towards A $\beta$  to limit aberrant catabolism of other natural targets of the enzyme using phage display methods.

## **Summary of Research Completed**

Summary of work performed on Aim 1: We were unable to conduct peptidomic profiling of neprilysin substrates as the graduate student conducting these studies was unable to generate randomized phage libraries and was also unable to engineer and express inactivated neprilysin mutants. We continue to conduct these studies as undergraduate research projects.

Summary of work performed on Aim 2: Given the failure to complete Aim 1, the studies of Aim 2 could not be conducted.

As described in previous progress reports, unanticipated experimental difficulties prompted us to initiate novel computational studies to better understand the substrate-binding site of the enzyme, and guide our subsequent experimental studies (which continued throughout the entire funding period and continue to be ongoing after the project end date). As part of these studies we have published a comprehensive review entitled "Neprilysin Inhibitors Provide Insight into the Specificity of the Enzyme and its Potential for Alzheimer's Disease Therapy" in *Frontiers of Drug Design and Discovery*. This review examines the structural and biochemical characterization of neprilysin-inhibitor interactions in order to provide insight into metalloendoprotease function and is now in press (see item 20). In addition, we have submitted another manuscript describing our completed modeling studies that assess binding modes of A $\beta$  in the active site of neprilysin. This manuscript, " $\beta$ -amyloid and neprilysin computational docking studies identify critical residues implicated in binding specificity" was submitted to an ACS journal, *The Journal of Chemical Information and Modeling* (submitted 9/2013 – see item 20). The submission was considered to be acceptable with minor revisions, and the revised version will be submitted in the coming weeks. The successful publication of these studies, supported by our CURE grant, are expected to support future efforts at soliciting extramural funding and provided guidance in directing our on-going mutagenic studies of neprilysin (and other metalloendoproteases) so that we may engineer a more selective form of these enzymes via phage display studies.

**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

\_\_\_X\_\_\_ No

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

\_\_\_\_\_ Yes

\_\_\_X\_\_\_ 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, and an abbreviated title of the

publication. For example, if you submit two publications for Smith (PI for Project 01), one publication for Zhang (PI for Project 03), and one publication for Bates (PI for Project 04), the filenames would be:

- Project 01 – Smith – Three cases of isolated
- Project 01 – Smith – Investigation of NEB1 deletions
- Project 03 – Zhang – Molecular profiling of aromatase
- Project 04 – Bates – Neonatal intensive care

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. Neprilysin inhibitors provide insight into the specificity of the enzyme and its potential for Alzheimer's Disease therapy.	Pope, D. and Cascio, M.	Frontiers in Drug Design and Discovery	12/2012	<input type="checkbox"/> Submitted <input checked="" type="checkbox"/> Accepted <input type="checkbox"/> Published
2. $\beta$ -amyloid and neprilysin computational docking studies identify critical residues implicated in binding specificity	Pope, D, Madura, JD, and Cascio, M	Journal of Chemical Information and Modeling	9/2013	<input checked="" 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 X \_\_\_\_\_

If yes, please describe your plans:

**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.

None

**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.*

# BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Michael Cascio, Ph.D.		POSITION TITLE Associate Professor	
eRA COMMONS USER NAME cascio			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Cornell University, Ithaca, NY	B.A.	1981	Chemistry & Biology
Columbia University, NY, NY	M.A./Ph.D.	1988	Biochem. & Mol. Biophys.
Scripps Research Institute, La Jolla, CA	Postdoc	1990	Mol. & Cell Biology
Yale University, New Haven, CT	Postdoc	1993	Mol. Biophys. & Biochem.

## A. Personal Statement

The main objective of the proposed project is to use a combination of photocrosslinking and mass spectrometry to directly map drug-binding sites in the serotonin transporter, and allow for modeling of these sites and rational design of new therapeutics. My role in this project is to conduct the photocrosslinking studies and subsequent enrichment and mass spectrometric studies. The primary focus of our lab is structure-function studies to characterize the glycine receptor, and we have recently initiated studies examining neurotransmitter transporters in collaboration with Drs. Madura, Surratt, and Lapinsky (i.e., the studies proposed herein). My lab has extensive experience using mass spectrometry, both as a structural tool in studies of ion channels, and as a proteomics tool to identify mitochondrial and ER proteins whose expression levels are modified upon oxidative stress in Parkinson's models. We also use mass spectrometry as a lipidomics tool to identify lipids that modulate membrane protein structure and function. We have been recently funded to conduct studies on engineering neprilysin as a potential Alzheimer's Disease therapeutic. These studies include proteomic analysis of neuroactive peptides that are substrates for wild-type and site-directed mutants of neprilysin. I currently have 4 graduate students and a single post-doc in my lab.

## B. Positions and Honors

2009 – present Associate Professor, Department of Chemistry and Biochemistry, Duquesne University

2007 – 2009 Associate Professor, Department of Microbiology and Molecular Genetics (formerly Molecular Genetics and Biochemistry) University of Pittsburgh School of Medicine

1998 – 2007 Assistant Professor, Department of Molecular Genetics and Biochemistry University of Pittsburgh School of Medicine

1994 - 1997 Research Assistant Professor, Department of Molecular Genetics and Biochemistry, University of Pittsburgh School of Medicine

1990 - 1993 Postdoctoral Fellow, Dept. of Molecular Biophysics and Biochemistry Howard Hughes Medical Institute, Yale University  
Advisor: Robert O. Fox, Ph.D.

- 1988 – 1990 Postdoctoral Fellow, Department of Molecular Biology Research Institute of Scripps Clinic  
 Advisor: N.B. Gilula, Ph.D.
- 1982 - 1988 Graduate Research Assistant, Dept. of Biochemistry and Molecular Biophysics  
 Columbia University, Thesis Advisor: B.A. Wallace, Ph.D.

**Professional Societies** Biophysical Society (1999 – present)  
 American Chemical Society (2007 – present)  
 ASBMB (editorial board member for *J. Biol. Chem.*; 2007-2013t)

**C. Selected publications** (5 of 53 total)

Cheng, M.H., Coalson, R.D. and **Cascio, M.**, (2008) Molecular Dynamics Simulations of Ethanol Binding to the Transmembrane Domain of the Glycine Receptor: Implications for the Channel Potentiation Mechanism. *Proteins*. 71, 972-981.

Liu, Z., Ramanoudjame, G., Liu, D., Fox, R.O., Jayaraman, V., Kurnikova, M., and **Cascio, M.** (2008) Overexpression and Functional Characterization of a Mutated Form of the Extracellular Domain of Human Homomeric  $\alpha 1$  Glycine Receptor. *Biochemistry*. 47, 9803-9810.

Goss, J.R.\*, **Cascio, M.\***, Goins, W.F., Huang, S., Krisky, D.M., Clarke, R.C., Johnson, J.W., Yoshimura, N., Gold, M.S., and Glorioso, J.C. (2011) HSV delivery of a ligand-regulated endogenous ion channel gene to sensory neurons results in pain control following channel activation. *Molecular Therapy*. 19, 500-506.

\*co-first authors

Divito, E.B., Davic, A.P., Johnson, M.E., and **Cascio M.** (2012) Electrospray ionization and collision induced dissociation mass spectrometry of primary fatty acid amides. *Anal Chem*. 84, 2388-2294.

Divito E.B., and **Cascio M.** (2013) Metabolism, Physiology, and Analyses of Primary Fatty Acid Amides. *Chem. Reviews* 113, 7343-7353.

**D. Research Support - Projects Ongoing or Completed During the Last 3 Years:**

NIH R21 MH098127 (Cascio, M. and Lapinsky, D.)

5/1/13 - 4/30/15

Photoprobes for identifying potential anti-depressant and anti-anxiety medications

The major goal of this proposal is to use photolabeled citalopram and fluoxetine to map their binding sites in the serotonin transporter using mass spectrometry.

NIH R01 NS053788 (Saxena, S.)

4/1/07 – 4/30/13

Determination of glycine receptor structure using FT-ESR

The major goal of this grant is to measure distances between introduced site-specific spin labels in the glycine receptor in different allosteric states to understand receptor function.

PA Dept. of Health CURE award # 4100050894-G1000083 (Cascio, M.)

1/1/10-12/31/13

Engineering  $A\beta$  selective enzymes for treatment of Alzheimer's Disease

The major goal of this grant is to engineer proteolytic enzymes to selectively degrade the amyloidogenic peptide  $A\beta$  using phage display and mass spectrometry.

NIH 2R15NS038443 (Cascio, M.)

5/1/09 - 5/31/13

High Efficiency Screening of Bioactive Lipids

The major goal of this analytical chemistry proposal is to screen bioactive lipids using highly efficient, high-throughput methodologies.