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.

1. **Grantee Institution:** Drexel 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):** Anne Martella

4. **Grant Contact Person's Telephone Number:** (215) 895-6471

5. **Grant SAP Number:** 4100050893

6. **Project Number and Title of Research Project**: 10 - *The Role of miRNAs in Modulating Alzheimer's Disease Risk*

7. **Start and End Date of Research Project:** 1/1/2010 - 6/30/2012

8. **Name of Principal Investigator for the Research Project:** Aleister Saunders, PhD

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:

   $ 110,921

   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
Russo, Andi	Research Assoc.	47	$23,500

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
Saunders, Aleister	PI	5
Lippa, Carol	Co-PI	5
Patel, Neha	Graduate Student	50%

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_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:
None	☐NIH ☐ Other federal (specify:_____) ☐ Nonfederal source (specify:_)		$	$

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

Yes__X_____ No_____

If yes, please describe your plans:

NIH R21 submission planned

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

We are interested in determining if other rare variants may lead to changes in miRNA-mediated regulation of gene expression. Specific interest is in genes that are associated with Alzheimer's disease and other neurologic disorders.

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____X___ No_____

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

	Undergraduate	Masters	Pre-doc	Post-doc
Male	2			
Female			1	
Unknown				
Total	**2**		**1**	

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic	2		1	
Unknown				
Total	**2**		**1**	

	Undergraduate	Masters	Pre-doc	Post-doc
White				
Black				
Asian	2		1	
Other				
Unknown				
Total	**2**		**1**	

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

    Yes_____ No____X___

    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___X____ No_____

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

    We established a system of recruiting Alzheimer's patients from our memory disorders clinic for this study. This lay the groundwork for future studies that will utilize this patient population for research studies that complement the memory disorders clinic's work in diagnosing and managing symptoms of memory loss.

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_X_____

    If yes, please describe the collaborations:

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

Yes_____ No___X____

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___X_____

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

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.

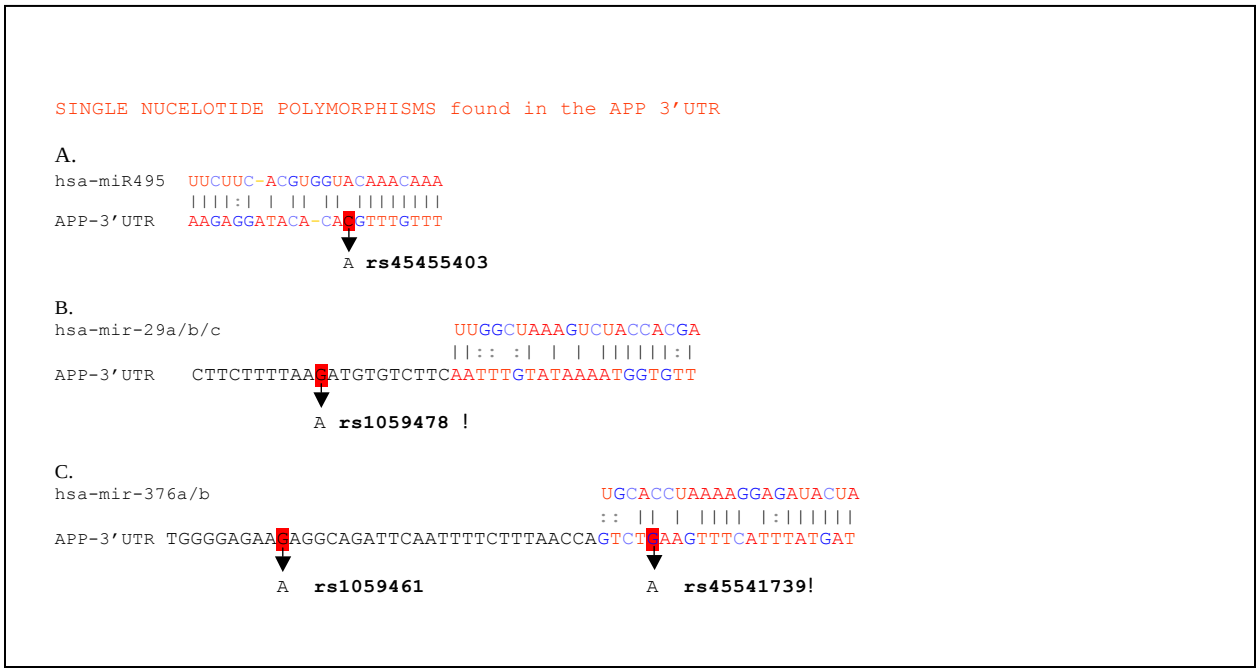
Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance 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 (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.

GOAL: Determine if the polymorphism, rs45455403, leads to increased APP expression and therefore increased risk of developing Alzheimer's disease.

Figure 1 Genetic variation in the 3'UTR of *APP*



Aim 1: Identify common polymorphisms in the human *APP* 3'UTR. We utilized two experimental approaches to identify genetic variation in the 3'UTR of *APP*. First we directly sequenced the 3'UTR in families that display genetic linkage on chromosome 21 to AD. Since the *APP* gene is located on chromosome 21, individuals that have disease predisposing or enhancing polymorphisms should be enriched in this sample. The sequencing results for *APP* 3' UTR region in the chromosome 21-linked families revealed no mutations. We extended this 3' UTR sequencing effort to include at least one proband in each family that comprise the entire NIMH sample (n=449). These efforts resulted in the identification of a rare SNP (rs454455403; minor allele frequency 0.021) in one African American family (FAM: 50368) comprising two affected individuals (90C00627- Onset Age=66 & age=71, 90C00782 - Onset Age =57 & age = 72) that are heterozygous for SNP rs45455403. Sequence context of rs45455403 revealed that the polymorphism lies one bp from the predicted seed region of a putative hsa-miR-495 target site (Figure 1A). Sequencing these 449 individuals from the NIMH AD Genetics Initiative sample identified no other polymorphisms. We therefore searched the human genome SNP database for SNPs located in the 3'UTR of *APP*. We identified two other SNPs, rs45541739 and **rs1059478** that are located in predicted target sites for miR-376a/b and miR-29a/b/c,

respectively. Figures 1B and 1C visualize the sequence context of these SNPs in relationship to the predicted miRNA target site. Interesting, similar to rs45455403, rs45541739 is also only found in African Americans. Together we have identified three polymorphisms that we will test to determine if the minor allele disrupts miRNA-mediated *APP* regulation (Aim 2) and increase risk for developing AD (Aim 3).

Aim 2: Test the effect of these polymorphisms on miRNA-mediated regulation. Given that rs45455403 lies immediately adjacent to the putative miR-495 target site, we tested if this SNP may alter miR-495 mediated APP expression regulation. Using Q-RT-PCR and total brain RNA obtained from a Caucasian male (age = 81 yrs) we confirmed that miR-495 is expressed in normal human brain tissue (Figure 2). Next, we cloned the entire *APP* 3' UTR (containing the major allele "C" of rs45455403) into a position immediately 3' of the firefly luciferase reporter gene. Co-transfection of this reporter vector in naïve HEK 293 cells along with a miR-495 over-expression vector lead to a significant decrease in luciferase activity (~50% ;$p < 0.001$; Figure 3) compared to reporter constructs where, either the miR-495 seed region was disrupted by mutation or reporter construct lacking *APP* 3'UTR, thus confirming miR-495 can bind to the *APP* 3' UTR and regulate gene expression. Inhibiting the over-expressed miR-495 using a anti-miR-495 inhibitor caused a significant increase in luciferase expression compared to a non-silencing control inhibitor (Figure 4).

Over expression of miR-495 also significantly decreased APP protein levels (~50%; $p < 0.01$; Figure 5) and *APP* mRNA levels (~40%; $p < 0.001$; Figure 6) compared to cells transfected with an empty-vector. Over-expression of miR-106a was used a positive control since it has previously been shown to regulate endogenous APP levels without affecting *APP* mRNA levels. Over-expression of miR-125b had no significant effect on APP levels as expected since *APP* contains no predicted miR-125b target sites. These results demonstrate that the *APP* 3'UTR contains a productive miR-495 target site and can control APP expression levels.

To determine if rs45455403 might alter miR-495 mediated regulation of *APP* expression, we mutated the miR-495 target site within the *APP* 3'UTR to replace the rs45455403 major allele (C) with the minor allele (A) (Figure 7). In addition, we also replaced the rs45455403 major allele with a (T) which should increase complementarity between the target site and miR-495. We co-transfected these luciferase vectors along with a miR-495 over-expression vector in naïve HEK 293 cells and observed that the miR-495 target site harboring the rs45455403 minor allele (A) disrupts miR-495 mediated reporter gene expression observed with the major allele (Figure 8). The miR-495 target site engineered to increased complementarity with a (T) substitution increases miR-495 mediated repression. This allele specific regulation is intriguing given that the major and minor alleles confer no changes in the complementarity between the target site and miR-495.

To gain further insight into the mechanism of this allele specific miR-495 regulation we mutated position 9 of the mature miR-495. This position is analogous to the rs45455403 position in the *APP* 3'UTR in that it is one bp away from the predicted seed region (Figure 9). Mutation of miR-495 resulted in decreased repression luciferase activity compared to wild-type miR-495 (Figure 10). As expected, over-expression of mutated miR-495 also resulted in decreased repression of APP protein levels compared to wild-type miR-495 (data not shown). These results demonstrate that miR-495 position 9 confers complementarity independent specificity to regulation of *APP* miR-495 target site.

We have demonstrated allele specific disruption of miRNA regulation of APP expression.

This suggests a novel pathogenic mechanism for AD whereby disruption of miRNA/APP mRNA interaction would lead to increased APP levels and eventually AD. We are currently investigating the effects of rs45541739 and rs35871145 in a similar fashion.

Aim 3: Determine if polymorphisms found in the predicted miRNA target sites of *APP* are over-represented in AD patients versus normal, aged controls. At the time of submission of last year's report we were in the process of genotyping the samples that we had collected to that point, ~137. We have completed this genotyping and have found that the rs45455403 polymorphism is found individuals affected with AD and unaffected individuals. We have identified 7 individuals that are heterozygous for this genetic variation. Of these 7, 2 are a diagnosis of AD, 1 has a diagnosis of mild-cognitive impairment (MCI) and 4 are unaffected. The prevalence of this allele (~2.5%) is what we expected from our initial studies. The range of ages for the AD and MCI patients is 78 -89 years old; while the unaffected individuals had an age range of 44 – 73 years old with an average age of 62 years old. Since AD is an age-dependent disease, unaffected individuals of a similar age range must be utilized. However we had difficulty obtaining these individuals initially. Since June 2011 we have continued to recruit AD patients and controls, this time focusing on obtaining older unaffected individuals. We have just completed collecting an additional ~100 individuals making it economically feasible to genotype this individuals. We will use other funds to complete these experiments.

At the Alzheimer's Association International conference where I presented our findings from this study. After my talk, I was approached by two program officers from the NIH (NINDS and NIA) who were very intrigued by our findings. From these conversations they encouraged us to submit our planned R01 to NIH. Also one of these program officers told me of an individual who had DNA from over 1000 African American Alzheimer's patients and controls. I talked to this scientist on the same day and we are in the process of establishing a collaboration where we will be able to determine the rs45455403 genotype for all of these individuals. Finally I was also approached by an editor of a high impact factor journal asking me to submit this work to the journal, which we are planning to do in the next two-three months.

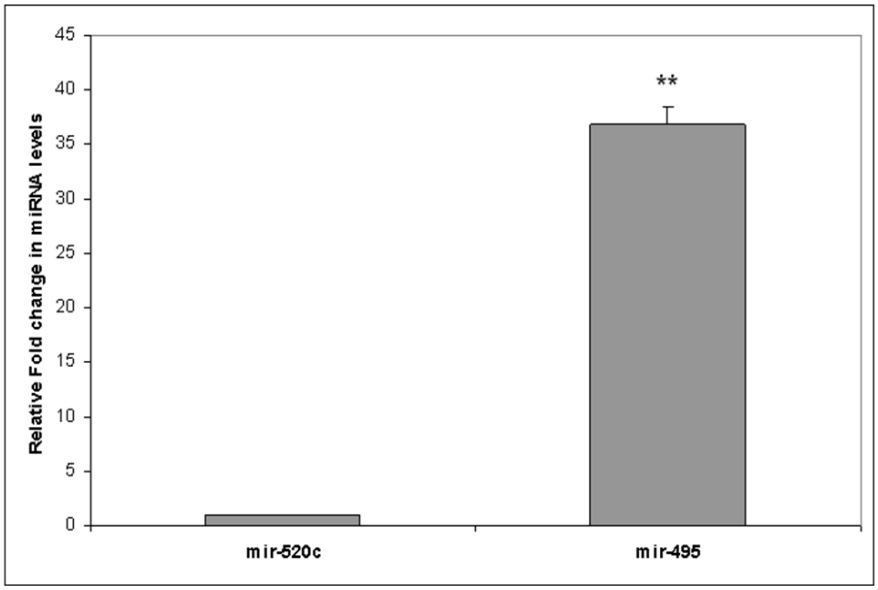


Figure 2: miR-495 expression in normal human brain. miR-495 RNA levels compared to RNU44 RNA levels. miR-520c has been reported to not be expressed in brain.

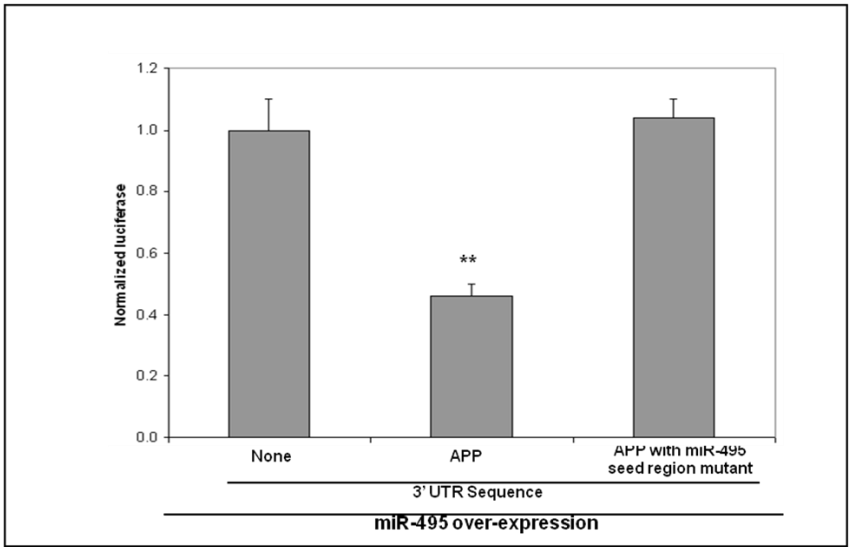


Figure 3: miR-495 over-expression binds to its putative wild-type target sequence, but not the mutated sequence, in APP 3'UTR and regulates reporter gene expression in Naïve 293 cells.

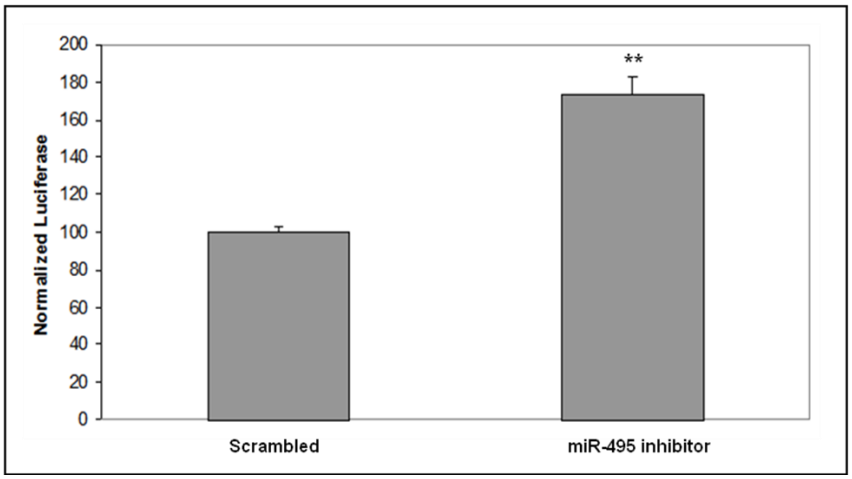


Figure 4: Inhibition of miR-495 increases reporter gene expression.

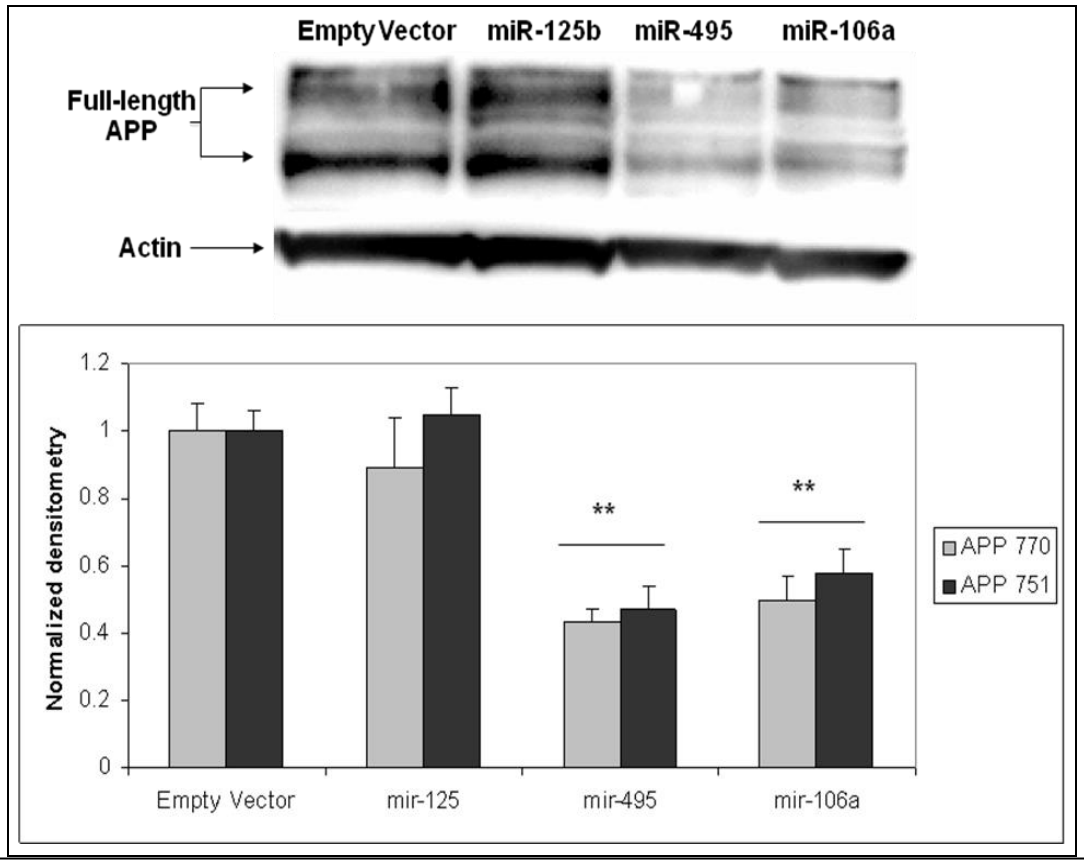


Figure 5: miR-495 over expression significantly decreases endogeneous APP protein levels in Naïve HEK 293 cells. miR-106a is used as a positive control, miR-125b is used as a negative control.

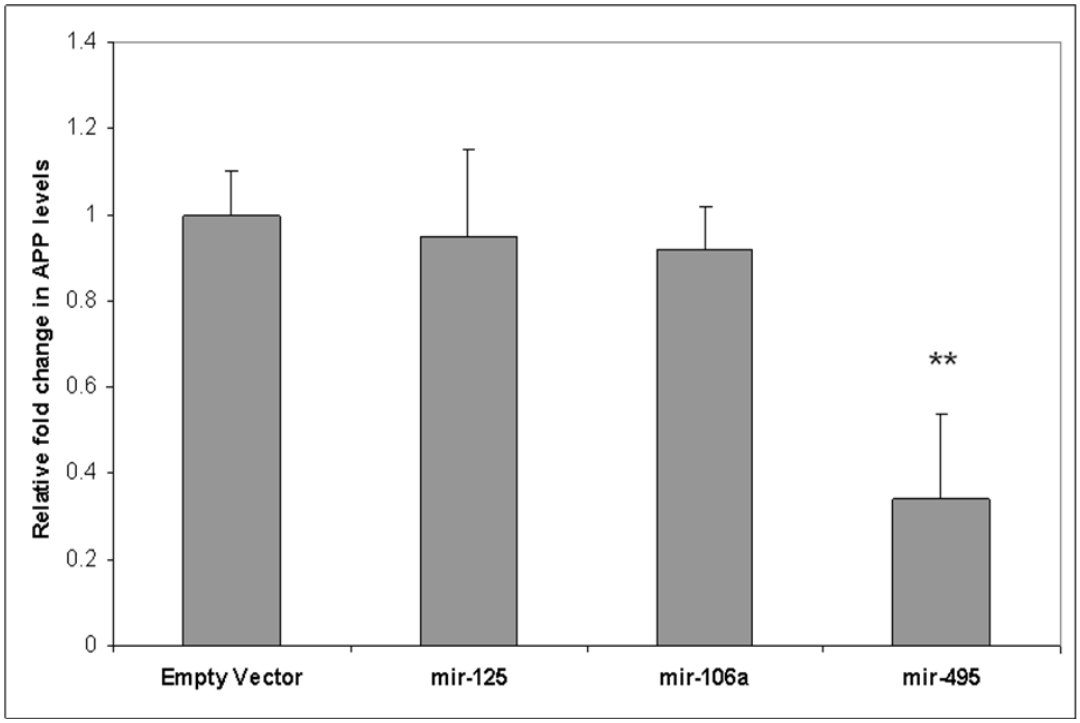


Figure 6: miR-495 over expression significantly decreases APP mRNA levels in Naïve 293 cells. miR-495 over-expression reduces APP mRNA levels unlike miR-106a which has no effect on APP mRNA levels.

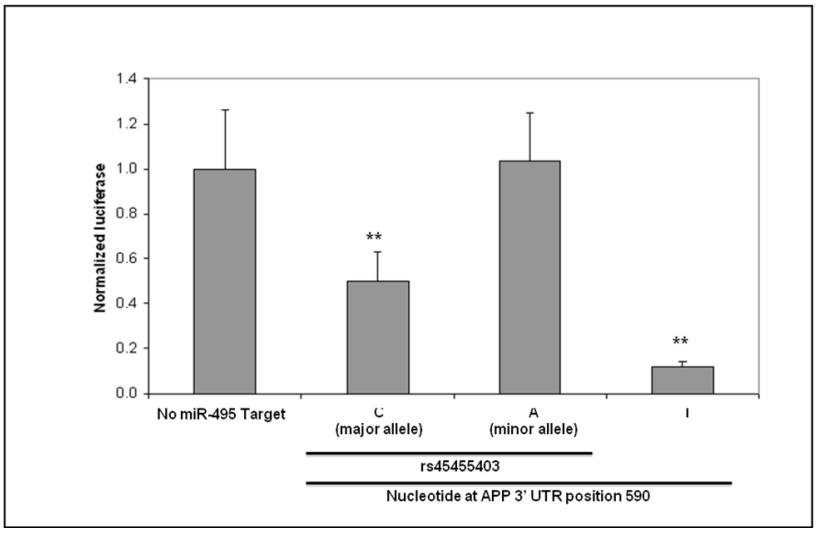


Figure 7: The minor allele of rs45455403 disrupts miR-495 mediated regulation of APP 3'UTR controlled luciferase expression. The APPP 3' UTR was mutated at position 590 from "C" to either "A", the minor allele of rs45455403, or to "T", predicted to be complementary to the corresponding miR-495 base.

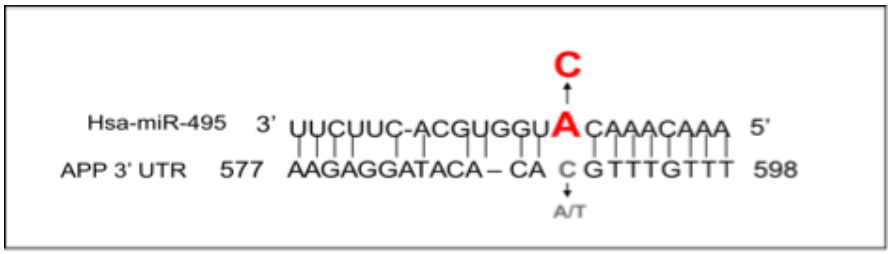


Figure 8: To assess if the allele specific regulation of luciferase activity may also result in allele specific regulation of APP protein levels, we mutated Position 9 of miR-495 since mutating the genomic copy of the *APP* 3'UTR is not possible. Position 9 of the miRNA is predicted to be the miRNA nucleotide corresponding to the rs45545403 allele.

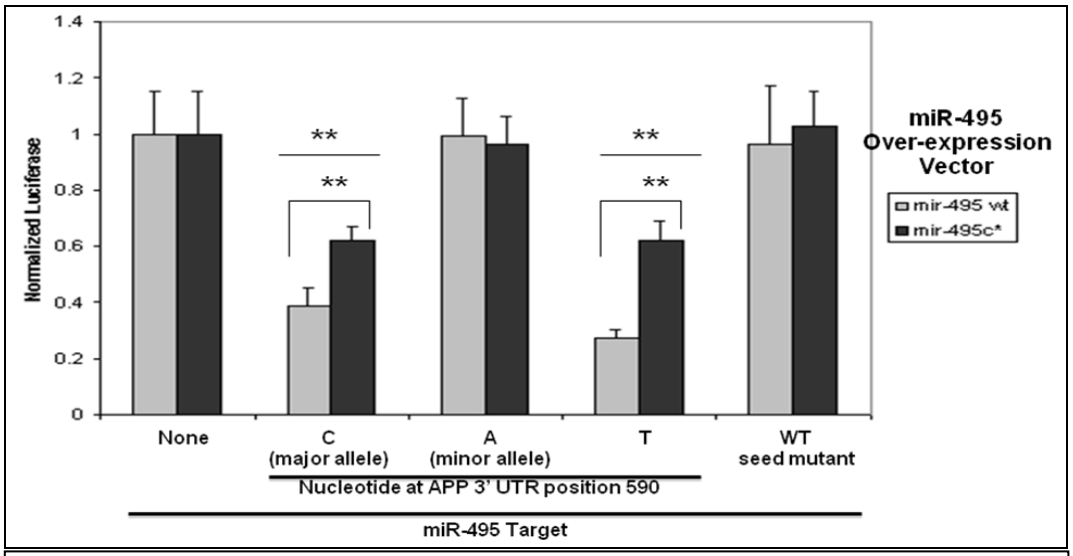


Figure 9: Over-expression of the miR-495 position 9 mutant suppresses miR-495 mediated luciferase expression compared to miR-495 wild type.

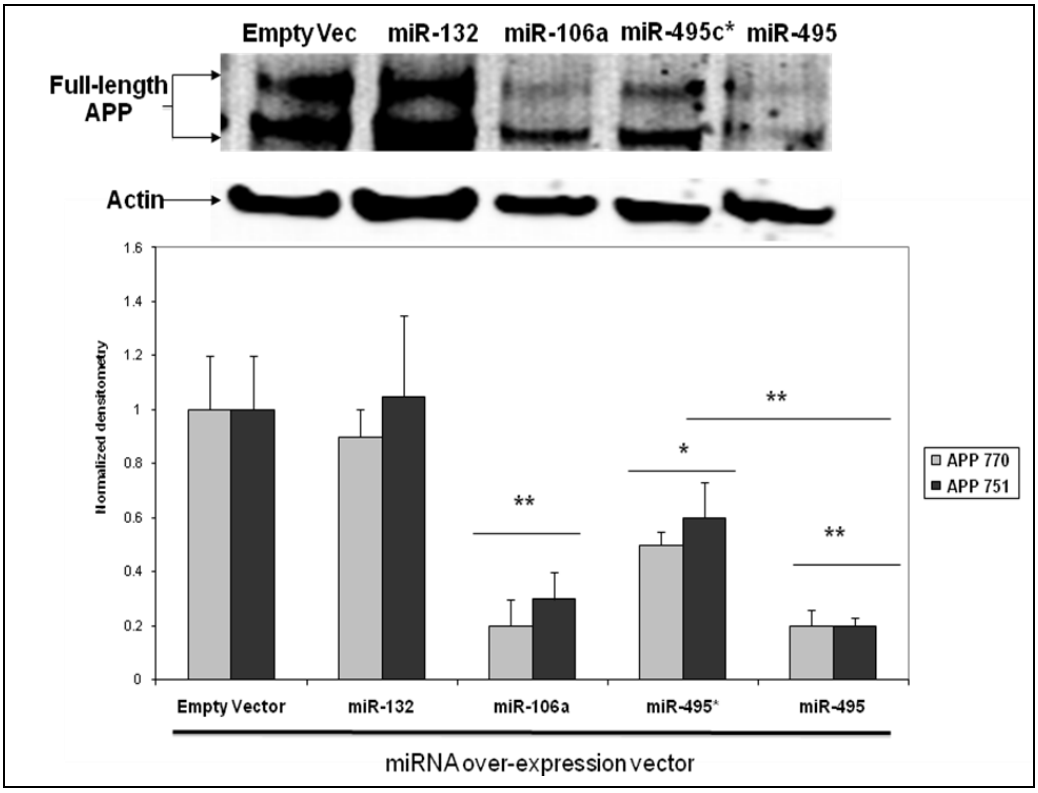


Figure 10: Over-expression of the miR-495 "C" (miR-495*) mutant suppresses miR-495 mediated repression of endogeneous APP levels in Naïve 293 cells compared to miR-495 wild type over-expression.

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
X_____No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__X__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
____ 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. None				☐Submitted ☐Accepted ☐Published

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

Yes___X____ No_____

If yes, please describe your plans:

We are completing our collection of unaffected individuals that meet our age criterion. Once we have completed this we will be able to determine if this polymorphism increases the risk of AD.

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.

We have demonstrated that disruption of miRNA mediated regulation of APP expression by a polymorphism in the APP gene leads to increased APP expression. APP expression increases are known to result in increased risk of developing Alzheimer's disease. We are unable to conclude at this time if this particular polymorphism leads to an increased risk of developing AD, however we hope to reach a conclusion in the near future. These findings

though, would allow for early prediction of individuals that would develop disease, something that is missing for all but the most extreme cases. In addition, the identification of a new mechanism that leads to the development of Alzheimer's disease may also allow for the identification of new approaches for therapeutic intervention.

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.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Aleister J. Saunders, Ph.D.	Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Pennsylvania State University	B.S.	05/90	Biochemistry
University of North Carolina at Chapel Hill	Ph.D.	09/96	Biochemistry
Harvard Medical School/Mass. General Hosp.	Post-doc	12/97	Genomics
Harvard Medical School/Mass. General Hosp.	Post-doc	12/01	Genetics

B. Positions and Honors

1987-1990 Research Assistant, Dept. of Chemistry, Pennsylvania State University
1988- 1990 Research Assistant, Physiology Dept., University of Pittsburgh Medical School
1990-1996 Graduate Student, Dept. Biochemistry and Biophysics, Univ. North Carolina, Chapel Hill
1990-1991 Teaching Fellow Dept. Biochemistry and Biophysics, Univ. North Carolina, Chapel Hill
1997-2001 Research Fellow, Harvard Medical School/Massachusetts General Hospital
2002 Instructor in Neurology, Harvard Medical School/Massachusetts General Hospital
2002-2008 Assistant Professor, Department of Bioscience & Biotechnology, Drexel University
2004-2008 Assistant Professor, Department of Biochemistry, Drexel University College of Medicine
2007-2008 Adjunct Assistant Professor, Department of Neurobiology, Drexel University College of Medicine
2008-present Associate Professor, Department of Bioscience & Biotechnology, Drexel University
2008-present Associate Professor, Department of Biochemistry, Drexel University College of Medicine
2008-present Adjunct Associate Professor, Department of Neurobiology, Drexel University College of Medicine
2008-2009 Interim Associate Department Head, Department of Biology
2009-2012 Associate Department Head, Department of Biology
2012-present Associate Dean for Research and Graduate Education, College of Arts & Sciences

Honors

1988 National Science Foundation, Undergraduate Research Fellowship
1994 Petroleum Research Fund, Research Grant Awardee
1999 National Institute of Aging; National Research Service Awardee
1999 Massachusetts Alzheimer's Disease Research Center Awardee

B. Peer-reviewed Publications (selected)

1. Bertram L, Blacker D, Mullin K, Keeney D, Jones J, Basu S, Yhu S, McInnis MG, Go RC, Vekrellis K, Selkoe DJ, Saunders AJ, Tanzi RE." Evidence for genetic linkage of Alzheimer's disease to chromosome 10q" Science 290(5500):2302-3 (2000).

2. Puglielli L, Ellis BC, Saunders AJ, Kovacs DM. Ceramide Stabilizes β-Site Amyloid Precursor Proteincleaving Enzyme 1 and Promotes Amyloid β-Peptide Biogenesis. J Biol Chem. 2003 278(22):19777-19783

3. Engstrom G, Rajagukguk R, Saunders AJ, Patel CN, Rajagukguk S, Merbitz-Zahradnik T, Xiao K, Pielak GJ, Trumpower B, Yu CA, Yu L, Durham B, Millett F. Design of a ruthenium-labeled cytochrome c derivative to study electron transfer with the cytochrome bc1 complex. Biochemistry. 2003 42(10):2816- 2824.

4. Saunders AJ, Bertram L, Mullin K, Sampson AJ, Basu S, Jones J, Kinney D, MacKenzie-Ingano L, Yu S, Albert MS, Moscarillo TJ, Go RCP, Bassett SS, Daly MJ, Laird NM, Becker DK, Wang G, Velicelebi G, Tanzi RE, Blacker D. Genetic Association of Alzheimer's disease with multiple polymorphisms in Alpha-2-Macroglobulin. Hum. Mol. Genet. 2003, 12(21):2765-2776.

5. Saunders AJ, Tanzi RE. Welcome to the Complex Disease World: Alpha2-Macroglobulin and Alzheimer's Disease. Exp Neurol. 2003, 184(1):50-53.

6. Zhang C, Khandelwal P, Cuellar T, Cosentino C, Sarangi S, Tanzi RE, Lee J, Saunders AJ "Identification of Ubiquilin1 as an APP metabolism regulator using an AICD-based functional screen" Molecular Neurodegeneration (2007) 2(1):15.

7. Patel N, Hoang D, Miller N, Rogers JT, Huang Q, Saunders AJ. "MicroRNAs can regulate human APP levels." Molecular Neurodegeneration 2008, 3(10) PMCID: PMC2529281.

8. Zhang C, Saunders AJ. An Emerging Role for Ubiquilin 1 in Regulating Protein Quality Control System and in Disease Pathogenesis. Discov Med. 2009 (40):18-22.

9. Ansaloni S, Leung B, Saunders AJ. TrkB isoforms differentially effect AICD-mediated gene expression. Int J Alzheimers Dis. 2011 Feb 24;2011:729382.

10. Chakraborty R, Vepuri V, Mhatre SD, Paddock BE, Miller S, Michelson SJ, Delvadia R, Desai A, Vinokur M, Melicharek DJ, Utreja S, Khandelwal P, Ansaloni S, Goldstein LE, Moir RD, Lee JC, Tabb LP, Saunders AJ, Marenda DR. Characterization of a Drosophila Alzheimer's Disease Model: Pharmacological Rescue of Cognitive Defects.. *PLoS One.* published 06 Jun 2011 10.1371/journal.pone.0020799

11. Hooli BV, Mohapatra G, Mattheisen M, Parrado AR, Roehr JT, Shen Y, Gusella JF, Moir R, Saunders AJ, Lange C, Tanzi RE, Bertram L.Role of common and rare APP DNA sequence variants in Alzheimer disease. Neurology. 2012 Apr 4. PMID: 22491860

12. Mhatre SD, Paddock BE, Saunders AJ, Marenda DR. Invertebrate Models of Alzheimer's Disease. J Alzheimers Dis. 2012 Aug 9. PMID: 22886023

13. Ansaloni S, Leung BP, Dubey A, Saunders AJ. Tyrosine kinase receptor B isoforms alter APP and BACE endogenous levels independently of BDNF. Advances in Alzheimer's Disease 2012; 1(3): 93-101. doi:10.4236/aad.2012.13012

14. Reza MA, Mhatre SD, Morrison JC, Utreja S, Saunders AJ, Breen DE, Marenda DR. Automated analysis of courtship suppression learning and memory in *Drosophila melanogaster.* Fly (Austin). 2013 Apr 1;7(2). PMID: 23644900