THE UNIVERSITY OF TEXAS
RIO GRANDE VALLEY
UTRGV.EDU

# Putting an Emphasis on Research in the Curriculum: Independent Research IV as the keystone for BMED students at the UTRGV

**8-18-2017**

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# Independent Research


- Students will learn the basic principles of research with their faculty mentors on different research projects
- The foundation of these courses focuses on research which ensures that students will gain training in research methods and conduct research projects. Students will use the knowledge and skills throughout their university and future professional careers.
- Benefits: students engage in research while obtaining course credit toward their bachelor's degree and their research will lead to significant contributions to the research literature and address critical issues in healthcare

# Independent Research-IV: Objectives (BMED3224)

I. Students will obtain an understand of the fundamental principles of biomedical research (e.g., biomarker discovery)

II. Students will be able to develop hypotheses, study design, carry out experiments and interpret data for a question related to research projects

III. Students will be able to access, read and gain insight from reading primary literature

# Independent Research IV: Course Pre-Requisites

- Admission to the BMED program and completion of Independent Research I-III

# Students will be able to

- integrate knowledge of previous BMED courses with current translation research
- initiate translational research proposals and how to submit translational research grant
- prepare review papers and/or research papers
- submit scientific paper and/or research grant by the end of semester

# Independent Research IV: Grading/Evaluation

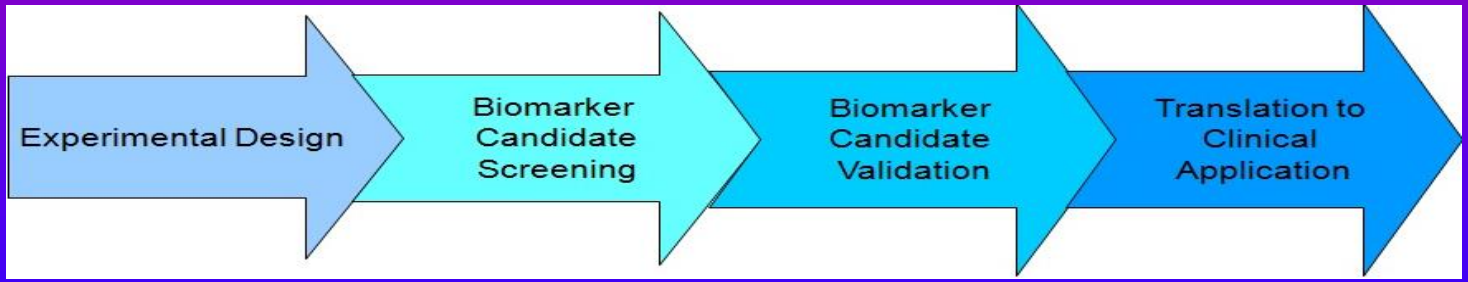

- Class Participation 10%
- Abstract or summary 10%
- Current findings (Tables) 30%
- Final review paper 20%
- Final presentation 30%
- Bonus points: 5 points for 1st place and 3 points for 2nd place (two students)

# Summary and Suggestions

- Have students on the same research project from year 1 and continue to year 2, 3 and 4
- Must be intentional about development of writing skills
- Result in student/faculty publications and presentations

# Biomarker Discovery

as an indicator of normal biological processes, etiology, pathogenic, diagnosis, prognosis or pharmacological responses to a therapeutic intervention



# Biomarker Uses and Applications

- Biomarkers include tools and technologies that can aid in understanding the
  - Prediction
  - Cause
  - Diagnosis
  - Progression
  - Regression and
  - Outcome of various diseases

Source: The Journal of the American Society for Experimental NeuroTherapeutics
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC534923/

# Academic Achievements together with my students - I

**Table 1. Research Projects, Students Participate in the Past and Current (Partial list)**

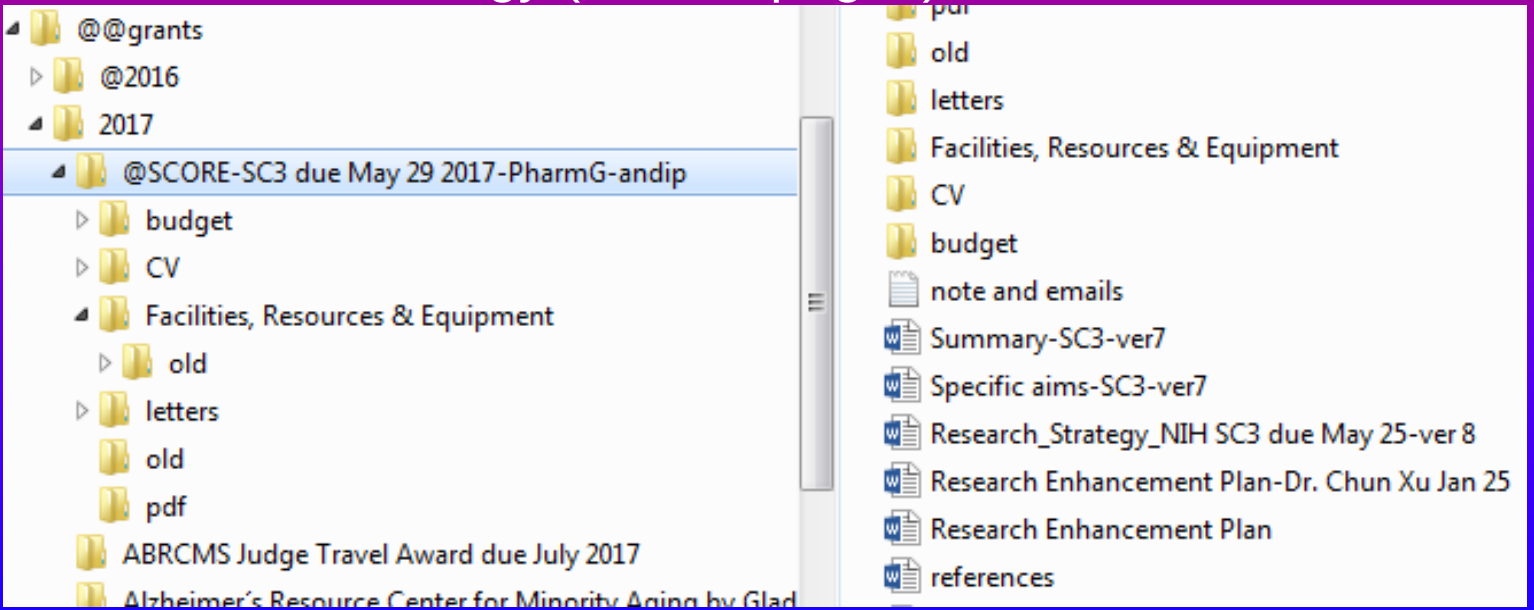
| Projects | Students (S) | Project Status |
|---|---|---|
| **Past** | | |
| Novel Somatic Copy Number Alteration Identified for Cervical Cancer in the Mexican American Population | Ordonez J- graduate S<br>Palmer L- medical S<br>Lara K - undergraduate S | *Medical Science* 2016, 4(3): 12 http://www.mdpi.com/2076-3271/4/3/12 |
| Pharmacogenetics of antidepressants, a review of significant genetic variants | Reyes-Barron C- medical S<br>Delozie A, medical S | *Clinical Depression* 2016 2(2):1 |
| Genome-wide methylome analyses in schizophrenia and bipolar disorder | Camarillo C-postdoc.<br>Ordonez J - a graduate S | *Biomed Research International* 2015, Feb, 4, s201587 |
| Pharmacogenomics for antipsychotic drugs | 5 BMED undergraduate S(Cho M, Contreras A, Garza A, Olvera S, Castillo D) | *Bipolar Disorder*, open access 2017, 3(1)1000117 |
| The DNA methylome and transcriptome of different brain regions in SCZ and BD | Ordonez J - a graduate S | *PLOS ONE*, 2014, 28;9(4):e9587 |
| BCL9 and C9orf5 are associated with negative symptoms in schizophrenia: meta-analysis of two genome-wide association studies Study | Villla E- graduate S<br>Cruzv C-a medical S | *PLOS ONE*, 2013, 8(1), e51674 |
| **Current** | | |
| 1. Whole exome sequencing for ADHD | Arulselvam S- undergraduate S | 50% completed |
| 2. Whole exome sequencing for epilepsy | Ramirez Y- undergraduate S | Present in ASHG conference Oct. 2017; 60% completed |
| 3. Recruitment of patients with psychiatric disorders (e.g., BP, SC and/or depression) | Tovar H, Abshier J, and Lozano S-graduate/undergraduate S | Ongoing research (a family with 9 members (4 affected) recruited |
| 4. Disease etiology and biomarker discovery for BP and SC | Tovar H and Weary C-graduate/undergraduate S | Ongoing research |
| 5. DNA methylation and LncRNA involved in developments of SC, BP | 4 undergraduate S | ongoing research |
| 6. Gene discovery for AD and MDD | Abshier J and Wear C-undergraduate S | Will submit within half month |
| 7. Genetic variants identified for hypertension | Tovar H- graduate S<br>Gonzalez V & Hinojosa P - undergraduate S | Will submit within one month |

# Academic Achievements together with my students -II

1. Actively involved in preparing research grant (e.g., NIH-R15, SC3)
2. Having publications in peer reviewed journals
3. Having credits from reviewing manuscripts for a number of peer reviewed journals

# 1. Research Grant


- Abstract/summary
- Search scientific publications
- Specific aims (hypothesis, objectives and aims)
- Research strategy (6 or 12 pages)…



# A Mini Gran Proposal

- A title, affiliation, key words (5-6 words)
- Abstract (1/2 page) (Week 4)
- Introduction (previous findings on the topics, objectives, hypothesis, specific aims, 2-4 pages), (Week 5-7)
- Approach (2-3 pages, workflow) (Week 8-10)
- Expect results (1/2-1 page) (Week 11)
- Strength/limitations and future direction (2/3-1 pages), revision, revision, proofreading (week 12-13)
- Literature cited and submission steps (Week 13)

# 2. A Mini Review Paper: Why we need to write a review paper

Because there has been an information explosion in science over the last 20 years and even scientists themselves don't have time to read all the original articles to stay on top of their fields. Many scientific journals now feature short articles of “review papers” on new or controversial areas of research, such as *Trends in Genetics*.

# Steps of Writing A Review Paper


- A title, affiliation, key words (5-6 words)
- Abstract (1/2 page) (Week 4)
- Introduction (previous findings on the topics, lack of issue we need to address, 2-3 pages) (Week 5-6)
- Method (1/2-1 page, workflow) (Week 7)
- Current findings (2-3 pages) (Week 8-10)
- Conclusion, future directions (1/2-1 pages) → revision, revision, proofreading (week 11-12)
- Literature cited and submission (Week 13)

# Publications

Bipolar Disorder: Open Access
ISSN: 2472-1077

Cho et al., Bipolar Disord 2017, 3:1
DOI: 10.4172/2472-1077.1000117

Mini Review OMICS International

## The Impact of Drug and Gene Interaction on the Antipsychotic Medication for Schizophrenia

**Michelle Cho[1], Adriana Contreras[1], Ashley Garza[1], Samantha Olvera[1], David Castillo[1], Gabriel de Erausquin[2] and Chun Xu[1]***

[1]Department of Health and Biomedical Science, University of Texas Rio Grande Valley, Brownsville, Texas, USA
[2]Department of Neurology and Psychiatry, University of Texas Rio Grande Valley, Brownsville, Texas, USA

**First five authors are our BMED undergraduate students**

medical sciences

MDPI

*Article*

## Novel Somatic Copy Number Alteration Identified for Cervical Cancer in the Mexican American Population

Alireza Torabi [1], Javier Ordonez [2], Brenda Bin Su [4], Laura Palmer [3], Chunxiang Mao [3], Katherine E. Lara [3], Lewis P. Rubin [3] and Chun Xu [3,*]

Bipolar Disorder: Open Access

Cho et al., Bipolar Disord 2017, 3:1
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# The Impact of Drug and Gene Interaction on the Antipsychotic Medication for Schizophrenia

**Michelle Cho[1], Adriana Contreras[1], Ashley Garza[1], Samantha Olvera[1], David Castillo[1], Gabriel de Erausquin[2] and Chun Xu[1]***

[1]*Department of Health and Biomedical Science, University of Texas Rio Grande Valley, Brownsville, Texas, USA*
[2]*Department of Neurology and Psychiatry, University of Texas Rio Grande Valley, Brownsville, Texas, USA*

## Abstract

**Objective:** Schizophrenia, a neuropsychiatric disorder, is known to be neurodevelopmentally progressive. Due to the extensive interindividual variability found in the responses of patients, management of schizophrenia has proven to be challenging. This interindividual variability to treatment could be justified by the variation of the enzymes in charge of metabolizing medications, especially those associated with cytochrome P450. Since genetic factors influence the phenotypic responses to drugs, researchers are involved in identifying schizophrenic genetic factors, which could impact responses and severe effects for commonly known neuroleptic drugs known as pharmacogenetics. In order to predict drug response at the personal level, genetic variants that determine drug effects need to be identified.

**Methods:** We have chosen to investigate gene targets for risperidone and clozapine, two commonly administered drugs for the treatment of schizophrenia. The aim of this review is to contribute in the understanding of genetic influences on drug responses of risperidone and clozapine in schizophrenia. We reviewed original primary research articles, meta-analysis, and review publications on drug and gene interaction on the treatment of schizophrenia. Our main findings focused on schizophrenia, pharmacogenetics and cytochrome P450.

**Results and conclusion:** After filtering our results to human species and English language, a total of 45 scientific articles were used for this review. A promising direction for future research in schizophrenia treatment lies behind the identification of the specific genetic contributors that affect drug response.

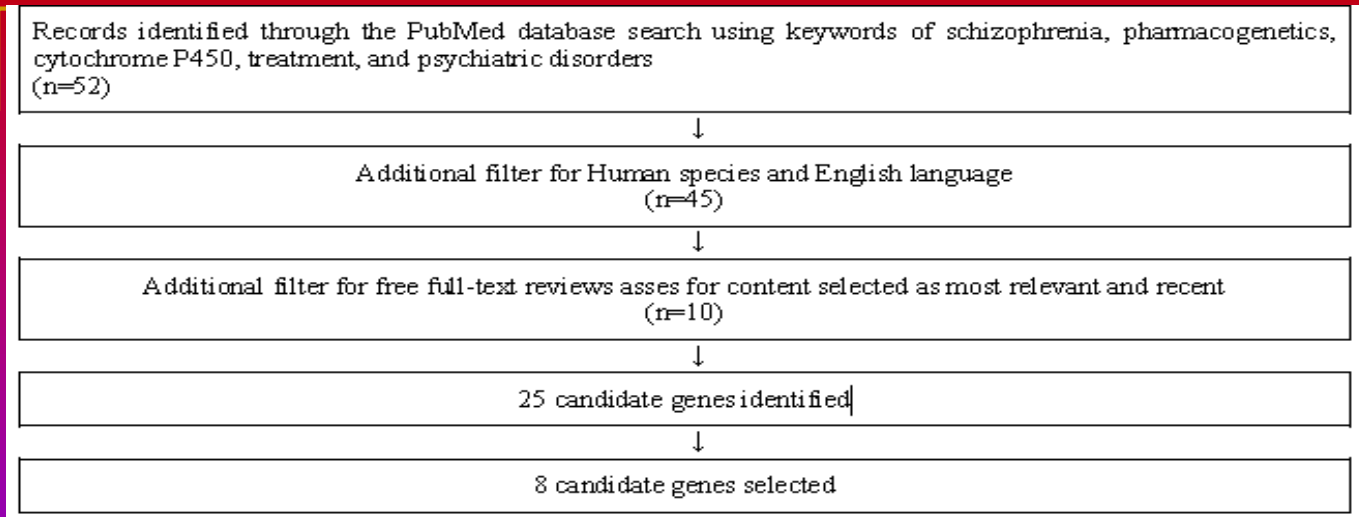
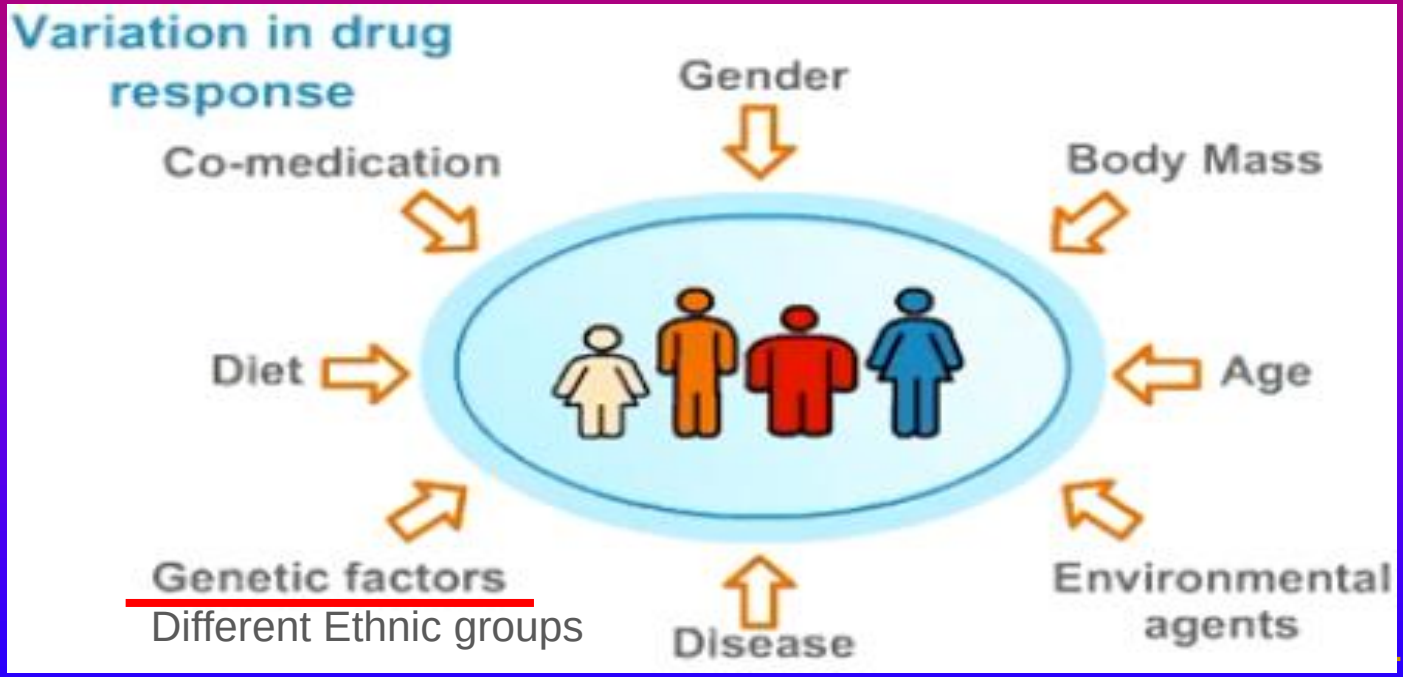



**Figure 1:** Workflow of publications used for this review paper.

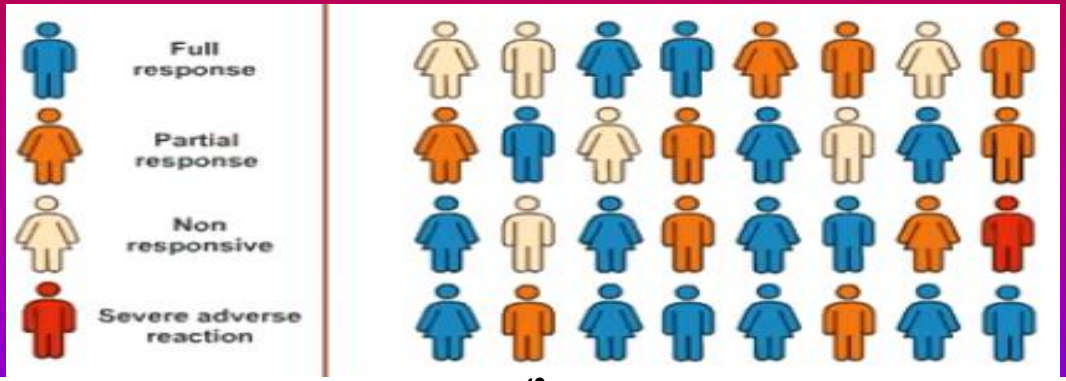
| | | | | | |
|---|---|---|---|---|---|
| TR2A | His452Tyr (rs6314) | A (n=661)<br>C (n=503)<br>H<br>AS (n=504) | 0.121<br>0.079<br>N/A<br>0.005 | • $Ca^{+2}$ mobilization ↓ (Zhang and Malhotra [20])<br>• Tyr variant is associated with reduced calcium release and reduced ability to activate phospholipases (Zhang and Malhotra [20])<br>• Tyr variant showed lowered antipsychotic binding affinity and ↓ drug potency (Arranz et al. [35], n=274; Masellis et al. [31], n=185; Arranz et al. [36], n=153)<br>• Tyr allele was significantly associated with poor response to clozapine treatment compared to the His allele (Arranz et al. [35], n=274; Masellis et al. [31], n=185; Arranz et al. [36], n=153) | Clozapine and Risperidone |
| | T102C (rs6313) | A (n=661)<br>C (n=503)<br>H<br>AS (n=504) | 0.393<br>0.436<br>N/A<br>0.412 | • C allele of T102C was more prevalent among non-responders for Clozapine (Arranz et al. [35], n=274)<br>• For risperidone response, there is a significant association between the C/C genotype and better response (Lane et al. [37], n=100; Kim et al. [38], n=100) | |
| | A-1438G (rs6311) | A (n=661)<br>C (n=503)<br>H<br>AS (n=504) | 0.409<br>0.437<br>N/A<br>0.412 | • G/G genotype was less likely to respond to clozapine (Arranz et al. [35], n=274, Chen et al. [39], n=128) | |
| TR2C | Cys23Ser (rs6318) | A (n=661)<br>C (n=503)<br>H<br>AS (n=504) | 0.299<br>0.117<br>N/A<br>0.012 | • Patients with Ser allele were more likely to respond to clozapine treatment compared to patients who are Cys/Cys homozygotes (n=162) | Clozapine |

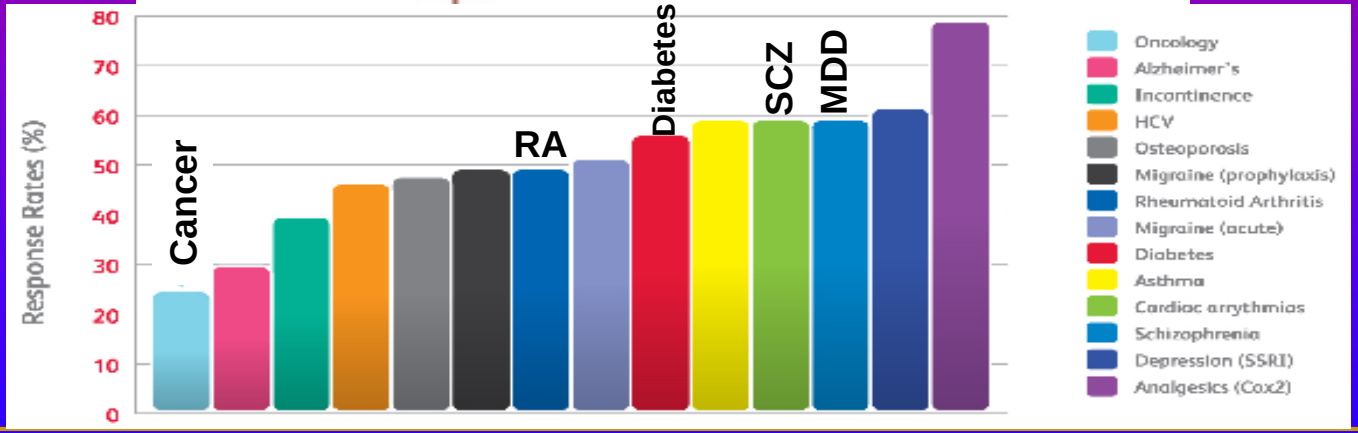
# Pharmacogenetics
# Applications of Genomic Medicine

**Pharmacogenetics**: to study of genetic influences on an individual's response to drugs



# Inter-Individual Differences in Drug Responses




Trend molecular medicine 2002, 7:201

# Why Pharmacogenetics?

- Adverse drug reactions (ADRs): one of the top 5 leading causes of death & illness; 2 million people suffer ADR; 4-30% of all hospital admission; >100,000 deaths (Lazarou et al.l1998, Sultana et al., 2013)
- ADRs: costs > 4 billion $US annually in the US (Steimer 2002)
- G

**At least 60% of ADRs are preventable – reported by WHO 2008**

| Drug ( | | | |
|---|---|---|---|
| Imipran | | | |
| Isoniaz | | | |
| Warfar | | | |
| 5-fluorouracil (Adrucil) | Cancer | Severe immune suppression | DPD |
| Clarithromycin (Biaxin) | Antibiotic | Heartbeat irregularity | KCNE2 |
| Azathioprine (Imuran) | Rheumatoid arthritis | Severe immune suppression | TPMT |

# 3. Reviewing Manuscripts

- BioMed Central (BMC) Neuroscience 2017 Manuscript ID: BR – 2017: “Novel functional variants at the GWAS-implicated loci might confer risk to major depressive disorder, bipolar affective disorder and schizophrenia” revised by a BMED student, Garza Arnulfo
- Preventive Medicine Reports, 2017 Manuscript ID: PMEDR-17-27: “Metabolic syndrome, self-reported health and behavioral factors in Americans aged 40 and over” revised by a BMED student

# Comments for the Manuscript

**Title: Novel functional variants at the GWAS-implicated loci might confer risk to major depressive disorder, bipolar affective disorder and schizophrenia**

The authors conducted a research by focus on unravelling the mechanisms of genetic variation, gene expression, other genomics parameters in association with cognitive function and neuropsychiatric disorders based on previous studies. Authors report novel findings that expand the repertoire of functional variation in human genome, recognize the targeted genes and provide an evidence relevant to disease-associated effects of the identified rSNPs on cognition including on bipolar affective disorder, major depressive disorder and schizophrenia.
There are several concerns and minor changes that the authors should address that will improve this manuscript prior to publication:

**Minor changes**

In addition to a number of comments and suggestions in the text, following you will see more minor changes

1. Abstract on page 2, authors should provide a full name of GWAS
2. It confused on diagnostic groups since in abstract, authors mentioned BP, SC, however, there are more diagnostic groups in the tables
3. Table 1 is not only rSNP associated with cognitive but also other traits (BP, SC)
4. Authors emphasize on cognition, however, they also study other traits
5. Page 6, line 141, authors should provide a full name for UTR
6. Page 6, line 148-150, authors should explain what is the relevant of study expression difference of colorectal and breast cancer cell lines to identify rSNPs for neuropsychiatric traits
7. Page 7, line 164, authors should offer a full name of MAF, the first time in the text, not on page 22, line 535

# Benefits of publishing, grant writing and reviewing manuscripts as an undergraduate students

- To help improve writing and research skills
- To experience the scholarly publication process
- To connect with professors and researchers
- To display leadership and initiative
- To inform a future career path

# In your CV, you will write…

**Selected Publications (Total: 50 Publications * as corresponding authors)**

**40.** **Xu C**, Ozbay F, Wigg K et al (2003) Evaluation of adrenergic receptors □2A and □1C and Gilles de la Tourette Syndrome. *Am J Med Genet*. May 15;119B(1):54-9

**41.** **Xu C**, Goodz S, Sellers EM et al (2002) CYP2A6 Genetic Variation and Potential Consequences. *Advanced Drug Delivery Review* 54, 1245-1256.

**42.** **Xu C**, Rao YS, Xu B et al (2002) An in vivo pilot study characterizing the new CYP2A6*7, *8, and *10 alleles. *BBRC* 290: 318-324

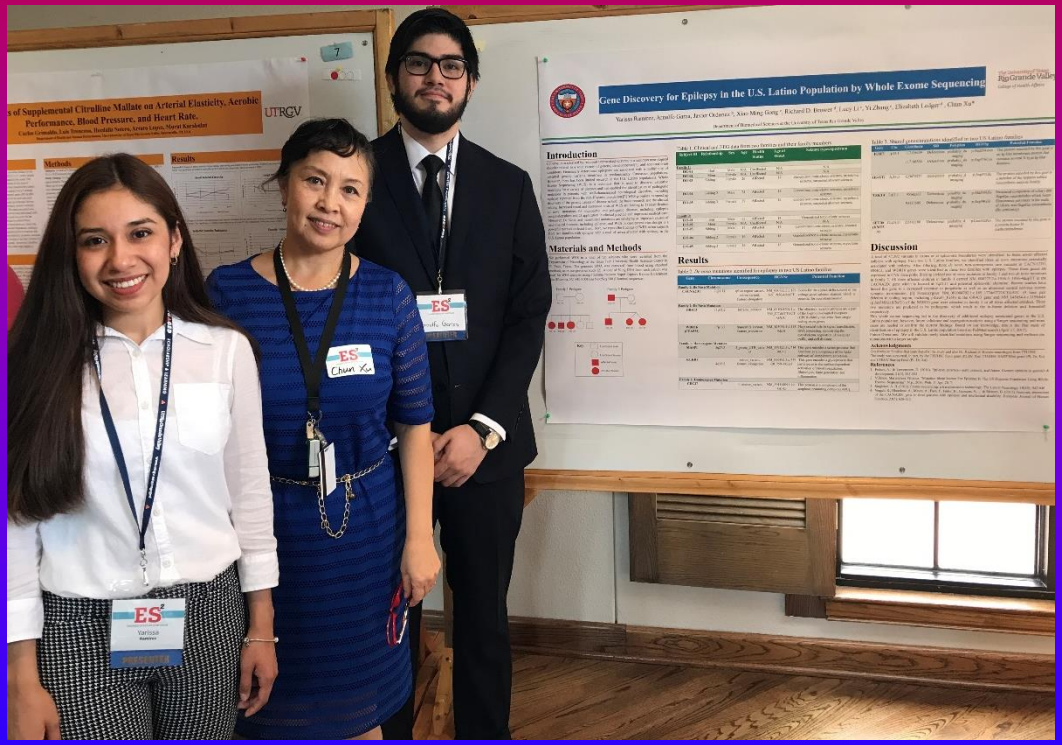
**43.** Dai Y, **Xu C**, Holmberg M et al (2001) Linkage analysis suggests a region of importance for multiple sclerosis in 3p14-13. *Genes Immun*. Dec;2(8):451-4

**Service for Scientific Journals**

As an external reviewer for

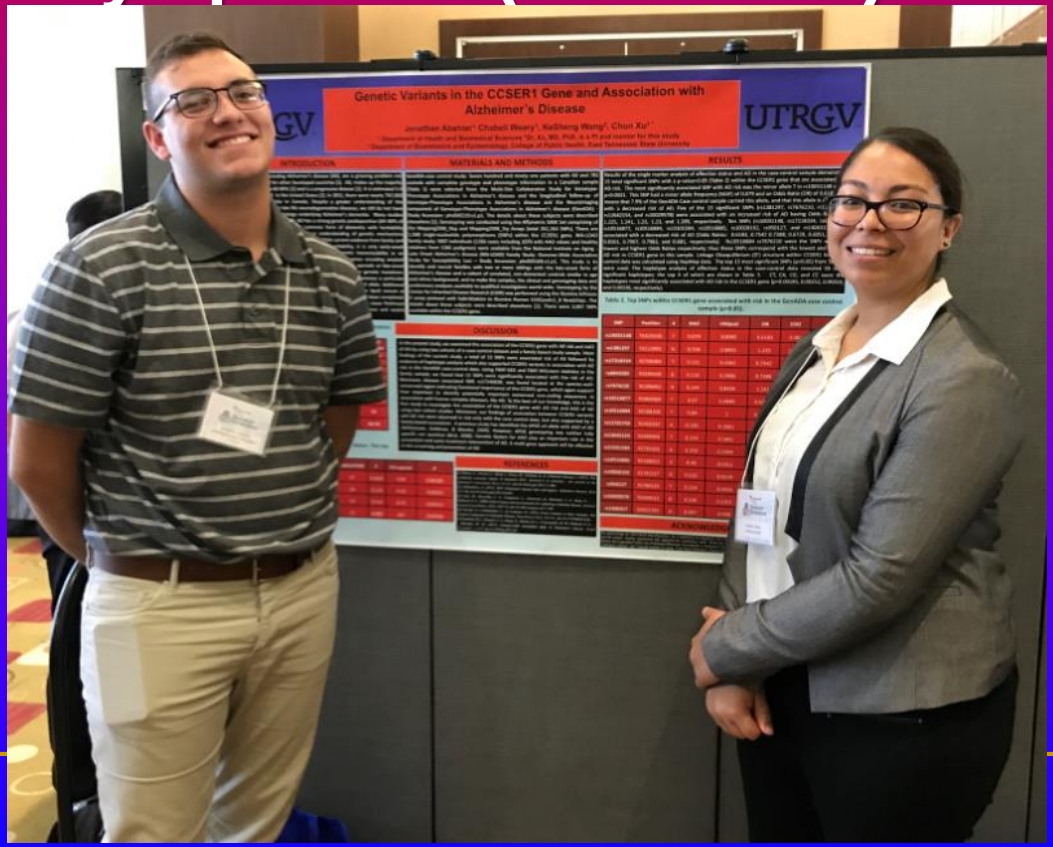
1. BMC Neuroscience 2017 Manuscript ID: BR - 2017
2. Preventive Medicine Reports, 2017 Manuscript ID: PMEDR-17-27

# Two posters presented at the Engaged Scholar Symposium (4-19-2017)

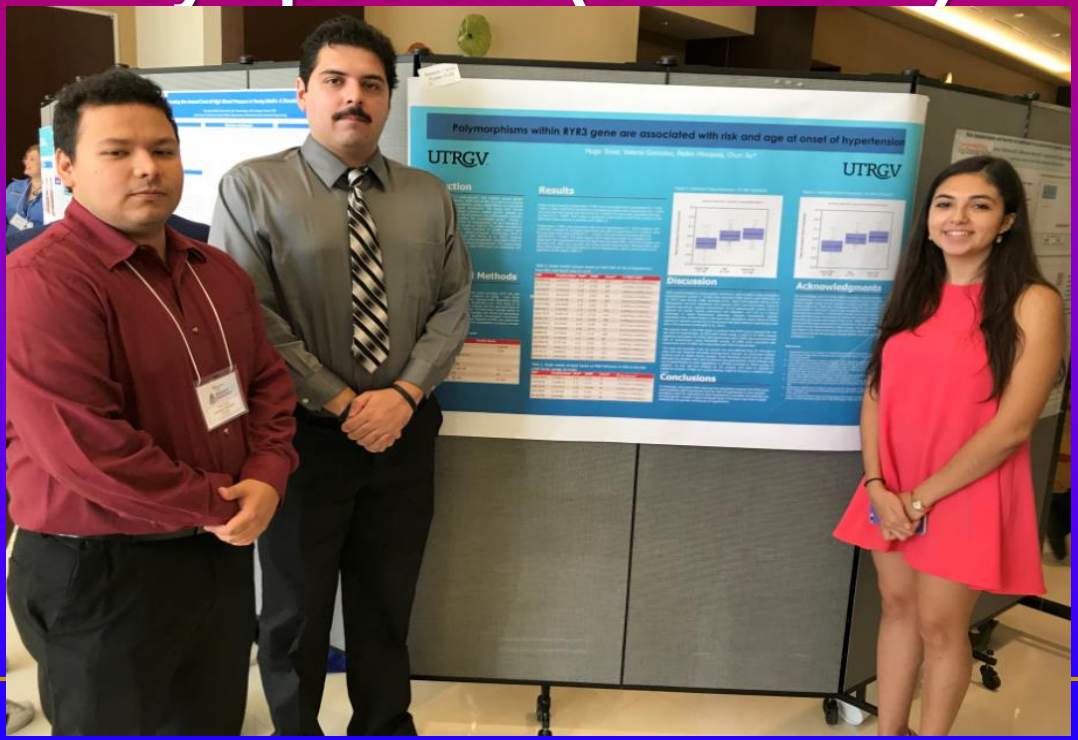


# Study of Alzheimer's Disease has been selected for an oral presentation at the UTRGV-School of Medicine Research Symposium (8-12-2017)

# A poster presentation at the UTRGV-School of Medicine Research Symposium (8-12-2017)



# Study of Hypertension has been won the 1st place for posters at the UTRGV-School of Medicine Research Symposium (8-12-2017)



# Thank you

# Questions and comments