APPLICANT BIOGRAPHICAL SKETCH

Use only for individual predoctoral and postdoctoral fellowships, dissertation research grants (R36),and Research Supplements to Promote Diversity in Health-Related Research (Admin Suppl). DO NOT EXCEED FIVE PAGES.

NAME OF APPLICANT: Marshall Huang

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: PSTP Trainee

EDUCATION/TRAINING *(Most applicants will begin with baccalaureate or other initial professional education, such as nursing. Include postdoctoral training and residency training if applicable. High school students should list their current institution and associated information. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	START DATE MM/YYYY	END DATE *(or expected end date)* MM/YYYY	FIELD OF STUDY
Cornell University, College of Agriculture and Life Sciences (Ithaca, NY)	B.S.	08/09	05/13	Biological Sciences, Nutritional Sciences
University of Pittsburgh School of Medicine (Pittsburgh, PA)	M.D.	08/13	05/18	Medicine

NOTE: The Biographical Sketch may not exceed five pages. Follow the formats and instructions below.

A. Personal Statement

My long-term research goal is to elucidate the cellular and molecular mechanisms behind neurodegenerative processes. My undergraduate and medical school training have provided me with a strong background in cellular biology and neuroscience. While at Cornell University, my passion to study neurodegenerative diseases led me to Dr. Fenghua Hu's lab. There, I worked to determine the how a haplo-insufficiency of progranulin leads to frontotemporal lobar degeneration. Through this experience, I not only learned many essential molecular biology techniques, but also the theory behind them.

While at the University of Pittsburgh School of Medicine, I joined Dr. Robert Friedlander's lab in order to continue my work on neurodegeneration. As a renowned neurosurgeon who is heavily involved in both basic science research and clinical work, I found him to be the ideal mentor for my career aspirations. In addition, his group focuses on the pathophysiology of Huntington's disease, a goal I find both interesting and clinically significant. I have completed three years of medical school and a research year as a part of the Physician-Scientist Training Program. I was awarded the Walter L. Copeland Medical Student Scholar Fellowship in order to fund my research.

In recent years, finding effective treatments for neurodegenerative diseases has become increasingly urgent. Considering that the average age of our population is steadily increasing and that age is the greatest risk factor for neurodegeneration, we will likely see a dramatic rise in the incidence of these diseases in the near future. While I am concerned about all forms of neurodegeneration, Huntington's disease (HD) is of particular interest to me. Unlike Alzheimer's or Parkinson's disease, HD is virtually always attributable to a single genetic defect, which has led to the development of many accurate cell and animal models. This offers a unique opportunity to study disease pathogenesis and evaluate potential therapeutic interventions in a system that is highly translatable to humans.

Through my project, I aim to characterize the function of huntingtin protein in the mitochondria. Considering that many studies have linked mitochondrial dysfunction to neurodegeneration, I expect that this knowledge will elucidate the role of the critical protein that causes HD and one aspect behind mutant-huntingtin mediated neurodegeneration. Although my research is focused on HD, I hope that our findings reveal commonalities in the pathophysiology of several neurodegenerative diseases. My ultimate goal is to discover a connection between multiple causes of neurodegeneration and design a protective agent that is able to protect the brain from age-related degeneration. As a physician-scientist, I hope to not only improve the lives of my patients but also contribute globally by conducting patient-oriented clinical and basic science research.

B. Positions and Honors

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	END DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Graduate Research Student	05/15	05/16	Neurodegeneration and mitochondrial pathology	University of Pittsburgh	Robert Friedlander, MD
Undergraduate Research Student	01/12	05/13	Cell and Molecular Biology	Cornell University	Fenghua Hu, PhD
Undergraduate Research Student	06/11	09/11	Chemistry and Chemical Biology	Cornell University	Francis DiSalvo, PhD
Undergraduate Research Student	01/11	05/11	Plant Pathology and Plant-Microbe Biology	Cornell University	Michelle Cilia, PhD

Academic and Professional Honors

List any academic and professional honors that would reflect upon your potential for a research career and qualifications. Include all scholarships, traineeships, fellowships, and development awards. Indicate sources of awards, dates, and grant or award numbers. List current memberships in professional societies, if applicable.

Professional Memberships and Leadership Positions

2014 – 2015 Neurosurgery Interest Group, Founder and President

2014 – 2015 American Association of Neurological Surgeons Student Chapter, Founder

2014 – 2015 Student Interest Group in Neurology, President

Academic Honors / Awards

2015 – 2016 Walter L. Copeland Medical Student Scholar Fellowship

2015 – 2016 Physician Scientist Training Program

2014 Dean's Summer Research Project

2013 Magna Cum Laude, Cornell University

2010 – 2013 Dean's List

C. Contributions to Science (for predoctoral students and more advanced candidates only; high school students, undergraduates, and postbaccalaureates should skip this section)

The frontotemporal lobar degeneration risk factor, TMEM106B, regulates lysosomal morphology and function

A haploinsuffciency of progranulin (PGRN) is a common cause of frontotemporal lobar degeneration with ubiquitin positive inclusions of TDP-43 (FTLD-U), the second most common cause of early onset dementia.

Genome-wide association studies have also found that single nucleotide polymorphisms in the TMEM106B gene are a risk factor for FTLD-U, particularly in conjunction with PGRN mutations. This project investigated the functions of TMEM106B and its relationship to PGRN.

My role involved culturing T98G, N2A, and HEK293T cell lines for use in a variety of experiments. In order to determine if there was a direct interaction between TMEM106B and PGRN, I pulled down TMEM106B, along with anything complexed to it, from purified cell lysate with co-immunoprecipitations (Co-IP) and measured the protein concentrations by western blot. I also used the western blot to measure changes in PGRN levels after varying levels of TMEM106B expression.

We found that overexpression of TMEM106B resulted in the accumulation of enlarged lysosomes, impaired the degradation of endocytic cargoes, and elevated levels of PGRN. In addition, we found that TMEM106B is localized in the late endosome/lysosome compartments and its levels are regulated by lysosomal activities. We concluded that our molecular and cellular characterization of TMEM106B supports a role of TMEM106B in regulating lysosomal morphology and function. Considering that PGRN also functions in lysosomes, we believe that lysosomal dysfunction has critical role in the progression of FTLD-U.

Brady OA, Zheng Y, Murphy K, **Huang MJ**, Hu F. The frontotemporal lobar degeneration risk factor, TMEM106B, regulates lysosomal morphology and function. *Human Molecular Genetics*. 2013; 22(4):685–695. (peer-reviewed)

Structurally ordered intermetallic platinum–cobalt core–shell nanoparticles with enhanced activity and stability as oxygen reduction electrocatalysts

This project aimed to optimize the performance and durability of nanocatalysts for the oxygen reduction reaction (ORR) in fuel-cell applications. Instead of traditional carbon-supported platinum (Pt/C) nanoparticles, we were interested in creating structurally ordered intermetallic nanoparticles. In an attempt to create a stable catalyst with the highest ORR, we experimented with many combinations of elements.

My role in this project was to determine the best method to synthesize nanoparticles with a combination of platinum (Pt) with iron (Fe), nickel (Ni), and cobalt (Co). The ratios that I most commonly worked with were PtFe, PtNi, PtCo, $PtFe_{.2}Ni_{.8}$, $PtFe_{.5}Ni_{.5}$, and $PtFe_{.8}Ni_{.2}$. After synthesizing and annealing the nanocatalysts, I used x-ray diffraction to determine the structure. The samples were then tested durability and ORR activity. Our lab eventually found that ordered nanoparticles with Pt_3Co intermetallic cores and a 2–3 atomic-layer-thick platinum shell were more durable and active than Pt/C nanoparticles after 5,000 cycles. We concluded that these ordered intermetallic core-shell nanocatalysts could be used for the ORR in future fuel-cell applications.

Research Papers

1. Iorio-Morin C, Kano H, **Huang M**, Lunsford LD, Simonová G, Liscak R, Cohen-Inbar O, Sheehan J, Lee CC, Wu HM, Mathieu D. Histology-stratified tumor control and patient survival following stereotactic radiosurgery for pineal region tumors: a report from the International Gamma Knife Research Foundation. World Neurosurg. 2017 Jul 24. [Epub ahead of print] PubMed PMID: 28751141.

2. **Huang MJ**, Kano H, Mousavi SH, Niranjan A, Monaco EA 3rd, Arai Y, Flickinger JC, Lunsford LD. Stereotactic radiosurgery for recurrent vestibular schwannoma after previous resection. J Neurosurg. 2017 May;126(5):1506-1513. PubMed PMID: 27471891.

3. Mousavi SH, Niranjan A, Akpinar B, **Huang M**, Kano H, Tonetti D, Flickinger JC, Dade Lunsford L. Hearing subclassification may predict long-term auditory outcomes after radiosurgery for vestibular schwannoma patients with good hearing. J Neurosurg. 2016 Oct;125(4):845-852. PubMed PMID: 26745482.

4. Mousavi SH, Niranjan A, **Huang MJ**, Laghari FJ, Shin SS, Mindlin JL, Flickinger JC, Lunsford LD. Early radiosurgery provides superior pain relief for trigeminal neuralgia patients. Neurology. 2015 Dec 15;85(24):2159-65. PubMed PMID: 26561286.

5. Brady OA, Zheng Y, Murphy K, **Huang M**, Hu F. The frontotemporal lobar degeneration risk factor, TMEM106B, regulates lysosomal morphology and function. Hum Mol Genet. 2013 Feb 15;22(4):685-95. PubMed PMID: 23136129

D. Scholastic Performance

Predoctoral applicants: Using the chart provided, list by institution and year all undergraduate and graduate courses with grades. In addition, in the space following the chart, explain any marking system if other than 1-100, A, B, C, D, F, or 0-4.0 if applicable. Show levels required for a passing grade.

Postdoctoral applicants: Using the chart provided, list by institution and year all undergraduate courses and graduate scientific and/or professional courses germane to the training sought under this award with grades. In the space following the chart, explain any marking system if other than 1-100, A, B, C, D, F, or 0-4.0 if applicable. Show levels required for a passing grade.

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	OTHER COURSE TITLE	GRADE