BIOGRAPHICAL SKETCH

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NAME: Huang, Miller

eRA COMMONS USER NAME (credential, e.g., agency login): m3huang

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Berkeley	BS	12/2003	Bioengineering
University of California, San Diego	PhD	06/2011	Molecular Pathology
University of California, San Diego	Postdoctoral	07/2011-01/2012	Pathology (mentor: David Cheresh)
University of California, San Francisco	Postdoctoral	03/2012-06/2015	Neurology (mentor: William Weiss)

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

A. Personal Statement

During my postdoc training, I developed human stem cell based models for medulloblastoma and neuroblastoma. Using human induced pluripotent stem cells (iPSC) from a healthy adult, I differentiated towards neuroepithelial stem (NES) cells or trunk neural crest cells (tNCC), mis-expressed MYCN and implanted orthotopically into immunocompromised mice (cerebellum for NES cells and renal capsule for tNCC). Within 3-4 months post-injection, all mice exhibited signs of tumor formation and had to be euthanized. Tumors were analyzed by histology and RNA-seq to validate the NES cell-derived tumors resembled medulloblastoma (compared to other pediatric brain tumors) and the tNCC-derived tumors resembled neuroblastoma (compared to other neural crest derived tumors). I have also utilized the models to categorize candidate mutations as either drivers or passengers in each disease. For my independent laboratory, I plan to utilize these model systems to continue validating candidate mutations as drivers or passengers. In addition, I envision my model can be used for chemical and genetic screens (e.g. CRISPR interference) to identify candidate therapeutic vulnerabilities for tumors with genotypes that are resistant to standard of care.

B. Positions and Honors

Employment

2011-2012	UC San Diego	Post-Doctoral Scholar (under David A Cheresh)
2012-2015	UC San Francisco	Post-Doctoral Scholar (under William A Weiss)
2015-2017	UC San Francisco	Instructor
2017-2019	UC San Francisco	Assistant Adjunct Professor
2019-present	USC/Children's Hospital Los Angeles	Assistant Professor

Honors

2007-2010	Molecular Pathology of Cancer T32 Training Grant
2013	NIH F32 Postdoctoral Fellowship (declined)
2013-2016	American Cancer Society Postdoctoral Fellowship
2013-2015	Alex's Lemonade Stand Foundation Young Investigator Award
2015	AACR Scholar-in-Training Award
2016-present	NIH/NCI K99/R00 Pathway to Independence Award
2016	Lerner Family Foundation Travel Award
2017	UCSF REAC award
2018	Lerner Family Foundation Early Career Travel award

C. Contributions to Science

1. **Modeling medulloblastoma (MB) using human pluripotent stem cells.** Currently, MB models are restricted to genetically engineered mouse models (GEMM), human cell lines and primary tumors from patients. To understand which genes are involved in MB tumorigenesis, GEMMs provide some clue but human and mouse cells of the same type have shown differences in genetic requirements for transformation (e.g. CMYC and H-RAS are sufficient to transform mouse but not human fibroblasts). Current human cell models such as cell lines and primary tumors are already transformed. In contrast, my human stem cell based model of MB can be routinely used to address how genetic mutations alone or in combination influence a normal neuroepithelial stem cell since the genetic background is cleaner and there is an isogenic control cell line to compare against. In addition, the control cell line is critical when testing therapy and performing compound/genetic screens to identify targets that affect tumor cells but not normal cells. Human stem cells also allow modeling of patient-relevant chromosomal abnormalities, a difficult task in GEMM as mouse and human chromosomes do not align.

    a. **Huang M***, Tailor J*, Zhen Q, Gillmor AH, Miller ML, Weishaupt H, Chen J, Zheng T, Nash EK, McHenry LK, An Z, Ye F, Takashima Y, Clarke J, Ayetey H, Cavalli FMG, Luu B, Moriarity BS, Ilkhanizadeh S, Chavez L, Yu C, Kurian KM, Magnaldo T, Sevenet N, Koch P, Pollard S, Dirks P, Snyder MP, Largaespada DA, Cho YJ, Phillips JJ, Swartling FJ, Morrissy AS, Kool M, Pfister SM, Taylor MD, Smith A, Weiss WA. Engineering genetic predisposition in human neuroepithelial stem cells recapitulates medulloblastoma. ***Cell Stem Cell*** (2019).

2. **Modeling neuroblastoma (NB) using human pluripotent stem cells.** I have also developed a human stem cell based model of NB. Of the advantages I described in #1 of a human stem cell based model over GEMM, the ability to model chromosomal copy number changes in NB is particularly important. Sequencing studies of high-risk NB have found few recurring single nucleotide variations but identified recurring subchromosomal alterations (e.g. deletion of 1p, 11q and gain of 17q) suggesting that the vast majority of NB patient tumors is driven by these large chromosomal alterations. To aid the development of my model for NB, I optimized a protocol to differentiate human pluripotent stem cells toward trunk neural crest cells (cell of origin for NB).

    a. Huang M, Miller ML, McHenry LK, Zheng T, Zhen Q, Ilkhanizadeh S, Conklin BR, Bronner ME, Weiss WA. Generating trunk neural crest from human pluripotent stem cells. *Scientific Reports.* (2016)

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/bibliography/47060547/

D. Research Support

ACTIVE

4R00CA197484-03 (Huang) 9/16/2019 – 8/31/2022 9.00 calendar
NIH/NCI $146,902
Identification of novel cooperating partners of MYCN in neuroblastoma tumorigenesis

The major goals of this project are to define the role of deletion of chromosome 1p in MYCN-driven neuroblastoma tumorigenesis and to identify critical genes within chromosome 1p that act as tumor suppressors in MYCN-dependent tumorigenesis

COMPLETED (within last 3 years)

K99CA197484-01 (Huang) 07/01/2016-06/30/2019
NIH/NCI
Identification of novel cooperating partners of MYCN in neuroblastoma tumorigenesis

The goal of this proposal is to develop a human stem cell based model of neuroblastoma that will be used to identify cooperating partners of MYCN in tumorigenesis