

## YU-HUI WONG, Ph.D.

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Brain Research Center  
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Female born on April 10, 1979

### PERSONAL STATEMENT

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Currently working as an independent researcher in the Brain Research Center of NYCU; demonstrating the ability to successfully balance between academic and educational commitments. Pursue a varied and challenging position that will enable me to consolidate my professional experience, expand my knowledge and provide opportunities for personal and professional growth.

### EDUCATION

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1997.04-2001.07	B.S. in Life Sciences, National Yang-Ming University, Taipei, Taiwan
2001.09-2003.07	M.S. in Neuroscience, National Yang-Ming University, Taipei, Taiwan (Dean's Award, School of Life Sciences, NYMU)
2003.09-2009.12	Ph.D. in Neuroscience, National Yang-Ming University, Taipei, Taiwan (Mentor: Ming-Ji Fann, Ph.D.)

### POSITIONS and EMPLOYMENTS

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2010.08-2014.07	Postdoctoral Fellow, Department of Molecular and Cell Biology, University of California, Berkeley, USA (Supervisor: Mu-ming Poo, Ph.D.)
2014.08-2016.01	Postdoctoral Fellow, Brain Research Center, National Yang-Ming University, Taipei, Taiwan
2016.02-present	Assistant Research Fellow, Brain Research Center, National Yang Ming Chiao Tung University, Taipei, Taiwan
2020.08-present	Adjunct Assistant Professor, Department of Life Sciences and Institute of Genome Sciences, National Yang Ming Chiao Tung University, Taipei, Taiwan

### CURRENT RESEARCH

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Our laboratory is working on identifying the molecular mechanisms underlying how a pluripotent cell develops into a defined cell type of human brain, such as neurons, microglia, retinal ganglion cells and other neural lineages. This has allowed us to generate functional brain cells with high consistency at scale from human iPSCs, including patient-derived iPSCs or those carrying disease-specific mutations by CRISPR/Cas9 technology, offering novel avenues for the development of human *in vitro* models to support research and drug discovery.

In the past four years, we used human iPSCs derived from familial and sporadic patients of Alzheimer's disease (AD) to study disease mechanisms and to screen novel drugs for treatment. We differentiated the AD-iPSC lines into the neuronal lineage to examine whether these neurons have mature phenotypic and physiological properties, as well as AD-like biochemical features. We also established a novel protocol enabling differentiation of human microglia-like cells from hiPSCs in high

purity, which is used to investigate the neuroinflammatory phenotypes of AD. In the future, AD-iPSC derived neurons and glial cells, plus 3D organoids, harboring disease properties will be used as humanized models to study the mechanisms underlying AD pathogenesis, as well as to evaluate potential drugs for AD treatment.

## RESEARCH EXPERIENCES

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### 2001.09-2009.12      **Molecular and Cellular Mechanisms of Neural Development**

- General molecular experiments and biochemical assays (gene cloning, RT-PCR, western blot, etc.)
- General cell biological experiments (mammalian cell culture, immunocytochemistry, etc.)
- *In vivo* chick embryo manipulation (*in ovo* electroporation, immunohistochemistry, etc.)
- Phenotype analyses of transgenic mouse embryos

### 2010.08-2014.07      **Mechanisms and Regulation of Neurotrophin Transport and Secretion**

- *In vitro* live-cell imaging (time-lapse recording of single molecule tracking, FRET imaging, calcium imaging, and image analysis, etc.)
- General cell biological experiments (primary neuronal culture, immunocytochemistry, etc.)
- *In vivo* rat embryo manipulation (*in utero* electroporation, section and time-lapse imaging, immunohistochemistry, etc.)
- Viral vector package (lentivirus)

### 2014.08-present      **Modeling of Human Neurological Disorders Using Induced Pluripotent Stem Cells**

- *In vitro* modeling of AD using patients' iPSCs (human iPSC culture, neuron & microglia differentiation, 3D brain organoid, genome editing with CRISPR/Cas9 technology, etc.)
- Evaluation of drug candidate using AD-iPSCs (*in vitro* AD pathological phenotype assays)

## PUBLICATIONS

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### Theses

Functional study of Protogenin signaling in the embryonic development. Ph. D. dissertation, National Yang-Ming University, Taipei, Taiwan (12/2009).

### Articles (Peer-reviewed)

- Human iPSC-derived neurons as a platform to decipher the mechanisms behind brain aging. Chao CC, Shen BW, Tzeng TY, Kung HJ, Tsai TF and **Wong YH\***. (2021) *Biomedicines* 9(11):1635; doi.org/10.3390/biomedicines9111635. (IF=6.1; R/C=65/295, biochemistry & molecular biology) (\* [Corresponding](#))
- Efficient conversion of human induced pluripotent stem cells into microglia by defined transcription factors. Chen SW, Hung YS, Fuh JL, Chen NJ, Chu YS, Chen SC, Fann MJ and **Wong YH\***. (2021) *Stem Cell Reports* 16(5): 1363-1380; doi: 10.1016/j.stemcr.2021.03.010. (IF=7.8; R/C=5/31, cell & tissue engineering) (\* [Corresponding](#))
- Muscle atrophy-related myotube-derived exosomal microRNA in neuronal dysfunction: Targeting both coding and long-noncoding RNAs. Yang CP<sup>#</sup>, Yang WS<sup>#</sup>, **Wong YH<sup>#</sup>**, Wang KH, Teng YC, Chang MH, Liao KH, Nian FS, Tsai JW, Hwang WL, Lin MW, Tzeng TY, Wang PN, Campbell M, Chen LK, Tsai TF\*, Chang PC\* and Kung HJ\*. (2020) *Aging Cell* e13107; doi: 10.1111/accel.13107. (IF=9.3; R/C=4/66, geriatrics & gerontology) (<sup>#</sup> [First author](#))

Assessing the therapeutic potential of *Graptopetalum paraguayense* on Alzheimer's disease using patient iPSC-derived neurons. Wu PC, Fann MJ, Tran T, Chen SC, Devina T, Cheng IH, Lien CC, Kao LS, Wang SJ, Fuh JL, Tzeng TT, Huang CY, Shiao YJ\* and **Wong YH\***. (2019) *Sci. Rep.* 9, 19301; doi:10.1038/s41598-019-55614-9. (IF=4.4; R/C=19/126, multidisciplinary sciences) (\*  
**Corresponding**)

GSKIP-mediated anchoring increases phosphorylation of Tau by PKA but not GSK3beta via a cAMP/PKA/GSKIP/GSK/Tau axis signaling in cerebrospinal fluid and iPSC cells of Alzheimer disease. Ko HJ#, Chiou SJ#, **Wong YH#**, Wang YH, Lai YL, Chou CH, Wang C, Loh JK, Lieu AS, Cheng JT, Lin YT, Lu PJ, Fann MJ, Huang CY\* and Hong YR\*. (2019) *J. Clin. Med.* 8(10), pii: 1751; doi.org/10.3390/jcm810175. (IF=4.2; R/C=35/313, medicine, general & internal) (#**First author**)

Cdk12 regulates neurogenesis and late-born neuronal migration in the developing cerebral cortex. Chen HR, Juan HC, **Wong YH**, Tsai JW and Fann MJ\* (2017) *Cereb Cortex.* 27(3):2289-2302. (IF=5.4; R/C=36/289, neurosciences)

Activity-dependent BDNF release via endocytic pathways is regulated by complexin and synaptotagmin-6. **Wong YH**, Lee CM, Xie W, Cui B and Poo MM\* (2015) *Proc Natl Acad Sci U S A.* 112(32):E4475-84. (IF=11.2; R/C=7/126, multidisciplinary sciences) (#**First author**)

Protogenin prevents premature apoptosis of rostral cephalic neural crest cells by activating the  $\alpha 5\beta 1$ -integrin. Wang YC, Juan HC, **Wong YH**, Kuo WC, Lu YL, Lin SF, Lu CJ and Fann MJ\* (2013) *Cell Death Dis.* 4:e651. (IF=8.5; R/C=37/195, cell biology)

Self-amplifying autocrine actions of BDNF in axon development. Cheng PL, Song AH, **Wong YH**, Wang S, Zhang X and Poo MM\* (2011) *Proc Natl Acad Sci U S A.* 108(45):18430-5. (IF=11.2; R/C=7/126, multidisciplinary sciences)

Protogenin defines a transition stage during embryonic neurogenesis and prevents precocious neuronal differentiation. **Wong YH**, Lu AC, Wang YC, Cheng HC, Chang C, Chen PH, Yu JY and Fann MJ\* (2010) *J Neurosci.* 30(12):4428-39. (IF=6.2; R/C=33/289, neurosciences) (#**First author**)

CDK13/CDC2L5 interacts with L-type cyclins and regulates alternate splicing. Chen HH, **Wong YH**, Geneviere AM and Fann MJ\* (2007) *Biochem Biophys Res Commun.* 354(3):735-40. (IF: 3.6; rank: 24/71, biophysics)

(\***Corresponding author**) (#*These authors contributed equally.*)

(*IF and rank by JCR 2021*)

### **Manuscripts (in preparation or submission)**

- ER stress accelerates the onset of Alzheimer's Disease-like phenotypes in APP D678H mutant iPSC derived neuron.

Deniva T, **Wong YH**, Hsiao CW and Cheng IH\*.

(under review of the *Journal of Neurochemistry*)

- Efficiently induced human retinal ganglion-like cells provide a platform for studying ethambutol-induced optic neuropathy.

Liou HC, Chen SW, Wu PC, Cheng HJ, Fann MJ and **Wong YH\***.

(in preparation)

- Protogenin regulates Hox gene expression and vertebral patterning through Wnt signaling pathway. Hung YS, Fann MJ, **Wong YH\*** and Yu JY\*.

(in preparation)

- Peripheral TREM2 and soluble TREM2 mRNA expression are associated with the cognitive decline in mild dementia due to Alzheimer's disease.

Lee WJ, Chen NJ, Tsai JW, **Wong YH**, Yang YH and Fuh JL\*.

(submitted to the *Journal of Neuroinflammation*)

(\***Corresponding author**)

## **Patents**

- Methods of producing microglia and uses thereof. (Inventor & Applicant; Appl. No: 62/872,360; US provisional; Jul 10 2019 filed)

## **Oral Presentations** (in 5 years)

(Invited talks at the international meetings and seminars)

- 2020.10.21 Age-related myotube-derived exosomal microRNA in neuronal dysfunction. The Sixth ICAH-NCGG Symposium, Hsinchu, Taiwan
- 2019.10.31 Modeling Alzheimer's disease *in vitro* and evaluating novel drugs for treatment using human iPSC-derived neural cells. The 3<sup>rd</sup> Vinmec International Conference on Cell & Gene Therapy, Hanoi, Vietnam
- 2019.10.30 Assessing the therapeutic potential of Chinese herbal medicines on Alzheimer's disease using patient iPSC-derived neurons. Hanoi Medical University, Hanoi, Vietnam
- 2017.09.16 Modeling Alzheimer's disease *in vitro* and evaluating novel drugs for treatment with human induced pluripotent stem cells. International Conference of Developmental Biology, Stem Cells and Regenerative Medicine, Taipei, Taiwan

## **Conference Abstracts** (in 5 years)

- 2020.09.12 Efficient generation of functional microglia-like cells from human induced pluripotent stem cells by defined transcription factors. (poster) Interdisciplinary Neuroscience Congress, Taipei, Taiwan
- 2019.08.23 Efficient generation of functional microglia-like cells from human induced pluripotent stem cells by defined transcription factors. (poster) International Conference of Developmental Biology, Stem Cells and Regenerative Medicine, Taipei, Taiwan
- 2019.07.17 Direct conversion of human induced pluripotent stem cells into functional microglia-like cells by defined transcription factors. (<https://doi.org/10.1016/j.jalz.2019.08.024>) Alzheimer's Association International Conference, Los Angeles, USA
- 2017.09.16 Modeling Alzheimer's disease *in vitro* and evaluating novel drugs for treatment with human induced pluripotent stem cells. (selected short talk & poster) International Conference of Developmental Biology, Stem Cells and Regenerative Medicine, Taipei, Taiwan

## **GRANTS**

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### **Research Grants**

- Untangling cell type-specific roles and associated genetic risk variants in Alzheimer's disease using human induced pluripotent stem cells (計畫主持人, 計畫編號: CI-111-4, 財團法人嚴慶齡醫學基金會, 111/1/1~111/12/31, NT\$210,000)
- To study the genetic risk variants and environmental factors for Alzheimer's disease and to screen novel drugs for treatment using human induced pluripotent stem cells (hiPSCs) (計畫主持人, 計畫編號: MoST 108-2320-B-010-042-MY3, 科技部, 108/8/1~111/7/31, NT\$4,194,000)
- Characterization of the effects of *Graptopetalum paraguayense* and *Vitis thunbergii* var. *taiwaniana* in the alleviation of Alzheimer's disease-related phenotypes using patient-derived induced pluripotent stem cells (計畫主持人, 計畫編號: CI-108-2, 財團法人嚴慶齡醫學基金會, 108/1/1~108/12/31, NT\$230,000)
- Untangling cell type-specific roles and associated genetic risk variants in sporadic Alzheimer's disease using human induced pluripotent stem cells (hiPSCs) (計畫主持人, 計畫編號: MoST 107-2635-B-010-001-, 科技部, 107/8/1~108/7/31, NT\$820,000)

To study the underlying mechanisms of Alzheimer's disease (AD) and screen novel drugs for treatment using human induced pluripotent stem cells (iPSCs) as an *in vitro* model (計畫主持人，計畫編號：CI-107-1，財團法人嚴慶齡醫學基金會，107/1/1~107/12/31，NT\$300,000)

### **Industry-University Cooperative Research Project**

建立 PSEN1\_A246E 和 LRRK2\_G2019S 突變之人類誘導型多能幹細胞 (計畫主持人，計畫編號：109J036，昱星生物科技股份有限公司，109/8/1~110/1/31，NT\$666,667)

人類誘導型多能幹細胞衍生神經元之產生 (計畫主持人，計畫編號：108J048，昱星生物科技股份有限公司，108/10/1~109/1/31，NT\$57,529)

Grape King Biotech Co., Ltd. commissioned the drug tests using human neurons derived from induced pluripotent stem cells of patients with Alzheimer's disease. (計畫主持人，計畫編號：107J033，葡萄王生技股份有限公司，107/7/1~108/1/31，NT\$1,241,000)

### **Joint Research Grants**

Involved in the grant “腦的退化：「骨骼肌-到-腦」軸調控老化之身心衰退” (協同研究人員，台灣腦科技發展及國際躍升計畫 2021-2024，科技部，總主持人：王培寧教授)

Involved in the grant “大腦可塑性在身心衰退的創新機轉” (協同研究人員，台灣腦科技發展及國際躍升計畫 2019-2020，科技部，總主持人：王培寧教授)

Involved in the grant “特色領域卓越中心 - 陽明大學腦科學中心” (協同研究人員，教育部深耕計畫 2018-2022，總主持人：王署君教授)

Involved in the grant “A multimodal approach of microglia mediated neuroinflammation in Alzheimer's disease: from bench to clinical” (協同研究人員，Research Program for Neuroscience 2017-2019，科技部，總主持人：傅中玲教授)

## **ACADEMIC SERVICE**

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### **BRC, NYCU (國立陽明交通大學腦科學研究中心)**

- 協助陽明交通大學腦科學中心教育部深耕計畫 107 / 108 / 109 年度結案報告 (Dec 2018/2019/2020/2021)
- 協助安排 BRC 腦科學中心月會專題演講 (Apr 2020, Dec 2020, Aug 2021, Apr 2022)
- 協助 BRC 腦科學頂尖論壇暨專家外審座談會 (Jun 2019)
- 協助 BRC 程淮榮客座教授專題演講暨學生座談會 (Jul 2019)
- 協助 BRC 年度腦功能健檢活動 (Oct 2019)
- 協助 BRC 教育部深耕計畫撰寫 (Oct 2017 – Jan 2018)

### **Others**

- Office of Student Affairs, Graduate Program in Molecular Medicine, School of Life Sciences, NYCU (2022.02-present)
- Admission committee of graduate students (Department of Life Sciences and Institute of Genome Sciences, NYCU, 2021)
- Committee member of Ph.D. candidate progress report (Department of Life Sciences and Institute of Genome Sciences, NYMU, 2020)
- Admission committee of undergraduate students (Interdisciplinary Program for Undergraduates, NYMU, 2020)

- Committee member of Ph.D. candidate qualifying exams (Department of Life Sciences and Institute of Genome Sciences, NYMU, 2019)

## TEACHING and STUDENT TRAINING

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2021.09-present	Scientific Literature Reading and Analysis I (2 hr/week, Undergraduate, Department of Life Sciences and Institute of Genome Sciences, NYCU)
2020.09-present	Career Development and Preparation (2 hr/week, Undergraduate, Department of Life Sciences and Institute of Genome Sciences, NYCU) 獲 109 年度「良師益友獎」
2021.09-2022.01	Seminar on Molecular Medicine (2 hr/week, Graduate Program in Molecular Medicine, School of Life Sciences, NYCU)
2021.05	Graduate course (4 hr) on ESC/iPSC development & applications
2020.09-2021-06	Seminar course (2 hr/week, Master degree, Department of Life Sciences and Institute of Genome Sciences, NYCU)
2020.06	Graduate course (2 hr) on hiPSC technology & applications for neurological diseases
2016.07-present	Graduate and undergraduate student training: <u>Shih-Wei Chen 陳是瑋</u> , enrolling as a Ph.D. student in the Department of Life Sciences and Institute of Genome Sciences, NYCU (Sep 2021) 獲 110 年度「科技部補助大專校院培育優秀博士生獎學金」NT\$40,000/month for 4 years <u>Ting-Hui Xie 謝婷卉</u> (Undergraduate, 2021-2022) <u>Hsiang-Chi Liou 柳湘琪</u> (Master, 2017-2019) <u>Yi-Chun Liu 劉羿君</u> (Master, 2017-2019) <u>Tran Thanh Tu</u> (Master, USTH Vietnam, 2017-2018) <u>Doan Thao Nguyen</u> (Undergraduate, USTH Vietnam, 2017)

## PROFESSIONAL SOCIETIES and OTHER EXPERIENCES

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### Memberships

- 2021-present Member of The International Society for Stem Cell Research (ISSCR)  
2019-present Member of Taiwan Society for Stem Cell Research  
2017-present Member of Taiwanese Society of Developmental Biology  
2003-present Member of Society for Neuroscience, USA

### Journal Reviewer

- 2018-present Reviewer for PLOS ONE  
2015-present Reviewer for Developmental Neurobiology