MINEE-LIANE CHOI

INVITED TALK 3

Organoid-Based Drug Testbed Using AI for Brain Disorders

Minee L. Choi[1*]

[1] Department of the Brain & Cognitive Sciences, KAIST, Daejeon: 34141, Republic of Korea

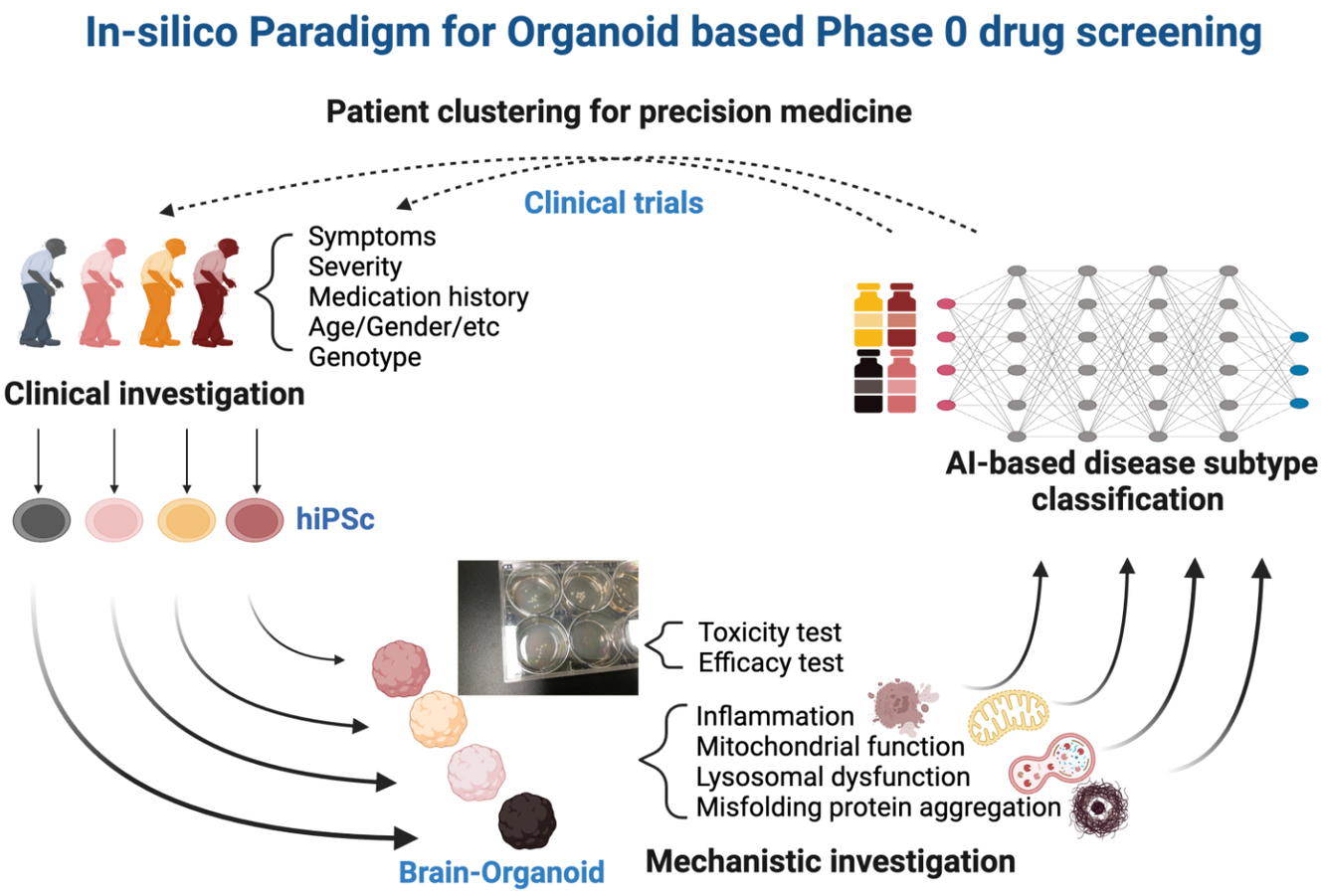
***Corresponding author:** minee.choi@kaist.ac.kr

Abstract

Parkinson's disease (PD) is a progressive and currently incurable neurodegenerative disorder characterized by significant clinical heterogeneity. It is increasingly recognized that different cellular mechanisms may drive the disease in different individuals. Identifying the mechanistic subtypes in patients would enable a precision medicine approach, whereby targeted therapies could be applied to address the specific pathological mechanisms. However, defining the underlying cellular mechanisms in each patient has been challenging due to the limited accessibility of brain cells from living individuals.

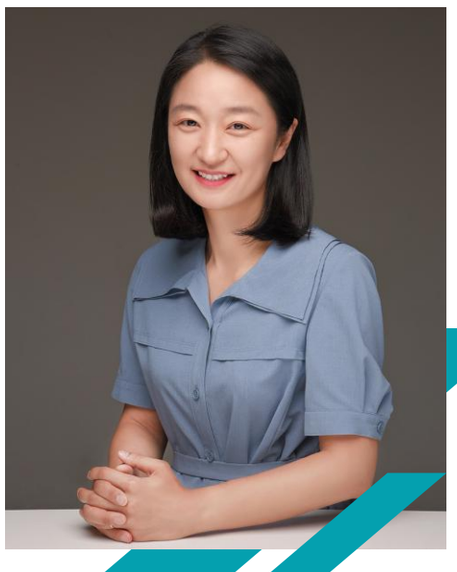
By utilizing induced pluripotent stem cell (iPSC) organoid technology, we have embraced the 'disease in a dish' paradigm to study patient-specific brain cells. This approach has facilitated the development of preclinical models derived directly from individuals with PD. Our method has demonstrated exceptional accuracy in predicting molecular subtypes while maintaining broad generalizability. Using deep neural networks, we analyzed two types of raw imaging data alongside data extracted from a widely used high-content imaging platform. Notably, our results indicated that analyzing raw data without predefined features can effectively predict cellular subtypes, revealing novel biological insights into the disease.

The successful application of deep learning to characterize cellular subtypes in PD marks a significant breakthrough in understanding the complexity of this disorder. These advancements hold great potential for developing an AI-driven validation pipeline capable of predicting the efficacy of novel therapeutic agents targeting specific molecular pathways in individual patients. This approach has the potential to significantly reduce the time and cost of clinical trial preparation for neurodegenerative diseases.



Keywords: Neurodegenerative disorders, hiPSC, Organoid, AI, Precision Medicine

CURRICULUM VITAE



Name:	Minee L. Choi
Academic positions:	Assistant Professor
Workplace:	KAIST
Address:	W13, R502-5, 291 Daehak-ro, Yuseong-gu, Daejeon 34141, Republic of Korea
Email:	minee.choi@kaist.ac.kr
Expertise:	Patient-derived iPSC, Parkinson's disease, Lewy Body Dementia, Organoid, Mitochondrial Dysfunction, AI

Education History

[Doctorate]	2008-2013	Department of Clinical Neurosciences, University of Cambridge, UK
[B.A/MMSc]	1998-2005	College of Medicine, Hanyang University, Republic of Korea

Professional Background

2023-present	Assistant Professor at the Department of Brain and Cognitive Sciences, KAIST, Republic of Korea
2017-2022	Research Fellow at the Francis Crick Institute, UK (laboratory secondment)
2014-2022	Post-Doctoral Research Fellow at the UCL Queen Square Institute of Neurology, University of London, UK
2012-2013	Research Associate at the UCL Wolfson Institute for Biomedical Research, University of London, UK

Selected Awards and Honors

1.	2024	KAIST Outstanding Lecture Award
2.	2023	KAIST Q-DAY Special Prize; Creative lecture award
3.	2010	Imogen Rose Prize; Best first-year report award of the Department of Clinical Neurosciences, University of Cambridge
4.	2008	Cambridge Overseas Trust; PhD scholarship (2008 – 2012)
5.	2008	Mogam Foundation Overseas Student Fund Award

Selected Publications

1. D'Sa K, Evans JR, Virdi GS, Vecchi G, Adam A, Bertolli O, Fleming J, Chang H, Leighton C, Horrocks M, Athauda D†, **Choi ML†**, Gandhi G† "Prediction of mechanistic subtypes of Parkinson's using patient-derived stem cell models" *Nature Machine Intelligence*, 11 Aug (2023) **†Equally contributed**
2. **Choi ML**, Chappard A, Singh BP, Maclachlan C, Rodrigues M, Fedotova E, Berezhnov AV, De S, Peddie C, Athauda D, Virdi GS, Zhang W, Evans JR, Angelova PR, Esteras N, Morris K, Tosatto L, Little D, Gissen P, Collinson L, Klenerman D, Abramov AY, Horrocks MH, Gandhi S **"**Pathological structural conversion of α-synuclein at the mitochondria induces neuronal toxicity" *Nature Neuroscience* 25, 1134–1148 (2022).
3. Angelova PR***, Choi ML*,** Berezhnov AV, Horrocks MH, Hughes CD, De S, Rodrigues M, Yapom R, Little D, Dolt KS, Kunath T, Devine MJ, Gissen P, Shchepinov MS, Sylantyev S, Pavlov EV, Klenerman D, Abramov AY, Gandhi S "Alpha synuclein aggregation drives ferroptosis in Parkinson's disease: an interplay of iron, calcium and lipid peroxidation" *Cell death & Differentiation*. 27, 2781-2796 (2020) (*Equally contributed).
4. Hughes CD***, Choi ML*,** Ryten M, Hopkins L, Drews A, Botía JA, Iljina M, Rodrigues M, Gagliano SA, Gandhi S, Bryant C, Klenerman D "Picomolar concentrations of oligomeric alpha-synuclein sensitizes TLR4 to play an initiating role in Parkinson's disease pathogenesis" *Acta Neuropathologica* 137(1), 103-120 (2019).
5. Ludtmann MHR, Angelova PR, Horrocks MH, **Choi ML**, Rodrigues M, Baev AY, Berezhnov AV, Yao Z, Little D, Banushi B, Al-Menhali AS, Ranasinghe RT, Whiten DR, Yapom R, Dolt KS, Devine MJ, Gissen P, Kunath T, Jaganjac M, Pavlov EV, Klenerman D, Abramov AY, Gandhi S "α-synuclein oligomers interact with ATP synthase and open the permeability transition pore in Parkinson's disease" *Nature Communications* 9(1), 1–16 (2018)