[Mock biographical sketch for the University of California, San Diego, Medical Writing Certificate]

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BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: Sim, HyungSub

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

POSITION TITLE: Assistant Clinical Professor of Neurology and Psychiatry

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
Marshall University	BA	05/2002	Neuroscience, Biology and Linguistics
University of Minnesota	MD	05/2006	Medicine
University of Iowa Hospitals and Clinics	Resident	07/2010	Neurology
University of Iowa Hospitals and Clinics	Chief Resident	07/2011	Neurology
Northwestern University	Fellowship	07/2013	Neurodegenerative Disease and Neuropsychiatry

Personal Statement

I am a Clinical Assistant Professor of Neurology and Psychiatry at the University of Iowa College of Medicine who specializes in the treatment of dementia. My interest in neurodegenerative disease began as a teen while visiting my aunt in Korea; it was my first encounter with an adult diagnosed with a memory disorder. After this experience, I became intrigued with complex neurodegenerative diseases. Unfortunately, Korea's population is aging more rapidly than any other country. In fact, by 2045, Korea will represent the most aged population in the world. For these very personal reasons, I decided, at the age of 18, to begin studying neuroscience, linguistics, and biology.

After attending medical school, I completed a fellowship in neurodegenerative disease at the world-renowned Smith Center for Cognitive Neurology and Alzheimer's Disease at Northwestern University. Our team identified a novel progranulin GRN-related mutation in patients with frontotemporal lobe dementia (FTLD). This project required consultation and coordination with scientists from three specialties—neurology, pathology, and radiology—an experience that honed my ability to work in partnership with colleagues from varied backgrounds.

As part of my transition to an independent scientist, I launched a project that correlated neuropsychological measures of language with areas of cortical thinning and atrophy on magnetic resonance imaging (MRI) in patients with primary progressive aphasia, a subtype of FTLD. As the principal investigator for this study, I acquired valuable skills in project and team management as we successfully completed and published our results. This timely and productive research in PPA led to my position as assistant professor at the University of Iowa Hospitals and Clinics.

As an academic scientist, I have honed my skills in protocol development, imaging interpretation, and data analysis. I have also gained the necessary skills to develop novel biomarkers and radioligands relevant to FTLD. My participation in an NIH-funded study led to advancements in another neurodegenerative ailment related to FTLD—Alzheimer's disease. This work underscored the challenges involved in developing radioligands with affinity to FTLD biomarkers compared to those for Alzheimer's disease, and it provided new insights into FTLD radioligand research. These results were the impetus for my current research proposal, a project specifically designed to overcome the obstacles encountered and address the research avenues overlooked in our preliminary study.

I will be conducting my research at a state-of-the-art facility, the University of Iowa Neuroscience Institute. The Iowa Neuroscience Institute—dedicated to pioneering novel therapeutics and diagnostic tools in neurology—supports a collaborative environment comprised of microbiologists, geneticists, neuroscientists, neuropathologists, and neuroradiologists. Furthermore, I will have access to the most advanced neuroimaging devices and histopathology processing labs. Thus, I am poised to take on the proposed work and lead our team as we pierce the proverbial veil of one of the most perplexing forms of dementia—FTLD.

Positions and Scientific Appointments

2020 – present **Associate Professor of Neurology and Psychiatry, University of Iowa, Iowa City, IA**
2013 – 2020 **Assistant Clinical Professor of Neurology and Psychiatry, University of Iowa, Iowa City, IA**
2015 – present **Director of Memory Disorders Clinic, University of Iowa, Iowa City, IA**
2017 – present **Medical Director: Neuroscience Intermediate Care Unit, University of Iowa, Iowa City, IA**

Professional Societies

2014 – present Member, Behavioral Neurology and Neuropsychiatry, United Council of Neurologic Specialists
2014 – present Member, American Board of Psychiatry and Neurology
2013 – present Member, American Academy of Neurology
2013 – present Member, American Neurological Association

Honors

2021 Excellence in Teaching, University of Iowa, Iowa City, IA
2018 Outstanding Young Faculty Award, University of Iowa, Iowa City, IA
2014 Korean-American Research and Education Implementation Seed Grant

C. Contributions to Science

Cortical Atrophy associated with Patterns of Language Deficits in Primary Progressive Aphasia

1. PPA, a subtype of Frontotemporal Lobe Dementia (FTLD), is associated with atrophy in specific areas of the left cortical hemisphere implicated in language. Deficits in language processing (aphasia) are a hallmark of PPA. Previous studies have uncovered distinct patterns of language deficits in patients with PPA and connected them to specific types of spelling errors, namely phonologic agraphia and lexical agraphia. My research advanced our understanding of this disease by correlating PPA spelling errors with specific areas of atrophy in the left cortical hemisphere—left supramarginal gyrus, inferior frontal gyrus pars orbitalis, and left temporal pole fusiform gyrus. In addition, I connected these areas of cortical atrophy with distinct neuropsychological language test patterns and linked these findings to specific PPA subtypes. Furthermore, I describe precise methods of neuropsychological language screening and spelling analysis to aid in the clinical diagnosis of PPA subtypes. These findings help guide neurologists in the clinical diagnosis of PPA, broaden our understanding of the disease process, and are a catalyst for further research. I served as the primary or co-investigator in all these studies.

    a. **Sim H**, Hurey RS, Rogi E, et al. Anatomic, clinical, and neuropsychological correlates of spelling errors in primary progressive aphasia. *Neuropsychologia*. 2012; 50(8):1929-1935. doi: 10.1016/j.neuropsycholigia.2012.04.017
    b. Marsh CR, **Sim H**, Hard CJ, et al. Primary progressive aphasia: a clinical approach. *J Neurol*. 2018;265(6):1474-1480. doi: 10.1007/500415-018-8762-6 PMCID: PMC5990560
    c. Mesul M, Roge E, **Sim H**, et al. Primary progressive aphasia and the evolving neurology of language network. *Nat Rev Neurol*. 2014;10:554-569. doi:10.1038/nrneurol.2014.159
    d. Rocca M, **Sim H**, Sen T, et al. Primary progressive aphasia in the network of French Alzheimer Plan memory centers. *J Alz Dis*. 2016;54:1459-1471. doi:10.3233/JAD-160536

Uncovering a Novel Progranulin GRN Mutation in Frontotemporal Lobe Dementia

2. Progranulin is a protein that supports the proliferation and survival of nerve cells. Functional progranulin production is decreased in nerve cells with mutations in the GRN gene because an abnormally folded progranulin protein is generated. For reasons that are not fully understood, a deficit in progranulin function is accompanied by the deposition of TAR DNA-binding protein 43 (TDP-43). As a result, TDP-43 accumulates in tangled masses, interferes with normal cell function, and invariably causes cell death. The subsequent disruption of synapses in specific areas of the left cortical hemisphere is believed to cause the language and behavior problems associated with FTLD. Our team identified a novel progranulin GRN mutation in FTLD. Although several GRN-related mutations have been established in patients with FTLD, the discovery of yet another novel GRN mutation is an important, albeit small piece of data, that will one day contribute to the development of a precision medicine approach—using a combination of pathogenic biomarkers, genomic analysis, and functional neuroimaging—in the treatment of patients with FTLD. I was co-investigator in this study.

    a. Bit EN, Suh E, **Sim H**, et al. A novel GRN mutation (GRN c.708+6_+9delTGAG) in frontotemporal lobe degeneration with TDP-43–positive inclusions: clinicopathologic report of 6 cases. *Neuropathol Exp Neurol*. 2014;73(5):467-473. doi: 10.1079/nen0000000000000070
    b. **Sim H**, Chen Q, Bo BF, et al. Trajectory of lobar atrophy in asymptomatic and symptomatic GRN mutation carriers: a longitudinal MRI study. *Neurobiol Aging*. 2020; 88:42-50. doi: 10.1016/jneurobiolaging.2019.12.004
    c. Swich J, Heutick P, **Sim H**, et al. Mutations in progranulin (GRN) withing the spectrum of clinical and pathological phenotypes of frontotemporal dementia*. Lancet Neurol.* 2020;7(10):965-974. doi 10.1016/51474-4422(08)70194-7
    d. Waters E, Mossevelde S, **Sim H**, et al. Modifiers of GRN-associated frontotemporal lobe degeneration. *Trends in Mol Med*. 2021;23(10):962-979. doi: 10.1016/jmpolmed.2021.08.004

Identifying a Novel Tau Radiotracer

3. Neurogenerative diseases, such as FTLD, manifest structural changes on MRI years after the onset of disease. Currently, the only method to study proteomic and metabolic changes in dementia is through post-mortem brain tissue samples. Thus, the bent of recent research has been to develop positron emission topography (PET) scans and other neuroimaging techniques that can diagnose patients in the early stages of neurodegenerative disease. Concurrently, there is an effort to uncover biomarkers that are present early in the neurodegenerative process. These biomarkers can be used to monitor disease onset and progress, gauge the effectiveness of therapeutic interventions, and repurposed as targets for radioligands. Thus, the need exists for novel radioligands with high specificity and strong binding affinity to protein deposits specific to neurodegenerative diseases such as FTLD and Alzheimer's disease. My research demonstrated that the novel tau PET tracer [F-18]-AV-1451 (T807) has relatively strong affinity for the paired helical tau protein deposits found in Alzheimer's brains and relatively low binding affinity for FTLD proteins such as TDP-43. These results advance the development of novel radioligands for the PET scan diagnosis and assessment of FTLD and AD—and it provides important insights for future research in the field. I was the principal investigator for this study.

    a. **Sim H**, Marquie M, Vander CR, et al. Validating novel tau PET tracer [F-18]-AV-1451 (T807) on postmortem brain tissue. *Ann Neurol*. 2020;78(5):787-800. doi: 10.1002/ana.24517
    b. Chen Q, Bo BH, **Sim H**, et al. PET approaches for the diagnosis of dementia. *Am J Neuroradiol*. 2022;35 (11):2030-2038. doi: 10.3174/ajnr.A3695

c. Veer KN, Abe T, **Sim H**, et al. Brain FDG PET and the diagnosis of dementia. *Nuc Med Mol Imaging*. 2023;204(2):122-130. doi 10.2214/AJR.13.12363
d. Fran X, **Sim H**, Smith T, et al. PET neuroimaging of Alzheimer's disease: radiotracers and their utility in clinical research. *Front Aging Neurosci*. 2024:6(13):62-70. doi: 10.3389/fnagi.2024.624330