An Phu Tran Nguyen, Ph.D.
Assistant Professor, Department of Biological Sciences
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EDUCATION

University of Tuebingen (Baden-Wuerttermberg, Germany)   **March 2015**
Ph.D., Biology
Thesis title: "Lysosomal degradation of α-Synuclein: Analysis *in vivo* and *in vitro*"

University of Angers (Maine-et-Loire, France)   **June 2009**
M.Sc., Life Science
Thesis title: "Molecular mechanisms of phagocytosis: Phospholipase D activity's regulation by ARF6 during phagocytosis"

University of Angers (Maine-et-Loire, France)   **June 2007**
B.Sc., Life Science
Thesis title: "Contribution to Sodium channel study by molecular biology approaches"

RESEARCH EXPERIENCE

Research Scientist, Van Andel Institute (Michigan, USA)   **2018-2023**
Department of Neurodegenerative Science
Advisor: Professor Darren Moore
Disease mechanisms of LRRK2 variants
- Develop rodent models of LRRK2-induced neurodegeneration using Helper- dependent human adenovirus 5 (HdAd5).
- Develop rat models to assess neurodegenerative phenotypes and mechanism(s) of the LRRK2 familial Roc-COR mutations, R1441C and Y1699C using human adenovirus 5 (Ad5).
- Analyze biochemical properties and neurotoxicity of LRRK2 common coding variants associated with Parkinson's disease. Develop rat models to assess the mechanisms of the LRRK2 risk mutation, e.g G2385R, in mediating neurodegenerative phenotypes using human Ad5.
Disease modification of LRRK2
- Evaluate disease-modifying effects of expression of Rab-specific phosphatase (PPM1H) or transcription factors (PROX1 and CUX1) in experimental models of neurotoxicity and neurodegeneration.
Contributions of LRRK2 mutations to protein aggregation
- Assess the contribution of LRRK2 mutations to wild-type Tau pathology and degeneration in humanized hTau transgenic mice.
- Assess the requirement of LRRK2 to development Aβ neuropathology and neurodegeneration in APP/PSEN1 transgenic mice.
- Develop mouse models of α-Synuclein propagation in forebrain using α-Synuclein pre-formed fibrils.
Funding:
- West Michigan Neurodegenerative Diseases (MiND) Pilot Funding (PI: Tran Nguyen)
- Developed technologies, data, ideas and was involved as key Research Scientist for multiple grants: Micheal J. Fox Foundation (PI: Moore), R01NS120489 NIH/NINDS (PI: Moore), "Gibby & Friends vs Parky" Parkinson's Disease Research Project Award (PI: Moore/Kanaan), Parkinson's Foundation Stanley Fahn Junior Faculty Award (PI: Martin/Moore)

Postdoctoral Fellow, Van Andel Institute (Michigan, USA)   **2014-2018**
Department of Neurodegenerative Science
Advisor: Professor Darren Moore

- Developed a rat model of LRRK2-induced neurodegeneration using human adenovirus 5 (Ad5) gene transfer technology.
- Demonstrated that G2019S LRRK2 induced neurodegeneration in Parkinson's disease in a kinase and GTPase manner.
- Demonstrated that pharmacological inhibition of LRRK2 kinase protected against dopaminergic cell death in Ad5-induced G2019S LRRK2 rat model. Developed collaboration with pharmaceutical industry (Sanofi).
  This work resulted in one publication in Proceedings of the Academy of Sciences of the United States of America **(Nguyen et al., 2020)** and one publication in Neurobiology of Disease **(Tsika et al., 2015)**
- Evaluated the interaction of LRRK2 and Tau in mediating neurodegeneration in mouse models of Parkinson's disease. Demonstrated that G2019S LRRK2 promotes neuron-to-neuron transmission of Tau protein in mouse brain.
  This work resulted in a publication in Human Molecular Genetics **(Nguyen et al., 2018)**

Funding:

- American Parkinson Disease Association Postdoctoral Fellowship (PI: Tran Nguyen)
- Developed technologies, data, ideas and was involved as key post-doctoral researcher for multiple grants: Micheal J. Fox Foundation (PI: Moore), R01NS091719-01A1 NIH/NINDS (PI: Moore), Sanofi-Aventis (PI: Moore), Parkinson's disease Foundation (PI: Moore)

Ph.D. Student,   **2010-2014**
Boehringer Ingelheim Pharma Ltd. (Baden-Wuerttemberg, Germany)
CNS Disease Research
Advisors: Dr. Thomas Ciossek and Professor Boris Ferger
University of Tuebingen (Baden-Wuerttemberg, Germany)
Institute of Medical Genetics and Applied Genomics
Advisor: Professor Olaf Riess

- Generated Tet-inducible mouse models (Pcp2 promoter) overexpressing C-terminal truncated α-Synuclein (1-120) in cerebellar Purkinje cells. Assessed impacts of overexpressing α-Synuclein on protein turnover in cerebellum, cerebellar pathology and mouse locomotor behavior.
- Generated Tet-inducible cell lines (HEK293T-TRex, M17, SH-SY5Y) overexpressing C-terminal truncated α-Synuclein (1-120). Assessed impacts of mutation chaperone-mediated autophagy motif on alpha-Synuclein protein turnover in cell lines.
- Coordinated public-private collaboration between Boehringer Ingelheim Pharma and the University of Tuebingen.

Funding:

- Marie Curie Actions Doctoral Fellowship (PI: Tran Nguyen)

Master's Student, University of Strasbourg (Bas-Rhin, France)   **2009**
Institute of Cellular and Integrative Neuroscience
Advisor: Dr. Nancy Grant

- Assessed mechanism of regulation of Phospholipase D (PLD) activity by small GTPases during FcγR-mediated phagocytosis. Demonstrated that the small GTPase ARF6 regulated PLD activity and triggered production of phosphatidic acid during phagocytosis in RAW 264.7 macrophages.

This work resulted in two publications in Journal of Immunology **(Corrotte et al., 2010 and Tanguy et al., 2019)**

GRANTS AND FELLOWSHIPS

West Michigan Neurodegenerative Diseases Pilot Funding   **2022-2023**

"Elucidating the role of Rab phosphorylation in mutant LRRK2-induced neurodegeneration in Parkinson's disease"

Research grant (with value of $100,000 per year for one year) awarded by West Michigan Neurodegenerative Diseases (MiND) program to support early-stage collaborative research projects identifying genetic and epigenetic changes that may play roles in neurodegenerative diseases, such as Parkinson's and Alzheimer's.

American Parkinson's Disease Association Postdoctoral Fellowship   **2017-2018**

"Elucidating the contribution of GTPase activity to mutant LRRK2-induced neurodegeneration in Parkinson's disease"

Fellowship (with value of $35,000 per year for one year) awarded by the American Parkinson's Disease Association to support post-doctoral scientists whose research holds promise to provide new insights into the pathophysiology, etiology and treatment of Parkinson's disease.

Marie Curie Actions Doctoral Fellowship   **2010-2013**

"Lysosomal degradation of α-Synuclein: Analysis *in vivo* and *in vitro*"

Fellowship (with equivalent value of $35,000 per year for three years) awarded by the European Commission to promote academic-industrial partnership and to facilitate early-stage researcher mobility.

PUBLICATIONS

Published in peer-reviewed journals

1. Dues DJ, **Nguyen APT**, Becker K, Ma J and Moore DJ. Hippocampal subfield vulnerability to α-synuclein pathology precedes neurodegeneration and cognitive dysfunction. NPJ Parkinsons Dis, Aug 29;9(1):125, **2023**.

2. Fernández B, Chittoor-Vinod V, Kluss J, Kelly K, Bryant N, **Nguyen APT**, Bukhari S, Smith N, Ordóñez A, Fdez E, Chartier-Harlin M, Wilson M, Montine T., Moore DJ, West AB, Cookson M, Nichols J and Hilfiker S. Evaluation of current methods to detect cellular Leucine-rich repeat kinase 2 (LRRK2) kinase activity. J. Parkinson Dis, May 20, **2022**.

3. **Nguyen APT**, Tsika E, Kelly K, Levine N, Chen X, West AB, Boularand S, Barneoud P and Moore DJ. Dopaminergic Neurodegeneration Induced by Parkinson's Disease-Linked G2019S LRRK2 is Dependent on Kinase and GTPase Activity. Proc Natl Acad Sci USA, 117(29):17296-17307, **2020**.

4. Tanguy E*, **Nguyen AP***, Bader MF, Grant NJ, Vitale N. Regulation of Phospholipase D by Arf6 during FcγR-mediated Phagocytosis. J Immunol, 202(10):2971-2981, **2019**. (*co-author)

5. **Nguyen APT**, Daniel G, Valdés P, Islam MS, Schneider BL, Moore DJ. G2019S LRRK2 enhances the neuronal transmission of tau in the mouse brain. Hum Mol Genet, 27(1):120-134, **2018**.

6. **Nguyen AP** and Moore DJ. Understanding the GTPase Activity of LRRK2: Regulation, Function, and Neurotoxicity. Adv Neurobiol, 14:71-88, **2017**.

7. Tsika E, **Nguyen AP**, Dusonchet J, Colin P, Schneider BL, Moore DJ. Adenoviral-mediated expression of G2019S LRRK2 induces striatal pathology in a kinase-dependent manner in a rat model of Parkinson's disease. Neurobiol Dis., 77:49-61, **2015**.

8. Corrotte M, **Nguyen AP**, Harlay ML, Vitale N, Bader MF, Grant NJ. Ral isoforms are implicated in Fc gamma R-mediated phagocytosis: activation of phospholipase D by RalA. J Immunol, 185(5):2942-50, **2010**.

Manuscripts in preparation

9. **Nguyen AP**, Levine N, Boularand S, Barneoud P and Moore DJ. Chronic dosing with a novel small-molecule LRRK2 kinase inhibitor, RA10597329, protects against neurodegeneration in a Parkinson's disease rat model overexpressing G2019S LRRK2.
10. **Nguyen AP**, Levine N, Polinski N, Young S and Moore DJ. A novel viral rat model of dopaminergic neurodegeneration mediated by the Parkinson's disease-associated mutations G2019S and G2385R in LRRK2 gene.
11. **Nguyen AP**, Moser R, Cunningham L, Bryant N, West AB, Moore DJ. Common coding variants in LRRK2 associated with Parkinson's disease risk modulate LRRK2-dependent Rab10 phosphorylation.
12. **Nguyen AP**, Scudamore O, Riess O, Ferger B, Hengerer B and Ciossek T. Mutation in chaperone-mediated autophagy motif does not affect C-terminal truncated a-Synuclein turnover in cells and mouse brain.
13. Dues DJ, Ma Y, **Nguyen APT**, Offerman A, Beddows I and Moore DJ. Formation of templated inclusions in a forebrain α-synuclein mouse model is independent of LRRK2.

PRESENTATIONS

Oral presentations

1. Invited speaker, Department of Biological Sciences, College of Letters and Science, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin. Mechanisms of LRRK2-induced neurodegeneration in vivo: role of enzymatic activities and protein aggregation. **2023.**
2. Invited speaker, International Research Conference on Neurodegenerative Diseases 2022, Omaha, Nebraska. Parkinson's disease risk variant, G2385R LRRK2, enhances Rab phosphorylation, neurotoxicity and neurodegeneration. **2022.**
3. Invited speaker, Dopamine 2022, Montreal, Quebec. Mechanisms of LRRK2-induced neurodegeneration in vivo: role of enzymatic kinase and GTPase activities. **2022.**
4. Invited speaker, Robert Wood Johnson Medical School, Institute for Neurological Therapeutics, New Brunswick, New Jersey. Mechanisms of LRRK2-induced neurodegeneration in vivo: role of enzymatic activities and protein aggregation. **2022.**
5. Short talk selected from abstracts, Grand Challenges in Parkinson's disease, Grand Rapids, Michigan. Common coding variants in LRRK2 associated with Parkinson's disease risk modulate LRRK2-dependent Rab10 phosphorylation. **2021.**
6. Invited speaker, 5th Annual Udall Center for Parkinson's Disease Research Symposium, Ann Arbor, Michigan. Mechanisms of LRRK2-induced neurodegeneration in vivo: role of kinase and GTPase enzymatic activities. **2019.**
7. Invited speaker, Society of Neuroscience annual meeting, Chicago, Illinois. Impact of pathogenic or endogenous LRRK2 on tau metabolism, pathology and neurodegeneration in mouse brain. **2015.**

Poster presentations

1. **Nguyen AP**, Moser R, Cunningham L, Bryant N, West AB, Young S and Moore DJ. Parkinson's disease risk variant, G2385R LRRK2, enhances Rab phosphorylation, neurotoxicity and neurodegeneration. Society of Neuroscience annual meeting. San Diego, California, USA, **2022.**
2. **Nguyen AP**, Moser R, Cunningham L, Bryant N, West AB and Moore DJ. Common coding variants in LRRK2 associated with Parkinson's disease risk modulate LRRK2-dependent Rab10 phosphorylation. Grand Challenges in Parkinson's disease. Grand Rapids, Michigan, USA, **2021.**
3. **Nguyen AP**, Tsika E, Levine N, and Moore DJ. Mechanisms of LRRK2-induced neurodegeneration *in vivo*: role of kinase and GTPase enzymatic activities. Grand Challenges in Parkinson's disease. Grand Rapids, Michigan, USA, **2019.**
4. **Nguyen AP**, Tsika E, Levine N, and Moore DJ. Mechanisms of LRRK2-induced neurodegeneration *in vivo*: role of kinase and GTPase enzymatic activities. Gordon Research Conference. Sunday River, Maine, USA, **2019.**

5. **Nguyen AP**, Tsika E, Levine N, and Moore DJ. Mechanisms of LRRK2-induced neurodegeneration *in vivo*: role of kinase and GTPase enzymatic activities. Society of Neuroscience annual meeting. San Diego, California, USA, **2018.**
6. **Nguyen APT,** Daniel G, Tsika E, Levine N, Valdés P, Schneider BL, Moore DJ. Mechanisms of LRRK2-induced neurodegeneration *in vivo*: role of enzymatic activity and protein aggregation. Grand Challenges in Parkinson's disease. Grand Rapids, Michigan, USA, **2017.**
7. **Nguyen APT,** Daniel G, Tsika E, Levine N, Valdés P, Schneider BL, Moore DJ. Mechanisms of LRRK2-induced neurodegeneration *in vivo*: role of enzymatic activity and protein aggregation. Gordon Research Conference. Sunday River, Maine, USA, **2017.**
8. **Nguyen APT,** Daniel G, Islam S, Valdés P, Schneider BL, Moore DJ. Impact of LRRK2 expression on tau solubility, phosphorylation, neuronal propagation and tau-mediated neurodegeneration in mouse brain. Grand Challenges in Parkinson's disease. Grand Rapids, Michigan, USA, **2016**.
9. **Nguyen APT,** Daniel G, Schneider BL, Moore DJ. Exploring the Interaction of LRRK2 and Tau in Mediating Neurodegeneration in mice**.** Grand Challenges in Parkinson's disease. Grand Rapids, Michigan, USA, **2015.**
10. **Nguyen APT** and Ciossek T. Generating of Tet-regulation models *in vivo* and *in vitro* overexpressing C-terminal truncated α-Synuclein. Satellite Meeting of the International Society for Neurochemistry. Naxos, Greece, **2011.**

SERVICE AND OUTREACH
Research grant review
Israel Science Foundation, **2021**
Scientific publication review
Genes, **2022**
British Journal of Pharmacology, Genes and Diseases, Frontier in Aging Neuroscience, **2021**
Neurobiology of Disease, **2020**
Acta Neuropathologica, Pharmacological Research, Human Molecular Genetics, **2019**
Biochimica et Biophysica Acta, Acta Neuropathologica, **2018**
Leadership
Member, Postdoctoral Leadership Committee, Van Andel Institute, **2015-2016**
Professional memberships
Society for Neuroscience, Member, **2015-present**
NEURASYNC consortium (European academic-industrial initial training network on α-Synuclein-related brain diseases), Member, **2010-2014**
Editorial Board of Frontiers in Aging Neuroscience, Review Editor, **2021**

MENTORING EXPERIENCE
Dylan Dues, Van Andel Institute Graduate School, Graduate student,
Department of Neurodegenerative Science, **2018-present**
Rafael Bena de Araujo, Van Andel Institute Graduate School, Rotation student
Department of Neurodegenerative Science, **2022**
Lindsey Cunningham, Van Andel Institute Graduate School, Rotation student
Department of Neurodegenerative Science, **2016**
Bassem Akladios, University of Ulm, Master's student
CNS Disease Research, **2010**

TEACHING EXPERIENCE

Stereology demonstration for the teaching module: "Molecular Neurodegeneration", Van Andel Institute Graduate School, **2017-2019**