BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Malyshka, Dmitry

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

POSITION TITLE: Graduate Research Assistant

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
Drexel University	BS / MS	05/2017	Chemistry / Biophysical Chemistry
The Ohio State University	MD / PhD	Expected 05/2026	Medicine and Biomedical Sciences

A. Personal Statement

As someone always interested in the why of things, it is no wonder I ended up choosing chemistry as my undergraduate field on my way to pursuing medicine and research. The field aims to explain both the macroscopic and the microscopic world around us, satisfying a curiosity deep within me. I found chemistry especially interesting when applied to biological systems, in awe by the elegance of explaining the driving forces of life as a united yet immeasurably complex ensemble of chemical and physical reactions. Understanding human physiology and pathology from this viewpoint was especially rewarding, as seeing how an appreciation of truly fundamental processes can drive our medical knowledge and future therapies effectively married my innate curiosity and budding medical interests. It is this mindset that pushed me to choose my research paths and my future career as a physician-scientist.

My undergraduate research delt with understanding protein dynamics and their potential relation to apoptosis, exposing me to a wide variety of biophysical and biochemical techniques both through first-hand experiences and a thorough exploration of literature across my five years of unpaid research in the Schweitzer-Stenner lab. My extensive work allowed me to become a published author, and I cherish the many opportunities I got to present my work both on the national and international stages. Through it all, I gained confidence as a scientist and solidified my decision to pursue research as a career path. In need of further research training and coupled with multiple clinical experiences that exposed me to medicine, I settled on continuing my path at the Medical Scientist Training Program (MSTP) of the Ohio State University.

Through my first two years at OSU's College of Medicine, I encountered multiple patients with dementia and was shaken by how this disease can ravage both an individual and their family. It is these experiences that led me to consider Alzheimer's disease (AD) research. The more I looked at the field, the more questions I had, and I was especially staggered by the field's lack of therapy or understanding behind even the most basic of pathological processes. This ignited my inquisitiveness and led me to join the lab of Dr. Jeff Kuret, where I plan to channel my ever-growing curiosity and passion to push the field's molecular understanding of the disease. Along the way, I plan to obtain valuable experience in scientific communication (including scientific writing alongside visual and oral presentations), experimental design (including hypothesis testing along with rigor and reproducibility), laboratory techniques (ranging from biochemical assays and cryo-electron microscopy to computational biology), and mentoring (in the form of supervising and teaching any incoming undergraduate and graduate students).

My ultimate goal is to become a physician-scientist serving at an academic medical center, contributing impactful science to the field of neurology as a leader of a well-funded laboratory. These goals have grown naturally during my growth as a scientist and the first half of the MSTP program at The Ohio State University, and I believe that the laboratory and mentorship of Dr. Jeff Kuret afford me the perfect environment to gain the valuable skills needed to succeed in these aspirations. With this in mind, I seek this fellowship to fund me during the critical and formative years in my development as a physician-scientist.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2013	Lead Chemist (intern), MultiFlex Plating Co. (PA)
2014	Research and Development Scientist (intern), iCeutica, Inc. (PA)
2015 – 2018	Lab Scientist, SMA Medical Labs (PA)
2017 – 2018	Research Assistant (unpaid), Drexel University (PA)
2018 – present	MSTP Student, Medical Scientist Training Program, Ohio State University (OH)

Other Experiences and Professional Memberships

2013 – 2017	Student Member, American Chemical Society (ACS)
2014 – 2015	Vice President, ACS Student Chapter, Drexel University
2014 – 2015	Premedical Volunteer, Hospital of the University of Pennsylvania
2014 – 2017	Tutor for Introductory and Advanced Chemistry Courses, Drexel University
2014 – 2018	Member, Biophysical Society
2018 – 2019	Member, Ultrasound Student Interest Group
2018 – present	Medical Student Volunteer, Columbus Free Clinic
2018 – present	Member, Medical Scientist Student Organization
2019 – 2020	Vice President, Students for Integrative Medicine
2020 – 2021	Vice President, Infectious Diseases Student Interest Group

Honors

2013	Maryanoff Summer Research Fellowship
2016	Bruce and Cynthia Maryanoff Research Prize
2017	Robert O. Hutchins Endowed Chemistry Research Prize
2019	MSTP Leadership and Academic Achievement Award
2020	OSU Distinguished University Fellowship

C. Contributions to Science

1. Undergraduate Research

My experience in the Schweitzer-Stenner lab as a BS/MS student led to multiple contributions in the field of apoptosis-related structural dynamics of cytochrome *c*. Cytochrome *c* is usually found in the mitochondria as a part of the electron transport chain; yet, its release from the mitochondria (through a variety of potential pathways) and subsequent binding to cytosolic factors is seen as an apoptotic point-of-no-return. As such, understanding this has tremendous biological implications for diseases that can subvert normal apoptotic responses such as cancer. Cytochrome *c*'s release is reliant on the presence of and interaction with cardiolipin (a phospholipid with two phosphate headgroups found mainly on the inner mitochondrial membrane) as well as a gain of peroxidase activity. In the Schweitzer-Stenner lab, I investigated multiple phenomena resulting from this vital interaction between cytochrome *c* and cardiolipin.

Evidence for Doubly Ionized State of the Cardiolipin Headgroup Under Physiological Conditions. Under the Maryanoff Summer Research Fellowship in 2013, I explored the ionization state of cardiolipin under physiological conditions. This work was driven by the fact that the primary mode of interaction between cytochrome *c* and cardiolipin is electrostatic in nature, and yet there was no scientific consensus about the ionization state of the latter. There was substantial literature supporting either a doubly or singly ionized states. With no conclusive evidence for either, application of appropriate global kinetic models to the system was precluded. I aimed to ameliorate this situation by combining biophysical and computational methods to investigate the ionization state of cardiolipin. I was able to combine infrared spectroscopy and computational chemistry to derive convincing evidence for a doubly ionized state. While relatively simple, this work's importance in the field cannot be understated, exemplified by it now being cited over twenty times. I was excited to present this work at the 59th Biophysical Society meeting in poster form.

a. **Malyshka D**, Pandiscia L, Schweitzer-Stenner R. Cardiolipin containing liposomes are fully ionized at physiological pH. An FT-IR study of phosphate group ionization. *Vibrational Spectroscopy*. 2014;75: 86-92. DOI: 10.1016/j.vibspec.2014.10.003

Exploration of Cytochrome *c* and its Heme Group's Dynamics Using Resonance Raman Spectroscopy. With the question of protonation state out of the way, I moved onto exploring the protein's dynamics in contact with cardiolipin using vibrational spectroscopy. This work added the lab's concomitant exploration of cytochrome *c* dynamics utilizing fluorescence quenching and anisotropy measurements as well as circular dichroism and electronic absorbance measurements. Resonance Raman spectroscopy offered an exciting way to explore the

dynamics of the heme group at the center of the molecule. However, I kept running into a major issue of my protein reducing under the laser beam due to the presence of small amounts of redox-active ferrocyanide, a byproduct of purification. While this precluded any direct analysis, I adapted this issue into a tool to assess the conformational changes of the protein itself – rooted in the fact that the conformational changes associated with the cardiolipin interaction inhibited photoreduction. We were able to further verify this method in the context of a global kinetic model developed in the Schweitzer-Stenner lab. Upon performing accompanying spectroscopic studies and biochemical assays, we were able to provide novel mechanistic insight behind gain of peroxidase activity at various pH values, rounding out the field's current understanding of cytochrome *c*'s binding and conformational dynamics. This work, at various stages, was presented at three consecutive Biophysical Society meetings (60^{th}-62^{nd}) as well as 6^{th} Georgian Bay Meeting on Bioinorganic Chemistry in Canada, where it was received very well.

a. **Malyshka D**, Schweitzer-Stenner R. Ferrocyanide-Mediated Photoreduction of Ferricytochrome *c* Utilized to Selectively Probe Non-native Conformations Induced by Binding to Cardiolipin-Containing Liposomes. *Chemistry – A European Journal*. 2017; 23(5): 1151-1156. DOI: 10.1002/chem.201604992
b. Milorey B, **Malyshka D**, Schweitzer-Stenner R. pH Dependence of Ferricytochrome c Conformational Transitions during Binding to Cardiolipin Membranes: Evidence for Histidine as the Distal Ligand at Neutral pH. *Journal of Physical Chemistry Letters*. 2017; 8 (9): 1993-1998. DOI: 10.1021/acs.jpclett.7b00597
c. Milorey B, Schweitzer-Stenner R, Kurbaj R, **Malyshka D**. pH-Induced Switch between Different Modes of Cytochrome c Binding to Cardiolipin-Containing Liposomes. *ACS Omega*. 2019; 4(1): 1386-1400. DOI: 10.1021/acsomega.8b02574

Mechanistic Insight into Ferrocyanide-mediated Photoreduction of Cytochrome *c*. After graduating from Drexel University (in my gap year), I continued in a small unpaid research role at the Schweitzer-Stenner lab while working full-time elsewhere. Due to my limited time, I pursued a project where I applied my biophysical chemistry knowledge to derive a theoretical model behind ferrocyanide-mediated photoreduction of cytochrome *c*. I then experimentally tested and validated my model, resulting in a comprehensive exploration of the phenomenon behind my second publication. While this work may not be directly biomedically applicable, I am incredibly proud of my ability to marry my broad theoretical knowledge with mechanistic derivation and validation.

a. **Malyshka D,** Schweitzer-Stenner R. Photoreduction of Ferricytochrome c in the Presence of Potassium Ferrocyanide. *Photochemical and Photobiological Sciences*. 2018; 17: 1462-1468.

2. Graduate Research

At Ohio State University, I joined the lab of Dr. Jeff Kuret, who has historically studied tau protein as it relates to Alzheimer's disease. As a rotation student in the summer of 2019, I was responsible for overseeing the collection and analysis of cryoEM data on tau filaments produced by an in-house *in vitro* model. After joining the lab in February of 2020, I followed-up on my efforts to determine the structure of the filaments. This ultimately yielded a structure, and my experience in structural biology and preliminary data have allowed me to shape my thesis project, centered around applying structural biology to derive novel insight into various tauopathies. My preliminary data was presented in poster form at Wexner Medical Center's 2021 Research Day as well as the Molecular Biophysics Training Program's Fourth Annual Symposium in 2021 and received well.

D. Additional Information: Research Support and/or Scholastic Performance

Drexel University Undergraduate Science Coursework (BS)		
YEAR	COURSE	GRADE
2012	Evolution & Organism Diversity	AP
2012	Majors Chemistry I, II, & III	AP
2012	Calculus I, II, & III	AP
2012	Fundamentals of Physics I	AP
2012	Cells and Genetics	A
2012	Quantitative Analysis	A+
2012	Multivariate Calculus	A+
2013	General Chemistry III	A+
2013	Quantitative Analysis Lab	A
2013	Linear Algebra	A+
2013	Fundamentals of Physics II	A+
2013	Principles of Cell Biology	A
2013	Everyday Chemistry	A+
2013	Fundamentals of Physics III	A
2013	Majors Organic Chemistry I	A+
2013	Thermodynamics & Kinetics	A+
2013	Differential Equations	A+
2014	Principles of Molecular Biology	A
2014	Majors Organic Chemistry II	A
2014	Software Skills for Chemists	A
2014	Physical Chemistry Lab I	A
2014	Computer-Aided Drug Design	A-
2014	Majors Organic Chemistry III	A
2014	Physical Chemistry IV	B+
2014	Physical Chemistry Lab II	A
2014	Analytical Chemistry I	A
2015	Atom & Molecular Spectroscopy	A+
2015	Qualitative Organic Chemistry	A
2015	Thermodynamics (Physics)	A
2016	Biochemistry Lab	A-
2016	Analytical Chemistry II	A-
2016	General Psychology I	B+
2016	Gross Anatomy I	A-
2016	Gross Anatomy I Lab	B+
2017	Gross Anatomy II	C+
2017	Gross Anatomy II Lab	A-
2017	Vector Calculus	A+
2017	Biochemistry	B+
2017	Inorganic Chemistry Lab	A-
Drexel University Graduate Coursework (MS)		
2015	Inorganic Chemistry II	A-
2015	Organic Chemistry II	A-
2015	Physical Chemistry II	A
2015	Biophysical Chemistry	A+
2015	Physical Chemistry I	A+
2015	Chemical Info Retrieval	A-
2016	Inorganic Chemistry III	A
2016	Inorganic Chemistry I	A+
2016	Polymer Chemistry I	A

Drexel University – BS GPA: **3.89**; MS GPA: **3.90**

The Ohio State University

Medical Coursework (MD)		
YEAR	COURSE	GRADE
2018 - 19	Medical Sciences I	S
2019 - 20	Medical Sciences II	S
The Ohio State University Graduate Coursework (PhD)		
2018	Ind. Study in Biomed. Sci.	S
2019	Ind. Study in Biomed. Sci.	S
2019	Concepts in Biomed. Sci.	A
2020	Research Prob. Solving	S
2020	Methods in BMI	A
2020	Patient Cent. Research	S
2020	Fundam. of Grant Writing	A
2020	Electron Microscopy Lab	A
2021	Adv. Biochem. / Biophysics	A
2021	Prof. Issues in Biomed. Sci.	S
2018 - 21	MSSO Seminar	S

The Ohio State University – GPA: **4.0**

Undergraduate and graduate courses at Drexel University are graded with letter grades A-F, with a +/- system in place to distinguish the bottom and top 3% in the letter bracket. GPA is calculated on a traditional 4-point scale after taking the +/- system into account (e.g. A counts as 4.0, A- counts as 3.7).

Graduate coursework at the Ohio State University is graded with letter grades A-F or as S/U (for Satisfactory/Unsatisfactory, with a 70% threshold). Some courses that would have received A-F grading were switched to S/U due to COVID-related academic changes.

Medical school coursework at the Ohio State University's College of Medicine is graded as S/U (for Satisfactory/Unsatisfactory, with a 70% threshold). Listed coursework includes the entirety of the didactic medical curriculum.

MCAT Score (2017): **514**
USMLE Step 1 Score (2020): **240**

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Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Kuret, Jeff

eRA COMMONS USER NAME (credential, e.g., agency login): Kuret03

POSITION TITLE: Professor of Biological Chemistry and Pharmacology

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, Los Angles (UCLA), CA	B.S.	06/1978	Biochemistry
Stanford University, Stanford, CA	Ph.D.	06/1984	Pharmacology
Medical Sciences Inst., Dundee University, U.K.	Postdoc.	11/1986	Biochemistry

A. Personal Statement

I am well prepared to serve as sponsor of this project and dissertation advisor for Dmitry Malyshka. First, I manage a laboratory that focuses on Alzheimer's disease and other dementing illnesses of the elderly, with 25 years of experience working with tau protein. We seek to clarify aggregation mechanisms using biochemical/biophysical methods, to develop aggregation antagonists as potential therapeutic agents using biochemical/computational approaches, to create small-molecule probes for protein aggregates using synthetic chemistry methods, and to characterize the AD expression phenotype using systems biology approaches. As a result, my laboratory works with research concepts and specialty reagents (tau expression constructs, human brain-derived specimens, recombinant protein preparations, radioligands, etc) that are directly relevant for this project. For example, this year we inaugurated the *Interdisciplinary Resource Network on Biologically Active Tau Aggregate Polymorphs from Alzheimer's Disease and Related Dementias* (U24 AG072458; J. Kuret mPI) that aims to boost research rigor by disseminating purified and benchmarked tauopathy-derived aggregates to researchers around the country. Second,

Second, I am firmly committed to doctoral training. Since arriving at The Ohio State University (OSU) College of Medicine in 1998 I have mentored 21 doctoral students (including four MD/PhD students) through projects that employ a combination of computational, biochemical, and structural biological approaches. I also am in my ninth year as Co-Director of the OSU Interdisciplinary Biophysics Graduate Program, which is the premier graduate program in quantitative biology on this campus, and am mPI of a campus-wide NIGMS-funded T32 program (GM118291) focused on Molecular Biophysics. In these capacities I recruit graduate students to campus and also work with other program directors to deliver Responsible Conduct of Research training to multiple campus T32-supported and interdisciplinary graduate programs. In addition, having completed Entering Mentoring training through the Center for the Improvement of Mentored Experiences in Research (CIMER), I support campus-wide efforts to improve mentor training by acting as a workshop facilitator under the auspices the OSU Office of Postdoctoral Affairs.

I am excited about the synergy between this project and my own research and training efforts, and am committed to its success.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2013 – present Co-Director, OSU Biophysics graduate program
2002 – present Professor, Ohio St. University College of Medicine, Columbus, OH
1998 – 2002 Associate Professor (Tenured), Ohio St. University College of Medicine, Columbus, OH
1995 – 1998 Investigator, Northwestern University Alzheimer's Disease Center
1990 – 1994 Senior Staff Investigator, Cold Spring Harbor Laboratory
1988 – 1990 Staff Investigator, Cold Spring Harbor Laboratory

Other Experience and Professional Memberships

2018 – 2021 Member, Graduate Council
2020 – 2021 Chair, Graduate Council
Review Panel, member

2012 – 2013 *Drug Discovery for the Nervous System* (DDNS), NIH
2007 – 2013 *Molecular Probes* (MNPS-C), NIH
2007 – present Scientific Review Board, *Alzheimer's Disease Drug Discovery Foundation*
2006 – 2010 *Synapse, Cytoskeleton, & Trafficking* study section (SYN), NIH
1997 – present Initial Review Board of the Medical and Scientific Advisory Council, Research Grant Program, Alzheimer's Association.

Review Panel, ad-hoc member; last 5 years

2021	ZAG1 ZIP-P(J2)	*AD Risk Factors*
	ZAG1 ZIJ-P(O1)	*Harmonization of AD and Related Dementias (AD/ADRD) Genetic, Epidemiologic, & Clinical Data to Enhance Therapeutic Target Discovery*
2020	ZN1 SRB-H 14R	*White matter lesion etiology of dementia in the U.S. including in health disparity populations*
	MDCN-P (56)	*Molecular and Cellular Causal Aspects of Alzheimer's Disease*
2019	MDCN-E (57)	*Selective Cell and Network Vulnerability in Aging & AD*
	ZAG1 ZIJ-P (O2)	*AD and related Dementias*
2018	ZAG1 ZIJ-P (J4)	*AD and related Dementias* (Service as panel chair)
	MDCN-E (57)	*Selective Cell and Network Vulnerability in Aging & AD*
	ZAG1 ZIJ-P(03)	*Analysis of Data from NIA's Alzheimer's Disease Sequencing Project Follow-Up Study (U01)*
2017	ZAG1 ZIJ-6 (J2)	*AD sequencing follow up Study (U01)*
	ZIJ-U (A1)	*Exosomes: From Biogenesis & Secretion to the Early Pathogenesis of AD*
	MDCN-E (56)	*Capturing Complexity in the Molecular & Cellular Mechanisms Involved in the Etiology of AD*
	SRB-E (13)	*Leveraging Existing Resources for Research on Lewy Body Dementia*
	SRB-A(10)	*Frontotemporal Degeneration (FTD) Sequencing Consortium Review*
	ZIJ-P (01)	*Additional Sequencing for the AD Sequencing Project (U01)*
2016	BDCN-Q (02)	*Chronic Dysfunction & Integrative Neurodegeneration*

Editorial
2009/2012 Associate Editor, *Journal of Alzheimer's Disease*
2009 – 2021 Editorial board, *International Journal of Alzheimer's Disease*
2009 – 2014 Editorial board, *Journal of Biological Chemistry*
2010 – present Editorial board, *Current Alzheimer Research*

Honors
2004 & 2015 Elizabeth Gross award: *for excellence in biophysics teaching, mentoring, and research*
2009 Elan Pharmaceuticals/Institute for the Study of Aging award: *for novel approaches to Alzheimer's disease drug discovery*

C. Contribution to Science

1. My first contribution to the study of protein aggregate molecular pathology was to discover that certain monoclonal antibodies frequently used to assess neurofibrillary pathology on autopsy (e.g., Alz50 and MC1) were conformation selective. The findings were especially impactful because they were made at a time when leaders in the field argued that tau filaments lacked organized substructure or ordered folding. From this time forward, conformation-sensitive antibodies became powerful tools for assessing tau aggregation state in neurodegenerative diseases, and became popular probes for assessing the aggregation state of other proteins, including Aβ. I served as the primary investigator in this study, leading all aspects of it.
   a. Carmel, G., Mager, E.M., Binder, L.I., & Kuret, J. (1996) The structural basis of Alz50 selectivity for Alzheimer's disease pathology. *J. Biol. Chem*. **271,** 32789-32795.
2. My second contribution was to develop quantitative electron microscopy and laser light scattering methods for analyzing protein aggregation kinetics. Previous work in the field emphasized thioflavin dye fluorescence for quantitative work and electron microscopy for only qualitative analysis. The new methods allowed the field

to move beyond low resolution analysis of aggregation time courses, so that tau aggregation kinetics could be dissected at the level of elementary rate constants.

a. Necula, M. & Kuret, J. (2004) Electron Microscopy as a Quantitative Method for Investigating tau Fibrillization. *Anal. Biochem*. **329,** 238-246
b. Necula, M. & Kuret, J. (2004) An improved laser light scattering assay for investigating tau fibrillization. *Anal. Biochem*. **333,** 205-215
c. Chang, E. & Kuret, J. (2008) Detection and Quantification of Tau Aggregation Using a Membrane Filter Assay. *Anal. Biochem*. **373,** 330-336. PMCID: PMC2359897.
d. Huseby, C.J. & Kuret, J. (2016) Analyzing tau aggregation with electron microscopy. *Meth. Mol. Biol*., **1345,** 101-12

3. My laboratory applied the new methods summarized above to gain fundamental insights into the mechanism of tau aggregation, including the effects of post-translational modifications and alternative splicing on tau aggregation propensity. The results have extended the positive correlation between tau aggregation propensity and disease to the level of individual isoforms. They also deduced the role of secondary processes in controlling aggregate size distribution.

a. Congdon, E.E., Kim, S., Bonchack, J., Songrug, T., Matsavinos, A., & Kuret, J. (2008) Nucleation dependent tau fibrillization: the importance of dimerization and an estimation of elementary rate constants. *J. Biol Chem.* **283,** 13806-13816. PMCID: PMC2376241.
b. Zhong, Q, Congdon, E.E., Nagaraja, H.N., & Kuret, J. (2012) Tau isoform composition influences the rate and extent of filament formation. *J. Biol. Chem.* **287,** 20711-20719. PMCID: PMC3370253.
c. Huseby, CJ, Bundschuh, R, & Kuret, J. (2019) The role of annealing and fragmentation in human tau aggregation dynamics. *J. Biol. Chem.* **294,** 4728-4737 PMCID: PMC6442056
d. Yang, J, Agnihotri, MV, Huseby, CJ, Kuret, J & Singer SJ (2021) A theoretical study of polymorphism in VQIVYK fibrils. *Biophys. J.* **120,** 1-21. PMID: 33571490

4. Although hyper-phosphorylation of tau Ser/Thr residues is an established trigger of tau misfunction and aggregation, tau modifications extend to Lys residues as well, raising the possibility that different modification signatures depress or promote aggregation propensity depending on site occupancy. In a collaborative proteomic study, we found the major detectable Lys modification to be methylation. The data established Lys methylation as part of the normal tau post-translational modification signature in human brain, and suggested that it can function in part to protect against pathological tau aggregation.

a. Thomas, S.N., Funk, K.E., Wan, Y., Liao, Z., Davies, P., Kuret, J., & Yang A.J. (2012) Dual modification of Alzheimer's disease PHF-tau protein by lysine methylation and ubiquitylation: a mass spectrometry approach. *Acta Neuropathol.* **123,** 105-117. PMCID: PMC3249157.
b. Funk, K.E., Thomas, S.N., Schafer, K.N., Cooper G.L., Liao, Z., Clark, D.J., Yang, A.J., & Kuret, J. (2014) Lysine methylation is an endogenous post-translational modification of tau protein in human brain and a modulator of aggregation propensity. *Biochem. J*. **462,** 77-88.
c. Cooper, G.L, Huseby, C.J., Chandler, C.N., Cocuron, J.-C., Alonso, A.P., & Kuret, J. (2018) A liquid chromatography tandem mass spectroscopy approach for quantification of protein methylation stoichiometry. *Anal. Biochem*. **545,** 72-7.
d. Huseby CJ, Hoffman CN, Cooper GL, Cocuron JC, Alonso AP, Thomas SN, Yang AJ, Kuret J (2019) Quantification of Tau Protein Lysine Methylation in Aging and Alzheimer's Disease. *J. Alzheimers Dis.* **71,** 979-991

5. Finally, my laboratory discovered the first molecular marker for granulovacolar degeneration. Although observed in human brain specimens since 1912, the molecular composition of these abnormally large vacuolar bodies within the cytoplasm of select nerve cells had been unknown. From this time forward, it has been possible to detect and quantify GVD with as much confidence as plaques and tangles. The data point toward a common mechanism underlying the formation of all three major pathologies associated with AD (plaques, tangles, and GVD bodies).

a. Ghoshal, N., Smiley, J.F., DeMaggio, A.J., Hoekstra, M.F., Cochran, E.J., Binder, L.I., & Kuret, J. (1999) A New Molecular Link Between the Fibrillar and Granulovacuolar Lesions of Alzheimer's Disease. *Am. J. Pathol*. **155,** 1163 – 1172.
b. Kannanayakal , T.J., Tao, H., Vandre, D.D., & Kuret J. (2006) Casein kinase-1 isoforms differentially associate with neurofibrillary & granulovacuolar degeneration lesions. *Acta Neuropathol.* **111,** 413-421

c. Funk, K.E., Mrak, R.E., & Kuret, J. (2011) Granulovacuolar Degeneration Bodies of Alzheimer's Disease Resemble Late-stage Autophagic Organelles. *Neuropath. Applied Neurobiol.* **37,** 295-306. PMCID: PMC3037976.
d. Funk, K.E. & Kuret, J. (2012) Lysosomal fusion dysfunction as a unifying hypothesis for Alzheimer's disease pathology. *Int. J. Alzheimer Dis.* **2012:**752894. PMCID: PMC3437286.

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/jeff.kuret.1/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

U24 AG072458 Eisenberg/Kayed/Keene/Kuret (MPI) 07/01/21 – 06/30/26
NIH/NIA
Interdisciplinary Resource Network on Biologically Active Tau Aggregate Polymorphs from Alzheimer's Disease and Related Dementias
This cooperative agreement supports the isolation, biophysical characterization, molecular probe specificity, and nation-wide dissemination of brain-derived tau aggregate polymorphs from Alzheimer's disease and Alzeimer's disease related dementias.

R01 AG065380 Obrietan/Hoyt (MPI) 08/01/20 – 03/31/25
NIH/NIA
AD pathogenesis and the desynchronization of cortico-limbic circadian rhythms
This project tests the hypothesis that pathological Aβ disrupts the cricadian clock in forebrain leading to desynchrony among synaptic circuits and cognitive decline.
Role: Co-I; preparation and vetting of Aβ aggregates for biological experimentation.

RF1 AG054018 Kuret (PI) 06/01/17 – 03/31/22
NIH/NIA
Structure and Genesis of tau aggregates
This project will quantify secondary processes in tau aggregation, identify mechanism of binding of small molecules to tau aggregates, and clarify the mechanism of action of non-covalent tau aggregation inhibitors

RF1 AG054018-S1 Kuret (PI) 06/15/20 – 03/31/22
NIH/NIA
Structure and Genesis of tau aggregates
This supplement uses CryoEM methods to investigate the effects of aggregation inducer Geranine G on synthetic tau filament structure.

Ongoing Training Support

T32 GM118291 Bundschuh/Kuret/Magliery (MPI) 07/01/17 – 06/30/22
NIH/NIGMS
Molecular Biophysics predoctoral training at The Ohio State University
This training program brings together molecular biophysics researchers spread out among more than 20 departments spanning five colleges.

Completed Research Support

R21 NS092396 Kuret (PI) 08/01/16 – 07/31/19
NIH/NINDS
Imaging agents for Synucleinopathy Drug Discovery
This lead optimization study seeks to identify candidate radiotracers for pre-mortem detection and staging of Lewy Body dementia and Parkinson's disease