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## BIOGRAPHICAL SKETCH

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NAME Nicholas T. Seyfried	POSITION TITLE Assistant Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) NSEYFRIED			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Boston College, Chestnut Hill MA	B.S.	09/95-05/99	Biochemistry
University of Oxford, United Kingdom	PhD	09/01-12/04	Biochemistry
University of Georgia, Athens GA	postdoc	12/04-12/06	Mass Spectrometry
Emory University School of Medicine, Atlanta GA	postdoc	12/06-08/10	Neuroproteomics

### A. Personal Statement

My research is currently focused on the development of mass spectrometry based techniques for: i) the high throughput quantitative analysis of proteins from complex biological samples including post-mortem human brain tissue ii) Identification and quantification of protein post-translational modifications including, ubiquitination, phosphorylation, methylation and acetylation iii) Proteomic biomarker discovery in cerebral spinal fluid, blood and platelets in Alzheimer's disease (AD), frontotemporal dementia (FTD) and other related neurodegenerative disorders.

### B. Positions and Honors

#### Positions:

1999-2001 Research Assistant, Department of Neurosurgery, Harvard Medical School, Boston, MA  
2010- Assistant Professor, Department of Biochemistry, Emory School of Medicine, Atlanta, GA  
2010- Director, Emory NINDS-Neuroscience Proteomics Core Facility

#### Honors:

2003-04 Arthritis Research Campaign D.Phil. Studentship  
2004 British Society for Matrix Biology Travel Award  
2007-09 NIH T32 NRSA Fellowship in Translational Neurology  
2009-10 NIH F32 NRSA Fellowship (National Institute of Aging)

#### Other Experience and Professional Memberships:

2005- American Society for Mass Spectrometry  
2007- Society for Neuroscience  
2012- American Society for Neurochemistry  
2012- Associate Editor *Journal of Integrated- OMICS (JIOMICS)*  
2007-2008 GeorgiaBio Emerging Leaders Network (ELN) business relations committee  
2010-2011 ad hoc reviewer for *Journal of Proteome Research*  
2011 ad hoc reviewer for *Journal of Biological Chemistry*  
2011 ad hoc reviewer for *PlosOne*  
2012 ad hoc reviewer for *Human Molecular Genetics*

### C. Peer-reviewed Publications

#### Most relevant to the current application

1. Seyfried NT, Atwood 3<sup>rd</sup> JA, Yongye A, Almond A, Day AJ, Orlando R and Woods RJ. (2007) Fourier transform mass spectrometry to monitor hyaluronan-protein interactions: Use of hydrogen/deuterium amide exchange. *Rapid Commun. Mass Spectrom.* 21:121-131.

2. Baker DL, **Seyfried NT**, Li H, Orlando R, Terns RM, and Terns MP. (2008) Determination of protein-RNA interaction sites in the Cbf5-H/ACA guide RNA complex by mass spectrometric protein footprinting. *Biochemistry* 47:1500-1510.
3. **Seyfried NT**, Huysentruyt LC, Atwood 3<sup>rd</sup> JA, Seyfried TN and Orlando R. (2008) Up-regulation of NG2 proteoglycan and interferon induced transmembrane proteins 1 and 3 in mouse astrocytoma: A membrane proteomics approach. *Cancer Letters* 263: 243-52. PMID: 2726046
4. **Seyfried NT**, Xu P, Duong DM, Cheng D, Hanfelt J and Peng J. (2008) Systematic approach for validating the ubiquitinated proteome. *Analytical Chemistry* 80: 4161-4169. PMID: 2673951.
5. Xu P, Duong DM, **Seyfried NT**, Cheng D, Xie Y, Robert J, Rush J, Hochstrasser M, Finley D, Peng J. (2009) Quantitative proteomics reveals the function of unconventional ubiquitin chains in proteasomal degradation. *Cell*. 137:133-45. PMID: 2668214.
6. **Seyfried NT**, Gozal YM, Dammer EB, Xia Q, Duong DM, Cheng D, Lah JJ, Levey AI and Peng J. (2010) Multiplex SILAC analysis of a cellular TDP-43 proteinopathy model reveals protein inclusions associated with SUMOylation and diverse polyUb chains. *Molecular and Cellular Proteomics* 9:705-18. PMID: 2860236.
7. Herskowitz JH, **Seyfried NT\***, Duong DM, Xia Q, Rees HD, Gearing M, Peng J, Lah JJ, and Levey AI (2010) Phosphoproteomic analysis in human frontal cortex reveals site-specific changes in GFAP and NDRG2 phosphorylation in frontotemporal lobar degeneration *J. Proteome Research* 9: 6368-79. PMID: 2997170. \*Co-first author.
8. Franco M, **Seyfried NT\***, Brand AH, Peng J and Mayor U. (2011) A novel strategy to isolate neuronal ubiquitin conjugates reveals a wide role for ubiquitination in synaptogenesis *Molecular and Cellular Proteomics* 10: M110.002188. PMID: 3098581. \*Co-first author
9. Herskowitz, JH, **Seyfried, NT**, Gearing, M, Peng, J, Levey, AI, and Lah, JJ. (2011) Rho kinase II phosphorylation of the lipoprotein receptor LR11/SorLa alter amyloid- $\beta$  production. *Journal of Biological Chemistry* 286:6117-27. PMID: 3057792.
10. Dammer EB, Na CH, Xu P, **Seyfried NT**, Duong DM, Cheng D, Gearing M, Rees H, Lah JJ, Levey AI, Rush J, and Peng J. (2011) Polyubiquitin linkage profiles in three models of proteolytic stress suggest etiology of neurodegenerative disease *Journal of Biological Chemistry*, 286:10457-65. PMID: 3060499.
11. Gozal YM, **Seyfried NT**, Gearing M, Glass JD, Heilman CJ, Wu J, Duong DM, Cheng D, Xia Q, Rees HD, Fritz JJ, Cooper DS, Peng J, Levey AI, Lah JJ. (2011) Aberrant Septin 11 is Associated with Sporadic Frontotemporal Lobar Degeneration. *Mol Neurodegeneration*. 6:82. PMID: 3259087.
12. Donovan LE, Higginbotham L, Dammer EB, Gearing M, Rees HD, Xia Q, Duong DM, **Seyfried NT**, Lah JJ, and Levey AI (2012) Analysis of a membrane enriched proteome from post-mortem human brain tissue in Alzheimer's disease. *Proteomics Clin. Appl.* 6: 201-11.
13. **Seyfried NT**, Gozal YM, Donovan LE, Herskowitz JH, Dammer EB, Xia Q, Ku L, Chang J, Duong DM, Rees HD, Cooper DS, Glass JD, Gearing M, Tansey MG, Lah JJ, Feng Y, Levey A, Peng J (2012) Quantitative analysis of the detergent-insoluble brain proteome in frontotemporal lobar degeneration using SILAC internal standards. *J. Proteome Research*. 11: 2721-38. PMID: 3357000
14. Herskowitz JH Gozal YM, Duong DM, Dammer EB, Gearing M, Ye K, Lah JJ, Peng J, Levey AI, and **Seyfried NT** (2012) Asparaginyl endopeptidase cleaves TDP-43 in brain. *Proteomics*.15-16:2455-63
15. Dammer EB, Fallini C, Gozal YM, Duong DM, Rossoll W, Xu P, Lah JJ, Levey AI, Peng J, Bassell GJ and **Seyfried NT** (2012) Coaggregation of RNA-binding Proteins in a Model of TDP-43 Proteinopathy with Selective RGG Motif Methylation and a Role for RRM1 Ubiquitination. *PLoS One*, 7:e38658, PMID 3380899
16. Wu F, Wu J, Nicholson AD, Echeverry R, Haile W, Catano M, An J, Lee AK, Duong DM, Dammer EB, **Seyfried NT**, Tong FC, Votaw JR, Medcalf R and Yepes M (2012) Tissue-Type Plasminogen Activator Regulates the Neuronal Uptake of Glucose in the Ischemic Brain. *J. Neuroscience* 32:9848-9858.PMID: 3437989
17. Kallappagoudar S, Dammer EB, Duong DM, **Seyfried NT**, Lucchesi JC. (2013) Expression, purification and proteomic analysis of recombinant histone H4 acetylated at lysine 16. *Proteomics*. in press

18. Dammer EB, Duong DM, Diner I, Gearing M, Feng Y, Lah JJ, Levey I, and **Seyfried NT** (2013) A Neuron Enriched Nuclear Proteome Isolated from Human Brain *J. Proteome Research* (in press).
19. Donovan LE, Dammer EB, Duong DM, Hanfelt JJ, Levey AI, **Seyfried NT** and Lah JJ (2013) Exploring the potential of the platelet membrane proteome as a source of peripheral biomarkers for Alzheimer's disease. *Alzheimer's Research & Therapy* (in press).
20. Wu F, Nicholson AD, Haile WB, Torre E, An J, Chen C, Lee AK, Duong DM, Dammer EB, **Seyfried NT**, Tong FC, Votaw JR, Yepes M. (2013) Tissue-type plasminogen activator mediates neuronal detection and adaptation to metabolic stress. *J Cereb Blood Flow Metab.* (In press)
21. Zhang H, Park SH, Pantazides BG, Karpiuk O, Warren MD, Hardy CW, Duong DM, Park SJ, Kim HS, Vassilopoulos A, **Seyfried NT**, Johnsen SA, Gius D, Yu DS (2013) SIRT2 directs the replication stress response through CDK9 deacetylation. *Proc Natl Acad Sci.* Aug 13;110:13546-51
22. Go YM, Roede JR, Walkers D, Duong DM, **Seyfried NT**, Orr M, Liang Y, Pennell KD, Jones DP (2013) Selective targeting of the cysteine proteome by thioredoxin and glutathione redox systems. *Mol Cell Proteomics.* In press

#### **Additional publications (in chronological order)**

1. Joki T, Heese O, Nikas DC, Bello L, Zhang J, Stine KK, **Seyfried NT**, Abe T, Chen LB, Carroll RS and Black PM. (2000) Expression of cyclooxygenase-2 in human gliomas and in vitro inhibition by a specific COX-2 inhibitor, NS-398. *Cancer Research* 60: 4926-4931.
2. Joki T, Machluf M, Atala A, Zhu J, **Seyfried NT**, Dunn IF, Abe T, Carroll RS and Black PM. (2001) Continuous release of endostatin from microencapsulated engineered cells for tumor therapy. *Nature Biotechnology* 19: 35-39.
3. **Seyfried NT**, Blundell CD, Day AJ and Almond A. (2005) The preparation and application of biologically active fluorescent hyaluronan oligosaccharides. *Glycobiology* 15: 303-312. PMID: 15496500.
4. **Seyfried NT**, McVey GF, Almond A, Mahoney DJ, Dudhia, J and Day, AJ. (2005) Expression and purification of functionally active hyaluronan-binding domains from human cartilage link protein, aggrecan and versican; formation of ternary complexes with defined hyaluronan oligosaccharides. *J. Biol. Chem.* 280: 5435-5448.
5. **Seyfried NT**, Day AJ and Almond A. (2006) Experimental evidence for all-or-none cooperative interactions between the G1-domain of versican and multivalent hyaluronan oligosaccharides. *Matrix Biology* 25: 14-19.
6. Kuznetsova SA, Issa P, Perruccio EM, Zeng B, **Seyfried NT**, Fielder HL, Day AJ, Wight TN, and Roberts DD. (2006) Induction of Cell Surface Versican-Thrombospondin-1 Complexes during ER Stress in Vascular Smooth Muscle Cells. *J Cell Sci.* 119: 4499-4509.

## **D. Research Support**

### **Ongoing Research Support**

NIRG-12-242297 Alzheimer's Association

11/1/2012 – 10/31/2014

#### **Early Changes in the Brain Proteome and Alzheimer's Disease Risk**

The main aim of this project is to employ a unbiased quantitative proteomics approach to establish a link between brain specific protein expression levels in the synapse rich fractions from individuals with preclinical AD and symptomatic AD.

**Role:** Principal Investigator

5P50AG025688-08

The Emory Alzheimer's Disease Research Center

5/1/2012-4/30/2013

**Emory ADRC Pilot award:** The main aim of this project is to employ proteomics approach to define early changes in brain specific protein expression levels from the detergent-insoluble and synapse rich fractions of individuals with asymptomatic AD and definite AD.

**Role:** Principal Investigator

## **Completed Research Support**

MJFF Grant

09/6/2011-09/05/2012

### **Estimating neuroprotective effects of nigral AAV-NRTN using selective reaction monitoring to quantitatively measure p-erk1/2 signaling strength in nigral DA neurons**

Michael J. Fox Foundation for Parkinson's Disease Research. Successful completion of these studies will provide new and valuable information on how this targeted mass spectrometry approach might be useful to quantify other proteins and their post-translational modifications in healthy or diseased brain in an antibody-independent manner.

**Role:** Co- Investigator

ADFF Grant

01/1/2011-12/31/2011

### **CSF biomarkers of FTL-D-TDP and FTL-D-TAU – A multi-center study.**

The Alzheimer's Drug Discovery Foundation (ADDF) and The Association for Frontotemporal Dementias (AFTD). Specific Aims: 1) Validation of identified CSF biomarkers that distinguish between FTL-D-TDP and FTL-D-TAU in a multi-center design, 2) Identification of novel CSF biomarkers associated with FTL-D-TAU.

**Role:** Co-Investigator

1F32 AG032848-01A1

04/01/2009-08/31/2010

### **Characterizing TDP-43 isoforms in neurodegenerative disease**

Frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS) are severe neurodegenerative disorders that together affect approximately 200,000 people in the United States. The study of TDP-43 will provide deeper understanding into the pathogenesis of these diseases and potentially lead to novel therapeutic strategies. This study provided the first detailed characterization of TDP-43 isoforms either isolated from FTL-D-U brain tissue or expressed in culture.

**Role:** Principal Investigator