BIOGRAPHICAL SKETCH

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NAME: YATES, NATHAN

eRA COMMONS USER NAME (agency login):

POSITION TITLE: Associate Professor

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)	Completion Date MM/YYYY	FIELD OF STUDY
Allegheny College, Meadville, PA	BS	06/1988	Chemistry
University of Florida, Gainesville, FL	PHD	05/1993	Analytical Chemistry
University of Virginia, Charlottesville, VA	Postdoctoral Fellow	11/1995	Bio-analytical Chemistry

A. PERSONAL STATEMENT

My 25 plus years of experience with mass spectrometry have afforded me numerous opportunities to advance academic, government, and industrial science through the development and application of new molecular analysis methods. Advances in mass spectrometry are inextricably linked to the rapid growth in scientific discoveries and data. The ultimate goal of my work is to bring these new experimental innovations to the broader scientific community. As an industrial and academic scientists, I have led collaborative efforts to design new instrumentation and data analysis tools that impact important areas of science. At Merck and Co. Inc., my work centered on the development new medicines, the discovery of protein biomarkers, and the translation of diagnostic assays to the clinic. My academic research program at the University of Pittsburgh is highly collaborative and interdisciplinary, bringing together experts in protein biochemistry, mass spectrometry, and informatics. As the Director of a campus-wide center for mass spectrometry, I have the opportunity to collaborate with investigators whose research programs span from understanding basic biology to developing new therapies and approaches for treating disease.

In the current application I will provide scientific guidance and expertise in protein mass spectrometry as the Director of the Biomedical Mass Spectrometry Center in the Schools of Health Sciences at the University of Pittsburgh (www.bioms.pitt.edu). The center is a campus-wide shared facility dedicated to advancing the use and application of mass spectrometry in basic and/or translational research. A highly motivated and well trained staff fully utilize 12 modern mass spectrometers and train researches at all levels, from first-time users to experts in the field. I will provide input on the experimental approach and experimental design that is taken. In addition, I will also assist with the review of the data, interpretation of the results, and publication of the experimental findings.

1. Huang F, Zeng X, Kim W, Balasubramani M, Fortian A, Gygi SP, Yates NA, Sorkin A. Lysine 63-linked polyubiquitination is required for EGF receptor degradation. Proc Natl Acad Sci U S A. 2013 Sep 24;110(39):15722-7. PubMed PMID: 24019463; PubMed Central PMCID: PMC3785728.
2. Antony ML, Lee J, Hahm ER, Kim SH, Marcus AI, Kumari V, Ji X, Yang Z, Vowell CL, Wipf P, Uechi GT, Yates NA, Romero G, Sarkar SN, Singh SV. Growth arrest by the antitumor steroidal lactone withaferin A in human breast cancer cells is associated with down-regulation and covalent binding at cysteine 303 of β-tubulin. J Biol Chem. 2014 Jan 17;289(3):1852-65. PubMed PMID: 24297176; PubMed Central PMCID: PMC3894360.
3. Fang Q, Inanc B, Schamus S, Wang XH, Wei L, Brown AR, Svilar D, Sugrue KF, Goellner EM, Zeng X, Yates NA, Lan L, Vens C, Sobol RW. HSP90 regulates DNA repair via the interaction between XRCC1 and DNA polymerase β. Nat Commun. 2014 Nov 26;5:5513. PubMed PMID: 25423885; PubMed Central PMCID: PMC4246423.
4. MacDonald ML, Ding Y, Newman J, Hemby S, Penzes P, Lewis DA, Yates NA, Sweet RA. Altered glutamate protein co-expression network topology linked to spine loss in the auditory cortex of

schizophrenia. Biol Psychiatry. 2015 Jun 1;77(11):959-68. PubMed PMID: 25433904; PubMed Central PMCID: PMC4428927.

B. POSITIONS AND HONORS

Positions and Employment

1995 - 2001	Senior Research Chemist, Department of Molecular Design and Diversity, Merck & Co. Inc., Rahway, NJ
2004 - 2010	Research Fellow, Department of Medicinal Chemistry, Merck & Co. Inc., Rahway, NJ
2004 - 2010	Senior Research Fellow, Department of Molecular Profiling, Merck & Co. Inc., Rahway, NJ
2010 - 2011	Scientific Director, Department of Exploratory and Translational Science, Merck & Co. Inc., Rahway, NJ
2011 -	Associate Professor, Department of Cell Biology, University of Pittsburgh, Pittsburgh, PA
2011 -	Director, Biomedical Mass Spectrometry Center, University of Pittsburgh, Pittsburgh, PA

Other Experience and Professional Memberships

1988 -	Member, American Chemical Society
1992 -	Member, American Society of Mass Spectroemtry
2006 - 2009	Member, The Association for Biomolecular Resource Facilities
2011 - 2012	Member, United States Human Proteomics Organization

Honors

1991	Kenan Analytical Chemistry Award, Union Carbide
1993	Shell Fellowship in Chemistry, Shell Oil Company
1994	Fellowship, Science and Technology Agency of Japan (declined), STA/NSF
2006	New Jersey Early Career Award in Mass Spectrometry, New Jersey ACS
2012	Distinguished Analytical Scientist, Chemical and Pharmaceutical Structure Analysis

C. Contribution to Science

1. ACADEMIC AND INDUSTRIAL EXPERIENCE IN MASS SPECTROMETRY: My research has focused on the development of mass spectrometry as an important bio-analytical tool for life sciences research and drug discovery. I received my graduate and post-doctoral training in the laboratories of Professors Richard A. Yost at the University of Florida and Donald F. Hunt at the University of Virginia. During this time, I also had an opportunity to work in the research and development laboratories at Finnigan Corporation (now Thermo-Fisher) under the direction of Dr. George Stafford. Drs. Yost, Hunt, and Stafford are all recipients of the prestigious award for “Distinguished Contributions to Mass Spectrometry” that recognizes a singular and significant achievement in the field. The unifying theme of my work with these pioneers was to develop and apply the tandem mass spectrometry capabilities of a new type of mass spectrometer, the quadrupole ion trap. It is personally satisfying that these efforts helped contribute to the acceptance and commercialization of ion trap mass spectrometers as a new and disruptive technology for proteomic analyses. During my tenure at Merck, I invented Differential Mass Spectrometry (dMS), an efficient mass spectrometry based strategy for comparing complex biological systems that permits un-biased analysis of all ions detected in full scan mass spectra. Working with a team of software engineers, I helped integrate the dMS approach into the Elucidator proteomic analysis suite that was sold commercially and eventually purchased by Microsoft. Throughout my career I have been fortunate to participate in team science and make contributions that have impacted the widespread use of mass spectrometry.
   a. Yates NA, Bradshaw SC, Yost RA, Tucker DB. , inventors. Thermo-Fisher, assignee. Method of operating an ion trap mass spectrometer to determine the resonant frequency of trapped ions. United States 5,128,542. 1991.
   b. Kim RM, Manna M, Hutchins SM, Griffin PR, Yates NA, Bernick AM, Chapman KT. Dendrimer-supported combinatorial chemistry. Proc Natl Acad Sci U S A. 1996 Sep 17;93(19):10012-7. PubMed PMID: 11607705; PubMed Central PMCID: PMC38327.

c. Sachs JR, Wiener MC, Yates NA. , inventors. Merck & Co. Inc., assignee. Mass spectrometry data analysis techniques. United States 6,906,320. 2004.

d. Paweletz CP, Wiener MC, Bondarenko AY, Yates NA, Song Q, Liaw A, Lee AY, Hunt BT, Henle ES, Meng F, Sleph HF, Holahan M, Sankaranarayanan S, Simon AJ, Settlage RE, Sachs JR, Shearman M, Sachs AB, Cook JJ, Hendrickson RC. Application of an end-to-end biomarker discovery platform to identify target engagement markers in cerebrospinal fluid by high resolution differential mass spectrometry. J Proteome Res. 2010 Mar 5;9(3):1392-401. PubMed PMID: 20095649.

2. DEVELOPMENT AND APPLICATION OF DIFFERENTIAL MASS SPECTROMETRY IN BASIC RESEARCH AND DRUG DEVELOPMENT: As a Scientific Director in the Department of Exploratory and Translational Sciences at Merck and Co. Inc., I invented and commercialized Differential Mass Spectrometry (dMS), a label free technique for measuring the global expression of proteins in complex biological systems. The dMS approach provides an efficient MS based strategy for the un-biased analysis of all ions detected in full scan mass spectra, not just ions that have corresponding tandem mass spectra and peptide sequences. The dMS platform has been used to discover protein-based biomarkers for Alzheimer's disease, diabetes, and cancer. In collaboration with Rosetta Biosoftware, the dMS approach was commercialized as part of the Elucidator™ proteomics analysis suite that was later acquired by Microsoft Corporation. At the University of Pittsburgh, I have continued to advance the dMS techniques and applied our new cloud computing based analysis tools to a number of basic and translational studies in neuroscience, oncology, and aging research.
   a. Yates NA, Deyanova EG, Geissler W, Weiner MC, Sachs JR, Wong KK, Thornberrry NA, Roy RS, Settlage RE, Hendrickson RC. Identification of peptidase substrates in human plasma by FTMS based differential mass spectrometry. International journal of mass spectrometry. 2007 January 01; 259(1-3):174-183.

   b. Zhao X, Deyanova EG, Lubbers LS, Zafian P, Li JJ, Liaw A, Song Q, Du Y, Settlage RE, Hickey GJ, Yates NA, Hendrickson RC. Differential mass spectrometry of rat plasma reveals proteins that are responsive to 17beta-estradiol and a selective estrogen receptor modulator PPT. J Proteome Res. 2008 Oct;7(10):4373-83. PubMed PMID: 18785765.

   c. Mazur MT, Cardasis HL, Spellman DS, Liaw A, Yates NA, Hendrickson RC. Quantitative analysis of intact apolipoproteins in human HDL by top-down differential mass spectrometry. Proc Natl Acad Sci U S A. 2010 Apr 27;107(17):7728-33. PubMed PMID: 20388904; PubMed Central PMCID: PMC2867874.

   d. Fang Q, Inanc B, Schamus S, Wang XH, Wei L, Brown AR, Svilar D, Sugrue KF, Goellner EM, Zeng X, Yates NA, Lan L, Vens C, Sobol RW. HSP90 regulates DNA repair via the interaction between XRCC1 and DNA polymerase β. Nat Commun. 2014 Nov 26;5:5513. PubMed PMID: 25423885; PubMed Central PMCID: PMC4246423.

3. BASIC AND TRANSLATIONAL APPLICATIONS OF TARGETED PROTEOMICS ASSAYS: My laboratory has developed targeted proteomic assays for the quantification of biologically relevant peptides and proteins that are based on the pioneering work of Professors Chris Enke and Richard Yost who invented the triple stage quadrupole mass spectrometer and demonstrated the use of selected reaction monitoring (SRM) for ultra-trace level analysis. Targeted proteomic assays were recently recognized by the journal Nature Methods, as “The 2012 Method of the Year” for their ability to support hypothesis driven studies. My laboratory actively develops and applies targeted proteomics in basic and translational research. In a collaboration with the University of Pennsylvania, we developed a multiplexed selected reaction monitoring mass spectrometry assay to measure proteins associated with lipoprotein metabolism and compared the fractional synthetic rates for two proteins determined by the classical GC-MS method with the peptide based LC-SRM methods. We then applied this technique to other proteins involved in lipoprotein metabolism whose kinetics are not readily measured using the classical antibody based methods. In collaboration with the Department of Psychiatry at the University of Pittsburgh, we developed assays to measure more than 250 proteins in the auditory cortex of post mortem brain. We have also developed multiplexed assays to measure 140 mitochondrial proteins in preclinical models and human samples. Finally we have developed ultra-sensitive affinity purification methods to detect low abundance peptide hormones in plasma. Targeted proteomic assays provide a unique opportunity to advance mass spectrometry as a clinic ready technology for measuring biologically relevant molecules with absolute molecular specificity.
   a. Lee AY, Yates NA, Ichetovkin M, Deyanova E, Southwick K, Fisher TS, Wang W, Loderstedt J, Walker N, Zhou H, Zhao X, Sparrow CP, Hubbard BK, Rader DJ, Sitlani A, Millar JS, Hendrickson RC.

Measurement of fractional synthetic rates of multiple protein analytes by triple quadrupole mass spectrometry. Clin Chem. 2012 Mar;58(3):619-27. PubMed PMID: 22249652.

b. Huang F, Zeng X, Kim W, Balasubramani M, Fortian A, Gygi SP, Yates NA, Sorkin A. Lysine 63-linked polyubiquitination is required for EGF receptor degradation. Proc Natl Acad Sci U S A. 2013 Sep 24;110(39):15722-7. PubMed PMID: 24019463; PubMed Central PMCID: PMC3785728.

c. Chappell DL, Lee AY, Castro-Perez J, Zhou H, Roddy TP, Lassman ME, Shankar SS, Yates NA, Wang W, Laterza OF. An ultrasensitive method for the quantitation of active and inactive GLP-1 in human plasma via immunoaffinity LC-MS/MS. Bioanalysis. 2014 Jan;6(1):33-42. PubMed PMID: 24341493.

d. MacDonald ML, Ding Y, Newman J, Hemby S, Penzes P, Lewis DA, Yates NA, Sweet RA. Altered glutamate protein co-expression network topology linked to spine loss in the auditory cortex of schizophrenia. Biol Psychiatry. 2015 Jun 1;77(11):959-68. PubMed PMID: 25433904; PubMed Central PMCID: PMC4428927.

4. INFORMATICS AND MASS SPECTROMETRY SOFTWARE DEVELOPMENT: An important component of my research has been the development of software, algorithms, and data analysis platforms that advance and simplify the acquisition, interpretation, and utilization of mass spectrometry data. Early in my career I worked in the research and development laboratories at Finnigan Corporation (now Thermo-Fisher) and developed expertise in programming instrument control languages that extended the capabilities of a new type of mass spectrometer, the quadrupole ion trap. It was this experience that helped me realize how much data and information is produced by mass spectrometers, and how much of it goes unexamined or unused. A central theme of my work has been to develop software tools that delve into the richness of mass spectrometry data and extracts new information. At UVA, I wrote instrument control programs that automated the acquisition of MS/MS spectra on an early prototype of an electrospray ion trap. This approach was later commercialized as data dependent acquisition and remains one of the primary methods for collecting proteomics data. At Merck, I developed software tools for the analysis of complex combinatorial libraries that enabled the screening for new drug targets. I also developed algorithms for performing Differential Mass Spectrometry that were commercialized used to discover molecular biomarkers. At the University of Pittsburgh, I launched CHORUS (www.chorusproject.org) a non-profit community controlled data analysis solution that currently allows more than 1000 users from 100 labs around the world to store, share, and analyze mass spectrometry on a cloud computing platform. I find the interface between bio-analytical chemistry and software development to be a fantastically exciting place to work, and envision that “easy to use” data analysis environments will be the key enabling technology that brings the power of mass spectrometry to the life sciences and health care community.

   a. Yates N, Wislocki D, Roberts A, Berk S, Klatt T, Shen DM, Willoughby C, Rosauer K, Chapman K, Griffin P. Mass spectrometry screening of combinatorial mixtures, correlation of measured and predicted electrospray ionization spectra. Anal Chem. 2001 Jul 1;73(13):2941-51. PubMed PMID: 11467539.

   b. Mehl JT, Cummings JJ, Rohde E, Yates NN. Automated protein identification using atmospheric-pressure matrix-assisted laser desorption/ionization. Rapid Commun Mass Spectrom. 2003;17(14):1600-10. PubMed PMID: 12845586.

   c. Wiener MC, Sachs JR, Deyanova EG, Yates NA. Differential mass spectrometry: a label-free LC-MS method for finding significant differences in complex peptide and protein mixtures. Anal Chem. 2004 Oct 15;76(20):6085-96. PubMed PMID: 15481957.

   d. Meng F, Wiener MC, Sachs JR, Burns C, Verma P, Paweletz CP, Mazur MT, Deyanova EG, Yates NA, Hendrickson RC. Quantitative analysis of complex peptide mixtures using FTMS and differential mass spectrometry. J Am Soc Mass Spectrom. 2007 Feb;18(2):226-33. PubMed PMID: 17070068.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/nathan.yates.1/bibliography/47384989/public/?sort=date&direction=ascending

D. RESEARCH SUPPORT

Ongoing Research Support

2014/04/01-2019/03/31

1 R01AR065445-01, NIH
Huard (PI)
Bone Abnormalities & Healing Defect in Muscular Dystrophy
This proposal aims to determine the nature of skeletal system defects and characterize whether the progressive bone histopathology observed in a mouse model of muscular dystrophy is driven by stem cell abnormalities. Dr. Yates will direct the proteomic analyses of a series of stem cell pools.
Role: Co-Investigator

2014/04/01-2019/03/31
2 R01MH071533-11 , NIH
Sweet (PI)
Plasticity of Auditory Cortical Circuits in Schizophrenia
The purpose of this application is to apply modern quantitative proteomic techniques to the analysis of post-mortem brain tissue from subjects with schizophrenia.
Role: Co-Investigator

2013/07/01-2018/06/30
1 P01 AG043376-01A1 , NIH/NIA
Robbins (PI)
Cell Autonomous and Non-Autonomous Mechanisms of Aging
Dr. Yates will direct all proteomic approaches to identify factors secreted by senescent cells, stem cells and circulating factors for all three projects.
Role: Co-Investigator

2014/04/01-2016/03/31
R21 EB017184 , NIH
Isenberg (PI)
Bioengineering Tracheas through Targeting Activated CD47
This proposal will investigate newly-identified signaling pathways and the role that they play in limiting cellular and tissue regeneration, engraftment and tracheal angiogenesis.
Role: Co-Investigator

2010/08/01-2015/07/31
P30 CA047904 24, NIH/NCI
Davidson (PI)
Cancer Center Support Grant (Cancer Biomarkers Facility)
The major goals of this project are to develop and apply mass spectrometry based proteomics for the discovery and translation of cancer biomarkers.
Role: Co-Investigator

2014/07/01-2015/06/30
S10 OD018071-01
YATES, NATHAN Andrew (PI)
Request for triple quadrupole mass spectrometer for the University of Pittsburgh
Role: PI