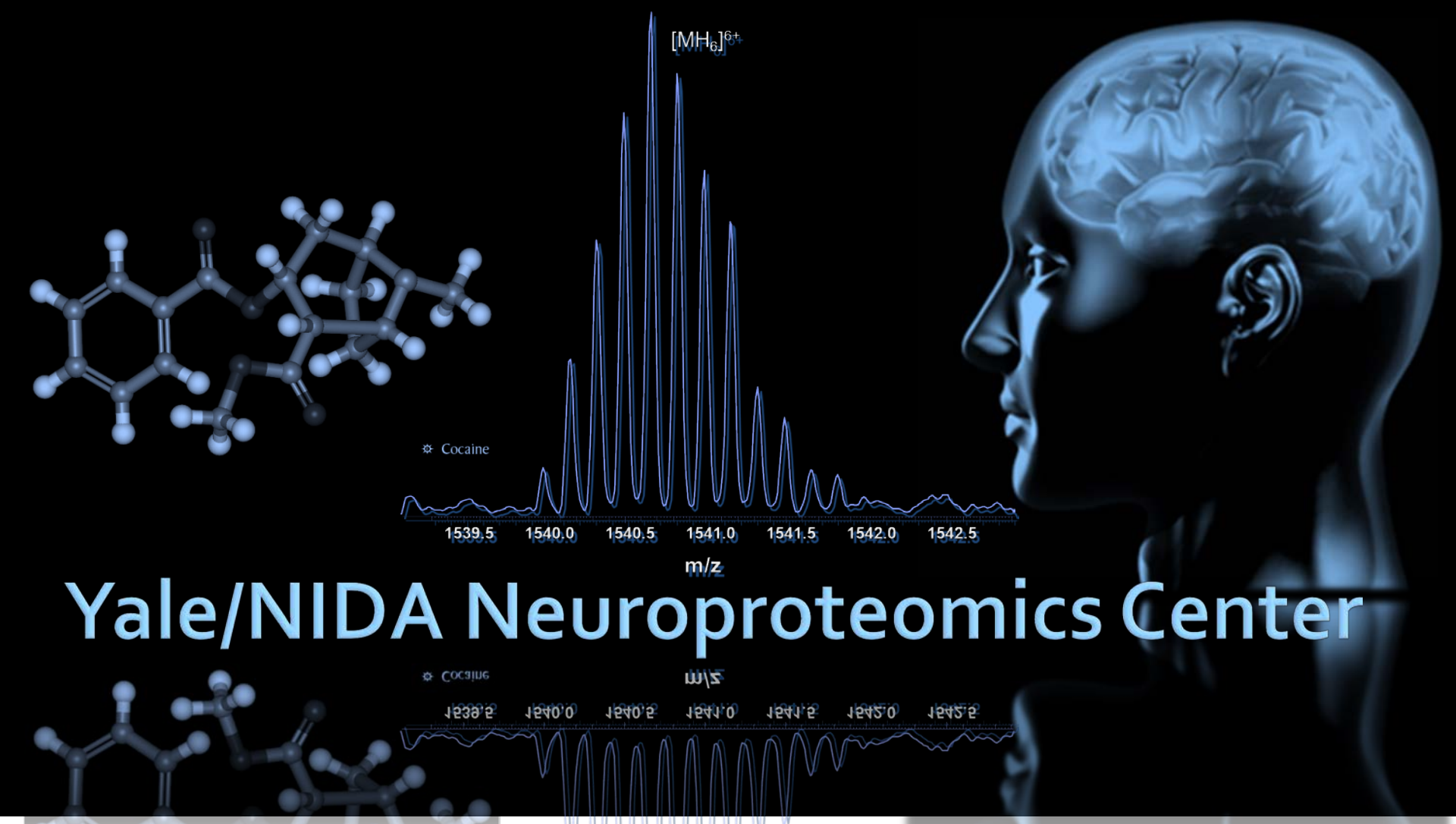


Yale/NIDA Neuroproteomics Center

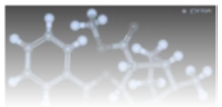
Administrative Core
Co-Directors
Angus Nairn & Ken Williams

Welcome from Deputy Dean Carolyn Slayman

"On behalf of Yale Medical School, I am delighted to welcome the External Advisory Board to today's meeting. Like other top research universities, Yale is experiencing a rapid upswing in interest in neuroproteomics and other areas of proteomics. Existing faculty are increasingly incorporating protein profiling and studies of post-translational protein modifications into their research; new faculty are being recruited with expertise in proteomics tools; and as in the past, the Keck Lab is helping to lead the way by making these new tools available, not only to Yale researchers, but also to biomedical scientists at other institutions around the country."

"Yale has made major investments in proteomics. Since 2003, the Medical School has spent $17 million to house, help equip, and support the Keck Lab. In spite of the financial challenges that now face medical schools and universities across the country, we plan to continue investing in proteomics to the best of our ability."

Welcome from Deputy Dean Carolyn Slayman



“Today’s meeting will give you an overview of some of the research that is underway in the Yale/NIDA Neuroproteomics Center. You will hear from 7 Yale scientists, 4 scientists from other universities, and 5 senior members of the Keck Laboratory; all working together to use advanced proteomics tools to probe fundamental questions in neuroscience. I am certain that you will enjoy the program, and we look forward to your feedback on how to make it even stronger.”

Advisory Board Meeting
Yale/NIDA Neuroproteomics Research Center

- **Program Outline:**
  - **Brief Overview of Center**
  - **Core Technologies presented by 6 Directors**
  - **Progress of established research projects presented by 6 Center investigators**
  - **Progress of 3 Pilot Project s presented by 3 “alumni”**
  - **Progress/plans for a new Pilot Project by current awardee**
  - **(Optional) At close of meeting there will be tours of Neuroproteomics Center Cores located in the Keck Labs**
  - **Advisory Board Meeting with Angus Nairn & Ken Williams**
  - **14 talks, morning and lunch break: will try to maintain schedule. If I stand up when you’re talking, your talk has extended into the 5 min Q&A section at end of each talk.**
- **Goal:**
  - **Seek advice from Advisory Board on improving the Center**

Yale/NIDA Neuroproteomics Research Center

- Theme: “Proteomics of Altered Signaling in Addiction”
- Co-Director Ken Williams
  - Founder (1980) & Co-Director, Keck Laboratory
    - Associate Director, Proteomics Core, Northeast Biodefense Center
    - Professor (Adjunct) Research, Mol. Biophysics & Biochemistry
  - Office located in MS/Proteomics Cores @ 300 George St
- Co-Director Angus Nairn
  - Charles Murphy Professor of Psychiatry and Pharmacology
  - Office in CT Mental Health Center near many Neuroproteomics Center investigators in Dept. of Psychiatry
- Background:
  - Center funding (2004 – 2009, 2009 – 2014): now in existence for 8.7 years, or almost 4 years since last competing renewal
  - Year Nine funding, 6/12 through 5/13, DC: $981K
  - Center grant funds core services provided to center investigators. building of YPED database, biotechnology research, Pilot Project grants

Yale/NIDA Neuroproteomics Center Has Five Cores

Administrative	Ken Williams	Mol. Biophys. Bioch.	Co-Directors
	Angus Nairn	Psychiatry	

Bioinformatics & Biostatistics	Kei-Hoi Cheung	Anesthesiology (Medical Informatics)	Director
	Perry Miller		Assoc. Director
	Mark Shifman		Yale Protein Expression Database (YPED)
	Mark Gerstein & Can Bruce	Mol. Biophys. Bioch.	Bioinformatics
	Rob Bjornson & Nick Carriero	Computer Science	High Performance Computing
	Hongyu Zhao	Epidemiology	Biostatistics

Three Service Cores in the Yale/NIDA Neuroproteomics Center

Protein Profiling & Identification, Biophysics, & Phosphoinositide Analysis	Kathy Stone	Mol. Biophys. Bioch.	Director
	Chris Colangelo	Mol. Biophys. Bioch.	Protein Profiling
	Pietro De Camilli	Cell Biology	Phosphoinositide Analysis
	Ewa Folta-Stogniew	Mol. Biophys. Bioch.	Biophysics

Protein Post-Translational Modifications	Erol Gulcicek	Mol. Biophys. Bioch.	Director
	TuKiet Lam	Mol. Biophys. Bioch.	FTICR-MS

Targeted Proteomics	Chris Colangelo	Mol. Biophys. Bioch.	Director
	Janet Crawford	Mol. Biophys. Bioch.	Peptide Synthesis in Support of MRM Technology

Internal Advisory Board (IAB)
Yale/NIDA Neuroproteomics Center

	Name	Departments & Sections
1	Dr. Carolyn Slayman	Deputy Dean for Academic and Scientific Affairs, Yale School of Medicine; Sterling Professor Genetics; Professor, Physiology
2	Dr. Jose Costa	Vice Chair, Pathology & Yale Cancer Center; Professor Pathology & Medicine
3	Dr. Anthony Koleske	Professor, Molecular Biophysics and Biochemistry; & Neurobiology
4	Dr. William Sessa	Dir Div of Bio Sciences, Vice Chair, Department of Pharmacology and Int Med Cardiology
5	Dr. Robert Sherwin	C. N. H. Long Professor of Int. Med; Section Chief Int. Med. Endocrinology; PI on Yale's (NIH) Clinical and Translational Science Award (CTSA)
6	Dr. Tobias Walther	Associate Professor, Cell Biology
7	Dr. Heping Zhang	Susan Dwight Bliss Professor of Biostatistics; Prof Statistics; Prof Public Health, Child Study Ctr & Statistics

External Advisory Board (EAB)
Yale/NIDA Neuroproteomics Center

	Name	Department	Institution
1	Dr. Brian Chait	Prof., Laboratory of Mass Spectrometry	Rockefeller U.
2	Dr. James Eberwine	Co-Director , PENN Genome Frontiers Institute	U. Pennsylvania
3	Dr. Edward Hawrot	Assoc. Dean, Biology Program; Prof. Med. Sci.	Brown Medical School
4	Dr. Peter Kalivas	Distinguished University Professor, Neurosciences	Medical University of South Carolina
5	Dr. Peter McPherson	James McGill Prof., Neurology and Neurosurgery	Montreal Neurological Institute
6	Dr. David Muddiman	Dir. Keck FT-ICR Mass Spectrometry Lab, Prof. Chem.	North Carolina State U.
7	Dr. Andrey Rzhetsky	Institute of Genomics and Systems Biology	University Chicago
8	Dr. Paul Tempst	Prof. Molecular Biology	Memorial Sloane Kettering Cancer C.

Synergies Between the Neuroproteomics Center & Keck Lab

Synergies:

- Nine mass spectrometers purchased by Keck since 2004 for >$6 million support the service cores in the Neuroproteomics Center
- Protein Profiling & Identification, PTM, & Targeted Proteomics cores are located within 7,500 ft^2 Keck MS/Proteomics Resource
- NIDA Bioinformatics, Biophysics, Biostatistics, & HPC Core sections are located within the corresponding Keck Resources
- Keck Protein Chemistry and Genomic Resources provide complementary technologies that are not available through the Center.
- Improved technologies developed in Neuroproteomics Center are leveraged by their rapid availability to >1,000 PI users of Keck Lab
  - ✓ Rat/Mouse Brain LC-MRM Assay for 112 proteins will soon be released through Keck Lab

Synergies Between the Neuroproteomics Center & Keck Lab

- **Center Investigators strongly supported the last two SIGs awarded to Keck**

Year	Instrument	#Projects	#NIDA Projects	%NIDA Projects
2010	AB Sciex 5500 QTRAP (LC-MRM, $490K)	20	10	50%
2011	LTQ Orbitrap Elite (LFQ, SILAC, P-Proteomics, $780K)	51	27	53%

- **In 2012 the Center joined *with* Keck to successfully request funding ($626K) from the School for an AB Sciex Triple TOF 5600 that carries out the exhaustive MS/MS sequencing required to develop LC-MRM assays, and that also supports SWATH & iTRAQ analyses carried out in Keck and in the Center.**

Neuroproteomics Center Accomplishments Since Last Competing Renewal (6/2009)

- **New Instrumentation**
  - Three new mass spectrometry systems in 3 years
- **Grant Application**
  - Pending $560K SIG for “6500 QTrap Mass Spectrometer ”
- **New Technologies**
  - Designed comprehensive workflow for development of routine LC-MRM & LC-SWATH “proteome” assays
- **YPED** has been substantially expanded and improved
  - Serves as Center & Keck database, supports 1,313 users at 325 institutions

Yale/NIDA Neuroproteomics Center Mission Statement

- **The theme of the Center, "Proteomics of Altered Signaling in Drug Addiction" will bring together exceptionally strong Yale programs in cellular and molecular neuroscience, neuronal signaling, and in molecular actions of psychostimulants and psychotropic drugs in the brain to identify adaptive changes in protein expression and regulation that are related to the actions of drugs of abuse.**

- **The Center will improve existing technologies as well as develop new proteomics technologies that can be applied in a quantitative manner to biological questions related to the actions of drugs of abuse on cellular signaling, specifically in the neuronal substrates of addictive drug action.**

- **The Center will provide training, and recruit new and younger investigators, into the area of proteomics, and recruit investigators into studies of addictive drug action.**

NIDA Center Investigators - 2009

Yale – CNNR, Physiology, Pharmacology, Genetics, Child Study

- Thomas Biederer*
- Sreeganga Chandra
- Pietro DeCamilli
- Richard Lifton
- Paul Lombroso
- Len Kaczmarek
- Stephen Strittmatter
- Susumo Tomita
- Dan Wu

Yale - Psychiatry

- Ralph DiLeone
- Angus Nairn*
- Marina Picciotto*
- Sam Sathyanesan
- Arthur Simen
- Rajita Sinha*
- Jane Taylor*
- Zoron Zimolo*

UT Southwestern, U.Conn, Chicago, Rockefeller, Stanford

- James Bibb*
- Elizabeth Eipper*
- William Green*
- Paul Greengard*
- Robert Malenka*

*NIDA PI or drug action/abuse researcher

NIDA Center Investigators - 2013

Yale – CNNR, Physiology, Pharmacology, Genetics, Child Study, MBB

- Thomas Biederer*
- Sreeganga Chandra
- Pietro DeCamilli
- Richard Lifton
- Paul Lombroso
- Len Kaczmarek
- Stephen Strittmatter
- Susumo Tomita
- Dan Wu
- Michael Koelle
- Jesse Rinehart

Yale - Psychiatry

- Ralph DiLeone
- Angus Nairn*
- Marina Picciotto*
- Jane Taylor*
- Zoron Zimolo*

Alumni - Colorado Michigan St, S Dakota Pittsburgh, Baylor

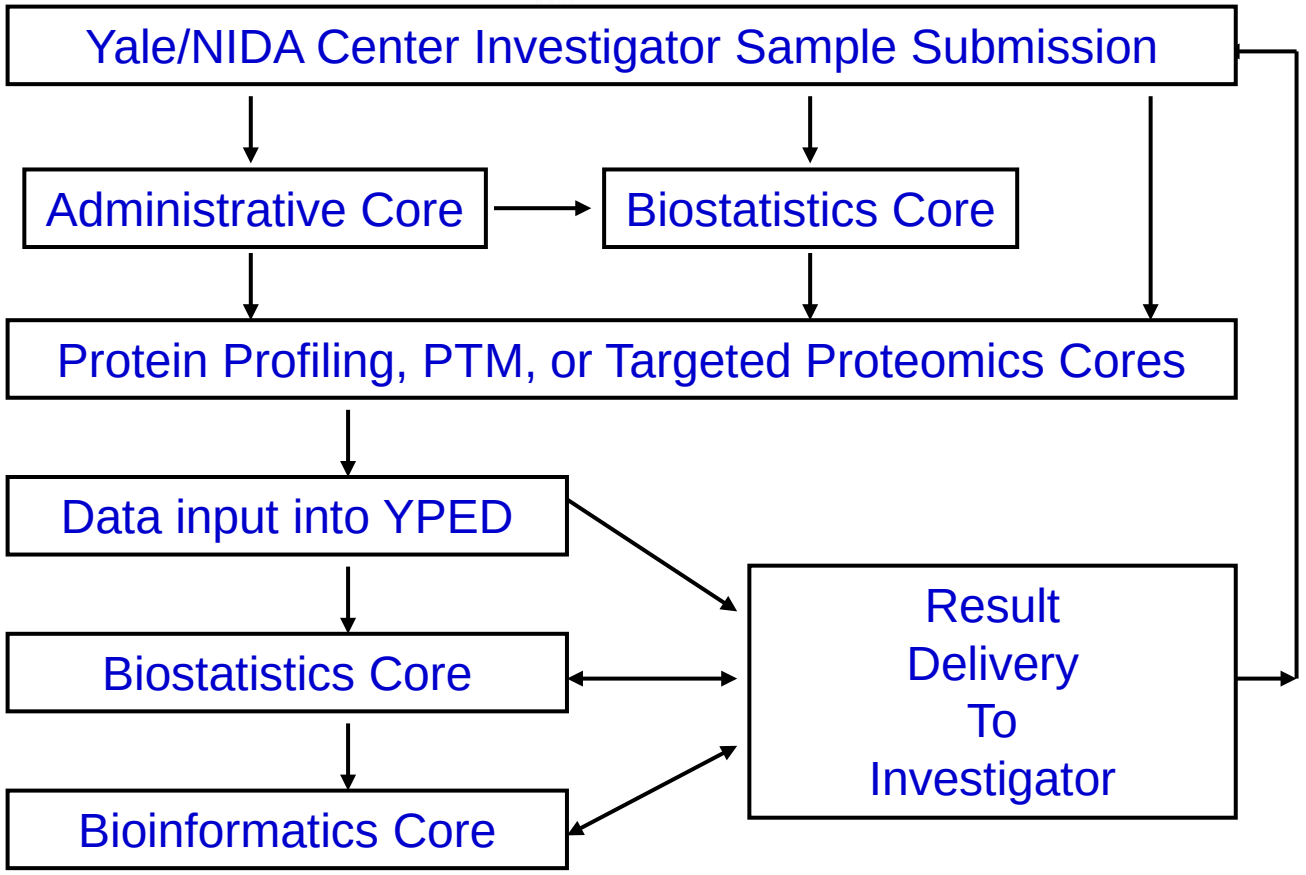
- Tristan McClure-Begley*
- A.J. Robison*
- Sam Sathyanesan
- Mary Torregrossa*
- Nilesh Tannu*

UT Southwestern, U Conn, Chicago, Rockefeller, Wake Forest, Indiana, U Mass, Mt Sinai

- James Bibb*
- Elizabeth Eipper*
- William Green*
- Paul Greengard*
- Scott Hemby*
- Ken Mackie*
- Maria Morabito*
- Eric Nestler*
- Lakshmi Devi*

*NIDA PI or drug action/abuse researcher

NIDA Center Project Development

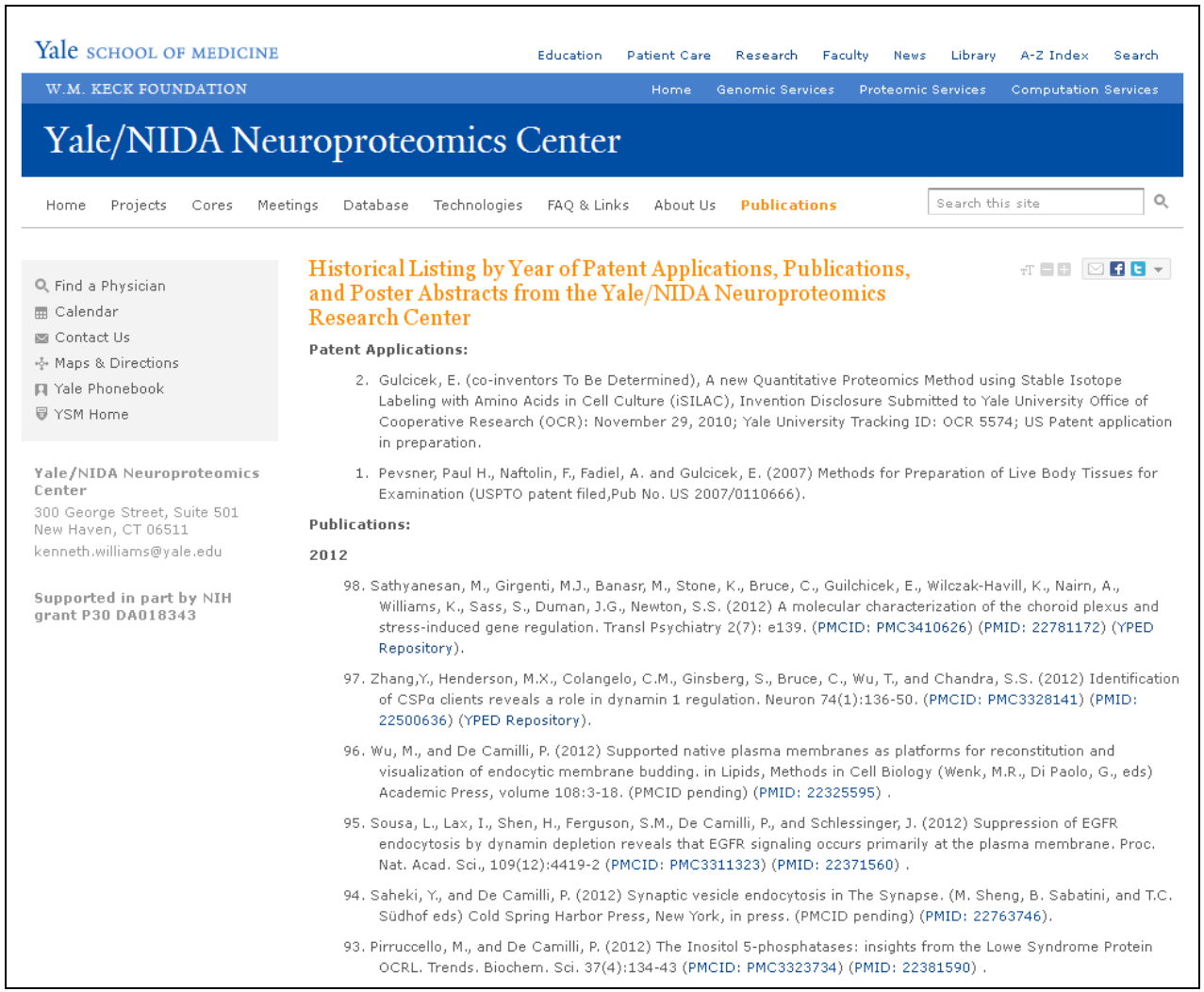


Yale/NIDA Neuroproteomics Center Core Usage in 2012

	# Services	#Investigators
MS/Proteomics		
Digests	524	12
LC-MS/MS Protein ID	626	13
LC-MS/MS Phospho Site ID	147	5
Profiling: LFQ	98	3
Profiling: iTRAQ	16	3
Profiling: SILAC	42	2
Profiling: DIGE	19	3
LC-MRM	886	7
LC-MS/MS "Proteome" Seq. on 5600	109	4
SWATH	160	4

Biophysics		
SEC-Laser Light Scattering	18	3
Isothermal Microcalorimetry (ITC)	36	1
SPR/Biacore T100	63	2
Phosphoinositide Analysis	680	3
Biostatistical Analysis	208	5
Bioinformatics Analyses	155	4

NIDA Center Website and Publications



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New Haven, CT 06511
kenneth.williams@yale.edu

Supported in part by NIH grant P30 DA018343

Historical Listing by Year of Patent Applications, Publications, and Poster Abstracts from the Yale/NIDA Neuroproteomics Research Center

Patent Applications:

2. Gulcicek, E. (co-inventors To Be Determined), A new Quantitative Proteomics Method using Stable Isotope Labeling with Amino Acids in Cell Culture (iSILAC), Invention Disclosure Submitted to Yale University Office of Cooperative Research (OCR): November 29, 2010; Yale University Tracking ID: OCR 5574; US Patent application in preparation.

1. Pevsner, Paul H., Naftolin, F., Fadiel, A. and Gulcicek, E. (2007) Methods for Preparation of Live Body Tissues for Examination (USPTO patent filed,Pub No. US 2007/0110666).

Publications:

2012

98. Sathyanesan, M., Girgenti, M.J., Banasr, M., Stone, K., Bruce, C., Guilchicek, E., Wilczak-Havill, K., Nairn, A., Williams, K., Sass, S., Duman, J.G., Newton, S.S. (2012) A molecular characterization of the choroid plexus and stress-induced gene regulation. Transl Psychiatry 2(7): e139. (PMCID: PMC3410626) (PMID: 22781172) (YPED Repository).

97. Zhang,Y., Henderson, M.X., Colangelo, C.M., Ginsberg, S., Bruce, C., Wu, T., and Chandra, S.S. (2012) Identification of CSPα clients reveals a role in dynamin 1 regulation. Neuron 74(1):136-50. (PMCID: PMC3328141) (PMID: 22500636) (YPED Repository).

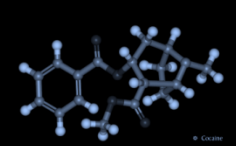
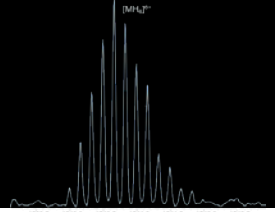
96. Wu, M., and De Camilli, P. (2012) Supported native plasma membranes as platforms for reconstitution and visualization of endocytic membrane budding. in Lipids, Methods in Cell Biology (Wenk, M.R., Di Paolo, G., eds) Academic Press, volume 108:3-18. (PMCID pending) (PMID: 22325595) .

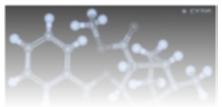
95. Sousa, L., Lax, I., Shen, H., Ferguson, S.M., De Camilli, P., and Schlessinger, J. (2012) Suppression of EGFR endocytosis by dynamin depletion reveals that EGFR signaling occurs primarily at the plasma membrane. Proc. Nat. Acad. Sci., 109(12):4419-2 (PMCID: PMC3311323) (PMID: 22371560) .

94. Saheki, Y., and De Camilli, P. (2012) Synaptic vesicle endocytosis in The Synapse. (M. Sheng, B. Sabatini, and T.C. Südhof eds) Cold Spring Harbor Press, New York, in press. (PMCID pending) (PMID: 22763746).

93. Pirruccello, M., and De Camilli, P. (2012) The Inositol 5-phosphatases: insights from the Lowe Syndrome Protein OCRL. Trends. Biochem. Sci. 37(4):134-43 (PMCID: PMC3323734) (PMID: 22381590) .

➢**61 Publications since last competing renewal submitted 2/2009 and 10 Submitted manuscripts & manuscripts in revision 9 manuscripts in preparation**

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Program

2013 Meeting of the Yale/NIDA Neuroproteomics Center

Talk	Speakers	Institution	Core or Project Title	Start Time	Min
Continental Breakfast – All Attendees Invited/Poster presenters should mount their posters.				7:30 AM	30
1	Ken Williams & Angus Nairn	Yale U.	Center Overview	8:00 AM	20
2	Kathy Stone	Yale U.	Protein Profiling and Identification Core Sections	8:20 AM	20
3	Erol Gulcicek	Yale U.	Protein Post-Translational Modification & Profiling Core	8:40 AM	20
4	Kei Cheung	Yale U.	Bioinformatics and Biostatistics Core	9:00 AM	20
5	Ewa Folta-Stogniew	Yale U.	Biophysics Core Section	9:20 AM	20
	Break		Morning Coffee Break	9:40 AM	20
6	Rob Kitchen	Yale U.	Toward Improved Label-free Quantification of MS/MS Spectra Using Predicted Proteomes Based on Second-generation RNA-Sequencing	10:00 AM	30
7	Thomas Biederer	Yale U.	Identification and Analysis of Protein Complexes Mediating Synapse Formation	10:30 AM	30
8	Sreeganga Chandra	Yale U.	Neuronal Substrates Required for Synapse Maintenance	11:00 AM	30
9	Pietro DeCamilli	Yale U.	Endocytic Mechanisms and Phosphoinositide Metabolism at Synapses	11:30 AM	30
Buffet Lunch & Poster Session – All Attendees Welcome/Poster presenters should stand near their posters.				12:00 PM	30
10	Chris Colangelo	Yale U.	Targeted Proteomics Core: Comprehensive Workflows for the Development of LC-MRM and SWATH Proteome Assays	12:30 PM	20
11	Betty Eipper	U. Conn.	Effects of Cocaine on Kalirin Phosphorylation and Function	12:50 PM	30
12	Marina Picciotto/Tristan McClure-Begley	Yale U./ U. Colorado	Defining the nAChR Interactome	1:20 PM	30
13	Alfred J. Robison	Michigan State U.	Neuronal Subtype-Specific Effects of the Transcription Factor ΔFosB on Synaptic Physiology	1:50 PM	30
14	Mary Torregrossa	U. Pittsburgh	Identification of Proteins that are Differentially Activated by Drug Cue Memory Extinction and Reconsolidation using Phosphoproteomics	2:20 PM	30
15	Angus Nairn	Yale U.	Current and Future Challenges in Neuroproteomics	2:50 PM	30
(Closed) Internal and External Advisory Committee Meeting with Angus Nairn and Ken Williams, and (optional) tours of NIDA/Neuroproteomics Center for attendees and speakers				3:20 PM	40