

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Dykstra, Linda A.	POSITION TITLE William Rand Kenan Distinguished Professor Depts. Psychology; Pharmacology; Curriculum in Neurobiology		
eRA COMMONS USER NAME dykstra			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Hope College, Holland, MI	B.A.	1966	Mathematics/Psychology
University of Chicago, Chicago, IL	M.A.	1968	English Literature
University of Chicago, Chicago, IL	Ph.D.	1972	Psychopharmacology
University of North Carolina, Chapel Hill, NC	Postdoctoral	1973	Pharmacology

**A. Personal Statement**

**Research Focus:** Research in my laboratory focuses on investigations of the analgesic effects of opioids as well as the development of tolerance to and dependence upon opioids and other related compounds (R37-DA02749-32). Recently, my laboratory has expanded its interest in this area through a collaborative project investigating systems for transdermal drug delivery of the opioid agonist, buprenorphine (R21-DA0269980). Investigations in my laboratory employ an integrative strategy that combines genetic, pharmacological and behavioral approaches to the investigation of pain and analgesia.

**Training Focus:** Currently, I serve as the director of two different training programs. One of those programs, Training in Research on Drug Abuse (T32-DA02744), is in its 22<sup>nd</sup> year of support, with continued support for an additional 3 years. This program provides research training in areas related to the neurobiology of drugs of abuse. In addition to directing this program, I have served as the major research advisor for over 20 predoctoral students, 15 postdoctoral fellows and numerous undergraduates who have worked within my laboratory. The other program that I direct, SPIRE or Seeding Postdoctoral Innovators in Research & Education is one of the longest running Institutional Research and Academic Career Development Award (IRACDA) programs supported by NIGMS. This integrated program provides training in both research and teaching for postdoctoral fellows in the biomedical sciences. Training in research is provided within laboratories at the University of North Carolina at Chapel Hill. Training in teaching is provided in partnership with four partner universities within the state of North Carolina that have demonstrated a commitment to the training, encouragement and assistance to students from groups underrepresented in the biomedical and behavioral research enterprise of the nation.

**B. Positions and Honors****Positions and Employment**

1970-1972 NIMH Predoctoral Research Fellow, Univ. of Chicago  
 1972-1973 NIDA Postdoctoral Research Fellow, Univ. of North Carolina, Dept of Pharmacology  
 1973-1984 Assistant/Associate/Full Professor of Psychology and Pharmacology, Univ. North Carolina  
 1984-present William Rand Kenan Distinguished Professor; Psychology and Pharmacology, Univ. North Carolina  
 1996-2008 Dean of Graduate School, Univ. North Carolina

**Visiting Appointments:**

1979 Assistant Professor, Harvard University, Laboratory of Psychobiology  
 1985/06 Professor, University of Michigan, Dept. Pharmacology  
 2001/02 Professor, Duke University, Dept. of Cell Biology

**President or Chair of Professional Groups**

1988 Chair, Psychopharmacology Division, American Psychological Association  
 1997/98 President, College on Problems of Drug Dependence

Principal Investigator/Program Director (Last, First, Middle): Dykstra, Linda

- 2005/06 Chair, Behavioral Pharmacology Division, American Society of Pharmacology & Experimental Therapeutics
- 2006/07 President, Association of Graduate Schools; American Association Universities
- 2007/09 Chair, Board of Directors, North Carolina Association Biomedical Research
- 2008/10 Sec/Treasurer, Neuropharmacology Division, American Society of Pharmacology & Experimental Therapeutics

#### **Membership on Advisory Committees**

- 1983/87 NIH Clinical and Behavioral Review Group
- 1991/94 National Advisory Council on Drug Abuse
- 2002-current Executive Board, North Carolina Association Biomedical Research
- 2004-2008 Advisory Board, Graduate Record Exam, Educational Testing Services;

#### **Honors**

- 1967-1968 Ford Foundation Fellowship in the Humanities
- 1977-1987 Research Scientist Development Award, NIH
- 1988-1998 Research Scientist Award, NIH
- 1988-1998 NIH/NIDA MERIT Award
- 1991 Elected Member, American College of Neuropsychopharmacology
- 1991 Appointed: William Rand Kenan Distinguished Professor
- 2004 Mentorship Award, CPDD
- 2005 Marian W. Fischman Lectureship Award

### **B. Selected peer-reviewed publications**

(Publications selected from over 150 peer-reviewed publications)

- Picker, M.J., Daugherty, D., Henry, Fredrick E., Miller Laurence L., & Dykstra, L.A. (In Press) Metabotropic glutamate antagonists alone and in combination with morphine: Comparison across two models of acute pain and a model of persistent, inflammatory pain. *Behav Pharmacol*
- Dykstra, L.A., Fischer, B.D., Balter, R.E., Henry, F.E., Schmidt, K.T., Miller, L.L. (2011) Opioid antinociception, tolerance and dependence: Interactions with the N-methyl-D-aspartate (NMDA) system in mice. *Behav Pharmacology* 22 (5&6): 540-547 MSID#3305204
- Miller, L.L. Picker, M.J., Schmidt, K.T. and Dykstra, L.A. (2011) Effects of morphine on pain-elicited and pain-suppressed behavior in CB1 knockout and wildtype mice. *Psychopharmacology* 215 (3): 455-465. PMID
- Fischer, B.D., Ward, S.J., Henry, F.E. and Dykstra, L.A. (2010) Attenuation of morphine antinociceptive tolerance by a CB1 receptor agonist and an NMDA receptor antagonist: interactive effects. *Neuropharmacology* 58: 544-550
- Ward, S.J., Rosenberg, M.B., Dykstra, L.A. and Walker, E.A. (2009) The CB1 antagonist SR141716 blocks cue-induced reinstatement of cocaine seeking and attenuates extinction behaviors predictive of relapse in mice. *Drug and Alcohol Dependence* 105: 248-255, 2009. PMID: 19679410
- Miller, L.L., Ward, S.J. and Dykstra, L.A. (2008) Chronic unpredictable stress enhances cocaine conditioned place preference in CB1 receptor knockout mice. *Behavioral Pharmacology*, 19:575-581. PMID: 18690112
- Fischer, B.D., Miller, L.L., Henry, F., Picker, M.J. and Dykstra, L.A. (2008) Increased efficacy of mu-opioid agonist-induced antinociception by metabotropic glutamate receptor antagonists in C57BL/6 mice: Comparison with (-)-6-phosphonomethyl-deca-hydroisoquinoline-3-carboxylic acid (LY235959). *Psychopharmacol.* 198: 271-278. PMID: 18392754
- Ramsey, A.J., Laakso, A., Cyr, M., Sotnikova, T.D., Salahpour, A., Medvedev, I.O., Dykstra, L.A., Gainetdinov, R.R. and Caron, M.G. (2008) Genetic NMDA receptor deficiency disrupts acute and chronic effects of cocaine but not amphetamine. *Neuropsychopharmacology* 33(11): 2701-2714. PMID: 18185498
- Fischer, B.D., Zimmerman, E.I., Picker, M.J. and Dykstra, L.A. (2008) Morphine in combination with metabotropic glutamate receptor antagonists on schedule-controlled responding and thermal nociception. *J. Pharmacol. Exp. Ther.* 324: 732-739. PMID: 17982001
- Ward, S.J., Walker, E.A. and Dykstra, L.A. (2007) Effect of cannabinoid CB1 receptor antagonist SR141716A and CB1 receptor knockout on cue-induced reinstatement of Ensure and corn-oil seeking in mice. *Neuropsychopharmacology* 32(12):2592-600. PMID: 17392737

Principal Investigator/Program Director (Last, First, Middle): Dykstra, Linda

- Fischer, B.D. and Dykstra, L.A. (2006) Interactions between an NMDA antagonist and low-efficacy opioid receptor agonists in assays of schedule-controlled responding and thermal nociception. *J. Pharmacol. Exp. Ther.* 318:1300-1306. PMID: 16772537
- Allen, R.M., Carelli, R.M., Dykstra, L.A., Suchey, T.L., Everett, C.V. (2005) Effects of the competitive NMDA receptor antagonists, (-)-6-phosphonomethyl-deca-hydroisoquinoline-3-carboxylic acid (LY235959), on responding for cocaine under both fixed and progressive ratio schedules of reinforcement. *J. Pharmacol. Exp. Ther.* 315: 449-457. PMID: 16024734
- Medvedev, I.O., Bohn, L.M., Gainetdinov, R.R., Caron, M.G. and Dykstra, L.A. (2005) Characterization of conditioned place preference to cocaine in isogenic dopamine transporter knockout mice. *Psychopharmacology* 180: 408-413. PMID: 15719221
- Carroll, F.I., Thomas, J.B., Dykstra, L.A., Granger, A.L., Allen, R.M., Howard, J.L., Pollard, G.T., Aceto, M.D. and Harris, L.S. (2004) Pharmacological properties of JDTC: A novel  $\mu$  opioid receptor antagonist. *Eur. J. Pharmacol.* 501: 111-119 PMID: 15464069
- Bohn, L.M., Gainetdinov, R.R., Sotnikova, T.D., Lefkowitz, R.J., Dykstra, L.A. and Caron, M.G. (2003) Enhanced Rewarding Properties of Morphine, but not Cocaine, in  $\beta$ arrestin-2 Knockout Mice. *J. Neurosci.* 23: 10265-10273. PMID: 14614085
- Dykstra, L.A., Granger, A.L., Allen, R.M. Xiaoyan Zhang and Kenner C. Rice (2002) Antinociceptive effects of the selective delta opioid agonist, SNC 80, alone and in combination with mu opioids in the squirrel monkey titration procedure. *Psychopharmacology* 163; 420-429. PMID: 12373443
- Allen, R.M. and Dykstra, L.A. (2000) N-methyl-D-aspartate receptor antagonists potentiate the antinociceptive effects of morphine in squirrel monkeys. *J. Pharmacol. Exp. Ther.* 298: 188-297. PMID: 11408554
- Allen, R.M. and Dykstra, L.A. (2000) Role of morphine maintenance dose in the development of tolerance and its attenuation by an NMDA receptor antagonist. *Psychopharmacol.* 148: 59-65. PMID: 10663418
- Allen, R.M. and Dykstra, L.A. (2000) Attenuation of mu-opioid tolerance and cross-tolerance by the competitive NMDA receptor antagonist, LY23595, is related to tolerance and cross-tolerance magnitude. *J. Pharmacol. Exp. Ther.* 295:1012-1021. PMID: 11082436

### C. Research Support

R37-DA02749-32 (Merit Award) Dykstra, L. (PI) 01/01/05 – 12/31/11

Opioid Analgesics: Pharmacological and Behavioral Factors

The specific research goals of this grant are based on evidence that the effects of opioid analgesics can be modulated by interactions between opioid and N-methyl-D-aspartate (NMDA) and/or metabotropic glutamate (mGlu) receptor systems. The experiments proposed in this application explore the mechanisms underlying these effects further by investigating interactions between these systems using an integrative strategy that combines genetic, pharmacological and behavioral approaches.

T32-DA 07244-21 Dykstra, Linda A. (PI) 07/01/10 – 6/30/15

Predocutorial Training in Interdisciplinary Research on Drug Abuse

This program provides interdisciplinary, graduate training in areas related to drug and alcohol abuse for predoctoral students pursuing careers either in basic biomedical research or in more clinically-related research on drug abuse. This training grant is currently in its 4<sup>th</sup>, 5-year period.

K12 GM00678-09 Dykstra, Linda A. (PI) 09/01/08 – 08/31/12

SPIRE (Seeding Postdoctoral Innovators in Research & Education)

The SPIRE program is an Institutional Research and Academic Career Development Award (IRACDA) for postdoctoral fellows in the biomedical sciences. It is delivered through the University of North Carolina at Chapel Hill in partnership with five historically minority universities within the state of North Carolina. The program provides postdoctoral fellows with research training as well as professional development and a year of hands-on teaching experience at minority-serving undergraduate institutions.

R21-DA026980-01 Narayan, R. (PI); Dykstra (co-investigator) 08/01/09 – 07/31/11

Autonomous Treatment of Opioid Abuse AARA

Principal Investigator/Program Director (Last, First, Middle): Dykstra, Linda

The specific goal of this award is to implement a microneedle system that can be used for transdermal drug delivery of the opioid agonist buprenorphine. Once an appropriate system is developed, it will be tested for in vivo activity in mice. Measures include antinociception and suppression of opioid withdrawal.