## 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 | POSITION TITLE |
|---|---|
| Mactutus, Charles F. | Professor |
| eRA COMMONS USER NAME<br>mactutus | |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | YEAR(s) | FIELD OF STUDY |
|---|---|---|---|
| St. Lawrence University, Canton, NY | B.S. | 1975 | Psychology |
| Kent State University, Kent OH | M.A. | 1977 | Psychology |
| Kent State University, Kent OH | Ph.D. | 1979 | Exp.Psychol./Statistics |
| Johns Hopkins University, Baltimore, MD | Postdoc. | 1979-1981 | Neurotoxicol./Pharmacol |

### A. Personal Statement.

Dr. Mactutus is currently Professor of Psychology, having recently been elected as a Fellow of *American Association for the Advancement of Science*, a society of which he has been a member since 1979. He has served as Department chair, 2005-2008, during which time he helped to shepherd the faculty through three top-ten nationally ranked accomplishments. Dr. Mactutus extended his background in Experimental Psychology with post-doctoral training in Neurotoxicology and Pharmacology at The Johns Hopkins University, and served as a scientist in the intramural program at NIH(NIEHS) for six years before joining the academic ranks. Dr. Mactutus has been a PI on NIH grants from the NIEHS, NICHD, and NIDA, and has participated on other NIH grants funded through NIDA, NIMH and NIA. Dr. Mactutus has been a charter member of an NIH Study Section, and has served on others, as well as serving the U.S.E.P.A. as a Scientific Advisory Panel member on Developmental Neurotoxicity. He is an active ad hoc reviewer and currently serves on the editorial boards of the *International Journal of Developmental Neurobiology and HIV/AIDS-Research and Palliative Care*.

Beginning with the introduction of a new preclinical model for noninvasive chronic intravenous administration of drugs of abuse during pregnancy, and a systematic dose-response study of cocaine pharmacokinetics, Dr. Mactutus and his group were first to identify a true teratogenic effect (i.e., the neurons being most susceptible to disruption at the time of their genesis) in the central nervous system for the attentional disorders in offspring following recreational maternal cocaine use. Specifically, we identified an apoptotic cascade and the major molecular components underlying the teratogenic effect of cocaine in the central noradrenergic system.

Through a series of 30 publications, we have identified a new mechanism (and potential therapeutic approach) for HIV/drug abuse, resulting in two U.S. patent applications, 11/913,519 and 12/620,170. The basis for the therapeutic approaches derives from our mechanistic studies of the neurotoxic response(s) to the HIV-1 viral proteins, TAT and gp120, as well as the HIV-1 transgenic rat, and the consequent cognitive dysfunction characteristic of NeuroAIDS and pediatric AIDS.

The present application is an exciting extension of our research program to the broader issue of motivated behavior, and pursues a better understanding of the interactions between overlapping reward and homeostatic neurocircuits for motivational systems with a mechanistic focus on select dopaminergic neuroadaptations in the central nervous system. Dr. Mactutus and his team have expertise with behavioral, neurochemical, and pharmacological techniques to assess the integrity of catecholaminergic systems, and the dopaminergic system in particular. Further, it is of note that Drs. Mactutus, Booze, Askenov, and Harrod have long-standing relationships working together in a highly productive manner and represent an ideal team for the conduct of this research program.

**Positions and Honors.**

## Professional Experience:

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|---|---|
| 1981-1983 | Staff Fellow, Laboratory of Behavioral and Neurological Toxicology, NIH-National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, NC. |
| 1983-1986 | NIH Senior Staff Fellow, Laboratory of Behavioral and Neurological Toxicology, NIH, NIEHS, Research Triangle Park, NC. |
| 1984-1986 | Head, Developmental Neurobiology Workgroup, Laboratory of Behavioral and Neurological Toxicology, NIH-NIEHS, Research Triangle Park, NC. |
| 1987-1987 | Assistant Prof. of Medicine, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA. |
| 1988-1988 | Sabbatical. |
| 1989-1991 | Assistant Professor of Psychology, University of North Carolina-Greensboro, Greensboro, NC (1989); High Point College, High Point, NC (1989-1990); Bennett College, Greensboro, NC (1990-1991). |
| 1991-2001 | Associate Professor, Div. of Pharmacology Experimental Therapeutics, College of Pharmacy/ Tobacco &Health Research Institute/Grad Ctr Toxicol. University of Kentucky, Lexington, KY. |
| 2001-2002 | Professor, Div. of Pharmaceutical Sciences, College of Pharmacy/Tobacco and Health Research Institute/Grad Ctr Toxicol., University of Kentucky, Lexington, KY. |
| 2002-Present | Professor of Psychology, Dept. of Psychology, University of South Carolina, Columbia, SC. |
| 2005-2008 | Chair, Department of Psychology, University of South Carolina, Columbia, SC. |

## Awards and Other Professional Activities:

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|---|---|
| 1994-1998: | Chair, Publications Committee, Neurobehavioral Teratology Society |
| 1993-1999: | Editorial Board, *Neurotoxicology and Teratology* (two 3-yr terms) |
| 2004-present: | Editorial Board, *International Journal of Developmental Neuroscience* |
| 2007: | University of South Carolina Educational Foundation Research Award |
| 2008: | *Alpha Sigma Lamba* – Distinguished leadership and service to Adult Learners in Higher Ed. |
| 2008. | Best Mentor Award – Psychology Graduate Student Association. |
| 2009-present: | Editorial Board, *HIV/AIDS - Research and Palliative Care* |
| 2010-present: | Fellow, *American Association for the Advancement of Science* |
| Ongoing: | Manuscript Reviews: *Am. J. Psychol.*; *Behav. Neurosci.; Behav. Processes*; *Brain Res.*; *Devel. Psychobiol.*; *Environ. Hlth. Persp.*; *Hormones & Beh*; *Int. J. Dev. Neurosci.; JEP: ABP*; *J. Neurosci.*; *J. Pharmacol. Exp. Therap.; Life Sci., Neuropsychopharmacol; Neurotoxicol.*; *Neurotoxicol. Teratol.*; *Obstet. Gynecol.*; *Pharmacol. Biochem. Behav.*; *Physiol. Behav.*; *Physiol. Psychol.*; *Psychopharmacol.*; *Toxicol. Appl. Pharmacol.* |

## Federal Government Advisory Committees:

| | |
|---|---|
| 1996: | NIH/NIMH, Chair, SEP--Molecular, Cellular, & Developmental Neurosci. Review Committee |
| 1996-97: | NIH/NIDA, B-START grant reviewer |
| 1997: | NIH/NIDA, Neurophysiology and Neuroanatomy study section, ad hoc reviewer. |
| 1998-2004: | U.S.E.P.A, Scientific Advisory Panel, Developmental Neurotoxicity. |
| 9/99-9/00: | NIH/CSR, ALTX1 study section, ad hoc reviewer |
| 11/00: | NIH/NIDA, Special Emphasis Panel – "…Drug Abuse Studies in the Mouse" |
| 2001: | NIH/NIDA, B-START grant reviewer |
| 10/02-6/03: | NIH/CSR, BBBP1 Study Section – ad hoc member |
| 4/05: | NIH/NIDA, Special Emphasis Panel, "Translational Drug Abuse Developmental Centers" |
| 7/03-6/07: | NIH/CSR, BRLE Study Section – charter member |
| 6/07: | NIH/NIDA, Special Emphasis Panel, "Translational Drug Abuse Developmental Centers" |
| 10/08; 06/09 | NIH/CSR, DBD Study Section – ad hoc member |
| 10/11: | NIH/NIDA, Special Emphasis Panel, "Medications Development Program Projects for Substance-Related Disorders (P01)" |
| 03/2013: | NIH/NIDA, Special Emphasis Panel ZDA1-NXR-B-15, |
| 03/2013: | NIH/CSR, Special Emphasis Panel ZRG1-AARR-C-22, |
| 07/2013: | NIH/CSR, NAED study section, ad hoc member. |

**B. Selected peer-reviewed publications.** *(Significant and most relevant 15 publications, out of a total of 100+ peer-reviewed publications)*

**Relevant to the current application**


1. Moran LM, Booze RM, Mactutus CF. Time and Time Again: Temporal Processing Demands Implicate Perceptual and Gating Deficits in the HIV-1 Transgenic Rat. J Neuroimmune Pharmacol. 2013 Sep;8(4):988-97. PMID: 23690140.
2. Moran LM, Booze RM, Webb KM, Mactutus CF. Neurobehavioral alterations in HIV-1 transgenic rats: evidence for dopaminergic dysfunction. Exp Neurol. 2013 Jan;239:139-47. PMID: 23063600.
3. Moran LM, Aksenov MY, Booze RM, Webb KM, Mactutus CF. Adolescent HIV-1 transgenic rats: evidence for dopaminergic alterations in behavior and neurochemistry revealed by methamphetamine challenge. Curr HIV Res. 2012 Jul;10(5):415-24. PMID: 22591365
4. Mactutus CF, Harrod SB, Hord LL, Moran LM, Booze RM. Prenatal IV Cocaine: Alterations in Auditory Information Processing. Front Psychiatry. 2011;2:38. PMID: 21747770.
5. Patel DA, Booze RM, and Mactutus CF. Prenatal cocaine exposure alters progenitor cell markers in the subventricular zone of the adult rat brain. *International Journal of Developmental Neuroscience,* 30(1):1-9, 2012. PMID: 22119286.


**Additional recent publications of importance to the field (in reverse chronological order)**


6. Bertrand SJ, Mactutus CF, Aksenova MV, Espensen-Sturges TD, Booze RM. Synaptodendritic recovery following HIV Tat exposure: Neurorestoration by phytoestrogens. J Neurochem. 2013 Jul 22. doi: 10.1111/jnc.12375. [Epub ahead of print] PMID: 23875777.
7. Bertrand SJ, Aksenova MV, Mactutus CF, Booze RM. HIV-1 Tat protein variants: Critical role for the cysteine region in synaptodendritic injury. Exp Neurol. 2013 248:228-35. PMID: 23811015
8. Lacy RT, Mactutus CF, and Harrod SB. Prenatal IV nicotine exposure produces a sex difference in sensorimotor gating of the auditory startle reflex in adult rats. *International Journal of Developmental Neuroscience,* 29(2):153-161, 2011. PMID: 21145386.
9. Fitting S, Booze RM, Hasselrot U, Mactutus CF. Dose-dependent long-term effects of Tat in the rat hippocampal formation: a design-based stereological study. *Hippocampus.* **20(4):**469-480, 2010. PMID: 19489004.
10. Ferris MJ, Frederick-Duus D, Fadel J, Mactutus CF, Booze RM. *In vivo* microdialysis in awake, freely moving rats demonstrates HIV-1 Tat-induced alterations in dopamine transmission. *Synapse.* 2009, 63(3):181-185. PMID: 19086089.
11. Fitting S, Booze RM, Mactutus CF. Neonatal intrahippocampal injection of the HIV-1 proteins gp120 and Tat: differential effects on behavior and the relationship to stereological hippocampal measures. Brain Res. 2008 Sep 26;1232:139-54. PMID: 18674522
12. Harrod SB, Mactutus CF, Fitting S, Hasselrot U, Booze RM. Intra-accumbal Tat1-72 alters acute and sensitized responses to cocaine. Pharmacol Biochem Behav. 2008 Oct;90(4):723-9. PMID: 18582493
13. Fitting S, Booze RM, Gilbert CA, Mactutus CF. Effects of chronic adult dietary restriction on spatial learning in the aged F344 x BN hybrid F1 rat. Physiol Behav. 2008 Feb 27;93(3):560-9. PMID: 18035382
14. Fitting S, Booze RM, Hasselrot U, Mactutus CF. Differential long-term neurotoxicity of HIV-1 proteins in the rat hippocampal formation: a design-based stereological study. Hippocampus. 2008;18(2):135-47. PMID: 17924522.
15. Ferris MJ, Mactutus CF, Booze RM. Neurotoxic profiles of HIV, psychostimulant drugs of abuse, and their *con*certed effect on the brain: current status of dopamine system vulnerability in NeuroAIDS. *Neurosci Biobehav Rev.* 2008, 32(5):883-909. Review. PMID: 18430470.

Research Support (ongoing or completed in the last three years).

**Ongoing**

HD043680 PI 12/01/02 - 07/31/17
NIH-NICHD
Maternal HIV: Developmental Neurotoxicity
Using a translational model of the core components of cognition relevant to pediatric HIV-1/AIDS as well as to HIV-1-associated neurocognitive disorders (HAND), the long-term goal is to identify and validate novel neurotherapeutics to “tune” the cognition domains afflicted by HIV-1.

R01 DA013137 (Booze) Co-PI 09/01/99-11/30/15
NIH-NIDA
HIV/Cocaine Neurotoxicity in Females
The ultimate goal of this research is to identify the critical neurological targets of HIV infection and to develop innovative pharmacological strategies for preventing cognitive and motor dysfunction following HIV infection in drug abusing women. Dietary phytoestrogens (soy isoflavones) are under investigation as novel adjunctive therapy for HIV-1 in women.

R01 DA021287 (Harrod) Co-PI 4/15/07 - 03/31/14
NIH-NIDA
Prenatal IV nicotine: Long-term vulnerability to stimulant drugs.
The major goal of this project is to investigate the effects of gestational nicotine on subsequent cocaine and methamphetamine self-administration and conditioned place preference in treated and non-treated offspring during adolescence and adulthood.

R03 DA031604 PI 04/01/11-03/31/14
NIH-NIDA
Methamphetamine and HIV-1: NMDAR/D1 mediated neurologic effects
The present research proposal will investigate the role of D1R/NMDAR interactions in the overlapping pathway of METH/HIV-1 protein neurotoxicity. The broad goal of the research is to elucidate the molecular basis of METH/HIV-induced cognitive deficits.

**Completed**

R03 DA026721 (Zhu) Consultant 04/01/09-06/30/12
NIH-NIDA
Role of Dopamine Transporter: HIV-1 Tat Protein and Nicotine Sensitization
The long-term goal of the present research proposal is to elucidate the underlying neurobiological mechanisms of Tat-induced dysfunction of mesolimbic dopamine system contributing to nicotine dependence.

R03 DA024275 (Zhu) Co-I 05/15/09-10/30/11
NIH-NIDA
Role of DARPP-32: Individual Responsiveness to Nicotine
This proposal will test the hypothesis that environmental enrichment (EE) changes DA receptor-mediated cAMP/PKA signaling, in turn modifying the effects of NIC on DARPP-32, and these changes will contribute to differences in NIC-induced behavioral sensitization observed as a function of EE.

DA013965 PI (sub) 06/01/02-01/31/09
NIH-NIDA
Prenatal Cocaine Exposure and Attentional Dysfunction
The project will test the hypothesis that the attentional impairment seen following prenatal cocaine exposure results from changes in catecholaminergic systems in prefrontal cortex and/or anterior cingulate cortex, and that targeting these systems with potential therapeutic agents will ameliorate the attentional impairments.