BIOGRAPHICAL SKETCH

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NAME: Daniel J. Morgan

eRA COMMONS USER NAME (credential, e.g., agency login): MORGANDA

POSITION TITLE: Associate Professor and Associate Vice Chair

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Grinnell College, Grinnell IA	B.A.	1993-1997	Biology
Rutgers University, Piscataway NJ	Ph.D.	1997-2004	Neuroscience
University of Washington, Seattle WA	Postdoctoral	2004-2007	Kinase Signaling
Indiana University, Bloomington IN	Postdoctoral	2007-2010	Cannabinoid Signaling

A. Personal Statement

The primary focus of my laboratory is to understand the mechanisms responsible for endocannabinoid signaling in human health and disease including cannabinoid tolerance, drug addiction, and metabolic homeostasis. Currently my group is funded by NIDA to assess the mechanisms responsible for cannabinoid tolerance (DA044999). This work involves assessing the contribution and molecular mechanisms of c-Jun N-terminal kinase (JNK) signaling in tolerance for different cannabinoid drugs. We are also actively engaged in work to understand the mechanisms responsible for sex differences between male and female mice in the response and tolerance to cannabinoids. This work involves using different strains of mutant mice that express either desensitization or internalization-resistant forms of the cannabinoid type 1 receptor. Members of my group commonly use methods in behavioral pharmacology to assess acute, inflammatory, and chronic pain in mice and molecular pharmacological approaches to assess cannabinoid receptor function and signaling. These pain testing approaches include the tail-flick and hotplate tests to measure acute pain, the formalin test to measure inflammatory pain, and the von Frey, Hargraeve's, and acetone tests to measure mechanical and thermal sensitivity in mice with chronic pain from chemotherapy exposure or nerve injury. We also use the elevated plus maze, forced swim test, conditioned place preference, and ultrasonic vocalizations to measure affective components of chronic pain. Lab members use molecular approaches such as qRT-PCR, Western Blotting, radioligand binding, and agonist-stimulated G protein activation to probe receptor expression and function.

A second project that we are interested in involves understanding the role of neuropeptide signaling in the regulation of pain and motivated behaviors such as drug addiction and feeding. This work focuses on assessing the role of small neuropeptides derived from a protein precursor protein called proSAAS. ProSAAS-derived peptides have been shown to signal through two recently deorphanized G protein-coupled receptors, GPR171 and GPR83, to modulate body weight, feeding behavior, morphine tolerance and reward, and anxiety behaviors. Our current work involves examining acute, inflammatory, and chronic pain as well as morphine tolerance in mutant mice lacking proSAAS. Finally, a third project involves assessing the impact of decursinol, the active anti-inflammatory and antinociceptive natural product component from the Korean Angelica Gigas Nakai plant, in acute, inflammatory, and chemotherapy-evoked chronic pain. Current work on this project involves assessing whether tolerance develops to the pain-relieving effects of decursinol and also whether co-administering this natural compound with chemotherapy might prevent development and "chronification" of neuropathic pain. My goals also include providing the highest level of mentorship to my trainees and to help recruit and develop women

and members of underrepresented groups so that they can obtain tenure track faculty positions in academia or equivalent senior positions in biotechnology or the pharmaceutical industry.

B. Positions and Honors

Positions

1996	Summer Intern, Iowa State University, Ames, IA
1997-2004	Graduate Assistant and Postdoctoral Fellow, Rutgers University, Piscataway, NJ
2004-2007	Senior Fellow, University of Washington School of Medicine, Seattle, WA
2007-2010	Postdoctoral Fellow, Indiana University, Bloomington, IN
2010-2015	Research Scientist, Indiana University, Bloomington, IN
2012-2020	Assistant Professor, Penn State University, Hershey, PA
2020	Associate Professor (with Tenure), Penn State University, Hershey, PA
2020-present	Adjunct Associate Professor, Penn State University, Hershey, PA
2020-present	Associate Professor (with Tenure) and Associate Vice Chair of Biomedical Sciences, Joan C Edwards School of Medicine at Marshall University, Huntington, WV

Honors

1993-1997	Trustee Honor Scholarship-Grinnell College.
1997-1999	NIH IMSD Minority Development Fellowship- Rutgers.
2000	Champions Scholarship-Rutgers
2005-2007	Cardiovascular Pathology Training Fellowship-University of Washington
2006	American Society for Cell Biology Travel Award
2009	NIDA Early Career Investigator Travel Award
2010	Chicago Society for Neuroscience Postdoctoral Poster Award
2011	Julius Axelrod Symposium Award
2013-2015	Satvir Tevethia Junior Faculty Research Scholar Award
2014	Winter Brain Conference Travel Award Fellow
2014	CSHL/NIDA Cellular Biology of Addiction Short Course Travel Award
2017	Jackson Laboratories Genetics of Addiction Short Course Travel Award

Other Experience and Professional Societies

1998-present	Member, Society for Neuroscience
2010-present	Member, American Society for Pharmacology and Experimental Therapeutics (ASPET)
2009-present	Member, International Cannabinoid Research Society
2014	Ad hoc grant reviewer for Austrian Science Fund.
2014	Ad hoc reviewer for European Journal of Pharmaceutical Science and PLOS One
2014-2016	Ad hoc reviewer, special issue guest editor for Progress in Neuro-Psychopharmacology and Biological Psychiatry
2016	Ad hoc grant reviewer for Health Research Council of New Zealand.
2016-present	Member, ASPET Neuropharmacology Executive Committee
2016	Travel Fellow Committee, Winter Conference on Brain Research
2017-present	Program Committee, Winter Conference on Brain Research
2017-present	Ad hoc reviewer for Neuropharmacology, British Journal of Pharmacology, Scientific Reports, Acta Pharmacologia Sinica, ACS Neuroscience, and Drug and Alcohol Dependence
2018	Program Committee and Session Chair, International Cannabinoid Research Society
2018-present	Ad hoc reviewer for Alcoholism: Clinical and Experimental Research
2019-present	Ad hoc reviewer for Pain, Neuroscience Letters, Pharmacology, Biochemistry, and Behavior, and European Journal of Pharmacology
2019	Canadian Institutes of Health College of Reviewers (Cannabis Team Grant Study Section)
2019	Panel Member, Congressionally Directed Medical Research Programs, Spinal Cord Injury Research Program (SCIRP)
2019	Penn State Hershey Leadership Academy for Excellence in Academic Medicine
2019-present	Panel Member, Florida Department of Health Biomedical Research Programs
2020-present	Editorial Board, Pharmacology Research & Perspectives
2020-present	Editorial Board, Frontiers in Molecular Neuroscience
2020	Secretary/Treasurer-Elect, ASPET Neuropharmacology Executive Committee

C. Contributions to Science

"My Biography" at NCBI:

http://www.ncbi.nlm.nih.gov/sites/myncbi/daniel.morgan.1/bibliography/45974986/public/?sort=date&direction=ascending

My graduate work focused on understanding the role of neuropeptide processing and signaling. I characterized the distribution of proSAAS transcript and the processing of the proSAAS protein precursor during development. I produced proSAAS knock-out (KO) mice lacking this novel neuropeptide and demonstrated that this neuropeptide is involved in regulating body weight, anxiety-like behaviors, and cocaine response.

A. Lei Y, Xin X, **Morgan D**, Pintar J and Fricker, LD. (1999) Identification of mouse CPX-1, a novel member of metallocarboxypeptidase gene family with highest similarity to CPX-2. *DNA and Cell Biology*. **18**: 175-185. (PMID: 10073577).

B. **Morgan DJ**, Mzhavia N, Peng B, Pan H, Devi LA and JE Pintar. (2005) Embryonic gene expression and pro-protein processing of proSAAS during rodent development. *Journal of Neurochemistry*. **93**: 1454-63. (PMID: 15935061).

C. **Morgan, DJ**, Wei, S, Gomes, I, Czyzyk, TA. Mzhavia, N, Pan, H., Devi, LA, Fricker, LD, Pintar, JE. (2010) The propeptide precursor proSAAS in involved in fetal neuropeptide processing and body weight regulation. *Journal of Neurochemistry*. **113**: 1275-1284. (PMCID: PMC3510705).

D. Berezniuk, I., Sironi, J., Rodriguez, R.M., Zee, M.L., Pintar, J.E., **Morgan, D.J.**, Wetsel, W.C., Fricker, L.D. (2017). ProSAAS-derived peptides are regulated by cocaine, and contribute to the physiological effects of cocaine administration in mice. *Journal of Neurochemistry*. **143**: 268-81. (PMCID: PMC5693316).

My postdoctoral work focused on G protein-coupled receptor and intracellular signaling pathways involved in mediating sperm motility and capacitation. During my first post-doctoral fellowship with Stan McKnight I used knock-in mice expressing a chemical-genetic mutation in protein kinase A to examine the temporal requirements for this kinase in the capacitation and acquisition of bicarbonate-stimulated motility. During the first year of my second post-doctoral fellowship with Ken Mackie, I demonstrated that Δ^9-THC inhibits sperm motility and ATP production. While training with Ken I also learned how to make antibodies for G protein-coupled lipid receptors such as GPR119.

A. **Morgan DJ**, Weisenhaus M, Shum, S, Su, T, Zheng, R, Zhang C, Shokat, KM, Hille, B, Babcock, DF, and GS McKnight. (2008). A chemical-genetic approach to the study of PKA in specific tissues: Analysis of sperm capacitation. *Proceedings of the National Academy of Sciences*. **104**: 20740-20745. (PMCID: PMC2634883).

B. **Morgan, DJ**, Muller, CH, Murataeva, NA, Davis, BJ, and Mackie, K. (2012). Delta-9-tetrahydrocannabinol (Δ^9-THC) attenuates bicarbonate-stimulated sperm motility and male fecundity. *British Journal of Pharmacology*. **165 (8)**: 2575-83. (PMCID: PMC3423255).

C. Miller, S, Hu, SS, Leishman, E, **Morgan, D**, Wager-Miller, J, Bradshaw, HB, and Straiker, A. (2017). A GPR119 signaling system in the murine eye regulates intraocular pressure in a sex-dependent manner. *Investigative Ophthalmology and Visual Science*. **58 (7)**: 2930-38. (PMCID: PMC5469424).

My most recent work as a senior postdoctoral fellow, research scientist, and new assistant professor has focused on understanding the mechanisms responsible for tolerance to cannabinoid drugs. During this phase of my career I have demonstrated that mice expressing a desensitization-resistant form of CB_1 are acutely more sensitive to cannabinoids and develop tolerance to cannabinoids more slowly. We are also actively engaged in examining the role of JNKs in tolerance to cannabinoid drugs such as Δ^9-THC.

A. **Morgan DJ,** Davis, BJ, Kearn, CS, Marcus, DA, Cook, AJ, Wager-Miller, J, Straiker, AS, Myoga, MH, Karduck, J, Leishman, E, Sim-Selley LJ, Czyzyk, TA, , Bradshaw, HB, Selley, DA Mackie, K. (2014). Mutation of putative GRK phosphorylation sites in the cannabinoid receptor 1 (CB1) confers resistance to cannabinoid tolerance and hypersensitivity to cannabinoids in mice. *Journal of Neuroscience*. **34 (15):** *5152-63*. (PMCID: PMC3983798).

B. Nealon, CM, Henderson-Redmond, AN, Hale, DE, and **Morgan, DJ.** (2019). Tolerance to WIN55,212-2 is significantly delayed in desensitization-resistant S426A/S430A mice. *Neuropharmacology*. **148**:151-159. (PMCID: PMC6535342).

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C. Blanton, H.L., Breslford, J., DeTurk, N., Pruitt, K., Narasimhan, M., **Morgan, D.J.**, and Guindon, J. (2019). Cannabinoids: Current and Future Options to Treat Chronic and Chemotherapy-Induced Neuropathic Pain. *Drugs*. **79 (9)**: 969-995. (PMID:31127530).

D. Henderson-Redmond, A.N., Nealon, C.M., Davis, B.J., Yuill, M.B., Sepulveda, D.E., Blanton, H., Zee, M.L., Haskins, C.P., Marcus, D.J., Mackie, K., Guindon, J., and **Morgan, D.J.** c-Jun N terminal kinase signaling pathways mediate cannabinoid tolerance in an agonist-specific manner. *Neuropharmacology*. In Press. (PMID: 31758947)

My laboratory is also interested in how cannabis substance use disorder develops and also how the opioid and endocannabinoid signaling systems modulate alcohol, opiate, and food addiction. My laboratory has found increased Δ^9-THC dependence and ethanol consumption in mutant S426A/S430A mutant mice with enhanced endocannabinoid signaling. We have also found increased ethanol drinking in humanized mice expressing the MOR A118G polymorphism.

A. Henderson-Redmond, AN, Guindon, J, and **Morgan DJ**. (2016). Roles for the endocananbinoid system in ethanol-motivated behavior. *Progress in Neuro-psychopharmacology and Biological Psychiatry*. **65,** 330-9. (PMCID: PMC4679600).

B. Marcus, D.J., Zee, M.L., Davis, B.J., Haskins, C.P., Andrews, M.J., Amin, R., Henderson-Redmond, A.N., Mackie, K., Czyzyk, T.A., **Morgan D.J.** (2016). Mice expressing a "hyper-sensitive" form of the cannabinoid receptor 1 (CB1) are not obese or diabetic. *PLOS One*. **11(8)**: e0160462. (PMCID: PMC4976987).

C. Marcus, D.J., Henderson-Redmond, A.N., Zee, M.L., Amin, R., Farnsworth, J.C., Andrews, M.J., Davis, B.J., Mackie, K., and **Morgan, D.J.** (2017). Mice expressing a "hyper-sensitive" form of the cannabinoid receptor 1 (CB1) show modestly alcohol preference and consumption. *PLOS One*. **12(4):** e0174826. (PMCID: PMC5398885).

D. Henderson-Redmond, A.N., Lowe, T., Kline, A.M., Tian, X.B., **Morgan D.J.** (2018). Increased ethanol drinking in "humanized" mice expressing the mu-opioid receptor A118G polymorphism are mediated through sex-specific mechanisms. *Brain Research Bulletin*. **138:** 12-19. (PMCID: PMC5796878).

I have a long-standing interest in the mechanisms of mu opioid receptor (MOR) signaling and tolerance to MOR agonists. We have recently shown that JNK signaling is involved in chronic tolerance to the antinociceptive and antiallodynic effects of morphine in a chemotherapy-induced model of neuropathic pain. We also find evidence of unidirectional cross-tolerance and additive antinociceptive effects between morphine and the CB2 selective agonist, JWH133.

A. Marcus DJ, Zee, ML, Hughes, A, Yuill, MB, Hohmann, AG, Mackie K, Guindon, J, and **Morgan DJ**. (2015). Tolerance to the antinociceptive effects of chronic morphine requires c-Jun N-terminal kinase. *Molecular Pain*. **11**: 34. (PMCID: PMC4465431).

B. Henderson-Redmond, A.N., Yuill, M.B., Lowe, T., Kline, A.M., Zee, M.L., Guindon, J., and **Morgan, DJ.** (2016). Morphine-induced anti-nociception and reward in "humanized" mice expressing the mu opioid receptor A118G polymorphism. *Brain Research Bulletin*. **123:** 5-12. (PMCID: PMC4848164).

C. Yuill, M.B., Zee, M.L., Marcus, D.J., and **Morgan D.J.** (2016). Tolerance to the anti-nociceptive and hypothermic effects of morphine are mediated by multiple isoforms of c-Jun N-terminal Kinase. *Neuroreport*. **27:** 392-6. (PMCID: PMC4808337).

D. Yuill, MB, Hale, D, Guindon, J, and **Morgan, DJ.** (2017). Functional interactions between opioids and the cannabinoid receptor 2 agonist JWH-133 in inflammatory pain. *Molecular Pain*. **13**: 1-15. (PMCID: PMC5593227).

D. Research Support:

Active:

R01 DA044999, Morgan (PI) 09/01/18-01/31/23
NIH/NIDA
Mechanisms of cannabinoid tolerance.
The goal of this study is to determine whether JNK-mediated Δ^9-THC tolerance is mediated through direct phosphorylation of the CB_1 receptor.
Role: PI

Completed Research Funding:

R21 DE028650, Hu (PI) 04/01/18-01/31/23
NIH/NIDCR
The role of chronic cannabis and its two major psychoactive ingredients in papillomavirus-associated oropharyngeal disease.
The goal of this study is to determine whether Δ^9-THC, cannabidiol, or inhaled cannabis enhance papillomavirus virulence in oropharyngeal disease.
Role: Co-investigator

SAP#4100079742, Morgan (PI) 07/01/18-06/30/19
PA State Dept. of Health CURE Tobacco Settlement Funds
Agonist-specific mechanisms of cannabinoid tolerance.
The goal of this project is to provide Bridge funding for the re-submission of 1R01 DA044999.
Role: PI

K01 DA037355, Morgan (PI) 02/01/15-01/31/18
NIH/NIDA
Desensitization and downregulation of CB1 during cannabinoid tolerance.
The goal of this study is determine whether desensitization of downregulation of CB1 is responsible for JNK-mediated Δ^9-THC tolerance.
Role: PI

R21 DA036385, Morgan (PI) 07/15/13-06/30/16
NIH/NIDA
Characterization of a novel JNK-mediated mechanism of cannabinoid tolerance.
The goal of this study is to determine the form of JNK responsible for mediating tolerance to Δ^9-THC and to identify transcriptional targets of JNK responsible for this process.
Role: PI

SAP #4100057673, Morgan (PI) 07/15/13-12/31/15
PA State Dept. of Health CURE Tobacco Settlement Funds
Does enhanced cannabinoid receptor 1 (CB1) signaling increase the risk of drug abuse?
The goal of this study is to determine whether reward and dependence for alcohol and morphine are increased in mice with enhanced cannabinoid signaling.
Role: PI