CURRICULUM VITAE

Blaise M. Costa, B.Pharm, M.Pharm, Ph.D.

Tenured Professor and Discipline Chair for Pharmacology Department of Biomedical Sciences Virginia College of Osteopathic Medicine (VCOM) Center for One Health Research Faculty, Virginia-Maryland College of Veterinary Medicine. Virginia Tech, VA

CONTACT INFORMATION

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EDUCATION

- Bachelor of Pharmacy, 1995-1999 MGR Medical University, Chennai, India
- Master of Pharmacy in Pharmacology, 1999-2001 MGR Medical University, Chennai, India
- Doctor of Philosophy (Ph.D.) in Psychopharmacology, 2001-2005 National Institute of Mental Health And Neurosciences (NIMHANS), Bangalore, India Dissertation: Molecular dynamics of NMDA ionotropic glutamate receptors

• Postdoctoral fellowships

The Royal Society International Research Fellowship, University of London School of Pharmacy, UK, 2005 -2006

Max Planck Institute of Brain Research, Frankfurt, Germany, Department of Neurochemistry, 2006 -2007

University of Nebraska Medical Center, Omaha NE, Department of Pharmacology and Experimental Neuroscience, 2007-2010

LICENSES AND CERTIFICATES

• Registered Pharmacist, India, License#TNPC-5899A1, Reg. date: Apr 9, 2001 –present

ACADEMIC APPOINTMENTS

- 2010-2013; Senior Research Fellow, Department of Pharmacology and Experimental Neuroscience, University of Nebraska Med Center, Omaha, NE
- 2013-2017; Assistant Professor of Pharmacology, Edward Via Virginia College of Osteopathic Medicine, Blacksburg, VA
- 2015 –present; Center for One Health Research Faculty, Department of Biomedical Sciences and Pathobiology, Virginia-Maryland College of Veterinary Medicine, Virginia Tech, VA
- 2017-2022; Associate Professor of Pharmacology, Edward Via Virginia College of Osteopathic Medicine, Blacksburg, VA

• 2022-present; Tenured Professor and Discipline Chair for Pharmacology, Edward Via Virginia College of Osteopathic Medicine, Blacksburg, VA

TEACHING EXPERIENCE

Medical Pharmacology (didactic)

- MED 7160 Musculoskeletal System Pharmacology Course, lecturer 2013 present
- MED 7165 Neurological System and Special Senses Pharm Course, lecturer 2014 present
- MED 7165 Autonomic Pharmacology Simulation Course, 2022 present
- MED 7170 Cardiovascular and Pulmonary Sys, lecturer & course director, 2013 present
- MED 7175 Gastrointestinal and Renal Sys, lecturer & course director from 2013 present
- MED 7180 Reproductive and Endocrine Sys lecturer & course director from 2013 present
- MED 7160 Comprehensive Review, Pharm Course director 2021 present

Case Based Learning (CBL)

- Antimicrobials for Bone & Joint infections, Pharm course director from 2013 present
- Urinary Tract Infections, Pharm course director from 2020 present
- Gastrointestinal Infections, Pharm course director from 2020 present
- Inflammatory Disorders and Osteoarthritis, Pharm course director from 2020 present

Graduate courses

• 2019- present; Structure and function of ion channels and electrophysiology course to graduate students, at COHR.

PROFESSIONAL AFFILIATIONS

- 2007 Member, Society for Neuroscience
- 2013 Member, American Heart Association
- 2016 Member, The American Society for Pharmacology and Experimental Therapeutics (ASPET)

HONORS AND AWARDS

- 2022 Awarded tenure & promoted to full professor
- 2021 VCOM researcher of the year award
- 2015, 18&19 Golden apple award for excellence in teaching, sigma sigma phi VCOM
- 2010 UNMC-Unemed stimulus to expedite NMDAR drug discovery & patents process
- 2010 Annual performance stipend for extraordinary contribution to the project
- 2009 UNMC-Unemed new invention notification award
- 2009 Eli Lilly NMDA receptor drug discovery collaboration award
- 2007 UNMC annual postdoctoral travel award, Omaha, NE
- 2007 Max Planck Society short-term training fellowship, Germany
- 2005 The Royal Society International Exchange Researcher Award, UK
- 2001 PhD position through nationwide entrance examination for one seat at NIMHANS
- 2001 Best outgoing student during masters from JSS Department of Pharmacology
- 1995 Admitted for B.Pharmacy course through state-wide entrance examination

PROFESSIONAL SERVICE

- 2020 present Associate editor Journal of Alzheimer's Disease
- 2017 present Invited to review NIH R-series grants

Ad-hoc reviewer

- Science Direct
- Journal of Pharmacology and Experimental Therapeutics
- American Chemical Society
- Journal of Medicinal chemistry
- Journal of Clinical Medicine
- Journal of Biomedicine and Biotechnology
- Journal of Neurochemistry International
- PLOS One
- Neurotoxicity
- Molecules
- MDPI Cells
- Journal of Molecular Graphics and Modelling
- Journal of Biomolecular Structure and Dynamics

MENTORING ACTIVITIES

Graduate student mentor

- 2019 -2021, Co-chaired graduate student (Lina Kwapisz) dissertation committee Department of Biomedical Sciences and Pathobiology, VMCVM, Virginia Tech Dissertation: Pharmacology of a Novel Biased Allosteric Modulator for NMDA Receptors
- 2022- present, Co-chair graduate student (De'Yana Hines) dissertation committee School of Biomedical Engineering and Sciences, Virginia Tech Dissertation: To identify the role of brain lymphatic systems in cranial osteopathic manipulative therapy on animals models of Alzheimer's disease.

Undergraduate or post graduate student mentor

(students who worked >1000hrs in the lab are listed below, *co-authored at least one publication)

- Lucas Kane* 07/2013 -07/2015, Computational modeling of NMDAR modulation binding sites
- Douglas Bledsoe* 12/2015 -07/2018, Electrophys of novel NMDAR allosteric modulators.
- Caroline Campbell* 10/2016 06/2017, Behavioral & biochem analysis of rat model of AD.
- Mike Mykins* 06/2017 06/2018, Immunohistochemistry of AD rat brain tissue & analysis.
- Tyler Lucas* 06/2017 -04/2019 Behavioral & immunoassays of AD rat brain tissue & analysis.
- Bryanna Vacca* 06/2018 6/2019 Electrophysiology of novel NMDAR allosteric modulators.
- Tullia Johnston* 07/2018 6/2019 Electrophysiology of novel NMDAR allosteric

modulators.

- Brittney Mehrkens* 07/2019 1/2021, Biochem analysis of transgenic rat model of AD
- Patrick Rafael 09/2020 -7/2021 Primary neuron & astrocytes culture and immunoassays
- Alyssa Ingram 5/2021 -7/2022 Primary neuron culture and immunoassays
- Seth Boehringer* 6/2021 –present, Electrophysiology of novel NMDAR allosteric modulators.
- Nakia Philip 7/2022 present, Generating disease causing GRIN mutations and biochemistry

Research training for medical students

(VCOM students who made a significant contribution or *co-authored a manuscript are listed below)

- 2018 19, one VCOM student. Anushri Wagner
- 2019-20, three VCOM students. Rehan Razzaq*
- 2020-present, four VCOM students each academic year

INSTITUTIONAL SERVICE

- 2013 -present, interviewed 30-40 students each year for admission at VCOM
- 2013 –present, academic advisor for 12 medical students each year
- 2013 present, poster judge for research day as needed
- 2015 -18 & 2022 Via wellness committee
- 2017 Multicultural or Diversity Committee faculty panel member
- 2020 present, serve on faculty search committee as needed
- 2022- Institutional environmental and biosafety committee
- 2022 -Pharmacology curriculum oversite committee

GRANTS and CONTRACTS

Completed awards as PI or co-PI (co-investigator awards not listed)

- 2015, American Heart Association (AHA) Scientist Development Award, National, Identifying Molecular Determinants of Novel Drug Target in NMDA Receptor. \$308, 0000. Blaise Costa (PI -VCOM). Total \$308,000 for 2016-2020.
- 2015, VCOM One Health, The role of tri-heteromeric (GluN1/2/3) NMDA receptors in stroke and its mitigation. Blaise Costa (PI-VCOM), Bradley Klein (CVM). About 13% requested amount was funded (\$5,835).
- 3. 2016, VCOM One Health, The role of tri-heteromeric (GluN1/2/3) NMDA receptors in stroke and its mitigation. Blaise Costa (VCOM co-PI) and Bradley Klein (CVM Co-PI). Total \$41,013.
- 4. 2016, VCOM REAP, Clearance of Brain Metabolic Waste in a Natural Animal Model of Alzheimer's disease by Cranial Osteopathic Manipulation. Blaise Costa (co-PI VCOM, Hope Tobey (VCOM), Gunnar Brolinson (VCOM) & Bradley Klein (CVM). Total \$45,000.
- 5. 2017, VCOM REAP, Clearance of Brain Metabolic Waste in a Natural Animal Model of Alzheimer's disease by Cranial Osteopathic Manipulation. Blaise Costa (co-PI VCOM, Hope Tobey (VCOM), Gunnar Brolinson (VCOM) & Bradley Klein (CVM). Total \$49,966.

- 6. 2017, VCOM One Health, The role of tri-heteromeric (GluN1/2/3) NMDA receptors in stroke and its mitigation. Blaise Costa (VCOM co-PI) and Bradley Klein (CVM Co-PI). Total \$42,500.
- 7. 2019, VCOM One Health, Mechanisms and Neuroprotective Effects of Triheteromeric NMDA Receptor Modulators. Blaise Costa (VCOM co-PI) and Bradley Klein (CVM Co-PI). Total \$49,994.
- 8. 2019, American Osteopathic Association (AOA), Clearance of Brain Metabolic Waste in a Natural Animal Model of Alzheimer's disease by Cranial Osteopathic Manipulation. Blaise Costa (co-PI VCOM, Hope Tobey (VCOM), Gunnar Brolinson (VCOM) & Bradley Klein (CVM). Total \$125,000.
- 2020, VCOM One Health, Identification and Characterization of Mechanically Distinct Novel Anti-Viral Agents Blaise Costa (VCOM), Andrea Bertke (CVM). \$14,000. Funded. This was only ~16% of the requested fund (\$100,000).
- 2020 VCOM –ICTAS, Pharmacological Characterization of NMDA Receptor Modulators Using Engineered Microenvironments Representing Brain Disorders Blaise Costa (VCOM) & Jenny Munson (VT BEAM). Total \$98,142.
- 11. 2022, VCOM-ICTAS, To define the pharmacology of agonist concentration biased NMDA receptors modulators. Blaise Costa (VCOM) and Dr.Pam VandeVord (VT BEAM). Total \$47,000

Active Awards as PI or MPI

- 1 R15 AT010789-01A1 Costa (PI) 07/01/2021 06/30/2024 Sponsor: National Institutes of Health, National Center For Complementary and Alternative Medicine To identify the role of brain lymphatic systems in cranial osteopathic manipulative therapy on animals models of Alzheimer's disease. PI: Costa Total award: \$480,000 Award-receiving institution: VCOM
- Internal seed grant, Costa & VandeVord (MPI) 7/1/2023 6/30/2024 Sponsor: Virginia Tech ICTAS & VCOM REAP To Study Traumatic Brain Injury Induced Oscillation of Glutamate Pendulum & Chemical Clamps to Hold. MPI: Costa & VandeVord Total award: \$80,000

PUBLICATIONS

Patents on Experimental Therapeutic Agents (US Patents and Trademark Office)

- 1. 2018, Biased NMDA Receptor Modulators and uses thereof. PCT/US2019/061308. Role: Inventor
- 2. 2012, Novel positive and negative allosteric aromatic ring modulators for composition of matter and methods of use. International publication number: <u>WO2012/019106</u>. Role: Co-inventor

Peer-Reviewed Journal Articles

 Boehringer SC, Johnston TV, Kwapisz LC, VandeVord PJ, Costa BM. CNS4 causes subtype-specific changes in agonist efficacy and reversal potential of permeant cations in NMDA receptors. *Pharmacol* *Res Perspect.* 2023 Jun;11(3):e01107. doi: 10.1002/prp2.1107. PMID: 37283007; PMCID: PMC10245146.

- Costa BM, Kwapisz LC, Mehrkens B, Bledsoe DN, Vacca BN, Johnston TV, Razzaq R, Manickam D, Klein BG. A glutamate concentration-biased allosteric modulator potentiates NMDA-induced ion influx in neurons. *Pharmacol Res Perspect.* 2021 Oct;9(5):e00859. doi: 10.1002/prp2.859. PubMed PMID: 34476911; PubMed Central PMCID: PMC8413904.
- **Costa BM**. NMDA receptor modulation and severe acute respiratory syndrome treatment. *F1000Res*. 2021;10. doi: 10.12688/f1000research.73897.1. eCollection 2021. PubMed PMID: 36544563; PubMed Central PMCID: PMC9745209.
- France G, Volianskis R, Ingram R, Bannister N, Rothärmel R, Irvine MW, Fang G, Burnell ES, Sapkota K, Costa BM, Chopra DA, Dravid SM, Michael-Titus AT, Monaghan DT, Georgiou J, Bortolotto ZA, Jane DE, Collingridge GL, Volianskis A. Differential regulation of STP, LTP and LTD by structurally diverse NMDA receptor subunit-specific positive allosteric modulators. *Neuropharmacology*. 2021 Oct 19;:108840. doi: 10.1016/j.neuropharm.2021.108840. [Epub ahead of print] PubMed PMID: 34678377.
- Anandakrishnan R, Tobey H, Nguyen S, Sandoval O, Klein BG, **Costa BM**. Cranial manipulation affects cholinergic pathway gene expression in aged rats. **J Osteopath Med.** 2022 Jan 10;122(2):95-103. doi: 10.1515/jom-2021-0183. PMID: 34995434.
- Tobey H, Lucas T, Paul S, Berr S, Mehrkens B, Brolinson PG, Klein B, Costa BM Mechanoceutics Alters Alzheimer's Disease Phenotypes in Transgenic Rats: A Pilot Study. J Alzheimers Dis. 2020;74(2):421-427. doi: 10.3233/JAD-191071. PubMed PMID: 32039851.
- Bledsoe D, Vacca B, Laube B, Klein BG, Costa B. Ligand binding domain interface: A tipping point for pharmacological agents binding with GluN1/2A subunit containing NMDA receptors. *Eur J Pharmacol.* 2019 Feb 5;844:216-224. PubMed PMID: 30553788.
- Tobey H, Lucas T, Bledsoe D, Mykins M, Campbell C, Berr S, Sasser T, Helm R, Brolinson PG, Klein B, Costa BM Effect of Cranial Osteopathic Manipulation on Aged Rat Model of Alzheimer's Disease. *J American Osteopathic Association* 2019 Oct 15. doi: 10.7556/jaoa.2019.121. PMID: 31613309.
- Irvine MW, Fang G, Sapkota K, Burnell ES, Volianskis A, **Costa BM**, Culley G, Collingridge GL, Monaghan DT, Jane DE. Investigation of the structural requirements for N-methyl-D-aspartate receptor positive and negative allosteric modulators based on 2-naphthoic acid. *Eur J Med Chem*. 2019 Feb 15;164:471-498. PubMed PMID:30622023.
- Bledsoe D, Tamer C, Mesic I, Madry C, Klein BG, Laube B, Costa BM. Positive Modulatory Interactions of NMDA Receptor GluN1/2B Ligand Binding Domains Attenuate Antagonists Activity. *Front Pharmacol.* 2017 May 9;8:229. doi:10.3389/fphar.2017.00229. eCollection 2017. PubMed PMID: 28536523
- Kane LT, **Costa BM**. Identification of Novel Allosteric Modulator Binding Sites in NMDA Receptors: A Molecular Modeling Study. *J Mol Graph Model*, 2015.61:p.204-213

- Irvine MW, Fang G, Eaves R, Mayo-Martin MB, Burnell ES, **Costa BM** et al. Synthesis of a Series of Novel 3,9-Disubstituted Phenanthrenes as Analogues of Known N-Methyl-d-aspartate Receptor Allosteric Modulators. *Synthesis*, 2015 March 19; 47(11):1593.
- Gautam V, Trinidad JC, Rimerman RA, Costa BM, Burlingame AL, Monaghan DT. Nedd4 is a specific E3 ubiquitin ligase for the NMDA receptor subunit GluN2D. *Neuropharmacology.2013* Nov;74:96-107.
- Collingridge GL, Volianskis A, Bannister N, France G, Hanna L, Mercier M, Tidball P, Fang G, Irvine MW, **Costa BM**, Monaghan DT, Bortolotto ZA, Molnár E, Lodge D, Jane DE. The NMDA receptor as a target for cognitive enhancement. *Neuropharmacology.* 2013 Jan;64:13-26.
- Costa BM, Yao H, Yang L, Buch S. Role of Endoplasmic Reticulum (ER) Stress in Cocaine-Induced Microglial Cell Death. *J Neuroimmune Pharmacol.* 2013 Jun;8(3):705-14.
- Irvine MW, Costa BM[¥], Volianskis A, Fang G, Ceolin L, Collingridge GL, Monaghan DT, Jane DE. Coumarin-3-carboxylic acid derivatives as potentiators and inhibitors of recombinant and native N-methyl-D-aspartate receptors. *Neurochem Int.* 2012 Sep;61(4):593-600.¥ equally contributed as first author
- Costa BM, Irvine MW, Fang G, Eaves RJ, Mayo-Martin MB, Laube B, Jane DE, Monaghan DT. Structure-activity relationships for allosteric NMDA receptor inhibitors based on 2-naphthoic acid. *Neuropharmacology.* 2012 Mar;62(4):1730-6.
- Irvine MW, Costa BM[¥], Dlaboga D, Culley GR, Hulse R, Scholefield CL, Atlason P, Fang G, Eaves R, Morley R, Mayo-Martin MB, Amici M, Bortolotto ZA, Donaldson L, Collingridge GL, Molnár E, Monaghan DT, Jane DE. Piperazine-2,3-dicarboxylic acid derivatives as dual antagonists of NMDA and GluK1-containing kainate receptors. *J Med Chem.* 2012 Jan 12;55(1):327-41. .¥ equally contributed as first author
- Buch S, Yao H, Guo M, Mori T, **Costa B**, Singh V, Seth P, Wang J, Su TP. Cocaine and HIV-1 interplay in CNS: cellular and molecular mechanisms. *Curr HIV Res.* 2012 Jul;10(5):425-8.
- Monaghan DT, Irvine MW, **Costa BM**, Fang G, Jane DE. Pharmacological modulation of NMDA receptor activity and the advent of negative and positive allosteric modulators. *Neurochem Int.* 2012 *Sep;61(4):581-92.*
- Costa BM, Irvine MW, Fang G, Eaves RJ, Mayo-Martin MB, Skifter DA, Jane DE, Monaghan DT. A novel family of negative and positive allosteric modulators of NMDA receptors. *J Pharmacol Exp Ther.* 2010 Dec;335(3):614-21.
- *Costa BM, Feng B, Tsintsadze TS, Morley RM, Irvine MW, Tsintsadze V, Lozovaya NA, Jane DE, Monaghan DT. N-methyl-D-aspartate (NMDA) receptor NR2 subunit selectivity of a series of novel piperazine-2,3-dicarboxylate derivatives: preferential blockade of extrasynaptic NMDA receptors in the rat hippocampal CA3-CA1 synapse. J Pharmacol Exp Ther. 2009 Nov;331(2):618-26. *corresponding author

- Delev D, Pavlova A, Heinz S, **Costa BM**, Chandra T, Poetsch B, Seifried E, Oldenburg J. Modelling and expression studies of two novel mutations causing factor V deficiency. *Thromb Haemost.* 2008 Nov;100(5):766-72.
- Costa BM, Sowdhamini R, Pradhan N. Comparative analysis of different competitive antagonists interaction with NR2A and NR2B subunits of N-methyl-D-aspartate (NMDA) ionotropic glutamate receptor. *J Mol Model.* 2005 Nov;11(6):489-502. doi: 10.1007/s00894-005-0258-5. Epub 2005 Jun 1. PubMed PMID: 15928921.
- Costa BM, Bhattacharyya D, Sowdhamini R, Pradhan N. Structural consequences of D481N/K483Q mutation at glycine binding site of NMDA ionotropic glutamate receptors: a molecular dynamics study. *J Biomol Struct Dyn.* 2005 Feb;22(4):399-410. doi: 10.1080/07391102.2005.10507012. PubMed PMID: 15588104.
- Costa BM, Sowdhamini R, Rao MR, Pradhan N. Evolutionary trace analysis of ionotropic glutamate receptor sequences and modeling the interactions of agonists with different NMDA receptor subunits. J Mol Model. 2004 Dec;10(5-6):305-16. doi: 10.1007/s00894-004-0196-7. Epub 2004 Oct 22. PubMed PMID: 15597199.

PubMed key: <u>https://www.ncbi.nlm.nih.gov/myncbi/18II7wm0VP5/bibliography/public/</u>

Non-Peer reviewed publications

• Registering 18FDG/PET Mouse and AMYViD/PET-CT Rat Studies to Brain VOI Atlases This article is available at the <u>Bruker website</u>.

PUBLISHED ABSTRACTS

• Presented more than 100 abstracts at local, national or international meetings in the past 20 years

ORAL PRESENTATIONS

• Routinely give talks at local, state and national level meetings, seminars and conferences.

SYSTEM INNOVATION AND QUALITY IMPROVEMENT ACTIVITIES

- 2018 Collaboration with the University of Virginia Radiology & Medical Imaging Center, developed protocol to quantify amyloid-beta plaques in rat model of Alzheimer's disease (AD).
- This protocol is widely used to perform Amyvid (Florbetapir F¹⁸) PET imaging in rat models of AD. See non peer-reviewed publication section for more details.

EXTRACURRICULAR ACTIVITIES

- 2023 Blacksburg draper mile run (5m58s)
- 2021-23 Hokie half marathon (13.1 miles, best 106min) VCOM runners representative
- 2018-19, Played in NRU retired soccer players' team. Won championship in Spring 2019
- 2017 Assistant coach for NRU U10 girls rec soccer team
- 2017 American Red Cross blood donor
- 2014 Runner-up in Virginia Tech annual badminton tournament -doubles