Caroline Machado Kopruszinski

- **Professional title(s) and appointments**

  Research Assistant Professor, Pharmacology

  Research Assistant Professor, Neurology

  Research Assistant Professor, Neuroscience – GIDP

  Research Assistant Professor, Comprehensive Center for Pain & Addiction

- **Research interests and areas of expertise**

  Research interests

  Dr. Caroline Machado Kopruszinski's research focuses on identifying the neurobiological mechanisms that drive headaches, migraine chronification, post-traumatic headache, and chronic pain, with a particular emphasis on sex differences in pain susceptibility. Her laboratory investigates peripheral and central signaling pathways, including neuropeptides, immune mediators, and neuroendocrine factors, that modulate sensory neuron excitability, trigeminal pain processing and headache chronification using translational preclinical models.

  A major focus of her research is understanding the biological mechanisms underlying female-prevalent pain disorders, factors that lead to chronification of pain states and their comorbidities. Her work investigates sex-dependent mechanisms regulating nociceptor sensitization and pain susceptibility in translational preclinical models, using complementary behavioral, electrophysiological, molecular and pharmacological approaches to define mechanisms underlying migraine, post-traumatic headache, and other chronic pain disorders. By integrating discoveries from preclinical models with human samples and tissues, her research aims to identify novel therapeutic targets and advance precision medicine strategies to manage these pain conditions and prevent pain chronification.

  Areas of expertise:

  - Translational pain research
  - Migraine, headache, and orofacial pain neurobiology
  - Chronic pain mechanisms, with emphasis on the trigeminal system

- Sex differences in pain susceptibility
- Translational preclinical models of migraine, headache, orofacial, and extracephalic pain
- Animal behavior
- Experimental surgical procedures in animal models
- Ex vivo functional studies of trigeminal neurons
- Molecular and pharmacological approaches to elucidate mechanisms of pain modulation

- **Education and degrees**

BS in Pharmacy science: Campos de Andrade University Center (UNIANDRADE), Brazil, 2006-2010

MS in Pharmacology: Federal University of Paraná (UFPR), Brazil, 2010-2012

PhD in Medical Pharmacology (visiting Scholar): University of Arizona (UA), USA, 2014-2015

PhD in Pharmacology: Federal University of Paraná (UFPR), Brazil, 2012-2016

- **Awards and honors**

2023 - 2025 Recipient - U.S. Department of Defense CDMRP Award (PR230220), U.S. Department of Defense

2022 Recipient - Frontiers in Headache Research Scholarship, American Headache Society Annual Meeting, American Headache Society

2021 Honorable Mention, University of Arizona Outstanding Postdoctoral Scholar Award, University of Arizona

2020 - 2022 Recipient - Amgen Competitive Program in Migraine Research Award (Principal Investigator), Amgen

2019 IHS financial travel grant award - 19th Congress of the International Headache Society - IHS, Dublin/Ireland

2019 Recipient - Frontiers in Headache Research Scholarship, American Headache Society Annual Meeting, American Headache Society

2017 Recipient - AstraZeneca Internal Postdoctoral Project and Scholarship Award (8th Call), AstraZeneca

2015 IASP financial travel grant award - 16th World Congress on Pain, IASP - International Association for the Study of Pain, Yokohama-Kanto/Japan

2014 IASP financial travel grant award - 15th World Congress on Pain, IASP - International Association for the Study of Pain, Buenos Aires-BA/Argentina

2014 Recipient - Doctoral Exchange Scholarship, Federal University of Paraná/University of Arizona, Coordination of Superior Level Staff Improvement (CAPES)

2013 Recipient - Best Poster Award , NeuPSIG - International Congress of Neuropathic Pain

- **Publications or links to publication profiles (Google Scholar)**

Publications link Pubmed:
https://pubmed.ncbi.nlm.nih.gov/?term=kopruszinski%5Bauthor%5D&sort=date

Publications link Google scholar:
https://scholar.google.com/citations?user=6mhGQIMAAAAJ&hl=pt-BR

List of publications:

1. Tanaka K, **Kopruszinski CM,** Luo S, Moutal A, Lee G, Bharadwaj V, Ismail K, Anderson T, Martin LF, Antenucci N, Neugebauer V, Dodick DW, Navratilova E, Porreca F. Identification of a central CGRP circuit for trigeminal V1-mediated migraine-like pain in mice. Brain. 2026 Jun 24:awag217. doi: 10.1093/brain/awag217. PMID: 42339700
2. Lillo Vizin RC, **Kopruszinski CM,** Lee G, Moutal A, Anderson T, Dodick DW, Schwedt TJ, Navratilova E, Porreca F. Sexually dimorphic mediation of experimental post-traumatic headache by orexin receptor signaling. Pain. 2026 Jun 16. doi: 10.1097/j.pain.0000000000004035. Online ahead of print. PMID: 42302125
3. Antenucci N, Shanmugam S, Mazzitelli M, Tanaka K, **Kopruszinski C,** Ponomarev I, Navratilova E, Porreca F, Neugebauer V. Sex-dependent central amygdala physiology after supradural CGRP exposure is associated with

migraine-like behaviors. J Headache Pain. 2026 Jun 6. doi: 10.1186/s10194-026-02417-9. Online ahead of print. PMID: 42251283

4. Lillo Vizin RC, **Kopruszinski CM.** Chronotype and primary headaches: What a population-based study reveals. Headache. 2026 May;66(5):1021-1022. doi: 10.1111/head.70094. Epub 2026 Mar 28. PMID: 41902423

5. de Boer I, **Kopruszinski CM.** 2025 Highlights in sex and gender differences in migraine. Cephalalgia. 2026 Feb;46(2):3331024261417385. doi: 10.1177/03331024261417385. Epub 2026 Feb 13. PMID: 41685540

6. Vizin RCL, **Kopruszinski CM,** Oyarzo JN, Dodick DW, Broide RS, Brideau-Andersen AD, Brin MF, Anderson T, Navratilova E, Porreca F. OnabotulinumtoxinA inhibits dysregulation of descending pain modulation following mild traumatic brain injury in mice. J Headache Pain. 2025 Oct 16;26(1):216. doi: 10.1186/s10194-025-02159-0. PMID: 41102655

7. Spagnol FJ, Zortea JM, Gomes LC, da Luz FMR, Baggio DF, Lejeune VBP, Ferreira LEN, **Kopruszinski CM,** Chichorro JG. Dipyrone induces sex-dependent latent sensitization in a preclinical model of medication overuse headache. Eur J Pharmacol. 2025 Nov 5;1006:178173. doi: 10.1016/j.ejphar.2025.178173. Epub 2025 Sep 15. PMID: 40962013

8. Stratton HJ, Dolatyari M, **Kopruszinski C,** Ghetti A, Maciuba S, Bowden G, Rivière P, Barber K, Dodick DW, Edorh E, Dumaire N, Moutal A, Navratilova E, Porreca F. A prolactin-targeting antibody to prevent stress-induced peripheral nociceptor sensitization and female postoperative pain. Proc Natl Acad Sci U S A. 2025 May 20;122(20):e2501229122. doi: 10.1073/pnas.2501229122. Epub 2025 May 12. PMID: 40354542

9. Kopruszinski CM, Linley JE, Thornton P, Walker AS, Newton P, Podichetty S, Ruparel RH, Moreira de Souza LH, Navratilova E, Meno-Tetang G, Gurrell I, Dodick DW, Dobson C, Chessell T, Porreca F, Chessell I. Efficacy of MEDI0618, a pH-dependent monoclonal antibody targeting PAR2, in preclinical models of migraine. Brain. 2025 Apr 3;148(4):1345-1359. doi: 10.1093/brain/awae344. PMID: 40036725

10. Navratilova E, **Kopruszinski CM,** Oyarzo J, Barber KR, Anderson T, Dodick DW, Schwedt TJ, Porreca F. Sex differences in effectiveness of CGRP receptor antagonism for treatment of acute and persistent headache-like pain in a mouse model of mild traumatic brain injury. Cephalalgia. 2025

Feb;45(2):3331024251321087. doi: 10.1177/03331024251321087. PMID: 39980371

11. Guzman G, **Kopruszinski CM,** Barber KR, Lillo Vizin RC, Dodick DW, Navratilova E, Porreca F. Chronification of migraine sensitizes to CGRP in male and female mice. Cephalalgia. 2025 Feb;45(2):3331024251317446. doi: 10.1177/03331024251317446. PMID: 39945018

12. Lillo Vizin RC, Ito H, **Kopruszinski CM,** Ikegami M, Ikegami D, Yue X, Navratilova E, Moutal A, Cowen SL, Porreca F. Cortical kappa opioid receptors integrate negative affect and sleep disturbance. Transl Psychiatry. 2024 Oct 4;14(1):417. doi: 10.1038/s41398-024-03123-3. PMID: 39366962

13. **Kopruszinski CM,** Lee G, Martin LK, Barber KR, Moutal A, Dodick DW, Navratilova E, Porreca F. A male-specific mechanism of meningeal nociceptor sensitization promoting migraine headache. Cephalalgia. 2024 Sep;44(9):3331024241281493. doi: 10.1177/03331024241281493. PMID: 39233656

14. Singh S, **Kopruszinski CM,** Watanabe M, Dodick DW, Navratilova E, Porreca F. Female-selective mechanisms promoting migraine. J Headache Pain. 2024 Apr 24;25(1):63. doi: 10.1186/s10194-024-01771-w. PMID: 38658853

15. Lillo Vizin RC, **Kopruszinski CM,** Redman PM, Ito H, Rau J, Dodick DW, Navratilova E, Porreca F. Unraveling the directional relationship of sleep and migraine-like pain. Brain Commun. 2024 Feb 18;6(2):fcae051. doi: 10.1093/braincomms/fcae051. eCollection 2024. PMID: 38444905

16. Fiatcoski F, Jesus CHA, de Melo Turnes J, Chichorro JG, **Kopruszinski CM.** Sex differences in descending control of nociception (DCN) responses after chronic orofacial pain induction in rats and the contribution of kappa opioid receptors. Behav Brain Res. 2024 Feb 29;459:114789. doi: 10.1016/j.bbr.2023.114789. Epub 2023 Nov 29. PMID: 38036264

17. Rudolph M, **Kopruszinski C,** Wu C, Navratilova E, Schwedt TJ, Dodick DW, Porreca F, Anderson T. Identification of brain areas in mice with peak neural activity across the acute and persistent phases of post-traumatic headache. Cephalalgia. 2023 Nov;43(11):3331024231217469. doi: 10.1177/03331024231217469. PMID: 38016977

18. **Kopruszinski CM,** Porreca F, Chichorro JG. Editorial: Chronic orofacial pain. Front Pain Res (Lausanne). 2023 Jan 4;3:1086256. doi: 10.3389/fpain.2022.1086256. eCollection 2022. PMID: 36688086

19. **Kopruszinski CM,** Watanabe M, Martinez AL, de Souza LHM, Dodick DW, Moutal A, Neugebauer V, Porreca F, Navratilova E. Kappa opioid receptor agonists produce sexually dimorphic and prolactin-dependent hyperalgesic priming. Pain. 2023 Jun 1;164(6):e263-e273. doi: 10.1097/j.pain.0000000000002835. Epub 2022 Nov 29. MID: 36625833

20. **Kopruszinski CM,** Vizin R, Watanabe M, Martinez AL, de Souza LHM, Dodick DW, Porreca F, Navratilova E. Exploring the neurobiology of the premonitory phase of migraine preclinically - a role for hypothalamic kappa opioid receptors? J Headache Pain. 2022 Sep 30;23(1):126. doi: 10.1186/s10194-022-01497-7. PMID: 36175828

21. Ito H, Navratilova E, Vagnerova B, Watanabe M, **Kopruszinski C,** Moreira de Souza LH, Yue X, Ikegami D, Moutal A, Patwardhan A, Khanna R, Yamazaki M, Guerrero M, Rosen H, Roberts E, Neugebauer V, Dodick DW, Porreca F. Chronic pain recruits hypothalamic dynorphin/kappa opioid receptor signalling to promote wakefulness and vigilance. Brain. 2023 Mar 1;146(3):1186-1199. doi: 10.1093/brain/awac153. PMID: 35485490

22. Watanabe M, **Kopruszinski CM,** Moutal A, Ikegami D, Khanna R, Chen Y, Ross S, Mackenzie K, Stratton J, Dodick DW, Navratilova E, Porreca F. Dysregulation of serum prolactin links the hypothalamus with female nociceptors to promote migraine. Brain. 2022 Aug 27;145(8):2894-2909. doi: 10.1093/brain/awac104. PMID: 35325034

23. Ikegami D, Navratilova E, Yue X, Moutal A, **Kopruszinski CM,** Khanna R, Patwardhan A, Dodick DW, Porreca F. A prolactin-dependent sexually dimorphic mechanism of migraine chronification. Cephalalgia. 2022 Mar;42(3):197-208. doi: 10.1177/03331024211039813. Epub 2021 Sep 12. PMID: 34510920

24. **Kopruszinski CM,** Turnes JM, Swiokla J, Weinstein TJ, Schwedt TJ, Dodick DW, Anderson T, Navratilova E, Porreca F. CGRP monoclonal antibody prevents the loss of diffuse noxious inhibitory controls (DNIC) in a mouse model of post-traumatic headache. Cephalalgia. 2021 May;41(6):749-759. doi: 10.1177/0333102420981688. Epub 2021 Feb 20. PMID: 33615840

25. **Kopruszinski CM,** Thornton P, Arnold J, Newton P, Lowne D, Navratilova E, Swiokla J, Dodick DW, Dobson C, Gurrell I, Chessell IP, Porreca F. Characterization and preclinical evaluation of a protease activated receptor 2 (PAR2) monoclonal antibody as a preventive therapy for migraine. Cephalalgia. 2020 Dec;40(14):1535-1550. doi: 10.1177/0333102420966581. Epub 2020 Nov 1. PMID: 33131305

26. **Kopruszinski CM,** Navratilova E, Swiokla J, Dodick DW, Chessell IP, Porreca F. A novel, injury-free rodent model of vulnerability for assessment of acute and preventive therapies reveals temporal contributions of CGRP-receptor activation in migraine-like pain. Cephalalgia. 2021 Mar;41(3):305-317. doi: 10.1177/0333102420959794. Epub 2020 Sep 26. PMID: 32985222

27. **Kopruszinski CM,** Swiokla J, Lee YS, Navratilova E, VanderVeen L, Yang M, Liu Y, Miyazaki T, Schmidt WK, Zalevsky J, Porreca F. Preclinical Assessment of the Analgesic Pharmacology of NKTR-181 in Rodents. Cell Mol Neurobiol. 2021 Jul;41(5):949-960. doi: 10.1007/s10571-020-00816-3. Epub 2020 Feb 27. PMID: 32107752

28. Chen Y, Moutal A, Navratilova E, **Kopruszinski C,** Yue X, Ikegami M, Chow M, Kanazawa I, Bellampalli SS, Xie J, Patwardhan A, Rice K, Fields H, Akopian A, Neugebauer V, Dodick D, Khanna R, Porreca F. The prolactin receptor long isoform regulates nociceptor sensitization and opioid-induced hyperalgesia selectively in females. Sci Transl Med. 2020 Feb 5;12(529):eaay7550. doi: 10.1126/scitranslmed.aay7550. PMID: 32024801

29. Dos Reis RC, **Kopruszinski CM,** Nones CFM, Aguiar DA, Chichorro JG. The opposing contribution of neurotrophin-3 and nerve growth factor to orofacial heat hyperalgesia in rats. Behav Pharmacol. 2020 Feb;31(1):27-33. doi: 10.1097/FBP.0000000000000503. PMID: 31577558

30. **Kopruszinski CM,** Navratilova E, Vagnerova B, Swiokla J, Patwardhan A, Dodick D, Porreca F. Cannabinoids induce latent sensitization in a preclinical model of medication overuse headache. Cephalalgia. 2020 Jan;40(1):68-78. doi: 10.1177/0333102419865252. Epub 2019 Jul 16. PMID: 31311288

31. **Kopruszinski CM,** Dos Reis RC, Rae GA, Chichorro JG. Blockade of peripheral endothelin receptors abolishes heat hyperalgesia and spontaneous nociceptive behavior in a rat model of facial cancer. Arch Oral Biol. 2019 Jan;97:231-237. doi: 10.1016/j.archoralbio.2018.10.038. Epub 2018 Nov 2. PMID: 30408737

32. **Kopruszinski CM,** Dos Reis RC, Gambeta E, Acco A, Rae GA, King T, Chichorro JG. Blockade of endothelin receptors reduces tumor-induced ongoing pain and evoked hypersensitivity in a rat model of facial carcinoma induced pain. Eur J Pharmacol. 2018 Jan 5;818:132-140. doi: 10.1016/j.ejphar.2017.10.045. Epub 2017 Oct 22. PMID: 29069579

33. Souza RF, Oliveira LL, Nones CFM, Dos Reis RC, Araya EI, **Kopruszinski CM,** Rae GA, Chichorro JG. Mechanisms involved in facial heat hyperalgesia induced by endothelin-1 in female rats. Arch Oral Biol. 2017 Nov;83:297-303. doi: 10.1016/j.archoralbio.2017.08.015. Epub 2017 Aug 30. PMID: 28865353

34. Gambeta E, **Kopruszinski CM,** Dos Reis RC, Zanoveli JM, Chichorro JG. Facial pain and anxiety-like behavior are reduced by pregabalin in a model of facial carcinoma in rats. Neuropharmacology. 2017 Oct;125:263-271. doi: 10.1016/j.neuropharm.2017.07.035. Epub 2017 Aug 2. PMID: 28778832

35. Araya EI, Nones CFM, Ferreira LEN, **Kopruszinski CM,** Cunha JMD, Chichorro JG. Role of peripheral and central TRPV1 receptors in facial heat hyperalgesia in streptozotocin-induced diabetic rats. Brain Res. 2017 Sep 1;1670:146-155. doi: 10.1016/j.brainres.2017.06.004. Epub 2017 Jun 9. PMID: 28606782

36. Xie JY, De Felice M, **Kopruszinski CM,** Eyde N, LaVigne J, Remeniuk B, Hernandez P, Yue X, Goshima N, Ossipov M, King T, Streicher JM, Navratilova E, Dodick D, Rosen H, Roberts E, Porreca F. Kappa opioid receptor antagonists: A possible new class of therapeutics for migraine prevention. Cephalalgia. 2017 Jul;37(8):780-794. doi: 10.1177/0333102417702120. Epub 2017 Apr 4. PMID: 28376659

37. Dos Reis RC, **Kopruszinski CM,** Nones CF, Chichorro JG. Nerve growth factor induces facial heat hyperalgesia and plays a role in trigeminal neuropathic pain in rats. Behav Pharmacol. 2016 Sep;27(6):528-35. doi: 10.1097/FBP.0000000000000246. PMID: 27392124

38. **Kopruszinski CM,** Xie JY, Eyde NM, Remeniuk B, Walter S, Stratton J, Bigal M, Chichorro JG, Dodick D, Porreca F. Prevention of stress- or nitric oxide donor-induced medication overuse headache by a calcitonin gene-related peptide antibody in rodents. Cephalalgia. 2017 May;37(6):560-570. doi: 10.1177/0333102416650702. Epub 2016 May 19. PMID: 27206958

39. Gambeta E, **Kopruszinski CM,** Dos Reis RC, Zanoveli JM, Chichorro JG. Evaluation of heat hyperalgesia and anxiety like-behaviors in a rat model of orofacial cancer. Neurosci Lett. 2016 Apr 21;619:100-5. doi: 10.1016/j.neulet.2016.03.001. Epub 2016 Mar 4. PMID: 26952973

40. **Kopruszinski CM,** Reis RC, Bressan E, Reeh PW, Chichorro JG. Vitamin B complex attenuated heat hyperalgesia following infraorbital nerve constriction in rats and reduced capsaicin in vivo and in vitro effects. Eur J Pharmacol. 2015 Sep 5;762:326-32. doi: 10.1016/j.ejphar.2015.05.063. Epub 2015 Jun 3. PMID: 26048309

41. Martins GG, Lívero FA, Stolf AM, **Kopruszinski CM,** Cardoso CC, Beltrame OC, Queiroz-Telles JE, Strapasson RL, Stefanello MÉ, Oude-Elferink R, Acco A. Sesquiterpene lactones of Moquiniastrum polymorphum subsp. floccosum have antineoplastic effects in Walker-256 tumor-bearing rats. Chem Biol Interact. 2015 Feb 25;228:46-56. doi: 10.1016/j.cbi.2015.01.018. Epub 2015 Jan 20. PMID: 25616030

42. Hummig W, **Kopruszinski CM,** Chichorro JG. Pregabalin reduces acute inflammatory and persistent pain associated with nerve injury and cancer in rat models of orofacial pain. J Oral Facial Pain Headache. 2014 Fall;28(4):350-9. doi: 10.11607/ofph.1317. PMID: 25347171

43. Cruz LS, **Kopruszinski CM,** Chichorro JG. Intraganglionar resiniferatoxin prevents orofacial inflammatory and neuropathic hyperalgesia. Behav Pharmacol. 2014 Apr;25(2):112-8. doi: 10.1097/FBP.0000000000000024. PMID: 24557321

44. **Kopruszinski CM,** Reis RC, Chichorro JG. B vitamins relieve neuropathic pain behaviors induced by infraorbital nerve constriction in rats. Life Sci. 2012 Dec 10;91(23-24):1187-95. doi: 10.1016/j.lfs.2012.08.025. Epub 2012 Aug 24. PMID: 22940269

- **Professional memberships and leadership roles**

  Memberships:
  American Headache Society (AHS)
  International Headache Society (IHS)
  International Association for the Study of Pain (IASP)
  Society for Neuroscience (SfN)

- Contact information

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- Updated CV

Attached

- Recent accomplishments, news, pictures, or other information you would like highlighted