ARTICLE
Digital Timeline Assignment of Key Opioid Research Articles Spanning Five Decades

Alexis S. Hill
Biology Department, College of the Holy Cross, Worcester, MA 01610.
https://doi.org/10.59390/TVRA6768

Learning to read scientific literature is a crucial component of an undergraduate science education. Undergraduate science students learn to analyze data, read primary literature, and integrate knowledge across articles into a cohesive understanding of a field of study. Often, a class includes students with varying experience reading primary literature, making it difficult to develop assignments that are adequately approachable yet challenging for every student. Here I describe a three-part assignment for an intermediate level neurobiology course that seeks to address this concern. Each student was first assigned a single article in the field of opioid research, which they summarized in an entry for a digital timeline. Second, students presented their timeline entries to the class, and the compiled digital timeline was made publicly available online. In the third part of the assignment, students wrote a brief perspective paper. Here, students explained how their assigned article fit into the field of study using their classmates' timeline entries, along with the option to include additional references outside of the timeline. This three-part assignment sought to provide a supportive yet challenging project for students at all levels. The project was designed as a non-disposable assignment, aligned with additional learning goals and pedagogical practices, including interdisciplinary awareness, writing-to-learn, and inclusive pedagogy. Versions of this assignment have been used for both in-person and remote instruction.

Key words: primary literature; writing-to-learn; inclusive pedagogy; non-disposable assignment; remote instruction

A key component of an undergraduate science education is the development of a foundational understanding of how scientific inquiry is conducted, including the ability to read and analyze primary literature within a field of study. In intermediate level courses that serve students at multiple stages of this learning process, it can be difficult to design assignments that are adequately approachable yet challenging for all students.

The primary goal of this assignment is to expose students to primary literature within the broad context of a field of study that spans decades, including techniques from multiple disciplines and contradictory data. This assignment links course material with experimental design and critical analysis, while students build a historical account of how individual experiments and articles fit within a broader context.

To create an assignment that would be appropriate for students with different levels of prior experience reading primary literature, this three-part assignment was designed with opportunities for feedback and student choice. Each part of the assignment was designed with increasing difficulty such that students could apply concepts and skills learned during one part of the assignment to the next part. Instructor feedback was used to help guide students in this process. Student choice was also incorporated into the assignment, specifically to encourage more advanced students to challenge themselves beyond the minimum assignment requirements. Together, these practices follow an inclusive, asset-based pedagogical approach, with a goal to provide enriching learning opportunities for all students in the class (Florian, 2015).

The assignment was constructed in a manner that aligns with other pedagogical goals. The American Association for the Advancement of Science (AAAS) *Vision and Change* core competencies include the interdisciplinary nature of science within biology subfields, with other science disciplines, and with society more broadly (AAAS, 2010). Additionally, this course is part of the integrative core curriculum of the neuroscience program at Holy Cross, which also has an explicit learning goal of interdisciplinary awareness (Basu et al., 2021). The topic of opioid research was chosen because it is one of the course topics that highlights "interdisciplinary relationships", in that understanding the functions of opioids requires techniques that span across disciplines, including biology (such as receptor trafficking), chemistry (such as x-ray crystallization), and psychology (including models of addiction-related behavior). Articles were chosen by the instructor to integrate several levels of analysis in neuroscience inquiry, while reinforcing key themes from the course, including molecular structure of receptors, intracellular signaling pathways, neuronal physiology, neural circuits, and animal behavior.

Scientific writing is an important communication skill for students to develop. When incorporated into course assignments, scientific writing has been shown to increase scientific literacy and confidence (Brownell et al., 2013). Writing-to-learn is a pedagogical tool through which students use writing to learn or reinforce course material (Rivard, 1994). Furthermore, this assignment was designed such that the instructor's role is not solely as a grader, but also as a collaborator, helping students edit their writing before it is shared with the rest of the class. Assignments that are collaborative in nature have been shown to increase student motivation and satisfaction (Chinn and Hilgers, 2000).

In the past several years, many groups have published exciting new ways to teach students how to read literature, in flipped and project-based classes, such as the Consider, Read, Elucidate hypotheses, Analyze and interpret data, and Think of the next Experiment (CREATE) method (Hoskins et al., 2007) and Process Oriented Guided Inquiry Learning (POGIL) (Murray, 2014). Yet, some faculty have been hesitant to adopt these new practices, which may require attendance at faculty development workshops or shifts in teaching style and may be perceived to take significant time and effort to implement (Miller and Metz, 2014). The assignment described here can be integrated with many teaching styles and can require little to no class time.

Versions of this assignment have been used for two semesters of an Intermediate Neurobiology course at a small undergraduate liberal arts college. The assignments were used during a traditional in-person semester (Fall 2018, 11 students) and remotely (Spring 2020, 25 students). Each class consisted of second- through fourth-year students and was intended to provide an entryway into primary literature, while allowing more challenging options for advanced students.

METHODS AND RESULTS

Assignment Part 1

Students were instructed to generate a timeline entry for an assigned article. Timeline entries consisted of a brief summary of the article (five sentence maximum), a representative figure from the article (one to two figure panels), and a caption for the figure (one to two sentences). An example timeline entry can be seen in Figure 1, a screenshot from the timeline that was generated. The full timeline from Spring 2020 is at the following URL: https://bit.ly/2VnXIP5. As can be seen at this URL, the timeline consists of a separate page for each student entry and provides an overview of key papers related to opioid research.

A full list of the 25 articles used for this assignment (Spring 2020) are listed in the Appendix. Articles were chosen to meet the following criteria: (1) spanned multiple decades (1973-2019), (2) utilized a variety of techniques and levels of analysis, including chromatography, x-ray crystallography, electrophysiology, immunohistochemistry, and animal behavior, (3) included some findings that had been presented in class, (4) included sets of articles from the same research group, (5) included some articles with conflicting results, and (6) included some authors from groups that have been historically marginalized in STEM.

Each student was assigned one article by matching an alphabetized list of student names and a chronological list of articles (students with last names at the beginning of the alphabet were assigned earlier papers). In a larger class, this assignment could be designed with students working in groups, where each group is assigned one or more articles.

The audience for this assignment was the other students in the class— readers with background neurobiology knowledge, but who had not read the same article.

Students were invited, but not required, to set up individual meetings with the instructor to discuss their article

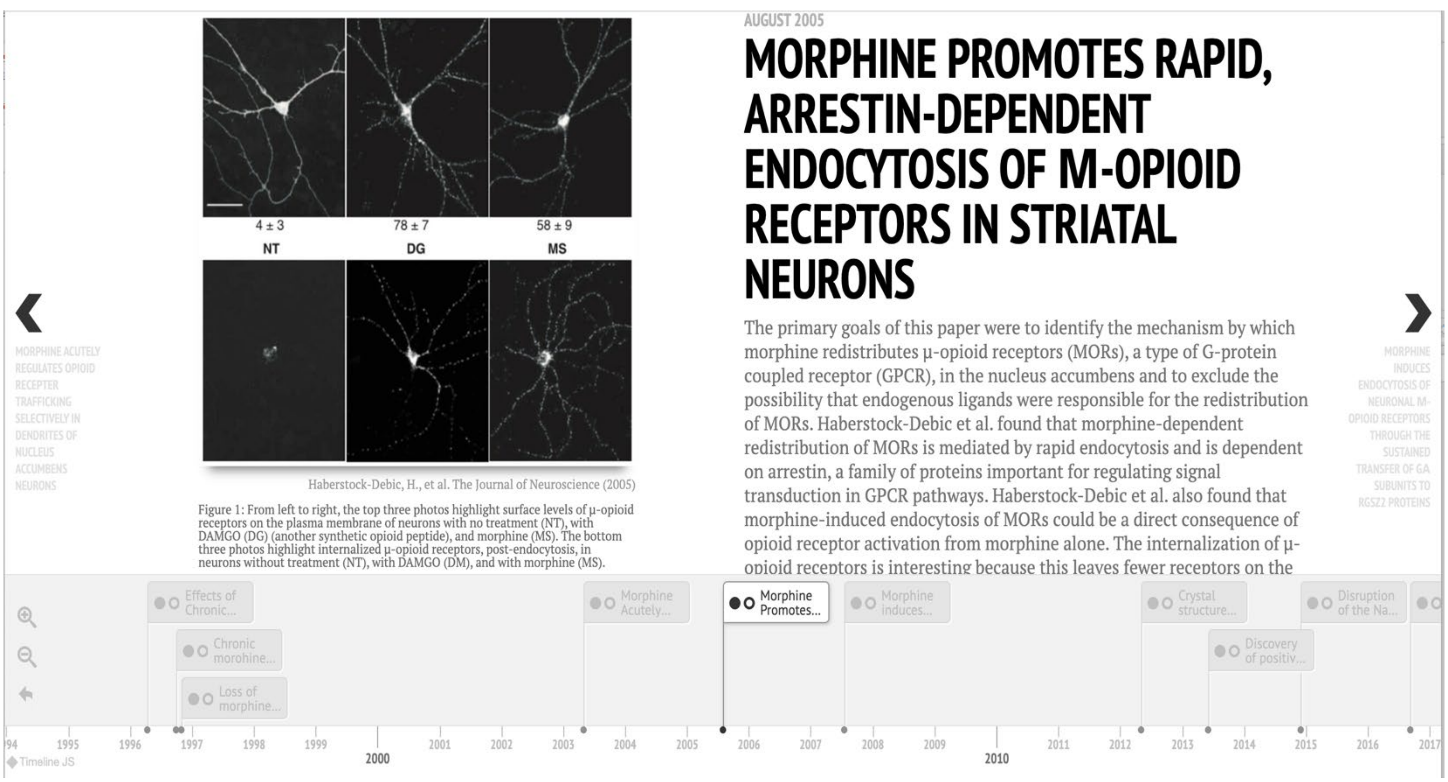

Figure 1. A screenshot of a timeline entry, including figure and figure caption (left), article title (top right in bold), summary (right) and timeline overview (across the bottom). Image Copyright 2005 Society for Neuroscience (Haberstock-Debic et al., 2005).

in its entirety or to ask specific questions. Students assigned long articles were also encouraged to meet with the instructor to determine whether to focus their summary on specific findings within the article. In Spring 2020, 10 out of 25 students met with the instructor at this stage of the assignment.

When students turned in their timeline entries to the instructor, the entries were graded, and the instructor provided feedback to each student. Feedback included grammatical and factual corrections, comments on writing style, and guidance regarding representative figure panel selection. In Spring 2020, some students were required to fix errors; several students chose figure panels that did not align with their figure captions, and two timeline entries included factual mistakes. Editing was optional for the rest of the students. Edited timeline entries were not regraded.

Students then uploaded their timeline entries into a shared Google Sheet, made from a TimelineJS template. TimelineJS is a free, open source, user-friendly mechanism to create digital timelines, developed by the Knight Lab at Northwestern University. The Google Sheet template can be downloaded, along with instructions and additional information from their website (https://timeline.knightlab.com). When in-person, students added their entries to the timeline all together in a computer lab, during the last ten minutes of a class period. When remote, the timeline was generated by students individually outside of class time.

Assignment Part 2

After the timeline was generated, students presented their entries to the class. In the class of eleven students, all presentations were given during a single fifty-minute class period. Each student gave a three-minute presentation of their timeline entry, while it was projected in front of the class. Each student then also answered one to two questions from classmates or the instructor. For the class of 25 students, the plan was for five groups of students to each give five- to seven-minute group presentations summarizing the main conclusions of a set of articles within the timeline. However, this portion of the assignment was cancelled in Spring 2020 due to technological, scheduling and other challenges associated with the COVID19 pandemic. Another alternative would be to have students record presentations that could be shared and viewed by students outside of class.

Assignment Part 3

Students were then assigned to each write a short perspective paper (600-900 words, excluding references), putting the findings from their assigned article into the context of the rest of the timeline. Students were directed to use the timeline to identify articles that were closely related to their assigned article. In the perspective paper, students were required to include citations of at least five articles from the timeline, and citing additional references was optional. Students were again encouraged, but not required, to meet with the instructor, to discuss any aspect of this part of the assignment.

In Spring 2020, eleven students (out of 25) completed this part of the assignment with the minimum requirement of citing five timeline articles. Eleven students cited additional timeline articles (for a total of six through eleven cited articles), and three students cited additional sources outside of the timeline.

DISCUSSION

The three-part framework of this assignment aims to provide an accessible yet challenging learning opportunity for students with varying levels of prior experience with primary literature. Prior proficiency in reading primary literature is not required. Many students may be challenged in the first part of the assignment, yet with the instructor's help, gain experience reading primary literature, which they can then apply when completing later parts of the assignment. Students who have prior experience reading primary literature may be able to complete the first part of the assignment without much difficulty, but then be challenged when they need to integrate information from several articles in the third part of the assignment.

In the third part of the assignment, more than half of the students went beyond the minimum requirement by opting to incorporate additional cited papers within and beyond the class generated timeline. These students typically used additional articles to support relevant points. One student took a particularly creative approach, weaving in a broader context from a book about people and cultural factors that have influenced the opioid crisis (Quinones, 2015). (Excerpts from this book were initially included in the course syllabus but were cut when several class meetings were cancelled during the COVID19 pandemic.) Only three students used sources outside of the timeline. In future semesters, the handout describing the assignment may be edited to more strongly encourage students to seek additional sources. This may include more guidance as to how to find additional sources, in order to further encourage students to push themselves in this respect.

This assignment produced a digital timeline website that was shared publicly (using the same URL included here in the Methods and Results section). This project is thus a non-disposable assignment (NDA), in that student coursework is viewed not only by the instructor, but by others within and beyond the classroom. Such assignments add value to the world outside of the classroom, which in turn increases the value of the assignment to the student (Seraphin et al., 2019). The assignment described here has the potential to be widely shared with relevant communities. The Spring 2020 Timeline was shared via Twitter, which provides a convenient platform to share this type of assignment with interested users. Several graduate students and Principal Investigators shared the post with colleagues, highlighting the usefulness of this timeline as an introduction to opioid research, or the usefulness of the digital timeline tool itself. As of April 2021, the Spring 2020 Timeline URL has been accessed via Twitter 394 times. Some NDAs are designed to create Open Educational Resources (OERs), some of which are not only used, but also revised, by the public (Wiley and Hilton III, 2018). Although digital timelines created thus far through this assignment have not been set up for public revision, this is a possibility for the future.

The joint goal of creating a digital timeline engendered a collaborative spirit to this project. During the in-person semester, when students were together while adding their timeline entries to the shared Google Sheet and presenting their entries, students appeared excited and supportive of each other. This aspect of the assignment appeared to create comradery and a sense of joint success, as has been previously reported in cooperative group work (Johnson et al., 2014). Although students received individual grades that were not dependent on each other, they were aware throughout the assignment that they were producing a timeline together as a group. This aspect of the assignment could be incorporated into remote instruction, especially as many students have become familiar with using shared Google Sheets and platforms for virtual presentations.

The following learning goals for this assignment may be assessed in the future:

- Practice critical reading of primary literature.
- Develop scientific writing skills, with an emphasis on clarity and brevity.
- Reinforce neuroscience concepts and experimental techniques.
- Enhance understanding of how individual techniques, experiments, and articles contribute to the broader context of an interdisciplinary scientific field.

Anecdotal student responses suggest that this assignment was successful in reinforcing course material and also in motivating students beyond the scope of the assignment. Multiple students reported to the instructor that the assignment helped their comprehension of key course topics, including intracellular G protein-coupled signaling pathways and neuronal circuit functions. In the Spring 2020 class, there were two second-year students who are part of an honors program for which they are required to pick a thesis topic during their third year. Both students approached the instructor several months after the course, with plans to write their honors theses on topics stemming from this assignment.

In conclusion, this assignment provides a framework for teaching analysis of primary literature and scientific writing to undergraduate students with a range of prior experience. The assignment lends itself easily to exploring interdisciplinary topics, utilizes a writing-to-learn approach, creates a non-disposable work product, and can be implemented when teaching in-person or remotely.

REFERENCES

AAAS (2010) Vision and Change: A Call to Action. In. Washington, DC: AAAS. doi: 10.1187/cbe.10-03-0044

Basu AC, Hill AS, Isaacs AK, Mondoux MA, Mruczek REB, Narita T (2021) Integrative STEM education for undergraduate neuroscience: Design and implementation. Neurosci Lett 746:135660. doi: 10.1016/j.neulet.2021.135660

Brownell SE, Price JV, Steinman L (2013) A writing-intensive course improves biology undergraduates' perception and confidence of their abilities to read scientific literature and communicate science. Adv Physiol Educ 37(1):70-79. doi: 10.1152/advan.00138.2012

Chinn PWU, Hilgers TL (2000) From Corrector to Collaborator: The Range of Instructor Roles in Writing-Based Natural and Applied Science Classes. J Res Sci Teach 37(1):3-25. doi: 10.1007/978-94-017-0165-5_18

Florian L (2015) Inclusive Pedagogy: A transformative approach to individual differences but can it help reduce educational inequalities? Scott educ rev 47(1):5-14. Available at https://pdfs.semanticscholar.org/1464/371af971eb6502bb7eed9adef86aa0f18151.pdf?_ga=2.35773731.203313355.1672874388-2027292468.1672874388.

Haberstock-Debic H, Kim KA, Yu YJ, von Zastrow M. (2005) Morphine promotes rapid, arrestin-dependent endocytosis of mu-opioid receptors in striatal neurons. J Neurosci. 25(34):7847-57. doi: 10.1523/JNEUROSCI.5045-04.2005

Hoskins SG, Stevens LM, Nehm RH (2007) Selective use of the primary literature transforms the classroom into a virtual laboratory. Genetics 176(3):1381-1389. DOI: 10.1534/genetics.107.071183

Johnson DW, Johnson RT, Smith KA (2014) Cooperative Learning: Improving University Instruction by Basing Practice on Validated Theory. J Excel Coll Teach 25(3&4):85-118. Available at https://eric.ed.gov/?id=EJ1041374.

Miller CJ, Metz MJ (2014) A comparison of professional-level faculty and student perceptions of active learning: its current use, effectiveness, and barriers. Adv Physiol Educ 38(3):246-252. doi: 10.1152/advan.00014.2014

Murray TA (2014) Teaching students to read the primary literature using POGIL activities. Biochem Mol Biol Educ 42(2):165-173. doi: 10.1002/bmb.20765

Quinones S (2015) Dreamland: the true tale of America's opiate epidemic. New York, NY: Bloomsbury Press. doi: 10.1093/pubmed/fdz047

Rivard LP (1994) A Review of Writing to Learn in Science: Implications for Practice and Research. J Res Sci Teach 31(9):969-983. doi: 10.1002/tea.3660310910

Seraphin SB, Grizzell JA, Kerr-German A, Perkins MA, Grzanka PR, Hardin EE (2019) A Conceptual Framework for Non-Disposable Assignments: Inspiring Implementation, Innovation, and Research. Psychol Learn Teach 18(1):84-97. doi: 10.1177/1475725718811711

Knight Lab. TimelineJS. Evanston, IL: Northwestern University. Available at https://timeline.knightlab.com

Wiley D, Hilton III JL (2018) Defining OER-Enabled Pedagogy. IRRODL 19(4). doi: 10.19173/irrodl.v19i4.3601

Received June 17, 2021; revised October 13, 2021; accepted October, 13, 2021.

Acknowledgements: Thank you to Alo C. Basu for helpful comments on this manuscript.

Address correspondence to: Dr. Alexis S. Hill, Department of Biology, College of the Holy Cross, 1 College St., Worcester, MA 01610. Email: ahill@holycross.edu

APPENDIX
ARTICLES USED FOR OPIOID RESEARCH TIMELINE (IN CHRONOLOGICAL ORDER)

Pert CB, Snyder SH. (1973 Mar 9) Opiate receptor: demonstration in nervous tissue. Science. 179(4077):1011-4. doi: 10.1126/science.179.4077.1011. PubMed PMID: 4687585.

Simon EJ, Hiller JM, Edelman I. (1973 Jul) Stereospecific binding of the potent narcotic analgesic (3H) Etorphine to rat-brain homogenate. Proc Natl Acad Sci U S A. 70(7):1947-9. doi: 10.1073/pnas.70.7.1947. PubMed PMID: 4516196; PubMed Central PMCID: PMC433639.

Hughes J, Smith TW, Kosterlitz HW, Fothergill LA, Morgan BA, Morris HR. (1975 Dec 18) Identification of two related pentapeptides from the brain with potent opiate agonist activity. Nature. 258(5536):577-80. doi: 10.1038/258577a0. PubMed PMID: 1207728.

Simantov R, Snyder SH. (1976 Jul) Morphine-like peptides in mammalian brain: isolation, structure elucidation, and interactions with the opiate receptor. Proc Natl Acad Sci U S A. 73(7):2515-9. doi: 10.1073/pnas.73.7.2515. PubMed PMID: 1065904; PubMed Central PMCID: PMC430630.

Iwatsubo K, Clouet DH. (1977 Aug) Effects of morphine and haloperidol on the electrical activity of rat nigrostriatal neurons. J Pharmacol Exp Ther. 202(2):429-36. PubMed PMID: 886472.

Nowycky MC, Walters JR, Roth RH. (1978) Dopaminergic neurons: effect of acute and chronic morphine administration on single cell activity and transmitter metabolism. J Neural Transm. 42(2):99-116. doi: 10.1007/BF01675349. PubMed PMID: 206664.

Matthews RT, German DC. (1984 Mar) Electrophysiological evidence for excitation of rat ventral tegmental area dopamine neurons by morphine. Neuroscience. 11(3):617-25. doi: 10.1016/0306-4522(84)90048-4. PubMed PMID: 6717805.

Trulson ME, Arasteh K. (1985 Aug 7) Morphine increases the activity of midbrain dopamine neurons in vitro. Eur J Pharmacol. 114(1):105-9. doi: 10.1016/0014-2999(85)90530-8. PubMed PMID: 2931290.

North RA, Williams JT, Surprenant A, Christie MJ. (1987 Aug) Mu and delta receptors belong to a family of receptors that are coupled to potassium channels. Proc Natl Acad Sci U S A. 84(15):5487-91. doi: 10.1073/pnas.84.15.5487. PubMed PMID: 2440052; PubMed Central PMCID: PMC298884.

Di Chiara G, Imperato A. (1988 Jul) Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. Proc Natl Acad Sci U S A. 85(14):5274-8. doi: 10.1073/pnas.85.14.5274. PubMed PMID: 2899326; PubMed Central PMCID: PMC281732.

Miyake M, Christie MJ, North RA. (1989 May) Single potassium channels opened by opioids in rat locus ceruleus neurons. Proc Natl Acad Sci U S A. 86(9):3419-22. doi: 10.1073/pnas.86.9.3419. PubMed PMID: 2566172; PubMed Central PMCID: PMC287144.

Johnson SW, North RA. (1992 Feb) Opioids excite dopamine neurons by hyperpolarization of local interneurons. J Neurosci. 12(2):483-8. PubMed PMID: 1346804; PubMed Central PMCID: PMC6575608.

Sim LJ, Selley DE, Dworkin SI, Childers SR. (1996 Apr 15) Effects of chronic morphine administration on mu opioid receptor-stimulated [35S]GTPgammaS autoradiography in rat brain. J Neurosci. 16(8):2684-92. PubMed PMID: 8786444; PubMed Central PMCID: PMC6578746.

Sklair-Tavron L, Shi WX, Lane SB, Harris HW, Bunney BS, Nestler EJ. (1996 Oct 1) Chronic morphine induces visible changes in the morphology of mesolimbic dopamine neurons. Proc Natl Acad Sci U S A. 93(20):11202-7. doi: 10.1073/pnas.93.20.11202. PubMed PMID: 8855333; PubMed Central PMCID: PMC38308.

Matthes HW, Maldonado R, Simonin F, Valverde O, Slowe S, Kitchen I, Befort K, Dierich A, Le Meur M, Dollé P, Tzavara E, Hanoune J, Roques BP, Kieffer BL. (1996 Oct 31) Loss of morphine-induced analgesia, reward effect and withdrawal symptoms in mice lacking the mu-opioid-receptor gene. Nature. 383(6603):819-23. doi: 10.1038/383819a0. PubMed PMID: 8893006.

Haberstock-Debic H, Wein M, Barrot M, Colago EE, Rahman Z, Neve RL, Pickel VM, Nestler EJ, von Zastrow M, Svingos AL. (2003 May 15) Morphine acutely regulates opioid receptor trafficking selectively in dendrites of nucleus accumbens neurons. J Neurosci.;23(10):4324-32. PubMed PMID: 12764121; PubMed Central PMCID: PMC6741100.

Haberstock-Debic H, Kim KA, Yu YJ, von Zastrow M. (2005 Aug 24) Morphine promotes rapid, arrestin-dependent endocytosis of mu-opioid receptors in striatal neurons. J Neurosci. 25(34):7847-57. doi: 10.1523/JNEUROSCI.5045-04.2005. PubMed PMID: 16120787; PubMed Central PMCID: PMC6725258.

Rodríguez-Muñoz M, de la Torre-Madrid E, Sánchez-Blázquez P, Garzón J. (2007 Jul 17) Morphine induces endocytosis of neuronal mu-opioid receptors through the sustained transfer of Galpha subunits to RGSZ2 proteins. Mol Pain. 3:19. doi: 10.1186/1744-8069-3-19. PubMed PMID: 17634133; PubMed Central PMCID: PMC1947952.

Manglik A, Kruse AC, Kobilka TS, Thian FS, Mathiesen JM, Sunahara RK, Pardo L, Weis WI, Kobilka BK, Granier S. (2012 Mar 21) Crystal structure of the μ-opioid receptor bound to a morphinan antagonist. Nature. 485(7398):321-6. doi: 10.1038/nature10954. PubMed PMID: 22437502; PubMed Central PMCID: PMC3523197.

Burford NT, Clark MJ, Wehrman TS, Gerritz SW, Banks M, O'Connell J, Traynor JR, Alt A. (2013 Jun 25) Discovery of positive allosteric modulators and silent allosteric modulators of the μ-opioid receptor. Proc Natl Acad Sci U S A. 110(26):10830-5. doi: 10.1073/pnas.1300393110. PubMed PMID: 23754417; PubMed Central PMCID: PMC3696790.

Livingston KE, Traynor JR. (2014 Dec 23) Disruption of the Na+ ion binding site as a mechanism for positive allosteric modulation of the mu-opioid receptor. Proc Natl Acad Sci U S A. 111(51):18369-74. doi: 10.1073/pnas.1415013111. PubMed PMID: 25489080; PubMed Central PMCID: PMC4280615.

Manglik A, Lin H, Aryal DK, McCorvy JD, Dengler D, Corder G, Levit A, Kling RC, Bernat V, Hübner H, Huang XP, Sassano MF, Giguère PM, Löber S, Da Duan, Scherrer G, Kobilka BK, Gmeiner P, Roth BL, Shoichet BK. (2016 Sep 8) Structure-based discovery of opioid analgesics with reduced side effects. Nature. 537(7619):185-190. doi: 10.1038/nature19112. PubMed PMID: 27533032; PubMed Central PMCID: PMC5161585.

Schmid CL, Kennedy NM, Ross NC, Lovell KM, Yue Z, Morgenweck J, Cameron MD, Bannister TD, Bohn LM. (2017 Nov 16) Bias Factor and Therapeutic Window Correlate to Predict Safer Opioid Analgesics. Cell. 171(5):1165-1175.e13. doi: 10.1016/j.cell.2017.10.035. PubMed PMID: 29149605; PubMed Central PMCID: PMC5731250.

Hill R, Disney A, Conibear A, Sutcliffe K, Dewey W, Husbands S, Bailey C, Kelly E, Henderson G. (2018 Jul) The novel μ-opioid receptor agonist PZM21 depresses respiration and induces tolerance to antinociception. Br J Pharmacol. 175(13):2653-2661. doi: 10.1111/bph.14224. PubMed PMID: 29582414; PubMed Central PMCID: PMC6003631.

Kudla L, Bugno R, Skupio U, Wiktorowska L, Solecki W, Wojtas A, Golembiowska K, Zádor F, Benyhe S, Buda S, Makuch W, Przewlocka B, Bojarski AJ, Przewlocki R. (2019 Dec 8)

Functional characterization of a novel opioid, PZM21, and its effects on the behavioural responses to morphine. Br J Pharmacol. 2019 Dec;176(23):4434-4445. doi: 10.1111/bph.14805. PubMed PMID: 31347704; PubMed Central PMCID: PMC6932942.