

EDITORIAL

Progress in Neuropharmacology of Anesthetics and Analgesics for the Improvement of Medical Treatment

General anesthetics are important drugs in perioperative medicine, which work on the nervous system to induce a comprehensive state for surgeries or invasive medical procedures. The use of modern general anesthetics is a revolutionary medical affair; however, the precise mechanism of how general anesthetics induce their pharmacological effects, mainly including sedation, unconsciousness, immobility and analgesia is still not fully understood. This myth constitutes one of the most intriguing scientific questions [1, 2]. For medical purpose, our knowledge of anesthetic pharmacology definitely can improve the safety of patients and help to develop novel and better general anesthetics. Most reviews in this thematic issue are about emerging pharmacology of general anesthetics on various biological levels, including molecular targets, neural circuits and systemic behaviors.

In the review by Daniel Mulkey *et al.* [3], the authors comprehensively discuss the contributions of astrocyte in general anesthesia, which is a recently identified modulator in the central nervous system that is involved in the action of general anesthetics [4]. In the review by Platholi and Hemmings [5], the authors review the cellular and molecular mechanisms of transient and persistent general anesthetic alterations of synaptic transmission and plasticity, which is critically important to higher-order brain functions such as learning and memory in general anesthesia. For the review by Donghang Zhang *et al.* [6], c-fos staining is commonly used to identify the activated neurons during sleep and/or wakefulness, as well as in various physiological conditions in the central nervous system. Identifying c-fos expression is also a direct and convenient method to explore the effects of general anesthetics on the activity of neural nuclei and circuits. The authors first summarize the actions of general anesthetics on neural nuclei and circuits based on c-fos expression. This review may provide a useful resource for further studies on neural nuclei and circuits in general anesthesia. As a following in-depth perspective, the review by Hailong Dong *et al.* [7] discusses the neural substrates for regulation of sleep and general anesthesia, which is one of the underlying mechanisms shared by sleep and general anesthesia. Besides the above-mentioned articles in this thematic issue, another review by Lai-Wo Stan Leung and Tao Luo [8] is also relevant, which fully discusses cholinergic modulation of general anesthesia and indicates that brain cholinergic neurons can regulate the immune and inflammatory response after surgical operation and anesthetic exposure. In summary, these reviews discuss our recent understanding about the actions of general anesthetics in the central nervous system from various levels such as ion channel, neurotransmitter receptors, cellular types, neural nuclei and circuits. Such knowledge may help us to better understand how general anesthetics modulate our brain and improve the quality of anesthesia and its recovery.

Besides general anesthesia, this thematic issue also contains some novel perspectives in analgesic pharmacology, particularly based on new ion channels. In the review by Lu Huang *et al.* [9], the authors fully discuss the advantages and limitations of the translational perspectives of K2P (Two-pore domain potassium) channels in pain medicine and provide outstanding questions for future studies in the end. Besides this article in this thematic issue, another review in the previous issue by Daniel Cook and Peter Goldstein [10] is also relevant, which summarizes some non-canonical molecular targets for novel analgesics, such as ryanodine receptors (RyRs) and hyperpolarization-activated cyclic nucleotide-gated (HCN) channels. All these molecular targets are of great significance for the development of novel non-opioid analgesics.

In summary, this thematic issue contains review articles that comprehensively discuss the emerging pharmacology of anesthetics and analgesics.

REFERENCES

- [1] Kennedy, D.; Norman, C. What don't we know? *Science*, **2005**, *309*(5731), 75.
<http://dx.doi.org/10.1126/science.309.5731.75> PMID: 15994521
- [2] Hemmings, H.C., Jr; Akabas, M.H.; Goldstein, P.A.; Trudell, J.R.; Orser, B.A.; Harrison, N.L. Emerging molecular mechanisms of general anesthetic action. *Trends Pharmacol. Sci.*, **2005**, *26*(10), 503-510.
<http://dx.doi.org/10.1016/j.tips.2005.08.006> PMID: 16126282
- [3] Mulkey, D.K.; Olsen, M.L.; Ou, M.; Cleary, C.M.; Du, G. Putative roles of astrocytes in general anesthesia. *Curr. Neuropharmacol.*, **2022**, *20*(1), 5-15.
PMID: 33588730
- [4] Perouansky, M.; MacIver, M.B.; Pearce, R.A. Wake up, Neurons! Astrocytes calling. *Anesthesiology*, **2019**, *130*(3), 361-363.
<http://dx.doi.org/10.1097/ALN.0000000000002589> PMID: 30707121
- [5] Platholi, J.; Hemmings, H.C., Jr Effects of general anesthetics on synaptic transmission and plasticity. *Curr. Neuropharmacol.*, **2022**, *20*(1), 27-54.
PMID: 34344292
- [6] Zhang, D.; Liu, J.; Zhu, T.; Zhou, C. Identifying c-fos expression as a strategy to investigate the actions of general anesthetics on the central nervous system. *Curr. Neuropharmacol.*, **2022**, *20*(1), 55-71.
PMID: 34503426
- [7] Dong, H. Neural substrates for regulation of sleep and general anesthesia. *Curr. Neuropharmacol.*, **2022**, *20*(1), 72-84.
<http://dx.doi.org/10.2174/1570159X19666211214144639> PMID: 34906058
- [8] Leung, L.S.; Luo, T. Cholinergic modulation of general anesthesia. *Curr. Neuropharmacol.*, **2021**, *19*(11), 1925-1936.
<http://dx.doi.org/10.2174/1570159X19666210421095504> PMID: 33882810

- [9] Huang, L.; Xu, G.; Jiang, R.; Luo, Y.; Zuo, Y.; Liu, J. Development of non-opioid analgesics targeting two-pore domain potassium channels. *Curr. Neuropharmacol.*, **2022**, 20(1), 16-26.
PMID: 33827408
- [10] Cook, D.C.; Goldstein, P.A. Non-canonical molecular targets for novel analgesics: Intracellular calcium and HCN channels. *Curr. Neuropharmacol.*, **2021**, 19(11), 1937-1951.
<http://dx.doi.org/10.2174/1570159X19666210119153047> PMID: 33463473

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