International Clinical and Medical Case Reports Journal
Research Article (ISSN: 2832-5788)

Beyond Local Anesthesia: The Emerging Roles of Procaine and Lidocaine in Neural Regulation, Inflammation, and Cancer Biology

NAZLIKUL, H.[1,2,3*], URAL NAZLIKUL F.G.[4], REUTER U.R.M.,[6,7], OETTMEIER, R.[8], ACARKAN , T.[9], TAMAM, Y.[10,11] , ORAK, M.[12], BILGIN, M.D.[13,14]

Abstract

Neural Therapy with Procaine and Lidocaine in Regulatory Medicine: Potential Applications in Oncology

Neural therapy using procaine and lidocaine is a promising approach in regulatory medicine and is attracting growing interest in oncology. By influencing the autonomic nervous system (ANS) and supporting anti-inflammatory, epigenetic, and immunomodulatory effects, these local anesthetics may also act on the tumor microenvironment and could have a role in cancer prevention and treatment.

Procaine has demonstrated antioxidant, epigenetic, and anti-inflammatory effects that may support immune function and inhibit tumor growth. Lidocaine complements these properties by inhibiting the NF-κB signaling pathway, reducing pro-inflammatory cytokine production, and enhancing T-cell activity, thereby potentially contributing to improved antitumor immune responses.

Given their favorable tolerability, relatively low cost, and broad range of potential applications, procaine and lidocaine may represent valuable complementary components of multimodal cancer treatment strategies. However, further well-designed clinical studies are required to evaluate their efficacy in oncology systematically and more clearly define their therapeutic potential.

Keywords: Neural therapy, procaine, lidocaine, tumor microenvironment, autonomic nervous system.

[1]President of IFMANT (International Federation of Medical Associations of Neural Therapy), Schattenhalb, Switzerland ORCID: 0000-0002-9746-5220

[2]President of BNR (Scientific Neural Therapy and Rehabilitation Association), Istanbul, Turkey

[3]Faculty of Medicine, Department of Biophysics, Istanbul University of Health and Technology, Istanbul, Turkey

[4]Department of Physical Medicine and Rehabilitation, Istanbul Health and Technology University, Istanbul, Turkey Orcid: 0000-0002-0921-3359

[5]President of the Association for Scientific Complementary Medicine and Regulation (BTR), Istanbul, Turkey

[6]Professorship of Naturopathy, University of Applied Sciences, Anhalt, Germany

[7]Klinik im Leben, D-07973 Greiz, Germany, orcid.org/0000-0001-6357-6320

[8]Alpstein Clinic, CH-9056 Gais/AR, Switzerland Orcid: 0009- 0003- 4365-2084

[9]Independent Physician, Istanbul, Turkey Orcid: 0000-0002-3464-853X

[10]University Of Health Sciences, Adana City Health Practıce And Research Centre, Department Of Internal Medicine / Department Of Neurology, Turkey Orcid: 0000-0002-9886-2017

[11]President of AATRTF (European-Asian Federation of Complementary and Regulatory Medicine) Istanbul, Turkey

[12]Professor of Emergency Medicine, Faculty of Medicine, Dicle University, Diyarbakir, Türkiye, Orcid: 0000-0002-0931-3359

[13]Professor, Department of Biophysics, Graduate School of Health Sciences Aydın Adnan Menderes University, Aydın, Türkiye

[14]Aydın Adnan Menderes University Faculty of Medicine, Department of Biophysics, Aydın, Turkey, ORCID: 0000-0003-0754-0854

Citation: *NAZLIKUL, H., URAL NAZLIKUL, F. G., REUTER, U. R. M., OETTMEIER, R., ACARKAN, T., TAMAM, Y., ORAK, M., BİLGİN, M. D. Beyond Local Anesthesia: The Emerging Roles of Procaine and Lidocaine in Neural Regulation, Inflammation, and Cancer Biology. Int Clinc Med Case Rep Jour. 2026;5(10):1–29. DOI: https://doi.org/10.5281/zenodo.23372295*

Received Date: 05 July, 2026; **Accepted Date:** 24 September, 2026; **Published Date:** 13 October, 2026

***Corresponding author:** Prof. Dr. med. Hüseyin NAZLIKUL, President of IFMANT (International Federation of Medical Associations of Neural Therapy), Schattenhalb, Switzerland ORCID: 0000-0002-9746-5220;
President of BNR (Scientific Neural Therapy and Rehabilitation Association), Istanbul, Turkey;
Faculty of Medicine, Department of Biophysics, Istanbul University of Health and Technology, Istanbul, Turkey

Copyright: © Hüseyin NAZLIKUL, Open Access 2026. This article, published in Int Clinc Med Case Rep Jour (ICMCRJ) (Attribution 4.0 International), as described by http://creativecommons.org/licenses/by/4.0/

1. INTRODUCTION

The treatment of cancer requires a multimodal approach that goes beyond purely tumor-focused therapy and accounts for the organism's overall biological regulation. Neural therapy, particularly with the local anesthetics procaine and lidocaine, offers an innovative approach to modulating the autonomic nervous system (ANS), reducing inflammation, and influencing the tumor microenvironment.

This article examines the mechanisms of action of neural therapy, highlights the similarities and differences between procaine and lidocaine, and discusses their potential roles in the prevention and therapeutic management of cancer.[1-9]

1.1 What Is Neural Therapy?

Neural therapy is a scientifically based regulatory medical procedure that considers the autonomic nervous system a central regulator of physiological processes. It was developed on conventional medical principles and is therefore not considered a complementary medical method.[1,5,10]

Through the targeted injection of local anesthetics such as procaine or lidocaine into specific regions of the body, so-called “interference fields” or neuromodulatory triggers are neutralized, autonomic dysfunctions are corrected, and endogenous healing processes are activated.[1, 9-16] Neural therapy is used for both diagnostic and therapeutic purposes in a wide range of conditions, including chronic pain and systemic disorders.[16-20]

1.2 The Role of the Autonomic Nervous System in Neural Therapy

The autonomic nervous system (ANS), comprising the sympathetic and parasympathetic nervous systems, regulates vital physiological functions such as heart rate, blood pressure, digestion, and immune responses.[1,5, 21- 26]

The sympathetic nervous system (SNS) plays an essential role in immune defense by regulating the development, activation, and function of immune cells.[27-31] Stimulation of adrenergic receptors (ARs) on immune cells influences their survival, proliferation, circulation, and cytokine production, all of which are essential components of immune surveillance.[27]

Within the framework of neural therapy, the ANS is targeted to correct autonomic imbalances and reduce stress-induced sympathetic overactivity.[21,22,32-38] Restoration of homeostasis may promote regenerative and reparative processes within the organism.[1, 2, 11, 38]

Furthermore, neural therapy may support communication between the peripheral and central nervous systems by modulating bidirectional signaling and thereby influencing regulatory processes.[38-42] The underlying mechanisms of action of neural therapy are schematically illustrated in Figure 1.

Recent studies indicate that dysregulation of the ANS is a central feature of many immune-mediated inflammatory diseases (IMIDs). Chronic systemic inflammation is associated with dysregulation of the stress response, suggesting an important neuroimmune dialogue in the pathophysiology of IMIDs.[20,27]

The available literature indicates that chronic systemic and regional inflammation represents an essential factor in disease progression in IMIDs. Regional inflammation and immune deficiency may promote organ-specific damage, whereas systemic inflammation is associated with increased morbidity and mortality because it involves multiple organ systems.[27]

Based on these findings, novel strategies to restore ANS and SNS homeostasis could be developed as safe, cost-effective approaches to managing IMIDs. Such strategies may not only reduce comorbidities but may also contribute to improved life expectancy in affected patients.[27]

The treatment of IMIDs primarily focuses on controlling inflammatory processes, modulating the immune response, and alleviating symptoms. In addition to immunosuppressive agents and biologics, regulatory therapeutic approaches, such as neural therapy and anti-inflammatory interventions, may be promising adjunctive strategies for managing these disorders.[27]

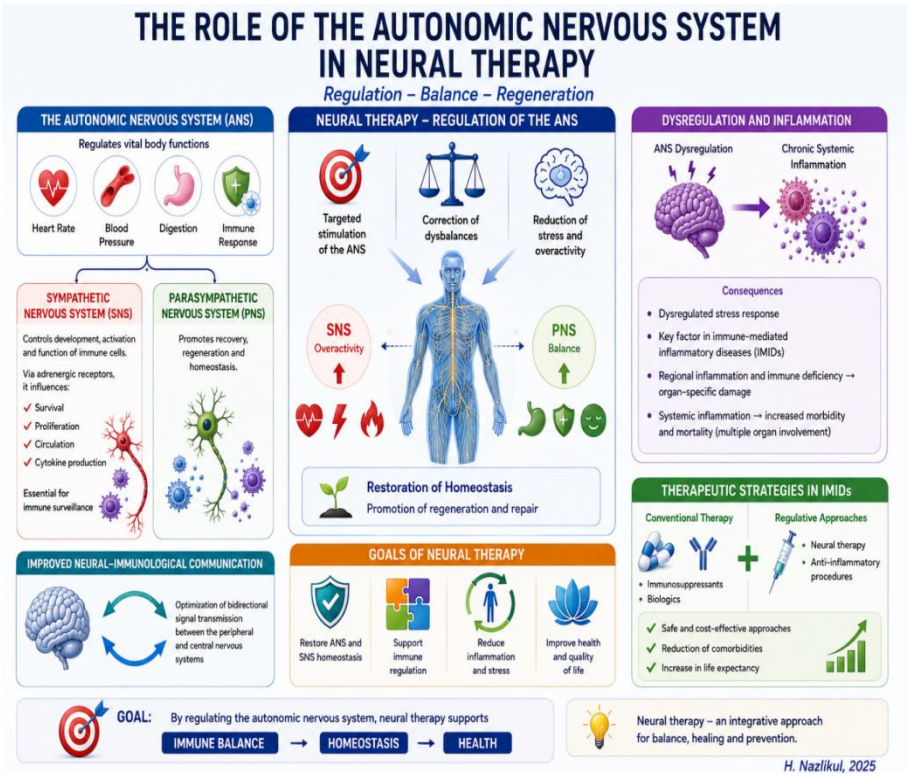


Figure 1: Role of the autonomic nervous system in neural therapy. *Schematic representation of the potential regulatory effects of neural therapy on the balance between sympathetic and parasympathetic activity, as well as on neuroimmune communication, inflammatory regulation, and the restoration of homeostasis*

1.3 Relationship Between the Nervous, Immune, and Endocrine Systems

Interaction Between the Nervous and Immune Systems

- The nervous system modulates immune responses through direct innervation of lymphoid organs and the release of neurotransmitters.[45-52]
- Chronic stress, mediated through the autonomic nervous system (ANS), can suppress immune function and enhance inflammatory processes.[22, 52]

Interaction with the Endocrine System

- The ANS regulates endocrine gland function through the hypothalamic–pituitary axis.[1,3,38]
- Neural therapy may influence hormone production by modulating the ANS, particularly cortisol secretion, which plays a key role in inflammatory and immune processes. [1,13, 38, 52]

Bidirectional Communication

- Bidirectional communication exists between the peripheral nervous system (PNS) and the central nervous system.[52–56] Peripheral signals, such as those arising from inflammation or tissue injury, are transmitted to the CNS via afferent neural pathways. In turn, the CNS exerts regulatory effects on immune and inflammatory processes through the ANS.[22,38,52] The complex interactions between the nervous and endocrine systems are schematically illustrated in Figure 2

.

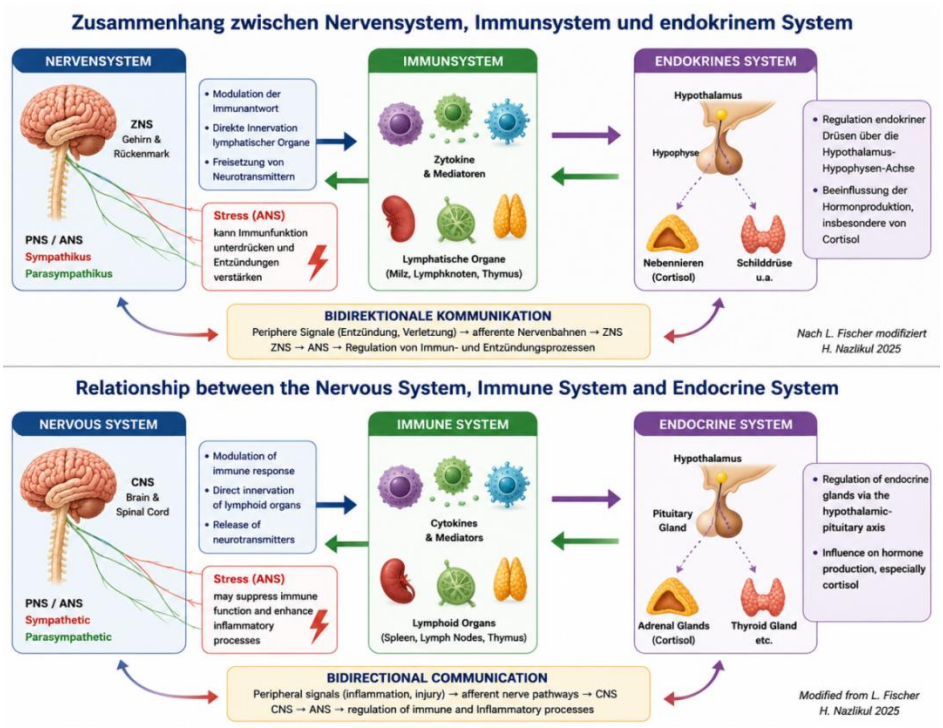


Figure 2: Interactions between the nervous, immune, and endocrine systems. *Schematic representation of bidirectional neuroimmune–endocrine communication and its role in immune responses, inflammatory regulation, stress responses, and hormonal homeostasis. Modified from L. Fischer; H. Nazlikul, 2025.*

1.4 Biophysical Medicine and Regulatory Medicine

Neural therapy is closely associated with biophysical and regulatory medicine, as both approaches aim to restore the body's natural homeostasis. In biophysical medicine, the human organism is regarded as a complex electromagnetic system in which cellular communication and function are critically dependent on bioelectrical signals.

Procaine and lidocaine play an important role in this context, as their membrane-stabilizing and neuromodulatory effects may specifically influence the regulation of physiological processes.

2. PHARMACOLOGICAL BASIS: COMPARISON OF PROCAINE AND LIDOCAINE

2.1 Procaine

Properties

- Procaine is a short-acting ester-type local anesthetic that acts primarily by blocking voltage-gated sodium channels. It is rapidly metabolized by plasma cholinesterases.[19, 38, 57-61]

Additional Effects

- **Anti-inflammatory effects:** Procaine inhibits the release of pro-inflammatory cytokines, including TNF-α and IL-6.[19, 38, 40, 52, 61]
- **Epigenetic effects:** Procaine may act as a histone deacetylase inhibitor, thereby potentially contributing to the reactivation of tumor suppressor genes.[19, 38, 40, 52, 59]
- **Regulation of membrane potential:** Procaine stabilizes the cell membrane and improves the function of ion-dependent mechanisms.[19, 38, 40, 52, 59]
- **If microcirculation is compromised**, it can lead to inadequate supply of nutrients and oxygen to surrounding cells and impede the removal of metabolic waste products.[19,38,40] This highlights the critical role of microcirculation in maintaining cellular health and function.

Limitations

- **Short half-life:** Due to its rapid metabolism, the duration of action is limited.
- **Allergic reactions:** Metabolism to para-aminobenzoic acid (PABA) may trigger allergic reactions.[52, 61]

2.1.1 Mechanisms of Action of Procaine in Neural Therapy

In neural therapy, procaine is valued not only as a local anesthetic but also for its regulatory effects on the nervous and immune systems.[1,3,38]

Inhibition of Sodium Channels

- Procaine blocks nerve impulse conduction, thereby reducing pain and spastic muscle contractions.[52, 62]

Anti-inflammatory Effects

- Procaine inhibits pro-inflammatory cytokines such as TNF-α and IL-6 and reduces oxidative stress. [19,38,39,52]
- Procaine inhibit the replication of SARS-CoV-2 ,influenza A virus, Herpes Simplex Virus, the growth of Aspergillus species and exert antimicrobial properties during coinfection with influenza A viruses and A. Fumigatus.[63-66]

Epigenetic Modulation

- Procaine influences DNA methylation patterns and may thereby promote the expression of tumor suppressor genes.[19,38, 67-71]

Regulation of the Autonomic Nervous System

- Procaine promotes a balance between sympathetic and parasympathetic activity, supporting its application in stress-related disorders and chronic pain conditions.[1,3,28,52]

Improvement of Microcirculation

- Procaine enhances blood flow in treated tissues, thereby supporting tissue regeneration.[72,73]

Neutralization of Interference Fields

- Through targeted injection into trigger points or scar tissue, pathological impulses that may contribute to the persistence or exacerbation of chronic disorders are neutralized [3,5,37,38]

2.1.2 Therapeutic Applications of Procaine in Neural Therapy

- **Pain relief:** Procaine is specifically used in the treatment of trigger points, scars, and chronic pain conditions.
- **Treatment of interference fields:** Targeted injection may interrupt pathological reflex mechanisms, thereby positively influencing chronic disorders.[38,52,74]
- **Regulation of the autonomic nervous system:** Procaine may help correct stress-induced autonomic imbalances.[38,52]
- **Oncological applications:** Due to its epigenetic effects and its potential to modulate the tumor microenvironment, procaine is increasingly being investigated and applied within the context of integrative oncology.[19,38,40,61,72,75]

2.2 Lidocaine

Properties

Lidocaine is a longer-acting amide-type local anesthetic with a mechanism of action similar to that of procaine, but with a longer half-life and a more pronounced analgesic effect.

Additional Effects

- **Anti-invasive effects:** In vitro studies have demonstrated that lidocaine can inhibit the migration and invasion of cancer cells *(7, 16, 38, 75-82).*
- **Immunomodulatory effects:** Lidocaine may stimulate T-cell activity and inhibit immunosuppressive macrophages *(7, 16,49, 76-79).*
- **Anti-inflammatory effects:** Lidocaine may reduce systemic inflammatory markers such as C-reactive protein (CRP) *(7, 16, 38, 75-82).*
- **Limitations**
- **Increased risk of adverse effects:** Overdosage is associated with an increased risk of cardiovascular toxicity and lidocaine is more toxic than procaine*(83-88*)
- **Limitations of use:** Lidocaine requires precise dosing and administration to minimize the risk of adverse effects *(83-88).*

2.2.1 Therapeutic Applications of Lidocaine

Intravenous lidocaine infusions and lidocaine patches are effective and generally safe in the management of various chronic and neuropathic pain syndromes. Furthermore, evidence suggests that the perioperative use of lidocaine may reduce the risk of developing chronic postoperative pain syndromes.[90]

Inhibition of Cytokine Production and Immunomodulation

- **Lidocaine reduces the release of pro-inflammatory cytokines:** At therapeutic concentrations, lidocaine dose-dependently inhibits both spontaneous and TNF-α-stimulated secretion of IL-8 and IL-1β in HT-29 and Caco-2 cell lines.[91-96]

- **Stimulation of anti-inflammatory mediators:** Lidocaine promotes the secretion of IL-1 receptor antagonist, thereby exerting a dual effect: inhibiting pro-inflammatory cytokines and enhancing anti-inflammatory responses.[7,49,91]
- **Regulation of Nuclear Factor-κB (NF-κB)**
- **Inhibition of NF-κB:** Lidocaine reduces NF-κB activation, thereby modulating the production of pro-inflammatory cytokines and T-cell proliferation.[7,95-98]
- **Reduction of NF-κB nuclear translocation in T cells:** The proliferation of anti-CD3-stimulated peripheral blood T cells (PB T cells) is significantly inhibited, while NF-κB nuclear translocation is reduced following lidocaine treatment.[7,99-101]

3. PROCAINE AND LIDOCAINE IN ONCOLOGY

Procaine and lidocaine have traditionally been used as local anesthetics; however, in recent years, increasing attention has been directed toward their potential applications in the prevention and treatment of cancer. The potential mechanisms of action of procaine and lidocaine in the oncological context are systematically illustrated in Figure 3.

3.1 Combination of Procaine and Chemotherapy

- The combination of procaine and carboplatin has been described as one of the most effective strategies for reducing global DNA methylation levels in colorectal cancer cells.[102]
- Procaine may help reduce the cytotoxicity and adverse effects associated with chemotherapy and radiotherapy.[19,37,38,103-106]

3.2 Lidocaine in Oncology

In addition to its analgesic effects, lidocaine exhibits potential immunomodulatory and anti-inflammatory properties, making it a promising candidate for further investigation in integrative oncology.[7]

Note: This article provides a comprehensive overview of the mechanisms of action of neural therapy and the pharmacological properties of procaine and lidocaine. In addition, their potential roles in preventive and therapeutic medicine, particularly in oncology, are discussed.

4. MECHANISMS OF ACTION OF PROCAINE

4.1 Inhibition of Sodium Channels

Procaine blocks voltage-gated sodium channels in cell membranes, thereby interrupting nerve conduction and producing a local anesthetic effect. In addition to its analgesic properties, procaine may exert antiproliferative effects, as sodium channels play an important role in cellular proliferation and tumor progression.[19,38,61, 69-72]

4.2 Antioxidant Properties

Procaine exhibits pronounced antioxidant properties that may neutralize free radicals and reduce oxidative stress. Because oxidative stress plays an important role in tumorigenesis, procaine may potentially exert protective effects against DNA damage and cancer-promoting mutations.[19,38,61,72]

4.3 Inhibition of DNA Methylation

Procaine exhibits epigenetic effects by inhibiting DNA methyltransferase activity, potentially leading to the reactivation of tumor suppressor genes. Aberrant DNA methylation patterns are a

characteristic feature of many cancer cells and contribute to tumor progression. Therefore, procaine-induced reduction of DNA methylation may exert antiproliferative effects.[7,38,109-113]

Another study demonstrated that procaine reduces genomic 5-methylcytosine content, thereby inhibiting cancer cell growth.[109]

4.4 Anti-inflammatory Effects

Procaine may reduce the expression of pro-inflammatory cytokines, thereby attenuating chronic inflammation. Since chronic inflammation is an established risk factor for tumor development, procaine may have a potential role in the prevention and treatment of inflammation-associated cancers.[19,38-40, 61,72]

4.5 Application of Procaine in Cancer Prevention

A systematic analysis by Grandhi and Perona[114] examined procaine's potential efficacy in preventing cancer recurrence after surgical interventions.

Given its potential to influence mechanisms associated with aging and cellular senescence—including oxidative stress, inflammation, DNA methylation, autophagy, and tumor-protective mechanisms—Gradinaru et al.[61] classified procaine as a potential geroprotective agent.

4.6 Reduction of Inflammation

Through its anti-inflammatory effects, procaine may reduce chronic inflammation and thereby protect against the development of malignant diseases. This effect is associated with the inhibition of pro-inflammatory cytokines and modulation of the immune response.[19,38-40,72]

4.7 Protection Against DNA Damage

Through its antioxidant properties, procaine may protect against DNA damage caused by free radicals and oxidative processes. Since DNA damage can induce mutations that contribute to tumorigenesis, procaine may play a potential role in mechanisms involved in DNA protection.[19,38-40,72, 109,113]

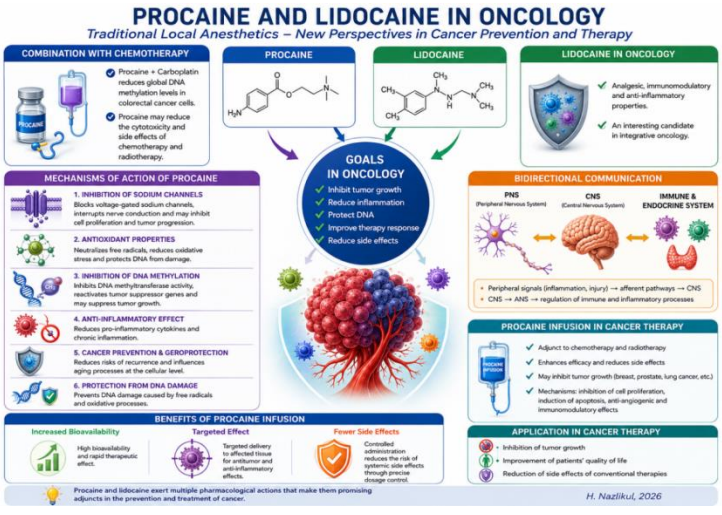


Figure 3: Potential mechanisms of action of procaine and lidocaine in the oncological context. *Schematic representation of the reported pharmacological and biological mechanisms, including potential anti-inflammatory, immunomodulatory, epigenetic, and antiproliferative effects, as well as possible interactions with established oncological treatment modalities. The approaches shown should be understood as complementary mechanisms and do not replace established standard oncological therapy.*

5. APPLICATION OF PROCAINE IN CANCER THERAPY – PROCAINE INFUSION: SPECIFIC BENEFITS AND APPLICATIONS

Procaine may be used as an adjunct to conventional cancer treatments such as chemotherapy and radiotherapy. Through its epigenetic, anti-inflammatory, and antioxidant effects, procaine may enhance the efficacy of these treatments while reducing treatment-related adverse effects.[3,19,38,61] Several studies suggest that procaine may inhibit the growth of various types of cancer, including breast, prostate, and lung cancer. These effects may involve a combination of inhibition of cell proliferation, induction of apoptosis, and suppression of angiogenesis.[3, 4, 11, 19,20, 38, 39, 40, 52,61, 115-117]

5.1 Mechanism of Procaine Infusion

Procaine infusion refers to the intravenous administration of a procaine solution to achieve systemic effects. This approach allows for homogeneous, systemic distribution of the drug and maintains therapeutic concentrations in the bloodstream.[19,38,61,118,19] The application of procaine infusion in the oncological context is schematically illustrated in Figure 4. The underlying potential mechanisms of action and their possible relevance to supportive oncological therapy are discussed in detail below.

5.2 Benefits of Procaine Infusion

- **Increased bioavailability:** Intravenous administration provides high bioavailability and allows a rapid onset of therapeutic effects.[1,3,10,19, 38, 61]
- **Targeted effects:** Following intravenous administration, procaine may reach affected tissues and potentially exert its antitumor and anti-inflammatory effects.[3,19,38,61, 63-65]
- **Potential for reduced adverse effects:** Controlled intravenous administration allows precise adjustment of the dose and may thereby help reduce the risk of systemic adverse effects.[3,19,38,61, 64]

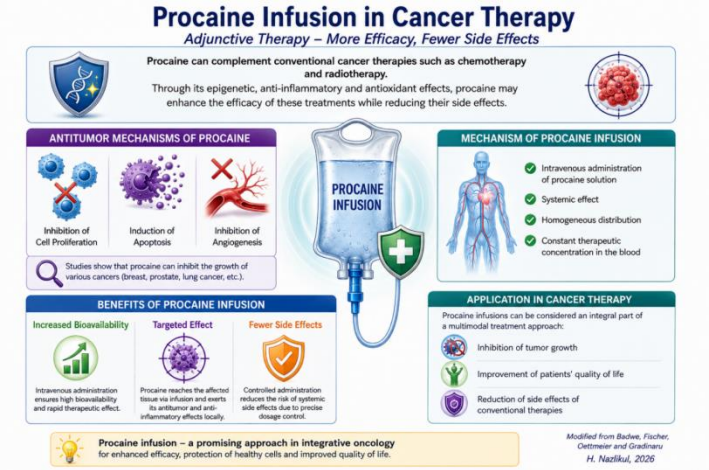


Figure 4: Procaine infusion as a potential adjuvant approach in the oncological context. *Schematic representation of the intravenous administration of procaine and its discussed potential antitumor, anti-inflammatory, and cytoprotective mechanisms. The figure also illustrates possible complementary effects within multimodal oncological treatment concepts. Procaine infusion should be considered a complementary approach and does not replace established standard oncological therapy.*

5.3 Application in Cancer Therapy

Procaine infusions may be part of a multimodal treatment approach combining conventional and complementary therapeutic strategies. Their use may potentially contribute to the inhibition of tumor growth, improvement of patients' quality of life, and reduction of adverse effects associated with conventional cancer therapies.[19, 61]

6. PHARMACOLOGICAL PROPERTIES OF LIDOCAINE

Lidocaine is an amide-type local anesthetic that inhibits the generation and conduction of nerve impulses by blocking voltage-gated sodium channels.[3,7,16,49,50, 76-79, 122-129] In addition to its local anesthetic effects, lidocaine exerts systemic effects that may be relevant in various therapeutic contexts.

6.1 Mechanisms of Action of Lidocaine

- **Inhibition of sodium channels:** Lidocaine reduces neuronal excitability by blocking voltage-gated sodium channels, thereby accounting for its analgesic effects.
- **Reduction of inflammation:** Lidocaine inhibits the activation of NF-κB, a key transcription factor involved in the production of pro-inflammatory cytokines.[7,16, 49,50, 76-79]
- **Epigenetic effects:** Lidocaine may influence epigenetic modifications, including DNA methylation in cancer cells, thereby potentially promoting the expression of tumor suppressor genes.[3,19,38,61,120-123]
- **Inhibition of tumor cell migration:** Lidocaine may inhibit tumor cell migration and metastatic processes by modulating the function of cell adhesion molecules and metalloproteinases.[120-123-129]
- **Modulation of the immune system:** Lidocaine may inhibit immunosuppressive cell populations, such as M2 macrophages, and stimulate T-cell activity, thereby potentially enhancing the antitumor immune response.[124-129]

6.2 Lidocaine in Neural Therapy

In neural therapy, lidocaine is used to modulate the autonomic nervous system and to neutralize pathological interference fields. The principal therapeutic objectives include:

- **Regulation of the autonomic nervous system:** Lidocaine may help restore the balance between sympathetic and parasympathetic activity, thereby supporting physiological homeostasis *(Nazlikul et al., 2022; Nazlikul et al, 2025; Ural Nazlikul et al, 2025).*
- **Pain relief:** Lidocaine is used for trigger-point injections and in the treatment of chronic pain, while its anti-inflammatory properties may further enhance its analgesic *effects.*[38,127,128]
- **Improvement of microcirculation:** Vasodilation in treated areas may enhance local blood flow, thereby contributing to tissue regeneration.[124-128]

6.3 Lidocaine and Cancer: Therapeutic Perspectives

Lidocaine has demonstrated promising properties in the oncological setting, both as a supportive therapeutic intervention and as a compound with potential direct antitumor effects:

- **Inhibition of tumor growth and metastasis:**
    - Studies suggest that lidocaine may inhibit cancer cell

proliferation and promote apoptotic processes in tumor cells.

- It may influence the tumor microenvironment by inhibiting pro-inflammatory and pro-metastatic signaling pathways.[7]

- **Improvement of response to cancer therapies:**
  - Lidocaine may act synergistically with chemotherapeutic agents by increasing tumor cells' susceptibility to treatment.[7]
- **Protection against therapy-induced neurotoxicity:**
  - Lidocaine possesses potential neuroprotective properties that may contribute to reducing chemotherapy-induced neuropathy.[7]

A multicenter randomized clinical trial demonstrated that perioperative peritumoral infiltration with **0.5% lidocaine** significantly improved **5-year disease-free survival (DFS)** and **overall survival (OS)** in patients with early breast cancer. These findings highlight the potential role of lidocaine in limiting metastatic processes, potentially through the blockade of voltage-gated sodium channels and modulation of inflammatory signaling pathways.[7,129,130]

7. SCIENTIFIC STUDIES AND EVIDENCE

7.1 In Vitro Studies

In vitro studies have demonstrated that procaine and lidocaine may inhibit the growth and proliferation of various cancer cell lines. These findings provide important insights into the potential mechanisms of action and therapeutic effects of these agents in cancer treatment.[110, 111]

7.2 In Vivo Studies

In vivo studies using animal models suggest that procaine and lidocaine may slow tumor growth and improve survival. These findings support further investigation of these agents as potential adjuncts to cancer therapy.

7.3 Clinical Studies

Although the preclinical data are promising, clinical evidence in humans remains limited. Further well-designed clinical studies are required to systematically evaluate the safety and efficacy of procaine and lidocaine in patients with cancer.

7.4 Safety and Adverse Effects

7.4.1 General Safety

Procaine and lidocaine are generally considered safe when administered appropriately and under medical supervision. They are usually well tolerated, with mild local reactions at the injection site among the most commonly reported adverse effects.

7.4.2 Potential Adverse Effects

At high doses or when administered improperly, systemic adverse effects may occur, including dizziness, nausea, and cardiac arrhythmias. Therefore, procaine infusions should be administered exclusively by appropriately trained and experienced healthcare professionals.

8. MECHANISMS OF NEURAL THERAPY AND THEIR POTENTIAL INFLUENCE ON CANCER

8.1 Regulation of the Autonomic Nervous System

Neural therapy modulates the autonomic nervous system, particularly by promoting a functional balance between sympathetic and parasympathetic activity. This may reduce stress-induced cortisol secretion, which can exert immunosuppressive effects and may thereby contribute to cancer progression.[38,52,72]

The potential mechanisms of action of neural therapy in the oncological context are presented schematically and systematically in Figure 5. The figure provides an overview of the different levels of action and illustrates their functional interrelationships.

8.2 Effects on the Tumor Microenvironment

Procaine and lidocaine may influence the tumor microenvironment through the following mechanisms:

- **Inhibition of inflammation:** Both agents may reduce the release of pro-inflammatory mediators, thereby potentially contributing to tumor growth inhibition.
- **Modulation of pH:** Procaine may influence metabolic acidosis in the tumor microenvironment, thereby potentially contributing to the inhibition of tumor growth.

8.3 Epigenetic Modulation

Procaine may act as an epigenetic regulator by inhibiting DNA methylation in tumor cells and promoting the expression of tumor suppressor genes. These effects may inhibit cancer cell proliferation and enhance apoptotic processes.

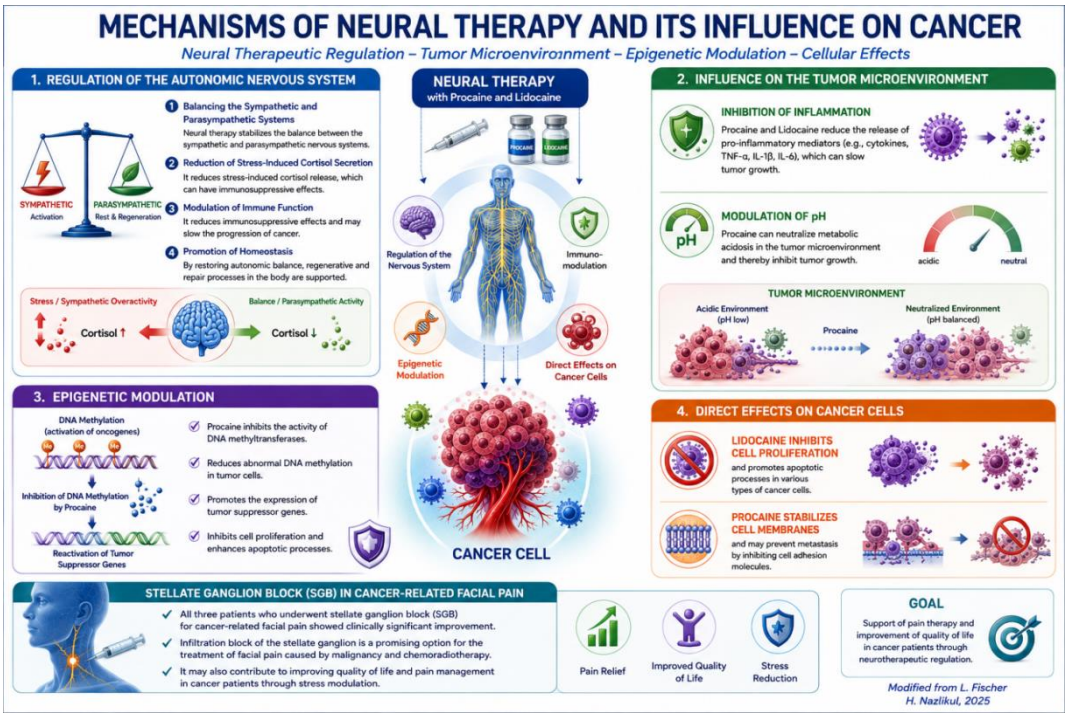


Figure 5: Potential mechanisms of neural therapy in the oncological context. *Schematic representation of different regulatory mechanisms of neural therapy with procaine and lidocaine, including modulation of the autonomic nervous system, potential effects on the tumor microenvironment, epigenetic regulatory mechanisms, and direct cellular effects. In addition, stellate ganglion block for cancer-related pain is illustrated as a potential component of an integrative pain management approach.*

8.4 Direct Effects on Cancer Cells

- **Lidocaine inhibits cell proliferation** and promotes apoptotic processes in various cancer cell types.
- **Procaine stabilizes cell membranes** and may inhibit metastatic processes by interfering with cell adhesion molecules.

Clinically significant improvement was observed in all three patients who underwent stellate ganglion block (SGB) for the treatment of cancer-related facial pain. Stellate ganglion infiltration block may represent a promising therapeutic option for facial pain associated with malignancy and chemoradiotherapy. In addition, by modulating stress-related autonomic regulation, SGB may contribute to improved pain management and quality of life in patients with cancer.[52,131]

9. THERAPEUTIC APPLICATIONS IN CANCER TREATMENT

9.1 Pain Relief

Neural therapy with procaine and lidocaine may alleviate chronic pain frequently associated with cancer. Targeted treatment of trigger points and improvement of local microcirculation may contribute substantially to these analgesic effects.

9.2 Adjunctive Immunomodulation

- **Procaine may modulate immune responses through its regulatory effects on the autonomic nervous system.**
- **Lidocaine may attenuate tumor-associated immunosuppressive mechanisms** and potentially enhance the effectiveness of immunotherapeutic approaches.

9.3 Potential Preventive Effects

Repeated applications of neural therapy could help maintain a more stable biological and regulatory milieu. However, whether this translates into a reduced risk of tumor recurrence requires confirmation in appropriately designed clinical studies.

10. CONCLUSION AND FUTURE RESEARCH

10.1 Clinical Studies and Current Evidence

Procaine in Cancer Treatment

Studies suggest that procaine inhibits tumor cell growth and improves responsiveness to chemotherapy. A study by Smith et al. (132) reported that procaine significantly reduced DNA methylation in breast cancer cells.

In health services research on cancer patients, particularly in 30 years of clinical application as evidenced by Reuter and Oettmeier, demonstrates the effectiveness of this treatment.[132, 133]

Lidocaine and Its Antimetastatic Properties

Zhou et al.[134] and Zhang et al.[135] reported that lidocaine inhibited the migration and invasion of prostate cancer cells. Further studies suggest that lidocaine may exert synergistic effects when combined with conventional cancer therapies.

Preclinical Studies

- Zhang et al.[135] demonstrated that lidocaine inhibited the migration and invasion of prostate cancer cells.

Clinical Applications

- Lidocaine is increasingly used in perioperative settings to reduce postoperative pain and has also been investigated for its potential role in reducing metastatic risk.

10.2 Discussion: Neural Therapeutic Regulatory Medicine with Procaine and Lidocaine

Neural therapy is a regulatory medicine approach that targets the autonomic nervous system (ANS) as a central regulator of physiological and healing processes. Through the targeted injection of local anesthetics such as procaine and lidocaine, pathological neuromodulatory triggers (“interference fields”) may be neutralized, autonomic imbalances modulated, and endogenous regulatory and healing processes supported.

These substances exert both local and systemic effects, including:

- **Modulation of the autonomic nervous system**
- **Improvement of microcirculation**
- **Anti-inflammatory effects**

Coordination and Communication Between the ANS and the Immune System

The ANS interacts closely with the immune system and modulates a variety of immunological processes:

- **Regulation of cytokines:** The sympathetic nervous system (SNS) modulates the production of pro-inflammatory cytokines such as TNF-α and IL-6, whereas the parasympathetic nervous system (PNS) contributes to anti-inflammatory regulatory responses.
- **Innervation of lymphoid organs:** The ANS influences immune responses through direct innervation of lymphoid organs, including the spleen, lymph nodes, and thymus.
- **Stress regulation:** Chronic stress may contribute to immune suppression through sustained activation of the SNS. By promoting restoration of ANS homeostasis, neural therapy may support a more balanced functional immune response.

Figure 6 schematically illustrates the coordination and bidirectional communication between the autonomic nervous system (ANS) and the immune system. The figure summarizes the principal interactions and highlights the complex neuroimmune regulatory mechanisms involved.

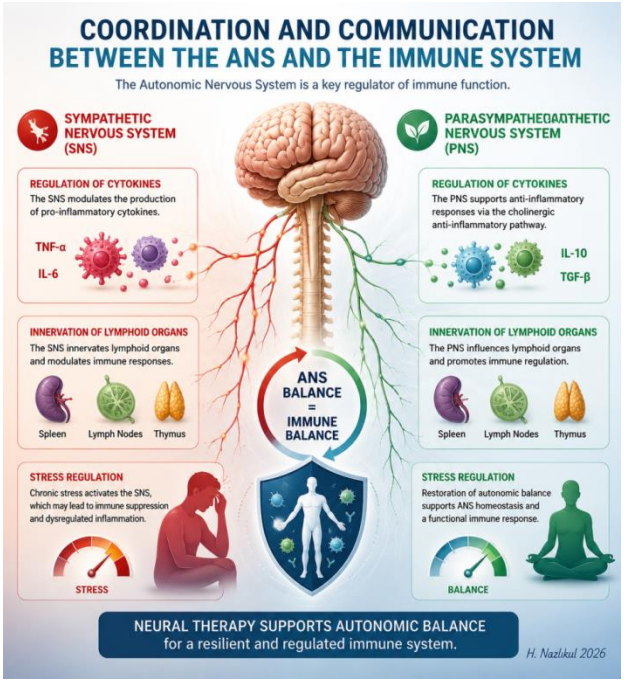


Figure 6: Coordination and bidirectional communication between the autonomic nervous system and the immune system. *Schematic representation of sympathetic and parasympathetic regulation of immune processes, including cytokine modulation, neural influence on lymphoid organs, and stress regulation. Functional autonomic balance contributes to neuroimmune homeostasis and the regulation of inflammatory processes.*

10.3 Procaine and Lidocaine: Therapeutic Potential and Economic Advantages

1. Procaine

- **Mechanisms of action:** Procaine exhibits anti-inflammatory, antioxidant, and epigenetic properties. It inhibits pro-inflammatory cytokines such as TNF-α and IL-6, neutralizes free radicals, and influences DNA methylation, potentially reactivating tumor suppressor genes.
- **Therapeutic applications:** Procaine is used in neural therapy for pain management, improvement of microcirculation, and regulation of autonomic dysfunction. In oncology, its effects on the tumor microenvironment may contribute to tumor-inhibitory mechanisms.
- **Economic advantages:** Procaine is inexpensive and can be used in a broad range of clinical applications, making it an economically attractive option for pain and inflammation management.

2. Lidocaine

- **Mechanisms of action:** Lidocaine inhibits NF-κB activation, reduces pro-inflammatory cytokine production, and modulates T-cell proliferation. It may also inhibit cancer cell migration and invasion and help regulate autonomic nervous system balance.
- **Therapeutic applications:** In addition to its use in neural therapy, lidocaine is used perioperatively in oncology to reduce postoperative pain and has been investigated for its potential to inhibit metastatic processes.
- **Economic advantages:** Lidocaine is cost-effective and has a broad range of clinical applications, making it a suitable candidate for larger clinical trials and potential integration into routine clinical practice, as supported by evidence.

10.4 Need for Further Research

Although preclinical data support the potential biological effects of procaine and lidocaine, further large-scale clinical studies are required to systematically evaluate their efficacy and safety in oncology and neural therapy.

Recommended areas for future research include:

- Long-term effects of neural therapy on cancer progression and survival outcomes
- Mechanisms underlying the potential tumor-inhibitory effects of procaine and lidocaine
- Potential synergistic interactions between neural therapy and conventional cancer treatments

10.5 Conclusion and Outlook

Procaine and lidocaine are established local anesthetics with a broad spectrum of therapeutic applications. Their integration into neural therapy offers a potentially cost-effective regulatory approach for managing chronic disorders, supporting oncological care, and modulating neuroimmune processes.

Further scientific investigation and carefully evaluated clinical applications may help clarify the full therapeutic potential of these agents, to improve patients' quality of life and determine whether they can help reduce the risk of tumor recurrence.

Procaine and lidocaine represent promising candidates for further investigation in the prevention and treatment of cancer. Their biological effects extend beyond conventional analgesia and include potential

immunomodulatory, anti-inflammatory, and epigenetic mechanisms. While procaine is of particular interest because of its epigenetic and anti-inflammatory properties, lidocaine has attracted increasing attention for its potential effects on tumor cell migration and invasion.

Summary and Perspective

- **Procaine offers a particularly interesting perspective through its potential epigenetic mechanisms of action.** Modulation of DNA methylation may contribute to the reactivation of tumor suppressor genes, thereby influencing regulatory processes relevant to tumor growth and cell proliferation.
- **Lidocaine is increasingly attracting scientific interest beyond its conventional role as a local anesthetic.** Experimental findings indicate potential antimetastatic properties, particularly through modulation of cell migration, invasion, and other tumor-biologically relevant signaling pathways.
- **Within the framework of neural therapy, procaine and lidocaine therefore acquire a broader scientific dimension.** Their potential neuroregulatory, anti-inflammatory, immunomodulatory, and epigenetic effects open new perspectives for integrative and multimodal oncological treatment concepts.

For modern oncology, this means that **neural therapy should not be regarded as a substitute for established oncological treatments, but rather as a potential complementary regulatory approach whose clinical relevance should be systematically investigated through further high-quality preclinical and clinical studies.**

Future Perspectives

- **The next crucial step is generating robust clinical evidence.** Prospective, randomized, and adequately powered clinical trials are required to systematically investigate and scientifically validate the safety, dosing, indications, and clinical efficacy of procaine and lidocaine in the oncological setting.
- **Integration into multimodal treatment concepts appears particularly promising.** Combining neural therapeutic regulatory approaches with established oncological therapies may offer new opportunities to reduce treatment-related burden, improve quality of life, and potentially enhance overall therapeutic outcomes.
- **The convergence of neuroregulation, immunomodulation, and biophysical regulatory mechanisms opens an expanded field of research.** In particular, the interplay between the autonomic nervous system, immune responses, inflammatory regulation, the tumor microenvironment, and epigenetic mechanisms should become an increasing focus of translational research.
- **In the long term, neural therapy may therefore acquire a new scientific perspective within integrative oncology:** not as an alternative to evidence-based cancer treatment, but as a potentially complementary regulatory approach within individualized, multimodal treatment strategies.
- The key question for future research is therefore not only whether procaine and lidocaine exert biological effects beyond

local anesthesia, but also **which of their regulatory mechanisms can be translated into reproducible clinical benefits—and which patient populations are most likely to derive meaningful additional benefit from them.**

DECLARATION OF CONFLICTS OF INTEREST

Declaration of Conflicts of Interest

The authors declare that they have **no conflicts of interest** related to this publication and no **competing interests** to disclose.

The authors confirm that **no competing financial interests** are associated with this work.

No human or animal studies were conducted by the authors for this contribution. The studies mentioned in this publication adhere to the **ethical guidelines** specified in their respective sources.

Funding Statement

This research **received no specific funding** from **public, commercial, or nonprofit organizations**.

Author Contributions

Prof. Dr. Hüseyin NAZLIKUL and **Prof. Dr. Fatma Gülcin URAL NAZLIKUL** contributed equally to the conception, scientific development, and intellectual content of the article *"**Procaine and Lidocaine Beyond Anesthesia: Linking Neural Regulation, Neuroinflammation, and Cancer Biology**"*

Both authors contributed their extensive clinical and scientific expertise in neural therapy, regulatory medicine, pain medicine, neurophysiology, and autonomic regulation. Emphasis was placed on the joint analysis of the mechanisms of action of procaine and lidocaine beyond their conventional local anesthetic effects, particularly regarding modulation of the autonomic nervous system, neuroinflammatory processes, immune regulation, and potential interactions with the tumor microenvironment.

Both authors also contributed equally to bringing neural therapeutic approaches together with multimodal and integrative cancer treatment strategies, and to carefully interpreting the scientific evidence behind them.

Both authors contributed equally to all major scientific and conceptual aspects of the manuscript and share responsibility for the relevant content.

Prof. Dr. Uwe REUTER and Dr. Ralf OETTMEIER , together with Prof. Dr. Hüseyin NAZLIKUL, generously shared their scientific expertise in developing the manuscript. Their contributions focused especially on procaine-based infusion, the pharmacological properties of procaine and lidocaine, and their potential applications in oncology. They carefully reviewed and thoughtfully evaluated the relevant literature, while also bringing in their expertise and previous publications in these fields. Their valuable work helped strengthen the pharmacological and scientific foundation of the relevant sections of the manuscript.

Prof. Dr. Yusuf Tamam and Prof. Dr. Murat Orak made substantial scientific contributions to this manuscript. Prof. Dr. Yusuf Tamam provided particular expertise in evaluating neurological complications in patients with cancer and supporting their clinical management. Prof. Dr. Murat Orak contributed his expertise to the sections on cancer-related pain management and oncological emergencies. Both authors helped critically evaluate the relevant literature, refine the manuscript scientifically, and prepare and improve the figures and illustrations. Their expertise and

clinical experience helped strengthen the work's interdisciplinary approach, scientific quality, and clinical relevance.

Dr. Tijen ACARKAN, PhD, contributed to the manuscript by conducting a focused review of the literature on the relevant pathophysiological mechanisms. She also helped evaluate and contextualize the scientific processes most relevant to the article's subject.

Prof. Dr. M. Dinçer Bilgin contributed to the scientific development of the manuscript, particularly by evaluating the biophysical mechanisms underlying cancer and its treatment. He provided critical insights and recommendations regarding the biological and biophysical effects of chemotherapy and radiotherapy, including treatment-related complications. He also participated in the critical review, scientific revision, and validation of the manuscript, contributing to its scientific accuracy, interdisciplinary coherence, and overall quality.

Acknowledgements

The authors would like to express their heartfelt gratitude to **Prof. Dr. Lorenz FISCHER** and **Dr. Hans BAROP** for their outstanding, longstanding contributions to the scientific development and international recognition of Neural Therapy.

Over the years, both have helped move Neural Therapy toward a more scientifically grounded, structured, and standardized medical approach. Their contributions extend well beyond their publications and written work. Through their continued dedication to medical education, their training of generations of physicians, and their active participation in national and international Neural Therapy organizations, congresses, and scientific forums, they have helped build and strengthen the field's scientific foundations.

Their dedication to integrating clinical experience with scientific reasoning, fostering professional exchange, and promoting high standards in education and clinical practice has helped shape the scientific framework on which contemporary Neural Therapy continues to develop.

The authors would also like to extend their warm appreciation to Prof. Dr. **Lorenz FISCHER** and **Dr. Hans BAROP**, honoring not only their scientific contributions but also their decades of dedicated work advancing, teaching, and supporting the international development of Neural Therapy.

We express our deepest appreciation and gratitude for their enduring contribution to the scientific foundation and future of Neural Therapy.

We would like to express our special appreciation to **Prof. Dr. Rajendra A. Badwe** and his research team for their pioneering clinical study investigating the peritumoral administration of lidocaine in patients with early breast cancer.

Published in the Journal of Clinical Oncology (2023), their findings offer important clinical evidence that local anesthetics may have biological and clinical relevance in oncology beyond their traditional role in anesthesia.

This study is especially meaningful to us because it offers a fresh scientific perspective on observations we've made in clinical practice over the years. It also helps us better understand how local anesthesia, neuroinflammatory processes, the tumor microenvironment, and disease outcomes may be connected.

We particularly acknowledge the research team's contribution to bringing clinical evidence into a field previously explored largely through experimental investigations, thereby opening new avenues for interdisciplinary research.

REFERENCES

1. Engel, R., Barop, H., Giebel, J., Ludin, S. M., & Fischer, L. (2022). The influence of modern neurophysiology on the previous definitions of “segment” and “interference field” in neural therapy. *Complementary medicine research*, *29*(3), 257-267.
2. Vinyes, D., Muñoz-Sellart, M., & Fischer, L. (2023). Therapeutic use of low-dose local anesthetics in pain, inflammation, and other clinical conditions: a systematic scoping review. *Journal of clinical medicine*, *12*(23), 7221.
3. Barop, H. (2017). *Textbook and atlas of neural therapy: diagnosis and therapy with local anesthetics*. Georg Thieme Verlag.
4. Nazlikul, H., Ural Nazlikul, F. G., Acarkan, T., Özkan, N., & Türk, A. (2026). Regulation Instead of Symptom Management: The Role of Neural Therapy in Modern Sports Medicine Concepts. *J International Journal of Public Health Research and Epidemiology*, *2*(3), 15.
5. Nazlİkul, H., Ural, F. G., Öztürk, G. T., & Öztürk, A. D. T. (2018). Evaluation of neural therapy effect in patients with piriformis syndrome. *Journal of back and musculoskeletal rehabilitation*, *31*(6), 1105-1110.
6. URAL NAZLIKUL, F. G., NAZLIKUL, H., ÖZKAN, N., ACARKAN, T., TAMAM, Y., ORAK, M., & BILGIN, M. Long-Term Effects of Neural Therapy in Fibromyalgia–A Retrospective Multicenter Analysis Effectiveness of Neural Therapy in Patients with Fibromyalgia. *IntClinc Med Case Rep Jour*.
7. Badwe, R. A., Parmar, V., Nair, N., Joshi, S., Hawaldar, R., Pawar, S., ... & Gupta, S. (2023). Effect of peritumoral infiltration of local anesthetic before surgery on survival in early breast cancer. *Journal of Clinical Oncology*, *41*(18), 3318-3328.
8. Nazlikul, H., & Nazlikul, F. G. U. (2026). Sacroiliac Joint or Iliosacral Joint. In *Neuraltherapeutic Medicine: An Evolution of Neural Therapy* (pp. 575-593). Cham: Springer Nature Switzerland.
9. Nazlikul, H., Ural Nazlikul, F. G., & Tamam, Y. (2025). The Significance of Thoracic Blockages for the Autonomic Nervous System–Neural Therapy and Its Clinical Relevance. Recent Adv Clin Trials. 2025; 5 (1); 1-17. DOI: 10.33425/2771-9057.1054. *Volume*, *5*, 2.
10. Nazlikul, H., & Ural, F. (2026). The diaphragm: recognizing functional disorders and treating them effectively with neural therapy and manual medicine Das Zwerchfell: Funktionsstörungen erkennen und wirksam behandeln mit Neuraltherapie und manueller Medizin. *Manuelle Medizin*, *64*(Suppl 1).
11. Fischer, L. (2019). Neural Therapy: Neurophysiology, Injection Technique and Therapy Proposals. *4th, Completely Revised Edition.*
12. Fischer, L., Ludin, S. M., Thommen, D., & Hausammann, R. (2010). Application for the adoption of interference field therapy (neural therapy according to Huneke) into the health benefit basket of the compulsory health insurance. *Submitted to the Swiss Federal Office of Public Health.*

13. Fischer, L. (2026). Communication in the Neuroimmune System. In *Neuraltherapeutic Medicine: An Evolution of Neural Therapy* (pp. 273-284). Cham: Springer Nature Switzerland.
14. Shiratori Tusita, L. N., & Fischer, L. (2023). Chronic therapy-resistant neck pain in a fifty-year-old man: the role of partially impacted third molars–case report and new pathophysiological insights. *Complementary Medicine Research*, *30*(3), 270-274.
15. Kronenberg, R. M., Ludin, S. M., & Fischer, L. (2018). Severe Case of Chronic Pelvic Pain Syndrome: Recovery after Injection of Procaine into the Vesicoprostatic Plexus—Case Report and Discussion of Pathophysiology and Mechanisms of Action. *Case reports in urology*, *2018*(1), 9137215.
16. Cassuto, J., Sinclair, R., & Bonderovic, M. (2006). Anti-inflammatory properties of local anesthetics and their present and potential clinical implications. *Acta Anaesthesiologica Scandinavica*, *50*(3), 265-282.
17. Vinyes, D., Muñoz-Sellart, M., & Fischer, L. (2023). Therapeutic use of low-dose local anesthetics in pain, inflammation, and other clinical conditions: a systematic scoping review. *Journal of clinical medicine*, *12*(23), 7221.
18. Lopes, C. A., & Fischer, L. (2023). A case of severe trigeminal neuralgia: recovery by means of stellate ganglion block with procaine. Discussion of possible mechanisms of action. *Journal of International Medical Research*, *51*(4), 03000605231164479.
19. Oettmeier, R., Nazlikul, H., Pinilla Bonilla, L., Ural Nazlikul, F., & Reuter, U. (2025). More than One Century: Intravenous Procaine Therapy-a Systematic Review. *Int Clinc Med Case Rep Jour*, *4*(12), 1-25.
20. Ural Nazlikul, F. G., & Nazlikul, H. (2025). Diaphragmatic dysfunctions and their treatment: neural therapy and manual medicine as effective approaches. *Int Clinc Med Case Rep Jour. 2025; 4 (1): 1*, *8*.
21. Jänig, W. (2006). The integrative action of the autonomic nervous system. *Neurobiology of homeostasis*.
22. Jänig, W. (2014). Sympathetic nervous system and inflammation: a conceptual view. *Autonomic Neuroscience*, *182*, 4-14.
23. Jänig, W., & Baron, R. (2006). Is CRPS I a neuropathic pain syndrome?. *Pain*, *120*(3), 227-229.
24. Jänig, W. (2016). Neurocardiology: a neurobiologist's perspective. *The Journal of physiology*, *594*(14), 3955.
25. Schaible, H. G. (2014). Nociceptive neurons detect cytokines in arthritis. *Arthritis research & therapy*, *16*(5), 470.
26. Vinyes, D., Muñoz-Sellart, M., Colilles, G. A., & Gurevich, M. I. (2025). Inyecciones de Procaína en Puntos de Tensión Miofascial para el Tratamiento de Trastornos de Ansiedad: Serie de Casos.
27. Bellinger, D. L., & Lorton, D. (2018). Sympathetic nerve hyperactivity in the spleen: causal for nonpathogenic-driven chronic immune-mediated inflammatory diseases (IMIDs)?. *International Journal of Molecular Sciences*, *19*(4), 1188.
28. Bellinger, D. L., & Lorton, D. (2022). Sympathetic nerves and innate immune

system in the spleen: Implications of impairment in HIV-1 and relevant models. *Cells*, *11*(4), 673.

29. Bellinger, D. L., Nance, D. M., & Lorton, D. (2013). Innervation of the immune system. *The Wiley-Blackwell Handbook of Psychoneuroimmunology*, 24-72.
30. Jänig, W. (2014). Sympathetic nervous system and inflammation: a conceptual view. *Autonomic Neuroscience*, *182*, 4-14.
31. Lubahn, C. L., Lorton, D., Schaller, J. A., Sweeney, S. J., & Bellinger, D. L. (2014). Targeting α-and β-adrenergic receptors differentially shifts Th1, Th2, and inflammatory cytokine profiles in immune organs to attenuate adjuvant arthritis. *Frontiers in immunology*, *5*, 346.
32. Bai, R., Chen, N., Li, L., Du, N., Bai, L., Lv, Z., ... & Cui, J. (2020). Mechanisms of cancer resistance to immunotherapy. *Frontiers in oncology*, *10*, 527366.
33. Nazlikul, H. (2010). Neurovegetativum, Blockaden und manuelle Medizin. *Manuelle Medizin*, *48*(6), 435-439.
34. Nazlikul, H. (2010). Thorakale Blockaden und Wirkung der Neuraltherapie in Kombination mit manueller Therapie. *Manuelle Medizin*, *48*(5), 329-338.
35. Nazlıkul, H. (2016). REFLEKS SEMPATİK DİSTROFİ TEDAVİSİNDE NÖRALTERAPİ UYGULANMASI ÇÖZÜM OLABİLİR. *Bilimsel Tamamlayıcı Tıp Regülasyon ve Nöral Terapi Dergisi*, *10*(1), 1-4.
36. Nazlıkul, H. (2015). NAZLIKUL'A GÖRE LİMBİK SİSTEMİN NÖROJENİK YANITININ, NÖRALTERAPİ VE UYGULAMALI KİNEZİYOLOJİ (AK) BÜTÜNLÜĞÜ İÇİNDE ÇÖZÜMÜ. *Bilimsel Tamamlayıcı Tıp Regülasyon ve Nöral Terapi Dergisi*, *9*(2), 1-6.
37. Nazlikul H. Nöralterapi Ders Kitabı [Neural Therapy Textbook]. 4. Baskı. İstanbul: Nobel Tıp Kitabevleri; 2024.
38. Nazlikul H, Ural Nazlikul FG, eds. Nöralterapi Atlası: Temel ve İleri Uygulamalar [Atlas of Neural Therapy: Basic and Advanced Techniques]. 1. Baskı. Ankara: Ankara Nobel Tıp Kitabevleri; 2026. ISBN: 978-625-8919-09-7.
39. Papathanasiou, G. S. (2020). Local anesthetics and Covid19 associated acute respiratory distress syndrome: a new therapeutic indication. *Clin. Res. Open Access*, *6*(10.16966), 2469-6714.
40. Reuter, U. R., Oettmeier, R., & Nazlikul, H. (2017). Procaine and procaine-base-infusion: a review of the safety and fields of application after twenty years of use. *Clin Res Open Access*, *4*(1).
41. NAZLIKUL, H., & NAZLIKUL, F. G. U. (2023). Regülasyon Tıbbında Nöralterapi ve Manuel Terapi Uygulamalarının Yeri. *Turkiye Klinikleri Sports Medicine-Special Topics*, *9*(1), 8-14.
42. Nazlikul, H., & Gülçin Ural Nazlikul, F. (2025). Diagnostik und Therapie der ersten Rippe: eine neue Technik. *Manuelle Medizin*, *63*(2), 123-128.
43. Nazlikul, H., & Nazlikul, F. G. U. (2026). The Cervical Spine. In *Neuraltherapeutic Medicine: An Evolution of Neural Therapy* (pp. 505-527). Cham: Springer Nature Switzerland.
44. Bustamante, C., Pinilla, L., & Amaris, O. (2023). An approach to acute SARS-CoV-2 management with complementary Neuraltherapeutic medicine: a Case report.

Clinical Medicine Insights: Case Reports, *16*, 11795476231159584.

45. Tracey, I., & Mantyh, P. W. (2007). The cerebral signature for pain perception and its modulation. *Neuron*, *55*(3), 377-391.
46. Morris, T., & Tracey, J. Lidocaine: its effects on wound healing. *Br. J. Surgery. 64: 902*, *903*.
47. Brooks, J., & Tracey, I. (2005). From nociception to pain perception: imaging the spinal and supraspinal pathwaysRadiology (50). *Pain Practice*, *5*(4), 384.
48. Tamam, Y., Yokuş, B., Tamam, C., Yüceer, H., Karahan, S., Em, B., ... & Tüzün, E. (2023). The effect of lidocaine on the experimental model of streptozotocin-induced Alzheimer's disease. *Archives of Neuropsychiatry*, *60*(1), 68.
49. Tamam, Y., Tamam, C., Goksel, A., Tamam, B., & Nazlikul, H. (2017). Peripheral lidocaine injection (neural therapy) in the treatment of migraine in pregnancy. *Journal of the Neurological Sciences*, *381*, 946.
50. Tamam, Y., Özdemir, H., Gedik, A., Tamam, C., & Nazlıkul, H. (2025). Efficacy of peripheral lidocaine application in the treatment of neurogenic detrusor overactivity in multiple sclerosis patients. *Journal of the Neurological Sciences*, *480*.
51. URAL NAZLIKUL, F. G., NAZLIKUL, H., ÖZKAN, N., ACARKAN, T., TAMAM, Y., ORAK, M., & BILGIN, M. Long-Term Effects of Neural Therapy in Fibromyalgia–A Retrospective Multicenter Analysis Effectiveness of Neural Therapy in Patients with Fibromyalgia. *IntClinc Med Case Rep Jour*.
52. Fischer, L., Barop, H., Ludin, S. M., & Schaible, H. G. (2022). Regulation of acute reflectory hyperinflammation in viral and other diseases by means of stellate ganglion block. A conceptual view with a focus on Covid-19. *Autonomic Neuroscience*, *237*, 102903.
53. Fischer, L., de la Vega, K. P., & Fleckenstein, J. (2013). Neuraltherapie: Injektion an das Ganglion stellatum. *Zeitschrift für Komplementärmedizin*, *5*(06), 27-32.
54. Fleckenstein, J., Neuberger, E. W., Bormuth, P., Comes, F., Schneider, A., Banzer, W., ... & Simon, P. (2021). Investigation of the sympathetic regulation in delayed onset muscle soreness: Results of an RCT. *Frontiers in Physiology*, *12*, 697335.
55. Pfister, & Fischer. (2009). Die Behandlung des komplexen regionalen Schmerzsyndroms der oberen Extremität mit wiederholter Lokalanästhesie des Ganglion stellatum. *Praxis*, *98*(5), 247-257.
56. Türk, A., & Nazlikul, H. (2024). Stellat Gangliyon Blokajı ve Kardiyovasküler Hastalıklarda Nöralterapi Yaklaşımı= Stellate Ganglion Blockade and the Role of Neural Therapy in Cardiovascular Diseases. *Kalp, Damar ve Ödem; Beslenme ve Egzersiz içinde. İÜC Üniversite Yayınev, İstanbul*, S115-124.
57. Aslan, A. (1960). Procaine therapy in old age and other disorders (Novocaine factor H3). *Gerontologia Clinica*, *2*(3), 148-176.

58. Lüth, P. (1960). A review of procaine-therapy in elderly individuals. *Journal of Gerontology*, *15*(4), 395-399.
59. Bai, F., Michel, R., & Rossignol, P. (1984). Effects of procaine on the oxidative phosphorylation of brain mitochondria from senescent rats. *Mechanisms of ageing and development*, *26*(2-3), 277-282.
60. Grădinaru, D., Margină, D., & Borșa, C. (2009). In vitro studies regarding the antioxidant effects of procaine, Gerovital H3 and Aslavital. *Revue Roumaine de Chimie*, *54*(9), 761-766.
61. Gradinaru, D., Ungurianu, A., Margina, D., Moreno-Villanueva, M., & Bürkle, A. (2021). Procaine–the controversial geroprotector candidate: new insights regarding its molecular and cellular effects. *Oxidative medicine and cellular longevity*, *2021*(1), 3617042.
62. Scholz, A. (2002). Mechanisms of (local) anaesthetics on voltage-gated sodium and other ion channels. *British journal of anaesthesia*, *89*(1), 52-61.
63. Häring, C., Jungwirth, J., Schroeder, J., Löffler, B., Engert, B., & Ehrhardt, C. (2023). The local anaesthetic procaine prodrugs ProcCluster® and procaine hydrochloride impair SARS-CoV-2 replication and egress in vitro. *International journal of molecular sciences*, *24*(19), 14584.
64. Häring, C., Schroeder, J., Jungwirth, J., Löffler, B., Henke, A., Engert, B., & Ehrhardt, C. (2024). ProcCluster® and procaine hydrochloride inhibit the replication of influenza A virus in vitro. *Frontiers in Microbiology*, *15*, 1422651.
65. König, S., Schroeder, J., Heinekamp, T., Brakhage, A. A., Löffler, B., Engert, B., & Ehrhardt, C. (2024). ProcCluster® and procaine hydrochloride inhibit the growth of Aspergillus species and exert antimicrobial properties during coinfection with influenza A viruses and A. fumigatus in vitro. *Frontiers in Cellular and Infection Microbiology*, *14*, 1445428.
66. Jungwirth, J., Siegert, L., Gauthier, L., Henke, A., Krämer, O. H., Engert, B., & Ehrhardt, C. (2025). The Procaine-Based ProcCluster® Impedes the Second Envelopment Process of Herpes Simplex Virus Type 1. *International journal of molecular sciences*, *26*(15), 7185.
67. Villar-Garea, A., Fraga, M. F., Espada, J., & Esteller, M. (2003). Procaine is a DNA-demethylating agent with growth-inhibitory effects in human cancer cells. *Cancer research*, *63*(16), 4984-4989.
68. Sun, Y., Li, Y., Bao, Y., Meng, S., Sun, Y., Schumann, G., ... & Shi, J. (2020). Brief report: increased addictive internet and substance use behavior during the COVID-19 pandemic in China. *The American journal on addictions*, *29*(4), 268-270.
69. Schumann, S., Scherthan, H., Frank, T., Lapa, C., Müller, J., Seifert, S., ... & Eberlein, U. (2020). DNA damage in blood leukocytes of prostate cancer patients undergoing PET/CT examinations with [68Ga] Ga-PSMA I&T. *Cancers*, *12*(2), 388.
70. Schumann, N. A., Mendonça, A. S., Silveira, M. M., Vargas, L. N., Leme, L. O., de Sousa, R. V., & Franco, M. M. (2020). Procaine and S-adenosyl-l-homocysteine affect the expression of

genes related to the epigenetic machinery and change the DNA methylation status of in vitro cultured bovine skin fibroblasts. *DNA and Cell Biology*, *39*(1), 37-49.

71. Schumann, U., Zhang, H. N., Sibbritt, T., Pan, A., Horvath, A., Gross, S., ... & Preiss, T. (2020). Multiple links between 5-methylcytosine content of mRNA and translation. *BMC biology*, *18*(1), 40.
72. Oettmeier, R., & Pinilla Bonilla, L. B. (2026). The Systemic Use of Procaine. In *Neuraltherapeutic Medicine: An Evolution of Neural Therapy* (pp. 615-633). Cham: Springer Nature Switzerland.
73. Perls, T. (2013). The reappearance of procaine hydrochloride (Gerovital H3) for antiaging. *Journal of the American Geriatrics Society*, *61*(6).
74. Saha, F. J., & Wander, R. (2014). Das Störfeld als neuromodulativer Trigger auf allen Ebenen. *Deutsche Zeitschrift für Akupunktur*, *57*(2), 6-9.
75. Myles, P. S., Peyton, P., Silbert, B., Hunt, J., Rigg, J. R., & Sessler, D. I. (2011). Perioperative epidural analgesia for major abdominal surgery for cancer and recurrence-free survival: randomised trial. *Bmj*, *342*.
76. Hollmann, M. W., Ritter, C. H., Henle, P., De Klaver, M., Kamatchi, G. L., & Durieux, M. E. (2001). Inhibition of m3 muscarinic acetylcholine receptors by local anaesthetics. *British journal of pharmacology*, *133*(1), 207-216.
77. Hollmann, M. W., Herroeder, S., Kurz, K. S., Hoenemann, C. W., Struemper, D., Hahnenkamp, K., & Durieux, M. E. (2004). Time-dependent inhibition of G protein–coupled receptor signaling by local anesthetics. *Anesthesiology*, *100*(4), 852-860.
78. Picardi, S., Lirk, P., Boeckh, R., & Hollmann, M. W. (2015). Adjuvanzien in der modernen Anästhesie–Lidocain. *AINS-Anästhesiologie· Intensivmedizin· Notfallmedizin· Schmerztherapie*, *50*(05), 322-327.
79. Muth-Selbach, U., Hermanns, H., Stegmann, J. U., Kollosche, K., Freynhagen, R., Bauer, I., & Lipfert, P. (2009). Antinociceptive effects of systemic lidocaine: involvement of the spinal glycinergic system. *European journal of pharmacology*, *613*(1-3), 68-73.
80. Lirk, P., Berger, R., Hollmann, M. W., & Fiegl, H. (2012). Lidocaine time-and dose-dependently demethylates deoxyribonucleic acid in breast cancer cell lines in vitro. *British journal of anaesthesia*, *109*(2), 200-207.
81. Kranke, P., Jokinen, J., Pace, N. L., Schnabel, A., Hollmann, M. W., Hahnenkamp, K., ... & Weibel, S. (2015). Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *Cochrane Database of Systematic Reviews*, (7).
82. Weibel, S., Jokinen, J., Pace, N. L., Schnabel, A., Hollmann, M. W., Hahnenkamp, K., ... & Kranke, P. (2016). Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. *British journal of anaesthesia*, *116*(6), 770-783.
83. Becker, J. E., Price, J. L., Leonard, D., Suris, A., Kandil, E., Shaw, M., ... & Adinoff, B. (2020). The efficacy of

lidocaine in disrupting cocaine cue-induced memory reconsolidation. *Drug and alcohol dependence*, *212*, 108062.

84. Becker, D. E., & Reed, K. L. (2012). Local anesthetics: review of pharmacological considerations. *Anesthesia progress*, *59*(2), 90-102.
85. Zink, W., Steinfeldt, T., & Wiesmann, T. (2020). Bestandsaufnahme der Lokalanästhetika 2020. *Der Anaesthesist*, *69*(5), 301-313.
86. Smok, A. (2020). *Einfluss von Lidocain auf die sympathisch vermittelte Vasokonstriktion an der unbehaarten Pfotenhaut der Ratte* (Doctoral dissertation, Dissertation, Düsseldorf, Heinrich-Heine-Universität, 2020).
87. Bruning, G., Gerontopoulou, S., & Woitalla-Bruning, J. (2025). Sicherer Umgang mit Lokalanästhetika. *Phlebologie*, *54*(06), 234-235.
88. Grifka, J., Götz, J., Fenk-Mayer, A., & Benditz, A. (2023). Injektionstherapie bei Zervikal-und Lumbalsyndromen: Grundlagen, Indikationen und allgemeine Durchführung. *Die Orthopädie*, *52*(12), 1017-1024.
89. Zink, T. (2003). *Extrakapsuläre Kataraktextraktion unter Oberflächenanästhesie mit Tetracain (1%): Tropfen-Gel* (Doctoral dissertation, lmu).
90. Yousefshahi F, Predescu O, Asenjo JF. The efficacy of systemic lidocaine in the management of chronic pain: A literature review. Anesth Pain Med. 2017;7(3):e44732. doi: 10.5812/aapm.44732
91. Lahav, M., Levite, M., Bassani, L., Lang, A., Fidder, H., Tal, R., ... & Chowers, Y. (2002). Lidocaine inhibits secretion of IL-8 and IL-1 β and stimulates secretion of IL-1 receptor antagonist by epithelial cells. *Clinical & Experimental Immunology*, *127*(2), 226-233.
92. Lang, A., Horin, S. B., Picard, O., Fudim, E., Amariglio, N., & Chowers, Y. (2010). Lidocaine inhibits epithelial chemokine secretion via inhibition of nuclear factor κB activation. *Immunobiology*, *215*(4), 304-313.
93. Cassuto, J., Sinclair, R., & Bonderovic, M. (2006). Anti-inflammatory properties of local anesthetics and their present and potential clinical implications. *Acta Anaesthesiologica Scandinavica*, *50*(3), 265-282.
94. Sadaf, S., Malik, N. A., Kousar, R. R., & Haq, H. D. (2025). Efficacy of nebulized lidocaine, salbutamol, and beclomethasone plus salbutamol in post-COVID ARDS patients on non-invasive ventilation; a randomized controlled trial. *Anaesthesia, Pain & Intensive Care*, *29*(8), 890-896.
95. Lahat, A., Horin, S. B., Lang, A., Fudim, E., Picard, O., & Chowers, Y. (2008). Lidocaine down-regulates nuclear factor-κB signalling and inhibits cytokine production and T cell proliferation. *Clinical & Experimental Immunology*, *152*(2), 320-327.
96. Lirk, P., Berger, R., Hollmann, M. W., & Fiegl, H. (2012). Lidocaine time-and dose-dependently demethylates deoxyribonucleic acid in breast cancer cell lines in vitro. *British journal of anaesthesia*, *109*(2), 200-207.
97. Liepinsh, E., Skapare, E., Kuka, J., Makrecka, M., Cirule, H., Vavers, E., ... & Dambrova, M. (2013). Activated

peroxisomal fatty acid metabolism improves cardiac recovery in ischemia-reperfusion. *Naunyn-Schmiedeberg's archives of pharmacology*, *386*(6), 541-550.

98. Kuka, M., & Iannacone, M. (2018). Viral subversion of B cell responses within secondary lymphoid organs. *Nature Reviews Immunology*, *18*(4), 255-265.
99. Piegeler, T., Dull, R. O., Hu, G., Castellon, M., Chignalia, A. Z., Koshy, R. G., ... & Minshall, R. D. (2014). Ropivacaine attenuates endotoxin plus hyperinflation-mediated acute lung injury via inhibition of early-onset Src-dependent signaling. *BMC anesthesiology*, *14*(1), 57.
100. Ma, L., Cong, W., Zhang, H., Zhang, W., Zhan, Y., Liu, Y., ... & Zhao, L. (2025). Lidocaine inhibits the proliferation of non-small cell lung cancer and exerts anti-inflammatory effects through the TLR-9/MyD88/NF-κb pathway. *DNA and Cell Biology*, *44*(3), 161-171.
101. Zhang, S., Li, Y., & Tu, Y. (2021). Lidocaine attenuates CFA-induced inflammatory pain in rats by regulating the MAPK/ERK/NF-κB signaling pathway. *Experimental and therapeutic medicine*, *21*(3), 211.
102. Sabit, H., Samy, M. B., Said, O. A., & El-Zawahri, M. M. (2016). Procaine induces epigenetic changes in HCT116 colon cancer cells. *Genetics research international*, *2016*(1), 8348450.
103. Djordjevic, B. (1983). Variable interaction of heat and procaine in potentiation of radiation lethality in mammalian cells of neoplastic origin. *International Journal of Radiation Biology and Related Studies in Physics, Chemistry and Medicine*, *43*(4), 399-409.
104. Chamaraux-Tran, T. N. (2019). *Effets antitumoraux des anesthésiques locaux dans le cancer du sein* (Doctoral dissertation, Université de Strasbourg).
105. Goneppanavar, U., & Kaur, J. (2021). Anesthesia and Cancer Recurrence. In *Textbook of Onco-Anesthesiology* (pp. 13-41). Singapore: Springer Singapore.
106. Kwong, D. L., Sham, J. S., Au, G. K., Chua, D. T., Kwong, P. W., Cheng, A. C., ... & Choy, D. D. (2004). Concurrent and adjuvant chemotherapy for nasopharyngeal carcinoma: a factorial study. *Journal of clinical oncology*, *22*(13), 2643-2653.
107. Yamane, K., Naozaki, Y., & Worarad, K. (2020, December). Physiology and promotion of seed germination in ornamental peach. In *III Asian Horticultural Congress-AHC2020 1312* (pp. 197-202).
108. Brueckner, B., & Lyko, F. (2004). DNA methyltransferase inhibitors: old and new drugs for an epigenetic cancer therapy. *Trends in pharmacological sciences*, *25*(11), 551-554.
109. Schumann, N. A., Mendonça, A. S., Silveira, M. M., Vargas, L. N., Leme, L. O., de Sousa, R. V., & Franco, M. M. (2020). Procaine and S-adenosyl-l-homocysteine affect the expression of genes related to the epigenetic machinery and change the DNA methylation status of in vitro cultured bovine skin fibroblasts. *DNA and Cell Biology*, *39*(1), 37-4
110. Villar-Garea A, Fraga MF, Espada J, Esteller M (2003). Procaine is a DNA-Demethylating Agent with Growth-

inhibitory Effects in Human Cancer Cells. Cancer Res 63: 4984–4989.

111. Villar-Garea A (2005). Epigenetic transcriptional repression of tumour suppressor genes and its reversion by drugs. Doctoral thesis. Chemical Sciences. Department of Biochemistry and Molecular Biology, University of Valencia, Mayo, USA.
112. Tada M, Imazeki F, Fukai K, Sakamoto A, Arai M, et al. (2007). Procaine inhibits the proliferation and DNA methylation in human hepatoma cells. Hepatol Int 1: 355–364.
113. Sabit H, Samy MB, Said O, El-Zawahri MM (2016). Procaine Induces Epigenetic Changes in HCT116 Colon Cancer Cells. Genetics Research International 2016: 8348450.
114. Grandhi, R. K., & Perona, B. (2020). Mechanisms of action by which local anesthetics reduce cancer recurrence: a systematic review. *Pain Medicine*, *21*(2), 401-414.
115. NAZLIKUL, H., NAZLIKUL, F. U., BILGIN, M., ACARKAN, T., ÖZKAN, N., & TAMAM, Y. Neural Therapy in Migraine: Clinical Evidence for a Holistic Therapeutic Approach–Analysis of 464 Cases. IntClinc Med Case Rep Jour. 2025; 4 (4): 1-7. *DOI: https://doi. org/10.5281/zenodo, 15262178.*
116. Jılta, O., Açanal, M. H., Velayi, M., Jilta, G. Y., & Nazlıkul, H. (2025). Effects of neuraltherapy in post-traumatic paraplegia: A case study of significant and permanent improvement in a cat. *Journal of Istanbul Veterinary Sciences*, *9*(1), 15-22.
117. Ural, F. G., Öztürk, G. T., & Nazlıkul, H. (2017). Evaluation of neural therapy effects in patients with lateral epicondylitis: a randomized controlled trial. *Ankara Medical Journal*, *17*(4), 260-266.
118. Seifen, A. B., Ferrari, A. A., Seifen, E. E., Thompson, D. S., & Chapman, J. (1979). Pharmacokinetics of intravenous procaine infusion in humans. *Anesthesia & Analgesia*, *58*(5), 382-386.
119. Jan, R., Akim, A., Zafar, M. N., Sung, Y. Y., & Muhammad, T. S. T. (2020). Breast cancer: a global concern, diagnostic and therapeutic perspectives, mechanistic targets in drug development. *Advanced Pharmaceutical Bulletin*, *11*(4), 580.
120. Piegeler, T., Votta-Velis, E. G., Liu, G., Place, A. T., Schwartz, D. E., Beck-Schimmer, B., ... & Borgeat, A. (2012). Anti-metastatic potential of amide-linked local anesthetics: Inhibition of lung adenocarcinoma cell migration and inflammatory Src signaling independent of sodium channel blockade. *Anesthesiology*, *117*(3), 548.
121. Piegeler, T., Votta-Velis, E. G., Bakhshi, F. R., Mao, M., Carnegie, G., Bonini, M. G., ... & Minshall, R. D. (2014). Endothelial barrier protection by local anesthetics: ropivacaine and lidocaine block tumor necrosis factor-α–induced endothelial cell Src activation. *Anesthesiology*, *120*(6), 1414.
122. Piegeler, T., Schläpfer, M., Dull, R. O., Schwartz, D. E., Borgeat, A., Minshall, R. D., & Beck-Schimmer, B. (2015). Clinically relevant concentrations of lidocaine and ropivacaine inhibit TNFα-induced invasion of lung adenocarcinoma

cells in vitro by blocking the activation of Akt and focal adhesion kinase. *BJA: British Journal of Anaesthesia*, *115*(5), 784-791.

123. Zhang, C., Xie, C., & Lu, Y. (2021). Local anesthetic lidocaine and cancer: insight into tumor progression and recurrence. *Frontiers in oncology*, *11*, 669746.
124. Sun, D., Li, Y. C., & Zhang, X. Y. (2021). Lidocaine promoted ferroptosis by targeting miR-382-5p/SLC7A11 axis in ovarian and breast cancer. *Frontiers in pharmacology*, *12*, 681223.
125. Liu, C., Yu, M., Li, Y., Wang, H., Xu, C., Zhang, X., ... & Guo, X. (2021). Lidocaine inhibits the metastatic potential of ovarian cancer by blocking NaV1. 5-mediated EMT and FAK/Paxillin signaling pathway. *Cancer medicine*, *10*(1), 337-349.
126. Zhang, H., Qu, M., Guo, K., Wang, Y., Gu, J., Wu, H., ... & Miao, C. (2022). Intraoperative lidocaine infusion in patients undergoing pancreatectomy for pancreatic cancer: a mechanistic, multicentre randomised clinical trial. *British journal of anaesthesia*, *129*(2), 244-253.
127. Takaishi, K., Kitahata, H., & Kawahito, S. (2013). Local anesthetics inhibit nitric oxide production and L-arginine uptake in cultured bovine aortic endothelial cells. *European Journal of Pharmacology*, *704*(1-3), 58-63.
128. Haraguchi-Suzuki, K., Kawabata-Iwakawa, R., Suzuki, T., Suto, T., Takazawa, T., & Saito, S. (2022). Local anesthetic lidocaine-inducible gene, growth differentiation factor-15 suppresses the growth of cancer cell lines. *Scientific reports*, *12*(1), 14520.
129. Sessler, D. I., Bao, X., Leiman, D., Song, J., Chittenden, J., Voelkner, A., ... & Gadsden, J. (2025). A phase I study of the pharmacokinetics, pharmacodynamics, and safety of liposomal bupivacaine for sciatic nerve block in the popliteal fossa for bunionectomy. *The Journal of Clinical Pharmacology*, *65*(4), 441-451.
130. Ostović, H., Šimac, B., Pražetina, M., Bradić, N., & Peršec, J. (2025). The effect of intravenous lidocaine, ketamine, and lidocaine–ketamine combination in colorectal cancer surgery: a randomized controlled trial. *Anesthesia & Analgesia*, *140*(1), 67-76.
131. Darabad, R. R., Kalangara, J. P., & Woodbury, A. (2020). Case series: cancer-related facial pain treated with stellate ganglion block. *Palliative Medicine Reports*, *1*(1), pmr-2020.
132. Small, A., Fetiveau, M., Smith, R., & Colditz, I. (2021). Three studies evaluating the potential for lidocaine, bupivacaine or procaine to reduce pain-related behaviors following ring castration and/or tail docking in lambs. *Animals*, *11*(12), 3583.
133. Ungurianu, A., Margina, D., Borsa, C., Ionescu, C., von Scheven, G., Oziol, L., ... & Moreno-Villanueva, M. (2020). The Radioprotective Effect of Procaine and Procaine-Derived Product Gerovital H3 in Lymphocytes from Young and Aged Individuals. *Oxidative Medicine and Cellular Longevity*, *2020*(1), 3580934.
134. Xu, L., Mu, X., Liu, M., Wang, Z., Shen, C., Mu, Q., ... & Wang, W. (2023). Novel thieno [2, 3-b] quinoline-procaine hybrid

molecules: A new class of allosteric SHP-1 activators evolved from PTP1B inhibitors. *Chinese Chemical Letters*, *34*(8), 108063.

135. Zhang, J. G., Zhong, L. F., Zhang, M., & Xia, Y. X. (1992). Protection effects of procaine on oxidative stress and toxicities of renal cortical slices from rats caused by cisplatin in vitro. *Archives of toxicology*, *66*(5), 354-358.