

The amide local anesthetic lidocaine in cancer surgery— potential antimetastatic e...

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Introduction

Surgery is a main part of the treatment of most cancers. In 2015, 80% of the 15.2 million new diagnosis cases of cancer needed surgery ([1](#)). However, the perioperative period might be critical: the long-term follow-up of a cohort of 1,173 patients who underwent mastectomy for breast cancer suggested a bimodal recurrence pattern with an early broad peak at about 18 months after surgery and a second one at about 60 months. If the second peak might be the natural outcome of the breast cancer disease, the first one might result from an early escape of cancer cells from dormancy as well as for recurrence driven by surgery ([2](#)). Several competing hypotheses have been proposed to explain this phenomenon ([3](#)): surgery might lead to pro-tumorigenic inflammatory changes during the perioperative period, such as increased levels of pro-inflammatory cytokines, prostaglandins, or catecholamines, which might also affect the competence of parts of the innate immune system, such as natural killer (NK) cells, which are crucial for the detection and disintegration of circulating tumor cells (CTCs) ([4](#)). The surgical stimulus might also increase levels of growth factors like vascular endothelial growth factor (VEGF), basic fibroblast growth factor, transforming growth factor beta (TGF- β), heparin-binding epidermal growth factor *-like growth factor*, or *platelet-derived growth factor*, which have all been linked to tumor growth and metastasis ([5-7](#)). By inducing this pro-inflammatory environment in combination with its effects on immune surveillance, surgery itself might therefore enhance cancer cell dissemination and escape from immune surveillance and other hallmarks of cancer such as entrapment, invasion, migration, adhesion, or increasing of NETs ([3](#)). Added to the fact <https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

that primary tumor removal may promote tumor cell dissemination ([8](#), [9](#)), those effects could enhance establishment of new metastatic foci or accelerate growth of micrometastases ([5](#)).

As anesthesia is a key element of the perioperative period, it has been hypothesized that it could possibly also have an influence on cancer recurrence after surgery. On the one hand, some anesthetic and analgesic drug receptors are overexpressed in tumor tissues and are associated with metastasis ([10](#)). On the other hand, several retrospective studies have suggested an impact of anesthesia on cancer survival ([11](#)); notably, regional anesthesia might be associated with a reduced risk of cancer relapse or recurrence in some studies, although there are also studies reporting no effect ([12](#) - [14](#)). One of the proposed hypotheses to explain these observations may be related to the anti-inflammatory effects of local anesthetics (LAs) affecting proliferation, migration, or invasion of cancer cells as well ([15](#) - [17](#)). This review aims at summarizing different properties of amide-linked LAs bearing the potential to exert antitumor or antimetastatic effects. Lidocaine might be of particular interest, as this LA can be used intravenously for multimodal analgesia ([18](#)). Perioperative intravenous (IV) lidocaine has already been shown to reduce postoperative pain and opioid requirements ([19](#)), appears to be safe, and might not only reduce inflammatory markers but also the length of hospitalization, e. g., after colorectal surgery ([20](#)). The drug might therefore be an ideal candidate for a clinical trial evaluating the effects of amide-linked LAs on recurrence after cancer surgery.

Anti-Inflammatory Effects of LAs *In Vitro* and *In Vivo*

Anti-inflammatory effects of LAs are well-known and have been studied extensively ([21](#)). However, the influence of LAs on the integrity of the endothelial barrier might be crucial for a possible inhibitory effect on the generation of metastasis during the perioperative period ([14](#)). CTCs—released into the circulation from the primary tumor during surgical removal of the latter—are able to form new (microscopic) metastatic lesions ([22](#), [23](#)), which will finally determine the patient's fate, even after a complete surgical removal of the primary tumor ([24](#), [25](#)). Endothelial barrier function is mostly regulated by Src protein tyrosine kinase (Src) and the activation of the enzyme will lead to a loss in endothelial barrier integrity *via* phosphorylation of its main substrate caveolin-1 at tyrosine 14 and several subsequent signal transduction pathways finally leading to the disruption of tight junctions and an increase in neutrophil adhesion and transmigration ([26](#), [27](#)), which might also be able to ease the extravasation of CTCs from the circulation ([28](#)). Intercellular adhesion molecule-1 (ICAM-1) is crucial for the adhesion and transmigration of neutrophils to the endothelium, thus aggravating the inflammatory response ([29](#), [30](#)). Additionally, phosphorylation of ICAM-1 is not only Src-dependent but also leads to an increase in neutrophil binding and transmigration ([31](#)). Src is activated by certain inflammatory cytokines, such as tumor necrosis factor alpha (TNF α), which is released at increasing concentrations—possibly due to surgical stress—during the perioperative period ([32](#), [33](#)). Therefore, the endothelial barrier might be impaired and the formation of new metastatic sites might be favored ([14](#), [34](#)). However, there is evidence that the amide LAs, such

as lidocaine and ropivacaine, might be able to attenuate the inflammatory response in the endothelium, which might then lead to a preservation of endothelial barrier integrity ([35](#), [36](#)). In a model of experimental acute lung injury triggered by tracheal instillation of bacterial lipopolysaccharide, ropivacaine was able to attenuate the formation of pulmonary edema and neutrophil transmigration, most certainly by decreasing Src and ICAM-1 expression in rats and mice ([37](#), [38](#)). Data from *in vitro* experiments using human lung microvascular endothelial cells incubated with TNF α and ropivacaine or lidocaine suggested that the drugs might be able to preserve endothelial barrier function by inhibiting signal transduction by the cytokine receptor TNFR1, which subsequently also lead to less Src and ICAM-1 activation and/or phosphorylation ([39](#)).

Neutrophil transmigration has also been demonstrated to be a factor influencing CTC extravasation and metastasis, as the CTCs might use the activated leukocytes as some sort of “ facilitator” for their own transmigration by binding of cancer cell ICAM-1 to neutrophilic CD11b (integrin α M) ([40](#), [41](#)). Therefore—at least in terms of CTC extravasation—it might be beneficial that LAs seem to impair neutrophil activation and priming ([42](#) - [44](#)).

Anti-Inflammatory = Antimetastatic?

There is a large overlap between inflammatory signaling pathways found to be crucial in inflammation as well as in cancer ([17](#), [45](#), [46](#)). For instance, Src kinase is also involved in signal transduction leading to cancer cell migration, cytoskeleton changes, invasion, proliferation, and the

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extravasation of CTCs ([45](#), [47](#) - [49](#)). Src activation and ICAM-1 phosphorylation in cancer cells can not only be induced by incubation with TNF α but also be blocked by clinically relevant concentrations of lidocaine and ropivacaine ([16](#)). Furthermore, the inhibition of Src activation by amide LAs also has an impact on the activation of Akt and focal adhesion kinase ([15](#)), a pathway which might also have a crucial role in triple negative breast cancer and is currently investigated for the development of new targeted therapies ([48](#)). A decrease in TNF α -induced secretion of cancer cell matrix metalloproteinase 9—an enzyme necessary for the degeneration of the extracellular matrix by malignant cells ([50](#))—in combination with a subsequent decrease in invasiveness *in vitro* has also been linked to the inhibition of Src activation by the LAs ([15](#)). Interestingly though, depending on the cell type used, the observed effects on cancer cell invasiveness have both been shown to be either independent (Src-dependent mechanism in non-small-cell lung cancer cells) or dependent (sodium channel variant Na_v 1.5 in colon cancer cells) on the blockade of the voltage-gated sodium channel (VGSC) ([16](#), [51](#)). Cancer growth might also be affected by LAs, as lidocaine has been shown to induce apoptosis and suppress tumor growth in human breast tumor cells ([52](#)) as well as in other tumor cells *in vitro* ([15](#), [16](#), [53](#) - [57](#)). Interestingly, it might also be able to sensitize breast cancer cells against chemotherapeutic drugs ([58](#)).

Besides these already well-established *in vitro* effects, a very recent study showed encouraging results regarding a possible inhibition of tumor growth by lidocaine in a xenograft model *in vivo* ([54](#)): cells originating from a

human hepatocellular carcinoma cell line have been injected subcutaneously into immunocompromised mice, which then have been subject to treatment with lidocaine (30 mg/kg) twice a week injected into the peritoneal cavity. Compared to control, lidocaine treatment was able to reduce the growth of the tumor. Furthermore, it was also found to be as effective as treatment with cisplatin (3 mg/kg, once per week) and was even able to increase the sensitivity of the tumor against cisplatin, which the authors related to an increased induction of apoptosis by the LA ([54](#)). In another study, the phenomenon of enhancing the effectiveness of a chemotherapeutic agent has been linked to the fact that lidocaine was demonstrated to induce demethylation of deoxyribonucleic acid in breast cancer cells, thus interfering with the cells' epigenetics, i. e., their regulation of gene expression ([59](#)).

In humans, many studies retrospectively analyzed the effects of the use of regional anesthesia and LAs in patients undergoing cancer surgery. Several studies showed a potential beneficial effect ([12](#), [60](#) - [62](#)), while others did not ([63](#) - [66](#)). So far, no data from adequately powered randomized controlled trials (RCTs) are available and therefore the authors of a recent Cochrane review concluded that there is currently only "inadequate" evidence for a potential beneficial effect of the perioperative use of regional anesthesia in cancer patients ([67](#)). However, these inconclusive findings might, at least in part, be explainable by the large heterogeneity of studies, tumors, and patients alike ([14](#)). Moreover, the intermediate outcomes of RCT so far have been encouraging: in a pilot study utilizing blood samples

from patients undergoing breast cancer surgery (NCT 00418457), the serum of women anesthetized with propofol and paravertebral block induced more apoptosis in a triple-negative breast cancer cell line compared to serum derived from women exposed to sevoflurane and an opioid-based regimen ([68](#)). In addition, these two different anesthetic techniques might also have an impact on serum concentrations of factors contributing to tumor progression after surgery: propofol plus paravertebral block increased the level of TGF- β , whereas sevoflurane together with opioids increased the level of VEGF-C 24 h after surgery ([69](#)). But as both TGF- β and VEGF-C are involved in the regulation of tumorigenesis ([70](#), [71](#)), these findings are insufficient to favor any of those two techniques.

Effects on the Immune System: Implication for Malignant Diseases

The Central Role of the Immune System in Cancer

Immunosurveillance by the innate immune system plays a crucial role in the early stages of carcinogenesis and is a promising target to treat breast cancer ([72](#), [73](#)). NK cells drive this process and play a key role in detecting abnormal growth and subsequent activation and recruitment of other immune cells to eliminate cancer cells ([74](#)). Moreover, NK dysfunction can lead to breast cancer progression ([75](#)), and restoring NK activity is currently under investigation as part of the treatment regimen for breast cancer ([76](#)). A derangement of immune processes is a common event during the perioperative period and might lead to severe disturbances, e. g., of NK cell function with subsequent enhanced dissemination of CTCs ([77](#)), as NK cell activity can be impaired for up to 7 days after breast cancer surgery ([78](#)).

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Furthermore, surgery shifts the balance of T-helper (Th)1/Th2 toward the Th2 humoral response, a phenomenon which also exerts pro-tumor actions ([79](#), [80](#)).

Impact of LAs on Cell-Mediated Immunity

The impact of LAs on antitumor immunity and NK cell function is still contradictory. Thus, a meta-analysis comparing the effect of spinal or epidural anesthesia with general anesthesia failed to demonstrate any enhancement of NK cell function after neuraxial anesthesia, due to a significant degree of heterogeneity of the five eligible studies ([81](#)).

However, the choice of the anesthetic technique might still have an impact on NK cell function: according to a pilot study from the already mentioned RCT evaluating patients undergoing breast cancer surgery with two different anesthetic regimens (propofol + paravertebral block vs. sevoflurane + opioids only, NCT 00418457), serum of women anesthetized with propofol plus paravertebral block for breast cancer surgery impaired the antitumor activity of NK cells much less than that of women exposed to sevoflurane and opioids ([68](#)). Turning more specifically to lidocaine, this LA might also affect NK cell activity differently, depending on the concentration used: from the early 1980s until the 2000s, *in vitro* studies have shown that lidocaine might compromise NK cell activity, but the experimental concentrations tested were high (from 0.2 to 5 mg/ml whereas a level of 5 µg/ml is toxic) and were not compatible with concentrations found after a systemic use of the drug ([82](#) - [84](#)). However, more recently Ramirez et al. have shown that lidocaine at lower and clinically relevant concentrations (10^{-8} to 10^{-6} M)

may instead preserve cytotoxicity of isolated human NK cells ([85](#)). Whether LAs might also affect other immune cells, e. g., lymphocytes, remains controversial: proliferation of Jurkat cells, an immortalized human T lymphocyte cell line commonly used to study T cell signaling or the expression of various chemokines, was decreased by lidocaine *via* the induction of apoptosis ([86](#), [87](#)) or *via* a dose-dependent inhibition of the cytokines IL-2 and TNF- α ([88](#)). It is difficult to translate those *in vitro* results to a clinical immunosuppressive effect of lidocaine because Jurkat cells are derived from the peripheral blood of a patient with T cell leukemia and express the uncontrolled characteristics of cancer cells ([89](#)). More physiologically, lidocaine also had an immunosuppressive effect on isolated mouse T cells derived from Peyer's patches ([90](#)) and reduced the secretion of pro-inflammatory cytokines in freshly isolated peripheral blood T cells ([88](#)). In addition, lidocaine inhibited the differentiation of Th1 cell responses of mice dendritic cells ([91](#)). However, all these experiments again used excessive lidocaine concentrations and therefore a translation into daily clinical use might be rather difficult. On the contrary, under clinical conditions, Yardeni et al. have shown that intraoperative IV lidocaine in combination with patient-controlled epidural analgesia was able to preserve lymphocyte response to phytohemagglutinin-M compared with a control group receiving only normal saline. This suggests that lidocaine might be able to reduce immune dysfunction as induced by the surgical stimulus ([92](#)). These results were later confirmed by Wang et al. who have shown that IV lidocaine might also preserve the balance of Th1/Th2 after radical hysterectomy for cervical cancer, whereas Th1/Th2 imbalance might favor

tumor cells to escape immune surveillance and clearance ([93](#)). All those clinical data suggested an enhanced effect of lidocaine on immunity and might support its clinical use during the perioperative period. While intraoperative IV lidocaine failed to confirm an opioid sparing effect after breast cancer surgery in two studies ([94](#), [95](#)), those same trials have shown a decrease of the incidence and severity of persistent postsurgical pain at the same time ([95](#), [96](#)). One of the hypotheses argued by the authors to explain those results is the impact of the anti-inflammatory properties of lidocaine.

Because the *in vitro* results remain unclear and the clinical mechanisms of action of lidocaine on immune functions are unsettled, it seems urgent to design a clinical trial to study the impact of IV lidocaine on immune function and cancer surveillance and follow the patient to see if an immune modulation during surgery may have an impact on outcome after breast cancer surgery.

“ From Bench-to-Bedside” Application for IV Lidocaine in Oncology?

We have summarized above a lot of promising data—in particular detailed evidence of plausible direct and putative mechanisms of action—to support a new use of lidocaine in oncologic patients as it bears the potential to serve as a “ repurposing candidate” drug ([97](#)).

First of all it is a well-known drug, commonly used in multimodal analgesia ([98](#)) with a well-established and evaluated toxicologic and pharmacokinetic profile for this purpose ([99](#) - [101](#)).

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However, a number of steps have to be undertaken before repurposing IV lidocaine for oncologic diseases. Unfortunately, there is no reliable clinical evidence of its oncological effects available right now. Therefore, we urgently need randomized controlled clinical trials to test the hypothesis of lidocaine's antitumor effects at clinically relevant doses as suggested by the large amount of *in vitro* and *in vivo* evidence.

So far, the oncological properties of lidocaine were mainly assessed by retrospective studies or secondary analyses of patients enrolled in published clinical trials which were not powered and designed to study other effects or outcome parameters ([14](#)). In order to test the hypothesis that lidocaine might have an antitumor or antimetastatic effect, patients would have to be randomized to receive IV lidocaine at relevant doses for perioperative analgesia or placebo. Possible outcome measures could, for instance, be the disease-free survival after a long-term follow-up or the impact of lidocaine on inflammatory or NK cytotoxic functions after surgery. Identifying subgroups of procedures and surgeries where patients are responsive to lidocaine would be useful to demonstrate a protective effect of this LA against recurrence and metastasis. This strategy might help to avoid the inconsistent results of studies on protective effect of regional anesthesia ([14](#)). Thus, patients undergoing colorectal or breast cancer surgery could be of interest as those surgeries imply a high risk of local or distant relapse, even after achieving a complete surgical resection ([102](#)). Additionally, some phenotypes of those cancers overexpress one of the main targets of

lidocaine: the VGSC which might also be involved in the process of metastasis ([103](#)).

Conclusion

Due to its large therapeutic margin, strong anti-inflammatory properties and potential beneficial impact on the innate immune surveillance system, lidocaine might be an ideal candidate for drug repurposing in cancer, which might potentially affect the patients' outcome dramatically. Besides the already proven favorable effects of perioperative IV lidocaine application on, e. g., post-operative pain and inflammation, patients with (breast) cancer might also benefit from an antimetastatic effect, ideally associated with a subsequent increase in recurrence-free and overall survival. However, due to the fact that there is currently not enough clinical evidence to support this hypothesis, we urgently call for clinical trials evaluating the effects of perioperative lidocaine during cancer surgical period to answer the question once and for all: is there a beneficial effect or not?

Author Contributions

Both authors contributed equally to this work.

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Sullivan R, Alatisse OI, Anderson BO, Audisio R, Autier P, Aggarwal A, et al. Global cancer surgery: delivering safe, affordable, and timely cancer surgery. *Lancet Oncol* (2015) 16(11): 1193–224. doi: 10. 1016/S1470-2045(15)00223-5

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

2. Retsky M, Demicheli R, Hrushesky W, Baum M, Gukas I. Surgery triggers outgrowth of latent distant disease in breast cancer: an inconvenient truth? *Cancers (Basel)* (2010) 2(2): 305–37. doi: 10. 3390/cancers2020305

[CrossRef Full Text](#) | [Google Scholar](#)

3. Tohme S, Simmons RL, Tsung A. Surgery for cancer: a trigger for metastases. *Cancer Res* (2017) 77(7): 1548–52. doi: 10. 1158/0008-5472. CAN-16-1536

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

4. Ramirez MF, Ai D, Bauer M, Vauthey JN, Gottumukkala V, Kee S, et al. Innate immune function after breast, lung, and colorectal cancer surgery. *J Surg Res* (2015) 194(1): 185–93. doi: 10. 1016/j. jss. 2014. 10. 030

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

5. Abramovitch R, Marikovsky M, Meir G, Neeman M. Stimulation of tumour growth by wound-derived growth factors. *Br J Cancer* (1999) 79(9–10): 1392–8. doi: 10. 1038/sj. bjc. 6690223

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

6. Curigliano G, Petit JY, Bertolini F, Colleoni M, Peruzzotti G, de Braud F, et al. Systemic effects of surgery: quantitative analysis of circulating basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF) and transforming growth factor beta (TGF-beta) in patients with breast cancer who underwent limited or extended surgery. *Breast Cancer Res Treat* (2005) 93(1): 35–40. doi: 10. 1007/s10549-005-3381-1

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

7. Hormbrey E, Han C, Roberts A, McGrouther DA, Harris AL. The relationship of human wound vascular endothelial growth factor (VEGF) after breast cancer surgery to circulating VEGF and angiogenesis. *Clin Cancer Res* (2003) 9(12): 4332–9.

[Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

8. Choy A, McCulloch P. Induction of tumour cell shedding into effluent venous blood breast cancer surgery. *Br J Cancer* (1996) 73(1): 79–82. doi: 10.1038/bjc.1996.14

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

9. McCulloch P, Choy A, Martin L. Association between tumour angiogenesis and tumour cell shedding into effluent venous blood during breast cancer surgery. *Lancet* (1995) 346(8986): 1334–5. doi: 10.1016/S0140-6736(95)92345-4

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

10. Connolly C, Madden SF, Buggy DJ, Gallagher HC. Expression of anaesthetic and analgesic drug target genes in excised breast tumour tissue: association with clinical disease recurrence or metastasis. *PLoS One* (2017) 12(5): e0177105. doi: 10.1371/journal.pone.0177105

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

11. Sekandarzad MW, van Zundert AAJ, Lirk PB, Doornebal CW, Hollmann MW. Perioperative anesthesia care and tumor progression. *Anesth Analg* (2017) 124(5): 1697–708. doi: 10.1213/ANE.0000000000001652

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

12. Exadaktylos AK, Buggy DJ, Moriarty DC, Mascha E, Sessler DI. Can anesthetic technique for primary breast cancer surgery affect recurrence or

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

metastasis? *Anesthesiology* (2006) 105(4): 660–4. doi: 10.1097/00000542-200610000-00008

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

13. Weng M, Chen W, Hou W, Li L, Ding M, Miao C. The effect of neuraxial anesthesia on cancer recurrence and survival after cancer surgery: an updated meta-analysis. *Oncotarget* (2016) 7(12): 15262–73. doi: 10.18632/oncotarget.7683

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

14. Piegeler T, Hollmann MW, Borgeat A, Lirk P. Do amide local anesthetics play a therapeutic role in the perioperative management of cancer patients? *Int Anesthesiol Clin* (2016) 54(4): e17–32. doi: 10.1097/AIA.000000000000119

[CrossRef Full Text](#) | [Google Scholar](#)

15. Piegeler T, Schlapfer M, Dull RO, Schwartz DE, Borgeat A, Minshall RD, et al. Clinically relevant concentrations of lidocaine and ropivacaine inhibit TNFalpha-induced invasion of lung adenocarcinoma cells in vitro by blocking the activation of Akt and focal adhesion kinase. *Br J Anaesth* (2015) 115(5): 784–91. doi: 10.1093/bja/aev341

[CrossRef Full Text](#) | [Google Scholar](#)

16. Piegeler T, Votta-Velis EG, Liu G, Place AT, Schwartz DE, Beck-Schimmer B, et al. Antimetastatic potential of amide-linked local anesthetics: inhibition
<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

of lung adenocarcinoma cell migration and inflammatory Src signaling independent of sodium channel blockade. *Anesthesiology* (2012) 117(3): 548–59. doi: 10.1097/ALN.0b013e3182661977

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

17. Votta-Velis EG, Piegeler T, Minshall RD, Aguirre J, Beck-Schimmer B, Schwartz DE, et al. Regional anaesthesia and cancer metastases: the implication of local anaesthetics. *Acta Anaesthesiol Scand* (2013) 57(10): 1211–29. doi: 10.1111/aas.12210

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

18. Collinsworth KA, Kalman SM, Harrison DC. The clinical pharmacology of lidocaine as an antiarrhythmic drug. *Circulation* (1974) 50(6): 1217–30. doi: 10.1161/01.CIR.50.6.1217

[CrossRef Full Text](#) | [Google Scholar](#)

19. Weibel S, Jokinen J, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, et al. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. *Br J Anaesth* (2016) 116(6): 770–83. doi: 10.1093/bja/aew101

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

20. Herroeder S, Pecher S, Schonherr ME, Kaulitz G, Hahnenkamp K, Friess H, et al. Systemic lidocaine shortens length of hospital stay after colorectal

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

surgery: a double-blinded, randomized, placebo-controlled trial. *Ann Surg* (2007) 246(2): 192–200. doi: 10. 1097/SLA. 0b013e31805dac11

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

21. Hollmann MW, Durieux ME. Local anesthetics and the inflammatory response: a new therapeutic indication? *Anesthesiology* (2000) 93(3): 858–75. doi: 10. 1097/00000542-200009000-00038

[CrossRef Full Text](#) | [Google Scholar](#)

22. Bellahcene A, Castronovo V, Ogbureke KU, Fisher LW, Fedarko NS. Small integrin-binding ligand N-linked glycoproteins (SIBLINGs): multifunctional proteins in cancer. *Nat Rev Cancer* (2008) 8(3): 212–26. doi: 10. 1038/nrc2345

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

23. Glodblatt SA, Nadel EM. Cancer cells in the circulating blood. *Cancer Prog* (1963) 92: 119–40.

[Google Scholar](#)

24. Cristofanilli M, Budd GT, Ellis MJ, Stopeck A, Matera J, Miller MC, et al. Circulating tumor cells, disease progression, and survival in metastatic breast cancer. *N Engl J Med* (2004) 351(8): 781–91. doi: 10. 1056/NEJMoa040766

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

25. Piegeler T, Winder T, Kern S, Pestalozzi B, Schneider PM, Beck-Schimmer B. Detection of circulating tumor cells in patients with esophagogastric or pancreatic adenocarcinoma using the CellSearch(R) system: an observational feasibility study. *Oncol Lett* (2016) 12(2): 1513-8. doi: 10.3892/ol. 2016. 4809

[CrossRef Full Text](#) | [Google Scholar](#)

26. Hu G, Minshall RD. Regulation of transendothelial permeability by Src kinase. *Microvasc Res* (2009) 77(1): 21-5. doi: 10.1016/j.mvr. 2008. 10. 002

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

27. Muller WA. Mechanisms of leukocyte transendothelial migration. *Annu Rev Pathol* (2011) 6: 323-44. doi: 10.1146/annurev-pathol-011110-130224

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

28. Garcia-Roman J, Zentella-Dehesa A. Vascular permeability changes involved in tumor metastasis. *Cancer Lett* (2013) 335(2): 259-69. doi: 10.1016/j.canlet. 2013. 03. 005

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

29. Basit A, Reutershan J, Morris MA, Solga M, Rose CE Jr, Ley K. ICAM-1 and LFA-1 play critical roles in LPS-induced neutrophil recruitment into the alveolar space. *Am J Physiol Lung Cell Mol Physiol* (2006) 291(2): L200-7. doi: 10.1152/ajplung. 00346. 2005

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

30. Hu G, Vogel SM, Schwartz DE, Malik AB, Minshall RD. Intercellular adhesion molecule-1-dependent neutrophil adhesion to endothelial cells induces caveolae-mediated pulmonary vascular hyperpermeability. *Circ Res* (2008) 102(12): e120–31. doi: 10. 1161/CIRCRESAHA. 107. 167486

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

31. Liu G, Vogel SM, Gao X, Javaid K, Hu G, Danilov SM, et al. Src phosphorylation of endothelial cell surface intercellular adhesion molecule-1 mediates neutrophil adhesion and contributes to the mechanism of lung inflammation. *Arterioscler Thromb Vasc Biol* (2011) 31(6): 1342–50. doi: 10. 1161/ATVBAHA. 110. 222208

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

32. Riedel B, Browne K, Silbert B. Cerebral protection: inflammation, endothelial dysfunction, and postoperative cognitive dysfunction. *Curr Opin Anaesthesiol* (2014) 27(1): 89–97. doi: 10. 1097/ACO. 0000000000000032

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

33. Schmidt A, Bengtsson A, Tylman M, Blomqvist L. Pro-inflammatory cytokines in elective flap surgery. *J Surg Res* (2007) 137(1): 117–21. doi: 10. 1016/j. jss. 2006. 05. 040

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

34. Piegeler T, Beck-Schimmer B. Anesthesia and colorectal cancer – the perioperative period as a window of opportunity? *Eur J Surg Oncol* (2016) 42(9): 1286–95. doi: 10. 1016/j. ejso. 2016. 05. 004

[CrossRef Full Text](#) | [Google Scholar](#)

35. de Klaver MJ, Buckingham MG, Rich GF. Lidocaine attenuates cytokine-induced cell injury in endothelial and vascular smooth muscle cells. *Anesth Analg* (2003) 97(2): 465–70. doi: 10. 1213/01. ANE. 0000073162. 27208. E9

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

36. de Klaver MJ, Weingart GS, Obrig TG, Rich GF. Local anesthetic-induced protection against lipopolysaccharide-induced injury in endothelial cells: the role of mitochondrial adenosine triphosphate-sensitive potassium channels. *Anesth Analg* (2006) 102(4): 1108–13. doi: 10. 1213/01. ane. 0000200310. 39031. 1f

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

37. Blumenthal S, Borgeat A, Pasch T, Reyes L, Booy C, Lambert M, et al. Ropivacaine decreases inflammation in experimental endotoxin-induced lung injury. *Anesthesiology* (2006) 104(5): 961–9. doi: 10. 1097/00000542-200605000-00012

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

38. Piegeler T, Dull RO, Hu G, Castellon M, Chignalia AZ, Koshy RG, et al. Ropivacaine attenuates endotoxin plus hyperinflation-mediated acute lung
<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

injury via inhibition of early-onset Src-dependent signaling. *BMC Anesthesiol* (2014) 14: 57. doi: 10.1186/1471-2253-14-57

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

39. Piegeler T, Votta-Velis EG, Bakhshi FR, Mao M, Carnegie G, Bonini MG, et al. Endothelial barrier protection by local anesthetics: ropivacaine and lidocaine block tumor necrosis factor-alpha-induced endothelial cell Src activation. *Anesthesiology* (2014) 120(6): 1414-28. doi: 10.1097/ALN.000000000000174

[CrossRef Full Text](#) | [Google Scholar](#)

40. Wu QD, Wang JH, Condron C, Bouchier-Hayes D, Redmond HP. Human neutrophils facilitate tumor cell transendothelial migration. *Am J Physiol Cell Physiol* (2001) 280(4): C814-22. doi: 10.1152/ajpcell.2001.280.4.C814

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

41. Lin YC, Shun CT, Wu MS, Chen CC. A novel anticancer effect of thalidomide: inhibition of intercellular adhesion molecule-1-mediated cell invasion and metastasis through suppression of nuclear factor-kappaB. *Clin Cancer Res* (2006) 12(23): 7165-73. doi: 10.1158/1078-0432.CCR-06-1393

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

42. Fischer LG, Bremer M, Coleman EJ, Conrad B, Krumm B, Gross A, et al. Local anesthetics attenuate lysophosphatidic acid-induced priming in human

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

neutrophils. *Anesth Analg* (2001) 92(4): 1041-7. doi: 10. 1097/00000539-200104000-00044

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

43. Picardi S, Cartellieri S, Groves D, Hahnenkamp K, Gerner P, Durieux ME, et al. Local anesthetic-induced inhibition of human neutrophil priming: the influence of structure, lipophilicity, and charge. *Reg Anesth Pain Med* (2013) 38(1): 9-15. doi: 10. 1097/AAP. 0b013e31827a3cbe

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

44. Hollmann MW, Gross A, Jelacin N, Durieux ME. Local anesthetic effects on priming and activation of human neutrophils. *Anesthesiology* (2001) 95(1): 113-22. doi: 10. 1097/00000542-200107000-00021

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

45. Kim MP, Park SI, Kopetz S, Gallick GE. Src family kinases as mediators of endothelial permeability: effects on inflammation and metastasis. *Cell Tissue Res* (2009) 335(1): 249-59. doi: 10. 1007/s00441-008-0682-9

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

46. Kobayashi H, Boelte KC, Lin PC. Endothelial cell adhesion molecules and cancer progression. *Curr Med Chem* (2007) 14(4): 377-86. doi: 10. 2174/092986707779941032

[CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

47. Guarino M. Src signaling in cancer invasion. *J Cell Physiol* (2010) 223(1): 14–26. doi: 10.1002/jcp.22011

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

48. Massihnia D, Galvano A, Fanale D, Perez A, Castiglia M, Incorvaia L, et al. Triple negative breast cancer: shedding light onto the role of pi3k/akt/mtor pathway. *Oncotarget* (2016) 7(37): 60712–22. doi: 10.18632/oncotarget.10858

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

49. Kawai N, Tsuji S, Tsujii M, Ito T, Yasumaru M, Kakiuchi Y, et al. Tumor necrosis factor alpha stimulates invasion of Src-activated intestinal cells. *Gastroenterology* (2002) 122(2): 331–9. doi: 10.1053/gast.2002.31023

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

50. Lenglet S, Mach F, Montecucco F. Matrix metalloproteinase-9: a deleterious link between hepatic ischemia-reperfusion and colorectal cancer. *World J Gastroenterol* (2012) 18(48): 7131–3. doi: 10.3748/wjg.v18.i48.7131

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

51. Baptista-Hon DT, Robertson FM, Robertson GB, Owen SJ, Rogers GW, Lydon EL, et al. Potent inhibition by ropivacaine of metastatic colon cancer SW620 cell invasion and Nav1.5 channel function. *Br J Anaesth* (2014) 113(Suppl 1): i39–48. doi: 10.1093/bja/aeu104

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

52. Chang YC, Liu CL, Chen MJ, Hsu YW, Chen SN, Lin CH, et al. Local anesthetics induce apoptosis in human breast tumor cells. *Anesth Analg* (2014) 118(1): 116–24. doi: 10.1213/ANE.0b013e3182a94479

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

53. Chang YC, Hsu YC, Liu CL, Huang SY, Hu MC, Cheng SP. Local anesthetics induce apoptosis in human thyroid cancer cells through the mitogen-activated protein kinase pathway. *PLoS One* (2014) 9(2): e89563. doi: 10.1371/journal.pone.0089563

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

54. Xing W, Chen DT, Pan JH, Chen YH, Yan Y, Li Q, et al. Lidocaine induces apoptosis and suppresses tumor growth in human hepatocellular carcinoma cells in vitro and in a xenograft model in vivo. *Anesthesiology* (2017) 126(5): 868–81. doi: 10.1097/ALN.0000000000001528

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

55. Jiang Y, Gou H, Zhu J, Tian S, Yu L. Lidocaine inhibits the invasion and migration of TRPV6-expressing cancer cells by TRPV6 downregulation. *Oncol Lett* (2016) 12(2): 1164–70. doi: 10.3892/ol.2016.4709

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

56. Wang HW, Wang LY, Jiang L, Tian SM, Zhong TD, Fang XM. Amide-linked local anesthetics induce apoptosis in human non-small cell lung cancer. *J Thorac Dis* (2016) 8(10): 2748–57. doi: 10. 21037/jtd. 2016. 09. 66

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

57. Le Gac G, Angenard G, Clement B, Laviolle B, Coulouarn C, Beloeil H. Local anesthetics inhibit the growth of human hepatocellular carcinoma cells. *Anesth Analg* (2017) 125(5): 1600–9. doi: 10. 1213/ANE. 0000000000002429

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

58. Li K, Yang J, Han X. Lidocaine sensitizes the cytotoxicity of cisplatin in breast cancer cells via up-regulation of RARbeta2 and RASSF1A demethylation. *Int J Mol Sci* (2014) 15(12): 23519–36. doi: 10. 3390/ijms151223519

[CrossRef Full Text](#) | [Google Scholar](#)

59. Lirk P, Berger R, Hollmann MW, Fiegl H. Lidocaine time- and dose-dependently demethylates deoxyribonucleic acid in breast cancer cell lines in vitro. *Br J Anaesth* (2012) 109(2): 200–7. doi: 10. 1093/bja/aes128

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

60. Schlagenhauff B, Ellwanger U, Breuninger H, Stroebel W, Rassner G, Garbe C. Prognostic impact of the type of anaesthesia used during the excision of primary cutaneous melanoma. *Melanoma Res* (2000) 10(2): 165–9. doi: 10. 1097/00008390-200004000-00009

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

61. Biki B, Mascha E, Moriarty DC, Fitzpatrick JM, Sessler DI, Buggy DJ. Anesthetic technique for radical prostatectomy surgery affects cancer recurrence: a retrospective analysis. *Anesthesiology* (2008) 109(2): 180-7. doi: 10.1097/ALN.0b013e31817f5b73

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

62. Christopherson R, James KE, Tableman M, Marshall P, Johnson FE. Long-term survival after colon cancer surgery: a variation associated with choice of anesthesia. *Anesth Analg* (2008) 107(1): 325-32. doi: 10.1213/ane.0b013e3181770f55

[CrossRef Full Text](#) | [Google Scholar](#)

63. Myles PS, Peyton P, Silbert B, Hunt J, Rigg JR, Sessler DI, et al. Perioperative epidural analgesia for major abdominal surgery for cancer and recurrence-free survival: randomised trial. *BMJ* (2011) 342: d1491. doi: 10.1136/bmj.d1491

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

64. Ismail H, Ho KM, Narayan K, Kondalsamy-Chennakesavan S. Effect of neuraxial anaesthesia on tumour progression in cervical cancer patients treated with brachytherapy: a retrospective cohort study. *Br J Anaesth* (2010) 105(2): 145-9. doi: 10.1093/bja/aeq156

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

65. Lacassie HJ, Cartagena J, Branes J, Assel M, Echevarria GC. The relationship between neuraxial anesthesia and advanced ovarian cancer-related outcomes in the Chilean population. *Anesth Analg* (2013) 117(3): 653-60. doi: 10.1213/ANE.0b013e3182a07046

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

66. Cummings KC III, Xu F, Cummings LC, Cooper GS. A comparison of epidural analgesia and traditional pain management effects on survival and cancer recurrence after colectomy: a population-based study. *Anesthesiology* (2012) 116(4): 797-806. doi: 10.1097/ALN.0b013e31824674f6

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

67. Cakmakkaya OS, Kolodzie K, Apfel CC, Pace NL. Anaesthetic techniques for risk of malignant tumour recurrence. *Cochrane Database Syst Rev* (2014) 11: CD008877. doi: 10.1002/14651858.CD008877.pub2

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

68. Jaura AI, Flood G, Gallagher HC, Buggy DJ. Differential effects of serum from patients administered distinct anaesthetic techniques on apoptosis in breast cancer cells in vitro: a pilot study. *Br J Anaesth* (2014) 113(Suppl 1): i63-7. doi: 10.1093/bja/aet581

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

69. Looney M, Doran P, Buggy DJ. Effect of anesthetic technique on serum vascular endothelial growth factor C and transforming growth factor beta in women undergoing anesthesia and surgery for breast cancer.

Anesthesiology (2010) 113(5): 1118–25. doi: 10. 1097/ALN.

0b013e3181f79a69

[CrossRef Full Text](#) | [Google Scholar](#)

70. Fabregat I, Fernando J, Mainez J, Sancho P. TGF-beta signaling in cancer treatment. *Curr Pharm Des* (2014) 20(17): 2934–47. doi: 10.

2174/13816128113199990591

[CrossRef Full Text](#) | [Google Scholar](#)

71. Wang CA, Tsai SJ. The non-canonical role of vascular endothelial growth factor-C axis in cancer progression. *Exp Biol Med (Maywood)* (2015) 240(6): 718–24. doi: 10. 1177/1535370215583802

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

72. Stoll G, Ma Y, Yang H, Kepp O, Zitvogel L, Kroemer G. Pro-necrotic molecules impact local immunosurveillance in human breast cancer.

Oncoimmunology (2017) 6(4): e1299302. doi: 10. 1080/2162402X. 2017.

1299302

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

73. Kroemer G, Senovilla L, Galluzzi L, Andre F, Zitvogel L. Natural and therapy-induced immunosurveillance in breast cancer. *Nat Med* (2015) 21(10): 1128–38. doi: 10. 1038/nm. 3944

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

74. Gillard-Bocquet M, Caer C, Cagnard N, Crozet L, Perez M, Fridman WH, et al. Lung tumor microenvironment induces specific gene expression signature in intratumoral NK cells. *Front Immunol* (2013) 4: 19. doi: 10. 3389/fimmu. 2013. 00019

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

75. Mamessier E, Pradel LC, Thibult ML, Drevet C, Zouine A, Jacquemier J, et al. Peripheral blood NK cells from breast cancer patients are tumor-induced composite subsets. *J Immunol* (2013) 190(5): 2424–36. doi: 10. 4049/jimmunol. 1200140

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

76. Shenouda MM, Gillgrass A, Nham T, Hogg R, Lee AJ, Chew MV, et al. Ex vivo expanded natural killer cells from breast cancer patients and healthy donors are highly cytotoxic against breast cancer cell lines and patient-derived tumours. *Breast Cancer Res* (2017) 19(1): 76. doi: 10. 1186/s13058-017-0867-9

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

77. Ben-Eliyahu S, Page GG, Yirmiya R, Shakhar G. Evidence that stress and surgical interventions promote tumor development by suppressing natural killer cell activity. *Int J Cancer* (1999) 80(6): 880-8. doi: 10. 1002/(SICI)1097-0215(19990315)80: 6 <880:: AID-IJC14> 3. 0. CO; 2-Y

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

78. McCulloch PG, MacIntyre A. Effects of surgery on the generation of lymphokine-activated killer cells in patients with breast cancer. *Br J Surg* (1993) 80(8): 1005-7. doi: 10. 1002/bjs. 1800800824

[CrossRef Full Text](#) | [Google Scholar](#)

79. Cata JP, Wang H, Gottumukkala V, Reuben J, Sessler DI. Inflammatory response, immunosuppression, and cancer recurrence after perioperative blood transfusions. *Br J Anaesth* (2013) 110(5): 690-701. doi: 10. 1093/bja/aet068

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

80. Ogawa K, Hirai M, Katsube T, Murayama M, Hamaguchi K, Shimakawa T, et al. Suppression of cellular immunity by surgical stress. *Surgery* (2000) 127(3): 329-36. doi: 10. 1067/msy. 2000. 103498

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

81. Conrick-Martin I, Kell MR, Buggy DJ. Meta-analysis of the effect of central neuraxial regional anesthesia compared with general anesthesia on

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

postoperative natural killer T lymphocyte function. *J Clin Anesth* (2012) 24(1): 3-7. doi: 10. 1016/j. jclinane. 2011. 09. 001

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

82. Krog J, Hokland M, Ahlburg P, Parner E, Tonnesen E. Lipid solubility- and concentration-dependent attenuation of in vitro natural killer cell cytotoxicity by local anesthetics. *Acta Anaesthesiol Scand* (2002) 46(7): 875-81. doi: 10. 1034/j. 1399-6576. 2002. 460719. x

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

83. Renzi PM, Ginns LC. Effect of lidocaine on natural killer activity: rapid inhibition of lysis. *Immunopharmacol Immunotoxicol* (1990) 12(3): 417-37. doi: 10. 3109/08923979009006471

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

84. Takagi S, Kitagawa S, Oshimi K, Takaku F, Miura Y. Effect of local anaesthetics on human natural killer cell activity. *Clin Exp Immunol* (1983) 53(2): 477-81.

[PubMed Abstract](#) | [Google Scholar](#)

85. Ramirez MF, Tran P, Cata JP. The effect of clinically therapeutic plasma concentrations of lidocaine on natural killer cell cytotoxicity. *Reg Anesth Pain Med* (2015) 40(1): 43-8. doi: 10. 1097/AAP. 0000000000000191

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

86. Boselli E, Duflo F, Debon R, Allaouchiche B, Chassard D, Thomas L, et al. The induction of apoptosis by local anesthetics: a comparison between lidocaine and ropivacaine. *Anesth Analg* (2003) 96(3): 755-6. doi: 10.1213/01.ANE.0000047201.85815.9D

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

87. Werdehausen R, Braun S, Essmann F, Schulze-Osthoff K, Walczak H, Lipfert P, et al. Lidocaine induces apoptosis via the mitochondrial pathway independently of death receptor signaling. *Anesthesiology* (2007) 107(1): 136-43. doi: 10.1097/01.anes.0000268389.39436.66

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

88. Lahat A, Ben-Horin S, Lang A, Fudim E, Picard O, Chowers Y. Lidocaine down-regulates nuclear factor-kappaB signalling and inhibits cytokine production and T cell proliferation. *Clin Exp Immunol* (2008) 152(2): 320-7. doi: 10.1111/j.1365-2249.2008.03636.x

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

89. Schneider U, Schwenk HU, Bornkamm G. Characterization of EBV-genome negative "null" and "T" cell lines derived from children with acute lymphoblastic leukemia and leukemic transformed non-Hodgkin lymphoma. *Int J Cancer* (1977) 19(5): 621-6. doi: 10.1002/ijc.2910190505

[CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

90. Kawasaki T, Kawasaki C, Sata T, Chaudry IH. Lidocaine suppresses mouse Peyer's patch T cell functions and induces bacterial translocation. *Surgery* (2011) 149(1): 106–13. doi: 10. 1016/j. surg. 2010. 03. 024

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

91. Jeon YT, Na H, Ryu H, Chung Y. Modulation of dendritic cell activation and subsequent Th1 cell polarization by lidocaine. *PLoS One* (2015) 10(10): e0139845. doi: 10. 1371/journal. pone. 0139845

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

92. Yardeni IZ, Beilin B, Mayburd E, Levinson Y, Bessler H. The effect of perioperative intravenous lidocaine on postoperative pain and immune function. *Anesth Analg* (2009) 109(5): 1464–9. doi: 10. 1213/ANE. 0b013e3181bab1bd

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

93. Wang HL, Yan HD, Liu YY, Sun BZ, Huang R, Wang XS, et al. Intraoperative intravenous lidocaine exerts a protective effect on cell-mediated immunity in patients undergoing radical hysterectomy. *Mol Med Rep* (2015) 12(5): 7039–44. doi: 10. 3892/mmr. 2015. 4235

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

94. Terkawi AS, Durieux ME, Gottschalk A, Brenin D, Tiouririne M. Effect of intravenous lidocaine on postoperative recovery of patients undergoing mastectomy: a double-blind, placebo-controlled randomized trial. *Reg* <https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

Anesth Pain Med (2014) 39(6): 472–7. doi: 10. 1097/AAP.

0000000000000140

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

95. Grigoras A, Lee P, Sattar F, Shorten G. Perioperative intravenous lidocaine decreases the incidence of persistent pain after breast surgery.

Clin J Pain (2012) 28(7): 567–72. doi: 10. 1097/AJP. 0b013e31823b9cc8

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

96. Terkawi AS, Sharma S, Durieux ME, Thammishetti S, Brenin D, Tiouririne M. Perioperative lidocaine infusion reduces the incidence of post-mastectomy chronic pain: a double-blind, placebo-controlled randomized trial. *Pain Physician* (2015) 18(2): E139–46.

[PubMed Abstract](#) | [Google Scholar](#)

97. Pantziarka P, Bouche G, Meheus L, Sukhatme V, Sukhatme VP, Vikas P. The repurposing drugs in oncology (ReDO) project. *Ecancermedicalscience* (2014) 8: 442. doi: 10. 3332/ecancer. 2014. 442

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

98. Dunn LK, Durieux ME. Perioperative use of intravenous lidocaine.

Anesthesiology (2017) 126(4): 729–37. doi: 10. 1097/ALN.

00000000000001527

[CrossRef Full Text](#) | [Google Scholar](#)

<https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

99. McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: a systematic review of randomized controlled trials. *Drugs* (2010) 70(9): 1149–63. doi: 10.2165/10898560-000000000-00000

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

100. Mooney JJ, Pagel PS, Kundu A. Safety, tolerability, and short-term efficacy of intravenous lidocaine infusions for the treatment of chronic pain in adolescents and young adults: a preliminary report. *Pain Med* (2014) 15(5): 820–5. doi: 10.1111/pme.12333

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

101. Daykin H. The efficacy and safety of intravenous lidocaine for analgesia in the older adult: a literature review. *Br J Pain* (2017) 11(1): 23–31. doi: 10.1177/2049463716676205

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)

102. Pantziarka P, Bouche G, Sullivan R, Ilbawi AM, Dare AJ, Meheus L. Perioperative therapies – enhancing the impact of cancer surgery with repurposed drugs. *Eur J Surg Oncol* (2017) 43(11): 1985–8. doi: 10.1016/j.ejso.2017.08.010

[CrossRef Full Text](#) | [Google Scholar](#)

103. Martin F, Ufodiana C, Watt I, Bland M, Brackenbury WJ. Therapeutic value of voltage-gated sodium channel inhibitors in breast, colorectal, and <https://assignbuster.com/the-amide-local-anesthetic-lidocaine-in-cancer-surgery-potential-antimetastatic-effects-and-preservation-of-immune-cell-function-a-narrative-review/>

prostate cancer: a systematic review. *Front Pharmacol* (2015) 6: 273. doi:
10.3389/fphar.2015.00273

[PubMed Abstract](#) | [CrossRef Full Text](#) | [Google Scholar](#)