The thromboxane A₂ pathway and its components are implicated in the regulation of tumor cell angiogenesis, migration, invasion, metastasis and apoptosis.

Scientific studies report cyclooxygenase-2 is up-regulated in many different types of cancer including breast, cervix, colon, esophagus, glioma, head and neck, lung, melanoma, pancreas, prostate, stomach and thyroid.

Levels of urinary 11-dehydrothromboxane B₂ reflect activity of components of the thromboxane A₂ pathway impacting thromboxane A₂ generation. Test results may be of use to the healthcare provider in the diagnosis, prognosis and therapeutic management of patients with cancer.

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**Peer reviewed publications citing the thromboxane A₂ pathway and urinary 11-dehydrothromboxane B₂ (11-DHTXB2)**

<table>
<thead>
<tr>
<th>Date</th>
<th>Journal</th>
<th>Report Type</th>
<th>Human/Animal</th>
<th>Subject</th>
<th>11-DHTXB2 Test cited</th>
</tr>
</thead>
</table>

1. **Circulating Prostaglandin Biosynthesis in Colorectal Cancer and Potential Clinical Significance**
   2015 • Biomedicine • Clinical Research • Human • 15 control/ 20 patients • 11-DHTXB2

   “CRC progression is accompanied by a pronounced elevation of systemic TXA₂ biosynthesis.”
   “Measurement of urinary TXA₂ metabolites such as 11-dehydro TXB₂ might provide the best estimate of systemic TXA₂ biosynthesis in vivo”

2. **Activation of the Thromboxane A₂ Pathway in Human Prostate Cancer Correlates with Tumor Gleason Score and Pathologic Stage**
   2006 • European Urology • Clinical Research • Human • 46 lesions studied

   “These findings identify the TXA₂ pathway as a potential target for PCa prevention or treatment or both.”

3. **The Role of Cyclooxygenase-2 in Cell Proliferation and Cell Death in Human Malignancies**
   2010 • Int J Cell Biology • Review Article • Human

   “Amongst the different mediators of inflammation, the cyclooxygenases (COXs) clearly appear to be implicated in cancer.”
4. **Role of COX-2, thromboxane A₂ synthase, and prostaglandin I₂ synthase in papillary thyroid carcinoma growth**  
   2005 • Modern Pathology • Clinical Research • 15 cases • Human  
   
   “COX-2 is expressed in many types of cancers including colon, pancreas, stomach, lung, breast, prostate, cervix, head and neck, esophagus, bladder, glioma, and melanomas. Recent studies have shown that COX-2 is expressed in thyroid lesions.”

5. **Epigenetic deregulation of the COX pathway in cancer**  
   2012 • Progress in Lipid Research • Review Article  
   
   “Epigenetics acts as a bidirectional control of the COX pathway that gauges and modulates the impact of exogenous and endogenous factors at multiple levels.”

6. **Differential Expression of Thromboxane Synthase in Prostate Carcinoma: Role in Tumor Cell Motility**  
   2004 • Am J Pathology • Clinical Research • Human • 40 specimens  
   
   “The present study is the first report detailing the endogenous expression of TxS in human prostate cancer cells and its potential involvement in PCa cell motility and perineural invasion.”

7. **Thromboxane synthase expression and correlation with VEGF and angiogenesis in non-small cell lung cancer**  
   2014 • Biochimia et Biophysica ACTA • Clinical Research • 46 specimens  
   
   “This study confirms previous observations of the role of TXS in NSCLC using an in-vivo model, providing further support for the potential of TXS inhibition as a therapeutic strategy in the disease.”

8. **The thromboxane synthase and receptor signaling pathway in cancer: an emerging paradigm in cancer progression and metastasis**  
   2011 • Cancer Metastasis Rev • Review Article • Cancer  
   
   “Increased cyclooxygenase (COX)-2 expression has been described in a variety of human cancers, which has focused attention on TXA₂ as a downstream metabolite of the COX-2-derived PGH₂.”  
   “It is a great importance to further determine whether and how prostanoids, such as TXA₂, mediate the effects of COX-2 in cancer, potentially leading to a more targeted approach for cancer prevention and treatment.”
9. **Examination of thromboxane synthase as a prognostic factor and therapeutic target in non-small cell lung cancer**
   2011 • Molecular Cancer • Clinical Research • Human

   “Thromboxane synthase (TXS) metabolises prostaglandin H2 into thromboxanes, which are biologically active on cancer cells. TXS over-expression has been reported in a range of cancers, and associated with a poor prognosis.”

   “Measurement of TXB2 levels in human plasma would be indicative of circulating levels in the blood. Thromboxane B2 levels were found to be significantly (p<0.01) higher in plasma samples taken from patients with NSCLC, relative to age-matched controls (3307 ± 189 pg/mL versus 2201 ± 317 pg/mL; n= 49 NSCLC patient, 19 cancer-free controls.”

10. **Inhibition of the arachidonic acid metabolism blocks endothelial cell migration and induces apoptosis**
    2004 • ACTA Neurochir • Clinical Research • Human

    “These data suggest that inhibitors of thromboxane synthase influence migration and apoptosis in both human glioma cells and human endothelial cells. An anti-invasive treatment strategy using this class of compounds may therefore not only sensitize glioma cells to conventional treatments inducing apoptosis but may also be supported by an anti-angiogenic effect.”

    “We demonstrated that this enzyme is expressed in gliomas in vitro and in vivo and that specific thromboxane synthase inhibitors block migration, which is paralleled by a decrease of thromboxane B2 (Thx B2) formation.”

11. **Communicating clinical research to reduce cancer risk through diet: Walnuts as a case example**
    2014 • Nutrition Research Practice • Review Article • 11-DTXB2

    “Both the walnut and fish diets inhibited prostaglandin E metabolite (PGEM) and 11-dehydro thromboxane B2, but had no effect on IL-1β, IL-6, TNF-α, CRP, or the number of circulating lymphocyte subsets.”

    “A plant-based diet is associated with decreased risk for cancer and other chronic diseases, due in part to reduced chronic inflammation.”

12. **Case-Control study of aspirin use and risk of pancreatic cancer**
    2014 • Cancer Epidemiol Biomarkers Prev • Clinical Research • Human • 690 Controls/362 Cases

    “We observed a significant inverse relationship between aspirin use and risk of pancreatic cancer.”
13. **Aspirin and Cancer**

2016 • JACC • Review Article • Human

“The protective effects of low-dose aspirin against cancer appear to reflect the prevention of early neoplastic transformation throughout the alimentary tract, as well as an antimetastatic action. Both effects may be explained by the antiplatelet effect of low-dose aspirin.”

14. **Targeting arachidonic pathway by natural products for cancer prevention and therapy**

2016 • Sem Can Bio • Clinical Research

“Curcumin, resveratrol, apigenin, anthocyanins, berberine, ellagic acid, eugenol, fisetin, ursolic acid, [6]-gingerol, guggulsterone, lycopene and genistein are well known cancer chemopreventive agents which act by targeting multiple pathways, including COX-2.”

15. **Neuroblastoma-related inflammation**

2013 • OncoImmunology • Research Study • Mice

“The anticancer effects of aspirin have been suggested to depend on the inhibition of platelet activation, directly stemming from a reduction in TXA2 levels. This would be paralleled by a reduction in the metastatic potential of cancer cells and in the levels of COX2, by angiogenesis inhibition as well as by the attenuation of pro-inflammatory pathways involving, among several mediators, PGE2.”

16. **Curcumin anticancer studies in pancreatic cancer**

2016 • Nutrients • Review Article

“We also demonstrated that curcumin inhibited the proliferation and enhanced the apoptosis of MIA PaCA-2 cells, through the suppression of NF-kB-activation.”

17. **Role of platelets in inflammation and cancer: novel therapeutic strategies.**

2014 • Basic & clinical pharmacology & toxicology • Review Article • 11DHTXB2

“The results of clinical studies have shown that the antiplatelet drug aspirin reduces the incidence of vascular events and colorectal cancer.”

“Low-dose aspirin treatment (which is associated with a preferential inhibition of platelet COX-1) causes a 70-80% reduction of urinary 11-dehydro-TXB2 and 2,3-din-or-TXB2 excretion.”
18. **Platelet activation in patients with colorectal cancer.**
2005 • Prostaglandins Leukot Essent Fatty Acids • Clinical Research • 20 Subjects • Human • 11DXTXB2

“Enhanced platelet activation occurs in colorectal cancer patients. Permanent inactivation of platelet COX-1 by low dose aspirin might restore anti tumor reactivity.”

19. **Effects of celecoxib on prostanoid biosynthesis and circulating angiogenesis proteins in familial adenomatous polyposis**
2012 • J Pharmacol Exp Ther • Clinical Research • Human • 9 Controls/9 Subjects – 11-DHTXB2

“Intestinal tumorigenesis was associated with enhanced urinary TX-M levels, but unaffected by celecoxib, suggesting the involvement of a COX-1-dependent pathway, presumably from platelets.”

20. **The cyclooxygenase-2/thromboxane A2 pathway; a bridge from rheumatoid arthritis to lung cancer?**
2014 • Can Let • Review Article • Human • 11-DXTXB2

“It is possible that COX-2 derived TxA2 could be monitored for the early detection of LC in RA patients, and targeting this molecular pathway may decrease the risk of LC in patients with RA.”

21. **Platelets, cyclooxygenases and colon cancer**
2014 • Sem in Oncol • Review Article

“Activated platelets, in response to tissue damage, induce a proinflammatory program involving the aberrant expression of cyclooxygenase (COX)-2.”

“The central role of platelet activation in cancer development is sustained by the analysis of clinical studies with aspirin showing an anticancer efficacy by the drug, even at the low doses used for the prevention of atherothrombosis.”

22. **Cigarette smoking, cyclogenyase-2 pathway and cancer**
2011 • Biochimica Biophysica Acta • Review Article

“Cigarette smoke exposure can induce COX-2 expression and activity, increase PGE2 and TxA2 release, and lead to an imbalance in PGI2 and TxA2 production in favor of the latter.”
23. **Thromboxane A2 exerts promoting effects on cell proliferation through mediating cyclooxygenase-2 signal in lung adenocarcinoma cell**
   2014 • J Cancer Res Clin Oncol

   “The present study has for the first shown that dual TXA2 modulators and the single blocker of TXAS or TXA2R offer a similar inhibitory role in lung adenocarcinoma cell proliferation and that the tumor-promoting effects of COX-2 can largely be relayed by TXA2.”

24. **Role of thromboxane A2 in the induction of apoptosis of immature thymocytes by lipopolysaccharide**
   2005 • Clin Diagn Lab Immunol • Clinical Research • Mice

   “These studies indicate that TXA(2) mediates a portion of apoptotic thymocyte death caused by LPS.”

25. **Thromboxane A2 exerts promoting effects on cell proliferation through mediating cyclooxygenase-2 signal in lung adenocarcinoma cells**
   2014 • J Can Res Clin Oncol • Clinical Research

   “The present study has for the first shown that dual TXA2 modulators and the single blocker of TXAS or TXA2R offer a similar inhibitory role in lung adenocarcinoma cell proliferation and that the tumor-promoting effects of COX-2 can largely be relayed by TXA2. Thus, TXA2 should be regarded as a critical molecule in COX-2 mediated tumor growth and a valuable target against lung cancer.”

26. **Aspirin use and reduced risk of pancreatic cancer**
   2016 • Cancer Epidemiol Biomarkers Prev • Clinical Research • Human • 794 Controls/761 Cases

   “Regular use of aspirin thus appears to reduce risk of pancreatic cancer by almost half.”

27. **The role of aspirin in cancer prevention**
   2012 • Nat Rev Clin Oncol • Review Article • Human

   “Recently published secondary analyses of cardiovascular trials provide the first randomized evidence that daily aspirin use may also reduce the incidence of all cancers combined, even at low doses (75-100 mg daily)”

   “10% reduction in overall cancer incidence beginning during the first 10 years of treatment could tip the balance of benefits and risks favourably in average-risk populations.”

   **Thromboxane A₂ pathway schematics**