

## Aspirin's Expanding Role in Cardiovascular Health, Inflammation Control, and Cancer Prevention

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To the Editor,

We read with great interest the article by Yang et al., titled "Aspirin prevents metastasis by limiting platelet TXA<sub>2</sub> suppression of T cell immunity," highlighting aspirin's potential in reducing cancer metastasis.<sup>1</sup> The suppression of TXA<sub>2</sub>-mediated activation of the ARHGEF1 protein is critical in T cell receptor signaling. Such signaling suppression compromises T cell activation and immune surveillance, and facilitates cancer cell metastasis. By blocking TXA<sub>2</sub> production, Aspirin reinstates effective T cell immune responses, thereby significantly decreasing metastatic potential.

This promising effect of Aspirin adds to its well-established multifaceted therapeutic effects that we wish to highlight in this letter. Aspirin has long been utilized in cardiovascular medicine primarily for its anti-thrombotic effects. By irreversibly inhibiting cyclooxygenase-1 (COX-1), it reduces the production of thromboxane A<sub>2</sub> (TXA<sub>2</sub>), thus diminishing platelet aggregation and preventing thrombosis.<sup>2</sup> Clinically, aspirin significantly contributes to cardiovascular protection, acting both prophylactically in high-risk individuals and therapeutically in preventing coronary artery and stent thrombosis.

At higher doses, Aspirin also exhibits significant anti-inflammatory effects by inhibiting cyclooxygenase-2 (COX-2) enzymes, thereby reducing the production of pro-inflammatory prostaglandins and subsequently decreasing systemic inflammation, including levels of inflammatory markers such as C-reactive protein (CRP). Elevated CRP has been linked to enhanced tumorigenesis; therefore, aspirin's capacity to mitigate chronic inflammation might indirectly impede cancer progression, over and above its beneficial role in cardiovascular prevention.<sup>3</sup>

In addition, recent evidence suggests aspirin use may significantly reduce the risk of colorectal cancer recurrence in some patients.<sup>4</sup> A 3-year randomized placebo-controlled trial revealed low-dose aspirin administration has shown promising results in its ability to reduce the recurrence rate by altering the PI3K pathway.<sup>5</sup> Furthermore, the anti-inflammatory and immunomodulatory properties of aspirin have proven useful in improving long-term outcomes in breast cancer survivors.<sup>6</sup> These findings show the role aspirin currently plays in the world of oncology beyond metastasis.

Despite its remarkable therapeutic potential, aspirin usage is not without risks. Potential adverse effects include gastrointestinal irritation, increased risk of bleeding, renal dysfunction, and hypersensitivity reactions, necessitating careful patient selection and dosage considerations. Given aspirin's affordability and accessibility, it could represent an invaluable addition to the arsenal against cardiovascular disease, chronic inflammation, and cancer metastasis. However, comprehensive clinical trials are essential to determine optimal dosing and fully delineate aspirin's risk-benefit profile.

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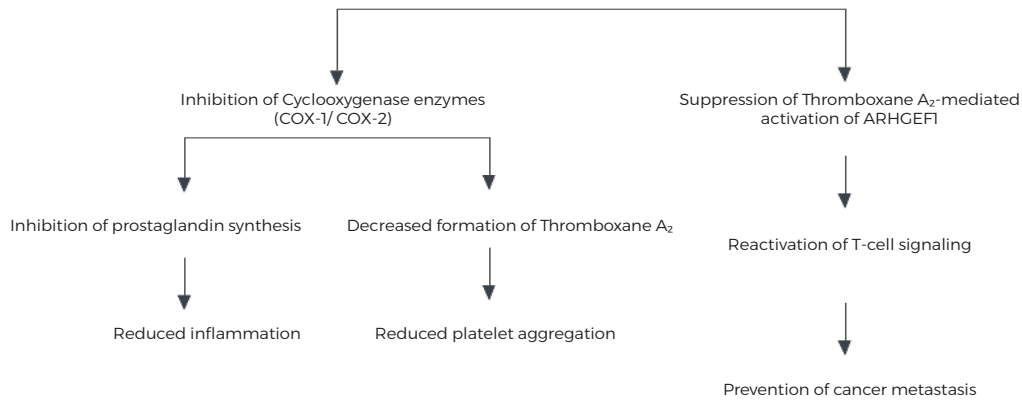
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## Mechanisms of Therapeutic Actions of Aspirin (Acetylsalicylic Acid)



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