

## The Impact of the “Yogic Lifestyle” on Cancer Prognosis and Survival: Can we Target Cancer Stem Cells with Yoga?

### Abstract

Cancer has recently been known to originate from stem cell-like cells, called cancer stem cells (CSCs). Their unique properties of self-duplication, multiplication, as well as migration give the CSC resistance over conventional cancer therapies. Newer therapies are in developmental stage to target these stem cell-like populations and become the vanguard of future treatments. Several complementary and alternative treatments have been used in cancer management as an adjunct to conventional therapy to improve the overall quality of life and reduce recurrence. Yoga stands as the third most popular of all complementary and alternative medicine treatments currently used in cancer patients today. Preliminary results show that yoga modulates neural, hormonal, and immune functions at a cellular level. The scope of this commentary is to discuss the current evidence-based medicine on yoga and its effect on CSCs.

**Keywords:** Cancer, stem cells, yoga, treatment

### Introduction

Targeted cancer treatment is the new focus in research for management of patients to improve overall outcome.<sup>[1,2]</sup> In spite of recent advances, there has been no evidence that the prevalence of cancer has decreased.<sup>[3]</sup> These special stem cell-like cancer cells have the ability to originate, spread, and cause recurrence of cancer in the body.<sup>[4,5]</sup> At the cellular level, aberrant expression of hormones, cytokines, and chemokines which include estrogens, androgens, tumor necrosis factor (TNF), and notch and tumorigenic signals such as nuclear factor-kappa B (NF- $\kappa$ B) and Myc-1 enhance the growth of cancer stem cell (CSC).<sup>[5]</sup> A study by Heddleston *et al.*<sup>[6]</sup> describes how CSCs work through multiple mechanisms and networks such as their ability to restrict DNA damage during radiation or chemotherapy by reduction of reactive oxygen species (ROS) and enhanced activity of DNA checkpoint kinases.<sup>[7,8]</sup> In conclusion, it is believed that the CSC population survives with injury and continues to propagate the tumor by preventing DNA damage.

In yogic philosophy, prāna is the vital force in all living beings in the universe.<sup>[9]</sup> Prāna is the basic life principle that is responsible

for all kinds of movement (of thought as well as matter) and has the ability to expand and contract by itself.<sup>[10]</sup> Prāna represents the interface between energy and consciousness.<sup>[9]</sup> Yogic philosophy also appreciates that mind is more powerful than prāna and hence can direct the pranic flow.<sup>[9,10]</sup> The practice of yoga includes physical postures, breathing practices, and meditations.<sup>[11]</sup> It is known to alter immune and endocrine functions at the cellular level through influencing cell cycle, aging, oxidative stress, cell death, and several pathways of stress signaling.<sup>[12,13]</sup> Yoga has also been shown to affect natural killer cell (NK cell) function and alter stress and DNA damage in breast cancer patients receiving radiotherapy.<sup>[14,15]</sup>

### Cancer Stem Cell and the Role of Hypoxia

Hypoxia is necessary for stem cell survival.<sup>[16]</sup> Hypoxia enhances malignant potential of tumor cells by facilitation of tumor invasion and metastasis,<sup>[17]</sup> increased expression of drug resistance genes,<sup>[18]</sup> reduced expression of DNA repair genes,<sup>[19]</sup> and increased genomic instability.<sup>[20]</sup> Hypoxia-induced signaling is primarily mediated by hypoxia-inducible

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factor-1 (HIF-1a) molecule expressed by mammalian cells in response to hypoxia that regulates  $O_2$  homeostasis. HIF-1 has led to the concept of a “molecular target” of hypoxia in the development of cancer therapeutics.<sup>[21]</sup> Heddleston *et al.*<sup>[6]</sup> demonstrated that CSCs are critically dependent on hypoxia-induced factors for their survival, self-renewal, and growth. Presence of hypoxia in tumors can result in the promotion of CSC phenotypes even in the context of successful killing of other tumor cells and thus represents a challenge in therapy.<sup>[6]</sup> Experimental evidence puts an emphasis on micro-environmental conditions such as low-oxygen environments that govern CSC and suggests that the new targeted treatment modalities should be focused on influencing the niche of the CSC.<sup>[6]</sup> A strong correlation between tumor hypoxia and poor patient outcomes is seen in the presence of CSCs.<sup>[6]</sup>

### Yoga and Oxygenation

Yogic postures (asanas) and breathing techniques (pranayama) focus on airflow in the lungs, thus increasing their capacity, endurance, and efficiency.<sup>[22]</sup> Back-bending postures open the chest, improving both lung and heart functions.<sup>[22]</sup> A study<sup>[23]</sup> assessed blood oxygen saturation before, during, and after two yoga breathing techniques in 29 healthy male volunteers with ages ranging between 17 and 32 years. A significant increase ( $P < 0.01$ ) in oxygen saturation was observed in the high-frequency yoga breathing. Another study measured the impact of asanas and pranayama on blood oxygen saturation level. It was observed from the study that the groups differed significantly with an increase in oxygenation in the pranayama group.<sup>[23]</sup> Yoga practices have also been shown to improve ROS levels and oxidation status. A study was conducted on healthy male volunteers divided into two groups: yoga ( $n = 34$ ) and control groups ( $n = 8$ ). The yoga group practiced yoga asanas, pranayama, and meditation for 3 months and the control group followed a usual routine. Blood samples done before, during, and after 3 months of practice showed an increase in total antioxidant status ( $P < 0.001$ ), wherein glutathione peroxidase activity was increased ( $P < 0.001$ ) and plasma concentration level of malondialdehyde ( $P < 0.01$ ) and oxidized glutathione ( $P < 0.01$ ) decreased significantly after 3 months in the yoga group suggesting an improvement in oxidative stress, these molecules are markers for oxidative stress.<sup>[24]</sup>

Sudarshan Kriya (SK), which is a type of pranayama in which breathing is in three different rhythms,<sup>[25]</sup> has been shown to lower blood lactate levels and provides better antioxidant defense.<sup>[25]</sup> In another study,<sup>[26]</sup> the effect of SK was studied at the transcriptional level of the antioxidant enzymes. There was a significant increase in the expression of glutathione-S-transferase in practitioners of SK compared to the normal controls, along with a significant increase in anti-carcinogenic molecules such as anti-apoptotic COX-2

and heat shock proteins-70. It was also observed that age-related human telomerase reverse transcriptase and regulator proteins such as anti-apoptotic Bcl-2 showed an increasing trend in SK practitioners.<sup>[26]</sup>

### Modulation of Neural, Endocrine, and Immune Functions Through Yoga Therapy

Aberrant expression and activities of hormones, cytokines, and chemokines which include estrogens, androgens, and transforming growth factor-notch and tumorigenic signaling elements such as telomerase, NF- $\kappa$ B, and Myc-1 may enhance CSC survival and contribute toward the malignant potential of tumors.<sup>[27,12]</sup> The practice of yoga can bring a balance in the expression and activities of various hormones, cytokines, and tumorigenic signaling elements that help to reduce CSC survival, progression, and recurrence of the tumor. By increasing<sup>[28]</sup> NK cell activity, reducing plasma TNF- $\alpha$  levels following surgery, and modulating stress-induced DNA damage during radiotherapy in breast cancer patients, an improved prognosis can be expected.<sup>[29]</sup> Tseng *et al.*<sup>[30]</sup> demonstrated an increased lysis of CSC NK cells. This lysis was mediated by increased cytotoxicity as well as augmented secretion of interferon gamma (IFN- $\gamma$ ). They also established that inhibition of reversion of cells to a less-differentiated phenotype by blocking NF- $\kappa$ B or targeted knockdown of COX-2 in monocytes significantly augmented NK cell cytotoxicity and secretion of IFN- $\gamma$ .<sup>[30]</sup> A study on 45 dementia caregivers showed that brief daily yogic meditation led to a decreased NF- $\kappa$ B-related transcription of pro-inflammatory cytokines and decreased interferon response factors 1.<sup>[31]</sup> This may enhance NK cell activity indirectly.<sup>[31]</sup> The lifestyle changes associated with the yogic practice have been shown to increase NK cell activity in breast cancer patients.<sup>[28,32]</sup> A pilot study displayed that regular practitioners of yoga have lower cellular dysfunction perhaps due to reduced qualitative DNA damage and better restorative responses compared to control patients.<sup>[33]</sup> Long Parma *et al.*<sup>[34]</sup> reported the effect on inflammatory biological markers for twenty breast cancer survivors who participated in a 6-month yoga-based exercise program. Inflammatory markers such as interleukin-6 (IL-6), IL-8, TNF- $\alpha$ , and C-reactive protein were measured. The obtained results show the effectiveness of yogic asanas and pranayama exercises in improving body composition, but reported no significant changes in inflammatory markers or cytokines. Larger studies are needed to determine whether there are significant changes in inflammatory serum markers as a result of specific exercise modalities.<sup>[34]</sup>

### Future Aspects

The relationship between the 5000-year-old practice of yoga, based on ancient Vedic scriptures, and the newly discovered science of CSC inspires the researcher to examine the biological implications of ancient metaphysical

practices. More research and larger trials on various yogic techniques and types and stages of cancer could give us valuable information and also deeper understanding and functioning of CSCs. Yoga therapy may have a complementary effect with conventional modalities of treatment in preventing cancer progression and recurrence by increasing the susceptibility of CSCs to conventional treatment. Future research may focus on the study of lysis of CSC by specific yoga techniques posttreatment and the quantitative assessments of inflammatory mediators.

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### Conflicts of interest

There are no conflicts of interest.

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