

# Beta-endorphins and cancer: holistic insight

## Abstract

Endorphins are endomorphine produced in the pituitary gland. In the three types of endorphins, betaendorphins are abundant endorphin, a precursor of POMC (Proopiomelanocortin). Mechanisms of actions of betaendorphins includes analgesic, stress buster, anti-inflammatory, antiviral, and anti-tumor activity. It will be used in holistic preventive, therapeutic, palliative, and health promotive in management of cancer without adverse effects and inexpensive. This article highlights about the betaendorphins in holistic management of cancer.

**Keywords:** NF-KB, GABA, Dopamine, substance p, IFN- $\gamma$

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**Abbreviations:** PNS, peripheral nervous system; CNS, central nervous system; NF-kB, nuclear factor kappa-lightchain-enhancer of activated B cells; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; IFN- $\gamma$ , interferon gamma; GABA, Gama aminobutyric acid; VEGF, vascular endothelial growth factor; MMP-9, matrix mettaloproteinases-9; COX2, cyclo-oxygenase2; ROS, reactive oxygen species; EGF, epidermal growth factor; FGF, fibroblast growth factor; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; IFN- $\beta$ , interferon beta; IL-10, interleukin 10; TGF- $\beta$ , transforming growth factor-beta; PGE2, prostaglandin E2; UPA, urokinase plasminogen activator; IL-2, interleukin 2, IL-4, interleukin 4; IL-6, interleukin-6; IFN- $\gamma$ , interferon gamma; COX-1 COX2, cyclo-oxygenase 2; MMPs, matrix metallo proteinases; HIF-1 $\alpha$ , hypoxia- inducible factor alfa

## Introduction

Cancer is a leading cause of death worldwide due to external environmental factors such as tobacco, alcohol, chemicals (lead, arsenic, bismuth etc), dietary factors accounts 1/3 of all cancers and viruses(HPV, EBV). More than 90 percent of all cancers are due to external environmental factors. Chronic inflammation is considered as a seventh hall mark of cancer accounts 25 percent of all cancers. Current latest treatment of cancer includes surgery, chemotherapy, and radiotherapy, which have many adverse effects and poor prognosis. In cancer immunotherapy stimulating our own immune cells to act against cancer cells, which are antigenic in nature. Restricted to certain type of cancers such as head and neck cancers, breast cancers, and cervical cancers.

Endomorphins are endogenous opioids, neuropeptides produced in the pituitary gland. Betaendorphins, enkephalins, and dynorphins are three types of endorphins binds with  $\mu$ ,  $\kappa$ , and  $\delta$  receptors present on the immune cells and nervous system. Endorphins are produced during physical stress and pain. Endorphin receptors are increased during stressful conditions such as pain and inflammation binds haphazardly with endorphins. Endorphins are useful prognostic biomarkers in inflammation associated cancer.<sup>1-6</sup>

## Betaendorphins mechanisms of actions

An abundant endomorphin is betaendorphin binds with its  $\mu$  receptor present on the PNS (Peripheral nervous system) results in substance P inhibition, a neurotransmitter of pain, inflammation and in the CNS (Central nervous system) inhibits GABA, a inhibitory neurotransmitter of pain results in release of dopamine involved in analgesic activity and stress buster activity.<sup>7-16</sup> Betaendorphin binds

with its  $\mu$  receptors present on the innate and adaptive immune cells results in activation release opsonin, granzyme-B, IFN- $\gamma$ , and antibodies involved in anti-inflammatory, antiviral, and anti-tumor activity. Betaendorphins inhibit inflammatory mediators such as IL-1, TNF- $\alpha$ , IL-6, and COX-2, which activates NF-KB, a key transcription factor involved in tumor progression by cell proliferation (Cyclin D,E), cell survival (BCL-2, BCL-XL), angiogenesis (IL-8, COX-2, HIF-1 $\alpha$ ), genomic instability (ROS,RNS,AID), Immune modulation (IL-4, IL-5,IL-13,IL-10,TGF- $\beta$ ), invasion and metastasis (Mmp's2,9 and UPA).<sup>17-28</sup>

Betaendorphins inhibit NF-KB, a key transcription factor, which acts against P53, a tumor suppressor gene, a guardian of the genome mutated in many cancers. Betaendorphins also inhibit oxidative stress caused by free radicals such as ROS, RNS, which involve in cell aging, cell injury, DNA damage, and cell death. Clinical studies have shown that after beta-endorphin neuronal implantation, yoga and meditation, music therapy, and massage therapy in cancer patients improve the survival rate and prognosis of cancer patients by its anti-tumor activity by activating immune cells such as macrophages and NK cells and stress reduction.<sup>24,29-31</sup>

Betaendorphin is a holistic preventive, therapeutic, health promotive and palliative management of cancer without adverse effects and inexpensive.

## Conclusion and future perspective

Betaendorphins are natural, abundant endogenous opioid synthesize and stored in the pituitary gland. Because of its analgesic, anti-inflammatory, antiviral, and antitumor activity, it can be used in holistic management of cancer. Clinical research and trails of betaendorphins synthesis, mechanisms of actions, dose dependent duration of action, prognosis related to cancer will be helpful for better future holistic management of cancer.

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## Conflicts of interest

Authors declare that there is no conflict of interest.

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