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Opinion

Milk-Derived Stem Cells for Cancer Therapy

Shanti Choudhary*

College of Animal Biotechnology, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, Punjab, India

***Corresponding Author:** Shanti Choudhary, College of Animal Biotechnology, Guru Angad Dev Veterinary and Animal Sciences University, Ludhiana, Punjab, India.

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Milk consists of not only the nutritional components (carbohydrates, proteins, fats, vitamins, and minerals) but also the non-cellular (immunoglobulins, cytokines, and antimicrobials) and cellular (inflammatory cells, lactocytes, and stem cells) components. Nutritional components of milk provide growth and development for young ones and humans. Though the value of non-cellular components of milk is appreciated, the presence of its cellular component, stem cells in milk, is enigmatic. The evidence of stem cells in human milk was first reported by the team of Cregan and Hartman in the year 2007 [1]. Later the presence of stem cells in milk have been reported in human [2,3], murine [4], and bovine [5]. The mixture of human milk-derived cells was hematopoietic (CD34+, CD133+, and CD123+), mesenchymal (CD90+, CD44+, CD271+, and CD146+) [6], endothelial progenitors (CD105+), lactocyte (CD18+), myoepithelial (CK14/SMA+), and embryonic stem-like cells (OCT4+, SOX2+, NANOG+, and TRA 60-1+) [3]. An initial report of cow milk showed the presence of stem cell-like cells and progenitor cells. The study showed a subset (30-40%) of bovine milk-derived cells were mesenchymal (CD90+, CD73+, and CD105+) and pluripotent (SOX2+ and OCT4+) [5], though the nature of milk-derived stem cells (mdSC) to be mesenchymal remained inconclusive [3]. The recent discovery of the integration of mdSC with the brain of suckling mice pup [4] is intriguing and thus warrants further investigations. Identification and characterization of mdSC in dairy animals (cow and goat) in infancy may have a potential for future therapeutic applications like cell growth, tissue regeneration, angiogenesis and tumor suppression. In addition, the presence of stem cells in milk can be an important source for other therapeutic purposes [7,8]. The use of mdSC is advantageous not only because of the cheapest source of stem cell isolation but also due to the non-invasive method, easy to harvest, devoid of tissue rejection and free from ethical issues.

Mammary cancer is the most common cause of woman cancer in India and accounts for more than 25-32% of female cancer [9]. Per the Indian Council for Medical Research (ICMR) registry data of 2016, the cancer burden in India is estimated to be 1·45 million new cases each year and is expected to increase in coming years [10]. Every 4-minute one patient is diagnosed with breast cancer in India. The success rate of the patient survival after the treatment is only 60% and killing a patient every 13-minute. However, breast cancer might not be prevented but could be treated using a novel approach alone or in conjugation with the existing technology. Application of mdSC and its secretome to repair mammary tissue and inhibit tumor growth is novel. The use of stem cells for tissue regeneration is a promising alternative to treating existing clinical diseases. The capabilities of stem cells, such as mammary stem cells, to elicit in vivo growth of mammary tissue and inhibition of metastasis of mammary tumor cells are not known. Mesenchymal stem cells (MSCs) secrete growth factors having paracrine and trophic functions, such as the promotion of nerve innervations that plays a fundamental role in tissue regeneration. Among the various strategy to treat cancer, surgery is the first option where tumor mass is excised, and a hollow area is allowed to fill up by regenerating healthy tissue. Other options to treat cancer are radiotherapy

(kill tumors by damaging cancer cell DNA) and chemotherapy (use very toxic drugs to stop or slow down tumor growth). Nano-sized exosomes have been shown to exhibit a crucial regulator of cell-cell interaction [11]. Meanwhile, Exosomes target tumor niche where they get entry into cancer cells via are endocytosis or receptor-ligand interaction, then release cargoes and thus affect tumor cell survival, progression, and metastasis [12]. In addition to these, recent studies also showed that conditioned media (CM) of stem cells (or secretome) contain secreted growth factors that have an important role in various physiological processes such as anti-microbials, angiogenic, growth promoters, cell proliferation, including tissue regeneration [13-15]. Secreted factors of stem cells and conditioned media of the mammosphere contained transforming growth factor-beta (TGFβ), insulin-like growth factor 1 (IGF-1), and hepatocyte growth factor (HGF) [14]. TGF-β stimulates programmed cell death and inhibits cell cycle progression, thus suppressing mammary tumorigenesis [16]. Primarily, mesenchymal stem cells (MSCs) have been involved in many clinical applications due to their immunosuppressive nature. MSCs confers resistance to rejection by the host immune system after transplantation, in addition to promoting cell survival, inducing angiogenesis, and thus promoting the growth of tissue. There is compelling evidence to show that MSCs have a pro-tumorigenic role, and also, these cells have potent tumor-suppressive effects that have been exploited as cancer therapeutics. For example, cytotoxic effects of MSCs have been demonstrated by releasing TNF-Related Apoptosis-Inducing Ligand (TRAIL) that selectively induces apoptosis in cancer cells. The apoptotic effect of MSCs on other types of cancer cells has been shown by inhibiting the activation of the ERK/AKT pathway [17] or by downregulating PI3K/AKT pathway [18].

In conclusion, stem cell derived-multiple antigenic vaccine may find applications in treating cancer. Role of mdSC in treating cancer is yet far from reality.

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