

## *INTRODUCTION*

Stem cells are unspecialized unique cells that have two properties making them different from other cell types, *Self-renewal* - the ability to go through numerous cycles of cell division while maintaining the undifferentiated state and *Potency* - the capacity to differentiate into specialized cell types under certain conditions. They are of two general types, embryonic stem cells and adult stem cells( Scholer;et al .,2007)

Embryonic stem cells are derived from the epiblast tissue of the inner cell mass (ICM) of a blastocyst .They are pluripotent and can develop into each of the more than 200 cell types of the adult body when given sufficient and necessary stimulation for a specific cell type (Montoya., 2005).

Adult stem cell is an undifferentiated cell found in a tissue or organ. This cell type can renew itself and can also give rise to "mature" cell types that have characteristic shapes and specialized functions ( Port.,2008 ).

Adult stem cells exist in significant numbers in tissues with high regenerative capacity and high cellular turnover such as bone marrow (*located in the osteoblastic niche on the bone surface*), intestines(*located between differentiated paneth cells*) and skin( *located in bulge area of hair follicle*)( Hassan,et al.,2004).

The potential clinical application of stem cell is now Stem cell based therapy, offering renewable source of replacement of cell and tissue ,beneficial in diseases like Alzheimer ,Spinal cord injuries,burns and Diabetes. (Gupta,etal.,2008)

The cancer stem cell hypothesis proposes that certain tumors originate from and persist due to mutations in tissue stem cells that result in unregulated, immortal proliferation, and in this state are referred to as cancer stem cells (Reya, et al., (2001).

cancer stem cells may generate tumors through the stem cell processes of self-renewal and differentiation into multiple cell types. Such cells are proposed to persist in tumors as a distinct population and cause relapse and metastasis by giving rise to new tumors(Matsui ,et al.,2004)

CSCs have been described for the first time in leukaemia(*Bonnet, et al .,1997*) but recently CSCs are identified in several solid tumors, including cancers of the Brain (*Singh,et al .,2003*), breast (*Al-Hajj ,et al;2003*), colon(*Brien ,et al.,2007*), ovary(*Zhang , et al.,2008*), pancreas(*Li C, et al .,2007*) and prostate(*Maitland , et al.,2008*).

Worldwide, breast cancer is the most common type of cancer and the most common cause of cancer-related mortality among women. In the United States, approximately 212,920 new cases of invasive breast cancer, 61,980 in situ cases, and 40,970 deaths were expected to have occurred in 2008. In women, breast cancer accounts for 26% of new cases of cancer and 15% of cancer death (*Martin, et al.,2008*). In Egypt, breast cancer is the first solid malignant tumor in women representing 37.6% (*Mokhter et al., 2007*).

Many studies for evaluation of cancer stem cell hypothesis have been applied for breast cancer(*polyak .,2007*).

Tumor initiating phenotype was proposed by Clarke and colleagues who provided the first proof of existence of cancer stem cells in solid tumors . Their study showed that in nine human breast cancer samples, a minority of cells bearing the surface markers  $CD44^{+}/CD24^{-/low}$  were capable of generating tumors in NOD/scid mice even when implanted in low number. By contrast ,the other cancer cell populations,such as  $CD44^{+}/CD24^{-/low}$  failed to generate tumors even when implanted in higher numbers(*Honeth,et al .,2008*) .

The presence of putative breast cancer stem cells is shown both in primary tumors and distant metastases. All patients had a putative stem cell phenotype among the disseminated tumor cells (DTC )and most individual DTC showed such  $CD24^{-/low}/CD44^{+}$  phenotype.(*Balic,et al.,2006*)

Tumorigenic breast cancer cells that express high levels of CD44 and low or undetectable levels of CD24 ( $CD44^{+}/CD24^{-/low}$ ) are proved to be resistant to chemotherapy and therefore responsible for cancer relapse.( *Xiaoxian ,et al .,2008*)

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