Evidence states that in cancer, leukemia growth and propagation are determined by leukemia cells, which have the potential for self-renewal and are known as cancer stem cells (CSC) (1). Shortly hereafter, this phenomenon was identified that leukemia cells are composed of many immature undifferentiated cells to more specialized cells having limited ability to self-renew. With the passage of time and more research on CSCs, it was observed that these cells are not located in blood only because these cells were isolated and characterized from various tumors such as breast (1), brain (2), colon (3), pancreas (4), prostate (5), lung (6), neck & head tumor (7). Lately, researchers suggested that CSCs presence is the main reason for relapse of disease (8, 9). Chemotherapies can wipe out bulk of cancer cells, while fails to target CSCs. Moreover, early treatment increases the quantity of drug resistant CSCs which results in recurrence of the disease (10). Hence, the cancer theory of stem cell suggest that small groups of CSCs are present in tumors which promote and maintain tumor growth (11, 12). For example, breast cancer stem cells (BCSCs) progressively play a vital function in growth of BC and are involved in metastasis. CSCs have potential to self-renew and yield daughter cells which result in bulk tumor cells formation, while maintaining a self-replicating potential. The long lasting life time of stem cells makes them able to cause mutations in DNA. The cells ability to replicate also makes them candidates for origin of
tumor cells (13). Here, we tried to discuss the role of organ specific CSCs in the localized cancer progression and metastasis.

**BREAST CANCER STEM CELLS (BCSCS)**

According to the CSC studies, cancer arises from normal stem cells, in the breast and in other tissues which undergo oncogenic transformation (14). CSC display characteristics that can have fundamental importance for detection of breast cancer, prevention as well as treatment. CSC promote formation of cell motility, growth of blood vessel and therapy resistance (15) and also involved in metastasis of breast (16, 17). Breast CSCs progressively play a vital role in growth of BC and are involved in metastasis.

Breast CSCs are mainly composed of cells expressing the cancer stem cell surface protein marker CD44+ (20). BCSCs expressed ESA+/CD44+ and lacking the expression of CD2, CD3, CD10, CD16, CD18, CD31, CD64 and CD140b (Lin-) by flow cytometry (21). Moreover, recent studies has demonstrated that BC tumor cells give increase expression of CD44 and reduce expression of CD24 marker and are chemotherapy resistance (22).

Furthermore, scientists also have identified an additional marker and protein called ALDH, produced by CSCs and observed in tumors of patient biopsies, CD133 (prominin-1) (23), CD49fhi have been proposed as BCSC biomarkers. ALDH1, is present in normal mammary SCs and BCSC, an enzyme which is used for oxidation of the intracellular aldehydes (24). Lately, sulforaphane a compound derived from broccoli, can be crucial to prevent or treat breast cancer by targeting CSCs. Researchers has find out that sulforaphane targeted and killed CSCs can prevent growing of new tumors (25). In mammary gland, three lineages are generated by differentiated cells, which include alveolar epithelial cells; cells that produce milk, myoepithelial cells; contracted cells that covers alveoli and ducts and thirdly, ductal epithelial cells; cells lining the ducts. Till recently, due to lack of cell surface markers identification, isolation and characterization of breast CSs was limit in range (26).

**NON-HODGKIN LYMPHOMA STEM CELLS (NHLSCS)**

The CSCs has evidenced the presence of specific population of cell in cancers, moreover suggests that cancers are basically isolated from CSCs that are responsible for specific stem cells properties including self-renewal (11). Hence, the existence of CSCs has been proved in various cancers including acute myeloid leukemia. Thus, several surface markers, to isolate CSCs, has been discovered including colon, brain and breast (27).
Recently, it has been suggested that in non-Hodgkin lymphoma, lymphoma stem cells do not provide sufficient data to confirm presence of CSCs. So, the presence of lymphoma SCs remains unresolved (28). To detect the presence of CSCs, that have no identified surface marker for isolation of stem cell, side population analysis has been applied. The side population is majorly discovered as a stem cell population. Moreover, this analysis is particularly based on normal stem cells characteristic, which allows to protect themselves from cytotoxic agents (29).

Hodgkin lymphoma comprise of side population cells, they can give rise to larger cells similar to morphology of Reed-Sternberg cell, also reported that they are resistance to chemotherapy (30).

Both, non-Hodgkin and Hodgkin lymphoma presents identical gene organizations of clonal IGH in Reed-Sternberg cells. B-cell non-Hodgkin’s lymphomas are obtained either from lymphoid cells or from mature B-lymphocytes, which develops chromosomal translocations through errors in the IG gene remodeling processes during normal B-cell differentiation (31, 32).

**COLORECTAL CANCER STEM CELLS (CRCSCS)**

Evidence demonstrates that the presence of CRCSCs in colorectal cancer (CRC) contribute to progression of tumor, chemotherapy resistance and failure in therapeutic approach (3, 33). Tumor cells carrying CD133 marker has high resistance to chemotherapy (34). Self-renewal and tumorigenic property of colorectal CSCs population in colon cancers has been evidenced in various studies employing the CD133 surface marker (3, 33). CD133 is the most common CSCs marker characterized (35). CD133 is a five transmembrane glycoprotein which was for the first time found in hematopoietic stem and progenitor cells (36). CD133 is found in various tumors, including brain cancer (37), colon (38, 39), liver (40), ovary (41), bone (42) and still in progress. CD133 (+) in cancers has ability to initiate tumor growth (3, 33). CD133 (+) cells can develop tumors with extended self-renewal and differentiation capabilities and without phenotypic alterations after serial transplantation. Tumorigenic potential of CD133 (+) has also been confirmed in vitro study (33). On the contrary, CD133 (-) has no ability to form tumors.

Moreover, some others markers for detection and evaluation of CSCs and their role in clinical significance of CRC has been observed. These markers include CD44 which is expressed in many cancers which include colorectal cancer (43-45), CD166 (43-47), CD29 (47, 48), CD24 (38, 48, 49), Lgr5 (39, 48) nuclear beta-catenin (50), EpCam (51), ALDH1 (51, 52), CDCP1 and CXCR4 (38) and CC188 (53). The use of the combination of these markers to identify CSCs in colorectal cancers will uncover more about the function of CSCs and will also play a significant role in clinical usage.

**CHRONIC MYELOID LEUKEMIA (CML) STEM CELLS**

Chronic Myeloid Leukemia is a systemic disturbance of hematopoietic stem cell. Tyrosine Kinase Inhibitors (TKI) therapy fails to heal patients of CML even though having capability to cause rapid remission, which has been demonstrated for leukemic stem cells presence in CML (54).
The property of cells including self-renewal and raising heterogeneous CML SCs population of is somehow alike to normal hematopoietic SCs but only difference is of gene marker of BCR-ABL which is particular to CML. SCs of CML exist as inactive state. Recently, studies state that CML SCs are not completely dependent on BCR-ABL gene, for their survival purpose and are not fully addicted to this oncoprotein (56).

The presence of leukemic SCs was conformed and was unresponsive to imatinib, which support the disease and acts as a reservoir of leukemia cells (43, 56). It has been noticed that TKI has ability to target progenitors better as compare to imatinib as they have high affinity to BCR-ABL gene. Drugs similar to imatinib, are not successful to fully cure the illness, patient have tendency to generate resistance against chemo and radiotherapy and disease reoccurs once the drug is discontinue (54, 57).

Several subsets of CD34+ cells were isolated from CML patients, BCR-ABL mRNA presence was assessed in each of the subsets of CD34+ cells. BCR-ABL mRNA was determined in CD34+ CD38− and CD34+ CD38+ cells (58). CML SCs are reported as a tiny subpopulations of cells that express Lin−, CD34+, CD38− and CD90+ (59). Moreover, it is also suggested that CML SCs forms a small subpopulation of the Lin−, CD34+, CD38− and CD90+ (60). Hence, some substitute targeted potential therapies are required for the suppression of CML stem cells, which function either alone or in combination with TKI.

**OVARIAN CANCER STEM CELLS (OCSCS)**

The CSCs are a small groups of tumor cells which has capability to self-renew and give rise to other SCs, also these cells goes through bulk cell proliferation and differentiation to producing mature cancer cell leading to formation of secondary/tertiary tumors (21, 61).

The reason behind 90% of cancers originates from ovary surface epithelium is that stem cells reside this area. In early stage of ovarian cancer (OC), the number of epithelial ovarian CSCs was used to predict progression of the disease (62). First CSCs were isolated in leukemia cells that express CD34 marker (1). Afterwards, various different types of CSCs were discovered, in ovarian CSCs, colon (46) and prostate cancers (5) and were evidence in many ovarian cancer patient (63). Various CSCs share identical biomarkers, as in ovarian CSCs. So the development of therapies that target directly the biomarkers of CSCs can meliorate clinical result and patient's survival (64).

In ovarian CSCs, CD44 is chiefly expressed, CD44+/CD24− expression correlates with invasion and chemotherapy resistance (65, 66). CD24 expression affects metastasis and represents a pathetic prognostics in OC (67). Various different antibodies has been introduced against isoforms of CD44 (68). Relative high expression of surface marker CD117 was remarked in OC (63). Tumor cells carrying CD133 marker has high resistance to chemotherapy (34). Its expression mostly goes higher in advanced stages of OC than in benign stage or normal ovaries (64). The epithelial cell adhesion molecule (EpCAM) is a protein membrane that is expressed majorly in various different types of tumor, including ovary, neck, breast, pancreas, head, colon and lungs. EpCAM serves as therapeutic agent to ovarian cancer (69). Aldehyde dehydrogenase (ALDH) isoenzyme ALDH1A1 was discovered as marker of CSCs, as it is chemoresistance in the ovarian CSC (70). Various ALDH isoenzymes including ALDH1A3, ALDH3A2 and ALDH7A1 has very higher expression rate in ovarian cancers in comparison to normal healthy ovarian tissues (71). Hence, ALDH is a remarkable marker to analyze ovarian cancer stem cells (OCSCs) which are responsible for Ovarian cancer progression.
CONCLUSION

Cancer Stem Cells (CSCs) from the day of their discoveries, have been known a big hurdle in cancer cure but with the huge research on their molecular biology, these are known as the hope to develop cancer treatment strategies. CSCs in every localized tumor behave in almost a similar way but the major issue is their stemness characteristics. Several questions are remained unanswered till now like why a tumor organ develops cancer stem cells for them? Or it’s the stem cells of specific organ who transformed themselves toward cancer cells and then cancer development or there is another unknown mechanism? If the cancer stem cells are developed after the development of cancer in an organ then there are several hopes to find the solutions sooner but if the organ specific stem cells transformed themselves toward cancer cells and then these cells developed the localized cancer, then the story is a little bit more difficult to explore. Understanding the current studies, it can be concluded that we are unable to find out cure until we cannot understand the mechanism of CSCs origin and then their role in cancer development and progression.

CONFLICT OF INTEREST

The authors declare no conflict of interest with any person or organization.

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