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Editorial

Cancer Stem Cells in Breast Cancer: an Overview

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Breast cancer is the most common cancer between women and, despite all the progress made so far, breast cancer still show a significant mortality, morbidity and a high incidence of recurrence and treatment failure. Thus, understand the tumor initiation, progression and renewal is fundamental to achieve better treatment choices. A recent theory that could explain the formation of tumors is the stem cells hypothesis that says that tumors originate by compromised self-renewal process of both tissue and progenitor stem cells.

Cancer stem cells, as like as normal stem cells, show properties like self-renewal, multilineage differentiation, apoptotic resistance and angiogenic induction [1,2] and most likely contribute to cancer progression, spread and therapy failure. Recent studies suggest that some cancers, including breast cancer, are driven by cells with stem cell characteristics. A small population of cells that were described only recently and appear to have an important role in breast tumor are called breast cancer stem cells (BCSC). In 2003, Al Hajj and coworkers analyzed cell surface markers in samples of 9 patients diagnosed for breast cancer. They isolated a small population of cells with increased expression of CD44 and low/absent expression of CD24 and observed that cells $CD44^{+}/CD24^{-/low}$ were able to form a whole new tumor when injected in NOD/CID mice and also keep their tumorigenic potential after serially transplantation in mice [3].

In 2005, Ponti and coworkers confirmed that $CD44^{+}/CD24^{-/low}$ breast cancer cells show stem cell properties and demonstrated that breast tumorigenic cells, when cultured *in vitro*, were able to propagate as mammosphere [4]. The ability to form mammospheres when cultured is a surrogate assay for self-renew [5]. In addition, breast cancer with a higher proportion of $CD44^{+}/CD24^{-/low}$ correlates with poor overall survival, increased distant metastases and a shorter period without recurrence [6,7].

However, other studies have demonstrated that only $CD44^{+}/CD24^{-/low}$ may not be sufficient to distinguish the population of cells with cancer stem cell properties. Ginestier and coworkers (2007) demonstrated that aldehyde dehydrogenase 1 (ALDH1) could be a stem cell marker, since cells positive for ALDH1 were capable to initiate a tumor and shown stem cell properties. They also analyzed the expression of ALDH1 in 577 breast tumor samples from patients and observed that tumors positive for ALDH1 correlated with poor clinical outcome. However, the exact function of aldehyde dehydrogenase 1 in cancer stem cells remains unknown [8].

Wright et al. (2008) shown that breast CSC positive for Prominin 1 (CD133) - a cell-surface glycoprotein with two large glycosylated extracellular loops and five transmembrane domains - were capable to form breast tumors with as few as 100 cells, similar to $CD44^{+}/CD24^{-/low}$ CSCs, while those negative for CD133 were incapable to generate new tumors in mouse xenograft models. CSCs positive for CD133 also express stem cell genes, show drug resistance and have the ability to form mammospheres [9]. Taken together, these findings regarding CD133 lead to the consideration of CD133 as a cancer stem cell marker candidate. Other markers, like BMI1, are being studied as potential stem cell markers due to their role in cell growth, proliferation and self-renewal of cancer stem cells [10]. Despite the large number of publications in CSC field, additional studies are fundamental. It is important identify other reliable markers capable of isolating the CSCs in order to identify new therapies that can reduce and even eradicate breast CSCs.

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