Significance of cancer stem cells and its biomarkers in carcinogenesis and cancer therapy

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Dear Friends
Season's greetings!!

Cancer is among the disease that kills major population in the world and its chance of cure is directly linked to early detection and appropriate intervention. I would like to highlight the recent advances in origin of cancer and cancer therapy. Most patients with cancer die because of metastasis and treatment resistance. For Head & Neck and Eyelid/ Ocular carcinoma, the standard treatment is chemotherapy, surgery and radiotherapy. Studies have proven that removing as much as possible of the tumor does not mean cure because minimum amount of cells can lead to relapse. Question arises how this happens?

Not every cancer cell is capable of initiating tumor. Several theories have been proposed to explain the origin of cancer. Most recent one is Cancer Stem Cell theory which is based on recent advance studies on cancer molecular biology. The Progenitor cell hypothesis of cancer development suggests special cells the Cancer Stem Cells (CSCs) also called Tumor initiating or generating or sustaining cells, are subpopulation of cancer cells within tumor that resemble normal stem cells due to self-renewal capacity but unlike normal adult stem cells they have unlimited division[1,2]. CSCs not only have the capability of self-renewal but have poorly regulated differentiation and extraordinary proliferative property due to high level of DNA repairer mechanism, resistance to apoptosis, long life span[3] and metastasize to distant sites. These peculiar biological properties contribute to the possibility that CSCs are responsible for cancer recurrence, metastasis and chemo-radio resistance.

Process of self-renewal of CSCs is highly controlled by several singling molecules and growth factors[4]. The origin of cancer Stem Cells is still a matter of debate. Genomic instability causing spontaneous transformation of non-tumorogenic stem cells into CSCs may be a causative factor. The carcinogenesis is a multistep process related to accumulation of epigenetic and genetic alterations (mutations) in singling pathway, responsible for transformation of tissue resident stem cells into CSCs.

First human CSCs was identified by Dick's group (1994) in Leukemic cells and later Al-Hajj isolated CSCs in solid tumor (breast cancer) using specific cell surface biomarkers[2,5]. Now several biomarkers have been used to identify CSCs in many types of cancers like CD34 and CD38 for Myeloid leukemia, CD14 and ALDH for Breast cancer, CD133 for Brain, Ovary & Lung, CD44 for Head & Neck cancer, ABCB5 for melanomas and CD24 for Retinoblastoma, Glioma, Prostatic cancer. CD24 is a small heavily glycosylated, phosphatidyl-inisitol-anchored ucin-like surface protein which is alternative ligand for P-selectin, an adhesion molecule which is expressed by activated endothelial cells and platelets. Functionally it plays a critical role in metastasis of tumor cells through P-selection[6]. However, a universal biomarkers for these cells may not exist. Though biomarkers may vary among patients and also according to the type of cancer but existence of biomarkers for CSCs would be helpful for early detection as well as treatment of the disease.

If CSCs are not completely eliminated, minimal amount will repopulate a tumor. The current methods of chemo-radiotherapy treatment are poorly selective (the drugs damage not only tumor cells but normal cells also) causing ineffectiveness and serious adverse effects. Thus identification of CSCs by using biomarkers brings about important therapeutic impacts. The drug targeting selectively the CSCs would eradicate the tumor without allowing recurrence of cancer. There is also option to attack microenvironment that support the CSCs either by preventing angiogenesis or interfering in singling pathway.

Despite much evidence pointing to the existence of CSCs, the subject is still controversial and needs further extensive research.

References

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