“Scientific Pill” Cancer Stem Cells and Radiation Treatment.

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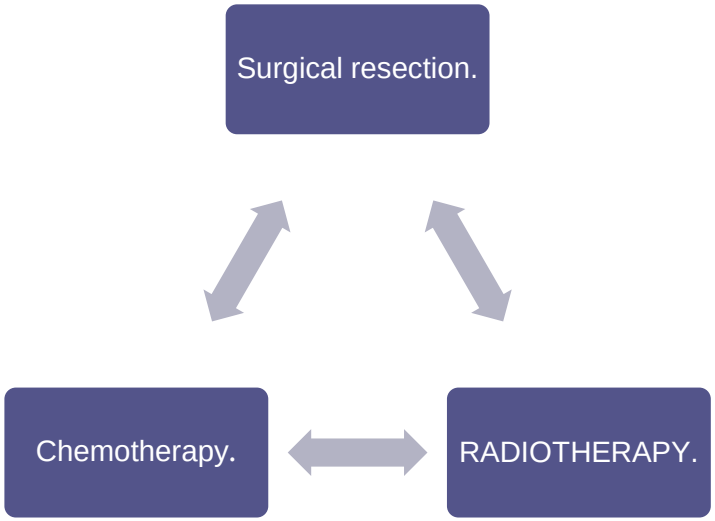
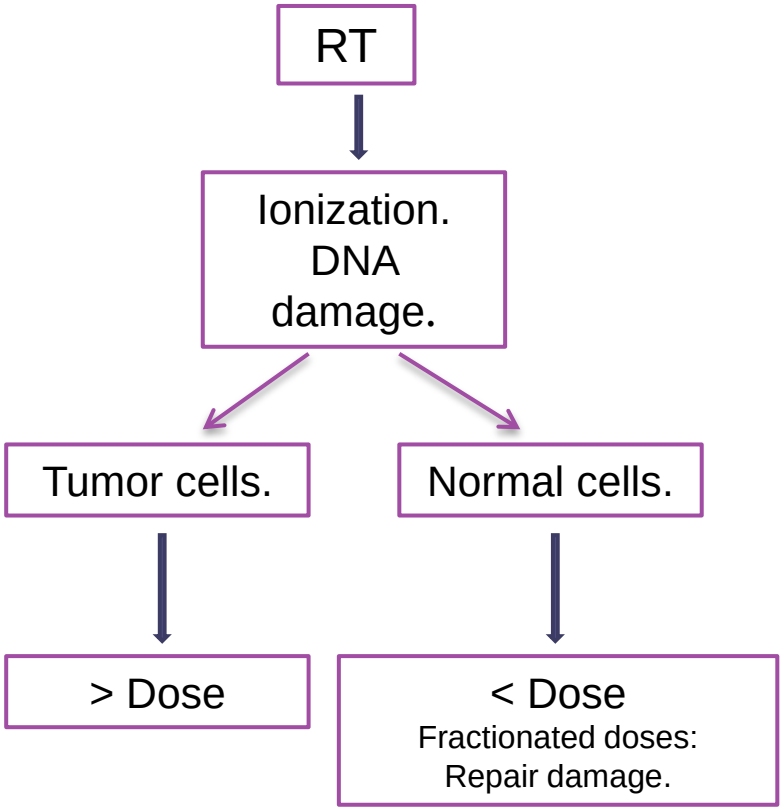
Radiotherapy (RT).

Cancer therapeutics pillars.

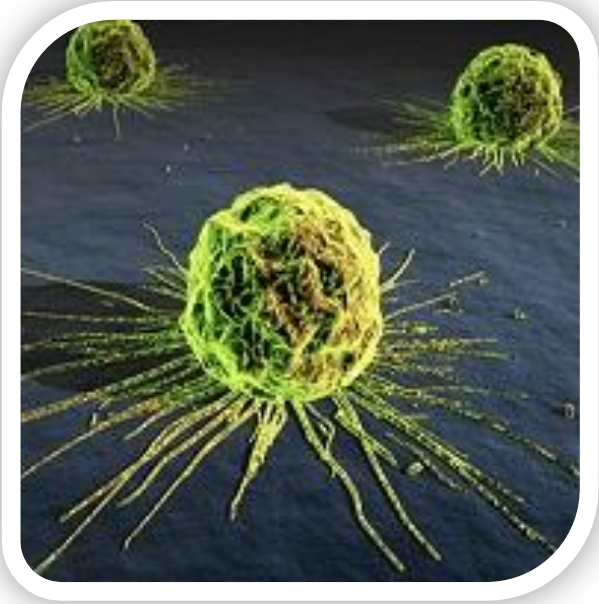




Cancer Stem Cells(CSC).

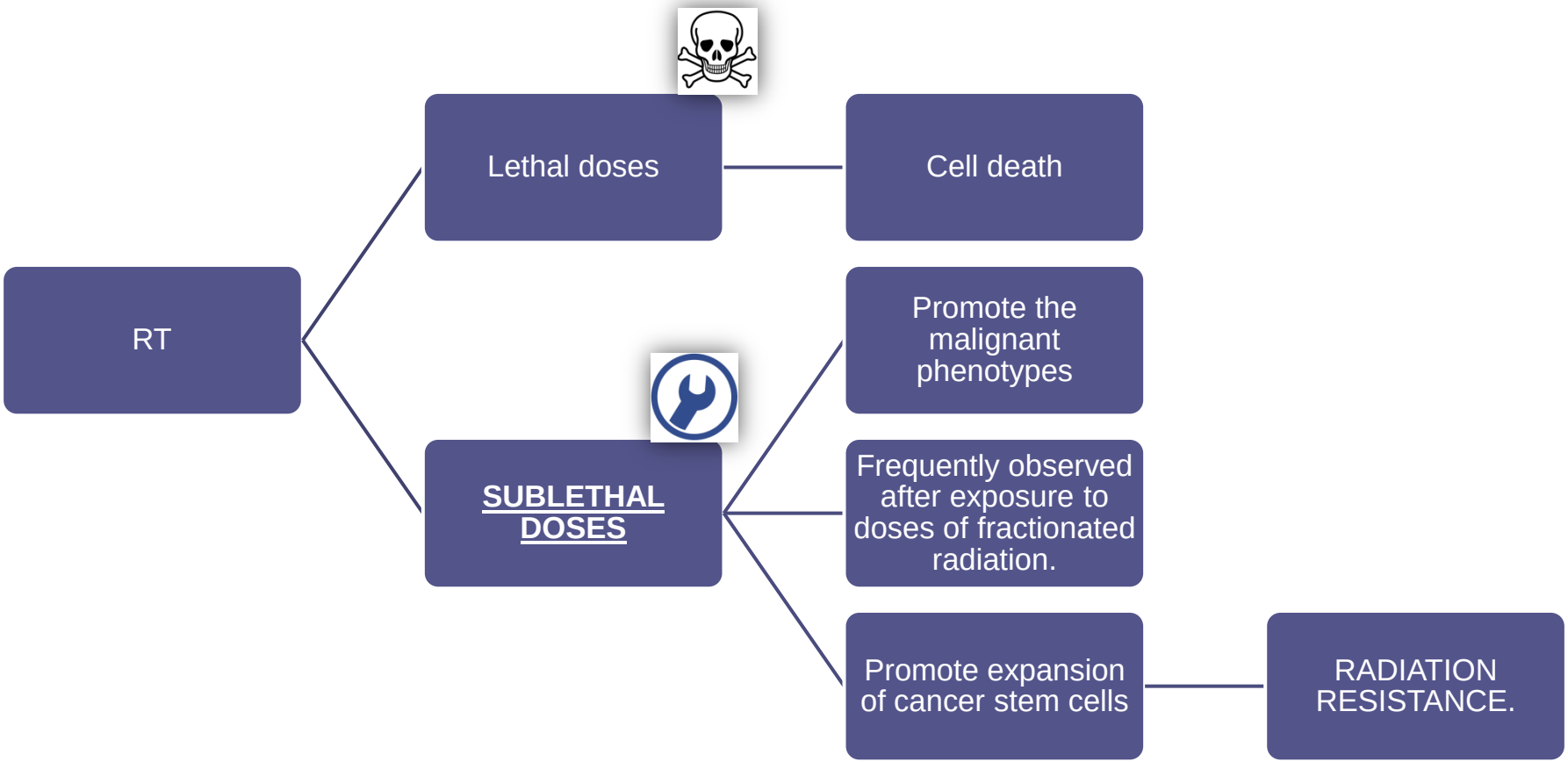
- Definition→ 3 characteristics.

  1. A selective capacity to initiate tumor and drive neoplasic proliferation.
  2. An ability to generate endless copies of themselves through self-renewal.
  3. The potential to give rise to more differentiated non-stem cell cancer progeny.



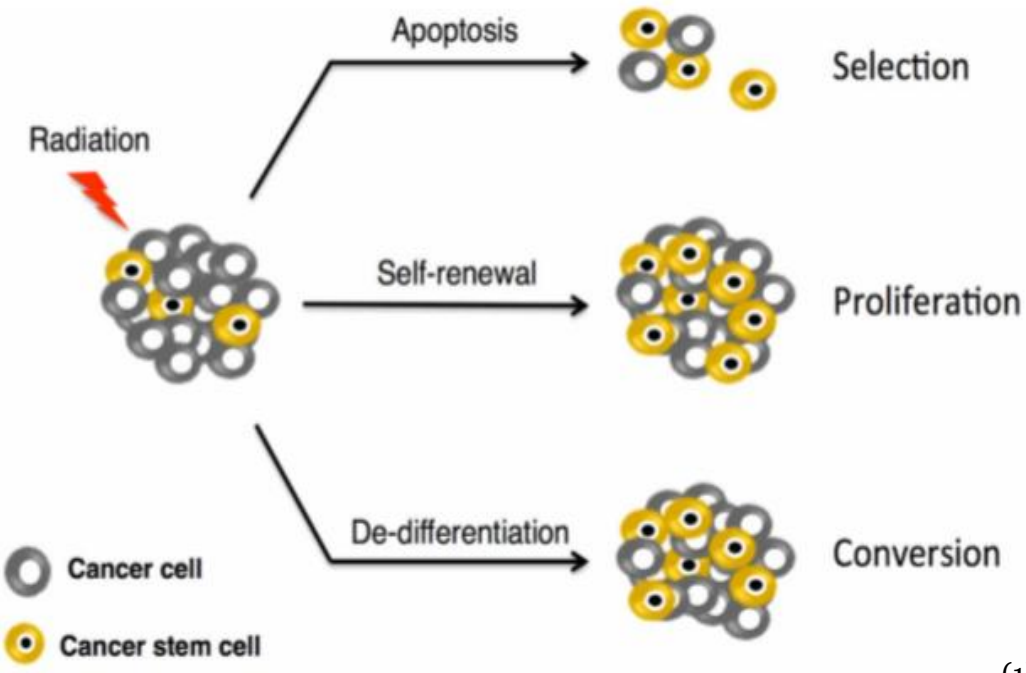
Detection and identification of CSC: a) Surface markers; b) Gene overexpression.

Population increase after irradiation CSC.



Population increase after irradiation CSC.

How? Hypothesis



(1)

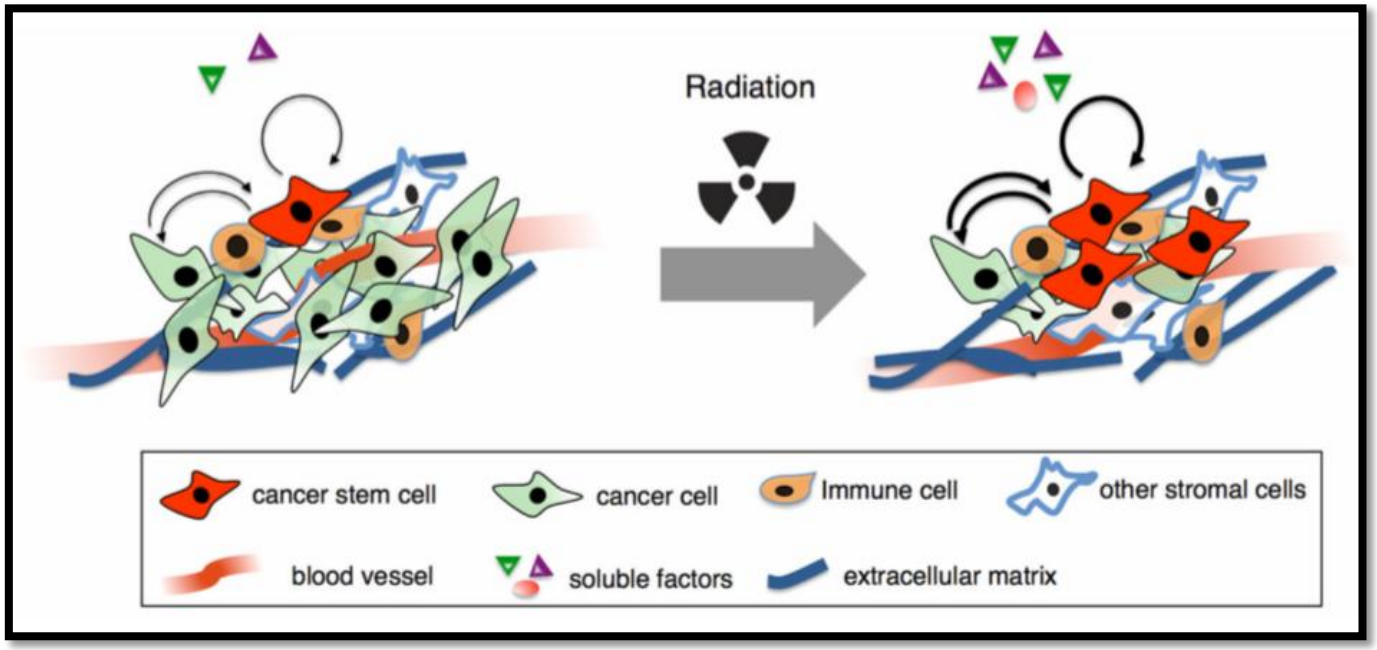
-CSC are more resistant to radiation than the rest of cancer cells.
-Preferential activation of the DNA damage response.

Exposure to sublethal radiation stimulates proliferation.

Adaptation to radiation of some cancer cells and acquire radio-resistance in association with self-renewal and tumorigenic capacity.

Microenvironment/CSC/Radiation.

- As anti-radiation mechanism, cells can undergo senescence.
- Radiationt-induced senescent cells secrete many soluble factors that could alter the behavior of neighboring cells.
- Cytokines and chemokines could provide a cancer-promoting microenvironment for their neighboring tumor and normal cells.



(1)

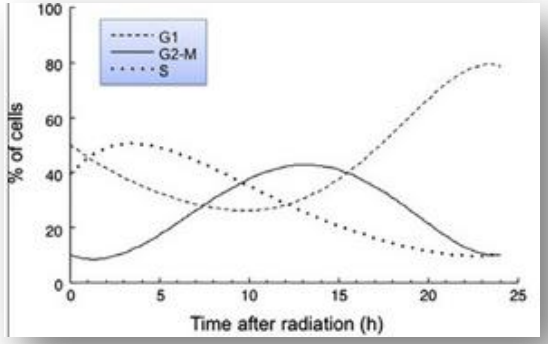
Mechanism of radiation resistance.

CSC's radioresistance → Tumor **RECURRENCE**

1. Redistribution.
2. Enhanced repair of DNA.
3. Upregulated cell cycle control mechanisms.
4. Reactive Oxygen Species (ROSs) and free radical scavenging.
5. Interaction with stromal environment.

Mechanism of radiation resistance.

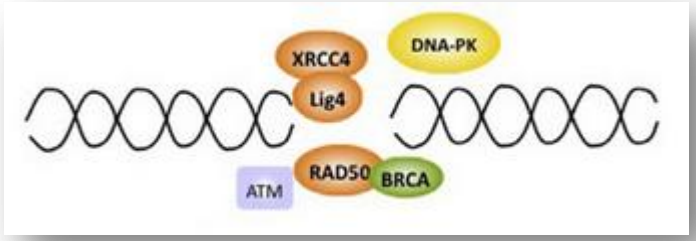
1. Redistribution.



(2)

Cells change their radiosensitivity as they traverse the division cycle. CSCs are usually in the **quiescent phase**.

2. Enhanced reparir of DNA.



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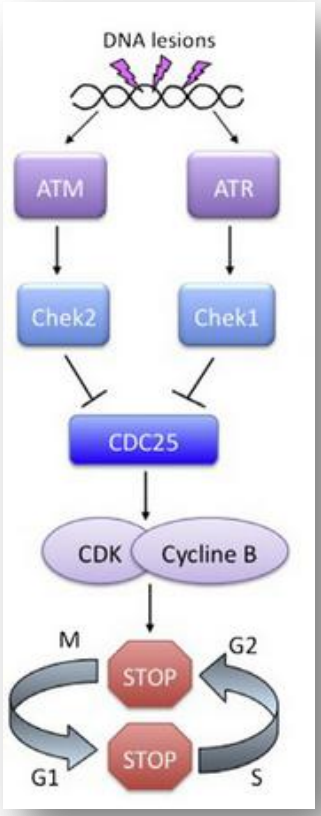
Fundamentally NHEJ. Recognition and reparation.

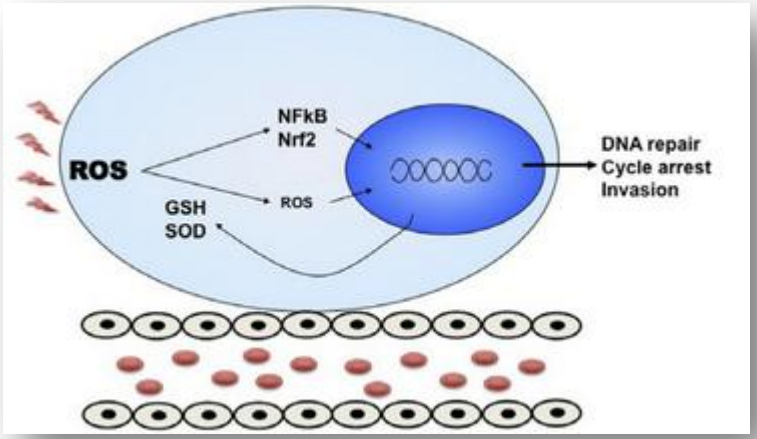
3. Upregulated cell cycle control mechanisms.



(2)

Mechanism of radiation resistance.

4. ROSs and free radical scavenging.



(2)

CSCs reside in a perivascular niche and are exposed to oxygen and high ROS levels.

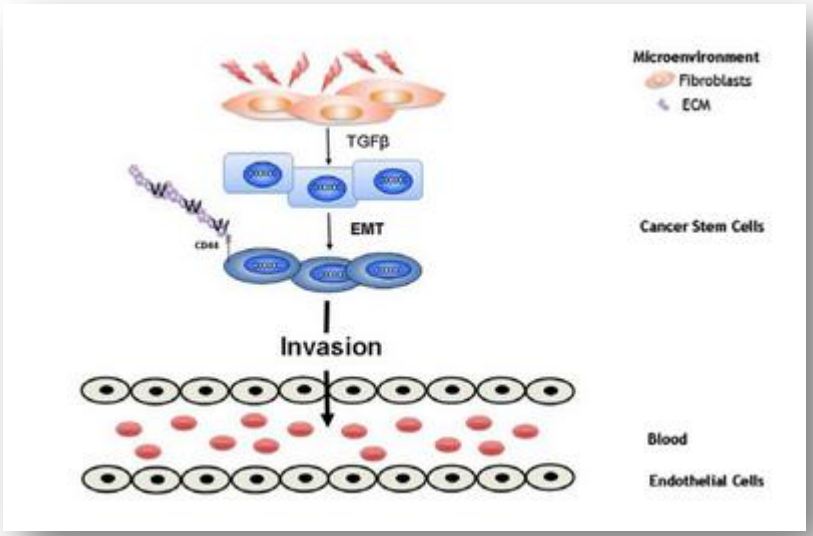
-ROS-scavenging enzymes:

-Superoxide dismutase(**SOD**).

-Glutathione (**GSH**).

-Activation of transcription factors that actives these enzymes.

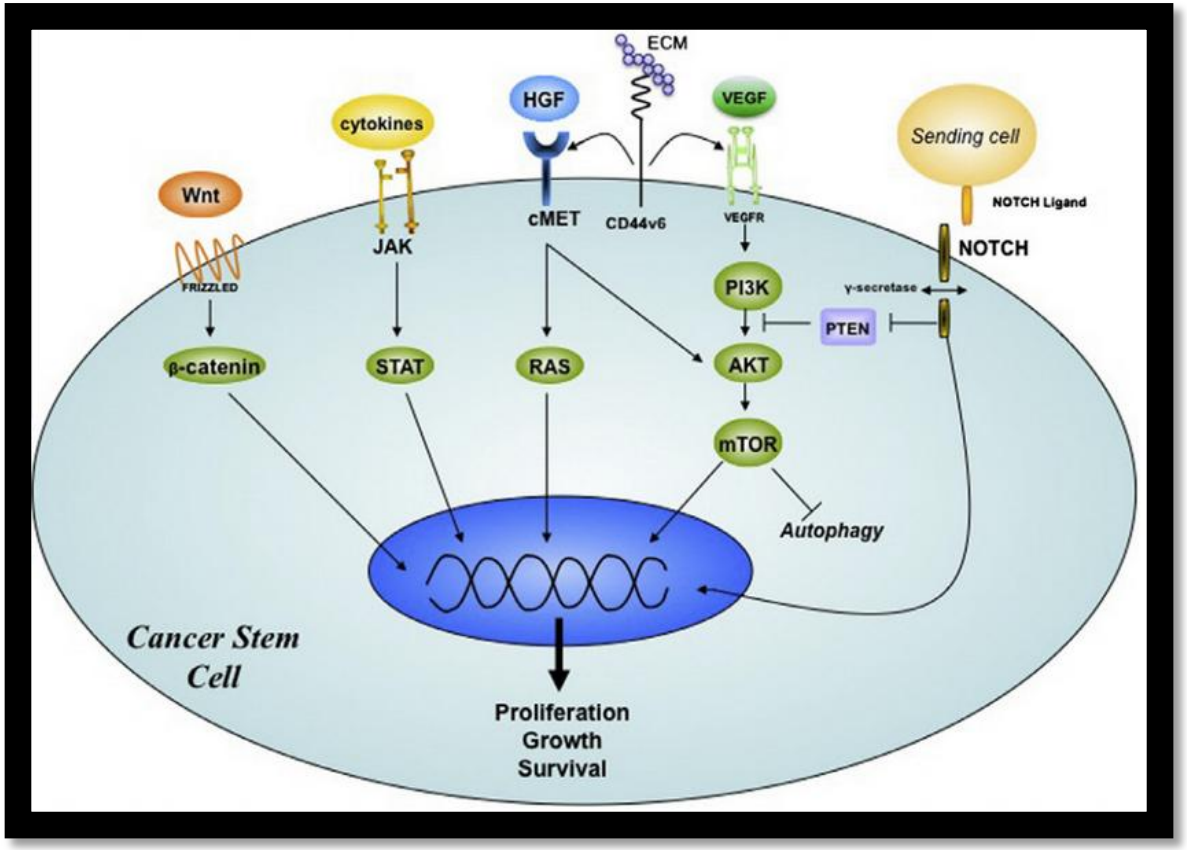
5. Interaction with stromal environment.



(2)

Changes in gene expression in the fibroblasts→ TGF-β→EMT

Therapeutical strategies to target CSCs.



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Bibliografía.

1.- Yongjoon S, Su-Jae L. Radiation treatment and cancer stem cells. Arch. Pharm. Res. 2015:(38): 408-413.

2.- Moncharmont C, Levy A, Gilormini M, et al. Targeting a cornerstone of radiation resistance: Cancer stem cell. Cancer Lett. 2012:(322): 139-147.

3.- Morrison R, M. Schleicher S, Sun Y, et al. Targeting the Mechanisms of Resistance to Chemotherapy and Radiotherapy with the Cancer Stem Cell Hypothesis. J Oncol. 2010: (2011): 13.