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Aggressive phenotype of triple-negative breast cancer stem cells (TNBC-CSC)

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Recent studies on surface receptors and gene expression of breast tumors have come up with a term Triple-Negative Breast Cancer (TNBC), creating a phenotype and disease quite distinct from that seen in Triple-Positive Breast Cancer (TPBC), which is a much more aggressive disease without tumor-specific treatment options. Although slightly responsive to chemotherapy, TNBC is more difficult to treat and generally insensitive to most available hormonal or targeted therapeutic agents. We constructed a population of TNBC and TPBC by stable transfection of 4T1 cells with the rat HER2 gene, ER gene and PgR gene to avoid non-specific immune responses, and sorting using flow cytometry. Cells were injected into mice and HT was achieved using gold nanoshells, and live animal imaging was used to non-invasively measure tumor growth. We uncovered two phenotypically distinct populations of cancer stem cells (CSC) based on the expression of CD24+/ALDH-1+/CD44 high cells, and demonstrated that they proliferate significantly faster than CD24-/ALDH-1-/CD44 low cells or wild type controls. Exposure of TNBC-CSC and TPBC-CSC to HT, RT or HT+RT result in differential release of Hsp72. Under all conditions tested, TPBC-CSC released significantly more Hsp72 than TNBC-CSC. Western blot analysis of the 1.17 g/ml density exosome fraction (obtained from sucrose gradient ultracentrifugation) revealed that TPBC-CSC contained significantly more Hsp72 within the exosomes than TNBC-CSC. Taken together this investigation determined that the use of combined HT+RT in combination with current anti-breast cancer chemotherapeutic, known as the triple modality will be beneficial to patients with TNBC.

Biography

Punit Kaur finished her BSc in 1999 with Botany, Zoology and Chemistry from Punjab University, Chandigarh, India. Then she went for Postgraduation (MSc) (1999-2001) in Microbiology from Guru Nanak Dev University, Amritsar, Punjab, India. Later she pursued for PhD (2001-2008) on the topic Experimental Medicine and Biotechnology from the Postgraduate Institute of Medical Education and Research, Chandigarh, India.

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