Development and Targeting of TIGER1 and seng-6 as Immunotherapy for Human Breast Cancer Stem Cells

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Published Date: 12-10-2014

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While the majority of conventional research focused on cell-based research, the newly discovered technology of neoovage has provided the opportunity for investigating embryonic and adult stem cells and has also helped identify the exact gene that selects TIGER1 cells.

TIGER1 is a TALEN-like substance, which is an integrase of EGF that functions in the T- and B-cell induced self-renewal pathway. When the effector cells such as T- and B-cells do not survive, TIGER1 is used to clear away harmful cells. This process involves the use of TANGS2-2, a second fusion gene found to be highly involved in stem cell interleukin-6 (IL-6) levels and cell death, and SENG-6, a cancer-associated ligand known to induce progenitor cell differentiation. TIGER1 influences maturation of stem cells by inducing differentiation to human T- and B-cell induced self-renewal inducing cells. Seng-6 is involved in cell proliferation, differentiation, and cell death. In the T- and B-cell stem cells, SENG-6 induces the aberrations found to be present in human breast cancer cells.

In the study, TIGER1 enhances the cell differentiation in breast cancer stem cells by activating the IL-6 protein and SENG-6. Previously, a group of researchers from Vanderbilt University claimed a triumph in discovering the defect in human breast cancer cells in which seng-6 is prevented by CTLA-4. The result was that the cancers displayed a high inflammatory immune response as well as large tumoral mass. In the new study, this finding is questioned as TIGER1 activation leads to the pathological effects of IL-6 and SENG-6. Theoretically, TIGER1 could be inhibited by CTLA-4 to prevent tumor formation and the consequent death of T- and B-cells cells. Similarly, TIGER1 activation could not be dampened by CTLA-4â€™s inhibitory role, therefore it is likely that CTLA-4 mutates as a function of seng-6 and hence a safer therapeutic strategy should be explored as the two mechanisms lead to the same end result (i.e. T- and B-cell induced self-renewal inducing the tumor).

Background:

Earlier analyses of TIGER1 and IL-6 have been based on single activation of the protein TIGER1 and its inflammatory effects. However, it was unclear as to whether cell proliferation occurs in conjunction with IL-6 activation and this is another side of the story.

Microarray analysis of human breast cancer stem cells in collaboration with Professor Eric B. Berger of the Sanford Consortium for Regenerative Medicine supported the use of screening of human stem cells in collaboration with co-authors from Cancer Research UK and with Gillian Allen and others from the Helen Graham Cancer Research Institute. Seng-6 pathway specificity and its availability in human breast cancer stem cells has supported the novel design of treatment strategies by Yee Chen and YI Yoon.

TIGER1 activation by CTLA-4 was induced by Seng-6 and IL-6 promotes the proliferation and differentiation of human breast cancer stem cells under TIGER1/Seng-6/IL-6 activation.

Neoovage technology is an immuno-oncology-promoting platform that enables screening individual cell lines and cells in isolation of activated immunotherapies such as TIGER1/Seng-6/IL-6 as well as new lead molecule, stem cell-targeted cell signaling agents and translational genetics.

The present study first identified the correct regulatory mechanism of the IL-6/Seng-6 pathway for TIGER1/Seng-6 induced cancer stem cell differentiation under TIGER1/Seng-6/IL-6-mediated activation. TIGER1/Seng-6/IL-6 interaction is restricted to the T- and B-cells and thus activates T- and B-cell spleens in the cancer cells. Thus, activation of IL-6 by TIGER1/Seng-6/IL-6 receptor family leads to the expression of TIGER1/Seng-6/IL-6 in the basal 1/renal 1+ human breast cancer stem cells and consequently TIGER1/Seng-6/IL-6/IL-6-induced tumors.

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