WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A REVIEW ON TARGETING CANCER STEM CELLS with NATURAL PRODUCTS

TARVIN PUNITHA KUMAR.T[1], DIVYA.K[2]

[1] B.PHARMACY
[2] PHARM.D.
DEPARTMENT OF PHARMACOLOGY.
DEPARTMENT OF PHARMACOLOGY, PALLAVAN COLLEGE OF PHARMACY, IYYENGARKULAM, KANCHIPURAM-631502.

ABSTRACT :

A subset of cancer cells known as cancer stem cells (CSCs) are in charge of the development, spread, and recurrence of cancer. One intriguing approach to cancer treatment is to target CSCs. The development of CSC-targeted therapeutics, including as CSC-specific markers, signaling pathway blockage, and epigenetic modification, is covered in this review along with the therapeutic significance of CSCs in the treatment of cancer. The review also emphasizes how natural ingredients like green tea catechins, resveratrol, and curcumin may be able to target CSCs and stop the spread of cancer.

Key words: Cancer stem cells, Targeted therapy, Natural products, Curcumin, Resveratrol

INTRODUCTION :

Despite advances in many therapeutic measures, cancer remains one of the most dangerous diseases that impact people globally. Drug resistance is one of the main issues with cancer treatment, and it has been discovered that cancer stem cells (CSCs) are one of the key mediators of resistance. Toxicological characteristics that restrict the life-extending potential of the majority of CT medications significantly impair their therapeutic efficacies. Chemosensitizers and drug delivery systems, two new technologies designed to enhance the effectiveness of CT medications, have not yet demonstrated clinical promise in the majority of cancer types. CSC-targeted treatments have received a lot of attention in recent years. In light of this, several promising novel treatment approaches that target CSCs directly, including CSC biomarker-mediated targeting,

Therapeutic Implications of CSCs in Cancer Treatment :

Many retrospective studies that question the current Response Evaluation Criteria in Solid Tumors (RECIST) guidelines for assessing the efficacy of cancer therapeutics in clinical trials have suggested that the failure to assess CSC response in patients receiving CT may be a factor contributing to tumor recurrence. In particular, it has been argued that the time-to-progression, progression-free survival, and tumor size parameters used to assess the therapeutic efficacy of pharmacological compounds are not reliable indicators of patient outcomes. New standards for assessing and standardizing response criteria in known stem cell-associated cancers are therefore being put out. Numerous intrinsic drug-resistance mechanisms in CSCs have the ability to render cytotoxic medicines inactive, which can lead to the recurrence of tumors.

CSC-Targeted Therapies :

1. CSC-specific markers: Using small compounds or monoclonal antibodies to target CSC-specific markers such CD44, CD133, and ALDH1.
2. Signaling pathway inhibition: Blocking signaling pathways like Wnt/β-catenin, Notch, and Hedgehog that are essential for maintaining CSCs.
3. Epigenetic modulation: Changing CSC-specific epigenetic alterations like histone modification and DNA methylation.

CSC-Directed Immunotherapy

1. CSC-specific vaccines: creating vaccinations that target antigens unique to CSCs, like WT1 or HER2.
2. Adoptive T-cell therapy: Using T cells, including CAR-T cells, that are particularly directed against CSCs.
3. Immunomodulatory treatments: Boosting anti-CSC immunity with immunomodulatory treatments, like checkpoint inhibitors.

CSC-Targeted Chemotherapy

1. CSC-specific chemotherapeutics: creating drugs like gemcitabine or salinomycin that target CSCs exclusively.
2. CSC-targeted nanoparticle delivery: Chemotherapeutics are delivered to CSCs exclusively via nanoparticles.
3. Combination chemotherapy: To improve anti-tumor activity, CSC-targeted chemotherapeutics are combined with traditional chemotherapeutics.

CSC-Based Cancer Treatment Strategies

1. CSC-directed therapy: This approach focuses on CSCs as the main treatment target.
2. Combining CSC-targeted treatments with traditional cancer treatments is known as CSC-targeted combination therapy.
3. CSC-based biomarker development: creating biomarkers that can identify CSCs specifically, enabling early cancer detection and tracking.

Genetic and Molecular Signatures of CSCs

In addition to helping identify possible molecular targets for NPs' therapeutic activity screening, the CSC genotype and phenotypic specification may result in prognostic indicators of tumor dissemination and recurrence. CSCs can be identified by analyzing surface Cell Adhesion Molecules (CAM) expression (immunophenotype) profiles, such as CD133, CD44, CD34, and CD24, using Fluorescence Activated Cell Sorting (FACS), immunofluorescent detection by confocal microscopy, tumor sphere forming assays, Hoechst dye exclusion in side-population (SP) cells, identification of signaling pathways, serial colony-forming unit assays, migration assays, and label-retention assays.

Transcription Factors :

1. SOX2: Overexpressed in different kinds of CSCs, this transcription factor preserves stem cell pluripotency.
2. OCT4: Overexpressed in CSCs from different types of cancer, this transcription factor controls stem cell self-renewal.
3. NANOG: Overexpressed in CSCs from different types of cancer, this transcription factor preserves stem cell pluripotency.

Cell Surface Markers

1. CD44: CSCs from a variety of malignancies, such as breast, colon, and prostate cancer, overexpress this cell surface marker.
2. Second, CSCs from a variety of malignancies, such as lung, colon, and brain cancer, overexpress the cell surface marker CD133.
3. ALDH1: CSCs from a variety of malignancies, such as breast, colon, and prostate cancer, overexpress this cell surface marker.

Signalling Pathways

1. Wnt/β-catenin pathway: This signaling pathway encourages cancer and self-renewal when it is activated in CSCs.
2. Notch signaling pathway: This signaling route encourages cancer and self-renewal when it is triggered in CSCs.
3. Hedgehog signaling pathway: This signaling route encourages cancer and self-renewal when it is triggered in CSCs.

Gene Expression Profiles :

Genes overexpressed in CSCs that promote stem cell pluripotency include SOX2, OCT4, and NANOG; genes overexpressed in CSCs that promote epithelial-to-mesenchymal transition (EMT) include TWIST, SNAIL, and SLUG; and genes overexpressed in CSCs that promote EMT include ABCG2 and MDR1.

MicroRNAs :

1. miR-21: A microRNA that encourages carcinogenesis and is overexpressed in CSCs.
2. miR-34a: A microRNA that suppresses carcinogenesis and is downregulated in CSCs.
3. miR-200c: A microRNA that prevents EMT and is downregulated in CSCs.

Developmental and Maintenance Signaling Pathways :

Wnt/β-catenin, Notch, and Hedgehog are examples of cellular signaling networks that control tissue homeostasis and embryonic development. Cellular signaling networks, including PI3K/Akt/mTOR, NF-κB, and STAT3, that control cell survival, proliferation, and metabolism.

WNT/β-catenin pathway

Proteins transmitting cellular signals, either in the closest cell-to-cell communication (paracrine) or communication within the same cell (autocrine), initiate the Wnt/-catenin pathway, which is a collection of signal transduction pathways. WNT/β-catenin signaling is triggered when WNT binds to the Frizzled receptor, which causes β-catenin to accumulate in the cytoplasm.

Notch pathway

Several Notch receptor types, including Notch1, Notch2, Notch3, and Notch4, make up the Notch pathway. The proteolytic cleavage of the receptor's cytoplasmic domain is initiated by the sequential contact and binding of Notch ligands (Delta-like-1, DLL3, DLL4, Jagged1, or JAG2) with NOTCH receptors (Notch1–4), ADAM/TACE, and-secretase. When Delta-like and Jagged surface ligands attach, A Disintegrin and Metalloproteinase (ADAM) proteases and secretase proteolytic enzymes cleave the ligand, activating Notch signaling.

Clinical Studies on Phytomedicines :

Few clinical trials assessing the safety and effectiveness of phytomedicines that target drug-resistant CSCs and cancer cells have been conducted recently. Zhebeigranules, a combination of three herbs, have been demonstrated to lower the proportions of CD34+, CD123+, and CD33+,CD123+ leukemia stem cells in patients with acute myeloid leukemia when used in conjunction with chemotherapy.

Curcumin

In patients with advanced colorectal cancer, a phase II clinical trial showed that curcumin, a polyphenol found in turmeric, slows the proliferation of cancer stem cells and triggers apoptosis.
Curcumin inhibits the Wnt/β-catenin signaling system, which targets cancer stem cells in breast cancer, according to a preclinical study.

Resveratrol

1. Resveratrol, a polyphenol found in grapes, has been shown in a phase I clinical trial to limit the formation of cancer stem cells and cause apoptosis in patients with colon cancer.
2. Resveratrol inhibits the Notch signaling system to target cancer stem cells in pancreatic cancer, according to a preclinical study.

Ginger

By blocking the NF-κB signaling system, ginger extract suppresses the proliferation of cancer stem cells and causes ovarian cancer cells to undergo apoptosis, according to a preclinical study.
Ginger extract has been shown in a phase II clinical research to lessen nausea and vomiting that cancer patients experience during chemotherapy.

Green tea catechins

1. A preclinical investigation shown that via blocking the PI3K/Akt signaling pathway, green tea catechins, in particular EGCG, limit the proliferation of cancer stem cells and cause apoptosis in prostate cancer cells.
2. In individuals with androgen-independent prostate cancer, green tea catechins have been shown in a phase II clinical trial to prevent the proliferation of prostate cancer cells.

Conclusion :

The creation of more potent and long-lasting cancer treatments may result from focusing on cancer stem cells, which are a crucial target for cancer therapy. Green tea catechins, resveratrol, and curcumin are examples of natural compounds that have demonstrated potential in preventing the growth of cancer by targeting CSCs. To thoroughly investigate the potential of these natural chemicals and create novel treatments that can specifically target CSCs, more research is required. Research into CSC-targeted therapeutics, including as CSC-specific markers, signaling pathway blockage, and epigenetic modification, is a promising field with enormous potential to enhance the effectiveness of cancer treatment.

REFERENCE :

1. Moselhy, J., Srinivasan, S., Ankem, M. K., & Damodaran, C. (2015). Natural products that target cancer stem cells. *Anticancer Research*, *35*(11), 5773-5788.
2. Gupta, P. K., Saraff, M., Gahtori, R., Negi, N., Tripathi, S. K., Kumar, J., ... & Kesari, K. K. (2021). Phytomedicines targeting cancer stem cells: Therapeutic opportunities and prospects for pharmaceutical development. *Pharmaceuticals*, *14*(7), 676.

3. Duan, H., Liu, Y., Gao, Z., & Huang, W. (2021). Recent advances in drug delivery systems for targeting cancer stem cells. *Acta Pharmaceutica Sinica B*, *11*(1), 55-70.
4. Gairola, K., Gururani, S., Bahuguna, A., Garia, V., Pujari, R., & Dubey, S. K. (2021). Natural products targeting cancer stem cells: Implications for cancer chemoprevention and therapeutics. *Journal of Food Biochemistry*, *45*(7), e13772.