



Wnt antagonism in cancer stem cells- targeting stemness of cancers via the Wnt-BETA catenin pathway

Sudha Warriar, PhD

Associate Professor
Group Head- Wnt Lab
PI- Cancer Stem Cells and Cardiovascular and Neuronal Regeneration
Manipal School of Regenerative Medicine, Manipal University
Bangalore, India
Adjunct Associate Professor
Curtin Medical School, Faculty of Health

Abstract

Cancer stem cells (CSCs) are hypothesized to be the pathological counterpart of normal somatic tissue stem cells. The CSC model proposes that tumours are hierarchically organised with a subset of tumour cells at their apex, which possess self-renewal and multilineage differentiation potential. Cancer stem cells, unlike the bulk of the cells within the tumor, are elusive to drug treatment and are unaffected on chemo and radiotherapy. These self-renewing cells are responsible for the flare up of cancer and remission long after treatment. Cancer stem cells have a capacity for unlimited self-renewal, as well as the ability to initiate and drive tumor progression in an animal model.

Activated Wnt/ β -Catenin signaling is a key feature of epithelial cancers and is critical for metastasis and epithelial-mesenchymal transition (EMT) , a signature trait of CSCs. We explored the effect of the Wnt antagonist, secreted frizzled related protein 4 (sFRP4) in CSCs in gliomas. We found that sFRP4 chemo-sensitizes GSC-enriched cells to commonly used drugs, by the reversal of EMT and by decreasing drug effluxers. sFRP4 acts at multiple levels of the Wnt- β -Catenin and the Wnt- calcium pathways in inhibiting CSCs. We also identified a novel mechanism of action of sFRP4. These findings could be exploited for designing better targeted strategies to improve chemo-response and eventually eliminate glioblastoma CSCs.

*For correspondence:

Competing interests: The authors declare that no competing interests exist.

Received: 2017-05-29

Accepted: 2017-06-29

Published: 2017-09-05

Copyright The Author(s) 2017. This article is published with open access by BioMedPress (BMP).

This article is distributed under the terms of the Creative Commons Attribution License (CC-BY 4.0) which permits any use, distribution, and reproduction in any medium, provided the original author(s) and the source are credited.

Keywords

Funding

References