

ONC201 may inhibit cancer stem cell self-renewals by altering their gene expression

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ONC201 may inhibit cancer stem cell self-renewals by altering their gene expression, according to a study published August 2, 2017 in the open-access journal *PLOS ONE* by Varun Vijay Prabhu from Oncoceutics, Inc., USA and colleagues.

Cancer stem cells survive after chemotherapy and radiation treatment and are associated with recurrence, metastasis and poor survival in clinical trials. Previous studies have shown that a small molecule known as ONC201 currently in advanced [cancer clinical trials](#), targets self-renewing colorectal cancer stem cells. However, little is known about the specific stem cell-related effects by which ONC201 inhibits cancer stem cells from renewing.

Prabhu and colleagues conducted a [gene expression analysis](#) of colorectal, prostate cancer and glioblastoma cell lines and patient-derived tissues that were both treated with ONC201. They found that ONC201 alters the gene expression of [cancer stem cell](#) markers and signaling pathways prior to killing the tumor cells, providing pharmacodynamic biomarkers of response. These changes were not observed in cells with acquired resistance to ONC201. Finally, the authors suggest that a pre-treatment gene expression signature of cancer stem cells might be able to help predict the response to ONC201.

These findings provide further evidence of ONC201 as an inhibitor of cancer stem cells and support ongoing clinical trials in prostate cancer and glioblastoma that have shown evidence of tumor shrinkage. Further

research could test these cancer stem cell [gene expression](#) at the RNA and protein level in circulating [tumor cells](#) and biopsies from patients on trial.

More information: Prabhu VV, Lulla AR, Madhukar NS, Ralff MD, Zhao D, Kline CLB, et al. (2017) Cancer stem cell-related gene expression as a potential biomarker of response for first-in-class imipridone ONC201 in solid tumors. *PLoS ONE* 12(8): e0180541. doi.org/10.1371/journal.pone.0180541

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