Biomedical Research & Therapy

ISSN: 2198-4093
www.bmrat.org

POSTER

# All-trans retinoic acid targets gastric cancer stem cells and inhibits patient-derived gastric carcinoma tumor growth

P H Nguyen, J Giraud, C Staedel, L Chambonnier, P Dubus , E Chevret, H Boeuf, X Gauthereau, B Rousseau, M Fevre, I Soubeyran, G Belleannée, S Evrard, D Collet, F Mégraud and C Varon

Faculty of Biotechnology Thai Nguyen Universtiy of Sciences, Thai Nguyen, Vietnam

## Abstract

Gastric carcinoma is the third leading cause of cancer-related death worldwide. This cancer, most of the time metastatic, is essentially treated by surgery associated with conventional chemotherapy, and has a poor prognosis. The existence of cancer stem cells (CSC) expressing CD44 and a high aldehyde dehydrogenase (ALDH) activity has recently been demonstrated in gastric carcinoma and has opened new perspectives to develop targeted therapy. In this study, we evaluated the effects of all-transretinoic acid (ATRA) on CSCs in human gastric carcinoma. ATRA effects were evaluated on the proliferation and tumorigenic properties of gastric carcinoma cells from patient-derived tumors and cell lines in conventional 2D cultures, in 3D culture systems (tumorsphere assay) and in mouse xenograft models. ATRA inhibited both tumorspheres initiation and growth in vitro, which was associated with a cell-cycle arrest through the upregulation of cyclin-dependent kinase (CDK) inhibitors and the downregulation of cell-cycle progression activators. More importantly, ATRA downregulated the expression of the CSC markers CD44 and ALDH as well as stemness genes such as Klf4 and Sox2 and induced differentiation of tumorspheres. Finally, 2 weeks of daily ATRA treatment were sufficient to inhibit gastric tumor progression in vivo, which was associated with a decrease in CD44, ALDH1, Ki67 and PCNA expression in the remaining tumor cells. Administration of ATRA appears to be a potent strategy to efficiently inhibit tumor growth and more importantly to target gastric CSCs in both intestinal and diffuse types of gastric carcinoma.

## Keywords

Cancer stem cells, all trans retinoic acid, gastric cancer

## Funding

*For correspondence:

hungnguyenphu@gmail.com

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

Received: 2017-06-23
Accepted: 2017-07-10
Published: 2017-09-05

Biomedical Research & Therapy

ISSN: 2198-4093
www.bmrat.org

## References

1. Nguyen, P.H., Giraud, J., Staedel, C., Chambonnier, L., Dubus, P., Chevret, E., Bœuf, H., Gauthereau, X., Rousseau, B., Fevre, M., et al. (2016). All-trans retinoic acid targets gastric cancer stem cells and inhibits patient-derived gastric carcinoma tumor growth. Oncogene.
2. Nguyen, P.H., Giraud, J., Chambonnier, L., Dubus, P., Wittkop, L., Belleannée, G., Collet, D., Soubeyran, I., Evrard, S., Rousseau, B., et al. (2017). Characterization of Biomarkers of Tumorigenic and Chemoresistant Cancer Stem Cells in Human Gastric Carcinoma. Clin. Cancer Res. Off. J. Am. Assoc. Cancer Res. 23, 1586–1597.


DOI 10.15419/bmrat.v4iS.301