

The FASEB Journal

The Journal of the Federation of American Societies for Experimental Biology



(The FASEB Journal. 2013;27:248.3)

© 2013 FASEB

248.3

An epigenetic perspective on pharmacologic ascorbate in colon cancer

Matthew Carl Kaiser¹, Praveen Rajendran², Mohaiza W Dashwood², Mark A Levine⁴, Alexander Michels², Balz Frei² and Roderick H Dashwood³

¹ Oregon State University, Corvallis, OR

² Linus Pauling Institute, Oregon State University, Corvallis, OR

³ Environmental and Molecular Toxicology, Linus Pauling Institute, Oregon State University, Corvallis, OR

⁴ NIDDK, National Institutes of Health, Bethesda, MD

Aim: There is growing interest in pharmacologic ascorbate (Asc) and its therapeutic properties (Levine *et al. Adv Nutr* 2011;2:78). We examined cell viability, histone deacetylase (HDAC) expression, and related protein modifications in cancer versus noncancer colon epithelial cells following exposure to Asc.

Methods: MTT assays were conducted in HCT116 colon cancer and CCD841 non-transformed colonic epithelial cells treated with 0.25 to 16 mM Asc or ascorbate-2-phosphate (AAp), in the presence and absence of catalase (CAT, 280 U/mg), or with 5 to 160 μ M H₂O₂. Cell lysates obtained 6 h and 24 h post-treatment were immunoblotted as reported by Rajendran *et al. Mol Cancer* 2011;10:68.

Results: In MTT assays, IC₅₀ data were as follows: 8 mM Asc (CCD841); 3 mM Asc (HCT116), >50mM AAp (HCT116), and 65 μ M H₂O₂ (HCT116). CAT protected against both Asc- and H₂O₂- induced cytotoxicity. At 6 h, Asc and H₂O₂ altered the expression of HDACs (HDAC4, HDAC6, SIRT3) and enhanced the acetylation of histone (H3, H4) and non-histone proteins (tubulin, p53).

Conclusions: Asc was more cytotoxic to colon cancer cells than non-cancer cells. Findings with the non-H₂O₂ producing compound AAp, and with CAT, implicated H₂O₂ in Asc-induced cytotoxicity. Asc was shown, for the first time, to alter epigenetic end-points related to HDAC changes in colon cancer cells.

Grant Funding Source: CA090890, CA090890, AT002034

[http://www.fasebj.org/cgi/content/meeting_abstract/27/1_MeetingAbstracts/248.](http://www.fasebj.org/cgi/content/meeting_abstract/27/1_MeetingAbstracts/248.3)

[3](http://www.fasebj.org/cgi/content/meeting_abstract/27/1_MeetingAbstracts/248.3)