Int J Radiat Oncol Biol Phys. 2001 May 1;50(1):27-36.

Nuclear expression of human apurinic/apyrimidinic endonuclease (HAP1/Ref-1) in head-and-neck cancer is associated with resistance to chemoradiotherapy and poor outcome.

Koukourakis MI, Giatromanolaki A, Kakolyris S, Sivridis E, Georgoulias V, Funtzilas G, Hickson ID, Gatter KC, Harris AL.

Source

Department of Radiotherapy and Oncology, University Hospital of Iraklion, Iraklion 71306, Crete, Greece. targ@her.forthnet.gr

Abstract

PURPOSE:

HAP1/Ref-1 endonuclease is involved in the repair of DNA strand breaks and in the activation of DNA binding of several transcription factors. HAP1 is also a potent activator of wild type p53. It therefore has multiple possible roles in the response of human cancer to radiotherapy and chemotherapy.

METHODS AND MATERIALS:

The nuclear expression of HAP1 and p53 proteins was studied by immunohistochemistry in paraffin-embedded material from 95 patients with locally advanced squamous cell head-and-neck cancer (HNC) treated with radical radiotherapy (38 cases with induction platinum-based chemotherapy and 57 with concurrent platinum chemoradiotherapy).

RESULTS:

HAP1 was present in the nuclei of normal epithelium and stromal cells. Loss of HAP1 nuclear expression was frequently noted in cancer cells. Tumors with high HAP1 nuclear expression (% of positive cells > mean; mean = 11%) were of good differentiation ($p = 0.06$) and presented frequently with advanced nodal disease ($p = 0.01$). High nuclear HAP1 expression was significantly associated with poor complete response rate ($p = 0.00001$), shorter local relapse-free interval ($p < 0.0001$), and poorer survival ($p < 0.0008$). HAP1 nuclear reactivity was inversely associated with p53 nuclear accumulation ($p = 0.003$). The inverse correlation between HAP1 expression and prognosis was independent of p53 status.

CONCLUSION:

HAP1 nuclear expression in HNC is inversely associated with p53 nuclear accumulation and directly related to resistance to chemoradiotherapy and poor survival. Further clinical investigation is required to confirm these findings.