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LETTER TO THE EDITOR

Clusterin inhibition to enhance tumor chemosensitivity in systemic tumors

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To the editor

I read with great interest the recent article by Cheng et al. [1]. Interestingly, inhibition of clusterin activity enhances the sensitivity to a number of other chemo-therapeutic agents in a number of other systemic malignancies besides lung carcinomas.

For instance, OGX-011 can be used to inhibit clusterin in renal cell carcinomas. This inhibition of clusterin enhances the sensitivity to and the anti-neoplastic effects of sorafenib [2]. The combination exerts marked synergism in decreasing proliferation in renal cell malignancies by virtue of significant down-regulation of phosphorylated Akt. Similarly, the use of antisense—oligo deoxynucleotides to inhibit clusterin accentuates the radio—sensitivity of bladder carcinomas [3]. Similarly, antisense oligonucleotides against clusterin have been shown to increase radio–chemosensitivity in prostate carcinomas [4]. The efficacy of androgen ablation is also accentuated following treatment with these antisense oligonucleotides.

Similarly, accentuated clusterin expression usually indicates a poor response to radiotherapy as well as chemotherapy in breast cancers. Down-regulation of clusterin increases the sensitivity to tamoxifen in ER anti-estrogen resistant breast cancer cells [5]. Similarly, in ovarian carcinomas, down-regulation of clusterin increases sensitivity to agents such as paclitaxel [6]. The down-regulation can be achieved by transfection of siRNA or by using OGX-011. This results in improved prognosis and a better clinical outcome in these tumors.

The above examples clearly illustrate the efficacy of clusterin targeting in increasing radio as well as chemosensitivity in a number of systemic tumors. Clearly, there is a need to develop further anti-clusterin therapy that may very well change the management of chemoresistamt malignancies in the near future.

References

1. Cheng CY, Cherng SH, Wu WJ et al (2012) Regulation of chemosensitivity and migration by clusterin in non-small cell lung cancer cells. Cancer Chemother Pharmacol 69:145–154
2. Kususda Y, Miyake H, Gleave ME, Fujisawa M (2012) Clusterin inhibition using OGX-011 synergistically enhances antitumour activity of sorafenib in a human renal cell carcinoma model. Br J Cancer 106:1945–1952
3. Yamanaka K, Gleave M, Muramaki M, Hara I, Miyake H (2005) Enhanced radiosensitivity by inhibition of the anti-apoptotic gene clusterin using antisense oligodeoxynucleotide in a human bladder cancer model. Oncol Rep 13:885–890
4. Gleave M, Miyake H (2005) Use of antisense oligonucleotides targeting the cytoprotective gene, clusterin, to enhance androgen- and chemo-sensitivity in prostate cancer. World J Urol 23:38–46
5. Cappelletti V, Gariboldi M, De Cecco L et al (2008) Patterns and changes in gene expression following neo-adjuvant anti-estrogen treatment in estrogen receptor-positive breast cancer. Endocr Relat Cancer 15:439–449
6. Hassan MK, Watari H, Han Y et al (2011) Clusterin is a potential molecular predictor for ovarian cancer patient's survival: targeting clusterin improves response to paclitaxel. J Exp Clin Cancer Res 30:113

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