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Combination effect of cetuximab with radiation in colorectal cancer cells

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ABSTRACT

Aims and background. Colorectal cancer (CRC) is one of the commonest malignant disorders and frequently associated with high expression of epidermal growth factor receptor (EGFR), resulting in advanced disease and a poor prognosis. In this study, we investigated the radiosensitizing effects of the selective EGFR inhibitor cetuximab in human CRC cell lines.

Methods. Four human CRC cell lines, CaCo-2, HCT-8, LoVo, and WiDr, were treated with cetuximab and/or radiation. The effects on cell proliferation and viability were measured by MTT and annexin-V staining, and clonogenic survival assay. The *in vivo* effect on the growth of CRC xenografts was assessed in athymic nude mice.

Results. Cetuximab in combination with radiation significantly inhibited the *in vitro* proliferation of CRC cells, with a concomitant increase in cell death, except in WiDr cells. Clonogenic survival assay confirmed that cetuximab worked as a radiosensitizer in three cetuximab-sensitivie CRC cells. However, no correlations were found between the radiosensitivity and EGFR expression level or mutation status of EGFR signaling molecules. In nude mice bearing CRC cell xenografts, cetuximab plus radiation significantly inhibited the tumor growth over either agent alone. Interestingly, the WiDr xenograft was also sensitive to cetuximab and/or radiation *in vivo*, suggesting host-mediated effects of cetuximab.

Conclusions. Cetuximab enhanced the radiosensitivity of CRC cells *in vitro* and efficiently inhibited xenograft tumor growth. This study provided a rationale for the clinical application of the selective EGFR inhibitor cetuximab in combination with radiation in CRC. Free full text available at www.tumorionline.it

Key words: colorectal cancer, EGFR, cetuximab, radiation.

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