Combination effect of cetuximab with radiation in colorectal cancer cells

Hye Kyung Shin¹, Mi-Sook Kim², Jin Kyung Lee³, Seung-Sook Lee⁴, Young Hoon Ji¹, Jong-II Kim², and Jae-Hoon Jeong¹

¹Division of Radiation Cancer Research, ²Department of Radiation Oncology, ³Department of Laboratory Medicine, and ⁴Department of Experimental Pathology, Korea Institute of Radiological and Medical Sciences, Seoul; ⁵Department of Food and Microbial Technology, Seoul Women’s University, Seoul, Korea

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-sensitive 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.tumoronline.it

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

Acknowledgments: This work was supported by the National Nuclear R & D Program of the Ministry of Education, Science and Technology, Republic of Korea.

Correspondence to: Mi-Sook Kim, MD, PhD, Department of Radiation Oncology, Korea Institute of Radiological and Medical Sciences, 215-4 Gongneung-dong, Nowon-Gu, Seoul, Republic of Korea 139-706. Tel +82-2970-1264; fax +82-2970-2412; e-mail mskim@kcch.re.kr, or Jae-Hoon Jeong, PhD, Division of Radiation Cancer Research, Korea Institute of Radiological and Medical Sciences, 215-4 Gongneung-dong, Nowon-Gu, Seoul, Republic of Korea 139-706. Tel +82-2970-1386; fax +82-2970-2462; e-mail jeongj@kirams.re.kr

Received October 19, 2009; accepted April 8, 2010.