pISSN 2287-2728
eISSN 2287-285X

CMH

Editorial

http://dx.doi.org/10.3350/cmh.2015.21.3.230
Clinical and Molecular Hepatology 2015;21:230-231

P53 expression in hepatocellular carcinoma: influence on the radiotherapeutic response of the hepatocellular carcinoma

Yu Rim Lee and Soo Young Park

Department of Internal Medicine, Kyungpook National University Hospital, Daegu, Korea

Keywords: Hepatocellular carcinoma; Radiotherapy; P53

See Article on Page 257

Hepatocellular carcinoma (HCC) is the second leading cause of cancer related death with increasing incidence.[1] The standard treatments of HCC consist of surgical resection, liver transplantation, radiofrequency ablation and transarterial chemoembolization. However, because a large proportion of HCC patients are diagnosed in advanced stage, long-term prognosis is disappointing with few available therapeutic modalities.[2,3]

Although Radiotherapy is not included in the Barcelona Clinic Liver Cancer (BCLC) algorithm, it has shown acceptable therapeutic efficacy as one of the therapeutic options for HCC patients.[4] However, as HCC often acquires radioresistance which are correlated with treatment failure,[5] only a small number of radionuclides, such as iodine-131, yttrium-90, rhenium-188 and holmium-166, have been used to the HCC treatment.[6,7] The P53 protein is a transcription factor related to DNA damage repair, growth arrest and apoptosis leading to uncontrolled proliferation, associated with more than 50% of human cancers.[8-10] P53 normally exists in low steady level, but the expression and activation of P53 increases after radiation. The P53 is thought to be one of the key elements involved in the response to radiotherapy.[8] Many studies have been conducted for elucidating relationship between P53 and effectiveness of radiotherapy in cancer and revealed that mutation or inactivation of P53 causes genetic instability, resulting in development of tumors and ineffectiveness of radiotherapy.[9-11]

In this issue, Gomes et al. reported influence of P53 on the radiotherapeutic response of the HCC. In this study, investigation of the effect of iodine-131 radiotherapy in three human HCC cell lines with different degrees of P53 expression was conducted to assess the influence of P53 on the HCC cell survival after radiation therapy. As a result, Hep3B2.1-7 cell line, which has a homozygous deletion in the TP53 gene, did not express P53, HepG2 expresses its normal form, and HuH7, which has a mutated codon, overexpressed P53. For HepG2 and HuH7 cell lines, an increase in P53 expression was observed after both external and internal radiation with I-131, especially in HuH7. Level of phosphorylated P53 was higher after external irradiation than internal radiation with highest levels of phosphorylation in HepG2 cell line. The

Abbreviations:
BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma

Corresponding author : Soo Young Park
Department of Internal Medicine, Kyungpook National University Hospital, 130 Dongdeok-ro, Jung-gu, Daegu 41944, Korea
Tel: +82-53-200-5519, Fax: +82-53-426-8773
E-mail: psyoung0419@gmail.com

Received : Aug. 7, 2015 / **Revised :** Aug. 27, 2015

Hep3B2.1-7 cells were less radiosensitive than other two cell lines. More radiosensitive cell lines, which exhibit a great decrease in cell survival (HepG2, HbH7) showed a higher expression of P53. Thus, P53 protein, encoded by the TP 53 tumor suppressor gene, might be an important factor in radiotherapeutic response in HCC, which is consistent with previous studies.[9,10]

Although P53 triggered most apoptotic cell death, in this study, cells died by late apoptosis/necrosis and necrosis. We must consider the possibility of the aggressiveness of radiation to cells or observation of cell death in later stage. Moreover, HepG2 cell line is more sensitive to both external and internal radiation than HuH7 cell line. It might be related to the character of HepG2 cell line which expressed the normal and more functional form of P53.

Further studies are warranted about more detail signaling pathways. It would be an important target for HCC treatment.

Conflicts of Interest

The authors have no conflicts to disclose.

REFERENCES

1. World Health Organization. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalende Worldwide in 2012. WHO web site, <http://globocan.iarc.fr/Default.aspx> Accessed Aug. 5, 2015.
2. Thomas MB, Zhu AX. Hepatocellular carcinoma: the need for progress. J Clin Oncol 2005;23:2892-2899.
3. Schwartz JM, Ham JM. Treatment of Hepatocellular Carcinoma. Curr Treat Options Gastroenterol 2003;6:465-472.
4. Toya R, Murakami R, Baba Y, Nishimura R, Morishita S, Ikeda O, et al. Conformal radiation therapy for portal vein tumor thrombosis of hepatocellular carcinoma. Radiother Oncol 2007;84:266-271.
5. Kim JJ, Tannock IF. Repopulation of cancer cells during therapy: an important cause of treatment failure. Nat Rev Cancer 2005;5:516-525.
6. Keng GH, Sundram FX. Radionuclide therapy of hepatocellular carcinoma. Ann Acad Med Singapore 2003;32:518-524.
7. Raoul JL, Boucher E, Rolland Y, Garin E. Treatment of hepatocellular carcinoma with intra-arterial injection of radionuclides. Nat Rev Gastroenterol Hepatol 2010;7:41-49.
8. Gudkov AV, Komarova EA. The role of p53 in determining sensitivity to radiotherapy. Nat Rev Cancer 2003;3:117-129.
9. Begg AC, Stewart FA, Vens C. Strategies to improve radiotherapy with targeted drugs. Nat Rev Cancer 2011;11:239-253.
10. Levine AJ, Oren M. The first 30 years of p53: growing ever more complex. Nat Rev Cancer 2009;9:749-758.
11. He M, Zhao M, Shen B, Prise KM, Shao C. Radiation-induced intercellular signaling mediated by cytochrome-c via a p53-dependent pathway in hepatoma cells. Oncogene 2011;30:1947-1955.