

Influence of recombinant human growth hormone (rhGH) on proliferation of hepatocellular carcinoma cells with positive and negative growth hormone receptors *in vitro*

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ABSTRACT

Aims and background. Recombinant human growth hormone (rhGH) is increasingly used in the clinic because it promotes the synthesis of proteins. However, rhGH is able to increase malignant transformation and tumor recurrence. The aim of this study was to investigate the effects of rhGH on hepatocellular carcinoma (HCC) cells with positive and negative growth hormone receptors (GHR) in order to guide its clinical application.

Methods and study design. Cells of the human HCC cell lines Bel-7402 (GHR+) and SMMC-7721 (GHR-) as well as human umbilical vein endothelial cell line ECV304 cells in the exponential growth phase were harvested and divided into experimental and control groups. After the human HCC cells were cultured alone or co-cultured with ECV304 cells under the different treatments, cell cycle phase, proliferation index, and expression levels of vascular endothelial growth factor (VEGF) mRNA and proteins were determined.

Results. In the Bel-7402 GHR+ cells treated with rhGH, both the percentage of cell in G₂-M phase and the proliferation index were higher than those of controls ($P < 0.05$); this was not the case in the SMMC-7721 GHR- cells treated with rhGH ($P > 0.05$). Although there was no difference in the cell doubling times between ECV304 cells co-incubated with Bel-7721 GHR- cells treated with rhGH and without rhGH, the doubling times of ECV304 cells co-incubated with Bel-7402 GHR+ cells, when treated with rhGH, were significantly shortened compared to those of controls ($P < 0.05$). The cell doubling times of ECV304 cells co-incubated with Bel-7721 GHR- or Bel-7402 GHR+ cells which were treated with bevacizumab were longer than those of controls and of cells with rhGH ($P < 0.05$). The VEGF mRNA and protein expression levels were higher in Bel-7402 GHR+ cells treated with different doses of rhGH than controls ($P < 0.05$ or $P < 0.01$); however, there was no statistically significant difference in the expression levels of VEGF mRNA and proteins between SMMC-7721 GHR- cells treated with rhGH and controls.

Conclusions. rhGH can induce VEGF secretion and stimulate proliferation of Bel-7402 GHR+ cells *in vitro*, but has little effect on the proliferation of SMMC-7721 GHR- cells, suggesting that rhGH may be applied safely to treatment for the catabolic state in patients with GHR-negative HCC. **Free full text available at www.tumorionline.it**

Key words: recombinant human growth hormone, receptors, vascular endothelial growth factor, hepatocellular carcinoma, co-culture, cell proliferation.

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