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An inhibition of cell growth was induced by therapeutic stem cells expressing a suicide enzyme and interferon-beta via their migratory capability in human hepatocarcinoma cells *In vitro*

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Recently, studies of stem cells in anticancer therapy have been regarded as an ingenious alternative having advantages over radiotherapy and/or chemotherapy. When genetically engineered with suicide genes and/or immunotherapeutic genes, stem cells can exhibit a potent therapeutic efficacy combined with their strong tumor tropism toward cancer cells. In the present study, we introduced genetically engineered stem cells (GESTECs) and evaluated their therapeutic efficacy against liver heaptocarcinoma cells, Hep3B. These GESTECs are neuronal stem cells engineered with a bacterial *cytosine deaminase (CD)* gene and a human *interferon-beta (IFN-b)* gene (HB1.F3.CD and HB1.F3.CD.IFN-b). *CD* gene is a suicide gene expressing *cytosine deaminase* that can convert a non-toxic prodrug, 5-fluorocytosine (5-FC), to an active form, 5-fluorouracil (5-FU), which has a powerful cytotoxic effect on cancer cells. Human *interferon-beta (IFN-b)* is a typical cytokine having an antitumor effect. Using RT-PCR, we confirmed *CD* and *IFN-b* gene expressions in GESTECs and the expressions of chemoattractant molecules such as SCF, CXCR4, c-kit, VEGF, and VEGFR2, in cancer cell lines. To determine the migratory ability of engineered stem cells, we performed a modified trasnwell assay in which HB1.F3.CD or HB1.F3.CD.IFN-b cells selectively migrated toward liver cancer cells due to the migrating capacity of neural stem cells toward various chemoattractants expressed by cancer cells. In the cytotoxicity test using co-culture system and MTT assay, HB1.F3.CD or HB1.F3.CD.IFN-b cells showed the significant inhibition of Hep3B cell growth following administration of 5-FC. More potent inhibitory effect on Hep3B cell growth was induced by HB1.F3.CD.IFN-b rather than by HB1.F3.CD alone, which means the synergic effect of *IFN-b* and 5-FU converted from 5-FC by *CD*. From the data presented in this study, we suggest that GESTECs expressing both CD and *IFN-b* may have a prominent advantage for treating human hepatocarcinoma with their coupling effect of fusion genes and selective tumor targeting of stem cells.

Biography

Kyung-A Hwang is doing her Ph.D. course at the Laboratory of Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University (Cheongju, Republic of Korea). Kyung-Chul Choi completed his Ph.D. from the University of British Columbia (Vancouver, BC, Canada) and postdoctoral studies from the Cornell University (Ithaca, NY, USA). He has published more than 100 papers in peer-review journals and is an Associate Professor and Department Head in the program of pre-veterinary medicine, College of Veterinary Medicine, Chungbuk National University.