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Potential use of therapeutic engineered stem cells expressing chemo- and immuno-therapeutic genes for selective target of human non-small cell lung carcinoma cells

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Genetically engineered stem cells (GESTECs) producing suicide enzymes and immunotherapeutic agents along with their strong tumor tropism have a definite therapeutic potential in anticancer treatment. Suicide enzymes can convert non-toxic pro-drugs to toxic metabolites that can reduce tumor growth. *Cytosine deaminase (CD)* is a suicide enzyme that changes a pro-drug, 5-fluorocytosine (5-FC) into a toxic agent, 5-fluorouracil (5-FU). As an immunotherapeutic agent, human *interferon-beta (IFN-b)* is a typical cytokine having an antitumor effect. In this study, we used human neural stem cells (HB1.F3) transduced with *E.coli CD* gene and human *IFN-b* gene as GESTECs (HB1.F3.CD or HB1.F3.CD.IFN-b) and evaluated whether these GESTECs were capable of migrating to human non-small cell lung carcinoma cells (A549) and of exerting the cytotoxicity against cancer cells *in vitro*. Using RT-PCR, we confirmed the expression of *CD* and *IFN-b* gene in these GESTECs and of chemoattractant molecules such as SCF, CXCR4, c-kit, VEGF, and VEGFR2 in A549 cell line. In a modified trasnwell migration assay, GESTECs (HB1.F3.CD or HB1.F3.CD.IFN-b) appeared to migrate selectively toward lung cancer cells. It can be attributed to the prominent migrating capacity of GESTECs toward various chemoattractants secreted by cancer cells. In addition, using co-culture system and MTT assay, we tested a therapeutic efficacy of GESTECs. When A549 and GESTECs were co-cultured in the presence of 5-FC, HB1.F3.CD or HB1.F3.CD.IFN-b cells showed the inhibition of cancer cell growth. Moreover, a stronger inhibitory effect on A549 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*. The results of this study have shown that GESTECs expressing CD or CD.IFN-b genes may migrate toward lung cancer cells selectively and exert anticancer capacity *in situ*. Consequentially, it is suggested that GESTECs can be a promising alternative anticancer therapy over radiotherapy and/or chemotherapy.

Biography

Bo-Rim Yi is doing her master 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.