Conclusions: Although further study will be needed, the non-integrating and self-replicating VEE RNA replicon system has the potential to make a great contribution to generating clinically applicable canine iPSCs.

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Effects of human neural stem cells transduced with cytosine deaminase and interferon-β on the growth of K562 human chronic myeloid leukemia cells in a xenograft model

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Introduction: Gene-directed enzyme/prodrug therapies have been found to be more advantageous compared to conventional cancer treatment method. One of these, a cytosine deaminase (CD)/5-fluorocytosine (5-FC) system, is known to induce apoptosis of cancer cells by converting 5-FC, a prodrug, to its metabolically active form, 5-fluorouracil. In this study, human neural stem cells (hNSCs) derived enzyme/prodrug therapy was used to treat leukemia. The parental hNSCs, HB1.F3, were engineered to express E. coli CD and/or human interferon-β.

Materials and Methods: To manufacture animal models xenografted with leukemia, K-562 cells (1×10^6) were mixed with Matrigel at 1:1 volume ratio of Matrigel to PBS in 100 μl and injected subcutaneously (*s.c.*) into the back of athymic nude mice. This animal study was performed for 24 daysafter hNSCs injections. When tumor volume reached 500 mm^3, CM-Dilpre-labeled hNSCs (4×10^6 cells per mouse) were injected subcutaneously adjacent to the tumor mass. Another group, CM-dil pre-labeled hNSCs (4×10^6cells per mouse) were injected intravenously. hNSCs were injected on the first day of each week. Two days after the injection of hNSCs, all mice received i.p. injections of 5-FC (500 mg/kg/day in 100 μl PBS) everyday for 24 days. At 24 h after the last 5-FC treatment, the mice were euthanized and tumor masses were harvested for molecular analysis.

Results: In a xenografted mouse model administered with hNSCs intravenously or subcutaneously, hNSC significantly inhibits the growth of tumor mass and extends survival date in the presence of a prodrug. In addition, HB1.F3.CD.IFN-β treatment group showed more anti-tumor effects compared with HB1.F3.CD treatment group, indicating that IFN- β may have a synergistic effects for directly killing leukemia tumors.

Conclusions: The present results represent that engineered hNSCs and prodrug treatment inhibited the proliferation of leukemia. These results suggest that gene therapy employing genetically engineeredstem cells expressing CD and IFN-β may be effective for treating leukemia.

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Hypoxia Mitigates Mitochondrial Damage and Oxidative Stress Induced by Cisplatin in Human Malignant Mesothelioma Cells

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Introduction: Hypoxia induces drug resistance in human cancers. Human malignant mesothelioma (HMM), an aggressive tumor associated with exposure to asbestos fibers, is resistant to various chemotherapeutic regimens. This study was performed to determine if mitochondria are involved in the hypoxia-induced drug resistance in HMM.

Materials and Methods: Two HMM cell lines, MS1 and H513, were cultured in complete RPMI 1640 medium. Hypoxic condition (0.1% O2) was achieved by an air chamber system (Billups-Rothenberg Inc., USA). Cells were treated with 10 μM cisplatin. Cytotoxicity was assessed by MTT assay. Apoptosis was determined by Annexin V/propidium iodide analysis. Mitochondrial membrane potential (MMP) and permeability were measured by JC-1 ratio and calcein fluorescence. Mitochondrial stress was evaluated using Mitotracker Red fluorescence. Mitochondrial DNA (mtDNA) damage was analyzed by amplification efficiency of long mtDNA fragment relative to mtDNA copy number. Oxidative stress was determined using various fluorochromes specific for reactive oxygen species (ROS). Ultrastructure of mitochondria was scrutinized by transmission electron