γδ T Cell Transports Adenovirus Vector for Prostate Cancer Cells

Introduction and Objective: Androgen deprivation therapy and cytotoxic chemotherapy are the mainstays of prostate cancer treatment. Given its frequent failure, new therapy that reduces prostate cancer progression would be a breakthrough in treating this disease. Gene therapy has been used in clinical cancer treatment. For gene therapy, recombinant adenovirus (Ad) vectors have been used to deliver foreign genes to target cells. Among Ads, Ad type 5 (Ad5), has been commonly used as Ad vectors. Ad5 requires the coxsackievirus and adenovirus receptor (CAR) on the cell surface as an initial receptor for infection. However, the expression of CAR on cancer cell is often down-regulated. To overcome this first hurdle, Mizuguchi et al. invented a novel type of Ad vector, which is chimeric type 5 and containing type 35 fiber proteins (Ad5/F35). Ad5/F35 vectors recognize human CD46 as a cellular receptor, for infection. The second hurdle is that, the majority of humans carry preexisting humoral and/or cellular immunity to Ad5 which may severely limit the use of Ad5 based vectors. Meanwhile, γδ T cell play a regulatory role in cancer growth, and γδ T cell is known to recognize and attack cancer cells via an interaction of NKG2D on γδ T cell and MIC A/B expressed on cancer cell. For the reasons, we investigated whether the γδ T cells can be a transporter for Ad5/F35 delivery in this study. Again, the aim of this study was improve the efficiency of Ad delivery for cancer cells.
Materials and Methods: The Ad5/F35-GFP, chimeric type 5 and type 35 fiber proteins expressing GFP was used. The γδ T cells was expanded from PBMC with the stimulation of Zoledronic acid and IL-2. GFP expression in γδ T cells and PC3 cells (prostate cancer cell line) transduced with Ad5/F35-GFP was determined by fluorescent microscope and Flow cytometer.
Results: Expression of CD46 (but not CAR) on γδ T cells was recognized. Infection rate of Ad5/F35-GFP to γδ T cells was approximately 50% at 48hr co-culture. During the co-culture with Ad5/F35-GFP and γδ T cells, NKG2D expression on γδ T cells has been preserved. After the co-culture of Ad5/F35-GFP infected γδ T cells and PC3 cells, GFP expression was recognized with 98% of PC3 cells.
Conclusion: γδ T cells can be used as a transporter for Ad5/F35-GFP. Our epoch-making carrier system might be a clue to improve the efficacy of Ad vector based cancer treatment.