Abstract No: 367 *Health Sciences*

Effective induction of cytotoxic T Lymphocytes by PMDC derived exosomes for development of adaptive cellular immunotherapy/cell-free vaccine

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Cancer immunotherapy aims at improving survival and quality of life of cancer patients. Since few years, many studies have focused on dendritic cell derived-exosomes (DC-Exo) which can be used as a novel source of vaccinations. Recently a great deal of interest has been raised in PMDC cell lines which have been established at the University of Niigata (Japan).PMDC05 was generated by using leukemia blast cells and PMDC11 was derived from PMDC05 by transduction of the CD80 gene. This study aims to evaluate the effectiveness of DC-Exo to induce cytotoxic T lymphocyte (CTL) responses and antitumor immunity. Exosomes were isolated from PMDC by using the ExoQuick-TC solution. These exosomes were pulsed with CMVpp65 peptide to induce CTLs. The toxicity of CTL which is induced by DC-Exo was determined by the cytotoxicity assay. The statistical relevance of the difference in CMVpp65 specific CTL generation by DC-Exo was evaluated by one-way ANOVA test.

Transduction of the CD80 gene into PMDC05 increased the expression of CD80 in PMDC11. In addition, expression of CD4, CD54, CD56, CD123 and HLA-DRco-stimulatory molecules were increased. However, the expression of CD80 was decreased in PMDC05. PMDC11- derived exosomes (DC11-Exo) showed an expression of CD63 and CD80, while the expression of CD80 was negative in PMDC05-derived exosomes. (DC05-Exo)CD80 is important for antigen-presentation and stimulation of CTL. DC05-Exo which was pulsed with CMVpp65 induced a moderate number (0.43%) of CTL. Interestingly, DC11-Exo showed the ability to induce a higher number of CTL (1.83%).This might be due to the uptake of exogenous antigen by DC-Exo,in turn stimulating antigen-specific CTL via the MHC complexes and co-stimulatory molecules on DC-Exo.

This study provides evidence that exosomes which were released from PMDC would be in a position to develop anti-tumor immune responses. Furthermore, the efficiency in expression of immune responses by DC-Exo might be due to antigen cross-presentation. Since DC11-Exo has the ability to generate antigen specific CTL, DC-Exo could be used for the development of a cell-free vaccine in the future.