Cytokine-based log-scale expansion of functional human dendritic cells from PBMC

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Abstract

[PURPOSE]: Dendritic cells (DCs) play a crucial role in maintaining the immune system. Though DC-based cancer immunotherapy has been suggested to hold potential to treat various malignancies, clinical efficacies are still insufficient in many human trials. We proved that this antitumor effect depends on the number of DCs (Kato T., et al. Neoplasia 2010), and it is necessary to prepare an enough number of DCs for effective treatments of tumors. In this study, therefore, we attempted to expand functional human DCs ex vivo with new technologies.

[Materials and Methods]: Peripheral blood mononuclear cells (PBMCs) were obtained from healthy volunteers and cancer patients. CD3-depleted PBMCs were expanded and differentiated into DCs in the presence of cytokine cocktails for several weeks by floating cultivation. Expanded DC properties were analyzed, and compared with those of conventional DC.

[RESULTS]: Total cells increased approximately 10 – 100 fold after 5 weeks culture and >80% of expanded cells expressed CD11c. Thus, by this method, 10 – 100 times more CD11c+ cells could be obtained than conventional procedures could. As are seen in conventional DCs, expanded DCs showed dendrites after maturation, and endocytotic activities. Expanded DCs also expressed HLA-DR, adhesion molecules, and co-stimulatory molecules and produced inflammatory cytokines as well as conventional DCs did. Functionally, MLR assay revealed that expanded DCs could stimulate allogenic T-cell proliferation to the same extent as conventional DCs.

[CONCLUSIONS]: We established a new culture method to expand human DCs. Expanded DC had properties that were required to obtain therapeutic gain. We expect that this technology will be able to contribute largely to both basic and clinical research of human cancer immunotherapy. DC expansion technology will improve therapeutic gain of cancer and alleviate patients’ burden of apheresis.