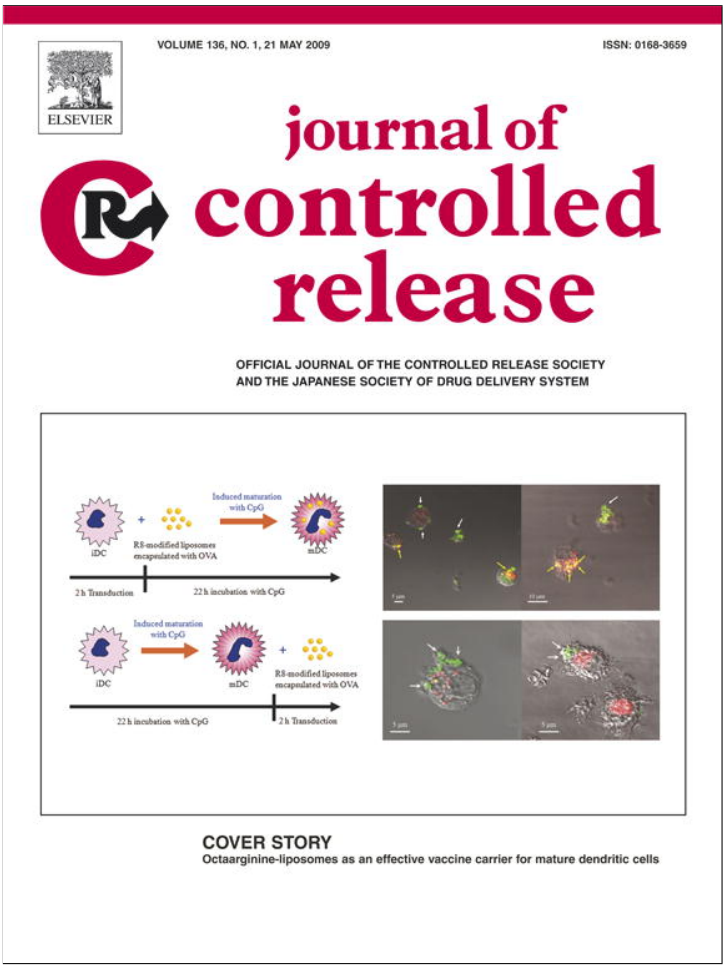

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Cover Story

Octaarginine-liposomes as an effective vaccine carrier for mature dendritic cells

Dendritic cells (DCs) have been used efficiently to induce immunity against tumors and viral infectious diseases. The unique ability of DCs to take up, process and present antigens (Ags), and to activate naive CD4+ and CD8+ T-cells raises the possibility of using DCs as "nature vaccines." The efficiency of Ag-loaded DCs to induce immunity against tumors and viral infectious diseases has been tested in a number of pre-clinical trials. Although DC-based immunotherapy is promising, optimization of DC-based vaccination protocols is necessary to enhance the success rate of future clinical trials. In most trials, Ags were loaded into DCs *in vitro* and the cells were then administered back to patients. It is known that immature DCs (iDCs) are good at capturing antigens, but not as efficient as mature DCs (mDCs) in stimulating T-cells. On the other hand, mDCs are not as good as iDCs in antigen uptake. Recently Professor Harashima's group demonstrated that liposomes modified with octaarginine, a cell-penetrating peptide, were efficiently taken up by iDCs and the encapsulated Ag were delivered to the cytosolic compartment. The group also showed that octaarginine-modified liposomes (R8-Lips) induced *in vitro* presentation of major histocompatibility complex-class I molecule (MHC-I) and elicit *in vivo* anti-tumor effect successfully.

An article in this issue by Professor Harashima and his group has demonstrated that R8-Lips were efficiently taken up into DCs, regardless of their maturation stage [1]. R8-Lips were also highly efficient in escaping from endosomes into cytosol to release a protein antigen. Interestingly, transduction of mDCs induced dramatically higher MHC-I presentation and robust Ag-specific cytotoxic T lymphocytes activity than transduction of iDCs. It is possible that in iDCs, internalized Ag are slowly degraded and inefficiently used for inducing MHC-I presentation. Transduction of mDCs with R8-Lip may allow DCs to process and present internalized Ag to T-cells using newly synthesized MHC-I. While it is too early to understand completely the mechanisms of substantially enhanced effect of R8-Lips through transduction of mDCs, this particular approach opens up new, more efficient possibilities in DC-based vaccination.

Reference

[1] A. Homhuan, K. Kogure, T. Nakamura, N. Shastri, H. Harashima, Enhanced antigen presentation and CTL activity by transduction of mature rather than immature dendritic cells with octaarginine-modified liposomes, J. Control. Release 136 (2009) 79–85.

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