GENE THERAPY

Exosomal therapy for established arthritis

Dendritic cells (DCs) that express the tryptophan-degrading enzyme indoleamine 2,3-dioxygenase (IDO), or exosomes derived from these cells, are immunosuppressive and anti-inflammatory, and could be a novel gene therapy approach for rheumatoid arthritis according to research by Paul Robbins and colleagues at the University of Pittsburgh, USA.

This research, which has now been published in *Arthritis & Rheumatism*, follows on from earlier work by this group. “We have reported previously that microvesicles, termed exosomes, produced by immunosuppressive DCs are as or more suppressive than the cells themselves,” says Robbins.

In this latest study, the researchers used adenoviruses to transduce bone-marrow-derived DCs so that they overexpressed IDO. “Given that the enzyme IDO has been reported to confer immunosuppressive effects if expressed

in tumor cells or DCs, we examined the immunosuppressive effects of DCs genetically modified to express IDO as well as exosomes derived from these cells,” explains Robbins. Intravenous injection of IDO-expressing DCs or exosomes reversed the progression of disease in mice with collagen-induced arthritis, whereas disease progression was unchanged in mice receiving control DCs or saline. Similarly, inflammation was reduced in a mouse model of antigen-specific inflammation (delayed hypersensitivity model) following hindpaw injection of IDO-expressing DCs or exosomes, but was

unchanged in recipients of control DCs.

“We demonstrated that IDO-expressing DCs are able to reverse established arthritis, as are the DC-derived exosomes,” Robbins says. “The most interesting result is the fact that exosomes from IDO-expressing DCs were so highly suppressive.”

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Original article Bianco, N. R. et al. Therapeutic effect of exosomes from indoleamine 2,3-dioxygenase-positive dendritic cells in collagen-induced arthritis and delayed-type hypersensitivity disease models. *Arthritis Rheum.* 60, 380–389 (2009).