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Effect of minicircle vector encoding anti-CD25/IL-10/CXCR3 fusion protein in allograft rejection model

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Objectives: We previously proposed minicircle vector technology as the potential platform for the development and production of new biologics. In this study, we have designed a novel target molecule for the treatment of allograft rejection and evaluated its feasibility as the therapeutic agent in this disease using minicircle vector system.

Methods: We engineered vectors to carry cassette sequences for anti-CD25, IL-10, and CXCR3 fusion protein, and then isolated minicircle vectors from the parent vectors. We verified the substantial production of anti-CD25/IL-10/CXCR3 fusion protein from minicircles and their duration in HEK293T cells and mice models. We also evaluated whether minicircle-derived anti-CD25/IL-10/CXCR3 has therapeutic effects in a skin allograft in mice model.

Results: We confirmed the production of anti-CD25/IL-10/CXCR3 from minicircle by its significant availability in cells transfected with the minicircle and in its conditioned media. After a single injection of minicircle by hydrodynamic injection via mouse tail vein, luminescence or red fluorescence was maintained until 40 days in the liver tissue, suggesting the production of anti-CD25/IL-10/CXCR3 protein from minicircles via protein synthesis machinery in liver. Mice treated with the minicircle encoding anti-CD25/IL-10/CXCR3 showed prolonged skin allograft survival times accompanied by improved immunologic regulation e.g., reduction of the lymphocyte population of Th1, Th2, Th17 and an induction of regulatory T cells.

Conclusions: These findings implied that self-generated anti-CD25/IL-10/CXCR3 protein drug by minicircle technology is functionally active and relevant for reducing allograft rejection. Minicircle vector system may be useful for the development of new biological drugs, avoiding manufacturing or practical problems.