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Self in vivo production of a synthetic biological drug, anti-IL-2Rα/IL-10 fusion protein using minicircles in skin allograft model

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Objectives: Anti-IL-2Rα monoclonal antibodies are typically used to prevent acute rejection in patients after transplantation. Minicircle DNA, one of the most remarkable gene therapy technologies of late, has the advantage of being small in size, non-viral, and free of unwanted immune responses such as no bacterial backbone. The aim of this study was to investigate the therapeutic effects of anti-IL-2Rα and IL-10, anti-inflammatory cytokine, in vitro and in vivo using a minicircle vector system.

Methods: Minicircle DNA was prepared by inserting the sequences for Basiliximab (anti-IL-2Rα) and IL-10 into the parental plasmid and removing the bacterial backbone. After minicircle DNA administration, protein production for anti-IL-2Rα and IL-10 was determined in HEK293T cell line and mice, and the therapeutic effect was evaluated in skin allograft rejection model.

Results: Minicircle DNA was transfected into the HEK293T cells and observed up to 30 days and detected the protein production in the conditioned media. In mice, in vivo imaging was used to confirm that DNA expression persists for up to 30 days after single administration. The produced protein was maintained in the blood for up to 10 days. Anti-IL-2Rα / IL-10 fusion protein increased survival effect more than single protein expressing anti-IL-2Rα or IL-10 in the skin allograft rejection model.

Conclusions: Anti-IL-2Rα / IL-10 fusion protein, which is synthesized in the body using minicircle DNA, has demonstrated an effective therapeutic effect on acute rejection after transplantation. We also demonstrated the potential of the minicircle DNA as a powerful biological agent to induce immune tolerance of grafts by combining various therapeutic target designs.