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Evaluation of an anti-inflammatory dendrimer to topically treat psoriasis

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Psoriasis is an auto-immune disease resulting from a chronic and exaggerated inflammation of the skin and hyperproliferation of keratinocytes. Conventional topical treatments for this disease, such as anti-inflammatory drugs, present low efficiency, and systemic administration of synthetic drugs or biologic immunomodulators can present severe side effects and/or are highly expensive. So, there is an unmet need for the development of new drugs that could provide sustainable therapeutic effects. In this study, we evaluated the potential efficacy of anti-inflammatory dendrimers for the topical treatment of psoriasis. Dendrimers are hyperbranched and perfectly defined macromolecules of nanometer size, constituted of branches grafted on a central core. IMD006, a phosphorus-based dendrimer capped with azabisphosphonate groups, has strong immuno-modulatory effects towards different immune cell types. We tested the effects of IMD006 in two psoriasis models: the imiquimod-induced murine model and a reconstructed human epidermis (RHE) model, in which cocktails of pro-inflammatory cytokines are used to induce psoriasis-associated changes. IMD006 presented dose-dependent therapeutic efficacies, significantly reducing lesions and histopathological changes associated with psoriasis. Moreover, we show that IMD006 is rapidly taken up by keratinocytes in 2D culture, decreasing their proliferation and increasing their differentiation. In keratinocytes in 2D culture, IMD006 associated with mitochondria, increased mitochondrial ROS production and ultimately lysosomal degradation of these organelles. Therefore, the anti-psoriatic effect of dendrimers is, at least in part, the result of a direct effect on keratinocytes. Our results demonstrate that anti-inflammatory dendrimers are good candidates for the topical treatment of psoriasis with a broad effect on multiple cell types involved in the development and progression of the disease.