

Supplementary Table S1. Examples of delivery modalities studied in relation to RNA therapeutics for certain dermatological conditions.

Clinical practice

| Dermatological condition | Delivery modality | Details |
|---------------------------------|--------------------------|---|
| Hypertrophic scars, keloids | Microneedles | siSPARC/Gtn-Tyr nanoplex-loaded HA microneedle patch ¹ |

Animal model(s)

| Dermatological condition | Delivery modality | Details |
|---------------------------------|--------------------------|---|
| Alopecia areata | Intralesional injection | Intralesional injection of anti-Tbx21 siRNA conjugated with cationised gelatin microspheres ² |
| Atopic dermatitis | Cream emulsion | Cream emulsion containing anti-CD86 siRNA. ² Intradermal injections using a gene gun were considered but not adopted, as such modality was believed to irritate inflamed skin, preventing repeated treatment. ³ |
| | Iontophoresis | Iontophoretic delivery of anti-interleukin 10 (IL-10) siRNA ⁴ |
| | Iontophoresis | Iontophoretic delivery of anti-sense oligonucleotides in respect of IL-10 ⁵ |
| Melanoma | Microneedles | Intradermal delivery of signal transducer and activity of transcription 3 (STAT3) siRNA ⁶ |
| | Subcutaneous injection | Subcutaneous injection of siRNA (siV599EB-Raf) containing melanoma cell line; ² subcutaneous injection of stable A375 |

| Dermatological condition | Delivery modality | Details |
|---------------------------------|--------------------------|---|
| | | melanoma cell line transduced with retroviral expression plasmid for shRNA ² |
| Psoriasis | Intradermal injection | Intradermal injection of short hairpin RNA (shRNA)-encoding lentiviral vectors against tumor necrosis factor- α (TNF- α) ² |
| | Ionic liquid formulation | Topical application of ionic liquid aggregates with siRNA targeting atypical inhibitor of nuclear factor κ B (I κ B) protein I κ B ζ (NFKBIZ) ⁷ |
| Squamous cell carcinoma | Intratumoral injection | Intratumoral injection of VEGF siRNA expressing plasmid DNA conjugated with cationised gelatine microspheres ² |
| (Delivery only) | Novel microneedle | Combination of sponge spicules and cationic flexible liposomes to form a novel microneedle ⁸ |

¹ YY Chun, WWR Tan, MIG Vos, et al. Scar prevention through topical delivery of gelatin-tyramine-siSPARC nanoplex loaded in dissolvable hyaluronic acid microneedle patch across skin barrier. *Biomater Sci.* 2022 Jul 12;10(14):3963-3971. doi: 10.1039/d2bm00572g.

² B Geusens, N Sanders, T Prow, et al. Cutaneous short-interfering RNA therapy. *Expert Opin Drug Deliv.* 2009 Dec;6(12):1333-49. doi: 10.1517/17425240903304032.

³ Ritprajak P, Hashiguchi M, Azuma M. Topical application of cream-emulsified CD86 siRNA ameliorates allergic skin disease by targeting cutaneous dendritic cells. *Mol Ther* 2008;16(7):1323-30. doi: 10.1038/mt.2008.91.

⁴ K Kigasawa, K Kajimoto, S Hama, et al. Noninvasive delivery of siRNA into the epidermis by iontophoresis using an atopic dermatitis-like model rat. *Int J Pharm.* 2010 Jan 4;383(1-2):157-60. doi: 10.1016/j.ijpharm.2009.08.036.

⁵ T Sakamoto, E Miyazaki, Y Aramaki, et al. Improvement of dermatitis by iontophoretically delivered antisense oligonucleotides for interleukin-10 in NC/Nga mice. *Gene Ther.* 2004 Feb;11(3):317-24. doi: 10.1038/sj.gt.3302171.

⁶ JT Pan, WY Ruan, MY Qin, et al. Intradermal delivery of STAT3 siRNA to treat melanoma via dissolving microneedles. *Sci Rep.* 2018; 8: 1117. doi: 10.1038/s41598-018-19463-2.

⁷ A Mandal, N Kumbhojkar, C Reilly, et al. Treatment of psoriasis with NFKBIZ siRNA using topical ionic liquid formulations. *Sci Adv.* 2020 Jul 22;6(30):eabb6049. doi: 10.1126/sciadv.abb6049.

⁸ XJ Liang, JL Zhang, HL Ou, et al. Skin Delivery of siRNA Using Sponge Spicules in Combination with Cationic Flexible Liposomes. *Mol Ther Nucleic Acids.* 2020 Jun 5;20:639-648. doi: 10.1016/j.omtn.2020.04.003.