Needle-Free Delivery of DNA Therapeutics for Immune Modulation and Activation

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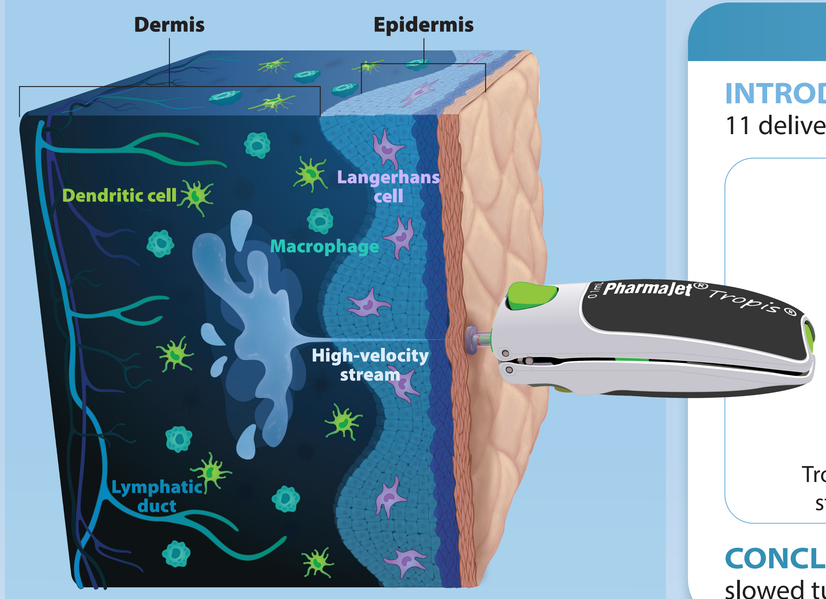
Introduction:

PharmaJet's needle-free delivery enhances the immune response of therapeutic DNA vaccines compared to traditional delivery approaches. Needle-free delivery enhances immune modulation in the treatment of autoimmune diseases and T cell activation in cancer, highlighting broad clinical and therapeutic potential.

Benefits of Intradermal (ID) Delivery

- ✓ Durable antibody response[1, 2, 3]
- ✓ Mucosal immunity[4]
- ✓ Cross-reactive antibodies[1, 4]
- ✓ T cell responses[2, 5]
- ✓ Amenable to self-administration



- The dermis contains a dense network of antigen presenting cells (APCs), including Langerhans cells, dermal dendritic cells, and macrophages.[6]
- Dendritic and Langerhans cells are key migratory APCs that prime T cells in lymph nodes.[7, 8, 9]
- Lymphatic ducts enable migration of antigens and APCs to lymph nodes.[9]

Delivery Matters

Dermal APCs promote follicular helper CD4+ T cell differentiation, germinal center formation, and B cell maturation for long-lived antibody responses and migrate to lymph nodes and bone marrow to present antigens via major histocompatibility complex (MHC) Class I and initiate CD8+ T cell responses.[3, 7, 8, 9]

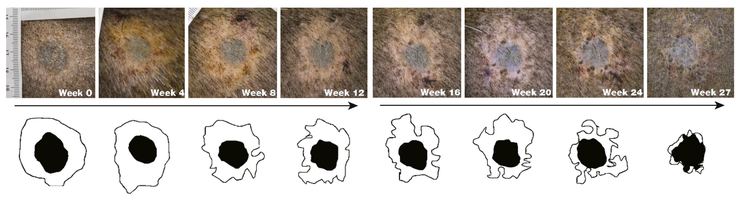
When treating autoimmune disease, therapeutic vaccines must avoid triggering inflammation, which can increase auto-reactive T cells and undermine efficacy.[10] Due to the direct access to APCs, the intradermal route with Tropis can enable delivery that is less inflammatory than intramuscular (IM) administration, which relies on an inflammatory response to recruit and activate immune cells.[11]

Immune Modulation and Tolerogenic Effect in Autoimmunity: Vitiligo[12]

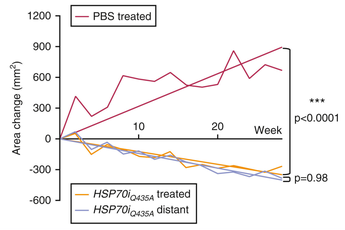
INTRODUCTION: Sinclair swine with spontaneous melanoma and vitiligo provide a clinically relevant autoimmune model assessing local immune modulation with HSP70iQ435A DNA delivered by 4 peri-lesional injections (single injection per week over a 4-week period), resulting in repigmentation.

Significant Progressive Repigmentation of Treated Vitiligo Lesions

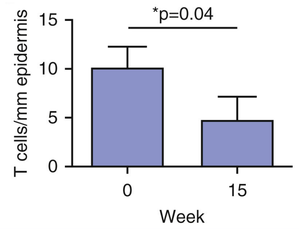
Observed from Week 0 to Week 27 (over ~6 months) using Needle-Free Delivery with Stratis® IM/SC ($p < 0.0001$)



Lesion Area Decrease in Treated and Distant Lesions vs. PBS Control



T Cell Infiltration Reduction in Lesions

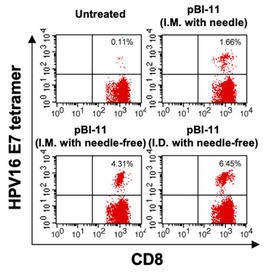


CONCLUSION: Intramuscular needle-free delivery of HSP70iQ435A DNA via Stratis promoted sustained repigmentation at treated and distant lesions, with reduced epidermal T cell infiltration and no systemic anti-HSP70 antibody response (data not shown), supporting localized immune modulation in autoimmune skin disease.

Immune Activation in Cancer: Intradermal HPV DNA Vaccine[5]

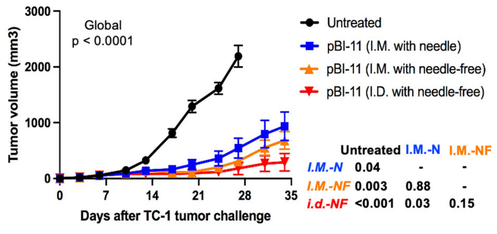
INTRODUCTION: A preclinical TC-1 tumor model was used to evaluate immune responses, tumor control, and survival following HPV DNA vaccine pBI-11 delivered by Tropis® ID needle-free injection and compared to IM needle and syringe (N/S) delivery.

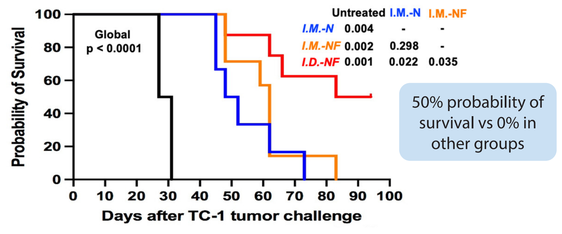
Increased CD8+ T Cells



Tropis ID needle-free delivery induced the strongest CD8+ T cell response (6.45%).

Therapeutic HPV Vaccine (pBI-11) Slowed Tumor Growth and Improved Survival



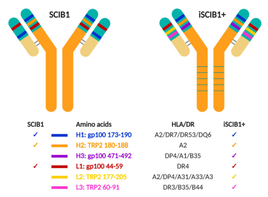


Tropis ID needle-free delivery significantly slowed tumor growth and improved survival compared to untreated and IM N/S groups.

CONCLUSION: Tropis ID needle-free delivery of pBI-11 induced potent immune activation (with the strongest CD8+ T cell responses) and significantly slowed tumor growth and improved survival compared to untreated and IM N/S groups, supporting its potential in therapeutic cancer vaccination.

Immune Activation: Clinical Impact in Cancer Immunotherapy[13, 14]

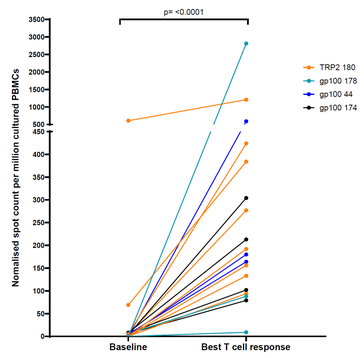
INTRODUCTION: The SCOPE trial evaluates SCIB1 and next-generation iSCIB1+ therapeutic vaccines combined with checkpoint inhibitors in patients with advanced melanoma. The SCIB1 arm using Stratis IM delivery showed strong immune and clinical responses. For iSCIB1+ Stratis delivery is being investigated and a new trial arm now evaluates intradermal delivery with Tropis to assess its impact on immune activation, durability, and clinical outcomes.



SCIB1: ImmunoBody® DNA vaccine, TRP-2, gp100; limited to specific HLA types.

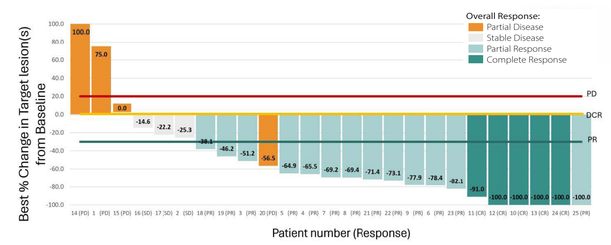
iSCIB1+: AvidiMab®-modified, includes additional melanoma epitopes, broadening HLA coverage.

Significant Increase in Specific T cells



Immune activation observed across multiple epitopes, demonstrating broad immunogenicity of SCIB1. Seventy percent (16 / 23) demonstrated a T cell response that corresponded with best overall response (change in target lesion size).

Overall Response Rate (ORR) at 6 Months



Seventy-two percent (18/25) ORR, 5 complete responses (CR), and 13 partial responses (PR) at 6 months.

CONCLUSION: SCIB1 induced significant ($p < 0.0001$) T cell responses in 70% of patients and melanoma lesion regression, achieving a 72% ORR. The ongoing SCOPE trial is evaluating iSCIB1+ delivered intradermally with Tropis to compare immune and clinical outcomes across delivery routes and to evaluate participant experience.

Conclusion:

Needle-free DNA vaccine delivery shaped immune outcomes in preclinical and clinical studies across autoimmune and oncology models. It also demonstrated immune activation for oncology vaccines, leading to an observed increase in CD8+ T cell responses, reduced lesion size, slowed tumor growth, and improved survival. Immune modulation was shown with decreased T cell infiltrates in both local and treated lesions and repigmentation over time. Intradermal delivery has shown additional immunologic and therapeutic benefits compared to IM delivery, as shown in the HPV DNA vaccine study.

1. Kumar, D. et al. (2025). Cellular immune breadth of an Omicron-specific, self-amplifying monovalent mRNA vaccine booster for COVID-19. NPJ Vaccines 10, 42. 2. Alberer, M. et al. (2017). Safety and immunogenicity of a mRNA rabies vaccine in healthy adults: an open-label, non-randomised, prospective, first-in-human phase 1 clinical trial. Lancet 390, 1511-1520. 3. West, H. C. & Bennett, C. L. (2017) Redefining the Role of Langerhans Cells As Immune Regulators within the Skin. Front Immunol 8, 1941. 4. Hernandez-Franco, J. F. et al. (2023). Intradermal Vaccination against Influenza with a STING-Targeted Nanoparticle Combination Adjuvant Induces Superior Cross-Protective Humoral Immunity in Swine Compared with Intranasal and Intramuscular Immunization. Vaccines (Basel) 11. 5. Peng, S. et al. (2023). Immune responses, therapeutic anti-tumor effects, and tolerability upon therapeutic HPV16/18 E6/E7 DNA vaccination via needle-free biojector. mBio 14, e0212123. 6. Kupper, T. S. & Fuhlbrigge, R. C. (2004). Immune surveillance in the skin: mechanisms and clinical consequences. Nat Rev Immunol 4, 211-222. 7. Best, S. R. et al. (2009). Administration of HPV DNA vaccine via electroporation elicits the strongest CD8+ T cell immune responses compared to intramuscular injection and intradermal gene gun delivery. Vaccine 27, 5450-5459. 8. Lind, A. et al. (2012). Intradermal vaccination of HIV-infected patients with short HIV Gag p24-like peptides induces CD4 + and CD8 + T cell responses lasting more than seven years. Scand J Infect Dis 44, 566-572. 9. Duffy, D. et al. (2012). Neutrophils transport antigen from the dermis to the bone marrow, initiating a source of memory CD8+ T cells. Immunity 37, 917-929. 10. Kim, A. et al. (2023). Vaccines for immune tolerance against autoimmune disease. Adv Drug Deliv Rev 203, 115140. 11. Liang, F. & Lore, K. (2016). Local innate immune responses in the vaccine adjuvant-injected muscle. Clin Transl Immunology 5, e74. 12. Henning, S. W. et al. (2018). HSP70iQ435A-Encoding DNA Repigments Vitiligo Lesions in Sinclair Swine. J Invest Dermatol 138. 13. Shaw, H. et al. (February 2025). A DNA plasmid melanoma cancer vaccine, SCIB1, combined with nivolumab + ipilimumab in patients with advanced unresectable melanoma: Efficacy and safety results from the open-label Phase 2 SCOPE Trial. [Poster presentation]. American Association for Cancer Research (Immuno-Oncology), Los Angeles, CA, United States. 14. Gardner, P. et al. (2025, January 13). Scancell: Poised for several pivotal clinical events in 2025 [Equity research report]. Trinity Delta. https://scancell.co.uk/wp-content/uploads/2025/01/SCLP-Update-250113-1.pdf

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