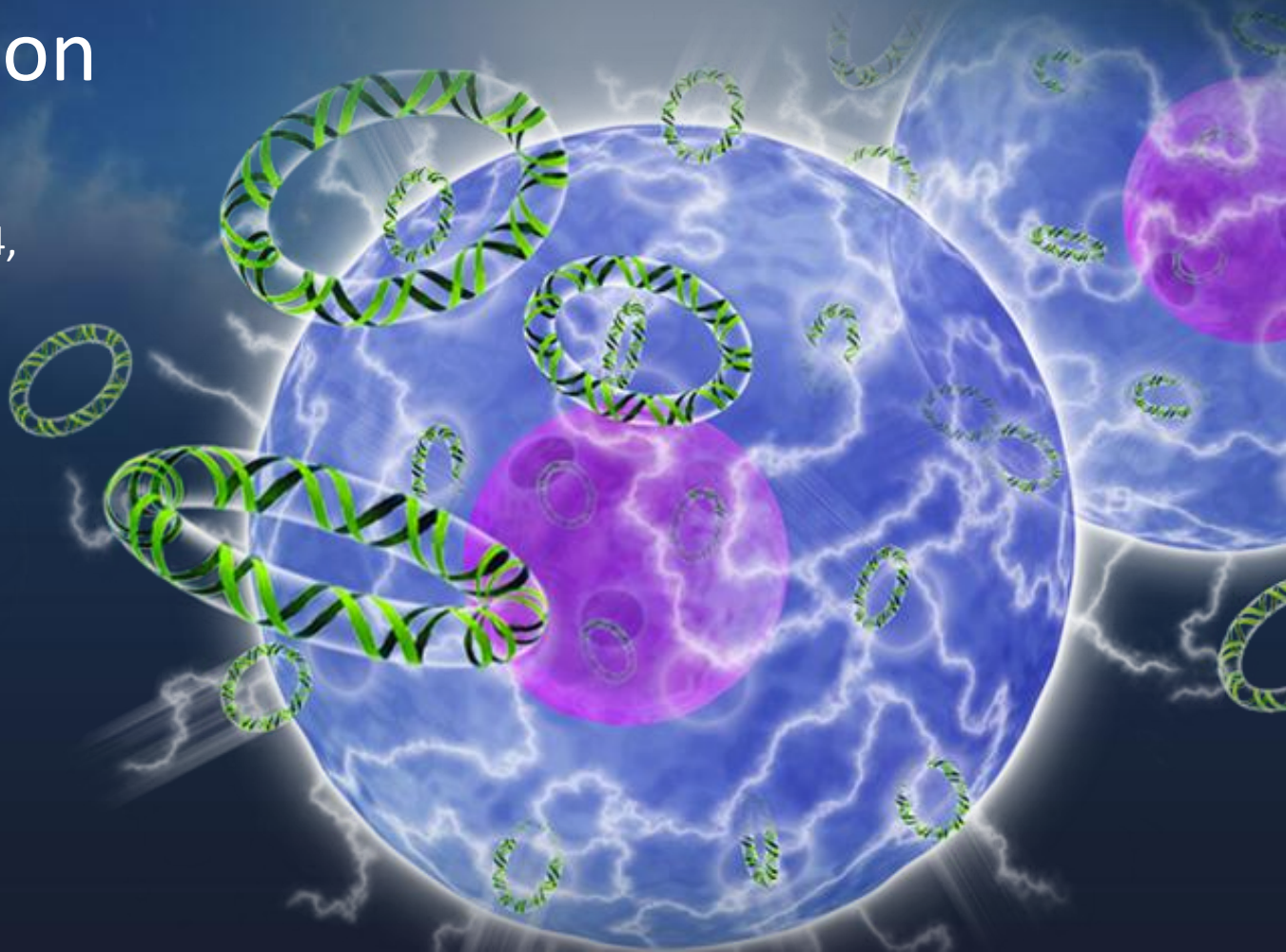
Generation of robust immunity following DNA vaccination enhanced by intradermal electroporation

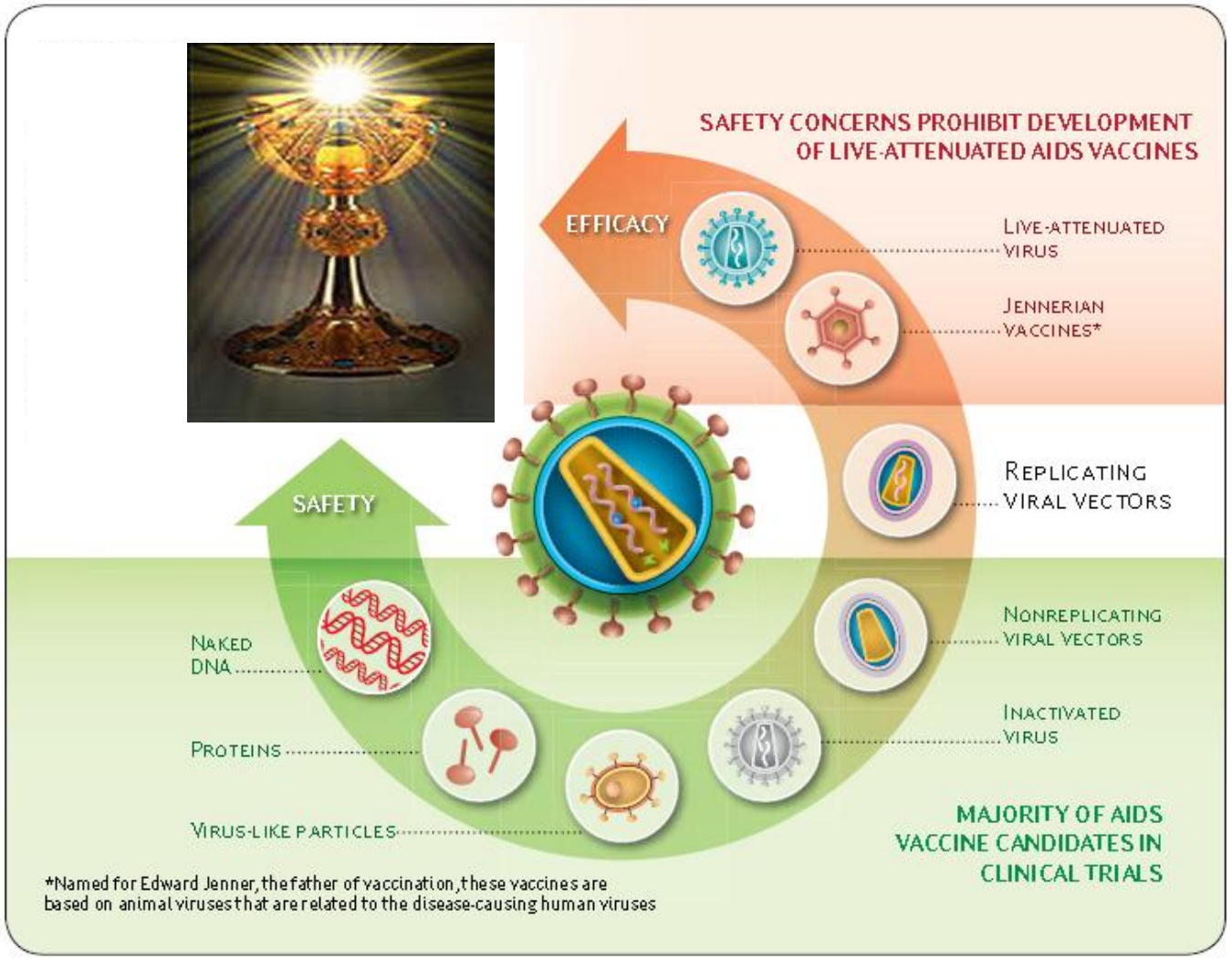


Cell & Gene Therapy 2014,
Las Vegas, NV

October 27–29, 2014

Trevor Smith, PhD

Vaccines: Safety vs. Efficacy

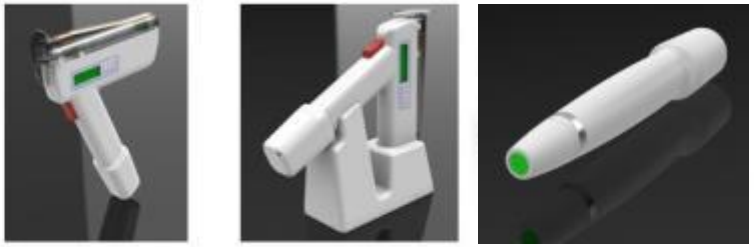


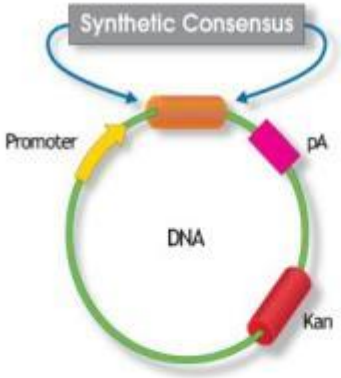
IAVI Blueprint for AIDS Vaccine Report, 2008

inovio

Inovio: Fulfilling the promise of DNA Vaccines

DNA Delivery Systems





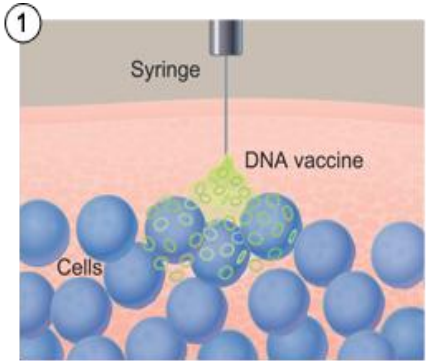
DNA Vaccine Platform

SynCon™ Optimized Vaccines

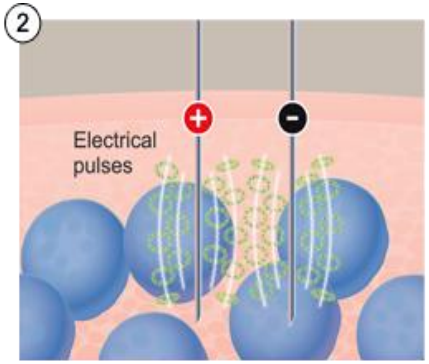
Manufacturing & Formulations
(Affiliate: VGXI, Inc.)

inovio

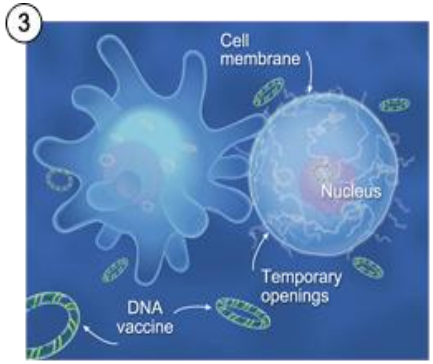
Enhanced DNA Delivery: *in vivo* Electroporation



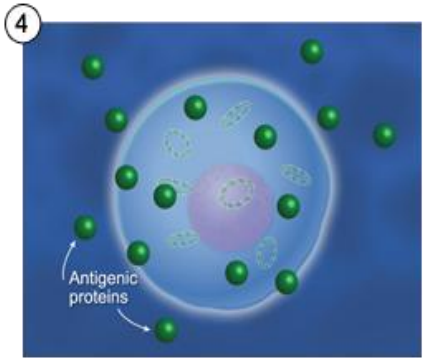
DNA vaccine delivered into muscle or skin.



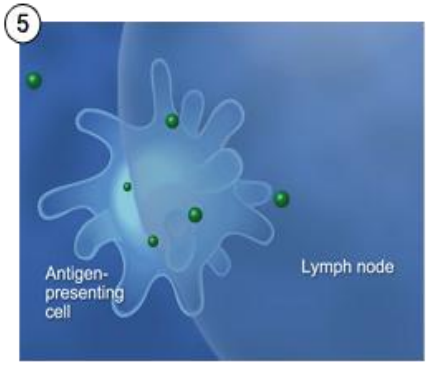
Electroporation: millisecond electrical fields applied.



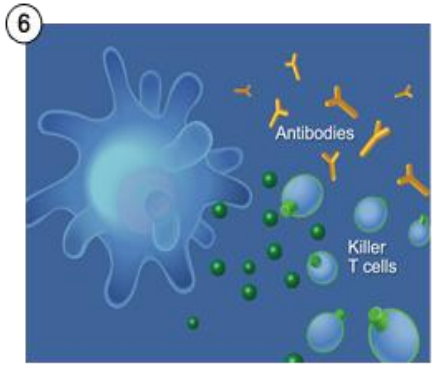
Temporary pores in cell membrane; significant cellular uptake of vaccine.



Cell membrane reseals. Cellular machinery uses the DNA code to produce one or more of the disease antigens coded by the DNA vaccine.



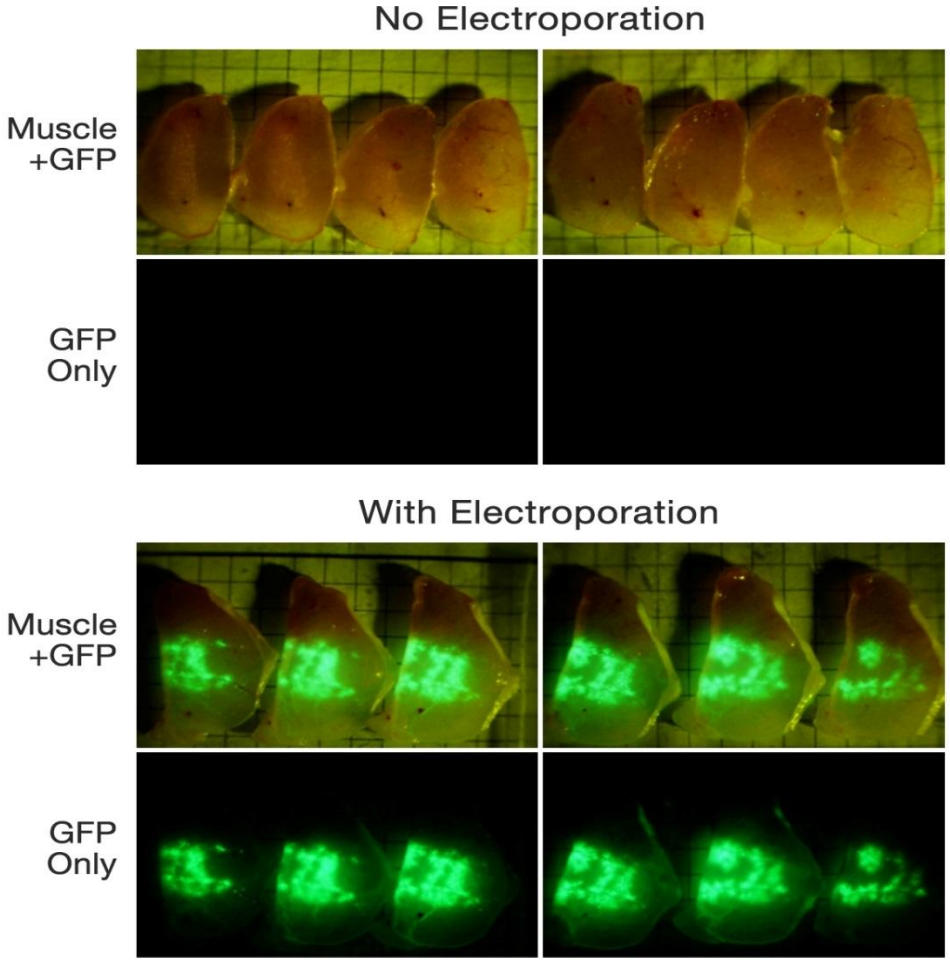
Antigen-presenting cells engulf the antigens and carry them to lymph nodes.



Antibodies or killer T-cells that can eliminate cancerous or infected cells are produced.

inovio

Electroporation Enhanced Transfection

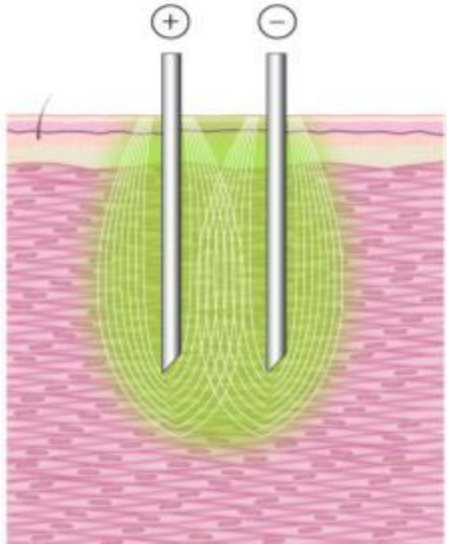


inovio

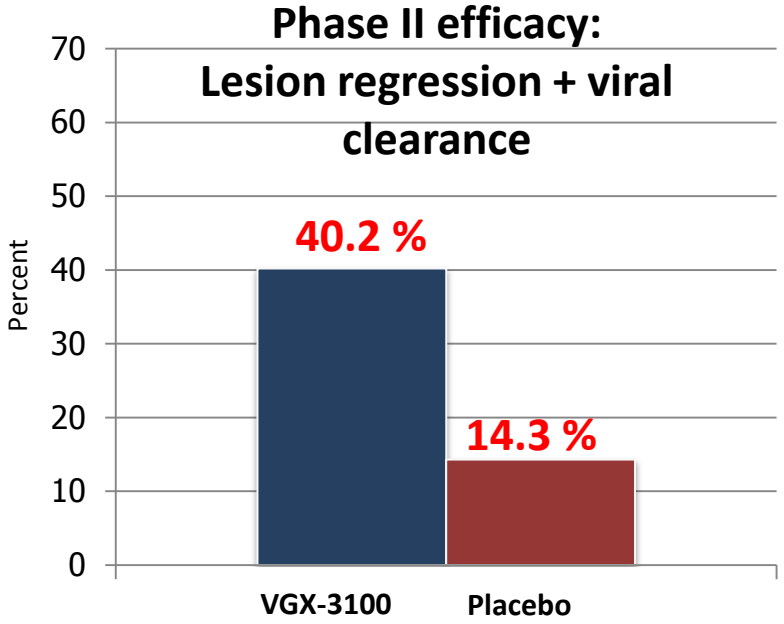
Sardesai and Weiner, Curr. Opin. Immunol. 2011

Muscle EP Device – In the clinic: CELLECTRA®-5P

IM-Electroporation



Number patients treated - 520+
Total immunizations - 1300+



Therapeutic Phase I

HPV-001 Inovio
HPV-002 Inovio
HIV-001 UPenn – PennVax B
HPV-004 Inovio (open IND)
HPV-005 Inovio (open IND)
HPV-006 Inovio (Open IND)

Prophylactic Phase I

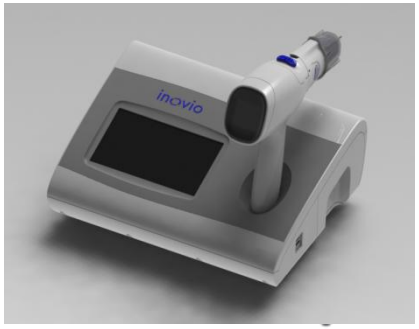
HIV-080 HVTN – PennVax B
FLU-001 Inovio (US)
FLU-001 Inovio (Korea)
RV-262 Army – PennVax B and G

Therapeutic Phase II

HPV-003 Inovio Cervical Dysplasia

VGX-3100 (HPV16/18 E6 & E7 oncoproteins)

Phase III Device

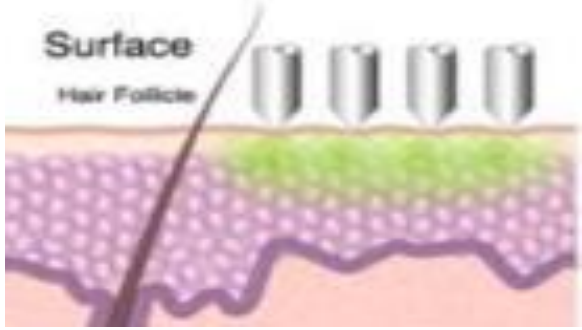


inovio

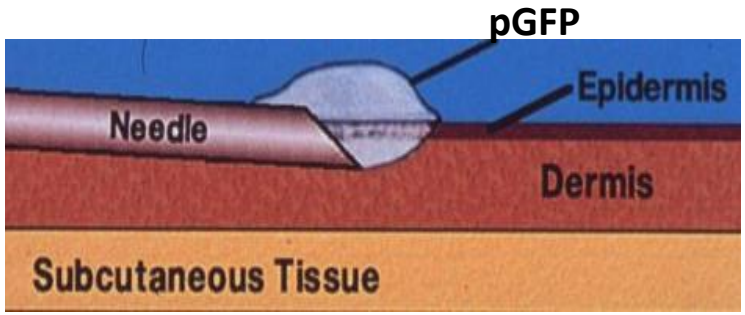
Skin EP Device – preclinical: SEP

Surface EP System

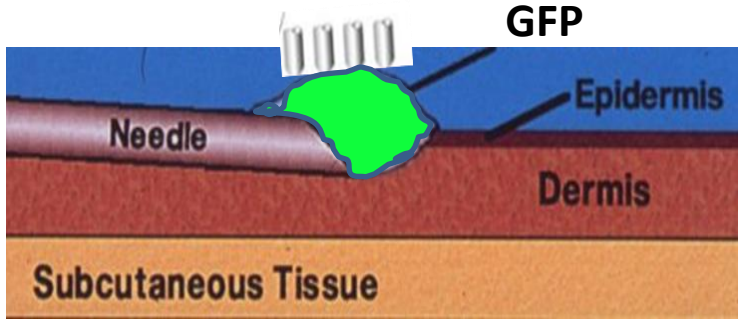
Intradermal Electroporation



ID injection + SEP procedure:



1. Mantoux injection to admin. pDNA

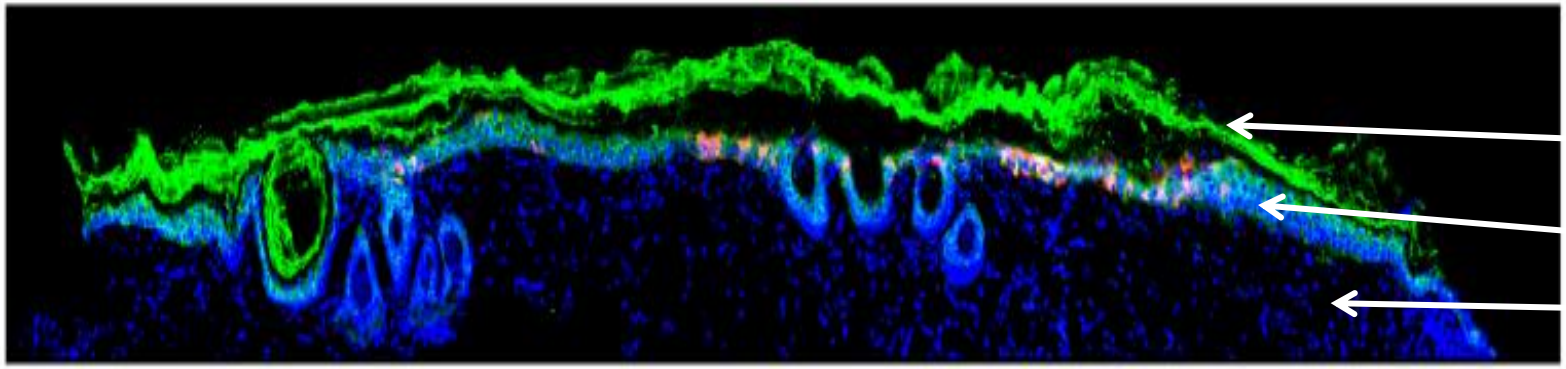


2. EP to allow pDNA transfection

inovio

Surface EP specifically targets the Epidermis

K10/RFP/Hoescht



inovio

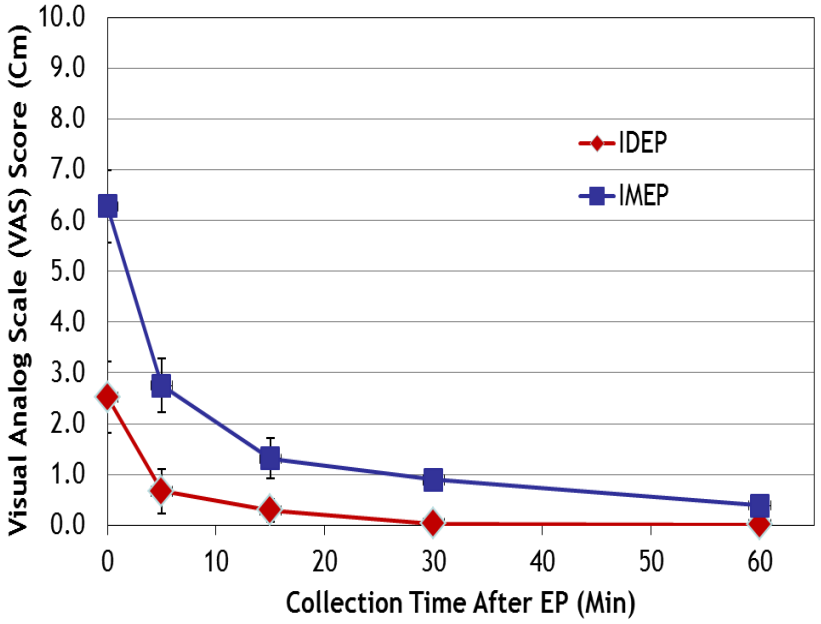
Smith TRF et al, Mol. Ther. – Methods & Clinical Dev. In press

Advantages of vaccinating in the skin

Accessibility

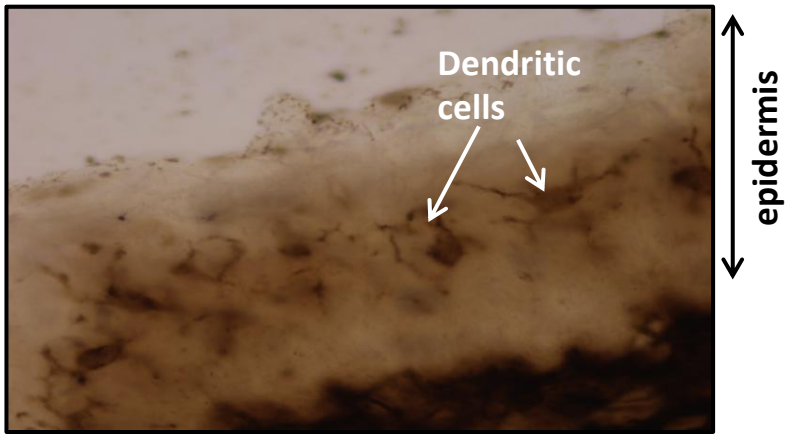
Monitoring

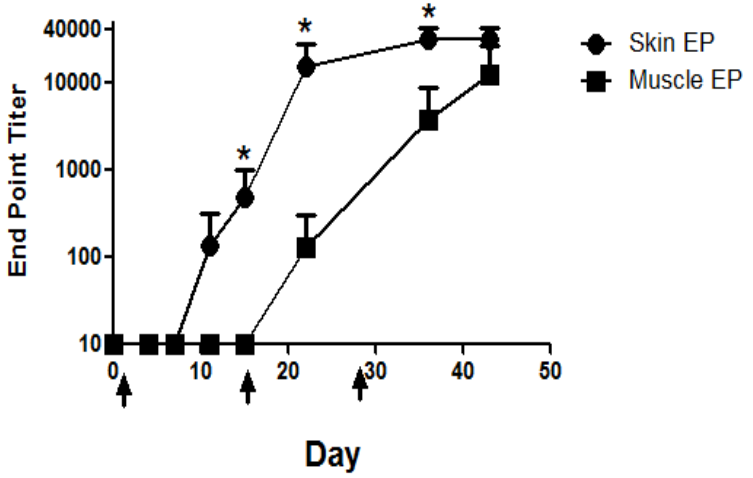
Tolerability:



Diehl MC et al, Hum Vacc. Imm. 2013

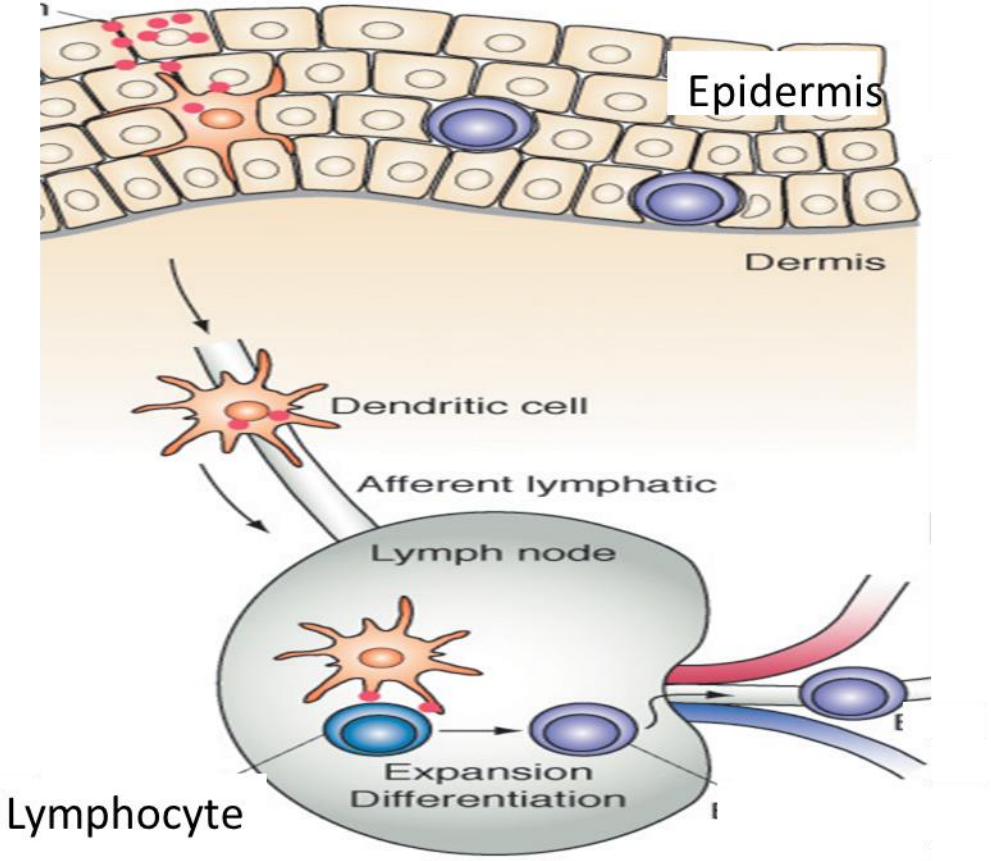
Immunocompetence:





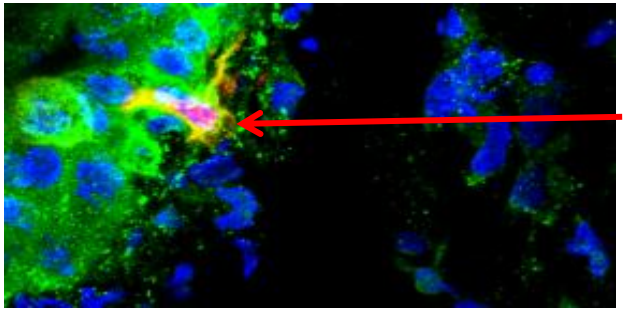
inovio

Proposed Mechanism



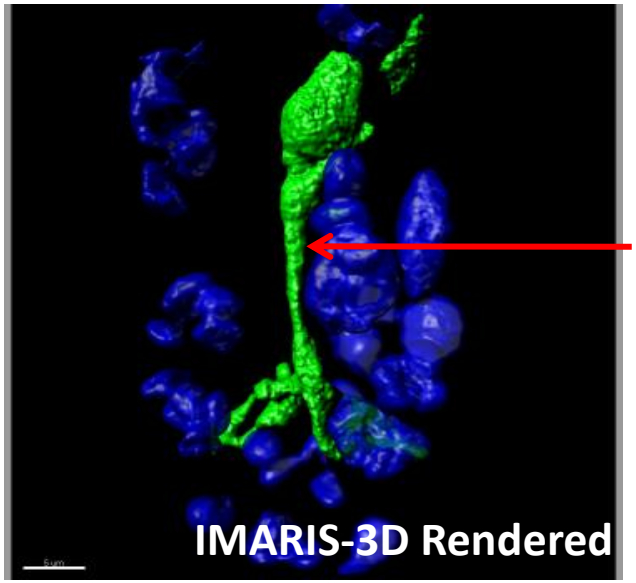
Directly transfecting Dendritic Cells

Epidermis:



RFP positive dendritic cell

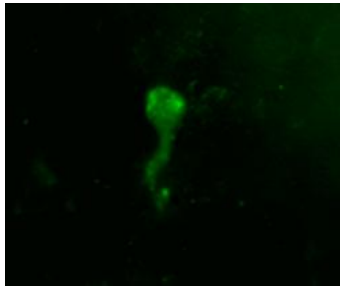
Dermis:



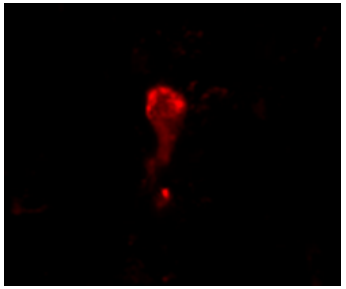
GFP positive dendritic cell

Dendritic cell staining in dermis:

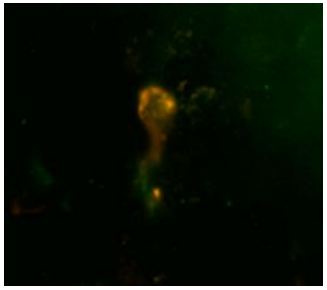
GFP



MsGp2



Color merged

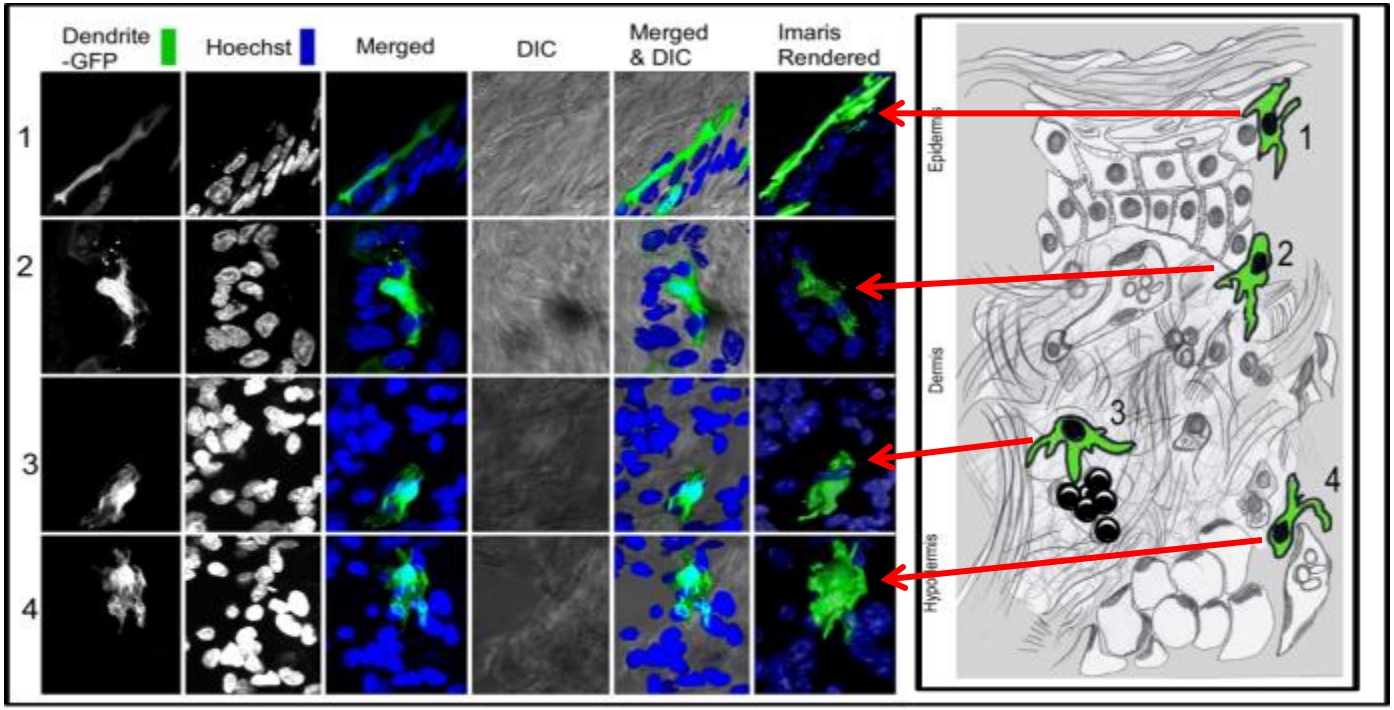


GFP
MsGp2

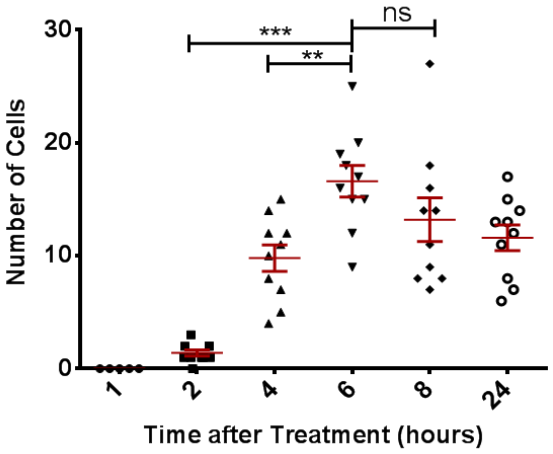
Amante D et al, Human Gene Therapy. In press

inovio

Kinetics of DC migration into the dermis



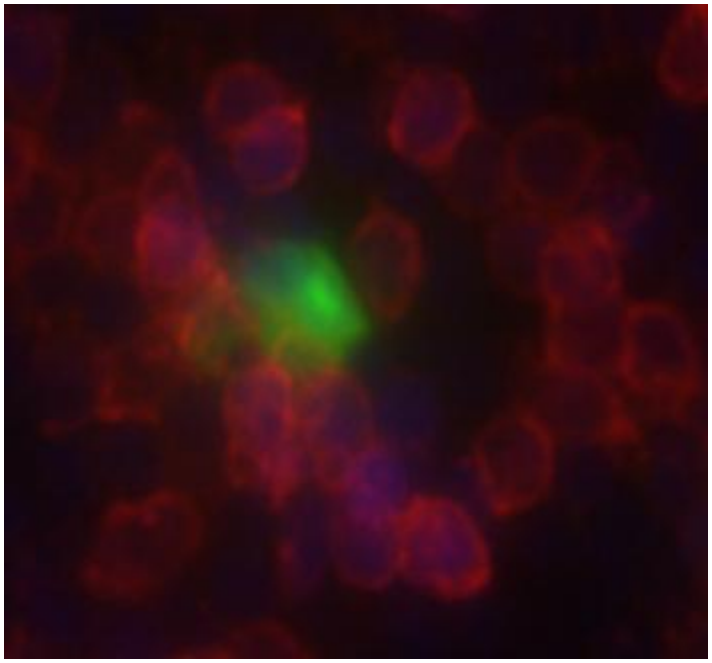
Number of GFP+ cells In the dermis:



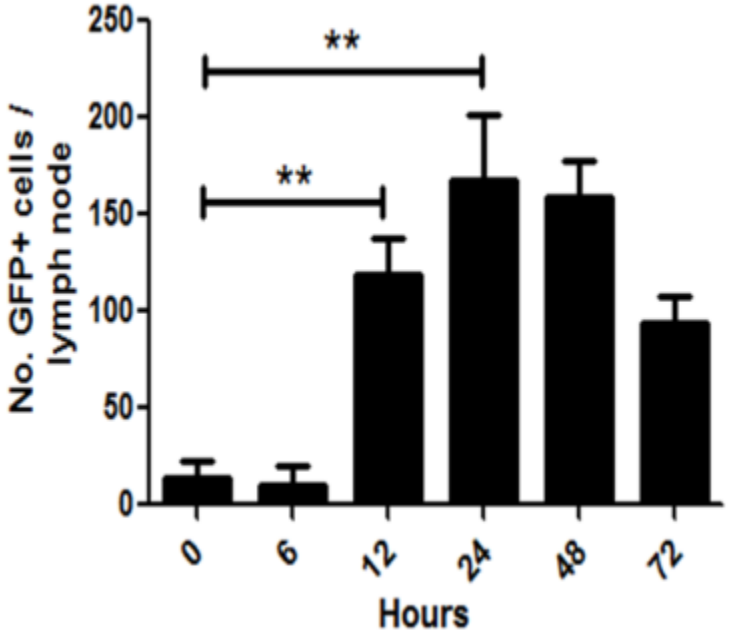
inovio

GFP+ cells in the draining lymph nodes

CD4/GFP/Dapi

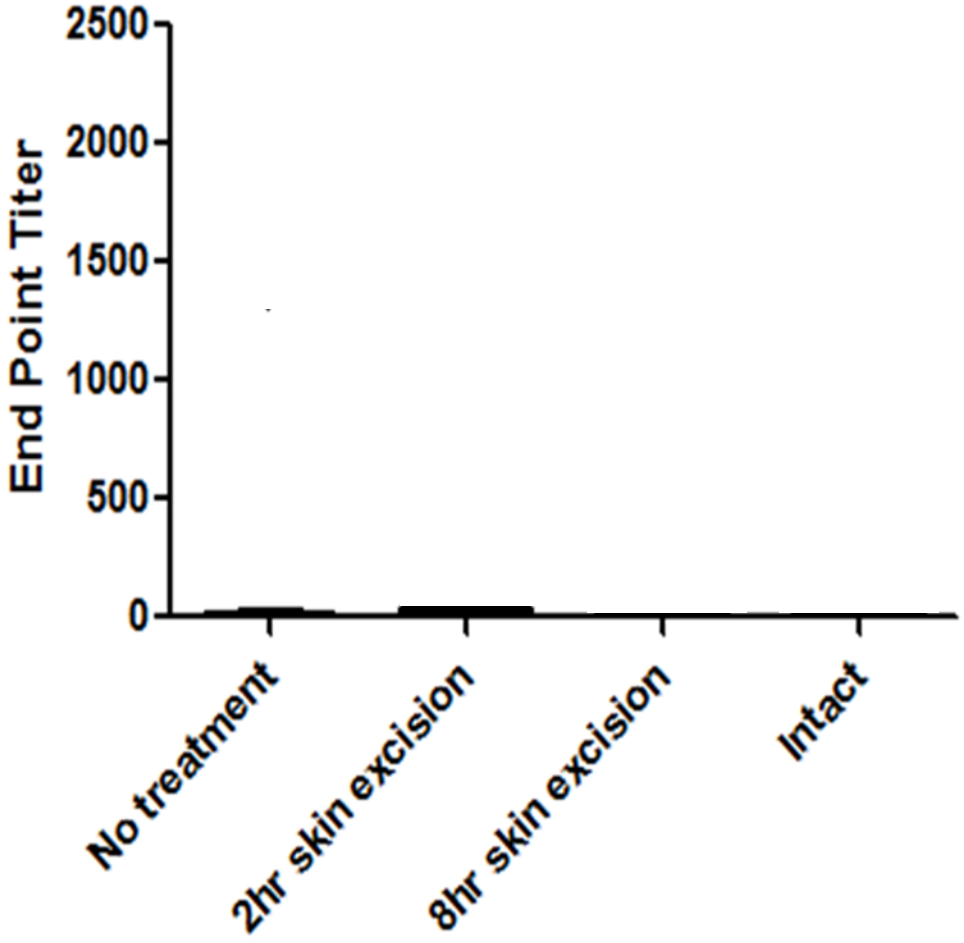


GFP+ cell in the T cell zone of the cortex in the inguinal lymph node



inovio

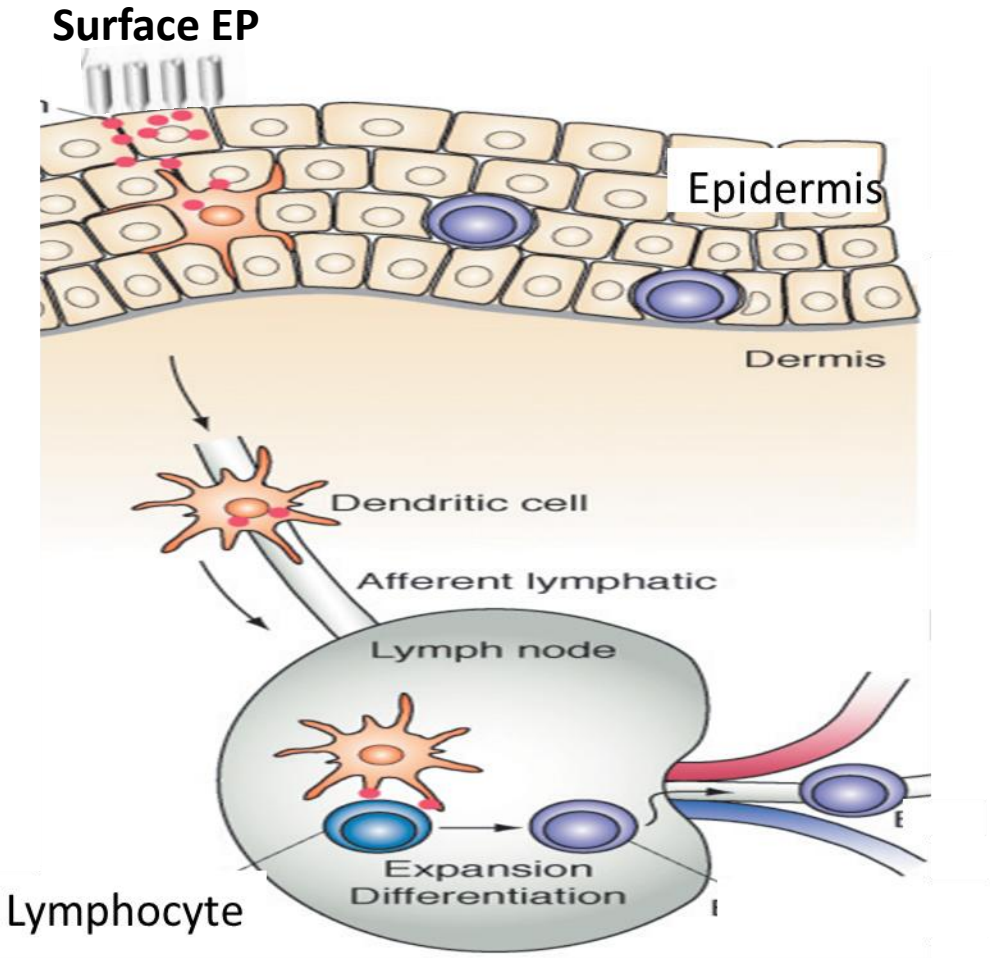
Treatment site excision and host immune responses



inovio

Summary

- **Transfection of epidermal DCs**
- **Migration into dermis**
- **Traffic to the DLN**



- **Prime Immune Response**

Vaccine Indications:

Influenza

Ebola

Travel vaccines

inovio

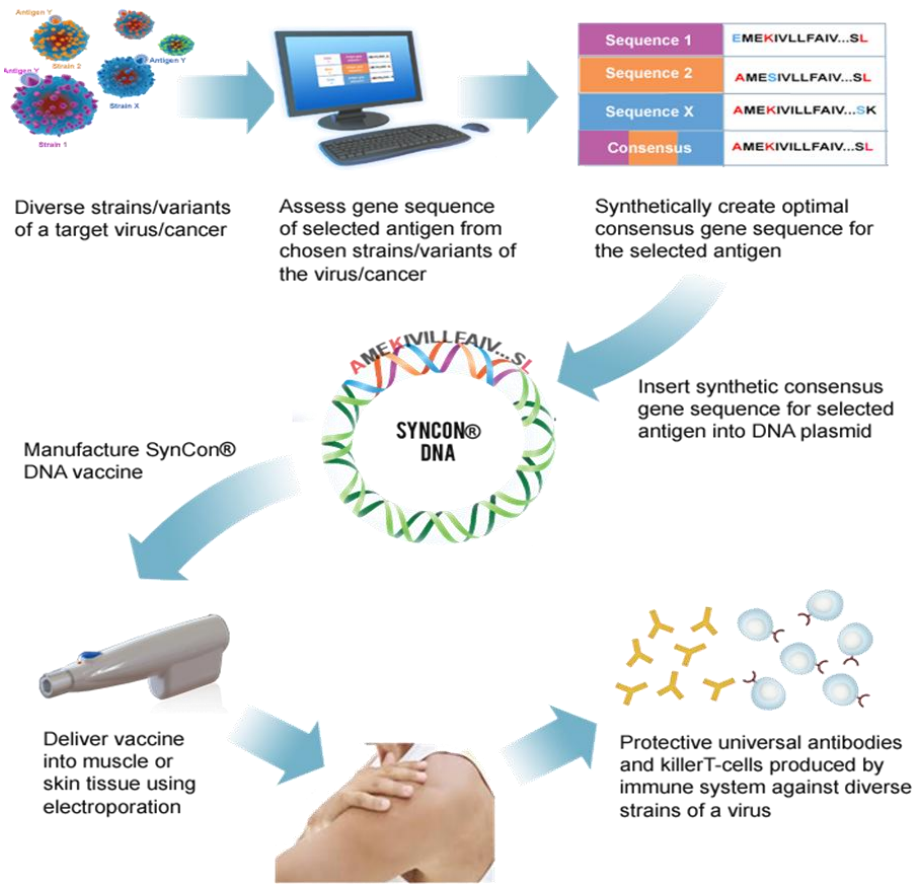
Acknowledgments

Kate Broderick
Jay McCoy
Janess Mendoza
Dinah Amante
Katherine Schultheis
Alan Gomez
Laurent Humeau
Niranjan Sardesai
J. Joseph Kim

Bill Kiosses

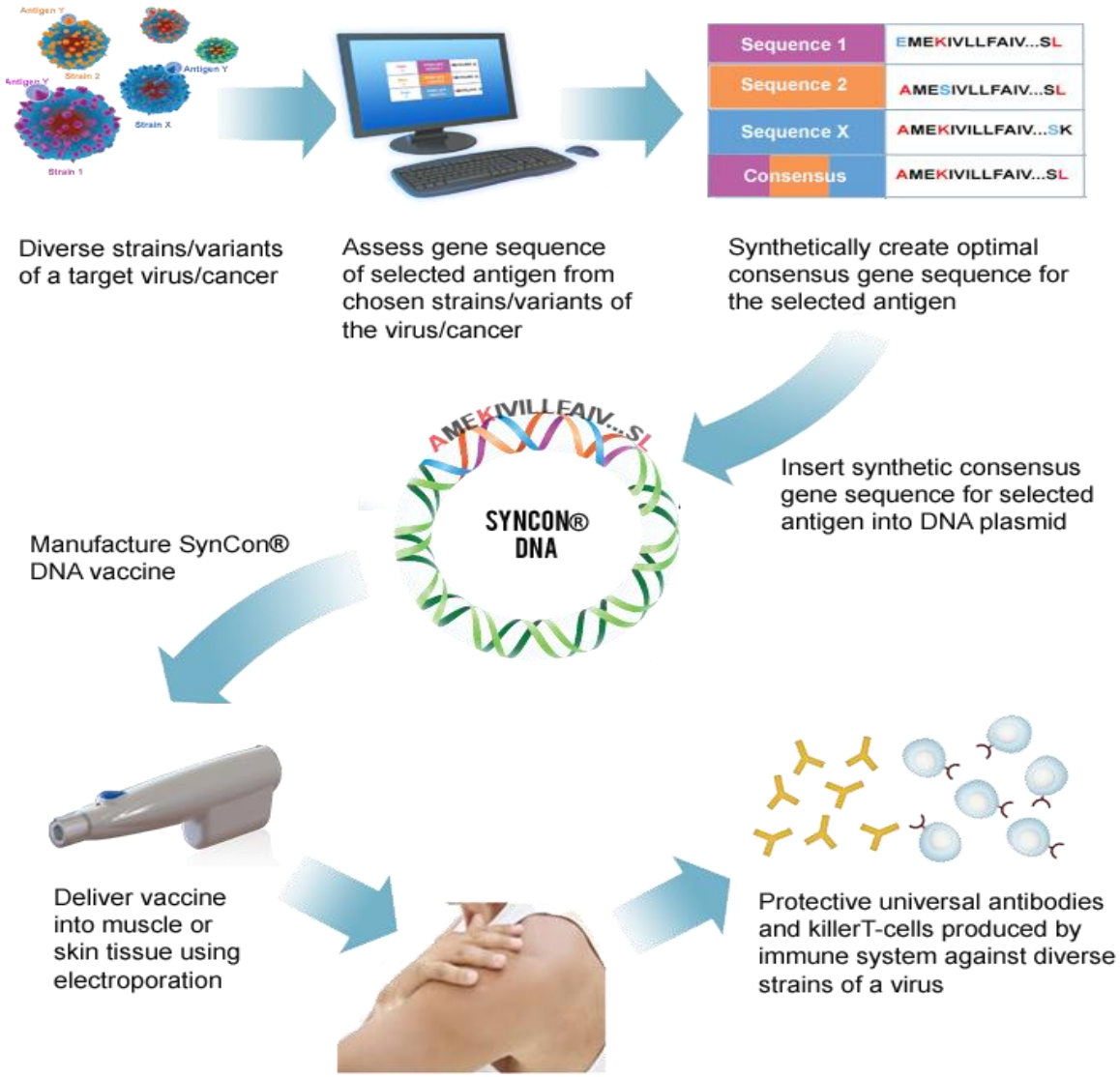
This work was supported in part by US Army grant W23RYX-8141-N604: #08023003 and US Army SBIR W81XWH-11-C-0051:# 1031550133.

Additional funding support from DTRA and NIH/NIAID

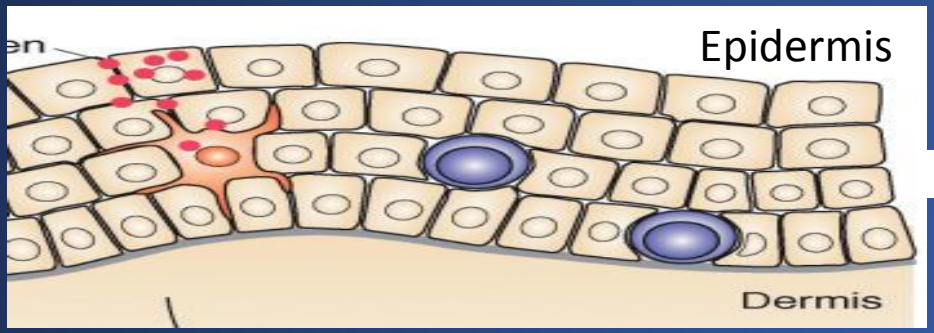


SynCon® DNA vaccine helps the immune system to recognize and break tolerance of cancer antigens/cells or achieve universal protection against multiple existing or newly emergent virus strains.

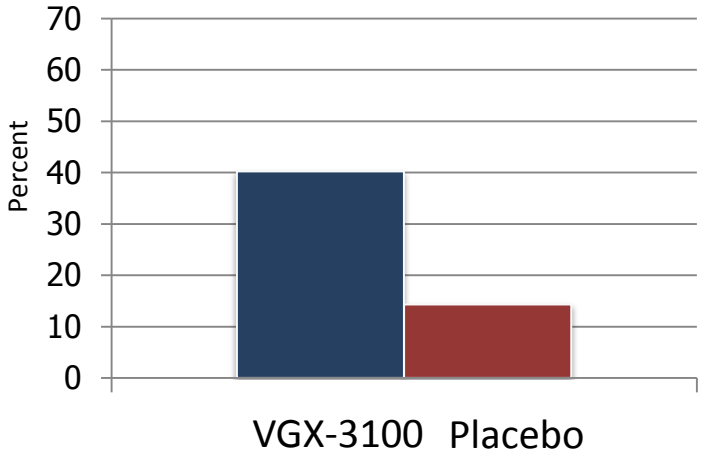
Inovio combines optimized DNA with safe & effective delivery to generate significant T cells with killing activity



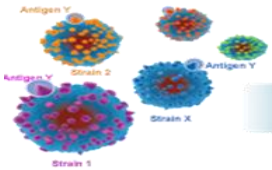
SynCon® DNA vaccine helps the immune system to recognize and break tolerance


Epidermis
Dermis

Overall Histopathologic Regression* and
Virological (HPV Type 16 or 18) Clearance Incidence
Per-Protocol** Population (N=142)



Inovio: Fulfilling the promise of DNA Vaccines



Diverse strains/variants of a target virus/cancer

Assess gene sequence of selected antigen from chosen strains/variants of the virus/cancer

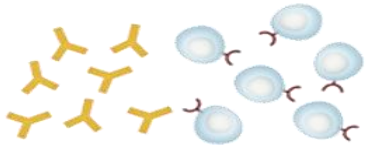
Sequence 1	EMEKIVLLFAIV...SL
Sequence 2	AMESIVLLFAIV...SL
Sequence X	AMEKIVILLFAIV...SK
Consensus	AMEKIVILLFAIV...SL

Synthetically create optimal consensus gene sequence for the selected antigen

Insert synthetic consensus gene sequence for selected antigen into DNA plasmid

Manufacture SynCon® DNA vaccine

Deliver vaccine into muscle or skin tissue using electroporation



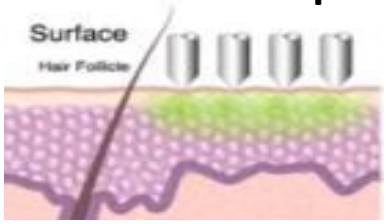
Protective universal antibodies and killerT-cells produced by immune system against diverse strains of a virus

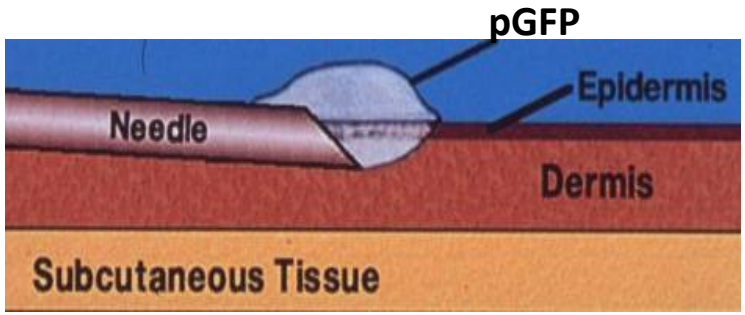
inovio

Skin EP Device – preclinical: SEP

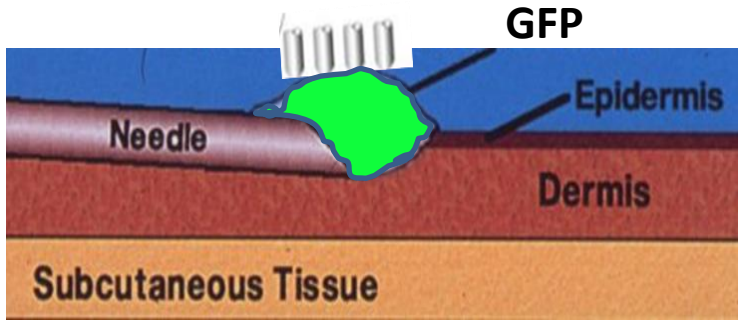
Surface EP System

Intradermal Electroporation



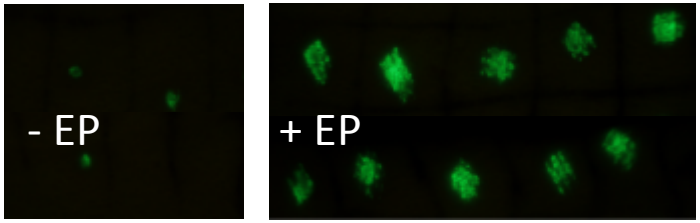


1. Mantoux injection to admin. pDNA

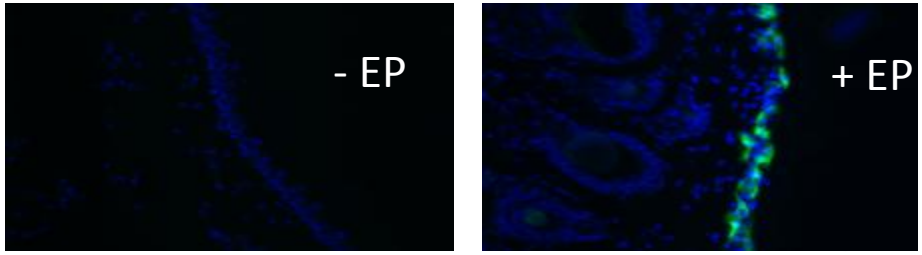


2. EP to allow pDNA transfection

GFP expression on skin surface



GFP expression in epidermis



inovio