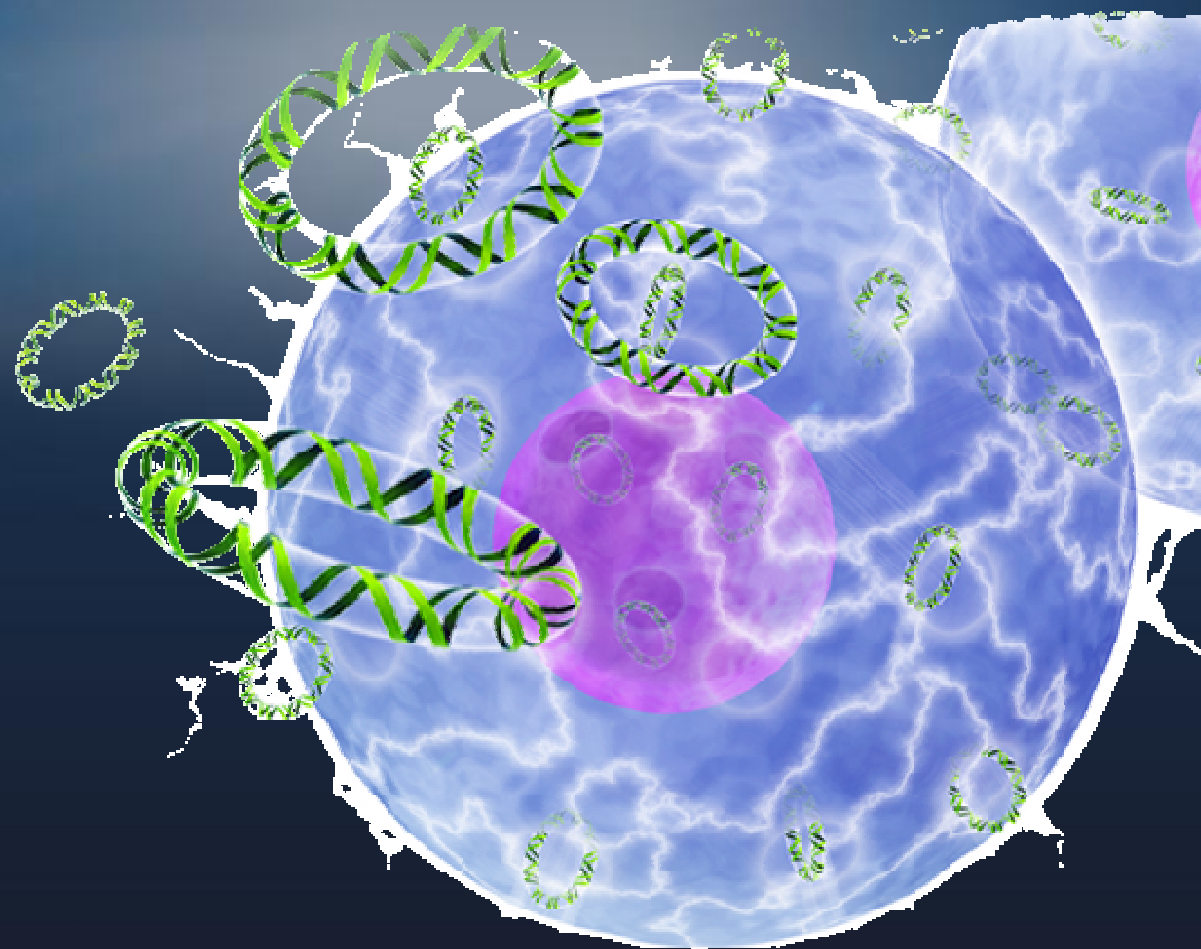


Enhanced delivery of DNA-based vaccines and immunotherapeutics through next-generation electroporation devices

Stephanie Ramos, Ph.D.
Inovio Pharmaceuticals

Cell & Gene Therapy, 2015
London, UK
August 10, 2015



Attractiveness of DNA Vaccines

Safer than live virus vaccines

- Cannot cause disease
- No significant side effects

Prevent and treat

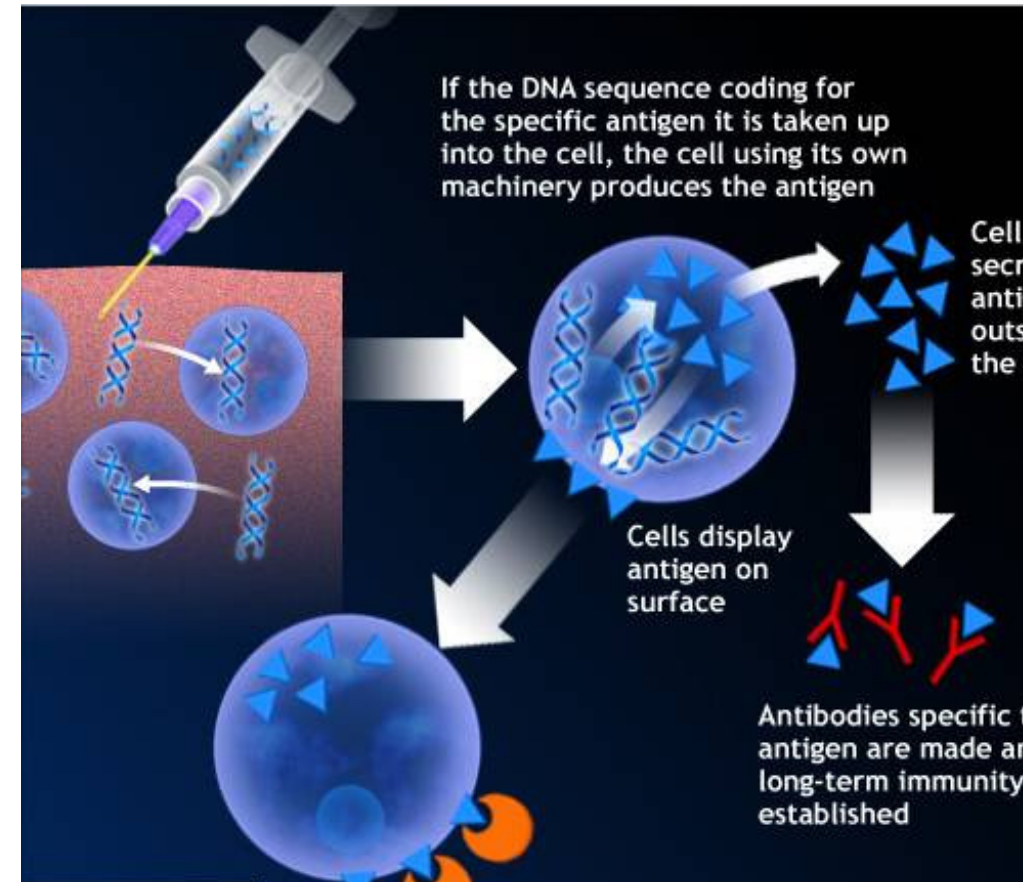
- Vastly expands market size
- Generate T cell & Antibody responses

Faster development

Easier to manufacture

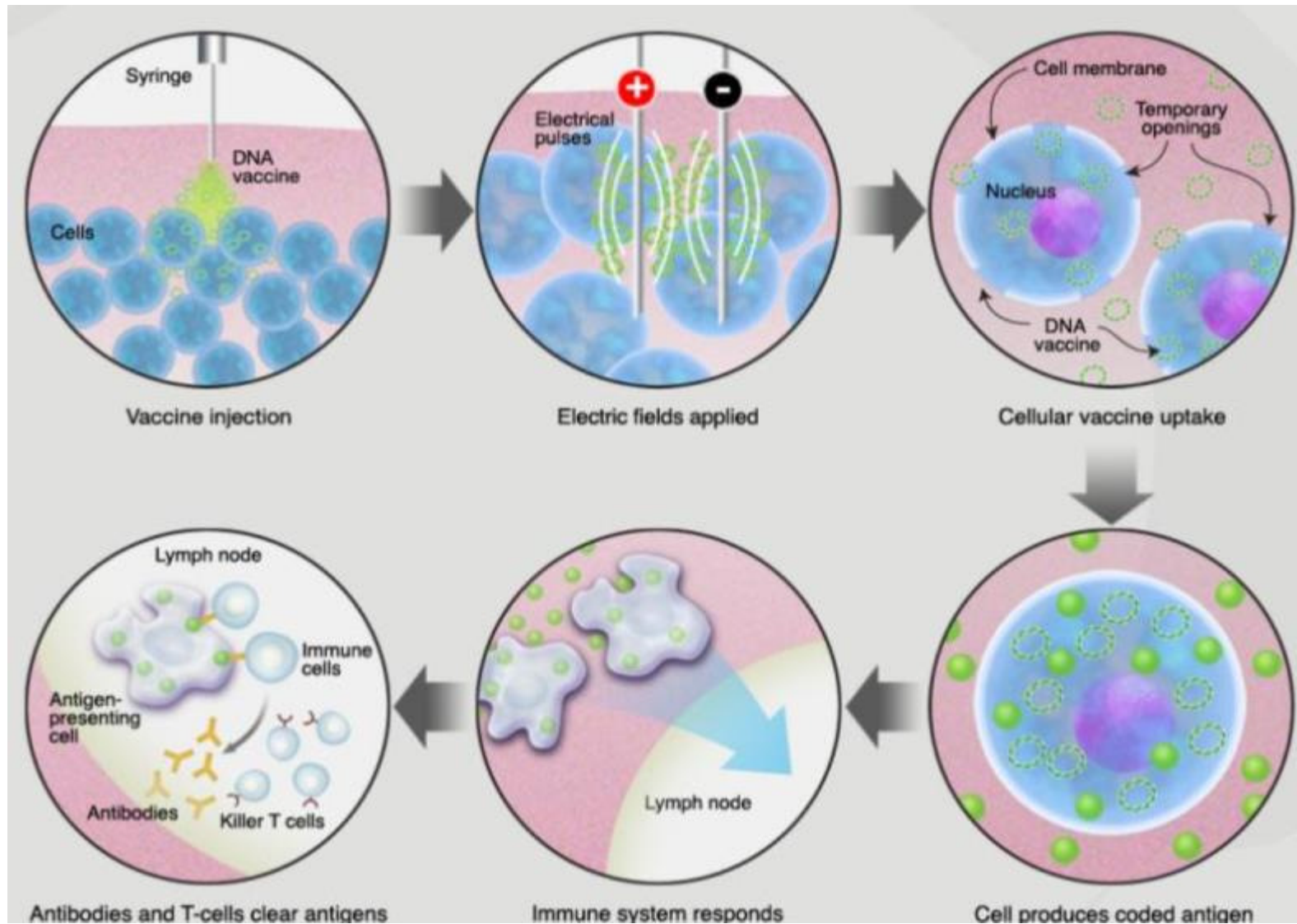
Combination vaccines possible

Key limitation of delivery being recently overcome with electroporation

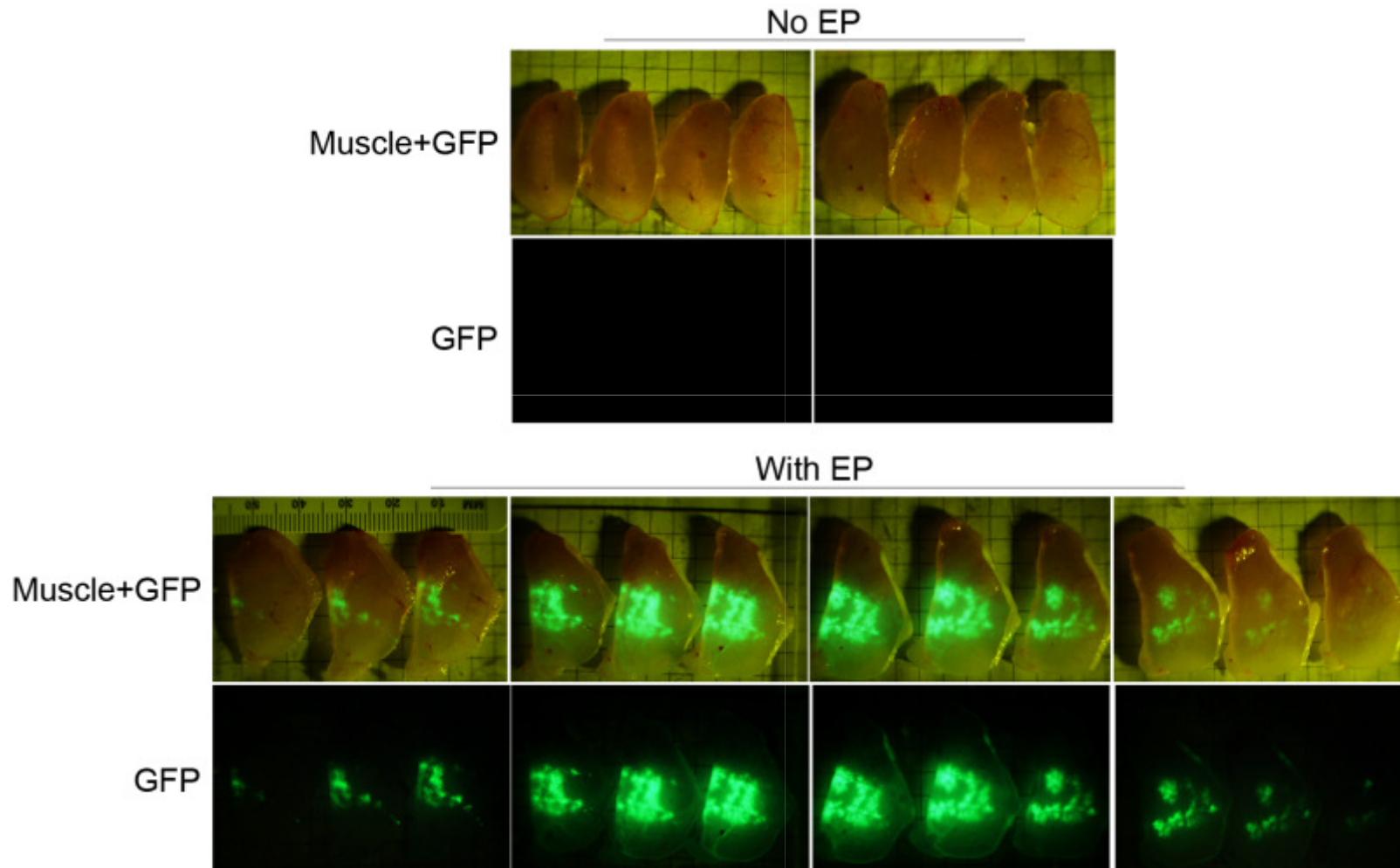


Electroporation is a key enabling technology

Enhanced DNA Delivery: Electroporation



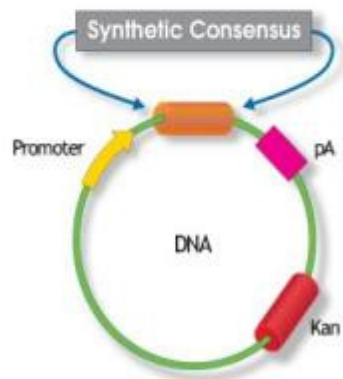
INOVIO: Electroporation Enhanced Transfection



Sardesai & Weiner, Curr Opin Immunol 2011

INOVIO: Fulfilling the Promise of DNA Vaccines

DNA Delivery Systems

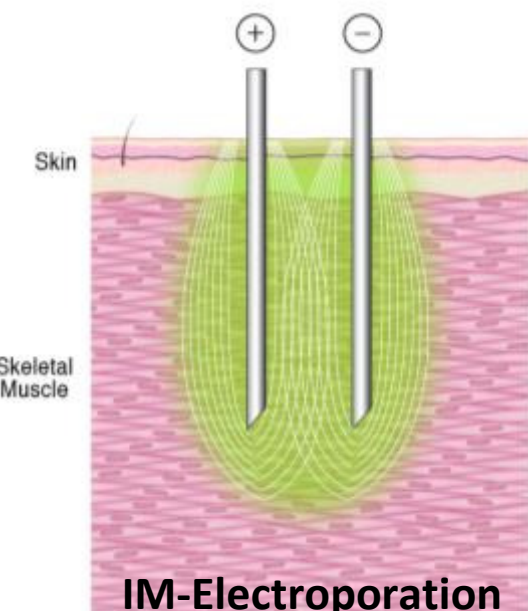


SynCon™ Optimized Vaccines



Manufacturing & Formulations
(Affiliate: VGXI, Inc.)

Muscle EP Device in the Clinic: CELLECTRA[®]-5P



Phase I/II Device



Phase III Device



Prophylactic Phase I

- FLU-001 US } (Flu)
- FLU-001 Korea } (Flu)
- HIV-080 } (HIV)
- RV-262 } (HIV)
- EBOV-001 (Ebola)

Therapeutic Phase I

- HIV-001 (HIV)
- HPV-001 } (HPV-associated CIN)
- HPV-002 } (HPV-associated CIN)
- HPV-004 } (HPV-associated cancers)
- HPV-005 } (HPV-associated cancers)
- HPV-006 } (HPV-associated cancers)
- TRT-001 (breast, lung, pancreatic cancers)
- PCa-001 (prostate cancer)
- VGX-6150-01 (chronic HepC)
- HBV-001 (chronic HepB)

Therapeutic Phase II

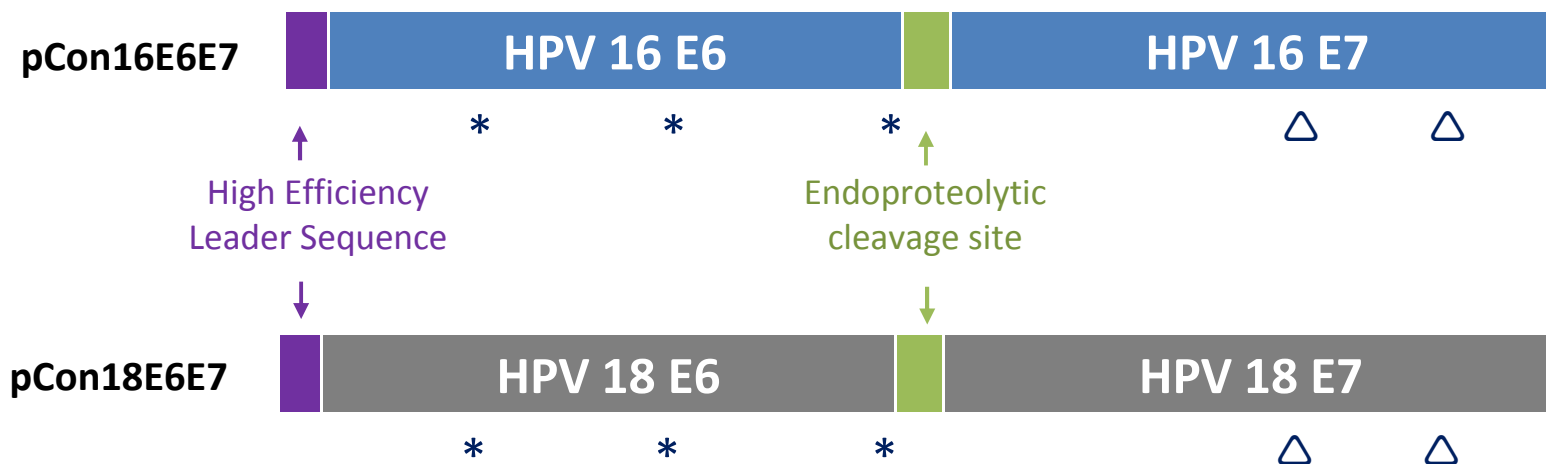
- HPV-003 (HPV-assoc cervical dysplasia)
- EORTC-1411 (HPV-associated cervical cancer)

Number of total patients treated - 550+
Number of total immunizations - 1450+

VIO's Clinical Experience

-3100: Non-Surgical Option for the Treatment of HPV-Specific High-Grade Cervical Dysp

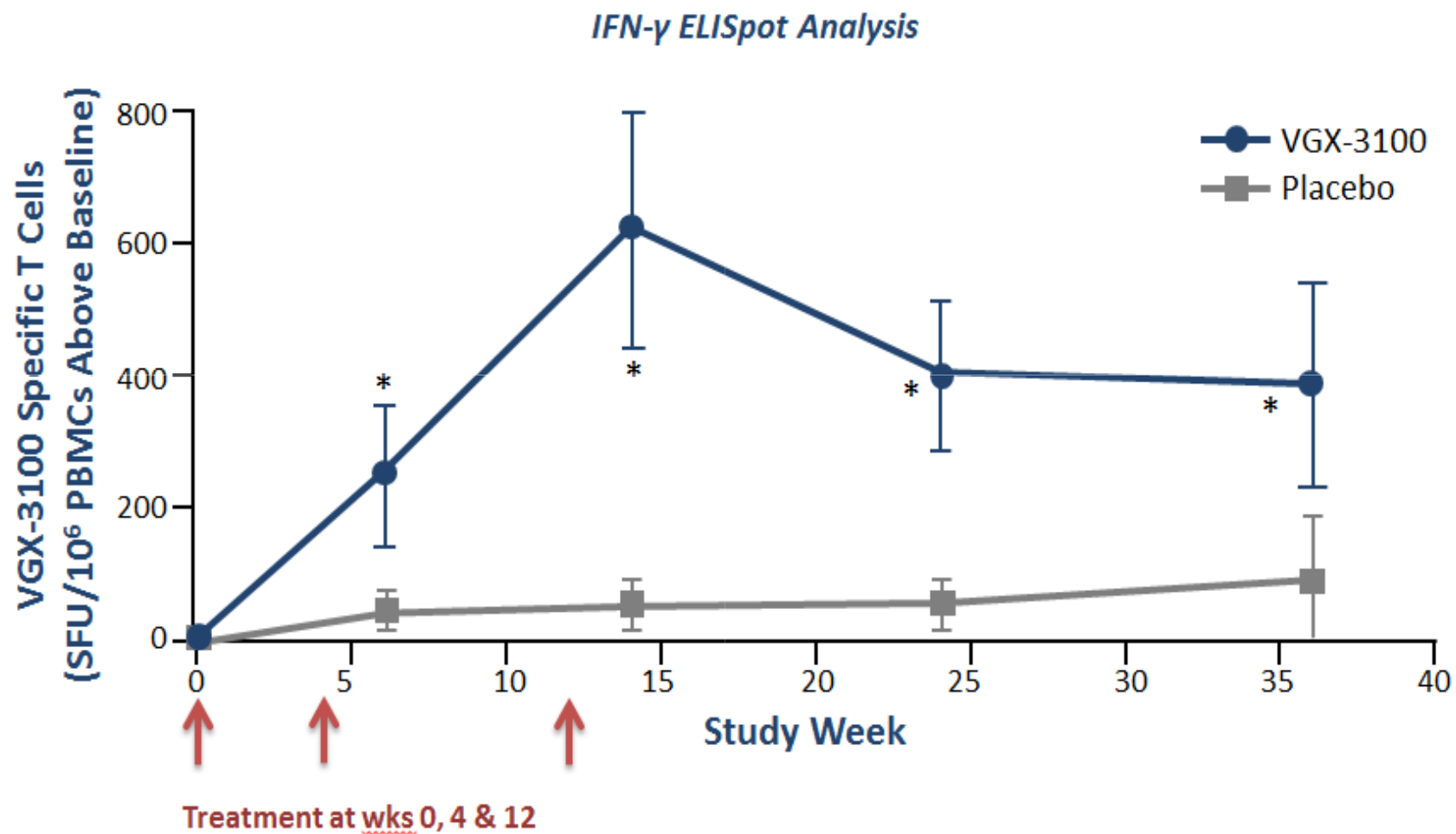
- Combination HPV16/18 E6/E7 DNA immunotherapy
- Two DNA plasmids delivered simultaneously via IM injection followed by IM electroporation (CELLECTRA[®]-5P)
- Capitalizes on Inovio's ability to drive the body's own immune system to seek and destroy pre-cancerous cells



△Mutations in Rb binding site

*Deletions or mutations important for p53 binding and degradation

VGX-3100 Phase II: Generation of Robust HPV-16 and HPV-18 T Cell Responses

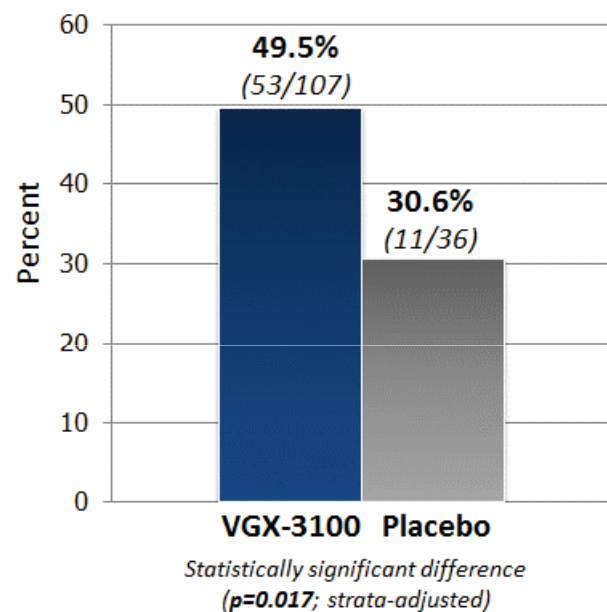


*Statistically significant; bars are 95% CI.
IFN = interferon.

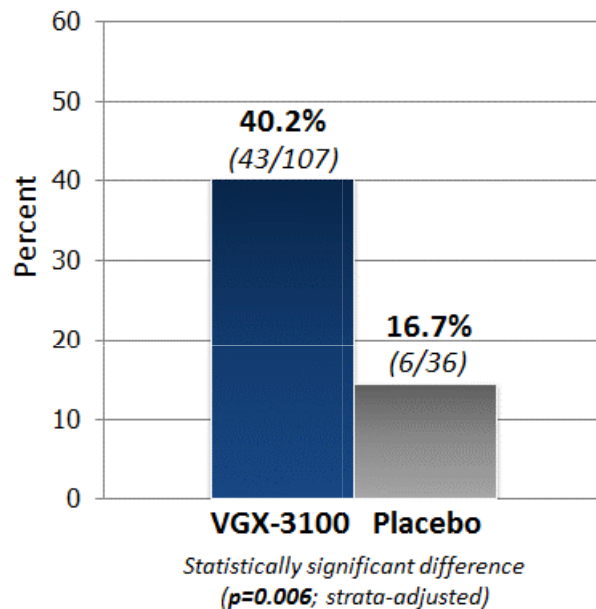
Inovio Pharmaceuticals: Proprietary Data

VGX-3100 Phase II: Clinically Significant Efficacy in the Treatment of Cervical Dysplasia

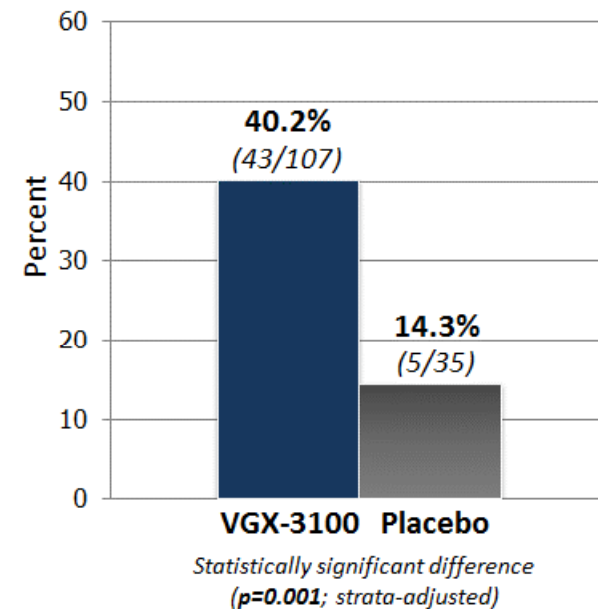
Pre-Specified 1^o Endpoint: Histopathologic Regression to CIN1 or Normal



Post-Hoc Analysis: Regression to Normal

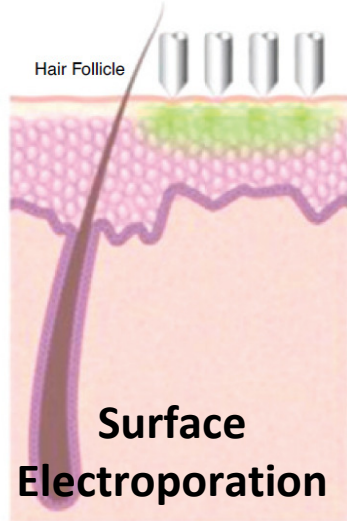


Histopathologic Regression to CIN1 or Normal AND Virological Clearance (HPV16 or 18) (n=143)



- ▶ Significant disease regression and viral clearance
- ▶ First report of clinical efficacy with a therapeutic naked DNA vaccine using electroporation delivery

Enhanced DNA Delivery to the Skin via Surface Electroporation



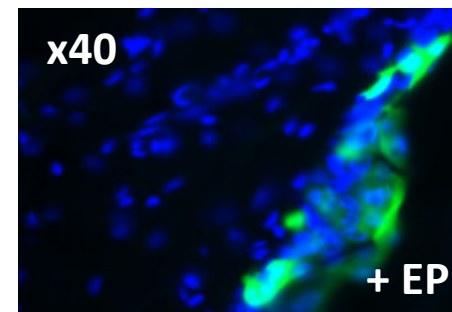
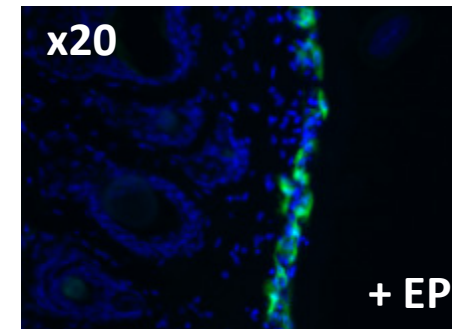
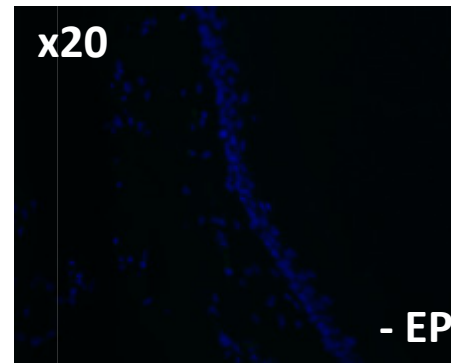
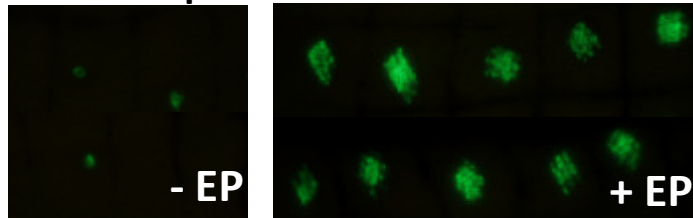
Tethered Surface EP System



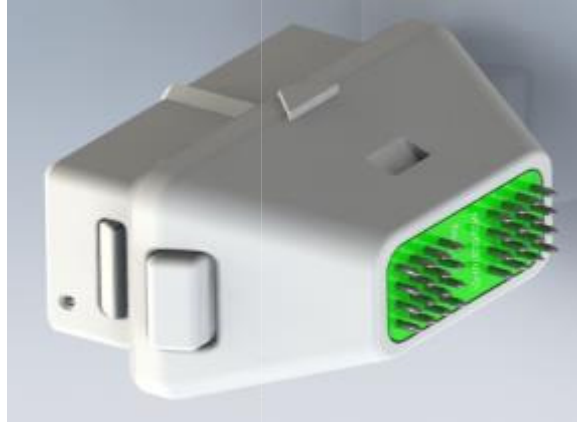
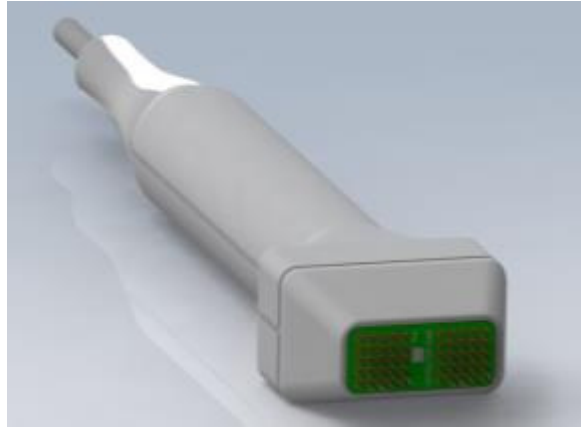
Surface EP System



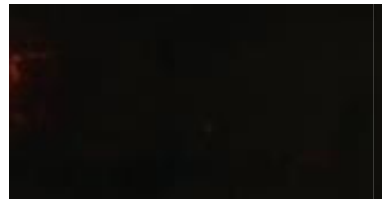
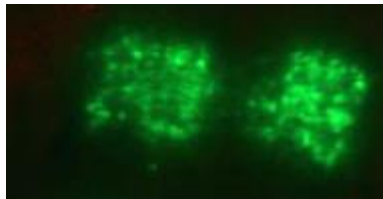
GFP expression on skin surface



Evolution of Surface EP to a Multi-head Device

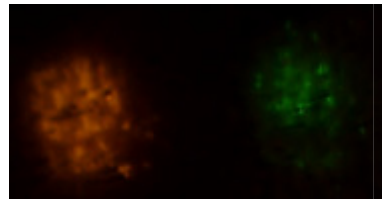
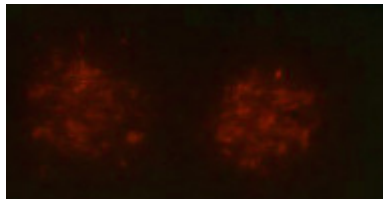


GFP only

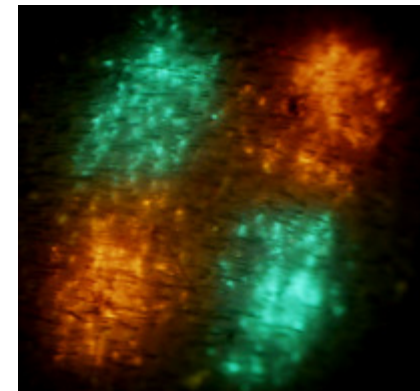


Injection only
(No EP)

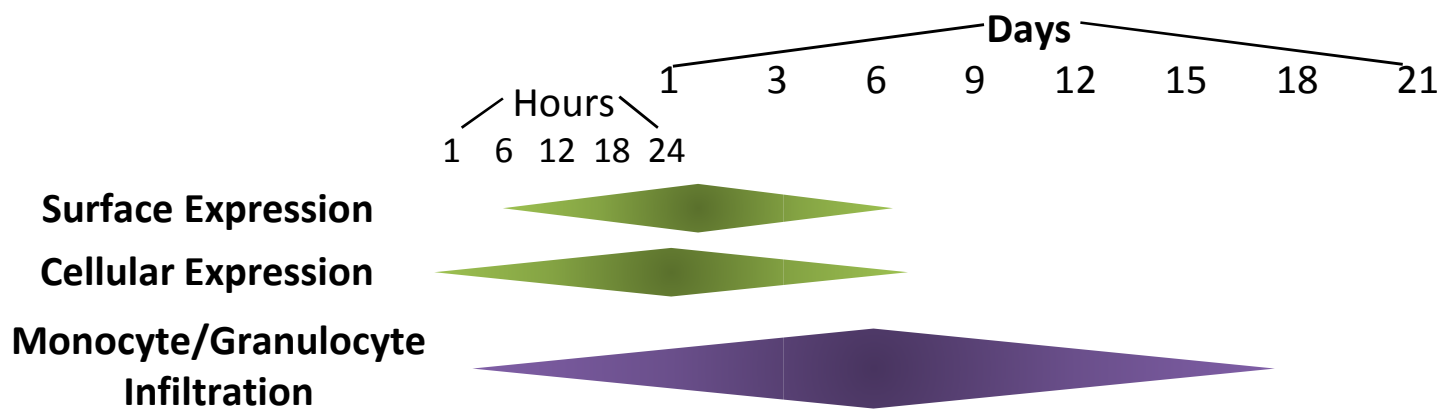
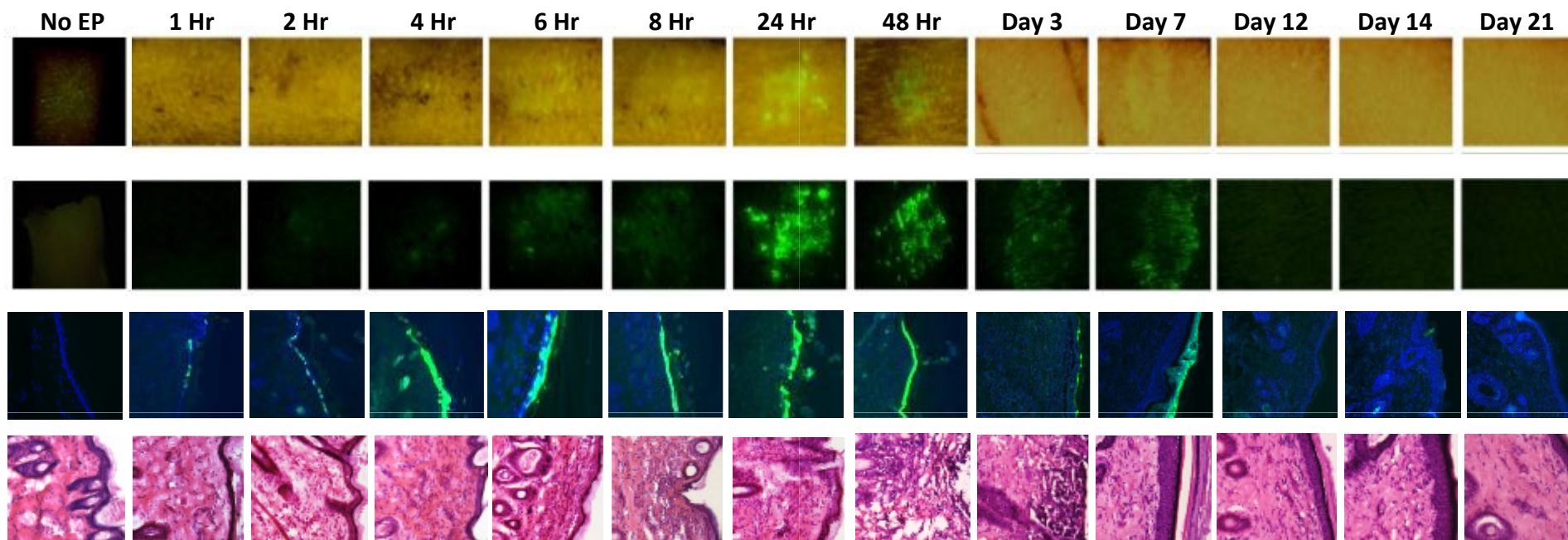
RFP only



RFP and GFP

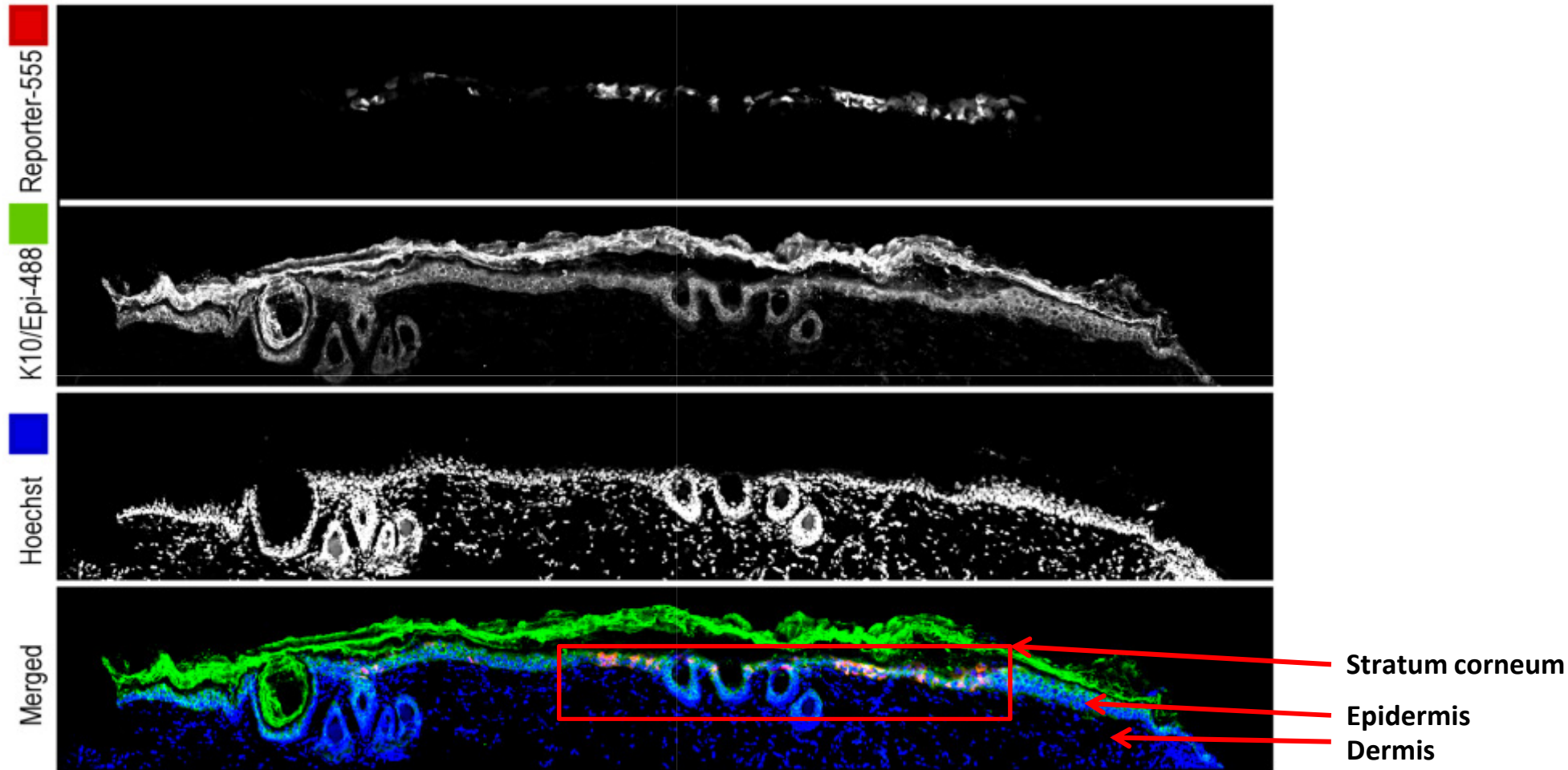


Expression Kinetics in Skin following SEP



Mendoza, Vaccines 2

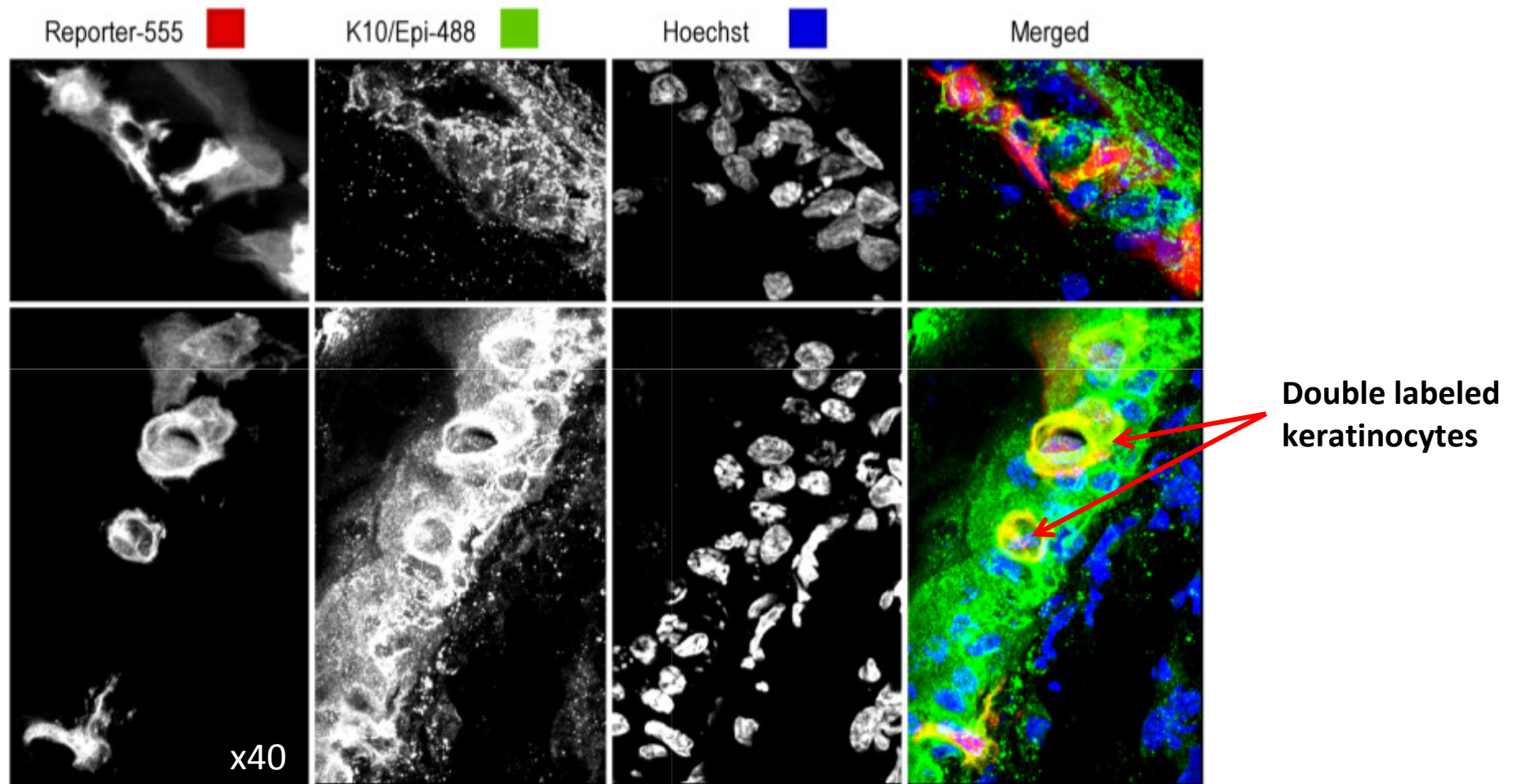
Directly Targeting the Epidermis with SEP



x10

Smith, Mol Ther Methods Clin Dev 2014

Directly Transfecting Keratinocytes with SEP



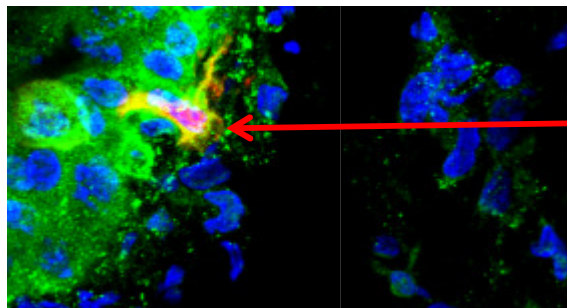
Mendoza et al, Hum Vacc Imm 2013

Directly Transfecting Dendritic Cells with SEP

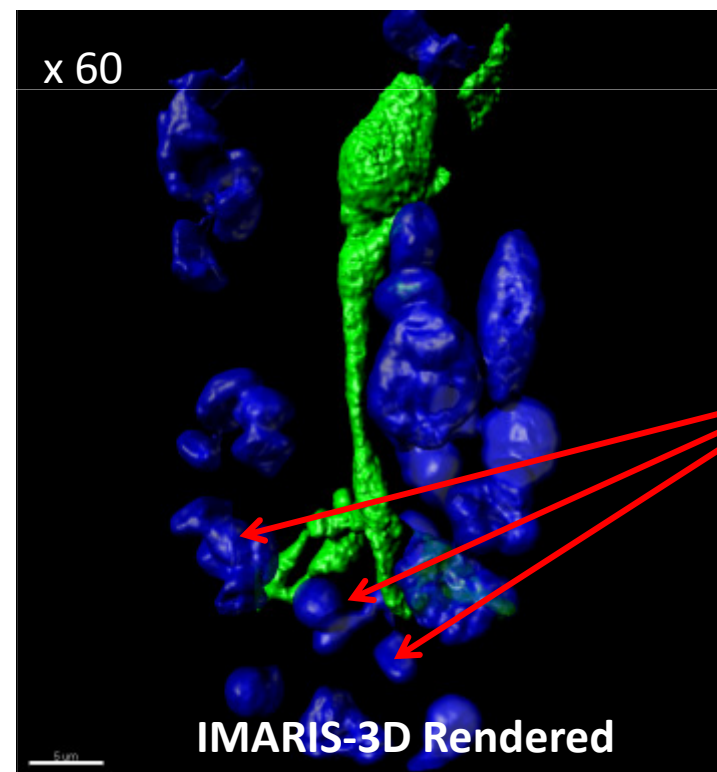
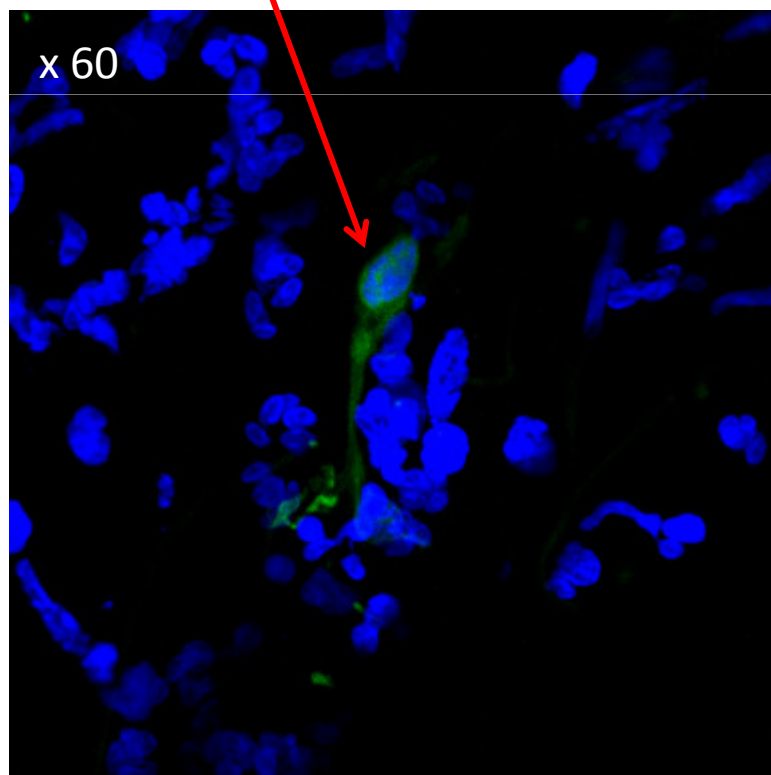
*Amante,
Hum Gene Ther Meth*

GFP positive
dendritic cell

x40



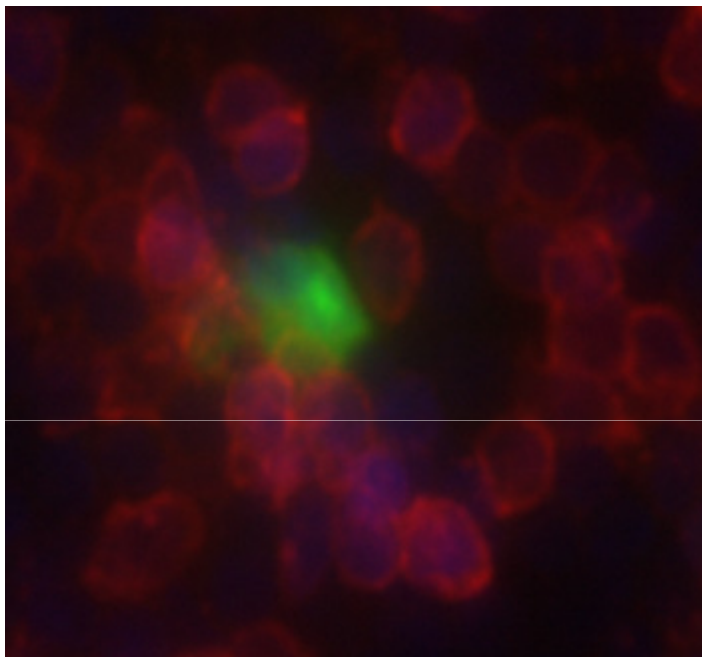
RFP positive
dendritic cell



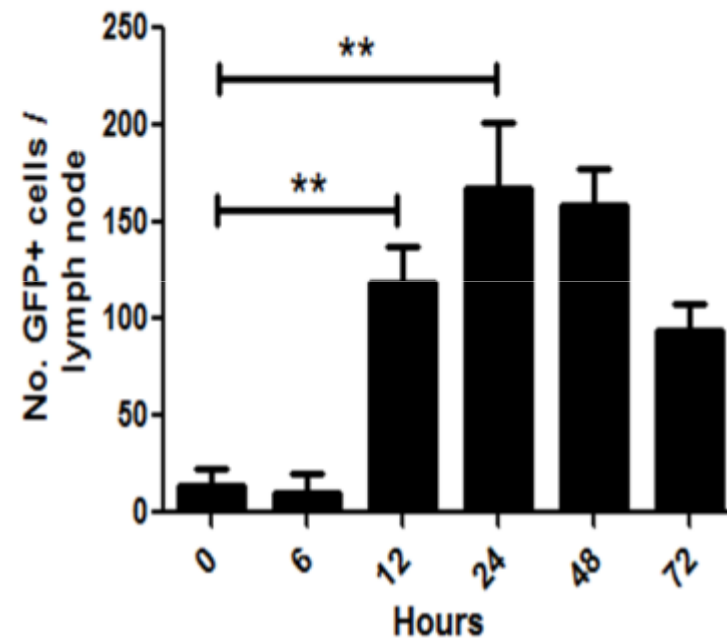
Lymphocytes interact
with transfected
dendritic cell

inov

Transfected Cell Migration into Draining Lymph Nodes



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



Minimally Invasive Dermal Electroporation – CELLECTRA®-3P

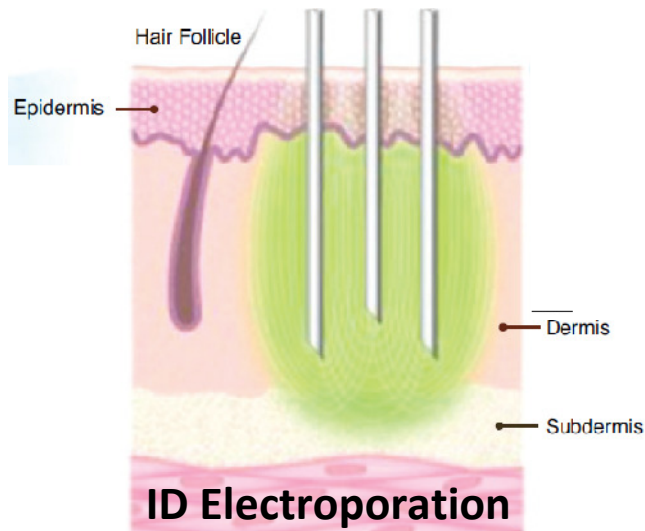
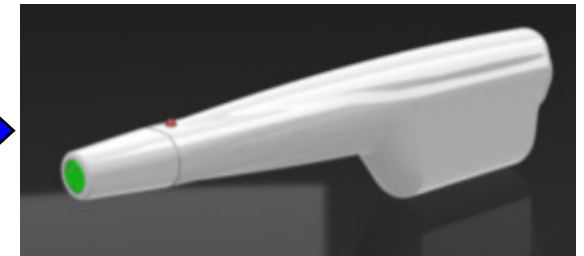
Tethered 3P System



Next Gen Tethered 3P System

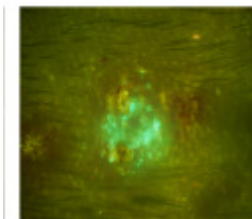
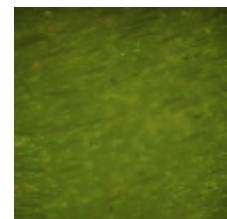


Portable Cordless 3P System

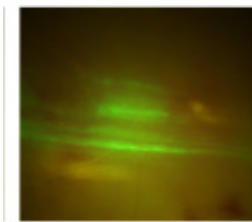
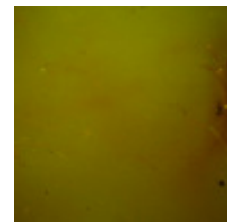


No EP

3P-EP

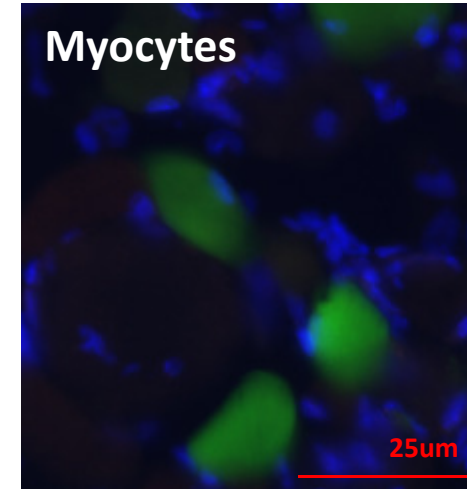
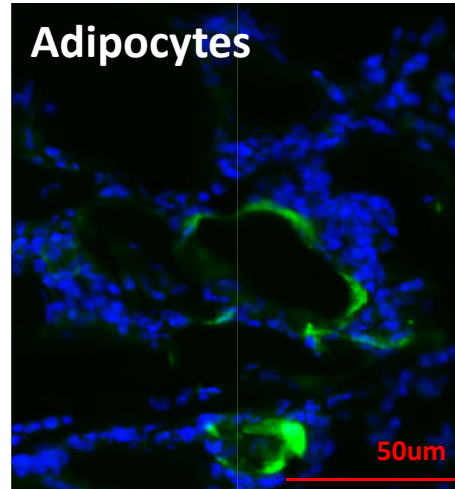
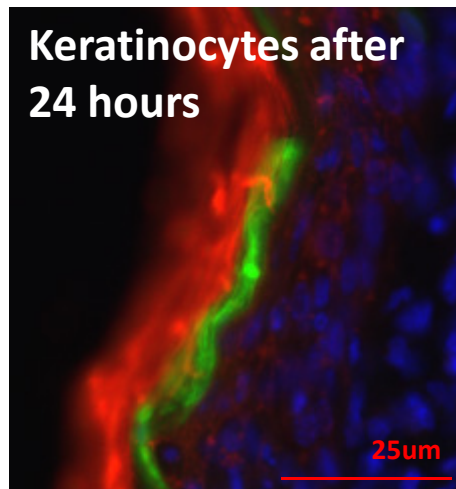
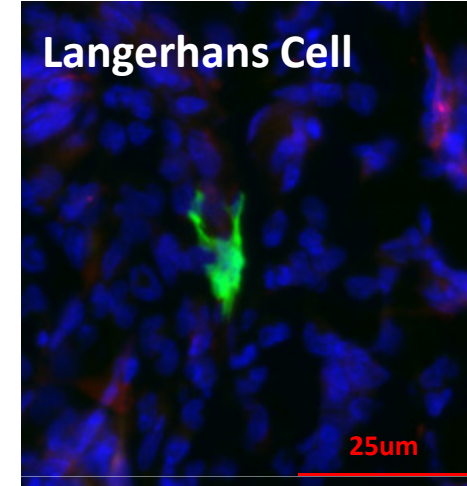
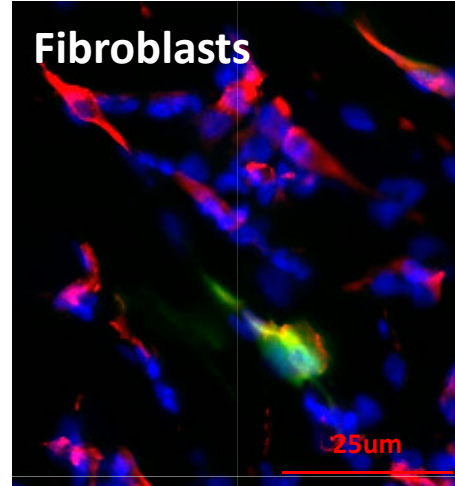


Skin surface




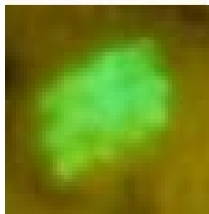
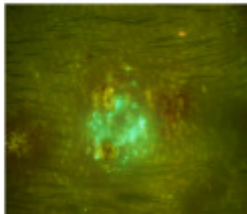


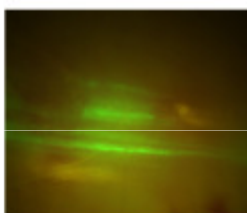

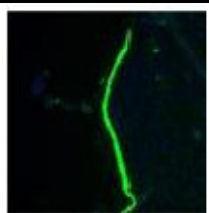
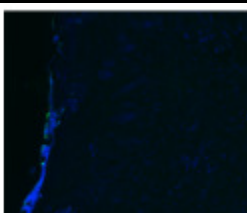

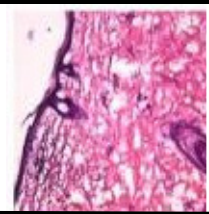
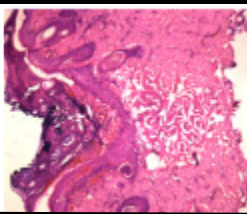
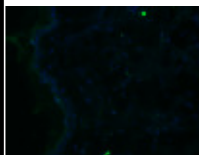
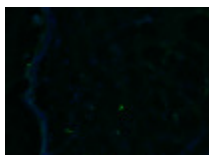
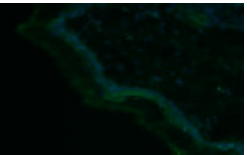




Skin underside

CELLECTRA[®]-3P targets a wide range of cell types in the skin



Same target tissue, different biological effect.....

	DNA Injection Only (No EP)	 SEP	 CELLECTRA-3P
Skin Surface			
Skin Underside			
Skin Section (DAPI stained)			
Skin Section (H&E stained)			
Skin Section (TUNEL stained)			

	DNA Injection Only (No EP)	 SEP	 CELLECTRA-3P
Epidermal Transfection	+	+++++	+++
Dermal/ Subdermal Transfection	-	-	+++++
Epidermis : Dermis Transfection Ratio	1:0	5:0	3:5
Necrosis	-	+	+++++
Apoptosis	-	++++	+++

Acknowledgments

inovia

INOVIO

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Amir Khan

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VGXI, Inc.

Dorothy Peterson

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W81XWH-11-C-0051:# 1031550133. Additional funding support from DTRA and NIH/NIAID

