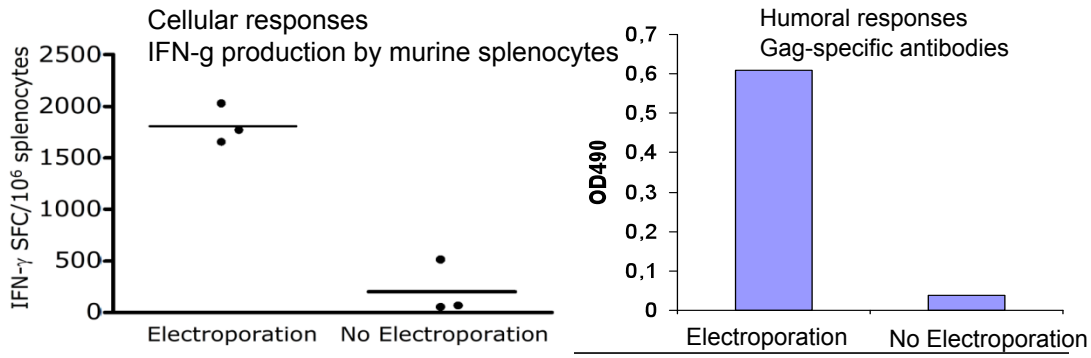
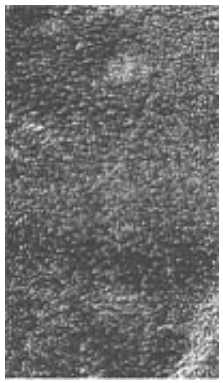
In vivo electroporation

Electroporation

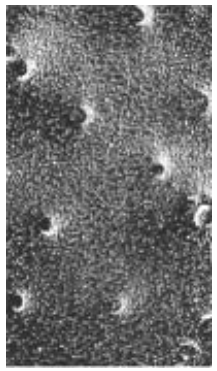
- Technique to enhance uptake of macromolecules into cells by application of electric pulses
- Widely used *in vitro* to facilitate transformation

- *In vivo* it enhances immune responses after DNA immunization, especially in small animals (mice)

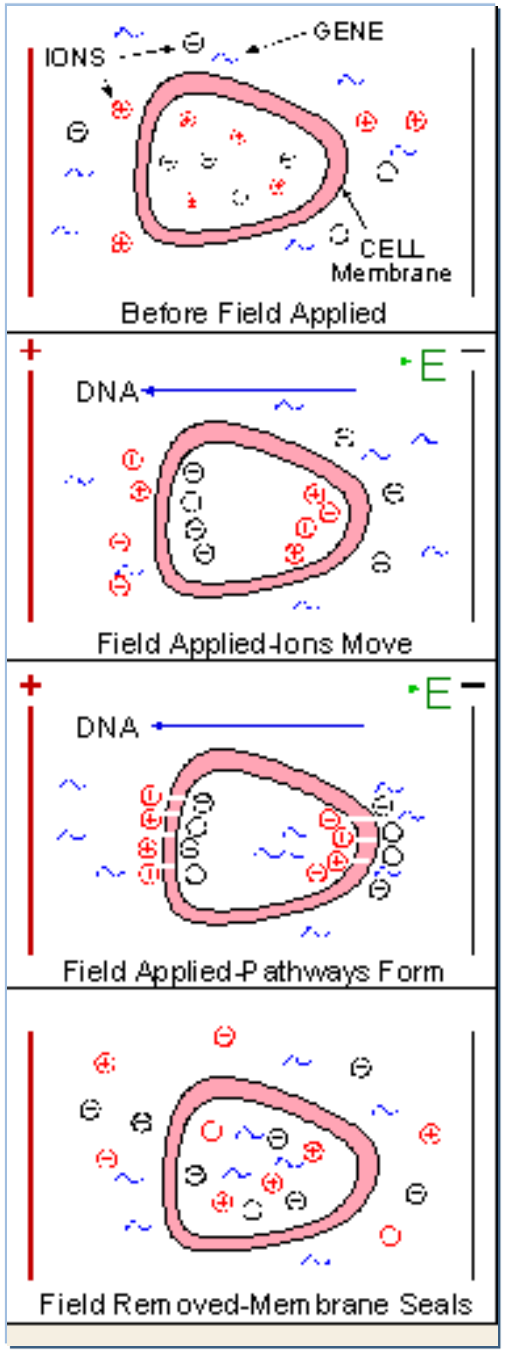




Electroporation



Illustrations from Inovio



Poor uptake of DNA

Cell membrane polarizes

Pores are formed
DNA is taken up

Pores are closed
in minutes

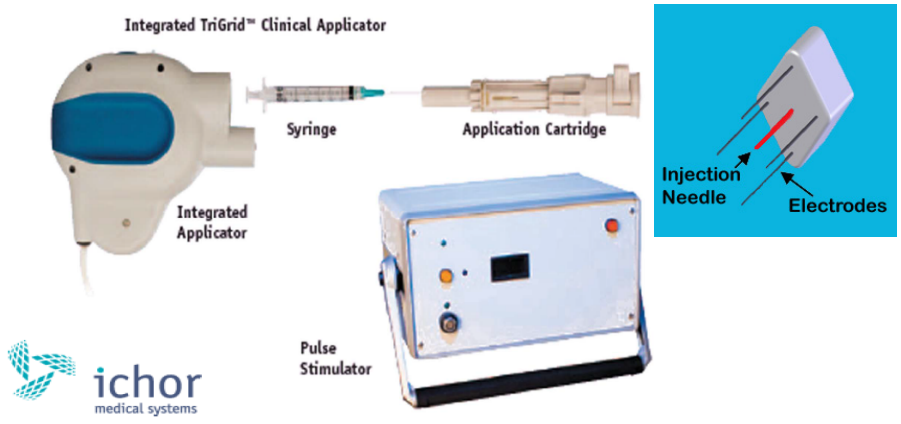
Clinical electroporation devices

Devices for plasmid DNA delivery indluding (a) **TriGrid** and (b) **CELLECTRA** with applicator (for intramuscular electroporation), (c) **DermaVax** (for transdermal electroporation) (1d) needless injection device

BioPharm International Supplements By: Rocky Cranenburgh
Oct 2, 2011 Volume 24, Issue 10, pp. s12-s18

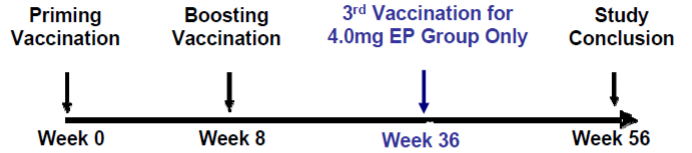
http://www.biopharminternational.com/biopharm/article/articleDetail.jsp?id=742599&sk=&date=&pageID=2

TriGrid™ In Vivo Electroporation Device



Intramuscular

ADVAX Electroporation Clinical Trial Design



Group/Route	Dose	Subjects
Placebo/EP	Saline	8
IM	4.0mg	8
Low EP	0.2mg	8
Mid EP	1.0mg	8
High EP	4.0mg	8

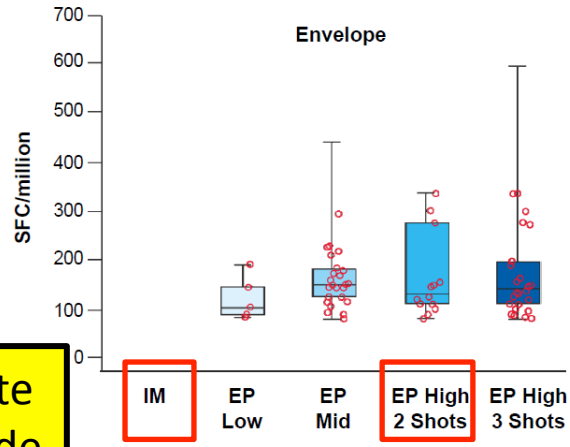
Healthy males and females aged 18-60 at low risk for HIV-1 infection

EP Improves IFNγ ELISpot Response Rate

Dose Group	Response Rate	
IM 4.0mg	0/8	0%
EP 0.2mg	3/8	37.5%
EP 1.0mg	7/8	87.5%
EP 4.0mg	6/8	75%
EP 4.0mg 3 shots	8/8	100%

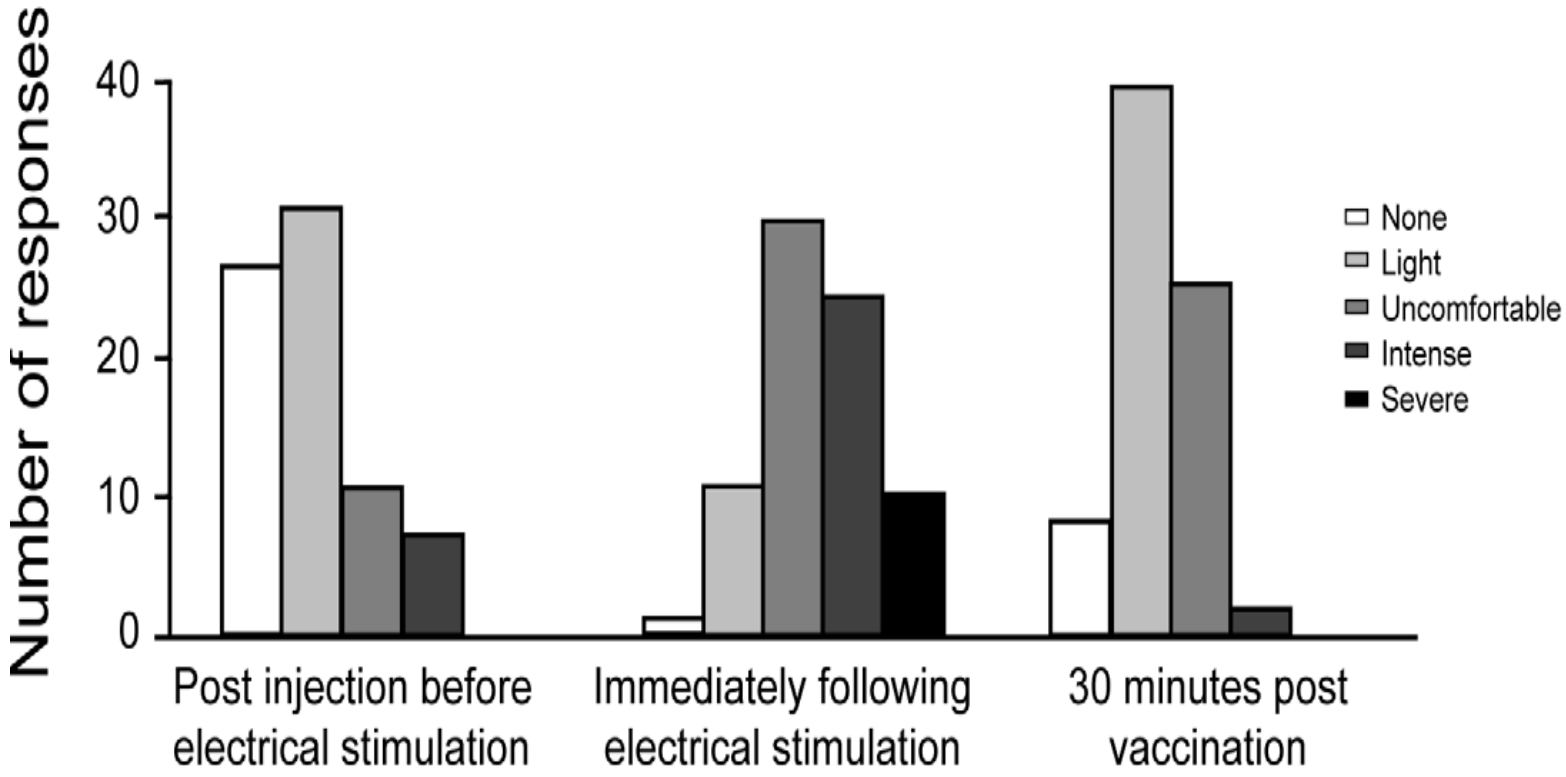
Higher response rate
Moderate magnitude

EP Boosts the Magnitude of the Dominant IFNγ ELISpot Response to Envelope



S. Vasan presentation 2009

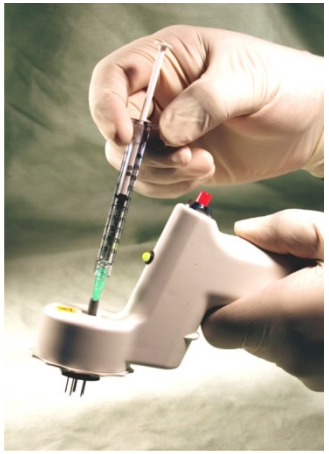
Discomfort

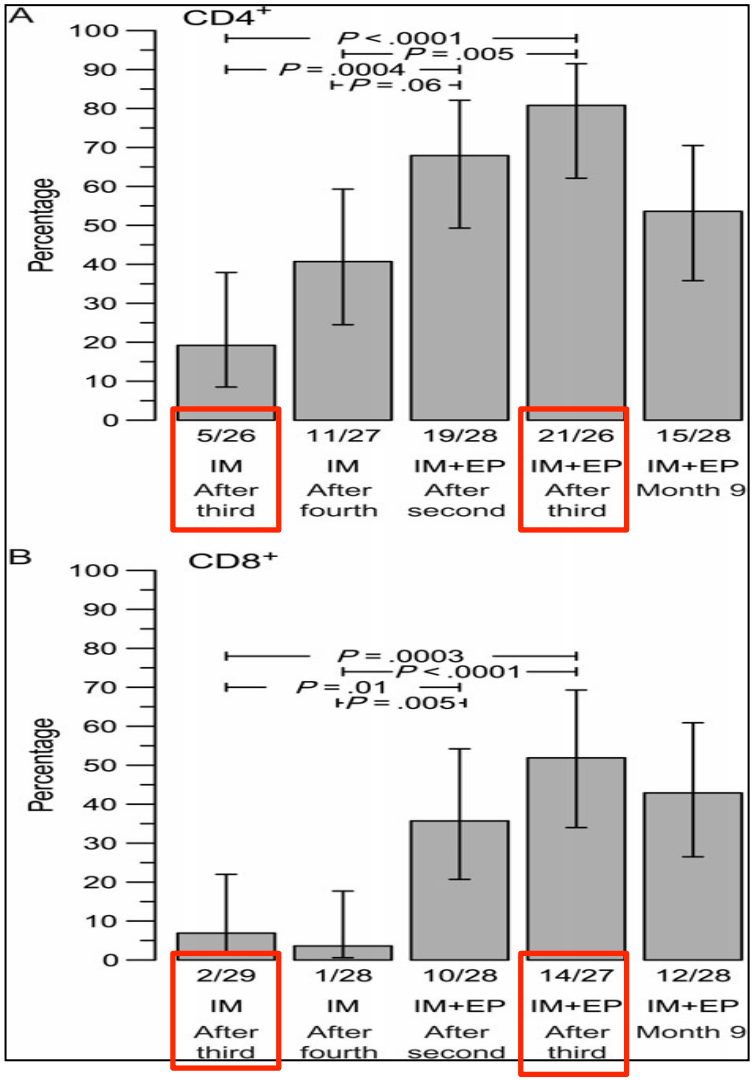

Number of responses
40
30
20
10
0
None
Light
Uncomfortable
Intense
Severe
Post injection before electrical stimulation
Immediately following electrical stimulation
30 minutes post vaccination

CELLECTRA Inovio

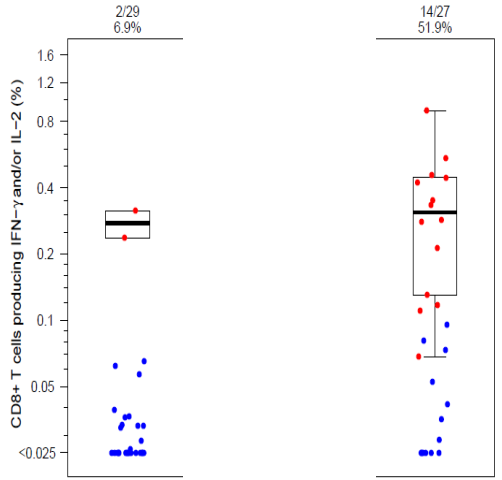
PennVax + IL-12 DNA
HVTN 70 without electroporation
HVTN 80 with electroporation
Immunization month 0, 1, **3**

Intramuscular





Higher response rate
Moderate magnitude

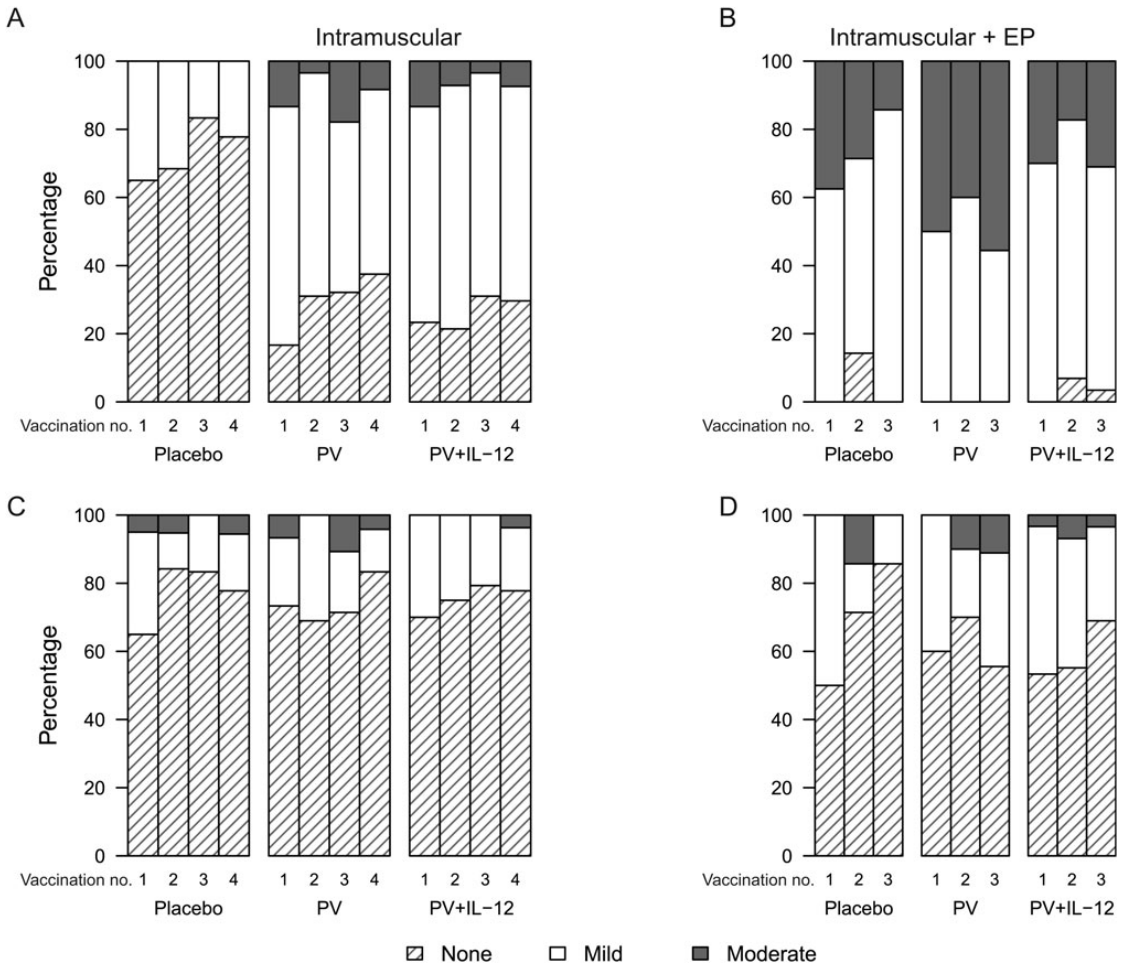


Kalams SA et al JID 2013:208

Discomfort

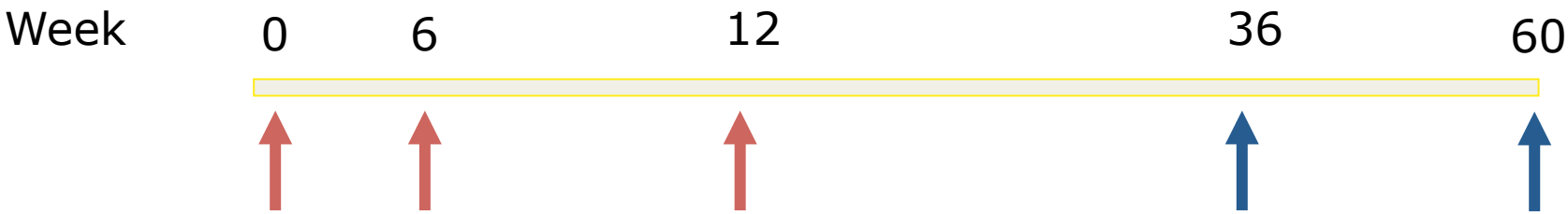
Local Pain

Systemic



HIVIS 07, n=27

phase 1 to TaMoVac II in Tanzania and Mozambique, n=186



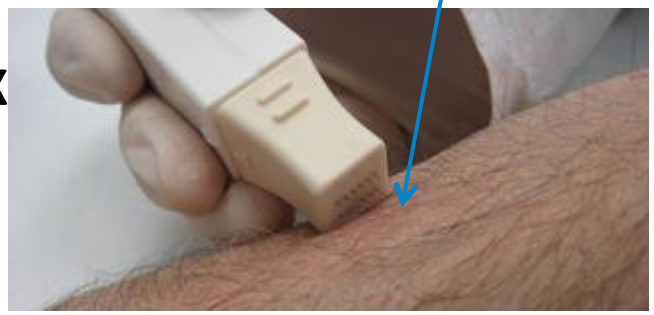
Plasmid HIV-DNA A, B, C

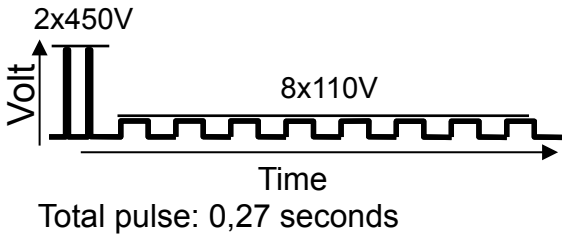
MVA-CMDR A, E

i.m.

Zetajet intradermal injection

Dermavax intradermal





Discomfort in HIVIS 07

78 visits with ZetaJet injections
51 visits with electroporation

ZetaJet i.d.

2* (0 – 5) during injection

0* (0 – 1) after 30 min

Electroporation i.d., DermaVax

3* (1 – 8) during injection

0* (0 – 1) after 30 min

Reactogenicity VAS (visual analog pain scale 0 - 10);

* median value, ()range

B Hejdeman personal information

TaMoVac II in Tanzania and Mozambique is ongoing with same schedule, n=198.

I.d. DNA immunization +/- electroporation completed.

I.d. electroporation well tolerated (personal communication)

RV262 Part A (Part B: Kenya, Tanzania and Uganda n=80, placebo controlled)

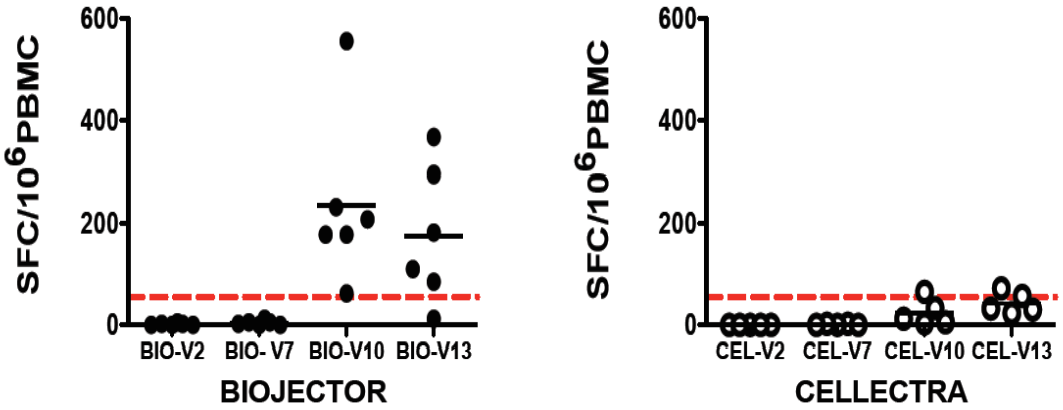
N=12; **intramuscular injections**

Prime DNA with **electroporation** (CELLECTRA) or **Biojector** 2000 month 0 and 1
Boost MVA-CMDR month 3 and 6

IFN-γ Elispot

PEPTIDE POOL	POST 1ST MVA			POST 2ND MVA			Cumulative		
	Bio-Ject	CELL-EP	Total	Bio-Ject	CELL-EP	Total	Bio-Ject	CELL-EP	Total
MVA-CMDR Gag	2/6	0/5	2/11	2/6	0/5	2/11	3/6	0/5	3/11
MVA-CMDR Env	6/6	1/5	7/11	5/6	2/5	7/11	6/6	2/5	8/11

MVA-CMDR ENV-PP (CM235)



J Courier 2011

Conclusion

- There are i.m. and i.d. electroporation devices in clinical studies
- There is enhancement of immune responses
- The electroporation ads to the immunization discomfort, but is tolerable

- Are the extra procedures and discomfort worth the increase in immune responses?