



HIV VACCINE  
TRIALS NETWORK

# Positive Responses with Adenovirus and Vaccinia (MVA) as vaccine vectors: The HVTN experience

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## MVA and Ad5 as Vectors in HVTN Trials

- HVTN 055 Therion MVA or MVA+FPV
- HVTN 065 GeoVax MVA or DNA+MVA
- HVTN 050 Merck Ad5 gag
- HVTN 502/503 Merck Ad5 gag/pol/nef
- HVTN 054 VRC Ad5 env/gag/pol
- HVTN 057 VRC DNA + Ad5 env/gag/pol
- HVTN 069 VRC DNA + Ad5 env/gag/pol
- HVTN 204 VRC DNA + Ad5 env/gag/pol



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## Three trials chosen

- All participants are vector naïve (vaccinia- or Ad5-naïve)
- Intracellular Cytokine Staining (ICS) T cell immunogenicity data has been collected in the same laboratory using the same peptides for *in vitro* stimulation (pools of global Potential T Cell Epitope (PTE) peptides)
- The study with the VRC Ad5 vaccine was chosen due to the above reasons, but the VRC vaccine product moving forward into clinical testing includes a DNA prime and then Ad5 boost



# Cautionary notes

- Vectors are not the only differences between these studies
  - Vector inserts encoding the HIV-1-proteins differ
  - Vaccination regimen differs: single dose vs. multi-dose vs. prime+boost
- PTE peptides used for immunogenicity assessment are not matched to the vaccine inserts
- These studies have not been designed to compare responses across trials, and therefore, the comparisons presented here cannot be used to determine superiority of one vaccine over another



# HVTN 054: Phase I Ad5 Dose Escalation

Vaccine: 1 dose of Ad5 (Vaccine Research Center)  
encoding Gag and Pol (clade B), Env (clades A,B,C)

Study Participants: n= 48, low Ad5 neutralizing Ab  
titers

Study Design:

Group 1: 20/4:  $10^{10}$  PU vaccine/placebo

Group 2: 20/4:  $10^{11}$  PU vaccine/placebo

Note that data from groups 1 and 2 are combined  
for this presentation.



# HVTN 055: Phase I FPV/MVA Dose Escalation

## Vaccines:

- rMVA-HIV env/gag + rMVA-HIV tat/rev/nef-RT
  - Dose escalation  $10^7$ ,  $10^8$ , and  $10^9$  pfu
- rFPV-HIV env/gag + rFPV-HIV tat/rev/nef-RT
  - Dose =  $10^9$  pfu

Alone or in combination in vaccinia-naïve HIV-uninfected participants

Vaccine provider: Therion Biologics Corp.



# HVTN 055: Five Treatment Groups

	MVA dose	Vaccination Schedule (Months)					
		0	1	3	5	7	
1*	NA	FPV	FPV	FPV	FPV	FPV	N=22
2	$10^7$	MVA	MVA	FPV	FPV	FPV	
3	$10^8$	MVA	MVA	FPV	FPV	FPV	
4	$10^9$	MVA	MVA	FPV	FPV	FPV	N=20
5	$10^9$	MVA	MVA	MVA	MVA	MVA	N=23

\*10 Vaccine recipients and 2 controls in each group for Part A.  
Part B adds an additional 25 vaccine recipients to groups 1, 4 and 5.



# HVTN 065: Phase I DNA/MVA Dose Escalation

## Vaccines:

- DNA encoding Gag, PR, RT, Env, Tat, Rev, Vpu
  - Dose escalation 0.3 and 3mg
- rMVA, gag, pol, env
  - Dose escalation  $10^7$  and  $10^8$  TCID<sub>50</sub>

Vaccinia-naïve HIV-uninfected participants

Vaccine provider: GeoVax, Inc.



# HVTN 065: Four Treatment Groups

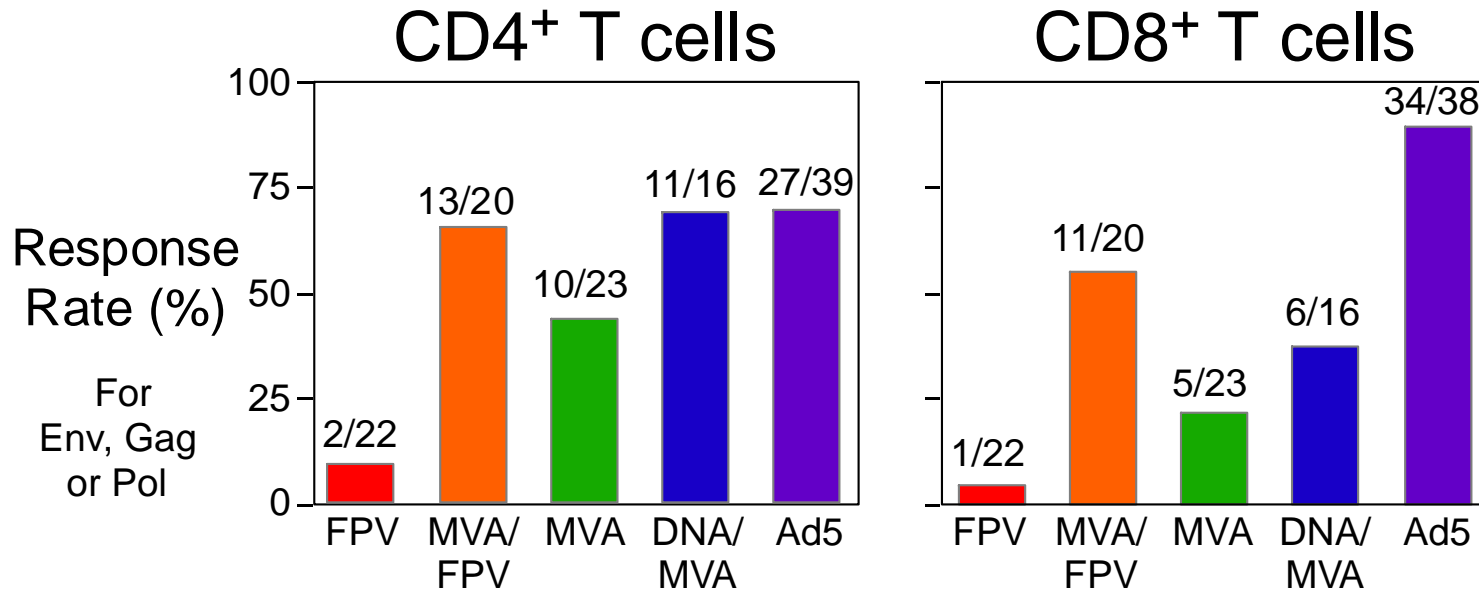
		Vaccination Schedule (Months)					
		Dose		Prime		Boost	
N*	N*	DNA	MVA	0	2	4	6
1	10	0.3	$10^7$	DNA	DNA	MVA	MVA
2	30	3	$10^8$	DNA	DNA	MVA	MVA
3	30	3	$10^8$	DNA	MVA	-	MVA
4	30	-	$10^8$	MVA	MVA	-	MVA

N=16

\*6 controls in each group



# Vaccination with MVA or Ad5 induces both CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses



### Vaccination details:

FPV\*  
0,1,3,5 mo  
10<sup>9</sup>

MVA  
0,1 mo 10<sup>9</sup>  
FPV\* boost  
3,5 mo 10<sup>9</sup>

MVA\*  
0,1,3,5 mo  
10<sup>9</sup>

DNA  
0,2 mo 3mg  
MVA boost  
4,6 mo 10<sup>8</sup>

Ad5  
0 mo  
10<sup>10</sup> group 1  
10<sup>11</sup> group 2  
groups  
combined

HVTN 055

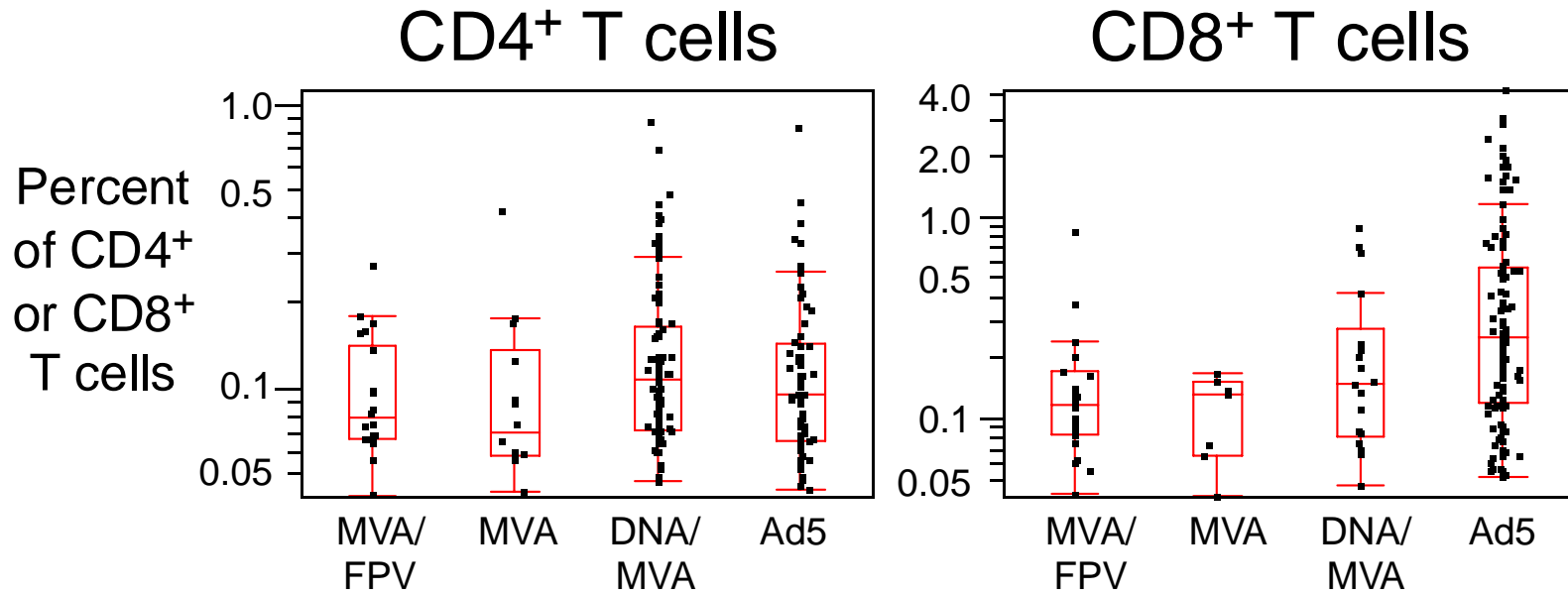
HVTN 065

HVTN 054

\*Only vaccinations given before immunogenicity testing are listed.



# Vaccination with MVA or Ad5 induces both CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses



### Vaccination details:

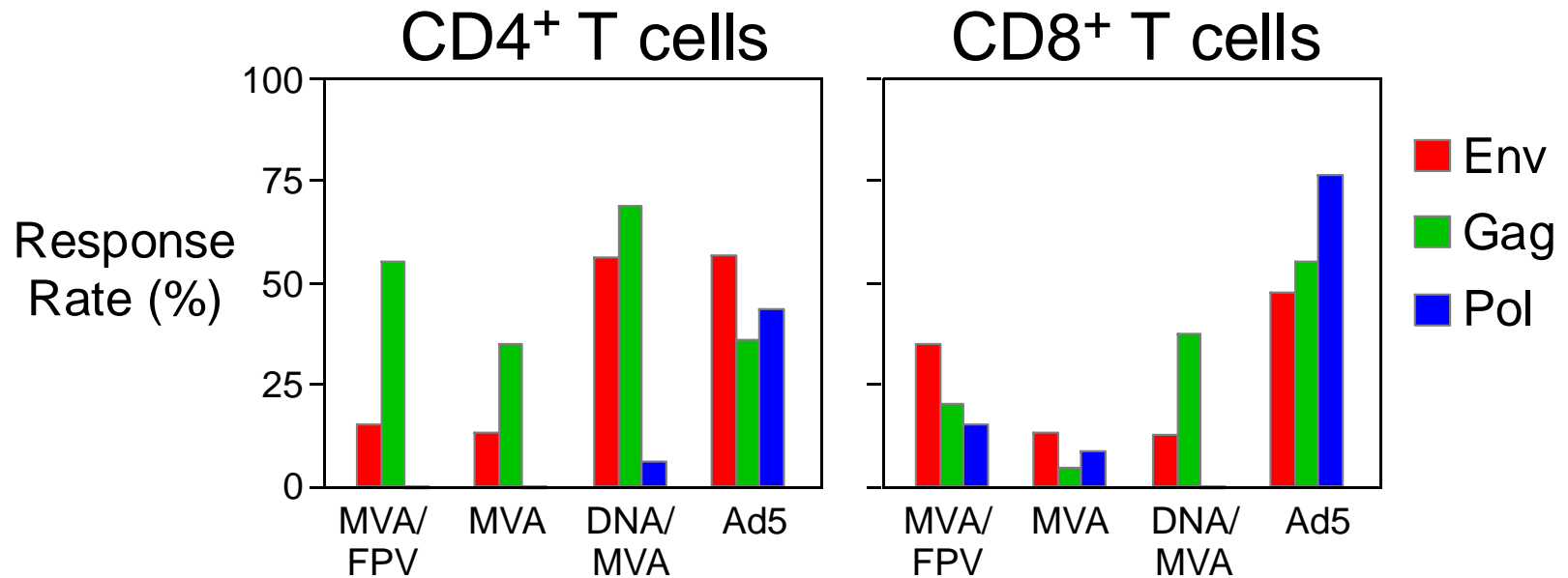
MVA	MVA*	DNA	Ad5
0,1 mo 10 <sup>9</sup>	0,1,3,5 mo	0,2 mo 3mg	0 mo
	10 <sup>9</sup>		10 <sup>10</sup> group 1
FPV* boost		MVA boost	10 <sup>11</sup> group 2
3,5 mo 10 <sup>9</sup>		4,6 mo 10 <sup>8</sup>	groups
			combined
HVTN 055		HVTN 065	HVTN 054

\*Only vaccinations given before immunogenicity testing are listed.

Positive responses for any peptide pool are shown.



# Responses to Env, Gag and Pol induced by vaccination with MVA or Ad5



MVA  
0,1 mo 10<sup>9</sup>

MVA\*  
0,1,3,5 mo 10<sup>9</sup>

FPV\* boost  
3,5 mo 10<sup>9</sup>

HVTN 055  
Env/Gag  
Tat/Rev/Nef-RT

DNA  
0,2 mo 3mg

MVA boost  
4,6 mo 10<sup>8</sup>

HVTN 065  
Env/Gag/PR/RT/  
Tat/Rev/Vpu

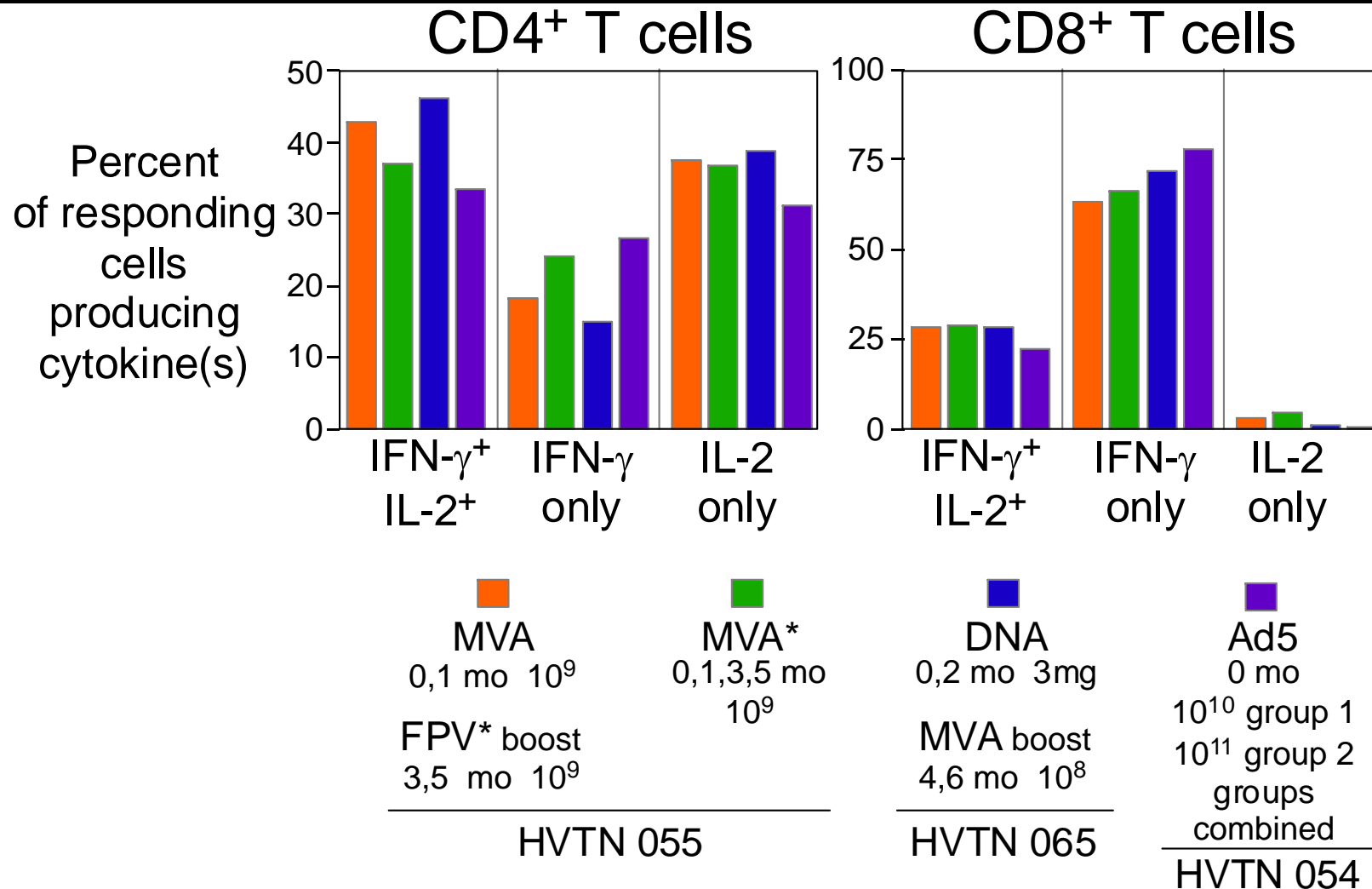
Ad5  
0 mo  
10<sup>10</sup> group 1  
10<sup>11</sup> group 2  
groups  
combined

HVTN 054  
EnvA/EnvB/EnvC  
Gag/Pol

\*Only vaccinations given before immunogenicity testing are listed.



# Similar cytokine distribution of cells induced by vaccination with MVA or Ad5



\*Only vaccinations given before immunogenicity testing are listed.

Positive responses for any peptide pool are included.



# Conclusions

- Vaccines including Ad5 or MVA as vectors induce CD4<sup>+</sup> and CD8<sup>+</sup> T cells producing IFN- $\gamma$  and/or IL-2
- The magnitudes of CD4 responses are similar; CD8 responses induced by a single dose of Ad5 have higher magnitudes (as high as 4%)
- Differences in responses to different HIV-1 proteins may be due to differences in vector insert design
- These promising positive results with MVA and DNA/MVA vaccines show that these vectors have good potential to elicit immune responses and that earlier less promising results with other MVA vectors were likely due to inferior vaccine insert design



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