

Improved modes of delivering a safe and highly immunogenic multigene, multiclade HIV-1 DNA plasmid vaccine boosted with HIV-1 MVA

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HIV immunogenicity study

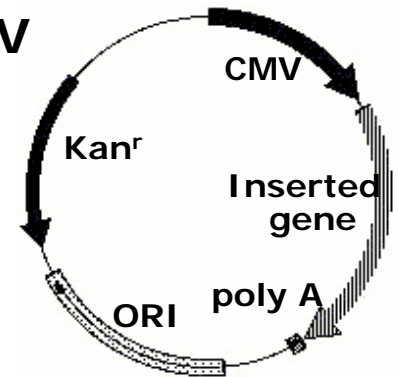
HIVIS

Objectives

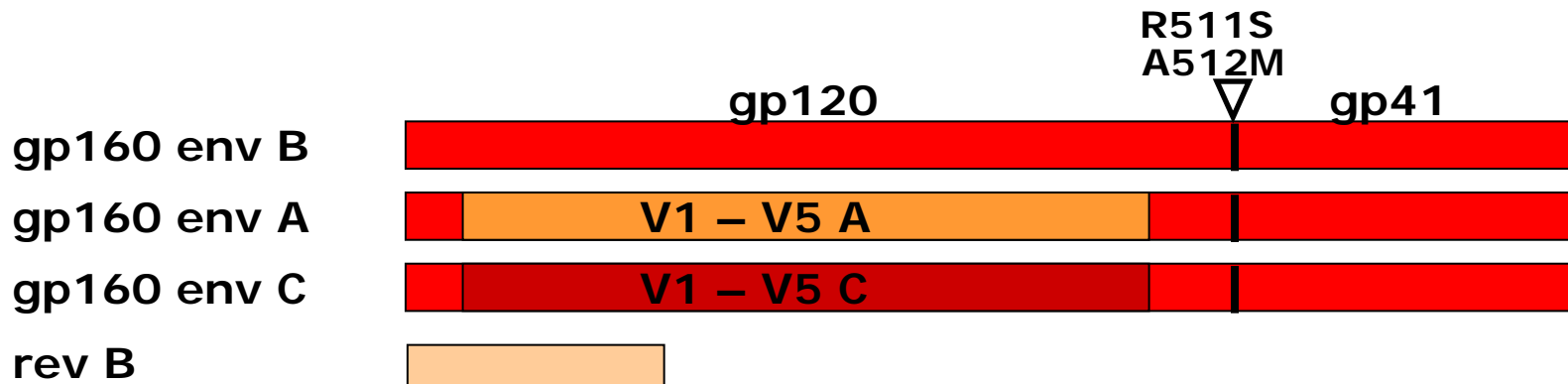
- To optimise the priming with HIV-1 DNA plasmids prior to HIV-1 Modified Vaccinia Ankara (MVA) boost
- To develop expertise and capability to study HIV-1 vaccines in Tanzania

7 plasmid HIV-1 DNA multigene/multiclade vaccine

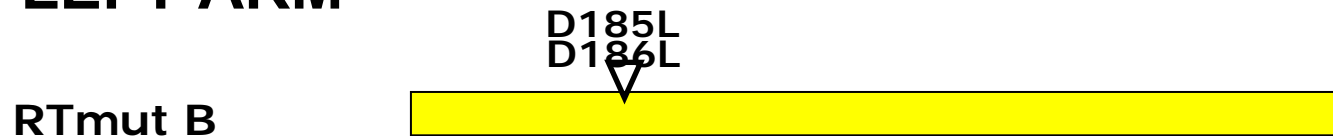
pKCMV



Developed by B Wahren, Dept virology, SMI, Karolinska Inst
Produced by Vecura



LEFT ARM



RIGHT ARM

DNA prime

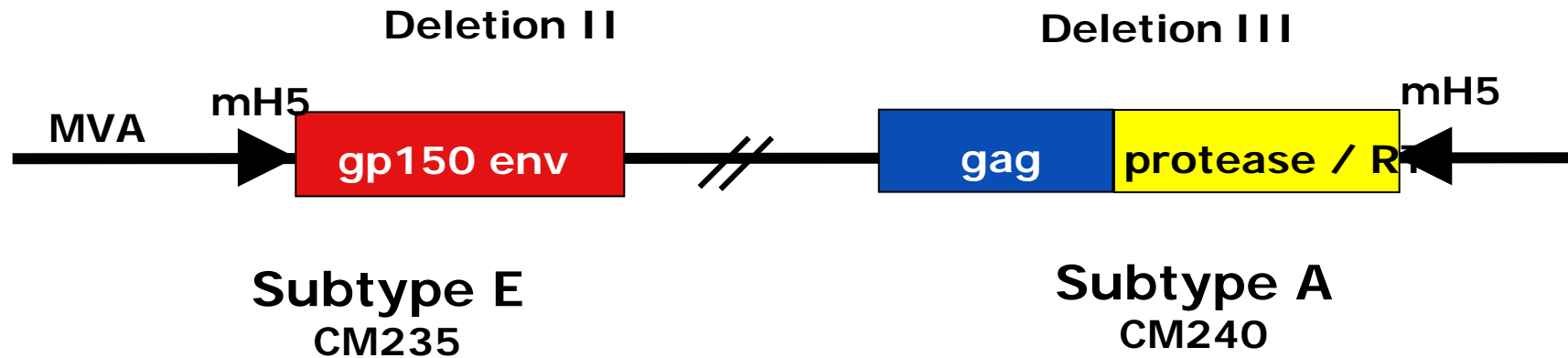
Three immunizations in the deltoid muscle or the skin above with Biojector

Group	Volunteers	Dose	Administration	Adjuvant
A	10	1 mg	Id	-
B	10	3.8 mg	Im	-
C	10	1 mg	Id	GMCSF* Left arm
D	10	2 mg	Im	GMCSF* Left arm

*Leukine® (sargramostim) Berlex, 0.5 ml - 150ug

MVA* / CMDR boost

Developed by P Earl and B Moss, Laboratory of Viral Diseases, NIAID, NIH
Produced by Walter Reed Army Institute of Research

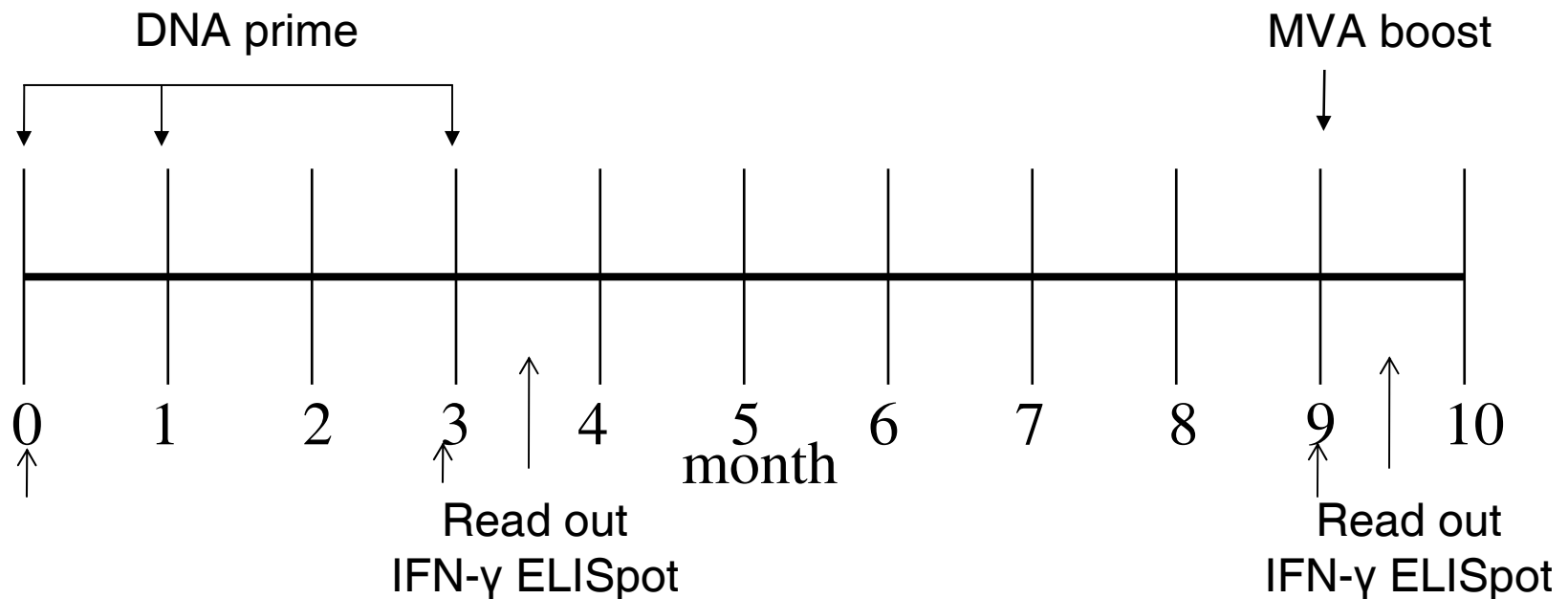


Volunteers were block re-randomized to

10^7 pfu id or
 10^8 pfu im

*Modified Vaccinia Ankara

HIVIS-Stockholm



Peptide pools	Gene	Length, overlap, homology
Gag I, II	P17(B), p 24(A)	15 mer, 10 aa, DNA
Env I, II, III	gp 120(A), gp 120(A/B), gp 41(B)	15mer, 10 aa, DNA
Gag WRAIR	p6, p7, p17, p24 (A)	15mer, 11 aa, MVA

Criteria for positive ELISPOT: > 55 spots/10⁶ cells and >4 x background (mean spots in medium-only wells)

Adverse Events

HIV-1 DNA prime

The vaccine alone was well tolerated.

Mild fatigue, 'influenza' like symptoms or headaches were common in the GMCSF arms

Two volunteers received only one DNA injection; one defaulted, one had an adverse event.

Two volunteers had grade 3 adverse events in im/GMCSF groups with symptoms typical of GMCSF (fatigue and fever)

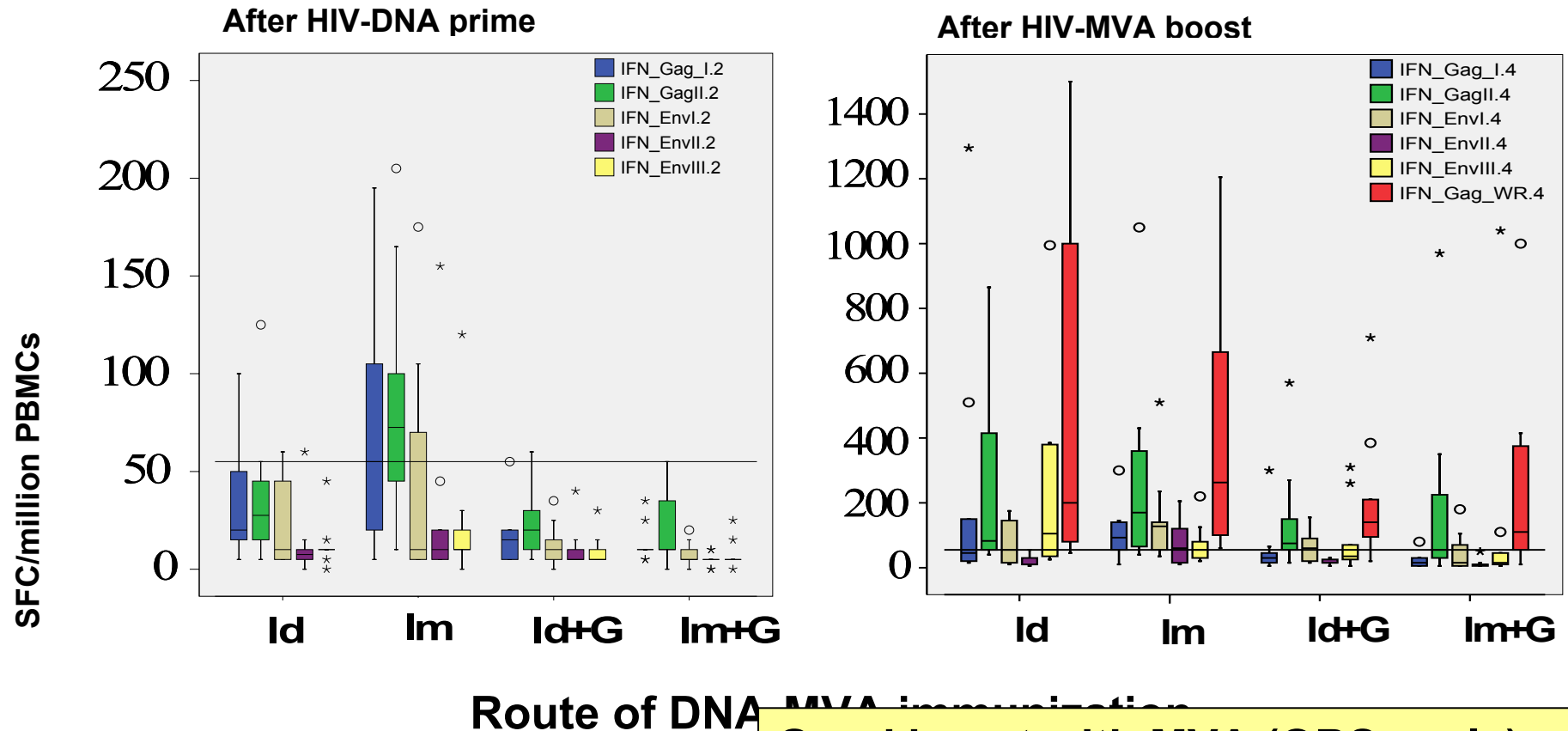
HIV-1 MVA boost

Very well tolerated

No laboratory adverse events

No diagnostic HIV seroconversion

IFN- γ ELISPOT in response to peptide pools



11/ 38 reacted after the prime

Im better than Id

Good boost with MVA (OBS scale)

Prime with Id same as Im after boost

No benefit of GMCSF

IFN- γ ELISPOT reactivity to peptide pools
2 weeks after HIV-1 MVA boost, n= 37
immunized 3 times with HIV- 1 DNA and once with HIV-1 MVA

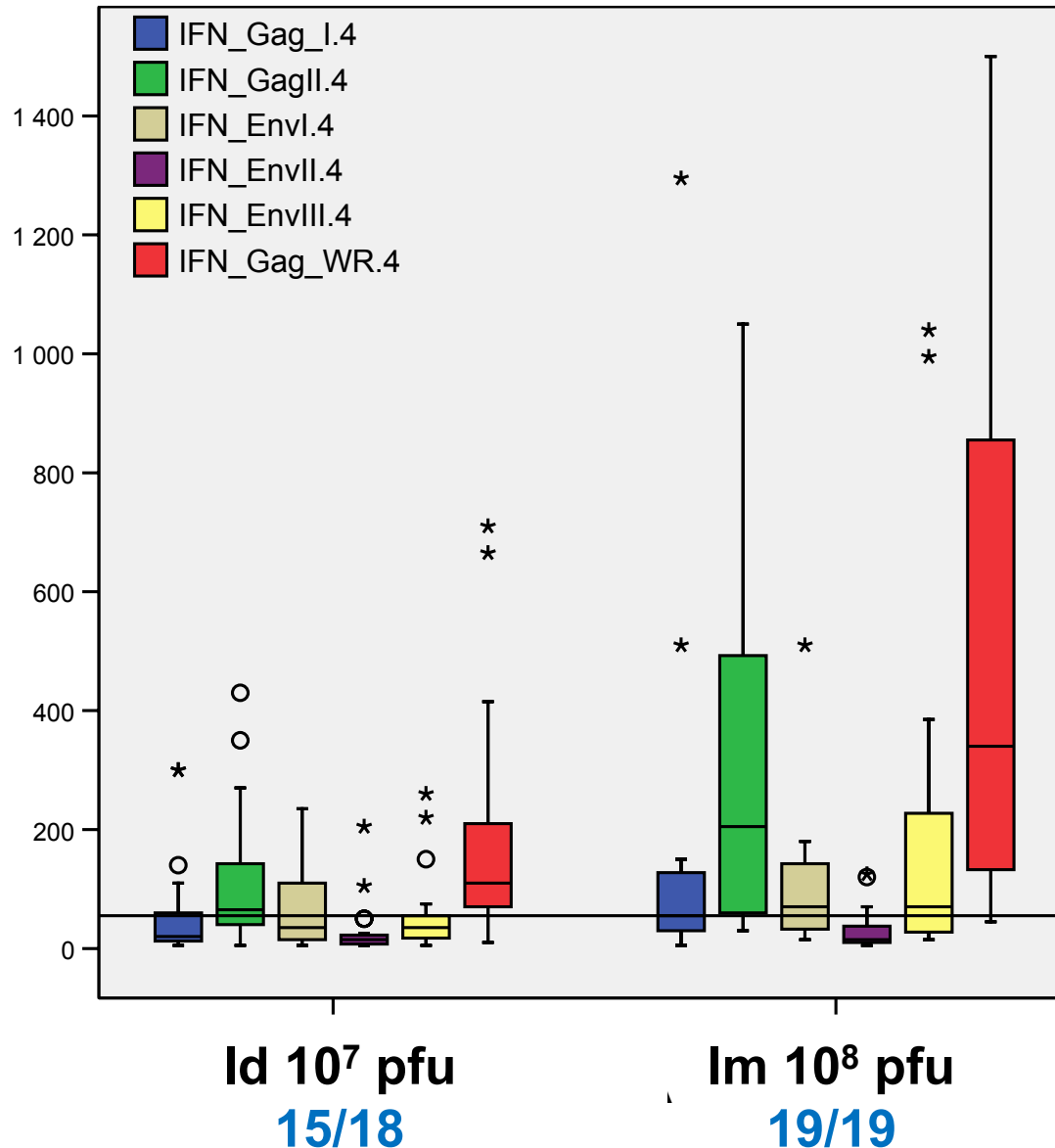
Gag or Env 34 (92%)

Any Gag 32 (86%)

Any Env 24 (65%)

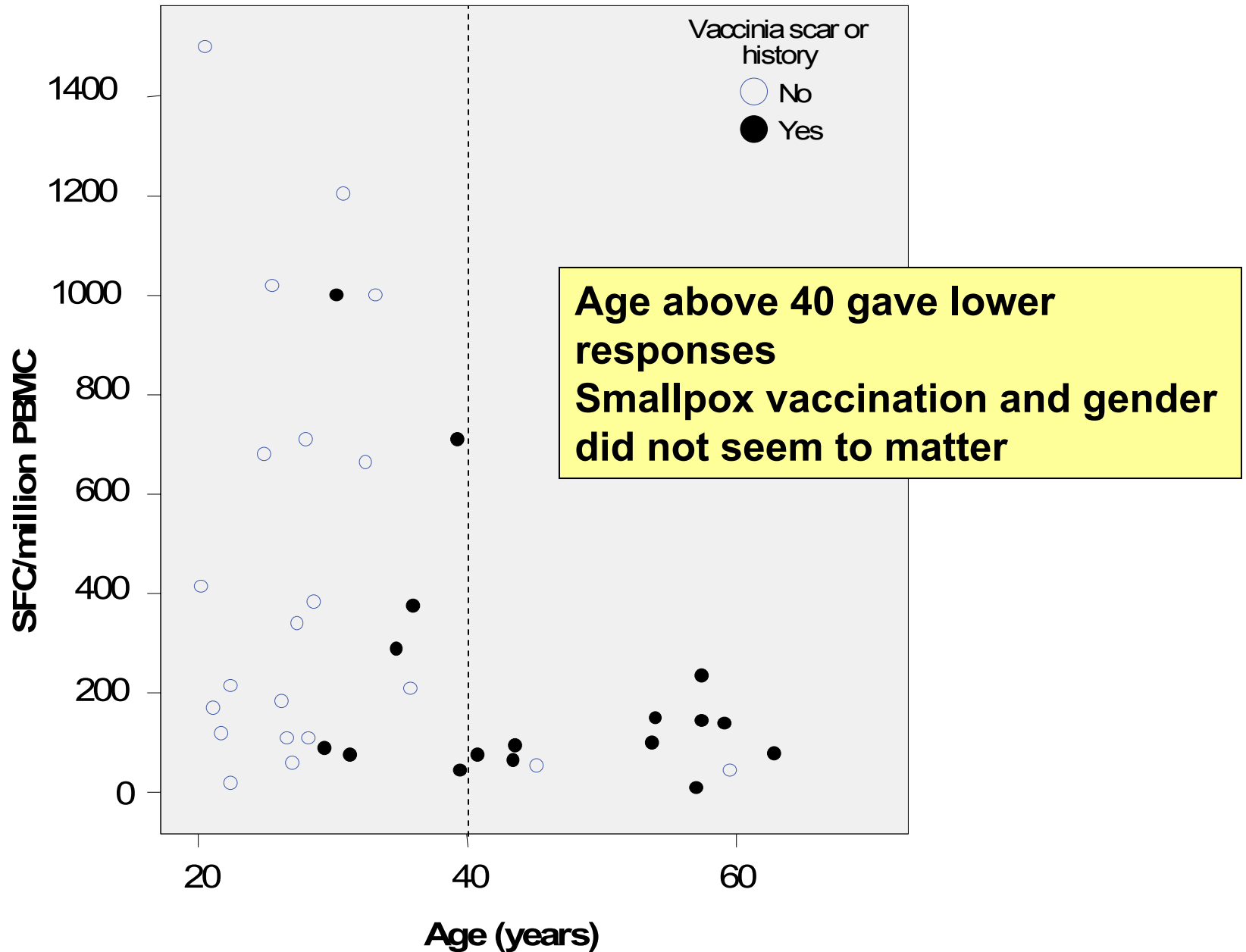
Gag and Env 22 (59%)

IFN- γ ELIspot by MVA mode of immunization



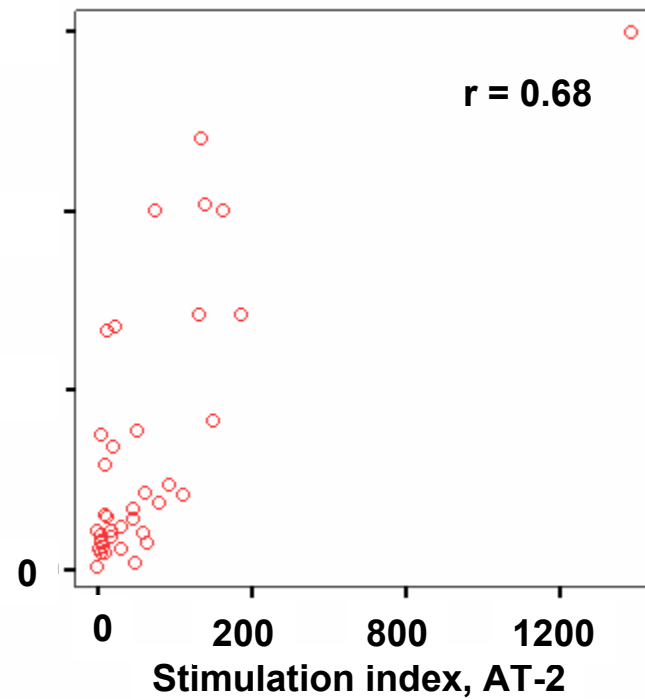
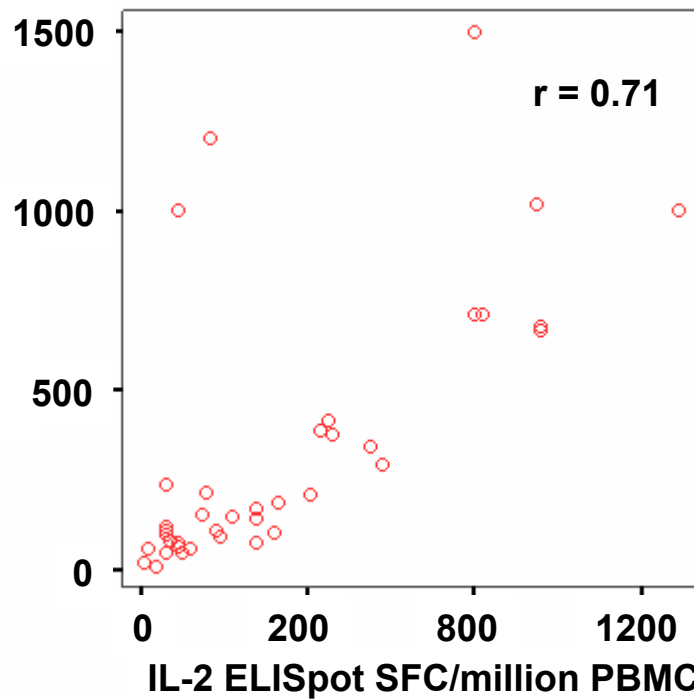
A higher dose of MVA im gave a better boost than a lower dose Id

IFN- γ ELISpot gag by prior smallpox vaccination



HIV specific responses in IFN- γ vs IL-2 ELISpot and lymphoproliferation

IFN- γ ELISpot
SFC/million PBMC



IFN-gamma ELISpot results were supported by
IL2-ELISpot and lymphoproliferation

Summary of HIV-1 specific immune responses after immunization with HIV-1 DNA and MVA

IFN- γ ELISpot	34/37 (92%)
IL-2 ELISpot	25/37 (68%)
Lymphoproliferation	35/38 (92%)

ELISpot and/or lymphoproliferation
37/38 (97%)

Non-responder: Male Age 57 years DNA I.m. + GMCSF MVA I.d. Smallpox vaccinated.

Conclusion

This HIV-1 DNA prime/MVA boost approach is:

Safe

Highly immunogenic with the best responses in:

- vaccinees under 40 years of age, receiving
- DNA Id (low dose) or Im (high dose) and
- MVA Im

(Despite common exposure to smallpox vaccination)

Warrants further – expanded - studies

HIVIS Study group

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