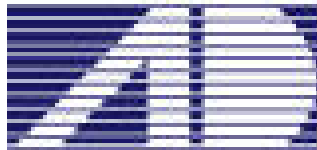


In Vivo Electroporation Enhances the Immunogenicity of ADVAX, a DNA-based HIV-1 Vaccine Candidate, in Healthy Volunteers



Aaron Diamond AIDS Research Center



ichor
medical systems

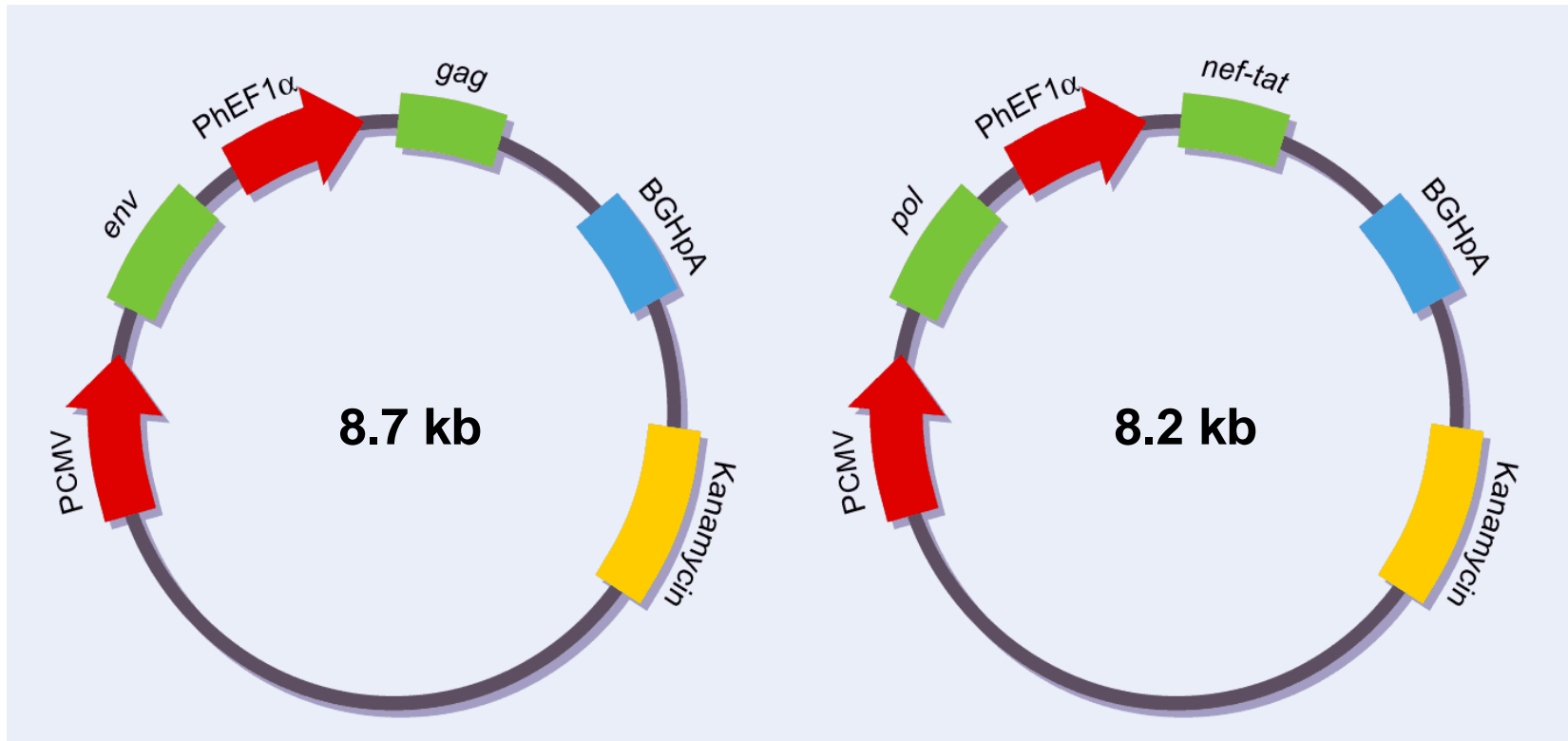


iavi International AIDS
Vaccine Initiative



the
collaboration
for AIDS vaccine discovery

ADVAX Clade B'/C DNA Vaccine



In Vivo Electroporation (EP) Enhances Humoral and Cellular Immunogenicity

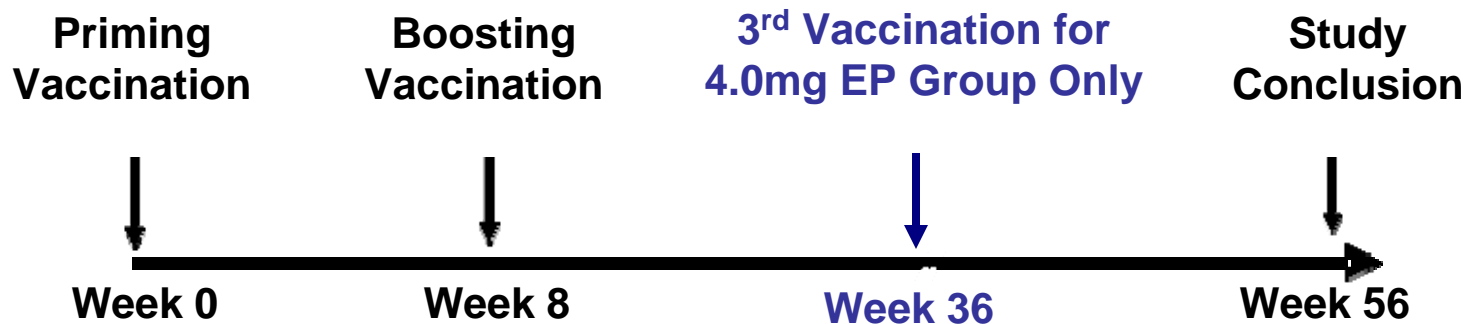
EP = *in vivo* propagation of electrical fields to enhance the intracellular uptake of DNA, resulting in:

- Higher transfection efficiency
- Higher antigen expression
- Enhanced cellular and humoral immunogenicity
- Recruitment of immune cells to injection sites
- Dose sparing of vaccine

EP enhances humoral responses to DNA vaccines by 1–2 logs, confirmed reproducibly with multiple antigens in mice and rabbits

Cellular responses increase by 2-4 fold

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

TriGrid™ In Vivo Electroporation Device

Integrated TriGrid™ Clinical Applicator



Integrated
Applicator



Syringe



Application Cartridge



Pulse
Stimulator



ichor
medical systems

TriGrid™ In Vivo Electroporation Procedure



Clinical Trial Progress and Safety To Date

Trial began October 2007

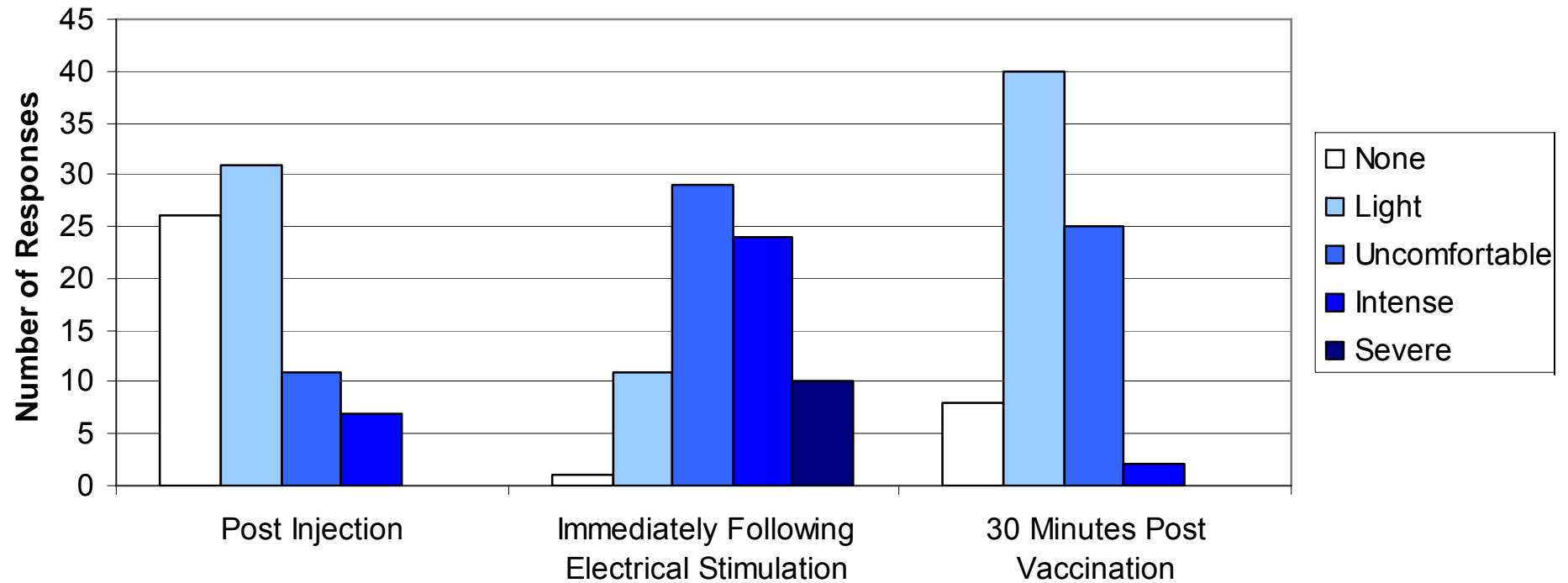
All 40 volunteers enrolled and all vaccinations complete

One SAE to date not related to vaccine

Safety labs unremarkable

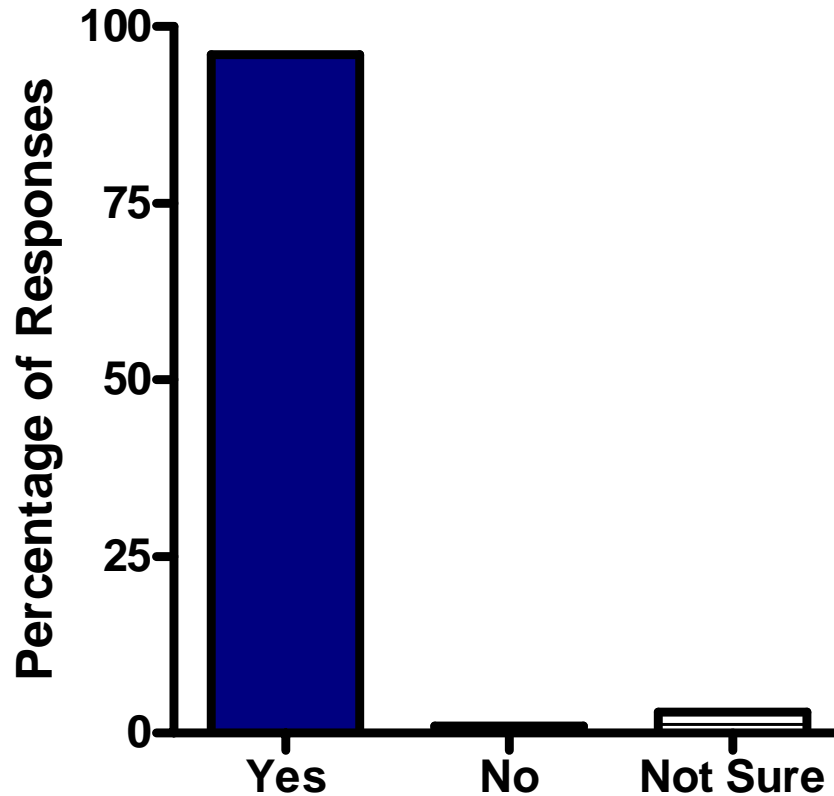
Last volunteer visit completed October 2009

Electroporation Tolerability



Total of 75 EP administrations in 32 volunteers

Electroporation Acceptability



EP is acceptable if it protects against a serious disease, such as HIV, for which there is no vaccine

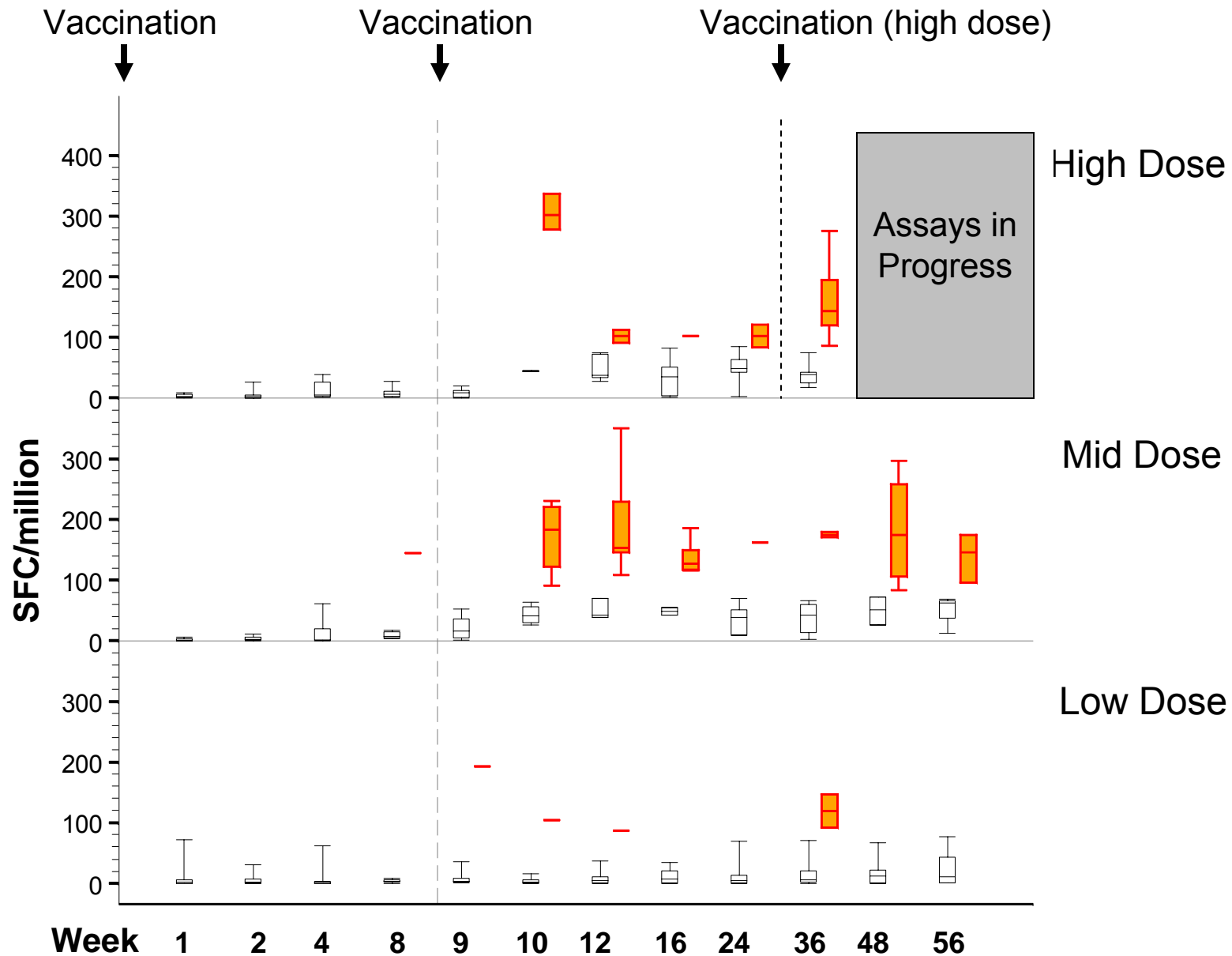
EP Improves IFN γ ELISpot Response Rate

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%

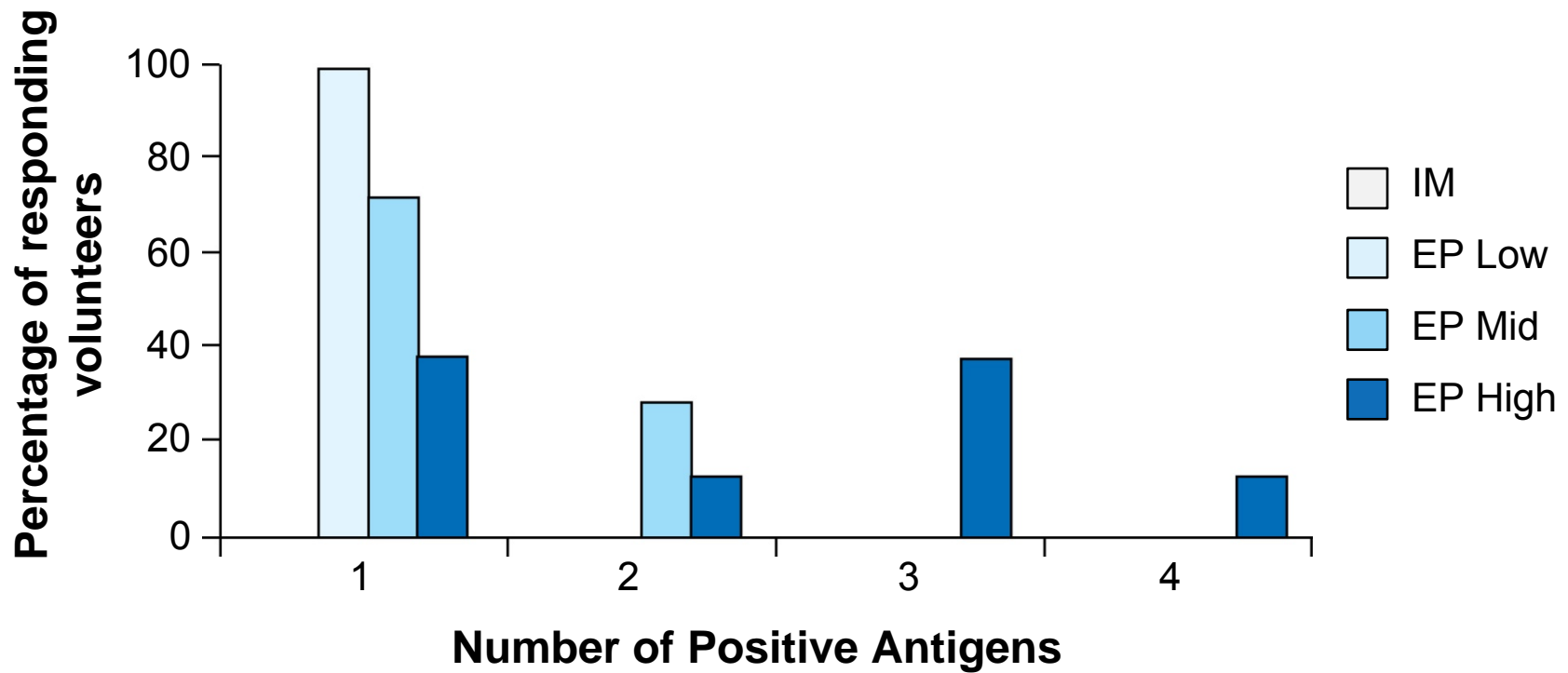
EP Improves IFN γ ELISpot Response Rate

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%

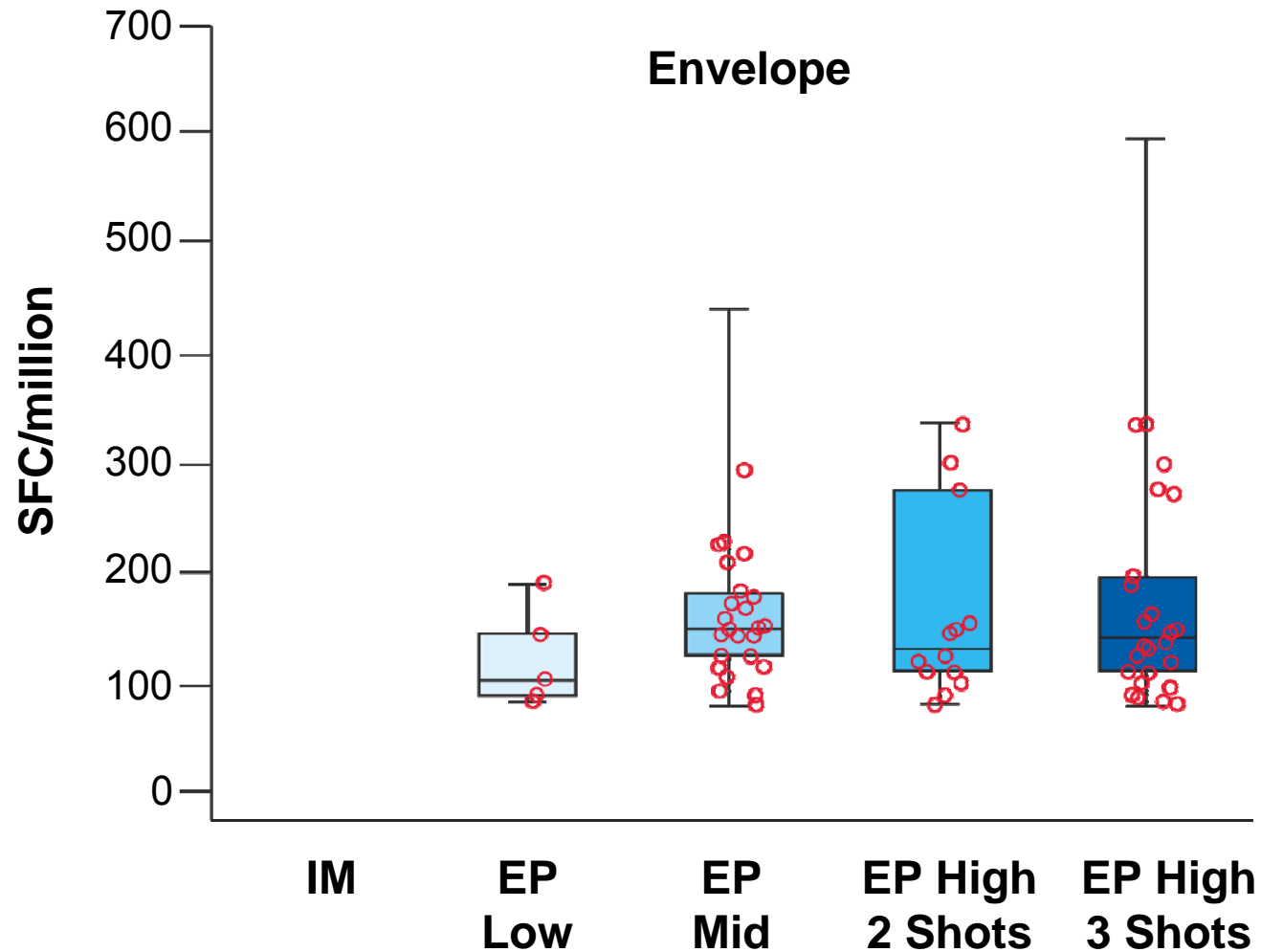
EP Induces Durable IFN γ ELISpot Responses



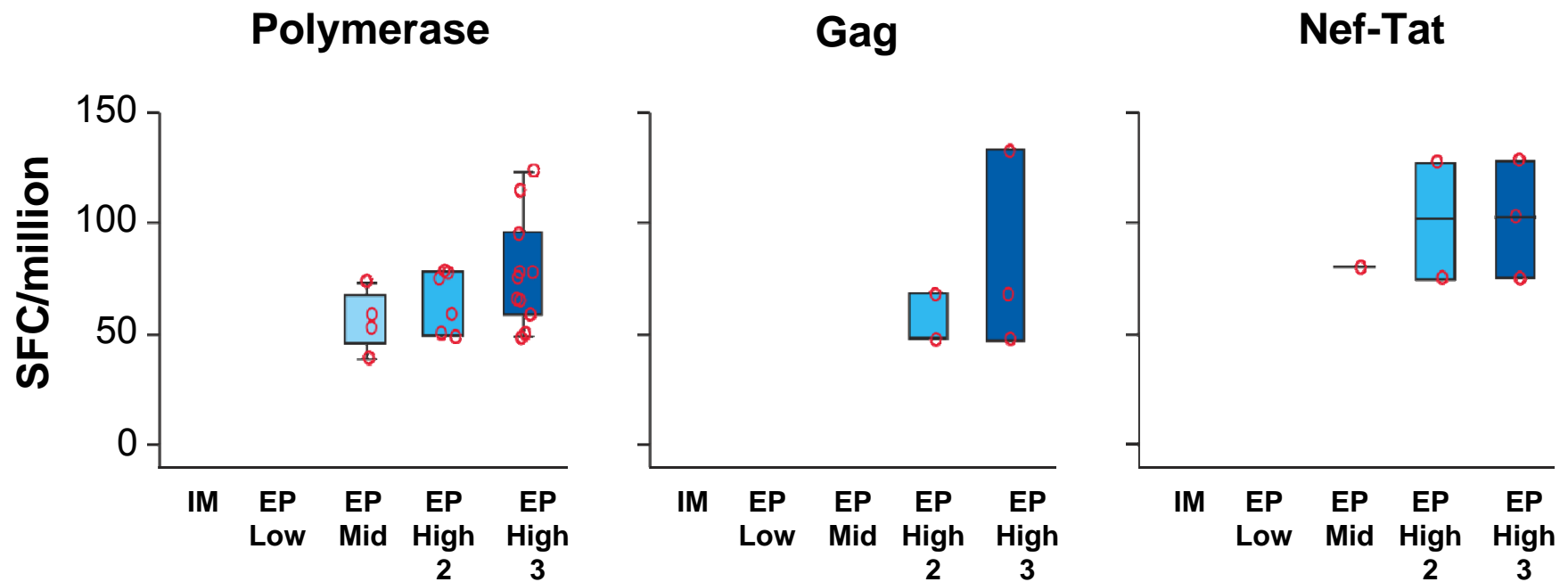
EP Increases the Breadth of the IFN γ ELISpot Antigen Response



EP Boosts the Magnitude of the Dominant IFN γ ELISpot Response to Envelope



EP Boosts the Magnitude of the Sub-Dominant IFN γ ELISpot Responses



ICCS Analysis of High Dose EP Volunteers at Peak ELISpot Response

Both CD4 and CD8 responses were elicited, with slight CD4 predominance

Co-secretion of IFN γ and IL-2 is evident in both CD4+ and CD8+ responses

Strong correlation with ELISpot Responses

Highest cytokine secretion in response to *env*, although the majority of responses were to more than one antigen

Conclusions

TriGrid™ EP delivery of ADVAX:

- Is safe, tolerable, and acceptable
- Improves the total IFN γ ELISpot response rate
- Improves the magnitude of IFN γ ELISpot responses
- Improves the breadth of IFN γ ELISpot responses
- Improves the duration of IFN γ ELISpot responses
- Induces IFN γ /IL-2 CD4+ and CD8+ T cell responses to multiple antigens

Acknowledgements

Our Dedicated Clinical Trial Volunteers

ADARC Clinical Team

David Ho
Arlene Hurley
Daniel Dugin

Rockefeller Clinical Team

Sarah Schlesinger
Marina Caskey
Johanne Andersen

IAVI Clinical Team

Pat Fast
Claudia Schmidt
Harriet Park
Angela Lombardo

ADARC Laboratory

Yaoxing Huang
David Gardiner
Mar Boente-Carrera
Roselle Vittorino
Faye Yu
Yang Song

IAVI HIL

Jill Gilmour
Jo Cox
Tony Tarragona
Dilbinder Gill
Lorna Clark
Hannah Cheeseman
Phil Bergin

ICHOR Medical Systems

Bob Bernard
Drew Hannaman
Ryan Betts
Barry Ellefsen
Claire Evans
Karen Dolter
Brian Livingston

EMMES, Inc.

Len Dally
Kelley Loghran
Carol Smith