

CIC 2014 CCI

December 2-4
2 - 4 décembre
OTTAWA

Canadian Immunization Conference
Conférence canadienne sur l'immunisation

Ebola virus vaccine VSV Δ G-EBOVGP - From design to delivery -

Judie Alimonti, Ph.D.

Public Health Agency of Canada

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Disclosure Statement



- I have no affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.

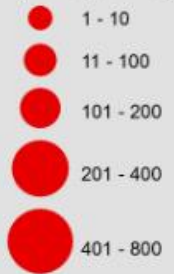
EBOLA OUTBREAK RESPONSE: REGIONAL CONFIRMED AND PROBABLE CASES

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

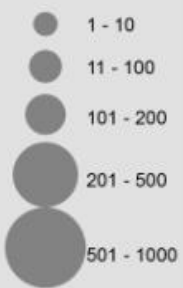


MAP DATE: 29 October 2014

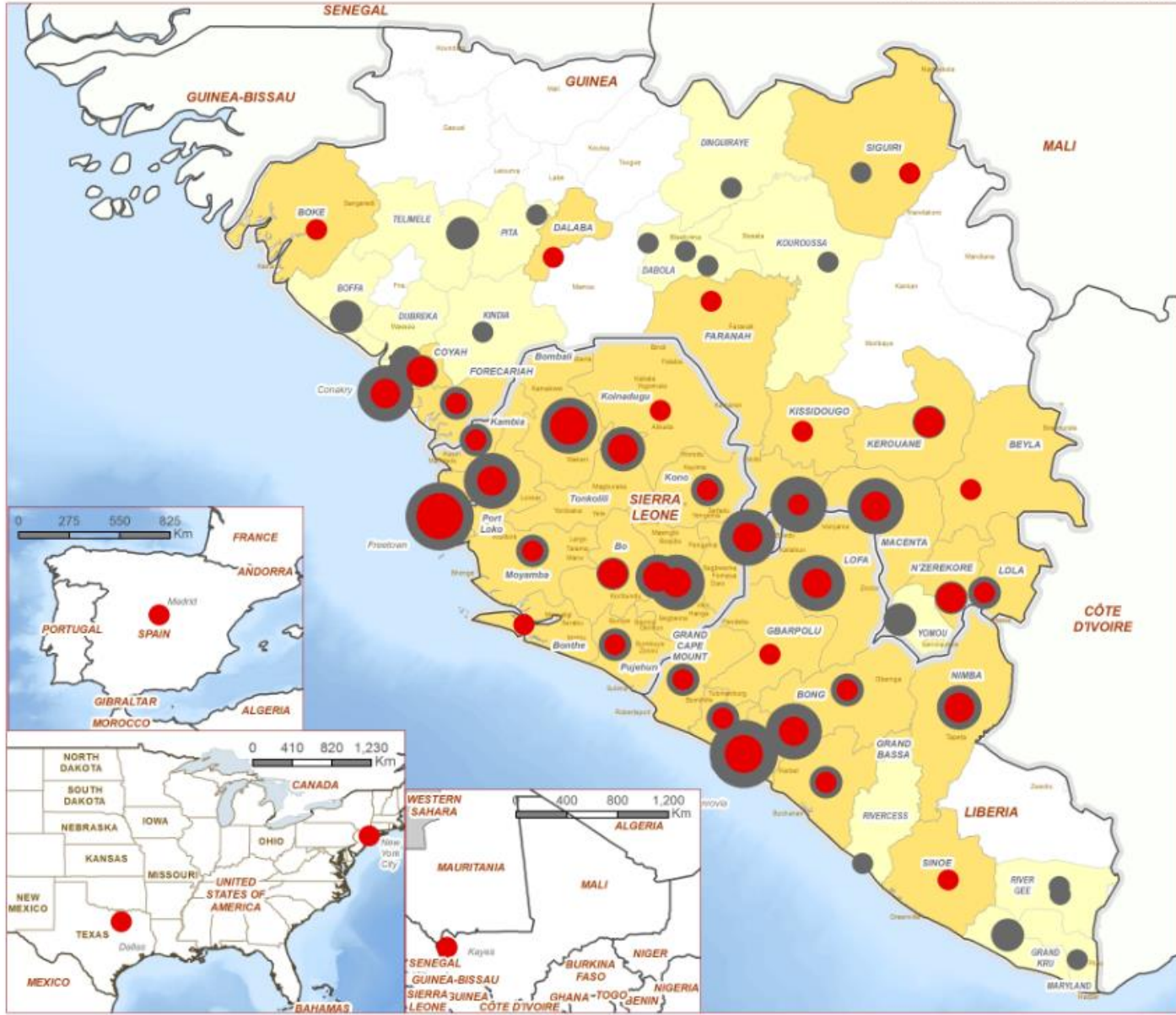
Recent Cases (21 Days Prior)



All cases



- NOT ACTIVE - No cases in previous 21 days
- ACTIVE - New cases in previous 21 days
- NEWLY INFECTED - New cases in previous 7 days (in previously uninfected areas)



Map Scale (A3): 1:3,700,000

1 cm = 37 km



Filoviridae Family

Genus	Species	Virus	No. human cases	No. events	Case Fatality Rate (%)
<i>Ebolavirus</i>	<i>Zaire Ebolavirus</i>	Ebola virus (EBOV)	1097	10	25-90
	<i>Sudan Ebolavirus</i>	Sudan Virus (SUDV)	792	7	41-71
	<i>Bundibugyo Ebolavirus</i>	Bundibugyo Virus (BDBV)	208	2	32-47
	<i>Reston Ebolavirus</i>	Reston Virus (RESTV)	13	3	0
	<i>Tai Forest Ebolavirus</i>	Tai Forest Virus (TAFV)	2	2	0
<i>Marburgvirus</i>	<i>Marburg Marburgvirus</i>	Marburg Virus (MARV)	470	9	23-90
		Ravn Virus (RAVV)			

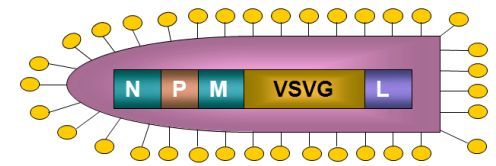
Ebola virus: (EBOV)

- Negative sense ss RNA virus
- Up to 90% case fatality rate in humans
 - » Onset of symptoms 2-21 days
 - » VHF: Fever, muscle aches, diarrhea, vomiting, haemorrhage, lymphocyte apoptosis
 - » Death due to multi-organ failure and shock
- Evidence for bats to be the natural reservoir
- Spread through close contact with bodily fluids or infected animals



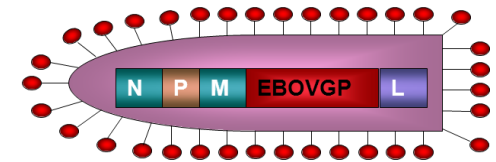
Vesicular Stomatitis Virus (VSV) Vector

- Rhabdovirus: ss (-) RNA
 - grows to high titres ($>10^9$ pfu/ml)
 - manipulated by recombinant DNA technologies
- generally not a human pathogen
 - no pre-existing immunity in humans
 - induces strong B & T cell responses



WT VSV

Glycoprotein
switched



VSV Δ G/EBOVGP



Route of Immunization

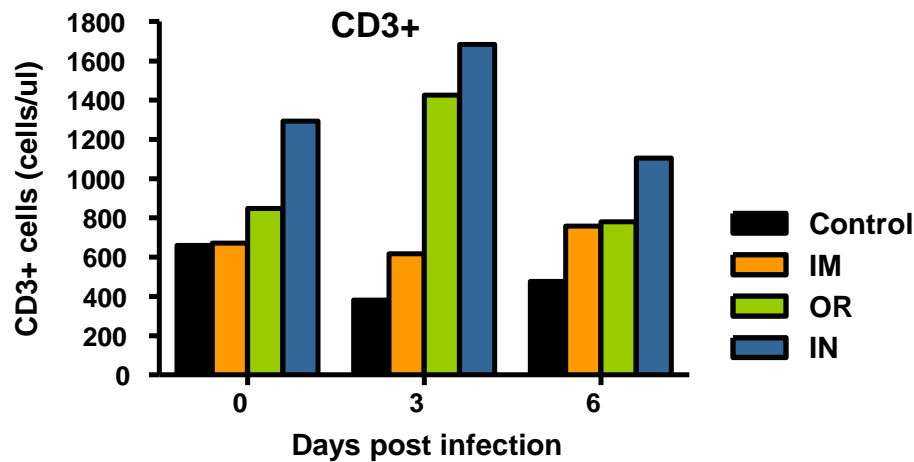


Cynomolgus
Macaques

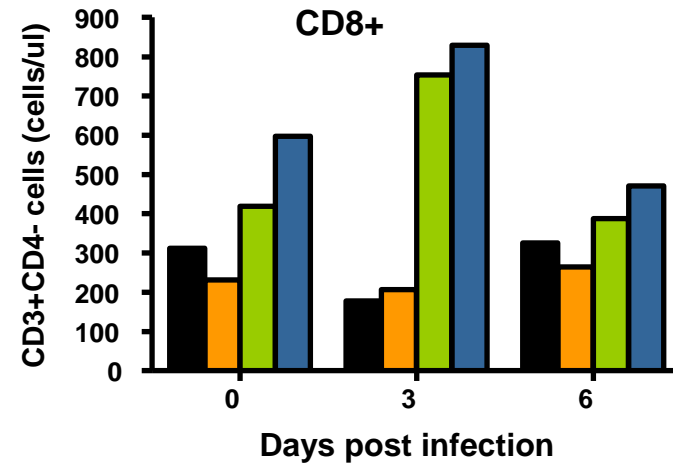
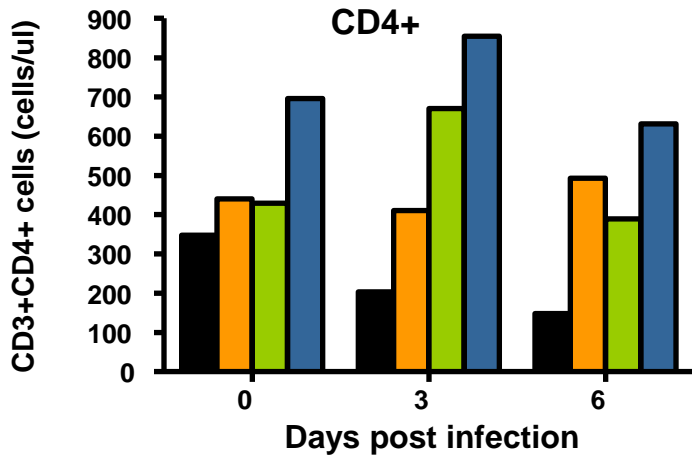
Vaccination Groups 2 x 10 ⁷ pfu	Challenge EBOV 1000 pfu	Survival
VSVΔG/MARVGP Control		
IM = intramuscular		0 / 2
VSVΔG/EBOVGP		
IM = intramuscular		2 / 2
OR = oral		4 / 4
IN = intranasal		4 / 4

2009 PLoS ONE 4:e5547

Absolute Lymphocyte Counts Post-challenge

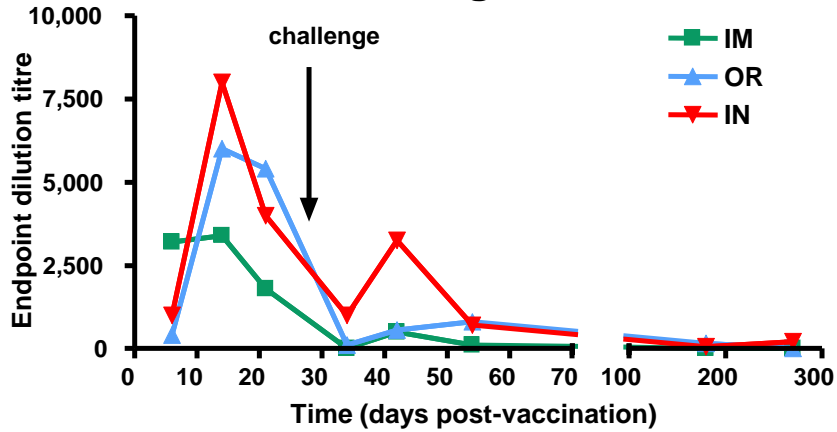


Flow cytometry
Immunophenotyping
Whole blood staining of lymphocytes

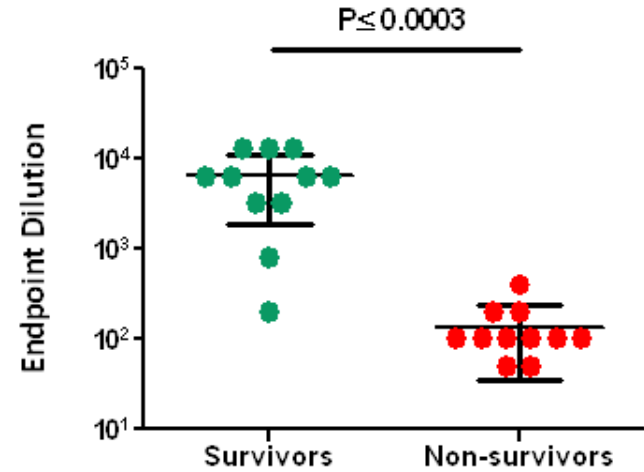


B cell Response: EBOV GP-specific IgG/M/A ELISA

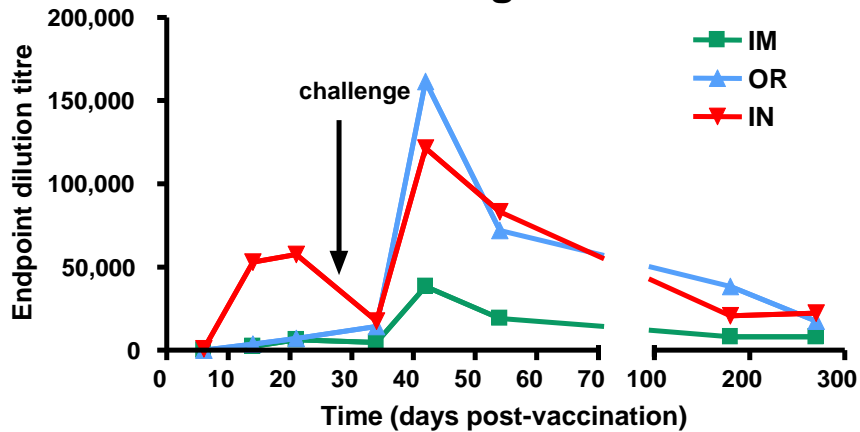
IgM



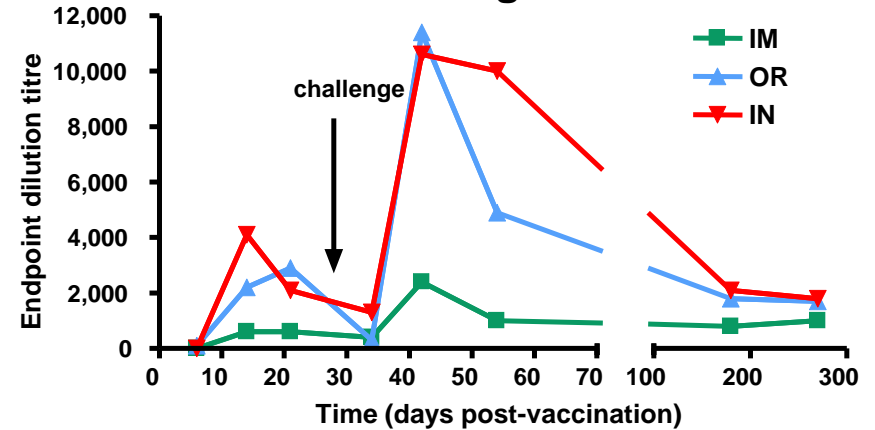
GP-IgG titre correlates with survival



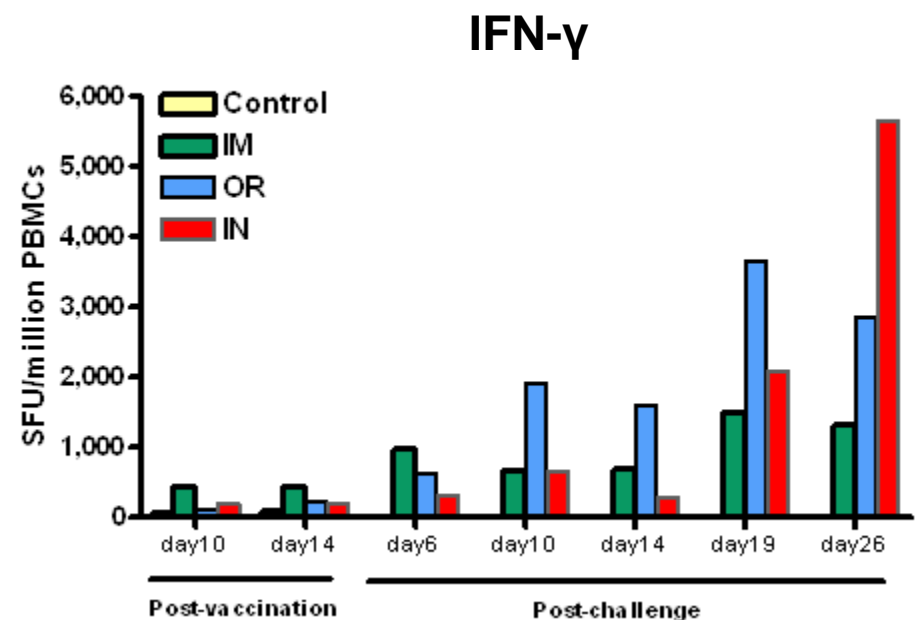
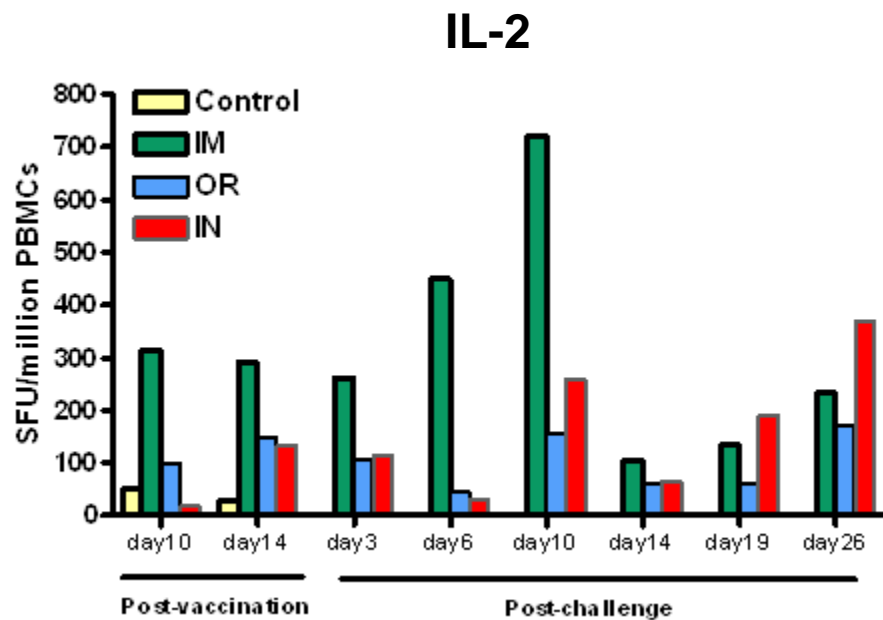
IgG



IgA



T cell Response: EBOV GP-Specific ELISPOT



VSV-EBOV as a Post-exposure Therapeutic

Challenge
EBOV 1000 pfu



Post-exposure tmt
 2×10^8 pfu

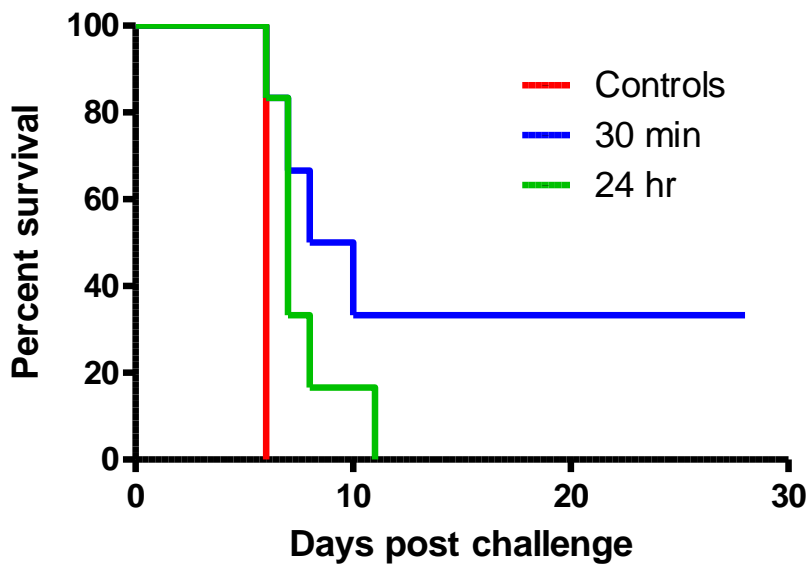
VSV-EBOV

Controls: untreated n=2

30 minute treatment n=6

24 hour treatment n=6

Post-exposure Survival



» VSV-EBOV

- Effective vaccine & post-exposure therapeutic

» Currently in phase I clinical trials

- Canada, USA, Germany, Switzerland

» Once approved for human use it can be used in outbreaks

- i.e.: ring vaccination; vaccination of health care workers

Thank you



PUBLIC HEALTH AGENCY of CANADA
AGENCE DE SANTÉ PUBLIQUE du CANADA

Special Pathogens Program

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Lisa Hensley
Peter Jahrling



Further Development & Manufacturing

Vaccine Clinical Trials

Cdn. Centre for Vaccinology
WRAIR
NIAID
USAMRIID



Vaccine Manufacturer