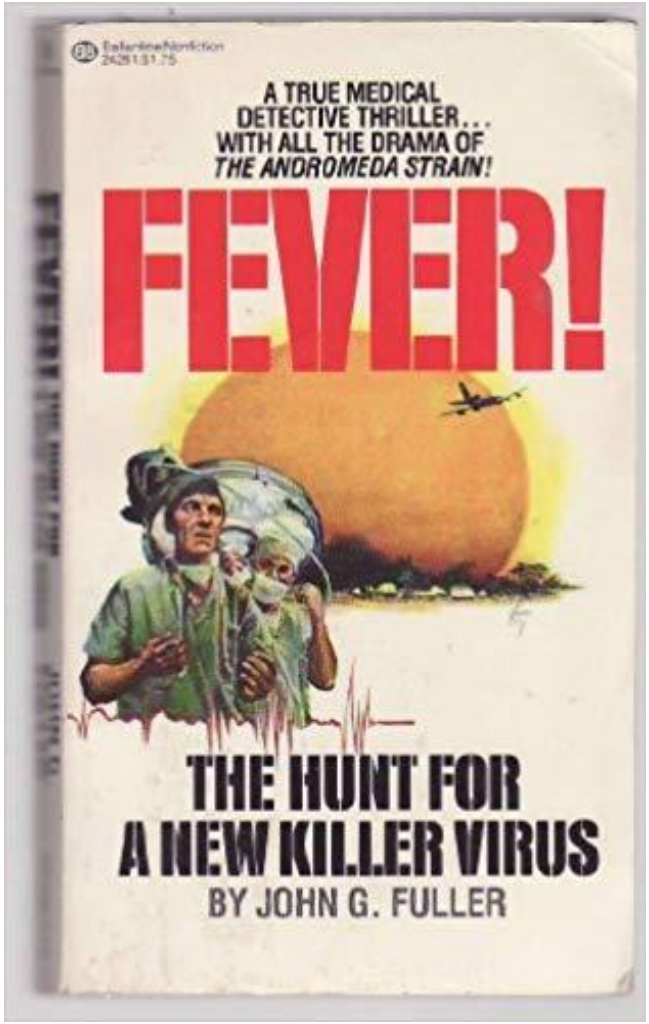
[Nearly] 50 years of Lassa fever: The road ahead

Robert F. Garry, PhD
Tulane University
Zalgen Labs

VIRAL HEMORRHAGIC FEVER CONSORTIUM

GVN
GLOBAL VIRUS NETWORK



February 1969 - deadly unidentified virus reported from remote African missionary hospital, two American nurses stricken and died within 10 days. Doctors stymied by mysterious symptoms of the killer: soaring temperature, painful backache, swelling of the throat and neck, discolored skin! Latest victim airlifted to special isolation ward at New York's Columbia Presbyterian Hospital, blood samples rushed to Yale's Arborvirus [*sic*] Laboratory, all-out search launches to discover an antidote. U. S. Public Health officials alarmed, virus has the potential to decimate the whole population, aviation officials consider cancellation of all jet travel to critical world areas.

THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE
Vol. 19, No. 4

Printed in U.S.A.

LASSA FEVER, A NEW VIRUS DISEASE OF MAN FROM WEST AFRICA

II. REPORT OF A LABORATORY-ACQUIRED INFECTION TREATED WITH PLASMA FROM A PERSON RECENTLY RECOVERED FROM THE DISEASE

EDGAR LEIFER, DAVID J. GOCKE, AND HENRY BOURNE
Department of Medicine, Columbia University College of Physicians and Surgeons, and The Presbyterian Hospital, New York, New York 10032

THE AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE
Vol. 19, No. 4
Copyright © 1970 by The American Society of Tropical Medicine and Hygiene
Printed in U.S.A.

LASSA FEVER, A NEW VIRUS DISEASE OF MAN FROM WEST AFRICA

III. ISOLATION AND CHARACTERIZATION OF THE VIRUS*

SONJA M. BUCKLEY AND JORDI CASALS
Yale Arbovirus Research Unit, Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Connecticut 06510, and The Rockefeller Foundation, New York, N.Y. 10020

TABLE 1

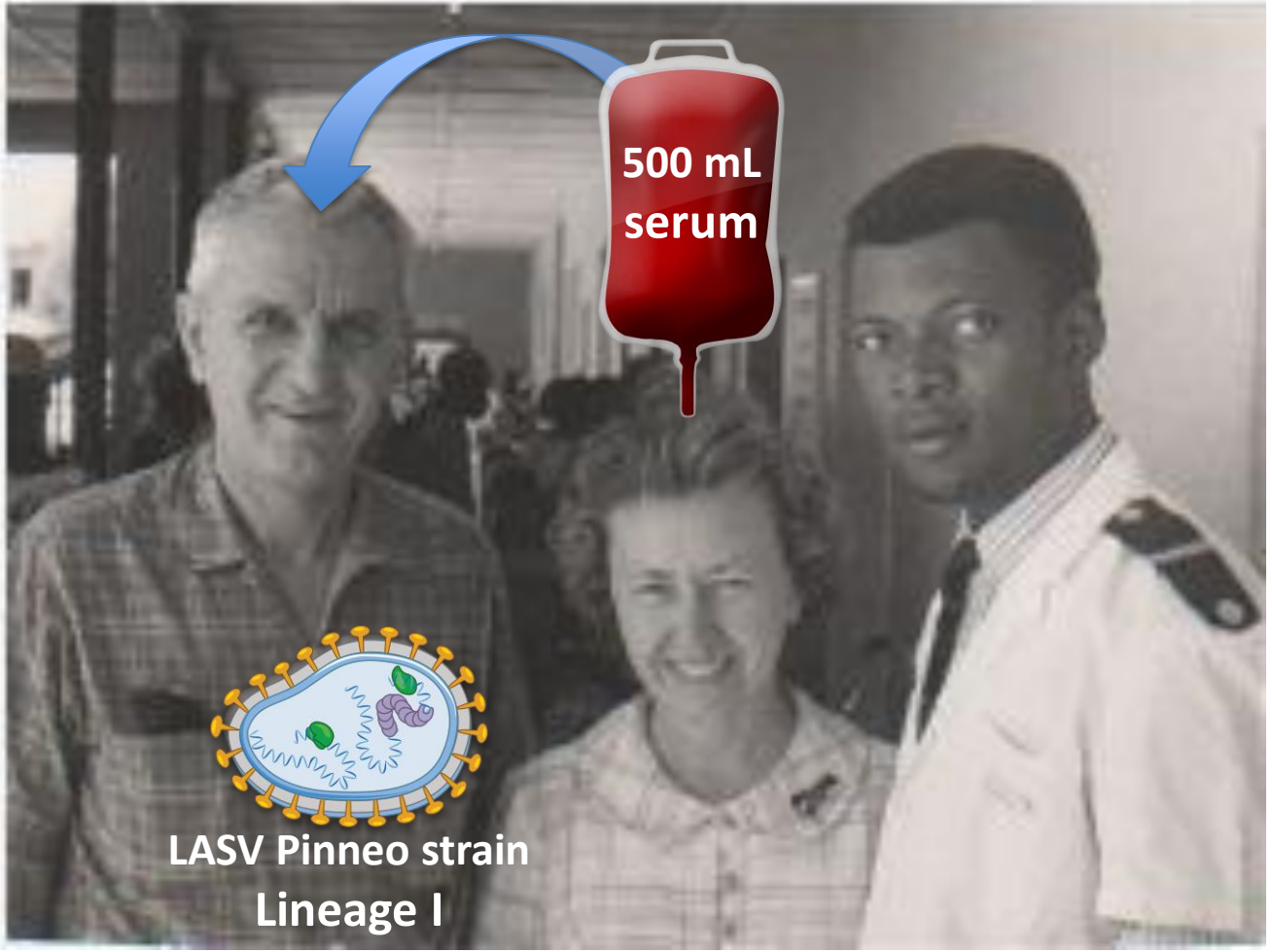
Source of materials, and isolations of Lassa virus

Patient	Sex	Locale of infection	Date of onset, 1969	Outcome of infection	Material, and date collected		Isolation in Vero cells
L.W.	F	Lassa, Nigeria	20 Jan.	Death, day 6	Serum, 26 Jan.	(day 6)	+
C.S.	F	Jos, Nigeria	3 Feb.	Death, day 10	Serum, 6 Feb.	(day 3)	+
					Serum, 13 Feb.	(day 10)	+
L.P.	F	Jos, Nigeria	20 Feb.	Recovery	Serum, 25 Feb.	(day 5)	+
					Serum, 5 March	(day 13)	+
					Pleural fluid, 5 March	(day 13)	+
					Serum, 6 March	(day 14)	+
					Serum, 20 March	(day 28)	0
					Serum, 29 March	(day 37)	0
J.C.	M	New Haven, Conn.	9 June	Recovery*	Serum, 16 June	(day 7)	+
					Serum, 18 June	(day 9)	+
					Urine, 18 June	(day 9)	+
					Throat washing, 18 June	(day 9)	+
					Throat washing, 23 June	(day 14)	+
					Urine, 26 June	(day 17)	+
					Urine, 11 July	(day 32)	+
N.Y.	F	—	In contact with L.P. in Nigeria, Feb. '69		Serum, 26 Feb. '69		0
C.C.	F	—	Stationed in Nigeria		Serum, 23 Sept. '68		0
Controls					Diluent		0

L.P.= Lily [Penny] Pinneo, RN

J.C.= Jordi Casals, MD

Penny with Jordi Casals and Raphael Adeyemi, a Nigerian Medical auxiliary, at the hospital in Jos, Nigeria, circa 1970.



JOURNAL OF VIROLOGY, May 1970, p. 651–652

Vol. 5, No. 5
Printed in U.S.A.

NOTES

Arenoviruses: Proposed Name for a Newly Defined Virus Group

WALLACE P. ROWE, FREDERICK A. MURPHY, GERNOT H. BERGOLD, JORDI CASALS, JOHN HOTCHIN, KARL M. JOHNSON, FRITZ LEHMANN-GRUBE, CEDRIC A. MIMS, ERIC TRAUB, AND PATRICIA A. WEBB

National Institute of Allergy and Infectious Diseases, Bethesda, Maryland; National Communicable Disease Center, Atlanta, Georgia; Instituto Venezolano de Investigaciones Cientificas, Caracas, Venezuela; Yale University School of Medicine, New Haven, Connecticut; New York State Department of Health, Albany, New York; Middle America Research Unit, Balboa Heights, Canal Zone; Hygiene-Institut der Philipps-Universität, Marburg/Lahn, Germany; John Curtin School of Medical Research, Canberra, Australia; and United Nations Food and Agricultural Organization, Ankara, Turkey

Received for publication 23 March 1970

The name "arenoviruses" is proposed for the newly defined taxonomic group containing lymphocytic choriomeningitis, Lassa, and the Tacaribe complex viruses.

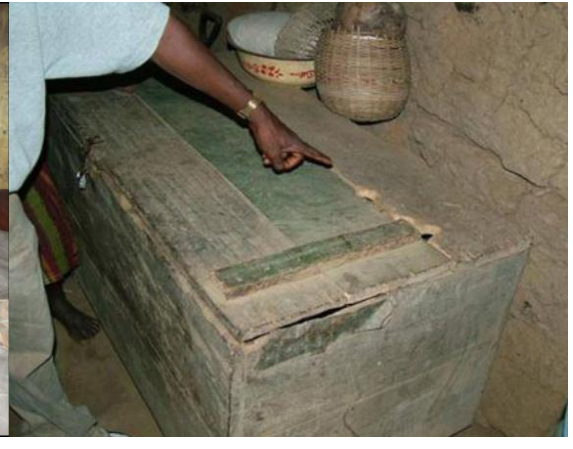
70% case fatality rate in patients presenting while viremic (Shaffer et al., 2014).

Lassa fever photos Dan Bausch, MPHTM, MD

Lassa fever is a zoonosis

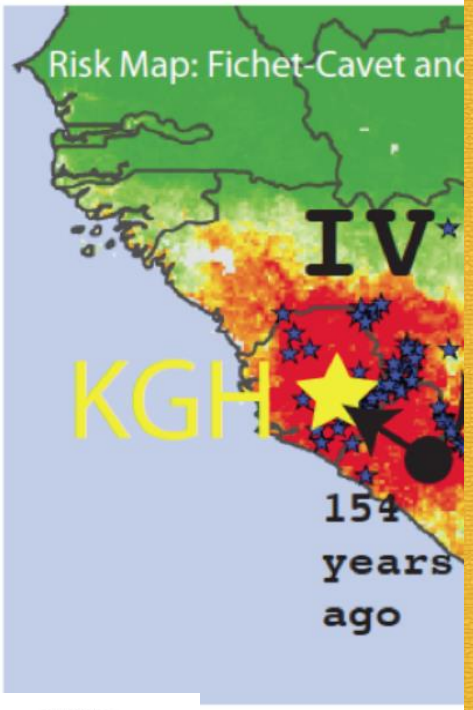
Mastomys natalensis (multimammate “rat”)

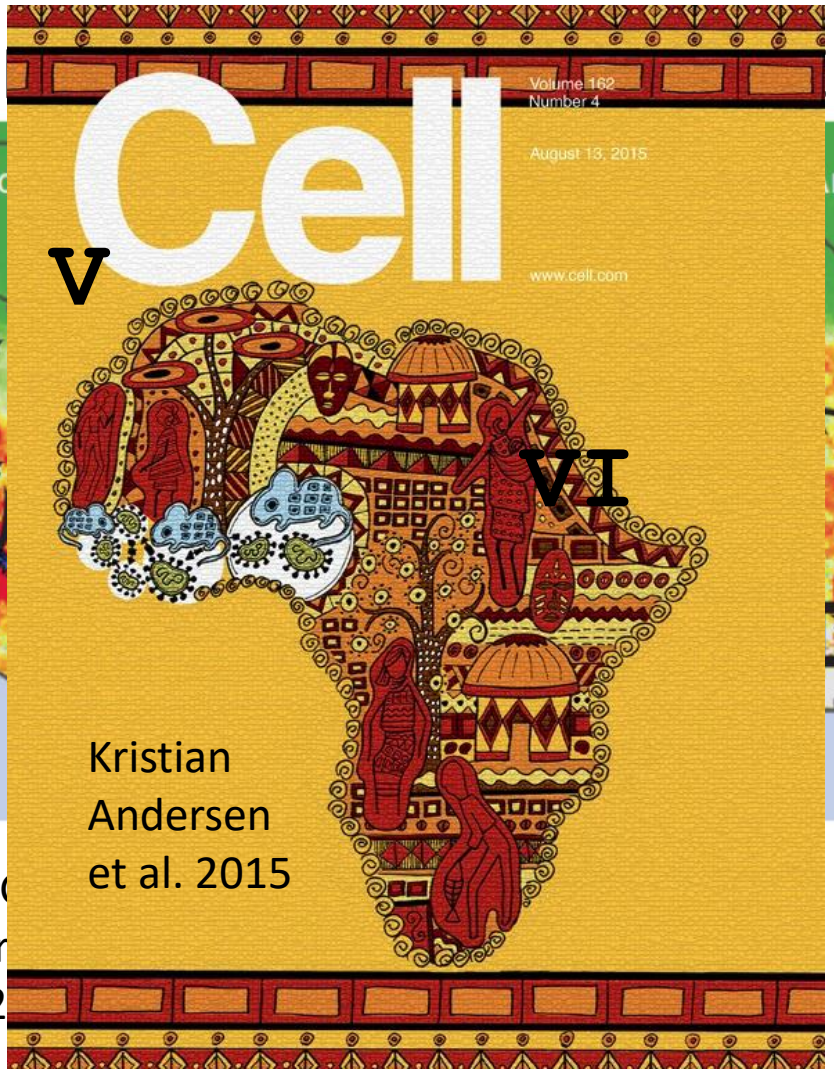
Photo credits:
Lina Moses, PhD
Tulane



Lassa fever is acquired through contact with excreta or the preparation of “rat” for food

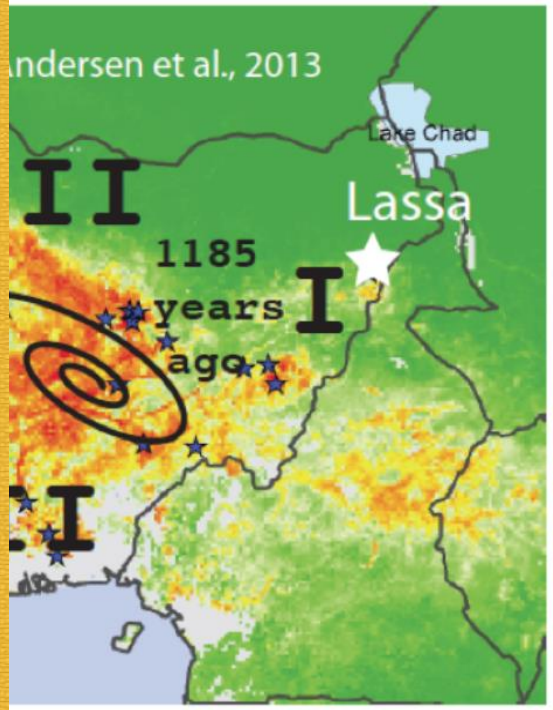
Whe





Kristian
Andersen
et al. 2015

Africa



Augustine
First EVD Sierr
May 25, 2

Christian Happi
First EVD Nigeria
July 20, 2014

Lassa fever program at Kenema Government Hospital

1970s and 1980s

Important site for Lassa fever research by CDC and others

1993

Blood Diamonds civil conflict forces suspension of Lassa program

2005

International team refurbishes Lassa Laboratory

2008

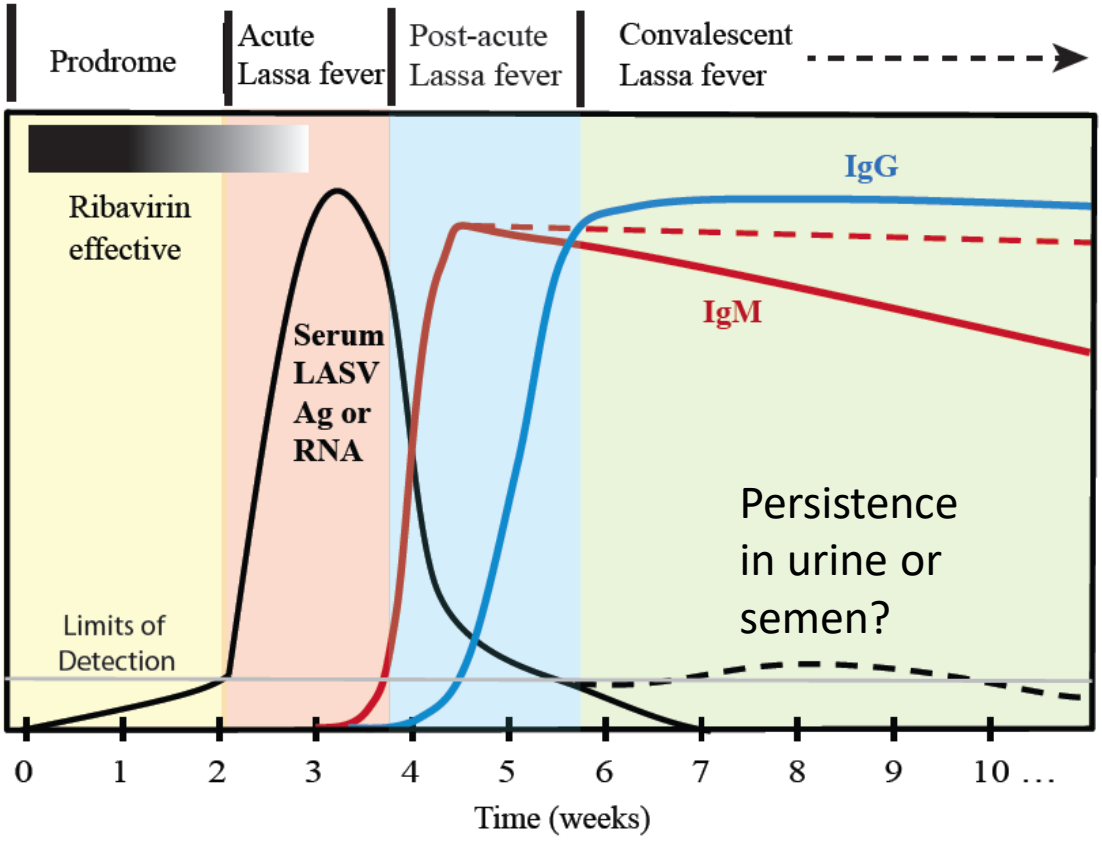
Establishment of recombinant Lassa ELISA diagnostics

2010

Introduction of ReLASV lateral flow immunoassays

Lassa fever diagnosis

LASV antigen, LASV RNA or antiLASV antibody



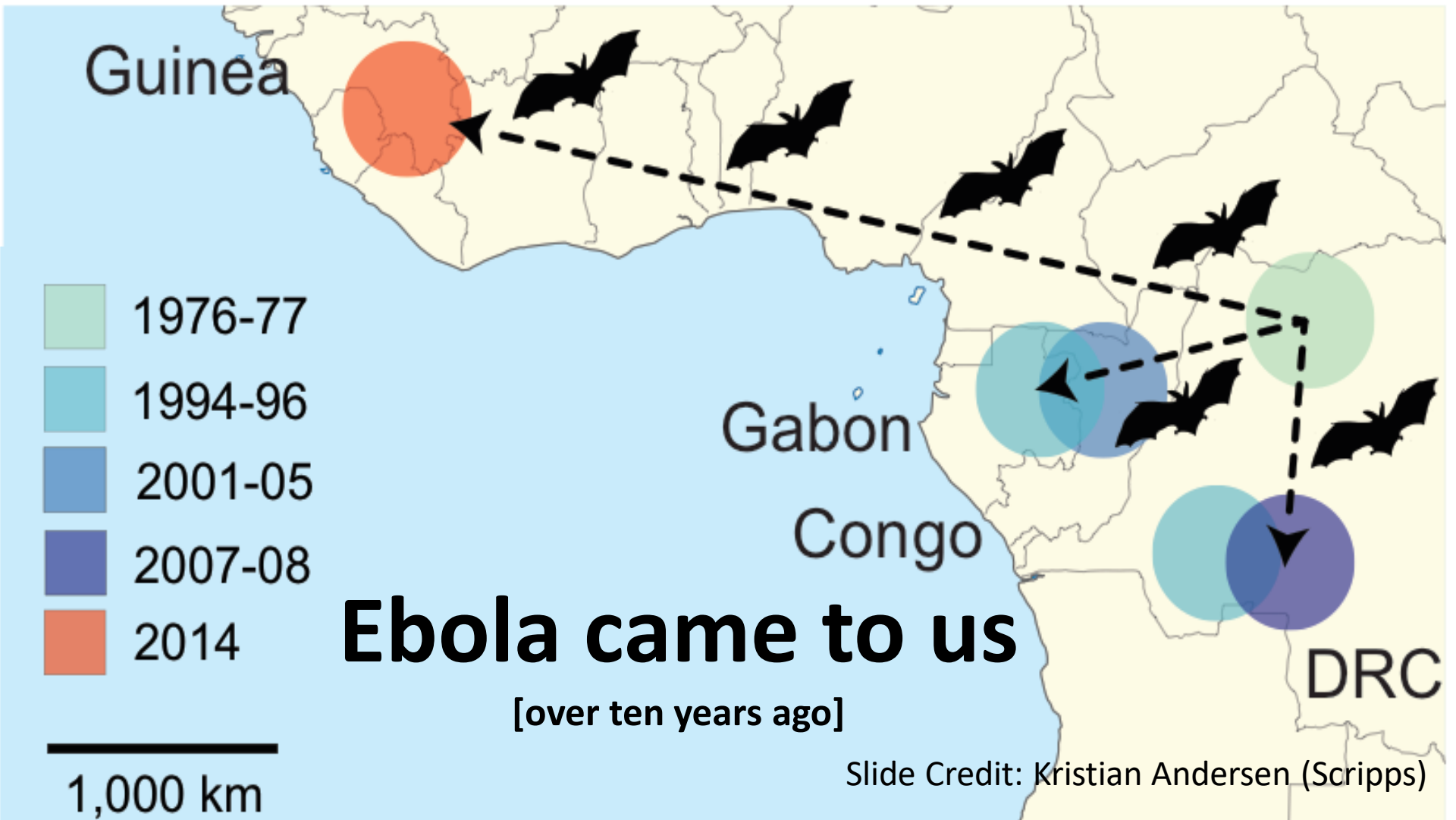
Lily (Penny) Pinneo (1917-2012)

RT-PCR

ReLASV Ag RDT

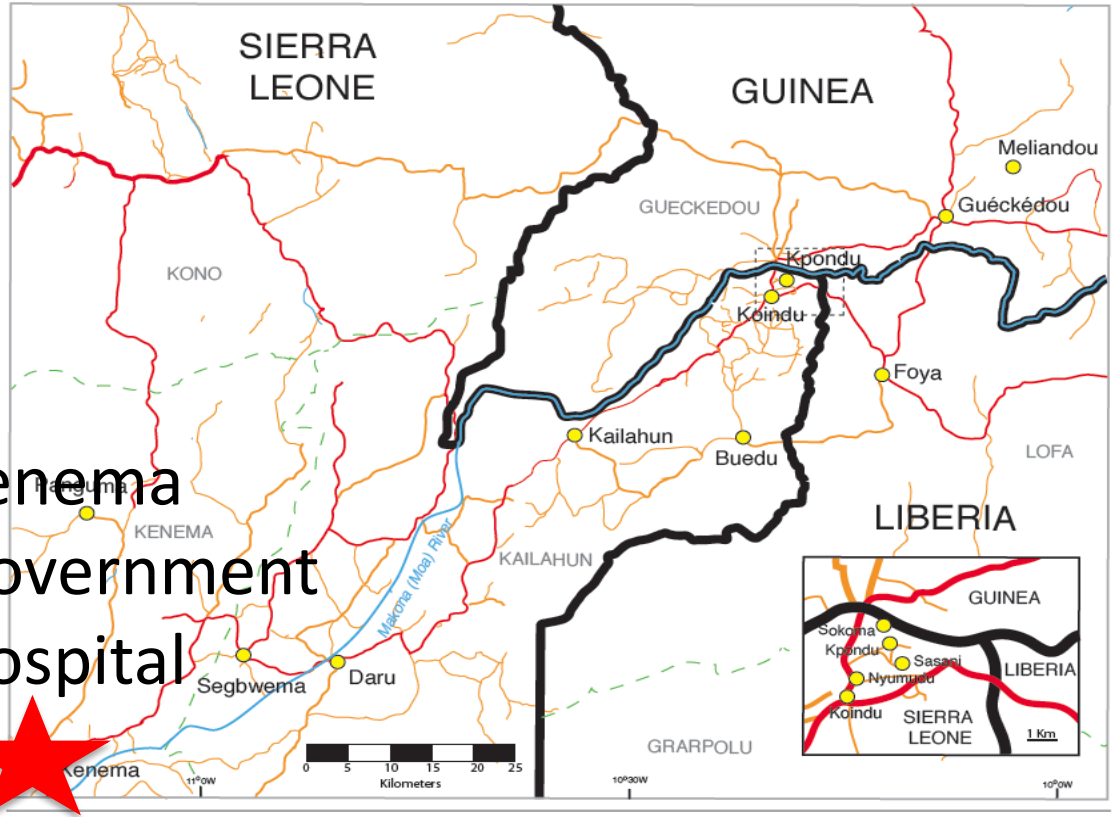
ReLASV Ag ELISA

Bond et al., Am J Trop Med Hyg. 2013 88:241-4.

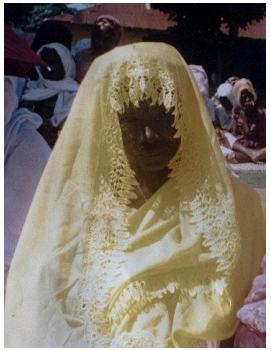


Slide Credit: Kristian Andersen (Scripps)

Kenema: Early epicenter of the 2013-16 Ebola Outbreak



Kenema Government Hospital

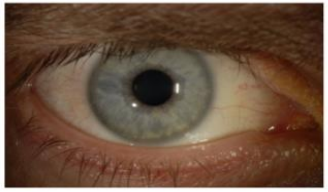


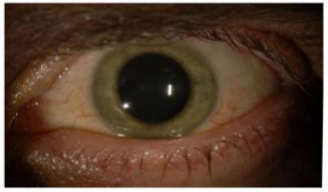
Healer

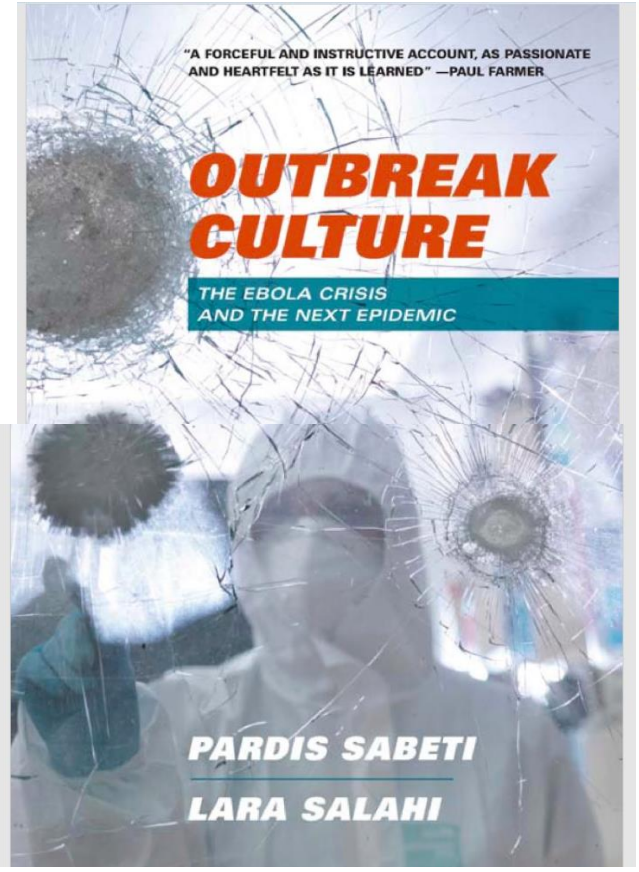
Dr. S. Humarr Khan

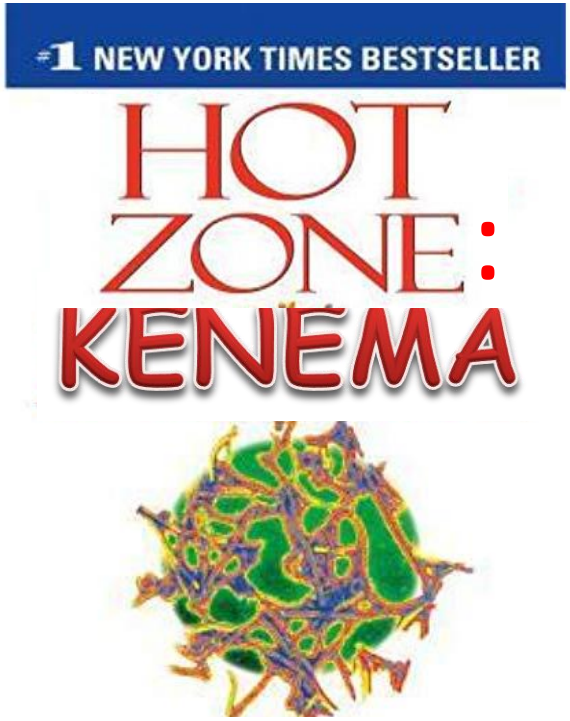
Nurse Will Pooley

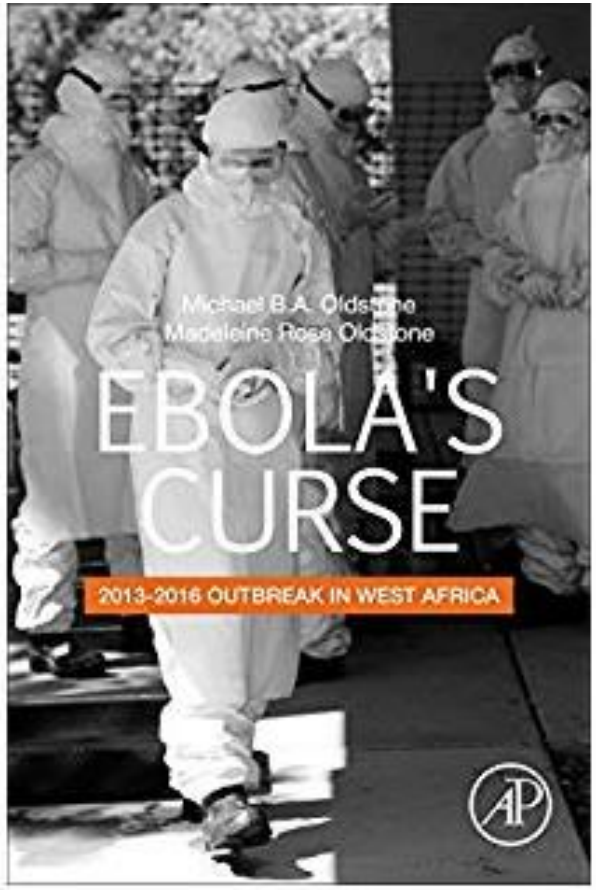
Dr. Ian Crozier

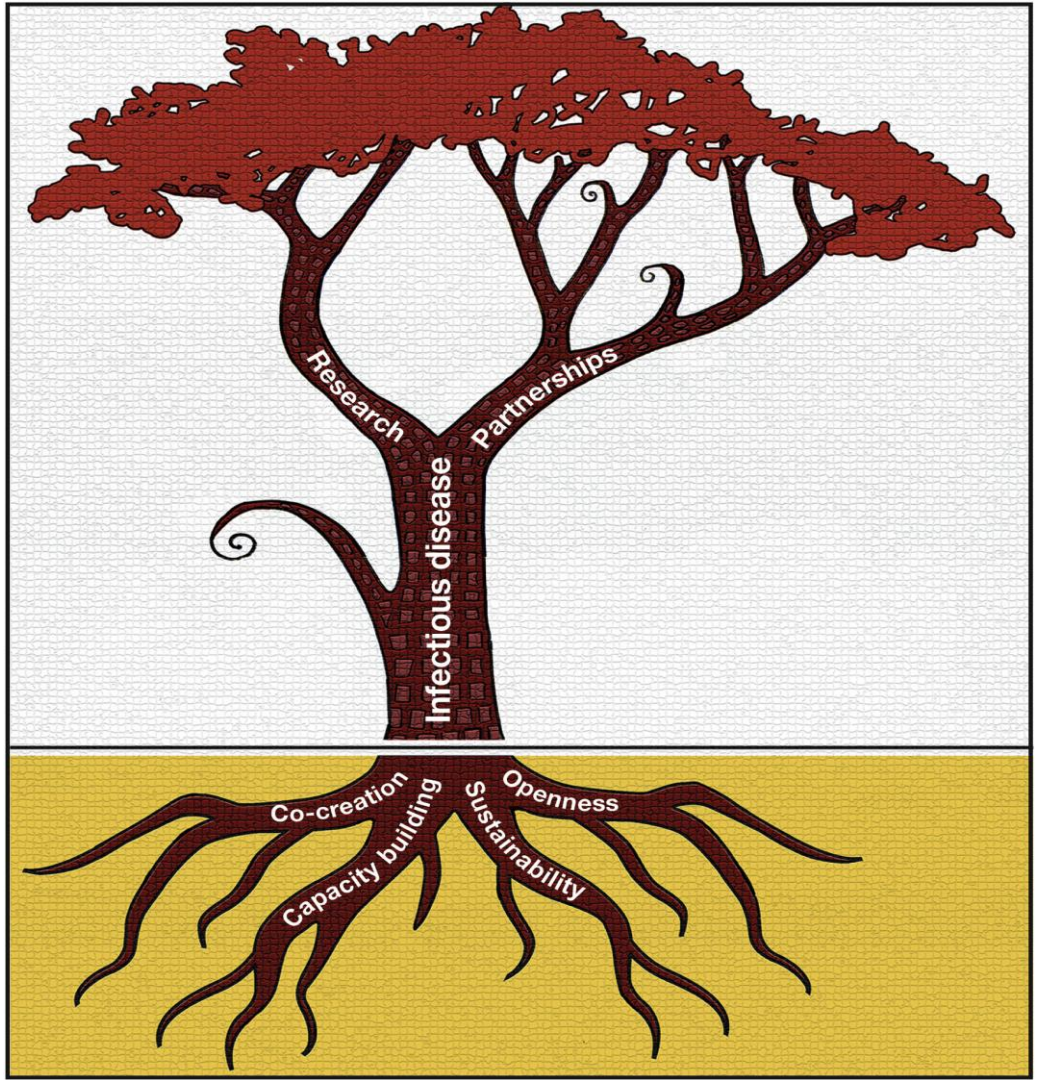





"A FORCEFUL AND INSTRUCTIVE ACCOUNT, AS PASSIONATE AND HEARTFELT AS IT IS LEARNED" —PAUL FARMER
OUTBREAK CULTURE
THE EBOLA CRISIS AND THE NEXT EPIDEMIC
PARDIS SABETI
LARA SALAHI


#1 NEW YORK TIMES BESTSELLER
HOT ZONE: KENEMA
THE TERRIFYING TRUE STORY OF EBOLA OUTBREAK IN WEST AFRICA
RICHARD PRESTON


Michael B.A. Oldstone
Madeleine Rose Oldstone
EBOLA'S CURSE
2013-2016 OUTBREAK IN WEST AFRICA
AP



Roots, Not Parachutes: Research Collaborations Combat Outbreaks

Nathan L. Yozwiak, Christian T. Happi, Donald S. Grant, John S. Schieffelin, Robert F. Garry, Pardis C. Sabeti, Kristian G. Andersen

Cell
Volume 166, Issue 1, Pages 5-8 (June 2016)
DOI: 10.1016/j.cell.2016.06.029

Photo credit: Allison Smither

May 14, 2014

ACEGID

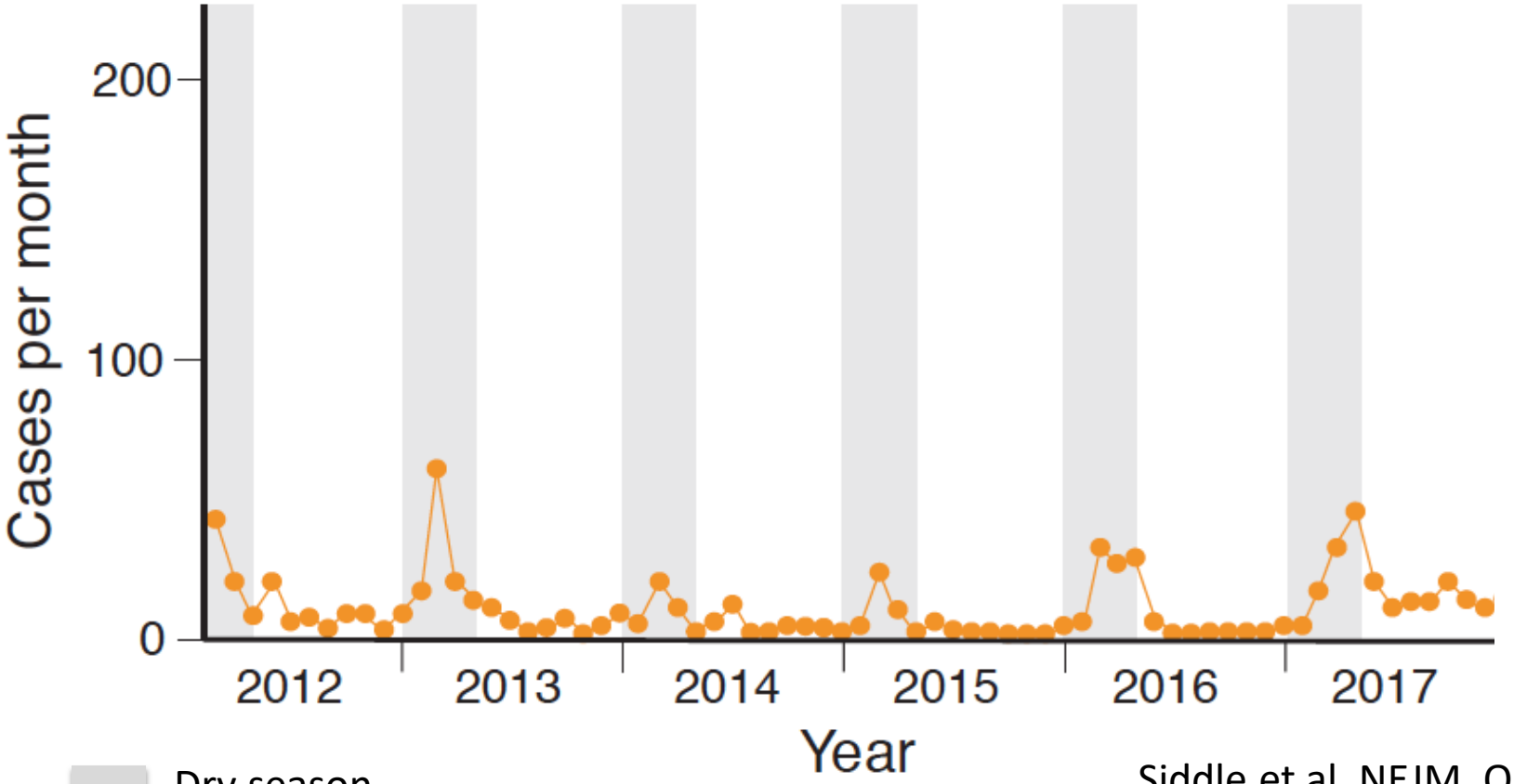
African Center of Excellence for Genomics of Infectious Diseases

Redeemer's University, Nigeria

r S.
umarr
han

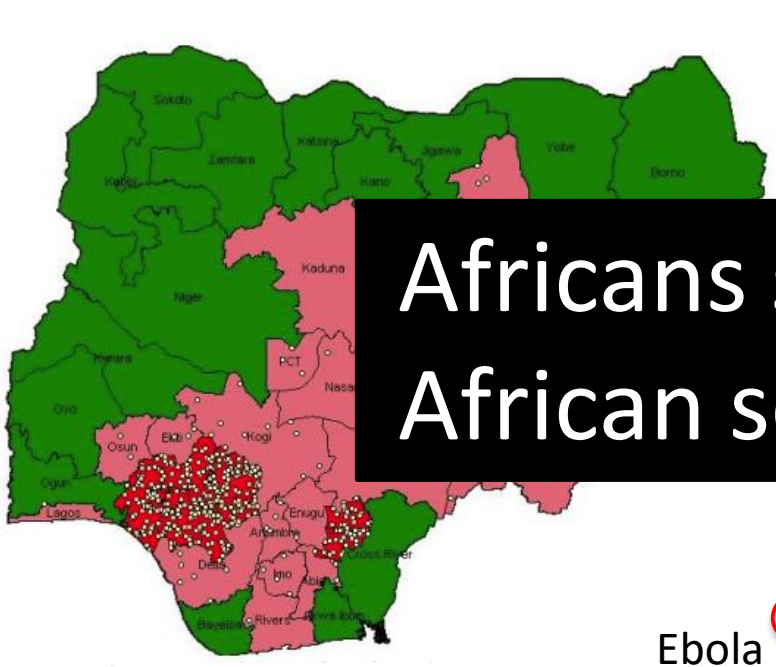
Dr
Pardis
Sabeti

“Confirmed” cases of Lassa fever in Nigeria

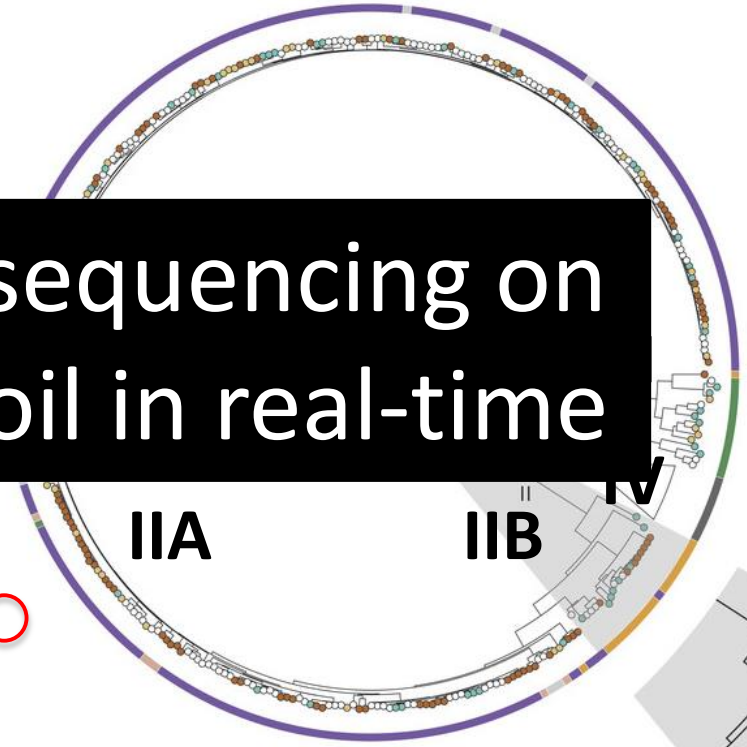


Siddle et al. NEJM, Oct. 17, 2018

21 (of 36) states have recorded at least one confirmed case



Africans sequencing on African soil in real-time



Region (outer ring and map):
- Southwestern Nigeria
- Southeastern Nigeria
- Northern Nigeria [III]
- Kogi State, Nigeria
- Nigeria: region not reported
- Outside Nigeria [IV]

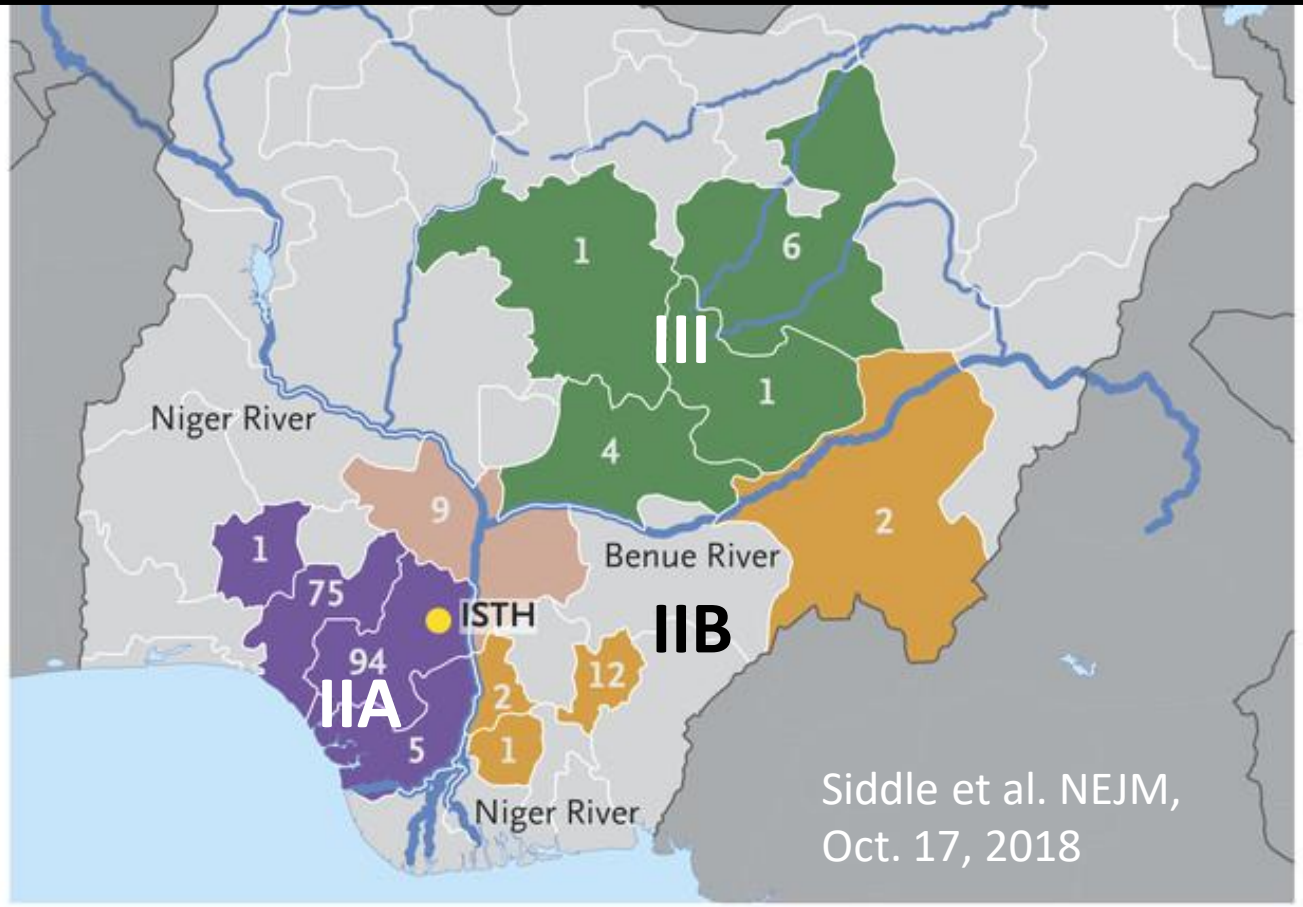
Season (tips):
- 2017–2018
- 2016–2017
- 2015–2016
- Previously published (pre-2015 seasons)

Ebola virus

1-50 confirmed cases
>50 confirmed cases
No confirmed cases
1 dot = confirmed case

States of origin (tips in inset):
- Ebonyi, southeastern Nigeria
- Taraba, southeastern Nigeria
- Anambra, southeastern Nigeria
- Delta, southwestern Nigeria
- Nigeria: previously published (pre-2015 seasons), no state reported

It’s all about the rodent transmission.



Katherine Siddle

Pardis Sabeti

Christian Happi

Christian Happi

GVN
GLOBAL VIRUS NETWORK

Sokoto
Zamfara
Katsina
Jigawa
Yobe
Borno
Kebbi
Kano
Kaduna
Bauchi
Gombe
Adamawa
Plateau
Kwara
Fct
Nasarawa
Taraba
Oyo
Osun
Ekiti
Kogi
Benue
Ogun
Ondo
Lagos
Edo
Enugu
Ebonyi
Cross River
Delta
Imo
Abia
Rivers
Akwa Ibom
Bayelsa

Legend

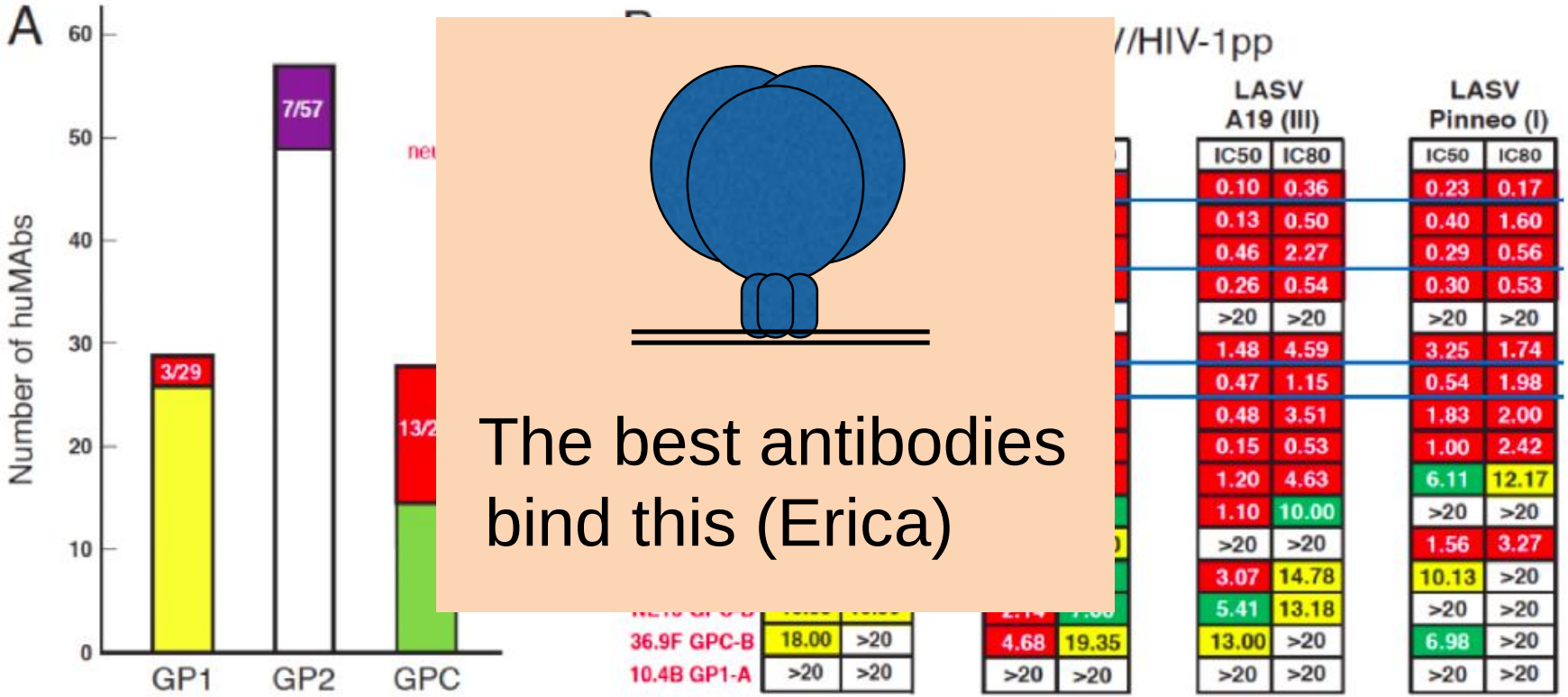
LGA Boundaries
Non Affected LGAs
States Boundary
LGAs with Suspected Cases

LGA by Number of Confirmed Cases
1-10
> 10

100 0 100 200 300 400 km


KGH Viral Hemorrhagic Fever Ecology Team
JUST BACK FROM NIGERIA

Most neutralizing human monoclonal antibodies target novel epitopes requiring both Lassa virus glycoprotein subunits



The best antibodies bind this (Erica)

James E. Robinson et al. *Nature Communications* **7** (2016) doi:10.1038/ncomms11544

Lassa virus B cell epitopes and how the work

Binding
blocks
dystrog
interac

ding here
on-
tralizing

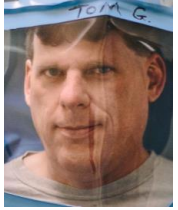
Bindi
block
fusion

ding
e blocks
on and
MP-1
interaction

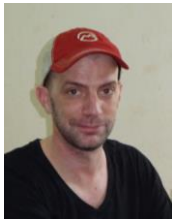
Erica and Kate

Human monoclonal antibody cocktail cures monkeys with late-stage Lassa fever

- 3 huMabs down-selected to 2
- Bispecific huMAbs work
- Effective at 1.5 mg/Kg against diverse lineages
- Rationally engineered Mabs in pipeline (Erica/Kate)



Tom Geisbert



Bob Cross

Chad Mire

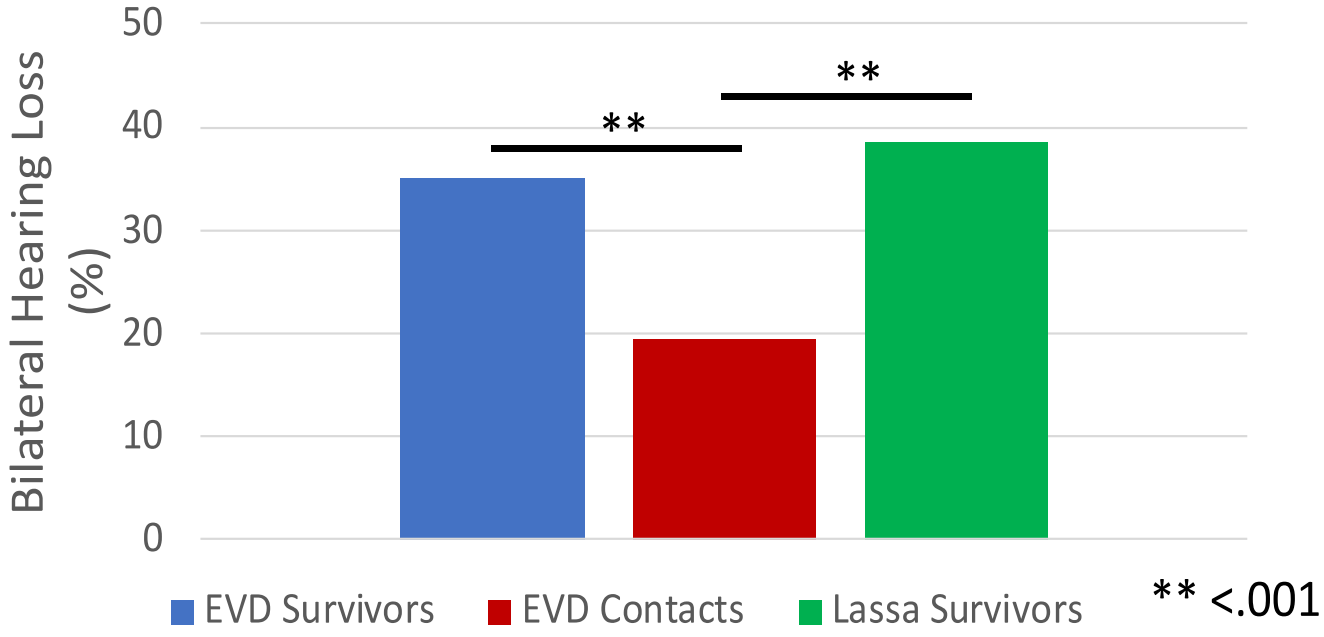
Luis Branco

Khan Center of Excellence (NIH- ICIDR)

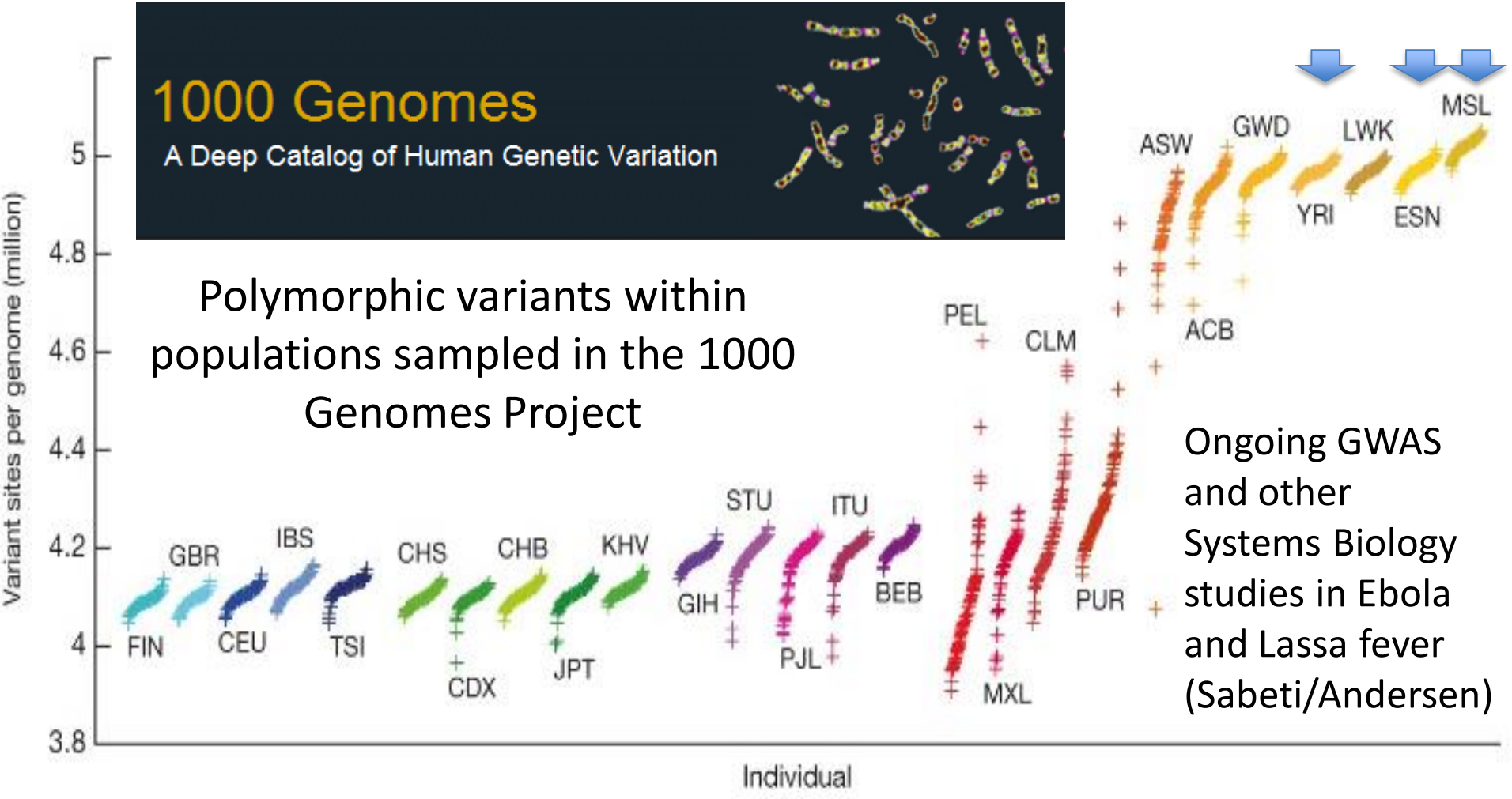
Dr. Donald S. Grant

Simbirie Jalloh

Bilateral Hearing loss in both Ebola and Lassa fever survivors

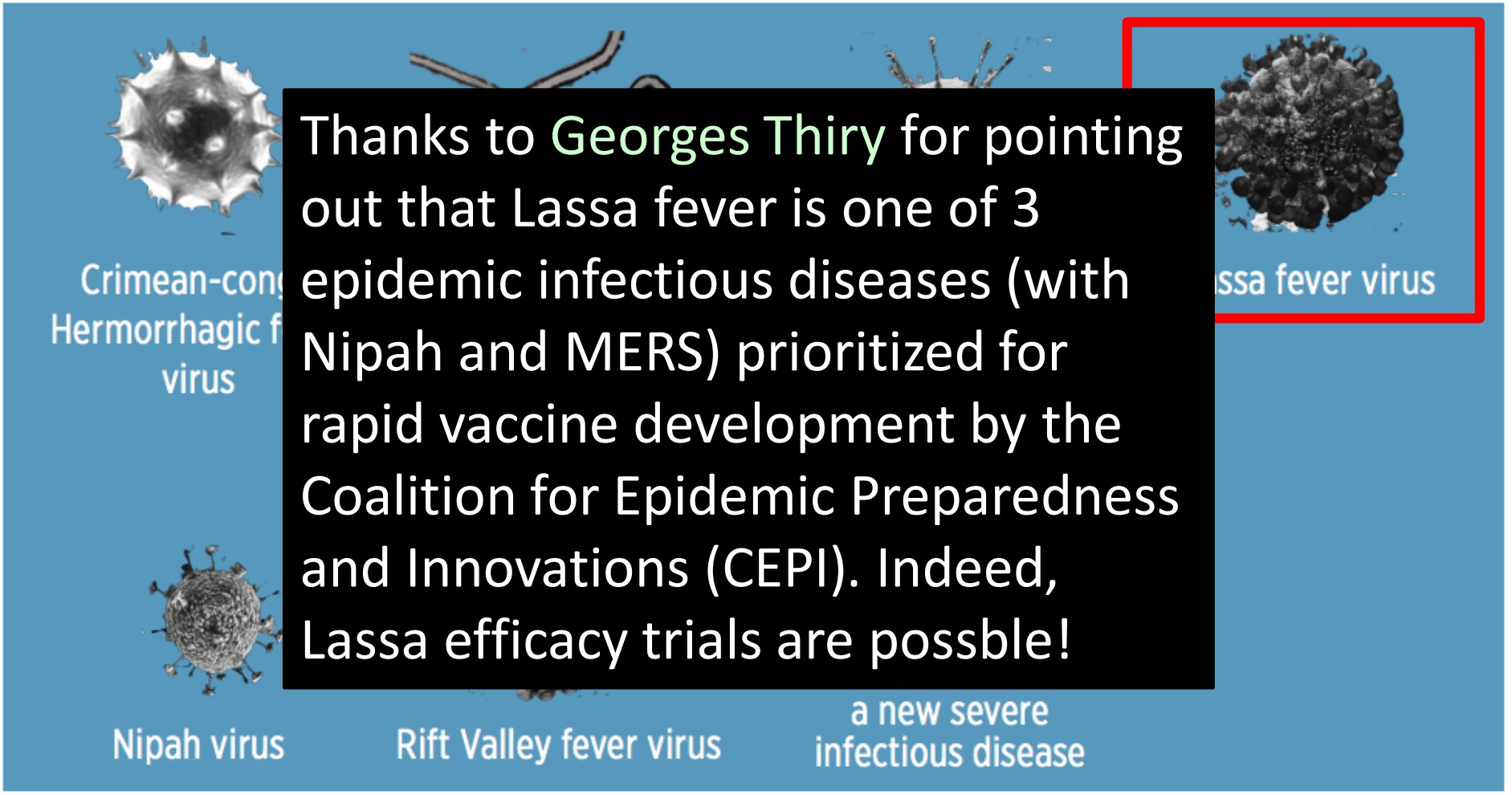


Hearing Loss Severity	Ebola Survivors (%) n = 342	Ebola Contacts n = 850	Lassa Survivors n = 57
Normal	222 (64.9)	685 (80.6)	35 (61.4)
Mild	105 (30.7)	149 (17.5)	5 (8.8)
Moderate	11 (3.2)	14 (1.7)	4 (5.3)
Severe	3 (0.9)	2 (0.2)	2 (3.5)
Profound	1 (0.3)	0 (0.0)	12 (21.1)



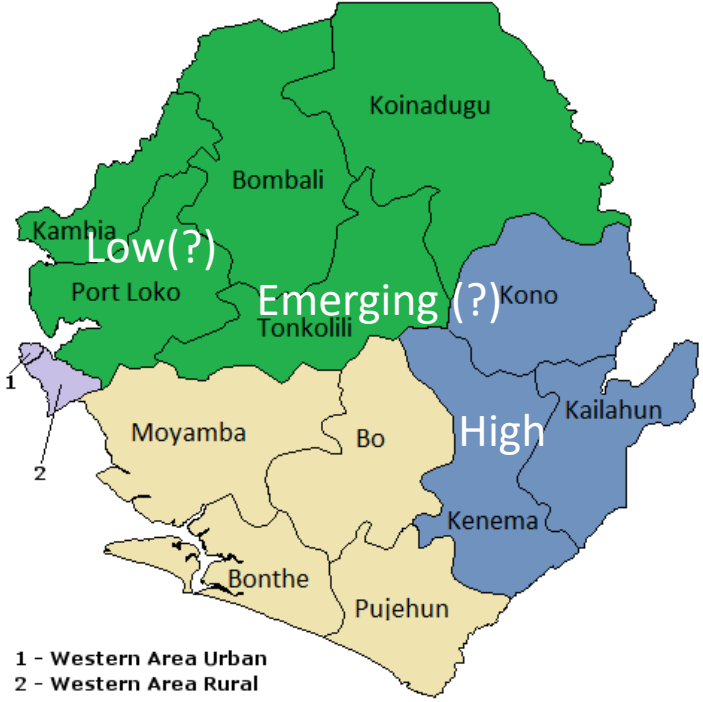
Nature 526, 68–74 (01 October 2015)

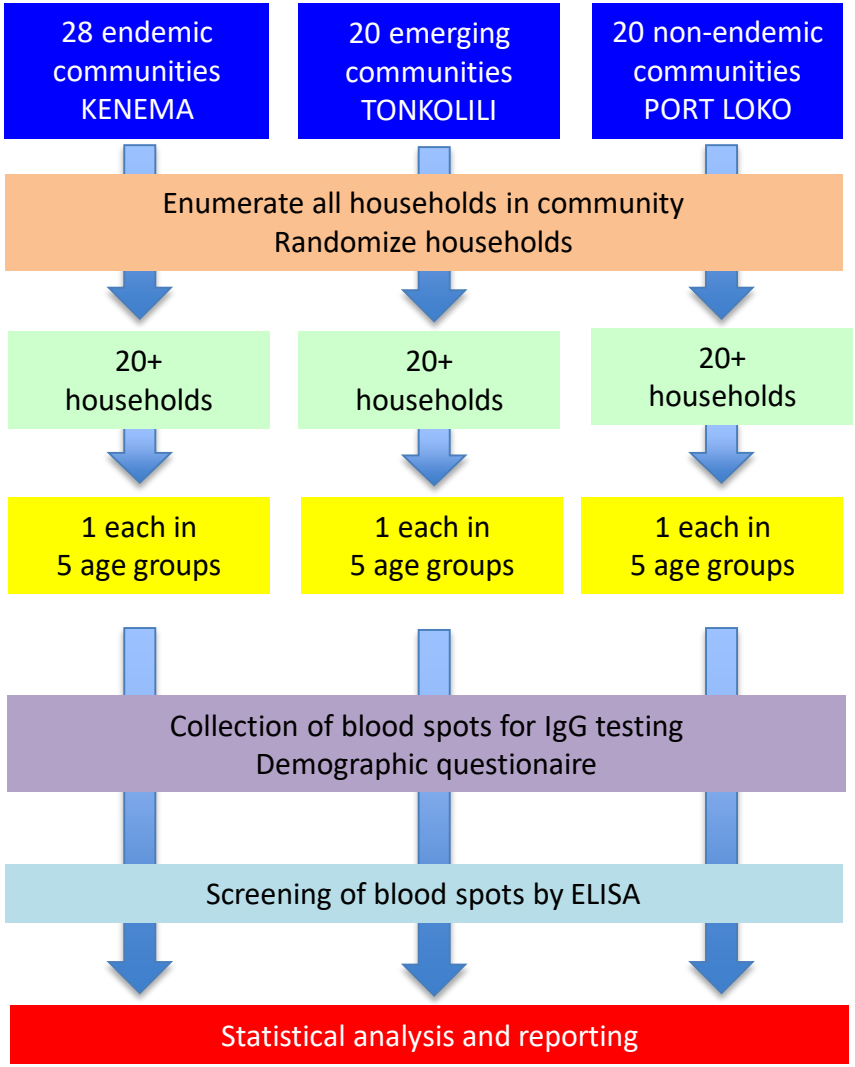
DISEASES TO BE URGENTLY ADDRESSED UNDER THE R&D BLUEPRINT



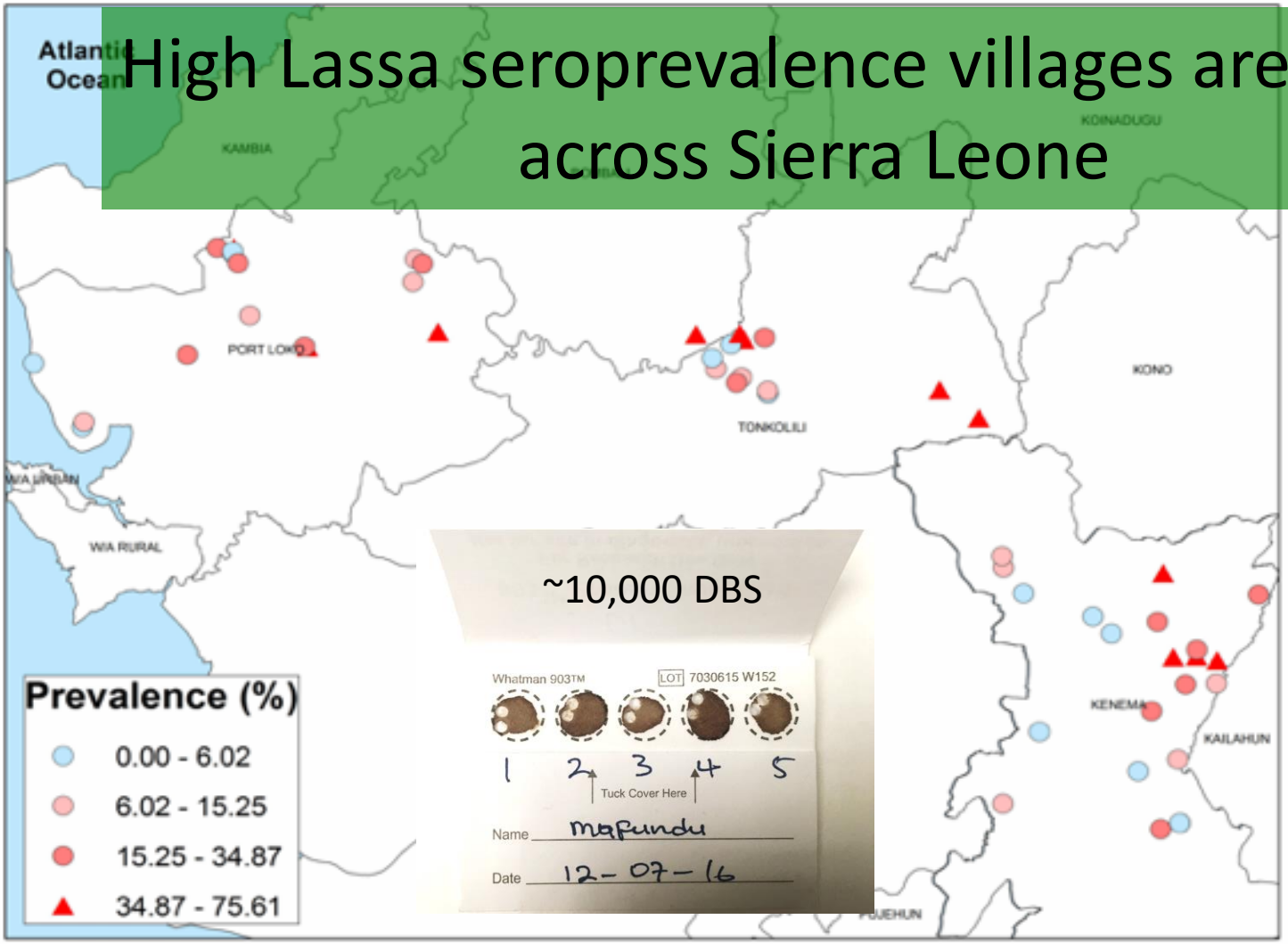
Thanks to Georges Thiry for pointing out that Lassa fever is one of 3 epidemic infectious diseases (with Nipah and MERS) prioritized for rapid vaccine development by the Coalition for Epidemic Preparedness and Innovations (CEPI). Indeed, Lassa efficacy trials are possble!

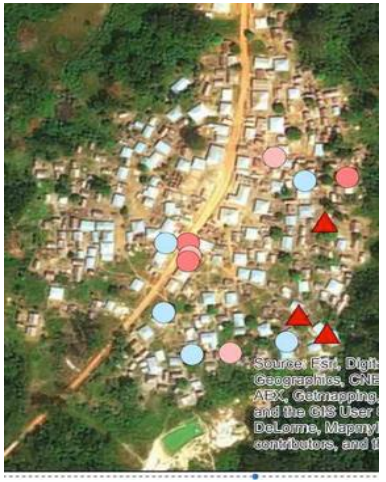
Ongoing antiLASV seroprevalence study in Sierra Leone





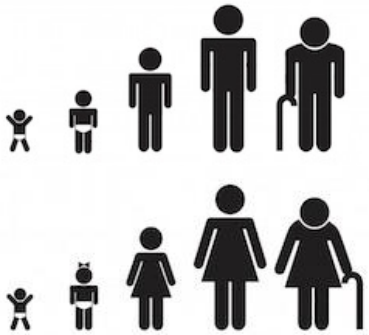
High Lassa seroprevalence villages are found across Sierra Leone



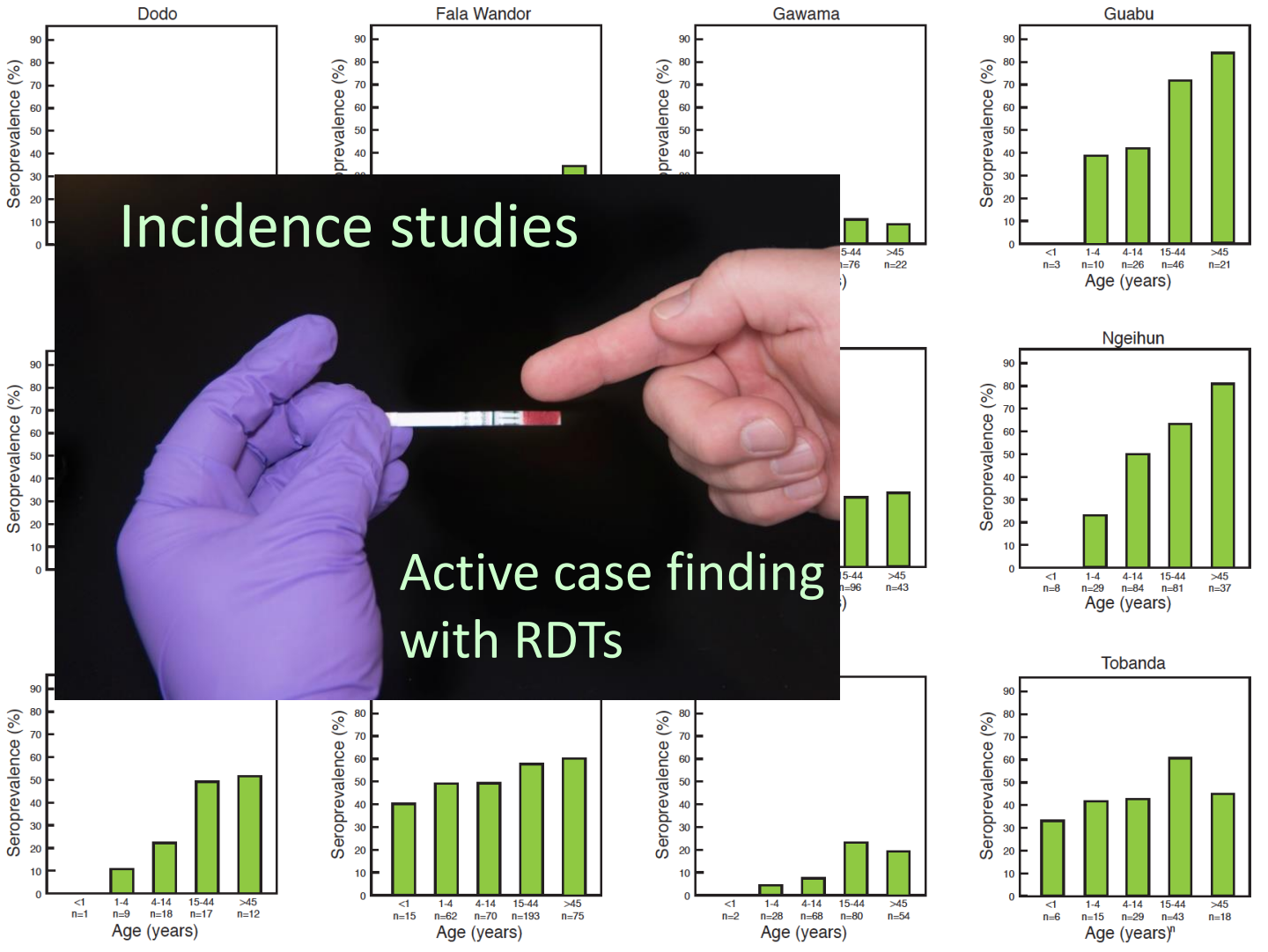


House level demographics and serology

LASV sero-prevalence by age



<1 1-4 5-14 15-44 >45



Kenema District: Gateway to the Go

GUINEA

SIERRA LEONE

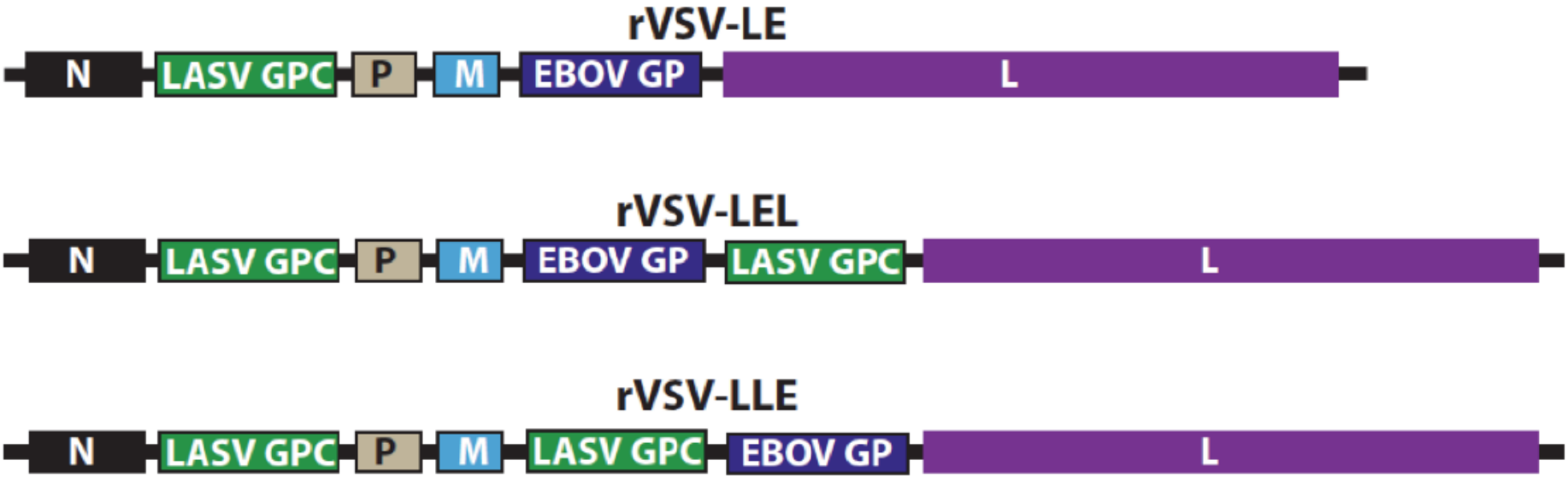
LIBERIA

COTE D'IVORE

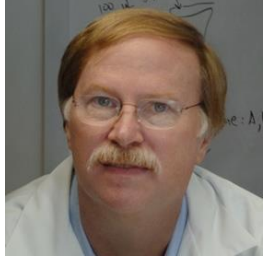
GHANA

TOGO

Single-vector, single injection, bivalent and trivalent rVSV vaccine candidates expressing stabilized LASV GPC and EBOV GP



VIRAL HEMORRHAGIC FEVER CONSORTIUM



Bob Garry - Tulane

Matt Boisen

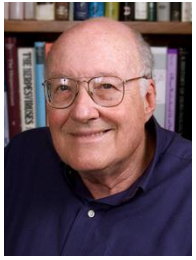
Luis Branco
Zalgen

James Robinson John Schieffelin
Tulane

Augustine
Goba
KGH

S. Humarr
Khan - KGH

Donald Grant KGH



Michael
Oldstone
Scripps

Mombu
Mamoh
KGH

Kristian
Andersen
Scripps

Erica
Saphire
&Kate
Hastie
Scripps

Pardis Sabeti
Harvard/
Broad

Tom Geisbert
Chad Mire & Bob
Cross UTMB

Christian Happi
Redeemers

In memoriam…


A
In Loving Memory of Dr.
SHEIKH H. KHAN
Born: 11th September 1974.
Died: 29th July 2014.
Former. Tulane-Lassa fever VHF-Doctor
Kenema Goverment Hospital RIP
Photo credit:
Pardis Sabeti


B
Photo credit:
Kristian Andersen


Mbalu
Fonnie


Alice
Kovoma


Mohamed
Fullah


Dr S. Humarr
Khan