Systems Vaccinology

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Global Vaccine Research and Immunization Forum

Hyatt Regency, Bethesda, Washington DC, March 4 – 6, 2014

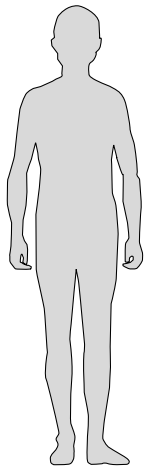
Topics

1. Systems Vaccinology: using the tools of systems biology to identify predictors of vaccine efficacy, and to discover new insights about protective immunity.

2. Gnostic predictors: extracting biological meaning from signatures.

3. Relevance for clinical trials

Vaccines as tools to probe the human immune system



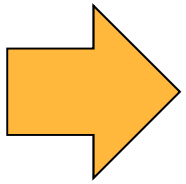
Young Healthy adults

Infants

Elderly

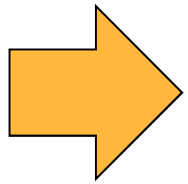
Malnourished

Immunocompromised

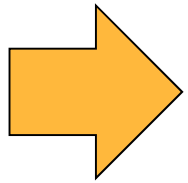


Yellow Fever vaccine
Influenza vaccines
Shingles vaccine
Pneumococcal vaccines
Meningococcal vaccines
Malaria vaccine
Tularemia vaccine

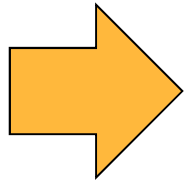
Measuring vaccine immunity



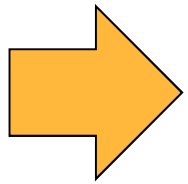
Serologic response



Flow cytometry
CyTOF



Cytokine assays

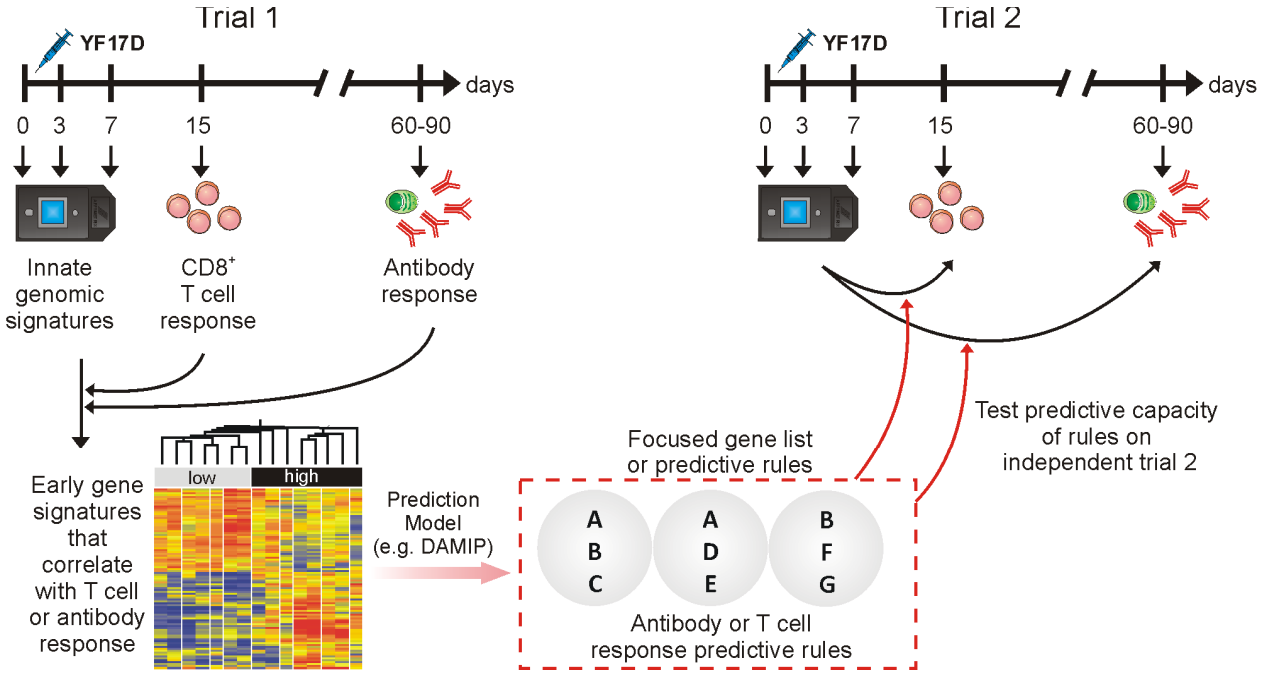


Transcriptomics
Micro RNAs
Metabolomics

nature immunology

Systems biology approach predicts immunogenicity of the yellow fever vaccine in humans

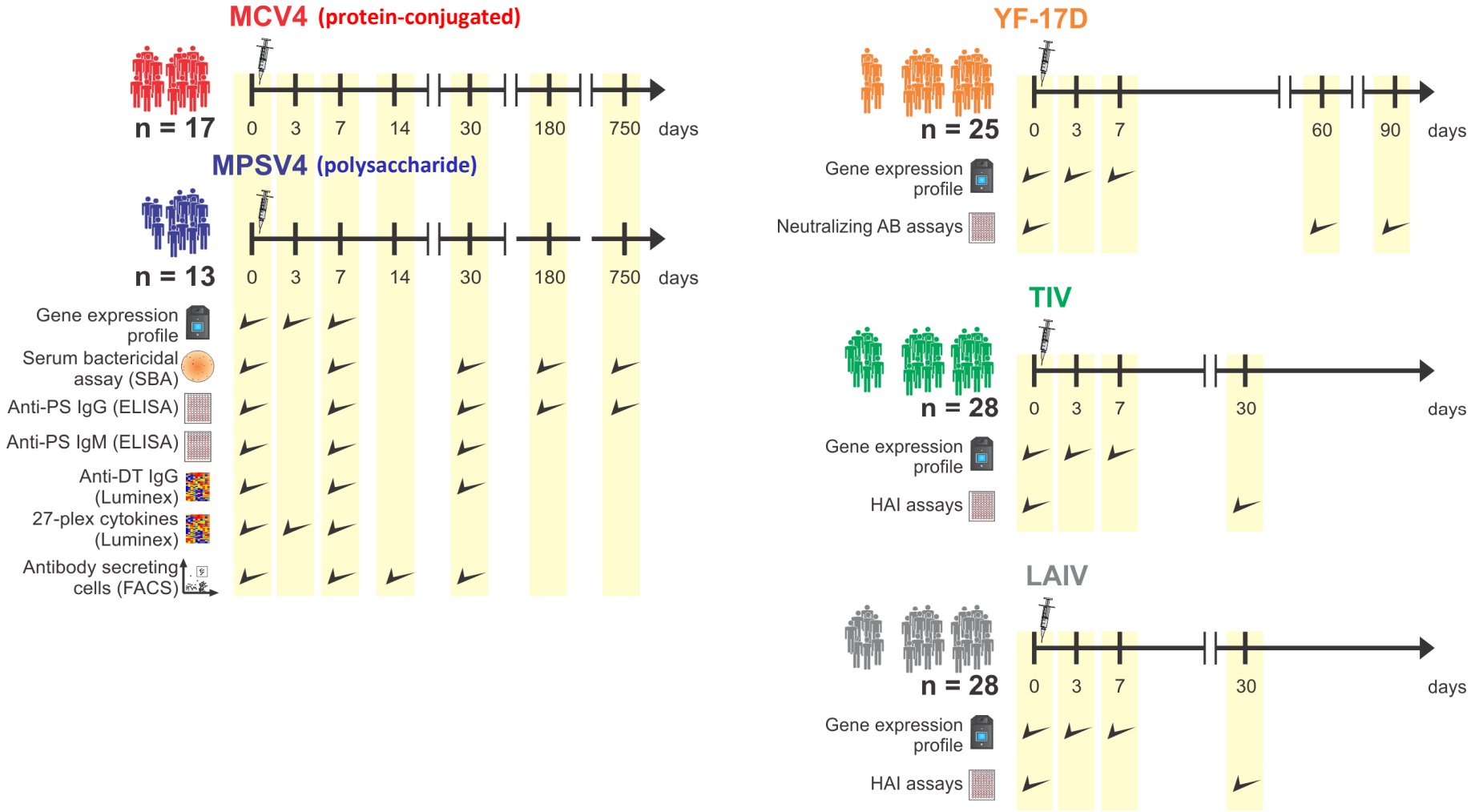
Troy D Querec[1,8], Rama S Akondy[1,8], Eva K Lee[2], Weiping Cao[1], Helder I Nakaya[1], Dirk Teuwen[3], Ali Pirani[4], Kim Gernert[4], Jiusheng Deng[1], Bruz Marzolf[5], Kathleen Kennedy[5], Haiyan Wu[5], Soumaya Bennouna[1], Herold Oluoch[1], Joseph Miller[1], Ricardo Z Vencio[5], Mark Mulligan[1,6], Alan Aderem[5], Rafi Ahmed[1] & Bali Pulendran[1,7]



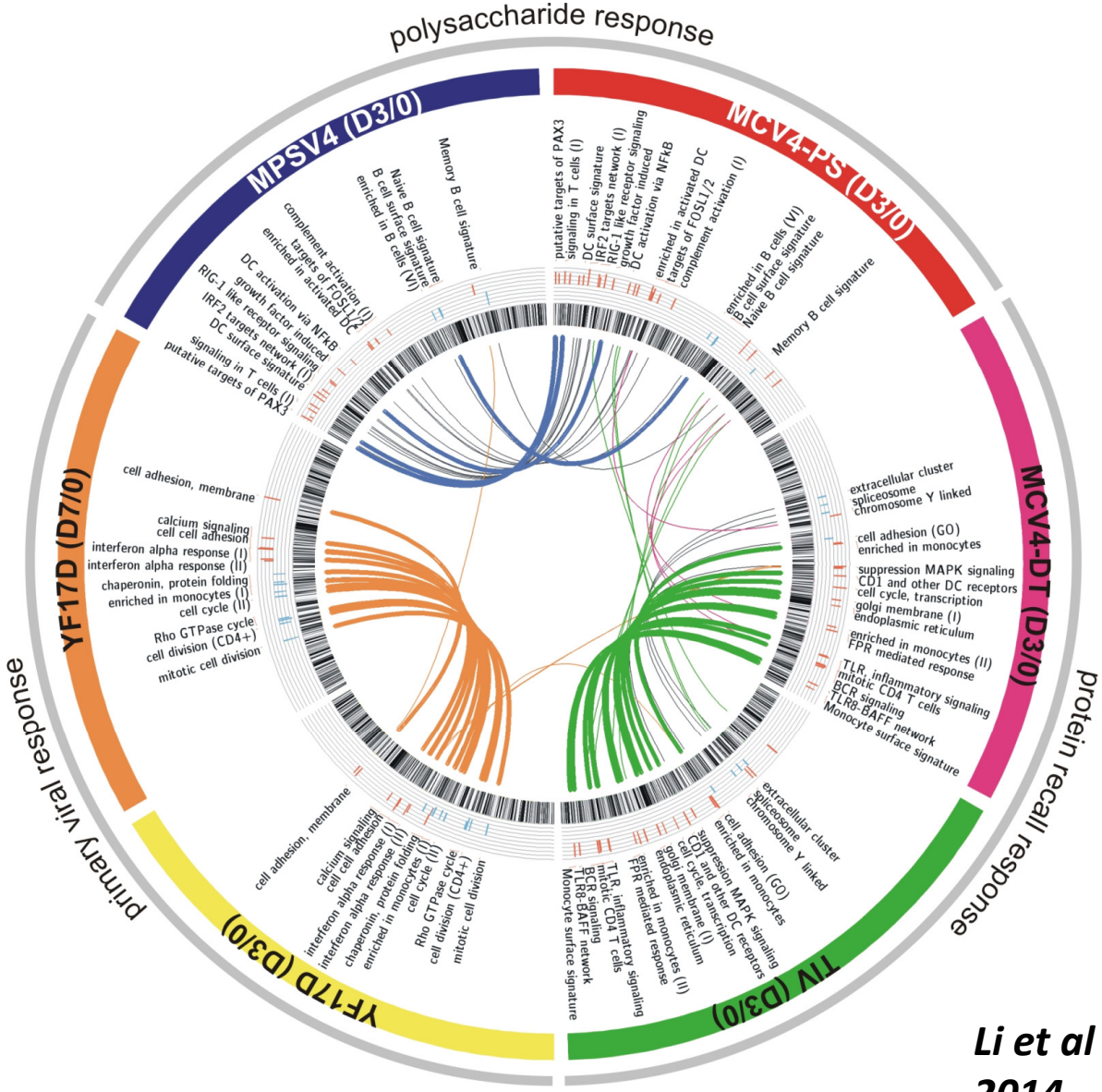
Systems biology of vaccination for seasonal influenza in humans

Helder I Nakaya[1,2], Jens Wrammert[1,3], Eva K Lee[4], Luigi Racioppi[5,6], Stephanie Marie-Kunze[1,2], W Nicholas Haining[7], Anthony R Means[6], Sudhir P Kasturi[1,2], Nooruddin Khan[1,2], Gui-Mei Li[1,3], Megan McCausland[1,3], Vibhu Kanchan[1,3], Kenneth E Kokko[8], Shuzhao Li[1,2], Rivka Elbein[9], Aneesh K Mehta[9], Alan Aderem[10], Kanta Subbarao[11], Rafi Ahmed[1,3] & Bali Pulendran[1,2,12]

Is there a “universal correlate”of antibody responses to any vaccine?



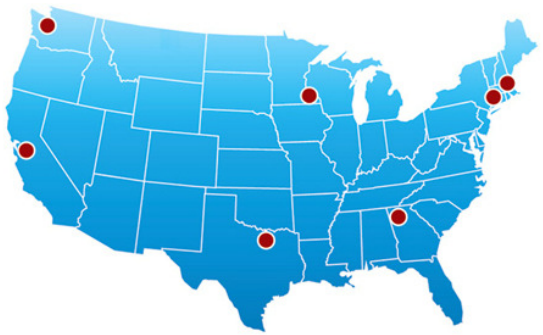
Day 3/0 antibody correlation



Li et al – Nature Immunology, 2014

HIPC Projects

Human Immunology Project Consortium



Baylor Research Institute

PRIMARY PROJECTS
PILOT PROJECTS
IOF PROJECTS

Project #:1U19AI089987-01

Title: Systems Analysis of Vaccine Responses in Healthy and Hyporesponsive Humans

PI: A. Karolina Palucka

Stanford University

PRIMARY PROJECTS
PILOT PROJECTS
IOF PROJECTS

Project #:1U19AI090019-01

Title: Vaccination and Infection: Indicators of Immunological Health and Responsiveness

PI: Mark M. Davis

Website: iti.stanford.edu

Yale University

PRIMARY PROJECTS
PILOT PROJECTS
IOF PROJECTS

Project #:1U19AI089992-01

Title: Defining Signatures for Immune Responsiveness by Functional Systems Immunology

PI: David A. Hafler (Contact), Erol Fikrig

Mayo Clinic

PRIMARY PROJECTS

Project #:1U01AI089859-01

Title: Bioinformatics Approach to Influenza A/H1N1 Vaccine Immune Profiling

PI: Gregory A. Poland

Emory University

PRIMARY PROJECTS
PILOT PROJECTS
IOF PROJECTS

Project #:1U19AI090023-01

Title: Systems Biological Analysis of Innate and Adaptive Responses to Vaccination

PI: Bali Pulendran

Dana-Farber Cancer Institute

PRIMARY PROJECTS
PILOT PROJECTS
IOF PROJECTS

Project #:1U01AI090043-01

Title: Crossprotective CTL Against Influenza

PI: Ellis L Reinherz

Seattle Biomedical Research Institute

PRIMARY PROJECTS
IOF PROJECTS

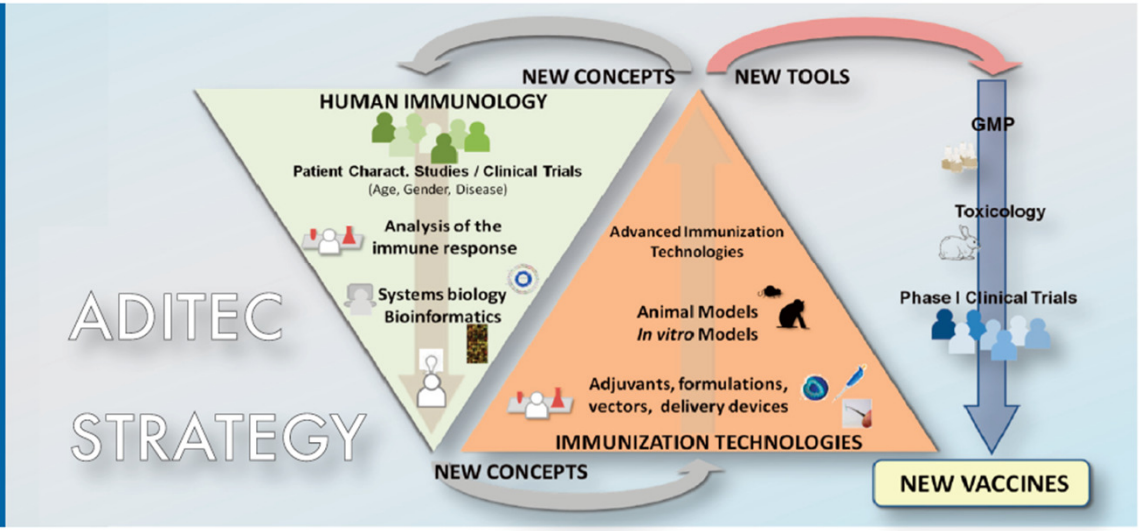
Project #:1U19AI089986-01

Title: Immune Profile and Network Analysis of Malaria Infection and Vaccination

PI: Kenneth D. Stuart (Contact), Margaret Juliana McElrath, Ruobing Wang

ADITEC Kick-off Meeting

Siena, October 7-8, 2011



Systems Immunology Consortium

BILL & MELINDA GATES foundation

Seattle BioMed
Freedom from Infectious Disease

EMORY UNIVERSITY

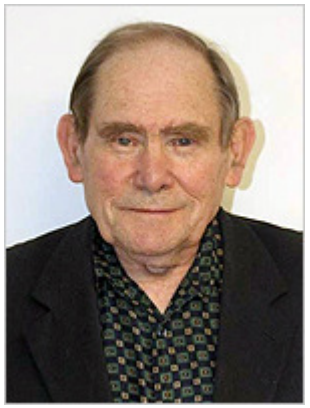
University of Cape Town · Universiteit Kaapstad · Yunivesithi yaseKapa

LELAND STANFORD JUNIOR UNIVERSITY
DIE LUFT DER FREIHEIT WEHT
1891

Goal:
Create a unified research platform for the analysis of vaccine trials and natural history studies

We are drowning in a sea of data and thirsting for knowledge

Low input,
High throughput,
No output Biology?



Sydney Brenner

What are we learning?

1. The impact of nutrient sensing and metabolic control on vaccine immunity

2. Control of vaccine immunity by the intestinal microbiome

nature immunology

Systems biology approach predicts immunogenicity of the yellow fever vaccine in humans

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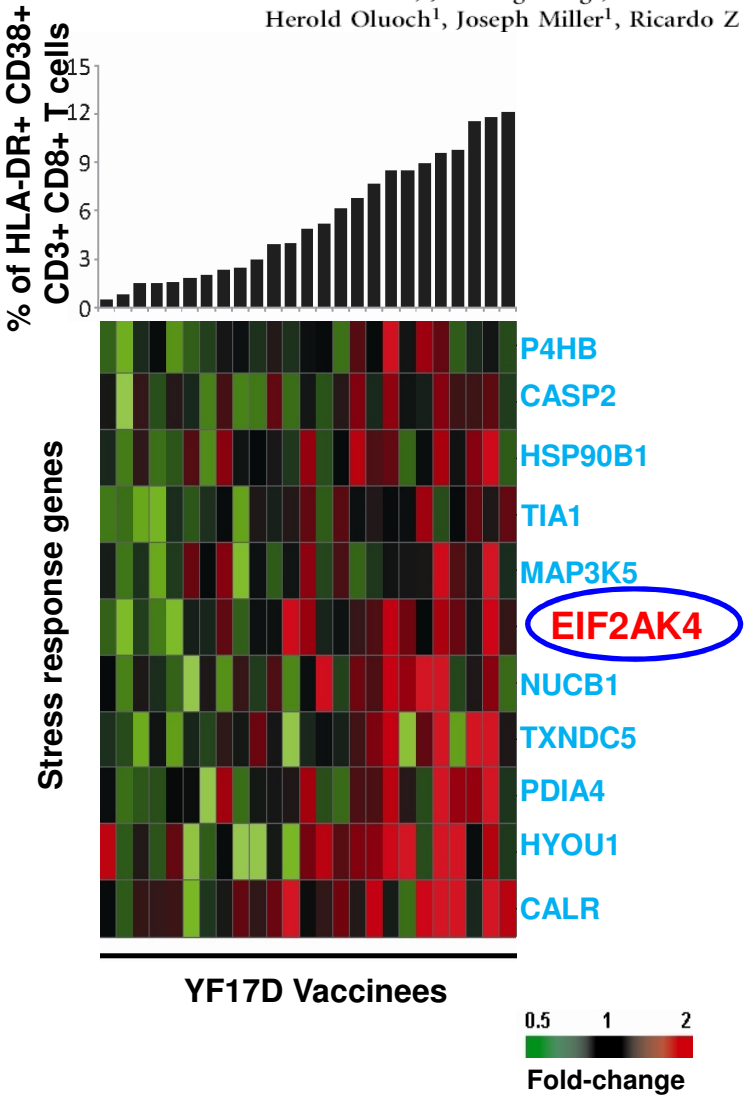
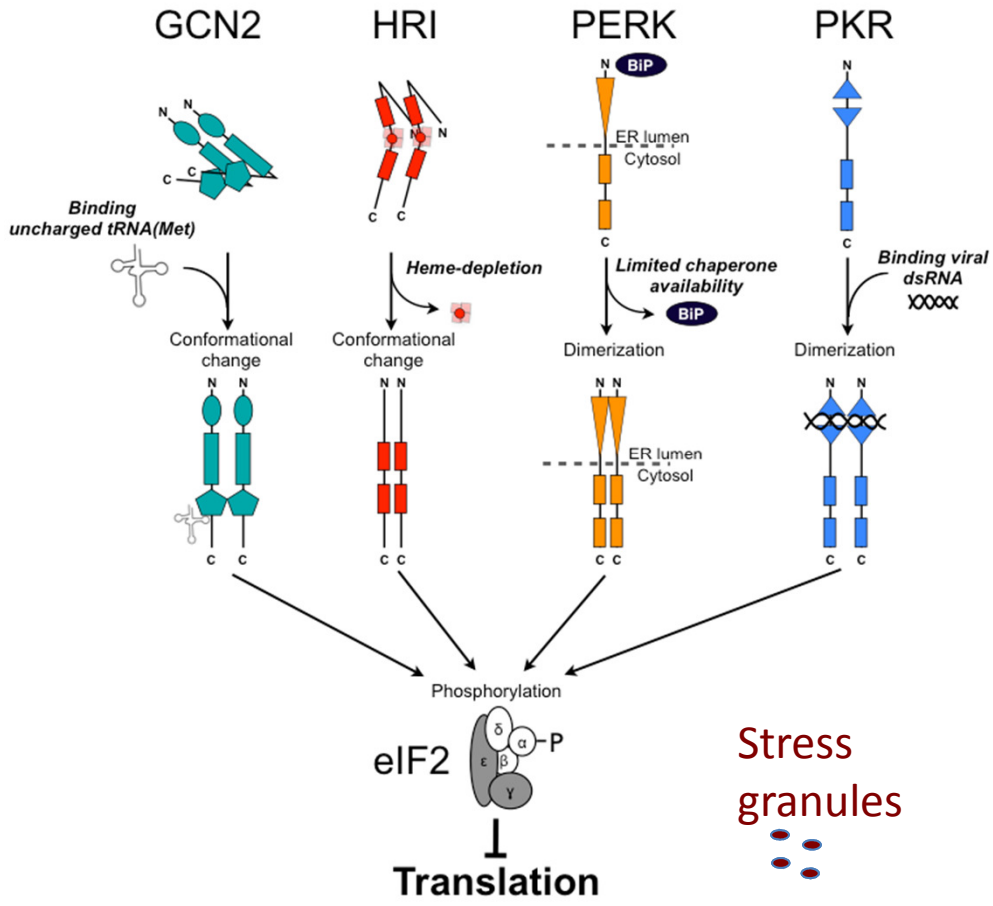




Science
AAAS

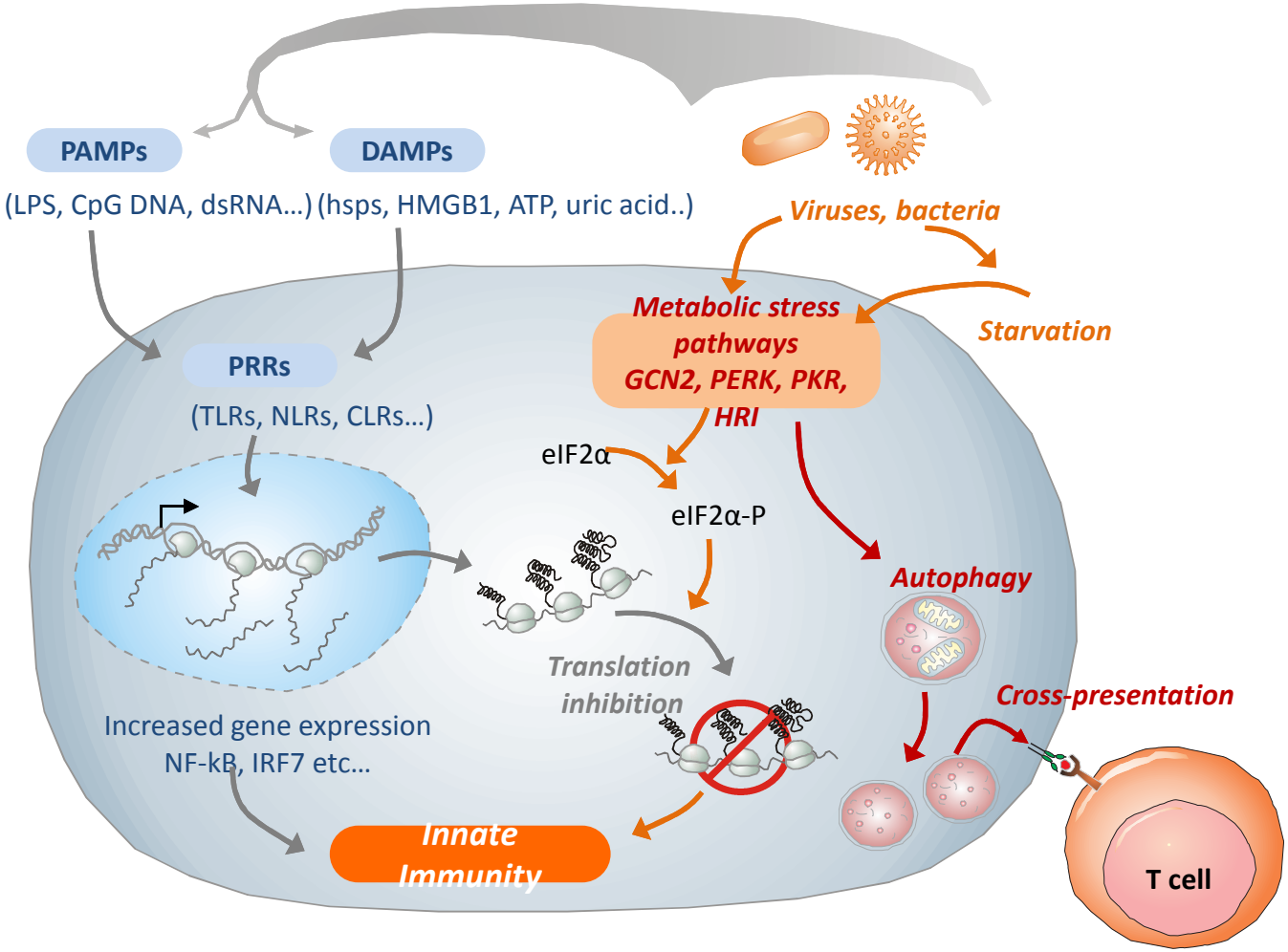
Vaccine Activation of the Nutrient Sensor GCN2 in Dendritic Cells Enhances Antigen Presentation

Rajesh Ravindran *et al.*

Science **343**, 313 (2014);
DOI: 10.1126/science.1246829

Rajesh Ravindran,[1]* Nooruddin Khan,[1,2]* Helder I. Nakaya,[1,3] Shuzhao Li,[1] Jens Loebbermann,[1] Mohan S. Maddur,[1] Youngja Park,[4] Dean P. Jones,[5] Pascal Chappert,[6,7] Jean Davoust,[6,7] David S. Weiss,[8] Herbert W. Virgin,[9] David Ron,[10] Bali Pulendran[1,3]†

The yellow fever vaccine YF-17D is one of the most successful vaccines ever developed in humans. Despite its efficacy and widespread use in more than 600 million people, the mechanisms by which it stimulates protective immunity remain poorly understood. Recent studies using systems biology approaches in humans have revealed that YF-17D–induced early expression of general control nonderepressible 2 kinase (GCN2) in the blood strongly correlates with the magnitude of the later CD8$^+$ T cell response. We demonstrate a key role for virus-induced GCN2 activation in programming dendritic cells to initiate autophagy and enhanced antigen presentation to both CD4$^+$ and CD8$^+$ T cells. These results reveal an unappreciated link between virus-induced integrated stress response in dendritic cells and the adaptive immune response.



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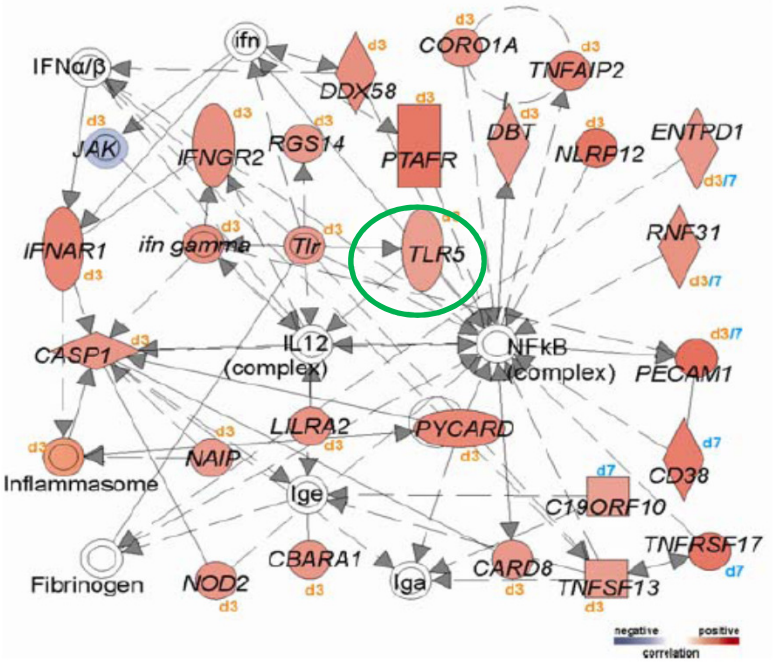
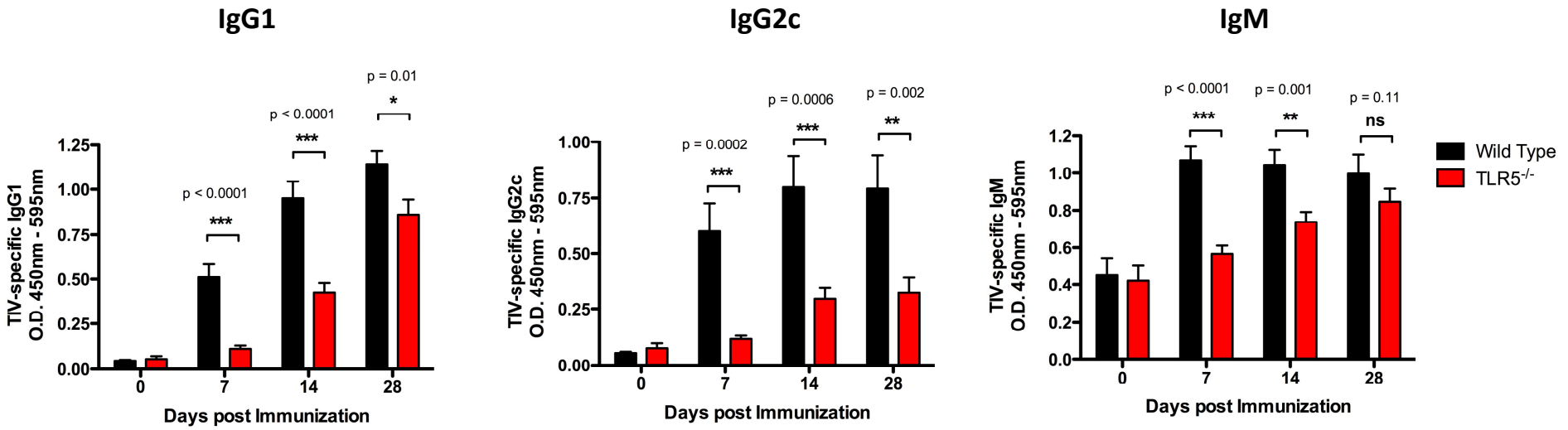
VOLUME 12 NUMBER 8 AUGUST 2011 NATURE IMMUNOLOGY

Early expression of TLR5 is positively correlated with productive antibody responses against influenza HA following vaccination with the seasonal inactivated flu vaccine



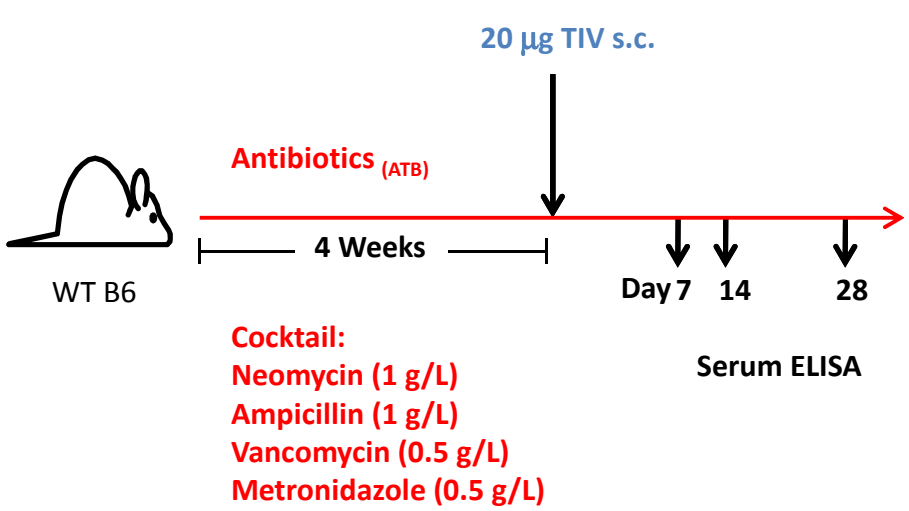
Natural Ligand for TLR5 is Flagellin

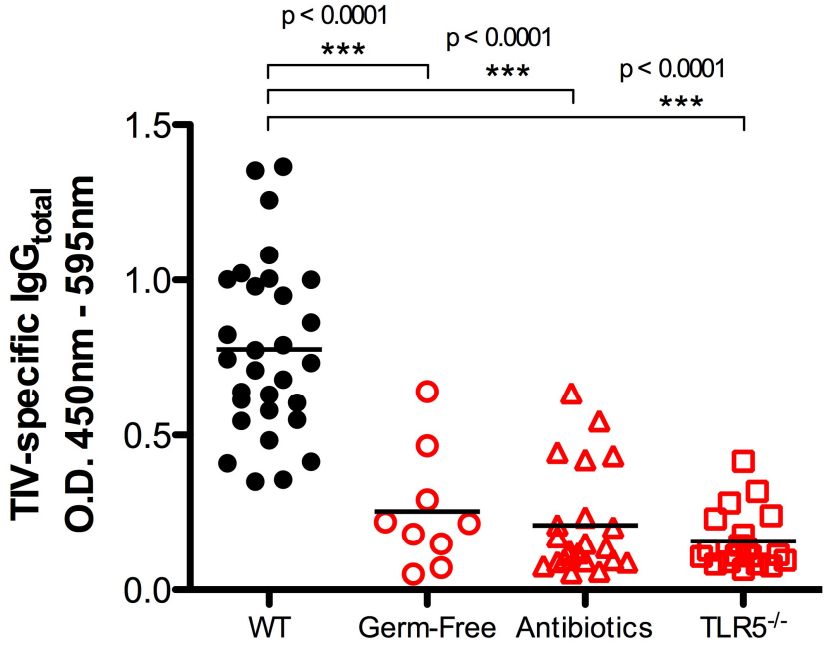
Antibody Response to vaccination with flu vaccination is dependent on TLR5



BUT, the flu vaccine itself lacks the capacity to stimulate TLR5 signaling

Is there a role for commensal microflora in mediating vaccine responses?

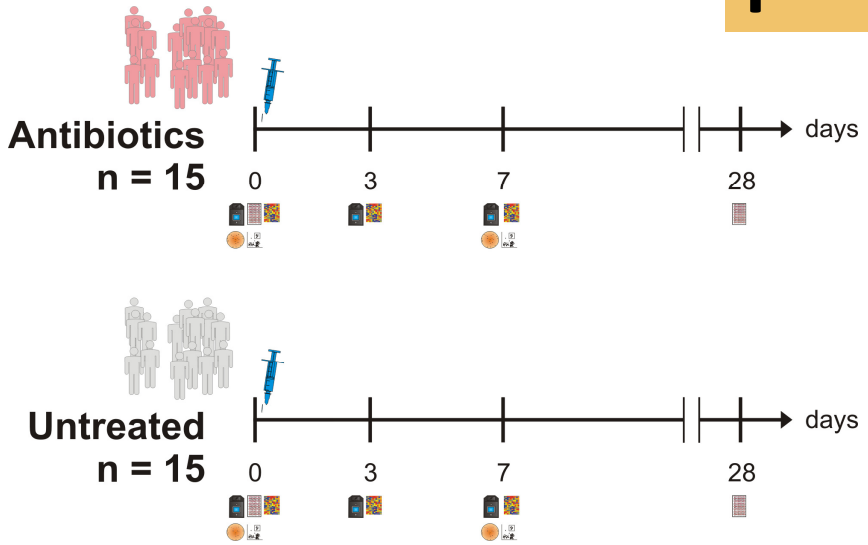




Implications for Human Vaccination Programs?

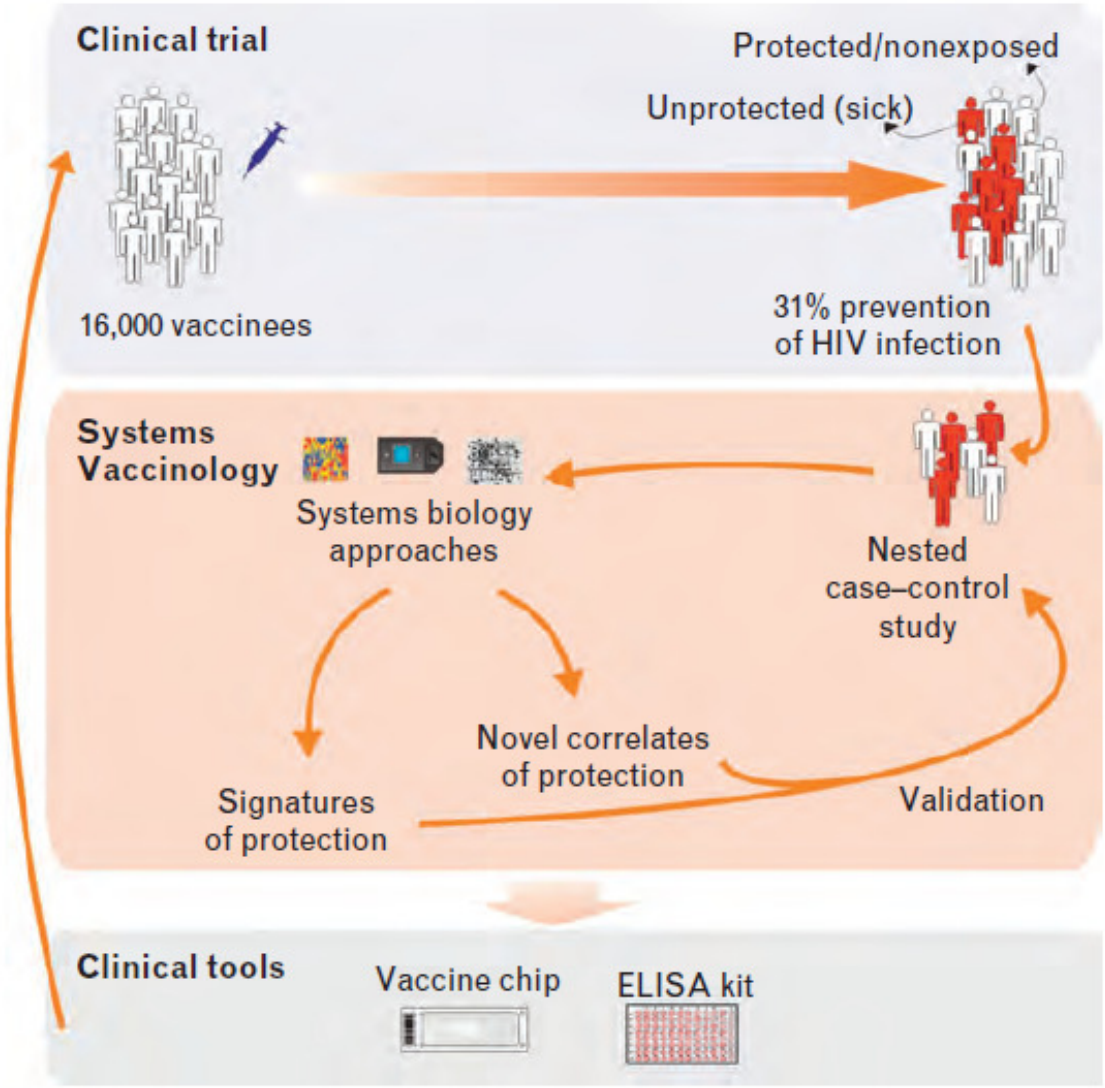
Vaccine Efficacy

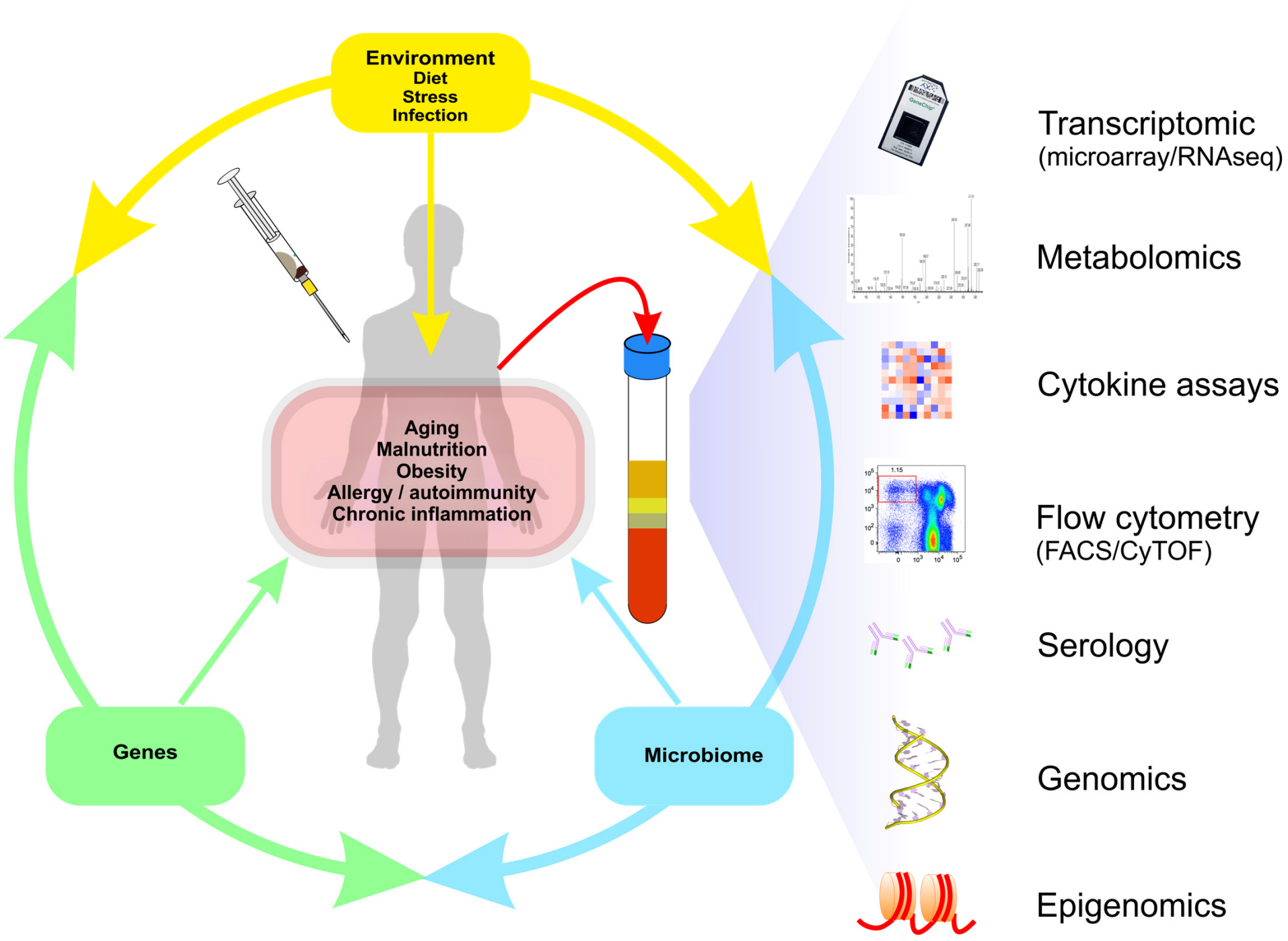
TLR5 polymorphisms



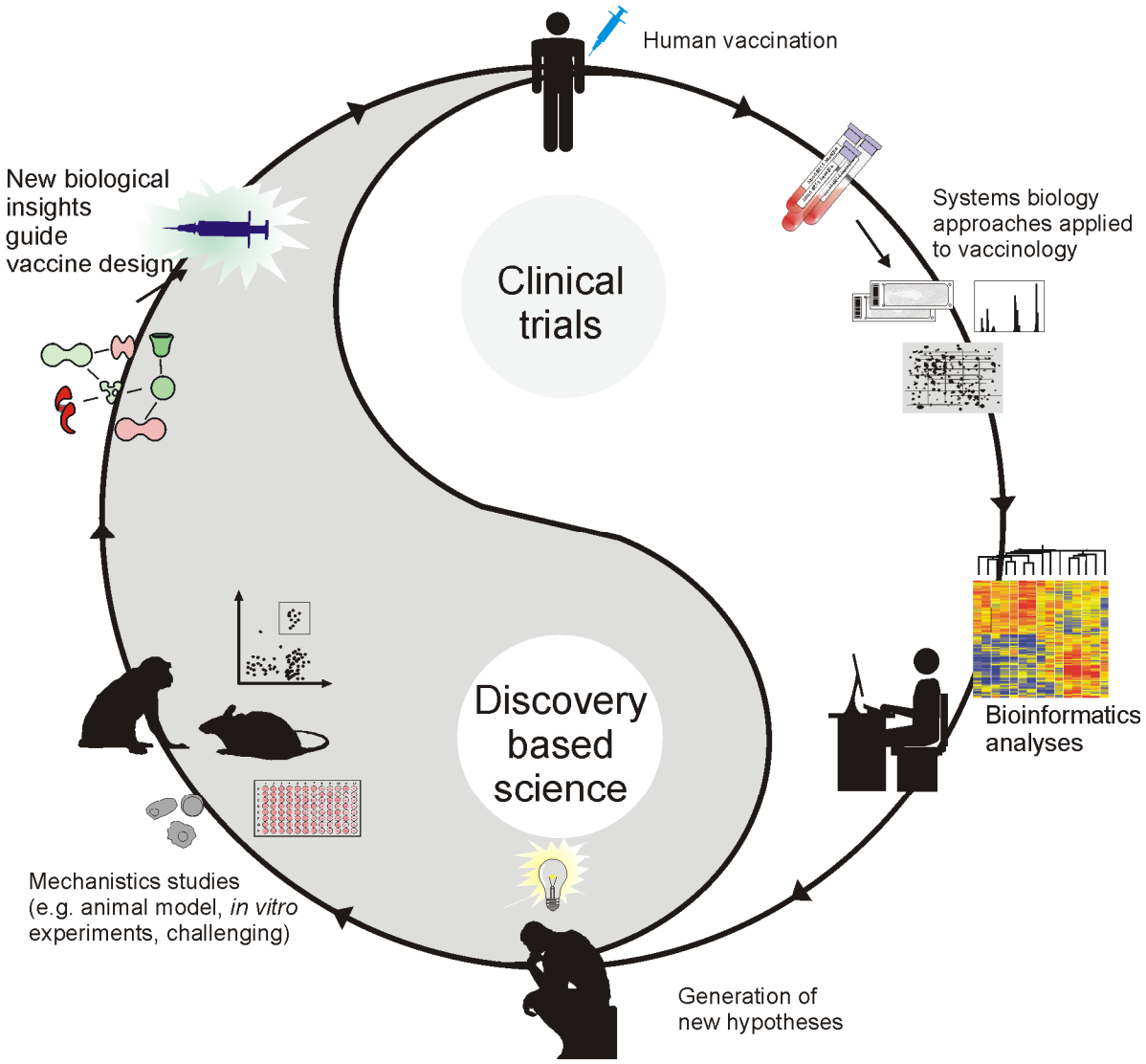
HAI d0 and d28
NGS – Microbiome (stool)

Potential applications for clinical trials




Environment
Diet
Stress
Infection
Aging
Malnutrition
Obesity
Allergy / autoimmunity
Chronic inflammation
Genes
Microbiome
Transcriptomic
(microarray/RNAseq)
Metabolomics
Cytokine assays
Flow cytometry
(FACS/CyTOF)
Serology
Genomics
Epigenomics

A framework for Systems Vaccinology



Immunity 2010

Acknowledgements

Emory Vaccine Center

Troy Querec

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Mark Mulligan

Rouphael Nadine

Francois Villinger

Traci Legere

Zarpheen Jinnah Sher

Eric Hunter

Cynthia Derdeyn

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Peng Xiao

Sharmila Reddy

Georgia Tech

Eva K. Lee

Dana-Farber

Nick Haining

NIAID-NIH

Kanta Subbarao

Yerkes Veterinary Staff:

Christopher Souder

Robert Sheffield

John Wambua

Carmen Nash

Stephanie Ehnert

National Institutes of Health

HIPC U19, CCHI U19 and IPIRC Flu center

BILL & MELINDA GATES foundation