

The Human Vaccines Project: Innovations to Accelerate Next Generation Vaccine Development

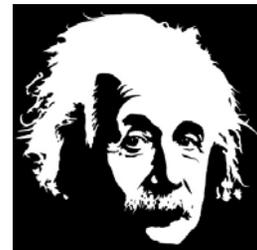
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“Insanity: doing the same thing over and over again and expecting different results”

-Albert Einstein



The Problem

The Old Paradigm is Failing

Money: \$ Billions

Time: Decades

Low Probability of Success

Opportunity Costs

A New Approach is Needed

The old paradigm of empiric-based vaccine development is not effective for major global diseases of the 21st century

Failed Vaccine and Immunotherapeutic Efficacy Trials

Last Decade:

- ❖ HIV
- ❖ TB
- ❖ Herpes Simplex
- ❖ Staph Aureus
- ❖ Melanoma
- ❖ Pancreatic Cancer
- ❖ Renal Cancer
- ❖ Prostate Cancer
- ❖ Others

Major Global Diseases for Which Globally Effective Vaccines Do Not Currently Exist....and **VERY FEW ARE LOW HANGING FRUIT**

Viral	Bacterial	Parasitic	Cancers	Other
Cytomegalovirus	Campylobacter	Chagas Disease	Breast Cancer	Allergies
Dengue, Chikungunya,	Chlamydia	Leishmaniasis	Colon Cancer	Alzheimer's
Epstein Barr	Helicobacter pylori	Malaria	Lung Cancer	Autoimmune Diseases
Hepatitis C	Shigella	Schistosomiasis	Melanoma	Metabolic Diseases
Herpes Simplex	Staphylococcus	Other Parasitic Diseases	Pancreatic Cancer	
HIV	Streptococcus A, B		Prostate Cancer	
Universal Influenza	Tuberculosis		Renal Cancer	
Respiratory Syncytial Virus	Other: Urinary Tract Infections		Other Cancers	
Rhinovirus				
Other Emerging Viral Diseases e.g. Ebola, Marburg; Zika; Lassa				

Vaccine Development is impeded by Pathogen-Specific AND Common (Trans-Vaccinology) Issues

- **Pathogen Specific Issues**
 - Antigen(s) required for protection?
 - Correlates of protection?

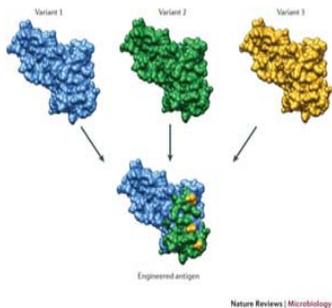
- **Trans-Vaccinology Issues**
 - Limitations of animal models
 - Limited understanding of human immune responses to vaccines
 - Population specific issues

Human Vaccines Project

The Opportunity

Technological revolution in the past decade has generated new tools that offer the potential to usher in a new era in global disease prevention

Structural and Computational Biology



Genomics and Immune Monitoring



Bioinformatics and Systems Biology



Immune-driven clinical breakthroughs

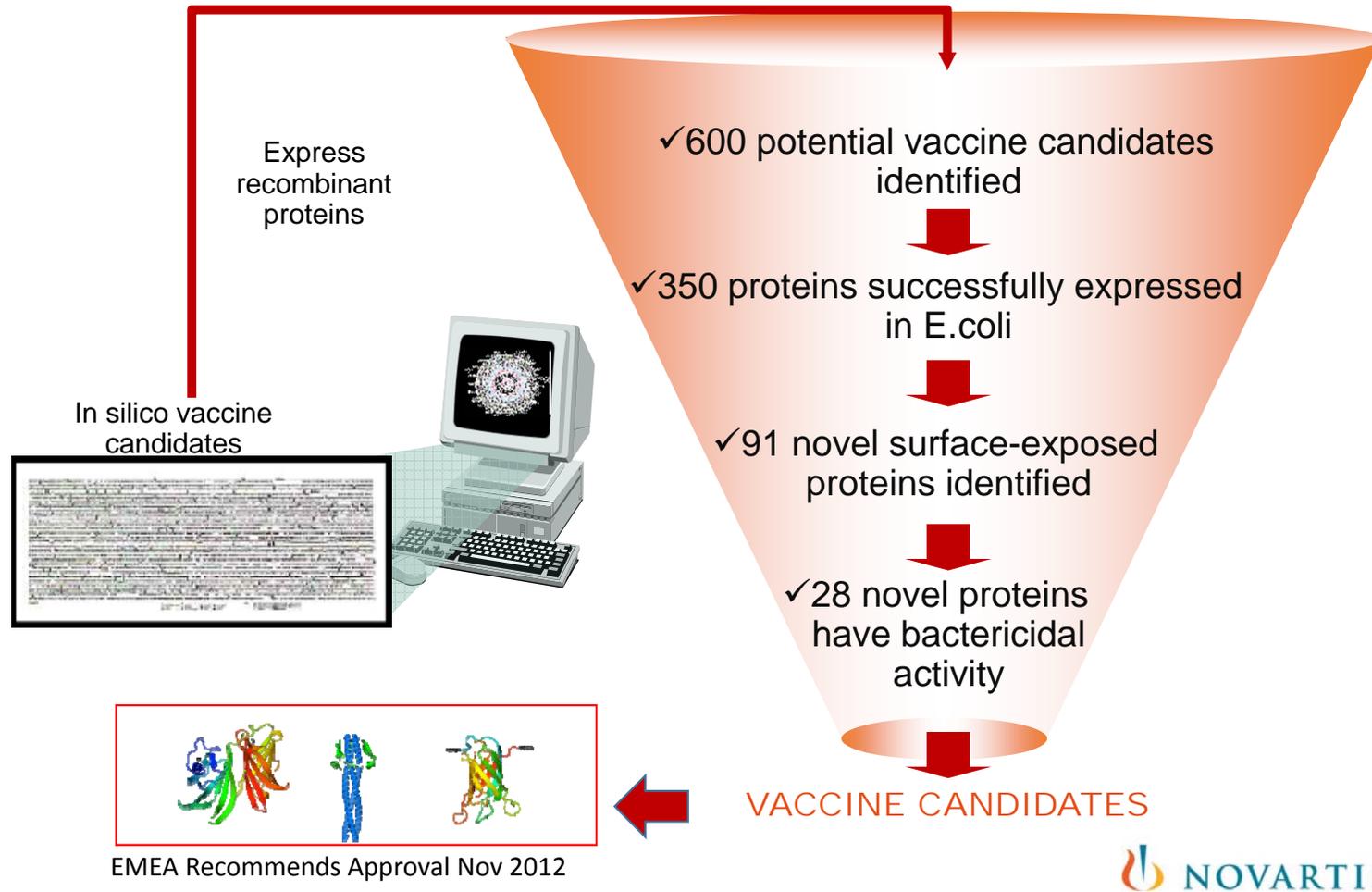


Antigen Discovery

Reverse Vaccinology; MassSpec-Immuno-peptidomics; Novel Platforms for Rapid Screening e.g. mRNA; Structural Vaccinology;

Vaccine Discovery Technologies

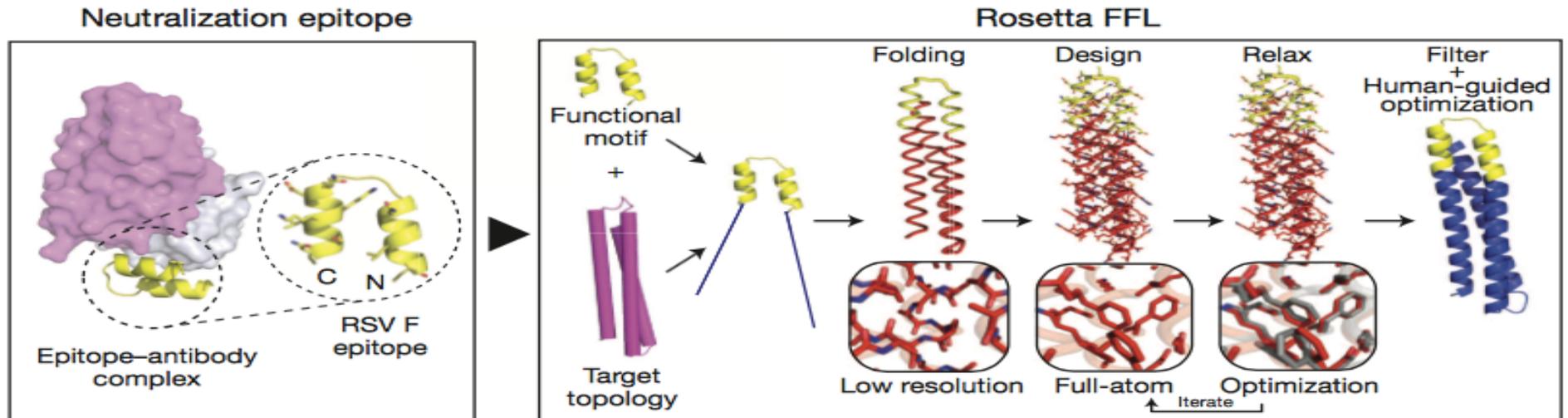
Reverse Vaccinology: Meningitis B



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Structural Vaccinology

Computational Biology: From Structure to Vaccine



Correia BE et al., Proof of principle for epitope-focused vaccine design. *Nature* 2014; 507:201-6.

Correlates of Protection

Human Challenge Models

Malaria Challenge Model in Humans Accelerates Malaria Vaccine R&D

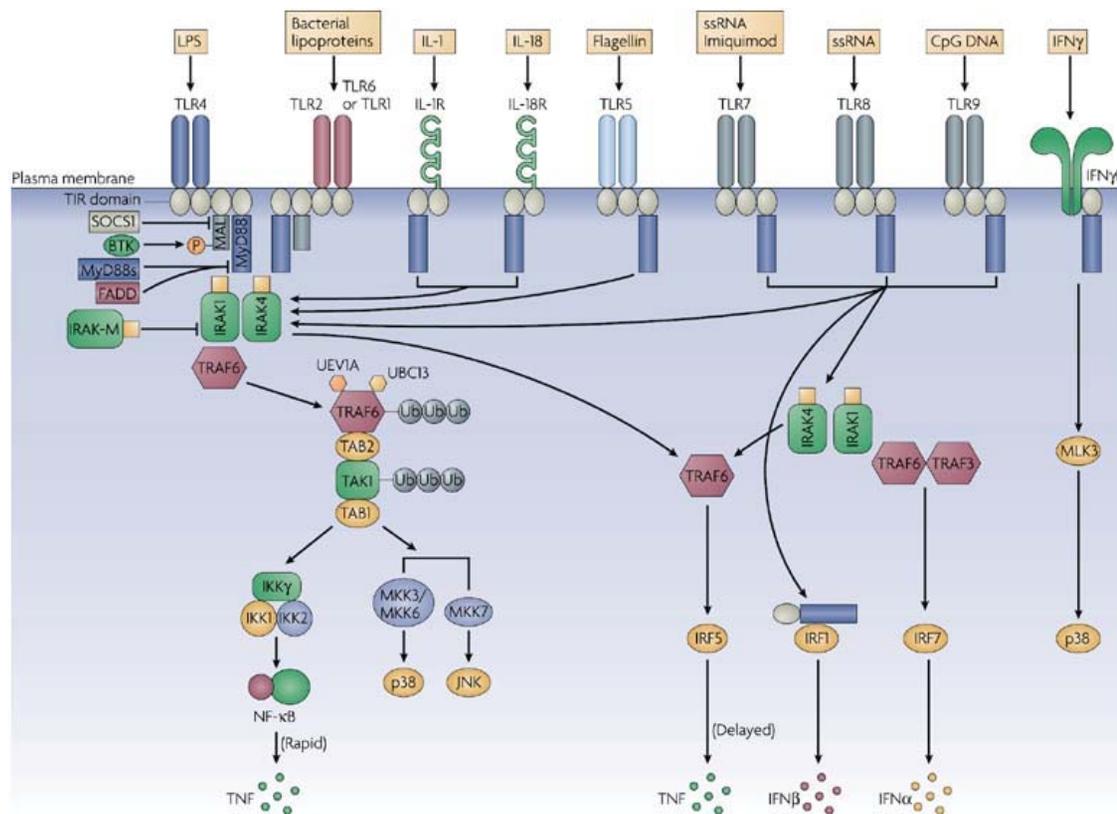


Novel Adjuvants

TLR-based Adjuvant Design

Vaccine Discovery Technologies

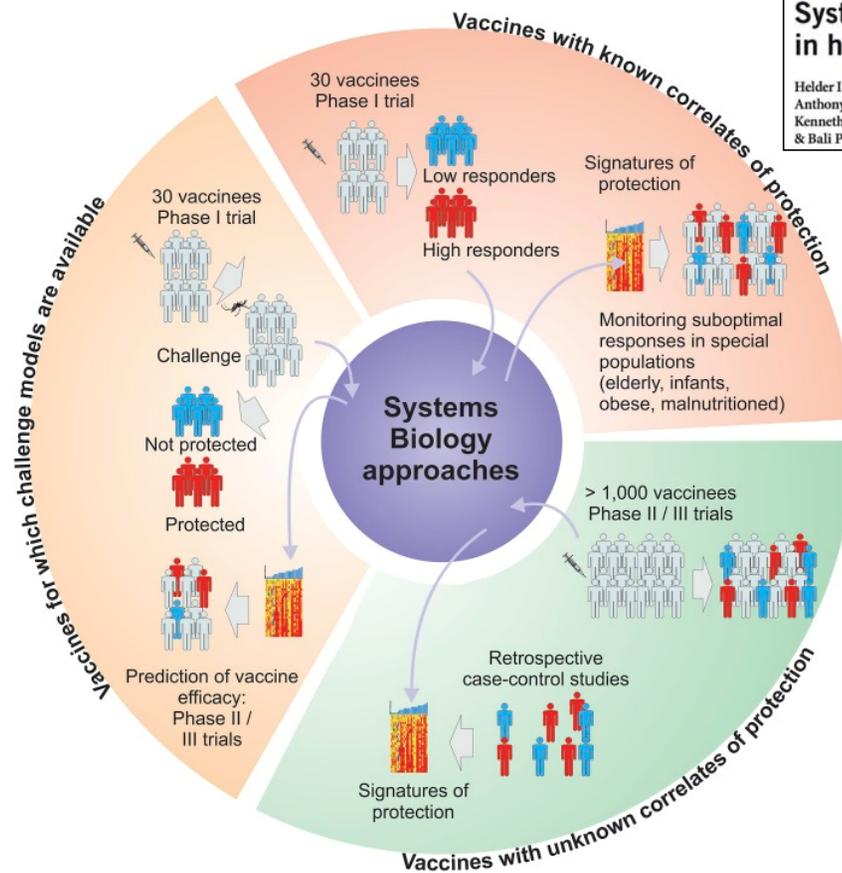
Innate Immunity, TLRs and Next Generation Adjuvants



Human Immune Monitoring

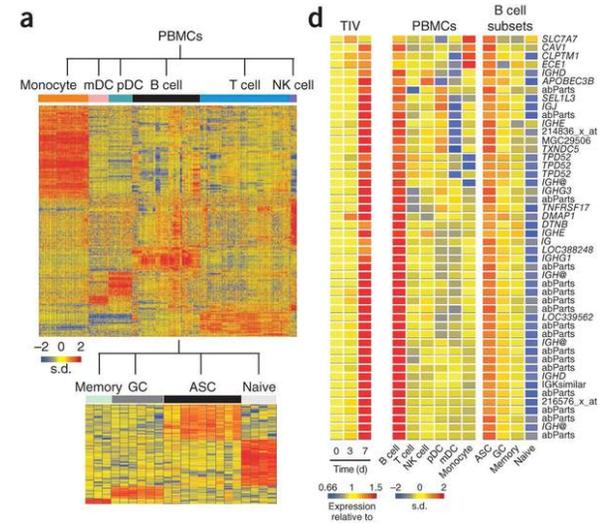
Single Cell Technologies; Tissue Sampling; Systems Vaccinology

Systems Vaccinology



Systems biology of vaccination for seasonal influenza in humans

Helder I Nakaya^{1,2}, Jens Wrammert^{1,3}, Eva K Lee⁴, Luigi Racioppi^{5,6}, Stephanie Marie-Kunze^{1,2}, W Nicholas Haining⁷, Anthony R Means⁸, Sudhir P Kasturi^{1,2}, Nooruddin Khan^{1,2}, Gui-Mei Li^{1,3}, Megan McCausland^{1,3}, Vibhu Kanchan^{1,3}, Kenneth E Kokko⁸, Shuzhao Li^{1,2}, Rivka Elbein⁹, Aneesh K Mehta⁹, Alan Aderem¹⁰, Kanta Subbarao¹¹, Rafi Ahmed^{1,3} & Bali Pulendran^{1,2,12}

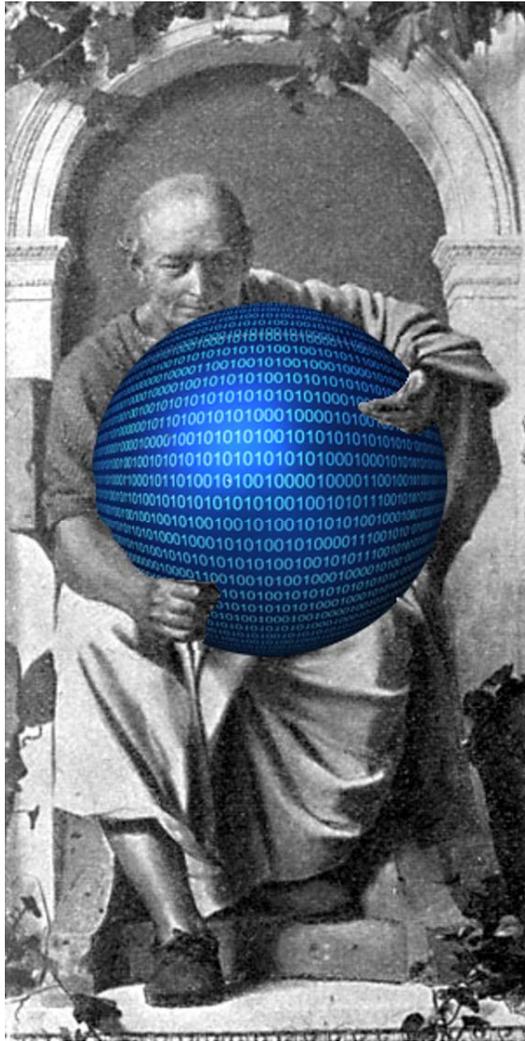


Nakaya et al., *Nat. Immunol.*, 2011
 Pulendran B, *PNAS*, 2014



Machine Learning

Bioinformatic Analytics of Big Data



CARPE DATEM

Human Vaccines Project

Genesis of the Project

How as a field can we harness recent technological innovations to accelerate the development of vaccines and immunotherapies against major global diseases, and improve the probability of success?



Accelerating Next-Generation Vaccine Development for Global Disease Prevention

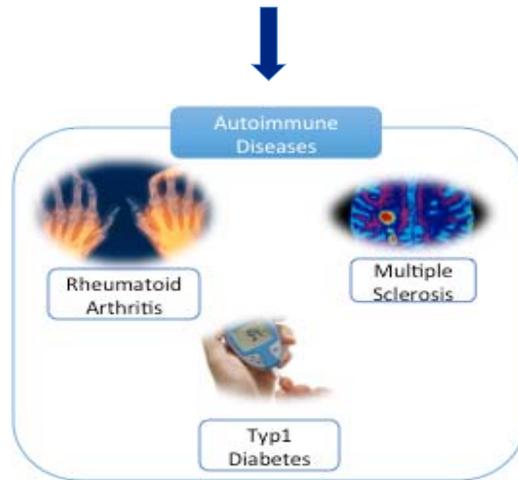
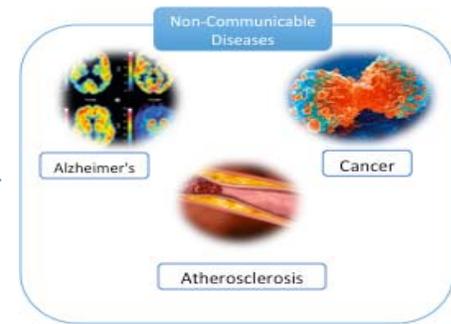
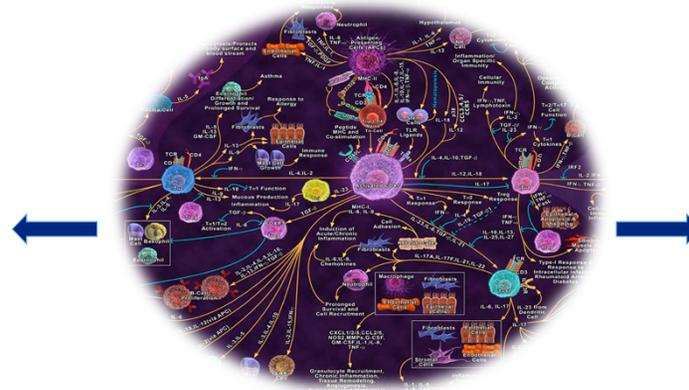
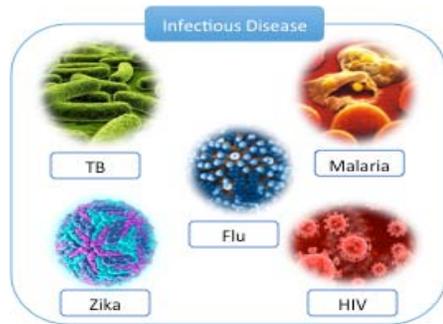
*Wayne C. Koff, Dennis R. Burton, Philip R. Johnson, Bruce D. Walker,
Charles R. King, Gary J. Nabel, Rafi Ahmed, Maharaj K. Bhan,
Stanley A. Plotkin*

Science 340: 1232910.doi; May 31, 2013

Human Vaccines Project

The Human Immune System

Decoding the human immune system holds the key to transformational advances in prevention and control of major diseases



Human Vaccines Project

Goals and Objectives

Decipher the Human Immunome

Technology-driven global consortium with the goal of accelerating development of vaccines and immunotherapies for major infectious diseases and cancers

- ❖ **Decipher the human immunome to enable rational design of vaccines and immunotherapies**
 - >1000 immunomes across different populations
 - Determine immune targets on infected and neoplastic cells for immune prophylaxis and therapy

Elucidate the Rules of Immunogenicity

- ❖ **Systematically determine how to generate long-lasting, effective immune responses in humans**
 - Conduct large numbers of iterative, clinical research studies in globally diverse populations
 - Undertake extensive genetic and immune monitoring and bioinformatics analyses
 - Directly link with pharma to ensure rapid translation to products

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New Paradigm for Global Health

A unique global discovery consortium to address the key challenges impeding the development of next generation vaccines and immunotherapies for major global diseases

- ❖ Pharma and Biotech Industry Partners
- ❖ Product Development Partnerships-NGOs, Foundations
- ❖ Academic Scientific Hubs
- ❖ Industry Partners in Artificial Intelligence and Machine Learning
- ❖ Developing Country Partners- Heterogeneous Populations
- ❖ Diversified Donors and Supporters- All partners are investors

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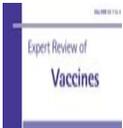
Progress



**Accelerating Next-Generation
Vaccine Development for Global
Disease Prevention**



**Towards a Human
Vaccines Project**



**Building the Human Vaccines Project:
Strategic Management
Recommendations**



**Deciphering the
Human Immunome**



**The Human Vaccines Project: A
Roadmap to Cancer Vaccine
Development**

- ❖ Idea first proposed 2013 *Science Magazine* 3Q, 2013
- ❖ Seed funding from Robert Wood Johnson Foundation, incubated at the International AIDS Vaccine Initiative (IAVI)
- ❖ La Jolla Scientific Workshop February 2014, endorsed by 35 leading scientists as “*meritorious, timely and potentially transformative*” in *Nature Immunology*
- ❖ World class Steering Committee assembled
- ❖ Scientific and business workshops completed
- ❖ Incorporated as an independent nonprofit 501(c)3, management team and founding Board assembled, 2015
- ❖ MacArthur Foundation funded regulatory project established to enable experimental medicine trials in globally diverse populations (2Q 2016)
- ❖ Collaborations/financial support from 6 pharma companies, 5 academic research centers established
- ❖ First scientific study launched (2Q 2016): Demo project on Human Immunome
- ❖ Bioinformatics and machine learning program launched (2Q 2016)
- ❖ Cancer vaccines program to be established (3Q 2016)
- ❖ Second demo project launched (4Q 2016): Rules of Immunogenicity

**Harnessing
Technological
Innovation to
Accelerate Vaccine
Development**

Summary

- Empiric approaches for vaccine development will likely be unsuccessful for major diseases of the 21st century
- Recent technological innovations offer the potential for the first time to “decode the human immune system” to significantly accelerate vaccine development and improve the probability of success

Human Vaccines Project

Impact

**New Paradigm for Immune
Driven Science & Product
Development**

**Accelerate Vaccines and
Immunotherapies for Major
Diseases**

A successful Human Vaccines Project will be transformational for global science, disease prevention and treatment

- ❖ **New product development paradigm:**
 - Reduce time, cost and risk of vaccines/immunotherapies
 - Rationally designed, highly targeted products
 - Novel immune signatures correlating with product safety and efficacy

- ❖ **“Decoded” immune system: a catalytic, open resource for global researchers**

- ❖ **Directly accelerate new and improved vaccines/immunotherapies:**
 - Major Global Killers: AIDS, TB, Malaria,
 - Emerging Diseases: Ebola, Pandemic Influenza
 - Neoplastic Diseases: Melanoma, Breast, Lung and Other Cancers

- ❖ **Vaccines and Therapies Tailored and Optimized for Key Populations**
 - Elderly
 - Developing World



Human Genome Project
2001



A new era of
Precision
Medicine



A new era of
Vaccines,
Immunotherapy and
Global Health

