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

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June 7, 2016

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

-Albert Einstein
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

The Old Paradigm is Failing
Money: $ Billions
Time: Decades
Low Probability of Success
Opportunity Costs

A New Approach is Needed
## Major Global Diseases for Which Globally Effective Vaccines Do Not Currently Exist….and VERY FEW ARE LOW HANGING FRUIT

<table>
<thead>
<tr>
<th>Viral</th>
<th>Bacterial</th>
<th>Parasitic</th>
<th>Cancers</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytomegalovirus</td>
<td>Campylobacter</td>
<td>Chagas Disease</td>
<td>Breast Cancer</td>
<td>Allergies</td>
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<td>Dengue, Chikungunya,</td>
<td>Chlamydia</td>
<td>Leishmaniasis</td>
<td>Colon Cancer</td>
<td>Alzheimer’s</td>
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<td>Epstein Barr</td>
<td>Helicobacter pylori</td>
<td>Malaria</td>
<td>Lung Cancer</td>
<td>Autoimmune Diseases</td>
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<tr>
<td>Hepatitis C</td>
<td>Shigella</td>
<td>Schistosomiasis</td>
<td>Melanoma</td>
<td>Metabolic Diseases</td>
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<tr>
<td>Herpes Simplex</td>
<td>Staphylococcus</td>
<td>Other Parasitic Diseases</td>
<td>Pancreatic Cancer</td>
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<tr>
<td>HIV</td>
<td>Streptococcus A, B</td>
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<td>Universal Influenza</td>
<td>Tuberculosis</td>
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<td>Respiratory Syncytial Virus</td>
<td>Other: Urinary Tract Infections</td>
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<td>Rhinovirus</td>
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<td>Other Emerging Viral Diseases e.g. Ebola, Marburg; Zika; Lassa</td>
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</table>
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
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-Immunopeptidomics; Novel Platforms for Rapid Screening e.g. mRNA; Structural Vaccinology;
In silico vaccine candidates

Express recombinant proteins

- 600 potential vaccine candidates identified
- 350 proteins successfully expressed in E.coli
- 91 novel surface-exposed proteins identified
- 28 novel proteins have bactericidal activity

EMEA Recommends Approval Nov 2012
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

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

Bioinformatic Analytics of Big Data
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?
Decoding the human immune system holds the key to transformational advances in prevention and control of major diseases.
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Goals and Objectives

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

- 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

- 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
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.
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Impact

New Paradigm for Immune Driven Science & Product Development

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