TRANSFORMING SCIENCE INTO GLOBAL HEALTH SOLUTIONS

The 21st Century Global Vaccine Revolution

Improving Health Outcomes for Millions of People Around the World

A new generation of vaccines is filling pressing and unmet global health needs.

But instead of preventing disease, many of the new vaccines – whether they're attacking HIV, tuberculosis, malaria or cancer – will be therapeutic and help prevent disease recurrence.

This is the 21st century's global vaccine revolution, and it's being accelerated by the transformative role of adjuvants, genetics and the immune system. The result: improved health outcomes for millions of people around the world.

The following five thought leaders – several from IDRI – access and analyze the progress and performance of new vaccines; they also make clear the challenges and barriers that confront researchers as they try to keep this critical scientific momentum going.

The Doors Are Wide Open For New Vaccines

By Steven G. Reed
Founder, President, and Chief Scientist, IDRI

It's shocking, but when we look back five years ago, there were no approved vaccine adjuvants in the United States.

Now the doors are opening and a new generation of vaccines is filling unmet needs that the first generation simply could not address.

Indeed, whether it's attacking HIV, tuberculosis, malaria – or cancer – today's vaccines have the potential to boost global health. But, instead of disease prevention, the vaccines of this decade will, in many cases, be therapeutic and help prevent disease recurrence. This means that a patient with prostate cancer can have surgery to remove a tumor, and then be vaccinated to sure the malignancy doesn't return or spread. Or a person with HIV can use a vaccine to keep AIDS at bay.

These vaccines would not possible without adjuvants, which give today's vaccines new potency and durability; and none of this could happen without our newfound insights into genetics and the immune system, which help us to understand the specific proteins to target.

The new vaccines also come at a most important time, because many diseases – like TB – seem to be increasingly resistant to drugs. Fortunately, vaccines are different than drugs, because they assault the immune system in a broad-based way. That said, many doctors are combining drugs and vaccines in a collaborative effort to deal with disease today. This allows us to keep the tools we currently have, while adding vital new ones to the mix.

In the end, when we look back on this period, I think it will be clear that the 21st century vaccine revolution dramatically improved health outcomes for millions of people around the world.

Changes in the Vaccine World Will Intensify

By Darrick Carter
Vice President of Adjuvant Technology, IDRI

There were well-established vaccines 10-20 years ago, but there was no real innovation or modernization. The biotechnology industry didn't see vaccines as a high-value market. Clean, recombinant proteins weren't used.

Virtually all vaccines were ground up, attenuated (weakened), or inactivated pathogen. Adjuvants with defined modes of action were missing. And there was very little on-site manufacturing or clinical trial capacity in developing countries.

Things have really changed since then. Today, the biotech business sees a market for vaccines, and some high-value segments of the market are even getting crowded. Immune therapeutics – which use vaccine products to be given as therapeutics after a disease is acquired – are taking hold. Clean proteins, or defined adjuvants, are being used in vaccine formulations.. Vaccine targets are changing from pathogen-oriented diseases to those related to cancers, high blood pressure and smoking cessation. And on-site manufacturing in emerging economies, plus clinical trial centers run by people from endemic countries, are increasingly becoming the norm.

Change will continue – and intensify – as we move forward through this decade.

Immune therapy will expand. Vaccine targets will diversify. Highly defined vaccines will be made to standards currently reserved for drugs, with known modes of action and immune correlates, or real measurable signs of immunity. And emerging countries will contribute their own new products, which are researched on-site, to the development pipeline.

The bottom line result, in my view, is expanded global wellness, which is a goal we're all working toward.

Making Strides in Next-Generation TB Vaccines

By Rhea N. Coler
Vice President of Preclinical Biology, IDRI

We've come a long way in the vaccine world.

The tuberculosis (TB) research field, for example, only began to receive serious attention and substantial resources in the mid-1990's. Since then, studies have highlighted the immense complexity of TB and underscored why we must continuously re-think how to optimize the design of TB vaccine candidates.

One important stride we've made in the development of next-generation TB vaccines has been the creation of adjuvants that stimulate effective, long-lived and appropriate immune responses. We've also developed a rich pipeline of new vaccine candidates. More than 16 candidate TB vaccines have entered clinical trials alone. Promising new biomarkers have emerged. Capacity for vaccine production and carrying out large-scale clinical trials is being developed in endemic countries. And basic information on safety and immune responses to a variety of first-generation TB antigens has been reported.

Now we need to conduct research that will be aided by both a comprehensive clinical trials infrastructure and the engagement of the scientific communities that are located in TB-endemic countries. We need to comprehensively apply innovations in vaccinology, adjuvant development, systems biology, genomics, bioinformatics, animal modeling, and contemporary immunologic and molecular tools to the outstanding questions concerning human immunity to TB.

We will need to push more innovative and heterogeneous TB vaccine candidates through the pipeline. In order to

get rapid results, Phase IIB studies will need to be conducted in highly selected populations. And difficult decisions will need to be made about how to move these candidates into populations in which the vaccine will have the most epidemiologic impact.

As we move into the next decade of TB vaccine research and development, we need to use out-of-the box approaches and advanced technologies. It's also more important than ever for researchers and their sponsors to work together in securing sufficient support and resources to achieve the ultimate goal of developing new, more effective TB vaccines.

Addressing the Barriers in Vaccine Discovery and Development

By Chris Wilson
Director of the Global Health Discovery & Translational Sciences Program
&
Chris Karp
Deputy Director of Host-Pathogen & Vaccine Discovery
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Some of our key vaccine priorities today include malaria, TB, HIV, cholera and visceral leishmaniasis. And we're trying to modify existing vaccines and create new ones with improved ease and lower delivery costs in critical areas that have serious research or solution gaps.

That said, there are several key research barriers that are impeding our progress in vaccine discovery and development.

- First, insufficient quality of newly researched vaccines and their ingredients and limited diversity of concepts and candidates being tested in the lab, or a mismatch between these two. We need more, diversified and top quality vaccine candidates
- Second, insufficient throughput to discover new targets for the immune system using modern methods, and applying them to pathogens with sizable genomes.
- Third, lack of understanding of how vaccines work, and how to predict which ones will work, without field-testing in large populations.
- Fourth, lack of clear understanding of how best to drive intended immune responses; or the inability to reliably drive robust responses in the mucosal immune system, key to vaccine success.
- Fifth, poverty of informative preclinical models and lack of head-to-head testing of competing concepts and candidates.
- Sixth, slow entry, insufficient throughput, and lack of head-to-head testing of candidates in human proof-of-concept (POC) trials.
- Seventh, regulatory partnerships to enable more efficient and earlier human POC testing.
- And eighth, unwillingness of grant reviewers, funders and decision makers to take informed risks appropriate for the magnitude of the problem being addressed and, conversely, to make dispassionate go/no-go decisions on further advancement based on solid, yet inevitably imperfect, data.

Despite these barriers, we are optimistic that the vaccine revolution, which has traveled so far, will continue its positive journey in the coming years. As a result, more people can be healthier in more places around the world.