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Minireview

Twenty-First Century Vaccinomics Innovation Systems: Capacity Building in the Global South and the Role of Product Development Partnerships (PDPs)

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Abstract

The availability of sequence information from publicly available complete genomes and data intensive sciences, together with next-generation sequencing technologies offer substantial promise for innovation in vaccinology and global public health in the beginning of the 21st century. This article presents an innovation analysis for the nascent field of vaccinomics by describing one of the major challenges in this endeavor: the need for capacities in "vaccinomics innovation systems" to support the developing countries involved in the creation and testing of new vaccines. In particular, we discuss the need for understanding how institutional frameworks can enhance capacities as intrinsic to a systems approach to health technology development. We focus our attention on the global South, meaning the technically less advanced and developing nations in Africa, Asia, and Latin America. This focus is timely and appropriate because the challenge for innovation in postgenomics medicine is markedly much greater in these regions where basic infrastructures are often underresourced and new or the anticipated institutional relationships can be fragile. Importantly, we examine the role of Product Development Partnerships (PDPs) as a 21st century organizational innovation that contributes to strengthening fragile institutions and capacity building. For vaccinomics innovation systems to stand the test of time in a context of global public health, local communities, knowledge, and cultures need to be collectively taken into account at all stages in programs for vaccinomics-guided vaccine development and delivery in the global South where the public health needs for rational vaccine development are urgent.

Vaccinomics Innovation Systems and Postgenomics Medicine

Vaccines are one of the most cost effective public health tools for tackling priority disease areas in developing countries (GAVI, 2010). The availability of sequence information from publicly available complete genomes (Altenhoff et al., 2011) and data-intensive sciences (Hey et al., 2009; Kolker, 2011), together with efforts to characterize the microbial world using next-generation sequencing technologies in the postgenomics era (Gilbert et al., 2010) offer substantial promise for innovation in vaccinology and global health in the beginning of the 21st century (Hotez and Pecoul, 2010; Kennedy and Poland, 2010). One particular envisioned advance is rational and mechanistically informed design of vaccines and directed use (e.g., customized at a subpopulation level) of vaccine-based public health interventions (Bagnoli and Rappuoli, 2006). Indeed, successful application of genomic technologies was first demonstrated in the innovation of a vaccine for *Neisseria meningitidis* serogroup B, reported in 2000 (Pizza et al., 2000). Since then, reverse vaccinology and other techniques associated with antigen identification and the ability to rapidly and cost effectively sequence genomes, have resulted in a vastly greater number of potential vaccine candidates than have been identified over the past 40 years. The analysis of entire sets of proteins expressed by a genome (the nascent field of proteomics) is likewise proving to be an important tool in antigen discovery and in understanding the role of the environment in regulating the pathophysiology of microorganisms (Scarselli et al., 2005; Serruto and Rappuoli, 2006). With the recent call made in September 2010 for the Human Proteome Project, we might anticipate further acceleration of the field of vaccinomics, the convergence of classical vaccinology with data intensive sciences and omics technologies.

Notably, this 21st century vaccine innovation system that utilizes genomics and proteomics in the discovery, development, and delivery of new vaccines, is comprised of an increasing number of actors and disciplinary fields. A complex

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and highly diverse set of actors including bioinformatics specialists, vaccinologists, immunologists, donor agencies, public health workers, clinical trial sites, government agencies, pharmaceutical industry, civil society, and many more, are all integral to the vaccinomics innovation process. Each of these actors requires basic infrastructural capacity to contribute to the innovation system. For example, university researchers require lab space, public health workers need transport, and government agencies depend on information and communication technology support.

This article presents an innovation analysis for the nascent field of vaccinomics by describing one of the major and hitherto neglected challenges in this endeavor: the need for capacities in "vaccinomics innovation systems" to support the developing countries involved in the creation and testing of new vaccines for global public health. In particular, we discuss the need for understanding how institutional frameworks can support minimum capacities as intrinsic to a systems approach to technology development. Institutions link the actors in an innovation system and facilitate knowledge production and communication between them. An integrated innovation system with enhanced capabilities for communication between actors is essential and timely to the field of vaccinomics where increased multidisciplinarity also demands more effective knowledge translation, communication, and diffusion.

We focus our attention on the global South, meaning the technically less advanced and developing nations in Africa, Asia, and Latin America. This focus is timely and appropriate because the challenge for innovation is markedly much greater in these regions where basic infrastructures are often underresourced and new or the anticipated institutional relationships can be fragile. Importantly, we examine the role of *Product Development Partnerships* (PDPs)—a concept that has attracted considerable interest in the field of global health—as an institutional innovation that contributes to strengthening fragile institutions and capacity building. Alongside the potential that PDPs offer for the 21st century vaccinomics innovation systems, there are important challenges that should be considered as well.

Building Global Health Capacities and PDPs for 21st Century Vaccine Innovation

Innovation systems for global health care, medicines, and devices have evolved significantly to take account of the global value and supply chains as well as an increased number of actors with a greater range and global spread of knowledge and expertise. Our understanding of innovation has moved from a linear model of knowledge production where innovation primarily occurs in academic and private laboratory settings, moving through a linear pipeline of product development, to more complex systems models. Importantly, the systems approach to innovation (Lundvall, 1992) recognizes processes of interactive learning and knowledge translation between actors. This complex and often tacit process of knowledge exchange and translation requires a sustainable and strong institutional framework to facilitate interaction (Freeman, 1987; Metcalf, 1995).

Adequate institutional frameworks contribute to the overall capacity for vaccine innovation in developing countries. This is no less applicable to the field of vaccinomics. In the context of vaccine innovation, capacity is the ability to perform functions, solve problems, and set and achieve technological objectives (Fukuda-Parr et al., 2002). Two elements are central to capacity building: adequate expertise and functional institutions. In the context of developing countries, the former is rarely adequate and relies on the funding and training provided by international development/health organizations. The latter tends be undermined and weakened by national structural problems, that is, aid dependency, unstable democracies, and lack of functional and responsive institutions (e.g., national regulatory authorities, local platforms for community engagement).

A core problem in developing countries is missing institutions or perverse institutions (Burnside and Dollar, 1997; North, 1990) that undermine the effectiveness of an innovation system, for example, those that lead to misinformation or the unintended diversion of resources. This is worsened by high turnover of personnel, weak institutional structures, and lack of transparency. In some cases, these institutional inadequacies have been addressed with the support of international organizations (e.g., World Bank, WHO, UN) by providing technical assistance (Wilson, 2007). Weak institutions and failure in knowledge communication can persist, however, because international aid programs often use a linear top-down approach (Brett, 2000) to institution building rather than a bottom-up approach that engages with local knowledge bases. Weak institutions and resulting insufficient capacities that fail to facilitate knowledge transfer and engagement between actors, including those at the community and policy level, can endanger a whole health program and health systems. Consequences range from insufficient enrollment of communities in clinical trials and low levels of uptake of the final vaccine product, to poor rates of success where disease control requires multiple interventions and strategies (e.g., malaria) (Keusch et al., 2010).

Public Private Partnerships (PPP) and more recently, a specific variant, PDPs, have emerged as new institutional innovations that have the potential to build capacities for vaccine innovation in developing countries. PDPs have arisen as solutions where the costs and risks associated with research act as barriers to product development. PDPs create long-term partnerships and build trust between specific actors (usually academia, industry, the public sector, and international agencies), toward the achievement of a common technological goal. They work as virtual nonprofit R&D organizations, outsourcing research activities to academic or private sector partners, while linking together expertise and providing public funding, technical oversight, and portfolio management. PDPs can leverage additional funds and negotiate terms with partners with regard to prices, preferential access and other aspects of benefit sharing. They usually focus on a specific technology (e.g., vaccines, drugs, or diagnostics) and work within a particular disease area. Recent research evidence from 122 health technology candidates in the combined PDP pipeline include 90 biopharmaceutical candidates and 32 diagnostic and vector control candidates (Grace, 2010). The International AIDS Vaccine Initiative (IAVI), for example, is a PDP that has attracted large amounts of donor funding. It aims to increase scientific and technological related capacities in the South, and institutional capacity through local ownership of vaccine development resulting from advocacy initiatives (Chataway and Hanlin, 2008). Table 1 lists other

Table 1. Examples of PDPs in Vaccine Development

PDP	*Objective*
The Meningitis Vaccine Project	To develop a low-cost vaccine for meningitis
PATH-VAC	To develop vaccines for Enteric Vaccine Initiative, Advancing Rotavirus Vaccine, Pneumococcal Vaccine Project, and Influenza Vaccine Project.
International Vaccine Institute	International center of research, training, and technical assistance for vaccines needed in developing countries (e.g., new oral cholera vaccine, Shanchol). Located in Korea
Path Malaria Vaccine initiative	To accelerate malaria vaccine development.
Pediatric Dengue Vaccine Initiative	To accelerate the development, evaluation, and sustained use of affordable dengue vaccines
IAVI	To ensure the development of safe, effective, accessible, preventive HIV vaccines
Medicines for Malaria Venture	To discover, develop, and deliver new, affordable antimalarial drugs
Institute for One World Health	R&D to combat infectious diseases in developing countries (e.g., Visceral leishmaniasis, Malaria, and Diarrheal disease)
Aeras	To develop new tuberculosis vaccines
The TB Alliance	To accelerate the discovery and development of new TB drugs

examples of PDPs that are involved in vaccine development. At a higher organizational resolution, the Figure 1 schematically maps out many of the partners involved in the IAVI PDP and their attendant roles.

In the case of South Africa, PDPs such as IAVI and the South African AIDS Vaccine Initiative (SAAVI), have demonstrated both the potential for, and challenges to this new approach to health innovation. Qualitative data from two clinical trial sites (Upton, 2011) reveal socioeconomic, cultural, political, and institutional constraints on effective mechanisms for knowledge communication between the researchers and the communities involved. The capacity of community members to absorb HIV/AIDS and vaccine science knowledge is crucial to the ethical and effective conduct of clinical trials. Equally important is the capacity of trial site researchers to understand the social and cultural factors that confound aims to achieve as wide a representation and retention of trial participants as possible across diverse populations over long periods of time. Moreover, in the case of HIV prevention clinical trials in developing country settings, the "law on the streets" may be quite different than the "law in the books" (Burris and Davis, 2009). Such functional disconnects in civil liberties of citizens may result in multiple, dynamic, and intersecting risk factors that warrant anticipatory governance and real-time monitoring of the social risks for clinical trial participants (Ozdemir, 2009).

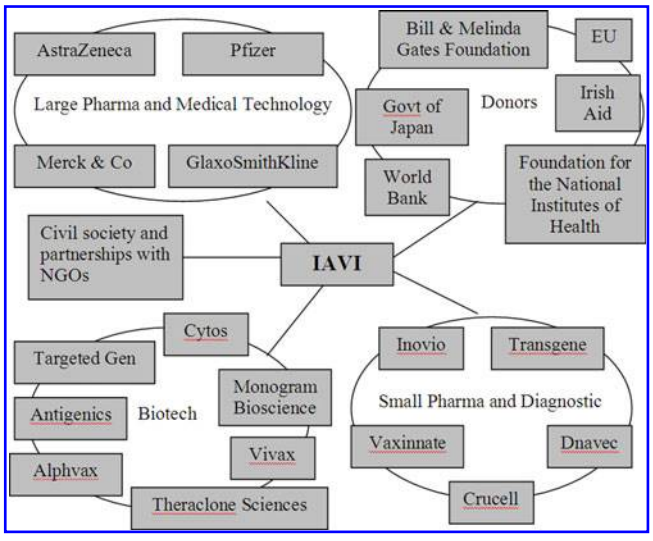

FIG 1. Collaborations within the International AIDS Vaccine Initiative (IAVI) PDP.

Insecurity underpins immediate priorities of food and employment in such contexts. Even so, given the high prevalence of HIV/AIDS in South Africa (UNAIDS, 2010), community members' motivation for involvement in community engagement activities and community interest in health innovation are evident. Challenges arise, however, from the high turnover of those involved causing "information decay" (Lesch et al., 2006). The problem in recruiting trial participants from marginalized and vulnerable populations is due, in part, to health beliefs and HIV/AIDS stigma. Ambivalence toward a positivist and scientific approach to HIV/AIDS and fears of association with the "white coats" from trial site clinics have cultural and historical roots. For example, the knowledge of past damaging medical interventions, such as the Tuskegee syphilis experiment (Marshall, 2005), and the legacy of racism under apartheid reinforced suspicions that clinical scientists were injecting black trial participants with the HIV virus (Upton, 2011). In addition government reticence in accepting responsibility for the wide range of factors contributing to the spread and treatment of HIV/AIDS (Nattrass, 2007) has contributed to such ambivalence. At the institutional level, conflicting accountabilities to donors and communities, due to priorities in developing science and technology capacity, threaten ethical and effective community engagement in the clinical trial process (Upton, 2011).

It has been recognized that building capacities at the national level for scientific diplomacy is important for knowledge exchange in an innovation system that involves global players and is working toward various vaccine solutions in the global South (Singer and Daar, 2001). We suggest, however, that the potential for developing PDP capacities also lies

in supporting communities in challenging negative social norms around target diseases such as HIV/AIDS and providing adequate funding for trial site resources (Upton, 2011). Communities can provide knowledge about their own histories and cultures, which can be usefully employed in strengthening the efforts of PDPs to build capacity. Opportunities to exchange that knowledge via national and global networks further promote learning and reflexive behavior and increase the potential for "shared health governance" (Ruger, 2010), which can also underpin a successful approach to PDP involvement in health innovation.

Conclusions and Forward Look

It is interesting to note that the fields of global health and global health governance have reached a critical juncture over the past few years (Kickbusch et al., 2010; Ozdemir et al. 2009; Pang et al., 2010). This is not only due to their visibility and the complexity of the challenges they pose. Presently, a chaotic set of actors and networks struggle to work toward improvements in global health while they remain very poorly coordinated. It is against this highly dynamic and complex background that the new field of vaccinomics is rapidly emerging. Vaccines and the field of vaccinomics represent a complex evolving 21st century data-intensive innovation that integrates the recent developments in genomics and proteomics with classical vaccinology in the postgenomics era. Current systems for the innovation and development of vaccines take place in a global context that demands collaboration among a wide variety of actors such as international agencies, national government agencies, communities, and the private sector. It is important to bear in mind that adequate capacities for vaccine innovation do not equate to the linear sum of these individuals, organizations, or their resources or expertise. Capacities crucially rely on the interaction of and exchange of expertise and knowledge in an institutional context that promotes learning and reflexive behavior. The latter relates to the ability of scientists (or other stakeholders in an innovation system) to be cognizant of how their own values and assumptions may contribute to, and influence the creation of meaning(s) from their own research. This is important as throughout the past century, science has been framed as if it is a value-free autonomous activity that is not affected by social systems or human values more generally. For sustainable 21st century vaccinomics innovation systems, we need to bear in mind that knowledge is coproduced by both science and social systems in which it is embedded (Jasanoff, 2006). To this end, PDPs are a *social institutional innovation* that can provide more formal and transparent structures on which to build long-term sustainable partnerships and trust, to reinforce or substitute for the often weak institutional frameworks that exist in developing countries.

The cases of IAVI and SAAVI in South Africa attest to the challenges that still prevail, despite the institutional frameworks advanced by PDPs (Upton, 2011). Social and cultural factors are at the core of capabilities and the successful establishment of institutions between actors in an innovation system. For vaccinomics innovation systems to stand the test of time in a context of global public health, local communities, knowledge and cultures need to be collectively taken into account at all stages in programs for vaccinomics-guided vaccine development and delivery in the global South where the public health needs for rational vaccine development are urgent.

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Author Disclosure Statement

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