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## The Global HIV Vaccine Enterprise\*

**Summary.** AIDS, which twenty-five years ago no one even knew it existed, has become the most serious infectious disease worldwide. The development of an HIV vaccine is one of the most difficult challenges that modern biomedical science is confronting. To address this challenge, scientists may need to organize themselves in a more intense, targeted, and collaborative effort, such as the one proposed by the Global HIV/AIDS Vaccine Enterprise. The enterprise concept proposes to complement the creativity of individual investigators with a collaborative system that ensures a more effective use of human and financial resources to produce new scientific knowledge. It also implies that the scientific knowledge can be harnessed in a targeted way to develop practical solutions to urgent global health problems, including explicit product development activities. Different modalities of the enterprise concept are being explored for the development of drugs to treat tuberculosis and vaccines to prevent malaria. [*Int Microbiol* 2005; 8(2):93-101]

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### The HIV/AIDS pandemic

AIDS was first reported in a short article published in 1981 in the *Mortality and Morbidity Weekly Report* of the US Centers for Disease Control and Prevention. [5]. The article described cases of *Pneumocystis carinii* pneumonia in five homosexual men in Los Angeles [13]. One month later 26 cases of Kaposi sarcoma among gay men were reported in the same newsletter [6], and that started a chain reaction with new cases of this acquired immunodeficiency being identified in different parts of the world.

After a period of initial confusion, the etiology of this new disease was clarified when Luc Montagnier [2] and Robert Gallo [12] provided complementary evidence indicat-

ing that a new retrovirus was associated with the disease that today is called AIDS. Very soon masses of information on HIV accumulated, building on an extensive body of knowledge on retroviruses, generated mostly from research supported in the 1970s as part of the so called "war on cancer". This is an extremely interesting example of how investments in a particular area of research can produce incredible benefits in a totally unexpected and unrelated field. With the isolation of HIV, diagnostic tests were rapidly developed, and the first serological test was licensed in 1985 [3]. Widespread serological screening made it possible to better understand the spread of the virus and to initiate a global response against that pandemic. In 1987 the first ant-HIV drug, AZT or zidovudine, was licensed [15]. This was the first of a long list of antiretroviral drugs that, used in combination, have dramatically changed the prognosis of people living with HIV/AIDS, at least in rich countries where people have access to these treatments.

In the last twenty-four years, HIV has continued its relentless spread and today it is estimated that around 40 mil-

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\*This article is based on the lecture pronounced by the author on occasion of the 105th General Meeting of the American Society for Microbiology (GSK International Leaders in Microbiology Lecture), June 5-9, 2005.

**Table 1.** Regional HIV/AIDS statistics and features, end of 2004\*

Region	Adults & children living with HIV	Adults & children newly infected	Adult prevalence rate (%) <sup>1</sup>	Adult & child deaths due to AIDS
Sub-Saharan Africa	25.4×10 <sup>6</sup> [23.4–28.4 × 10 <sup>6</sup> ]	3.1 × 10 <sup>6</sup> [2.7–3.8 × 10 <sup>6</sup> ]	7.4 [6.9–8.3]	2.3 × 10 <sup>6</sup> [2.1–2.6 × 10 <sup>6</sup> ]
North Africa & Middle East	540 000 [230 000–1.5 × 10 <sup>6</sup> ]	92 000 [34 000–350 000]	0.3 [0.1 - 0.7]	28 000 [12 000–72 000]
South & South-East Asia	7.1 × 10 <sup>6</sup> [4.4–10.6 × 10 <sup>6</sup> ]	890 000 [480 000–2.0 × 10 <sup>6</sup> ]	0.6 [0.4–0.9]	490 000 [300 000–750 000]
East Asia	1.1 × 10 <sup>6</sup> [560 000–1.8 × 10 <sup>6</sup> ]	290 000 [84 000–830 000]	0.1 [0.1–0.2]	51 000 [25 000–86 000]
Latin America	1.7 × 10 <sup>6</sup> [1.3–2.2 × 10 <sup>6</sup> ]	240 000 [170 000–430 000]	0.6 [0.5–0.8]	95 000 [73 000–120 000]
Caribbean	440 000 [270 000–780 000]	53 000 [27 000–140 000]	2.3 [1.5–4.1]	36 000 [24 000–61 000]
Eastern Europe & Central Asia	1.4 × 10 <sup>6</sup> [920 000–2.1 × 10 <sup>6</sup> ]	210 000 [110 000–480 000]	0.8 [0.5 - 1.2]	60 000 [39 000–87 000]
Western & Central Europe	610 000 [480 000–760 000]	21 000 [14 000–38 000]	0.3 [0.2–0.3]	6 500 [<8 500]
North America	1.0 × 10 <sup>6</sup> [540 000–1.6 × 10 <sup>6</sup> ]	44 000 [16 000–120 000]	0.6 [0.3 - 1.0]	16 000 [8 400–25 000]
Oceania	35 000 [25 000–48 000]	5 000 [2 100–13 000]	0.2 [0.1–0.3]	700 <1 700
TOTAL	39.4 × 10 <sup>6</sup> (35.9–44.3 × 10 <sup>6</sup> )	4.9 × 10 <sup>6</sup> (4.3–6.4 × 10 <sup>6</sup> )	1.1% (1.0–1.3%)	3.1 × 10 <sup>6</sup> (2.8–3.5 × 10 <sup>6</sup> )

\*Adapted from: World Health Organization (2005). Facts about HIV/AIDS-Global. [<http://w3.who.org/EN/Section10/Section18/Section348.htm#Global>]

<sup>1</sup>The proportion of adults (15 to 49 years of age) living with HIV/AIDS in 2004, using 2004 population numbers. The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.

lion people are living with HIV/AIDS in the world, and that more than 20 million people have already died of AIDS (Table 1). All of this from a disease that only 25 years ago we did not even know existed.

Of the estimated 40 million people living with HIV/AIDS in the world, 95% of them lives in developing countries, especially in Africa, which is home to 26 million people already infected with HIV. In at least six Sub-Saharan African countries, one in five adults are already infected with HIV, and in another ten countries 10 per cent of adults are infected. Contrary to popular belief, the epidemic is not under control. HIV continues to spread relentlessly at a rate of 14,000 new HIV infections every day [19].

The Joint United Nations Programme on HIV/AIDS, UNAIDS, has forecasted that from now until 2010 we could be adding some 5 million new infections every year. At the same time, we must recognize that we have some tools (although not the optimal ones) to try to prevent many of these infections. UNAIDS estimates that a comprehensive global response to the epidemic could reduce the number of new infections to less than 2 million per year. However, that comprehensive response would require an investment in

developing countries in the order of 15 to 20 billion dollars per year, which any of them cannot possibly afford. The sad reality is that fewer than one in five people at risk of HIV infection worldwide have access to prevention interventions, and less than 7 per cent of HIV-infected people have access to treatment.

Considering the logistical difficulties that the world is encountering in increasing and maintaining access to existing preventive interventions, an HIV vaccine may represent the best long-term solution for controlling the HIV/AIDS pandemic. It is indeed a long-term solution because developing an HIV vaccine remains one of the most difficult challenges confronting biomedical research today. As Ron Desrosiers commented in *Nature Medicine*, our struggle to develop an HIV vaccine can be compared to the mythical punishment of Sisyphus, condemned by the gods to roll a rock to the top of a mountain for eternity [10].

Confronting new scientific challenges in the search for an AIDS vaccine, and there are many, is usually frustrating, and some people wonder whether an HIV vaccine can be ever developed and whether scientists should give up that line of research and try to control this epidemic with other interventions, although they obviously are not the solution.

## The quest for an HIV vaccine

When HIV was identified as the causal agent of AIDS, the scientific community was optimistic in relation to the rapid development of an HIV vaccine. In fact, virologists have been very successful developing vaccines against many other viral diseases. That optimism led to a famous press conference in 1984, where Margaret Heckler, then the US secretary of Health, predicted that an HIV vaccine would be in clinical trials within the following two years. Secretary Heckler was right because in 1987 the first phase I trial of an HIV vaccine was initiated, using a baculovirus-derived gp160 manufactured by MicroGeneSys. What Mrs. Heckler did not know, as not any one knew at that time, was that HIV was much more complex than any virus or disease against which vaccines had been successfully developed.

The scientific issues about the difficulty in developing a HIV vaccine will not be discussed here, but they are mostly related to the fact that the immune response against HIV fail to control viral replication or progression to disease, and this is compounded by the extremely high rate of genetic variability of HIV, which facilitates escape of what otherwise could be an effective immune response. Nevertheless, and despite these scientific uncertainties, several candidate vaccines were developed and tested in human trials between 1986 and 1997. With renewed optimism, President Clinton proclaimed in 1997 the national goal of finding a vaccine for AIDS within the next ten years. He acknowledged, however, that that task was going to be difficult, and compared it with President Kennedy's call to put a man on the moon before the end of the 1960s. Despite important progress made since 1997, it has now become evident that President Clinton's deadline of 2007 will not be met.

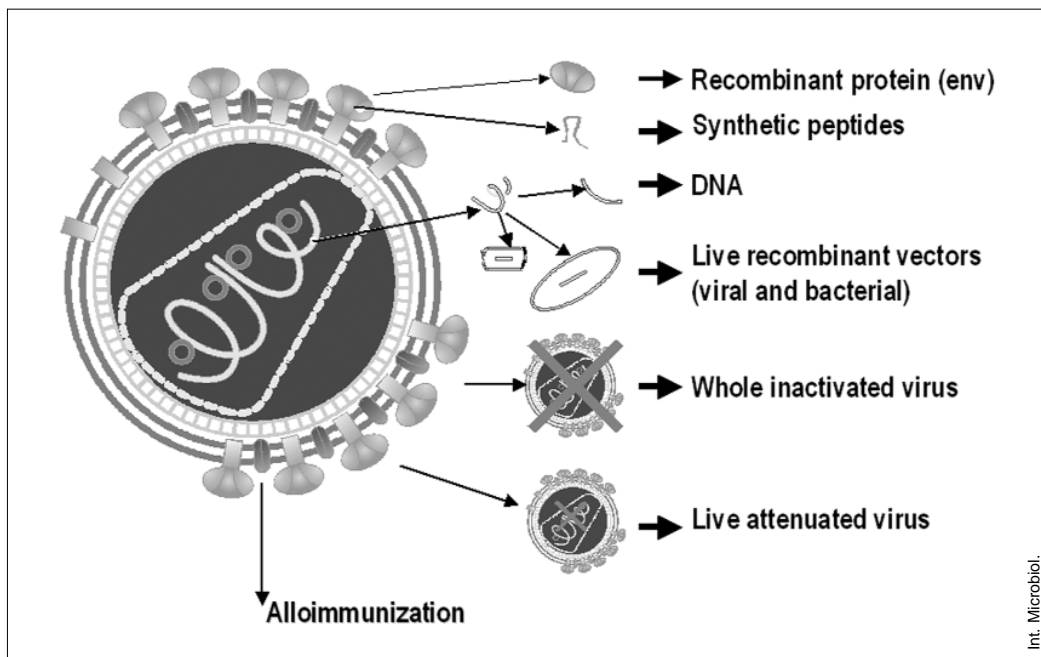
Vaccine studies are carried out in several phases. The first two phases consist of small trials whose aim is to confirm the safety and immunogenicity of the candidate vaccine as well as to determine the most effective dosage and schedule in a given population. Phase III trials, which test the vaccine for protective efficacy, are carried out only if the results of phases I and II have shown that the vaccine is safe and promising. In 2003 the HIV vaccine study conducted by VaxGen (Brisbane, California) was the first to conclude a phase III trial. Unfortunately, the candidate vaccine, a genetically engineered version of the HIV surface protein gp120, failed to provide any significant protection against HIV infection or disease [7]. These results had been predicted by many scientists, but "the proof is in the pudding", and there is no replacement for well conducted clinical trials to obtain definitive information on the efficacy of any vaccine.

## Three waves of vaccine paradigms and clinical trials, and current HIV vaccine concepts

Almost twenty years of research have led to the current HIV vaccine concepts shown in Fig. 1 [11]. Whole inactivated and live attenuated viruses, which are the classical approaches for viral vaccine development, are not being seriously considered for a human vaccine due to significant safety concerns. So, the majority of the candidate vaccines under development are based on subunit vaccines. Some of these subunit vaccines are based on the envelope proteins of HIV (especially gp120) or on selected epitopes of these proteins, and these vaccines are mostly aimed at inducing neutralizing antibodies. The VaxGen product that failed to induce protective immunity in phase III trials was based on a monomeric form of gp120. Other candidate vaccines use naked DNA or different bacterial or viral vectors, and they are designed to induce cell mediated immunity especially targeted to the internal more conserved proteins of HIV. And, some of these candidate vaccines are being explored in different prime-boost combinations, with the idea of inducing both humoral and cell-mediated immune responses

We can consider three waves of vaccine paradigms and clinical trials in the history of HIV vaccines. The first started with the discovery of the virus itself, and was based on the concept that neutralizing antibodies alone could be sufficient to induce protective immunity. Envelope-based vaccines were designed to induce neutralizing antibodies. This wave was completed in 2003, with the negative results of the gp120 phase III trials [7]. Overlapping the first wave, the second one started in the mid 1990's, with the recognition that cell-mediated immunity was a major component of the protective immune response against HIV infection, and this led to the development of DNA and vectored vaccines, three of which are now entering large scale trials, including poxvirus and adenovirus vectors in different prime-boost combinations. And we are now entering the third wave of HIV vaccine development, with the paradigm that we need new vaccine concepts and combinations, to induce more potent and durable humoral and cell-mediated immune responses, capable of preventing infection by primary isolates of different HIV subtypes.

From these almost twenty years of research, we have had some lessons. The first lesson is that the initial generation of envelope-based vaccines failed to induce protective immunity, and that novel envelope-based constructs will need to be developed and tested with the hope that they will induce the right quality and quantity of neutralizing antibodies. Like-



**Fig. 1.** Current HIV vaccine concepts. Based on WHO and UNAIDS.

wise, the first generations of T-cell vaccines, which are the majority in clinical trials today, only induce low level of immunity and of short duration. Additional research is needed to develop more potent vectors, especially those that can induce long-term memory. Two areas which are relatively unexplored, but that could provide some interesting leads in the future are those of mucosal and innate immunity. Finally, we are still struggling with the relevance of primate protection experiments in relation to potential protection in humans. We are not sure how to use these primate models as gate-keepers for moving candidate vaccines to clinical trials. Continuing HIV vaccine research doing more of the same with the hope that one day or other an effective safe vaccine will come out has no sense. New paradigms on how conduct HIV vaccine research must be explored.

## The Global HIV Vaccine Enterprise

In the context of one of major epidemics humankind is confronting, and searching for a new way of doing things, a group of twenty-four scientists, including two Nobel laureates (Harold Varmus and David Baltimore), proposed in June 2003 the creation of a global HIV vaccine Enterprise. The lead author of the paper was Rick Klausner, former director of the National Cancer Institute and current Executive Director for Global Health at the Bill & Melinda Gates Foundation, which has been one of the main driving forces of this initiative [14]. The article argues that the Enterprise is

needed because the present effort is not sufficient to produce a vaccine in the foreseeable future. This is because of the many scientific uncertainties that we are facing, and of insufficient investment, especially from the private sector. The article also outlines a new game plan for a more collaborative HIV vaccine discovery effort. Of course, we fully recognize, that it is not possible to plan for discovery, but we can indeed plan for the research that may accelerate discovery.

**Basic principles.** The severity of the AIDS pandemic and the need to maintain the momentum of our response to the pandemic is another major justification for the Enterprise, especially when the world is getting used to AIDS, which could become considered as just another “tropical disease” that does not affect “us”; or that the problem has already been solved with the development of antiretroviral therapies; and we also need to neutralize potential discouragement due to the perception that, perhaps, the development of an HIV vaccine is just not possible. Finally, the Enterprise is proposed because the urgency of the epidemic requires a more rapid vaccine development strategy, and this process involves very high costs, and very high risks that impose the need to identify new strategies for collaborative partnerships between the public and private sector and between industrialized and developing countries.

The Enterprise concept means a new way of thinking about problems, with the formulation of shared strategic plans, which have a level of “strategic vagueness” that should allow for self-learning and self correcting. It also means a new way of acting to solve problems, using common tools

and optimized resources, and supporting iterative activities that will lead to incremental knowledge. Finally, it means a new way of behaving as a global community of problem-solvers, that actively share information, that defer decisions to evidence rather than to advocacy, and that develop activities with the correct balance between collaboration and competition, both of which are major driving forces in the scientific endeavor.

The year 2003 was the period of conceptualization of the Enterprise, with the publication of the proposal in *Science*, and a follow-up meeting to refine the vision of the Enterprise. The year 2004 was spent in planning the implementation of the Enterprise vision, including the development of a joint Scientific Strategic Plan, and seeking the high level political support that will be necessary to obtain the resources to implement the identified priority activities. And in 2005 several activities are starting which include a new NIH Center for HIV/AIDS Vaccine Immunology (CHAVI), as well as a fresh infusion of funds from the Bill & Melinda Gates Foundation. The vision of the Enterprise was refined at a meeting convened by the authors of the Enterprise proposal plus a group of leading scientists, public health experts, and policy makers, which took place at the Airlie House in Warrenton, Virginia, in August 2003. The group agreed that the Enterprise would be developed, not as a new organization, but as an alliance of independent organizations (including funders and implementers) committed to accelerating the development of a preventive vaccine for HIV through the implementation of a jointly developed scientific plan, mobilization of additional resources, and greater collaboration among HIV vaccine researchers worldwide.

The Airlie House vision put the jointly developed scientific plan at the center of the proposed Enterprise, and this shared plan will be financially supported and technically implemented by a number of independent and autonomous institutions, with their own budget and using their own decision making mechanisms. So, as I indicated before, the Enterprise is not a new organization but an alliance of like-minded partners committed to accelerating the search for an AIDS vaccine.

The Enterprise is being developed, to some extent, following the model which was used to put together the successful Human Genome Project: many founders agreed on a scientific road map, voluntarily divided the work, and agreed also to an evolving set of production standards. The main features of the road map for the Global HIV Vaccine Enterprise are (i) the prioritization of the scientific challenges to be addressed as well as product development efforts, (ii) the rapid development of an implementation plan for all the components of the system, and (iii) the development of a plan that identifies the resources needed [14].

Several political bodies have already endorsed the Enterprise. In June 2004, the leaders of the industrialized countries (the G8) signed a communiqué expressing their belief that the time was right for the major scientific and other stakeholders to come together in a more organized fashion, and they endorsed the concept and called for the establishment of the Global HIV Vaccine Enterprise.

**Scientific Strategic Plan.** The scientific plan of the Enterprise was developed through a process of consultation in which six working groups involved more than 120 participants from 15 countries, and the plan was published in February 2005 in the open-access journal *Public Library of Science, Medicine* [8]. The plan summarizes the identified scientific priorities in the areas of vaccine discovery, laboratory standardization, product development and manufacturing, clinical trial capacity, regulatory considerations, and intellectual property issues. It also describes strategies and activities to implement the scientific agenda, including a discussion of the guiding principles of the Enterprise, a possible organizational structure, funding issues and political support. Although we are just beginning to implement the plan, some related activities are already starting, including the establishment of a permanent secretariat, to facilitate the coordinated funding and implementation of the plan by the different partners of the Enterprise alliance (Fig. 2).

**Activities from the Bill & Melinda Gates Foundation.** The Gates Foundation announced its decision to support the creation of centers or consortia focusing on vaccine discovery and laboratory standardization, which will work not as individual isolated groups, but as a network of institutions engaged in active and intense collaboration, according to the Global HIV/AIDS Vaccine Enterprise. With this model we hope to harness the best of both worlds, the creativity of individual investigators and the dimension, energy and sense of purpose of a big-science collaborative Enterprise.

In response to a call for proposals from the Gates Foundation to establish these targeted research centers, a number of pre-proposals (letters of inquiry) were received, focusing on one or a small number of new ideas, and bringing together the necessary variety, innovation and expertise to solve the specific problem proposed. A network analysis of the pre-proposals showed that many of the laboratories were highly interlinked among themselves, with a smaller number of unlinked groups which may represent those working outside of the research mainstream. The exchange of information is crucial for each laboratory to be as productive as possible, and to share reagents and procedures, so that data can

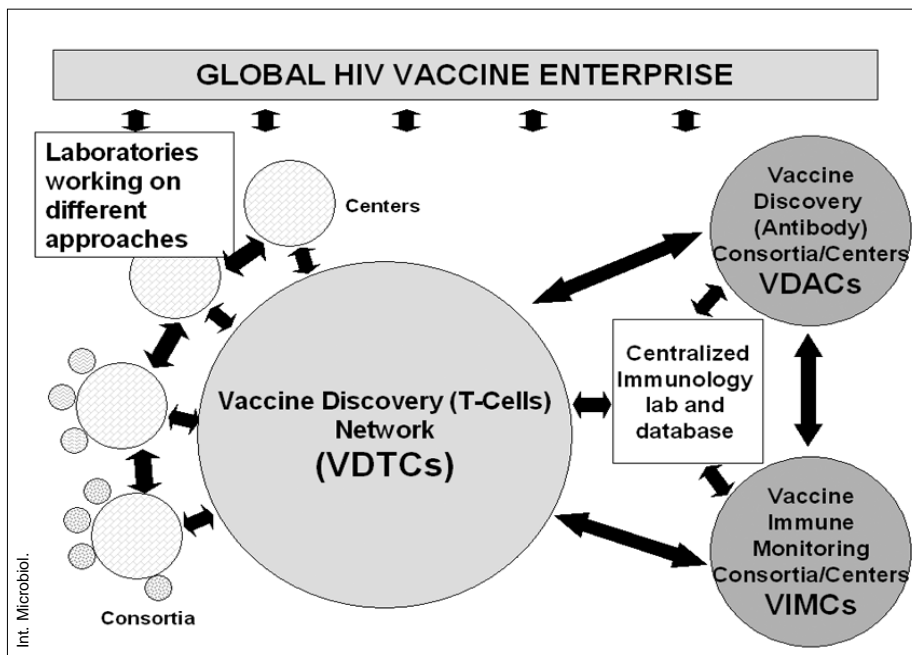


Fig. 2. Linkages between laboratories working on HIV vaccines.

be compared and, whenever necessary, analysed together [8]. A network of Clinical Research Training Centers in developing countries could help to ensure the quality of trials. In addition, a network of individuals and companies with manufacturing experience could link to consortia, centers and others providing them with process development and manufacturing expertise.

**Issues or tensions in the development of the Enterprise concept.** One tension which could arise in such an Enterprise project could be between what some people call “group thinking” and “individual thinking”. This tension has been presented occasionally as two different ways of doing science. One way is entirely based on the creativity of individual investigators working more or less in isolation on their own labs (what could be called the RO1 NIH culture). And the other way, where scientific exploration is guided by the collective wisdom of experts. History has taught us multiple times that current expert opinion is not always the right one. But, in fact, there is not real tension between these two ways of doing science; a more purposeful game plan can increase the individual creativity of researchers. In a war, soldiers are not sent to fight their own little battles. They are sent with a well prepared plan to optimize their individual efforts. And we are in a battle against AIDS.

The other tension, related to the first one, could be between investigator-driven basic research and targeted research, where the first is driven by curiosity and the search

for basic knowledge, and the later by the search for solutions. Again, there is no real tension. Both driving forces of science, the quest for fundamental understanding and the considerations for the use of the research results, are not only equally important but often they are also mutually energizing.

## Evolution of the scientific enterprise

With the ever increasing complexity of science, and the increasing difficulty of the problems to confront and to solve, scientific research has evolved into a highly complex enterprise with multiple partners that need to work in well coordinated fashion. That concept was recently discussed in the journal *Science* by Albert-László Barabási in a short commentary on the network theory and the emergence of the scientific enterprise (no relation with Global HIV Vaccine Enterprise) [1]. Barabási described how most great thinkers of the past published alone, although they built on each other's work and communicated with each other, as part of what Derek De Solla Price called “the invisible college” [9]. In the twentieth century, science became an increasingly collaborative enterprise, but usually of small groups, and the “invisible college” began to take formal shape and to become more visible.

More recent developments have led to larger collaborations, such as the International Human Genome Sequencing Consortium. Barabási recognized, however, that it was highly improbable that such large collaborations would come to dominate science, but he also recognized that most fields

need such collaborations and that the size of collaborative teams has increased, turning the scientific enterprise into a densely interconnected network driven by simple universal laws of efficiency that need to be understood, not ignored. One of the laws Barabási mentioned suggests that when forming a “dream team” an effort should be made to avoid the temptations to work mainly with friends that may not be the best scientists in the field, because that could eventually hurt the overall performance of the effort. In summary, the idealized image of the lonely investigator working in isolation in his or her lab, has now been replaced, or at least complemented, by a more collaborative effort such as the one suggested by the Global HIV Vaccine Enterprise.

The other argument frequently mentioned is that individual thinking is more creative than group thinking. However, that argument fails to capture the concept of “current scientific paradigm”, or “common science”, originally proposed by Thomas Kuhn [16]. Kuhn argued that the scientific community is extremely homogenous and very conservative. It is composed by members that go to the same schools, attend the same conferences, read the same journals, and that have their papers and grants peer-reviewed and hopefully accepted or approved by the same people. According to Kuhn, this situation creates a paradigm of “common science” that is not entirely conducive to innovation.

Pushing really innovative ideas, “out-of-the-box” ideas is actually risky. If they are ever funded (which is not often the case) they have a high risk of failure. But, on the other hand, the same community that is so risk-adverse, at the same time puts a high value on creativity and innovation. According to Kuhn, real scientific progress occurs when a new paradigm emerges that is more satisfactory than the current paradigm that drives the work of the scientific community. Then, Kuhn argued, when the new paradigm replaces the old one, scientists are rarely convinced to adopt the new ideas, and the new paradigm is fully adopted only when the old scientists die, and the younger scientists adopt the more satisfactory new paradigm which, with time, will become the “common science”, waiting to be superseded by a future paradigm change.

The other tension I mentioned before was between curiosity-driven research and use-driven research. It would be useful to give some background to this apparent dichotomy between basic and applied research. Some people credit this artificial separation of basic and applied to Vannevar Bush, who was the science adviser to President Franklin Delano Roosevelt, and who in 1945 published an influential report entitled “Science, the endless frontier” [4,20]. That report provided the blueprint used by the United States to develop its biomedical strategy and infrastructure after the Second World War. Bush recognized that basic science was

the engine that drives any future technological development, and he was concerned that if the basic science effort was not protected it would be rapidly “cannibalized” by the more pressing needs and rapid returns obtained from an applied research effort. That is how the linear model of research was formalized, in which basic research leads to applied research and development, and then to new products or processes.

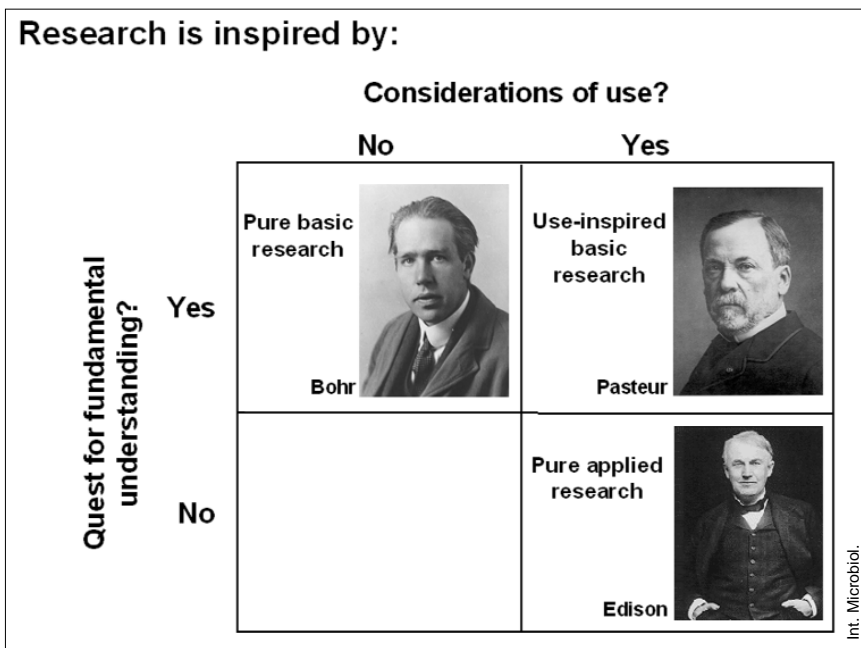
Bush’s linear model has been challenged by some authors, including the late Professor Donald Stokes, from Princeton, who was the author of an extremely interesting book entitled *Pasteur’s Quadrant* [18]. Stokes proposed, not a linear model of research progression, but a two dimensional conceptual plane, rescuing the importance of the so-called “use-inspired basic research”, or what Carlos Morel calls “strategic research” [17]. Stokes suggested that research could be inspired by the quest for fundamental understanding, by practical considerations of use, or by both, and these are represented in the different quadrants of Fig. 3. The upper left-hand cell includes basic research that is guided solely by the quest for understanding without thought for practical use. Stokes called this “the Bohr’s quadrant”, in view of how clearly Niels Bohr’s quest of a model atomic structure was a pure voyage of discovery.

The lower right-hand cell includes research that is guided solely by applied goals without seeking a more general understanding of the phenomena of a scientific field. Stokes found appropriate to call it “the Edison’s quadrant”, in view of how the brilliant inventor of Menlo Park, New Jersey, never pursued the scientific implications of his many very practical inventions. Many industries still pursue this type of research. The upper right-hand quadrant includes basic research that seeks to expand the frontiers of understanding but it is also inspired by considerations of use, and Stokes called it “the Pasteur’s Quadrant”, the title of his book. Note that Pasteur always considered basic and applied research as fruits from the same tree, the tree of science. In fact, most of the current biomedical research and the philosophy of the Enterprise are framed by Pasteur’s Quadrant, in which there is no tension between the quest for knowledge and the need to harness that knowledge to solve practical problems, such as the development of an HIV vaccine.

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### **Application of the “Enterprise” model to other global health problems**

Currently, two thirds of the world’s 6 billion people live in developing countries, and more than 1 in 6 persons live on less than US \$1.00 per day. In addition, millions of people die unnecessarily each year from diseases that are currently treat-



**Fig. 3.** Sources of research inspiration. Adapted from D.E. Stokes, *Pasteur's Quadrant* (1997).

able or preventable. Just three diseases—AIDS, tuberculosis and malaria—kill 6 million people annually. And access to existing, effective health interventions is severely limited for most of those in need, most of them living in developing countries.

The sad reality is that inadequate attention is paid to the health problems that affect the majority of the world's people: Medical research largely ignores the diseases that kill most people. Of the US \$70 billion spent annually on medical research, only 10 per cent is devoted to the diseases that cause 90 per cent of global diseases and death. Product development is primarily focused on rich world diseases. Of nearly 1,400 drugs approved in the last 25 years by the US Food and Drug Administration (FDA), only 20 were specifically for diseases that disproportionately affect the developing world.

Recognizing this situation, other collaborative Enterprise-like approaches are being implemented or discussed, to address at least two of the other main killers of mankind, tuberculosis and malaria. These include "The Global Alliance for TB Drug Development" and, still under initial planning, "The Malaria Vaccine Technology Roadmap".

## Concluding remarks

I want to conclude with a quote from my dear friend and colleague, Pascoal Mocumbi, Former Prime Minister of Mozambique, and now a very active participant and leader of two major health research initiatives, the European Com-

munity driven "European Developing Countries Clinical Trials Partnership" (or EDCTP), and the Global HIV/AIDS Vaccine Enterprise. Mocumbi admonishes us that "[...we are] now endangered by a failure to use our collective knowledge, wisdom and resources to bring essential medical advances to bear for the benefit of all our citizens." It is our social responsibility as scientists to do science, not only for the sake of science itself, but also for the sake of our fellow human beings that are suffering the burden of many infectious diseases that could be effectively controlled if we dedicated our time and efforts to that noble cause.

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### Iniciativa Conjunta por una Vacuna contra el SIDA

**Resumen.** El sida, cuya existencia era desconocida hace veinticinco años, se ha convertido en la enfermedad infecciosa más grave a escala planetaria. El desarrollo de una vacuna contra el virus de la inmunodeficiencia humana (HIV) es uno de los retos más difíciles que afronta la moderna ciencia de la biomedicina. Para ello, la comunidad científica ha de organizarse realizando un esfuerzo conjunto intenso y con un objetivo concreto, como el que propone la Iniciativa Conjunta por una Vacuna contra el Sida. El concepto de "iniciativa" trata de complementar la creatividad del investigador individual con un sistema de colaboración que asegure un uso más eficaz de los recursos humanos y financieros para generar conocimiento científico nuevo. Actualmente se están explorando diferentes modalidades del concepto de "iniciativa" para el desarrollo de fármacos para el tratamiento de la tuberculosis y de vacunas para prevenir la malaria. [*Int Microbiol* 2005; 8(2):93-101]

**Palabras clave:** vacuna contra el VIH · SIDA · iniciativa científica · epidemiología

### Iniciativa Conjunta por uma Vacina contra a AIDS

**Resumo.** A aids, cuja existência era desconhecida há vinte e cinco anos, se transformou na doença infecciosa mais grave a escala planetária. O desenvolvimento de uma vacina contra o vírus da imunodeficiência humana (HIV) é um dos desafios mais difíceis que enfrenta a moderna ciência da biomedicina. Para isso, a comunidade científica há de organizar-se realizando um esforço conjunto intenso e com um objetivo concreto, como o que propõe a Iniciativa Conjunta por uma Vacina contra a Aids. El concepto de "iniciativa" trata de complementar a criatividade do investigador individual com um sistema de colaboração que assegure mais um uso eficaz dos recursos humanos e financeiros para gerar conhecimento científico novo. Atualmente se estão explorando diferentes modalidades do conceito de "iniciativa" para o desenvolvimento de fármacos para o tratamento da tuberculose e de vacinas para prevenir a malaria. [*Int Microbiol* 2005; 8(2):93-101]

**Palabras chave:** vacina contra o HIV · AIDS · iniciativa científica · epidemiologia

