“Since all science is problem driven, it should be judged by the quality of the problems posed, and the quality of the solutions provided”
(Sydney Brenner, 1998)
We welcome the initiative of the Human Frontier Science Program (HFSP) presented by Japan, which is aimed at promoting, through international cooperation, basic research on biological functions. We are grateful for the informal opportunities our scientists have had to take part in some of the discussions of the feasibility study undertaken by Japan. We note that this study will be continued, and we would be pleased to be kept informed about its progress. – Declaration of the G7 Summit, Venice, 1987
EXECUTIVE SUMMARY

In the twenty years since its creation, the Human Frontier Science Program (HFSP) has established its unique role as a funding organization at the frontiers of the modern life sciences. In these efforts it has been extremely successful. While considerable efforts are undertaken around the world by organizations employing both public and private funds, often of an order of magnitude greater than that which HFSP will ever be able to offer, it has created for itself a unique niche to address the paradox that science is international while its institutions and funding organizations are mostly nationally or even regionally organized.

Against this background, the strategic aims of HFSP are to:

- Support innovative, cutting edge research at the frontiers of the life sciences
- Encourage high risk research
- Promote international collaboration in the spirit of science without borders
- Enable financial and intellectual independence for early career researchers
- Raise the profile of HFSP and its work through an intelligent communication strategy
- Foster inclusiveness by increasing participation by female scientists
- Sustain the means of achieving its distinctive mission in the face of the rising cost of research.

In line with these goals, international program grants as well as postdoctoral fellowships are and remain the pillars of its portfolio. The rigorous peer review by international committees will remain its hallmark.

Due to its one-of-a-kind position, HFSP can observe, and stimulate changes in fundamental biological research worldwide. Thus, it provides its member organizations with a window through which they can assess their national programs. It is a forum for discussion about best practices as well as a common test bed for new initiatives, many of which have been adopted by the national agencies. It can highlight communication problems between groups of scientists. Because its awardees are highly mobile, the Human Frontier Science Program is aware of global movements of talent, and through its prestigious awards HFSP will help in the recognition of new centers of excellence as they arise worldwide.

The frontiers of the life sciences are a rapidly moving target and thus resist clear identification. Nevertheless the broader issues can be readily defined. Biology has become quantitative and systemic due to major contributions from mathematics, physics, chemistry, the computer sciences and methodological developments in DNA-sequencing, imaging and light microscopy. These developments now permit meaningful research at higher levels of complexity in bridging the existing gap between molecular biology and ecology or biodiversity. No doubt, others, like the influence of climate change on biological systems, will be added in the future.

In recent years, HFSP has continuously reviewed its instruments and processes in order to measure its impact on grantees and host institutions. The reviews of 1996, 2001, 2007 and 2010 have invariably and consistently underlined the high quality of the program. Nevertheless, procedures and instruments have to be adapted while the life sciences progress in a process which can only be described as revolutionary. It is the aim of this Strategic Outlook to accommodate these developments and to use them to give future directions for this unique funding organization.
HISTORICAL BACKGROUND

The Human Frontier Science Program is a research funding organization, which aims to fund excellence in basic research in the life sciences by focusing on the support of the best researchers and ideas. Its unique ambition is to open the ever-moving frontiers of the life sciences through international program grants and through encouragement of young investigators and their early independence. It is and remains the only program, which, through its global membership, is able to achieve its goals irrespective of national concerns or considerations. It is the true spirit of frontier science, which always has been of an international nature.

HFSP was founded in 1989 through an initiative of former Japanese Prime Minister Yasuhiro Nakasone. His idea was to establish a funding organization for basic research in the life sciences. In his words, “HFSP was meant to be a 21st century, long/term global research program fostering international cooperation for the benefit of mankind, under which courageous researchers from throughout the world and the spirit of challenge would form teams to analyze and discover various complex mechanisms of living organisms”.

The issue of the emergence of complexity has since become a significant “frontier” in life science research.

Initially the focus was divided between molecular biology and brain research, the frontiers of science at that time. Prime Minister Nakasone had originally suggested the inclusion of studies on the ethical implications of recombinant DNA research, which had started to concern a wider audience in the middle of the 1980’s. However, this suggestion was subsequently put on hold when additional research showed that the risks of recombinant DNA research did not require the particular attention originally perceived. Nevertheless, the relationship between science and society remains a constant concern and will continue to guide HFSP activities.

The preparatory conferences, which led to the start of HFSP, also raised the issue of the emergence of complexity in the life sciences. Lack of knowledge and methods meant that the subject could not be properly addressed at the time, but it has since become a significant “frontier” in life science research. Nevertheless, because of the broad foresight of its founders, the program always emphasized the interdisciplinary nature of its funding perspectives thereby preparing it for the current challenges.

THE STRENGTHS OF HFSP

The work of HFSP rests on the issues of complexity in biology, on frontier research, on cross-border research across continents, on the quality of peer review and on the support of early independence of researchers. Taken together, these pillars make it distinctive
among funding agencies and therefore immensely valuable in the ever evolving world of science.

The issue of cutting-edge research at the frontiers of the life sciences

Frontier research is research at the cutting-edge of any given scientific field. The word “Frontier” may be associated with the exploration of the American West in the early 1800s (“Lewis and Clark”), the land beyond boundaries, the land of the unexpected and of unlimited opportunities. It takes enormous risks to step into the unknown and in this sense a “Frontier” is quite an appropriate goal for a research funding organization like HFSP and the kind of research it should support.

HFSP, in particular, has been given the task of promoting research into the “complex mechanisms of living organisms”. The status of research on living organisms can be traced to a few major breakthroughs, including Darwin’s hypothesis on the origin of species in 1859, the rediscovery of Mendel’s laws in 1900, the discovery of the physical nature of the gene by Watson and Crick in 1953, the invention of recombinant DNA technologies in and around 1970 and the completion of the sequence of the human genome in 2001. Since then it has become obvious that the expectations aroused prior to the completion of the genome sequence could not be met immediately. Apart from the fact that the genome carries more information than just protein coding sequences, living organisms obviously represent more than just the sum of their genes. Complexity in biology thus must be discussed in the context of higher levels of organization, including proteins, cells, organisms, populations and entire ecosystems. In this spirit the post-genome era imposes new challenges, which require biology to become integrative and quantitative.

Twenty years ago when HFSP was founded the frontier of biology could be defined as molecular biology. Later on it was realized that molecular biology alone does not guarantee the necessary depth of engagement, and, therefore, interdisciplinarity was added as a *sine-qua-non* of its activities. In fact, the boundaries of modern biology have become so broad that they require the integration of many fields such as the computer sciences, chemistry physics, mathematics and even engineering. Today, therefore, interdisciplinarity must be regarded as a given but without excellence and creativity is not sufficient to perform frontier research in biology.

The conduct of research in biology is rapidly changing. It has to harness and to integrate the new capabilities, such as databases, genome sequencing, novel microscopic technologies, to name just a few. A focus on reductionism and on “more-of-the-same”

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1 Lewis and Clark expedition, 1804-1806. Laid much of the groundwork for the expansion of the American West (see wikipedia.org/wiki/Lewis_and_Clark_Expedition)
type of research, albeit comparatively safe and reliable, is not likely to lead to fundamental breakthroughs anymore. A frontier is a moving target, and the issue of risk thus has to be analyzed anew every time HFSP is asked to fund a particular project: excellence and risk together have to remain the trademarks of the Human Frontier Science Program.

"A frontier is a moving target, and the issue of risk thus has to be analyzed anew every time HFSP is asked to fund a particular project."

How these matters can be dealt with and responded to by a funding organization has been the subject of a scientific conference dedicated to this subject, held in March 2010.

This “Frontier Conference” included 35 scientists from all over the world invited to represent many frontiers currently perceived to exist in the life sciences. The conclusions reached can be summarized as follows:

- the Life Sciences pose ever more challenges and opportunities for humankind
- interdisciplinarity is a necessary condition for progress in the life sciences but is not alone sufficient. Only combined with excellence and risk-proclivity does it define a frontier
- novel technologies, like the DNA-sequencing revolution, the improvement of imaging tools or the new developments in light-microscopy constantly redefine the field and accelerate progress in an unprecedented matter
- the relationship of mathematics and biology, unlike the one between mathematics and physics, is only in its infancy, still making it a challenge to reach beyond tautology and the trivial; nevertheless, current efforts already point far beyond the merely promising
- systemic, synthetic and quantitative approaches to biology thus require additional breakthroughs, not only in mathematics but also in information theory, in high-throughput chemistry, and in the computer sciences
- the science of genetics is on a continuing track of unimpeded success as seen not only for the classical yeast and animal models but also in the accelerating pace of developments in the understanding of the biology of plants
- the new possibilities in understanding complexity are beginning to penetrate even fields like the cognitive neurosciences, or ecology and biodiversity, which have not found intensive support by HFSP in the past
- the border lines between genetics, epigenetics and the environment are becoming more and more defined, permitting us to pose clearer questions as to their respective relationships
- Big Science has become a feature of modern biology thus posing challenges to a small funding organization like HFSP
- education in the interdisciplinary context of the life sciences has become increasingly important.

"HFSP believes unflinchingly in curiosity-driven research and in its particular power to rapidly increase our knowledge and thereby to contribute most efficiently to the innovation process."

These things seen and said HFSP will continue to resist the temptation to prescribe any particular subjects. It believes unflinchingly in curiosity-driven research and in its particular power to rapidly increase our knowledge and thereby to contribute most efficiently to the innovation process.

The issue of international research: science without borders

One particular, strength of HFSP is the possibility of supporting international program grants. This is another pillar, which distinguishes it from national or even supranational research councils like the European Research Council. The basis for scientific expertise cannot be broad enough today. To identify it within a national boundary may well be possible but is never guaranteed. HFSP offers the opportunity to rapidly jump such boundaries, to find a scientific partner almost anywhere in the world and to secure joint funding. National councils can develop such
possibilities, but only with considerable delays. It is amazing how, in retrospect, the Japanese government already recognized this issue two decades ago. These prerequisites have not changed at all. In fact they have become more and more relevant, and thus more than justify the existence of a research funding agency like HFSP.

The basis for HFSP’s international character is its membership. The current members of HFSP are Australia, Canada, France, Germany, Italy, India, Japan, New Zealand, Norway, the Republic of Korea, Switzerland, the United Kingdom of Great Britain and Northern Ireland, the United States of America and the European Union.

In a spirit of encompassing a world-wide community of scientists, HFSP is not only open for additional members but actively encourages countries to apply for membership as long as the country’s scientific capacity in basic research in fields represented in its current program meets its goals and perspectives.

The issue of inclusiveness

From early on, the founders of HFSP recognized that the potential for scientific discoveries is not restricted to scientists in later stages of their career. In contrast, experience teaches that unconventional ideas are more likely to be developed by junior researchers than by senior ones although there are exceptions to the rule. Many funding agencies in the world have neglected this issue. It was thus highly appropriate for the founding fathers (and mothers) of HFSP to foster early independence not only by setting up a program for postdoctoral fellows but also by emphasizing the role of junior researchers in program grants. This trend must and will continue.

In addition to supporting young researchers, Human Frontier Science Program is placing greater emphasis on increasing the number of women in HFSP activities. HFSP is not only working to increase the number of proposals submitted by women, which will hopefully lead to a more equitable balance in the funding profile, but also expanding the number of female reviewers and committee members.

Postdoctoral fellowships will remain the hallmark of HFSP. Nevertheless, even the best of people and the best of laboratories may require additional expertise from the outside, to improve on critical mass and effectiveness. Thus, small networks, as offered through HFSP’s Program Grants, are not in contrast to the concept of individual achievements.

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INDICATORS OF SUCCESS

In the spirit of transparency HFSP has always sought independent review to assess its achievements. The period from 2000-2005 was covered by the NIFU-STEP report, commissioned from the Norwegian Institute for Studies in Innovation, Research and Education. The portfolio changes introduced since the year 2000 were reviewed by a committee of high-level scientists (the Alberts Committee report, 2007) in early 2007. In preparation for the Intergovernmental Conference (IGC) in mid 2010, the Manchester Institute of Innovation Research was asked to assess the most recent performance of HFSP. It has assessed again the output, impact and appropriateness of HFSP’s funding schemes through a survey of awardees, a survey of host organizations, a bibliometric analysis and an integrative analysis of all the data collected.

The bottom line of all these assessments was and is that HFSP “occupies an important, unique niche in the world of science through its mode of supporting the

Discussion on trends in systems biology at the 2010 Awardees Meeting in Kerala, India

See full text at http://www.hfsp.org/about-us/reviews-hfsp

2 See full text at http://www.hfsp.org/about-us/reviews-hfsp
best innovative, international, interdisciplinary research”. For example, among the six Nobel Prize winners in 2009 in the fields of medicine and chemistry, three have been awardees of HFSP. In addition it is repeatedly stated that HFSP’s programs should continue to provide the conditions under which high risk and interdisciplinarity can flourish. Invariably, all these reports strongly urge participating member states to seriously consider increasing their financial commitments for future years.

The HFSP secretariat, in turn, pledges to continue its efforts for lean and efficient management, delivering a culture of trust to applicants and awardees, and remaining entirely open to professional interchanges with all its interlocutors, including members of its various review committees, councils and boards. In doing so it aims to continue being a role model in the increasingly globalizing world of research funding organizations.

COMMUNICATION AND PUBLIC RELATIONS

HFSP has always been dedicated to offering appropriate means of communication among its awardees and with the interested parts of the scientific community and society-at-large. Nevertheless it has remained largely unknown, even in scientific circles, not to mention the societal and political realm.

In order to improve its visibility, HFSP thus will undertake a variety of steps many of which are based on the revolutionary developments involving use of the world-wide web and the novel possibilities offered by the world of digitalization. These include:

• Continuing and expanding the annual awardees meetings and using them to enhance recognition of HFSP and its distinctive role. These unique multi-disciplinary meetings are forging an international body of talented scientists of all ages who are intellectually prepared for the possibilities of novel and exciting collaborations

• Creating an alumni organization, which HFSP wants to foster at the start but hopes to develop and maintain mainly through resources and efforts of the alumni themselves. Such a network will increase the corporate identity among awardees and increase substantially the visibility of the program

• Extending the visibility of and awareness about HFSP through improved communication via the website, with more information about the research funded by the Program and associated scientific policy issues, news about HFSP awardees, a special forum for alumni and by enhancing the Program’s presence at international meetings

HFSP’S OBJECTIVES FOR THE NEXT SIX YEARS

• Maintaining the uniqueness of HFSP in supporting high-risk international collaborations and individual researchers working at the frontiers of the life sciences

• Extending the frontiers: the “Frontiers” in modern biology are a rapidly moving target. HFSP

HFSPO President Prof. Akito Arima presents Dr. Karl Deisseroth with the 2010 Nakasone Award. In the background Prof. Ernst-Ludwig Winnacker, Secretary General of HFSPO.
acknowledges that these developments are crucial to its mission and will stimulate them through two new mechanisms, a bottom-up, HFSP-branded conference series and “Frontiers Conferences” to be held whenever necessary. With the advice of the Council of Scientists, HFSPO will invite scientific leaders in their field to review the state of the art and to define funding opportunities in the development of the life sciences. On the basis of these activities, HFSP guarantees a continuing emphasis on promoting and funding high-risk, world-class research in the life sciences.

- Strengthening the career support line of HFSP awardees by the introduction of a new program, the HFSP Investigator program, for the most talented CDA holders, who otherwise may fall back into dependent or semi dependent positions. This program would provide support for five years.

- Increasing the participation of female scientists at all levels of HFSP’s governance and activities.

- Continuing the inclusion of early-career scientists in program grants as a means of fostering early independence and broadening their research experience.

- Encouraging interaction between members of the HFSP community worldwide, including exploitation of new developments in digital communication and increasing visibility of the research funded by HFSP.

- Stabilizing its financial resources. Although Japan has indicated that it will continue to remain a leading contributor to HFSP, the organization will try to broaden its financial base through:
  
  o the development of a new key for the contributions of participating organizations, thereby compensating for the reduced proportion of the Japanese contribution; while acknowledging the key role of Japan in the Program
  
  o the addition of new members
  
  o the collaboration with public or private research funding organizations in the support of its programs.