THE INTERNATIONAL HUMAN FRONTIER SCIENCE PROGRAM ORGANIZATION

Three Decades of Unparalleled Success



The International Human Frontier Science Program Organization (HFSPO) is a story of extraordinary vision and a rare example of successful science diplomacy. First conceived in Japan in the 1980's, it was designed to stimulate collaboration among international research institutions. HFSPO was an experiment in more flexible program management allowing bottom-up initiatives that would be decided by an independent scientific structure and governed by an international board of trustees.

In 1986, a feasibility study for such an international endeavor was carried out by leading Japanese scientists under the auspices of the Japanese Prime Minister's Council for Science of Technology. This discussion was expanded in 1987 to include scientists from the G7 nations and the European Union, resulting in the "London Wise Men's Conference" in April 1987, which endorsed the suggestion. Prime Minister Nakasone of Japan proposed to implement HFSPO as the operational entity for the organization, at the Venice Economic Summit of the G7 countries and the European Commission in June 1987. The Economic Summit partners and the Chairman of the European Community welcomed the initiative. The newly created organization was charged with the following mission:

"To promote and fund basic research focused on the elucidation of the sophisticated and complex mechanisms of living organisms for the benefit of all humankind, through international cooperation."

In 1989, an International Scientists Committee further defined the organization, its activities, research areas and protocols. Later that year, the G7 governments agreed to implement HFSPO for three years, after which Members agreed to continue HFSPO.



The G7 Economic Summit in Venice 1987. From left to right: Wilfried Martens, Jacques Delors, Yasuhiro Nakasone, Margaret Thatcher, Ronald Reagan, Amintore Fanfani, François Mitterrand, Helmut Kohl and Brian Mulroney.



The meeting of the G7 Science Leaders 12-14 May, 2023, in Sendai/Japan (<u>https://www8.cao.go.jp/cstp/kokusaiteki/g7_2023/2023.html</u>)

HFSPO is unique: it supports innovative, frontier research in the life sciences, encourages high-risk, high-reward research and promotes international collaboration in the spirit of science without borders. HFSPO provides opportunities for the global scientific community to support frontier research in areas for which there are no prior studies, no data, and no guarantee for the concept.

The administrative offices of HFSPO, known as the Secretariat of the Program, were established in October 1989 in Strasbourg, France. The first President of the Program was Ambassador Miyazaki of Japan, the first Chairman of the Council of Scientists was Edward Rall of the United States USA and the first Secretary-General was Sir James Gowans, former Secretary of the UK Medical Research Council. The original HFSPO Members included the G7 countries plus the European Commission. Switzerland joined in 1990. Australia, the Republic of Korea, India, New Zealand, Norway Singapore, and Israel have joined since 2004, and South Africa joined in 2023.

More than 30 years following the highlevel endorsement of the G7 Summit that laid the foundation for HFSPO, the 2023 G7 Summit in Sendai, Japan, emphasized again the added value of HFSPO as a model to promote international talent mobility and circulation. The G7 Science Leaders reconfirmed that the Human Frontier Science Program (HFSP) "has promoted cutting-edge international joint research and human resource development, achieving siginficant results in the process" - recommending a continuation of this pioneering initiative.

HFSPO'S UNIQUE NICHE AND VALUE PROPOSITION

The Program provides exceptional value for Member nations by supporting exploratory research that individual nations might not otherwise fund. It operates on a central budget provided by its Members that remains under independent control, thereby removing the traditional 'red tape' common to bilateral or national programs. Thus, research institutions receive international money from HFSPO's annual budget, but the income does not carry a geographical tag.

HFSPO puts a high value on basic life science at the frontiers of knowledge, on international scientific cooperation, and on basic research as a driver of economic and social benefit. The HFSP niche complements the research priorities of its Members by providing international collaborations in areas and at times not covered by existing international agreements. Most HFSPfunded grant collaborations involve three or more countries and more than 95% of all grants involve intercontinental collaborations.

This is possible because HFSP Members share common values: They prize scientific integrity, excellence, bold innovation, and intercontinental collaboration. Members believe that co-operation and collaboration among diverse people, different points of view, and across disciplines builds creativity. Another very important aspect of HFSP regarding innovation is that any intellectual property remains with the inventors and is not released to HFSP as the funder. In every research study that HFSP supports, we accept the possibility of failure. We also know that innovations come through our willingness to embrace high-risk inquiry in the hope of achieving high-reward results. Often, HFSP grantees later succeed in gaining support from domestic funders based on the pioneering work they did under HFSP support.

THE PRESTIGE AND IMPACT OF HFSP-SUPPORTED RESEARCH

Since HFSPO's inception, more than 48,000 scientists have applied for HFSP research grants and each year, HFSP receives some 650-700 applications involving a total of 2,000-2,500 scientists. Since 1990, more than 21,000 early career scientists have applied for fellowship support and each year 500-600 postdoctoral researchers apply for HFSP fellowship support. Competition is rigorous and only the best, most exceptional frontier research proposals are supported.

HFSP-funded research ranks among the most impactful in the global scientific enterprise by advancing pure science and fueling the innovation economy. In the 30 plus years since HFSP's inception, research grantees have won 28 Nobel Prizes. Four out of the fourteen winners of the HFSP Nakasone Award were also recognized with Nobel Prizes, and since the inception of the Kavli Prize in Neuroscience, HFSP awardees have been among the winners every year. Likewise, HFSP grant investigators have won some of the most prestigious prizes from the Breakthrough Foundation, the Lasker Foundation, and the Canada Gairdner Foundation. In addition, HFSP scientists are recognized with major sciences prizes in Asia and Europe. Nearly every year an HFSP awardee is among the winners of the most recognized and prestigious prizes in science. HFSP-funded scientists are truly the pioneers of their fields pushing the frontiers of the life sciences to great insights and increased capability.



EXCEPTIONALLY PRODUCTIVE AND AUTHORITATIVE

The quality and influence of HFSPfunded research is reflected in the sheer number and prestige of the publishing record. Beginning in 2009, the year publishing companies introduced a funders field allowing authors to credit the organization that supported their research, HFSP scientific community has on average published 1,000 scientific articles per year. Bibliometric comparisons of HFSP against other national or international funding organizations – all much larger in size and operating budget demonstrate that HFSP scientific returns on investment are significantly higher. When looking at the share of HFSP papers cited by patents, as a proxy measure for uptake in innovation, the resulting data show that 9.6% of publications by HFSP fellows were cited between 2009-2011. This is by far and away higher than the world's share of papers in the life sciences (3.6%) and in research areas in the life sciences targeted by HFSP scholars (5.4%).

BASIC FRONTIER LIFE SCIENCE RESEARCH LEADING TO VALUABLE INNOVATIONS

HFSP-supported frontier basic science often breaks ground that leads to valuable innovations in the life sciences, new patents, and commercial enterprises.

SUPPORTING FRONTIER LIFE SCIENCE WITH OUR PROGRAMS

Research Grant Awards

HFSP supports frontier research in the life sciences through two types of research grants: **Research Grants - Program** are awarded to teams of two to four scientists at any stage of their careers who embark upon a new collaborative project. **Research Grants - Early Career** require team members be within five years of obtaining an independent position and not more than 10 years after completing their Ph.D.

HFSP research grants are awarded to interdisciplinary teams of two to four scientists working in different countries and preferably different continents. HFSP projects are based on the outstanding competence of the scientists, their innovative ways of thinking, and their willingness to take the risk to step outside the limits of their traditional research area and build new teams. These interdisciplinary collaborations have opened up new approaches for understanding the complex structures and regulatory networks of living systems and often include scientists from physics, chemistry, geology, material science, mathematics, nanoscience or psychology.

Fellowship Awards

HFSP offers two types of postdoctoral fellowships:

Long-Term Fellowships (LTF) are for applicants with a PhD in a biological topic who want to embark on a novel frontier project focusing on the life sciences. Cross-Disciplinary Fellowships (CDF) are for applicants who hold a doctoral degree in a nonbiological discipline (e.g., physics, chemistry, mathematics, engineering or computer sciences) and who have not worked in the life sciences before, but want to work on a novel frontier project in biology.

HFSP fellowships are for three years and provide an annual living allowance as well as a research and travel allowance. Child, parental leave and relocation allowances are provided where appropriate. HFSP fellowships must be taken up in a laboratory in a country different from the one where the PhD degree was conferred. Applicants from countries that are not HFSPO Members must pursue their fellowships in an HFSPO Member country. The programs for early career researchers have supported fellows from 71 different nationalities.



Developing RNA-based catalysts that revolutionize the discovery of bioactive peptides

Suga's 2017 HFSP grant research isolated two types of tRNAaminoacylating ribozymes from libraries based on an existing t-box riboswitch of *Bacillus subtilis glyQS*, which suggested a possible scenario of evolution of tRNA-aminoacylating ribozymes, primitive translation and T-box gene regulation systems. With this understanding, he was able to develop novel ribozymes, Flexizymes, that can charge tRNAs with amino acids, with the goal of reintroducing ribozymes into cellular metabolism, ultimately replacing protein enzymes. His discoveries have had major impacts in the biopharmaceutical industry, and he co-founded MiraBiologics.



Hiroaki Suga, Department of Chemistry, Tokyo University



Aviv Regev, The Broad Institute of MIT and Harvard

Single-cell genomics as the basis for personalized medicine

In 2005, an HFSP research grant team led by Regev investigated novel high-throughput set-ups for gene sequencing at the cellular level. Knowing the complex properties and dynamic behaviours of a cell provides the means to understand the physiology of an entire organism. She developed systems for analyzing tens of thousands of cells in a single experiment, which enabled the commercialization of this technology and its adoption worldwide. Now researchers are using these techniques to study the human body at the single-cell level, revealing new cell types with implications for health and disease. For example, single-cell studies of cancer provide new insights into tumour composition and drug resistance. A 2018 analysis of the global single-cell genome sequencing market is to reach USD 2.49 billion by 2025 with a compound annual growth rate of more than 14% during the forecast period. She was awarded the 2022 HFSP Nakasone Award.

Super-Resolution Microscopy That Can Image Actions in Living Cells

Nobel laureate Stefan Hell (HFSP Research Grant in 2017) developed a revolutionary super-resolution microscopy method called MINFLUX that allows permits imaging at a resolution the size of a small molecule and revealing unprecedented detail in imaging cellular structures. To demonstrate the power of these new developments, a precise cellular structure was needed, thus the Hell group teamed up with 2017 HFSP Young Investigator Jonas Ries, who had established superresolution reference standards as part of his HFSP grant.



Jonas Ries, European Molecular Biology Laboratory, Heidelberg

These reference structures consisted of nuclear pore complexes, channels that regulate transport between the nucleus and cytoplasm of cells, which the Ries group had labeled with super resolution-compatible fluorophores using the CRISPR/Cas9 technology. The MINFLUX microscope revealed the structure of these complex protein machines with unprecedented optical resolution. They demonstrated this was even possible in living cells, which paves the way for imaging molecular machines during their action.



Stefan Hell, Max-Planck-Institute for Biophysical Chemistry, Goettingen

HFSPO MEMBERS





Over the last more than 30 years, HFSPO has doubled the membership, welcoming new nations worldwide, committed with cutting-edge research in basic life sciences.

The current members of the International Human Frontier Science Program Organization (HFSPO) are the G7 nations, Australia, India, Israel, Norway, Republic of Korea, Singapore, South Africa, Switzerland, New Zealand and the non-G7 members of the European Union, who are represented by the European Commission.