ANNUAL REPORT

1 April 2021 — 31 March 2022

HFSP

International

Human Frontier Science Program

Organization

INTERNATIONAL HUMAN FRONTIER SCIENCE PROGRAM ORGANIZATION

The Human Frontier Science Program (HFSP) is unique, supporting international collaboration to undertake innovative, risky, basic research at the frontier of the life sciences. Special emphasis is given to the support and training of independent young investigators, beginning at the postdoctoral level. The Program is implemented by the International Human Frontier Science Program Organization (HFSPO), supported financially by Australia, Canada, France, Germany, India, Israel, Italy, Japan, the Republic of Korea, New Zealand, Singapore, Switzerland, the United Kingdom of Great Britain and Northern Ireland, the United States of America, and the European Commission. Since 1990, over 7500 researchers from more than 70 countries have been supported. Of these, 28 HFSP awardees have gone on to receive the Nobel Prize.

The cover image is of microtubule polymers undergoing treadmilling in silico (the colours represent time, from blue to gold). Image courtesy of HFSP Cross-Disciplinary Fellow and Career Development Award alumna Marija Zanic, together with EJ Lawrence and G Arpag, produced using the UCSF Chimera package.

https://www.hfsp.org/hfsp-news-events/reconstituting-microtubule-treadmilling-outside-cells

The following documents are available on the HFSP website www.hfsp.org:

- Joint Communiqués (Tokyo 1992, Washington 1997, Berlin 2002, Bern 2004, Ottawa 2007, Canberra 2010, Brussels 2013, London 2016, Tokyo 2019): https://www.hfsp.org/about/governance/membership

- Statutes of the International Human Frontier Science Program Organization: https://www.hfsp.org/about/governance/hfspo-statutes

- Guidelines for the participation of new members in HFSPO: https://www.hfsp.org/about/governance/membership

- General reviews of HFSP (1996, 2001, 2006-2007, 2010, 2018): https://www.hfsp.org/about/strategy/reviews

- Lists of 2022 awards: https://www.hfsp.org/awardees/newly-awarded

- Previous lists of awards, including titles and abstracts: http://www.hfsp.org/awardees/awards

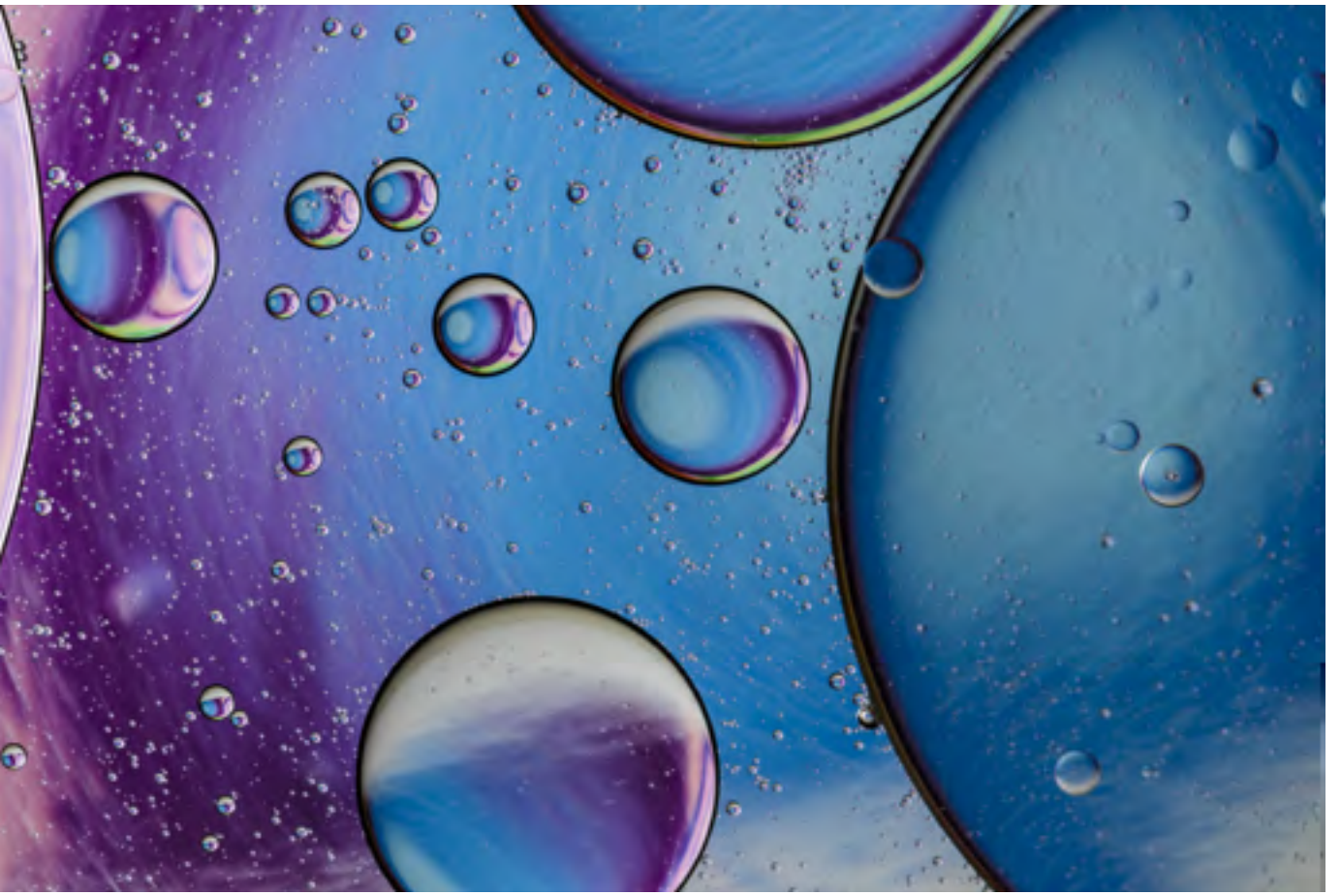
OUR SHARED VALUES

HFSPO is committed to supporting frontier life science research and engages with researchers in more than 50 different countries. In over 30 years of operations, the Organization has achieved an unparalleled record of success in funding ground-breaking discovery research that has advanced knowledge, created new research areas, and resulted in innovative and impactful applications.

Scientific excellence determines the selection of HFSP research projects, but for an internationally operating organisation it is paramount to be guided by equitable, diverse, and inclusive conditions because these are essential for achieving impactful outcomes and creating a sense of shared values among HFSPO staff, the Organization's Members and the global community of HFSP supported researchers.

HFSPO is committed to:

- taking into full consideration equity and inclusion in all aspects of its operations;
- encouraging good practice and raising awareness among reviewers and staff;
- maintaining a diverse geographic representation in all its statutory bodies and at the HFSP Secretariat in Strasbourg, France;
- supporting participation of female scientists as members of statutory bodies, and, in concertation with HFSPO Members, offering special support for women in science;
- reinforcing the application of good scientific practice at all stages of the HFSP programs and supporting the HFSPO Members in their efforts to raise awareness among the global scientific community.



In its fourth decade of operations, HFSPO will build on existing good practice and principles that guide local operations and international grant making.
We will seek even closer collaboration with our Members and the scientific community to establish an “esprit de corps” that underlies the standing and reputation of HFSPO and that is conducive to generating successful research outcomes across the world.

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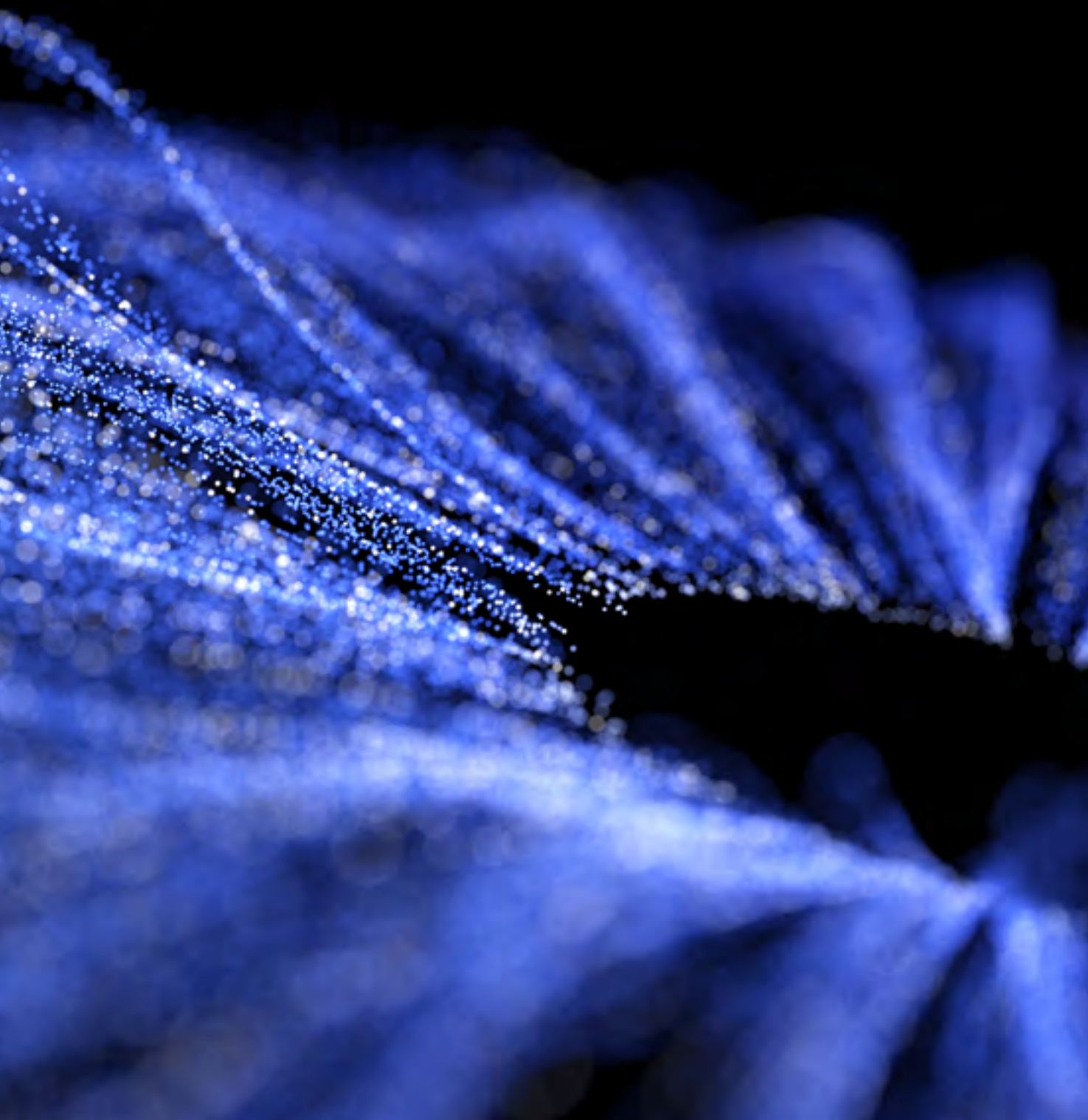
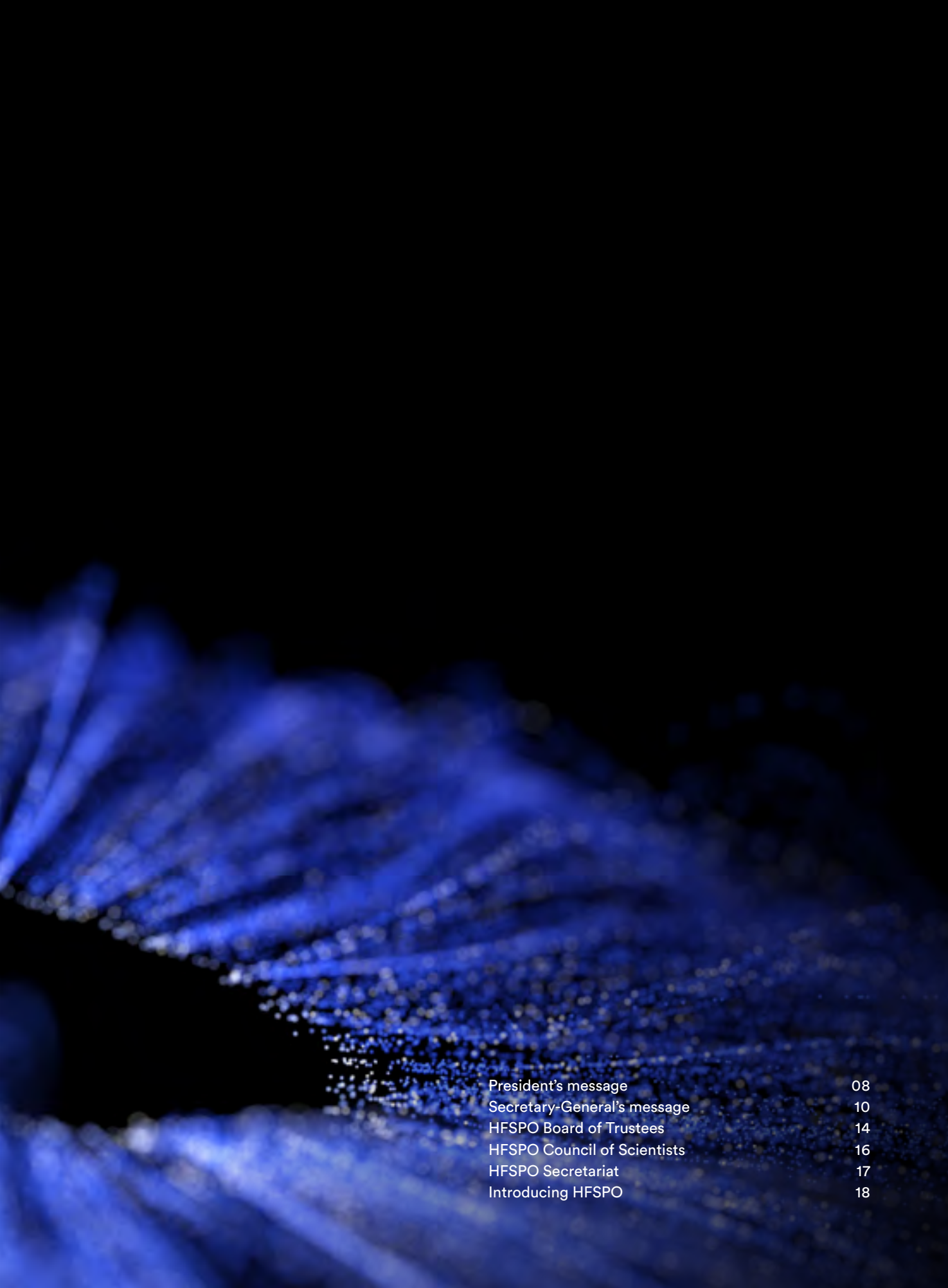
In addition to the annual report, HFSP will also publish a Science Digest presenting research highlights from HFSP research grant and fellowship awardees, together with summaries of recently awarded projects. The “HFSP Science Digest 2021” and future issues will be published as a separate document.

Introduction





PRESIDENT'S MESSAGE

The cherry blossom on Osaka University campus

> ***In the cherry blossom's shade, there's no such thing as a stranger***
>
> Kobayashi Issa

In Japan, we look forward through the long winter months to the season of cherry blossom and this year, for the first time since the Covid-19 pandemic broke out, we were able to walk under a shower of petals. As life science researchers, investigating the complex mechanisms of living organisms, it is our privilege, in cherry blossom season and indeed every day, to explore the magic of life.

Basic science, as we know, is hard work. It's about going to the lab every day, about continuing relentlessly until, if we're lucky, the cherry tree blossoms in a cluster of beautiful experiments which effect the breakthrough and move science on. Most often, it is the work of successive teams of scientists, inching knowledge forward from one generation to another, a community effort in which the success of one is progress for all.

At HFSP, we believe that the chances of serendipitous discovery are heightened by the mix of scientific cultures present in interdisciplinary teams where researchers are encouraged to find the best fit internationally for their project, taking a step sideways, with new collaborators on a new project, to discover something 'beautiful', truly new.

We hope that this year's new awards will give rise to some such beautiful experiments. On the starting block are an inspiring array of projects with fundamental questions: how fish use historical hydrodynamic motion cues in search and navigation tasks, what the link might be between brain development and aging, how to reconstruct a bee's buzz through micro-robots, how far the atmosphere is a living breathing ecosystem, what is the cellular and molecular basis of behavioural manipulation by viral infection or what are the social origins of rhythm, to cite just some examples. Taken together, new awards span the molecular biology of single cells to interactions among cells or organisms, to

evolutionary biology with potential for a better understanding of the consequences of environmental change. These projects involve men and women at different stages of their career, from the postdoc starting out to the seasoned researcher in a well-established lab, scientists working in 22 different countries.

Basic science pushes forward the frontiers of knowledge, and all HFSP projects answer fundamental biological questions, but basic science also builds a basis for applications that may contribute to solving medical, technical or environmental problems. Two years on, we see how HFSP supported research has played its part in the response to the Covid-19 pandemic: from Long-Term Fellow Shira Weingarten-Gabbay and her colleagues who shed light on an important source of T cell targets for potentially increased Covid-19 vaccine efficacy to HFSP grantee Michael Meyer-Hermann who provided advice to the government of the Federal Republic of Germany on the basis of mathematical models he developed for the course of the pandemic. In addition to applications, there are also start-ups, like the BioTech start-up launched by 2009 Long-Term Fellow, Alex Koglin, who produces vaccines and drugs on the basis of mRNA technology.

We, on the HFSP Board of Trustees, Council of Scientists and Review Committees, appreciate the opportunity that HFSPO gives us to work together with colleagues from around the world on a level playing field, where excellence in innovative life science research is the sole criterion for success. There, we perceive the full flowering of our national efforts in basic science in the global orchard of life science research and collaborate in supporting ambitious multilateral collaborations that would be difficult to accommodate at home.

We are supported in our task by the Secretary-Generals, who in three-year cycles, bring their own particular expertise to the implementation of the Program and running of the Secretariat. On 30 June 2021, we thanked Professor Warwick Anderson for his enduring contribution to reforming the administration of the Organization and on 1 July welcomed his successor, Professor Pavel Kabat, investing in him the hope that he will bring to bear his experience beyond the frontiers of biology to deepen and extend our roots in life science research. With him, we are preparing an ambitious new strategy to lead us into the next phase of development of the Program, for the next triennium (2024-2026) and beyond.

Cherry blossom fills the campus walkway of Osaka University today and I am reminded of the words of Nobel Laureate Elisabeth Blackburn, “We sometimes forget about the creative part of science. I think you need time to daydream, to let your imagination take you where it can… I’ve noticed among the creative, successful scientists who’ve really advanced things, that was a part of their life.”

I wish all our awardees, all those engaged in the risky venture of discovery, success and creativity on the frontiers!

Pavel KABAT, Yasutaka NAKASONE and Shigekazu NAGATA

SECRETARY-GENERAL'S MESSAGE

Pavel KABAT
Secretary-General of HFSPO

On 1 July 2021, I took up office as Secretary-General of HFSPO and I thank the President, the Board of Trustees and the HFSP scientific community for placing their trust in me for this position. I am honoured to succeed Professor Anderson after six years of his service and would like to express my thanks to him for his wise counsel in preparing me for the task of serving this unique Program and its community of scientists around the world.

The key to the Program's success may lie in its beginnings. These are grounded in the vision and experience of the late Prime Minister of Japan, Mr Yasuhiro Nakasone, who was born in 1918 at the close of the First World War, served in the Second World War, and rose to political prominence in the post war years, notably as Prime Minister from 1982 to 1987, when the Cold War still cast its shadow over hopes of lasting peace. It was in this divided world, at the Venice G7 Summit in 1987, that he launched the idea of HFSP, convincing his fellow G7 leaders of the need for a program in basic life sciences that would 'build up intellectual assets common to all humanity', tackling the problems of the world holistically by pulling together the highest scientific resources of every nation. At the same time, the initiative would be a powerful tool to build bridges over national and disciplinary borders, bringing together the people of the world through scientific collaboration.

Today, the world is still deeply divided, and the need to tackle common challenges collaboratively is even more pressing than before. My ambition, as we prepare to lay out a new strategy for HFSP for the coming years,

is to help make HFSP even more frontier and relevant to the problems and opportunities of the 21st century. But also an HFSP which is more equitable and inclusive, more reflective of the present global scientific and geopolitical landscape.

While the 20st century is widely known as the century of physics and chemistry, with the combustion engine, electricity, nuclear power, and internet being the mainstay examples of scientific and human progress, the 21st century is often hailed as *The Century of Biology*, or *The Age of Biology*, making HFSP all the more essential to the scientific enterprise. Bringing together the best minds around the world to tackle the key question *'What is life?'* through the exploration of the complex living systems and their inter-connected parts, HFSP may be better placed than others to stimulate scientific advance and to challenge new frontiers by focusing on *high risk - high gain* research based on ideas that are fresh, bold and innovative, grown from young creative minds with expertise in different fields, over different continents, and often without preliminary data. As such, HFSP is proven to be an unprecedented success.

HFSP projects draw on expertise from an ever-increasing range of disciplines beyond the life sciences to solve biological questions, and vice-versa. In order to respond to the transformational challenges of our time, such as climate change, biodiversity and food security, we need a new and deep engagement with the fundamental science of the living biosphere.

As a mathematician and earth system scientist, I am one of those looking to biology to unlock new depths of understanding and help resolve some of the most persistent uncertainties that earth system scientists have been facing. Planetary scale earth system science and climate science, with their traditionally mechanistic approaches drawing primarily on physics and high-powered supercomputers, need to engage with fundamental biology to provide insight into how life functions in the biosphere of land, ocean and the atmosphere. HFSP firmly believes that progress is made on the interface between disciplines and is fully committed to promoting such transdisciplinary approaches.

Frontier research is by nature 'edgy' or unconventional. Yet frontiers shift. Those areas, for example, synthetic biology, that were truly frontier not too long ago have now become mainstream. While it is HFSP's primary role to support and fund bottom-up ideas, it is also our task to stimulate new directions and map possible new territories. I am pleased that we were able to gather together a group of world leading scientists, among them many HFSP alumni and winners of prestigious prizes, including the Nobel Prize, to help us not only delineate how the frontiers of the life sciences have moved over the last decade but also provide a visionary perspective as to which scientific frontiers will need to be challenged in this 'century of biology'. Among these future frontiers, which I personally hope may be addressed, are, for example, how to harness artificial intelligence and big data in a productive partnership with fundamental process understanding in biology. Another is how cognitive science or psychology and fundamental (neuro)biology together can help us

understand what is driving our behaviour in responding to the most pressing environmental challenges and transformations of the 21st century. Among these challenges are biodiversity and food security. Imagine that the most important biological process on our planet, photosynthesis, which is incredibly inefficient in an otherwise very efficient and well-balanced nature in being able to utilise only a small percent of otherwise abundant light energy to produce the biomass, could be made doubly efficient, reducing the demand on land to produce food, by half. Try to imagine what a scientific discovery, resulting in the modest doubling of sunlight-to-biomass efficiency, would mean for food security and environmental sustainability in our 21st century world….

Frontier intellectual leadership is also required to maximize the benefit of science to society. One topic for our frontier discussions will be how to shorten the innovation cycle, bringing the outcomes and impacts of fundamental research more speedily into effect.

To date, HFSP has supported more than 3400 fellows and 1200 research grant collaborations involving some 4300 team members worldwide. Researchers from more than 70 countries have received HFSP support and funding so far. Many have gone on to become true frontier science leaders and to win prestigious international prizes, such as the Breakthrough Prize, the Brain Prize, the Leibniz Prize, the Kavli Prize, the NIH Director's New Innovator Award, the Canada Gairdner International Award or the Japan Prize. 28 of our grantees have gone on to win the Nobel Prize for Medicine or Physiology, Chemistry or Physics. These breathtaking results and successes over just 32 years of HFSPO's existence are a true tribute to HFSP's vision and mission, and proof that its formula has worked exceedingly well, beyond the boldest expectations of its founders. This is also a clear and convincing call for continued and increased commitment and support of the Program by its current and future Members, and by the international life science community at large.

I have no doubt that there are many more excellent innovative ideas to harvest around the world with the support of HFSP. For my part, as I begin my mandate as Secretary-General, I will keep the vision of our founders before me in the implementation of the Program - science for the advancement of knowledge and benefit for all humankind, science for peace.

Hirofumi NAKASONE and Pavel KABAT

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Pavel KABAT and Warwick ANDERSON

INTRODUCING HFSPO

The International Human Frontier Science Program Organization (HFSPO) is an international cooperation in life science research supported by the world's leading scientific countries. It promotes fundamental research in the life sciences with special emphasis on novel and interdisciplinary research, international and, in particular, intercontinental collaboration, and support for early career investigators.

HFSP funding complements national programs to enable collaborations in a scientific landscape that changes fast. Novel approaches from different disciplines hold great promise to address the most important problems in understanding complex life. The challenge for all scientists is to look beyond their original expertise and to broaden their horizons by working with collaborators they have never interacted with before and by moving into new fields of research. HFSP is at the forefront of such interdisciplinary, collaborative research. Through its different funding schemes, it supports frontier, potentially transformative 'out-of-the-box' proposals and encourages applications for high-risk/high-reward projects. Successful projects challenge existing paradigms by using novel approaches and techniques; they address important problems and barriers to progress in the field.

HFSP supports research into the complex mechanisms of living organisms, ranging from the biomolecular level to the whole organism and its physiology and behaviour. The life sciences have emerged as a leading scientific area in which approaches from physics, mathematics, chemistry, computer science and engineering converge to solve biological questions. HFSP aims to support frontier research by involving scientists from outside the life sciences as part of research collaborations and as postdoctoral fellows. To this end, the Program and Early Career Grants are specifically geared to fostering interactions between scientists from different disciplines and this is a major factor in the review of applications for these programs. In this context, HFSP supports Cross-Disciplinary Fellowships to equip young scientists from outside biology with the skills needed to tackle problems in the life sciences.

Since its establishment in 1989, HFSP has demonstrated the value of creating a framework for competitive, collaborative, international research

of the highest calibre and for providing early career scientists with the opportunity to emerge as talented researchers capable of shaping the science of the future.

Since 1990, more than 1200 research grants involving over 4300 scientists, and more than 3400 fellowships have been awarded. Researchers from more than 70 countries have received HFSP funding so far.

HFSPO implements its Program through the following mechanisms of research support, details of which can be found in the subsequent chapters:

Postdoctoral Fellowships

- **Long-Term Fellowships** – for young life scientists within three years of obtaining their PhD who wish to broaden their scientific experience in a foreign laboratory.
- **Cross-Disciplinary Fellowships** – specifically for scientists with a PhD in non-biological disciplines to bring new perspectives to research in the life sciences.

Research Grants

- **Early Career Grants** – grants for interdisciplinary teams of early career researchers who are within the first five years of their first independent position and located in different countries.
- **Program Grants** – for interdisciplinary teams of researchers in different countries at any stage of their career.

HFSP supports the next generation of researchers, who are in the strongest position to open new avenues of research, through the fellowship program and the Early Career Grant. Program Grant teams are also encouraged to include early career scientists with the result that a significant number of scientists under the age of 40 are included in awarded teams. Taken together, these early career researchers are awarded approximately 70% of annual HFSP funds.

HFSP is governed by the Board of Trustees composed of appointees from HFSPO Members, currently Australia, Canada, France, Germany, India, Israel, Italy, Japan, New Zealand, the Republic of Korea, Singapore, Switzerland, the United Kingdom of Great Britain and Northern Ireland, the United States of America and the European Commission.

Members of the HFSPO Council of Scientists are nominated by the HFSPO Members. They provide scientific advice to the Board of Trustees and select the winners of the HFSP Nakasone Award.
The Board is supported by the HFSPO Secretariat, located in Strasbourg, France, and directed by the Secretary-General. Its legal status is a not-for profit association established in Alsace (Grand Est), France.
The Member countries support HFSP through voluntary contributions which are agreed at a Triennial Conference of HFSPO Members.

Chapter 1

Fellowship Program

1.0
HIGHLIGHTS

65 postdoctoral fellowships, including 56 Long-Term Fellowships and 9 Cross-Disciplinary Fellowships, were awarded in March 2022 from 603 letters of intent submitted in May 2021. The final success rate based on the 493 reviewed letters of intent is 13%.

44% of the reviewed applications were from **female applicants**.

In the competition that ended in March 2022, **20%** of the reviewed applications were for the **Cross-Disciplinary** Fellowship Program.

Awardees were of **19 different nationalities** and chose **12 different host countries**.

In another neuroscience project, an Australian Cross-Disciplinary fellow, trained in physics, will **use cutting-edge quantum microscopy techniques** to study how electrical signals propagate in a neuron and across neuronal assemblies at the École Normale Supérieure Paris-Saclay, France.

An awardee from Brazil will move to the Gulbenkian Institute in Lisbon, Portugal, to study the **role of neuronal heme sensing in the metabolic adaptation to infection**. The fellow hypothesises that neurons sense labile heme, either directly or indirectly, and elicit sickness behaviour and an associated organismal hypometabolic state.

A Cross-Disciplinary fellow with a PhD in mechanical engineering will move from the Republic of Korea to the University of Texas at Austin, USA, to **develop a wireless focused ultrasound system for sono-optogenetics in freely behaving animals**. This will provide a powerful tool for cognitive or memory behavioural studies and could eventually aid identifying the causes of human depression through behavioural experiments.

1.1

THE AIMS OF THE HFSP FELLOWSHIPS

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 focussing on the life sciences.
- **Cross-Disciplinary Fellowships (CDF)** are for applicants who hold a doctoral degree in a non-biological discipline (e.g., physics, chemistry, mathematics, engineering or computer sciences), and who have not worked in the life sciences before, to work on a novel frontier project in biology.

All HFSP fellowships are for three years and provide an annual living allowance as well as a research and travel allowance. In addition, child, parental leave and relocation allowances are provided where appropriate.

All HFSP fellowships must be taken up in a laboratory in a different country to the one where the PhD degree was conferred. Applicants from a country that is not a member of HFSPO must hold their fellowship in a HFSPO member country.

HFSP fellowships are flexible, for example, awardees can defer the third year of their fellowship for up to two years and can also use the third year in a different country or in their home country. At the end of the fellowship, the awardees can request a six-month no-cost extension to spend any remaining funds in their host lab. At HFSPO we believe that such flexibility is crucial to allow fellows to make the most of their postdoctoral training.

1.2

SELECTION OF HFSP FELLOWSHIPS AWARDED IN MARCH 2022

The competition for 2022 fellowships was launched in May 2021, employing for the first time a two-step application process consisting of a letter of intent, followed by the submission of a full proposal. The largest group of applicants (25%) in the letter of intent stage was from non-member countries, illustrating the worldwide reach of HFSP (Figure 1.1 and Table 1.1), followed by candidates from Europe (those countries which are not individual members of HFSPO but represented by the membership of the European Commission), India, France and Italy. In total, 603 letters of intent were submitted, out of which 493 were eligible and took part in the complete review cycle. The reviewed applications were from applicants of 54 nationalities proposing to move to 26 host countries.

In March 2022, HFSPO announced fellowship awards to scientists of 19 different nationalities (see Table 1.1). 56 young researchers were awarded Long-Term Fellowships and 9 were awarded Cross-Disciplinary Fellowships.

HFSP fellows chose host labs in 12 countries, with 49% of fellows going to labs in the United States of America (Figure 1.2). Since 1990, HFSP fellows have been hosted in 23 countries.

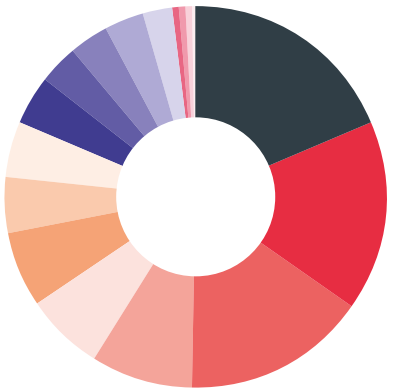


Figure 1.1

Number of fellowship applicants by nationality

92	Non-members*	17	UK
80	Europe**	17	USA
77	India	16	Korea
42	France	12	Canada
33	Dual nationalities	3	Australia
32	Italy	3	New Zealand
23	Germany	2	Switzerland
23	Israel	1	Singapore
20	Japan		

*92 applicants were from countries that are not members of the Organization.

**80 applicants were from countries of the European Union that are not individual members of HFSPO but are represented by the membership of the European Commission.

Table 1.1

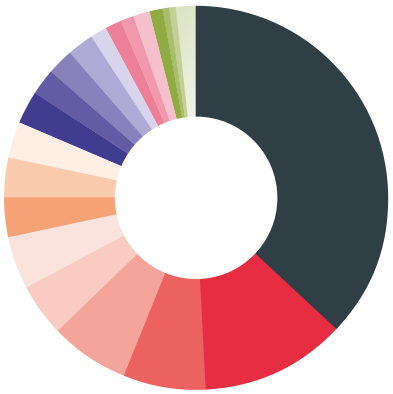
Nationalities of Long-Term (LTF) and Cross-Disciplinary (CDF) Fellowship applicants and awardees awarded in March 2022

Nationality	LTF applicants	LTF awardees	CDF applicants	CDF awardees	Total awardees
Australia	2		1	1	1
Canada	11	3	1		3 (3)
Europe	65	9	15	1	10 (1)
France	35	3	7	1	4 (3)
Germany	18	8	5		8 (3)
India	62	3	15		3
Israel	21	9	2	1	10 (3)
Italy	28	3	4	1	4 (3)
Japan	16	3	4		3 (3)
Korea	12		4	1	1
New Zealand	2		1		0
Singapore	1				0
Switzerland	1		1		0
United Kingdom	12	3	5	2	5 (3)
United States of America	12	1	5	1	2 (3)
Non-members (2)	67	3	25		3 (3)
Dual nationalities	28	8	5		8 (4)
TOTAL	393	56	100	9	65

(1) The European Long-Term Fellowship awardees come from Austria, Belgium, Netherlands (2), Poland, Slovenia and Spain (3). The European Cross-Disciplinary Fellowship awardee is from Poland.
(2) The applicants from non-member countries come from Algeria, Argentina, Bangladesh, Brazil, Chile, China, Cuba, Egypt, Georgia, Ghana, Iceland, Indonesia, Iran, Malaysia, Mexico, Pakistan, Philippines, Russia, South Africa, Taiwan, Tunisia, Turkey, Ukraine. The three awardees from non-member countries come from China (1) and Turkey (2).
(3) Additional awardees holding dual nationality are accounted for in the Dual nationalities row. For details see point (4) below.
(4) Among the eight awardees who hold dual nationalities, five are from HFSPO member countries: Israel/France (2), Israel/Germany, Japan/Canada, UK/Germany. The other three are from Argentina/Italy, Brazil/Angola and USA/Egypt.

Figure 1.2

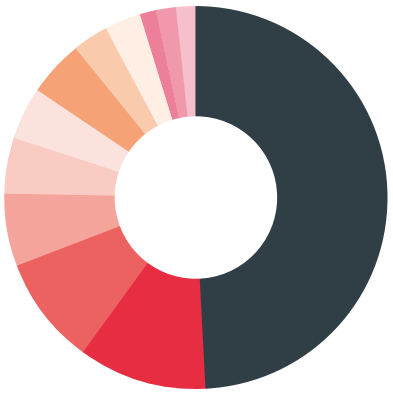
Host country of Long-Term and Cross-Disciplinary Fellowship applicants and awardees awarded in March 2022



Host country of 2022 applicants

183	USA	11	Italy
60	UK	10	Australia
34	Germany	7	Portugal
33	Switzerland	7	Singapore
22	France	6	Belgium
22	Spain	6	Israel
17	Denmark	6	Japan
16	The Netherlands	3	Ireland
15	Canada	3	New Zealand
13	Austria	7	Other*
12	Sweden		

* There were 7 applications for the following additional host countries: Chile (1), Finland (2), India (1), Korea (1), Luxembourg (1), Taiwan (1)



Host country of 2022 awardees

32	USA	3	France
7	Germany	2	The Netherlands
6	UK	2	Portugal
4	Switzerland	1	Canada
3	Australia	1	Belgium
3	Spain	1	Denmark

Table 1.2

Gender of Long-Term (LTF) and Cross-Disciplinary (CDF) Fellowship applicants and awardees awarded in March 2022

	Applications		Awards	
	LTF	CDF	LTF	CDF
Number of female scientists	184	35	22	3
	46.8%	35%	39.3%	33.3%
Number of male scientists	203	65	34	6
	51.7%	65%	60.7%	66.7%
Total number of scientists*	**387***	**100**	**56**	**9**

*Gender not provided by 6 Long-Term Fellowship applicants

1.3

THE HFSP FELLOWSHIP REVIEW COMMITTEE

NON-REVIEWING CHAIR
- **Marina PICCIOTTO**, Yale University School of Medicine, New Haven, USA

AUSTRALIA
- **Jacqueline MATTHEWS**, University of Sydney

CANADA
- **Daniel SCHRAMEK**, Mount Sinai Hospital, Toronto

EUROPEAN COMMISSION
- **Kirstine BERG-SORENSEN**, Technical University of Denmark, Lyngby, Denmark
- **Toni GABALDON**, Biomedical Research Institute and Centre for Genomic Regulation, Barcelona, Spain
- **Roland KANAAR**, Erasmus Medical Center, Rotterdam, the Netherlands
- **Vera VAN NOORT**, Catholic University of Leuven (KU Leuven), Belgium

FRANCE
- **Ana CUMANO**, Pasteur Institute, Paris
- **François FAGOTTO**, University of Montpellier

GERMANY
- **Victor SOURJIK**, Max Planck Institute for Terrestrial Microbiology, Marburg
- **Matthias TSCHÖP**, Helmholtz Center Munich / Technical University Munich

INDIA
- **Vatsala THIRUMALAI**, National Centre for Biological Sciences, Bangalore

ISRAEL
- **Michael KOZLOV**, Tel Aviv University

Marina PICCIOTTO

Chair of the HFSP Fellowship Review Committee

ITALY
- **Raffaele DE FRANCESCO**, National Institute of Molecular Genetics, Milan

JAPAN
- **Gohta GOSHIMA**, Nagoya University
- **Takashi TSUCHIMATSU**, University of Tokyo

NEW ZEALAND
- **Peter FINERAN**, University of Otago, Dunedin

OTHER
- **Jonathan WHITLOCK**, Norwegian University of Science and Technology, Trondheim, Norway

REPUBLIC OF KOREA
- **Sungjune JUNG**, POSTECH, Pohang

SINGAPORE
- **Hao YU**, National University of Singapore

SWITZERLAND
- **Thomas NEVIAN**, University of Bern

UNITED KINGDOM
- **Robert INSALL**, University of Glasgow
- **Scott WADDELL**, University of Oxford

UNITED STATES OF AMERICA
- **Marina PICCIOTTO**, Yale University School of Medicine, New Haven
- **Joseph PUGLISI**, Stanford University

DELEGATE FROM THE COUNCIL OF SCIENTISTS

The HFSPO Council of Scientists is responsible for overseeing the peer review process of HFSP funding programs. Each year a Council member participates in the review committee meetings as an observer with the role to monitor due diligence of the proceedings.
- **Anat BEN ZVI**, Ben-Gurion University of the Negev, Beer-Sheva, Israel

1.4

AWARDEES LISTS

Fellowships awarded in March 2022 (to be initiated during FY 2022)

Nationality of awardees in brackets, followed by the location of the host research laboratory.

1.4.1 CROSS-DISCIPLINARY FELLOWSHIPS

Quantum microscopy of neuron electric signals
HANLON Liam (Australia)
École Normale Supérieure Paris-Saclay, Gif-sur-Yvette, France

Development of wireless focused ultrasound system for sono-optogenetics in freely behaving animals
JEONG Jinmo (Korea)
The University of Texas, Austin, USA

An extreme approach to biomineralization: biomineral selection by extremophiles
KNOLL Pamela (USA)
University of Edinburgh, UK

Conformational changes in yeast vacuoles driven by membrane rigidity and protein jamming
LEVIN Ido (Israel)
University of Washington, Seattle, USA

Understanding and controlling the sub-motors of bacterial rotary nanomachines
RIEU Martin (France)
University of Oxford, UK

Tumour homing immune cells for cavitation therapy
SMITH Cameron (UK)
California Institute of Technology, Pasadena, USA

A multi-scale all-optical platform for the investigation of membrane potential dynamics
TORTAROLO Giorgio (Italy)
Swiss Federal Institute of Technology, Lausanne, Switzerland

Targeted protein degradation and electrophysiology to study the function of the proteasome
WHITTAKER Joanna (Poland)
University of Groningen, the Netherlands

Revealing the fundamental regulators of cell mechanical properties by single cell microfluidics
XU Catherine (UK)
Max Planck Institute for the Science of Light, Erlangen, Germany

1.4.2 LONG-TERM FELLOWSHIPS

Experimental control over sleep cognition via transcranial focused ultrasound
ADELHOEFER Nico (Germany)
Radboud University, Nijmegen, the Netherlands

An adaptive role of mammalian cortex in shaping innate visual behavior
ATLAN Gal (Israel/France)
University of California, San Francisco, USA

Assembly, dynamics, and plasticity of plastid translocon biogenesis
BAG Pushan (India)
The University of Tennessee, Knoxville, USA

Antigen recognition machineries of gamma delta T cells in the skin during health and disease
BIRAM Adi (Israel)
University of California, San Francisco, USA

Somatosensory processing in a cerebello-cortical loop for adaptive control
CROSS Kevin (Canada)
The University of North Carolina, Chapel Hill, USA

Cell size-dependent sex determination
D'ARIO Marco (Italy)
Stanford University School of Medicine, USA

Nutrient-regulated posttranslational modifications drive metastasis formation
DE LA CALLE ARREGUI Celia (Spain)
Vlaams Instituut Voor Biotechnology, Leuven, Belgium

Light induces lymph node activation via a sympathetic eye-to-lymph node pathway
DE VIRGILIIS Francesco (Italy)
University of Geneva, Switzerland

Circuits for perception of state of self and others
DOLENSEK Nate (Slovenia)
University of California, Berkeley, USA

Glucose regulation in nectarivorous birds
DOMER Adi (Israel)
University of California, Berkeley, USA

Symmetry breaking in multicellular self-organization: a quantitative imaging approach
DUNSING Valentin (Germany)
Institut de Biologie du Développement de Marseille, France

Functional proteome landscape of malaria parasite during the life cycle in host and vector
DZIEKAN Jerzy (Poland)
The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia

Monitoring and manipulating inter-organellar contact-sites during mycobacterial infection
EISENBERG-BORD Michal (Israel)
University of Cambridge, UK

Dissecting the structure-function consequences of mechanical stress on intact neural circuits
EL-QUESSNY Malak (USA/Egypt)
ICFO - The Institute of Photonic Sciences, Castelldefels, Spain

Dynamic threat assessment and signal integration by innate immune signaling complexes
FISCH Daniel (Germany)
Boston Children's Hospital, USA

Dopaminergic basis of learning temporal regularities in perceptual decisions
FRITSCHE Matthias (Germany)
University of Oxford, UK

Microtechnology-based limbic-cortex axis in 3D: modeling human neurodevelopment and disease
GARONE Maria Giovanna (Italy)
Murdoch Children's Research Institute, Parkville, Australia

Metabolic and cell–cell interactions of Helicobacter pylori and stem cells of the gastric glands
GEIER Benedikt (Germany)
Stanford University School of Medicine, USA

Uncovering the nuclear dynamics of telomeres upon replication stress
GONZALEZ MANJON Anna (Spain)
Children's Medical Research Institute, Sydney, Australia

Mapping the neuromodulatory heterogeneity in decision making
HAGIHARA Kenta (Japan)
Allen Institute for Brain Science, Seattle, USA

Understanding the neural mechanism underlying affiliative social behavior
HAYAT Hanna (France/Israel)
University of California, Los Angeles, USA

Biochemical and structural characterisation of the mycobacterial T4SS-like/T7SS conjugation system
HENNELL JAMES Rory (UK)
University Medical Center Hamburg-Eppendorf, Germany

Cell-specific functional connectivity of cerebellar outputs for locomotor learning
HERENT Coralie (France)
Champalimaud Centre for the Unknown, Lisbon, Portugal

Evolutionary, expression, and functional characterization of ancient putative chemosensors
HIMMEL Nathaniel (USA)
University of Lausanne, Switzerland

Characterizing how pioneer transcription factors and chromatin structure regulate genome activation
HOPPE Caroline (Germany)
Yale University, New Haven, USA

NAMUH -- A human genomic perspective on the evolution of chromosomal inversions
JAY Paul (France)
University of Copenhagen, Denmark

Metabolism as an integrator that coordinates morphogenesis in the developing mammalian embryo
JUNYENT ESPINOSA Sergi (Spain)
California Institute of Technology, Pasadena, USA

Homeostasis circuit for studying and treating gene dosage-dependent disorders
KATZ Noa (Israel)
Stanford University, Redwood City, USA

Neuronal heme sensing in metabolic adaptation to infection
KITOKO Jamil (Brazil/Angola)
Fundacao Calouste Gulbenkian, Lisbon, Portugal

Systematic characterization of SNPs in CREs associated with congenital heart disease
LINDENHOFER Dominik (Austria)
European Molecular Biology Laboratory, Heidelberg, Germany

Understanding ancient woolly mammoth gene function through multiplex gene editing
MAJEWSKI Dorothy (Canada)
Harvard Medical School, Boston, USA

Feeding or folding? Untangling the ecology of spatial patterning in microbial consortia
MEACOCK Oliver (UK)
University of Lausanne, Switzerland

Neural basis of relative aversive value coding in mice
MIRANDA Magdalena (Argentina/Italy)
Institute for Functional Genomics, Montpellier, France

Unraveling the molecular determinants of human ALS progression in spinal cord organoids
MIZRAHI Orel (Israel)
University of California San Diego, La Jolla, USA

Delineating control of translation upon iron starvation
MOLENAARS Marte (the Netherlands)
New York University School of Medicine, USA

Neuronal changes following pathogen infection: mechanisms underpinning sickness-related behaviors
MURIA Aurélie (France)
Technical University of Munich, Germany

Exploring the combinatorial space of plant immune receptors and pathogen signals
OFIR Gal (Israel)
Max Planck Institute for Developmental Biology, Tübingen, Germany

Spatial and temporal scales of serotonin neuromodulation
ÖZÇETE Özge Demet (Turkey)
Harvard Medical School, Boston, USA

Genome-wide profiling and targeted editing of chromatin state at double-strand breaks in cancer
PARNANDI Nishita (India)
The Francis Crick Institute, London, UK

Molecular mechanism of ERAD-M by in vitro reconstitution
PFITZNER Anna-Katharina (Germany)
Harvard Medical School, Boston, USA

The cellular and developmental genetic mechanisms underlying germline response to climate change
RAJAKUMAR Arjuna (Canada)
Whitehead Institute for Biomedical Research, Cambridge, USA

Revealing the control of epithelial mechanics during wound healing using in vivo force manipulation
ROGALLA Svana (Germany)
Basque Centre for Biophysics, Leioa, Spain

Deciphering the nature of genomic conflict using locus-specific chromatin perturbation and capture
RUDNIZKY Sergei (Israel)
Johns Hopkins University School of Medicine, Baltimore, USA

Influence of sleep memory consolidation on spinal neuroplasticity mechanisms in humans
SATO Sumire (Japan/Canada)
University of Toronto, Canada

Are endothelial cells regulated differently during limb regeneration than during development?
SAVAGE Aaron (UK)
Harvard University, Cambridge, USA

The ecological role of bacterial specialized metabolites in bacteria-microalgae interactions
SCHLEYER Guy (Israel/Germany)
Leibniz Institute for Natural Product Research and Infection Biology, Jena, Germany

Using computational models to link dynamics of brain plasticity with behavioral changes over time
SCHURR Roey (Israel)
Harvard University, Cambridge, USA

Unravelling the mechanisms of bis(monoacylglycero)phosphate synthesis and function in endolysosomes
SINGH Shubham (India)
Harvard University, Boston, USA

Functional cell atlas of neural crest cell contribution to newt development and regeneration
SUZUKI Miyuki (Japan)
California Institute of Technology, Pasadena, USA

Investigating the regulomic basis of major evolutionary transitions
TAYLOR Benjamin (UK/Germany)
Purdue University, West Lafayette, USA

Templated polypeptide synthesis inside a nanopore cavity
TOPARLAK Omer Duhan (Turkey)
University of Oxford, UK

Chemical and optogenetic approaches to identify and quantify the membrane sources of autophagosomes
UEMATSU Masaaki (Japan)
Cornell University, Ithaca, USA

Haemogenic gastruloids: a novel approach to generate and study blood stem cells in vitro
VAN DEN BRINK Susanne Carina (the Netherlands)
Hospital del Mar Medical Research Institute, Barcelona, Spain

Defining mechanisms of metabolic-epigenetic crosstalk that drive cancer initiation
XIAO Yi (China)
UT Southwestern Medical Center, Dallas, USA

Physiological functions and molecular mechanisms of neuronal ER-phagy
YPERMAN Klaas (Belgium)
Leibniz-Forschungsinstitut für Molekulare Pharmakologie, Berlin, Germany

Development of neural circuits for cooperative behavior in schooling fish
ZADA David (Israel)
University of California San Diego, La Jolla, USA

1.5

FELLOWSHIP PROFILE

2021 Cross-Disciplinary Fellowship

Rahul CHAJWA

Rahul Chajwa (India),
Department of Bioengineering, Stanford University, USA

HFSP project:

Birth, life and death of marine snow: real-time observations and biophysics of a sinking eco-system

Ecosystems on our planet are driven out of equilibrium with energy input from the sun resulting in a flux of matter across food chains, contributing to the global carbon cycle. This flux is remarkably vivid in the biological pump of our oceans, with gravity driving the downward flux of carbon in the form of marine snow, and microbes inhabiting and decaying it, thus regulating global climate. A predictive understanding of the hydrodynamic, biotic, and non-equilibrium aspects of this sinking microbial ecosystem is a notoriously challenging and globally relevant problem and is the central theme of my research.

My HFSP project is focused on studying marine snow as a novel class of sedimenting active matter, using a newly invented 'hydrodynamic treadmill' which helps us achieve an ecologically relevant setting, both in a stationary lab and on a floating research vessel. My host supervisor, Manu Prakash, and I are trying to understand the formation, sinking and decomposition of marine snow aggregates, through a controlled physical simulation of oceanic conditions in table-top experiments, along with numerical and analytical calculations. I'm applying my training as a physicist to shed light on the dynamical aspects of microbial life in the ocean, and to contribute insights that can help mitigate the negative impact of human activities on global climate.

Chapter 2

Research Grant Program

2.0
HIGHLIGHTS

32 research grants, including 25 Program and 7 Early Career were awarded in March 2022 from 716 letters of intent submitted in March 2021, indicating a 4.5% success rate.

Four out of the seven awarded Early Career teams are led by a female principal investigator.

The average age of awardee is 47 years for the Program grants and 36 for Early Career grants.

Research topics range from the lipid composition in synaptic membranes, horizontal gene transfer in protocells and physical genome regulation to the mechanics of plant cell walls, mental space travel and the microbiome of the atmosphere.

The Program grant team led by principal investigator Pavel Tomancak bridges evolutionary biology and tissue biomechanics in order to reveal the mechanisms by which the least understood elements of the cytoskeleton, intermediate filaments, have shaped the species-specific mechanics and development of epithelial tissues across phylogeny.

The Early Career grant team led by principal investigator Maria Cristina Crava will combine virology, neurophysiology and plant science to understand which neuronal and molecular mechanisms interact when a virus controls the behaviour of its host to ensure maximal dispersal.

2.1

THE AIMS OF THE HFSP RESEARCH GRANTS

HFSP research grants support basic research at the frontiers of life sciences, with emphasis on novel collaborations crossing national – often continental – and disciplinary boundaries. As biological research has become increasingly quantitative, major progress in answering basic questions requires interdisciplinary approaches, novel ways to use new technologies and innovative theoretical approaches. This is seen in the strong participation of scientists from disciplines outside the traditional life sciences, such as physics, chemistry, geology, computer science, material science, mathematics, nanoscience or psychology, in awarded HFSP research grants. 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 that characterize living organisms, their evolution and interactions.

HFSP supports frontier research through two types of research grants:

- **Research Grants - Program** are awarded to team members at any stage of their careers who embark upon a new collaborative project.

- **Research Grants - Early Career** (previously Young Investigator Grants) require that team members are within 5 years of obtaining an independent position and not more than 10 years since completing their PhD.

Both types of grants are awarded to interdisciplinary teams of two to four scientists having their laboratories in different countries and preferably different continents.

2.2

SELECTION OF HFSP RESEARCH GRANTS AWARDED IN MARCH 2022

For the competition launched in March 2021, 716 letters of intent were submitted. In March 2022, the HFSPO Board of Trustees approved 32 awards, 25 to Program Grant teams and 7 to Early Career teams.

Table 2.1
The breakdown of the two-step review process for the HFSP research grants is shown in the table below

	Program Grants	Early Career Grants	Total
Number of submitted letters of intent*	560	156	**716**
Number of full applications	47	21	**68**
Number of awarded projects	25	7	**32**
% of awarded projects, based on letters of intent	4.46	4.49	**4.47**
% of awarded projects, based on full applications	53.2	33.3	**47.1**
Number of members per awarded team, mean (range)	3.1 (2-4)	3.3 (3-4)	**3.1**
Cumulative total per year, mUSD	9.60	2.76	**12.36**

*Submitted letters of intent including those ineligible because of multiple co-publications among team members. This eligibility criterion was specific to this cycle and increased the number of ineligible teams from the usual 1-5 to 40.

Figure 2.1

The figure shows the development of submitted letters of intent and awards as well as success rate over the last 10 years

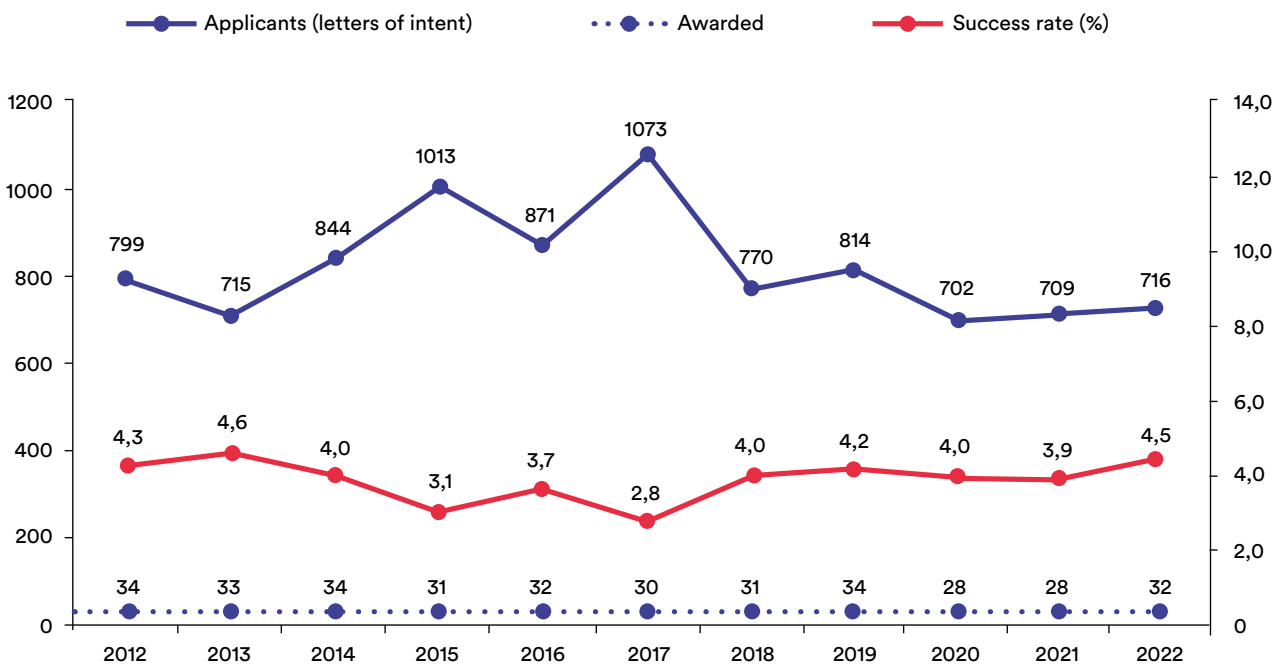


Table 2.2

The gender distribution for applicants and awardees differs between the Program and Early Career grants. This year, female applicants for the Early Career grants were more successful than male applicants in this category.

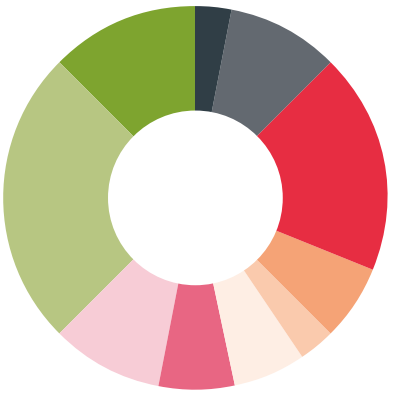
	Letter of intent		Awarded grants	
	Program	**Early Career**	**Program**	**Early Career**
Number of female scientists	443	135	20	9
	27.4%	32.6%	26%	39.1%
Number of male scientists	1167	279	57	14
	72.1%	67.4%	74%	60.9%
Total number of scientists	**1618***	**414**	**77**	**23**

*Gender not provided by 8 applicants for Program Grants

Figure 2.2

Countries in which awardees are working

Note that the numbers below may differ from other reports due to awardees having changed affiliation.



Principal Investigators

1	Australia	2	Israel
3	Canada	2	Italy
6	Europe*	3	Switzerland
2	Germany	8	UK
1	India	4	USA

*The principal investigators located in the countries of the European Union that are not individual members of HFSPO but are represented by the membership of the European Commission have their laboratories in the following countries: Austria (1), Denmark (1), Spain (3) and Sweden (1).

Co-Investigators

4	Australia	2	Italy
2	Canada	4	Japan
15	Europe*	1	Switzerland
3	France	6	UK
4	Germany	19	USA
3	Israel	5	Non-members**

*The co-investigators located in the countries of the European Union that are not individual members of HFSPO but are represented by the membership of the European Commission have their laboratories in the following countries: Austria (1), Belgium (2), Denmark (2), the Netherlands (4), Spain (2) and Sweden (4).

**For countries that are not members of the Organization, the co-investigators are located in China (1), Ecuador (1), Norway (2) and Peru (1).

2.3

THE HFSP RESEARCH GRANT REVIEW COMMITTEE

Tomomi SHIMOGORI
Chair of the HFSP Research Grant Review Committee

NON-REVIEWING CHAIR
- **Tomomi SHIMOGORI**, RIKEN Center for Brain Science (BSI), Wako, Japan

AUSTRALIA
- **Ryan LISTER**, Harry Perkins Institute of Medical Research, Perth
- **Robert PARTON**, University of Queensland, Brisbane

CANADA
- **Stephen W. MICHNICK**, University of Montreal (Deputy Chair)

EUROPEAN COMMISSION
- **Alessandra CAMBI**, Radboud University Medical Centre, Nijmegen, the Netherlands
- **Sebastian HAESLER**, Catholic University of Leuven (KU Leuven), Belgium
- **Marja-Leena LINNE**, Tampere University, Finland

FRANCE
- **Marie-France SAGOT**, University Claude Bernard, Lyon

GERMANY
- **Friedrich C. SIMMEL**, Technical University Munich, Garching

INDIA
- **Rashna BHANDARI**, Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad
- **Uma RAMAKRISHNAN**, NCBS - Tata Institute of Fundamental Research, Bangalore

ISRAEL
- **Roy BAR-ZIV**, Weizmann Institute of Science, Rehovot

ITALY
- **Antonio CELANI**, The Abdus Salam International Center for Theoretical Physics (ICTP), Trieste

JAPAN
- **Jun KITANO**, National Institute of Genetics, Mishima

REPUBLIC OF KOREA
- **Mi Sun JIN**, Gwangju Institute of Science and Technology (GIST)

NEW ZEALAND
- **Jasna RAKONJAC**, Massey University, Palmerston North

SINGAPORE
- **Hongyan WANG**, Duke-NUS Medical School

SWITZERLAND
- **Elisabeth Beate TRUERNIT**, ETH Zurich

UNITED KINGDOM
- **Tom BADEN**, University of Sussex, Brighton
- **Timothy SAUNDERS**, University of Warwick (until June 2021, University of Singapore)

UNITED STATES OF AMERICA
- **Karl MUNGER**, Tufts University School of Medicine, Boston
- **Anne PRINGLE**, University of Wisconsin, Madison
- **Jennifer ROSS**, Syracuse University

DELEGATE FROM THE COUNCIL OF SCIENTISTS

The HFSPO Council of Scientists is responsible for overseeing the peer review process of HFSP funding programs. Each year a Council member participates in the review committee meetings as an observer with the role to monitor due diligence of the proceedings.
- **Patricia BASSEREAU**, Institut Curie, Paris, France

2.4

AWARDEES LISTS

Research grants awarded in March 2022 (to be initiated in FY 2022)

Nationality is in parentheses when different from the country in which the lab is located.

2.4.1 RESEARCH GRANTS - PROGRAM

Mapping gut-to-brain transmission of prion protein

AGUZZI Adriano	Dept. of Neuropathology University of Zurich (UZH)	SWITZERLAND (ITALY)
THAISS Christoph	Dept. of Microbiology Perelman School of Medicine, University of Pennsylvania, Philadelphia	USA (GERMANY)

Spatial and deep neurolipidomics to reveal synapse diversity

AHRENDS Robert	Dept. of Analytical Chemistry University of Vienna	AUSTRIA (GERMANY)
ELLIS Shane	Dept. of Molecular Horizons/SCMB University of Wollongong	AUSTRALIA
KREUTZ Michael R.	Dept. of Neuroplasticity Leibniz Institute for Neurobiology Magdeburg	GERMANY
VERHELST Steven	Dept. of Cellular & Molecular Medicine Catholic University of Leuven (KU Leuven)	BELGIUM (THE NETHERLANDS)

Good vibes: how do plants recognise and respond to pollinator vibroacoustic signals?

BARBERO Francesca	Dept. of Life Sciences and Systems Biology University of Turin (UNITO)	ITALY
MATUS Tomas	Dept. of SysBio -Molecular Interactions and Regulation Institute for Integrative Systems Biology, Valencia	SPAIN
OBERST Sebastian	School of Mechanical and Mechatronic Engineering University of Technology, Sydney	AUSTRALIA

A bottom-up approach to understand how enzyme structural fluctuations accelerate multistep reactions

CHICA **Roberto**	Dept. of Chemistry and Biomolecular Sciences University of Ottawa	CANADA
GREEN **Anthony**	Dept. of Chemistry University of Manchester	UK
THOMPSON **Michael**	Dept. of Chemistry and Biochemistry University of California, Merced	USA

Assembly, mechanics and growth of plant cell walls

COEN **Enrico**	Dept. of Cell and Developmental Biology John Innes Centre, Norwich, UK	UK
COSGROVE **Daniel**	Dept. of Biology Pennsylvania State University Port Matilda	USA
DURAND-SMET **Pauline**	Dept. of Matter and Complex Systems Université Paris Diderot - Paris 7	FRANCE
SVAGAN (HANNER) **Anna**	Dept. of Fibre and Polymer Technology KTH Royal Institute of Technology Stockholm	SWEDEN

Dynamics of multilayer epithelial structures: Integrative mechanical characterization of epidermis

DAS **Tamal**	TIFR Centre for Interdisciplinary Sciences Tata Institute of Fundamental Research Hyderabad	INDIA
BI **Dapeng**	Dept. of Physics Northeastern University Boston	USA
SERWANE **Friedhelm**	Dept. of Physics University of Munich (LMU)	GERMANY

The walking fish: Integrating biomechanics, energetics and robotics to study water-land transition

DI SANTO **Valentina**	Dept. of Zoology Stockholm University	SWEDEN (ITALY)
IIDA **Fumiya**	Dept. of Engineering University of Cambridge	UK (JAPAN)
SHUBIN **Neil**	Dept. of Organismal Biology and Anatomy University of Chicago	USA

Bacterial genome editing systems as a driver of cancer mutations

GALUN **Eithan**	Dept. of Gene Therapy The Hadassah Medical Center Jerusalem	ISRAEL
DAGAN **Tal**	Institute of General Microbiology Kiel University (CAU)	GERMANY

Trichomes: uncovering principles of forming complex 3-dimensional shapes by cellular morphogenesis

GROSSNIKLAUS **Ueli**	Dept. of Plant and Microbial Biology University of Zurich (UZH)	SWITZERLAND
KONDO **Shigeru**	Dept. of Frontier Bioscience Osaka University Suita	JAPAN

Molecular determinants of evolutionary conservation in disordered protein regions

HOLEHOUSE **Alex**	Dept. of Biochemistry and Molecular Biophysics Washington University, School of Medicine St. Louis	USA (UK)
LEE **Hyun**	Dept. of Biochemistry University of Toronto, Faculty of Medicine	CANADA (KOREA)
WEIJERS **Dolf**	Lab. of Biochemistry Wageningen University	THE NETHERLANDS

Physical regulation of the genome

HOLT **Liam**	Dept. of Biochemistry and Molecular Pharmacology New York University School of Medicine	USA
LEVY **Emmanuel**	Dept. of Structural Biology Weizmann Institute of Science Rehovot	ISRAEL
TAKINOUE **Masahiro**	Dept. of Computer Science Tokyo Institute of Technology Yokohama	JAPAN

The evolution of sperm cell shape and motion

HUMPHRIES **Stuart**	Dept. of Life Sciences University of Lincoln	UK
FAUCI **Lisa**	Dept. of Mathematics Tulane University - SSE New Orleans	USA
SNOOK **Rhonda**	Dept. of Zoology Stockholm University	SWEDEN (USA)

Social origins of rhythm

KING **Stephanie**	School of Biological Sciences University of Bristol	UK
COOK **Peter**	Dept. of Psychology New College of Florida Sarasota	USA
MADSEN **Peter**	Dept. of Biology Aarhus University	DENMARK
RAVIGNANI **Andrea**	MPI for Psycholinguistics Nijmegen	THE NETHERLANDS (ITALY)

Using Dracula ants and multi-omic models to unravel the evolution of distributed metabolism

LEBOEUF **Adria**	Dept. of Biology University of Fribourg	SWITZERLAND (USA)
FISHER **Brian**	Dept. of Entomology California Academy of Sciences San Francisco	USA
TEUSINK **Bas**	Amsterdam Institute for Life and Environment Vrije University Amsterdam (VU)	THE NETHERLANDS

Unravelling the code of mitochondrial-nuclear communication

LEFKIMMIATIS **Konstantinos**	Dept. of Molecular Medicine University of Pavia	ITALY (GREECE)
DASKALAKIS **Nikolaos**	Dept. of Psychiatry McLean Hospital Belmont	USA (GREECE)
STADLER **Brigitte**	Interdisciplinary Nanoscience Center (iNANO) University of Aarhus	DENMARK (SWITZERLAND)

Regulation of neuronal physiology by the electromechanical effects of the action potential

LOIS **Carlos**	Dept. of Biology and Biological Engineering California Institute of Technology Pasadena	USA (SPAIN)
ROYLE **Stephen**	Dept. of Biomedical Sciences University of Warwick Coventry	UK
SEZGIN **Erdinc**	Women's and Children's Health Karolinska Institute Solna	SWEDEN (TURKEY)

Super-resolution multifunctional scanning ion conductance microscopy: tapping the cell's energy grid

MACHESKY **Laura**	Institute of Cancer Sciences Cancer Research UK Beatson Institute Glasgow	UK
SASAKI **Atsuo**	Dept. of Internal Medicine University of Cincinnati	USA (JAPAN)
TAKAHASHI **Yasufumi**	Nano Life Science Institute Kanazawa University	JAPAN

Unravelling the mechanisms of brain and behavioral elaboration in ecologically diverse butterflies

MONTGOMERY **Stephen**	School of Biological Sciences University of Bristol	UK
BACQUET **Caroline**	Dept. of Biotechnology Universidad Regional Amazónica IKIAM Tena	ECUADOR (CHILE)
EL JUNDI **Basil**	Dept. of Biology Faculty of Natural Sciences NTNU, Trondheim	NORWAY (GERMANY)
MARTIN **Arnaud**	Dept. of Biological Sciences The George Washington University Washington	USA (FRANCE)

Intracellular voltage control of directional cell migration

SÁEZ **Pablo**	Dept. of Biochemistry and Molecular Cell Biology University Medical Center Hamburg-Eppendorf Hamburg	GERMANY (CHILE)
GOV **Nir**	Dept. of Chemical and Biological Physics Weizmann Institute of Science Rehovot	ISRAEL
KRISHNAN **Yamuna**	Dept. of Chemistry University of Chicago	USA (INDIA)

New ways to generate color: light manipulation by crystal-forming pigments

STUART-FOX **Devi**	School of BioSciences University of Melbourne	AUSTRALIA
PALMER **Benjamin**	Dept. of Chemistry Ben-Gurion University of the Negev Beer-Sheva	ISRAEL (UK)
TZIKA **Athanasia**	Dept. of Genetics and Evolution University of Geneva	SWITZERLAND (GREECE)

Bridging biophysics and evolution: impact of intermediate filament evolution on tissue mechanics

TOMANCAK **Pavel**	Tomancak lab MPI of Molecular Cell Biology and Genetics (MPI-CBG) Dresden	GERMANY (CZECH REPUBLIC)
EXTAVOUR **Cassandra**	Dept. of Organismic & Evolutionary Biology, Molecular & Cellular Biology Harvard University, Cambridge	USA (CANADA)
HEISENBERG **Carl-Philipp**	Dept. of Life Sciences Institute of Science and Technology Austria Klosterneuburg	AUSTRIA (GERMANY)
HEJNOL **Andreas**	Dept. of Biological Sciences University of Bergen	NORWAY (GERMANY)

Bridging robotics and pollination: Reconstructing a bee's buzz through micro-robots

VALLEJO-MARIN **Mario**	Dept. of Biological and Environmental Sciences University of Stirling	UK (MEXICO)
JAFFERIS **Noah**	Dept. of Electrical and Computer Engineering University of Massachusetts, Lowell	USA

Mental 3D space-time travel in fission-fusion animal societies

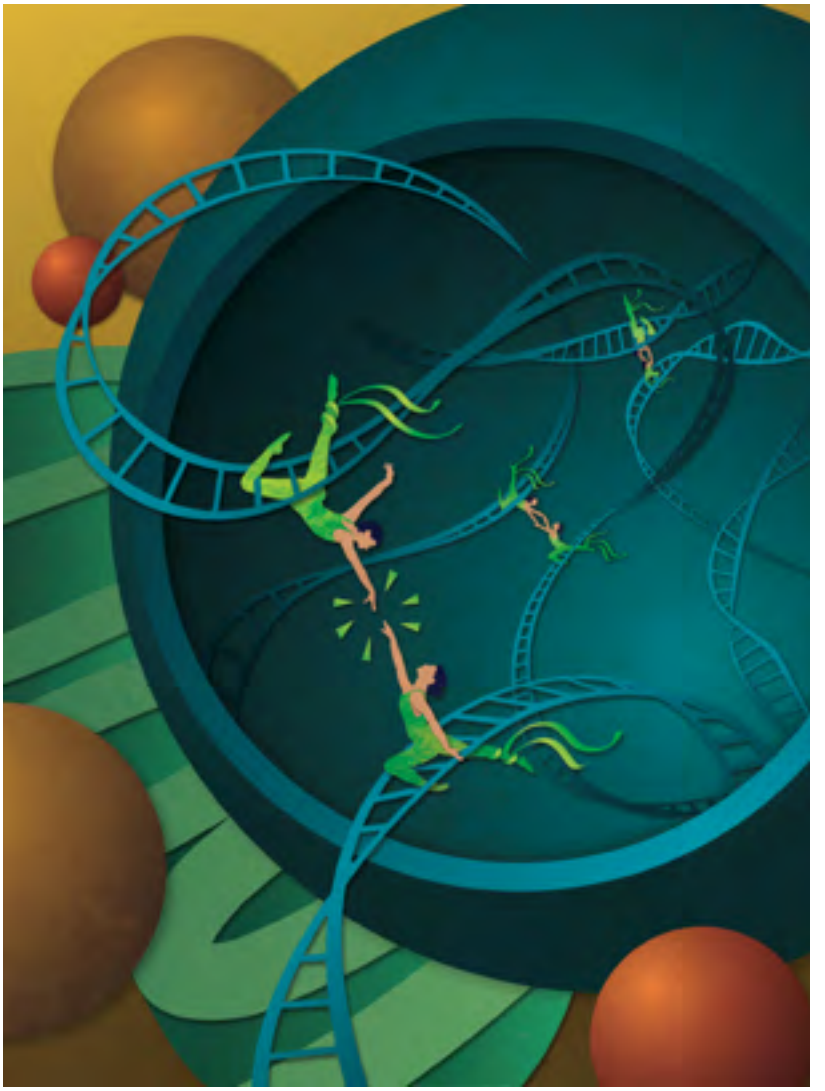
WAHLBERG **Magnus**	Dept. of Biology University of Southern Denmark (SDU) Odense M	DENMARK (SWEDEN)
MOSS **Cynthia**	Dept. of Psychological and Brain Sciences Johns Hopkins University Krieger School of Arts & Sciences Baltimore	USA
PEREMANS **Herbert**	Dept. of Engineering Management University of Antwerp	BELGIUM
VON BAYERN **Auguste**	Dept. of Behavioural Ecology. & Evolutionary Genetics MPI for Ornithology (MPIO) Seewiesen	GERMANY

Modeling electric fields at the heart of enzyme catalysis and function

WUTTKE **Stefan**	BCMaterial Basque Center on Materials, Applications and Nanostructures Leioa	SPAIN (GERMANY)
BOXER **Steven**	Dept. of Chemistry Stanford University	USA

Deciphering the link between brain development and aging

ZOU **Yimin**	Dept. of Neurobiology The University of California, San Diego La Jolla	USA
BOURNE **James**	Australian Regenerative Medicine Institute Monash University Clayton	AUSTRALIA
FUJIYAMA **Fumino**	Lab. of Histology and Cytology Hokkaido University Sapporo	JAPAN
HJERLING-LEFFLER **Jens**	Dept. of Medical Biochemistry and Biophysics Karolinska Institute Solna	SWEDEN



Michal Levo
(HFSP Long-Term Fellowship 2016)

In this illustration the acrobats represent distant genes that pair together in space, despite large genomic distances, and engage in coordinated gene activity.
Image by João Raimundo and Jeremy Guay at Peregrine Creative for Princeton University.

www.hfsp.org/hfsp-news-events/genomically-apart-acting-together-gene-coupling-living-embryos

2.4.2 RESEARCH GRANTS - EARLY CAREER

Cellular and molecular basis of behavioural manipulation by viral infection

CRAVA **Maria Cristina**	University Institute of Biotechnology and Biomedicine University of Valencia	SPAIN (ITALY)
GAMIR **Jordi**	Dept. of Agricultural and Environmental Sciences Universitat Jaume I de Castello Castello De La Plana	SPAIN
PRIETO-GODINO **Lucia**	Neural Circuits and Evolution Lab The Francis Crick Institute (UK Centre for Medical Research and Innovation) London	UK (SPAIN)
YON **Felipe**	Instituto de Medicina Tropical Universidad Peruana Cayetano Heredia Lima	PERU

Reconstructing water to land transitions in arthropod evolution combining atoms, genes and fossils

FERNANDEZ **Rosa**	Institute of Evolutionary Biology CSIC Barcelona	SPAIN
MUÑOZ-GARCIA **Ana Belen**	Dept. of Physics University of Naples, Federico II	ITALY (SPAIN)
ORTEGA-HERNANDEZ **Javier**	Dept. of Organismic and Evolutionary Biology Harvard University, Cambridge	USA (MEXICO)

Biofilm heterogeneity as an evolutionary mechanism for resilience to complex environments

FUSCO **Diana**	Dept. of Physics University of Cambridge	UK (ITALY)
RUIZ PESTANA **Luis**	Dept. of Civil and Architectural Engineering University of Miami Coral Gables	USA (SPAIN)
TROPINI **Carolina**	Dept. of Microbiology and Immunology and School of Biomedical Engineering University of British Columbia Vancouver	CANADA

The atmosphere: a living breathing ecosystem?

GOORDIAL **Jackie**	School of Environmental Sciences University of Guelph	CANADA
BRADLEY **James**	School of Geography Queen Mary University of London	UK
GREENING **Chris**	Dept. of Microbiology Monash University Clayton	AUSTRALIA
TREMBATH-REICHERT **Elizabeth**	School of Earth and Space Exploration Arizona State University, Tempe	USA

How fishes use historical hydrodynamic motion cues in search and navigation tasks

HERBERT-READ **James**	Dept. of Zoology University of Cambridge	UK
FAN **Dixia**	School of Engineering Westlake University, Hangzhou	CHINA
JODIN **Gurvan**	Dept. of Mechatronics SATIE UMR CNRS, Bruz	FRANCE

Crossing the barrier: horizontal gene transfer in synergistic protocells

O'FLAHERTY **Derek**	Dept. of Chemistry University of Guelph	CANADA
BONFIO **Claudia**	Supramolecular Science and Engineering Institute Centre International pour la Recherche aux Frontières de la Chimie Strasbourg	FRANCE (ITALY)
SPRUIJT **Evan**	Dept. of Physical Organic Chemistry Radboud University Nijmegen Medical Centre	THE NETHERLANDS

How do ecological network dynamics mediate the response of organisms to novel environments?

PILOSOF **Shai**	Dept. of Life Sciences Ben-Gurion University of the Negev Beer-Sheva	ISRAEL
DE DOMENICO **Manlio**	Digis - Digital Society Fondazione Bruno Kessler Trento	ITALY
HALL **James**	Dept. of Evolution, Ecology and Behaviour University of Liverpool	UK

2.5

RESEARCH GRANT PROFILE

2021 PROGRAM GRANT

Principal Investigator
Ke HU

- **Principal Investigator:** Ke Hu (People's Republic of China), Center for Mechanisms of Evolution, Arizona State University, Tempe, USA

- **Co-Investigator:** Kazuo Inaba (Japan), Shimoda Marine Research Center, University of Tsukuba, Japan

HFSP project: Understanding the cellular mechanics of coral bleaching

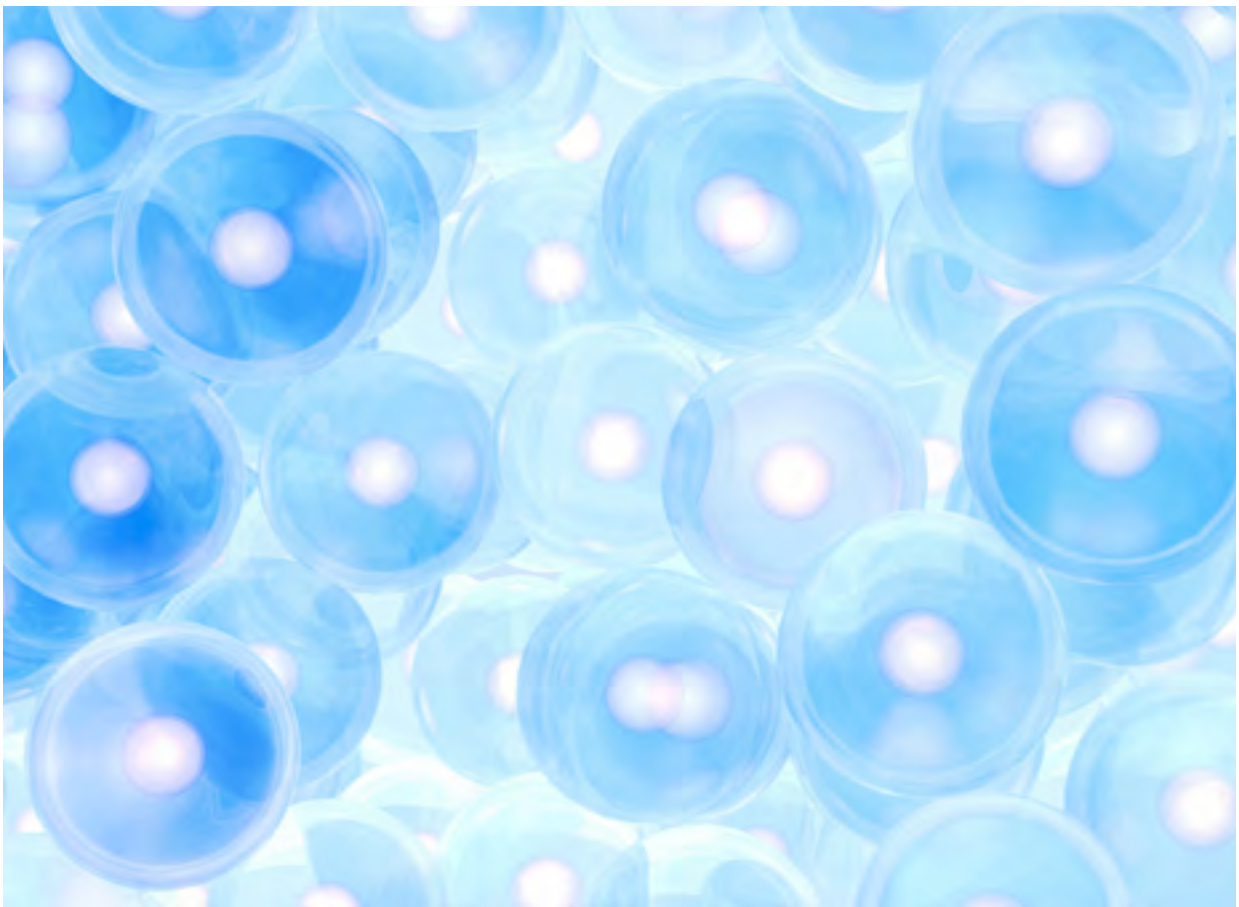
The life cycle of an intracellular symbiont includes host entry, intracellular proliferation, and host exit. Coral bleaching, triggered primarily by global warming, is caused by a massive exodus of the dinoflagellate *Symbiodinium* from its coral host. Sustained coral bleaching leads to coral death, destroying an essential foundation of the marine ecosystem. While the ecological importance of *Symbiodinium spps* has long been established, the mechanism of how the intracellular association with their hosts is established and dissolved is not understood.

In contrast to the lack of knowledge about mechanical interaction between *Symbiodinium* and the cnidarian spp host, much is known about how the symbiont-host interaction is established and abolished for apicomplexan parasites, which are a sister clade of the dinoflagellates in Aveolata. The apicomplexan parasite provides the main driving forces for both invasion (host entry) and egress (host exit), with these two processes sharing many molecular components. The vast majority of apicomplexans identified so far are obligate intracellular parasites of vertebrate and invertebrate hosts, but marine, photosynthetic relatives (Chromerids) that share important structural and genetic characteristics with both dinoflagellates and apicomplexans have been identified.

These findings not only further establish the link between these two deeply branched clades, but also strongly suggest the possibility of conservation of the cellular mechanisms of host-symbiont association/dissociation in these two groups.

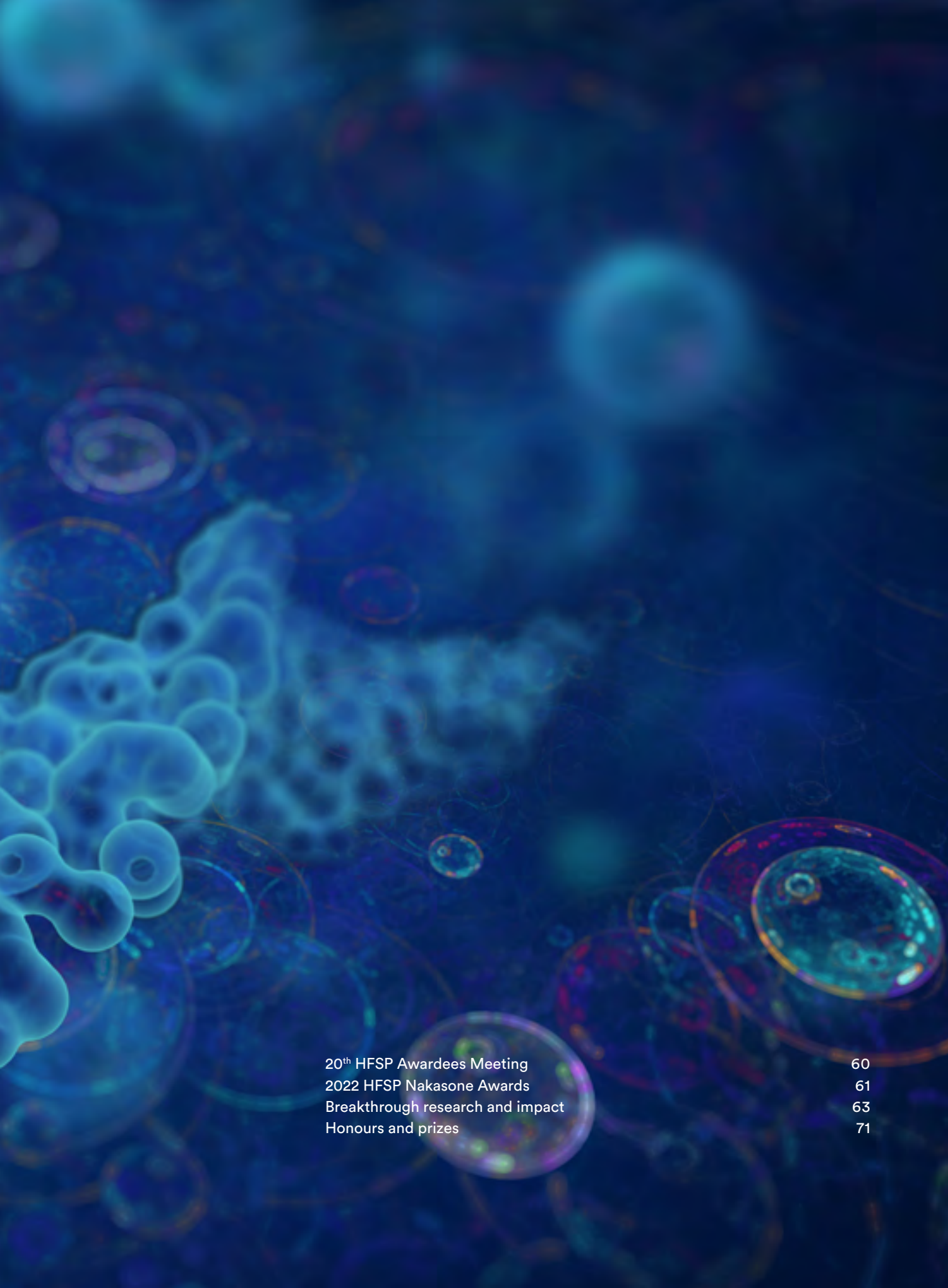
Together, the Hu and Inaba Labs will use their combined expertise in cell biology, parasitology, evolutionary biology and marine biology to explore the cell biological response and basis for coral bleaching, examine conservation of gene function between *Symbiodinium* and apicomplexans, and develop molecular genetic tools. The team will use the knowledge of symbiont-host interaction from the study of apicomplexans as the framework to elucidate whether coral bleaching is due to the rejection of the symbiont by the host or due to the active departure of the symbiont from the host (i.e., rejection of the host by the symbiont).

This evolution-guided strategy will allow the team to test whether two seemingly incongruent processes - the exodus of *Symbiodinium* from cnidarians and the egress of apicomplexan parasites from mammalian cells - share a common evolutionary origin and cellular mechanism.



Chapter 3

HFSP Science and Impact



3.0

20TH HFSP AWARDEES MEETING

The 2021 HFSP Awardees Meeting took place for the first time as an entirely virtual event from 5 to 8 July.

The meeting was hosted on a state-of-the-art interactive platform that provided a unique environment for scientific exchange with opportunities for networking via the live Q&A and the meeting hub. Talks were broadcast live from a studio in Paris and were made available on replay for three months following the meeting.

A record number of over 500 participants connected during the four days of the meeting, including HFSP awardees, together with members of their labs, alumni and HFSP committee members.

Highlights of the programme included meeting the winners of the 2021 HFSP Nakasone Award, Anthony Hyman and Clifford Brangwynne, and a presentation by special guest speaker Niklas Blomberg, Director of Elixir, who introduced the HFSP community to Elixir and the newly created Global Biodata Coalition. The programme also featured 40 talks and over 200 e-posters.

The studio setup for broadcasting the 2021 HFSP Awardees Meeting

3.1

2022 HFSP NAKASONE AWARDS

For the first time since its introduction, the 2022 HFSP Nakasone Award was made in two parts. The first award went to Aviv Regev of Genentech, a member of the Roche Group, South San Francisco, USA, for unravelling the biological processes controlling cellular phenotype through innovative computational, mathematical, and experimental approaches applied to single-cell genomics.

A second joint award went to Franz-Ulrich Hartl of the Max Planck Institute of Biochemistry, Martinsried, Germany, and Arthur L. Horwich of Yale University, New Haven, USA, for their discoveries revealing the functions and mechanisms of chaperone-mediated protein folding and the implication of their work in understanding human disease.

Aviv REGEV

The single-cell genomics revolution

Aviv Regev conceived a powerful suite of technologies to understand complex mechanisms at the level of an individual cell. Knowledge of its complex properties and dynamic behaviour provides the source for understanding the physiology of the organism. The cell is the fundamental unit of life, analogous to the molecule in chemistry. It is the entity with the capacity to function independently. Regev's key breakthrough was to experimentally, conceptually, and computationally make it possible to analyse individual cells on a grand scale, thereby supporting HFSP's mission of "basic research into the complex mechanisms of living organisms." Her work has produced fundamental new insights into an extraordinarily wide range of molecular systems and fields, including immunology, neurobiology, development, and cancer. In doing so, she has empowered scientists worldwide to answer the deepest and most general biological questions – how do cellular circuits function and rewire, and how do these dynamics underlie health and malfunction in disease?

Aviv Regev, a computational and systems biologist, was formerly a Professor of Biology at MIT and core member at the Broad Institute of MIT and Harvard (currently on leave since 2020), a Howard Hughes

Medical Institute Investigator, and the Chair of the Faculty, and the Director of the Klarman Cell Observatory and Cell Circuits Program at the Broad Institute. She remains a co-chair of the organising committee for the international Human Cell Atlas project and currently holds the position of Executive Vice President and Head of Research and Early Development at Genentech, a member of the Roche Group.

You can read more on the 2022 HFSP Nakasone Award to Aviv Regev here: https://www.hfsp.org/hfsp-nakasone-award/2022-aviv-regev

Proteins need folding machines to become functional

The ground-breaking discoveries made by F. Ulrich Hartl and Arthur L. Horwich established that many newly made proteins do not fold spontaneously but rather need the help of specialized folding machines, chaperones, to achieve their functional state. These molecular machines and their mechanics were illuminated primarily through the pioneering work by the laboratories of Hartl and Horwich. Their contributions are numerous, crucial, and profoundly complementary. Moreover, some of their most important early discoveries stemmed from their direct collaboration. These discoveries commenced in 1989 with the demonstration that protein folding in mitochondria requires a particular helper complex and continued with the systematic dissection of the mechanism of bacterial chaperonin, with both of the nominated researchers independently arriving at the critical insight that proteins fold within the encapsulated central cavity of that complex. The discovery of this fundamental biological principle helps to explain the phenotypes of human disease resulting from failure of protein homeostasis, including certain neurodegenerative disorders, and offers the prospect of developing novel therapies.

Franz-Ulrich HARTL

Arthur L. HORWICH

Franz-Ulrich Hartl is a biochemist who was appointed group leader at the Institute of Physiological Chemistry at the University of Munich in 1987. In 1991, he became associate member in the Program in Cellular Biochemistry & Biophysics at the Sloan Kettering Institute, New York, and member with tenure in 1993. He held additional posts at the Graduate School of Medical Sciences at Cornell University. From 1994 to 1997, he was Associate Investigator of the Howard Hughes Medical Institute. Since 1997, he is a director at the Max Planck Institute of Biochemistry, Martinsried, Germany.

Arthur L. Horwich trained in medicine and carried out his residency in paediatrics at the Yale New Haven Hospital before working at the Salk Institute in La Jolla. After a second postdoctoral position in the Department of Genetics at Yale University School of Medicine, he became Assistant Professor of Genetics, rising through the ranks to become full professor in 1995. Today, he remains a faculty member at Yale University School of Medicine. From 1990 to 2020, he was an Investigator of the Howard Hughes Medical Institute.

You can read more on the 2022 HFSP Nakasone Award to F. Ulrich Hartl and Arthur Horwich here: https://www.hfsp.org/hfsp-nakasone-award/2022-franz-ulrich-hartl-and-arthur-l-horwich

3.2

BREAKTHROUGH RESEARCH AND IMPACT

HFSP awardees' publications on breakthrough discoveries and novel approaches are regularly highlighted on the HFSP website. A few examples are described below (a more detailed account of breakthrough discoveries can be found in the 2021 HFSP Science Digest):

- **HFSP Program Grant holder Ronen Segev and colleagues showed that fish can navigate on land using an inverted submarine.** The team developed a fish operated vehicle - a wheeled terrestrial platform that reacts to the fish's movement characteristics, location, and orientation in its water tank to change the vehicle's position thus enabling fish to explore a terrestrial environment. Fish were tasked to 'drive' the vehicle towards a visual target in the terrestrial environment, and indeed were able to operate the vehicle, explore the new environment, and reach the target regardless of the starting point.

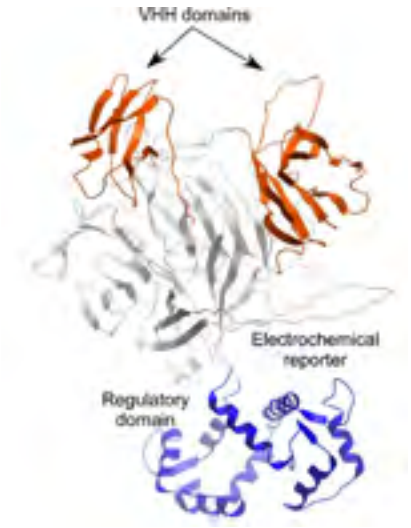
The fish operated vehicle
(photo credit: Shachar Givon and Matan Samina)

- **Grant awardee Yutetsu Kuruma working at the Japan Agency for Marine-Earth Science and Technology (JAMSTEC) has established a rapid and easy method to prepare artificial cells through optimizing a process using the droplet transfer method.** Artificial cell research attempts to fabricate cell-like entities from molecules and genes to apply as next-generation bioengineering or to elucidate the mystery of how cellular life emerged in the early earth environment. The cells are generally constructed by encapsulating a cell-free gene expression system (cell-free system) inside vesicles consisting of a phospholipid membrane, where several cellular functions can be reproduced inside. To do this, the formation of membrane vesicles in the laboratory at the same size scale as actual cells is the most important consideration. Although the general protocol of vesicle preparation has been shared, it is often difficult to form quality vesicles, especially for students or researchers who are non-experts in this field or technique. Since the bottom-up construction of cells is becoming a global trend in the field of synthetic biology, it is important to reduce technical barriers and increase the research population for the development of this research field.

- **HFSP Long-Term Fellows Talia Karasov and Derek Lundberg, together with their colleagues, are exploring diverse microbes that are hosted by agricultural and wild plants on and in their leaves.** In their project they seek to understand how the presence of surrounding commensal bacteria influenced disease progression by bacterial pathogens. Working on the model plant *Arabidopsis thaliana*, the team treated plants with different combinations of pathogenic and commensal *Pseudomonas* bacteria. The *Pseudomonas* strains were genetically barcoded with a unique DNA sequence before mixing the combinations, enabling all strains to be easily and unambiguously distinguished. The team then tracked the abundance of the diverse pathogenic and commensal bacterial strains while simultaneously monitoring plant health. They found that the commensal microbes often suppressed the proliferation and disease development caused by pathogenic bacteria, although not all plant genotypes benefited from the suppressive ability of the commensal microbes. Agricultural pathogens are a significant cause of global food insecurity and finding ways to combat pathogen spread remains a central challenge, particularly as climate change expands the range of many pathogens to higher latitudes. This study supports a role for surrounding microbes in combating disease. Ultimately, harnessing the plant microbiome to combat disease has potential to increase agricultural yields with minimal environmental impact.

Outcomes from HFSP supported research can have a lasting impact resulting from technological innovation and advanced insights into complex mechanisms.
Three examples of the impact of HFSP supported research are presented below:

Using synthetic biology to create next generation biosensors



A) A structural model of electrochemical biosensors of α-amylase based on circular permutated electrochemical enzyme glucose dehydrogenase. The model was generated using Alpha-Fold

B) Artificial methotrexate receptor system for based VHH and nanoCLAMP domains.

Supported by their 2018 HFSP Program Grant, Kirill Alexandrov and Evgeny Katz are combining electronic and natural systems into bioelectronic hybrids which have fascinated humans for centuries, with many imagined purposes both for the benefit of and detriment to mankind. HFSP funding enabled a multidisciplinary team to develop a range of bioelectronic sensors, most recently for methotrexate, a toxic chemotherapy drug requiring precise monitoring to avoid serious, life-threating side effects in cancer patients.

Their work on bioelectronic hybrids aims to transform a US$70 billion global diagnostic industry via new synthetic biology enabled biosensors that 'switch on' colour or electrical responses to drugs used in cancer, arthritis, and organ transplant treatments. This work is based on a modular approach to constructing small molecule biosensors – artificial proteins designed to capture biomarkers of choice and produce specific and sensitive responses. The research was carried out at the CSIRO-QUT Synthetic Biology Alliance (Australia), in collaboration with Clarkson University (USA) and Pathology Queensland (Australia) and primary funding was provided by HFSP.

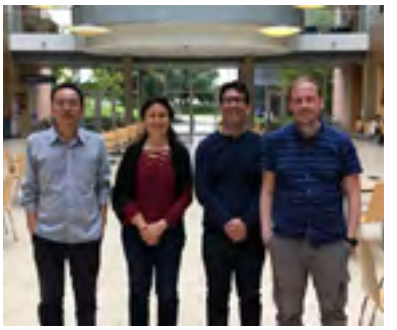
Over multiple collaborative projects, biosensors were developed and adapted to accurately measure protein biomarkers of stress such as α-amylase. Also, a range of small molecule biosensors was developed, including those for the immunosuppressant drugs cyclosporine A, tacrolimus and rapamycin, along with the anticancer drug methotrexate, which requires close monitoring to reduce toxicity and organ damage. Such protein biosensors have the potential to expand patient care by enabling sophisticated tests on cheaper lab equipment and new portable point-of-care devices, allowing therapeutic drug monitoring on less sophisticated equipment than available in small, regional or remote labs and hospitals. Future tests may also require smaller biological samples, the team having proved that a biosensor could accurately measure cyclosporine A levels in one microlitre blood samples.

Protein complexity and fragility makes construction and use of such protein biosensors difficult, but using a modular architecture helps alleviate the problem and could be adapted to potentially target any small molecule and not just to therapeutic drugs. The Clarkson team has also demonstrated the feasibility of advancing this technology to detect two different biomarkers at the same time.

The success of this project was based on the collaboration of scientists with expertise in different areas: synthetic biology, synthetic organic chemistry, and bioelectrochemistry. It is an exemplary collaboration that serves as a model for performing multi-disciplinary research. While the artificial enzyme preparation was carried out by an Australian team led by Prof. Alexandrov, bioelectrochemical study of the developed biosensor was performed by Dr. Smutok at Clarkson University. Both the US and Australian teams are continuing their successful work combining synthetic biology and bioelectronics and are expecting many more interesting and practically important results. The critical and continuous contributions of Dr. Artem Melman at Clarkson University, who passed away in November 2021, is gratefully acknowledged.

A multi-scale approach to understanding how cells convert physical forces into mechanical linkage

In 2016, Anna Akhmanova, Ben Goult, Jie Yan and Guy Tanentzapf were awarded an HFSP Program Grant, which led to the discovery of the long-sought connection between cell adhesion and the cell's microtubule cytoskeleton via a family of proteins called KANKs.



Jie YAN, Anna AKHMANOVA, Guy TANENTZAPF and Ben GOULT during their HFSP team meeting in Vancouver, Canada in May 2017

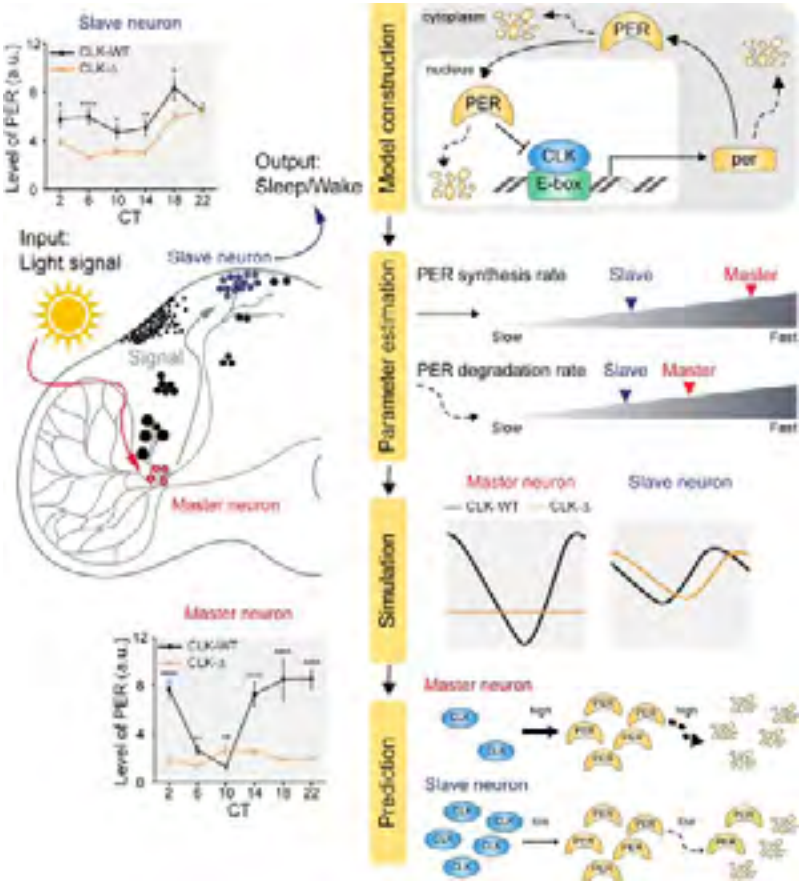
Most cells in the human body are held in place via attachments to a dense meshwork of proteins called the extracellular matrix. The adhesions to the matrix serve as sophisticated mechano-sensory structures, able to sense the physicality of the surroundings and convert these physical signals into biological signals. Understanding the remarkable versatility of the signalling outputs of these complexes as they respond to subtle changes in forces was the aim of the team's HFSP project.

The team studied how the core component in these complexes, the protein talin, responds to changes in force. They looked at this protein at the single molecule level (Yan lab), the structural and biochemical level (Goult lab) in cells using super resolution microscopy techniques (Akhmanova lab) and in the fruit fly, *Drosophila* (Tanentzapf lab). By studying how these proteins work on different scales, the team were able to define in detail how these mechanical linkages form and send signals into the cell.

Already in 2016, the team reported that one of the talin switches, through its interaction with KANK proteins, regulates the connection of adhesions to microtubules. Then in 2019, the team made a technological advance enabling the measurement of how forces alter the talin-KANK interactions, which showed that forces dramatically alter how these proteins interact.

In 2021, towards the culmination of their HFSP project, the team published three papers that together provide a novel view of the way that talin orchestrates the mechanical linkages and mechanosensing in cells. At the end of the HFSP award the team reflected on the successes of this grant, with over 20 publications resulting from the collaboration. The landscape for how cells sense mechanical forces has been transformed by the notion of this mechanical coding that cells are using to control their biological processes. With several papers in preparation based on the collaborations facilitated by the grant, the team will hopefully continue to work together in the future to build on the discoveries of the HFSP funded research.

How our circadian rhythm can be both strong and flexible



(left) The circadian clock operates as a network where the master pacemaker and slave oscillator are organized in a hierarchical manner. Although they generate rhythms via an identical transcriptional-translational feedback loop (TTFL) of PER proteins, the generated PER rhythms are different between them.

(right) By using a mathematical model describing the TTFL of the *Drosophila* circadian clock (top), we identified the differences between master and slave clock neurons (bottom).

HFSP Research Grant - Early Career holder Jae Kyoung Kim and colleagues used a combination of mathematical modelling and experiments to identify the difference in molecular clockworks of the master and slave clock neurons in *Drosophila*. Their work is based on the discovery of the molecular mechanism of the circadian clock which was recognised by the Nobel Prize in Physiology or Medicine in 2017. From what is known, it is not a single centralized clock that is responsible for our circadian cycles. Instead, it operates in a hierarchical network with a 'master pacemaker' and a 'slave oscillator'. The master pacemaker receives various input signals from the environment such as light. It then drives the slave oscillator that regulates various outputs such as sleep, feeding, and metabolism. Despite the different roles of the pacemaker neurons, they are known to share common molecular mechanisms that are well conserved in all lifeforms. For example, interlocked systems of multiple transcriptional-translational feedback loops (TTFLs) composed of core clock proteins have been extensively studied in fruit flies.

However, there is still much that we need to learn about our own biological clock. The hierarchically organised nature of master and slave clock neurons leads to a prevailing belief that they share an identical molecular clockwork. At the same time, the different roles they serve in regulating bodily rhythms also raise the question of whether they might function under different molecular clockworks.

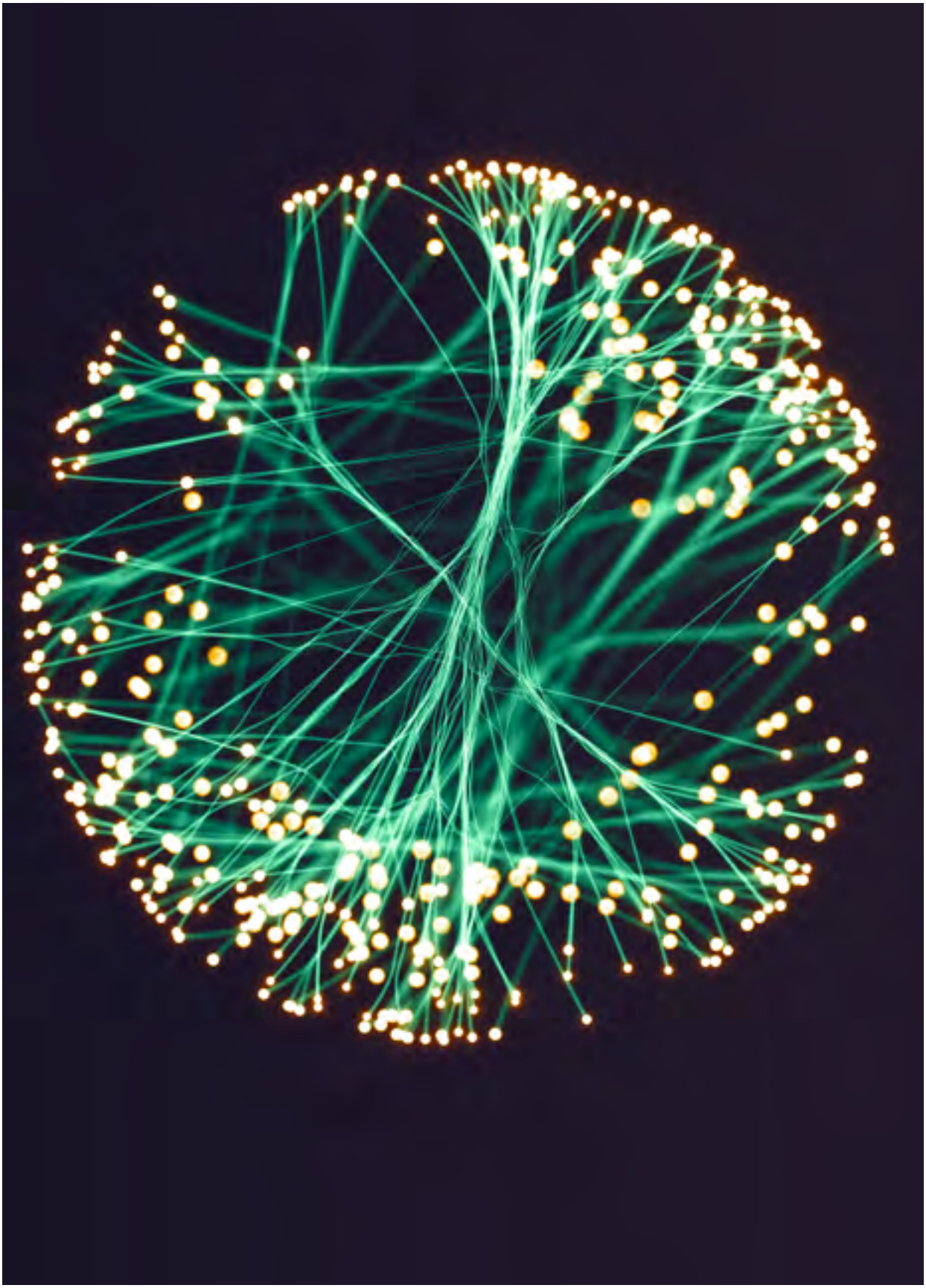
The team of researchers used a combination of mathematical and experimental approaches using fruit flies to answer this question and they found that the master clock and the slave clock operate via different molecular mechanisms. In both master and slave neurons of fruit flies, a circadian rhythm-related protein called PER is produced and degraded at different rates depending on the time of day. Previously, the team found that the master clock neuron (sLN_vs) and the slave clock neuron ($DN1_ps$) have different profiles of PER in wild-type and Clk-Δ mutant *Drosophila*. This hinted that there might be a potential difference in molecular clockworks between the master and slave clock neurons.

However, due to the complexity of the molecular clockwork, it was challenging to identify the source of such differences. Thus, the team developed a mathematical model describing the molecular clockworks of the master and slave clocks. Then, all possible molecular differences between the master and slave clock neurons were systematically investigated by using computer simulations. The model predicted that PER is more efficiently produced and then rapidly degraded in the master clock compared to the slave clock neurons. This prediction was then confirmed by follow-up experiments using animals.

Then, why do the master clock neurons have such different molecular properties from the slave clock neurons? To answer this question, the research team once again used the combination of mathematical model simulation and experiments. It was found that the faster rate of synthesis of PER in the master clock neurons allows them to generate synchronized rhythms with a high level of amplitude. Generation of such a strong rhythm with high amplitude is critical to delivering clear signals to slave clock neurons.

However, such strong rhythms would typically be unfavourable when it comes to adapting to environmental changes. These include natural causes such as different daylight hours across summer and winter seasons, up to more extreme artificial cases such as jet lag that occurs after international travel. Thanks to the distinct property of the master clock neurons, it is able to undergo phase dispersion when the standard light-dark cycle is disrupted, drastically reducing the level of PER. The master clock neurons can then easily adapt to the new diurnal cycle. Our master pacemaker's plasticity explains how we can quickly adjust to the new time zones after international flights after just a brief period of jet lag.

It is hoped that the findings of this study can have future clinical implications when it comes to treating various disorders that affect our circadian rhythm. Jae Kyoung Kim notes, "When the circadian clock loses its robustness and flexibility, the circadian rhythm sleep disorders can occur. As this study identifies the molecular mechanism that generates robustness and flexibility of the circadian clock, it can facilitate the identification of the cause of and treatment strategy for the circadian rhythm sleep disorders."



3.3

HONOURS AND PRIZES

Scientists who have received funding from HFSP are regularly awarded the most prestigious prizes in the life sciences in recognition of their ground-breaking research. Some of the top prizes in 2021 to researchers associated with HFSP are listed below:

- **The 2021 Nobel Prize in Physiology or Medicine** was awarded to David Julius, recipient of the 2017 HFSP Nakasone Award
- **The Gottfried Wilhelm Leibniz Prize** was awarded to former HFSP fellow **Asifa Akhtar**
- **The Albert Lasker Basic Medical Research Award** went to **Karl Deisseroth**, winner of the 2010 HFSP Nakasone Award
- **The Neuroscience Prize from the Gruber Foundation** went to HFSP research grant alumni **Christine Petit** and **Christopher A. Walsh**
- **The Breakthrough Prize in the Life Sciences** went to HFSP research grant holder **David Baker**

The recognition of HFSP funded scientists is an indication of the outstanding quality of the science that HFSP supports and of the Program's contribution to breakthrough advances and technological developments that have significant benefits for society.

Over the years, the scientists funded by HFSP have been recognized for their seminal work that in many cases has led to important tangible outcomes. HFSP alumni belong to an elite group of researchers who are regularly honoured by the most prestigious scientific distinctions, not least the Nobel Prizes, of which 28 have gone to HFSP alumni in the past 32 years.

HFSP grantees awarded the Nobel Prize

Nobel Laureate	HFSP Research Grant	Nobel Prize
Christiane NÜSSLEIN-VOLHARD	1993	1995 (Physiology or Medicine)
Rolf ZINKERNAGEL	1994	1996 (Physiology or Medicine)
Stanley PRUSINER	1994	1997 (Physiology or Medicine)
John WALKER	1996	1997 (Chemistry)
Steven CHU	1993	1997 (Physics)
Paul NURSE	1994	2001 (Physiology or Medicine)
Tim HUNT	1992, 1997	2001 (Physiology or Medicine)
John SULSTON	1991	2002 (Physiology or Medicine)
Peter AGRE	2000	2003 (Chemistry)
Linda BUCK	1995	2004 (Physiology or Medicine)
Avram HERSHKO	1998	2004 (Chemistry)
Roger KORNBERG	1990, 1993, 1997, 2000	2006 (Chemistry)
Roger TSIEN	1995	2008 (Chemistry)
Jack SZOSTAK	2001	2009 (Physiology or Medicine)
Venkatraman RAMAKRISHNAN	2000, 2009	2009 (Chemistry)
Ada YONATH	2003	2009 (Chemistry)
Jules HOFFMANN	1995	2011 (Physiology or Medicine)
Ralph STEINMAN	1996, 2006	2011 (Physiology or Medicine)
Randy SCHEKMAN	1991, 1995	2013 (Physiology or Medicine)
Thomas SÜDHOF	1995	2013 (Physiology or Medicine)
James ROTHMAN	1990, 1994, 2005	2013 (Physiology or Medicine)
Martin KARPLUS	2005	2013 (Chemistry)
Michael LEVITT	2008	2013 (Chemistry)
John O'KEEFE	1994	2014 (Physiology or Medicine)
Stefan HELL	2010	2014 (Chemistry)
Aziz SANCAR	1992	2015 (Chemistry)
Jeffrey C. HALL	1991, 2000	2017 (Physiology or Medicine)
Tasuku HONJO	1990	2018 (Physiology or Medicine)

The following section lists other recent awards and prizes to HFSP awardees and alumni from 2021 or earlier that have come to our attention in FY 2021[1]

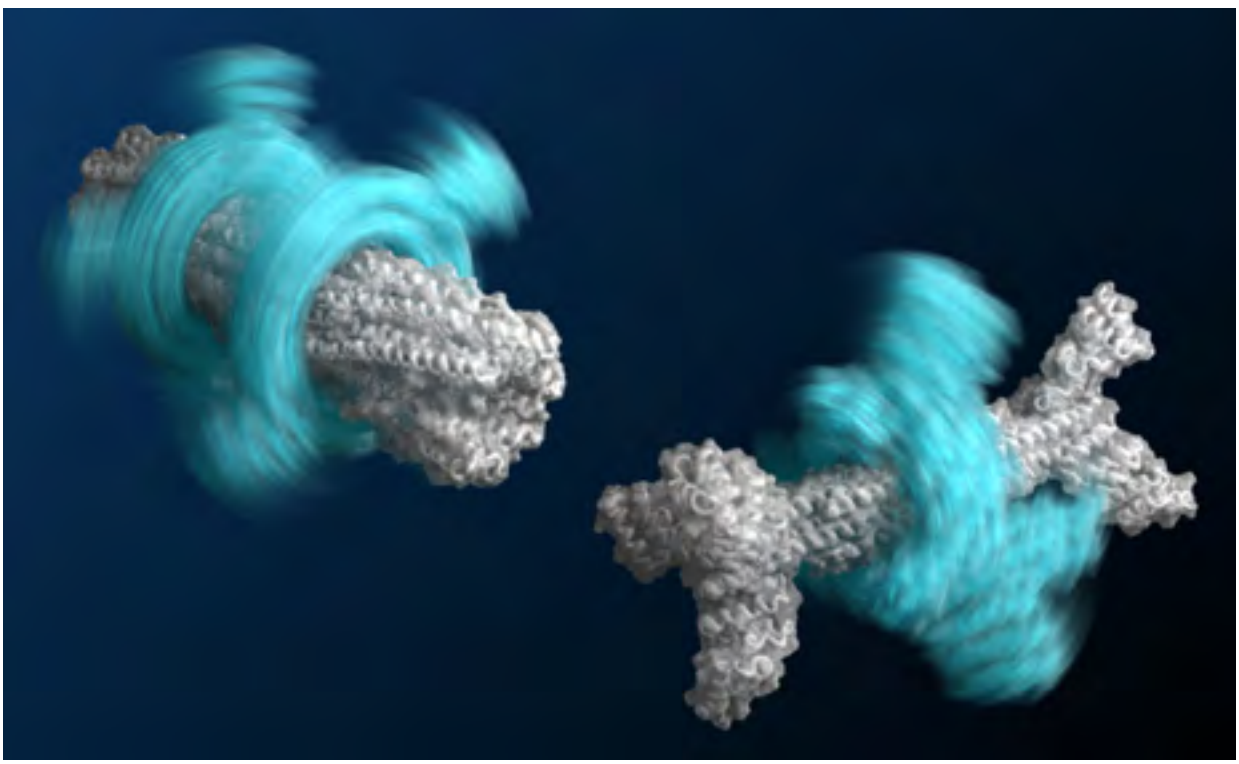
Name	Nationality	Current affiliation	HFSP award
Academie des Sciences - Grand Prix Charles-Léopold Mayer			
Carsten JANKE	Germany	Institut Curie, Paris, France	PG 2008
Academie des Sciences - Lamonica prize for Neurology			
Giovanni MARSICANO	Italy	University of Bordeaux, France	PG 2014
Bayer Science and Education Foundation - Hansen Family Award in Medical Sciences			
Kai JOHNSSON	Germany	Max Planck Institute for Medical Research, Heidelberg, Germany	PG 2004
Bettencourt Schueller Foundation - Prix Coups D'élan Pour La Recherche Française			
Mounia LAGHA	Algeria/ France	Institute of Molecular Genetics of Montpellier, France	LTF 2010, CDA 2015
Albert WEIXLBAUMER	Austria	Institute of Genetics and Molecular and Cellular Biology, Illkirch, France	LTF 2009
Breakthrough Prize Foundation - Breakthrough Prize- Life Sciences			
David BAKER	USA	University of Washington, Seattle, USA	PG 2019
CNRS - Prix Claude Paoletti			
Aline MUYLE	Belgium/ France	University of Lyon, France	LTF 2018
CNRS - Silver Medal			
Valentina EMILIANI	Italy	Vision Institute, Paris, France	PG 2010, 2016

1 Notes: RG=Research Grant (pre 2001); PG=Program Grant; YI=Young Investigator Grant; RG-P= Research Grant - Program; RG-EC=Research Grant - Early Career; LTF=Long-Term Fellowship; CDF= Cross-Disciplinary Fellowship; STF=Short-Term Fellowship. It should be noted that Research Grants were awarded up until 2001 when Program Grants and Young Investigator Grants were introduced. In 2020, the Program Grants and Young Investigator Grants were renamed Research Grants – Program and Research Grants – Early Career, respectively.
The Short-Term Fellowship program was terminated in 2010 and the Career Development Award (CDA) in 2019.

Name	Nationality	Current affiliation	HFSP award
Deutsche Forschungsgemeinschaft - Leibniz Prize			
Asifa AKHTAR	Germany	Max Planck Institute of Immunobiology and Epigenetics, Freiburg, Germany	LTF 1998
Eppendorf International - Eppendorf Award for Young European Investigators			
Tanmay BHARAT	UK	Sir William Dunn School of Pathology, University of Oxford, UK	RG-EC 2021
Ernst Schering Foundation - Ernst Schering Prize			
Aviv REGEV	Israel/USA	Genentech, San Francisco, USA	PG 2005, 2011
Gruber Foundation - Neuroscience Prize			
Christine PETIT	France	Institut Pasteur, Paris, France	RG 1999
Christopher A. WALSH	USA	Boston Children's Hospital, USA	RG 1995
Inamori Foundation - Kyoto Prize			
Robert G. ROEDER	USA	The Rockefeller University, New York, USA	RG 1992
Japan Academy - Japan Academy Medal			
Kei MIYAMOTO	Japan	Kindai University, Wakayama-ken, Japan	PG 2016
Japan Academy - Japan Academy Prize			
Atsushi MIYAWAKI	Japan	RIKEN Center for Advanced Photonics, Wako City, Japan	LTF 1995, PG 2002, 2005
Keio University Medical Science Fund - Keio Medical Science Prize			
Osamu NUREKI	Japan	University of Tokyo, Japan	PG 2001

Name	Nationality	Current affiliation	HFSP award
Lasker Foundation - Albert Lasker Basic Medical Research Award			
Karl DEISSEROTH	USA	Stanford University, USA	2010 HFSP Nakasone Award
Louis-Jeantet Foundation - Louis-Jeantet Prize			
Ton SCHUMACHER	The Netherlands	The Netherlands Cancer Institute, Amsterdam, the Netherlands	PG 2012
Max Planck Society - Otto-Hahn Medal			
Elena RECKZEH	Germany	Hubrecht Institute, Utrecht, the Netherlands	CDF 2021
Bogdan SIERIEBRIENNIKOV	Ukraine	New York University Langone School of Medicine, USA	LTF 2020
NIH - NIH Director's New Innovator Award			
Calin PLESA	Canada/ Romania	University of Oregon, Eugene, USA	LTF 2016
NIH - NIH Director's Pioneer Award			
Mikail SHAPIRO	USA	California Institute of Technology, Pasadena, USA	PG 2016
NIH - NIH Director's Transformative Research Award			
Zemer GITAI	USA	Princeton University, USA	YI 2008, 2013
Seok-Hyun YUN	Republic of Korea	Massachusetts General Hospital, Harvard Medical School, Cambridge, USA	PG 2016
Nobel Foundation - Nobel Prize in Physiology or Medicine			
David JULIUS	USA	University of California, San Francisco, USA	2017 HFSP Nakasone Award

Name	Nationality	Current affiliation	HFSP award
Pew Charitable Trusts - Pew Scholars in the Biomedical Sciences			
Alexander BISSON	Brazil	Brandeis University, Waltham, USA	RG-EC 2021
Edward CHOUCHANI	USA	Dana-Farber Cancer Institute, Boston, USA	LTF 2015
Molly SCHUMER	USA	Stanford University, USA	RG-EC 2020
Royal Society - Croonian Medal and Lecture			
Barry EVERITT	UK	Behavioural and Clinical Neuroscience Institute, Cambridge, UK	RG 1993, PG 2001
Wolf Foundation - Krill Prize			
Benyamin ROSENTAL	Israel	Ben Gurion University of the Negev, Beer-Sheeva, Israel	LTF 2014, YI 2019



Alex Courbet (2016 HFSP Long-Term Fellowship)

Computational design of the first synthetic protein rotary machines: overview of protein machine assembly. Artwork by ©Ian Haydon.

https://www.hfsp.org/hfsp-news-events/computational-design-first-synthetic-protein-rotary-machines

Mathew Shawkey (HFSP Research Grant - Program 2019)

How lizards change their colour. Agama atra lizard (photo by Michaël Nicolaï).

https://www.hfsp.org/hfsp-news-events/how-lizards-change-their-colour

Chapter 4

Finance

4.0
HFSPO'S REVENUE

HFSPO's funding model relies on the generous support of its 15 members: Australia, Canada, France, Germany, India, Israel, Italy, Japan, Republic of Korea, New Zealand, Singapore, Switzerland, the United Kingdom, the United States of America and the European Commission. Together, they agree on the individual and overall financial commitment to implement the Human Frontier Science Program.

In the last financial year, 97% of the budgeted contributions were collected. At the time of writing this report, the last outstanding payment from India has also been received. In light of the economic turmoil caused by the COVID pandemic, the Organization appreciates this exceptional stability of financial support, enabling it to maintain its support of frontier science around the world.

Table 4.1
Voluntary contributions to HFSPO in FY 2021

HFSPO Members	Pledged contribution (1)	Payments received in LC equivalent (2)	Budgeted contribution in USD equivalent (3)	USD equivalent of payments received (4)
Australia	1 686 000 AUD	1 114 450 AUD	1 282 617	835 441
Canada	2 180 000 CAD	2 179 713 CAD	1 729 198	1 725 355
European Commission	5 261 000 EUR	5 300 000 EUR	6 168 367	6 277 320
France	2 463 000 EUR	2 323 000 EUR	2 887 795	2 928 120
Germany	2 836 000 EUR	2 836 000 EUR	3 325 126	3 442 704
India	147 125 000 INR	-	2 010 231	-
Israel	1 056 000 ILS	1 056 000 ILS	316 035	325 000
Italy	500 000 EUR	500 000 EUR	586 235	570 170
Japan	2 271 314 000 JPY	2 271 314 000 JPY	20 499 705	21 396 140
Korea, Republic of	988 288 000 KRW	986 111 643 KRW	875 077	871 429
New Zealand	253 000 NZD	253 000 NZD	176 898	171 646
Singapore	776 000 SGD	776 000 SGD	577 037	573 288
Switzerland	610 000 CHF	610 000 CHF	646 118	691 265
United Kingdom	1 691 000 GBP	1 690 650 GBP	2 326 957	2 288 563
United States of America	12 000 000 USD	11 650 758 USD	12 000 000	11 650 758
TOTAL Contributions			**55 407 397**	**53 747 200**

(1) Pledged contributions in local currency in accordance with the Joint Communique issued by HFSPO Members in Tokyo, July 2019.

(2) Payments received in local currency equivalent correspond to payments received converted from the currency of payment to the currency of pledge at transaction date (date of receipt of funds).

(3) Budgeted contributions are pledged contributions converted to US dollars as per the approved budget consolidated in US dollars for FY 2021.

(4) USD equivalent of payments received are payments converted to US dollars at transaction date (date of receipt of funds).

This financial revenue is complemented by other income from asset management (interest and capital gain) which in FY 2021 constituted USD 2.3 million and some recovered funds in the order of USD 0.1 million. HFSPO's total revenues for the financial year 2021 totalled USD 56.0 million.

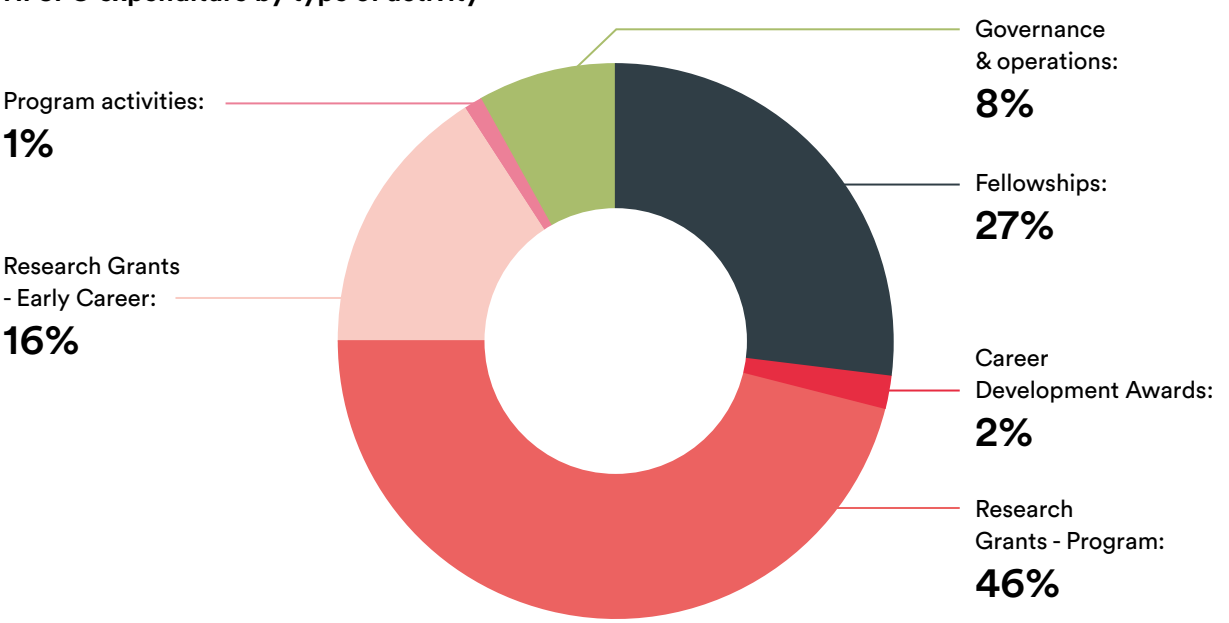
4.1

FY 2021 FINANCIAL SUMMARY

HFSPO was established to support and implement the scientific activities of the Program, and hence its cost structure is geared towards a maximal support of science.

In FY 2021, the scientific program accounted for 92% of the overall expenditure. Governance and operational costs to run the scientific program stand at 8%.

Figure 4.1.
HFSPO expenditure by type of activity



HFSPO'S ACTIVITIES

Income received totals USD 56.0 million which represents 98% of the amount budgeted.

Expenditures amount to USD 53.1 million and include:

- **Program awards and program activities** totalling USD 49.0 million:
  - — USD 24.4 million for Research Grants – Program (on budget)
  - — USD 8.5 million for Research Grants - Early Career (on budget)
  - — USD 14.5 million for Long-Term and Cross-Disciplinary Fellowships
  - — USD 1.3 million for Career Development Awards
  - — USD 0.3 million for program activities

- **Governance and operational costs** amounting to USD 4.1 million (on budget)

The net annual result for HFSPO's activities is a profit of USD 2.9 million.

GBC'S ACTIVITIES

HFSPO receives financial support from other life science research funding agencies to host and fund the activities of the Global Biodata Coalition (GBC), approved at the Board of Trustees meeting in November 2018. The decision to extend this support until 30 June 2023 was recently taken by the Board. During FY 2021, the support of the GBC by its funders amounted USD 690 thousand, and exceeded the expenditure by USD 361 thousand. These unspent funds are carried forward to FY 2022. The accumulated unspent funds since FY 2019 total USD 1.4 million.

These funds are administered by HFSPO in separate accounts. There are no direct administration charges to HFSPO, but the Secretary-General and the HFSPO Secretariat provide in-kind support in the form of contract management, payments and accounting services. This activity is to be cost-neutral for the Secretariat, without taking any funds from HFSPO Members' contributions.

The net consolidated balance from both HFSPO and GBC activities at year-end FY 2021 amounts to a gain of USD 3.3 million.

In Table 4.2 below, an overview of consolidated income and expenditure for HFSPO and GBC activities for FY 2021 are presented and compared with the approved budget, extending from 1 April 2021 to 31 March 2022.

Table 4.2

HFSPO's financial summary FY 2021 vs. FY 2020 – budget & actual (in thousand USD)

	BUDGET FY 2021	ACTUAL FY 2021	% Completion FY 2021	ACTUAL FY 2020	% Completion FY 2020
Contributions from HFSPO Members	55 407	53 747	97%	52 835	96%
Interests & capital gain	1 568	2 308	147%	840	110%
TOTAL INCOME	**56 975**	**56 055**	**98%**	**53 675**	**97%**
GOVERNANCE					
Meeting costs	10	-	0%	-	0%
Travel costs	65	-	0%	-	0%
Total Governance expenditure	**75**	**-**	**0%**	**-**	**0%**
PROGRAM					
Program Awards					
Research Grants - Program	24 415	24 415	100%	24 650	100%
Research Grants - Early Career	8 455	8 455	100%	8 450	100%
Fellowships	16 624	14 490	87%	14 515	92%
Career Development Awards	1 300	1 300	100%	2 600	96%
Total Program awards	**50 794**	**48 660**	**96%**	**50 215**	**97%**
Program activities	473	301	64%	148	41%
Total Program awards & activities	**51 267**	**48 961**	**96%**	**50 363**	**97%**

OPERATIONS

	BUDGET FY 2021	ACTUAL FY 2021	% Completion FY 2021	ACTUAL FY 2020	% Completion FY 2020
Human resources	3 046	3 030	99%	3 055	109%
Technical resources	484	590	122%	211	43%
Infrastructure resources	314	120	38%	98	82%
Communication, coordination	138	110	80%	117	61%
Contracts, fees and taxes	116	304	261%	221	95%
Total Operations	**4 099**	**4 153**	**101%**	**3 703**	**97%**
ASSESSMENT AND AUDIT					
Program assessment	-	-	-	-	-
Operational audit	-	-	-	-	-
TOTAL EXPENDITURE	**55 440**	**53 114**	**96%**	**54 066**	**0%**
NET HFSPO BALANCE	**1 535**	**2 941**		**-391**	
GBC's revenue	-	690	-	941	-
GBC's expenditure	-	329	-	292	-
NET GBC BALANCE		**361**		**649**	
NET CONSOLIDATED BALANCE	**1 535**	**3 302**		**259**	

In the spirit of science without borders, HFSP brings together international teams of researchers from around the globe and supports postdoctoral fellows to move to a laboratory in a new country. Since its inception, the Program has supported researchers from 70 different countries. Last year was no exception. As shown in table 4.3, awardees pursue their research in many different locations in the world.

Table 4.3
Geographical distribution of HFSP award payments by Members in FY 2021 (in thousand USD)

HFSPO Members	Research Grants	Fellowships	Career Development Awards	Total
Australia	1 013	308	100	**1 421**
Canada	1 425	204	-	**1 629**
European Commission	4 151	1 476	-	**5 627**
France	2 273	473	200	**2 946**
Germany	2 894	782	300	**3 976**
India	340	-	-	**340**
Israel	1 059	183	200	**1 442**
Italy	1 106	137	100	**1 343**
Japan	1 943	298	200	**2 442**
Korea, Republic of	357	-	-	**357**
New Zealand	249	-	-	**249**
Singapore	247	185	-	**432**
Switzerland	1 092	2 883	-	**3 975**
United Kingdom	3 950	1 575	-	**5 524**
United States of America	9 559	5 975	-	**15 534**
Non-Member	1 213	10	200	**1 423**
Total	**32 870**	**14 490**	**1 300**	**48 660**

4.2

SUMMARY STATEMENT OF ASSETS AND LIABILITIES

HFSPO's financial position is the balance between its assets and its liabilities. A positive position ensures that the payments to current awardees are guaranteed for the period of their award (three years) by HFSPO's available resources.

The summary statement below shows a simplified version of the balance sheet in euros (exchange rate, and other adjustments are not included) converted to US dollars for reporting purposes as of 31 March 2022.

Table 4.4
Assets and liabilities converted to US dollars as of 31 March 2022 (in thousand USD)

ASSETS	FY 2021
Cash	36 817
Long & short-term investments	49 000
Total Current assets	85 817
Prepaid expenses	239
Outstanding contributions	1 954
Total other current assets	2 193
Other assets	3 425
Total assets as of 31/03/2022	**91 435**

LIABILITIES	FY 2021
Accounts payable	683
Deferred income	14 943
Total current liabilities	15 626
Research Grants - Program	24 030
Research Grants - Early Career	8 110
Fellowships	17 665
Total committed awards	49 805
Retained earnings	13 076
Net income FY 2021	3 302
Net financial position (positive)	**9 626**
Total liabilities as of 31/03/2022	**91 435**

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