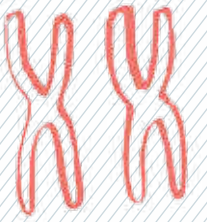
AXA RESEARCH FUND'S BOOK OF KNOWLEDGE

LIFE RISKS

AXA Research Fund
Through Research, Protection

Healthy aging



Antibodies

Protection services

Pandemic

Solidarity

Regenerative capacities

Immortality

Well-being

Neuroscience

Public debate

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The very nature of our business requires us to allocate time and resources to developing our knowledge and reinforcing the understanding and prevention of risks.

We made the choice to support fundamental research because it represents the substrate of scientific progress, because it may lead to revolutionary discoveries and because it challenges conventional ideas. An insurer knows that the greatest risks always appear suddenly from where they are least expected.

Our efforts have a philanthropic logic, not simply for generosity purposes but because we believe that preserving the independence and freedom of the researchers stimulates their creativity, protects their credibility and facilitates the sharing of their discoveries by all socio-economic stakeholders.

By betting on the strong engine of scientific progress and the construction of long-term approaches based on a good understanding of the world and intelligent risk management, we hope to contribute to a better future together.

Henri de Castries

FOREWORD BY JEAN-CHRISTOPHE MÉNIOUX

Chief Executive Officer, AXA Global Life

How would you describe the AXA Group's commitment to protecting society against risks to human life?

Today, life risks are becoming increasingly complex and uncertain. The AXA Group has one priority: to be close to the lives of our customers, understand the needs of each one and be able to meet their needs through appropriate protection. This means providing personalized assistance in managing the health of our customers based on their age and situation. This has become possible thanks to the technical skills of assessing and evaluating the potential risks faced by our customers. Our understanding of these risks, which is the core of our business, is precisely what has enabled us to become the worldwide leader in life insurance.

In an increasingly changing world, our understanding of risks must be constantly updated. To meet this challenge, we attach utmost importance to innovation, which allows us to embrace and welcome change. It is therefore a valuable opportunity to improve society, our business and the situation of our customers.
Health is an area particularly affected by change. Let us consider, for instance, medical progress. Nowadays, customers can easily decipher their genotype, which results in information asymmetry. Insurers therefore need to improve their knowledge to be able to bring real added value to customers through their expertise.

Protecting means first and foremost preventing risks. In today's society, we are witnessing a growing number of initiatives to protect the health of citizens. Thanks to progress, risk factors can be determined, for instance, by checking a person's heart rate or blood sugar level. The AXA Group participates in this approach by providing customers with support, such as health prevention applications, which enables them most importantly to prevent health risks. In this context, there is a perfect alignment between the interests of the customer and the insurer. There is no better coverage than coverage that has not been used, since the risks have been studied and avoided from the outset.

To achieve this, we devote time and resources to developing knowledge and preventing risks. Our commitment in this area is evident when considering the financial and human resources deployed by AXA in an effort to minimize the risks

"Protecting means first and foremost preventing risks.
That is why we devote time and resources
to developing knowledge and preventing risks."

of our customers. In particular, we have a department devoted to studying life risks. Doctors work closely with actuaries in order to integrate their medical expertise into reliable models. These make it possible to predict future risks, determine their extent and price insurance products to reflect the reality of risks, while remaining affordable for our customers.

How do you think the work of researchers funded by the AXA Research Fund will contribute to your knowledge of life risks?

Innovation is also born through encounter with knowledge developed outside the Group, which we must be able to gain in order to progress at the speed required by our times. That is why we are fortunate to have the opportunity to exchange with independent researchers funded by the AXA Research Fund.

Let us consider, for instance, longevity. We know, today, that life expectancy has increased and that the reality of individuals over 60 years of age has completely changed compared to the past. They are active individuals in a dynamic phase of life which needs to be organized and financed. Planning is essential, and in this new context, we have a role to play in shaping their future. It is true that the aging population has created an imbalance in the funding of pensions and, more specifically, a problem of resources. However, this is a context in which insurance can offer a solution.

Major projects, such as those of Prof. Jagger and Prof. Inoue, have provided us with information to help us understand what factors define an elderly person in good health, including their cognitive capacities or relationship network. Such information is key to any planning strategy in this phase of life.
For diseases such as Alzheimer's disease, which are real burdens to society from a human and financial point of view, it is very useful to expand our technical knowledge through innovative and promising projects, such as those of Prof. Hampel on early diagnosis and Prof. Preux on dementia. These are projects that help us reflect on solutions to better prevent the effects of dependence for our customers and their loved ones. The same is true for research on cancer, such as the work of Prof. Barbacid and Prof. Carmeliet. Due to the changing nature of our business, we are also interested in issues that are currently at the heart of society's concerns and could one day be covered by insurance. That is why we have everything to learn from projects on pandemics and antibiotic resistance, such as that led by Prof. Matic, or projects relating to risky behaviors and addictions.

To conclude, we must not forget the projects that are part of the digital revolution era, which allow diseases to be diagnosed and treated through innovative techniques, such as the use of nanoparticles. As a quick illustration, let us mention the work of Prof. Barakat on cardiovascular risks, which combines biology and engineering, or that of Prof. Fort, which uses modern bio-imaging techniques to improve diagnosis and treatment.

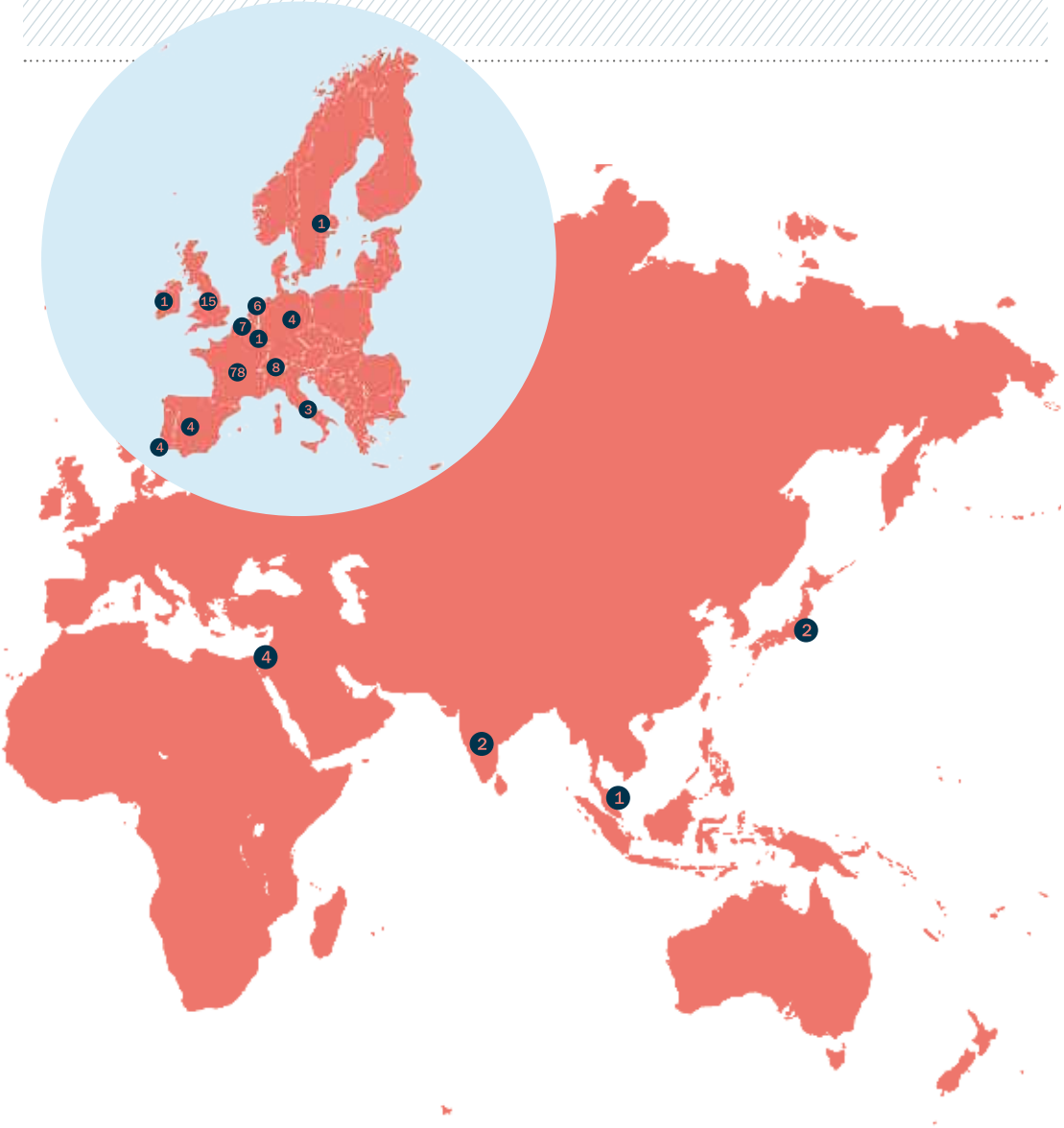
Once again, these are only examples. This Book of Knowledge contains more than 150 projects, which cover almost all current issues regarding the protection of human life. We do not yet know what tomorrow's risks will be, but it is reassuring to know that the researchers supported by the AXA Research Fund are already actively working to advance and share knowledge for a safer society.

OUR RESEARCHERS AROUND THE WORLD

This map only includes Fellows working on Life Risks

Belgium: Peter Carmeliet · Christina Chatzi · Nele Goeyvaerts · Sabine Langie · Pierre Maquet · Pierre Vanderhaeghen · Cameron Wyatt
Canada: Monica Cepoiu-Martin · Javier Clemente Casares
France: Abdul Barakat · Etienne Baulieu · Dipanwita Biswas · Chloé Boitard · Marie-Pierre Bonnet · Giulia Bucchioni · Matthias Bussonnier · Marina Caillet · Damien Carrel · Lauren Carrington · Zayna Chaker · Farah Chali · Caroline Claasen-Göntje · Pierre Clément · Pauline Colombier · Guillaume Corre · Mathieu Coureuil · Julien Courtin · Luisa De Cola · Margot Cucchetti · Antoine Decrulle · Alejandro Del Valle Suarez · Nathan Desdouits · Caroline Deshayes · Victoire de Lastours · Darja Dubravcic · Emmanuel Fort · Maria Daniela Garcia Castillo · Marine Garguilo · Grégoire Gessain · Tanvi Gore · Fabien Guegan · Harald Hampel · Muna Hilal · Petra Hlavacková · Eik Hoffmann · Daiki Horikawa · Baptiste Jaeger · Delphine Judith · Nadjia Kachenoura · Fernando Kasanetz · Frédéric Keck · Bjørg Elisabeth Kilavik · Guido Kroemer · Rajeev Kumar · Thomas Landrain · David Lebeaux · Yann Le Cunff · Joël Lemière · Ignacio López Ferreira · Elia Magrinelli · Tal Marciano · Ivan Matic · Robert Menard · France Meslé · Alice Meunier · Fabien Mézière · Juan Alberto Mondotte · Fabien Montel · Anne-Sophie Nicot · Cyrille Pauthenier · Rebeca Pérez de Diego · Pierre-Marie Preux · Miroslav Radman · Benoît Rey-Robert · Aude Rauscent · Mathieu Richard · Jean-Marie Robine · Benoît Robisson · Marina Rubio · Andrew Silvanus · Dea Slade · François Taddei · Cédric Thaury · Arabella Touati · Fanny Turlure · Anne-Claire Vergnaud · Stefania Zappettini
Germany: Frances Chen · Clémentine Garrouste · Marie Lagouge · Agata Starosta
India: Marcus James Taylor · Darius Koester
Ireland: Agata Blasiak
Israël: Ilana Blech · Arjan Boonman · Ofir Cohen · Adi Stern
Italy: Nicoletta Balbo · Giulia Bortolussi · Anna Julie Peired
Japan: Marco Candeias · Manami Inoue

Luxembourg: Bity Diene
Netherlands: Esther Aarts · Jennifer Cook · Maryam Kavousi · Julie Peron · Sizzle Vanterpool · Kiki Zanolie
Portugal: Pedro Coelho · Susana Gonçalves · Caetano Mendes · Albino Oliveira-Maia
Singapore: Andrea Glenn
Spain: Mariano Barbacid · Maria Blasco · Lucia Gutierrez Marruedo · Guiomar Solanas
Sweden: Thomas Helleday
Switzerland: Kalliopi Apazoglou · Christian Cajochen · Kinga Igloi · Melis Karaca · Mitsunori Nomura · Marie Pohl · Christina Schmidt · Antoine Viola
UK: Francesco Checchi · Matthew Collin · Florian Geier · Annie Ginty · Carol Jagger · Nicole Hondow · Gilles Kayem · Petra Klepac · Sophia Latham · Olivier Le Polain de Waroux · Lorna López · Amanda Nio · Natalia Salvadores · Matthew Tye · Raphael Wittenberg ·
USA: Ami Citri · Nicholas Croucher · Sophie Cypowyj · Oscar F. Silvestre · Yuval Itan · Maja Matis · Delphine Oudiette · Damien Roux · Virginia Spanoudaki.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THROUGH RESEARCH, PROTECTION

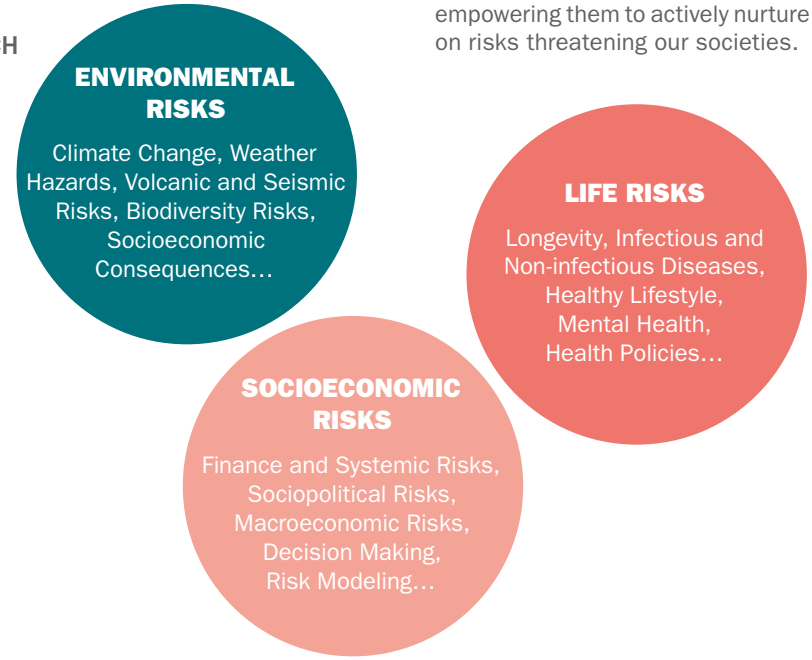
Science helps our societies and insurance companies to better protect people against risks.

Supporting scientific discoveries
As an insurer, it is part of AXA's corporate responsibility to be involved in building knowledge on risks in order to better prevent them and, if they do occur, to better protect people against their consequences. This knowledge is first produced by AXA experts using field data and in-house analysis. Nevertheless, in an increasingly changing world, our societies cannot rely solely on the past to explain the future, nor can we merely adapt existing models incrementally.

The AXA Research Fund supports independent academic research on risks in areas associated with the environment, life and society. It thus contributes to truly understand the current reality of such risks: today's research will help better protect tomorrow.

Helping researchers to nurture public debate
Supporting research goes beyond funding: AXA also helps researchers to popularize and disseminate their work and uses its corporate networks and communication resources to help selected scientists go one step further in sharing their knowledge with a broader audience, thus empowering them to actively nurture public debate on risks threatening our societies.

ELIGIBLE RESEARCH FIELDS



OUR FUNDING SCHEMES

The AXA Research Fund supports researchers both to better understand the risks we face and share their scientific discoveries for the benefit of society.

Support for academic innovation

Chairs up to €4M
Research institutions are offered help to attract top-tier international professors, notably through capital endowment.

Awards €250K
Mid-career researchers with extremely high potential for innovation in their fields are supported to develop and test their hypotheses, thus accelerating the pace of innovation.

Research Fellowships €120K
Each year, support is provided to some thirty talented young researchers at the outset of their careers (postdoctoral fellowships).

Support for dialogue between the academic world and society

Outlooks €250K
Innovative researchers with high potential for popularization are spurred to disseminate their findings to a wider audience through a variety of means, thus easing the dialogue with academic communities, policy makers, decision makers, experts, and other opinion-leaders (journalists, NGOs, etc.).

Joint Research Initiatives up to €300K
Under the leadership of a senior academic researcher, a collaborative framework is offered to academics with an AXA in-house expert team, providing essential elements for the success of their projects (data, field access, expertise, etc.). This framework aims at producing research publications in the open literature, available to everyone.

SELECTION PROCESS

Our grants are awarded following a transparent and robust selection process, which is overseen by our Scientific Board, mainly composed of famous senior academics.

The criteria used for the scientific and academic assessment of all applications are the following:

Academic excellence of the institution and the host laboratory

> Quality of its research: publication in scientific reviews, presence of internationally renowned researchers.

> Quality of the research environment and working conditions offered to researchers.

> Relationship to the international community: international impact of the research carried out.

Robustness of the project

> Consistency between the research project and the institution's long-term development policy.

> Operational strength and quality of the organization set up to support the project.

Academic excellence of the project

> Scientific originality and innovative nature of the project.

> The project's contribution to strengthening international networks.

> Academic excellence of the leading researcher (publications, prizes and awards, participation in colloquia, international scope of the applicant's career, etc.).

Build-up opportunity

> With equal levels of academic excellence, applications whose topic have received less funding or that come from emerging research centers may be given priority.

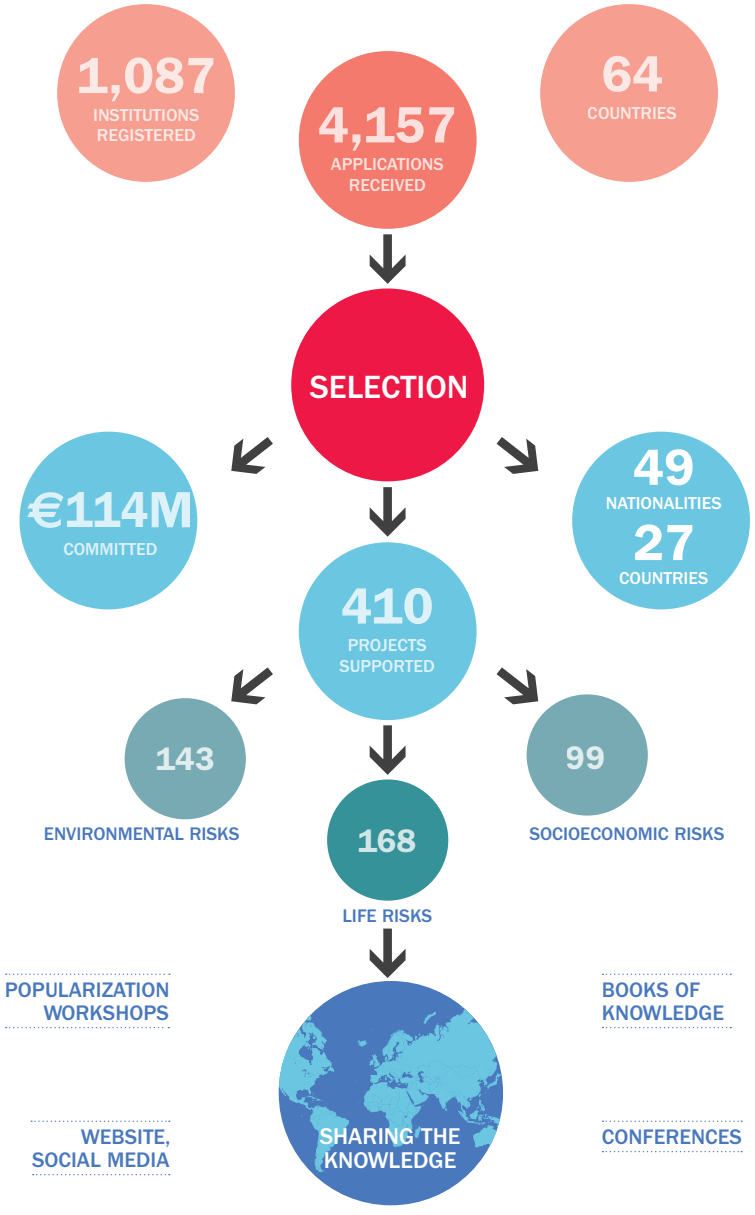
In order to ensure the largest diversity of candidates (profiles, countries and topics):

> Chairs and Fellowships are open to application through the host institution; each application is assessed by at least three recognized independent reviewers, who are able to give their opinion in complete freedom and anonymity.

> Nominees for Awards and Outlooks are proposed by topic-specific Search Committees formed on the basis of the "Open Grounds."

ALL FUNDING IS ULTIMATELY AWARDED BY THE AXA RESEARCH FUND SCIENTIFIC BOARD.

FIGURES AT A GLANCE



SCIENTIFIC BOARD

PRESIDENT

Professor Tom Kirkwood
Newcastle University, UK

Tom Kirkwood is Professor of Medicine and Associate Dean for Aging at Newcastle University, having previously been Director of the Institute for Aging and Health from 2004-2011. Educated in biology and mathematics at Cambridge and Oxford, he worked at the National Institute for Medical Research, where he formed and led a new research division until 1993, when he became Professor of Biological Gerontology at the University of Manchester. His research is focused on the basic science of aging and on understanding how genes as well as non-genetic factors, such as nutrition, influence longevity and health in old age.

He is a Fellow of the Academy of Medical Sciences and a Senior Investigator of the UK National Institute for Health Research. He was European President (Biology) of the International Association of Geriatrics and Gerontology, chaired the UK Foresight Task Force on "Healthcare and Older People" in 1995, led the project on "Mental Capital Through Life" within the recent Foresight program on Mental Capital and Well-Being. He was Specialist Adviser to the House of Lords Science & Technology Select Committee inquiry into "Aging: Scientific Aspects" and has served on the Councils of the Biotechnology and Biological Sciences Research Council (BBSRC) and the Academy of Medical Sciences.

Tom Kirkwood has published more than 300 scientific papers and won several international prizes for his research. He is a frequent contributor to television, radio and press discussion of scientific issues. His books include the award-winning *Time of Our Lives: The Science of Human Aging,* and *Chance, Development and Aging* (with Caleb Finch), but also *The End of Age* based on his BBC Reith Lectures in 2001.

The Scientific Board is composed of 14 respected individuals - researchers, international experts in their fields and AXA representatives. It is chaired by Professor Tom Kirkwood

ACADEMICS

Prof. Nihat Berker
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Prof. Maria A. Blasco
Director and Head of the Telomeres and Telomerase Group, National Cancer Research Centre (CNIO), Spain

Prof. Alessandra Casella
Professor of Economics, Columbia University and Research Associate, National Bureau of Economic Research, USA

Sylvie Lemmet
Director of the United Nations Environment Programme's Division of Technology, Industry and Economics, France

Prof. Lawrence Lessig
Roy L. Furman Professor of Law, Harvard Law School & Director of the Edmond J. Safra Center for Ethics, Harvard, USA

Dr. Valérie Masson-Delmotte
Research Director in Paleoclimatology, LSCE, France

Prof. Dominique Pestre
Professor, History of Science and Science in Society, EHESS, France

Prof. David Spiegelhalter
Winton Professor for the Public Understanding of Risk in the Statistical Laboratory, University of Cambridge, UK

AXA REPRESENTATIVES

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Chief Economist, AXA Group & Head of Research, AXA Investment Managers

Anne-Juliette Hermant
Global Head of Learning and Development, AXA Group

Alban de Mailly Nesle
Chief Risk Officer, AXA Group

Lucie Taleyson
Technical and Marketing Director, AXA Group Life Solutions

Véronique Weill
Chief Operating Officer and Member of the Management Committee, AXA Group

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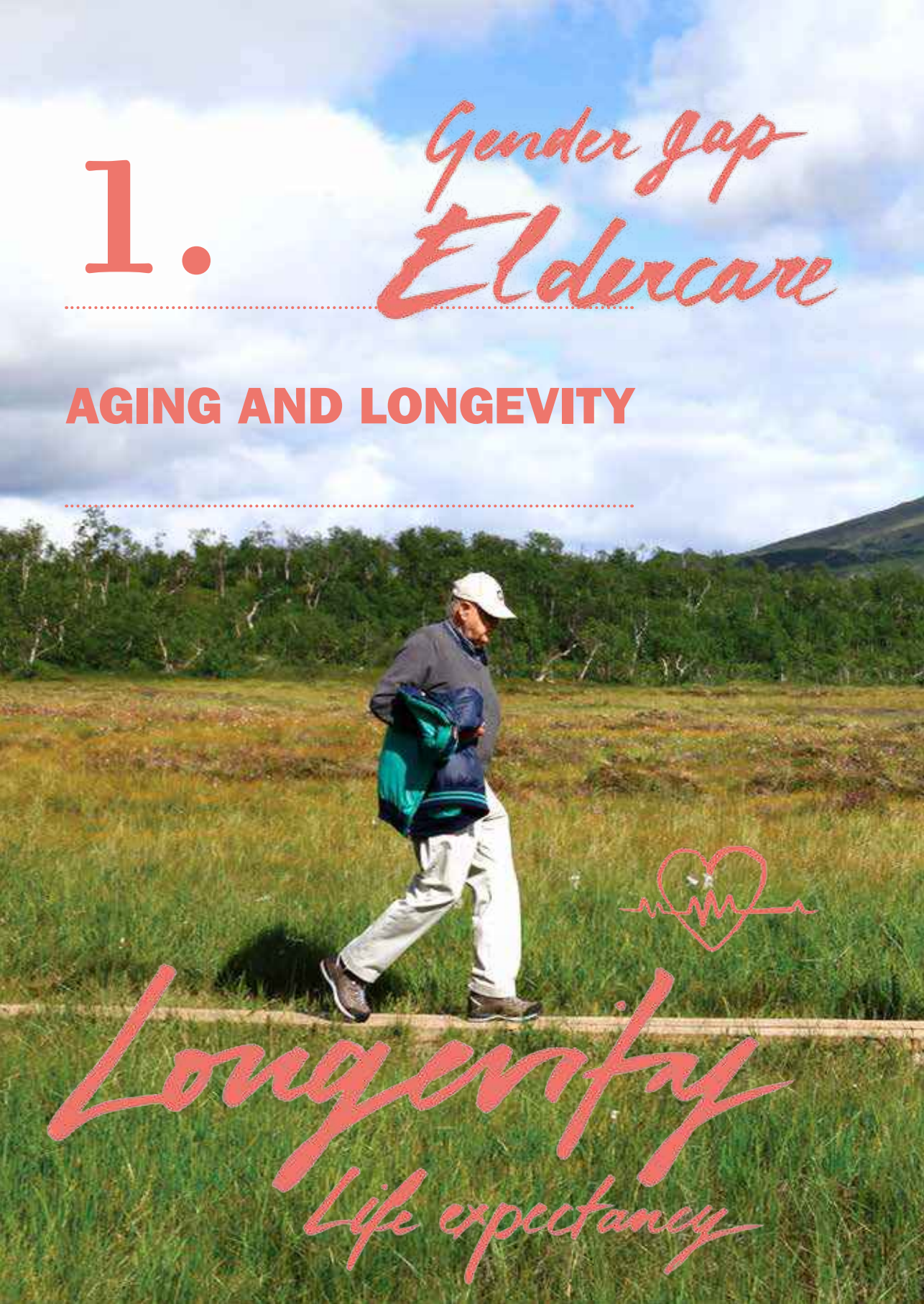
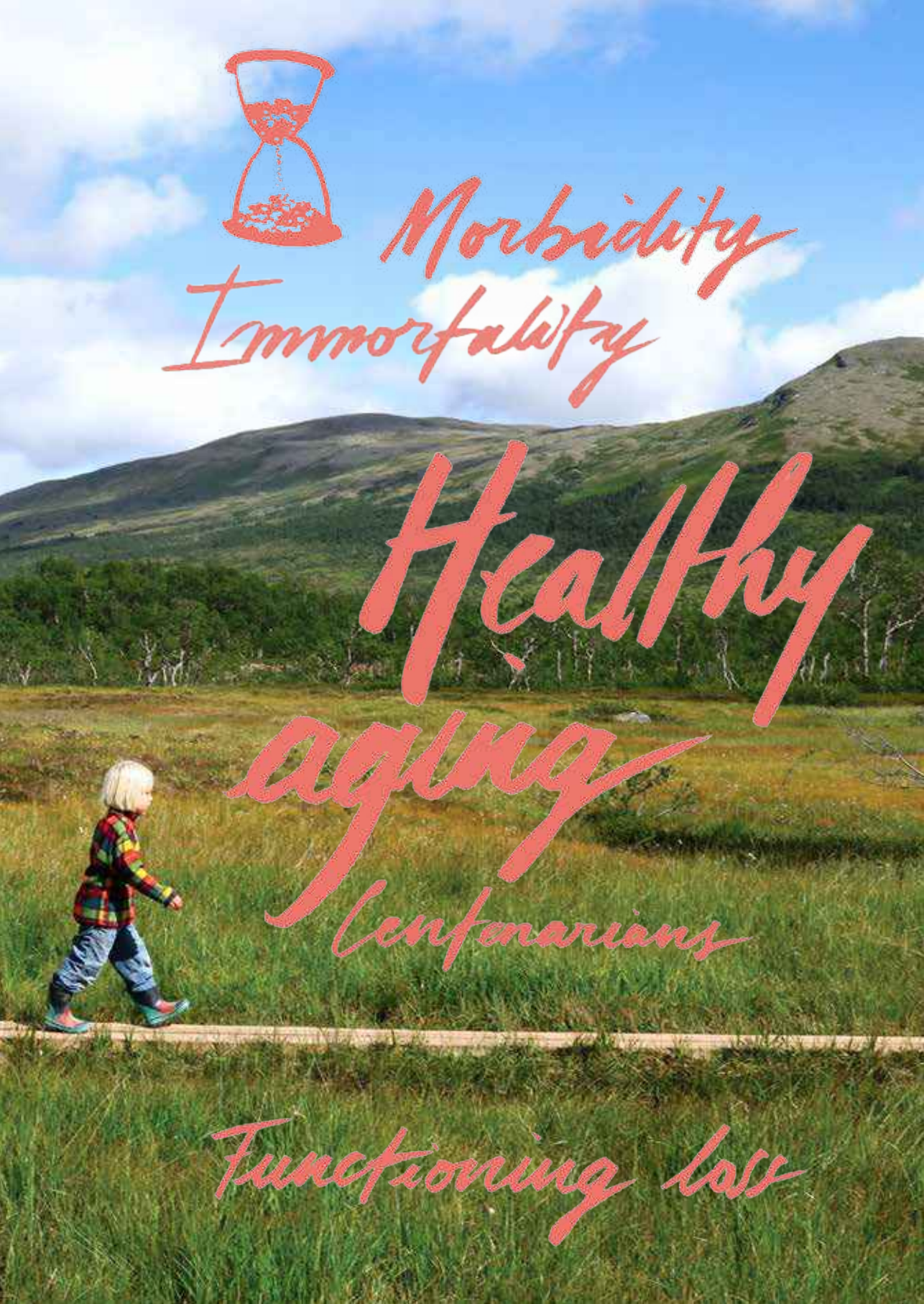
Gender gap
Eldercare

AGING AND LONGEVITY



Longevity
Life expectancy


Morbidity
Immortality
Healthy aging
Centenarians
Functioning loss


Morbidity
Immortality
Healthy aging
Gender gap
Eldercare
Centenarians
Functioning loss
Longevity
Life expectancy

INTRODUCTION TO AGING AND LONGEVITY

by Lucie Taleyson

Lucie Taleyson
Technical and Marketing Director,
AXA Group Life Solutions

Lucie Taleyson is the Head of the Technical and Marketing Department of AXA Group Life Solutions within AXA France. Previously, she was the Executive Assistant to Henri de Castries, the CEO of the AXA Group, and the Secretary of the Board of Directors. She joined AXA in 2006 as Head of Life Risks within the Group Risk Management Department.

We have witnessed an extraordinary rise in life expectancy for over a century, which currently increases on average by three months every year, not only at birth, but also at age 60. For example, the life expectancy at birth of French women is currently 85 years, compared to 49 years in 1900 (78 years compared to 45 years for French men). This is a global phenomenon. In a demographic context of low birth rates and limited immigration, this increase in life expectancy has resulted in an aging population. The latest scenarios of the UN estimate that between 2013 and 2050, the global population aged 60 and over will double and the population aged 80 and over will quadruple.

These changes will have a considerable impact on the insurance sector, particularly on the development of products that cover long-term risk, such as retirement or long-term care insurance, the purpose of which is to provide people with financial assistance for end-of-life risks. It is therefore critical not only for public authorities, but also for the insurance industry to gain a better understanding of the reasons for increased life expectancy and the causes of mortality, on the one hand, and the impact of aging, on the other hand. It is also essential to be able to anticipate the health conditions of the elderly.

Today, there is no consensus on the scenario of the compression of morbidity (according to which life expectancy without severe disability will increase faster than total life expectancy), or the opposite scenario, the expansion of morbidity (increase in the period of dependency at the end of life). This uncertainty is linked to the difficulty in defining life expectancy without disability. The funded studies will help provide more complete answers and develop common indicators on both the causes of mortality and the loss of functional autonomy and neurodegenerative diseases, in order to find appropriate responses to the challenge of aging.

IMMORTALITY IS ONLY ONE STEP AWAY

AXA Project
Biology of immortal and robust organisms

Professor Miroslav Radman
INSERM (France)
€300K (3 years)

Humans can adapt to the environment, but compared to some other species, we are not that flexible. For example, we could not live at a temperature of 80°C, and we could not survive more than four days without water. However, some organisms can live at boiling water temperatures, grow under strong radiation or do without water for 10 years. We know that such species are much better at fighting deadly stress than we are, but the reason is still unknown. Prof. Miroslav Radman is focusing his research on specific death-resistant organisms to understand how they protect their life machinery from falling apart.

His aim is to gain insight on how aging, or resisting the passage of time, occurs at the molecular level. Our body is made of organs, and organs are made of cells. Therefore, when cells age, organs and organisms also age.

Aging is functional deterioration mainly due to corrosion of biomolecules caused by oxygen free radicals. Such radicals are unavoidable since they are generated when our body produces energy—which is why we need to breathe. But they can also be found in air pollutants, food, water or drugs. Luckily, our cells have protection, repair and clean-up systems to counteract molecular damage. Like a skilled surgeon, special proteins repair DNA damage and replace damaged proteins. Radman points out that aging occurs when these life-protecting proteins are themselves damaged: they cannot repair the damage that accumulates, and the whole body ages and eventually dies.

Fascinated by robust and immortal species, Radman is studying how robust cells protect and repair themselves during oxidative stress. His approach has proved original and productive: he now believes that all organisms share the same chemistry of aging—protein damage—which is also the common cause of all age-related diseases, and that we may soon be able to prevent and treat the very cause of degenerative diseases. He has uncovered the mystery of robust species: their cells produce a molecular cocktail that protects cellular machinery from oxidative damage. Once its chemical composition is known, it could be used in humans to protect against age-related diseases and eventually delay aging. A potion for eternal youth may just be one step away.

Doctor Daiki Horikawa
Postdoctoral Fellow
INSERM (France)
€60K (1 year)

COULD THE WORLD'S TOUGHEST ANIMALS IMPROVE OUR BRAIN'S ROBUSTNESS?

Survival mechanisms in tardigrades against radiation and desiccation

So small and yet so helpful! Tardigrades are microscopic invertebrate animals that show considerable resistance to radiation and extreme dehydration, which cause oxidative stress in cells. Dr. Daiki Horikawa is studying protection and repair mechanisms against oxidative stress at the molecular level in the nervous system of tardigrades. This research could lead to a better understanding of how oxidative stress damages the human brain and how to prevent or even repair such damage.

Doctor Dea Slade
Postdoctoral Fellow
INSERM (France)
€120K (2 years)

A SHIELD AGAINST AGING

Anti-oxidation protection in Deinococcus radiodurans

Some organisms are extremely good at fighting oxidative stress, which is the main cause of aging. One is Deinococcus radiodurans, a tough bacterium that shows an impressive resistance when exposed to stressful events such as radiation and extreme dryness. By testing its antioxidant properties, Dr. Dea Slade is trying to understand its secret defense strategy. Her results may be of considerable help in uncovering the fundamental processes of cellular aging, with a potential impact on medicine and public health.

Antoine Decrulle
PhD Fellow
Université Paris Descartes (France)
€120K (3 years)

RISK MANAGEMENT IN BACTERIA AND IN OUR CELLS?

Intracellular control of asymmetry by designed RNA scaffolds for understanding cellular aging and risk management in single cells

Cells have their own "risk management" strategy: when dividing, they exclude "bad" components from one of the daughter cells. This asymmetrical distribution of damage plays a key role in keeping new cells preserved and increasing the fitness of the overall population. However, it is also believed to be responsible for the aging process. Antoine Decrulle is studying these strategies in order to understand the relationship between asymmetry and the aging process.

Guillaume Corre
PhD Fellow
INSERM (France)
€120K (3 years)

THE STRENGTH OF DIVERSITY

Phenotypic heterogeneity in isogenic cell populations: mechanisms and consequences

Differences between cells that share the same genes occur as a consequence of random molecular events. Diversification can improve adaptation to the environment but can also impact cell function and lifespan if the changes are inappropriate.

Doctor Marie Lagouge
Postdoctoral Fellow
Max-Planck-Institute for Biology of Aging (Germany)
€120K (2 years)

EXPRESS YOUR ENERGY!

The in vivo role of the RNA-binding protein SLIRP in mitochondrial function

Just as a computer needs electricity, our cells need energy, which is provided by mitochondria. Dr. Marie Lagouge is exploring the molecular machinery involved in mitochondrial production of energy, with a focus on mitochondrial genome expression, by studying the health condition of mice with disturbed machinery. Her research will improve the understanding of the mechanisms underlying many diseases linked to decline in cellular energy, such as age-related metabolic, cardiovascular and neurodegenerative disorders.

Florian Geier
PhD Fellow
Imperial College London (UK)
€120K (3 years)

CLUES FOR LONGEVITY IN OUR BLOOD

A metabolic analysis of longevity and aging in the model organism C. elegans

How long will you live? The answer may be found in your blood. Florian Geier is trying to identify which chemical compounds are associated with a long lifespan. By ingesting them, we might be able to greatly increase our life expectancy.

Zayna Chaker
PhD Fellow
Université Paris Descartes (France)
€120K (3 years)

A REGENERATION-FRIENDLY HORMONE

The role of IGF signaling in tissue homeostasis during aging: studying stem and progenitor cell behavior using mouse models of IGF1-R conditional mutagenesis and systems analysis

We age mainly due to a decline in the regeneration of our tissues. Insulin seems to contribute to cell renewal, maintaining regenerative potential throughout life. Zayna Chaker is studying the impact of insulin on the regulation of lifespan.

THE PROMISES OF AUTOPHAGY

AXA Project
Autophagy for longevity

Professor Guido Kroemer
INSERM (France)
€342K (3 years)

What is the role of "self-eating" in cells, and how does it impact health and longevity?
Commonly known as autophagy, this cleaning process helps fight stress damage, which is created in cells when they produce energy. If the damage is not repaired, protein aggregates tend to accumulate with a toxic effect on cells, eventually leading to their death. These proteins must therefore be eliminated. This elimination happens through autophagy, which protects cells against premature death.

Internationally recognized as a preeminent life scientist, Prof. Guido Kroemer has studied the positive role of autophagy in detail. By helping to remove oxidative damage, or dysfunctional parts of the cells—which is responsible for aging at cellular level—its action can increase lifespan. Kroemer has also focused on the role of autophagy in preventing neurodegenerative diseases, as it plays an essential role in cellular destruction of the protein aggregates responsible for these diseases.

We know that autophagy protects cells from premature death; however, as the underlying mechanisms are not yet fully understood, they are at the top of Kroemer's agenda.

He is also investigating what factors may play a significant role in autophagy, in order to stimulate and enhance the process. To begin, Kroemer is studying the potential regulators of autophagy at a chemical level.

However, he also suggests that there may be specific actions we can take to encourage this beneficial process at an individual level. We all know that a low-calorie diet is good for our health. But what we may not know is that this health benefit, according to Kroemer, is caused by an increase in the rate of autophagy. This is yet another good reason to eat a healthy diet and exercise more!

Doctor Maryam Kavousi
Postdoctoral Fellow
Erasmus Universiteit Rotterdam (Netherlands)
€120K (2 years)

AGING: WHAT'S YOUR SCORE?

"The Healthy Longevity Phenotype": definition, associated factors and prediction

Grow old and stay healthy: that's anyone's wish. While focusing on the definition of what constitutes healthy longevity, Dr. Maryam Kavousi seeks to identify the main prognostic factors for predicting an individual's aging trajectory.

She will concentrate on the contribution of lifestyle factors and biomarkers of disease and frailty to obtain a healthy longevity "score." Her research may contribute to filling the gap between the most advanced knowledge provided by aging research and future public policy.

Doctor Lorna López
Postdoctoral Fellow
The University of Edinburgh (UK)
€60K (1 year)

DO YOU HAVE A HEALTHY AGING BRAIN?

Genetic basis of cognitive aging: investigations through genetic variant association with white matter integrity

We all know an older relative or friend who seems to have aged exceptionally well. Dr. Lorna López sought to understand what makes each of us age differently. By focusing on the connections in the brain, she aimed to identify genes involved in age-related cognitive decline. Her analysis pointed to specific biological pathways that may influence the brain's white matter. López's results may bring a new biological understanding of aging and therefore better management and prevention of life risks.

Doctor Christina Schmidt
Postdoctoral Fellow
Universität Basel (Switzerland)
€120K (2 years)

SLEEP TIGHT, THINK RIGHT

Cerebral mechanisms underlying cognition-related time-of-day modulations in healthy aging: a functional neuroimaging approach

Spending nights working to meet a deadline is a situation most of us have experienced. However, being efficient the following day can be challenging. To unravel the mechanisms underlying this process, Dr. Christina Schmidt is investigating how sleep pressure and aging interact to alter cognitive performance by monitoring elderly people. Her results may affect the way our society schedules cognitive tasks throughout the day and, in the long run, help older people suffering from sleep-related issues.

Yann Le Cunff
PhD Fellow
Université Paris Diderot (France)
€120K (3 years)

ONE SPECIES, DIFFERENT AGING

Aging: a multi-scale approach

Aging is the result of a trade-off between reproduction and maintenance of the body. Yann Le Cunff is studying individual aging trajectories based on environmental conditions to build mortality curves at the population level.

EXPLAINING INDIVIDUAL DIFFERENCES IN AGING

AXA - Paris Descartes Chair
A systems approach to individual differences in longevity

Professor François Taddei
Université Paris Descartes
€1.25M (Temporary)

Why do some people die at age ten and others at 122? We are not equal when it comes to aging. Understanding what causes this difference between individuals is a major challenge for our greying society, which needs to develop prevention strategies as well as potential targets for treatment and medications.

To face this major challenge, the AXA Research Fund has decided to fund the AXA - Paris Descartes Chair on "A systems approach to individual differences in longevity." The Chair Holder, Prof. François Taddei, winner of several awards (INSERM, EURYI and HFSP, etc.) for his interdisciplinary approach to aging, is particularly well-suited to lead a multidisciplinary project that brings together excellent scientists from different backgrounds.

Using advanced demographic analysis, they are studying the variability of longevity between and within countries to identify which factors are the best predictors of life expectancy. Several elements, such as medical expenditure, socio-economic level and literacy, will be taken into account.

Instead of focusing on the mechanisms underlying the diseases that occur more frequently with age—a common approach in biology and medicine—Taddei is looking at the global mechanism of our internal clock, which seems to regulate aging, regardless of external factors.

Taddei and his colleagues are performing fundamental research in animal models to extract relevant mechanisms of aging, in order to explain differences at a molecular dynamics level. They could show, for instance, that even the laboratory's bacteria ages with similar dynamics to humans and many other species. These dynamics, which consist of an exponential acceleration ("Gompertz") phase followed by a plateau, can now be systematically studied to reveal environmental and genetic factors that affect the mortality curve. Their recent work shows that an increase in cellular investment in maintenance significantly delays aging in the model organism. Recent demographic data collected across the tree of life, from humans, animal models and plants, provide insight into the great diversity of aging patterns. Through lab experiments, Taddei and his team are now exploring the factors that modulate this complexity. Links between the human and animal models have already provided interesting insights. Their research will bring a more integrative view of inter-individual differences in longevity and may contribute to developing a scenario for the future of aging in Europe.

WHO IS MOST LIKELY TO LIVE ONE HUNDRED YEARS?

AXA Project
The Five Country Oldest Old Project (5-COOP)

Professor Jean-Marie Robine
INSERM (France)
€588K (2 years)

"May you live one hundred years," is a traditional birthday wish in many countries. And in fact, for reasons such as improved medical science and health-care and lifestyle choices, the number of people who live into their 90s and beyond is increasing dramatically. But is it truly a blessing to live so long? And what are the public-health policy implications as this population continues to grow? That's what a two-year project by an interdisciplinary, international research team aims to find out.

Headed by Prof. Jean-Marie Robine of the French Institute of Health and Medical Research (INSERM), the Five Country Oldest Old Project (5-COOP)is designed to more fully understand longevity in order to better anticipate the number and health status of the so-called "oldest old" over the coming decades. By surveying representative samples of centenarians in five countries, the project will examine such critical factors as the subjects' physical, sensory and cognitive capacities, the age at which chronic diseases begin and the frequency of such diseases as well as disabilities and other geriatric conditions, and the relationship between mortality and functional health status.

The five selected countries—Denmark, France, Japan, Sweden and Switzerland—were chosen because they offer high-quality data on mortality and/or health for centenarians, include a relatively high number of centenarians in their populations, and have excellent research teams. The multidisciplinary teams conducting the research include recognized experts in aging, geriatric medicine, social and preventive medicine, and public health.

In addition to forecasting the demographics of the oldest old, Robine's team expects to better understand the causes and patterns of the diseases that strike this seldom-studied population and to estimate the risk of dependence and physical or cognitive impairment. By examining health and social needs and the relationship between health and longevity, the results may help policy makers design appropriate public health strategies for the future.

HEALTHY LIFE EXPECTANCY

AXA Chair on Longevity and Healthy Active Life

Professor Carol Jagger
Newcastle University (UK)
€750K (Temporary)

Unlike wine, health does not tend to improve with age. That is why today's challenge is not just to increase life expectancy, but more to increase "health expectancy," the years of life that we spend in good health.

Prof. Carol Jagger, holder of the AXA Chair on Longevity at the internationally renowned Newcastle University, is studying multiple factors that contribute to successful aging: the way we cope with events, a positive attitude towards life and socioeconomic factors such as education, wealth, etc. She is particularly interested in diet, exercise and social interaction. Her research program aims to fully understand the mechanisms through which these good habits improve our healthy life expectancy.

Being free from diseases is a common measure of successful aging. However, one may argue that it is not realistic to think we can be completely free from diseases in our old years. Jagger has shown from the Newcastle 85+ Study that the reality is that, in late old age, people may have four or five diseases but can still live independently and have rich social lives. This highlights the importance of including the views of older people when defining health.

Nowadays, life expectancy is increasing, but life expectancy free of disability is increasing at a slower rate and appears to be declining in some European countries. This means that years with disability are increasing, resulting in an expansion of disability. Jagger states that just extending life in good health isn't enough. What matters more is that we extend life in good health by more than the increases in life expectancy in order to reduce unhealthy years. That is why she is focusing on a better understanding of factors that have a positive impact on aging.

Jagger's research will help establish future trends in aging in Europe, with an emphasis on finding the reasons for the large inequalities in healthy life expectancy that exist both between and within European countries and providing a vivid picture of population health over the coming two decades. Her findings will be relevant to public-policy planners who need to know whether extra years of life are healthy in order to plan to meet the demands that an aging population will make on health services, long-term care and pensions.

UNDERSTANDING THE SECRET OF LONGEVITY TO IMPROVE HUMAN SECURITY

AXA Chair on Health and Human Security

Professor Manami Inoue
The University of Tokyo (Japan)
€1.25M (Temporary)

How has Japan achieved the longest life expectancy at birth in the world? Ranked first in terms of life expectancy at birth for women since 1986, recording the highest ever worldwide figure of 86 years in 2008, Japan seems to hold the secret of longevity. Understanding what factors—particularly modifiable risk factors—have contributed to making the Japanese population healthy is important for global health policy, especially for countries struggling to improve public health.

The newly appointed Chair Holder is Prof. Manami Inoue. Awarded by authoritative academic societies in Japan (including the Japan Epidemiological Association and the Japan Cancer Association), she has worked in many prestigious institutions in Japan and gained in-depth knowledge of her country's longevity phenomenon.

The overall objective of her research is to gain a firm grasp of the interplay of selected risk factors in the burden of disease and injury in Japan over the past twenty years. Using comparable methodology and measurement metrics, she will study the distributions of risks across population subgroups based on age, sex, geography and socio-economic status, with a particular focus on aging.

Her results will be helpful for informing policies and programs that aim either to prevent disease and injury or to design responses to current natural disasters, such as earthquakes and their aftermath in Japan, and their effects on health.
Her findings will therefore be relevant for doctors, public health professionals, insurers and government decision makers. They will also be of interest to international organizations such as the WHO, with which University researchers have multiple ties, in generally helping to plan responses to major risks.

SCENARIOS FOR FUTURE MORTALITY

AXA Project
Mortality divergence and causes of death

Professor France Meslé
Institut National d'Études Démographiques (France)
€305K (3 years)

Significant differences in longevity in the modern world are regarded as unfair and unacceptable. However, the hope that medical progress and socio-economic advances will change this reality has faded away as we witness an increasing diversity among developed countries.

We know that many factors have an impact on longevity: the biological make-up of human beings, their evolving scientific and technological capabilities as well as their social, political, economic and cultural activities, at both individual and collective levels. But what are the actual causes that trigger death? And more importantly, could they be—at least partially—avoided? To answer to these crucial questions Prof. France Meslé and her team are studying the links between cause-of-death patterns and age mortality curves, with a particular focus on the midlife component as opposed to old-age mortality. Meslé is a leading international research in causes of death, particularly in European countries. Her project, although primarily demographic, is interdisciplinary as it requires clinical and epidemiologic approaches to mortality in order to understand all relevant information on causes of death.

Together with her team, she will create a large database of coherent time series of deaths for a hundred or so medical causes, assembling data from 20 countries over more than three decades. She will get a balanced view of Eastern and Western contexts and histories: France, West Germany, Spain, England and Wales, Japan and the US, on the one hand, and Russia, Ukraine, Belarus, the Baltic countries, Moldavia, Poland, the Czech Republic, Romania and East Germany, on the other. By using meaningful groups of causes, Meslé will be able to consider diseases amenable to health care, diseases related to risk factors, such as alcohol or tobacco, as well as more generally to distinguish between communicable and non-communicable diseases. The data analysis will therefore allow us to understand the extreme diversity of current situations in causes of death, across and within countries.
The results will widely impact health policy in industrialized countries, for a better fight against premature mortality and for improved health of the elderly. They will therefore help design possible scenarios for future mortality and health trends as well as rational evaluation tools and markers of policy makers to improve longevity.

VOICING OUT THE SILENT MARKERS OF ALZHEIMER'S

AXA-UPMC Chair on Alzheimer's Disease

Professor Harald Hampel
Université Pierre et Marie Curie (France)
€3M (Permanent)

Alzheimer's disease is one of the most significant risks for the growing population of elderly individuals and their families, with an estimation of 35.6 million people presently affected in the world. These numbers are expected to almost double every 20 years, to 65.7 million in 2030 and 115.4 million in 2050. As the most frequent neurodegenerative disease and a major worldwide epidemic, Alzheimer's presents a global challenge, with increasing strain on health-care systems and our societies.
The recently evidenced existence of a decade-long silent stage of the disease, with no clinical symptoms expressed, yet biological markers observable, creates opportunities for improving and accelerating early detection. To meet the need for diagnosis of Alzheimer's from the beginning, the AXA - UPMC Chair on Alzheimer's has been created with the aim of developing and validating new biomarkers to increase diagnostic accuracy at the totally asymptomatic stage and to better assess drug efficacy. Hosted by the highly specialized Institute for Memory and Alzheimer's Disease (IM2A) using the latest cutting-edge genetic, biochemical and neuroimaging technology available, the Chair will utilize the combined resources of several first-class scientific research teams in a rich variety of related research fields—from cognition to neuroimaging to genetics—working from bench to bedside. It will use quality and exhaustive cohorts of patients from all disease stages, managed through the IM2A infrastructure, which is a national reference center for several Alzheimer's and neurodegeneration-related clinical research programs and a leading institution worldwide. It will also benefit from a unique platform for integrating and processing multimodal biomarker information in order to extract specific algorithms for early presymptomatic detection.

The Chair and full university professorship will be permanently held by Prof. Harald Hampel, who is a word-leading researcher with vast expertise and reputation in neurology, psychiatry and cutting-edge neuroscience research. With 20 years of experience, he has successfully developed international research programs dedicated to Alzheimer's diagnosis and therapeutic algorithms.
Hampel's findings will provide significant new understanding of Alzheimer's Disease and related disorders, while building upon the scientific capabilities of biostatistical modeling, leading to breakthrough advances in improving both diagnosis and treatment using innovative biological markers.

Natalia Salvadores
PhD Fellow
The University of Edinburgh (UK)
€120K (3 years)

WHAT'S THE MATTER WITH ALZHEIMER'S?

Pathogenesis of Alzheimer's disease: The link between aging, vascular disease and cognitive decline

By 2050, the number of cases of Alzheimer's disease cases will quadruple. To discover new remedies, Natalia Salvadores is conducting an innovative investigation of the potential connection between Alzheimer's disease and neurovascular alterations due to aging.

Mitsunori Nomura
PhD Fellow
Ecole Polytechnique Fédérale de Lausanne (Switzerland)
€120K (3 years)

TGR5: A NEW TARGET TO TREAT ATHEROSCLEROSIS?

Bile acid signaling and age-related diseases: role of TGR5 in atherosclerosis

As the population becomes older, metabolic and cardiovascular diseases increase. Dr. Mitsunori Nomura has studied the role of the bile acid membrane receptor TGR5 in macrophages and its therapeutic potential to prevent atherosclerosis.

Susana Gonçalves
PhD Fellow
Instituto de Medicina Molecular (Portugal)
€120K (3 years)

PURSUING PROTEINS IN THE PARKINSON'S BRAIN

Unraveling the molecular basis of a synuclein dysfunction and the impairment of neurogenesis

In Parkinson's disease, alpha-synuclein protein, whose normal job is unknown, accumulates in neurons, affects their functioning and impairs the communication between neurons. Susana Gonçalves aims to discover its role, hoping to unravel a new treatment strategy.

DEMENTIA IN AFRICA: THROUGH RESEARCH COMES PROTECTION!

AXA Project
Dementia in Central African countries: epidemiology, follow-up and perspectives

Professor Pierre-Marie Preux
Université de Limoges/INSERM (France)
€242K (3 years)

Dementia is a loss of global cognitive ability that is severe enough to interfere with normal activities of daily living. It can affect various cognitive functions including memory, attention, language and logic. "Considering the aging population worldwide, dementia constitutes a major public health concern", states Prof. Pierre-Marie Preux. Both developed and developing countries are affected; however, few studies have been carried out in Africa.

In the Central African Republic and the Republic of Congo, Preux seeks to estimate the prevalence of dementia and its related syndromes and cognitive disorders (e.g., Alzheimer's disease). Preux also seeks to evaluate the risk factors associated with dementia (e.g., increasing age, hypertension, depressive symptoms, nutritional factors and lack of a primary education) and to determine whether genetic variations modify the risk of dementia in African populations. This is a transdisciplinary project that involves epidemiology (identifying the risk and protective factors, medical surveys, screening the markers of dementia), genetics (analyzing blood samples) and anthropology (observing the autonomy of the elderly, interviews, and studying how dementia is perceived by the surrounding people).

Preux will compare the situation in rural and in urban areas in order to identify the specific risk or lifestyle factors involved in dementia. "Understanding what causes the differences between dementia in developed and developing countries is a major challenge. However, it could enable us to determine new risk or protective factors as well as the history of these disorders and therefore help us establish appropriate strategies for care and control worldwide," explains Preux.
This transdisciplinary study (epidemiology, neurology, genetics and anthropology) will contribute to developing new hypotheses for the prevention of dementia. It could therefore be useful for informing policy makers and the general population—a perfect example of protection through research!

FIGHTING DEMENTIA AND DEPENDENCE

AXA Project
To combat dependence with a novel approach against the Tau protein abnormalities of dementia

Professor Etienne Baulieu
INSERM (France)
€373K (2 years)

Today, we live longer than ever before. In many ways, this is good news, but an aging population comes with a significant risk of age-related conditions, like Alzheimer's disease. A number of different forms of dementia are known to involve a protein in the brain called Tau. When Tau is abnormally shaped, it interferes with the correct functioning of neurons, eventually destroying them.

For this reason, Tau appears to be a good target both for detecting the risk of conditions like Alzheimer's and potentially finding treatments. Etienne Baulieu's team has already discovered that when the abnormal Tau is causing trouble in the brain, it is also seen interacting with a particular protein. The scientists suspect that this association could be at the root of such diseases. What if this interaction could be controlled or altered? Could we slow down the development of Alzheimer's disease? In other studies, the types of drugs capable of changing this protein interaction have already had success in protecting neurons. And, since Tau's "protein partner in crime" is found all over the brain, this may hold promise for developing therapies for certain neurodegenerative diseases.

As both researchers and families of patients with dementia know, these diseases progress with time, usually worsening over the course of five to fifteen years. For Baulieu, this time frame represents a window of opportunity to fight the onset of Tau-related diseases with a totally new approach. Targeting the interaction of the two proteins could help researchers find a way to delay the development of symptoms. It could even provide an early indicator of a person's risk of developing dementia, he believes. But first, to reach these goals, a very clear understanding of the way the proteins interact, on a variety of levels, is needed.

By the end of this century, some researchers believe that 50% of the global population will reach the age of 100, leaving them more susceptible to conditions linked to aging. The consequences of the dependence resulting from dementia-related illnesses is a painful and difficult challenge for patients, families and society alike. Baulieu's project aims to use a new approach to predict the development of disease and delay or even prevent the onset of devastating symptoms.

Doctor Nadjia Kachenoura
Postdoctoral Fellow
INSERM (France)
€60K (1 year)

AGING ARTERIES AND DECLINING COGNITIVE FUNCTIONS

Biomarkers of cerebral and arterial aging in functional MRI

With age come stiffer arteries, which, in turn, may be linked to declining brain functions. The goal of Dr. Nadjia Kachenoura's research is to find new indicators of arterial aging and to determine its consequences for the brain, especially when paired with traditional risk factors. Identifying accurate signs of cardiovascular and cerebral aging could enhance the use of non-invasive scans to predict, early on, disabling events such as strokes—and the early loss of cognitive functions they may cause.

Doctor Anna Julie Peired
Postdoctoral Fellow
Università degli Studi di Firenze (Italy)
€120K (2 years)

PROTECTING AGING KIDNEYS WITH VITAMIN A?

Renal progenitor cells in the prevention and regression of age-related renal failure

Over 30% of older people suffer from chronic kidney disease. This may have to do with renal progenitor cells: with age, fewer may be produced or able to mature, leaving the kidney less able to repair itself. Dr. Anna Julie Peired's research suggests that retinoic acid (RA), derived from vitamin A, counters these effects. If so, a vitamin A-rich diet or RA-based drugs could potentially delay or reverse age-related renal disease, reducing the need for costly therapies, like dialysis or kidney transplants.

Doctor Anne-Sophie Nicot
Postdoctoral Fellow
Ecole Normale Supérieure de Lyon (France)
€120K (2 years)

SAVING MUSCLE CAPITAL FOR AN INDEPENDENT LIFE

Regulation of protein aggregation in sarcopenia

The progressive loss of muscle mass in old age (sarcopenia) is the result of an imbalance between the production and deterioration of proteins within our muscles. This often in turn results in the loss of independence, making it a major health concern for our increasingly aging societies. Dr. Anne-Sophie Nicot is investigating the involvement of molecular players in muscle loss to better assess their impact on sarcopenia, in an effort to support new preventive and curative strategies.

Benoît Rey-Robert
PhD Fellow
Université de la Méditerranée (France)
€108K (3 years)

THE INTRICATE PROCESS OF AGING

Motor variability as a marker of the effects of aging on the neuro-musculo-skeletal system

Benoît Rey-Robert is studying alterations in the neurobiological system that are linked to aging and observable in behavior. His findings may help prevent the early deleterious effects of time on the neuro-musculo-skeletal system.

Tal Marciano
PhD Fellow
Ecole Nationale Supérieure de Techniques Avancées (France)
€120K (3 years)

OPTIMIZING EYE SURGERY WITH AN OPTIMIZED LASER

Optical properties of healthy, aging and pathological tissue of the anterior segment of the eye

In our aging population, eye surgery is on the rise. Tal Marciano aims to optimize a new ultra-short-pulse laser for age-related pathologies such as cataracts and glaucoma. He is simultaneously working on elucidating the factors that affect transparency of the eye, predicting the propagation of the laser beam in the tissue and developing a device for evaluating donated corneas. Mastering these elements holds promise for greater success and fewer side effects for increasingly common eye procedures.

Pauline Colombier
PhD Fellow
INSERM (France)
€120K (3 years)

A PAIN IN THE BACK

Intervertebral disc aging and degeneration: from pathophysiology to innovative treatments

To meet the needs of people affected by severe low back pain, Pauline Colombier is studying age-related degeneration of the interverterbral discs in an effort to develop treatments based on the promising approach of tissue engineering.

INSPIRED BY NATURE. TOWARDS IMAGING AND THERAPIES WITH SUPRAMOLECULAR CHEMISTRY AND NANOMATERIALS

AXA Chair on Supramolecular Chemistry

Professor Luisa De Cola
Université de Strasbourg (France)
€2.25M (Permanent)

Supramolecular chemistry might bear a mysterious name; however, it is among today's most sophisticated sciences. Located at the interface of chemistry, physics, biology and medical sciences, it has radically transformed how chemists view the world and work within it. Indeed, as the discipline made its entrance into laboratories, scientists no longer saw matter as being composed of separate atoms and molecules but as complex structures where the molecules interact with each other, leading to new properties. Such large molecular architecture is present all over Nature, and studying the way in which molecules are held together and "talk" to each other gives profound insight into the mechanisms of life. And as those processes are understood, they can also be reproduced with much simpler man-made molecules.

Supramolecular chemistry has proven to be a fundamental gateway to providing new therapeutic solutions to important health concerns, such as cancer and degenerative diseases. Numerous new molecules are designed and synthetized, then tested for potential activities on targets, such as cancer, Alzheimer's, HIV, autoimmune diseases, orphan diseases, allergies and obesity.

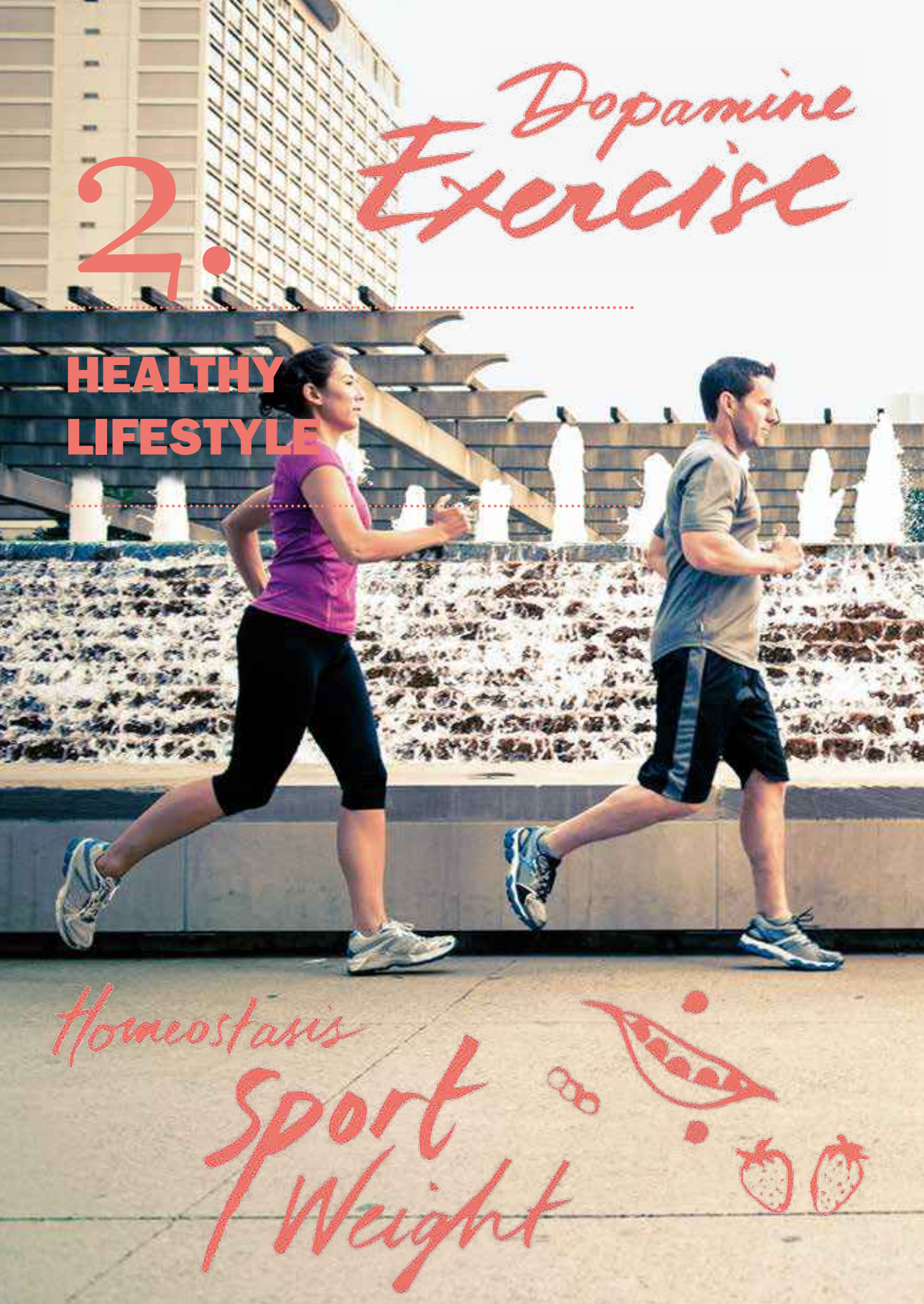
The University of Strasbourg, universally recognized as one of the world's leading centers for chemistry, was able to face the challenge of renewing the innovation led by Nobel-Prize winner Jean-Marie Lehn, by attracting Prof. Luisa De Cola, a world-class researcher in supramolecular chemistry.

Her presence will ensure the continuation of the University of Strasbourg's tradition of excellence and help lead the way for the next 30 years.

She will focus her research on nanomaterials and self-assembled systems and their emerging properties for *in vitro* and *in vivo* imaging and related bio-medical issues (therapeutic and diagnostics)—a highly relevant area of research where many breakthroughs can be expected in the near future.

De Cola's role will be to bridge the gap between fundamental research discoveries and industrial applications in order to defeat age-related diseases, such as cancer, and thus significantly contribute to long-term care and well-being in the future society of longevity.

NOTES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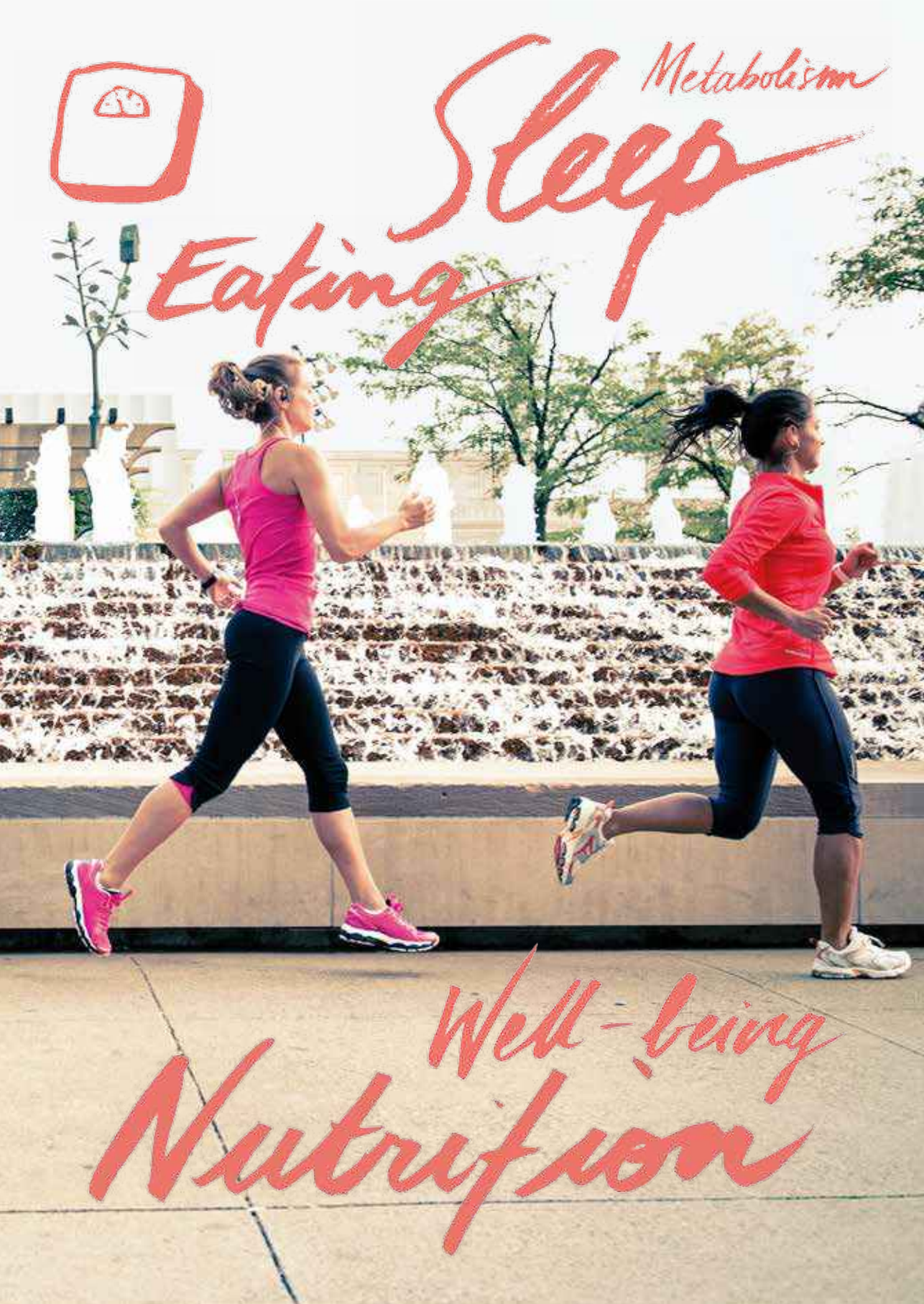
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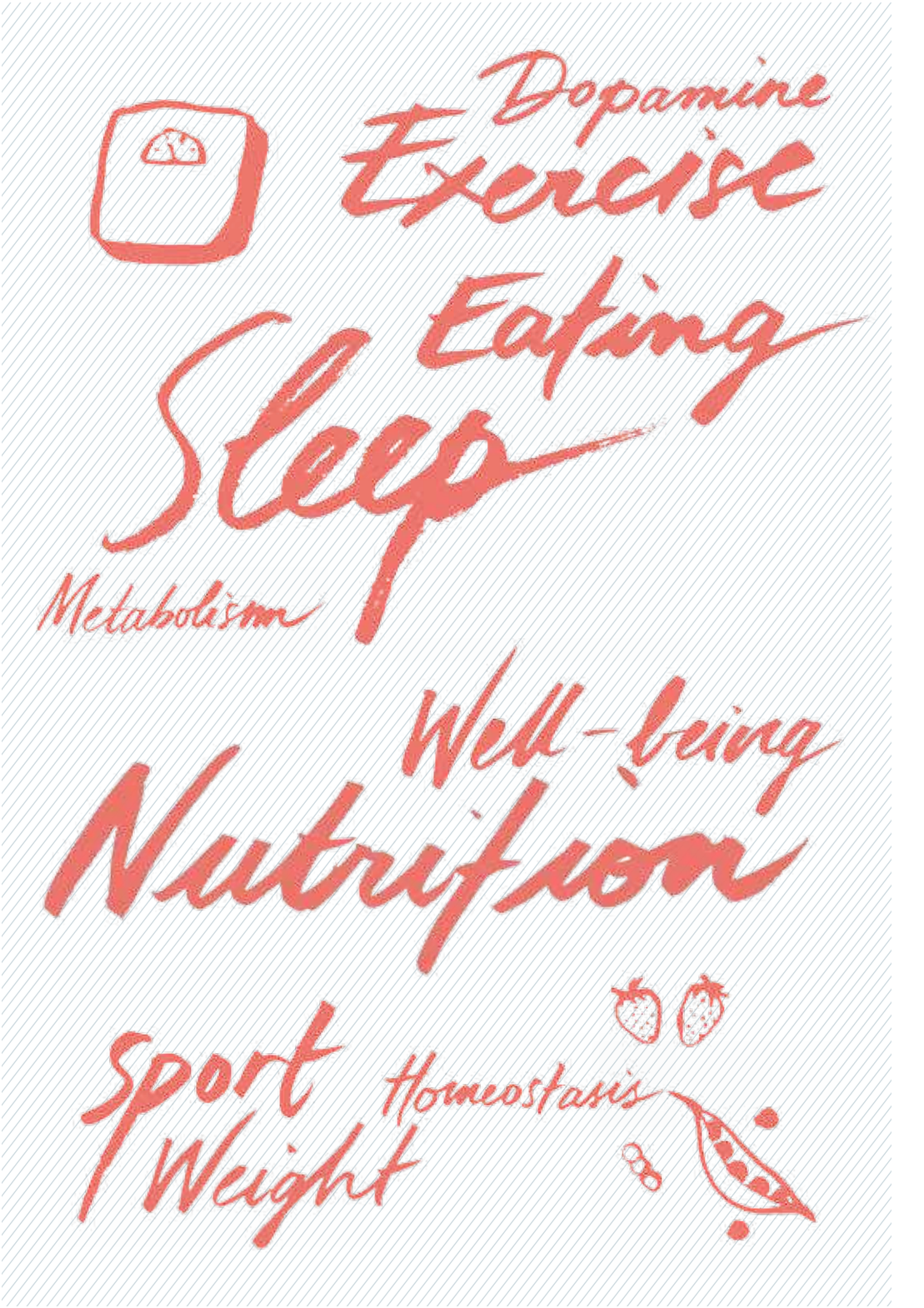
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INTRODUCTION TO HEALTHY LIFESTYLE

by Jean-Jacques Temprado

Jean-Jacques Temprado is currently Professor of Human Movement Sciences at Aix-Marseille University (France), in the Institute of Movement Sciences. His past research on coordination processes in the neuro-musculo-skeletal system has led him to develop a dynamical systems approach to age-related changes in complexity within and between brain, muscular and behavioral levels. He is currently Head Director of the Coord-Age project developed at Aix-Marseille University (AMIDEX).

Professor Jean-Jacques Temprado
Head Director of the Coord-Age project
Institute of Movement Sciences
Aix-Marseille University (France)

It is now widely demonstrated that, in addition to genetic and environmental factors, healthy lifestyle (HLS) strongly contributes to individual longevity, in particular by reducing the risk of chronic disease. HLS is based on (at least) three components: 1) a balanced diet, 2) intellectually and physically stimulating activities and 3) the preservation of social relations. In combination, they form the so-called "positive life habits."

AXA encourages research that contributes to a better understanding of the impact of positive life habits on successful aging, chronic and neuro-degenerative disease. Some examples of research projects that address these aspects can be found in this book.

Among the most current topics, many of them are related to the risks inherent in the aging of the neuro-musculo-skeletal system. For instance, understanding how individual sensory (but also cognitive, motor and physiological) functions are affected by aging is of primary importance for both researchers and clinicians. In another perspective, it appears that the mechanisms underlying food (dys)regulation should be studied both from the point of view of physiological disorders and from the (psychological) point of view of motivation. Indeed, how different types of food and presentation influence our eating behaviors and help fight against obesity remains poorly understood. Exercise, which is certainly the most powerful and least expensive way to prevent chronic disease and promote successful aging, has been the subject of a number of studies over the last decade. It is now clear that training programs for older adults must include both physical and mental activities. However, whether and how they can be combined to optimally improve or, at least, preserve functional capacities during aging would be worth further study.

Finally, another direction of research that is currently in expansion concerns the use of technology and intelligent tools to improve the quality of life of older adults or to increase the efficiency of surgery. This type of research is also encouraged by AXA.

Doctor Petra Hlavacková
Postdoctoral Fellow
CNRS (France)
€60K (1 year)

A DIGITAL BODYGUARD

Vigi-Sore – Conception of a technological device for the reduction or compensation of motor or mental handicap

Wheelchair users stay in the same position all day long, which is not without consequences. One of the most dreaded complications is pressure sores, due to prolonged overpressure between the body and the wheelchair. Dr. Petra Hlavacková participated in designing “Vigi-Sore,” a technological device that detects and locates areas of excessive pressure on the buttocks. It may provide relief for people suffering from pressure sores, and hospital stays could be reduced. Prevention would therefore also be a cure for the economy.

Amanda Nio
PhD Fellow
Cardiff Metropolitan University (UK)
€120K (3 years)

THE BEAT OF A WOMAN’S HEART

The role of exercise, aging and female sex hormones upon physiologic measures of cardiac structure and function in pre- and post-menopausal women

To clarify why women live longer than men, Amanda Nio is investigating the impact of female hormones and lifestyle. She is focusing on the heart, which is protected by estrogen (one of the main female sex hormones), and regular exercise.

Farah Chali
PhD Fellow
Fondation Garches (France)
€120K (3 years)

MILD EXERCISE TO INCREASE LIFE EXPECTANCY

Designing an innovative and beneficial exercise protocol, from mouse models to human SMA patients

New hope for people suffering from neuromuscular diseases could come from Farah Chali. She is studying the effects of physiological, cellular and molecular mechanisms activated by exercise on spinal muscular atrophy (SMA).

Caroline Claasen-Göntje
PhD Fellow
Ecole Nationale Supérieure des Mines de Paris (France)
€80K (2 years)

GUIDING THE SURGEON'S HAND

Smart motion sensor for navigated prosthetic surgery

Hip and knee arthroplasty is an increasingly common type of surgery. Caroline Claasen-Göntje’s aim was to develop a new intelligent tool that would guide the surgeon's movements along a planned trajectory when placing a prosthesis.

Doctor Cameron Wyatt
Postdoctoral Fellow
VIB (Belgium)
€120K (2 years)

FISHING FOR CLUES IN NEURONAL ACTIVITY

Assembly, function and maintenance of olfactory circuits

Zebrafish are gentle, silent, easy to keep, and fun to watch. The perfect pet. Like many neurobiologists, Dr. Cameron Wyatt likes them for another reason: they are a powerful model system for the study of vertebrate development and disease. He will use them to understand how neurons born in the olfactory system mature and integrate into the developing brain. One of the aims of the experiment, which studies both larvae and adult fish, is to see how the fate of the neurons is reflected in zebrafish behavior. Extended to humans, the results could help develop treatments for the repair of brain circuits involved in memory and learning. Disruption of these brain circuits is common in the elderly and in people with neurological disorders. The findings could then be useful for research on Alzheimer's, which currently affects 850,000 people in France.

Doctor Kalliopi Apazoglou
Postdoctoral Fellow
University of Geneva (Switzerland)
€120K (2 years)

HOW DOES DEPRESSION AFFECT THE SENSE OF SMELL?

Testing changes in olfactory processing as a biomarker of mood disorders

Serious depression, an illness that strikes up to 20% of the world's population, affects its victims in many ways. Dr. Kalliopi Apazoglou is exploring the correlation between depression and the sense of smell in both rodents and humans. The idea is to better understand how depression affects olfactory perception and its underlying neurophysiology. Hopefully, this will help in diagnosis by revealing malfunctions specific to the depressive state and may lead to simple, non-invasive odor tests as clinical tools.

Doctor Sabine Langie
Postdoctoral Fellow
Flemish Institute for Technological Research (VITO) (Belgium)
€120K (2 years)

HOW ENVIRONMENT INFLUENCES ALLERGY BEFORE AND AFTER BIRTH

Allergy: environmental and nutritional programming in childhood

What mothers-to-be eat and breathe can have an impact on the future baby, possibly leading to the development of allergic diseases. Dr. Sabine Langie hypothesizes that diet, lifestyle habits and air pollutants, for instance, can alter gene expression without changing DNA sequence (i.e., via altered DNA methylation patterns) leading to changes in the child's immune system. Identifying predictive biomarkers of allergic diseases could help create prevention strategies, in children or before pregnancy.

Mathieu Richard
PhD Fellow
Institut Curie (France)
€120K (3 years)

HOW DO HAIRS ENABLE US TO HEAR?

Collective motor oscillations from calcium feedback in a minimal acto-myosin system in vitro

Our hearing seems to be linked to the ability of hair cells in the inner ear to power mechanical oscillations, but it remains unclear exactly how this works. Using a novel approach, Mathieu Richard aims to create a bio-mechanical model.

Doctor Christina Chatzi
Postdoctoral Fellow
Université de Liège (Belgium)
€120K (2 years)

THE RISKS OF BISPHENOL A ON BRAIN DEVELOPMENT

Early and late effects of perinatal exposure to Bisphenol A on hippocampal development

Widely used in consumer goods, Bisphenol A (BPA) has raised widespread safety concerns, especially for fetuses and infants. By using sensitive cellular indicators to examine the effects of BPA on the development of the mouse hippocampus, Dr. Christina Chatzi's innovative approach aims to uncover endocrine disruption or neurotoxicity affecting life-long learning and memory. In addition to advancing understanding of the effects of BPA, the approach should apply to other environmental risks to brain development.

Giulia Bucchioni
PhD Fellow
Université de Picardie Jules Verne (France)
€120K (3 years)

HOW DO HUMAN EMOTIONS AND MOTOR SYSTEMS INTERACT TO CREATE EMPATHY?

Study of the motor correlate in the functional model of empathy for pain

Much remains to be understood about the links between our bodies and our emotions. Giulia Bucchioni's innovative project involves the search for correlations between empathy for pain, bodily posture and physiological indexes.

Doctor Esther Aarts
Postdoctoral Fellow
Radboud Universiteit Nijmegen (Netherlands)
€120K (2 years)

THE POWER OF FOOD

Food, brain, and distractibility: goal-directed versus habitual control of food intake

When there is delicious food in front of you, it can be hard to know when to stop eating. Dr. Esther Aarts is investigating what type of motivational control is associated with such poor eating habits. She focuses on the role of dopamine—the substance that regulates motivational control. Understanding how the power of food can unbalance motivational control in some individuals and not others could potentially lead to tailor-made treatments to fight the direct and indirect effects of being overweight.

Doctor Guiomar Solanas
Postdoctoral Fellow
Fundació Centre de Regulació Genòmica (Spain)
€120K (2 years)

DIET: GOOD FOR THE WAISTLINE, BUT ALSO FOR ANTI-AGING!

Macroenvironment influence on stem cell aging through circadian clock desynchronization

Stem cells are reserve cells that repair the tissues when they are damaged, like laying new bricks on a broken wall. Inside them, the molecular machinery of the circadian clock coordinates their function. Dr. Guiomar Solanas is one of the few scientists studying how the circadian clock progressively becomes uncoordinated in stem cells, shifting its accuracy as we age. Solanas seeks to establish a possible link between clock phase shifting and caloric restriction, which is known to delay aging.

Doctor Albino Oliveira-Maia
Postdoctoral Fellow
Instituto Gulbenkian de Ciência (Portugal)
€90K (1.5 years)

OBESITY: OF MICE AND MEN

Dopaminergic regulation of dietary learning

Dr. Albino Oliveira-Maia is studying the brains of mice to understand how the neurons that produce dopamine (a molecule that tells the body when it is satisfied) are associated with flavors and the delivery of nutrients to the stomach. He hopes to better understand the mechanisms linked to dysfunctional eating behaviors. Since obese people have modified brain dopamine circuits, similar to patients with addiction, this knowledge could advance medical care and research for both obesity and addiction.

Chloé Boitard
PhD fellow
National Institute for Agricultural Research – INRA (France)
€120K (3 years)

THIS IS YOUR BRAIN ON FAT

Effects of early-onset obesity on brain inflammation and cognitive abilities in rats

Chloé Boitard is investigating the impact of high-fat diet exposure on memory. Early obesity impedes brain function more drastically than adult obesity, suggesting vulnerability of the young brain to the detrimental effects of obesity.

SHEDDING MORE LIGHT ON AGING BIOLOGICAL CLOCKS

AXA Project

Impact of cataract surgery and intra-ocular lens replacement on endocrine and molecular circadian rhythms, sleep and cognitive function in older adults

Professor Christian Cajochen
University of Basel (Switzerland)
€300K (3 years)

The role of light extends well beyond vision. After long-distance flights for example, going outdoors into daylight helps lessen the effect of jet lag. That's because the light transmitted through the crystalline lens of the eye to certain cells in the retina impacts our inner biological clock, or circadian system. Exposure to daylight is needed for us to adjust our biological clock to actual, solar time, and therefore to synchronize and consolidate daily rhythms of many processes in our body. But what happens during the aging process, when the amount of light transmitted through the crystalline lens tends to decrease? Scientists know that the biological clock affects mood and behavior, but no one understands precisely how decreased light transmission affects the circadian system of the elderly. Nor is there much understanding of what happens when the crystalline lens is replaced by an artificial lens that blocks out certain types of light, for example during cataract surgery.

One of Europe's foremost sleep scientists, Prof. Christian Cajochen, wants to find out to what extent an aging crystalline lens contributes to disturbances in the body's circadian rhythm. The question is especially important because circadian rhythm disturbances have such a huge impact on the elderly – from hormonal rhythms, body core temperature and sleep to sleep-wake timing, cognition and mood.

Working with a team of European researchers, his project also focuses on the effects of lens replacement. Special attention is being paid to the effects of blue, relatively short light wavelengths, because replacement lenses often are designed to block blue light. The design is based on the theory that blue light might increase the risk for age-related macular degeneration. This matters because the photosensitive cells in the retina that affect the biological clock are especially sensitive to the blue, shorter wavelength part of the visible light spectrum. Research results could lead to the development of new therapies to treat the biological clock disruptions that impact the quality of life for innumerable elderly persons. The results could also lead to recommendations for ophthalmologists who prescribe replacement lenses for their elderly patients.

Doctor Antoine Viola
Postdoctoral Fellow
University of Basel
(Switzerland)
€120K (2 years)

FEELING SLEEPY? GO INTO THE LIGHT!

Effects of light on cognitive performance, circadian markers, autonomic nervous system and sleep homeostasis in healthy elderly men and women with different PER3 genotypes

Scientists have proven that exposure to bright polychromatic light at night can increase alertness and cognitive performance. Dr. Antoine Viola is among the first to investigate how people react to exposure to bright light based on their genetic predisposition. The PER3 gene comes in two forms: people with the longer version are more affected by sleep deprivation. The results could provide a means to enhance alertness and performance, but also new treatments for certain sleep disorders.

Doctor Kinga Igloi
Postdoctoral Fellow
University of Geneva
(Switzerland)
€120K (2 years)

BAD MEMORY? ONE SOLUTION IS SLEEP!

The role of reward in sleep-related memory consolidation and brain plasticity

Every day, an enormous amount of information reaches us, but only a tiny portion is incorporated into our memories. During sleep, recently acquired memories are strengthened through a replay mechanism. Dr. Kinga Igloi is investigating how motivational factors (i.e., rewards) influence the selection of newly memorized information for further consolidation. As lack of sleep is an increasing trend in our fast-paced society, Igloi's findings could also have major implications for public health.

Doctor Delphine Oudiette
Postdoctoral Fellow
Northwestern University
(USA)
€120K (2 years)

THE INTERPLAY BETWEEN SLEEP AND MEMORY IN AGING

Deficient memory processing during sleep: a possible factor in age-related memory impairment

As we grow older, memory and sleep quality usually decline. Due to the lack of studies on the correlation between these two phenomena, Dr. Delphine Oudiette decided to investigate whether memory loss during aging reflects (even partially) a decline in sleep quality. Oudiette is using novel methods to manipulate memory processing during sleep. An advance in the understanding of the relationship between memory, sleep and aging could contribute to improving memory in normal and pathological aging.

AGING, THE MIND AND SLEEP

AXA Project
Inter-individual differences in sleep homeostasis and circadian rhythmicity on cognition in older people

Professor Pierre Maquet
Cyclotron Research Center – University of Liège (Belgium)
€250K (3 years)

Who wouldn't agree that healthy aging goes hand in hand with a preserved mind? However, "many older people experience decrements in cognitive performance, which may result from age-related sleep alterations," says Prof. Pierre Maquet. These alterations are caused by a reduction in both drives for sleep: homeostatic and circadian. The interplay of these processes is complex and can vary between individuals. For example, the gene PER3 exists in different versions (called "alleles") amongst the population. The longer version makes people sleepier (i.e., increases their "sleep pressure") and reduces their cognitive performance after sleep loss. Maquet is studying how the circadian phase, homeostatic sleep pressure and their interaction influence cognitive function (i.e., mind function) in older people. Maquet's project involves volunteers between 55 and 75 years of age: 20 volunteers with the short PER3 allele and 20 volunteers with the long PER3 allele are participating in two separate visits. Each visit consists of two sessions of cognitive tasks under brain imaging: one before sleep time and the other after wake time. During one visit, the participants sleep at the laboratory between the two sessions, and during the other visit, the participants stay awake.

The great novelty in this project lies in the monitoring of both the circadian and the homeostatic factors. Circadian rhythms are measured through melatonin (the sleep hormone) content in samples of saliva taken each hour (except when people are sleeping). The homeostatic factor is monitored using two brain imaging techniques. One of these allows a direct probe of the local sleep pressure in the brain, which is very innovative.

Maquet's project aims at a better understanding of the mechanisms involved in changes in sleep and cognitive function. The effect of genetics on all the factors measured could provide a major contribution in terms of the practical application of chronobiology to changes in circadian and sleep control in older individuals. The results could be directly translated into health-promoting practices to increase sleep and cognitive performance in older people.

NOTES

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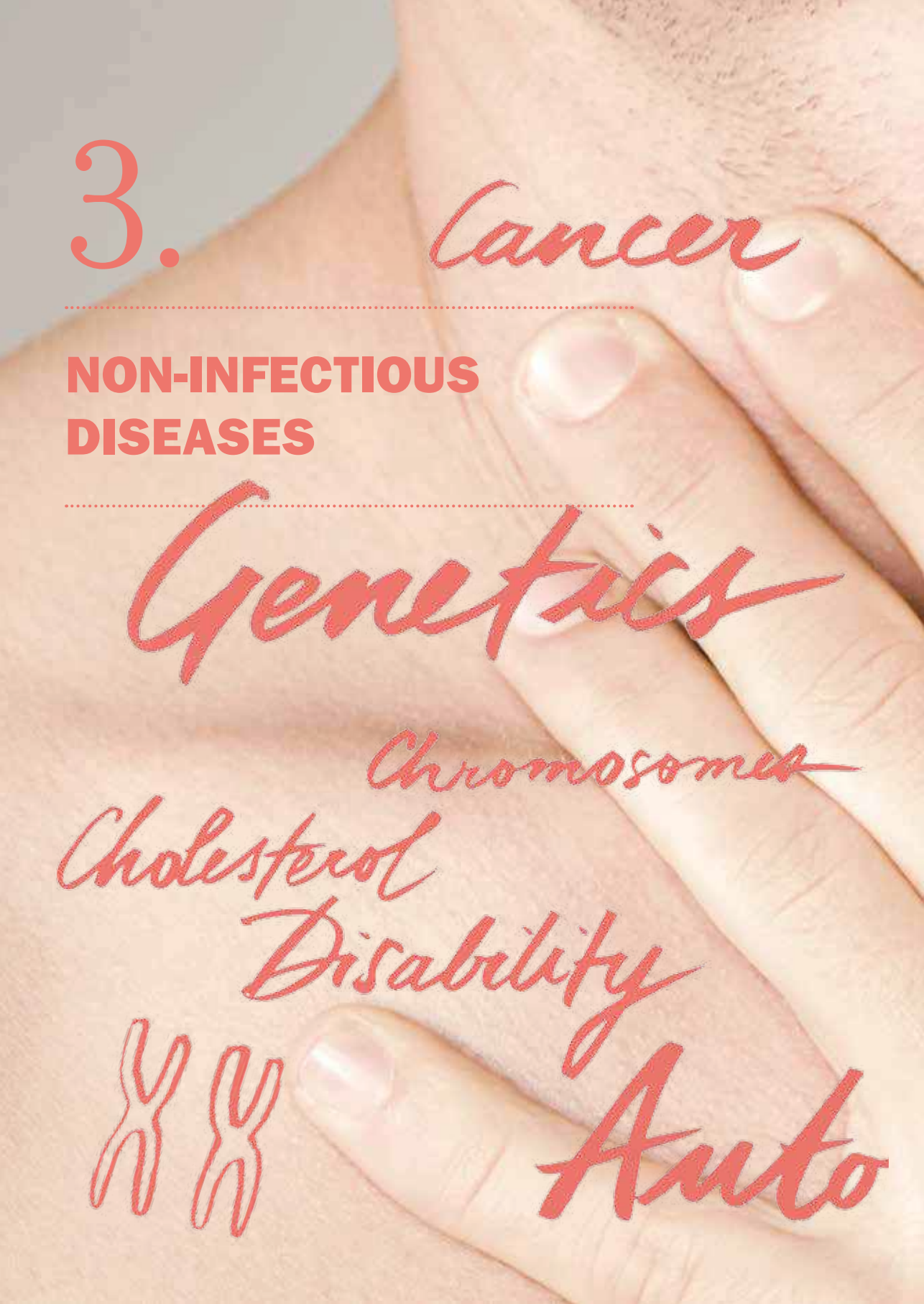
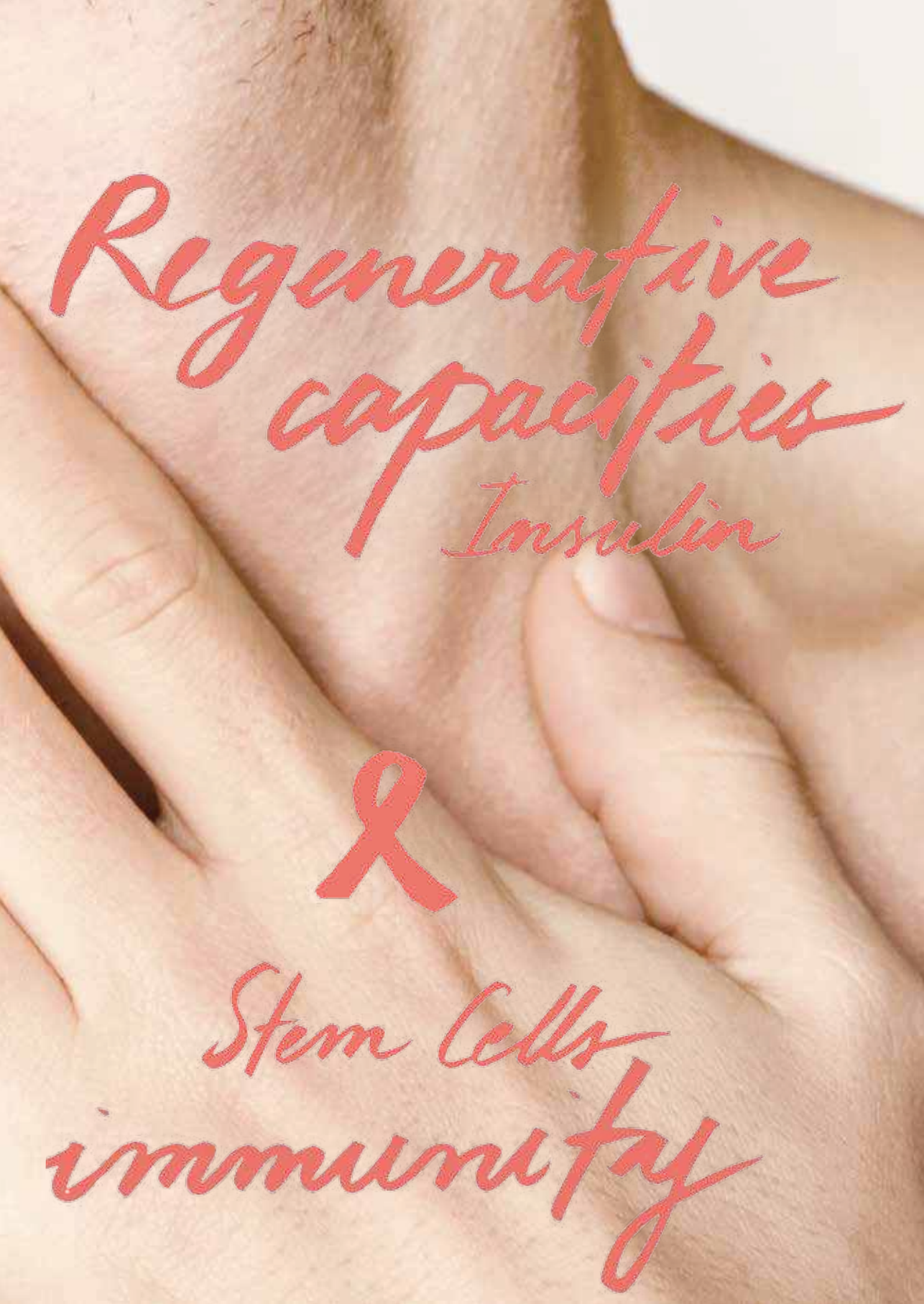
NON-INFECTIOUS DISEASES

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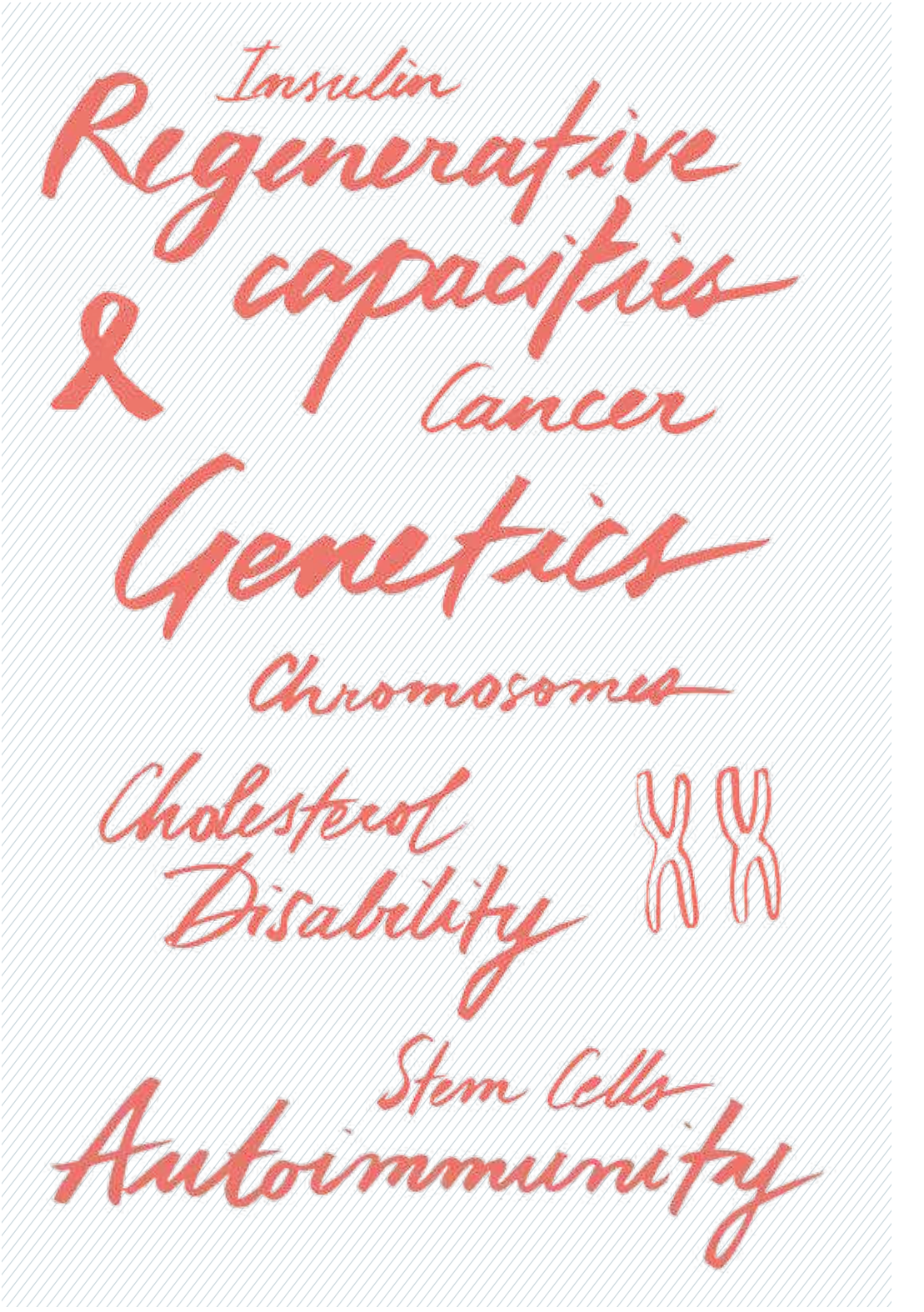
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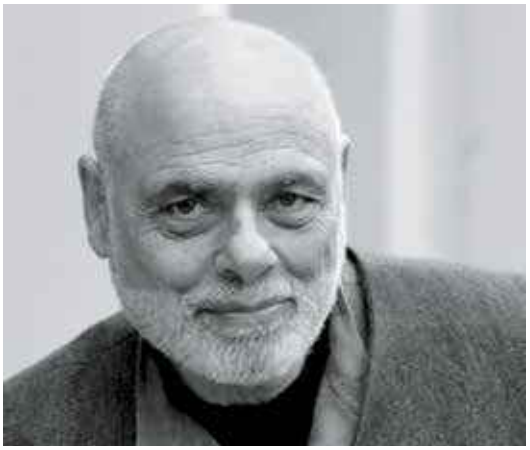
INTRODUCTION TO NON-INFECTIOUS DISEASES

by Irun R. Cohen



Professor Irun R. Cohen
Reviewer for the AXA Research Fund
Weizmann Institute of Science, Rehovot (Israël)

Irun R. Cohen, MD, is currently Professor of Immunology, Emeritus, at the Weizmann Institute of Science in Rehovot, Israël. His research on autoimmunity in health and disease has led to innovative therapies now in advanced clinical trials and to a renewed appreciation of the internal structure of the immune system.

Human diseases are the necessary outcome of two unavoidable facts of life: the living organism must first develop into a viable being, and then it has to maintain itself despite its inevitable dissolution, which is accelerated by interactions with the environment. Life, in short, is an ongoing struggle with the second law of thermodynamics, which dictates that all complex entities are difficult to produce and, once made, tend to fall apart.

Relatively simple creatures like bacteria escape dissolution and disease by constantly dividing into new daughter cells. However, our complex life cycle demands more complex solutions. At the *cellular* level, we require complex programs of primary formative development and differentiation, bolstered by the turnover, regeneration and re-differentiation of the stem cells needed to replace aged or damaged cells. At the *organ* level, we need to maintain life by healing mature but damaged organs and by organizing adaptive behavior as organized by the nervous system and other physiological systems. Organ maintenance relates to the judicious deployment of a healing *inflammatory response*. Unfortunately, the inflammatory response itself can damage the organism if it is applied at the wrong time, location, intensity or dynamics.

Taking this into account, we can classify the non-infectious diseases supported by the AXA Research Fund into two broad categories: diseases of development and diseases of maintenance.

Diseases of cell development and differentiation are expressed as *cancer, genetic diseases*, and *developmental aberrations*.

Diseases of maintenance relate to *inflammatory diseases*, inappropriate *nutrition* (starvation, obesity and imbalance), *autoimmunity*, *aging* and *trauma*. In recent years, medical science has become aware of the importance of the myriad of bacteria (and viruses?) that make up the *microbiome* to our health.

Biomedical research, as supported by the AXA Research Fund, constitutes one of human culture's responses to the fragile human condition.

Doctor Anne-Claire Vergnaud
Postdoctoral Fellow
Centre de Recherche en Nutrition Humaine d'Ile-de-France (France)
€60K (1 year)

AN APPLE A DAY: NUTRITION FOR PUBLIC HEALTH

French PNNS adequation score and risk for cancer

Lifestyle diseases, like obesity and certain cancers, are now so common that we speak in terms of an epidemic. Dr. Anne-Claire Vergnaud's goal is to identify the factors at play when adults gain weight and to determine the effect of nutrition public health programs on health. Her findings help clarify the interactions between diet, smoking and weight, for instance, and suggest that following official dietary advice may reduce the risk of early death. The impact on health policy and individual choices could be great.

Doctor Marco Candeias
Postdoctoral Fellow
University of Kyoto (Japan)
€120K (2 years)

BACK TO BASICS: A TRIP DOWN CANCER PATHWAYS

Studying cancer pathways in stem cells

The protein p53 can start or stop tumors depending on its mutation status and expression levels. Interestingly, Dr. Marco Candeias has revealed that levels of p53 proteins are regulated by… p53 itself! Or rather, by p53 mRNA, the intermediary that gives instructions to make p53 proteins. This molecule happens to protect the very proteins that it makes from destruction. Candeias' contribution to the central dogma of molecular biology could open new pathways for cancer treatments.

Doctor Fabien Montel
Postdoctoral Fellow
Institut Curie (France)
€60K (1 year)

TO FIGHT TUMORS USE THE FORCE, YOU SHALL

Tumor and micro-environment, role of pressure in tumoral growth

Cells feel stress too! Mechanical stress, that is. Physicist Dr. Fabien Montel has designed a system that uses liquid to apply pressure to tumors, which slows their growth. He has discovered why: in the center of the tumor, cell multiplication decreases. As soon as pressure is relieved, growth resumes. He will also investigate how pressure applied by tumors to their environment affects the surrounding healthy tissues, to determine whether the force exerted by the malignant tissue affects the healthy tissue.

Doctor Cédric Thaury
Postdoctoral Fellow
École Polytechnique (France)
€60K (1 year)

TAKING AIM AT TUMORS

Theoretical study of plasma expansion into a vacuum and of the acceleration of high energy ion beams during the interaction of a high intensity laser with a plasma

Radiation therapy using X-rays to kill cancer cells has disadvantages, like the inability to penetrate very far into the body. Dr. Cédric Thaury is working on alternatives: beams of high-energy particles—electrons or protons—that are fired at a tumor to destroy the cancerous cells. He is developing new tools, based on laser-plasma interaction, to produce and control these beams for precise, effective treatment of tumors with fewer side effects. Developing less costly systems would also allow for greater use of these therapies.

Doctor Maja Matis
Postdoctoral Fellow
Stanford University (USA)
€120K (2 years)

ALL PLANNED OUT

A proteomic approach to study cell migration during metastasis

Cells exhibit two opposite poles which direct vital actions. One of them is movement, which participates in metastasis in cancer. Dr. Maja Matis is exploring polarity by analyzing the proteins in fruit-fly cells. She aims to identify which proteins create polarity. It is likely that acting upon these proteins will impede migration and, in tumor cells, metastasis. Her findings may help identify which proteins are potential new targets for efficient and less toxic pharmaceutical treatments.

Joël Lemière
PhD Fellow
Institut Curie (France)
€120K (3.5 years)

THE MECHANISMS OF MOVEMENT

Study of endocytosis mechanisms on an experimental system that mimics a cell

How do cells move and change shape? Joël Lemière aims to understand cell behavior using a biomimetic system that artificially reproduces cell movement under controlled conditions. His results could be helpful in treating metastatic cancer.

TRACING THE VERY BEGINNING OF CANCER

AXA Chair on Molecular Oncology

Professor Mariano Barbacid
CNIO (Spain)
€2M (Permanent)

All the cells of our body permanently receive and emit signals that allow them to communicate and respond appropriately to their changing environment. External signals trigger cascades of reactions called “transduction pathways” that function in complex and regulated networks, thanks to interacting proteins. Some genes/signals play a crucial role in the control of cell proliferation, differentiation and death. A cell becomes malignant when, due to mutations in key genes it receives aberrant signals that lead to a disruption of the equilibrium between these three processes. The uncontrolled division of a malignant cell gives rise to a tumor. Cancer is a pathology of cellular signaling and communication.

One of the reasons why current treatments are relatively inefficient is the high complexity of the mechanisms of cancers and the plasticity of cancer cells, which allows them to become resistant to drugs. To meet the need for highly innovative research to discover new treatments, the AXA permanent Chair has been launched, held by the internationally renowned scientist Prof. Mariano Barbacid. He was notably among the first to discover and isolate the first human “oncogene”, a cancer-causing gene. The discovery revealed that cancer is a genetic disease caused by mutations in key genes.
Most cancers grow undetected for more than 90% of their existence and most often, at advanced stages, when they carry so many mutations that it is too late to understand the mechanism(s) of their formation. Understanding the very first steps of tumor formation is necessary for imagining rational approaches to prevent its progression.

The project will investigate in particular the K-Ras oncogene, which is mutated in one-fourth of human tumors, particularly lung, colorectal and pancreatic cancers, which are among the most deadly.
It will try to identify the proteins that are essential for tumor formation induced by the K-Ras. The ultimate goal of the project is to establish new therapeutic strategies that will inhibit tumor formation. The proteins involved in tumor formation will then be validated as targets through pharmacological approaches. The purpose is to develop a new generation of small compounds that would inhibit these proteins and provide the best therapeutic benefit with the least toxicity.

GETTING TO THE ROOT OF CANCER

AXA Project
Characterisation of the underlying mechanisms of aging and cancer

Professor Thomas Helleday
Karolinska Institutet (Sweden)
€381K (3 years)

Cancer touches many of us personally, and will do so even more often in the future: the number of new cases is expected to rise from 14 million in 2012 to 22 million within the next 20 years. If we hope to slow this trend, we must understand more about how cancer develops in the first place.

This is a very diverse family of diseases, which makes it hard to pin down any one trigger. But something most cancers have in common is genomic instability. This means that, for various possible reasons, the DNA of cancer cells has experienced a high rate of mutation, or change to the genetic code. Prof. Thomas Helleday believes that understanding what causes this instability in our genes will illuminate how cancer begins and provide new targets for therapies.

With over 100 mutations occurring each day, on average, it is vital for a cell to be able to repair these mistakes and avoid becoming cancerous. When the cell copies its DNA before cell division, the two strands of genetic material unwind, allowing the replication machinery to pass. If it encounters a damaged area of DNA, it may come to a halt, leaving a double-stranded break. Helleday's lab has identified the principal repair mechanism in these cases as homologous recombination (HR). Each of our chromosomes is lucky enough to have a partner carrying corresponding genetic information. If a break occurs in the DNA of one, the missing sequence can be copied from the other chromosome. This much is known, but many details of the process have yet to be revealed.

Helleday aims to identify new proteins involved in the HR repair mechanism and to unravel their precise roles. His strategy involves a particular relationship that may exist between the genes that produce them. Sometimes two genes interact in such a way that one may contain a mutation and the cell will still survive, but if both genes are mutated, the cell will die. Identifying this type of relationship can show where the role of one gene is backed up by another, thus revealing the function of each gene's protein product. Demonstrating just how homologous recombination normally works to repair DNA damage promises to provide fundamental information about the origins of cancer when things go wrong.

Doctor Lucia Gutierrez Marruedo
Postdoctoral Fellow
CSIC-Materials Science and Technology (Spain)
€120K (2 years)

TRACKING TINY WEAPONS AGAINST CANCER

Tracking of magnetic nanoparticle biodistribution

Nanotechnology holds great promise for medicine, but there are also many unknowns. Magnetic nanoparticles (MNPs), for example, can carry drugs directly to a tumor, but we don't know their ultimate fate in the body. Dr. Lucia Gutierrez Marruedo uses their magnetic properties to quantify MNPs in tissue and measure how they degrade over time. Knowing how they interact with the body could tell us about their performance and potential side effects and lead to tailored treatments for disease.

Doctor Oscar F. Silvestre
Postdoctoral Fellow
National Institute of Biomedical Imaging and Bioengineering (USA)
€120K (2 years)

NANOPARTICLES INTERACT WITH OUR CELLS

Tracking therapeutic nanoparticle dynamics and cytotoxic using cytometry and multimodal imaging

The frequent questions about nanoparticles are: can they be useful for us and are they toxic? Dr. Oscar Silvestre is testing the therapeutic potential of nanoparticles to treat cancer and their influence on cell function, detectable through gene expression, but also the influence of cells on these nanoparticles. Thanks to advanced tumor imaging and biological analysis, this study evaluates the application of nanoparticles in tumor therapy and may help predict eventual long-term health risks of their use.

Baptiste Jaeger
PhD Fellow
Université de la Méditerranée (France)
€108K (3 years)

LICENSE TO KILL

Natural killer cell education: acquisitions, anti-tumor properties, and tolerance to self

Baptiste Jaeger is studying blood cells that patrol our body to identify and remove tumor cells. Understanding how they differentiate between healthy and unhealthy cells may help develop drugs specifically targeting tumor cells.

Thomas Landrain
PhD Fellow
Université d'Evry-Val-d'Essonne (France)
€120K (3 years)

FROM CANCER TO EXPLOSIVES: THE MANY TALENTS OF BIOSENSORS

Smart Biosensors through RNA computing: computational design of RNA networks

Using biosensors made of circuits of the genetic material RNA, Thomas Landrain is creating tools to respond to a variety of molecular signals. The sensors could be triggered to kill tumors, for one, or even report the presence of landmines.

Doctor Virginia Spanoudaki
Postdoctoral Fellow
Stanford University (USA)
€120K (2.5 years)

3D IMAGING TECHNIQUES FOR CANCER MANAGEMENT

Enhanced molecular breast cancer imaging : 1 mm resolution positron emission tomography

Mammography is a widely used method for the detection and screening of non-palpable breast cancer; however it has a very high rate of false-positive detection (around 80%). Dr. Virginia Spanoudaki has worked on designing a high spatial resolution, breast-dedicated nuclear medicine imaging technique which provides three-dimensional images. This technique promises to improve breast cancer management and can be used in conjuction with existing breast imaging methods. The system is currently under evaluation.

Margot Cucchetti
PhD Fellow
INSERM (France)
€120K (3 years)

YOUR BODY CAN DEFEND ITSELF AGAINST CANCER. IT JUST NEEDS A LITTLE HELP!

Boosting the anti-tumoral properties of T lymphocytes via the CD28 costimulatory molecules

Our immune system defends us against external and internal threats. Among the natural bodyguards against internal threats such as cancer are the T-cells. Margot Cucchetti is studying how they help our bodies to defend themselves against cancer.

Doctor Nicole Hondow
Postdoctoral Fellow
University of Leeds (UK)
€120K (2 years)

NANOPARTICLE ATTACKS!

Assessing the biomedical risk of engineered nanoparticles: understanding the behavior of nanoparticles in physiological media and cells

Nanoparticles are in our daily life. In the food we eat, in sun creams we use, in clothes we wear. Does this mean we are in danger? To assess the risk, Dr. Nicole Hondow is focusing on how cells in our body react to intrusion by nanoparticles, instead of concentrating on nanoparticle toxicity. Despite appearing similar, cells show different levels of sensitivity to particles. Hondow is trying to understand what causes this difference. Her findings may lead to improvements in medical imaging and health care.

Ignacio López Ferreira
PhD Fellow
INSERM (France)
€120K (3 years)

CELL DAMAGE MANAGEMENT

Studies on the relationship between p53, cancer and aging

Cell integrity is crucial to our health. When a cell detects damage, it can either repair it and go on dividing, or stop cycling and it will age or die. Unfortunately, sometimes, the cell starts to divide unpredictably and can become cancerous. Ignacio López Ferreira is investigating the role of the p53 protein in the way cells analyze damage and trigger a suitable and sufficient response to manage the type and level of damage. These studies could help unravel how cancer and aging are related.

Tanvi Gore
PhD Fellow
CNRS (France)
€120K (3 years)

SONIC CURE FOR CANCER

Characterization of a new sub-cellular compartment involved in the production of biologically active Hedgehog, a molecule necessary for stem cell homeostasis

In industrialized countries, half of the people diagnosed with cancer are older than 65.
Tanvi Gore decided to tackle both cancer and aging at the same time, combining genetics, electron microscopy and live cell imaging.

Matthias Bussonnier
PhD Fellow
Institut Curie (France)
€120K (3 years)

TOWARDS IMMOBILIZATION OF CANCER CELLS?

Mechanics of the actin cortex in biomimetic and living systems

Cells move in our body. However, when movement involves cancer cells (e.g. during metastasis), it becomes dangerous. Matthias Bussonier aims to understand the mechanics that drive proliferation and spreading of cancer cells in the body.

STEPS TOWARDS REGENERATIVE MEDICINE

AXA Project
Identification and manipulation of molecular pathways relevant for age-dependent tissue regeneration

Professor Maria Blasco
CNIO (Spain)
€700K (3 years)

The somatic cells that constitute all tissues of the human body are specialized cells that have acquired a proper identity (blood cells, neurons, etc.) during the embryonic development. Despite this specialization, all our cells have the same genetic information in their nucleus. The differences between cells lie in the presence of tags of sorts, called “epigenetic marks” that can turn genes “on” (expression) or “off” (silence) in a way that is passed on during cell division. All cells of a tissue bear the same epigenetic pattern. It was admitted that differentiation was an irreversible process until the birth of Dolly in 1996, the first mammal to be cloned with a somatic cell.

Ten years later, Japanese scientists proved it was possible with a genetic cocktail to revert human somatic cells to cells that have properties of embryonic stem cells, the so-called “induced pluripotent stem (iPS) cells.” Pluripotent means that these cells have the potential to give rise to any cell of the body.

This breakthrough has great clinical implications, since these cells can, in principle, be produced from the patient’s own cells, thus avoiding the cloning of embryonic stem cells and the risk of immune rejection. It opens the way to personalized regenerative medicine and disease modeling.

The reversal of adult cells to iPS cells goes through nuclear reprogramming, a very complex process that involves erasing or resetting all the previous tags specific to each tissue. How this is achieved is largely unknown. Unraveling the age-related barriers to efficient reprogramming is the main objective of this AXA project led by Prof. Maria Blasco.

The research concerns the role of several factors during nuclear reprogramming mainly, the length of telomeres, the gatekeeper genes whose mutations predispose to cancer, the original reprogramming cocktail of genes, the gene silencing pathways. All this knowledge should improve the regeneration of tissues from older individuals, thus creating novel opportunities for the prevention and treatment of aging-associated diseases.

FIGHTING CANCER? STARVE BLOOD VESSELS

AXA Project
Exploration of endothelial cell metabolism during neovessel formation and the therapeutic potential

Professor Peter Carmeliet
VIB - Katholieke Universiteit Leuven (Belgium)
€963K (5 years)

As of today, aging and its associated progressive loss of physical integrity remains the prime risk factor in cancer development. As refined parasites, developing tumors hijack the vascular system of their hosts in order to promote their own growth. Prof. Peter Carmeliet aims to explore this from a rather novel angle. Indeed, a large number of cancer therapies inhibit the creation of new blood vessels caused by chemicals released from tumors; however, these strategies are reaching their limits. In particular, they present serious side effects, such as toxicity and resistance incurred by patients. Carmeliet suggests reversing the process: what if, instead of starving tumors by blocking their blood stock, we starved the blood vessels themselves by cutting off their power supply?

The idea is daring and risky. However, Carmeliet's team has been leading research in the field of vascular biology for the past 18 years, and their expertise will be much needed in this pioneering investigation. The energy usage of blood vessels has been very poorly studied. In fact, very little is known about the cells that line the inside of blood vessels. It is only known that, despite being in a prime position for accessing the oxygen that circulates in the blood, these specialized cells prefer to use anaerobic (oxygen-less) chemistry to generate energy. This very bizarre behavior may allow these cells to proliferate in non-vascularized areas – thereby letting tumors run wild with blood vessel proliferation (angiogenesis).

In consequence, better insights into energy supply to blood vessels and into the conditions which favor their proliferation are crucial to help design new strategies to block energy pathways. Thus starved, the blood vessels would no longer respond to the signals emitted by tumors, thereby accelerating the latter's isolation and inescapable death. The project is extremely challenging. However, with the support of Carmeliet's interdisciplinary team working in a very international environment using emerging technologies, it might open paths to entirely new therapeutic strategies for fighting the ever-growing plague of cancer.

Doctor Melis Karaca
Postdoctoral Fellow
University of Geneva
(Switzerland)
€60K (1 year)

OVERWEIGHT GAIN AND GLYCEMIA EQUILIBRIUM

Genetic abrogation of the amplifying pathway in pancreatic ß-cells: effects on diet-induced obesity

Dr. Melis Karaca is using mice to study the role of the pancreas in regulating the glucose content in blood (glycemia) and in overweight gain. Her results indicate that one specific protein, called GDH, is essential in pancreas function. She is investigating the importance of GDH regarding insulin secretion and the onset of obesity and type 2 diabetes. She aims to understand how efficient an insulin-secreting pancreatic cell should be to maintain normoglycemia and what adaptations of peripheral organs are induced by low cell efficiency.

Javier Clemente Casares
PhD Fellow
University of Calgary
(Canada)
€120K (3 years)

A NANOVACCINE FOR JUVENILE DIABETES

Re-establishing self-tolerance by targeting MHC class II-restricted autoimmunity

Juvenile diabetes is an autoimmune disease resulting from an attack that destroys pancreatic cells that secrete insulin. Javier Clemente Casares is studying a therapeutic approach that could lead to a nanovaccine for the disease.

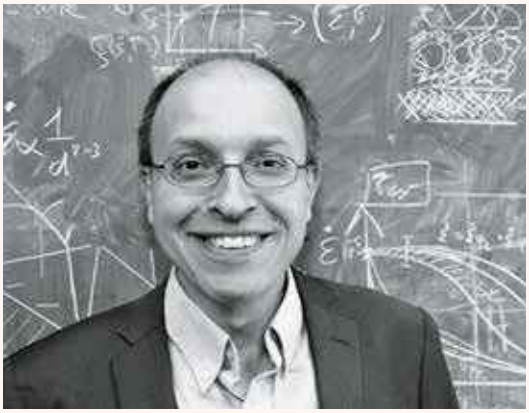
Doctor Marina Rubio
Postdoctoral Fellow
INSERM (France)
€60K (1 year)

STROKE HITS THE BOTTLE LINE

Critical influence of alcohol consumption on brain outcome following ischemic stroke and thrombolysis

Stroke is the second leading cause of death worldwide and the number one cause of acquired disability in adults. Dr. Marina Rubio is exploring the relationship between recovery and previous alcohol consumption as well as the impact of previous alcohol consumption on the only acute treatment for stroke — thrombolysis. Her results show, first, that chronic alcohol consumption provokes bigger stroke lesions and, second, that the beneficial effects of thrombolysis are lost after chronic alcohol exposure.

WHEN BIOLOGY MEETS ENGINEERING



AXA-Ecole Polytechnique Chair for Cardiovascular Cellular Engineering

Professor Abdul Barakat
Ecole Polytechnique (France)
€2M (Permanent)

Traditionally, medicine and engineering have lived in two different and separate worlds. Rooted in physics, chemistry and mechanics, engineers focused on the inanimate universe concentrating on biology, biochemistry and genetics, whereas medicine focused on the organic world. Now though, researchers from each world are beginning to see how much they each stand to benefit from the unique tools and approach of the other. Nowhere is this more true than in the ongoing battle against cardiovascular disease, the world's leading cause of mortality.

The creation of the AXA Chair for Cardiovascular Cellular Engineering at France's Ecole Polytechnique and the nomination of Prof. Abdul Barakat as its first holder constitute important steps forward in this new approach to cardiovascular disease. By applying modern engineering tools to cell biology, especially at the micro- and nano-scale, he is contributing to a better understanding of both normal and abnormal cellular functions. The chair will study the development and treatment of atherosclerosis through an interdisciplinary approach combining biology and engineering.

The two leading cardiovascular killers, coronary heart disease and stroke, both involve dysfunction of a particular type of cell called the endothelium, which constitutes the interface between the bloodstream and the arterial wall. When endothelial cells become dysfunctional, the arterial wall thickens—known as atherosclerosis—and the artery may be eventually blocked entirely. Genetic and lifestyle factors are involved, but so are mechanical factors and that's where engineering expertise can be critically important.

In their research into atherosclerosis, engineers such as Barakat and the members of his team are investigating how such mechanical considerations as pressure, frictional forces and stretch forces regulate endothelial cell function. This information is applied towards devising novel endovascular devices for enhancing the flow of blood through obstructed arteries. Another focus is examining the possibility of drug delivery against atherosclerosis via the intravenous injection of nanoparticles, a treatment that is highly targeted and non-invasive. Barakat's team aims to establish the mechanical environment needed for optimal delivery of nanoparticles to endothelial cells.

Doctor Rajeev Kumar
Postdoctoral Fellow
CNRS (France)
€90K (1.5 years)

REPRODUCTION: A COMPLEX PROCESS!

Investigating the mechanisms regulating recombination during meiosis

Meiosis is essential for fertility in sexually reproducing organisms. During meiosis, recombination between the mother's and father's chromosomes is critical for the faithful segregation of chromosomes. Dr. Rajeev Kumar's research aims to understand how the initiation of recombination is regulated in mammals. His work has identified key factors whose genetic ablation in mice leads to infertility. This study may provide a basic framework for delineating the molecular basis of certain cases of infertility and genetic disorders.

Marine Garguilo
PhD Fellow
Hôpital Raymond Poincaré (France)
€120K (3 years)

DROP THE PRESSURE

Determination of optimal PEEP level for speech under patient control in tracheostomized ventilator-dependant subjects

Tracheostomized patients require respiratory support for survival. Marine Garguilo is testing a new device, which, controlled by the patients, allows them to speak more fluidly while avoiding the risk of excessive pressure in the airways.

Doctor Gilles Kayem
Postdoctoral Fellow
University of Oxford (UK)
€60K (1 year)

SAVING MOTHERS

Assessing the risk of mortality in cases of near-miss maternal morbidity

Death during pregnancy and childbirth, although rare in modern countries, still exists. Dr. Gilles Kayem is investigating maternal near-miss events, in which the mother comes close to death but does not die. They can leave women heavily handicapped for the rest of their lives. Kayem's scrutiny of near-misses may give insight on how to avoid the rare, yet dramatic event of a healthy woman's death during childbirth, which will be beneficial for obstetric practitioners and health-care units.

Doctor Bjørg Elisabeth Kilavik
Postdoctoral Fellow
Université de la Méditerranée (France)
€60K (1 year)

READING MOVEMENT IN THE MIND

The use of intentional signals to switch on/off movement decoding in brain-machine interfaces

It is difficult to imagine anything more detrimental to one's independence than paralysis. Dr. Bjørg Elisabeth Kilavik's work may lead to a remarkable solution using brain-machine interfaces (BMIs). With BMIs, brain activity can be analyzed and used to generate movements by an external device (robot). She hopes to take it further by detecting the very *intention* to move, based on visual cues, allowing movement decoding to be switched on only when truly desired by the user. Efficient, portable BMI devices could one day change patients' lives.

Fabien Mézière
PhD Fellow
ESPCI (France)
€120K (3 years)

THE BONE WHISPERER

Modeling ultrasound propagation in cancellous bone: towards early diagnosis of osteoporosis and fracture risk assessment

Osteoporosis-related risks increase with aging. Fabien Mézière is currently developing an original tool for early diagnosis based on the spreading of ultrasound waves to allow early detection of lesions and porosity in the bones.

Doctor Giulia Bortolussi
Postdoctoral Fellow
International Centre for Genetic Engineering and Biotechnology (Italy)
€120K (2 years)

JAUNDICE AND BABIES

Neonatal jaundice: in vivo bilirubin neurotoxicity in a Ugt1 ko mouse model

75% of hospital readmissions of babies in their first week of life are due to jaundice. Severe jaundice can lead to permanent neurological damage and ultimately death. Limitations in animal and cellular models have narrowed the study of this disease. Thanks to a mutant mouse model that more closely mimics human jaundice, Dr. Guilia Bortolussi is performing molecular, tissue and behavioral analysis to better understand the molecular mechanisms that damage the brain and testing therapies that could improve brain protection.

Doctor Pierre Clément
Postdoctoral Fellow
Université de Versailles St-Quentin-en-Yvelines (France)
€60K (1 year)

CURING BLADDER HYPERACTIVITY IN SPINAL CORD INJURED PATIENTS USING GENE THERAPY?

Viral engineering for the treatment of neurogenic detrusor overactivity due to spinal cord injury: proof of concept study

Spinal cord injury causes bladder dysfunction and particularly incontinence. This debilitating condition is the leading cause of morbidity and re-hospitalization of paralyzed patients, and the current treatments are not fully satisfactory. Dr. Pierre Clément is studying the feasibility of introducing genetic material into the nervous pathways that control the bladder, using harmless viruses. This study is a first step towards the development of gene therapy for bladder hyperactivity due to spinal cord injury.

Marie-Pierre Bonnet
PhD Fellow
INSERM (France)
€120K (3 years)

BETTER CARE FOR MOTHERS

Postpartum Hemorrhage: epidemiological profile and assessment of anesthesia and intensive care practices in France

In France, postpartum hemorrhage remains the leading cause of maternal mortality, unlike in other high-income countries. Marie-Pierre Bonnet has described the epidemiological feature of postpartum hemorrhage and the components of anesthesia and critical care management in order to better understand this phenomenon specific to France. Her research could contribute to defining health-care policies in maternity hospitals, perinatal networks and at a national level as well as be extended to other cases of severe maternal morbidity.

SUPPORTING MEDICINE 2.0

AXA-ESPCI Chair in Biomedical Imaging

Professor Emmanuel Fort
ESPCI ParisTech (France)
€500K (Temporary)

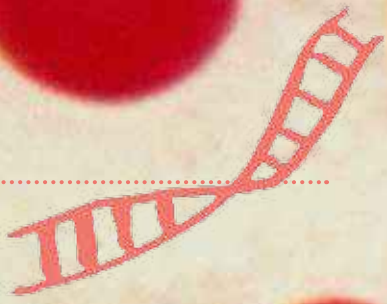
In some ways, modern medicine is like mending a moth hole in a knit sweater; you need to see each individual strand of yarn in order to precisely map damage and replace only the exact portion of each strand that's been eaten away. In medicine, rather than strands of yarn, it's about seeing individual molecules within individual cells and intervening at that extremely precise level. That's what makes nanotechnology and nanoparticles such exciting new frontiers. Situated at the intersection of quantum physics and biomedicine, nanotechnologies offer promising new directions for medical imaging for application in diagnoses and therapies.
Renowned for his research into the nature and behavior of wave/matter interactions, Prof. Emmanuel Fort is the newly appointed holder of the AXA-ESPCI Chair in Biomedical Imaging at ParisTech, the Paris Institute of Science and Technology. His lab is searching for ways to use nanotechnologies to make biomedical imaging much more precise than existing methods such as MRI.

Gold nanoparticles have been known for their healing properties since ancient Greece. The odd qualities of these nanoparticles are rich in possibilities for medical research for two reasons. For one, they serve as antennae, which capture and focus waves. Then, they scatter back the energy of these waves in the form of light or convert the absorbed energy into heat. The medical challenge is to exploit these features, especially the strong interaction with light.
Part of Fort's research uses the unique properties of these nanoparticles to image and destroy cancer tumors. When exposed to a particular wavelength of light, the particles emit light back. This enables a non-invasive, extremely high-definition biopsy, for example. What is more, because the nano-scale emitters can also produce heat, they could conceivably be used to very precisely "bake" cancerous cells, without affecting healthy ones.
Fort's research also focuses on cellular ultramicroscopy in which live cell activity can be observed with a nanometric resolution and a sensitivity down to a single molecule. Reaching these ultimate detection limits is most challenging but crucial to understanding the mechanisms involved in numerous diseases, such as Alzheimer's. Fort uses innovative principles to specifically improve the axial resolution and obtain 3D images of cells with a nanometer resolution.
Overall, Fort's goal is to create new types of imagery that marry diagnosis and therapy techniques into a single, unified form of treatment.

NOTES

4.

INFECTIOUS DISEASES



Immune System

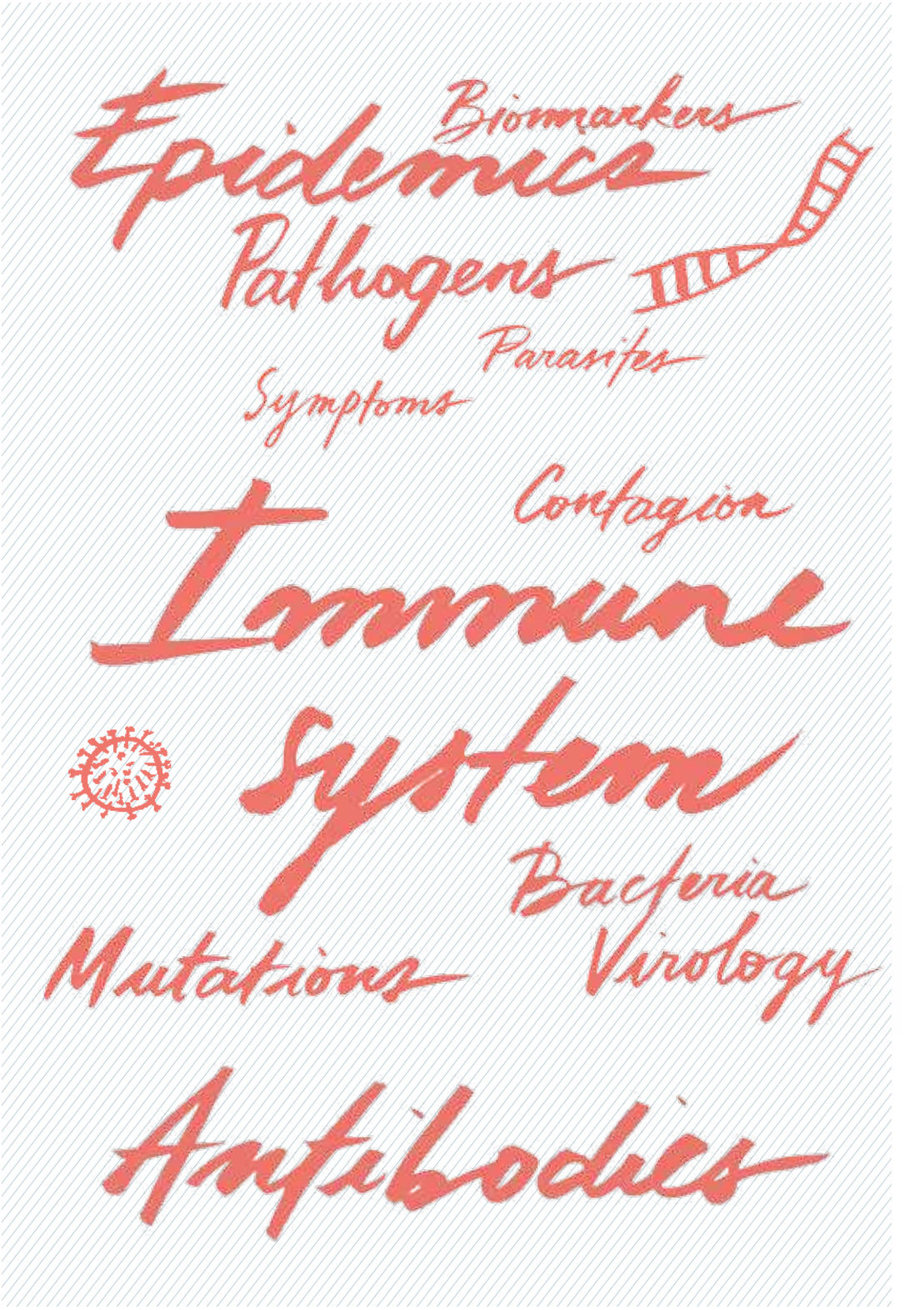
Bacteria

Contagion

Virology

Mutations


Epidemics
Pathogens
Antibodies
Symptoms
Parasites
Biomarkers


Biomarkers
Epidemics
Pathogens
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Symptoms
Contagion
Immune
System
Bacteria
Virology
Mutations
Antibodies

INTRODUCTION TO INFECTIOUS DISEASES

by Florence Niedergang

Florence Niedergang is a CNRS Research Director. She is Team Leader at Institut Cochin (INSERM U1016, CNRS UMR8104, Université Paris Descartes) and Co-director of the Infection, Immunity and Inflammation Department. Her work focuses on the mechanisms of internalization and activation of phagocytic cells in normal and pathological conditions such as infection by pathogens or during inflammation.

Dr. Florence Niedergang
Reviewer for the AXA Research Fund
Institut Cochin in Paris (France)

Infectious diseases are still responsible for about 30% of human deaths worldwide. In addition, according to the World Health Organization, one new disease appears in the world every year. With our modern lifestyle, characterized by the frequent and rapid movement of people around the world, new infectious diseases can spread very rapidly. Moreover, microorganisms show exceptional capacities of mutation and adaptation; and despite intensive efforts, treatments and in particular vaccines, are still lacking for many infectious diseases—especially those caused by viruses and intracellular parasites. The function of the immune system in normal and infectious conditions is still mysterious in many aspects, and it is essential to make progress in our understanding of the physiology of parasites and the reaction of their hosts.

Novel ideas, model systems and paradigms have recently been developed. Major changes in the toolbox of researchers, including massive analysis of data at the level of gene expression, epigenetic modifications or protein expression and functional regulation, have opened new paths for research, often requiring data mining and computational analysis. Because scientific progress needs to be fostered in many directions and often arises from an unexpected link between fundamental and applied research questions, AXA supports projects that focus on the physiology of pathogens or hosts, or on their interactions. Projects range from studies on viral particle assembly and production in host cells to the mechanisms of antibiotic resistance. Other projects aim to better understand the immune responses of cells or the organism as a whole or to identify genetic defects that cause increased susceptibility to specific pathogens. Mucosal surfaces, which are major portals of entry for pathogens, have recently gained significant attention.

There is no doubt that the projects supported by AXA have shed new light on various aspects of the intimate relationships between pathogens and their hosts.

INFLUENZA ON THE HUMAN DOORSTEP

AXA Project
Understanding lung dendritic cell function in resistance to influenza: from mouse to human

Professor Matthew Collin
Newcastle University (UK)
€570K (3 years)

Three times over the last century, the influenza A virus has caused major global pandemics with significant rates of disease and death. Even the less fierce, seasonal flu epidemics have their cost: recent estimates show that, in the United States, they cost the economy some 100 billion dollars. What's more, since small changes to the virus's genetic makeup occur constantly, our vaccines must be updated every year as we try to stay one step ahead of this pathogen.

Understanding better how the flu virus interacts with the human immune system would answer questions about how it manages to evade our defenses. This is the goal of a team led by Prof. Matthew Collin of Newcastle University. They started their investigation at the virus's first point of contact with our immune system: the lung dendritic cells.

The main role of dendritic cells (DC) is to take up foreign particles invading the body and process them for presentation on the cell surface—a signal that will activate other cells to launch an immune response. Using innovative bioinformatics tools, Collin's lab identified two subsets of human DC that appear to have distinct functions in resisting infection with influenza A. This was first observed in mouse models, which will also make it possible to determine the exact role of the DC subsets in fighting off the virus. To accomplish this, Collin will use a method called inducible depletion, meaning he will artificially trigger the regression of each of the mouse dendritic cell subsets in question, to determine the effect their absence may have on the immune response to influenza A.

The conclusions drawn from such mouse studies will need to be translated back into humans in order to shed light on the virus's ability to cause disease in people. Additional tests to achieve this important step will be carried out on human DC grown in the lab, as well as an innovative "humanized" mouse model with human lung DC grafts.

Ultimately, Collin's research should clarify to a much greater extent the precise role of our lung dendritic cells in launching a defense against influenza A infection. With this knowledge, more relevant strategies could be developed for designing vaccines—a current need that is sure to remain with us into the future.

Doctor Marina Caillet
Postdoctoral Fellow
Institut Pasteur
€120K (2 years)

A BRAND-NEW TYPE OF VIRUS TRANSMISSION

HTLV-1 viral biofilm: generation and transmission of a new infectious entity

A never-before-seen way for viruses to spread during an infection was discovered in Dr. Marina Caillet's lab. HTLV-1, a virus that causes both leukemia and a neurological disease, is able to exit the infected cell, enclosed in a protective cocoon of extracellular matrix proteins, called a viral biofilm. Caillet is studying this new form of transmission to understand how viral biofilms form and function. The answers may be relevant to other viruses such as HIV and could present new strategies for controlling infection.

Doctor Marcus James Taylor
Postdoctoral Fellow
National Centre for Biological Sciences (India)
€120K (2 years)

PEERING INTO THE IMMUNE RESPONSE

Examining the nanoscale biology of T-cell signaling

Fighting off infection requires communication among several cell types to trigger an immune response. But the power of traditional tools to discern the details is limited. Using high-resolution microscopy, Dr. Marcus James Taylor observes the very cell-surface molecules receiving the signal to launch an attack. By measuring their positions before and after activation and watching how they move in live cells, Taylor aims to provide fundamental information, on the nanoscale, about the immune system's molecular machinery.

Maria Daniela Garcia Castillo
PhD Fellow
Institut Curie (France)
€120K (3 years)

SEEKING PROTECTION AGAINST DEADLY TOXINS

Chemical genetics of Clathrin-independent endocytosis and retrograde transport—identification and molecular analysis of small molecule inhibitors of toxin entry into cells

Toxins, such as ricin or the bacterial Shiga-like toxins, can be deadly in the context of bioterrorism or infectious disease. Maria Daniela Garcia Castillo is working on identifying molecules able to protect our cells from their attack.

Grégoire Gessain
PhD Fellow
Institut Pasteur (France)
€120K (3 years)

A BETTER UNDERSTANDING OF BACTERIAL FOOD POISONING

Listeria monocytogenes interactions with intestinal immune cells: impact on bacterial dissemination and host response

Grégoire Gessain is studying our immune system's reactions to the dangerous foodborne bacterium, *Listeria.* His research on this common cause of food poisoning may reveal how it operates and how immune responses vary in different parts of the body.

Doctor Eik Hoffmann
Postdoctoral Fellow
Institut Curie,
INSERM (France)
€90K (1.5 years)

CELLULAR WARFARE: TRIGGERING AN IMMUNE REACTION

Receptor signaling coupled with antigen presentation in dendritic cells

Vital to our immune defense is the role of dendritic cells (DC) in capturing foreign particles, such as pathogens, in our tissues. They process the debris and display fragments on their surface— a signal that activates the next line of defense. Dr. Eik Hoffmann is studying detection molecules, or receptors, on the cell surface to show how DC trigger an immune reaction. His results show that both the type of receptor activated and the efficiency of pathogen processing dictate the immune response that follows.

Doctor Darius Koester
Postdoctoral Fellow
National Centre for Biological Sciences (India)
€120K (2 years)

FRIEND OR FOE? A MEMBRANE STORY

Deciphering the role of active remodeling of cortical actin on the spatiotemporal organization of cell surface molecules using an in vitro assay

As the door of your house, wide open to welcome friends but closed to prevent unexpected visits, the membrane opens to import nutrients into the cell, but stays closed to avoid infections. Dr. Darius Koester is working toward understanding its door code. Koester's project aims to rebuild and understand the machinery controlling the local membrane structures, and its changes over time. His work may help to develop efficient drug delivery systems or prevention treatments against pathogens that exploit membrane defects.

Doctor Yuval Itan
Postdoctoral Fellow
The Rockefeller University (USA)
€120K (2 years)

WHY DO SOME PEOPLE GET SICKER THAN OTHERS?

Genome-wide investigation of inborn errors of immunity to human infectious diseases

Within close human groups, catching a disease or not and the severity of the disease mostly depends on one's own genetic background. Dr. Yuval Itan wishes to unveil genetic predisposition to infectious diseases, individually and on a population-wide scale. He enquires to automate the identification of disease-favoring genes, to ultimately provide a wide array of computational tools for the diagnosis of genetic errors of the immune system, on the individual and population levels.

Doctor Juan Alberto Mondotte
Postdoctoral Fellow
Institut Pasteur (France)
€120K (2 years)

BRIGHT-EYED AND BUSHY-ANTENNAED

Dynamics of the RNAi-mediated antiviral immunity

Why exactly would anyone want to keep insects healthy? Malaria, dengue fever, yellow fever, sleeping sickness: these are but a few examples of diseases transmitted by insects. Yet Dr. Juan Alberto Mondotte could hold the key to making insects more resistant to the viruses they infect thousands with. By investigating their immune system, Mondotte hopes to understand the dynamics of insect immunity, opening a whole new range of perspectives for controlling both diseases and pests in agriculture.

Doctor Damien Roux
Postdoctoral Fellow
The Brigham and Women's Hospital (USA)
€90K (1.5 years)

PNEUMONIA-PROOFING HOSPITALIZED PATIENTS

Identification of bacterial factors involved in virulence and shared by main serogroups of Pseudomonas aeruginosa

Hospital-acquired infections are the fourth leading cause of patient death. The most prevalent is pneumonia, caused by the bacteria *Pseudomonas aeruginosa.* Dr. Damien Roux successfully identified the proteins responsible for the passage of bacteria from the environment and singled out the genetic mechanisms for the bacteria's acquired resistance to antibiotics. He is now investigating *Pseudomonas* infection in the lungs, often found in ventilator-associated pneumonia, which could lead to a new vaccine.

Doctor Ilana Blech
Postdoctoral Fellow
Hassadah Hebrew University Medical Center (Israël)
€60K (1 year)

THE ENEMY WITHIN

AIDS immunotherapy by T-cell vaccination (TCV)

Today, more than thirty-four million people are infected with HIV worldwide. Dr. Ilana Blech is exploring the role of patients' destructive autoimmune response to their own CD4 T-cells, which are essential to the immune system and depleted in AIDS. She is developing a vaccine against this autoimmune response which has already brought improvement in the symptoms of volunteer AIDS patients. With no side effects, it may be used to treat AIDS, in association with the usual antiretroviral therapies.

Doctor Arabella Touati
Postdoctoral Fellow
Université Victor Segalen Bordeaux 2 (France)
€120K (2 years)

TRACKING A COMMON CULPRIT: PNEUMONIA AND ENCEPHALITIS

Outbreaks of respiratory tract infections and emerging risk of encephalitis due to Mycoplasma pneumoniae: characterization by multiple genome analysis

A single bacterium, *Mycoplasma pneumoniaie*, may be involved in community-acquired pneumonia, acute attacks of asthma and even encephalitis, especially in children. The risk of severe outbreaks is high in confined settings like hospitals, and a fast response requires identifying the type of the bacterial isolate involved. Dr. Arabella Touati is developing a method to differentiate subtypes of *M. pneumoniaie* around the world that should work even if the isolates mutate over the course of an outbreak.

Doctor Mathieu Coureuil
Postdoctoral Fellow
INSERM (France)
€60K (1 year)

EVEN PATHOGENS CAN CROSS THE LINE!

Identification of the cellular receptor to Neisseria meningitidis

Our brain is so important that it is protected from infections by a special barrier that prevents infectious agents from penetrating. However, the bacterium that causes meningitis unfortunately has "a molecular key" to open it. Dr. Mathieu Coureuil is studying this molecular key and how it enables the bacterium to adhere to, open and cross the barrier. Not only will this study provide a greater understanding of a major disease, but it could also facilitate the development of new strategies for the delivery of drugs to the brain.

A BLURRY LINE BETWEEN HUMAN AND ANIMAL

AXA Project
Social representations of pathogens at the frontiers between species

Doctor Frédéric Keck
Collège de France (France)
€210K (3 years)

You may show your passport when you travel internationally, but infectious diseases do not respect borders. They do not always respect even species boundaries: over 200 zoonoses, diseases naturally transmissible between humans and animals, are known. And every time a new avian flu virus, for instance, is seen killing many birds, the first question we ask is: could it spread to humans?

While microbiologists are constantly at work on this subject, the issue involves much more than the microorganisms responsible for disease. Anthropologist Doctor Frédéric Keck leads a team conducting the first study comparing social factors in different cultures and contexts that influence animal-human disease transmission. They are exploring the frontiers between species: rather than an impermeable barrier, this is a zone where people exchange and interact with animals.
By training ethnographers to consider zoonoses, Keck hopes to benefit from these specialists' expertise of local culture to enrich our understanding of pathogen transmission. This may include knowledge of daily practices bringing people into close contact with animals, but also more abstract conceptions of species frontiers, where pathogens, animal spirits and human dead are thought to pass. Involving science historians will allow the team to understand how such animal/human distinctions have changed over time. Ethnographic studies in three cultural areas of Asia (Mongolia, Southeast Asia and Australia), will also reveal how they vary in space.
Acting as translators between different groups confronting these emerging diseases, Keck and colleagues analyze how global health surveillance systems are received on a local level, with the goal of establishing a dialogue between the two. Religious rituals or animal protection movements, for instance, may come into conflict with disease prevention measures that reaffirm species divisions. In this case, the moral foundations of those measures will be reassessed as well.

The goal is to have anthropologists at work on sites around the world, acting as "sentinels," agents on the ground who signal the presence of pathogens, but also as facilitators of an almost cooperative interaction between animals and humans. This work could bring us closer to effective global management of many largely preventable, but often neglected zoonoses.

Doctor Lauren Carrington
Postdoctoral Fellow
Institut de Recherche pour le Développement (France)
€120K (2 years)

MOSQUITOS COMPLAINING ABOUT HOT AND WET

Assessing the risk of chikungunya and dengue virus transmission in Europe: the effect of realistic environmental conditions on the vector competence of Aedes albopictus

Aedes albopictus is a highly competent mosquito vector of both chikungunya and dengue viruses, which can be fatal to humans. As the vector is particularly sensitive to temperature changes, Dr. Lauren Carrington will study how realistic daily fluctuations in temperature and humidity alter the capacity of *Ae. albopictus* to transmit the viruses under European conditions. Her results may improve vector control in urbanized areas, and predictions of future transmission risk of these viruses in Europe.

Caetano Mendes
PhD Fellow
Instituto Gulbenkian de Ciencia (Portugal)
€120K (3 years)

MOSQUITOES FOR PREVENTION OF DENGUE FEVER

Using natural bacteria to control disease transmission by mosquitoes: a quantitative approach

In a new effort to prevent dengue fever, mosquitoes carrying a life-altering bacterium are released to replace the wild population. Caetano Mendes is working on predicting the consequences of their release in affected areas of Rio de Janeiro.

Nathan Desdouits
PhD Fellow
Institut Pasteur (France)
€120K (3 years)

A SPOKE IN THE WHEEL OF DENGUE VIRUS INFECTION

Identification of new inhibition mechanisms against dengue virus

To confront the growing risk of dengue fever, Nathan Desdouits is focusing on the cavities exposed to a viral protein during fusion with human cells. Aiming a drug at these pockets could disrupt fusion and block infection by dengue and similar viruses.

Delphine Judith
PhD Fellow
Institut Pasteur (France)
€120K (3 years)

CHANGING CLIMATE, EMERGING DISEASE

Host factors involved in chikungunya virus infection

As the climate changes, insect-borne diseases like chikungunya risk spreading into new areas. Delphine Judith's research revealing the virus's basic mechanisms of infection should improve the hunt for new treatments and prevention methods.

Doctor Sophie Cypowyj
Postdoctoral Fellow
The Rockefeller University (USA)
€90K (1.5 years)

A GENETIC ORIGIN FOR CANDIDA INFECTIONS IN HEALTHY PATIENTS?

Inborn errors of IL-17 immunity in humans

Patients with immune deficiencies are often afflicted by persistent infections of the skin, mucous membranes and nails with a yeast, *Candida.* Otherwise healthy people can also be affected, though, and the tendency seems to run in families. The suspected culprit is a genetic defect and Dr. Sophie Cypowyj intends to identify it. Revealing a genetic origin for Candida susceptibility could not only improve treatments, but lead to a better understanding of the immune response to many fungal infections.

Doctor Fanny Turlure
Postdoctoral Fellow
INSERM (France)
€120K (2 years)

STOPPING A VIRUS IN ITS TRACKS

Contribution of human and viral factors to dengue virus assembly

As deadly as it can sometimes be, a virus is "just" a bit of genetic material, wrapped in a protein package. In order to fight the virus that causes dengue fever, Dr. Fanny Turlure wants to disrupt the step in its life cycle when this package assembles. To do so, she is focusing on the role of a packaging protein and the viral and human factors that interact with it. Elucidating the basics of virus assembly could lead to blocking it and a new approach to treatment for this disease threatening 2.5 billion people.

Doctor Fabien Guegan
Postdoctoral Fellow
Instituto de Medicina Molecular (Portugal)
€120K (2 years)

WHEN SLEEPING BECOMES FATAL

Long non-coding RNA control infectivity and transmission of Trypanosoma brucei parasites

Sleeping sickness is a fatal disease caused by trypanosome, a parasite transmitted by the tsetse fly. Dr. Fabien Guegan is studying how trypanosomes survive in the human blood using an ingenious strategy to evade the immune system called antigenic variation. He is also studying how this parasite adapts to extreme environmental changes, passing from human blood to the tsetse fly midgut. Understanding the adaptive strategies used by trypanosome will provide new avenues for developing treatments.

Doctor Caroline Deshayes
Postdoctoral Fellow
Université d'Angers (France)
€60K (1 year)

HEALING THE PAINS OF NEGLECT

Fighting the Buruli ulcer with innovative tools: from diagnosis to fundamental and therapeutic perspectives

Mycobacterium ulcerans, responsible for the Buruli ulcer, is a largely unknown flesh eater in the same family as the bacteria that cause tuberculosis and leprosy. In order to prevent the destructive effects of this disease on the skin, soft tissues, joints and bones of its victims—mostly children—Dr. Caroline Deshayes developed a new process to detect the toxin released by the bacteria in patients' tissues, which is useful for early diagnosis and capable of ensuring timely use of adequate treatment.

Cyrille Pauthenier
PhD Fellow
Université d'Evry-Val-d'Essonne (France)
€120K (3 years)

TAKING DRUG DESIGN INTO CELLS AND OUT AGAIN

Producing new antimicrobials and enhancing the current drugs polymorphism to fight drug resistance through a new metabolic engineering framework

Affordable, new antibiotics are needed and Cyrille Pauthenier hopes to engineer yeast cells to produce them for us. To avoid toxicity, the process will take place on the outside of the cell, making collection of the new drugs easy and harmless.

Sizzle Vanterpool
PhD Fellow
Maastricht University (Netherlands)
€120K (3 years)

PRETERM BIRTH AND A MOTHER'S ORAL HEALTH

Preventing preterm birth: the pathogenic role of oral microbes in preeclampsia and intrauterine infection

One reason for preterm birth, the main cause of perinatal death, could be maternal periodontitis, an oral infection, spreading to the uterus and placenta. Sizzle Vanterpool aims to develop a vaccine against the bacteria so dangerous for the unborn child.

Doctor Rebeca Pérez de Diego
Postdoctoral Fellow
Université Paris Descartes (France)
€105K (2 years)

COULD GENETICS EXPLAIN CERTAIN VIRAL INFECTIONS?

Childhood herpes simplex encephalitis (HSE): a novel primary immunodeficiency

When a healthy child falls ill with a rare, life-threatening viral disease, could there be a genetic reason? Primary immunodeficiencies (PIDs) are genetic disorders that leave a person susceptible to infections. A new kind of PID may play a role specifically in herpes simplex virus encephalitis, a terrible infection of the central nervous system. Dr. Rebeca Pérez de Diego aims to identify new PIDs that may be responsible—work that could lead to treatments restoring these children's missing immune function.

5.

NEUROSCIENCE, RISKY BEHAVIORS AND ADDICTIONS

cognitive functions

Mental disorders

Risky behaviors

Social attitudes

Drugs

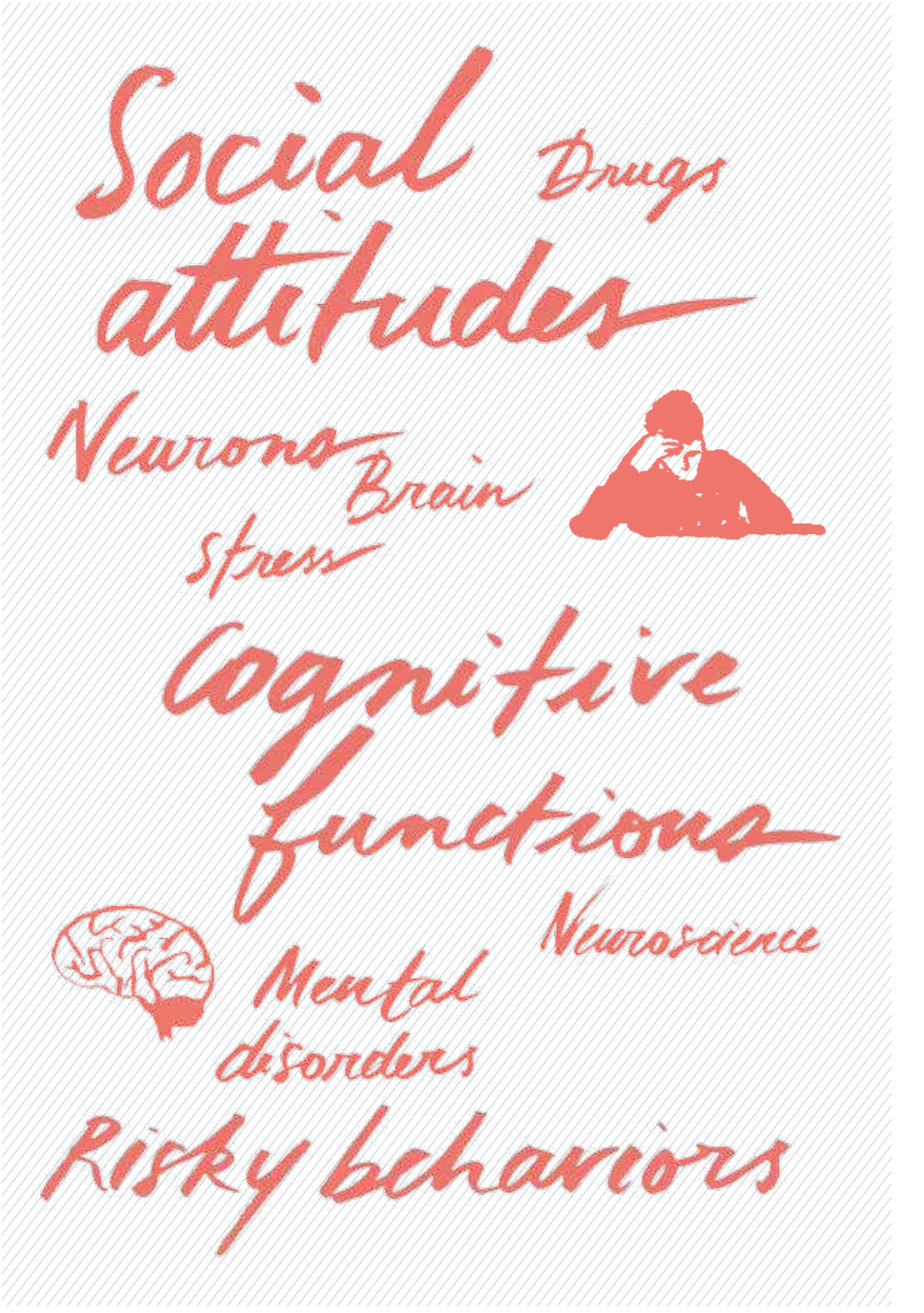
Neurons

Brain

Stress

Neuroscience

Depression


Social
Drugs
attitudes
Neurons
Brain
Stress
cognitive
functions
Neuroscience
Mental
disorders
Risky behaviors

INTRODUCTION TO NEUROSCIENCE, RISKY BEHAVIORS AND ADDICTIONS

by Philippe de Timary

Philippe de Timary
Professor of Psychiatry
Université Catholique de Louvain and Cliniques Universitaires Saint-Luc, Brussels (Belgium)

Philippe de Timary is Professor of Psychiatry at Université Catholique de Louvain and Cliniques Universitaires Saint-Luc in Brussels, Belgium. His research topics are mainly focused on the biological and behavioral factors involved in the developement of alcohol addiction.

Human beings are often exposed to stresses from their social environment and are not equally protected to resist these stresses, depending on genes, earlier exposure to stresses, and quality of social environment. A substantial proportion of the population will develop emotionally uncontrolled or risk-taking behaviors. These psychological symptoms are currently considered to result from an imbalance between overexpression of automatic processes in deep, subcortical brain regions and underactivity of control process at the level of the cortex. Although the burden of addictions and other mental health diseases on society is extremely high, the processes involved in their development are still poorly understood. However, rapid progress is being observed in these neuroscientific research fields. A fascinating aspect of research in this area is the extreme variety of the approaches to address scientific questions, as can be observed from the different projects that the AXA Research Fund has financed yet. Some studies will use animal models to examine the nature of abnormal processes happening on neurons, both at cellular and molecular levels in mental health diseases. This means first developing appropriate animal models of the disease and hence proper tools to study, for instance, the activity of the neurons in subcortical and cortical regions, using electrophysiological techniques, sometimes after a modification of the expression of genes to study the role of specific proteins in disease development. Other studies developed in humans make it possible, for instance, to measure brain activity in response to emotions or risk taking, with imaging techniques that are in constant progress and often coupled with genetic markers. Specific interest is given to processes observed during adolescence, a risky period where mental health disease frequently develops, especially when exposed to drugs. Through its visionary and generous policy, the AXA Research Fund is financing innovative and talented researchers in a field that is of paramount importance for the future of human societies.

Muna Hilal
PhD Fellow
Université Victor Segalen Bordeaux 2 (France)
€120K (3 years)

THE POWER BETWEEN YOUR NEURONS

The formation and maturation of synapses, synaptic plasticity and physiopathological implications

Contact points between neurons are more important than you may think: numerous brain diseases are linked to their dysfunction. Muna Hilal uses an array of techniques to understand how they work, making new therapeutic approaches possible.

Doctor Jennifer Cook
Postdoctoral Fellow
Radboud Universiteit Nijmegen (Netherlands)
€120K (2 years)

A "MIRROR" IN OUR BRAINS?!

Reconfiguring the mirror neuron system: individual differences and influences of social attitudes

Learning from trial and error can be slow and error-prone. In contrast, social learning (learning by watching others) can help us to pick up new information quickly without repeating mistakes that others have made. Dr. Jennifer Cook is investigating the brain regions involved in social learning to enquire whether social attitudes and social status affect a person's ability to learn via social means. Her results could help improve traditional teaching and perhaps even the treatment of people affected by autism, who may have difficulties with social learning.

Doctor Alice Meunier
Postdoctoral Fellow
Ecole Normale Supérieure (France)
€60K (1 year)

A NEURON IS BORN

Functions of hydrodynamic forces in neurogenesis

Even in adults, new brain cells continue to be born. Dr. Alice Meunier's creative method uses both biology and hydrodynamics to study the environment of these neurons-to-be. The coordinated movement of hair-like structures on the surface of neighboring cells circulates fluid in the brain and allows pro-growth molecules to wash over their targets. Understanding how these hair-like structures orient their beating is necessary if, one day, we hope to replace neurons in patients with neurodegenerative disease.

Doctor Julie Péron
Postdoctoral Fellow
University of Geneva (Switzerland)
€120K (2 years)

LISTEN AND YOUR BRAIN WILL ANSWER!

Electrophysiological activity of the ventral striatum in response to emotional prosody among patients suffering from resistant and chronic depression—ancillary study to the Pré-STHYM study

Depression is associated with strong negative emotions. In order to study the activity of the brain regions involved in emotional processing, Dr. Julie Péron is directly recording it in real time during brain surgery. Depression can be treated with deep brain stimulation which requires the implantation of stimulation electrodes in the patient's brain. Péron's innovative study could improve our understanding of depression and thus improve patients' lives.

THE CORTICAL NETWORK

AXA Chair in Neurosciences and Longevity

Professor Pierre Vanderhaeghen
Université Libre de Bruxelles (Belgium)
€3M (Permanent)

The brain is the most complex organ in our body and to a large extent is the key to our identity as human beings. It is the seat of intricate, multi-level interactions inherent to its function: from genes to neurons, from neurons to neural circuits, from neural circuits to perception, behavior, and consciousness. Yet despite the latest advances in neuroscience, getting a comprehensive view of brain development and function remains a major basic scientific question when considering the number of diseases left without any efficient therapeutic treatment. Beyond the suffering of more than 100 million people affected in Europe by a variety of brain diseases (including Alzheimer's and Parkinson's, autism, addiction, depression, epilepsy, migraines, mental and motor retardation, etc.), the total financial burden associated is estimated at 400 billion euros per year. In this context, the new AXA-ULB Chair in Neurosciences and Longevity clearly endeavors to address this major societal challenge.

ULB uses a multidisciplinary and innovative approach to synergize the best ULB neuroscience teams within the Neuroscience Institute (UNI), comprising scientists from different backgrounds, from genetics to psychology, neurobiology to clinical disciplines and even artificial intelligence. Such a broad approach is a first in Belgium. It is being carried out by Prof. Pierre Vanderhaeghen, the new Chair holder, specializing in the study of the cerebral cortex, a recently elected member of the European Molecular Biology Organization (EMBO), and notably awarded the Francqui Prize, the most prestigious award for Belgian scientists.

The first axis of his research will strive to uncover the mechanisms underlying the development of higher brain functions and how its alterations can lead to human diseases, while the second will try to use this knowledge to design innovative approaches towards brain repair.

An ambitious scientific program, a world renowned researcher and a brand new ULB Neuroscience Institute to host the Chair: this is an exciting combination with a great potential impact on healthy aging, prevention, understanding and treatment of brain diseases (including neurodevelopmental autistic syndromes and neurodegenerative disease such as Alzheimer's and stroke).

Doctor Annie Ginty
Postdoctoral Fellow
University of Birmingham (UK)
€120K (2 years)

THE STRESSFUL LIFE OF STUDENTS

Blunted physiological reactions to acute psychological stress: a novel marker of risky behavior, addiction, and poor health?

People who are biologically unaffected by stress seem to be at lower risk of cardiovascular disease. However, research has shown that such a low reaction is related to dependencies and maladaptive health behaviors (e.g. depression, bulimia). Dr. Annie Ginty is focusing on students in a stressful period of their life, to find out if low reactivity could be a biological marker of future dependencies and poor health. Her results could help develop cognitive, behavioral and pharmacological treatments.

Darja Dubravcic
PhD Fellow
Université Paris Descartes (France)
€120K (3 years)

HOW DOES NATURE DEAL WITH STRESS AND RISK

A quantitative sociobiological approach to fluctuating stress and resource management

Darja Dubravcic is studying how organisms deal with stressful situations and make decisions in an imperfect environment. Understanding their strategies may enable us to discover new means of adaptation and their costs and benefits.

Doctor Arjan Boonman
Postdoctoral Fellow
Tel Aviv University (Israël)
€120K (2 years)

BATS AND HUMANS: WHAT MAKES US TAKE RISKS?

The basis of individual risk-taking, using bats as a model

Why are some people more prone to taking risks? By observing a community of bats, Dr. Arjan Boonman is studying the combined influence of the four possible factors that drive risk taking: genetic, social, physiological and past experience. Bats, like humans, live in social structures where each of them makes individual behavioral decisions. Boonman will create a portrait of the typical risk seeker, providing a better understanding of the causes of risk taking in bats and therefore in humans.

Doctor Frances Chen
Postdoctoral Fellow
Albert-Ludwigs-Universität Freiburg (Germany)
€104K (2 years)

STRESSED OUT AND TAKING RISKS

Effects of stress on social and non-social risk taking

Are you a risk taker? That probably depends on both the situation and your biology. Dr. Frances Chen compares whether being alone or in a group when a stressful event occurs triggers different kinds of risk taking. She is also investigating whether oxytocin—a hormone relating to social interaction—influences people's willingness to take social risks. The knowledge gained from this rare pairing of complementary approaches may prove useful for medical professionals, managers faced with employee stress, or even people working with risk in their jobs.

Doctor Stefania Zappettini
Postdoctoral Fellow
INSERM (France)
€120K (2 years)

CAFFEINE AND PREGNANCY: A POTENTIAL RISK?

Deleterious consequences of caffeine consumption during pregnancy

Who doesn't appreciate a little caffeine pick-me-up now and then? If you're pregnant, though, it remains unclear if the stimulant is safe for the fetus. Dr. Stefania Zappettini's research could clarify that. Her lab discovered that, in mice, caffeine exposure led to seizures and long-term cognitive problems in offspring. Now, she aims to reveal more precisely how caffeine may affect the wiring of the developing brain—important information for public health, especially concerning the next generation.

Doctor Nicoletta Balbo
Postdoctoral Fellow
Università Bocconi (Italy)
€120K (2 years)

TEENS AND RISK: THE UNIVERSAL ELEMENTS OF SUBSTANCE ABUSE

Adolescent substance use: assessment of risk factors and risk prevention in a comparative perspective

Alcohol, tobacco, drugs: many people first try them as teens, which is also the age when substance abuse problems may begin. But the social and psychological factors behind them are unclear. Dr. Nicoletta Balbo is measuring teens' evalution of risk and identifying causes of substance use through statistical analyses of interacting risk factors. Rigorous, quantitative comparisons of multiple European countries like this are rare. Yet, identifying "universal" elements could lead to effective prevention strategies.

Agata Blasiak
PhD Fellow
University College Dublin (Ireland)
€120K (3.5 years)

TO REGROW A SPINAL CORD

Mechano-chemical modulation of axon outgrowth using a novel, high-throughput in vitro model system

Traumatic spinal cord injury is overrepresented among healthy young men. Agata Blasiak proposes a new approach, using nanomaterials, to understand how chemical and mechanical factors interact during the neuronal repair process.

Elia Magrinelli
PhD Fellow
INSERM (France)
€120K (3 years)

THE RISK OF ADDICTION IN OUR GENES

Challenging addictive behaviors in mouse models with abnormal corticostriatal projections

Our genes may make us more or less vulnerable to neuronal plasticity addiction. Elia Magrinelli is testing the role of a gene in the brain that may determine this risk and could serve as a predictor of susceptibility to addiction and a potential target for treatments.

Doctor Kiki Zanolie
Postdoctoral Fellow
Universiteit Leiden
(Netherlands)
€120K (2 years)

STATUS AND SENSIBILITY

"Why not?" The neural signature of social status in adolescence: implications for sensitivity to social rejection and risk-taking

Adolescence is a unique moment in life where acceptation from other teenagers becomes important. Dr. Kiki Zanolie is exploring the role played by social status—derived from a group in terms of physical attractiveness and good scores in sports and school — in case of rejection. Her hypothesis is that someone with a low status will react more heavily, often turning to risky behaviors. Zanolie's findings may contribute to identifying adolescents who are more at risk, allowing for early detection of behavioral problems to improve adolescents' well-being.

Doctor Andrea Glenn
Postdoctoral Fellow
Institute of Mental Health
(Singapore)
€81K (2 years)

ADAPTING TREATMENTS FOR JUVENILE DELINQUENCY?

Role of brain structure and function in juvenile delinquent and risk-taking behaviors and its impact on biological and psychosocial treatment efficacy

"Juvenile delinquency and risk-taking are a societal problem faced worldwide. Youth who engage in repetitive and persistent antisocial behavior are more likely to continue perpetrating crime and violence into adulthood," says Dr. Andrea Glenn. For the first time, the efficiency of combined treatments—biological (nutritional) and psychosocial (social skills training)—is tested in reducing problem behavior in youth, leading to more personalized treatments for youth who are at risk for criminal behavior.

Doctor Damien Carrel
Postdoctoral Fellow
ESPCI ParisTech (France)
€60K (1 year)

CANNABIS AND SCHIZOPHRENIA

Role of the cannabinoid CB1 receptor in neuronal remodeling in the adolescent brain and its implication in the transition to schizophrenia

Cannabis use during adolescence may accelerate the transition to psychosis in individuals predisposed to schizophrenia. Dr. Damien Carrel is studying the structural modifications of entire brain regions due to cannabis consumption in rats by concentrating on the morphology of their neurons. He aims to establish a link between these modifications and schizophrenic tendencies. His work could help us understand the risks of cannabis use during adolescence and thus contribute to preventing schizophrenia.

Doctor Fernando Kasanetz
Postdoctoral Fellow
Université Victor Segalen
Bordeaux 2 (France)
€90K (1.5 years)

UNDERSTANDING THE ROOTS OF ADDICTION

Cellular mechanism mediating the impairment in synaptic plasticity associated with the transition to addiction

Addiction does not happen to everyone. Focusing on the phase of transition from health to addiction, Dr. Fernando Kasanetz is investigating why some people develop a compulsive need for drug. By studying the initially disrupted inter-neuronal communication that follows cocaine intake, he showed that addiction is associated with the brain's inability to adapt to the effects of cocaine. Kasanetz is now exploring the cellular mechanisms that may explain maladaptive neuronal plasticity in addicts.

Doctor Ami Citri
Postdoctoral Fellow
Stanford University (USA)
€60K (1 year)

THIS IS YOUR BRAIN'S GENES ON DRUGS

The molecular genetic basis of addiction to drugs of abuse: dynamic transcriptional profiling of cocaine-induced gene expression in the Nucleus Accumbens

Why, when abuse of drugs has such devastating effects on people's lives, would anyone continue using them? Probably because cocaine and other drugs have a powerful influence on the brain, altering the circuits related to feelings of reward, and how the user remembers them. Dr. Ami Citri aims to identify which genes are turned on or off in one reward region of the brain, at different stages of addiction. If we could control this gene expression, we might be able to help people tackle their self-destructive behavior.

Julien Courtin
PhD Fellow
Université Victor Segalen Bordeaux 2 (France)
€120K (3 years)

THE WIRING OF FEAR

Role of cortical parvalbumin interneurons in fear behavior

How does our brain control fear and the behavior it drives? Julien Courtin's research on the prefrontal cortex suggests that inhibition of specific neuronal circuits could offer a solution for regulating disorders related to fear.

Doctor Aude Rauscent
Postdoctoral Fellow
INSERM (France)
€60K (1 year)

DRUG ADDICTION AND IMPULSIVITY—WHAT HAPPENS IN THE BRAIN?

Neurophysiological substrates of inter-individual vulnerability to cocaine dependence and its modulation by environmental conditions

There are few efficient therapeutical and preventive strategies against drug dependence, mainly because factors that contribute to the vulnerability to addiction remain unknown. Impulsivity is a marker of vulnerability to addiction. Dr. Aude Rauscent aims to understand whether differential stimulations interact with drug-induced plasticity in vulnerable and non-vulnerable animals. This project could help develop preventive strategies in vulnerable populations and therapeutical tools for patients.

6.

HEALTH POLICIES


Long-term care
Protection services
Retirement age
Political debate
Vaccination


Epidemiology
Policy makers
Financial risks
Long-term care
Protection services
Retirement age
Intergenerational Solidarity
Insurance
Political debate
Vaccination

INTRODUCTION TO HEALTH POLICIES

by Gérard de Pouvourville

Professor Gérard de Pouvourville
Director, ESSEC Institute for Health Economics and Management / Reviewer for the AXA Research Fund, Cergy Pontoise (France)

Gérard de Pouvourville is presently Chair Professor for Health Economics at ESSEC Business School. He has led a career as a researcher in the field of health care economics and management. His main contributions have dealt with hospital funding and management, physician payment scheme, health technology assessment and health policy.

Health insurance and prevention of health risk have always been a key policy issue in contemporary societies, because of the strong relationship between health and economic growth. Projects funded by AXA in this chapter are diverse in their aim: if benefits of welfare programs are a traditional question which is addressed in this chapter, others focus on specific dimensions of risks, with high relevance today for health policy makers.

Emerging health problems related to aging populations are addressed with two perspectives: how to provide good quality of care for seniors with mental illness and how to ensure sustainability of funding either through inter-generational solidarity or through private insurance systems.
Other projects focus on the unavoidable risks of medical treatments: medicine is a permanent trade-off between benefits and risks. Resistance to antibiotics and continuous changes in the ecology of germs are a growing challenge for all countries. There is also increased concern about side-effects of drugs in developed countries, some arguing that risk-aversion is growing to an extent that may inhibit innovation.
A third group of projects relate to the economic concept of externalities: transmissible infectious diseases are a case study of the negative involuntary effect of one's behavior on the group, whereas vaccination programs are the virtuous counterpart of the collective benefit of individual protection. If I accept vaccination at a minor risk of side effects, and if enough take the same risk, then the disease can be eradicated. The challenge is how to motivate individuals to take this risk, when the benefit is virtual, since I may not be exposed to the infection.

How does one deal with health issues and epidemics in a context of crisis, be it a natural disaster or an armed conflict? In this case, the risk of ill health may be a consequence and is aggravated by the crisis. There are enough examples of the prevalence of such situations in the world, where research work oriented towards policy recommendations will prove useful.

SIDE EFFECTS OF DRUGS
THE DARK SIDE OF ANTIBIOTICS

AXA Project
Effects of subinhibitory concentrations of antibiotics on the emergence of antibiotic resistance

Doctor Ivan Matic
INSERM (France)
€300K (3 years)

If you ask any French person what they think about antibiotics, there is a high probability that the answer will be: "They're not automatic." This catchy rhyme has been used successfully by the French health-care system in a national antibiotic awareness campaign launched in 2002.

The health-care administration and doctors were concerned that the overuse of antibiotics triggered resistance among a range of microbes. This problem caught the interest of Dr. Ivan Matic, who wanted to take a closer look at the issue. He observed that the massive use of this medication both by humans and in agriculture had an insidious impact on bacterial populations. Animal and human bodies do not retain a large portion of antibiotics. They are therefore released in nature and commonly found in soil and water. As a consequence, microbes often come into contact with low concentrations of antibiotics in the environment and adapt by developing resistance to them.

Matic will examine how these low concentrations of antibiotics affect the evolution of bacterial populations. He will specifically look at the evolution of *Escherichia coli*, a harmless bacterium that can be found in animal and human guts. However, some strains of this bacterial species are responsible for infectious diseases such as urinary tract infections, neonatal meningitis and hemorrhagic diarrhea.

A new experimental approach has been developed at INSERM to observe the physiological state and mutations induced by subinhibitory concentrations of antibiotics in individual living bacterial cells. The expected results will be useful for the pharmaceutical industry for designing new drugs with a low risk of developing resistance.

In 2007, 400,000 people living in Europe were infected with multidrug-resistant bacteria, which resulted in 2.5 million extra days spent in the hospital and 25,000 deaths. In order to combat this major public health and economic problem, public health organizations need such knowledge to regulate drug use.

Doctor Andrew Silvanus
Postdoctoral Fellow
Université de Versailles Saint-Quentin-en-Yvelines (France)
€60K (1 year)

ANTIBIOTIC RESISTANCE: FINDING NEW DRUGS FASTER

Pharmacodiversity oriented synthesis: a new tool for the rapid discovery of treatment for multidrug-resistant bacteria

The threat posed by drug-resistant bacteria and other microbes is increasing as new strains emerge. Yet, major pharmaceutical companies are not seeking new drugs to fight back. Dr. Andrew Silvanus is developing a faster, easier method of screening candidates for potential new "superdrugs": starting with natural substances containing molecular structures already known to fight infection, tweaking them in a variety of ways, and testing the results. Silvanus's work has the potential to accelerate vital antibiotic discovery.

Doctor Agata Starosta
Postdoctoral Fellow
Ludwig-Maximilians-Universität München (Germany)
€120K (2 years)

A NEW ANGLE ON ANTIBIOTICS

Development of novel antibiotics to overcome multi-drug-resistant bacteria: elongation factor P and the virulence pathway

The hunt for new antibiotics is in need of new targets. Instead of aiming to neutralize basic bacterial functions, Dr. Agata Starosta hopes to block their virulence, or ability to cause disease. Her lab has discovered a protein that is necessary for many bacteria to become pathogenic. By studying in detail the steps in this process, the structure of this new factor and how it operates with other molecules, her work could provide the basis for new drugs that attack these pathogens from a new angle.

Doctor Ofir Cohen
Postdoctoral Fellow
Weizmann Institute of Science (Israël)
€120K (2 years)

GETTING THE BETTER OF ANTIBIOTIC RESISTANCE

Studying multi-drug resistance implications of anti-sense-based regulatory structures in bacteria

As bacterial resistance to antibiotics is growing, Dr. Ofir Cohen aims to tackle this serious problem by exploiting a recently discovered switch mechanism capable of turning off certain bacterial genes. In particular, it seems to control genes associated with multi-drug resistance. By cataloguing these switches and their functions in multiple microorganisms, Cohen has shown that they are widespread across species and could provide an avenue to treat infections caused by dangerous bacteria that have already become resistant.

Victoire de Lastours
PhD Fellow
Université Paris Diderot (France)
€120K (3 years)

BACKSTABBING GERMS

Impact of fluoroquinolones on human commensal flora: dynamics of bacterial resistance and changes of the intestinal microbiota

To effectively cope with antibiotic resistance, Victoire de Lastours is studying commensal bacteria and exploring the mechanisms linked to emergence of resistance to antibiotics in the gastrointestinal tract, normal skin and nasal flora.

Doctor Adi Stern
Postdoctoral Fellow
Weizmann Institute of Science (Israël)
€60K (1 year)

STRIKING BACTERIA'S ACHILLES' HEEL

Inducing autoimmunity in bacteria

Just like humans, bacteria boast a sort of immune system that protects them from viruses. And, as for us, it can sometimes turn against them in an autoimmune reaction. Could we take advantage of this bacterial Achilles' heel to weaken these pathogens and make them more vulnerable to drugs? Dr. Adi Stern aimed to do just that by characterizing in detail this newfound bacterial system. In a world where antibiotic resistance is increasing, the ability to activate autoimmunity in bacteria would have critical applications.

Doctor Dipanwita Biswas
Postdoctoral Fellow
Université Joseph Fourier Grenoble 1 (France)
€120K (2 years)

A NEW APPROACH TO QUANTIFY THE EVOLUTION OF PARASITES

A synthetic system of molecular co-evolution

It is difficult to develop vaccines for human parasites such as HIV, influenza and hepatitis C because both the parasites and the immune system of the host evolve quickly. Dr. Dipanwita Biswas seeks to quantify the degree of predictability of this co-evolution by setting up a controlled model system that mimics the evolutionary dynamics between influenza and its host. Her results could help advance the development of vaccine design strategies that take viral mutations into account before they actually occur.

Marie Pohl
PhD Fellow
Institute of Medical Virology (Switzerland)
€120K (3 years)

SIDESTEPPING FLU RESISTANCE TO EXISTING DRUGS

Host factors for influenza A virus entry as novel drug target

To sidestep the increasing resistance of influenza A virus to existing drugs, Marie Pohl is targeting the human factors used by the virus to enter the cell. Drugs that block these factors may prove useful against flu and other viruses.

David Lebeaux
PhD Fellow
Institut Pasteur (France)
€120K (3 years)

LET'S CLEAN THE SURFACE

Antibiotic resistance in biofilms formed by pathogenic bacteria

65% of hospital-acquired infections, which claim 7,000 deaths in France every year, are due to agglomerates of bacteria that form on surfaces. David Lebeaux is studying the genetic mechanisms of their resistance to antibiotic treatments.

Doctor Pedro Coelho
Postdoctoral Fellow
Instituto Gulbenkian de Ciência (Portugal)
€120K (3 years)

THE RECYCLING OF ANTIBIOTICS

Loss of robustness as the key to drug repositioning

250,000 people die every year in the European Union because antibiotics could not cure their infection, due to a strong resistance of bacteria to different drug treatments. This is why Dr. Pedro Coelho will study bacteria that have lost robustness by changing their genetic code. Certain genes could be fragile, and therefore become new targets for existing drugs. His findings could lead to new treatments of infections that represent millions of human or animal cases around the world.

Clémentine Garrouste
PhD Fellow
Paris School of Economics (France)
€120K (3 years)

HOW MOTHERS-TO-BE WEIGH THE RISKS OF AMNIOCENTESIS

Pregnant women choices regarding the prenatal diagnosis of Down syndrome (amniocentesis)

Amniocentesis involves weighing the risk of giving birth to a child with Down Syndrome against the risk of losing a healthy child through an amniocentesis-related miscarriage. Clémentine Garrouste is examining how pregnant women handle this dilemma.

Benoît Robisson
PhD Fellow
INSERM (France)
€120K (3 years)

RIDDING DRUGS OF UNDESIRED SIDE EFFECTS

Predicting moonlighting proteins to prevent drug side effects

Undesired side effects, which threaten both patients and pharmaceutical companies, sometimes occur when a drug designed for a particular purpose affects proteins carrying unexpected functions. Benoît Robisson aims to identify such moonlighting proteins.

DEFEATING THE TROJAN HORSE OF MALARIA BEFORE IT ATTACKS

AXA Project

Malaria vaccines: a rational path toward identification of protective pre-erythrocytic stage vaccine candidates

Professor Robert Menard
Institut Pasteur (France)
€358K (3 years)

While malaria has been wiped out in many parts of the world, the disease continues to ravage and kill victims in Africa and Southeast Asia, causing an estimated 627,000 fatalities a year according to the World Health Organization. The complexity of the life cycle of the malaria parasite helps explain why scientists have not yet developed a vaccine to protect malaria victims, some 80% of whom are children. Now though, a research team headed by Prof. Robert Menard is seeking to uncover the still mysterious workings of the malaria parasite and in so doing, provide the fundamental understanding needed for vaccine development.

Widely recognized for his groundbreaking work stalking and even filming the malaria parasite in real time as it invades the human body, Menard is now focusing on the critical first step of the disease, when the Trojan Horse of malaria has entered the body but not yet launched its destructive cycle. This is when the malaria parasite is injected in the skin and enters the human bloodstream from a mosquito's saliva, but before it has reached the liver. Once the parasite reaches the liver, it infects and kills liver cells, then returns to the bloodstream to infect and kill red blood cells and the disease takes its often deadly toll.

Research has shown that it is possible to disrupt the parasite's life cycle during the relatively short first stage, and therefore prevent the ensuing attack on the red blood cells. But existing research results are merely empirical; no one yet understands how the mechanism works. This is what Menard and his team want to figure out and why their approach is so interesting. Understanding exactly how and why certain antigens protect against the malaria parasite would provide the fundamental knowledge needed to develop a vaccine.

What's more, using powerful molecular genetics and imaging techniques, Menard aims to take the process even further by actually testing antigens individually and evaluating their respective effectiveness. The goal is to identify the most effective antigen for use as the foundation for the malaria vaccine that has eluded medical science for so long.

Doctor Petra Klepac
Postdoctoral Fellow
University of Cambridge (UK)
€120K (2 years)

CONTROL OF IMMUNIZING INFECTIONS

International cooperation in disease control in the face of evolutionary risks

In our increasingly interconnected world, control and elimination of infectious diseases requires international and regional coordination of efforts. Dr. Petra Klepac's research combines epidemiological dynamics with the game theory of international agreements to find ways to increase cooperation and reach the regional vaccination coverage necessary for efficient control of infectious diseases and possibly their elimination. Results may impact public health, with relevance for both human and animal diseases.

Olivier Le Polain De Waroux
PhD Fellow
London School of Hygiene and Tropical Medicine (UK)
€120K (3 years)

MODELING THE PNEUMOCOCCAL DISEASE

Pneumococcal vaccination strategies for crisis-affected populations

Olivier Le Polain de Waroux is using mathematical models of pneumococcal disease transmission to explore different vaccination strategies on the burden of pneumococcal disease, based on data collected in Vietnam and Uganda. His findings may help populations who remain inadequately protected.

Doctor Nicholas Croucher
Postdoctoral Fellow
Harvard University (USA)
€120K (2 years)

UNDERSTANDING THE CLONING STRATEGY OF THE ENEMY

Population genomics of emerging pneumococcal clones in a vaccinated community

Dr. Nicholas Croucher is on the tracks of *Streptococcus pneumoniae*, a.k.a pneumococcus, a bacterium causing diseases such as pneumonia, septicemia and meningitis, which result in hundreds of thousands of deaths all over the world. Over past decades, several "clones" of this species have become resistant to antibiotics, and some have evolved to bypass recent vaccination efforts. Croucher will study how these "clones" evolve and adapt in response to such clinical interventions.

Doctor Nele Goeyvaerts
Postdoctoral Fellow
Universiteit Hasselt (Belgium)
€120K (2 years)

ALERT: CONTAGIOUS VIRUS DETECTED!

Mass action and contact network models for social mixing in infectious disease transmission modeling

The way people interact is crucial to understand the path taken by a disease in order to assess efficient containment strategies, according to Dr. Nele Goeyvaerts. She will link for the first time two different mathematical models to simulate person-to-person disease spread, one assuming people mix completely and randomly and one where each person becomes a node in a contact network. Her innovative approach may help to improve models of epidemic dynamics and produce effective tools for intervention.

Doctor Francesco Checchi
Postdoctoral Fellow
London School of Hygiene and Tropical Medicine (UK)
€60K (1 year)

HOW RUMORS CAN PREVENT THE SPREAD OF INFECTIOUS DISEASES

Improved detection of emergent infectious disease threats in the aftermath of armed conflicts and natural disasters

Almost 90% of the largest epidemics recorded worldwide between 1994 and 2004 occurred in settings of armed conflicts or natural disasters. Nowadays, according to Dr. Francesco Checchi, the design of Early Warning Alert and Response (EWARN) surveillance systems, particularly in emergencies, should rely on immediate alert and reporting instead of formal, heavily data-driven approaches. Checchi's field and desk-based evaluations of surveillance systems in Pakistan and elsewhere informed the new WHO guidelines for EWARN in emergencies.

Monica Cepoiu-Martin
PhD Fellow
University of Calgary (Canada)
€120K (3 years)

CARE SETTINGS: WHAT IS AT STAKE FOR THE ELDERLY?

Policy options for improving the quality of mental health care for seniors in long-term care and assisted living

Monica Cepoiu-Martin is analyzing factors that influence decision makers responsible for shaping the continuing care for seniors with mental health issues. Her evaluation of current policies and their outcomes may improve future policy options.

Doctor Sophia Latham
Postdoctoral Fellow
University of Liverpool (UK)
€120K (2 years)

INFECTIOUS DISEASE OUTBREAKS: WHEN TECHNOLOGIES BRING NEW UNCERTAINTY

New technologies - new uncertainties: the impact of emerging technologies on the management of infectious disease outbreaks

In an increasingly connected world, infectious diseases can spread rapidly amongst populations. Dr. Sophia Latham is studying how new technologies impact the decision-making process to restrict the impact of emerging infectious diseases. She has decided to focus on the additional uncertainty brought by new technologies, which can make decisions more complex and the outcomes less predictable. Her findings may facilitate better decision making, thus improving health, welfare and trade conditions.

HOW CAN PRIVATE LONG-TERM CARE INSURANCE SUPPLEMENT STATE SYSTEMS? THE UK AS A CASE STUDY

AXA Project

Professor Raphael Wittenberg
London School of Economics (LSE) (UK)
€300K (2.5 years)

Long-term care financing is a hot political issue in the United Kingdom. But what role can private insurance play in the future? Prof. Raphael Wittenberg and his colleagues have conducted a study to help decision makers address this question.

The number of people over age 65 is projected to rise by about 50% in the next 25 years in the United Kingdom, while the number aged 80 and over is set to more than double. This has raised concern over the future affordability of long-term care and pensions, fueling a debate about the appropriate balance between public and private funding.

So far, private long-term care insurance has not been very successful in the UK. There have been few enrollees in such products and most of the providers have ceased to offer them. "One problem seems to be that insurance products have not proved easy to price, because future trends in health and disability are uncertain. Another issue is that the publicly funded system is complicated, which may lead people to believe mistakenly that social care is free at point of use rather than means tested," explains Wittenberg.

Wittenberg and his colleagues at the PSSRU at the London School of Economics, Nuffield Trust, University of East Anglia and University of Barcelona, have been studying, with AXA Research Funding, the role private insurance could play in the future: how long-term care products could interact with state funding, what the expected life-time costs of care could be for older people, possible premiums and pay-outs and their attractiveness, and estimates of social care expenditure under different financing schemes. They have estimated, for example, that the average life-time costs of care for a person turning 65 in the UK in 2015 may be in the range £20,000 to £25,000 for a man and £40,000 to £50,000 for a woman without taking account of inflation.

They have reviewed published literature and consulted experts on long-term care insurance, looking at barriers, opportunities, and in particular what is or isn't working in other countries, and conducted extensive modeling. Their findings, many of which they presented at a successful workshop in January 2014, are expected to benefit decision makers in the private and public sectors.

Doctor Bity Diene
Postdoctoral Fellow
Université du Luxembourg (Luxembourg)
€40K (1 year)

HOW OLD DO YOU BUY?

Age-specific mortality, health and economic growth: an endogenized life expectancy

One's economic behavior strongly depends on age. Dr. Bity Diene aims to link age-related processes, such as demographic changes or saving and consuming behaviors, with public policies. Studying both developing and developed countries, Diene is analyzing national public health policies and their implications for individuals' economic behavior and growth. She may help us better understand how the ongoing changes in age-specific mortality influence economic dynamics both at individual and national levels.

Matthew Tye
PhD Fellow
University of Oxford (UK)
€120K (3 years)

ENTERING THE HOME TO LEARN HOW HOUSEHOLD DYNAMICS AFFECT AGING

Increasing longevity in Vietnam: strategies for long-term care – the intergenerational contract

As older populations continue to grow, we must better understand the factors that affect the well-being of the elderly. Matthew Tye will examine formal and informal care and support structures in Vietnam, including intergenerational relationships.

Alejandro Del Valle Suarez
PhD Fellow
Paris School of Economics (France)
€120K (3 years)

LESSONS FROM A MEXICAN REFORM

Essays on welfare and social protection. The impact of universal health insurance on welfare: evidence from Mexico's Seguro Popular

Alejandro del Valle Suarez is analyzing the labor market effects of government-subsidized health insurance. He has found that these programs improve the health of children while inadvertently encouraging women to join the labor force.

NOTES

APPENDIX

GLOSSARY

AGING AND LONGEVITY

Alpha-synuclein protein
A protein of unknown function found in the human brain that, in its dysfunctional form, is linked to neurodegenerative diseases like Parkinson's.

Autophagy
The process that deals with destruction of cells in the body, maintaining normal functioning by protein degradation and turnover of the destroyed cells' organelles for new cell formation.
Source: News-Medical.Net

Biomarkers
A measurable characteristic that indicates the severity or presence of a disease.
Source: Wikipedia

Free radicals
Atoms or molecules with an unpaired electron exposed in the outer shell, making them highly reactive with other substances.

Genome expression
Process by which the information contained in the genetic material of an organism (the genome) is turned into functional products, usually proteins.

Life expectancy
The number of years an individual is expected to live, according to statistical estimates taking into account sex, physical condition, occupation, etc.
Source: The Free Dictionary

Mitochondria
Structures within our cells that produce energy for cellular processes. They also contain their own genetic material.

Nanomaterials
Materials whose individual units have at least one dimension in the size range of 1 to 100 nanometers.

Oxidative damage
Damage that occurs in cells due to the action of highly reactive molecules (free radicals) interacting with and destabilizing its components.

Oxidative stress
Physiological stress on the body caused by the cumulative damage of highly reactive molecules (free radicals) inadequately neutralized by antioxidants; believed to be associated with aging.
Source: Merriam Webster

Progenitor cells
Early descendants of stem cells that can differentiate to form one or more kinds of cells, but cannot divide and reproduce indefinitely, and are often more limited than a stem cell in the kinds of cells they can become.
Source: Boston Children's Hospital

Receptor TGR5
A detection molecule on the cell surface triggered by bile acids. It is involved in inflammation related to hardening of the arteries, as well as insulin sensitivity and glucose regulation.

Sleep pressure
The feeling of need for sleep.

Stress damage
Accumulated damage to the components of cells caused by highly reactive molecules insufficiently neutralized by antioxidants; oxidative stress.

Supramolecular chemistry
A discipline at the interface of chemistry, physics, biology and medicine that views matter not as a collection of individual atoms, but as complex structures where molecules interact and create new properties. Understanding these processes in nature may allow them to be reproduced with simpler, man-made molecules.
Source: Luisa De Cola, cf. p. 34

HEALTHY LIFESTYLE

Arthroplasty
A surgical procedure to restore the integrity and function of a joint. A joint can be restored by resurfacing the bones or an artificial joint, called a prosthesis, may be used.
Source: Johns Hopkins Medicine Health Library

Bisphenol A
A carbon-based, synthetic compound found in certain plastics, used for consumer goods, and epoxy resins, used for the coating on the inside of food and beverage cans.

Circadian clock
A biochemical mechanism that provides organisms with an internal biological clock. It runs on a 24-hour cycle that coordinates with the day-night cycle and drives the circadian rhythm.

Circadian rhythm
A cycle, usually of 24 hours, in the physiological processes of living beings. Although naturally "built-in," it can be modulated by external factors such as sunlight or temperature and helps determine sleep, eating and other patterns linked to daily biological activities.

Circadian system
Complex regulatory network that influences the circadian clock and circadian rhythm of an organism.

DNA methylation patterns
Patterns of methylation on the DNA strand. Methyl groups are added to certain nucleotides of DNA, which can stably alter and regulate gene expression. When methylation occurs on a gene, it is turned off.

Gene
A gene is the basic physical and functional unit of heredity. Genes, which are made up of DNA, act as instructions to make molecules called proteins. Every person has two copies of each gene, one inherited from each parent.
Source: Genetics Home Reference

Macular degeneration
The progressive deterioration of a critical region of the retina called the macula. This disorder leads to irreversible loss of central vision, although peripheral vision is retained.
Source: The Free Dictionary

Nutrients
Nourishing substances used by organisms to survive, grow and repair themselves.

PER3
One member of a group of genes involved in circadian rhythms of locomotor activity, metabolism, and behavior.
Source: National Center for Biotechnology Information

Stem cells
A simple cell in the body that is able to develop into any one of various kinds of cells, such as blood cells, skin cells, etc.
Source: Merriam-Webster

NON-INFECTIOUS DISEASES

Angiogenesis
The process through which new blood vessels form from pre-existing vessels.
Source: Wikipedia

Centrosome
A cell structure that organizes filaments in the cytoplasm known as microtubules, elements of the cytoskeleton involved in cell division and movement of products within the cell.

Endothelium
The thin layer of cells that lines the interior surface of blood vessels.

Epigenetic marks
Features not directly governed by the genetic code, which include methylation of DNA and covalent modification of histone proteins. These groups modify the function of the tagged proteins and influence the way genes are expressed.
Source: Epigenesys

Epigenetic pattern
Patterns of epigenetic marks. They show which genes are turned “on” or “off.”

GDH (Glutamate dehydrogenase)
An enzyme involved in the metabolism of pancreatic beta cells and the secretion of insulin.

Genomic instability
Refers to a high rate of mutations in the DNA, a feature common to most cancers.
Source: Thomas Helleday, cf. p. 55

Glycemia
The concentration of glucose in the blood.
Source: News-Medical.Net

Homeostasis
The tendency of an organism or a cell to regulate its internal conditions, usually by a system of feedback controls, so as to stabilize health and functioning, regardless of the outside changing conditions.
Source: Biology Online

Homologous recombination
The process through which nucleotide sequences are exchanged between two similar or identical molecules of DNA. It is most widely used by cells to accurately repair harmful breaks that occur on both strands of DNA, known as double-strand breaks.
Source: Wikipedia

iPS cells (Induced pluripotent stem cells)
Adult cells that have been genetically reprogrammed to an embryonic stem cell-like state by being forced to express genes and factors important for maintaining the defining properties of embryonic stem cells.
Source: NIH Stem Cell Basics

K-Ras oncogene
The protein product of the normal K-Ras gene performs an essential function in normal tissue signaling. The mutation of a K-Ras gene can turn it into an oncogene—one with the potential to cause cancer.
Source: Wikipedia

Magnetic nanoparticles
A class of nanoparticles that can be manipulated using a magnetic field.

Meiosis
A special type of cell division necessary for sexual reproduction in eukaryotes, such as animals, plants and fungi, leading to the production of sperm and eggs.
Source: Wikipedia

Nanoparticles
A microscopic particle with at least one dimension less than 100 nm.
Source: Science Daily

Nanotechnology
The engineering of functional systems at the molecular scale.
Source: Center for Responsible Nanotechnology

Neurogenic detrusor overactivity
Bladder dysfunction resulting from a neurological condition, such as spinal injury or multiple sclerosis, that impairs communication between the bladder and the central nervous system, leaving the brain unable to regulate the detrusor muscles controlling urination.

Oncogene
A gene that has the potential to cause cancer.

Plasticity
The phenomenon allowing cells to undergo changes that transform them into other cell types. Although a normal part of development, one potential consequence of these cellular modifications is cancer.

Protein P53
A protein that acts as a tumor suppressor. It regulates cell division by keeping cells from growing and dividing too fast or in an uncontrolled way.
Source: Genetics Home Reference

Reprogramming
The erasing and remodeling of epigenetic marks, such as DNA methylation, during mammalian development.
Source: Wikipedia

Somatic cells
Specialized cells making up all tissues of the human body that have acquired a proper identity (blood cells, neurons, etc.) during embryonic development.
Source: Maria Blasco, cf. p. 59

T-cells
A type of white blood cell that is of key importance to the immune system and is at the core of adaptive immunity, the system that tailors the body's immune response to specific pathogens.
Source: MedicineNet

Telomeres
The segments at the end of each chromosome arm that regulate chromosomal replication at each cell division. Some of the telomere is lost each time a cell divides, and eventually, when the telomere is gone, the cell dies.
Source: Genetics Home Reference

Tracheostomized
Having undergone a tracheostomy, the creation of an opening through the neck, into the trachea, through which a tube may be inserted to maintain an effective airway and help a patient breathe.
Source: The Free Dictionary

Transduction pathway
A series of molecules, one activating the next, that allows a cell to sense a signal in its environment, transmit it to the inside of a cell, and trigger an appropriate response.

INFECTIOUS DISEASES

Antigenic variation
The mechanism by which an infectious organism alters its surface proteins in order to evade a host immune system response.
Source: Wikipedia

CD4 T-cells
A kind of white blood cell of the human immune system whose main role is to send signals of an invasion to other immune cells, which will attack the infectious particle.

Dendritic cells
Cells of the mammalian immune system that take up foreign particles invading the body and process them for presentation on the cell surface—a signal that will activate other cells to launch an immune response.
Source: Matthew Collin, cf. p. 72

HTLV-1
A retrovirus implicated in several kinds of disease, including a very aggressive form of leukemia and a neurological disorder.

Listeria
A genus of 10 species of bacteria, including *Listeria monocytogenes*, a major human pathogen that causes listeriosis, a serious, foodborne infection.

Periodontitis
A set of inflammatory diseases affecting the tissues surrounding and supporting the teeth. It is caused by microorganisms that adhere to and grow on the tooth's surfaces, along with an overly aggressive immune response.
Source: Wikipedia

Nutrients
Nourishing substances used by organisms to survive, grow and repair themselves.

Pathogen
An infectious agent, like a virus, bacterium or fungus, that can produce a disease in its host.

Trypanosoma
A group of single-celled parasites that require more than one host to complete a life cycle. They are most often transmitted by blood-feeding insects.

Zoonosis
An infectious disease that can be transmitted from animals to humans, or vice versa.

NEUROSCIENCE, RISKY BEHAVIORS AND ADDICTIONS

Autism
A general term for a group of complex disorders of brain development, characterized by difficulties in social interaction, verbal and non-verbal communication and repetitive behaviors. It can be associated with intellectual disability, difficulties in motor coordination and attention.

Nanomaterials
Materials whose individual units have at least one dimension in the size range of 1 to 100 nanometers.

Neuronal plasticity
Changes in neural pathways and synapses in the brain due to changes in behavior, environment, and neuronal processes.

Prefrontal cortex
Area of the brain situated at its front, just behind the forehead, in charge of abstract thinking, thought analysis and regulating behavior.

HEALTH POLICIES

Antigens
Any substance that causes your immune system to produce antibodies against it. An antigen may be a foreign substance from the environment (chemicals, bacteria, viruses, pollen), or be formed within the body, as with bacterial toxins.
Source: MedlinePlus

Commensal bacteria
Bacteria living in a symbiotic relationship with a host where the bacteria benefit, while the host is unaffected.

Escherichia coli
A group of bacteria, most strains of which are harmless, while others can cause serious infections of the urinary or respiratory tract, meningitis, diarrhea and others.

Moonlighting proteins
Proteins with more than one unique function.

Streptococcus pneumoniae
A bacterium causing diseases such as pneumonia, septicemia and meningitis that result in hundreds of thousands of deaths all over the world.
Source: Nicholas Croucher, cf. p. 99

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