

L'ORÉAL-UNESCO  
FOR WOMEN IN SCIENCE  
*2018*

20 AREAS OF  
SCIENTIFIC  
CHALLENGE  
YEARS FOR WOMEN IN SCIENCE





# SUMMARY

## *20 areas of scientific challenge*

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# EDITORIAL

## *20 years For Women in Science*

Science advances along a continuum, with discoveries large and small made through careful investigation or by chance in all corners of the world. These combine to increase our understanding of physical and biological processes, enabling us to uncover new ways of confronting challenges or even opening entirely new frontiers. Global connectivity has accelerated the discovery process, the dissemination of knowledge and the application of breakthroughs to make a difference in people's lives. New opportunities to fight disease, generate clean energy and enhance computing power have equipped scientists with new tools and energized their research.

In human health, discoveries in genomics and immunology at the end of the 20<sup>th</sup> century paved the way for tremendous progress in fighting disease over the past two decades. For example, the identification of more than 40 genes involved in breast cancer, including BRCA1&2 breast cancer suppressor genes, sparked research leading to a whole new classification of malignant diseases. These were based not on where the tumor was located, but rather on its genetic characteristics, and as a result, to targeted therapeutic approaches. Similarly, triple antiretroviral therapy based on new understanding of immune system behavior succeeded in bringing viral loads down to

undetectable levels in people infected with HIV. These breakthroughs have significantly improved survival rates: by 2014, AIDS-related deaths were down by 42% from their peak in 2004. Unprecedented global efforts were initiated to make therapy available worldwide, increasing the possibility of eradicating the disease.

International collaboration to solve problems increased as the global nature of the problems became clear: whether the threat involves biodiversity, air quality or influenza, actions in one part of the Earth have broad repercussions and demand new, concerted approaches. The World Wide Web provided an appropriate structure for global scientific collaboration, and computing power has increased exponentially since IBM's Deep Blue took the chess championship away from Garry Kasparov in 1997.

By 2003, an international consortium of scientists had completed the mapping of the human genome. Just four years later, the cost of sequencing an individual genome was under \$1,000. Genetic analysis is bringing new understanding to virtually all discovery areas, from agriculture to anthropology. Used on a series of remarkable recent paleontological discoveries, it is redefining the evolutionary history of the Earth's inhabitants, including humans.

Just as tools become available to appreciate the origins and properties of flora and fauna, the diversity of species is threatened by resource depletion, pollution and global warming. Scientists are playing a key role in cataloguing and investigating the properties of plants, work that may offer some protection against the destruction of fragile ecosystems. Some of the greatest repositories of plant genetic diversity are located in poorer countries; collaboration at a regional and global scale is helping to promote conservation.

Geographic interdependence has been matched, over the past 20 years, by a growing interdependence between scientific domains and the development of new territories at their interfaces. For example, information produced through genetic analysis can only be understood through advanced computing, which in turn requires ever stronger and lighter materials. The development of graphene, recognized with the 2010 Nobel Prize for Physics awarded to Konstantin Novoselov and Andre Geim, is now opening up entirely new possibilities for nanomaterials required for quantum computing.

We also see the growing importance of domains such as information technology and social sciences, which are vital to understanding the human condition, as well as the reasons for and consequences of human activities.

In this 20<sup>th</sup> year of the L'Oréal-UNESCO *For Women in Science* programme, we considered

the scientific production of the past two decades. We selected 20 areas of scientific challenge that have manifested over the past 20 years, attracting the skills and efforts of the world's leading scientists. Many of these scientists are women, and a number of them have been recognized with the L'Oréal-UNESCO *For Women in Science* Award. They work on all five continents, in biological and physical science, and are changing the world not only through their discoveries, but also by acting as role models to encourage more women to pursue their scientific aspirations.

These laureates' achievements have contributed significantly to scientific understanding of the world's pressing



*Professor Niveen Khashab, 2017 Laureate for Africa and the Arab States*



*Professor Indira Nath, 2002 Laureate for Asia-Pacific*

challenges. Their diverse intellectual capabilities are helping to solve the great social, economic and environmental issues of our time. Unfortunately, research is still deprived of the creative talents and diverse intellectual perspectives of half of humanity.

The research explored in the following pages ranges from the tiny cellular components of the human body to the dark matter of the universe, and addresses some of the most significant threats in the world today. Human health occupies a large space in scientific endeavors. Cancer, heart disease, pain and brain disorders such as Alzheimer's disease are high priorities in countries with aging demographics. Mosquito-borne diseases are significant concerns in the southern

hemisphere — a threat that gained global attention with the Zika virus two years ago — and are creeping northwards with the effects of climate change. Epidemics and pandemics keep scientists on high alert, particularly for viruses that jump from bird or animal species to humans. The phenomenal progress of the past two decades in HIV is also explored, along with the research it prompted in immune function more generally. In this respect, cancer therapies are now increasingly relying on immune system management. Additionally, we consider progress made in the development of new drugs and drug delivery systems.





*Professor Adeyinka Gladys Falusi, 2001 Laureate for Africa and the Arab States*

The evolution and perpetuation of the human race is an area where scientific discovery raises untold ethical and philosophical questions. We look at how scientists are approaching the challenge of hereditary diseases, particularly in places where populations tend, for reasons of social cohesion or isolation, to intermarry. We also look at reproduction, which has been progressively demystified through scientific advances with in vitro fertilization, gene editing and cloning (of species other than humans, for the moment). These advances are taking place at a time when the history of the human species is being rewritten thanks to genetic analysis of newly discovered remains, some of which have been preserved until recently under the permafrost. We are also witnessing the development of artificial intelligence as computers become so adept at processing different forms of information that they begin to learn independently and, it turns out, somewhat differently than humans.

On Earth, challenges of food security, biodiversity and pollution are closely interrelated. Climate change is placing additional pressure on scientists to find ways to preserve and improve agricultural production as land becomes less hospitable, reduce environmental pollution, and produce and store clean electricity efficiently using advanced materials. By 2017, India and China had become the top producers of solar and wind power. Experimentation on Earth is also unveiling some of the mysteries behind Earth's creation, with scientists at CERN finding evidence in 2012 of the Higgs Boson elementary particle that is considered responsible for creating mass in the universe.

We will explore discoveries that have contributed to advancing science in the 20 challenge areas. In each section, we introduce



*Professor Beatriz Barbuy, 2003 Laureate for Latin America*

you to some of the women scientists in medicine, biology, genetics, chemistry, astronomy and physics whose work has been recognized by the L'Oréal-UNESCO *For Women in Science* Award each year since the programme was inaugurated in 1998. You will meet Professors Jennifer Doudna and Emmanuelle Charpentier, who, in a transatlantic partnership, developed the CRISPR/Cas9 gene editing system; Professor Hualan Chen from Harbin China, whose research has brought innovative vaccines

against bird flu; Professor Jill Farrant from South Africa, whose work on resurrection plants brings hope for drought-resistant crops in Africa; and Professor Ameenah Gurib-Fakim, who inventoried medicinal plants on Mauritius, created the Centre for Phytotherapy Research and, in 2015, was elected President of Mauritius. These researchers, and the many others you will encounter here, are each determined to put their talents to work to preserve and improve life on Earth.



*Professor Deborah S. Jin, 2012 Laureate for North America*



# HIV/AIDS<sup>1</sup>

20 years ago, the AIDS epidemic was reaching its peak: HIV/AIDS was the leading cause of death worldwide in people aged 15 to 59; almost 25 million people had died from AIDS, and 40 million — over one percent of the global population — were living with HIV, including almost 2 million children (1, 2). In the developed world, treatment was still centered around AZT (zidovudine), which caused significant side effects and only kept the disease at bay temporarily. In the rest of the world, people succumbed quickly to the opportunistic infections, cancers, and wasting diseases their immune systems were unable to fight. People with HIV were barred from entering many countries, including the United States.

A major turning point occurred in 1996 when, at the Vancouver International AIDS Conference, Canadian pulmonary specialist Dr. Julio Montaner announced stunning results with a combined therapy of three anti-HIV drugs — AZT, didanosine, and nevirapine — that rendered the virus undetectable (3). People close to death with severe infections saw their viral load drop sharply and were literally able to get up from their hospital beds and resume their lives. Drug development over the next decade brought further improvements, as scientists achieved a better understanding of how the virus hijacks healthy cells, and found ways to stop its propagation and achieve lasting control. Today, treatment of HIV infection for many people consists of one pill a day, with minimal side effects. There is, however, still no definitive cure, and multiple vaccine trials have yet to produce a candidate for widespread use.

HIV/AIDS provoked revolutionary change in scientific enterprise. Research into how HIV evades and hampers immune response opened up entirely

new possibilities for the treatment of cancers and other diseases. People living with HIV demanded and won a place in research, changing the way clinical trials are run and improving access to experimental drugs. Education and prevention achieved new status as essential weapons to fight disease. And powerful new mechanisms for international collaboration accelerated scientific exchange, as well as improving access to treatments across the globe.

## *Know thine enemy*

The human immunodeficiency virus (HIV) was identified as the cause of the acquired immune deficiency syndrome (AIDS) in 1983 by virologists Françoise Barré-Sinoussi and Luc Montagnier at the Institut Pasteur in France (4). They were investigating retroviruses involved in a form of leukemia when they were asked to look at the possible role of a retrovirus in an alarming new, unknown disease that appeared to be aggressively affecting large numbers of homosexual men. Barré-Sinoussi spent months observing cells from a biopsy to understand how the virus emerged from cells, was transmitted into blood lymphocytes, and then replicated. She presented her findings on the virus at the US Centers for Disease Control and Prevention (CDC) in May 1983, enabling a link to be made between HIV and AIDS, and paving the way for the first diagnostic tests. Barré-Sinoussi continued her research on HIV at the Institut Pasteur, becoming head of the Retroviruses Unit in 1992. She and Montagnier, along with American virologist Frank Gallo, were awarded the 2008 Nobel Prize in Physiology or Medicine for their seminal contribution to combatting HIV/AIDS.



*Professor Quarraisha Abdool Karim, 2016 Laureate for Africa and the Arab States*

Barré-Sinoussi served as President of the International AIDS Society from 2012 to 2014.

## *Scientific activism and global collaboration*

Preventing or slowing the spread of HIV has presented challenges of a different kind. An enormous number of HIV/AIDS scientists have advocated for policy change, education, and community engagement, and have brought their expertise to low income countries, where the epidemic has been most devastating. Support for international efforts has come from both established and new global initiatives. UNAIDS was formed in 1996, bringing together different branches of the United Nations, along with the World Health Organization (WHO) and World Bank, to coordinate response, build technical capacity within countries, and identify international best practices in HIV prevention and care. Global surveillance has helped to identify emerging trends in the epidemic and mobilize resources. The Global Fund to Fight AIDS, Tuberculosis and Malaria, a public-private partnership established in 2002 with seed funding

from the Bill and Melinda Gates Foundation, has supplemented these efforts. Beginning in 2003, the US President's Emergency Plan for AIDS Relief (PEPFAR) has helped make HIV drugs available to poor countries and supported the establishment of counseling and prevention programs.

Over the past ten years, the drive to expand treatment availability has gained momentum as evidence accumulates that antiretroviral drugs dramatically reduce and even prevent transmission. The UN Millennium Goal of halting and reversing the spread of HIV/AIDS was reached in 2015, when mortality and infection rates reached a 20-year low (5). The previous year, the WHO reported that AIDS-related deaths had declined by 42% since their peak in 2004, with new infections among children halved to 220,000 (5). In 2014, more than 14 million people received anti-retroviral therapy (ART), a number climbing to 18 million by 2016 and 19.5 million by summer 2017 (5,6). WHO credits the development and global scale-up of access to ART as one of the most successful public health interventions of recent times. In many African countries, however, HIV



“Now is not the time to slow down responses or investments to the epidemic. If we don’t act, we could reverse the gains made to date.”

Professor Quarraisha Abdool Karim, 2016 Laureate for Africa and the Arab States

remains a powerful threat with an adult prevalence of 4.5% in 2014, compared to 0.5% in the Americas (6).

At the July 2017 International AIDS Conference on HIV Science in Paris, **Professor Quarraisha Abdool Karim**, Associate Scientific Director of the Centre for the AIDS Program of Research in South Africa (CAPRISA) warned attendees that “now is not the time to slow down responses or investments to the epidemic. If we don’t act, we could reverse the gains made to date” (7). **Professor Abdool Karim, a L’Oréal-UNESCO Laureate in 2016** for her invention of a tenofovir-based microbicide gel protecting women against HIV, joined other international science and policy leaders at the Paris Conference to launch the End AIDS Coalition, which aims to completely end the AIDS epidemic by 2030. The Coalition has identified five priorities for coming years: vaccine research, simpler ART drug formulations, research towards a functional or complete cure, funding models to apply strategies universally, and preventive and therapeutic measures tailored to at-risk groups (8).

A vaccine is, of course, the ultimate goal, but progress on this front has been slow. “*The whole problem with HIV compared to other viruses,*” says Biochemist Pamela Bjorkman, Professor at the California Institute of Technology, “*is that there are thousands or millions of strains even in a single*

*infected person. The virus mutates rapidly, making it really hard for the immune system to keep up.*” Studying a rare subset of HIV-infected people who make antibodies that neutralize more than 50 percent of available strains, Bjorkman uses powerful microscopes to identify features in the antibodies that could be used in a vaccine. In 2010, her team hypothesized that the distance between the antigen targets on the surface of HIV are too far apart to allow the Y-shaped antibody to hold on once mutation begins (9).

“*In 2015, we published a paper showing we could make artificial antibodies where the two arms of the “Y” are separated by the right distance that cross-link between the spikes on the surface of HIV and remain attached even if the virus mutates*” (10). These agents showed potent effects and Bjorkman’s team is now seeking to develop them for therapeutic use. **Bjorkman** combines biochemistry expertise with x-ray crystallography, electron microscopy, and 3D imaging techniques in her laboratory to better understand how the immune system recognizes viral targets. She **received the L’Oréal-UNESCO Award For Women in Science in 2006** in recognition of this work, which has had a major impact on cancer and auto-immune disease as well as HIV.



Professor Quarraisha Abdool Karim, 2016 Laureate for Africa and the Arab States

### Research by women to empower women in AIDS prevention

Putting prevention in the hands of women is central to addressing the challenge. Professor Abdool-Karim co-founded CAPRISA (Centre for the Aids Programme of Research in South Africa) in 2002, at the height of a period of AIDS denialism in South Africa. In partnership with Columbia University, with whom Abdool-Karim has collaborated since 1998 to build the science base in South Africa, CAPRISA undertakes globally relevant and locally responsive research into HIV pathogenesis, prevention, and epidemiology. Her team’s work on the SApiT trial of TB-HIV treatment shaped international guidelines on the clinical management of co-infected patients. Currently Vice-President,

Southern African region, of the African Academy of Sciences, Abdool Karim is committed to developing capacities to conduct scientific research and implement research findings in Africa. A primary preoccupation is designing sustainable strategies to introduce ART and prevention strategies in settings constrained by socio-cultural factors and resource shortages. Abdool Karim considers reaching teenage girls as key to accelerating progress against HIV/AIDS, and works closely with South African educational and family planning centers to equip young women with the tools they need to prevent infection. She also serves as Chair of the PEPFAR Adolescent Girls and Young Women Expert Working Group, part of the effort to share promising practices internationally.



Professor Pamela J. Bjorkman, 2006 Laureate for North America

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## 2 GENE EDITING

When it comes to disruptive technologies, genome editing far surpasses even home computing, offering the prospect of changing the very essence of everything from the food we eat to the characteristics of species, including humans. Basic understanding of genetic engineering dates back to ancient times, as evidenced in the domestication of any number of animals and plants. Watson and Crick discovered in 1953 that DNA forms a double helix, and Paul Berg developed a recombinant DNA (DNA from two species in the same molecule) technology in 1972. Since then, scientists have sought tools to manipulate genes in the laboratory, in order to produce changes more rapidly than through selective breeding. The 1980s saw plants (starting with tobacco) modified to become resistant to herbicides and pests, and mice genetically modified to study human diseases. Golden Rice, genetically altered to provide more Vitamin A, was developed in 2000.

The advent of genetically-modified organisms prompted a heated, ongoing debate around the benefits and risks for food production. Today, new genetic engineering technologies with potential for widespread application in humans are opening up an even more consequential questioning around the ethics of altering not just one individual's genetic structure, but the genomic inheritance of a whole population. While working towards eliminating diseases such as cystic fibrosis, sickle-cell anemia and muscular dystrophy from the human genome may appear as welcome progress, uncertainties remain about how these specific genes interact with other genes, and whether they could confer benefits in other areas. The sickle-cell gene, for example, is known to decrease susceptibility to malaria and is more prevalent in populations where malaria is endemic.

The completion of The Human Genome Project in 2003 prompted the formation that same year of the ENCODE (Encyclopedia of DNA Elements) international project to understand these functional relationships in the human genome. A first gene editing system, the Zinc Finger nucleases, was identified in 1991 (1) and was used to edit cultured cells in plant and animal models, essentially by removing or adding highly targeted DNA sequences. However, it was complex, expensive and known to make inaccurate cleavages of target DNA. In 2011, the TALEN system brought some improvements. However, the excitement and trepidation that now defines discourse around genetic engineering arose in 2012, with the development of CRISPR/Cas9, which has proven highly efficient in human, animal and plant cells, and is now used widely in genome manipulation experiments (2).

### *Transatlantic collaboration*

This latest precision gene-editing tool came to life when two scientists working on either side of the Atlantic Ocean discovered a way to replicate the mechanism used by particular bacteria to identify and remove the DNA of intruding viruses. **Professor Jennifer Doudna**, a structural biologist at the Howard Hughes Medical Institute and University of California at Berkeley, started looking at intriguing repeating sequences found in the genetic code of bacteria, known as “clustered regularly interspaced short palindromic repeats”, or CRISPRs. **Professor Emmanuelle Charpentier**, working in Europe, was analyzing pieces of bacterial DNA involved in drug resistance that moved around the genome and between cells. She became intrigued by the way *Streptococcus*



*Professor Emmanuelle Charpentier, 2016 Laureate for Europe*

*pyogenes* (a bacterium responsible for sore throats) defended itself against viruses that were attacking it. She found CRISPR sequences containing pieces of DNA that the bacteria had taken from the invading virus to immunize itself against further attack. Investigating how the bacteria managed to identify and remove a precise DNA sequence, Charpentier suspected that there may be interaction between RNA (ribonucleic acid) and DNA at the CRISPR site, an improbable hypothesis that was nevertheless confirmed through experimentation. A guide RNA containing the memorized intruder did, in fact, guide the Cas9 enzyme to destroy the particular DNA sequence of the virus. This finding led her, the following year, to collaborate with Professor Doudna on the development of the CRISPR/Cas9 system now employed in laboratories around the world. **Doudna and Charpentier were co-recipients of the 2016 L'Oréal-UNESCO Award For Women in Science** and, in 2015 won the Breakthrough Prize in Life Sciences, with significant funding from internet entrepreneurs including the heads of Apple, Facebook and Google.

Doudna and Charpentier recognized that the system raised ethical concerns. Within months of the publication of their results in 2012 (2), research papers from around the world were being submitted on different uses of CRISPR/Cas9 for genome engineering: in zebrafish, to improve pesticide resistance in wheat, in mouse studies of human diseases, and in monkeys, where it was shown that genetic changes made in embryos were evident in all cells, including eggs and sperm, and would therefore be passed on to future generations. Both scientists have become increasingly engaged in framing responsible use of the technology. In 2015, Doudna organized a meeting of scientists and bioethicists to discuss how genomic engineering could affect different domains. The group called for broad societal debate on the use of the technology and urged fellow scientists to refrain from using the technology to modify human embryos.





*Professor Jennifer Doudna, 2016 Laureate for North America*

“Over the next decade, I expect us to refine our understanding and use of CRISPR in a manner that allows us to drastically improve the lives of millions of people.”

*Professor Jennifer Doudna, 2016 Laureate for North America*

At the same time, they continue to help other scientists understand how to integrate CRISPR/Cas9 technology into their work. Currently, laboratories around the globe are using the system to edit T cells in mice so they attack cancerous tumors more effectively; to create malaria-resistant mosquitoes; to provide bananas with resistance to fungus; and even to reconstruct the evolution of species. Jennifer Doudna is pleased to see the rapidly evolving field of CRISPR gene editing benefiting human health, the environment and the economy. *“In biomedicine, CRISPR is advancing our ability to treat and potentially cure genetic diseases. For non-human applications, researchers are harnessing CRISPR in creative ways to develop more robust and nutritious food sources. Over the next decade, I expect us to refine our understanding and use of CRISPR in a manner that allows us to drastically improve the lives of millions of people.”*

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*Professor Jennifer Doudna, 2016 Laureate for North America*



# 3 CANCER

Hippocrates, the ancient Greek founder of western medicine, gave cancer its name after observing the crab-like shape of non-ulcerating tumors. 2,000 years later, the mystery of how cancer grows and spreads continues to challenge scientists. Since the pathological study of tumor tissue began a few hundred years ago, the naked human eye has been empowered by ever more powerful microscopes and imaging technologies, a process that accelerated with the development of x-rays in the early 20<sup>th</sup> century. Traditional theories that cancer spread through bodily liquids gave way to an understanding of the cellular replication processes involved in metastasis. Treatment strategies were developed and refined over time with techniques for minimally invasive surgery, targeted radiotherapy, and chemical methods of hormone blockade. Now, a steadily increasing number of chemotherapies show some success in reducing tumors, but produce highly varied responses from one person to the next, often with severe side effects.

At the turn of this century, the pace of cancer research began to increase dramatically, with funding rising to counter the projected health burdens of population aging. Over these last two decades, scientists in many fields, from medicinal chemistry and molecular genetics to microscopy and material science, have profoundly changed our basic understanding of cancer. The result is a vastly improved prognosis for patients and the promise of progress in avenues of new research for years to come.

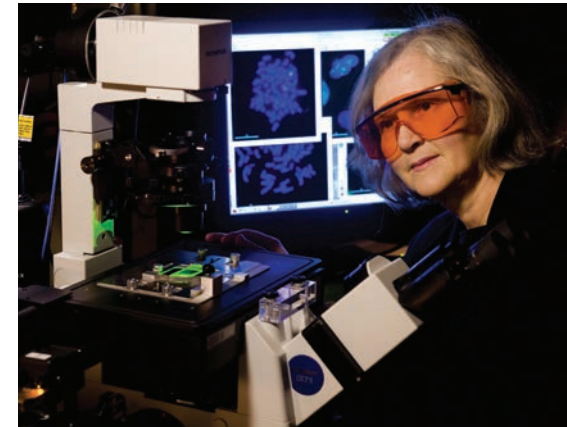
### *Cancer reclassified*

Until 1998, cancer was categorized based on the site at which the tumor first developed: people had breast cancer, stomach cancer, and so on, with the

understanding that these cancers could then spread to other parts of the body, most frequently the bones, lungs and liver. This approach received a major challenge in 1999 when Dr. Clara Bloomfield examined molecular characteristics of two cancers, leukemia and lymphoma, and discovered they were heterogeneous diseases requiring different treatment (1). The molecular defect found in one subgroup of leukemia patients was then so effectively counteracted by the drug imatinib that the US Food and Drug Administration (FDA) approved it just three months into the 2001 clinical trial (2). Dr. Bloomfield went on to receive the 2006 American Society for Clinical Oncology (ASCO) Distinguished Service award, and the WHO incorporated cytogenetics into its classification of these cancers in 2008 (3).

Proteins have become important in distinguishing cancer subtypes and providing targets for treatment. In 1999, the monoclonal antibody Herceptin was shown to dramatically increase survival in women with a particularly virulent form of breast cancer that leads to overproduction of the HER2 protein (4). At the time, molecular genetics was discovering chromosome translocations and genetic changes that were important in both promoting the survival of cancer cells and causing their proliferation. Along with colleagues at the University of Melbourne, Australia, **Professor Suzanne Cory**, a medical biologist, put these insights to work in understanding how immune responses are regulated by apoptosis, the natural programme of cell death. She has continued her research into how cells decide whether to live or die.

The risk of cancer increases as we age, and a better understanding of the mechanisms involved in age-related risk provides hope of preventing cancer along with other age-related diseases. Telomeres



*Professor Elizabeth H. Blackburn, 2008  
Laureate for North America and 2009 Nobel  
Prize in physiology or medicine.*

are the protective tips at the end of chromosomes, which carry genetic material. As we age, telomeres wear down and are less able to protect chromosomes, making them more likely to malfunction and reducing their ability to replenish cells. **Professor Elizabeth Blackburn**, President of the Salk Institute for Biological Studies in San Diego until 2017, was awarded the Nobel Prize in Physiology or Medicine in 2009, alongside Professor Carol Greider from Johns Hopkins University, for their discovery of telomeres and telomerase in 1985. Telomerase is an enzyme that can slow and partially reverse damage to telomeres, and its levels are influenced by stress, exercise, nutrients and potentially new therapies. As a pioneer in the field of telomere biology, Professor Blackburn has opened up new possibilities for preventing age-related diseases such as cancer. Her work was recognized with the **L'Oréal-UNESCO Award For Women in Science in 2009**.

### *Cancer genetics*

Our emerging understanding of cancer is based on what two pioneering researchers, Hanahan and Weinberg, described to in 2000 as the six “hallmarks” cells acquire as they evolve to a cancerous state — self-sufficiency in growth signals; insensitivity to growth-inhibitory signals; evasion of programmed cell death; limitless replicative potential; sustained angiogenesis; and tissue invasion and metastasis (5, 6). Each of these capabilities opens up possibilities for thwarting

cancer development and progression, as well as suggesting potential targets for therapies.

After 2003, the world’s scientists gained free access to the complete mapping of the three billion DNA letters in the human genome sequenced by the 13-year international Human Genome Project. In cancer, attention has since been focused on discovering the structure of specific proteins and their role in the development of pathologies. This is a key step to identifying medications to impede their progress. A succession of drugs has been developed and tested to target mutations in specific proteins identified through “companion” tests that diagnose cancer based on its molecular structure.

### *Targeted and personalized therapies*

Building on the accomplishment of the Human Genome Project, the International Cancer Genomics Consortium began work in 2008 to describe genomic, transcriptomic, and epigenomic changes in 50 different tumor subtypes. By 2013, more than 200 types and subtypes of cancer had been recognized, and the stream of new knowledge and therapies continues to flow (7). Progress is being made in immunotherapy, with checkpoint inhibitors targeting proteins central to immune suppression producing durable response in a number of cancers. The antibody ipilimumab has displayed the ability to stimulate the immune system to attack cancer cells by removing a “brake” that controls immune response. The number of new treatments is also increasing rapidly: in 2014 alone, four new drugs were approved for chronic lymphocytic leukemia, while three new drugs were approved in 2015 for advanced non-small cell lung cancer, all targeting PD-1 and PD-L1 immune checkpoint proteins (8,9). Over the past ten years, personalized cancer treatment has become feasible: the genome of a specific tumour can now be decoded in a couple of days at a manageable cost and used to guide therapy. In the United States, the cancer death rate has fallen by 25% since the 1990s: two out of three patients now live at least five years after a cancer diagnosis (10).





“These new drugs have already produced huge benefits to patients, combatting the disease more effectively without producing crippling side effects on normal cells.”

Professor Suzanne Cory, 2001 Laureate for North America

For Professor Cory, now the Director of the Walter and Eliza Hall Institute of Medical Research in Melbourne, the announcement in April 2016 of the FDA approval of venetoclax for the treatment of certain patients with chronic lymphocytic leukemia (CLL) was a historic milestone. “The approval capped nearly 30 years of research that began when David Vaux, then a PhD student with Jerry Adams and myself at the Walter and Eliza Hall Institute, discovered that a protein called B-cell lymphoma 2 or BCL2 prevents physiological cell death. This discovery, published in *Nature* in 1988, represents the first realization that mutations blocking cell death contribute to cancer development (11). Today, venetoclax is being used in over 40 clinical trials for many types of cancer.”

Cory received the L’Oréal-UNESCO Award For Women in Science in 2001 for her contributions to our understanding of the genetic basis of cancers. Today she says: “Cancer genetics is providing a much deeper understanding of the molecular drivers of individual types of cancer and has led to the development of drugs specifically targeting these changes. These new drugs have already produced huge benefits to patients, combatting the disease more effectively without producing crippling side effects on normal cells.”

The genetic era has raised as many questions as it has answered. A central challenge today is in redesigning research and treatment systems to enable a next stage of discovery and translate that

to clinical benefit. This process involves international collaborations to identify subgroups of patients whose tumours have particular genetic characteristics likely to respond to a particular antibody. The payback will be seen in response rates much closer to 100 percent than the 30 to 50 percent that has in the past been sufficient to set a new gold standard for treatment.

**Immunofluorescence microscopy to improve cancer treatment**

Cancer is now understood as the endpoint of a progressive transformation of normal cells into malignant tumour cells. Visualizing the processes that occur within and between cells during this transformation is the foundation of recent progress. Working at the Max Planck Institute for Biophysical Chemistry in the German city of Göttingen, Professor Mary Osborn has developed immunofluorescence microscopy to enable observation of the intra- and inter-cellular mechanisms of disease, and identified certain proteins as useful markers in distinguishing tumor types and refining patient treatment. Professor Osborn received the L’Oréal-UNESCO Award For Women in Science in 2006 in recognition of the important applications made possible by her research.

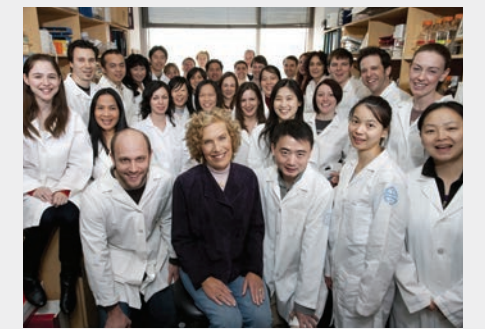
**Advancing therapy**

In 2010, two scientists received the L’Oréal-UNESCO Award For Women in Science for their contributions to advancing cancer therapies. At INSERM in Paris, molecular biologist Professor Anne Dejean-Assémat discovered that a protein — the retinoic acid receptor — is mutated in liver cancer, as well as in certain forms of leukemia and Hepatitis B infection. Her findings contributed to advances in differentiation therapy, where the objective is to turn the cancer cell back onto a non-malignant path rather than destroy it. Scientists at INSERM, where Professor Dejean-Assémat is Director of the Laboratory of Nuclear Organization and Oncogenesis, are now looking at features of the cell’s environment to identify exogenous as well as endogenous processes that enable anomalous cells to survive, grow, and metastasize.

Across the Atlantic at New York City’s Rockefeller University, cell biologist Elaine Fuchs was recognized for her work on the ways stem cells in the skin communicate with immune and other cells, and how this communication can malfunction, enabling cancer cells to hijack the mechanisms that stem cells rely on to replenish dying cells and repair wounds. Fuchs pioneered a reverse genetics technique exploring protein function and the consequent evolution of the disease, in order to uncover the genetic basis of a number of skin cancers.



Professor Anne Dejean-Assémat, 2010 Laureate for Europe



Professor Elaine Fuchs, 2010 Laureate for North America

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## 4 HEREDITARY DISEASE

Close-knit communities offer a number of advantages in terms of social cohesion, mutual support and the perpetuation of cultural traditions. They can also bring increased health risks as the genetic pool, including genes responsible for certain diseases, is restrained. In the Canadian province of Québec, for example, people in the Saguenay region have extremely high incidence of four genetic diseases that are very rare in other parts of the world. One in every 22 people carry one copy of the genetic mutation for autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS), which causes often crippling leg stiffness, developmental delays and neuropathy, among other symptoms. The mutation is thought to originate in one or several of the few thousand original French settlers who colonized New France in the 17<sup>th</sup> century. The region remained isolated for centuries and, while large families assured growth, the population is strikingly homogenous even today (1-4).

The area is now one of several hot spots around the world for scientific exploration of hereditary diseases. These populations offer tremendous opportunities to study the involvement of genetic mutations in common health problems as well: the mutation for spastic ataxia also appears to play a role in Parkinson's disease. In essence, the study of tight-knit communities is enabling significant progress on understanding gene-gene and gene-environment interactions as contributors to disease. Advances in genomic sequencing make it possible to identify genotype-phenotype correlations focusing on autozygosity, which is the hallmark of consanguinity: being descended from the same ancestors.

### *Consanguinity in Arab countries*

The population of the Saguenay region in Quebec presents a relatively rare example of consanguinity in the New World. However, it is estimated that over 1 billion people currently live in countries where consanguineous marriages are customary (5), notably across the Arab World. In 2003, the Centre for Arab Genomic Studies (CAGS) was established to characterize and prevent genetic disorders in Arab countries based on recent advances in human genetics. **Lihadh Al-Gazali, Professor of Clinical Genetics and Pediatrics** at the United Arab Emirates (UAE) University, pioneered genetics research in the region in the 1990s, work that **was recognized in 2008 when she received the L'Oréal-UNESCO Award For Women in Science**. Her interest was piqued by the numerous children with hereditary disorders she saw in her native Iraq and in the United Kingdom where she worked with a tight-knit Pakistani community during her training in pediatrics. The counseling service she established when she settled in the United Arab Emirates (UAE) in the 1990s was a precocious step towards integrating genetics into a conservative Arab society.

Al-Gazali has worked to characterize disorders common in the UAE and established a registry to monitor birth defects in the country. With collaborators at the CAGS and internationally, she has identified more than 40 autosomal recessive disorders that appear specific to the UAE (6). The CAGS report from 2012 found that 60% of genetic disorders in the Arab world were autosomal recessive, and over 25% were autosomal dominant. Almost 35% involve congenital malformations and chromosomal abnormalities. Half appear to occur in a single Arab country or population (7). Several disease conditions, such as hemoglobin disorders, hypertension, diabetes mellitus, and Down



*Professor Lihadh Al Gazali, 2008 Laureate for Africa and the Arab States*

Syndrome have reached epidemic proportions in the region.

In neighboring Tunisia, **Habiba Bouhamed Chaabouni, Professor of Medical Genetics** at the University of Tunis, has identified cultural, economic, geographic and other factors associated with consanguineous marriages. The country's consanguinity rate is 32% and genetic disorders are a national health problem. Importantly, she finds that marriages within a community, even when the spouse is not directly related, also produce high level of homozygosity, likely as longstanding patterns increase the genetic similarity among individuals in these communities. Chaabouni undertook genetic testing in the families of children with given autosomal recessive diseases, including familial Mediterranean fever, spinal muscular atrophy, hearing loss and Bardet-Biedel Syndrome. Taken altogether, in related couples, homozygous genotype was found in 97.5% of patients with one of the diseases; in unrelated couples, homozygous genotype was found in 70.5% (8).

### *Genetic counseling: finding the appropriate approach*

Chaabouni, who **received the 2006 L'Oréal-UNESCO Award For Women in Science**, established Tunisia's first genetic counseling service in 1981. In a country such as Tunisia, where the population is well educated and abortion of an affected fetus is legal, genetic counseling and prenatal diagnosis can play a significant role in reducing the incidence of hereditary diseases. In the UAE, Al-Gazali likewise established a genetics clinic and began diagnosing disorders and providing counseling. Working in a context where abortion is illegal raises important challenges and renders education on genetics, and an understanding of its role in diseases, all the more important, both among the general public and health professionals. Pre-implantation genetic diagnosis, using technology similar to in vitro fertilization, provides an option, though it is costly and not always effective. CRISPR-Cas9 gene editing may one day open further possibilities.



“In the next decade, work in the vast field of epigenetics will very likely enable us to identify the switches that control gene activation and suppression. This brings hope for treating a great number of genetic diseases.”

*Professor Habiba Bouhamed Chaabouni, 2006 Laureate for Africa and the Arab States*

Chaabouni and Al-Gazali recognize the pressing need to raise public awareness and address ethical, legal and social issues that may arise from genetic applications. Within that is the challenge for the scientific community to gear their efforts to understanding the balance between the risks and benefits of consanguinity.

Scientists in the Arab region are now collaborating closely through the CAGS to assemble an open access database of genetic diseases that will enable a better understanding of hereditary diseases, train health professionals in diagnostic techniques and establish modern laboratory facilities. Pioneers such as Chaabouni and Al-Gazali are playing an important role in creating the academic infrastructure to develop expertise in research and counseling in Arab countries.

Chaabouni fully expects genome sequencing to remain in the headlines over the next decade, and hopes that the technology will be democratized, so that it can be made available in less wealthy countries. “The mastery of tools for the correction of detected anomalies and their clinical consequences in individual carriers will depend on the precision of this genomic knowledge,” she says. “And scientific interest does not stop at the structure of the gene,” she emphasizes. “There is equal attention to the intracellular mechanisms that modify gene expression. In the next decade,

*work in the vast field of epigenetics will very likely enable us to identify the switches that control gene activation and suppression. This brings hope for treating a great number of genetic diseases.”*

However, Chaabouni insists that prevention of hereditary diseases will remain the most accessible and economical means of improving public health. “Educating populations and building awareness among health professionals is essential,” she insists. “Pertinent genetic counseling can mean more to a family than months of laboratory research. Clinical genetics and genetic counseling are the best messengers to link scientific research with its beneficiaries.” Chaabouni is driven to reduce the suffering that arises when genes express themselves negatively. “My career in science,” she says, “has been guided by three fundamental duties: to understand the situation in front of me, whether in the hospital, the laboratory or the classroom, and figure out its cause; to transmit knowledge and information to the appropriate individuals; and to come up with a solution adapted to the particular case, according to the means available.”



*Professor Habiba Bouhamed Chaabouni, 2006 Laureate for Africa and the Arab States*

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# 5 BRAIN DISORDERS

Degenerative brain diseases have an enormous impact: memory, thought, behavior and the ability to talk and move can all be compromised. Neuroscience seeks to understand how the brain processes the constant stream of information about our environment, and makes enough sense of it to respond appropriately. Brain cells in the outer layer of the brain receive and integrate thousands of inputs from different regions of the brain, using electrical and chemical signals to communicate. Brain disorders occur when signals are blocked or garbled in these communication channels. Understanding these channels and the neurons responsible for making sense of information is key to improving the lives of people with problems ranging from mental illness to addiction, epilepsy, the effects of stroke and brain injury, along with degenerative diseases like Alzheimer's.

Given the challenges of an aging population, an opioid epidemic and the effects of mental illness on the productivity and well-being of societies, brain research has finally become a priority. In 2013, the G7 launched a Global Action Against Dementia, committing to increase funding and collaboration on research with a goal of finding effective therapies by 2025 (1). In the same year, former US President, Barack Obama, launched the Brain Initiative, which focuses on the development of new tools to study the brain (2). The Human Brain Project in the UK and Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative in the US are working to build a computer model of the brain and map the dynamic activity of the brain's 86 billion neurons. In 2016, the International Brain Initiative was announced at the United Nations General Assembly, uniting scientists, government, foundations and private companies to accelerate progress (1).

As part of the US BRAIN Initiative, researchers at the Allen Institute of Brain Science are working with mice to develop a usable database categorizing all the different neurons in the brain. Lydia Ng, director of technology for the database, expects that modeling the cell types to see how they are put together will enable scientists to understand all the activity involved in perceiving something and acting on that perception (3). Hongkui Zeng leads the Allen Mouse Connectivity Atlas project, combining molecular, anatomical and physiological approaches to decipher the brain's circuitry and enable development of approaches to treat brain diseases and disorders. Using light microscopy, Dr. Zeng has already noted interesting patterns and variations in the intensity of connections between brain regions, which could yield valuable future research paths (4).

**Neurobiologist Brigitte Kieffer at the Douglas Institute Research Center, McGill University, Montréal, Canada,** sees a future where knowledge gained about brain circuitry from animal studies, combined with imaging studies in human populations, will lead to far more targeted diagnosis and treatment of all types of brain disorder, from depression to addiction to Alzheimer's disease. *"The problem with the brain,"* she says, *"is that we cannot be invasive and diagnose a problem based on biological samples; we rely on psychological evaluations that reveal symptoms, not the biological causes. Efforts today aim to address the biology of brain diseases by exploring what happens at the level of neuronal communication. In particular, we aim to understand how neurons form brain networks or circuits that coordinate their activities to produce behaviour. From there, we should be able to develop treatments that target dysfunctional circuits involved in producing specific symptoms."*



Professor Christine Van Broeckhoven, 2006 Laureate for Europe

## **Alzheimer's disease**

Alzheimer's disease was first described in 1906 by Dr. Alois Alzheimer, who associated memory loss and psychological changes in a patient with abnormalities noted during autopsy in the nerve cells in brain. Alzheimer's progressively destroys the synapses that enable communication between neurons and eventually kills the neurons. As people live progressively longer lives, it is now one of the major health and social challenges worldwide. The most recent estimated figures (2015) published in the World Alzheimer Report (1) suggest that there are 46 million people living with dementia today, a figure that is set to increase to 131.5 million by 2050. Almost half of those with Alzheimer's require high levels of care (5), often for many years.

Despite its early description, it was only in the late 1970s and 80s that Alzheimer's was recognized as the most common form of dementia. An international association, the Alzheimer's Association, was founded, and more recently, research into the disease has gained significant momentum. Current treatment approaches target

the buildup of amyloid plaques, similar to those seen in the brains of people suffering with Down's Syndrome. These appear to arise from a genetic mutation in a particular protein (see below: Finding mutations). Drugs that are currently in use or being tested in clinical trials aim to prevent or reduce the production of these beta-amyloid proteins, suggesting that we may at least be able to delay the progression of the disease.

At the 2017 Alzheimer's Association International Conference in London, Researchers Against Alzheimer's reported an increasing number of drugs under development, approximately half of which target amyloid build-up in the brain, with the other half focusing on neurotransmitter activity and inflammation. The current expectation is that combining these approaches may offer far better results than the modest effects observed with existing drugs. There is a sense of optimism that within ten years, science will have developed an armamentarium with which to combat this disease.





“Efforts today aim to address the biology of brain diseases by exploring what happens at the level of neuronal communication.”

Professor Brigitte Kieffer, 2014 Laureate for Europe

#### Addiction

The communication channels involved in neurodegenerative diseases also play a significant role in addiction. Research has succeeded, over the past 20 years, in identifying the molecular sites involved in all the main drugs of abuse, from heroin and cocaine to alcohol and nicotine, and understanding the chemical reward systems such as dopamine and noradrenaline that are activated in addiction. In 1992, Brigitte Kieffer, neurobiologist and Scientific Director at Montreal’s Douglas Institute Research Centre, was the first to clone and isolate the gene for an opioid receptor in the brain, opening an entire research field geared toward understanding the molecular basis of opioid-controlled behaviours. This enabled major advances in pain, addiction and mood disorder research. **Kieffer was elected a member of the French Academy of Sciences in 2013, and received the L’Oréal-UNESCO Award For Women in Science in 2014.** At the Kieffer Laboratory, newly established at the Douglas Research Centre, her team is combining non-invasive brain imaging and in vivo molecular imaging to connect neuronal signaling with brain network activities. In particular, they are seeking to identify where and how receptors control neuronal signaling and functional connectivity in the living brain to regulate behaviour.

A major challenge in translating these advances into clinical benefit lies in the current lack of connection between problem diagnosis based on a broad range of symptoms, and the far more specific influence of different signaling pathways. Kieffer welcomes current efforts to re-classify mental disorders into subdimensions of behavior that correspond with known neurobiological processes. *“Take motivation, for example. Many psychiatric diseases involve motivational deficits, and neuroscience has discovered many of the neurotransmitters and networks important to motivation. It may be interesting to identify and target motivational deficits, and their biology, as one of the potential biological problems, when one wants to understand and develop treatments for addiction or depression. This is where the field is heading.”*

#### Finding mutations

As leader of the Neurodegenerative Brain Diseases group at the Flanders Interuniversity Institute for Biotechnology in Belgium, molecular geneticist **Christine van Broeckhoven** collaborates with networks of neurology researchers internationally to uncover the genetic causes of dementia. **She received the L’Oréal-UNESCO Award For Women in Science in 2006** for her significant contributions to investigating the genetic bases of neurodegenerative disorders. She won the European Inventor Award in 2011 for developing new methods of identifying genes and proteins in Alzheimer’s sufferers that may serve as therapeutic targets. Chromosome 21 was an early focus of exploration,

(6) and earned her the Potamkin Prize in 1993, awarded by the American Academy of Neurology and considered the “Nobel Prize of Alzheimer’s research”. The award recognized her discovery that patients with Down’s Syndrome (who have three rather than the normal two copies of chromosome 21) developed amyloid plaques similar to those observed in Alzheimer’s disease. Through her later work, van Broeckhoven discovered a mutation in the amyloid precursor protein genes on chromosome 21 (7). In Alzheimer’s patients, this mutation causes proteins to aggregate in brain tissue. This discovery is an important step in identifying drugs to prevent or stop progression of the disease.



Professor Christine Van Broeckhoven, 2006 Laureate for Europe

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# MOSQUITO-BORNE DISEASES <sup>6</sup>

When we think about the deadliest animals in the world, mosquitoes may not come immediately to mind, but their ability to spread disease causes millions of deaths every year. These vector-borne diseases account for more than 17% of all infectious diseases, from malaria to dengue and yellow fever. Mosquitoes are certainly not the only vectors — ticks and sandflies also have the ability to transmit pathogens and parasites — but they are by far the most common and dangerous. In the face of challenges such as drug-resistant malaria, the increasing incidence of dengue, and the appearance of new diseases such as the Zika virus, the WHO regards improved measures for mosquito control as the best line of defense (1).

However, after widespread use of insecticides reduced the public health threat posed by mosquitoes in the late 1960s, control programmes were reduced or abandoned. Recent efforts to regain a degree of control face the additional challenges of resistance to insecticides. Furthermore, changing land use and rising temperatures are expanding hospitable environments for mosquitoes. As a result, the worldwide incidence of dengue fever has risen 30-fold over the past 50 years (2,3), for example.

Dengue virus is spread by mosquitoes and, at its most severe, causes fatal hemorrhagic fever. Children are particularly susceptible to severe disease. There are currently no drugs available to protect against dengue. Dengue fever has not attracted the attention of viruses that are more prevalent in developed countries, although the situation is changing as the disease expands and the worst-affected countries become viable markets for drug therapies. Research is underway to understand mechanisms involved in the

transmission of the virus and its impact on human cells.

## *Zika draws global attention*

Zika is drawing attention to the complex relationships between viruses. Recent mouse studies have found that mice with antibodies to dengue or West Nile virus suffer more severely from infection with the Zika virus (4). Zika is not new: the virus has made sporadic limited appearances since 1947. Neither was it, until the most recent outbreak in Brazil, considered very threatening. But something — and many suspect interaction with dengue — was causing far more serious damage to the fetuses of infected mothers, resulting in microcephaly (small brains and heads) and the development of Guillain-Barré, a severe neurological complication.

Zika is the first mosquito-borne disease known to cause a birth defect, and the challenge of caring for babies born with Zika-induced microcephaly will be a major concern in the years to come. The virus is also associated with miscarriage and stillbirth. In February 2016, WHO proclaimed Zika a public health emergency. The disease has continued to spread internationally, although Zika is no longer considered a threat of “international” concern (4). Approaches to addressing the spread and effects of the virus run the gamut from mosquito control to guidance and support for families with affected children. It is estimated that half the world’s population is exposed to the mosquito species, *Aedes Aegypti*, which carries both the Zika and dengue virus, and few of these people are immune to the disease.



*Professor Andrea Gamarnik, 2016 Laureate for Latin America*

## *Why dengue affects humans and not the mosquitoes that transmit the virus*

Working at the Molecular Virology Laboratory, Fundación Instituto Leloir, in Buenos Aires, Argentina, **molecular virologist Andrea Gamarnik** is leading research into the behavior of dengue virus as it cycles between mosquitoes and humans. In research published in 2017, she and her colleagues found that the dengue virus evolves a mechanism to regulate the production of viral non-coding RNAs differently in mosquitoes and humans, with a significant impact on the strength of the virus in each host (5).

In research to identify potential antiviral targets, Gamarnik’s laboratory has characterized elements of the dengue RNA genome and proteins that permit virus entry into host cells. It is expected that improving response to dengue will require a combination of efficient antivirals and therapies aimed at cellular targets. **Gamarnik was awarded a national fellowship by the L’Oréal-UNESCO For Women in Science programme in Argentina in 2009 and went on to become a 2016 L’Oréal-UNESCO Laureate in 2016.** It was

recognized that her work had potential applications in Zika virus that had just emerged as a new and frightening threat.

*“The Zika virus was an enormous challenge for the scientific community”* says Gamarnik. *“We did not know how the virus was transmitted, we did not have any diagnostic tools, and the neurological complications in newborns were completely unexpected.”* Scientists quickly learned that Zika was not only transmitted by mosquitoes, but also through sexual contact, and from mother to child. *“Information about different aspects of Zika virus pathogenesis was generated by unprecedented international collaboration,”* she stresses. *“In my laboratory, we focused on understanding the molecular mechanisms of Zika virus replication in the infected cell. That generated a lot of information about the molecular biology of the virus; what’s most exciting is that strategies to control Zika virus are now in place.”*



“Information about different aspects of Zika virus pathogenesis was generated by unprecedented international collaboration.”

*Professor Andrea Gamarnik, 2016 Laureate for Latin America*

### Malaria

Another mosquito, Anopheles, is primarily responsible for transmitting malaria parasites. Approximately 30 of the nearly 500 species of Anopheles mosquitoes are vectors of major significance. According to the WHO, an estimated 219 million people worldwide were infected by malaria in 2010, and 660,000 died (6). The disease is widespread in tropical regions, with approximately 90% of cases occurring in Africa. Encouragingly, the number of deaths dropped by 30% between 2010 and 2015, with even more impressive decreases in children under five. Rapid diagnostic testing, introduced widely over the past decade, has made it easier to distinguish swiftly between malarial and non-malarial fevers, enabling timely and appropriate treatment. Artemisinin-based combination therapies are highly effective against the most prevalent and lethal types of malaria (6,7).

The story of artemisinin’s discovery is a reminder that the natural world holds solutions to most of the problems it creates, if we have the patience to find them. Tu Youyou studied traditional Chinese medicine and was recruited to lead a secret project commissioned by Chairman Mao Zedong in 1967 to find a cure for malaria. She led her team on a quest through over 500 ancient books and discovered that sweet wormwood had been used in malaria around 400 AD. Tu also found ancient references to how the wormwood should be prepared to activate the artemisinin. She tested the resulting drug on herself first before releasing it

into clinical trials, and published results anonymously in 1977. In 2015, Tu Youyou won the Nobel Prize for Physiology or Medicine. She has neither a medical degree nor a doctorate, and has never worked outside China (8).

### Mosquito control

Mosquito control is the primary way to prevent and reduce transmission of these diseases. Larvae can be killed by reducing standing water or treating water with larvicides. Insecticide-treated mosquito nets are the cornerstone of malaria prevention efforts. Over the last five years, the use of treated nets in sub-Saharan Africa has increased significantly: in 2015, an estimated 53% of the population at risk slept under a treated net, compared to 30% in 2010 (9).

Due to mosquito’s increasing resistance to insecticides, and the dangers of insecticides to human health, scientists are investigating alternatives such as naturally occurring toxins that affect the insect but not plants or people (see Box). Most recently, the states of Florida and California have been experimenting with the release of male mosquitoes (*Aedes Aegypti*, the carrier of the Zika virus) that carry a bacterium that prevents mosquito eggs from hatching. The aim is to make the species infertile. In an unexpected turn of events, Google has joined the effort in California, in an effort to take their debugging skills beyond software into the insect world (10).



*Professor Alejandra Bravo, 2010 Laureate for Latin America*

### Finding alternatives to insecticides

**Dr. Segenet Kelemu**, a biologist and plant pathologist, leads the International Centre for Insect Physiology and Ecology (ICIPE), based in Nairobi, Kenya. ICIPE serves as one of the regional centers of the Stockholm Convention to minimize the use of organic pollutants in the management of disease vectors in Africa. The Convention is an international treaty that came into effect in 2004, with funding from the European Union and the Convention Fund. **Recognized with the L’Oréal-UNESCO Award For Women in Science in 2014**, Kelemu’s aim is to develop vector control strategies that do not pollute the environment or induce resistance, and are affordable to populations across Africa.

In Mexico, **Alejandra Bravo, Laureate 2010 and Professor at the Institute of Biotechnology in Cuernavaca**, is looking to naturally occurring Cry toxins from strains of *Bacillus thuringiensis* that could serve as substitutes for chemical insecticides. These toxins have the advantage of selectively targeting only the insect, with no harmful effects on plants or people. Her research involves tracking the intracellular response of mosquito cells to these toxins to understand how they kill the larvae. She is also exploring how the Cry toxin might be modified to work on a broader range of insects.



*Doctor Segenet Kelemu, 2014 Laureate for Africa and the Arab States*

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# 7 EPIDEMICS AND PANDEMICS

In the popular video game, *Plague Inc.*, released in 2012, players develop an infectious pathogen with the intention of spreading it across the globe and annihilating the human race. Players choose the pathogen's place of origin, route of transmission and symptoms, and the game is a race between the spread of the disease and scientific efforts to develop treatments and vaccines. Playing the game, it becomes clear that airborne pathogens spread most easily and that milder symptoms can enable a disease to affect many people before work begins on vaccines and cures. The game's UK developer, James Vaughan of Ndemis Creations, took great efforts to incorporate valid, real world epidemiological transmission models into *Plague Inc.*, and with 100 million downloads since its release, the game's entertaining approach to raising public awareness about pandemics has proven extremely infectious (1).

Of course, the very serious risks and challenges posed by epidemics and pandemics are no game. Outbreaks of both habitual epidemic disease (such as influenza) and rarer, traditionally localized diseases (like Ebola fever) are now able to fan out rapidly around the world with the aid of mass international travel. The WHO refers to viral-based disease outbreaks like influenza and the 2003 SARS epidemic as "hit and run" occurrences that take medical authorities by surprise and attack with unpredictable severity (2). Certainly, the past two decades have already provided numerous occasions to practice and improve scientific responses to and leadership on instances of virulent communicable disease.

## *Animal origins*

Humans can be infected with diseases originating in birds or mammals, particularly viruses. These animal-borne diseases do not generally transmit easily between human beings, but under certain conditions can become highly contagious and cause severe human disease outbreaks, as was the case in the recent Ebola epidemic in Africa.

The Ebola hemorrhagic fever virus is transmitted from wild animals and then spread from person to person. Limited outbreaks have historically occurred in remote Central African villages, but in 2014-2016, human-to-human transmission accelerated to create an epidemic in five West African countries that affected more people and caused more fatalities than all previous Ebola outbreaks combined. While the epidemic was declared over in late 2016, new cases emerged in the Democratic Republic of Congo in May 2017, a reminder that diseases can be controlled but only rarely eradicated. Vaccines currently being tested are showing promising results (3).

In 1997, human infections with the A(H5N1) influenza virus were first reported in Hong Kong during an outbreak in poultry. Over the past 20 years, A(H5N1) and other avian viruses dubbed "bird flu" have spread globally, typically moving from Asia to other parts of the world and infecting millions of domestic fowl (4). Avian viruses have also become a major public health concern: they cause severe disease in humans and have the potential to mutate to become more easily transmissible. An influenza pandemic occurs when an avian or mammalian virus emerges with the ability to cause human infection and transmission in a population lacking immunity. It was conditions like these were responsible for the rapid spread and deadly toll of history's worst ever influenza pandemic in 1918-19, which killed over 40 million



*Professor Hualan Chen, 2016 Laureate for Asia-Pacific*

people worldwide. A century later, the growth of global trade and travel means that a localized epidemic can transform into an international pandemic very rapidly, with little time to prepare a response.

In 2003, the then unknown severe acute respiratory syndrome (SARS) virus spread across 37 countries in less than a month. Like seasonal flu, the virus was transmitted through airborne particles, but proved far deadlier, killing almost 10% of infected individuals. Fortunately, in this case, SARS' rapid spread was matched by the speed of counter-efforts facilitated by today's infrastructure of international collaboration, coordination, and information. The virus receded by the end of 2003, following global action coordinated by WHO (4).

The rapid international response to SARS is a good example of how the world's scientific community can react effectively to the outbreak of a virulent, unknown disease. Initially, WHO issued a global alert regarding a new, atypical pneumonia in February 2003, just one month after the first cases appeared in Hong Kong and Vietnam. Global

tracking swiftly followed, with additional cases soon reported in Singapore and Canada. In March, WHO called on laboratories in nine countries to jointly research the cause of SARS and develop a diagnostic test. This enabled researchers to share investigations of clinical samples in real time. By April of 2003, Canadian scientists were able to sequence the genome of the coronavirus believed to be responsible for SARS, allowing WHO to disseminate confirmation of the etiology of the new pathogen. At the same time, WHO recommendations to limit travel and adopt screening and disinfection measures were implemented across affected countries. By July 2003, local transmissions had been stopped in Hong Kong, Beijing, Taiwan and Toronto, and travel advisories were lifted, effectively marking the end of the epidemic. Eventually, the SARS virus was traced back to bats (6).



“The success of vaccination strategies largely relies on having good information about the field viruses and the capacity to update the vaccines.”



Professor Hualan Chen, 2016 Laureate for Asia-Pacific

When the H1N1 influenza virus (originating in swine) was declared a global pandemic in June 2009, an effective vaccine was approved for use by September of the same year. Disease surveillance pinpointed particularly vulnerable population groups and prioritized them for vaccination: by November 2009, around 65 million people worldwide had been vaccinated (7). Coupled with exposure, vaccine coverage provides a good deal of protective immunity. Following the H1N1 pandemic, studies found that 20% to 40% percent of affected populations experienced some immunity (8). However, the swine flu pandemic is still thought to have killed tens, if not hundreds, of thousands of people internationally (9).

Globally, the coordinated response to such threats has developed substantially over the past two decades, with WHO assuming a central role in surveillance, alerts and guidance for prevention and treatment, as well as the deployment of vaccines and therapies when they become available. This work relies first and foremost on the efforts of scientists investigating diseases as they emerge in local environments. Professor Hualan Chen is one of these experts, heading the National Avian Reference Laboratory at the Chinese Academy of Agricultural Sciences in Harbin, China.

In 2013, when human infections with the A(H7N9) bird flu virus were reported in China, Chen’s team tested soil, water and poultry to help identify and close farms and markets where the virus was present. In the laboratory, Chen creates hybrid flu viruses to understand emerging strains, work that enabled her to develop two innovative vaccines. It is an ongoing challenge to stay on top of emerging viruses, involves careful work in the field and the laboratory, and is always a race against time (see box below). “*Avian influenza viruses always mutate,*” says Chen, “*and some of the mutations can help the virus to escape the immunity induced by the vaccines. The success of vaccination strategies largely relies on having good information about the field viruses and the capacity to update the vaccines.*”

*Importantly, the interconnectedness of global populations that enables the spread of disease is matched by an international scientific infrastructure capable of rallying with impressive speed to address outbreaks. Chen has great hopes for these efforts, while recognizing the immense effort required: “Extensive monitoring and evaluation can enable us to find the harmful viruses as soon as they emerge, and then take action to control or eliminate them before they cause problems to animals or humans.”*

Professor Chen continues to track the evolution of A(H7N9). A total of 1,558 laboratory-confirmed human infections with the virus have been reported since early 2013. As seen in previous years, the number of weekly reported cases in 2017 decreased over the summer months. However, the number of human infections with avian influenza A(H7N9) and the geographical distribution in the fifth epidemic wave (which began on 1 October, 2016) is

greater than earlier waves. This suggests that the virus is spreading, and emphasizes that intensive surveillance and control measures in both the human and animal health sector remain crucial. In 2013, Professor Chen was named one of Nature magazine’s “Top ten scientists who matter” and, in 2016, received the L’Oréal-UNESCO Award For Women in Science (10).



Professor Hualan Chen, 2016 Laureate for Asia-Pacific

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# FOOD SECURITY IN AFRICA 8

What do plants need to survive? A school child will tell you they need five essential ingredients: air, light, soil, water and the right temperature. The miracle is that the world's plants manage to survive in spite of extreme local variations in the quantity of each of these ingredients. In polar conditions, plants like the snow saxifrage of the Arctic are covered in insulating hairs against the cold; they grow huddled together, close to the ground to reduce weather damage. In warmer, drier desert conditions, native plants deprived of water can enter periods of suspended animation that cease whenever moisture reappears, at which point the plant springs back to life.

This ability to thrive in extreme conditions is now being harnessed by scientists to help ensure that the crops humans need to survive can continue flourishing amid rapidly changing conditions, in particular climate change and land-use pressures. Sub-Saharan Africa is at the forefront of these efforts: droughts are increasingly frequent, and the United Nations predicts that 90 million hectares of land will be affected by 2060 (1). Currently, low agricultural productivity contributes to the undernourishment of nearly a quarter of Africa's population (2).

In the 1960s, the Green Revolution significantly increased agricultural output across most of the world. Africa, particularly sub-Saharan Africa, was much less successful at implementing new techniques in irrigation, fertilization and production. Over the past 20 years, this gap with other regions in the developing world has grown, and climate change and global warming are now bringing further challenges. Shorter, warmer and drier growing seasons are already leading Africa's farmers to adjust when they sow seeds, and yields of staple crops such as maize and beans are at risk of significant decline with further temperature

increases. The United Nations Environment Programme (UN Environment) says climate change could reduce maize yields across southern Africa by as much as 30% by 2030 (3).

In 2006, the Alliance for a Green Revolution in Africa (AGRA) was formed to fulfill the vision of an Africa that can feed itself and, given its size and promise, the world. AGRA, chaired until recently by former UN Secretary-General Kofi Annan, works with African farmers to sustainably boost production by supporting access to credit and markets, improving soil health, and investing in crop varieties with greater resilience to environmental stress and resilience to pests and disease. AGRA's current president, Rwandan entomologist Dr. Agnes Kalibata — widely considered to be one of the most successful Agriculture Ministers in sub-Saharan Africa before assuming her role at AGRA — is working hard to reverse decades of underinvestment in rural areas, with support from international donors. She considers better prospects for agriculture in Africa as critical to addressing not only food supply but also high rural unemployment, particularly among young people, a major cause of rapid urbanization across the continent.

## *Seeds of renewal*

Increasing food supply and making food production reliable in ecosystems that are increasingly fragile due to climate change involves a range of solutions, from predictable pricing to better roads and transport, to more accessible credit, widespread irrigation, and improved pest control. Access to good seeds is critical, as is selective breeding to increase drought and pest resistance. AGRA investments in plant breeding have now developed more than 600 new, more resistant crop varieties and helped to establish



*Professor Jennifer Thomson, 2004 Laureate for Africa and the Arab States*

village-based agro-dealers who make seeds available to small farmers. Work is also underway on new blends of fertilizer formulated to suit local soil types (4).

**Jennifer Thomson, Emeritus Professor in the Department of Molecular and Cell Biology at South Africa's University of Cape Town**, has devoted her career to developing transgenic food plants that are more tolerant to local environmental stressors like disease, pests, drought, heat and soil conditions. A pioneer in the genetic modification of plants, Thomson's research has enabled smallholder farmers in Africa to successfully grow insect-resistant cowpea, disease-free bananas, virus-protected cassava, drought-tolerant maize and vitamin-enriched sorghum. She helped draft South Africa's 2013 National Biotechnology Strategy and was appointed by the Minister of Science and Technology to the National Advisory Council on Innovation. **In 2004, Thomson's work was recognized with the L'Oréal-UNESCO Award For Women in Science**; she was elected President of the Organization For Women in Science for the Developing World (OWSD) in 2016.

Maize is a staple across sub-Saharan Africa, but crops are frequently devastated by disease and drought. Thomson's work with her Cape Town colleague, **plant molecular physiologist Professor Jill Farrant**, is producing more resistant maize varieties. Farrant is the world's leading expert on "resurrection plants" that go long periods without water and spring back to life with seasonal rains. In stark contrast to more developed countries, 96% of Africa's farmland depends on rain instead of irrigation, and there is evidence rainy seasons are becoming later and shorter (5). Unlike most plant species, which have water-storage structures or long roots to reach ground water, resurrection plants faced with extended dry periods change their metabolism to achieve a stable, crystalline glass-like cellular state that can be maintained for months and even years. Once water is available, the shriveled plant bursts back to life. There are some 130 known varieties of resurrection plant in the world, and Farrant is trying different breeding techniques, from conventional methods to gene editing, to activate the "resurrection" gene in food staples such as maize.



“When I started working on resurrection plants in 1994,” Farrant says, “it soon became clear to me that there were a lot of similarities in the mechanisms used by orthodox seeds and vegetative tissues of resurrection plants to tolerate desiccation.” In 2017, her team published a study in *Nature Plants* (6) that she considers the best evidence yet that “seed-like” genes are switched on during the desiccation of vegetative tissues in resurrection plants. Working with Professor Henk Hilhorst of Wageningen University in the Netherlands, Farrant sequenced the genome of the resurrection species, *Xerophyta viscosa*, and also produced a model that may ultimately enable the production of drought tolerant cereals. “In many commercial crops,” Farrant explains, “the genes required for desiccation tolerance are present, but largely silenced during development. I am hoping we can “un-silence” the genes required for desiccation tolerance and produce desiccation tolerant and storable seeds.”

Both Farrant and Thomson are focused on the particular challenges of Africa’s smallholder farmers. During a recent TED Talk, Farrant asserted: “My vision is for the subsistence farmer: I’m targeting crops that are of African value” (7). **Farrant is a member of the Academy of Science of South Africa, The World Academy of Sciences for the advancement of science in developing countries (TWAS), and received the L’Oréal-UNESCO Award For Women in Science in 2012** for her contribution to the understanding of plant ecophysiology. Importantly, she and her fellow scientists recognize public reluctance to

“My vision is for the subsistence farmer: I’m targeting crops that are of African value.”

*Professor Jill Farrant, 2012 Laureate for Africa and the Arab States*



*Professor Jill Farrant, 2012 Laureate for Africa and the Arab States*

embrace genetically modified foods and are striving to increase understanding of the science involved. Thomson, in turn, has written three books that explain the technology behind genetic modification (GM), examine the issues and concerns surrounding GM crops and their environmental impact, and highlight their contribution to food security in Africa (8-10). Her presentations at the World Economic Forum in Davos, Switzerland, and at the UN, have helped rally support for African agricultural development and underscored the sector’s pressing challenges.

In 2015, the international community set 17 goals as part of the 2030 Agenda for Sustainable Development. The second goal on the Agenda is ending hunger, achieving food security and improved nutrition, and promoting sustainable agriculture. The dedication of scientists in Africa and the organizations supporting their efforts offer significant hope that small farmers — half of the world’s population — can gain access to the tools they need to achieve this goal.

Women make up the majority of smallholder farmers, representing 70% of sub-Saharan Africa’s population. Indeed, women are considered to hold the greatest potential for driving improvements, as they are increasingly playing a central role as farmers, leaders and scientists in finding ways to sustain and increase food production under difficult conditions. International support, renewed commitment from African leaders, and scientific progress are bringing new optimism for the future.

New momentum to find solutions to Africa’s food crisis has drawn Ethiopian-born **biologist Segenet Kelemu** back to the continent after 25 years in Latin America at the International Centre for Tropical Agriculture (CIAT) in Cali, Columbia. At CIAT, Professor Kelemu trained graduate students who later made important contributions to improving agriculture in China. She decided to bring her expertise in crop disease resistance and adaptation back to Africa, where in 2013, she became Director General of the International Centre for Insect Physiology and Ecology (ICIPE) in Nairobi, Kenya. Overseeing a staff of 400 and approximately 60 graduate students, Kelemu focuses on developing eco-friendly pest and disease

vector management strategies, and spreading the use of these new technologies. Her work with ICIPE emphasizes links between the problems of pests and vectors, environmental degradation, food insecurity, poverty and disease, and the central role of smallholder farmers in bringing about improvement. Professor Kelemu’s contribution to these challenges has been widely recognized. In 2011, she became the first African to be awarded with the US Academy of Sciences Developing World Prize for Agricultural Sciences, and **in 2014, she received the L’Oréal-UNESCO Award For Women in Science**. In 2015, she was elected a Fellow of the World Academy of Sciences (11).



*Professor Segenet Kelemu, 2014 Laureate for Africa and the Arab States*

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## 9 HEART DISEASE: REDUCING GENDER AND GEOGRAPHIC DIVIDES

Researchers are patient by nature, conducting experiments that take time to produce effects and must be reproduced multiple times before a discovery can be proclaimed with confidence and enter into the repository of scientific knowledge. In cardiovascular disease, major discoveries have required that patience to endure over decades.

Heart attacks and strokes have been the major causes of death worldwide since infectious diseases came under better control. However, it was only when results of the Framingham Heart Study (initiated by the US Public Health Service in 1947) were analyzed after more than a decade that the main contributors to cardiovascular risk could be identified with some authority. High blood cholesterol and blood pressure, diabetes and cigarette smoking topped the list. These have been the cornerstones of prevention efforts since that time, leading to substantial drops in incidence and mortality from cardiovascular disease (1). Since 1960, heart disease death rates in the US have dropped by almost two thirds and stroke rates by more than three quarters (2).

### *Not just a man's disease*

The Framingham Study also identified male gender as a risk factor, a finding that served to perpetuate the idea of cardiovascular disease as a men's issue. Major clinical trials on risk factor reduction were conducted exclusively on men. Even as late as 1999, doctors were found to conduct investigations of heart disease in women at half the rate of those conducted among men, and women were less likely to receive bypass surgery and angioplasty, standard treatments for

blocked arteries. The seminal study of aspirin to reduce the risk of heart attack involved more than 22,000 men and no women (3).

Research over the past 20 years has helped to narrow the gender gap. A major boost came when, in 1991, cardiologist Bernadine Healy was appointed head of the US National Institutes of Health, and funding expanded for studies of women and heart disease. Among the most important is the Women's Health Study on Vitamin E and aspirin in primary prevention of heart disease and cancer, through which researchers Julie Buring, Nancy Cook and I-Min Lee from Harvard University have followed (and continue to follow) some 40,000 women since 1995. These scientists reported in 2005 that low-dose aspirin significantly lowered the risk of stroke in women, but (in contrast to men) brings no benefit to reducing heart attack risk (4). Research has also shown that heart disease symptoms manifest differently in women and men. Nanette Wenger, Cardiologist at the Emory University School of Medicine, co-authored the seminal 1993 report "Cardiovascular Disease in Women" that emphasized the importance of prevention: 40% of all coronary events in women are fatal (5). In 2007, Wenger co-authored the 2007 Guidelines for Preventing Cardiovascular Disease in Women. In 2009, she received the Lifetime Achievement Award from the American College of Cardiology.

### *Prevention*

Individual and public health efforts to prevent heart disease by promoting improved diets and exercise and reduced smoking rates and salt intake



*Professor Grace Olaniyan-Taylor, 1998 Laureate from Africa*

have been boosted by a wide range of highly effective drugs to lower harmful cholesterol, reduce blood pressure and treat diabetes. Portable defibrillators have made an appearance in public spaces to enable citizens to perform life-saving resuscitation on anyone suffering sudden cardiac arrest. Automatic external defibrillator training was included in the American Red Cross basic CPR course from 1999. Surgical bypass procedures now commonly use minimally invasive and even robotic techniques, leading to fewer complications, faster recovery and enabling people to live for many more years. The first robot-assisted bypass surgery was performed in 2006, with surgical instruments and a camera placed inside the patient's chest through three small openings. Pacemakers to regularize heartbeat in atrial fibrillation are implanted routinely, with recent progress in extracting and replacing devices that stop working. Balloon angioplasty neatly and unobtrusively opens passageways through plaques that clog coronary arteries (6).

The stents used to keep clogged coronary arteries open have transformed from bare metal designs that posed risks of infection or hypersensitivity, to embrace new materials and models that elute drugs to help slow restenosis. Dr. Anne Strohbach of Ernst-Moritz-Arndt University, and Dr. Raila Busch of the German Centre for Cardiovascular Research are currently working on the use of polymers as stent platforms and coating matrices for drug-eluting stents in coronary vascular interventions. A new generation of biodegradable polymers offers hope of reducing adverse events such as blood clotting and hypersensitivity reactions. Strohbach and Busch are currently interested in how the biocompatibility of polymers might best be assessed and measured (7).



“But women are still not being given the opportunity to excel. Governments should start thinking seriously about how they can help women.”

*Professor Grace Olaniyan-Taylor, 1998 Laureate from Africa and Arab States*



*Professor Grace Olaniyan-Taylor, 1998 Laureate from Africa*

#### *Life with heart disease*

Success in reducing mortality from cardiovascular disease means that increasing numbers of people are living with, rather than dying from, the disease. According to the American Heart Association, there are currently 82 million people in the US living with cardiovascular diseases, including the after-effects of heart attacks or strokes (8). Along with increased prevention efforts, researchers and clinicians are now focusing on ways to improve the outcomes of cardiac interventions, so that people are better able to resume autonomous and productive lives.

Cardiac rehabilitation, provided in hospital following an intervention, or in the community in the weeks and months after discharge, has been found to make a significant difference. Nanette Wenger co-chaired the 1995 Guideline Panel on Cardiac Rehabilitation for the US Agency for Health Care Policy and Research, a particularly rewarding task, as the culmination of several decades of research and advocacy to move rehabilitation beyond the experimental phase (9). For researchers, the ultimate reward for years of patience and hard work is to produce real and widespread change. As Wenger stated upon publication of the guidelines: “*The enormous satisfaction today is that it is an accepted component of the continuum of cardiac care, with cardiac rehabilitation being a Class IA recommendation in all contemporary cardiovascular clinical practice guidelines.*”

#### *Global challenges*

While global death rates from cardiovascular disease have fallen dramatically, from approximately 393 per 100,000 people in 1990 to 286 in 2015, significant geographical divides have appeared. The prevalence of coronary heart disease, atrial fibrillation, heart failure and stroke are now highest in sub-Saharan Africa, Eastern and Central Europe and Central Asia (10). **Emeritus Professor Grace Olaniyan-Taylor**, a biochemist at Ibadan University in Nigeria specialized in lipid metabolism, helped to clarify the epidemiology of cardiovascular disease in Africa. Her studies comparing the manifestations of cardiovascular disease in different ethnic groups have helped expand knowledge of risk factors, including nutritional and socio-economic factors. Importantly, she was able to show that cholesterol

levels are determined by diet, exercise and other lifestyle factors, rather than race. This was crucial to removing barriers to the use of effective cholesterol-lowering medication. Olaniyan-Taylor was in 1998, among the first recipients of the **L'Oréal-UNESCO Award For Women in Science**, and the second woman ever to be inducted into the Nigerian Academy of Science. She continues to work to promote education in science among African women. “Enrollment of female students has risen gradually in both arts and science at our university,” she said at a conference on science education in developing countries, “but women are still not being given the opportunity to excel. Governments should start thinking seriously about how they can help women.”(11).



*Professor Grace Olaniyan-Taylor, 1998 Laureate from Africa*

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# 10 BIODIVERSITY

One of the most concerning aspects of species extinction is that we will never know just how many are being lost. There are likely 10 times more species on Earth than the 13 million or so that have been identified to date, and even this is a very rough estimate. What seems clear is that the rise of the human species' ability to “transform the whole biosphere” is, in the words of Michel Loreau, winner of the Ecology Institute Prize in Terrestrial Ecology in 2005, as big a threat to global biodiversity as “a massive extra-terrestrial body colliding with the Earth” would be (1).

Biodiversity loss has accelerated under pressures such as overexploitation of species, pollution, climate change, and the degradation, fragmentation, and destruction of habitats through agriculture and forestry activities, coastal development, canal and dam construction, and use of fresh water for irrigation and industry (2). Human introduction of invasive species has been a major cause of extinctions, particularly on islands. The increasing attention on biodiversity conservation over the past few decades follows concerted and effective efforts to reduce diversity: only 30 crops provide an estimated 90% of the world population's current caloric requirements. Wheat, rice and maize alone provide approximately half the calories consumed globally; even among these crops, genetic diversity is decreasing (3).

These concerns are not new. In 1971, UNESCO launched the Man and Biosphere Programme to promote the sustainable use and conservation of biological diversity and natural resources, largely through the creation of biosphere reserves. However, the field of biodiversity and conservation science has gained credibility and strength over the past few decades. A key moment came in 1992

with the United Nations Convention on Biological Diversity, which involved national commitments to reduce biodiversity loss. The United Nations Environment Programme (UN Environment) has taken a role in monitoring ecosystem health and sharing expertise. Food supply is a major focus. Marieta Sakalian, a UN Environment ecosystems expert, is working to preserve biodiversity in local food sources, which can be abandoned in favor of cash crops when traditional techniques of growing and preparing local plants are lost. Understanding threats to pollinators such as bees is another priority, with bees undergoing significant decline worldwide. A recent study found that light at night decreased pollinator visits to flowers enough to produce a 13% drop in fruit production (4).

Commercial activity is the key driver of biodiversity loss and businesses are being encouraged to participate in the global effort to exploit natural resources more sustainably. In 2015, the Supply Chain platform was launched to track corporate progress on reducing deforestation. It monitors approximately 450 companies (including giants such as Nestlé, Starbucks and Unilever) that produce, trade or retail products linked to palm oil, soy, timber and cattle, considered the “big four” commodities driving the loss of tropical forest habitats. The platform makes data widely available to encourage responsible sourcing (5).

The treasure trove of potentially useful (and marketable) compounds waiting to be discovered is encouraging conservation and exploration of plant species. In Costa Rica, the National Biodiversity Institute trained rural residents to collect plant specimens and has been able to collect over 3 million identified specimens over 20 years.



Doctor Ameenah Gurib-Fakim, 2007 Laureate for Africa and the Arab States

Plant species are the principle source of medicines and represent promising solutions to current challenges such as antibiotic resistant bacteria and more effective cancer therapies. 69% of new drugs in the past 25 years were either natural products, semi-synthetic drugs derived from natural products, or natural product mimics (1). The anti-cancer compound, taxol, was found in the Pacific yew tree, leading to a whole new class of drugs, and sirolimus, produced from a bacterium found in soil on Easter Island, is used to prevent rejection of organ transplants, treat a number of tumor types and as a coating for arterial stents (1).

Mauritius is one of the world's major “hot spots” of diversity, and **Professor Ameenah Gurib-Fakim** took on the daunting task of compiling the first inventory of aromatic and medicinal plants on the island. Her study, completed in 1994, described the properties of these plants and collected traditional knowledge on their use from

local villagers. **In 2007, her work was recognized with the L'Oréal-UNESCO Award For Women in Science.** In 2009, she created the Centre for Phytotherapy Research (later called the Centre International de Développement Pharmaceutique) to analyze plants for their health, nutritional and cosmetic applications. In a 2014 talk, Gurib-Fakim stated: “Every time a forest comes down... there's a potential lab going down with it”(6).

In a turn of events that surprised her more than anyone, Professor, now Her Excellency Gurib-Fakim, was elected President of the Island of Mauritius in 2015 (7). That she is the first woman president of the island is already an achievement. More importantly, she is the first biodiversity scientist to become president anywhere in the world, and is using her new position to raise awareness of climate change and promote investments in science in Africa. She has gained support from the Bill and Melinda Gates





“Every time a forest comes down... there’s a potential lab going down with it.”

Doctor Ameenah Gurib-Fakim, 2007 Laureate for Africa and the Arab States

Foundation to create ten PhD research positions on the island (8). A major concern, now more than ever, is to promote the use of African medicinal plants and protect intellectual property surrounding their development. She was, in 2005, one of the founders of the Association for African Medicinal Plants Standards that brings together African researchers and manufacturers to develop and commercialize remedies based on medicinal plants (9). In 2009, the Association launched the African Herbal Pharmacopoeia, a collection of monographs providing information and technical data on some 50 important African medicinal plants, aiming to promote their development and use internationally, and thereby their conservation locally.



Professor Gloria Montenegro, 1998 Laureate for Latin America

The Chilean flora is an important genetic resource, with 46% of its plants being endemic (only found in Central Chile). The traditional use of plants for medicinal purposes among native populations was documented by early settlers and these were found to have multiple medicinal effects: anti-inflammatory, diuretic, antimicrobial and antibiotic, antifungal, antimalarial and antioxidant. Drinking herbal infusions is still commonplace among local populations.

**Gloria Montenegro, Professor of Botany at the Pontificia Universidad Católica de Chile**, collects, categorizes and studies Chile’s endemic plants, which has led to the discovery and patenting of natural products. **In 1998, she was one of the first recipients of the L’Oréal-UNESCO Award For Women in Science**, in recognition of this work and its application in rehabilitating areas hit by natural disasters. Concerned for the conservation and sustainability of native medicinal plants, she developed theoretical and mathematical models of plant regeneration after harvesting, based on seasonal dynamics, growth rate and the position of renewal buds. *“This information allows us to assemble all the information required for sustainable harvesting,”* she says, *“knowing the time that every species would take to recover the biomass loss.”* She then set out to transfer this knowledge to the people working to harvest the plants. *“We travelled across the country and throughout Latin America organizing workshops for local people involved in using our native species.”*



Professor Gloria Montenegro, 1998 Laureate for Latin America

More recently, Montenegro turned her attention from plants to honey. While many honeys are made from the nectar of a wide variety of plants, she found a few unifloral honeys with native plant origins and identified which plants had been used the most intensively (10). The study of the botanical and geographical origin of honey has its own name, melissopalynology, and involves complex microscopic analysis of honey sediments and pollen grain. An increasing number of researchers worldwide are now focusing on improving our ability to characterize honey.

Montenegro and her colleagues have determined the particular composition of the honey and

assessed its medicinal properties; some had antibacterial activity that held promise as an alternative treatment for multi-drug-resistant bacteria. The properties of the honey were found to be closely related to the source of pollen used by honeybees. Their next challenge is to build scientific evidence of its effects. *“Our work has increased motivation to maintain beehives and protect honeybees from harmful chemicals, benefitting both bees and their keepers. We work closely with beekeepers, who are generally quite poor in my country, and add value to their products by certifying their properties through the university.”*

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# 11 IMMUNE FUNCTION

The virtues of cleanliness came under attack around 1990 when researchers showed that children exposed to dirt and germs in early life were less likely to develop allergies and asthma. The findings fit with trends noted by epidemiologists that allergic diseases are more common in developed countries where children are less likely to grow up on farms and with multiple siblings, both good sources of bacteria (1, 2). Children in developed countries are also more likely to receive antibiotics at a young age. This “hygiene hypothesis” holds that exposure to germs in early life strengthens the immune system and prevents the development of a hypersensitive immune system that mounts attacks against the body itself, possibly resulting in allergies and autoimmune diseases.

In the early 2000s, research suggested that humans had become dependent on microbes through evolution, that they were “old friends” without which the immune system could not function well (3). While there are still many debates among scientists about the role of various factors in immune function, there is growing appreciation for the careful balance that enables the immune system to be protective, but not so protective that it causes harm. It must be able to tolerate a little dirt. More recent thinking around allergies, particularly to food, involves introducing small quantities of the substance gradually to induce tolerance. Recommendations about feeding foods such as peanuts and strawberries to babies have been revised to promote gradual introduction.

In 2012, research on mice identified how the hygiene hypothesis might work, showing that mice exposed to bacteria had a decrease in the number of invariant natural killer T cells (NKT cells) - these fight infection but can also turn against the body in an auto-immune reaction (4). Exposure to

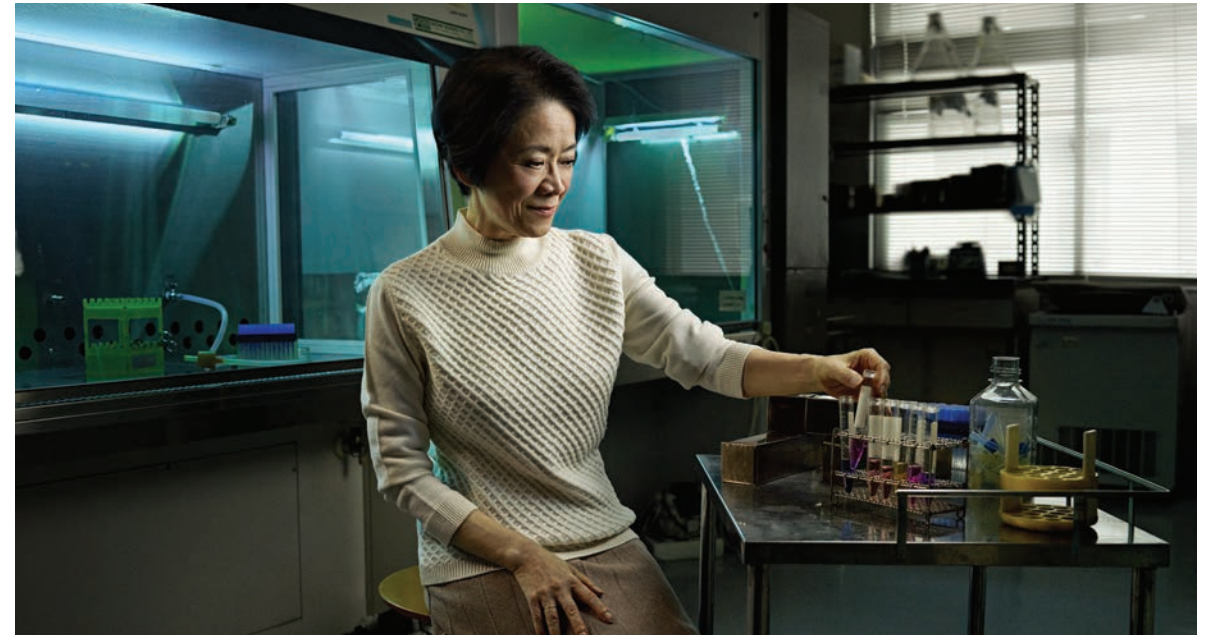
microbes that normally colonize the mucosa of the respiratory system, gut, and skin are now thought to play a role in preventing diseases as varied as type I diabetes, multiple sclerosis, neurodegenerative disease, depression and schizophrenia (5, 6).

## *Activating immunity*

These ideas about how the immune system develops evolved in parallel with new ideas about how immune response is activated. Previously, scientists worked according to a “self-non-self” theory, whereby the immune system was activated when it detected something “foreign” to the body itself. The change in direction came in 1994, when Polly Matzinger, an immunologist with the National Institutes of Health in the US, suggested that immune response was, instead, triggered by an alarm signal that could even be set off without the presence of foreign entities, by distress in the body’s own cells. This theory is called the “Danger Model” (7). Defining the distress is a challenge: what kinds of stress will signal the alarm? And how can medical interventions prompt immune activity? And how can they stop overactive response?

Such questions launched a quest for mechanisms involved in signaling danger that has led to the phenomenal expansion of treatment possibilities for everything from diabetes to inflammatory bowel disease to cancer over the past 20 years.

In 2011, Ralph Steinman was awarded the Nobel Prize in Physiology or Medicine for identifying dendritic cells, a type of cell involved in the immune system, as the essential link between acquired and innate immune system functionality. Back in 1908, the Prize was shared by Ilya Metchnikov, who proposed an innate immune



*Professor Kayo Inaba, 2014 Laureate for Asia-Pacific*

system of cells that immediately defend the body and kill microbes, and Paul Ehrlich. He focused on the workings of the acquired immune system cells that recognize invaders from past contact and confer long-lasting immunity. Steinman discovered that dendritic cells are at once “sentinels” that capture pathogens, “sensors” for infection and, once activated, “conductors” of the “immune orchestra” (8).

The two systems, innate and acquired, employ a complex communication system to coordinate interactions between external pathogens and allergens, and internal organs and cells. Substantial research has been undertaken with the goal of altering immune response by working through T cell receptors, discovered in 1984 by Canadian biophysicist Tak Mak, and proteins that bind to foreign molecules and determine which cells to attack and which to tolerate (9).

## *The immune system and cancer*

The cells of the immune system migrate throughout body tissues. Dendritic cells in particular are mostly found in the airway and skin, where they can capture antigens at their point of entry. Specific types of T cells migrate around searching for antigens on dendritic cells. When they find one, they receive the signal that activates immune response. **Japanese immunologist Kayo Inaba**

worked alongside Steinman to explain how dendritic cells capture the antigen and present it to T cells (8). Inaba also collaborated with Steinman on a ground-breaking experiment to demonstrate the anti-tumor activities of dendritic cells, which they removed from mice, loaded with antigen, and re-infused. These “primed” dendritic cells conferred strong protective immunity (8). This represented a dramatic change, as tumors were not previously thought to be potential targets for immune response, and opened new doors to immunotherapy. Inaba is one of the world’s leading scientists on dendritic cell research, a leader in the use of mouse studies in cancer immunotherapy and, in 2003, became the University of Kyoto’s first woman Dean. **She was awarded the L’Oréal-UNESCO Award For Women in Science in 2014** for her discoveries of immune system mechanisms against viral, bacterial and cellular threats.

Immunotherapy in the context of cancer treatment aims to establish a highly effective anticancer immune response that will successfully control the growth and spread of the cancer. The goal is to activate, or undo the suppression of, the immune response, while preventing an excessive response that leads to symptoms similar to those seen in autoimmune diseases. In 1995, Mak published a landmark paper on the discovery of the function of



the immune checkpoint protein CTLA-4, thereby opening the way for immunotherapy/checkpoint inhibitors as a means of cancer treatment (10).

A large number of specific immune checkpoint blocking agents are now being developed and tested, with very promising results not just in one, but in many types of cancer. Immunotherapy has evolved at the same time as targeted therapies, which produce outstanding results for a brief time, but inevitably grow ineffective as resistance develops (11). In contrast to this piecemeal approach of initiating a new targeted treatment each time resistance develops, some consider that tumor immunotherapy offers long-lasting benefits that will greatly prolong cancer survival (12). Activating T-cell receptors means that each person would benefit from their own personalized immune response to cancer.



Professor Laurie Glimcher,  
2014 Laureate for North America

“With the advent of molecular tools, it has been possible to study these with more precision and thereby lay the ground for future therapeutics.”

Professor Indira Nath, 2002 Laureate for Asia-Pacific

**Professor Laurie Gilmcher** was longstanding head of one of the world’s top immunology programmes at the Harvard School of Public Health. In October 2016, she became President and CEO of the Dana-Farber Cancer Institute. **She was awarded the L’Oréal-UNESCO Award For Women in Science in 2014** for her seminal discoveries of key factors that drive activation in the immune system, including the ER stress signal. Her immunological experiments have explored a wide range of diseases, including asthma, HIV, inflammatory bowel disease and osteoporosis. Gilmcher’s latest research is advancing the field of cancer immunotherapy. In research published in 2015 in *Cell*, Gilmcher identified a gene in dendritic cells that is activated by ovarian cancer, resulting in the cells’ inability to mount an effective response against the tumor. “Deactivating” the gene was found to restore dendritic cell function and trigger an immune response against ovarian tumors. In another 2015 study, published in *Nature Immunology*, Gilmcher’s team identified two proteins that play a critical role in eosinophil development and could be specifically targeted. This unlocks new possibilities for the treatment of asthma.

**Emeritus Professor of Immunology, Indira Nath**, in New Delhi, began her work on the cellular immune response in leprosy in the 1970s, when some 4.5 million people in India suffered from leprosy. Her research played an important role in identifying deficiencies in the immune response that led patients to develop the most serious form of leprosy. This discovery constituted a significant advance towards the development of treatments and vaccines. She was elected a Fellow of TWAS (Third World Academy of Sciences) in 1995, **received the L’Oréal-UNESCO Award For Women in Science in 2002**, and the Chevalier de l’Ordre National du Mérite in France in 2003. Her work encouraged early detection and better treatment, meaning that the terrible disfigurements that were once commonplace are now rare. Since 1995, multidrug therapy (MDT) treatment has been made available through the WHO, donated by foundations and private companies, free of charge to all patients worldwide. This has helped to achieve a dramatic decrease in the global disease burden: from 5.2 million people with leprosy in 1985, to 805,000 people in 1995, 753,000 in 1999, and 176,000 people with leprosy at the end of 2015 (13).



Professor Indira Nath,  
2002 Laureate for Asia-Pacific

Given recent progress in immunology, Dr. Nath considers that regulation of the immune response and inflammatory processes involved in disease are now better understood. “*Immune responses to control infection, transplantation and autoimmunity in the last decades have taught us lessons in which cell types and products are involved,*” she says. “*With the advent of molecular tools, it has been possible to study these with more precision and thereby lay the ground for future therapeutics.*”

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# ARTIFICIAL INTELLIGENCE <sup>12</sup>

A term first coined in 1956, artificial intelligence (AI) is defined as the ability of a computer to independently replicate intellectual processes typical of humans. It continues to both inspire great hopes of enabling us to solve problems that human intelligence cannot, and provoke fears that humans may become servants to machines in the process. As computer science has progressed, bringing the world to our smartphones and new driverless cars to our roads, the technology's limitations have also become more apparent: it performs the tasks it has been programmed to achieve effectively, but has insufficient capacity to cope with new situations. In 2011, when the IBM computer Watson competed against the champions of the American TV quiz show, "Jeopardy!", its designers discovered that the real challenge was not equipping Watson with the knowledge of trivia needed for the show, but enabling the computer to understand the announcer's questions (1). People understand words even when they are used in different sequences or couplings, just as we recognize objects despite variations in size or perspective. Variation is a computer's weak spot.

Over the past two decades, scientists working to overcome the deficits of computing have abandoned the field's traditional "top-down" approach (where a computer is pre-programmed with rigid rules) to adopt a "bottom-up" paradigm that uses many principles from contemporary research into human brain function to develop "neural networks" of computers that learn new "behaviors" on their own. Researchers are now looking into human learning, sensory perception and memory in order to improve these neural networks. An AI company called DeepMind Technologies, founded by Demis Hassabis, a British AI expert and neuroscientist, came to the attention of software giants in 2013 when its

neural network taught itself to play video games — very well — through trial and error coupled with reinforcing feedback from behavioral psychology. This demonstrated that for computers to solve problems, they need to be able to actively learn. Hassabis used his neuroscience background to apply knowledge about how the human brain works to the development of his neural network. One central idea stemmed from the fact that in the brain, memory and forward planning are intertwined: amnesia patients, for example, struggle to imagine future events. While learning to play a game, the DeepMind neural network reviewed past experience to extract lessons for improved success (2). Hassabis is now working with Google to understand where and how DeepMind's technology can be best applied.

In medicine, platforms such as IBM's Watson for Oncology integrate many neural networks to process natural language, generate hypotheses, and integrate this information with medical databases to create recommendations. Models have been developed to assess risk for cardiovascular disease, complications from treatment, and disease recurrence (3,4).

Professor Fei-Fei Li, an American electrical engineer, focuses on visual perception and the neural mechanisms that enable a meaningful interpretation of the visual world. She draws on the study of human neuroimaging in her work to develop intelligent algorithms that enable robots to contextualize visual information. As head of Stanford's AI and vision laboratories, Li built a 15 million-image dataset called ImageNet in 2009 that is designed to train deep learning image recognition algorithms (5). ImageNet is now used in an annual competition to develop algorithms that enable computers to accurately recognize images. Faster computing speed and better coding



*Professor Michelle Simmons, 2017 Laureate for Asia-Pacific*

have brought exponential increases in accuracy. For example, in 2014, Li and her students produced a model that could describe images in natural human-like sentences (6).

## **Human-robot interaction**

American professor Cynthia Breazeal is a pioneer in the field of social robotics, which seeks to integrate robots into the fabric of daily life as companions, carers and entertainers, occupations that require social and emotional intelligence. In the 1990s, she created the pioneering robot, Kismet, and leads MIT's Personal Robots group, which is currently launching Jibo, the first "family robot." Jibo recognizes faces and voices, picks up on emotional cues, and constantly learns as it is exposed to new things. In this way, it quickly becomes as capable at reading stories to children as it is at ordering Chinese food. Jibo is programmed to display spontaneity and unpredictability, which adds to its appeal. To design Jibo, Breazeal studied developmental psychology and cognitive development, along with animal behavior and cartoon animation. Jibo's

verbal enunciation, vocal modulations, facial expressions and body language, as well as its ability to process emotions in speech and respond appropriately, show how social robotics has already progressed far beyond commercial computer voice software (7).

Elsewhere, software developed by Boston-based Egyptian computer scientist Rana el Kaliouby scans people's faces and then geometrically analyzes the position of the mouth, nose, eyes, eyebrows, along with skin texture, to read emotion. Kaliouby began her work in facial recognition software at the Autism Research Centre in Cambridge, Massachusetts, where she was developing tools to help people with autism recognize social cues (8).

## **Overcoming language barriers**

The leap in quality bringing computer-human interaction to a new level is very recent and largely attributable to advances in language technologies. Improving computer understanding of speech and language requires substantial quantities of data to



# “Quantum computing will help us understand how nature works at the chemical level.”



Professor Michelle Simmons, 2017 Laureate for Asia-Pacific

be entered into systems, thereby enabling them to gain accuracy in matching spoken words with transcriptions, or sentences from one language to another. Statistical methods in natural language technologies rely on software searching multiple recordings matched with transcriptions, and calculating statistical odds of a particular combination of sounds meaning one thing over another. This has enabled drops in the error rate in machine transcription from approximately 25% five years ago to 6% today.

In 2007, Google switched to a statistics-based system for translation, with a database built by combing through a trillion web pages and pairing versions in different languages. Newer upgrades have arisen via interactive machine translation systems, where people improve the translations from which machines learn. This approach has led to the vastly improved translations now offered by systems such as Google Translate, which serves over 500 million monthly users and translates 140 billion words per day (9).

As computer science grows ever more ambitious in taking on tasks routinely performed by people, the phenomenal complexity of human senses, cognition, memory, communication and learning become ever more obvious. The latest developments at DeepMind indicate that

computers might, when set free from human teachers, develop their own distinct learning styles. A subset of AI – known as machine learning – focuses on the ability of computers to learn autonomously from data. Following a victory in 2016 over one of the world’s best players of Go, the famously complex Asian board game, DeepMind’s AlphaGo computer programme was redesigned to leapfrog the human mentoring stage and identify new Go strategies on its own, guided only by incentives to win. Researchers were able to watch the new AlphaGo Zero programme proceed through typical novice Go player stages, taking different routes to improving its abilities. In just a few days, it advanced far beyond the performance that had enabled it to beat Go’s reigning human player (10).

## Quantum computing

Whether applied to images, emotion or language processing, neural computer networks require heavy-duty computing power to train systems and enable them to continue learning and arriving at solutions. Advances rely on ever faster information processing. **In 2017, Professor Michelle Simmons**, founding member and Director of the Centre of Excellence for Quantum Computer Technology in Sydney, Australia, **was recognized with the L’Oréal-UNESCO Award For Women in Science** for her leadership in the area of “super” or

quantum computing. While classical computing has become ever faster, future improvements are limited by the binary nature of computer bits, either 0 or 1. In quantum computing, the basic unit of encoded information, the quantum bit or qubit, can also be a superposition and entanglement of 0 and 1, enabling many calculations to be performed simultaneously. This gives quantum computers the potential to be substantially more powerful than today’s supercomputers. The goal is to find an efficient way to manipulate single atoms to build qubits that can process information predictably without interference.

Speaking towards the end of 2017, Professor Simmons emphasizes the benefits of quantum computing for industries that are data intensive, require complex calculations, or sort through vast amounts of data. *“I can envisage a day where quantum computing assists with real time traffic control, longer-term weather prediction, enhanced facial recognition, lower delivery costs, optimized drug design, and highly personalized medicine. Quantum computing will help us understand how nature works at the chemical level.”*



Professor Michelle Simmons, 2017 Laureate for Asia-Pacific

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# 13 ENERGY

Electricity seemed almost magical when it was first introduced at the end of the 19<sup>th</sup> century, but quickly became indispensable and taken for granted by a large swathe of humanity. Today and moving forward, the appetite for electrically powered goods and services appears insatiable. One after another, low or zero-energy items such as telephone land lines, books and photo albums are being replaced by electronic devices. In just the last 25 years, mobile phone penetration globally has risen from nothing to 93% (1), with each phone containing a battery that needs to be charged on a regular basis. This tendency presents a double-edged scientific challenge: to increase the energy efficiency of this growing array of appliances, while producing ever more electricity in a manner that does not contribute to CO<sub>2</sub> emissions, one of the major factors contributing to climate change. Scientific developments over the past two decades have led to revolutionary progress on both fronts.

Before considering some of these advances, it is helpful to review the basic language of electricity that is used in scientific efforts and evaluations of their results. The Watt is the basic unit of power and describes the rate at which a given appliance consumes energy. A kiloWatt hour (kWh) is a unit of energy equal to a thousand Watt-hours, where one Watt-hour is a unit of energy equivalent to one watt of power expended for one hour. Far larger measurements have also entered the electricity lexicon: the megaWatt (MW), equal to 1 million Watts, and gigaWatt (GW), equal to 1 billion Watts. Progress on efficiency involves decreasing the Watt-hours required to produce the same benefit.

## *Seeing the light*

Energy saving campaigns, coupled with hefty bills, can help guide individual household choices that have a significant impact on demand for electricity. This includes, for example, ceiling fans that use 60 Watts instead of central air conditioning that uses 3500 Watts; or foregoing the clothes dryer that needs 5000 Watts for the clothesline that only needs clothes pegs. However, the major benefits observed in the past 20 years have arisen from improving the efficiency of electricity-dependent technologies. The humble light bulb provides an idea of the scale of this progress.

The incandescent light bulb uses a great deal of electricity to produce heat rather than light. The search for more efficient solutions dates back even before the energy crisis of the 1970s to the development of neon tubes coated with phosphors — the neon lights so common in 20th century offices. It was only after 1990, however, that compact fluorescent light bulbs providing consistent lighting at a reasonable price became commercially available. They used approximately 75% less electricity than incandescent bulbs. The second great leap in efficient home lighting technology came with progress on white light-emitting diodes, or LEDs. These are semiconductors that convert electricity into light. In 2003, the first residential LED bulb came to market. Uptake was initially slow due to compatibility problems with existing light fixtures, but user-friendly LED products that came to market after 2011 spurred substantial expansion in the market and significant drops in price. LED bulbs fit into standard sockets, use approximately 80% less electricity than incandescent bulbs, last approximately 25 times longer, and have become commonplace for home use. Today, scientists (see box below) are experimenting with organic LEDs:

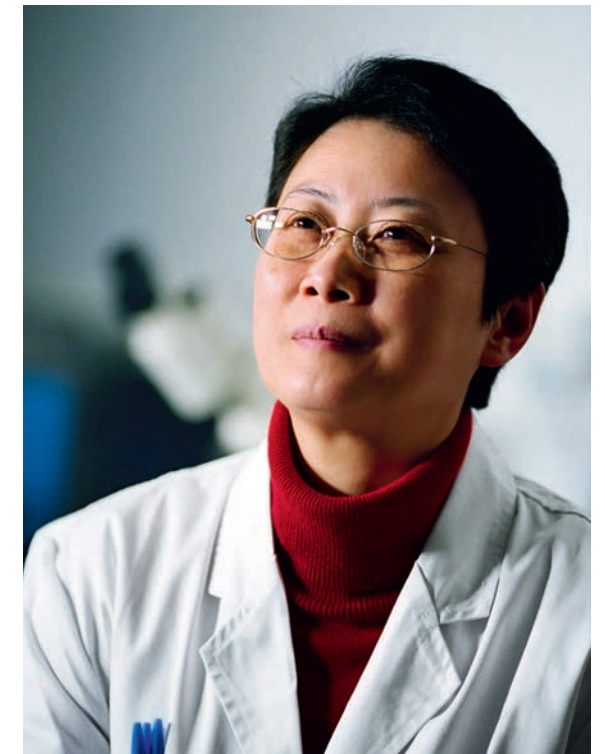
light-emitting diodes (LEDs) that use small organic molecules as their active element and can be fabricated on flexible layers, opening up entirely new possibilities for light emission.

## *Harnessing the light*

The relationship between light and electricity runs both ways. It was Albert Einstein who first formulated the photon theory of light, demonstrating how light shining on a metal surface could free electrons from that surface, creating electricity. The first silicon photovoltaic cell that converted sunlight into electrical power was made at Bell labs in 1954 by Daryl Chapin, Calvin Fuller and Gerald Pearson. The challenge since then has been to improve the efficiency of these solar cells in converting the sun's energy into electricity.

Silicon solar cells can only capture a narrow band of the light spectrum and therefore only convert some 16% of sunlight into electricity. (2) Improving the efficiency of solar panels involves identifying and assembling materials that can harvest the sun's energy better than silicon photovoltaic cells. New technologies include cells with layers of light harvesters that each gather energy from a separate slice of the solar spectrum. One promising technology, developed through collaboration between Tssutomu Miyasaka at Toei University in Yokohama, Japan, and Henry Snaith at Oxford University, began in 2008 (3), is a coating based on minerals called perovskites made from inexpensive ingredients (lead and ammonia), that are highly efficient at converting sunlight to electricity. It can be painted onto thin, flexible materials such as plastic, and could help to create an inexpensive and lightweight solar panel. Researchers are now working on how to prevent the material from breaking down when it gets wet.

Prices of solar panels were approximately 100 times more expensive 30 years ago. By 2013, solar electricity was cheaper than retail electricity in many countries. Major companies, including Walmart, IKEA, Google and Facebook, are now turning to solar power to meet their electricity needs (4). Solar's evolution has been so fast that the International Energy Agency raised its target for solar penetration by 2050 by almost 50%.



*Professor Vivian Wing-Wah Yam, 2011 Laureate for Asia-Pacific*

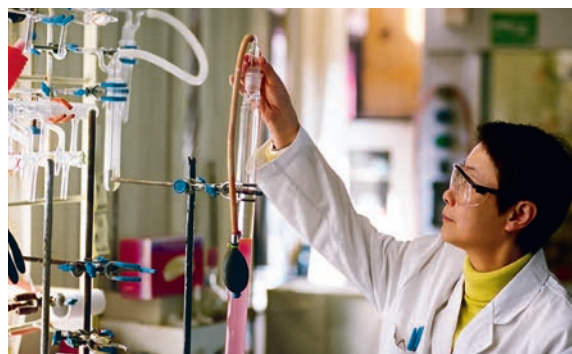
In particular, regions that faced the largest energy deficits are turning directly to solar and other renewable forms of energy. Between 2000 and 2014, the number of people lacking access to electricity worldwide dropped from 1.3 billion to 1.06 billion. Rural electrification has increased from 63% to 73%, much of it produced “off-grid” by sources such as solar and wind. (5) The top five solar power farms are located in China and India. China, beset by smog and experiencing the impacts of climate change, has committed to dramatically reducing its use of fossil fuels to only 20% of total energy by 2030 (6). The proportion of global electricity derived from renewable sources rose from 10.3% in 2015 to 11.3% in 2016, preventing the emission of 1.7 gigatonnes of CO<sub>2</sub> (7).

## *The age of the battery*

Better conversion rates of solar energy into electricity stand to meet energy needs sustainably in the future. However, a major challenge to the takeover of solar from fossil fuels remains – we must be able to ensure that the electricity is



“I do hope will make a great impact and contribution towards solving the energy issue that society faces today.”



Professor Vivian Wing-Wah Yam, 2011 Laureate for Asia-Pacific

available where and when it is needed. What happens when the sun sets (or the wind dies down)? Further progress depends on scientists' ability to bring the kind of revolutionary progress seen in solar energy production to energy storage systems, such as the battery.

Elon Musk, CEO of Tesla and Space X, has emerged as the world's key promoter of advances in the development of better and cheaper energy-dense batteries. Tesla is the world's biggest consumer of lithium-ion batteries. In May 2015, Tesla launched the Powerwall and Powerpack rechargeable lithium-ion battery packs, providing residential solar customers with a viable storage option, and meeting the solar power industry's need for high volumes of battery packs. Hawaii's electric utility is now using 272 Tesla power packs to store solar energy for use at night, eliminating the need for diesel-powered back-up generators (8).

The lithium-ion battery was first created in 1980 by John Goodenough and Stanley Whittingham at Oxford University, and was integrated into a multitude of modern devices. At the Cockrell School of Engineering, University of Texas, Goodenough and his colleague, Portuguese physicist Maria Helena Braga, have continued to improve on safety, energy storage capacity and charging speed by switching from a liquid electrical conductor to a solid-state glass compound. Braga began working on solid glass electrolytes in Portugal, developing a glass that is cheap and easy to manufacture. She worked with Goodenough to perfect the technology. In research published in December 2016 (9), Goodenough and Braga

report that these new batteries have at least three times as much energy density as current lithium-ion batteries. Charging time is also reduced from hours to minutes, and retains conductivity even at temperatures of -20 Celsius (10). Electricity storage in batteries not only solves the problem of intermittency in power generation, it also enables the expansion of renewable forms of energy into areas dominated by fossil fuels, notably vehicles.

#### A movable solar feast

Battery capacity determines how far drivers can go between charges in an electric car. The larger the kilowatt-hour (kWh) of the battery pack, the longer the distance. A 24 kWh battery pack allows the vehicle to travel approximately 130 km between charges, while an 85 kWh pack delivers a 425 km driving range. The Toyota Prius was launched in 1997 in Japan as the world's first commercially mass-produced hybrid car, and became available worldwide in 2000. Over the next ten years, major car manufacturers produced a small number of all-electric cars but undertook no mass production or marketing. In 2006, Tesla Motors released its Roadster, an expensive all-electric sports car. Over the next two years, governments in a number of countries committed to supporting and promoting the expansion of electric vehicles. In 2008, Nissan launched its affordable electric car, the LEAF, which could travel 160 kilometers on a full charge. Tesla responded with the Model S in 2012, which has a range of over 400 km per charge. By the end of 2016, more than 250,000 LEAFs and more than 10 million Toyota hybrid vehicles had been sold worldwide. All major automakers currently have electric cars under development (11).

Chemist Vivian Wing-Wah Yam at the University of Hong Kong, has been working on both sides of the light-energy equation, with research that could help to design materials that better harvest and convert light into energy, and make more efficient use of energy to produce light. Her research focuses on new classes of photoactive materials (materials used with solar cells to absorb light) combining metal atoms and organic molecules that absorb or emit light. To produce light, Yam is experimenting with organic light-emitting diodes (OLEDs) that can be deposited on clear plastic, glass or other materials to produce a brighter light more efficiently. “We have developed new classes of color-and light-generating atoms,”

she says, “and new strategies to assemble them that can be used in fabricating OLEDs but also have biomedical and environmental applications as sensors. I hope my research will make a great impact and contribution towards solving the energy issue that society faces today”. Her discovery of materials with unique light absorption properties also holds promise for improving the harvesting and conversion capacity of solar cells, as a complement to silicon. In 2001, Yam became the youngest member to be elected to the Chinese Academy of Sciences. **In 2011, she was recognized with the L'Oréal-UNESCO For Women in Science Award.**



Professor Vivian Wing-Wah Yam, 2011 Laureate for Asia-Pacific

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# ASSISTED REPRODUCTION

Two decades ago, a Scottish sheep named Dolly made headlines around the globe. Named after American country-western singer Dolly Parton, the sheep was the world's first clone: an animal reproduced from the DNA of a single source. Scientists removed DNA from an egg, and fused the egg with the nucleus of a cell from a donor sheep, so that only the donor DNA was carried on. The egg was replaced in a surrogate's uterus and in July 1996, Dolly was born (1). The achievement marked a seminal moment in the ongoing transformation of that most basic of functions: the reproduction of life and transmission of the genetic heritage of species. Dolly was living proof that conception could be taken from the bedroom to the laboratory.

Scientific interest in cloning focuses on a range of challenges, from producing replacement body parts to perpetuating endangered species, and even bringing extinct species back to life (2). Experimentation has also led to a new scientific understanding of ways to overcome problems in human reproduction, from difficulties in conception to the transmission of hereditary diseases.

The demystification of reproduction has generated more ethical debate than any other contemporary area of scientific discovery, and scientists tread very cautiously in applying any newfound knowledge to humans. There has been significantly less inhibition in the use of new reproductive technologies in animals. Over the last 20 years, selective livestock cloning has become a major business, offering everything from faster racehorses to cattle without horns. Genetic manipulation is also being explored in animals. In the past five years, researchers have produced a strain of pigs genetically resistant to infection with a common respiratory virus, and a breed of cattle resistant to Mad Cow Disease (3).

## *Genes are not the whole story*

One result of animal cloning experiments is that we are now realizing how much genes are influenced by their environment. Epigenetics is a field of inquiry born from observations that genetic material evolves differently depending on environmental conditions. As cloning studies progressed, it became apparent that, despite clones having identical DNA, a wide variety of environmental factors influenced whether a particular gene was turned on or off in an individual clone. This has considerable implications for the genetic makeup of the natural world's sexually reproducing, non-cloned species. The environmental factors that affect genes can range from conditions in the mother's uterus to nutrition, lifestyle, and exposure to pollutants and hazards, as well as many more factors that are not fully understood. So far, this science, called epigenetics, has improved our understanding of the epidemiology of chronic conditions such as hypertension and type 2 diabetes, conditions that most often appear in middle age but have their origins in utero. The "Barker hypothesis," named after British epidemiologist David Barker, holds that an adverse pre-conception and intrauterine environment is associated with the epigenetic malprogramming of the fetus, and a predisposition to various specific metabolic disorders in later life (4,5). One major impact of epigenetics has been the establishment of solid causal links between developmental deficits and fetal exposure to alcohol, leading to widespread campaigns to discourage drinking during pregnancy.

## *Advances in human reproduction*

The most famous name in human reproductive technology is Louise Brown, born in 1978 in the United Kingdom following in vitro fertilization (IVF). Louise was the world's first "test-tube" baby. Her birth was the culmination of scientific work ongoing since the late 1950s, when **Dr. Anne McLaren** and colleagues at the Royal Veterinary College in London demonstrated the feasibility of inseminating mouse embryos in a test tube and placing them in the uterus of a surrogate mother (6,7). Dr. McLaren continued to work on embryo transfer techniques throughout her career; **her contributions to paving the way for human assisted reproduction were recognized with the 2001 L'Oréal-UNESCO Award For Women in Science.**

The European Society of Human Reproduction estimates that over five million babies worldwide have now been born following IVF (8). Through IVF, harvested eggs and sperm are introduced in vitro to initiate fertilization. Once the embryo is between two and six days old, it is transferred to the mother or surrogate's uterus where it implants within the uterine lining and is carried through pregnancy. Technologies have also been developed to help counter male infertility, where a common problem is sperm that cannot penetrate the egg. When the egg is removed from the body for IVF, a procedure called intra-cytoplasmic sperm injection (ICSI), developed by Professor Andre Van Steirteghem in the early 1990s, can be used to insert the sperm directly into the egg, ensuring that fertilization has taken place before replacing the embryo into the uterus (9). The procedure is necessary when using eggs that have been frozen, as these develop a harder shell. In Europe, ICSI now accounts for two thirds of assisted conceptions (10).



*Doctor Anne McLaren, 2001 Laureate for Europe*

## *Genetic diagnosis*

People at high risk for transferring genetic diseases may opt for IVF so that the egg and sperm (and in some countries, the embryo) can be tested for the faulty gene prior to fertilization or implantation in the uterus. The first application of pre-implantation genetic diagnosis was reported in 1989 by Dr. Alan Handyside and colleagues at Hammersmith Hospital in London (11). Early on, the technique was used for single gene and sexual disorders but has since expanded to test for a far wider range of genetic diseases. Many countries prohibit genetic testing of pre-implantation embryos, meaning that testing occurs immediately after an ICSI procedure. Researchers are now exploring non-invasive pre-implantation diagnostic techniques; they are also recognizing that some abnormalities self-correct in early embryonic life (12). A new genetic splicing technique called CRISPR-Cas9 may soon make it possible to eliminate or deactivate the disease-causing gene at the embryonic stage (13).



### Preserving eggs and embryos through freezing

Techniques to harvest eggs have progressively improved, and the possibility of extracting and freezing eggs is now offered to many women who require radiation or chemotherapy for cancer at a young age. It has become possible to donate eggs and embryos, which can also be preserved through freezing. A major reason for the growing popularity of these services is the incompatibility between social trends that see women delaying childbirth to pursue professional opportunities, and the biological fact that eggs become less viable and more prone to abnormalities as women age.

The first pregnancy resulting from frozen eggs was reported in 1986 by Dr. Christopher Chen (14), but it was only in 1999 that Dr. Lilia Kuleshova, an expert physicist in cryobiology, achieved a flash-freezing process called human egg vitrification. After thawing, fertilization and implantation, this process resulted in a live birth (15). Studies show frozen eggs have similar pregnancy rates to “fresh” or recently retrieved eggs, and babies born from frozen eggs appear to have no more risk of malformations or other disorders than naturally conceived infants (16).

A major side effect of assisted reproductive technologies (ART) has been the rise in multiple pregnancies, as several fertilized eggs are reintroduced into the uterus assuming that not all will survive. Twin and triplet births involve greater risk of complications, and efforts have been made to increase the success rate of implanting a single embryo with better chances of survival. A 2006 study in Canada showed that double embryo transfer was used in 55% of ART procedures: twins were ten times more likely to be born before term and at low birth weights (17). The study was a wake-up call in the world of ART. Between 1997 and 2014, the rate of single embryo transfers increased significantly in an effort to minimize the risks associated with multiple pregnancies. In Europe, assisted reproductive technology use has been monitored since 1997. Pregnancy rates, or the percentage of attempts that result in pregnancy, are now around 35% for IVF and 33% for ICS: rates from donated eggs are approximately 50% (8).

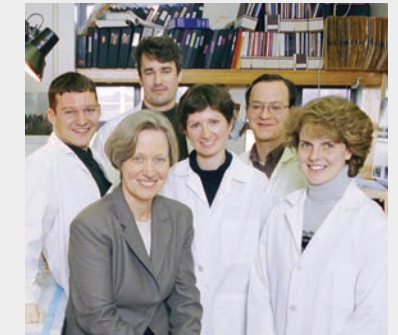


Professor Christiane Nüsslein-Volhard, 2006 Laureate of a Special Award 1995 Nobel Prize in physiology or medicine

**Professor Christiane Nüsslein-Volhard** has dedicated much of her career to studying how genes control embryonic development in flies and fish. She and collaborators Professors Eric Wieschaus and Edward Lewis, were awarded the Nobel Prize for Physiology or Medicine in 1995 for their discovery of genes that established the body plan of fruit flies, a discovery that enabled understanding of the genetic control of early embryonic development in all species, including humans. Christiane Nüsslein-Volhard has been Director of the Max Planck Institute of Developmental Biology in Germany since 1986 and has, in this and other positions, worked hard to promote gender equity in science by helping women balance research and family responsibilities. **In 2006, she combined a special award from the UNESCO-L'Oréal For Women in Science** with her own funds to create the Christiane Nüsslein-Volhard Foundation, which offers grants to young female scientists for baby sitters and household help.

**Professor of Molecular Biology and first woman President of Princeton University, geneticist Shirley Tilghman**, was part of the team that cloned the first mammalian gene. **She received the 2002 L'Oréal-UNESCO Award For Women in Science** for this work. Tilghman's research has focused on analyzing genes whose expression pattern is determined by whether the gene is inherited from the mother or father. She was a founding member of the US National Institute of Health's National Advisory Council of the Human Genome Project, and has ventured into the thorny debates around stem cell research and the ethics of gene editing. In a recent lecture at Princeton, Tilghman explored the ethical and moral issues of the latest developments in gene editing, stressing the need to proceed delicately (18). *“This is quite an extraordinary moment,”* she said. *“The only other moment in my career in microbiology when I can remember this kind of controversy and scientific attention to a new technology was when the field of recombinant (artificially engineered) DNA was arriving on the scene, and that was in the late 1970s.”* In her view, the most important question is whether gene editing will treat individual patients, limiting the impact to one person, or be used to alter germ line cells that will also affect subsequent generations. To date, Tilghman and the medical community are united in calls to prohibit the engineering of our human genetic inheritance.

*“This is quite an extraordinary moment when the field of recombinant (artificially engineered) DNA was arriving on the scene, and that was in the late 1970s.”*



Professor Shirley Tilghman, 2002 Laureate for North America

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# 15 UNDERSTANDING THE UNIVERSE

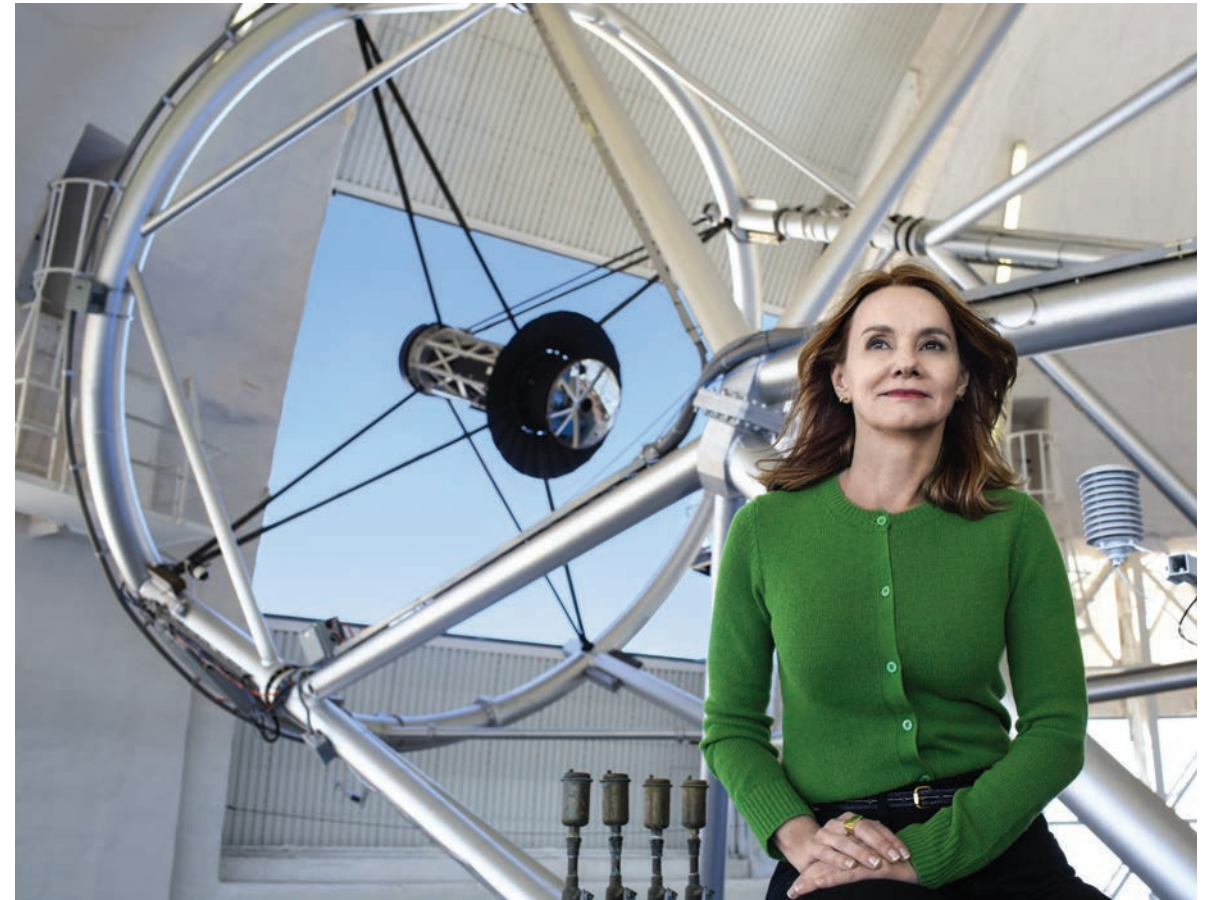
In considering the nature of our universe, physicist Peter Higgs in 1964 discussed the existence of an omnipresent particle forming a field through which all matter travels, and that is ultimately responsible for creating mass. This theorized particle became known as the Higgs boson and formed an important part of the Standard Model of Particle Physics, a theory describing all known fundamental particles and forces in our universe. Although it enabled the properties of particles to become better understood, the Higgs boson remained a theory for many years, rather than a measurable entity.

In 1997, two experiments were approved in Switzerland at the European Organization for Nuclear Research, or CERN as it is better known, to prove the existence of this particle: ATLAS and CMS, both of which take place within CERN's Large Hadron Collider (LHC). Over 3,000 physicists from 38 countries have been involved in the ATLAS project since it began. Their aim is to study nature at its most fundamental level, identify its basic building blocks and understand how they interact. Within CERN's Large Hadron Collider, which measures 27 km in circumference, two beams of protons collide, each carrying enough energy to produce particles with masses that are ten times greater than any known particle. Within the collider, the ATLAS particle detector was built to identify all the particles produced at the point where the proton beams collide. Accelerators can measure the types of particle released by high energy collisions, such as electrons and protons, and assess their direction and momentum, as well as the energy they release.

A central goal of the ATLAS project was to identify the Higgs boson as the missing piece in the Standard Model which states the existence of other particles and their ability to combine together and form matter. The Standard Model theorized the need for a boson, a type of subatomic particle. Unlike other sub-atomic particles such as electrons, neutrons and protons, which cannot occupy the same space on an atom, this boson can share space because it is more like a force than a particle. It was theorized that without the Higgs field, the universe would be composed of particles moving around at the speed of light and no atoms would exist. The intensity of a particle's interaction with the Higgs field influences the particle's mass, making it possible for two particles of the same size to have different masses.

**Rajaâ Cherkaoui El Moursli, Professor of Physics at Mohammed V University in Rabat,** participated in the ATLAS experiment and describes the working environment as the experience of a lifetime. *"The level at which people collaborate at CERN is remarkable, and this despite the tremendous diversity in nationalities, gender, race, religion, cultural quirks, status or political views. The focus is on what each person can contribute to solve the problem you're working on."* El Moursli **received the 2015 L'Oréal-UNESCO Award For Women in Science** for her key contribution to one of physics' greatest discoveries.

In 2012, ATLAS scientists reported finding evidence of a particle that was consistent with the Higgs boson. The force of the collision produced in ATLAS was strong enough to enable part of the



*Professor Thaisa Storchi Bergmann, 2015 Laureate for Latin America*

Higgs field to be measured before it decayed. Further experiments and measurements undertaken over the next year confirmed that the properties of the particle and the way it interacted with other particles matched those of a Higgs boson. *"Once the Higgs boson particle was discovered,"* says El Moursli, *"speculation about other theories stopped and the door was opened to further discoveries."* In 2013, Peter Higgs and Francois Englert, theoretical physicists who predicted the existence of the Standard Model Higgs boson, were awarded the Nobel Prize in Physics.

### *The next frontier*

Once the Higgs boson, the last missing particle in the Standard Model, was discovered, physicists increasingly turned their attention to the roughly 96% of the known universe that is not described by the Standard Model: Dark Matter and Dark

Energy. The guiding theory here is that before the Big Bang, the four forces that rule the universe — gravity, electromagnetism, and weak and strong nuclear force — were unified in a single symmetrical Superforce. This was shattered by the Big Bang, producing a highly unsymmetrical universe made up of planets, asteroids, etc. The Large Hadron Collider is now the site of further experimentation to create Dark Matter, a form of invisible matter. The Collider underwent two years of repair and upgrade following the ATLAS experiments, and scientists now hope it has the energy and magnetic fields required to make protons split into their most elusive sub-particles. Plans have also been developed to expand the Collider to a circumference of around 100 km.

The nature of dark matter remains one of the most important unresolved issues in astrophysics. Experimentation at CERN is pursuing theoretical models that explain dark matter as an exotic



“The level at which people collaborate at CERN is remarkable, and this despite the tremendous diversity in nationalities, gender, race, religion, cultural quirks, status or political views.”

*Professor Rajaâ Cherkaoui El Moursli, 2015 Laureate for Africa and the Arab States*



*Professor Rajaâ Cherkaoui El Moursli, 2015 Laureate for Africa and the Arab States*

massive particle, but there is no evidence yet that such particles exist. Another possible explanation has been gaining ground with discoveries made by NASA scientists in the past few years, that dark matter is made of black holes formed as the universe came into existence. Astrophysicist Alexander Kashlinsky at NASA led a team of astronomers in 2005 to explore a background glow of infrared light that exhibited patchiness in part of the sky. This and later observations led them to consider that galaxies may be embedded within a vast sphere of black holes (1).

**Brazilian Astrophysics Professor Thaisa Storchi Bergmann** has been observing super-massive black holes, millions of times more massive than the sun, which are found at the centre of nearly all currently known galaxies. She describes her work as “archeology of the universe”, studying traces of gas and dust found in the

vicinity of these black holes, along with x-rays and other electromagnetic waves that may be produced by events that happened billions of years ago and are only now making their way to Earth. In 1993, she discovered a super-massive black hole at the center of the galaxy called NGC 1097. Like many others, its nucleus was surrounded by rings of gas, providing the first evidence of an “accretion disk” of matter spinning around the galaxy core (2). She has continued to study the galaxy for 30 years. It may be many more before it can be experimentally verified, however, the discovery of the Higgs boson lent new force to international collaboration on understanding the fundamental question of how we, and everything around us, came to be. **Bergmann received the L’Oréal-UNESCO Award For Women in Science in 2015** for her groundbreaking work on super-massive black holes in the centers of galaxies, their associated regions of dense gas, dust and young stars, and the role of black holes in the evolution of galaxies.

Moroccan physicist Rajaâ Cherkaoui El Moursli, Professor of Physics at Mohammed V University in Rabat, contributed to the simulation and construction of the electromagnetic calorimeter in the ATLAS detector. She is Vice President of the Mohammed V University in Rabat, Morocco, where she leads work on the consolidation of a Distributed Analysis Support Team (DAST) for the ATLAS collaboration, focusing on analysis in top quark and Higgs boson physics. The scientist and her team of nuclear physicists contributed to the construction, simulation, test and launch of the Electromagnetic Calorimeter, one of ATLAS’s sub-

particle detectors, composed of sublayers of detectors that were each designed to detect specific particles. El Moursli’s team from Rabat, Casablanca, Oujda and Stockholm was in charge of building an electromagnetic calorimeter to detect all gamma rays and electrons. She has built on her CERN work to pursue important collaborations with scientists in Europe, and primarily France, in the development of nuclear physics expertise in Morocco. In particular, she recruited colleagues to teach in the Master’s programme on radiotherapy that she created to train professionals to provide cancer radiation therapy in centers across Morocco.



*Professor Rajaâ Cherkaoui El Moursli, 2015 Laureate for Africa and the Arab States*

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# 16 PAIN RELIEF

Pain is our body's way of protecting itself from damage, a signal to move our hand away from the fire. It is also triggered by the mechanisms involved in inflammation following injury or infection, and by nerve damage, both of which produce pain that can become chronic. Today, pain is increasingly garnering attention from researchers, international organizations and governments. Between 20% and 30% of populations in developed countries suffer from persistent or chronic pain, with significant impacts on their quality of life and ability to work. Pain is the most common reason people seek help from physicians, even though pain that lacks an obvious cause might be dismissed as being "in your head," while relief may come at the cost of addiction to pain-killing drugs. Pain is a perennial part of existence, and humanity has always sought to better understand and develop more effective ways of controlling it (1).

## *What causes pain?*

Traditionally, pain was considered a symptom of disease or injury, and treatment focused on identifying and addressing the underlying problem. The exponential growth in pain research over the past few decades paints a somewhat more complex picture. We now know that pain responses involve complex neurotransmitter and feedback loops within pain conducting systems. Receptors can begin to send pain signals in response to things that do not normally cause pain (2).

Previously, when a physiologic explanation for pain could not be found, the assumption was that the pain was psychological, a perspective that has given way to a more holistic approach. Fibromyalgia, which affects women more than men, and affects between one and five percent of the population, was long considered a

psychosomatic condition, as it involved no obvious injury or organic disease. Contemporary treatment of fibromyalgia and other neuropathic pain conditions seeks to understand what takes place when pain is experienced. Claudia Sommers, Professor of Neurology at Germany's University of Würzburg and a member of the International Association for the Study of Pain, embarked on her study of neuropathology in order to "see what somatic disease actually looked like" (3). In her investigation of patients with fibromyalgia, Sommers and her colleagues looked at the body's peripheral nerve systems and, in 2013, detected loss of function and physiological abnormalities (4). While they have yet to determine what causes these, the findings of their study prompted a windfall in research: in 2016-17, there were 50 new studies on fibromyalgia being published each month (5). Sommers' laboratory is exploring, in collaboration with a European Union funded consortium, the role of microRNAs in pain to understand why some people develop neuropathic pain after an injury and others do not. Many genetic factors have been found to influence pain sensitivity. The researchers are also investigating the role of cytokines in pain, substances secreted by certain immune system cells that have an effect on other cells (6).

Inflammatory pain is caused by "cross-talk" between the immune and nervous systems, signaling that some part of the body has suffered damage and needs protection. Both pain causing (proalgesic) and pain relieving (analgesic) molecules are involved in the complex processes that lead to tissue repair (7). In 2002, pharmacology researcher Camilla Svensson at the Karolinska Institute in Sweden made the important discovery that long-term inflammation in the joints triggers a group of cells in the central nervous system to amplify or prolong that pain



*Professor Lourdes Cruz, 2010 Laureate for Asia-Pacific*

(8,9). This would explain why pain in conditions such as rheumatoid arthritis persists even after medications have reduced inflammation. Svensson's group is now investigating links between these cells and persistent pain, in the hope of developing new drugs to relieve chronic inflammatory pain. Svensson was recognized in 2013 as a Future Research Leader by the Swedish Foundation for Strategic Research.

People's experience of pain varies, and therefore understanding these differences may help to uncover alternative strategies for pain alleviation. It would appear that genetic and epigenetic (the interaction of genes and environment) factors play a role in pain vulnerability and affect the brain networks involved in chronic pain. Current and evolving knowledge around pain is leading to strategies that address both peripheral and central pain mechanisms.

## *Relieving pain*

Nonsteroidal anti-inflammatories and acetaminophen are considered the basics of pain relief. They are now known to operate through mechanisms beyond reducing inflammation, producing an effect on the pain receptor and signaling process too. Certain antidepressants have analgesic qualities, as do some anticonvulsant medications, notably for nerve pain. The analgesic effect of antidepressants is independent of their

effect on depression, and various factors are potentially involved in their effect on pain. For example, they may alter the level of opioids produced by the body and/or block some of the channels involved in pain signaling and sensitization to pain.

The most powerful pain relievers augment the activity of receptors that are present in the body from the outset. The body's opioid system is a crucial network for lessening pain-related signal transmission. Opioid receptors are found in the brain and spinal cord, and in the peripheral nervous system. When a person takes an opioid medication, it increases this innate analgesic effect. Opioids have been used in pain relief for thousands of years and are effective against even the most severe forms of pain. In 1959, Dr. Paul Janssen developed the synthetic opioid, fentanyl, a potent analgesic one hundred times stronger than morphine. It was quickly adopted for use as an intravenous anesthetic. Controlled-release formulas and delivery mechanisms have seen these powerful painkillers adopted for use in chronic pain. The fentanyl patch was developed in the mid-1990s (10).

The problem with opioids is that they are also highly addictive. OxyContin, a drug derived from the opioid oxycodone, developed in the early 20<sup>th</sup> century, was marketed in the United States beginning in 1996. By 2001, it was the best-selling





“Solving the biology of the brain: that’s the focus, and functional imaging enables us to look at the whole brain and see connectivity patterns involved in pain and addiction.”

Professor Brigitte Kieffer, 2014 Laureate for Europe

narcotic pain reliever in the country and soon after, the most widely abused prescription drug of all time. More recently, fentanyl has been responsible for a startling rise in fatal overdoses: the US saw a 73% jump in deaths from 2014 to 2015; in Vancouver, Canada, fentanyl was detected in 81% of illicit drug deaths in the first nine months of 2017, representing a 143% increase in deaths in just one year (11).

The current opioid epidemic is prompting efforts to find new non-addictive interventions to manage chronic pain. Promising avenues include the development of a new generation of powerful but non-addictive opioid analgesics that enable opioids to work on pain without activating the “reward” effects that lead to addiction. Clinical trials are now underway (12). Other research is coupling opioids with agents to reduce the development of tolerance and dependence.

Neurobiologist Professor Brigitte Kieffer has conducted groundbreaking work on the brain mechanisms involved in pain, mental illness and drug addiction (see page 25). She was the first, in 1992, to isolate and clone the gene for an opioid receptor in the brain; her work in France and now as Scientific Director of the Douglas Mental Health Research Centre in Montreal, Canada, is helping to understand how opioid receptors can be activated

to reduce pain while minimizing the risk of addiction. “*Solving the biology of the brain: that’s the focus,*” she said in a recent interview, “*and functional imaging enables us to look at the whole brain and see connectivity patterns involved in pain and addiction.*”

### Cannabinoids

The human brain also has cannabinoid receptors in the pain-processing area of the brain, spinal cord, and peripheral nervous system. Supplementing natural cannabinoids with medical marijuana formulations provides a moderate analgesic effect. Higher doses are associated with a psychoactive, intoxicating effect (or “high”). Researchers have been developing formulations and delivery mechanisms that provide the pain relief without the high. In the early 2000s, a formula that could be sprayed in the mouth was developed, containing cannabidiol extracted from cannabis and tetrahydrocannabinol (THC), cannabis’ primary psychoactive component. Synthetic forms of THC have also been used for pain associated with multiple sclerosis. Many countries have, in the past 20 years, established medical marijuana programmes, which legalize its use under medical supervision.



Professor Lourdes Cruz, 2010 Laureate for Asia-Pacific

**Lourdes Cruz, Professor at the Marine Science Institute at the University of the Philippines,** began studying snail toxins in the 1970s, seeking to identify which components of snail venom were toxic for humans. Her work led to the discovery of conotoxins, which act on calcium channels that

release pain signals. Conotoxins have been used to develop a new non-addictive, non-opioid painkiller that, injected in spinal fluid, inhibits the pain pathway to the brain. **Her discoveries were recognized with the L’Oréal-UNESCO Award For Women in Science in 2010.**

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# 17 NEW MATERIALS

Humans' distinct ability to find and transform materials into useful objects has slowly but surely revolutionized what we do every day and how we interact with each other and the world around us. From the mining, smelting and casting of the bronze age to the current silicon, or "digital" age, understanding the properties of materials and how to manipulate them has helped to create the world we live in today. Along the way, consumption of materials has increased dramatically: between 1980 and 2010, global consumption, notably of metals and minerals, nearly doubled. Resource scarcity therefore presents a pressing challenge for today's societies and future generations.

Materials science was only recognized as a distinct discipline in the 1950s, and the real growth in materials research has occurred in the 21<sup>st</sup> century. The field is necessarily multidisciplinary, as chemical, physical and biological scientists collaborate with engineers to find and create diverse materials with specific properties, and bring these together into a functional piece. The ambition is to create materials with combinations of functional properties that do not currently exist, in order to serve very specific purposes: a material that is at once transparent, flexible and impermeable; or both smudge and crack resistant; or resistant to oxidation with high electrical conductivity. It is a pragmatic science, which also takes cost-effectiveness into account, in order to ensure that a material is viable for use in manufacturing products.

*"What is both very exciting for us as materials researchers, and also a little frustrating, is that the real impact of materials occurs when they turn into something that you actually carry around in your pocket,"* said Professor Julia Phillips, member of the National Science Board in the US, at the October 11 2017 Materials Day Symposium at MIT (1). University programmes emphasize

multidisciplinarity in order to integrate practical concerns into research programmes. Today, scientists may begin by imagining the combinations of properties that would be needed to enable or improve a particular function, and work to synthesize or assemble molecules to meet those needs.

They may also work in a more traditional discovery mode. New laboratory capabilities in computer simulation and advanced microscopy are helping scientists to solve questions that confounded earlier generations. For example, Professor Nicola Spaldin set out on a quest for magnetic ferroelectric materials, also known as multiferroics, that combined ferromagnetic and ferroelectric properties, meaning that an electric field can induce a magnetic polarization and vice versa in a material. The interplay between electricity and magnetism (evident when the needle of a compass moves when a current nearby is switched on or off) is well known, however the question was could they, and did they, coexist in real materials? Spaldin created computer models of virtual magnetic ferroelectrics to study their properties. She published a theoretical paper in 2000 (2), explaining where the contradiction between ferromagnetism and ferroelectricity arose and suggesting ways of working around it. The paper garnered only limited attention at the time, but over the past 15 years, it has come to be recognized as the basis of rapid advances in the field.

Spaldin had the opportunity to test her predictions by synthesizing multiferroics in the lab, collaborating with a group at Berkeley led by Ramamoorthy Ramesh to produce thin films of a multiferroic material called bismuth ferrite. Publication of the discovery in *Science* in 2003 (3) led to an explosion of research, the identification of further multiferroics, and the discovery of further properties in these materials. Multiferroics have applications in electronics, data storage and

transfer and, notably, quantum computing. In electronic devices, multiferroics can reverse polarization in response to low-power electric fields, and hold their polarized state without continuous power. This presents a significant advance over materials that require heat-generating and power-using electrical currents.

Professor Spaldin anticipates that the discovery of new uses will continue. *"There are additional applications of multiferroics that we had not thought of at all when we started our research,"* she says. *"Multiferroic surfaces seem to be quite efficient catalysts for water purification, for example, which is exciting since they are non-toxic and quite cheap and easy to produce."* As a basic scientist, Professor Spaldin finds it rewarding when discoveries prove to be useful. *"It's important for society not to forget that many important developments start out very far from applications,"* she cautions; *"Basic research should not be neglected."*

The devices we carry around with us today, and machines that carry us around, were made possible by advances in materials science, from the superalloys used in jet engines to the strained superlattices used in magnetic recording and lasers to the silicon in laptops and smartphones.

## *Silicon to silicene*

Silicon entered our lives in the form of transistors that would become the basis of the digital era and the semiconductor industry. Chemical modification of silicon enabled significant advances. In 1994, scientists published their first theoretical report on the thinnest possible form of silicon, heralding the progressive shrinking of microprocessor components. Within ten years, it seemed that further progress with silicon would be difficult (4). In 2004, a possible replacement material, graphene, was first described: its inventors, André Geim and Konstantin Novoselov from the University of Manchester, were awarded the Nobel Prize in Physics for their work. Graphene is the thinnest substance ever made. It is hundreds of times stronger than steel and yet flexible and malleable, conducts electricity faster than any other known material at room temperature and



*Professor Nicola Spaldin, 2017 Laureate for Europe*

converts light into a current (5). The first integrated circuit based on a graphene transistor was built by IBM researchers in June 2011. However, it proved ill-suited to some functions. In 2012, French scientists, including materials scientist Guy Le Lay, succeeded in developing silicene sheets from silicon atoms. They sought to make graphene behave like a semiconductor, so that it would be compatible with existing silicon-based circuitry, and enable production of even smaller electronics (6).

These advances are significant, and major efforts are underway to overcome the difficulties of working with such thin materials. Graphene research even has its own superhero icon, Mr G, to champion the cause (5). The difficulties are a reminder of the fundamentally pragmatic nature of materials science: its impact does not manifest until it results in something manufacturers can work with and people use in daily life.

## *Transport and energy*

In the aerospace and automotive sectors, the quest for ever lighter-weight materials has led to the development of aluminum alloys, titanium alloys and composite materials. In commercial airlines,



“My dream is to use the materials we develop to make the world we live in a better place.”

*Professor Zhenan Bao, 2017 Laureate for North America*

fuel economy has improved on average by 1% per year and is directly related to changes in the materials employed in airplane manufacture (7). In the automotive sector, a 10% reduction in the weight of a vehicle allows for a 6% increase in fuel economy. The last 25 years have seen reductions in car weight of up to 70%, due to new materials such as aluminum and magnesium alloys and carbon fiber compositions. The Ford pick-up truck lost 700 pounds (317.5 kg) in its 2015 switch to an all-aluminum alloy bed (8).

#### *Innovation in plastics*

A polymer is defined very broadly as a useful chemical made of many repeating units linked in one- two- or three-dimensional networks. Rayon and nylon are early manufactured polymers. Many polymers are composed of hydrocarbons (natural gas, coal or oil) or silicon, though biopolymers are made from natural feed stocks with biodegradable properties. Natural polymers include spider silk and hair starch, cellulose and rubber. Cellulose is the most abundant natural polymer and, with current technologies, can be used to make a vast range of products, from clothing to medical devices and pharmaceuticals. **Professor Tatiana Birshtein at the Russian Academy of Sciences in St. Petersburg, recognized with the L'Oréal-UNESCO Award For Women in Science in 2007,** has contributed to understanding the structures of a vast range of large molecules, allowing scientists to predict how they will behave under different conditions.

The combination of new materials and technologies such as laser 3D scanning is opening exciting new prospects for combining, applying and shaping



*Professor Tatiana Birshtein, 2007 Laureate for Europe*

materials in novel ways. One area is prosthetics, where these advances will help to create custom fit devices. Materials are being developed to be at once lighter and more resistant, control perspiration, and reduce odor and bacteria growth. They may also integrate sensors to provide dynamic feedback. Advances in materials used to probe brain activity may also one day help activate those prosthetic limbs. At MIT in the US, Associate Professor in Materials Science and Engineering, Polina Anikeeva, and her colleagues developed soft polymer-based devices to stimulate and record activity of brain and spinal cord tissue without provoking a foreign body response from brain tissue. Her laboratory has progressively improved the multi-functional fibers. They comprise elements that serve as conductive electrodes to record brain function, a transparent copolymer cladding to deliver light and stimulate neurons, and microfluid channels to deliver drugs that affect neural activity. The result is a rubbery device as thin as a human hair. Anikeeva and her colleagues have been able to implant these nanowire-mesh coated fibers in mice, delivering a light signal to the spinal cord and observing the signal travel down the sciatic nerve to the back-leg muscle. Anikeeva believes that eventual applications could include combatting spinal cord injury (9).



*Professor Zhenan Bao, 2017 Laureate for North America*

**Zhenan Bao, Professor in the Department of Chemical Engineering at Stanford University in the US,** is working on organic electronic materials that are flexible, stretchable, biodegradable and can heal themselves. Her aim is to replicate the skin's ability to sense and transmit a signal to the brain that could cover a prosthesis and allow a patient who has lost a limb to feel the sense of touch again. **Professor Bao was awarded the L'Oréal-UNESCO Award For Women in Science in 2017** for the development of this unique polymer skin. In 2015, the journal Nature named her as one of the top 10 people who had an important impact on science that year. “My dream,” she says, “is to use the materials we develop to make the world we live in a better place, whether it is for electronics that improve human health or for cleaner energy.”

**Mildred Dresselhaus (1930-2017), Professor Emerita at the Massachusetts Institute of Technology,** was known as the “Queen of carbon science”. She pioneered research into the electronic properties of materials, and, in particular, of carbon, introducing innovative tools for the analysis and development of nanoscale structures. A former President of the American Physical Society, **Prof. Dresselhaus’ tremendous contributions were recognized with the L'Oréal-UNESCO Award For Women in Science in 2007,** the Kavli Prize in Nanoscience in 2012, and the Presidential Medal of Freedom in 2014. She will be remembered by all as a pioneering scientist and advocate for women in science.



*Professor Mildred Dresselhaus, 2007 Laureate for North America*

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# 18 DRUG DISCOVERY AND DELIVERY

It's called Nature's medicine chest, the wealth of compounds in plants, animals, and other organisms that have the power to relieve symptoms and cure disease in humans. Scientists have long pursued the challenge of identifying these naturally occurring bioactive compounds and turning them into therapeutic agents, a process that involves isolating the compound's active ingredient and synthesizing it to improve its biological activity and reliability. Quite often, a compound will work on different body systems and the full range of its actions will only be revealed over significant periods of time. The process of synthesizing a given agent brings a better understanding of how it works and can highlight potential uses. Another important source of information lies in the ancient traditions of diverse cultures, which can help to illuminate therapeutic uses for naturally-occurring substances.

Exemplifying this process, **Margaret Brimble, Chair of Organic and Medicinal Chemistry at the University of Auckland in New Zealand**, has spent years looking at shellfish toxins and other natural products, isolating and synthesizing compounds that may be helpful in conditions ranging from traumatic brain injury to cancer and stroke. This work takes patience: Brimble's laboratory synthesized the compound trofinetide, which can alleviate brain injury, some 14 years ago. In 2017, she told us: *"I'm happy to report that trofinetide has now been successful in early clinical trials for Rett Syndrome and Fragile X syndrome, and the drug should reach the market in late 2018. This is very exciting, as the drug will be used to treat a genetic disease that affects the brain mainly in women and was discovered in a female academic's lab!"*. The route from

identification and synthesis of a compound in the laboratory to availability in the clinic to treat patients is long and full of obstacles.

Identifying potential therapies is only one side of the challenge. The other is finding potential drug targets, which requires an intensive understanding of the mechanisms underlying the health problem or disease concerned. Progress in the past few decades in understanding disease mechanisms, supported by tremendous computing power, has accelerated and expanded efforts to find new drug targets and enabled more effective exploration of existing targets. In 2002, the number of reported targets reached more than 1,500 from approximately 500 in 1996, and is continuing to grow rapidly (1). Knowledge of these targets can help to determine the mechanism of drug action at the molecular level, guide new drug design, and reveal promising further searches for new targets. It has also led to the identification of previously unknown targets for existing drugs. For example, interactions between the nervous, respiratory and cardiovascular systems can mean that a drug will target a receptor that impacts on more than one system (1).

Even once a target is found, the failure rate in identifying compounds that might have the desired effect is huge: fewer than two in 1,000 compounds even make it to the first stage of trials in the laboratory and in animals. Fewer still are ever tried in humans. One in 5,000 compounds might make it to market (2). Once there, it is likely to work in fewer than half of the people who take it.

Knowledge gained through the Human Genome Project, and subsequent discoveries of genes and proteins involved in disease, are bringing dramatic changes to the traditional model of drug

development. *"The challenge of matching the activity of a compound to a therapeutic target still relies on systematically constructing a structure-activity relationship profile,"* Brimble emphasizes. *"However, the process has been improved substantially by developments in computer-aided drug design."* **Brimble's work was recognized in 2007 with the L'Oréal-UNESCO Award For Women in Science.**



*Professor Margaret Brimble, 2007 Laureate for Asia-Pacific*

Proteins have gained interest as targets for various therapies. In 2009, **Professor Ada Yonath, Director of the Helen and Milton A. Kimmelman Center for Biomolecular Structure and Assembly of the Weizmann Institute of Science** in Israel, received the Nobel Prize in Chemistry along with Venkatraman Ramakrishnan and Thomas Steitz for their studies on the structure and function of ribosomes, which explained how the genetic code is translated into proteins. This research provided crucial insight into the mode of action of antibiotics. Ribosomes are the cell's protein factories and the three-dimensional models developed by Professor Yonath and her team, using x-ray crystallography, showed how different antibiotics bind to ribosomes. This binding is central to understanding antibiotic resistance and developing advanced antibiotics. **In 2008, Professor Yonath received the L'Oréal-UNESCO Award For Women in Science** for her studies of protein biosynthesis disruption by antibiotics.

## Drug delivery

Concurrent with the identification of new compounds and targets, the past 20 years have opened up whole new therapeutic possibilities through advances in the way drugs are delivered to targets. Drugs can be taken in different ways: orally, inhaled, implanted, injected and transdermally (via patches). For chronic conditions, a range of new injectable devices, prefillable syringes, pen injectors, electronic patch injectors and depot injectable delivery methods are all making significant headway in the growing area of drug self-administration.

The most significant recent advances have been in nanoparticle design and biomaterials that permit tightly calibrated rates of degradation. Synthetic and natural polymers are used for the controlled release and targeted delivery of drugs. Injectable drugs embedded in polymer carriers can allow for slower absorption of the drug, which reduces the number of doses a person has to take and can minimize acute side effects. More recently, "smart" polymers have been developed to respond to external stimuli such as changes in pH or



*Professor Ada Yonath, 2008 Laureate for Europe, 2009 Nobel Prize in chemistry*



“With drug delivery systems, we can achieve sustained release, thereby overcoming the highs and lows associated with conventional drug delivery.”

*Professor Molly Shoichet, 2015 Laureate for North America*

temperature, and can even respond to magnetic or electrical fields (3). Polymer carriers have already been developed to deliver drugs against cancer, rheumatoid arthritis, diabetes and hepatitis.

**Molly Shoichet, Professor of Chemical Engineering and Applied Chemistry, Chemistry and Biomaterials & Biomedical Engineering at the University of Toronto in Canada** is working with colleagues to develop these intelligent materials. “*Smart drug delivery systems enable us to deliver drugs more effectively to the target tissue,*” she told us in a recent interview. “*This means we can deliver more drug to the affected tissue with fewer side effects on the rest of the body. This can be achieved by injecting the drugs precisely where they need to be, or by taking advantage of targeting molecules to deliver the drugs via the circulatory system. With drug delivery systems, we can achieve sustained release, thereby overcoming the highs and lows associated with conventional drug delivery.*”

In cancer, a persistent problem has been the damage to healthy cells from powerful anti-tumor drugs. In conventional chemotherapy, many healthy cells are also killed, causing suppression of the immune system, irritation in the digestive tract, and accelerated hair loss. Nanoparticle drug delivery systems present exciting opportunities for safer and more effective anti-cancer drug therapy. Targeted

delivery systems are becoming more important with the emergence of potent and specific biological therapeutics. Hydrogels and other polymer-based carriers have also been developed to provide safe passage for pharmaceuticals through inhospitable regions of the body. In 2004, Satchi-Fainaro et al. published results of studies on the first polymer-antiangiogenic (anti-tumor growth) carrier with a linker designed to allow release of the drug in the presence of a particular protein known to be elevated in tumor cells. They showed that the drug selectively released in the tumor cells, and that it delivered prolonged activity without the nerve toxicity previously observed during its use. This was likely because the delivery system prevented it from crossing the blood-brain barrier (4).

Most recently, polymer-nanoparticle composites have been developed incorporating an inorganic nanoparticle that responds to light or externally-applied magnetic fields to target tumor sites in cancer and reduce the toxicity of anti-cancer agents to normal cells. These inorganic particles can also serve as contrast agents to enable image-guided drug release and provide information about the location of the drug delivery system. Positron emission tomography (PET) and magnetic resonance imaging (MRI) can also be used to observe how drugs are distributed to precise sites. Additionally, polymers are now being developed that are capable of recognizing molecules and directing intracellular delivery (5).



*Professor Molly Shoichet, 2015 Laureate for North America*

**Molly Shoichet, Professor of Chemical Engineering and Applied Chemistry, Chemistry and Biomaterials & Biomedical Engineering at the University of Toronto in Canada,** is working with colleagues to engineer intelligent biomaterials that can be used to target and destroy more cancer cells by redirecting more of the drug dose towards tumor sites and reducing side effects.

The blood-brain barrier is a particular interest in Shoichet's work. “*The blood-brain barrier limits our ability to deliver drugs to the brain, spinal cord and retina by intravenous or oral delivery*” she explains. “*One way to overcome the blood-brain barrier is to find a way to break down the*

*barrier. Another way is to simply go around the barrier and deliver molecules directly to the brain tissue. We are pursuing the latter and have had success in models of disease for stroke, spinal cord injury and blindness. We are investigating both cell and drug delivery strategies using innovative hydrogels to achieve success.*” **Professor Shoichet received the 2015 L'Oréal-UNESCO Award For Women in Science** in recognition of her work on methods to deliver biotherapeutics to the central nervous system and her complementary work on the creation of 3D patterns in hydrogen carriers (6).



*Professor Molly Shoichet, 2015 Laureate for North America*

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# 19 POLLUTION

Human activity has pushed the planet beyond its natural limits, with serious consequences. Air pollution has reached critical levels, with 98% of cities in low and middle-income countries failing to meet WHO guidelines on air quality (1), resulting in smog alerts and growing incidences of asthma, eye and skin irritation. In developed countries, the passenger car sitting in traffic spewing exhaust remains the most prevalent feature of the urban landscape, and carbon dioxide (CO<sub>2</sub>) emissions from transport continue to rise despite stringent emission standards (2). Garbage has also become a noxious side effect of the materialism that defines modern life. Despite efforts to encourage recycling of materials such as glass, tin, plastic and paper, even the most conscientious European countries have difficulty exceeding the 50% recycling mark (3). Plastic debris sits in landfills and is found in every major ocean. Some 8 million tonnes of plastic enter the oceans annually, (4) and it is predicted that by 2050, there could be more plastic in the oceans than fish. (5) In fact, plastic pollution levels have been suggested as a “geological indicator” of the earth’s current state, what scientists call the Anthropocene (human-altered) era (6).

## *Can we clean up our planet?*

Clean energy technologies and biodegradable materials may help to slow the rate at which the pollution and waste increases, but we still face the considerable challenge of undoing the damage done. Around the world, scientists are turning their attention to ways of detoxifying the environment and eliminating waste.

## *Air pollution*

Researchers can now envisage cleaning urban air, even outdoors. In 1972, Professor Akira Fujishima of the University of Tokyo published a study showing that, when exposed to light, titanium dioxide, used in paint, sunscreen, and food coloring, as well as thousands of other products, can split water into oxygen and hydrogen, mimicking photosynthesis in plants (7). This discovery has exciting applications in environmental remediation as powdered titanium dioxide will gradually purify water, when illuminated by sunlight. The process, called photocatalysis, can also potentially be used to clean air if the compound is integrated into building materials; even indoors, standard lighting is sufficient to activate titanium dioxide’s decomposition of pollutants. In 2000, photocatalysis got its own journal, discussing applications such as water storage tanks, window glass, concrete for roadways and bathroom fixtures (it also eliminates odors).

Researchers are also exploring other air-cleaning innovations, such as the use of electrostatic fields that ionize airborne smog particles to create fresh air. One experiment in the Netherlands was able to clean 30,000 cubic meters of air per hour (8). At California’s Stanford University, materials scientists are investigating polymers that could potentially be used in window screening to filter incoming air (9).

## *Water*

Birds coated in oil from ocean tanker spills appear regularly on television news. Now, scientists are finding a novel way to help them. An oil spill near the coast of Norway in 2009 gave marine environmental technologists at the Sintef research



*Professor Niveen Khashab, 2017 Laureate for Africa and the Arab States*

institute a chance to test a new way of cleaning up oil from seawater: peat moss. It absorbs and encapsulates oil, so that it can be easily removed from the surface of the water (10). In Ireland, chemical engineer Anne Morrissey at the University of Dublin is focusing on the removal of waterborne contaminants using absorptive substances and photocatalysis. She is also exploring the use of graphene and graphene composites in water treatment (11). Other researchers are experimenting with surface coatings that can be positively charged to attract and absorb pollutants from water, enabling production of low-cost water treatment systems. At the Swinburne University of Technology in Melbourne, Australia, research engineer Karyn Jarvis is investigating the use of quartz particles coated with a plasma-polymerized allylamine film to absorb the often toxic industrial dyes that are present in many waterways (12). Jarvis is particularly concerned by the decontamination of water in rural areas, disaster zones, and developing countries, where the large-scale water purification techniques used in richer urban centers are not practicable.

## *The plastics problem*

Large-scale production of synthetic organic polymers, commonly known as plastics, only began around 1950. In developed countries, plastics now account for more than 10% of solid waste. None are biodegradable. Recycling is

promoted, but has done little to displace primary plastic production. Globally, only 9% of plastics are recycled (13). Incineration of plastic waste is a major source of air pollution, releasing toxic gases.

One way to deal with polymer pollution is pyrolysis, a chemical recycling process that converts plastics into high quality oil for use in engines and power generation (petroleum is, after all, the main source ingredient of plastic). The plastics are heated in the absence of oxygen, producing liquid oil, leaving only a small amount of solid residue. Shafferina Dayana, a chemical biologist at the University of Malaya in Kuala Lumpur, has been studying the suitability of the liquid oil created by pyrolysis as a fuel. It has a higher calorific value (calories are a measure of energy) than the wood-based oil used in conventional diesel, and does not require refinement before use (14).

The growing body of evidence supporting the benefits of pyrolysis is also creating a new industry. In Niagara Falls, New York, the Plastic2Oil plant opened in 2009 and can process 40 tonnes of unsorted plastic a day, inexpensively converting 86% of it into clean liquid fuel. Moderate heat and lack of oxygen are used to break down the polymers into gases and oil. By 2012, the plant had recycled millions of pounds of plastic waste that would otherwise have been landfilled, and, in that year alone, produced 1,200,940 litres of fuel





Professor Niveen Khashab, 2017 Laureate for Africa and the Arab States

(15). Elsewhere, Australian Priyanka Bakaya has founded a company, PK Clean, to bring pyrolysis technology to communities around the world. In 2016, PK Clean's first plant opened in the American state of Utah; a second will open in Nova Scotia, Canada in 2018. Over the summer of 2017, PK Clean and the Plastic Ocean Project traveled North America's Atlantic Seaboard from North Carolina to Bermuda to collect oceanic plastic waste at sea, which was then used to create fuel for the ships the project used. Bakaya sees tremendous potential for the technology in coastal communities, where considerable amounts of waste are deposited by the sea (16).

### Thinking ahead

Taking cues from the world's ongoing polymer crisis, some scientists are seeking to anticipate the long-term impact of new technologies before they take hold. Linda Gaines, a physicist and transportation systems analyst at the Argonne National Laboratory in the US state of Illinois, is looking ahead to the day when cars are primarily powered by lithium-ion batteries, which will create a significant demand for lithium and a new problem: what to do with the batteries when they reach end of life. Batteries for the automotive sector are being designed for performance rather than recyclability, making much of the knowledge

“New technologies are of course exciting and potentially very beneficial, but it always boils down to the proper use and then disposal of new technologies to protect our environment.”

gained around recycling of lead-acid batteries inapplicable. Gaines' approach is holistic, studying the entire life cycle of a technology from materials to production processes, usage, and eventual recycling or disposal (17).

**Organic chemist Niveen Khashab, from the King Abdullah University of Science and Technology in Saudi Arabia,** is addressing similar concerns around nanotechnology. She **received the L'Oréal-UNESCO Award For Women in Science in 2017** for her design of novel nanoparticles that can be used in the early detection of disease and targeted drug delivery systems. To address the potentially harmful effects of these nanoparticles on the environment, she recently developed a new generation of nanoparticles that naturally degrade when exposed to light. “*Even though we cannot see it with our own eyes, the accumulation of these really tiny entities can influence biological and chemical processes,*” Professor Khashab told us in a recent interview. “*We therefore need to consider factors such as degradability and recyclability. During the industrial revolution, there was no thought that carbon dioxide emissions would one day pose a major threat to our planet. New technologies are of course exciting and potentially very beneficial, but it always boils down to the ‘proper use and then disposal’ of new technologies to protect our environment.*”



Professor Fayzah Al-Kharafi, 2011 Laureate for Africa and the Arab States

As long as fossil fuels remain in use, maximizing efficiency and minimizing the negative effects of production remains a priority. In Kuwait, **Professor of Chemistry Fayzah Al-Kharafi** is exploring high temperature geothermal solutions to address the impact of corrosion on engine cooling systems, crude oil distillation units, tap water and metal. An electrochemist, she has researched the electrochemical behavior of aluminum, copper, platinum, niobium, vanadium,

cadmium, brass, cobalt and low carbon steel, and collaborated on the discovery of a class of molybdenum-based catalysts that improve gasoline octane without benzene by-products. “*The state of the world has to be treated with more attention and care,*” she says. Currently Vice-President of the World Academy of Sciences, **Professor Al-Kharafi's contribution was recognized with the 2011 L'Oréal-UNESCO Award For Women in Science.**

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# HUMAN EVOLUTION: RETHINKING HOW WE CAME TO BE WHO (AND WHERE) WE ARE

From a genomic perspective, any two people anywhere on earth are 99.9% identical (1). The 0.1% variation includes such traits as resistance to malaria in people of African descent, and represents adaptation to particular conditions over a long period of time. The mapping of the human genome and advances in genetic analysis are enabling researchers to discover many more of these adaptive traits, and creating unexpected new versions of the story of human evolution. Palaeontologists now suggest we discard the idea of linear evolutionary progress from arboreal ape to modern human, along with the conclusion that we are the culmination of millions of years of development. As Susan Anton of New York University puts it: *“We’re not the pinnacle of everything that happened in the past. We just happen to be the thing that survived”* (2).

The field of human evolution and its subfield of “ancient genomics” have made many advances over the past 20 years, thanks to increasingly sophisticated tools and a remarkable series of discoveries of fossil remains. We have found new examples of our most ancient ancestors, and unearthed more recent distant relatives we never knew we had (such as the one-meter tall, 60,000-year-old “hobbit,” *homo floresiensis*, discovered in Indonesia in 2003) (3). We have also uncovered new evidence of cousins to whom we may be closer than previously thought (such as the Neanderthal, present in humanity’s early existence). Additionally, we have extended the history of our own species, with discoveries of skeletons showing anatomically modern *homo sapiens* was living in the region of Morocco 300,000 years ago, contradicting the prevailing theory that early humans originated in East Africa (4).

The mapping of the human genome, completed in 2003, enables researchers to compare modern genomes with those of some of our ancient relatives. It also enables us to identify distinct DNA sequences in the history of human populations and has led to new theories about population mixing and the movement of humans across the globe throughout our history.

## Discoveries

Discovered in Ethiopia in 2009, the nearly complete bones of a 4.4 million-year-old female *Ardipithecus ramidus*, nicknamed “Ardi”, are the earliest remains of a human ancestor ever found, beating the long-famous “Lucy,” a 3.2 million-year-old proto-human found in Tanzania in 1974 (5). Observing Ardi, researchers found a combination of both primitive traits and characteristics shared exclusively with later hominids. Paleontological research (Ardi is too old to extract genetic material) indicates that she may be the last common ancestor of humans and chimpanzees, our closest living relative. Her features also suggest that chimpanzees and other African apes have each followed different evolutionary pathways — getting better at knuckle walking and swinging from trees, while humans improve their ability to walk on two feet — meaning that we can “no longer consider chimps as proxies for our last common ancestor” (6). Most recently, in late August 2017, two palaeontologists at Sweden’s Uppsala University announced they had discovered human-like footprints in Crete that, dated and verified, could completely upend the narrative of early human evolution. The footprints are said to be 5.7 million years old, and were made



*Professor Jennifer Graves, 2006 Laureate for Asia-Pacific*

at a time when all previous research puts our ancestors in Africa with Ardi and Lucy, walking on considerably more ape-like feet (7).

When it comes to discoveries from more recent time periods, genetic analysis can be put to work. In 2013, evolutionary geneticist Kay Prüfer and colleagues at Germany’s Max Planck Institute reported sequencing the genome of a Neanderthal woman from Siberia. Among other things, they were able to tell that mating among close relatives was common among her recent ancestors. Comparing her genome with modern human genomes, the researchers found evidence of gene flow events among early humans, Neanderthals and Denisovans, a mysterious Eurasian sister group to Neanderthals whose lineage was genetically established by a single 40,000-year-old finger bone fragment found in Siberia’s Denisova cave in 2010. Prüfer’s evidence showed that interbreeding between different hominin groups likely occurred, a conclusion that would have been dismissed before genetic analysis became possible 30 years ago (8). Further examples of the fluidity of both our knowledge and taxonomy schemes came to light in the Sima de los Huesos cave in Spain in 2014, when 28 hominin skeletons over 300,000 years old were discovered. Genome sequencing of the remains found them to be closely related to the lineage leading to genomes of the Denisovans. However, their teeth do not exhibit the large size characteristic of Neanderthals and Denisovans. A number of scenarios were put forward to explain

these findings. The hominin may be related to an ancestor common to both Neanderthals and Denisovans. It could represent a distinct group that later contributed DNA to Denisovans. Or another hominin population may have brought Denisovan-like DNA into the Sima de los Huesos hominin’s population or its ancestors (9).

Scientists at Harvard discovered unexpected echoes of past populations in the DNA of modern people, finding evidence of a now-extinct population in northern Eurasia that interbred with ancestors of both Europeans and Siberians, who later migrated to the Americas, establishing a much closer genetic connection between Native Americans and Europeans (10). The Inuit people of the Arctic, in turn, have a number of genetic variations that help them withstand cold temperatures and survive on the sources of food available in the far North. Genes that affect how fatty acids are processed and body fat distribution are different to more southern inhabitants. They are also quite similar to a DNA sequence found in the Denisovans (10). In July 2017, scientists found hints, in the evolutionary history of a salivary protein, that a “ghost” species of unknown ancient human ancestors may have contributed genetic material to ancestors of people living in sub-Saharan Africa today. The research adds to the growing body of evidence suggesting that sexual encounters between different archaic human species may not have been unusual (11).



### From past to present

We can expect to discover much more about the evolution of our species in the years to come. Vast amounts of genetic data, collected from both ancient fossils and modern populations, are being explored to identify periodic mutations and remnants of population genetic traits indicative of early adaptations. Kelley Harris, a postdoctoral fellow at the Department of Genetics at Stanford University, has modeled the genetic evolution of Neanderthals, finding that early Neanderthal-human hybrids would have experienced negative selection that discouraged breeding back with the parent species, but enabled Neanderthal DNA to enter the human population (12). She has also simulated the movement of early humans out of Africa, looking at adaptation to new environmental challenges, notably to ultra-violet light. She sees a possibility that different populations experienced diverse selective pressures affecting genome integrity (13).

*“Genome sequencing is revolutionizing our understanding of how all animals, including humans, evolved,”* says Jennifer Graves, Emeritus Professor at the Australian National University College of Science. *“It shows that we share many genes, and comparing their sequences allows us to piece together the evolution of humans from the most ancient primitive worm. Our ability to obtain DNA sequences from the fossils of humans and related primates is starting to fill gaps in knowledge about our recent past. We can even look, in our sequence, for the signatures of rapid change in genes (involved, for instance, in reasoning and speech) that played a big part in making humans human. It happened so quickly!”*

We still have much to learn about who we are and how we have evolved. While the combination of genetic analysis and paleontological evidence has allowed the study of human evolution to make great strides, data from the two fields is often in conflict, particularly with regard to time, population movement, and the occurrence of inter-homo hybridization. However, further revelations are never more than a microscope and an excavation away.

# “Genome sequencing is revolutionizing our understanding of how all animals, including humans, evolved.”

*Professor Jennifer Graves, 2006 Laureate for Asia-Pacific*



Evolutionary geneticist Jennifer Graves specializes in such quintessentially Australian animals as kangaroos, platypus and the Tasmanian devil. Australia’s long isolation from other continents makes it an ideal place to investigate adaptive genetic evolution and Graves’ group probes the distant shared inheritance of humans and marsupials, the ancient family of pouched mammals that dominate locally, to discover how genes, chromosomes and regulatory systems evolve and work in all mammals. Interested in the regulation of genes and X chromosome activation, Graves has undertaken gene mapping work in marsupials, which predate placental mammals and therefore provide valuable clues to mammalian evolution. Her laboratory has used this unique vantage point to explore the origin, function and fate of human sex genes and chromosomes, gaining notoriety along the way by predicting the disappearance of the Y chromosome that produces human males (14). The reasoning that led to this oft-cited finding is actually quite simple. Unlike mammals such as platypuses, whose sex chromosomes are the same strength, the human Y



*Professor Jennifer Graves, 2006 Laureate for Asia-Pacific*

chromosome is much smaller than the female X (it has at most 50 genes, while the X bears around 1600), and is still losing genes at the rate of nearly 10 per every million years. As Graves highlights, if this continues, it means that “the human Y chromosome should disappear in about four and a half million years” (15). Jennifer Graves is a Fellow of the Australian Academy of Science and, **in 2006, was named a L’Oréal-UNESCO For Women In Science Laureate.** She was awarded the Australian Prime Minister’s Prize for Science in 2017.

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