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SIXTH WORLD CONFERENCE ON
THE FUTURE OF SCIENCE™

Viruses: the Invisible Enemy

VENICE, SEPTEMBER 19-21, 2010

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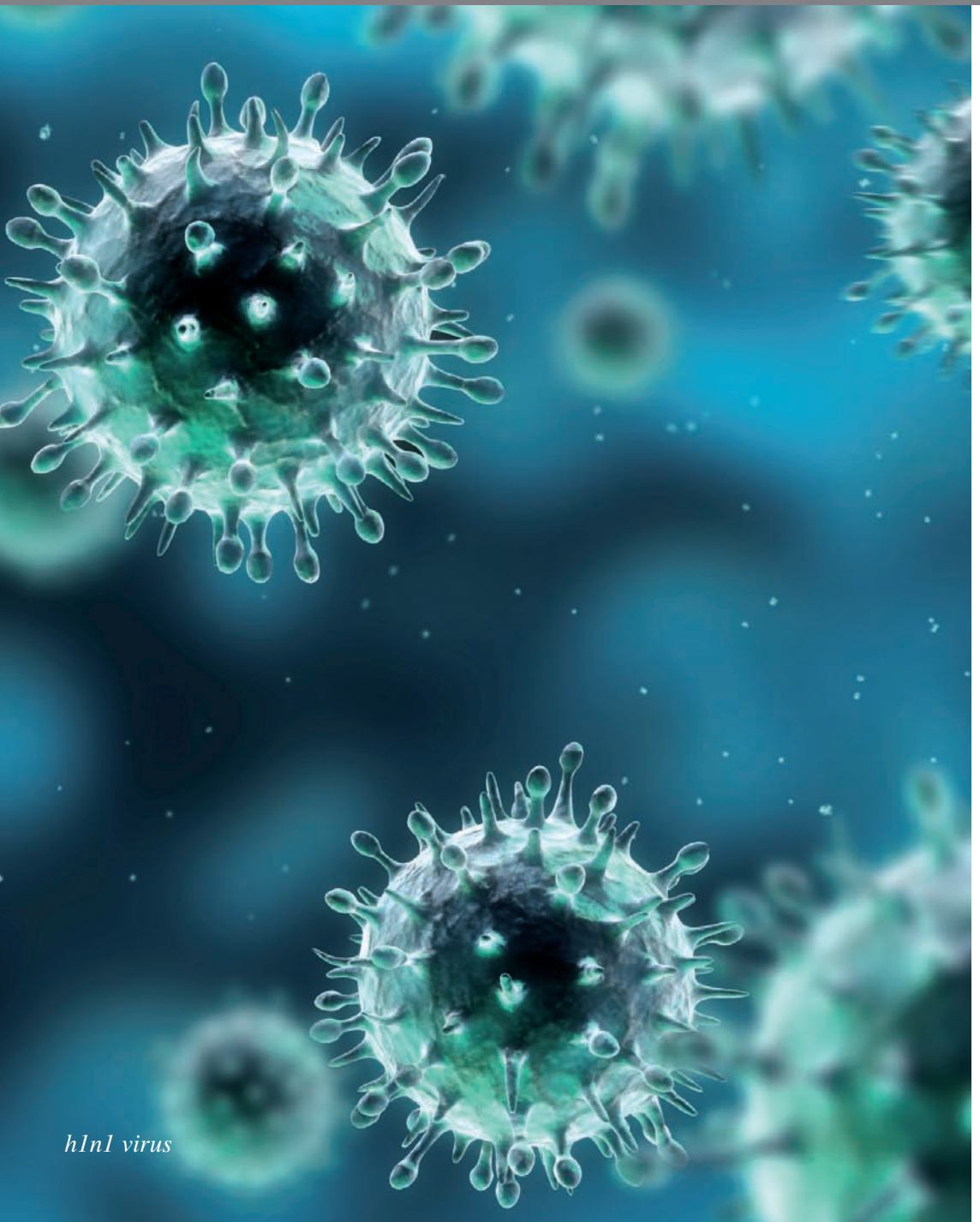

h1n1 virus

It is our great pleasure to welcome you all to the sixth World Conference on the Future of Science, "Viruses: the Invisible Enemy".

Viruses constitute one of the greatest challenges facing science and humanity today. They are infectious agents composed of packets of genetic material that have an extraordinary ability to survive, infect living organisms and replicate within them. Although their own evolutionary origins remain a mystery, viruses have been revealed as one of the great driving forces of evolution, because of their ability to transport fragments of DNA and RNA from cell to cell, from organism to organism. Viral fragments are foundin the genomes of almost all organisms, and viruses themselves are the most abundant biological entity on the planet. Although only about 5000 viruses have been described in any detail, it is known that billions of viral types exist; most are innocuous, and several are useful as vectors for therapies and in biomolecular research.

However if a single mutation occurs at a key point in a viral genome, the resulting new viral stain can destabilize the world. A good example was the recent emergence of a highly pathogenic strain of influenza A virus (avian flu), that caused panic worldwide for fear it would be highly infectious and lethal to humans. That scare proved unfounded, but we should never underestimate the danger that viruses pose: in the last century an estimated 120 million people died from smallpox 20 million from the influenza pandemic of 1918-1920, etc. In addition, viruses have fundamental roles in the development some forms of cancer, and must be considered in strategies to prevent and treat malignant diseases. But viruses not only cause human disease. Each year plant viruses are responsible for immense losses to agricultural production, and are an important contributing cause of famines. Effective means of combating plant viruses must therefore be part of the strategy to defeat hunger worldwide.

Notwithstanding the impact of viruses, insufficient resources are devoted to viral research, and interest in these mysterious biological entities dies down as soon as a viral scare or emergency passes. This Conference therefore wishes to promulgate an important message: the major economic, political and social impacts of viruses must be better recognised and better studied, making it possible to deploy the advanced techniques of biomolecular science and biotechnology to develop new vaccines and other ways to combat these small yet potent entities.

Not only scientists, but all concerned with the impact of viruses on society and the world will find the sixth World Conference on the Future of Science an authoritative source of updated information that will provide food for thought and for action.

Chiara Tonelli
Secretary General

Umberto Veronesi
President

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THE FUTURE OF SCIENCE™

Viruses: the Invisible Enemy

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Opening Lectures

Luc Montagnier
Living with viruses
Robert Gallo
Basic Science and HIV/AIDS: Perspectives from the Past and Prospects for the Future
Felice Casson
Science, Policy and Law

Luc Montagnier
2008 Nobel Prize in Medicine

Luc Montagnier has spent most of his scientific carreer in the study of viruses associated with chronic diseases. Among his achievements are the isolation, with his French team, of the viruses known as HIV 1 and HIV2, the first description of the apoptotic state of lymphocytes from patients with AIDS and seminal observations on the role of infectious cofactors in the disease.
Besides his involvement in the design of new types of protective and therapeutic AIDS vaccines, his current studies are aimed at the diagnosis and treatment of microbial and viral factors associated with cancers, neuro-degenerative and auto-immune diseases. As a strong advocate of preventive medicine, he is especially concerned with prolonging the active life of aging people.
Beyond his scientific interest in his deep involvement with helping developing countries acquire knowledge of and access to modern medicine and preventive medicine. As President of the World Foundation for Aids Research and Prevention, he has co-founded two centers for the prevention, treatment, research and diagnosis of AIDS patients in the Ivory Coast and Cameroon.
In 2008, he has been awarded the Nobel Prize for Physiology and Medicine.

LIVING WITH VIRUSES

Pathogenic microorganisms in this day of age are not only submitted to high selective pressure by the immune defences of theirs hosts, but also have to survive under highly active antiviral or antibiotic treatments. Not surprisingly, they have evolved in finding many ways to escape these hostile conditions, such as mutation of resistance, hypervariability of surface antigens, protective biofilms, latency inside cells and tissues.

Often, as with plague or cholera, epidemics have spread as a result of transportation. Today, although global surveillance systems and hygiene precautions could efficiently decrease these risks, we cannot exclude, as we have seen recently, outbreaks of new infections, difficult to put under control.

Moreover, germs have found new ways to silently invade our organisms whose immune system is not always fully operational, due to environmental factors.

In addition, our genome is full of ancient retroviruses whose unregulated expression could be harmful and lead to cancer or neurodegenerative diseases.

New molecular tools makes it now possible to detect these viral agents at an early stage in order to treat or prevent their harmful effects.

They should be made available to all human populations, whatever their economical situation.

Robert C. Gallo
Director and Professor, Institute of Human Virology,
University of Maryland School of Medicine, Baltimore, USA

Since 1996, Dr. Robert C. Gallo has been Director of the Institute of Human Virology at the University of Maryland School of Medicine. Previously (for 30 years) he was at the National Cancer Institute in Bethesda, MD. Dr. Gallo's career long interest has followed these themes: the study of the basic biology of human blood cells, their normal and abnormal growth, and the causes of abnormal growth whether excessive, e.g., leukemias or insufficient, e.g., immune deficiencies and the involvement of viruses in these abnormalities.
Dr. Gallo and his co-workers opened and pioneered the field of human retrovirology when in 1980 they discovered the first human retrovirus (HTLV-1) and with others showed it was a cause of a particular form of human leukemia. (This was the first, and to date, the only known human leukemia virus and one of the few known viruses shown to cause a human cancer). A year later he and his group discovered the second known human retrovirus (HTLV-2). Dr. Gallo and his colleagues also independently discovered HIV (the 3rd known human retrovirus), and provided the first results to show that HIV was the cause of AIDS. They also developed the life saving HIV blood test (1983-1984). Earlier (1978) Gallo discovered a variant of gibbon ape leukemia virus (Hall's Island strain) which causes T-cell leukemia.
The discoveries of all human retroviruses, including HIV, were to a great extent dependent on being able to grow human T-cells (lymphocytes) in the laboratory, and this was achieved by the use of a growth factor called Interleukin-2 or IL-2. Dr. Gallo and his co-workers discovered Interleukin-2 in 1976, thus setting the stage for all groups to culture human T-cells. Today IL-2 is used not only in laboratory experiments, but also in some therapies for cancer and AIDS. Gallo and co-workers also spent several years in the 1970ies working out detailed biochemical and immunological characteristics of human cellular DNA polymerases alpha, beta, and gamma as well as reverse transcriptase (RT) from several retroviruses in order to use RT as a sensitive and specific surrogate marker for retroviruses. It was particularly essential to distinguish the mitochondrial DNA polymerase (DNA pol. gamma) from RT because of their similar biochemical characteristics which ad led to many prior false claims for detecting human retroviruses.

In 1995 he and his colleagues discovered the first natural (endogenous) inhibitors of HIV, namely some of the beta chemokines. This discovery helped in the later discovery of the HIV co-receptor, CCR5, and opened up entire new approaches to treatment of HIV disease.
Also, Dr. Gallo, along with his colleague, D. Ablashi, discovered in 1986 the first new human herpes in more than twenty-five years, Human Herpes Virus-6 (HHV-6). This is now known to cause Roseola in infants and is a candidate for involvement in several other diseases.
Main Recognition
Dr. Gallo has been awarded 28 honorary doctorates from universities in the United States, Sweden, Italy, Israel, Peru, Germany, Belgium, Mexico, Argentina, Spain, Ireland, Jamaica and Greece. He is a member of numerous professional and honorary societies including the U.S. National Academy of Sciences, the Institute of Medicine of the U.S. National Academy of Sciences, the Royal Society of Medicine (Glasgow, Scotland), the Royal Society of Medicine (Brussels, Belgium), the Royal College of Physicians (Ireland) 2007, among several others, and a member of the National Inventors Hall of Fame.
He has received numerous major scientific honors and awards. What follows is a partial list. Uniquely the most prestigious U.S. award, the Albert Lasker Prize awarded twice (1982, 1986), General Motors Cancer Research Prize 1984, American Cancer Society Medal of Honor Award (1983), Gairdner Foundation International Award (Canada) 1987, The Japan Prize of Science and Technology (1988), Paul Ehrlich and Ludwig Darmstaedter Prize (Germany)1999, Principe de Asturias Award for Technical and Scientific Research (Spain) 2000, the World Health Award from President Gorbachev in Vienna in November 2001, the first Otto Herz Memorial Award for Basic Research on Malignant Processes (Israel) 1982, Hebrew University's Rabbi Shai Shacknai Memorial Price (Israel) 1985, the Tata Memorial Centre's Birla International Award (India) 1986, the Tevere Roma International Award (Italy) 1985, the Harvard Medical School Warren Alpert Foundation Award (1998), Israel's top prize, the Dan David Award (2009), and the National Library of Medicine Paul G. Rogers Medical Science Award (2010).
Dr. Gallo was the most cited scientist in the world 1980-1990, according to the Institute for Scientific Information (Science July 27, 1990, p. 358), and he was ranked third in the world for scientific impact for the period 1983-2002 (PNAS, November 15, 2005, vol102, no.46, 6569-16572). He has published close to 1,200 papers.

BASIC SCIENCE AND HIV/AIDS: PERSPECTIVES FROM THE PAST AND PROSPECTS FOR THE FUTURE

From 25 to 26 years ago (1983-84) HIV was first isolated at the Institute Pasteur (IP) by the Montagnier group, and by our group then at the National Cancer Institute (NCI) and shown to be the cause of AIDS. Several of our isolates of HIV were grown in continuous culture making an accurate global blood test possible as well as enabling HIV genomic analysis, cellular tropism, body distribution, modes of transmission, and variability (1984-85) by contributions from both groups. Other major advances soon followed, including the beginning of effective anti-viral therapy (a first in medicine) by another NCI group by 1986, and ultimately (by 1995) the huge advances in treating HIV and preventing mother to child transmission.

The lessons from this early period center on preparedness. In this report I will argue that despite the fact that the pace of discovery between 1982-85 was perhaps the fastest in medical history from the time of inception of a new complex disease and that basic science achieved two major practical advances (the blood test and effective anti-HIV therapy), nonetheless (1) we were far from prepared for the HIV epidemic; (2) most of the individuals or groups who made the early contribution did so almost by chance; (3) society regularly forgets the lessons of past major epidemics after an absence of some 20-30 years; and (4) we need multiple centers of excellence in virology that cover the breadth of human viral pathogens.

Three great needs remain: (1) drug delivery to developing nations (although this has been greatly aided by the U.S. PEPFAR program); (2) a "cure" so as no further therapy is needed by complete viral eradication or in the absence of a cure the continued development of new approaches to therapy because therapy is life-long and consequently can lead to side effects and HIV drug resistant mutants; and (3) a successful vaccine.
I will specifically describe the difficulties in HIV vaccine development but some important recent progress made at our Institute with a novel concept.

To summarize: the special challenges for a successful HIV vaccine are due to HIV DNA integration, HIV variation, and its early harm to the immune system. Though easy to describe, the challenge is uniquely difficult compared to past successful vaccines. However, most if not all current and past vaccine candidates have not taken these features of HIV into account.
What is needed and has been needed for over two decades are: (1) far more availability of primates and to a broader number of scientists; (2) an immune response which is sustained; (3) an immune response which is broad and results in sterilizing immunity or close to sterilizing immunity. Finally, I will describe the characteristics and progress, and remaining problems with a candidate vaccine developed at the Institute of Human Virology.

Felice Casson
Senator, Former Magistrate

He obtained a law degree from Padua University and entered the magistracy in 1980 as an investigating magistrate. He was subsequently appointed judge responsible for preliminary investigations and was public prosecutor in Venice from 1993 to 2005. He holds the top grade in the Italian Judiciary as Court of Cassation, with superior administrative functions.
He has been on leave since 2006 following his election to Parliament. In 2008 he was re-elected to the Senate and elected Vice-President of the Democratic Party Group.
As magistrate, among the many investigations conducted by Mr Casson, epescially in the field of terrorism, the fight against corruption, environmental security, the protection of workers and citizens from exposure to carcinogenic agents, are those on the Peteano massacre, disloyalty of the intelligence service and the State apparatus, terrorism and radical right-wing and international subversive organizations, global trade in warfare material, the GLADIO case, political corruption in the Veneto Region, the fire of La Fenice Theatre in Venice, the trials over deaths from VCM, PVC and asbestos in Marghera, investigation into environmental pollution, disorders caused by depleted uranium and radio spectrum pollution.
As senator, he was member of the following committees:
Committee on Elections and Parliamentary Immunity - Committee on the Prosecution of Government Members - Standing Commission on the Justice - Committee of Enquiry into Depleted Uranium - Committee on Workplace Deaths

In particular, he introduced and promoted bills on the fight against corruption and organized crime, the streamlining of civil and criminal law proceedings, safety and prevention measures for workers exposed to genotoxic, carcinogenic substances likes asbestos and VCM, environmental crime, population safety and the protection of crime victims.
He taught Law of Environment at the Venice Istituto Universitario di Architettura and the International Telematic University Uninettuno. He is a member of the scientifc board of the Venice International Academy of Environmental Sciences (IAES).
He authored several books, including:
Lo Stato violato, 1994 - Segreto di Stato e Ragion di Stato, 1992 - La fabbrica dei veleni, 2007

Abstract

SCIENCE, POLICY AND LAW

Over recent decades, science has become increasingly influential not only with respect to political and economic decisions, but also individual rights and the administration of justice. As a result of the interaction between science, policy and law, a new type of relationship has been established between "scientists" and the rest of the world.
In a democratic and liberal society, the uncertainties of science and the emergence of (more or less overt) conflicts of interest of various kinds require the political decision-takers and the judiciary to act with greater caution and respect, to guarantee basic individual human rights.
Transparent, complete and accurate information is required to protect the individual, and society itself, as the primary goods of every society, and must be based both on an increasingly broad expansion of consultation with the world of science, and on the consequent wider participation of citizens in the decision-making process.

Viruses in Evolution

Chairs: **Claudio Basilico, Chiara Tonelli**

Dorothy Crawford
Viruses: the invisible enemy revealed
Nathan Wolfe
Viral Forecasting
John Coffin
Endogenous viral sequences and their evolution

Animal and Plant Viruses

Ilaria Capua
Animals, humans and viruses: novel perspectives for managing global threats
Shivaji Pandey
Viruses, Insects and Hunger
Wilhelm Gruissem
The battle against plant viruses

Viruses and Mankind

Chairs: **Giuseppe Ippolito, Gianpiero Sironi**

Giuseppe Ippolito
Global burden of infectious diseases: not just numbers
Charles Rice
Hepatitis C: towards control and eradication
Adolfo García-Sastre
Pandemic influenza
Heinz Feldmann
Emerging Zoonotic Viruses: Response and Preparedness
Alberto Mantovani
Viruses and immunity: molecular pirates and the challenge of a global alliance
Rino Rappuoli
Vaccines to address the needs of 21st century society

Claudio Basilico

Department of Microbiology, NYU School of Medicine, New York

Dr. Claudio Basilico is the Jan Vilcek Professor of Molecular Pathogenesis and Chairman of the Department of Microbiology at NYU School of Medicine.
After training in virology in Italy and the U.S., he dedicated the earlier part of his scientific career to the study of oncogenic viruses and of how these viruses interact with the host cell machinery to induce malignant transformation of cells in culture and in vivo.
He also carried out pioneering studies on the mechanisms by which somatic cell mutations influence cell cycle progression and the gene and gene-functions which regulate cell division. In more recent years Dr. Basilico's work has mainly focused on the mechanisms through which signaling by growth factors and cognate receptors regulates cell proliferation and differentiation.
His studies on the regulation of expression and function of the FGF growth factor family have provided important information on the mechanisms by which these growth factors control embryonic developments, angiogenesis, limb and skeletal formation and play a role in some types of cancer. Dr. Basilico has served and continues to serve on the editorial board of numerous scientific journals as well as on the scientific advisory boards of academic institutions and biotechnology companies.

Chiara Tonelli

Professor of Genetics, Department of Biomolecular Sciences and Biotechnology, Università degli Studi di Milano, Italy.

Chiara Tonelli is Professor of Genetics at the University of Milan, Italy, and leader of the Plant Molecular Genetic Group of the Department of Biomolecular Sciences and Biotechnology at Milan. She is a member of the European Molecular Biology Organisation (EMBO). Her scientific interests range from fundamental aspects of plant biology to biotechnological applications. The major aim of her studies is to decipher the logic of transcriptional control and gene regulation in plants both during development and in interactions with the environment. She contributed to the identification and molecular characterization of regulatory gene families responsible for the coordinated control of flavonoid and anthocyanin metabolic pathways in plants. She discovered an interaction between duplicated genes, termed REED (reduced expression of endogenous duplications), in which the epigenetic mechanism of DNA methylation of promoter regions silences gene expression. More recently she discovered the first transcription factor specifically regulating stomata movements in plants, a finding that opens up new possibilities for improving crop survival and productivity in water scarcity conditions. Chiara has served on numerous scientific committees and science advisory boards in Italy and elsewhere. Currently she is a member of the Advisory Group for Food, Agriculture and Fisheries, and Biotechnology of the European Commission, and of the Expert Group for Food and Health Research, a board member of the European Plant Science Organisation (EPSO), and a member of the Research and Technological Transfer Committee of the University of Milan.
She serves as a reviewer for several scientific journals (Molecular Cell, Molecular and Cellular Biology, EMBO Journal, Plant Cell, Plant Journal, Plant Molecular Biology) and grant-awarding agencies (USDA, EMBO, TWAS, Human Frontier).
Since 2005 Chiara has been Secretary General of the World Conference on the Future of Science, a cycle of international conferences that gathers together eminent experts from various disciplines to discuss the implications of scientific progress and increase the awareness of society as a whole, not only of the benefits of science, but also of the problems and dilemmas that continuing scientific advance creates. Each year the Conference considers a different scientific theme of crucial significance to society, and examines the implications and benefits of progress in that area.

Dorothy Crawford

Professor of Medical Microbiology and Assistant Principal for Public Understanding of Medicine, University of Edinburgh, UK.

Dorothy Crawford qualified in medicine from St Thomas's Hospital, London, in 1968. She was awarded a PhD from Bristol University for studies on Epstein-Barr virus (EBV) in 1976. She became a member of the Royal College of Pathologists in 1981 and a Fellow of the College in 1991. After holding a Research Fellowship at University College, London, Dorothy was appointed Senior Lecturer and subsequently Reader in Virology at the Royal Postgraduate Medical School, London, where she gained an MD in 1987 and a DSc in 1992. She was appointed Professor of Medical Microbiology at the London School of Hygiene and Tropical Medicine in 1990.

Professor Crawford took the Robert Irvine Chair of Medical Microbiology at the University of Edinburgh in 1997, headed the School of Biomedical Sciences from 2004-2007, and was appointed Assistant Principal for Public Understanding of Medicine in 2007.

Professor Crawford was the first to identify EBV as the cause of B lymphoproliferative disease (BLPD) in the immunocompromised host and more recently to successfully treat this potentially fatal disease with T cell immunotherapy. She has published around 200 research papers.

She has also published two books on microbes for a general audience: The Invisible Enemy: A natural history of viruses (OUP 2000) and Deadly Companions: how microbes shaped our history (OUP 2007), and wrote a regular science column for the Scotsman newspaper from 2008-2009.

Professor Crawford was elected a Fellow of both the Royal Society of Edinburgh and the Academy of Medical Sciences in 2001 and awarded an OBE for services to medicine and higher education in 2005.

Abstract

VIRUSES: THE INVISIBLE ENEMY REVEALED

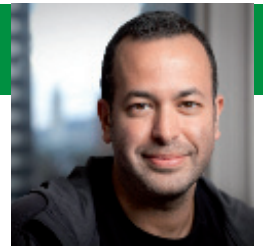
Viruses are tiny sub-microscopic entities whose structure was only elucidated after the invention of the electron microscope in the 1930s. We now know that viruses are by far the most abundant life form on Earth. Recent estimates suggest that there are in excess of ~5x1030 of them on the planet, that they are ubiquitous and staggeringly diverse. With around 100 million different types, they occupy every available niche including such inhospitable abodes as hot water springs, deep ocean trenches, the polar ice caps and acid lakes. One litre of sea water contains around a billion of them and in total the Earth's viruses lined up side by side would stretch across six galaxies.

Viruses, unlike any other life form, are not composed of cells but are particles consisting simply of a protein shell surrounding a piece of genetic material - either DNA or RNA. With no mechanisms for generating energy or making proteins, these particles are inert until they enter a living cell. Only then do they come to life and highjack the cell's machinery to produce thousands of daughter viruses. The smallest viruses have just three genes (compared to our ~20,000) but still they can infect, reproduce and spread in a matter of hours, sometimes causing life-threatening diseases. Clearly this minimalist lifestyle is highly successful.

All viruses are parasites but they have evolved remarkably varied and highly sophisticated survival strategies. Those that cause acute infections have perfected the technique of reproducing rapidly and moving on before they are wiped out by the host's immunity, whereas others have a more leisurely lifestyle. These have learnt to hide from their host's immune mechanisms and setup a persistent infection.

Rhinovirus, the common cold virus, causes an acute illness by infecting the cells lining the nose. Here it has learnt to tickle local nerve endings causing excess mucus secretion and sneezing, so projecting an aerosol spray of virus-laden mucus droplets into the atmosphere to maximise its spread. Aerosol spread works best among crowds and so the virus has evolved to cause symptoms mild enough to keep infected hosts up and about, travelling in packed trains and sitting in crowded classrooms.

The chicken pox virus also generally causes mild symptoms when it first infects. But this is a herpes virus, a family which are adept at spreading in sparse populations. The virus puts its energy into hiding in nerve cells, away from its host's immune system so that it can lodge for life in the same individual. It only reappears in old age to cause the painful rash of shingles and also to spread to younger family members who have not yet met the virus.



Nathan Wolfe
Lorry I. Lokey Visiting Professor in Human Biology, Stanford University;
Founder and CEO, Global Viral Forecasting, USA.

Dr. Nathan Wolfe founded Global Viral Forecasting (GVF), a hybrid company, to predict and prevent pathogen threats. GVF directs more than 100 scientists worldwide and is active in more than 20 countries.
Among Dr. Wolfe's discoveries are the origin of malaria and the first evidence of retroviruses jumping from nonhuman primates to humans. He has published extensively and his work has appeared in or been covered by Nature, Science, The New York Times, The Economist and Forbes, among others. He has received support of over $30m from Google.org, the NIH, Gates Foundation, Merck and the US Department of Defense. He serves on the editorial board of EcoHealth and is a member of DARPA's Defense Science Research Council.
Dr. Wolfe was awarded the prestigious NIH Director's Pioneer Award and is a National Geographic Emerging Explorer and World Economic Forum Young Global Leader. He was recognized as one of Popular Science's 'Brilliant 10,' and Rolling Stone's 'Top 100 Agents of Change.' He received his bachelor's degree from Stanford and his doctorate from Harvard and is currently the Lorry I. Lokey Visiting Professor at Stanford University.

Abstract

VIRAL FORECASTING

Current global disease control efforts focus largely on attempting to stop pandemics after they have already emerged. This fire brigade approach, which generally involves drugs, vaccines, and behavioral change, has severe limitations.
Just as we discovered in the 1960s that it is better to prevent heart attacks then try to treat them, over the next 50 years we will realize that it is better to stop pandemics before they spread and that effort should increasingly be focused on viral forecasting and pandemic prevention. In this talk I discuss how novel viruses enter into the human population from animals and go on to become pandemics.
I then discuss attempts by my own research group to study this process and attempt to control viruses that have only recently emerged. By creating a global network at the interface of humans and animals we are working to move viral forecasting from a theoretical possibility to a reality.

John Coffin
American Cancer Society Research Professor, Department of Microbiology,
Tufts University, Boston, USA

John M. Coffin is American Cancer Society Professor and Distinguished Professor, molecular Biology and Microbiology, Tufts University, Boston MA. He also serves as advisor on HIV and AIDS to the National Cancer Institute and to the HIV Drug Resistance Program (DRP), which he founded in 1997. He received his Ph.D. in Molecular Biology from the University of Wisconsin, Madison, in 1972, where he worked on retroviruses in the laboratory of Howard Temin.
He joined the Tufts faculty after 3 years with Charles Weissmann at the University of Zürich, Switzerland. In 1997, he was recruited to organize the DRP, of which he served as Director until 2005. He is well known for his work on retrovirus genetics, genome structure, and evolution, and is author of more than 150 peer-reviewed publications, and senior editor of Retroviruses, the definitive text on the subject. In 1999, he was elected to the National Academy of Sciences in recognition of his contributions to the field of retrovirology.

Abstract

ENDOGENOUS VIRAL SEQUENCES AND THEIR EVOLUTION

Throughout evolution, all living things have had to face the challenges of infectious agents - viruses, bacteria, parasites - and invent ways to deal with them. To survive, infectious agents must ways to counter these defenses, resulting in an eternal arms race. A full understanding of this arms race will help us to better understand the microbial enemy as well as provide important clues to development of new strategies for prevention and therapy of infection. With most infectious diseases, obtaining this understanding is hampered by the complete absence of a fossil record from which to construct an evolutionary history. Retroviruses, however, are a major exception to this general rule. Unlike all other entities infecting animals, retroviruses have the ability (and need) to integrate their genetic information, in the form of a DNA copy called the provirus, into the DNA of the host cell at more or less random locations.
An important consequence of this unique property is that occasional infection of the germ line leads to proviruses – called endogenous proviruses -, which are then inherited as part of the genetic composition of all descendants of the animal in which the integration occurred. Endogenous proviruses have been found in the DNA of all animals where they have been sought, including mammals and all other vertebrates, insects, mollusks, and many others. In humans, it has been estimated that there are about 80,000 endogenous proviruses, comprising about 8% of our total genetic makeup. In some species, including mice, chickens, cats, koalas, and others, endogenous viruses are still active and continue to be inserted into the genome, and can be important causes of disease. In humans, no active proviruses are known, their role in disease is uncertain, and they may all be extinct. In all cases, however, they provide an invaluable fossil record of the evolution of this large and important group of infectious pathogens.

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Because integration is at nearly random sites, and our genome is so large, if two proviruses are found at exactly the same location, they must be descendants of the same original integration event in a common ancestor of that species. Almost all proviruses in human DNA are found in the same place in chimpanzee DNA, meaning that they must be at least 5 million years old. Indeed, many are much older, occupying the same site in humans and new world monkeys, implying that the virus that gave rise to them must have existed at least 45 million years ago, and is long extinct as an infectious entity. Remarkably, even these very old fossils look very much like modern day viruses, meaning that all important events in their evolution took place in the very distant past. With the exceptions mentioned below, we know this for no other infectious agent, and many evolutionary biologists believe (incorrectly, I think) others to be much younger, because of the very rapid rate of evolution that some of them display over short time intervals.

By revealing important biologic properties of the ancestors of modern viruses, endogenous viruses can illuminate important events in the host-virus arms race. For example, many endogenous proviruses of mice can infect all mammals, except mice. The explanation for this apparent paradox is that the presence of a pathogenic virus in the genome strongly selected for a mutation in the mouse gene coding for the receptor - the cell surface protein that mediates viral entry, leaving the virus in the DNA no longer able to infect and spread in that species. In response, variants of the virus evolved that are now able to use the mutant form of the protein for entry. Remarkably, a virus called XMRV, which must have been derived from one of these endogenous mouse viruses, has recently been found in humans and may be associated with a variety of diseases, including prostate cancer and chronic fatigue syndrome.

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A few endogenous proviruses have also been co-opted to do something useful for their hosts. For example, in humans, the formation of the syncytiotrophoblast, a fused layer of cells that forms the surface of the placenta and prevents the passage of potentially harmful substances from mother to fetus, is mediated by the action of a gene found in an endogenous provirus. This gene had the original function of mediating virus entry bu fusing virus and cell membranes together, quite similar to the function it now serves in human development. Other endogenous proviruses can help protect their host from infection by similar viruses from outside by blocking access to specific receptors.

Until recently, retroviruses were thought to be the only entities to have generated this kind of a fossil record. Recently, however, a few sequences derived from genes of a group of viruses called Bornaviruses have been found in the DNA of humans and a few other species. As with retroviruses, these sequences demonstrate that this group of viruses is far older than evolutionary biologists have thought, and they also may provide some important function to their host, although we don't yet have any idea what that function may be.

Ilaria Capua

Director, OIE/FAO International Reference Laboratory for Newcastle Disease and Avian Influenza and OIE Collaborating Center for Diseases at the human-animal interface, Istituto Zooprofilattico Sperimentale delle Venezie, Italy.

She is currently Director of the Virology Department and of the National, FAO/ OIE Reference Laboratory for Avian Influenza (AI) and Newcastle disease (ND) and of the Collaborating Centre for Diseases at the Human–Animal Interface at the Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro (Italy). During her career as a veterinary virologist she has been nominated OIE and FAO expert for AI and ND. She has been involved in managing several AI outbreaks on a global scale, and in particular her group has supported African and Middle Eastern countries affected by the H5N1 crisis.

From 1997 to date she has been invited to give over 70 lectures as an international expert and as a guest lecturer at training courses in Europe, the US, Central and South America, Africa Australia and Asia.

She has been awarded the Houghton Lecture award in 2005 and the Promed 2006 Award. In 2007 she was among the winners of the Scientific American 50 prize and in 2008 Seed's Revolutionary Mind, for leadership in policy for promoting sharing of information at an international level.

From 1990 to date she has authored over 300 publications, predominantly on viral diseases of animals and zoonotic diseases including papers published in international refereed journals, papers and abstracts published in the proceedings of conferences, guest editorials, reviews, chapters of books and has co-authored two text books on avian influenza.

Her lab is currently coordinating 2 EU – funded projects, is a partner of additional 5 EU projects and is a WP leader in the EU Network of Excellence EPIZONE. Her group is involved in international activities funded by FAO and other international organisations.

ANIMALS, HUMANS AND VIRUSES: NOVEL PERSPECTIVES FOR MANAGING GLOBAL THREATS

The emergence and spread of the H1N1 pandemic 2009 virus has once again raised the issue of diseases emerging from the animal reservoir with pandemic potential. Prior to the emergence of this virus, the animal and human health crisis caused by influenza viruses of the H5N1 subtype had polarised attention of international organisations and donors on the need for improved veterinary infrastructure in developing countries and on the need for improved communication between thehuman and animal health sectors.

Significant investments in capacity building have resulted in the development of diagnostic laboratories and in the improvement of scientific know-how in the field of diagnostic virology. It is known that the animal reservoir (including arthropods) is the source of the majority of emerging pathogens which threaten global public health and also that most emerging pathogens originate (or cross the species barrier) in developing countries. It would therefore seem reasonable for the international community to capitalise on the investments that have been made as a result of the avian influenza emergency and expand the areas of diagnostic competence, possibly on a regional basis, to set up early warning systems and improved response capacities to manage diseases of public health relevance. In particular the infrastructure and knowledge base generated for managing the avian influenza crisis could be a basis for the development of a reliable diagnostic capacity for zoonotic vetorborne diseases such as West Nile Disease, Rift Valley Fever and for other highly lethal diseases such as rabies.

Possibly the biggest challenge we have is to find novel ways to maximise the use of the information which is generated as a result of the improved networking and diagnostic capacities. In the era of globalisation, emerging and re-emerging diseases of public health relevance are a concern to developing and developed countries and are a real threat due to the interdependence of the global economy. Communication and analysis systems available should be tailored to meet the global health priorities, and used to develop and constantly improve novel systems for the exploitation of information to generate knowledge, including a transdisciplinary approach between the medical and veterinary professions.

Shivaji Pandey
Director, Plant Production and Protection Division, FAO, Rome, Italy

Born and raised in India, where he also had his early education. Obtained his MS and Ph.D. in Plant Breeding and Plant Genetics from the University of Wisconsin, USA.
Worked for over 30 years in international agricultural research and development, serving as a scientist, Regional Representative for South America, Director of Maize Program, and Director of African Livelihoods Program at International Maize and Wheat Improvement Center (CIMMYT) in Mexico and in its outreach programs.
In 2005, joined Food and Agriculture Organization (FAO) of the United Nations as Director of Agricultural Support Systems Division (AGS).
In 2006, was appointed Director of Plant Production and Protection Division (AGP) at FAO, to lead work on increasing production and quality of all food and non-food crops to enhance food security and livelihoods especially of rural as well as urban poor. The work of the Division involves conservation and sustainable use of plant genetic resources, seed production, development and deployment of improved cultivars, use of appropriate agronomic practices, cropping systems, conservation agriculture, organic farming, and integrated pest management among others. International Treaties and Commissions such as ITPGRFA (International Treaty for Plant Genetic Resources for Food and Agriculture), GPA (Global Plan of Action), IPPC (International Plant Protection Commission), International Code of Conduct on Pesticides, and Rotterdam Convention also form parts of the Division's work.
Chairs the Inter-Departmental Working Group on Biotechnology at FAO which integrates research, development, and policy work on biotechnology of the Organization for agriculture, forestry, and fisheries.
Among honors and awards include D. Sc. from the Maharana Pratap University of Agriculture and Technology (India), Fellowship to the American Society of Agronomy, Fellowship to the Crop Science Society of America, and special recognitions from the governments of Bolivia, Colombia, Ecuador, and Vietnam.
Has authored or co-authored over 150 publications.

Abstract

VIRUSES, INSECTS AND HUNGER

Plant diseases cause annual losses of about US$ 60 billion, by lowering both quantity and quality of agricultural production. With over 800 recognized plant viruses, they are a major contributor to these losses, especially exacerbating food insecurity of the poorest of the poor. Approximately, 75% of the world's one billion hungry and poor live in rural areas, deriving their livelihoods from agriculture. Viral diseases cause serious losses in cassava, banana, rice, potato and other staple crops, affecting livelihoods of millions of poor in rural communities. Unfortunately, plant viruses in agriculture go beyond just lowering quantity and quality of production; they also hamper international trade through quarantine restrictions.

Plant viruses cause diseases with a range of symptoms. They are transmitted mainly through vector organisms such as insects and mites. The virus-vector relationship is specific for different diseases and is critical for disease management strategies. Some plant viruses are transmitted through seeds and through vegetatively propagated plant parts.

Disease diagnosis and virus identification are essential to exploit appropriate disease management strategies based on pathogen epidemiology and transmission mechanisms. Such strategies include use of virus-free planting material, appropriate cultural practices, integrated vector management and host plant resistance. Resistance breeding is effective against plant-to-plant transmission (seed and vector transmission), intracellular virus multiplication, and virus translocation and colonization of the plant.

The increase in emerging infectious plant diseases globally has been expressed in the form of 1) an increase in incidence, geographical or host range, or 2) changes in pathogenesis, or 3) newly evolving, or 4) newly discovered or identified plant diseases. Most emerging infectious plant diseases are caused by viruses.

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The range of mechanisms involved in this process of evolution and emergence of infectious viruses includes recombination and synergism between virus species, new vector biotypes, genome integration, host adaptation and long distance dispersal. These processes are consistently linked to major human-induced changes in the agricultural production system including crop introductions, crop intensification, germplasm movement, and introduction of new genotypes.

The risks associated with emerging viral diseases are higher in developing countries due to increased agricultural intensification within systems that have low capacities to design and implement appropriate control measures. Limitations are particularly prevalent in disease diagnosis and pathogen identification, surveillance and implementation of phytosanitary measures including plant quarantine (especially in conflict areas), production and utilization of virus-free material, application of appropriate cultural practices and vector control. FAO supports its member countries in development of appropriate policy, technological, regulatory, socio-economic, and political environment for improved disease management.

Wilhelm Gruissem
Professor, Department of Biology, Plant Biotechnology, ETH, Zurich, Switzerland

Wilhelm Gruissem has been full Professor of Plant Biotechnology in the Institute of Plant Sciences at the ETH Zürich (Swiss Federal Institute of Technology) since 2000. He was elected President of the European Plant Science Organization (EPSO) in 2006. At present he is Chair of the Department of Biology at ETH Zurich.

After obtaining his Ph.D. in 1979 he spent three years as a postdoctoral fellow at the University of Colorado in Boulder, USA. In 1983 he was appointed to the faculty of the University of California at Berkeley as professor of plant biology. He was Chair of the Department of Plant and Microbial Biology at UC Berkeley from 1993 to 1998, and from 1998 to 2000 he was Director of a collaborative research program between the Department and the Novartis Agricultural Discovery Institute in San Diego. Since 2001 he is Co-Director of the Functional Genomics Center Zurich. From 2004 to 2006 he was Chair of the Zurich-Basel Plant Science Center. In addition to his research on systems approaches to understand pathways and molecules involved in plant growth control, he directs a biotechnology program on trait improvement in cassava, rice and wheat.

Wilhelm Gruissem is elected Fellow of the American Association for the Advancement of Sciences, member of learned societies, Editor of Plant Molecular Biology, and serves on the editorial boards of several journals. He is co-editor of the acclaimed ASPB book 'Biochemistry and Molecular Biology of Plants'. He has received several prestigious awards, including a price from the Eiselen Foundation in Germany for his trait improvement work in cassava. In 2007 he was elected lifetime foreign member and Fellow of ASPB.

Abstract

THE BATTLE AGAINST PLANT VIRUSES

Like all other viruses, plant viruses are composed of a small DNA or RNA genome and a protein coat, and they depend on their host plants for replication and multiplication. But unlike many animal and human viruses that spread through aerosols, plant viruses depend on vector organisms such as insects or nematodes for transmission. In infected plants viruses spread by moving through plasmodesmata, the cytoplasmic connections between plant cells which are otherwise separated by a solid wall. Once viruses have infected plants, they are difficult to fight because chemical strategies are not effective. As the result, viruses cause many important plant diseases and are responsible for huge agricultural losses and often entirely destroyed crops. Plant breeders are continuously searching for resistance genes against viruses to protect our crop plants. But because viruses can also change their genome rapidly through recombination and mutations, they often evade resistance strategies and become virulent again.

So, why are plants not always infected by viruses? Unlike animals and human, plants do not produce antibodies that neutralize virus particles. It has been known for many decades, however, that prophylactic inoculation of plants with less virulent strains can be used to control viral diseases. This 'cross-protection' has uncovered an effective mechanism that plants have developed to shut off or 'silence' virus genes, and thereby prevent multiplication and spreading of the virus throughout the plant. Today we know that most eukaryotic organisms suppress foreign genetic elements, such as viruses or transposons, through a specific RNA turnover mechanism that is referred to as 'RNA silencing'. In higher plants, where more than 90% of viruses have a highly replicating RNA genome, the activity of the viral genome triggers the production of 21-25 nucleotide long small interfering RNAs (siRNAs), which bind to the virus RNAs and cause their efficient degradation. This makes it a potent defence mechanism against virus infection. In the battle between viruses and plants, however, viruses have also learned how to inactivate RNA silencing by expressing proteins that can bind siRNAs and therefore neutralize their protective function. But understanding the molecular mechanism of RNA silencing is now providing scientists and breeders new tools and strategies to combat plant viruses.

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Early attempts to genetically engineer virus resistance in crop plants relied on expressing viral coat proteins at high levels, which blocks the progression of virus infection. The protection of papaya against the papaya ringspot virus is the best-known example for the success of this strategy. More recently, genetic engineering of virus protection in crop plants is taking advantage of RNA-based strategies using siRNAs and another class of small RNAs, so called microRNAs (miRNAs), to interfere with virus replication and spread throughout the host plant. Together, these novel technologies are promising advances in our battle against plant viruses and efforts to protect our crop plants around the world.

Gianpiero Sironi

Department of Biomolecular Sciences and Biotechnology,
Università degli Studi di Milano, Italy.

Gianpiero Sironi graduated as M.D. at the University of Milan in 1962, where he then started his research work. He has been research assistant at the Karolinska Institutet, Stockholm, Sweden (1965-1966) and at the University of California at Berkeley (1969).
Since 1975 he has been full professor of Genetics at the University of Milano, where he has been Chairman of the Department of Genetics and Microbiology (1986-1990), Dean of the School of Biology (1990-1998), Chairman of the Ph.D. School in Genetics (1992-2001), Dean of the Faculty of Science (1998-2004) and Vice-Rector for Research (2004 – 2009).
He has been Chairman of the Conference of the Deans of the Schools of Biology of Italian Universities in 1990-1991 and President of the Italian Genetics Association (AGI) in 1990-1991.

His scientific interests, after an initial work on the induction of mutations in Drosophila, has dealt with various aspects of molecular genetics of bacteria, their plasmids, and bacterial viruses. Significant work has concerned the occurrence of prophage interference in lysogenic bacteria, the requirement of bacterial functions for phage multiplication and the physiology of a bacteriophage-plasmid element.

He is a member of Istituto Lombardo, Academy of Sciences and Humanities.
He retired form his University position in 2009, but is still interested in University life and its research activities.

Giuseppe Ippolito

Scientific Director National Institute for Infectious Diseases Lazzaro Spallanzani
Rome, Italy

Giuseppe Ippolito is the Scientific Director (since 1998) of the National Institute for Infectious Diseases (INMI) "Lazzaro Spallanzani" in Rome and Director (since 2009) of the WHO Collaborating Center for clinical care, diagnosis, response and training on Highly Infectious Diseases at INMI.
He graduated in Medicine (summa cum laude) at the University La Sapienza in Rome in 1978, and in 1981 he obtained his specialty degree in infectious diseases (summa cum laude). In 1984, he obtained a second specialty degree in Dermatology at the University "La Sapienza", Rome. He has also received a Masters Degree in Organization and Management of Health Institutions from the University of Tor Vergata, Rome, in 1997.
Within the L. Spallanzani Institute Giuseppe Ippolito served in various positions (Registrar and Senior Registrar) in the Infectious Diseases unit during the 1980s. In 1985, he joined the "Latium Region" Regional Authority as head of the AIDS epidemiology unit. In 1990 he was appointed Head of the AIDS Unit at INMI, and in 1993 he became Director of the AIDS Reference Center and the Unit for Infectious Diseases Epidemiology of the same institution; in 2000 he was appointed Director of the Department of epidemiology and preclinical research.
Giuseppe Ippolito served as member of several National bodies established by the Italian Ministry of Health: National Commission on AIDS (1998-present); Scientific Committee for the Research Project on Antiviral Treatments for AIDS (1992-1996); Scientific Committee for the Research Project on social and ethical aspects of AIDS (1994- 2002); Committee on Ebola and other Hemorrhagic fevers (1995-1996); Scientific Committee for CJV disease (1996); Co-coordinator of the Technical Committee for the management of risks related to the intentional use of biological, chemical and nuclear weapons (2001-2004); Committee on SARS (2003-2005); National Task force for influenza A/H1N1 (2009-2010). He was also a member of the Scientific Committee for the evaluation of Projects of Industrial Research for the Italian Ministry of Universities and Research (2005-2009), and he is currently a member of the Scientific Committee of the department of Medicine of the Italian Research Council.

He served on a number of international committees with the World Health Organization, the USA Centers for Diseases Control and Prevention, Health Canada, OECD, United Nations, NATO, G7+ Mexico -Global health Security Action Group, ILO, European Commission.
He has served as advisor and evaluator for several research and policy bodies, including the European Commission and the European Center for Diseases Control.
In the last 10 years, he coordinated 8 EU-funded projects, and is currently coordinating 4, all in the field of Emerging and Reemerging infections, biosecurity, preparedness and response; he has also been a partner or leader of 6 additional EU projects.
He is involved, as scientific coordinator, in international activities funded by the Italian Cooperation Office of the Italian Ministry of Foreign Affairs in Tanzania to strengthen the diagnosis and treatment of HIV/AIDS, tuberculosis, malaria, and emerging pathogens.
Over the years, Giuseppe Ippolito's research interests have been focused on: the Surveillance and control of nosocomial and occupational infections; epidemiology and prevention of HIV, HBV, HCV, Tuberculosis; Emerging ad re-emerging infections; biodefense, biosecurity and biosafety; alert, preparedness and response.
He has published as main author approximately 250 major papers (indexed by Index Medicus for a total Impact Factor of about 1300); 250 other peer-reviewed papers; 26 books, 30 book chapters, 44 reports and other publications for a general audience.
In 1998, he received the Charles C. Shepard Science Award from the Centers for Disease Control (CDC) for the study "A case-control of HIV seroconversion after percutaneous exposure".

GLOBAL BURDEN OF INFECTIOUS DISEASES: NOT JUST NUMBERS

At the beginning of the third millennium communicable diseases continue to cause worldwide -mostly in developing countries- the death of several million people each year with the greatest impact on morbidity and life expectancy. Communicable diseases do not respect national borders and the failure of control measures in one country can put neighbours and global health at risk.
There is evidence that the impact of these diseases is increasing due to continuing and worsening levels of poverty, the effect of population growth, the increase in man-made and natural disasters resulting in displacement of populations, the behavioural changes, the emergence of resistance to anti-infectives, climatic changes and deteriorating sanitation. Infectious diseases can be partially controlled through improved living conditions and effective public health and education systems.
The Global Burden of Disease (GBD) Study, established since 1992, is an assessment for evidence-based decisions in public health. The term was coined by epidemiologists and economists to study international variations in the patterns of disability-adjusted life expectancy (DALYs) for the World Bank.
Among the top 10 diseases for mortality and burden, 4 are infectious diseases. The methods to estimate health gaps changed over the years as the number of conditions (diseases, injuries and risk factors) considered. The GBD now quantifies the burden of about 500 sequelae of more than 100 major causes of death and disability disaggregated by eight geographic regions and ten age-sex groups, with projections to 2020.
The goal of GBD is now to systematically collect data for assessment of health status; to ensure that all estimates and projections were derived, in an indipendent way, on the basis of objective epidemiological and demographic methods; to measure the burden of disease using a metric that could also be used to assess the cost-effectiveness of interventions (Disability-Adjusted Life Years, or DALYs)

The latest round of GBD (2010 study) is in progress and the results will be published in 2011. The report will be based on improved methods allowing full use of the increasing amount of health data, particularly from developing countries, and will include a comprehensive and consistent revision of disability weights.
The data of GBD represent a policy framework to provide information for a coherent, comprehensive and accelerated response to communicable diseases, securing adequate resources to produce better health outcomes towards a sector-wide approach, setting a broad policy framework and establishing longer-term partnerships.
Now the term Global Burden is largely used also outside the GBD study and several estimates of "Burden" have been performed for several communicable diseases.
Examples related to viral infections, methodological aspect, use of data and their integration with social and political information will be presented and discussed.

Charles Rice

Professor, Laboratory of Virology and Infectious Disease; Scientific and Executive Director, Center for the Study of Hepatitis C, The Rockefeller University, NY, USA

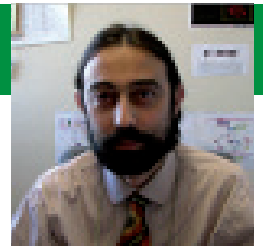
Dr. Rice is the Maurice R. and Corinne P. Greenberg Chair in Virology and serves as Head of the Laboratory for Virology and Infectious Disease at Rockefeller University. He is one of the world's most accomplished virologists and a prominent figure in research on members of the Flaviviridae including hepatitis C virus (HCV). Dr. Rice received his bachelor's degree from University of California Davis in 1974 and earned his Ph.D. from California Institute of Technology in 1981.

From 1986-2000, Dr. Rice was a faculty member at Washington University in St. Louis. His research team has helped to understand the biogenesis and structure of HCV-encoded proteins, discovered a highly conserved RNA element at the 3' terminus of HCV genome RNA, and produced the first infectious molecular clone of the virus-an essential tool for future studies on this important human pathogen. His laboratory has established efficient cell culture systems for studying HCV replication and evaluating antiviral efficacy. Dr. Rice has co-authored over 300 articles in the field of virology, serves as a reviewer for numerous journals, is a former editor of Journal of Virology, is a past President of the American Society for Virology, a Fellow of the American Association for the Advancement of Science, and a Member of the National Academy of Sciences.

Abstract

HEPATITIS C: TOWARDS CONTROL AND ERADICATION

Hepatitis C virus infection continues to be a worldwide health problem. Over the last two decades, research has focused on trying to establish tractable systems for studying virus replication and drug development. I will highlight recent work on HCV entry, RNA replication, virus assembly and emerging therapies. In addition, I will describe new tools for studying HCV biology, including HCV-permissive human hepatocyte micropatterned co-cultures, reporter systems that allow real time imaging of infectious processes, and new animal models.



Adolfo García-Sastre

Professor, Departments of Microbiology and Medicine; Director, Global Health and Emerging Pathogens Institute, Mount Sinai School of Medicine, New York, USA

Dr. García-Sastre is Professor in the Departments of Microbiology and Medicine and Director of the Global Health and Emerging Pathogens Institute at Mount Sinai School of Medicine in New York. He is also Principal Investigator for the Center for Research on Influenza Pathogenesis (CRIP), one of five NIAID Centers of Excellence for Influenza Research and Surveillance (CEIRS). For the past 20 years, his research interest has been focused on the molecular biology of influenza viruses and several other negative strand RNA viruses. During his postdoctoral training in the early 1990s, he developed for the first time, novel strategies for expression of foreign antigens by a negative strand RNA virus, influenza virus.

He has made major contributions to the influenza virus field, including 1) the development of reverse genetics techniques allowing the generation of recombinant influenza viruses from plasmid DNA (studies in collaboration with Dr. Palese); 2) the generation and evaluation of influenza virus vectors as potential vaccine candidates against different infectious diseases, including malaria and AIDS; 3) the identification of the biological role of the non structural protein NS1 of influenza virus during infection: the inhibition of the type I interferon (IFN) system; and 4) the reconstruction and characterization of the extinct pandemic influenza virus of 1918 (this paper was selected as paper of the year by Lancet). His studies provided the first description and molecular analysis of a viral-encoded IFN antagonist among negative strand RNA viruses. These studies led to the generation of attenuated influenza viruses containing defined mutations in their IFN antagonist protein that might prove to be optimal live vaccines against influenza. His research has resulted in more than 250 scientific publications and reviews. He was among the first members of the Vaccine Study Section of the NIH. In addition, he is an editor for Journal of Experimental Medicine, PLoS Pathogens and Journal of Virology and a member of the Editorial Board of Virology, Journal of General Virology and Virus Research. In 2009 he was elected Beijerink Professor by the Dutch National Academy of Sciences.

Abstract

PANDEMIC INFLUENZA

Human pandemic influenza viruses are characterized by the presence of an antigenically novel viral hemagglutinin which allows viral replication even in the presence of pre-existing influenza virus immunity.

Such hemagglutinins are derived from influenza virus strains that circulate in a non-human host animal. As viral strains adapted to non-human hosts are in general unable to transmit well in humans, pandemic influenza viruses require some levels of adaptation before being able to jump from one host to humans and initiate a pandemic. The novel pandemic H1N1 influenza virus, despite being genetically similar to other swine influenza virus, started the 2009 influenza human pandemic. We are investigating the genetic and molecular characteristics responsible for the success of the novel H1N1 virus in humans. Our results will be presented and discussed.

Heinz Feldmann

Laboratory of Virology, Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, Montana. USA

Dr. Feldmann graduated from Medical School and received his PhD in 1988 both from the University of Marburg, Germany. His postdoctoral research was conducted in the field of virology (filoviruses and hantaviruses) at the Philipps-University (Marburg, Germany) and the Special Pathogens Branch at the Centers for Disease Control and Prevention (Atlanta, USA). During his time in Marburg he was trained as an infectious disease specialist with focus on laboratory diagnostics. From 1999-2008, Dr. Feldmann held the position of Chief, Special Pathogens Program of the National Microbiology Laboratory, Public Health Agency of Canada (PHAC) (Winnipeg, Canada). Since 2008, he is the Chief, Laboratory of Virology at the Rocky Mountain Laboratories (RML), DIR NIAID, NIH (Hamilton, Montana), and the Chief Scientist of the RML BSL4 Laboratories. Heinz Feldmann is the laboratory expert on high containment viruses (BSL4) and serves as a consultant on viral hemorrhagic fevers and related pathogens for the World Health Organization and, thus, has field experience and expertise in outbreak management. He is a member of national and international professional societies, an editor for Archives of Virology, and serves on the editorial board of several virology journals. Dr. Feldmann is an external scientific reviewer for national and international organizations and serves as a scientific consultant for high containment laboratories. His professional interest is in the pathogenesis of hemorrhagic fever viruses, such as filoviruses, arenaviruses and bunyaviruses, and other special viral pathogens (high containment, BSL3 and BSL4). Dr. Feldmann was awarded with several honors including the 'Löffler-Frosch Award' from the German Society for Virology (DGV), the 'Dalrymple/Young Award' by the American Committee on Arthropod-Borne Viruses (ACAV), and the PHAC Research Merit Award.

EMERGING ZOONOTIC VIRUSES: RESPONSE AND PREPAREDNESS

Numerous viral diseases have emerged and re-emerged over the past decades. Aside from many others, the so called 'high containment' viruses in particular are a threat to our public health systems due to limited experience in case management and lack of appropriate resources. Many of these viruses are zoonotic in origin and remain a major challenge for animal and human health worldwide as evidenced by the emergence/re-emergence of influenza, SARS-CoV, Rift Valley fever virus and other exotic or more common pathogens. Many countries have established infectious disease centers with primary responsibility for disease surveillance, reference microbiology and quality assurance, preparedness and response to these threat agents. Rapid reference diagnostics is provided in most of these centers but on-site diagnostic capabilities are still underdeveloped and often hamper national and international outbreak investigations.

The animal/human health response mandate cannot be accomplished without a strong research component focused on pathogen biology, pathogenesis and immune response to provide the fundamental data and concepts for the development of antivirals, therapeutics and vaccines. Therefore, animal models that mimic disease become key elements for research operations. The reservoirs, if known, are often persistently infected with no or mild clinical symptoms and the distribution of the infectious diseases basically reflects the range and the population dynamics of the reservoir hosts. Studies in reservoir species are rare and animal models that mimic the reservoir host and the transmission of the pathogen to humans are limited. Small animal models, in particular the mouse, are the most feasible in high containment and they offer the most options for research due to greater access of immunological and genetic tools. However, their mimicry of human disease as well as their predictive value for therapeutic efficacy is often limited thereby making them, at best valuable initial screening tools for pathophysiology, treatment and vaccine studies. Future efforts need to focus on the development of more relevant small animal models through pathogen adaptation or by the use of genetically altered host or pathogen species. In parallel, the much needed immunological and genetic tools for new animal models need to be produced.

Alberto Mantovani
Professor, Università degli Studi di Milano; Scientific Director,
Istituto Clinico Humanitas, Milan, Italy

Scientific Director of Istituto Clinico Humanitas and President and founder of the Fondazione Humanitas per la Ricerca. . Professor of Pathology, School of Medicine, State University of Milan, Alberto Mantovani was born in Milan in 1948. He graduated (summa cum laude) in 1973 in Medicine at the University of Milan and in 1976 he specialized in Oncology at the University of Pavia. From 1973 to 1975 he had a scholarship at the Laboratory of Immunology and Chemotherapy at the Mario negri Institute in Milano. From 1973 to 1976 he was visiting fellow at the Department of Tumor Immunology of the Chester Research Institute in Belmont (GB). In 1978-1979 he was visiting fellow at the Laboratory of Immunodiagnosis, NIH, Bethesda (USA), with a Yamagiwa-Yoshida Scholarship of the UICC first and then with a NATO grant.

From 1979 to 1981 he was senior investigator, Department of Tumor Immunology and Chemotherapy, Istituto di Ricerche Farmacologiche "Mario Negri", Milan. In 1981 he became Chief of the Laboratory of Immunology, Istituto di Ricerche Farmacologiche "Mario Negri". From 1994 to 2001 he was full Professor of General Pathology, School of Medicine, University of Brescia, Italy.

From 1996 to 2005 he has lead the Department of Immunology and Cell Biology at the Istituto di Ricerche Farmacologiche "Mario Negri", Milan.

He was appointed numerous scientific awards, i.e. Biotec award (1998); the Marie T.Bonazinga Award by the Society of Leukocyte Biology (USA) (2000); the Guido Venosta Prize by the President of the Republic of Italy (2004); EFIS – Schering Plough 1st European Immunology Prize, Paris, France (2006); Galileo Galilei Prize for Research in Biomedical Sciences (2007); PISO Award (2007); Onoreficenza al Merito della Repubblica Italiana; the William Harvey Outstanding Scientist (2009). Member of various professional societies, e.g. European Molecular Biology Organization (EMBO); Henry Kunkel Society; the Faculty of 1000 Biology; and President of the International Cytokine Society. He has published more than 600 papers, mostly in high-ranking journals. Highly cited immunologist, the Institute for Scientific Information (ISI Thomson) ranked him as one of 100 most quoted immunologists in the world over the last 20 years.

VIRUSES AND IMMUNITY: MOLECULAR PIRATES AND THE CHALLENGE OF A GLOBAL ALLIANCE

Viruses know the immune system in an evolutionary sense much better than immunologists do. In their evolutions certain viruses (e.g. herpes viruses) have evolved strategies to subvert and divert components of the immune system. These include the expression of molecules which act as molecular traps (decoys) for cytokines and chemokines.
Therefore viruses have acted as molecular pirates in their evolutionary history. The challenge rests in learning lessons from viruses and exploiting their molecular armamentarium. At a different level, strategies to control viral and non viral diseases using immunization at a global level will be discussed. Emphasis will be on children morbidity and mortality, and on the global alliance for vaccines and immunization (GAVI).

Rino Rappuoli
Global Head, Vaccines Research, Novartis Vaccines and Diagnostics, Siena, Italy

Dr. Rino Rappuoli, PhD, is Global Head of Vaccines Research at Novartis Vaccines and Diagnostics, based in Siena, Italy. He earned his PhD in Biological Sciences at the University of Siena and has served as a visiting scientist at Rockefeller University in New York and Harvard Medical School in Boston.
He is member of European Molecular Biology Organization and foreign associate of the American National Academy of Sciences.
Published more than 450 works in peer-reviewed journals.
He introduced several novel scientific concepts, the names of which became popular. Examples are the concept that bacterial toxins can be detoxified by manipulation of their genes (genetic detoxification, 1987), the concept that microbes are better studied in the context of the cells they interact with instead of artificial laboratory conditions (cellular microbiology, 1996), the use of genomes to develop new vaccines (reverse vaccinology, 2000), the observation that the genome of a species (pangenome, 2005) is larger than the genome of an organism of the same species.
Several molecules he worked with became part of licensed vaccines. He characterized a molecule, CRM197, that today is the most widely used carrier for vaccines against H. influenzae, N. meningitidis and pneumococcus vaccines, and is used multiple times to vaccinate most children of the globe. Then he developed a vaccine against pertussis by engineering B. pertussis to produce a non toxic pertussis toxin antigen. This was the first rationally designed molecule approved for human use. Later he developed the first conjugate vaccine against meningococcus C that eliminated the disease in the UK in 2000. He pioneered the use of genomic information for vaccine development (reverse vaccinology). The first genome-derived vaccine against meningococcus B is now in Phase III clinical trials, several others are in earlier stages of development. Finally, in 1997 he obtained the regulatory approval for MF59, the first vaccine adjuvant approved for human use after the approval of aluminium salts in the 1920s. MF59 is now being used in many other experimental vaccines, the most advanced of which is a vaccine against pandemic influenza.

VACCINES TO ADDRESS THE NEEDS OF 21ST CENTURY SOCIETY

During the 20th century, vaccines have eliminated most of the childhood diseases with the major exceptions of the diseases caused by meningococcus and respiratory syncytial virus (RSV). What is the role of vaccination in the 21st century? The first target will be to develop vaccines for meningococcal meningitis, which is perhaps the last disease that in a few hours can attack and kill healthy children and young people, and RSV that affects virtually every single child in the first few months of life. Fortunately, thanks to several revolutionary technologies developed during the last 30 years, including conjugation, genomics and new adjuvants, we are in the final stages to conquer meningococcal meningitis and new approaches are being tested for RSV. The second and perhaps most important target of vaccination in the 21st century will be to take care of the global health problems of this century. These include taking care of the aging population, with new vaccines targeting the diseases typical of the elderly with an aging immune system, to control emerging antibiotic resistance, to preventing cancer, taking care of the diseases present only in countries affected by poverty, and taking care of emerging diseases such as pandemic influenza. Overall, vaccines in the 21st century will have an increased safety, and will be used as an insurance to ensure health across all ages, for the entire life.

Viruses, Cancer and Therapy

Italian Association for Cancer Research Symposium

Chairs: **Luigi Chieco-Bianchi, Maria Ines Colnaghi**

Robin Weiss
Viruses and Cancer
Genoveffa Franchini
Oncogenic retrovirus, chronic infection and cancer:
Viral strategies that favor viral persistence in humans
Harvey Alter
Chronic viral hepatitis and liver cancer
Inder Verma
Viruses as Allies of Man

Viruses and Society

Chairs: **Umberto Veronesi, Telmo Pievani**

Marc Ostfield
Transatlantic Partnerships to Counter Biological Threats
John Mackenzie
Societal drivers of disease emergence - the consequences of human actions and activities
Manuela Kron
Overcome a virus nightmare: why and how companies protect their people at all cost
Massimiano Bucchi
The visible virus: media representations of virus and pandemics

Closing

Umberto Veronesi, **Chiara Tonelli**

Luigi Chieco-Bianchi

Professor emeritus of Oncology, Department of Oncology and Surgical Sciences, University of Padova, Italy

Luigi Chieco-Bianchi is presently Professor Emeritus on Oncology at the Faculty of Medicine, University of Padova, Italy.
He graduated in Medicine with honorem at the University of Bari in 1957 and completed his training in Pathological Anatomy at University of Bari in 1960. In 1965 he moved to Univeristy of Padova as Assistant Professor in Pathological Anatomy, and was appointed in 1975 as Full Professor to the Chair of Oncology, a position he held until his retirement in 2005.
Professor Chieco-Bianchi has been Director of the Post-graduate School in Oncology and Coordinator of the Doctorat Program in Oncology, University of Padova.
As research fellow and visiting scientist he has worked in various prestigious institutions, namely Laboratoire de Gènètique, Institut du Radium-Fondation Curie, Paris (1958-59), Institut fur Krebsforschung, Deutsche Akademie der Wissenschaften, Berlin-Buch(1961),Dept. of Cell Biology, Weizmann Institute, Rehovoth (1963-64),National Cancer Institute, Bethesda (1973), Labs of Membrane Biology, Imperial Cancer Research Fund, London (1980), Dept. of Cancer Biology, School of Public Health, Harvard University, Boston (1993). Professor Chieco-Bianchi has been president of the International Association for Comparative Research on Leukemia and Related Diseases, of the Italian Cooperative Group on Immunology, and of the Italian Society of Cancerology; he has been member of the Scientific Council of the International Agency for Research on Cancer, Lyon, and member of the steering committee of the European Cancer Research Managers Forum, Brussels.
Prof Chieco-Bianchi 's research interests initially focused on the interplay between the host immune response and oncogenic mammalian retroviruses in experimental in vitro and in vivo mouse systems; in particular, he found that induced or innate immunological tolerance with deletion of antigen-specific T cell clones critically increases the tumorigenic potential of leukemia and sarcoma retroviruses. Prof. Chieco-Bianchi and his research group subsequently moved on to study the molecular biology of human oncogenic viruses. His current efforts are aimed at unravelling the mechanisms underlying the development of AIDS-associated tumors and the transforming capacity of human T cell leukemia virus type 1. This research is complemented by studies of the molecular epidemiology of human papillomavirus and human herpesvirus-8 and investigations targeted at identifying genetic and epigenetic alterations that drive neoplastic transformation and metastasis.

Maria Ines Colnaghi

Scientific Director AIRC, Italy

Ph.D. degree in Biology, University of Milan.
1966-1970 Research Associate, Experimental Oncology, Istituto Nazionale Tumori, Milano.
1970 to 1984 Vice Director of Experimental Oncology, Istituto Nazionale Tumori, Milano.
1984 to 1999 Director,of Experimental Oncology, Istituto Nazionale Tumori, Milano.
1992 to 1999 Head of the Department of Experimental Oncology, Istituto Nazionale Tumori, Milan.
2000 to date Scientific Director of Italian Association for Cancer Research.

Author of more than 300 publications, on various aspect of experimental oncology, including studies on chemical carcinogenesis, viral leukemogenesis and immunology of experimental and human tumors. A large part of Dr. Colnaghi's researches were focused on the development and application of monoclonal antibodies in oncology. During her career Dr. Colnaghi was: - Member of the Program Committee of the International Association for Breast Cancer Research. - Chairman of the Fellowship Committee of the European Association for Cancer Research. - President of the GCI (Group of Immunology Cooperation). - Secretary of the Italian Federation of the Immunological Societies. - Grant Reviewer for Italian Association for Cancer Research, for Italian MURST (Ministry University and Scientific and Technologic Research) and for Italian Ministry of health and others. - Member of the Editorial Board and/or referee for several International cancer journals.

Robin Weiss
Professor of Viral Oncology, Division of Infection and Immunity, University College London, UK

Robin A Weiss PhD, is Professor of Viral Oncology at University College London. He studied biology at UCL, and has spent most of his research career studying retroviruses, including the discovery of tumor virus genomes transmitted in a Mendelian manner in avian DNA. Robin has made significant contributions to our understanding of HIV and AIDS, which included the identification of CD4 as the cell surface receptor to which HIV binds and neutralising antibody responses to HIV and other viral infections. He has also conducted research on pig retroviruses as a potential infection hazard in xenotransplantation, and on AIDS-associated malignancies, particularly Kaposi's sarcoma and its herpesvirus. Robin was Director of Research at the Institute of Cancer Research, Royal Marsden Hospital, London, 1980-1999. He was elected a Fellow of the Royal Society in 1997. He was President of the Society for General Microbiology 2006-2009.

Abstract

VIRUSES AND CANCER

Approximately 20% of the human global cancer burden is caused by infectious agents and the majority of these are commonly occurring viruses. Perhaps the best known are the papilloma viruses that are associated with cancer of the cervix in women, but liver cancer, certain other carcinomas and sarcomas as well as several types of leukemia and lymphoma, are also caused by different types of virus.

We are gaining an increasing understanding of how oncogenic viruses cause malignant disease and this knowledge has provided important insights into the molecular biology of cancer in general. Cancer can be considered to be a relatively rare "side effect" of human tumor virus infection; there are multifactorial aspects of viral oncogenesis although the virus plays an essential role. The prevalence of the tumor virus and of the other co-factors help to explain why viral cancer rates vary in different parts of the world and even within different regions in Italy. Viral cancers occur more commonly in recipients of organ transplants and patients with AIDS so the immune system normally helps to suppress the development of viral tumors. The development of vaccines against hepatitis B virus and more recently papilloma viruses are effective in preventing infection and will therefore reduce the number of viral cancers in future years.

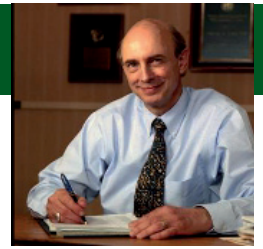
Genoveffa Franchini
Chief, Animal Models & Retroviral Vaccines Section, National Cancer Institute, Bethesda, USA

Dr. Genoveffa Franchini received her M.D. in 1977 from the University of Modena, Italy, and is the chief of the Animal Models & Retroviral Vaccines Section of the National Cancer Institute, USA. She is a world-renowned retrovirologist who has pioneered research on oncogenes and human retroviruses. Dr. Franchini has made significant achievements in retrovirology and translational approaches to prevent human retroviral infections. She has furthered the understanding of HTLV-1 pathogenesis, characterized new viral genes, and explored (Nature 2004) the affect of the host immune response (Nature 2010). Her interest in immunological mechanisms has bettered the understanding of vaccine protection, particularly in the SIV macaque model. Her accomplishments in HIV vaccine development have secured patent rights to the US Government on the use of poxvirus vectors alone or in combination with DNA. One of the vaccines developed and tested in Dr. Franchini's laboratory is in clinical trials in 16,000 volunteers in Thailand. Dr. Franchini's laboratory genetically characterized SIV (Nature 1987) and defined the regulatory function of HIV-1/2 and SIV genes (Science 1986, 1990). She first demonstrated the importance of Vpr in HIV-1 infectivity in macrophages (PNAS, 1990) and the SIV fusion peptide (Science, 1989). Her work in immunological mechanisms furthered the understanding of vaccine efficacy and protection (Nature Medicine, 2005). In the therapeutic arena, Dr. Franchini provided the first proof of principle that vaccination provides transient benefit to SIV-infected macaques (Nature Medicine, 2001), and she pioneered strategies to down-modulate regulators of immune response in HIV-1-infected individuals.

Abstract

ONCOGENIC RETROVIRUS, CHRONIC INFECTION AND CANCER: VIRAL STRATEGIES THAT FAVOR VIRAL PERSISTENCE IN HUMANS

Human T-cell leukemia/Lymphoma virus type 1(HTLV-1) infects about twenty million people worldwide. HTLV-1 is more frequent in some area of the world; for example 1% of the inhabitants of Kyushu, an island of Japan, are infected by HTLV-1.The virus was first isolated in the late Seventies at the National Cancer Institute from a patient that had Adult T-cell leukemia/Lymphoma (ATLL). HTLV-1 causes not only ATLL but also a neurological disease that results in paralysis of the lower limbs, designated Tropical Spastic Parapharesis/ HTLV-1 associated Myelopathy(TSP/HAM). However, disease occurs only in approximately 2% of the infected individuals in their life time. HTLV-1 is the first oncogenic retrovirus found in humans. Like the other known human retroviruses, such as the Human Immune Deficiency Virus type 1 and 2(HIV-1 and HIV-2) that cause Acquired Immune Deficiency (AIDS),HTLV-1 has a complex genome that encodes several structural and non structural proteins. HTLV-1 associated oncogenicity does not appear to be due to insertional mutagenesis. Rather, the expression of viral proteins in the virus-infected T-cells increases their survival and their ability to escape immune recognition. A current hypothesis for HTL1 leukemogenesis is that HTLV-1, by prolonging the life of the infected T-cells, may favor the accumulation of genetic lesions that ultimately cause the uncontrolled growth of T-cell and leukemia. Thus, the identification of the viral genetic determinant that prolong the life of the infected T-cells and favors viral persistence is important because it may provide several targets to inhibit virus spreading in the host and the subsequent cancer development.



Harvey Alter
Chief, Clinical Studies & Associate Director for Research,
Department of Transfusion Medicine, National Institute of Health, Bethesda, USA

Dr. Alter has spent most of his research career at the National Institutes of Health. He is currently designated Distinguished NIH Investigator and serves as Chief of Clinical Studies and Associate Director for Research in the Department of Transfusion Medicine.
Dr. Alter was co-discoverer of the Australia antigen that later proved to be the hepatitis B virus and was principal investigator in studies that identified non-A, non-B hepatitis, defined its chronic sequela and later showed its link to HCV.
His prospective studies of transfusion-associated hepatitis demonstrated how different donor interventions reduced hepatitis incidence from 30% in 1970 to near zero in 1997. In recognition of his research accomplishments, Dr. Alter was awarded the Landsteiner Prize, the highest award of the American Association of Blood Banks, the Inserm Medal from France, and the Clinical Lasker Award. He has been elected to both the National Academy of Sciences and the Institute of Medicine and is a Master of the American College of Physicians.

Abstract

CHRONIC VIRAL HEPATITIS AND LIVER CANCER

Most cases of liver cancer (hepatocellular carcinoma, HCC) are now known to be the result of chronic infection with the hepatitis B virus, the hepatitis C virus or a combination of these agents. In China, Southeast Asia, sub-Saharan Africa and southern Europe, the infection with the hepatitis B virus is the primary underlying cause whereas in Japan, the United States, most of Europe and the rest of the world, the hepatitis C virus is the predominant infectious agent able to induce this kind of cancer.
The progression from infection to cancer generally goes through a silent acute phase, followed by chronic inflammation, progressive fibrosis and cirrhosis.
Neither of the two viruses appear to be directly oncogenic, but the inflammatory microenvironment and the high level of genetic mutation that accompanies the evolution of cirrhosis are thought to facilitate the development of cancer. Alcoholism and other diseases that affect the liver, like hemochromatosis and non-alcoholic steatohepatitis, also can induce cirrhosis and HCC and may accelerate progression when they coexist with chronic hepatitis virus infection.
The longer the duration of infection, the more likely is the development of HCC. The majority of hepatocellular carcinoma related to infection with the hepatitis B virus occurs in adults who were infected at birth from a carrier mother. In contrast, infection with the hepatitis C virus is more frequent in young adulthood, through drug-related shared-needle usage and rarely, sexual transmission.

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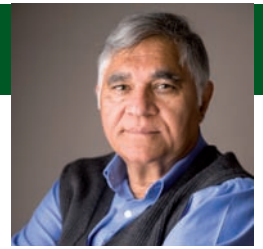
Infection through contaminated blood transfusions, once responsible for about 30% of cases, is now reduced to almost zero, due to the development of effective donor screening procedures. Both viral infections smolder usually for three or more decades before evolving into cancer. This is well demonstrated by the contrasting incidence of this kind of cancer in the US and Japan. Although both countries have a similar prevalence of infection with the hepatitis C virus, Japan has an 8-10 fold higher rate of hepatocellular carcinoma. Molecular clock studies now show that the predominant hepatitis C virus strain in Japan emerged and spread approximately 30 years before the most common strain in the US started to spread. These time differences suggest that the Japanese have been infected with the hepatitis C virus, on average, 30 years longer than Americans, and predicts that the rate of hepatocellular carcinoma in the US, and probably Europe as well, will increase dramatically over the next 2-3 decades (this concept is already being substantiated as the rate of hepatocellular carcinoma related to the hepatitis C virus has already increased 3 fold in the US since 1980).

Once hepatocellular carcinoma develops, small tumors (<3cm) can be treated by injection of alcohol or other toxins or with radiofrequency ablation. Larger masses that have not metastasized can be treated by surgical resection of the involved segment or lobe with or without chemotherapy. Unresectable lesions require liver transplantation.

While treatments for this kind of cancer have improved, the primary intervention is prevention. For hepatitis B virus, prevention is achieved by administering hepatitis B vaccine at birth, particularly in endemic regions. In non-endemic areas that do not have universal infant administration, vaccine should be given before early adolescence to prevent acquisition through sexual exposure.

There is no vaccine for hepatitis C virus currently available, but treatment for chronic hepatitis C is increasingly effective, with "cure" rates ranging from 45-50% to near 80% depending on viral genotype, and novel therapies are projected to increase cure rates significantly. It is thus essential to identify as soon as possible asymptomatic, infected persons with hepatitis C virus, so that they can be treated before cirrhosis and cancer ensue.



Inder Verma
Professor, Laboratory of Genetics, The Salk Institute for Biological Sciences,
La Jolla, CA, USA

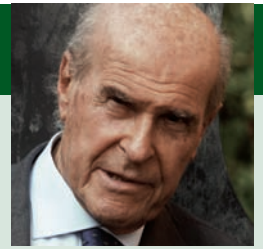
Inder M. Verma is a professor in the Laboratory of Genetics and holds the Irwin and Joan Jacobs Chair in Exemplary Life Science and American Cancer Society Professor of Molecular Biology. He received his PhD degree from the Weizmann Institute of Science, Rehovot, Israel in 1971, completed postdoctoral training with David Baltimore at Massachusetts Institute of Technology in 1974, and has been with the Salk Institute as Assistant Professor, Associate Professor and now Professor from 1974 to present. Dr. Verma is one of the world's leading authorities on the development of viruses for gene therapy vectors and uses genetically engineered viruses to insert new genes into cells that can then be returned to the body, where they produce the essential protein whose absence causes disease. Dr. Verma and Salk colleagues developed a gene therapy vector, based on a stripped-down version of HIV that can deliver genes to nondividing cells, which constitute the majority of the cells in our bodies. They have used this vector successfully to deliver the clotting factor gene to laboratory animals and to transfer a therapeutic gene to retinal cells to mice with an inborn deficiency. Dr. Verma's group is also studying two genes implicated in familial breast cancer, BRCA1 and BRCA2, and recently demonstrated that their action is linked to the cell's division cycle and that BRCA1 regulates gene activity.

Dr. Verma's scientific contributions have been recognized by a number of honors, including one of 25 lifetime American Cancer Society Professorships (1990), an Outstanding Investigator Award from the NIH (1988), membership in the Third World Academy of Sciences (1995), the National Academy of Sciences, India (1997), the National Academy of Sciences, USA (1997), the Institute of Medicine (1999), a Fellow of the American Academy of Arts and Sciences (2000), an Associate Member of the European Molecular Biology Organization, EMBO (1998) and election to the American Philosophical Society (2006) Vilcek Foundation Prize (2008), ASGT Outstanding Achievement Award (2009) Spector Prize (2010), and the Pasarow Award in Cancer Research (2010).

Abstract

VIRUSES AS ALLIES OF MAN

At the beginning of the third millennium, man has an opportunity to fulfill the cherished goal of improving the lot of humankind. Newer modalities of medicine are being practiced and daily new breakthroughs are being reported. I would like to talk about gene therapy, a form of molecular medicine, which will have a major impact on human health. At present, gene therapy is being contemplated for both genetic and acquired diseases.
These include hemophilia, cystic fibrosis, diabetes, cancer, Parkinson's, Alzheimer's, etc. In the case of genetic diseases, a wide variety of somatic, non-germinal tissues are being explored for the introduction of foreign genes with a view towards gene therapy. A prime requirement for successful gene therapy is the absence of any adverse effect on the recipient. A highly desirable delivery vehicle will be the one that can be generated at high amounts, integrate in non-dividing cells and have little or no associated immune problems. We have recently generated vectors based on a modified, non pathological, safe form of the AIDS virus that have the ability to introduce genes into both dividing and non-dividing cells. The vectors can introduce genes in a variety of cells and hosts.
Our current, third-generation viral vectors are devoid of six viral genes and therefore we consider them to be safe vectors. Using third generation lentiviral vectors we can introduce genes directly into brain, liver, muscle, hematopoietic stem cells, and more recently retina and a number of tumor cells. Our data shows that lentiviral vectors can not only efficiently deliver genes, but also have long term sustained production of the foreign protein. We have not observed any untoward immunological consequences due to the vector. My talk will discuss the use of vectors for a wide variety of genetic and acquired diseases. Additionally I will discuss the use of these viral vectors for studying complex biological systems. Finally I will discuss the social and ethical implications of genetic approaches to human health.



Umberto Veronesi

Scientific Director, European Institute of Oncology, Italy

Umberto Veronesi is a surgeon who has devoted the greater part of his professional life to exploring new pathways of research with the aim of improving the treatment and quality of life of cancer patients.
It was he who, at the National Cancer Institute in Milan, on the basis of controlled clinical trials, first contributed to the development of the conservative treatment of breast cancer. He was the first to demonstrate that in the case of small cancers of the breast it is safe to perform a wide resection followed by radiotherapy and, thereby preserve the breast, thus obviating the mutilating procedure of mastectomy. More recently he has developed new research using the sentinel node biopsy procedure to avoid axillary dissection when the lymph nodes are not involved.
In the last twenty years he has devoted his interests to breast cancer prevention, conducting two major randomized studies aimed at reducing the risk of breast cancer in normal women by means of retinoids and tamoxifen.
Very recently he has re-evaluated the procedures of postoperative radiotherapy after breast conserving surgery, introducing the technique of intraoperative radiotherapy.
By founding the International Melanoma Group he alerted pathologists and clinicians to the pressing need for international co-operation in melanoma research and devised and conducted trials which showed that prophylactic dissection of regional nodes in stage I disease could safely be avoided. Furthermore, he advocated a conservative approach to melanoma which has been adopted by the World Health Organisation Melanoma Group of which he was chief investigator for 20 years.
Veronesi has also dedicated his energies to initiating and promoting educational enterprises for the training of oncologists. In 1982, he founded the European School of Oncology, which has since become a point of reference throughout Europe and, in particular, an advisory body for the European Community. The European Society of Surgical Oncology, also founded by Umberto Veronesi, has, likewise undertaken an educational line which follows well in the wake of the guidelines set out by the School.

He was President of the International Union Against Cancer (UICC) until 1982, of the European Organization for Research and Treatment of Cancer from 1985 to 1988, and of the Federation of European Cancer Societies (FECS) from 1991 to 1993. He was founder and first President of the European Cancer Societies of Mastology.

He has been awarded "Honoris Causa" in Medicine by Argentinean (Buenos Aires, Cordoba), Brazilian (Rio Grande do Sul), Greek (Athens), Belgian (Antwerp), and Polish (Kracow) Universities. In May 2003 he was awarded "Honoris Causa" in Medical Biotechnologies from the University of Milan (Italy) and in March 2005 in Physics, also from the University of Milan. In December 2006 he was awarded "Honoris Causa" in Agricultural Sciences from the University of Naples (Italy) and in October 2007 he was awarded "Honoris Causa" in Medicine from University of Lleida (Spain). In November 2009 he was awarded "Honoris Causa" in Pedagogical Sciences from University of Genoa (Italy). In May 2010 he was awarded "Docteur Honoris Causa" from University of Antananarivo (Madagascar).
In March 2003 he was awarded the "2003 King Faisal International Prize" from Saudi Arabia.
In 1994 he was appointed President of the "Committee of Cancer Experts" of the Commission of European Communities.
Veronesi is the author of more than 755 scientific publications and 12 oncological treatises.
He was Scientific Director of the European Institute of Oncology - Milan, Italy from May 1994 to April 2000.
He was entrusted with the post of Minister of Health in the Italian Government from April 2000 to June 2001.
On July 1, 2001 he resumed the position of Scientific Director of the European Institute of Oncology. Since April 29, 2008 he has been a Senator of the sixteenth Italian Parliament.

Telmo Pievani

Professor, Philosophy of Science, University of Milan Bicocca, Italy.

Graduated in Philosophy of Science at the University of Milan, researcher in the field of Philosophy of Biology and Theory of Evolution, after Ph.D. researches in USA under the supervision of Niles Eldredge at the American Museum of Natural History in New York, he is now Associate Professor of Philosophy of Science at the University of Milan II – Bicocca, and vice-President of the Degree in Educational Sciences. His first monograph, about human evolution, "Homo sapiens and Other Catastrophes" (Meltemi, Rome, 2002), reached the 4° edition in few months. He is author also of: "Introduction to the Philosophy of Biology" (Laterza, Rome-Bari, 2005; Portuguese edition in press); "The Theory of Evolution" (Il Mulino, Bologna, 2006); "Creation without God" (Einaudi, Turin, 2006; Spanish edition 2009); "In Defence of Darwin" (Bompiani, Milan, 2007); "Born to Believe" (Codice Edizioni, Turin, 2008, with V. Girotto and G. Vallortigara). Engaged in several projects regarding communication of science, he is the Scientific Coordinator of Genoa Science Festival (www.festivalscienza.it) and Scientific Director of Rome Festival of Sciences. Member of the Scientific Board of Darwin Day Celebrations at the Natural History Museum of Milan, he is Director of "Pikaia", the first Italian website completely dedicated to evolution and philosophy of biology (www.pikaia.eu). He is fellow of: Italian Society of Evolutionary Biology; Istituto Veneto di Scienze, Lettere ed Arti; Scientific Board of "Umberto Veronesi" Foundation for the Progress of Sciences. He is member of the editorial boards of International journals such as Evolutionary Biology and Evolution: Outreach and Education. With Niles Eldredge and Ian Tattersall, he is the Curator of the International exhibition "Darwin 1809-2009" (Rome, Milan, Bari, 2009-2010; www.darwin2009.it). He writes for Il Corriere della Sera, and journals like Le Scienze, Micromega and L'Indice dei Libri.

Marc Ostfield

Director, Office of Policy and Global Issues, Bureau of European and Eurasian Affairs,
U.S. Department of State, Washington, USA.

Marc Ostfield is Director of the Office of Policy and Global Issues in the Bureau of European and Eurasian Affairs (EUR/PGI) at the U.S. Department of State where his offices focuses on counterterrorism, United Nations, human rights, environment, science, technology, health, crime, corruption, homeland security, strategic planning, and Congressional relations as they pertain to U.S. foreign policy with Europe and Eurasia. From 2002 to 2009, Dr. Ostfield was the Senior Advisor on Bioterrorism, Biodefense, and Health Security for the U.S. Department of State, Office of International Health and Biodefense. Over the course of his career, Dr. Ostfield has worked in more than 40 countries with U.S., European, and international organizations including the World Health Organization (WHO), the European Union, INTERPOL, the United Nations Development Programme (UNDP), UNICEF, and the World Bank -- and he previously directed the Behavior Change Communication Division of one of the largest USAID-sponsored global health programs. Recent publications include: "Pathogen Security: The Illusion of Security in Foreign Policy and Biodefense" (International Journal of Risk Assessment and Management, 2009), "Strengthening Biodefense Internationally: Illusion and Reality" (Biosecurity and Bioterrorism, 2008), "Biodefense: U.S. Vision of Broader Cooperation" (European Affairs, Spring 2007), and "Bioterrorism as a Foreign Policy Issue" (The SAIS Review of International Affairs, 2004). Dr. Ostfield has received a range of academic and professional honors, including multiple Superior Honor and Meritorious Honor awards from the U.S. Department of State, the Diplomacy Fellowship from the American Association for the Advancement of Science, the Javits Fellowship from the U.S. Department of Education, the 2007 Franklin Award for initiative in Counterterrorism, the 2006 Meritorious Unit Citation from the U.S. National Counterterrorism Center (NCTC), and the 2006 President's Volunteer Service Award for his community service as a volunteer firefighter since 1995. He holds a Ph.D. from the University of Pennsylvania's Annenberg School for Communication -- and speaks French, Arabic, Spanish, and Portuguese. .

Abstract

TRANSATLANTIC PARTNERSHIPS TO COUNTER BIOLOGICAL THREATS

This presentation will look at local and global risks from biological threats, and, in particular, some of the crucial issues at this intersection of science and security.
With very real concerns about the evolving threat of bioterrorism, this presentation will examine the key steps policy makers and scientists need to take in order to promote global scientific cooperation and simultaneously protect against those who would use biological agents to harm individuals and societies.
Emphasis will be on specific areas for creating or enhancing collaboration and partnerships between the U.S. and Europe to help transform the transatlantic and international dialogue and address these dual goals.
This presentation will describe ways that, with a comprehensive and international approach, we can reduce the threats from infectious diseases - whether naturally occurring, or the result of an accident or deliberate release.

John Mackenzie
Professor, Tropical Infectious Diseases, Curtin University, Australia

John Mackenzie is a Professor of Tropical Infectious Diseases and part-time Faculty Member at Curtin University, Western Australia, and is an Honorary Professor at the University of Queensland and Honorary Senior Principal Fellow at the Burnet Institute, Melbourne. He was formerly Professor of Microbiology and Tropical Infectious Diseases at the University of Queensland. He received his PhD in 1969 from the Australian National University where he worked with Professor Frank Fenner and Dr Robert Webster.
He was then a faculty member at the University of Western Australia for 22 years, working principally on influenza and mosquito-borne viral diseases. He was elected Secretary-General of the International Union of Microbiological Societies (IUMS) from 1999-2005, Fellow of the American Academy of Microbiology, and is a Past President of the Australian Society for Microbiology and the Asia-Pacific Society for Medical Virology. In 2002, he was appointed as Officer in the Order of Australia for services to public health research and to education, and in 2005, he was the inaugural recipient of the Academy of Science Malaysia's Mahathir Science Award for Excellence in Tropical Research. He serves on a number of international committees with the United Nations, World Health Organization (WHO) and other Non-Government Organizations.
He is a member of the steering committee of the Global Outbreak Alert and Response Network (GOARN), a member of the Technical Advisory Group of the WHO Asia-Pacific Strategy for Emerging Diseases, and a consultant to the new International Health Regulations (2005). Over the past year he has served as Chair of the IHR Emergency Committee for Influenza H1N1. His recent research interests have been in mosquito-borne virus diseases and emerging zoonotic viruses, and he has published over 300 major papers and research chapters on these and other research topics concerned with human and animal viral diseases.

Abstract

SOCIETAL DRIVERS OF DISEASE EMERGENCE THE CONSEQUENCES OF HUMAN ACTIONS AND ACTIVITIES

It is becoming increasingly clear that there is a strong human dimension to emerging and re-emerging diseases, and that most outbreaks or epidemics of emergent diseases are due in large part to human activities and/or human actions.
Thus a better understanding of the underlying causes or mechanisms that predispose to disease emergence is crucial for improving our ability to predict future disease outbreaks, and also to prevent or mitigate their emergence. In this context, it is important to recall that emerging viral diseases are defined as either novel diseases not previously recognised or known viral diseases which are increasing ,or which threaten to increase, in incidence or geographic range. The major human activities and actions which predispose to disease emergence are those which bring humans closer to the source of virus, or which increase the environmental opportunities for transmission.
These include changes in human demographics and urbanisation, changes in land use and agricultural practices, increases in globalisation of food supplies and trade, and the phenomenal increase in international travel and tourism. Added to these activities, genetic variation and mutations can change the transmissibility and/or the virulence of viruses.
Thus changes in human demographics , such as increased urbanisation as a consequence of a movement from rural to urban areas leading to the development of shanty towns, often without water or sewage resources, or increased population growth leading to over-crowding, poverty and migration, are examples of the activities which predispose to viral disease transmission and spread.

>>

Abstract

Similarly, changes in agricultural practices including intensive agriculture, deforestation, and increased irrigation also provide a potential for transmission as we struggle to feed an ever increasing world population. Indeed the globalisation of food supplies may also lead to virus transmission causing food poisoning.
Travel and tourism provide an excellent avenue for the rapid spread of viral diseases, bringing exotic viruses from distant continents, and spreading viral diseases across national borders.
Globalisation of trade may also spread mosquito vectors between continents, leading to the possibility of local transmission of exotic diseases.
For all of these, societal pressures for improved quality and quantity of safe food and water supplies, for exotic and distant places to go for business or holidays, and for the potential of an improved future with respect to jobs and education in increasingly large urban centres, all serve to increase the potential for the spread and transmission of known and novel viral disease threats.
Unfortunately, there are also examples were a breakdown of societal values can occur with increased transmission of some vaccine-preventable viral diseases, as exemplified by a reduction in public health programs leading to reduced levels of immunisation, resulting in the re-emergence of viral diseases such as measles and rubella.
In addition, a reduction in public health measures may also lead to inadequate vector control and thus increased incidence of mosquito-borne disease.
Finally, the economic consequences of emerging disease outbreaks can be significant, as seen from the emergence of SARS coronavirus in 2003 in China, and the spread of West Nile virus to North America in 1999.

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Abstract

OVERCOME A VIRUS NIGHTMARE: WHY AND HOW COMPANIES PROTECT THEIR PEOPLE AT ALL COST

Companies can be severely hit by an outbreak of flu pandemic that could spread around the world within a few weeks or months. Viral transmissibility, morbidity, mortality rates could vary from one country to the other.
Guidelines from Health organizations are taken extremely seriously.
The key objective of Nestlé, as well as many other companies in the world, is to safeguard the health of its employees and their families, maintain the safety and quality of its products, and minimize the potential disruption of a flu pandemic globally.
On these basis and from the example of the recent NH1H experience, Manuela Kron shows how Nestlé is equipped to provide its employees with the best possible support to face the crisis and to inform them, in good time, of any steps they need to take in the event of a flu pandemic. And the impact and some second level effects when a flu pandemic alarm goes off.

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Massimiano Bucchi (Ph.D. Social and Political Science, European University Institute, 1997) is Professor of Science and Technology in Society at the University of Trento, Italy.

He has published eight books, including Science and the media (London and New York, Routledge, 1998), Science in society. An Introduction to Social Studies of Science (London and New York, Routledge, 2004), Handbook of Public Communication of Science and Technology (with B. Trench, London and New York, Routledge, 2008), Beyond Technocracy. Citizens, Politics, Technoscience (New York, Springer, 2009) and several essays in international journals such as History and Philosophy of the Life Sciences, Nature, New Genetics and Society, Science and Public Understanding of Science.

He chairs the scientific committee of non profit research centre Observa Science in Society and has served as advisor and evaluator for several research and policy bodies, including the US National Science Foundation, the Royal Society, the European Commission and the European Food Safety Auhority.

He has carried out research and given seminars at several international institutions, such as the Royal Society, London School of Economics, University of California Berkeley, Royal Academy of Sciences Sweden, Science University Tokyo, Rikken Institute, American Association for the Advancement of Science and received several recognitions for his work, including the Mullins Prize awarded by the Society for Social Studies of Science (1997) and the Merck-Serono jury award for science books (2007).

He chairs the international committee organizing the 2012 World Conference on Public Communication of Science in Technology in Florence.

THE VISIBLE VIRUS: MEDIA REPRESENTATIONS OF VIRUS AND PANDEMICS

How do media deal with virus and pandemics? Using empirical data from the Science in the Media Monitor, the paper will focus on media dynamics in relation to virus alerts and related issues: e.g. media tendency to emphasize/dramatise these situations, the tendency to present expert advice in polarised, controversial form; finite 'cycles' of media attention that often tend to disregard subsequent, evolution/solution phases.
The question of 'naming' and labelling virus alerts in the media will also be addressed, particularly in relation to the recent case of H1N1 influenza virus.
Finally, the role of media dramatised public 'demonstrations' - e.g. the cases of Ministers or TV News Speakers eating chicken in front of TV cameras to reassure the audience during the 'bird flu' alert – will also be analysed.

Participants of First World Conference on the Future of Science believe it of vital importance that the world community realises we are on the threshold of a new era of knowledge. Science impacts all fields of human life and explosive growth of knowledge in areas such as genetics, astrophysics and information technology will lead to an even greater influence on human activities. Scientific knowledge offers us the possibility not only of improving the conditions of life for all, but also of radically changing the biological makeup of living organisms.

Humanity must be aware of the new freedoms and responsibilities these advances imply. Participants are also aware that this enhanced potential of science generates unanswered questions about its applications, and reasonable doubts about its possible misuse.

The signatories of this Charter believe science will continue to be vital for the progress and well-being of humanity; however the issues raised by scientific progress must be fully and openly debated by the whole of society.

THEY THEREFORE UNDERTAKE TO:

1. Create an alliance for scientific development - involving scientists, philosophers, theologians, politicians, industrialists, jurists, and all interested parties - which will oppose the isolation of science by promoting constructive dialogue between all forms of knowledge that respect human identity and dignity. Maximum priority must be given to harmonising the scientific and religious world views, reconciling ecology movements and science, and inserting scientific issues into political programmes worldwide.
2. Actively reaffirm the humanism of science, its intrinsic spirit of tolerance and incompatibility with absolutism in all its forms. Only if it reasserts these principles can science and other fields of endeavour hope to continue pursuing the fundamental aims of promoting civilisation and protecting human life. While basic research will expand the horizons of knowledge, applied research must be concerned with goals that are essential for the future of humanity, including the eradication of poverty and hunger, reduction of child mortality, conservation of ecosystems and bio-diversity, elimination of pollution, improvement of energy efficiency and reduction of fossil fuel use, reduction of the toll taken by HIV, malaria and cancer, provision of water for agriculture and uncontaminated water for drinking.
3. Promote scientific thought and the scientific method as a way of investigating and understanding the world, particularly among young people and in societies that have not attained an adequate level of material progress. The universal language of science and the rationality of the scientific method are unifying elements having the potential to bridge deep differences in culture, experience and faith, making constructive dialogue possible. The importance of encouraging interest in science in young children has been recognised by UNESCO, with its Declaration and Programme in Science and Technology Education.
4. Set up a permanent Authority for Science consisting of scientists, philosophers, theologians, industrialists, jurists, politicians and others, whose task will be to suggest the objectives and limits of scientific progress and to make rational proposals for the society of tomorrow. The Authority for Science will not be a group of super-technicians deciding in the name of all, but a committed team that systematically and conscientiously examines the problems posed and the opportunities offered by continuing scientific progress, and periodically submits its deliberations and conclusions to governments and public opinion.

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