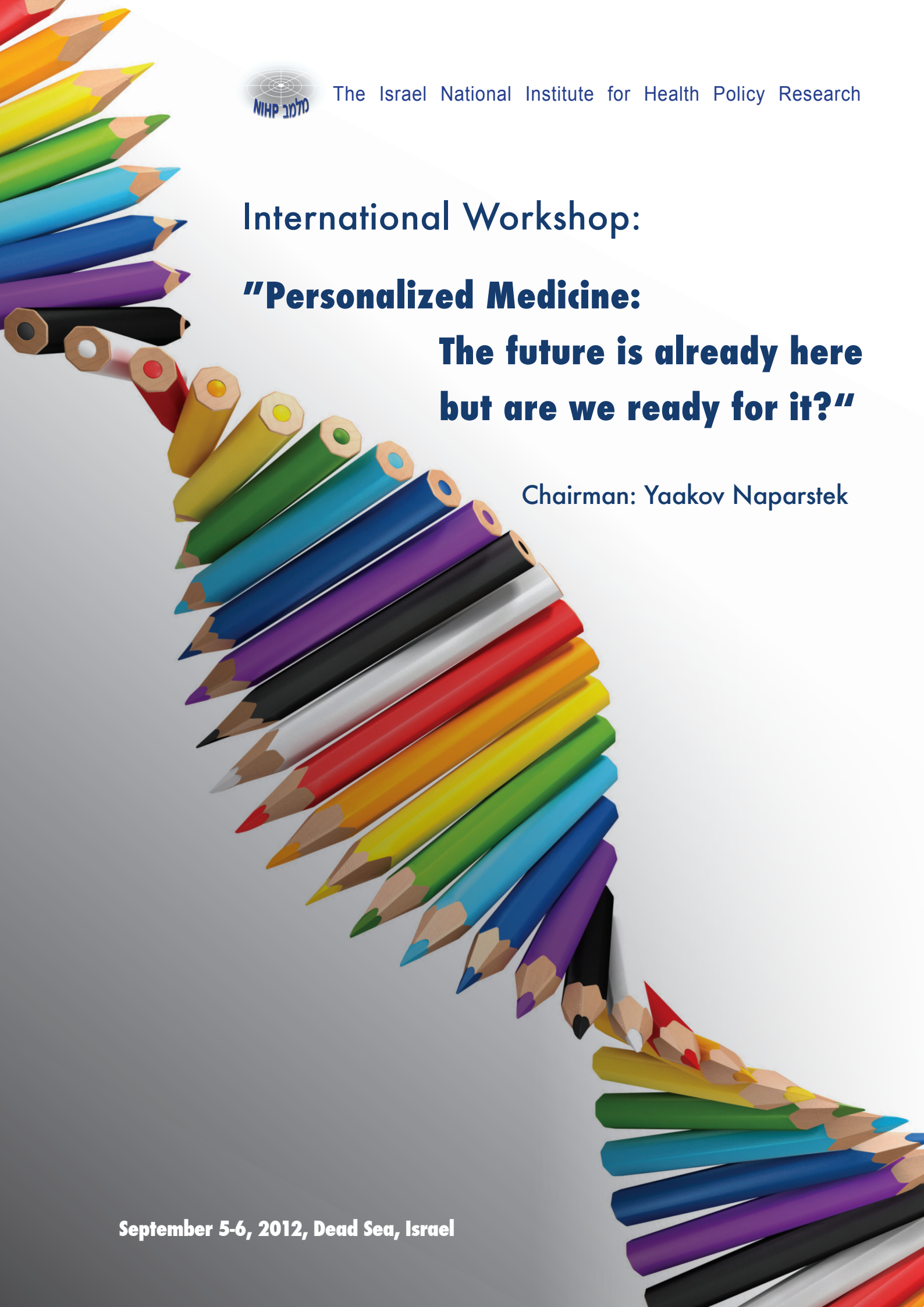
The Israel National Institute for Health Policy Research

International Workshop:

"Personalized Medicine: The future is already here but are we ready for it?"

Chairman: Yaakov Naparstek



September 5-6, 2012, Dead Sea, Israel

המכון הלאומי לחקר שרותי הבריאות ומדיניות הבריאות (ע"ר)
THE ISRAEL NATIONAL INSTITUTE FOR HEALTH POLICY RESEARCH

International Workshop:

Personalized Medicine:

The future is already here but are we ready for it?

September 5-6, 2012

Dead Sea, Israel

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Wednesday, September 5, 2012

09:00 - 10:00 ***Gathering & Morning Coffee***

10:00 - 13:00 **Opening Session – Chairperson: Yaakov Naparstek**
Greetings: Shlomo Mor-Yosef
Roni Gamzu

Yaakov Naparstek - *Why do we need another PM meeting?*
Gad Rennert - *Molecular Medicine - new promises, new problems*

Session A – Assessment of PM Technologies - Personalized Medicine vs. Comparative Effectiveness Research
Chairperson: Gad Rennert
Raju Kucherlapati - *Personalized Medicine in practice*
Eli Pikarsky - *Personalized diagnostics - A paradigm shift in the treatment of cancer patients*
Yossi Caraco - *Personalized Medicine for the non-oncology patient: what should we do to ensure rational implementation?*

Discussion

13:00 - 14:00 ***Lunch***

14:00 - 16:30 **Session B – PM and Health Economy - Is small the new big?**
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Alicia Granados - *Development and future of Personalized Medicine. Some challenges from the industry perspective*
Jacob Glazer - *In a world of Personalized Medicine, how (if at all) can doctors be evaluated?*
Osnat Luxenburg - *Regulatory aspects of Personalized Medicine*

Discussion

16:30 - 17:00 ***Coffee Break***

17:00 - 19:00 **Session C – Bioethical and Legal Aspects of PM - Whose genome is it anyway?**
Chairperson: Avinoam Reches
Ephrat Levy-Lahad - *The other Ps in Personalized Medicine – permission and provision of genomic information,*
Efrat Ram-Tiktin - *Patients and disease stratification – implications on equity and (in)equality*
Shai Lavi - *Personalized Medicine – A legal perspective*

Discussion

20:30 - 22:30 ***Dinner & Entertainment***

Thursday, September 6, 2012

09:00 - 11:00 **Session D – Barriers in Implementing Personalized Medicine**
Chairperson: Eddy Karnieli
Geoffrey Ginsburg - *Barriers to implementing genomics into clinical practice*
Edward Abrahams - *The barriers to Personalized Medicine's development and adoption*
Haim Bitterman - *Personalized Medicine – perspectives of a health care organization*

Discussion

11:00 - 11:30 ***Coffee Break***

11:30 - 13:00 **Session E – Parallel work groups:**
Assessment; Health Economy; Bioethics; Implementation

13:00 - 14:00 ***Lunch***

14:00 - 16:30 **Closing Session –**
Chairperson: Shlomo Mor-Yosef

Presentation of Position Papers
Concluding Remarks:
Roni Gamzu
Yaakov Naparstek

Coffee to Go

Dear Colleagues,

It is my great pleasure to welcome you to our workshop - "Personalized Medicine: The future is already here but are we ready for it?" which is being held under the auspices of The Israel National Institute for Health Policy Research.

One of the major scientific breakthroughs of the 21st Century has been the deciphering of the human genome, leading to a tremendous development in our understanding of the molecular basis of a large number of diseases. The past few years have seen the development of new drugs tailored to the individual patients by use of this genomic information. This has become defined as "Personalized Medicine".

Despite the success of this approach, there are number of issues and obstacles attempting to implement Personalized Medicine within the healthcare system.

- The interpretation of the diagnostic genomic data obtained from patients and even more so from healthy individuals and its effect on clinical therapy is still not clear.
- It appears that the classical clinical trial design, based on the statistical analysis of large populations, ignoring the specific characteristics of sub-groups, should be reevaluated.
- It is not clear whether the introduction of personalized medicine into the health services, will increase or decrease the total expenditure on health and if it increases who should cover it: the patient or the public.
- Personalized medicine will clearly lead to an increased emphasis on "orphan diseases" and the healthcare system will have to cope with a large number of expensive drugs benefitting a small number of patients.
- The easy accessibility to genomic data - by "direct to consumer" genetic testing may benefit the individual towards a proactive health attitude. Alternatively it may lead to unjustified harmful personal and medical decisions.
- The easy accessibility to genomic data also raises concerns regarding the use and misuse of the data by the health system as well as non-health care organizational entities.
- Whatever the answers are, medical schools as well as medical professional societies must be prepared to educate and train physicians how to implement and utilize the personalized medicine model into their daily clinical practice.

It is clear that personalized medicine is here to stay, but if it is to be employed successfully within the healthcare system, these issues must first be addressed.

The success of this workshop will be in its ability to draft a White Paper proposing solutions for the regulatory, economic, ethical and social challenges embedded in personalized medicine, which may then be implemented in the Israeli healthcare system.

I wish us all a fruitful and productive workshop

Yaakov Naparstek, MD
Workshop Chairman

List of Speakers

1. **Dr. Edward Abrahams,** PhD, President, Personalized Medicine Coalition, Washington DC, USA

2. **Prof. Haim Bitterman,** MD, Chief Physician, Clalit Health Services, Israel

3. **Prof. Yossi Caraco,** MD, Head, Clinical Pharmacology Unit. Director, Hadassah Clinical Research Center, Division of Medicine, Hadassah University Hospital Jerusalem, Israel

4. **Prof. Roni Gamzu,** MD, The Director General of the Ministry of Health, Israel

5. **Dr. Geoffrey Ginsburg,** MD, PhD, Director, Genomic Medicine, Duke Institute for Genome Sciences & Policy. Executive Director, Center for Personalized Medicine, Duke University Health System. Professor of Medicine and Pathology Duke University School of Medicine, Durham, USA

6. **Prof. Jacob Glazer,** PhD, The Faculty of Management, Tel Aviv University, Israel and the Department of Economics, Boston University, USA

7. **Dr. Alicia Granados,** MD, PhD, PH, Chair Board of Trustees of Autonomous University of Barcelona, UAB. Head of Global Evidence Definition/ Health Technology Assessment. Global Medical Affairs. Genzyme a Sanofi company, Spain

8. **Prof. Eddy Karnieli,** MD, Director Inst Endocrinology, Diabetes & Metabolism, Rambam medical Center and Director, Galil Center Medical Informatics,Telemedicine and Personalized Medicine Rappaport Faculty of Medicine, Israel

9. **Prof. Raju Kucherlapati,** PhD, Paul C. Cabot Professor of Genetics, Professor of Medicine, Harvard Medical School, Boston, MA, USA

10. **Prof. Shai Lavi,** PhD, Director, Edmond J. Safra Center for Ethics, Faculty of Law, Tel Aviv University, Israel

11. **Prof. Ephrat Levy-Lahad,** MD, Director, Medical Genetics Institute, Shaare Zedek Medical Center, Hebrew University Medical School, Jerusalem, Israel

12. **Dr. Osnat Luxenburg,** MD, MPH, MBA, Director of Medical Technology and Infrastructure Administration, Ministry of Health, Israel

13. **Prof. Shlomo Mor-Yosef,** MD, Chairperson, The Israel National Institute for Health Policy Research; Director General of The National Insurance Institute of Israel, Israel

14. **Prof. Yaakov Naparstek,** MD, Professor & Chairman, Department of Medicine, Hadassah University Hospital, Jerusalem, Israel

15. **Prof. Eli Pikarsky,** MD, PhD, Department of Pathology and the Lautenberg Center for Immunology and Cancer Research, The Hebrew University-Hadassah Medical School, Israel

16. **Dr. Efrat Ram-Tiktin,** PhD, Department of Philosophy, Bar Ilan University, Israel

17. **Prof. Avinoam Reches,** MD, Department of Neurology at Hadassah Hospital, The Hebrew University in Jerusalem, Israel

18. **Prof. Gad Rennert,** MD, PhD, Director, Clalit National Cancer Control Center and Personalized Medicine Program, Israel

19. **Prof. Joshua Shemer,** MD, Full Professor, Internal Medicine, Sackler Faculty of Medicine, Tel Aviv University; Chairman, Assuta Medical Centers in Israel; Director, Israeli Center for Health Technology Assessment in Health Care (ICTAHC), The Gertner Institute for Epidemiology and Health Policy Research, Tel Hashomer, Israel

20. **Dr. Mark Trusheim,** Visiting Scientist and Executive-in-Residence, MIT Sloan School of Management, USA

Abstracts

The Barriers to Personalized Medicine's Development and Adoption

Dr. Edward Abrahams

As we wrote in *The Case for Personalized Medicine*, “The long arc of medical history has been one in which diagnostic capability has evolved from the metaphysical, to the anatomical, to the cellular, and ultimately to the molecular level. Now that diseases can be sub-classified using evidence well beyond what is visibly obvious into categories that presage the course of disease and its likely response to treatment, there is an obligation to act on that information.” But the transition to personalized medicine requires overcoming numerous hurdles after the complexities of the science of human biology have been determined.

After defining personalized medicine and explaining how it can and will improve patient care as well as the health systems that incorporate it, I will discuss how misaligned regulations, guidelines, investment incentives, and perceptions must be changed to accelerate the development and adoption of new personalized medicine.

Personalized medicine – perspectives of a health care organization

Prof. Haim Bitterman

"Clalit" is one of the four health care organizations that, together, provide medical coverage to 100% of the country's population. Clalit is the largest organization (53% market share), and it operates all aspects of modern medical care via its more than 1,400 primary, secondary, and tertiary community clinics and 14 hospitals. Clalit was one of the first organizations that adopted new technologies in cancer risk stratification (e.g. testing for BRCA), and selection of cancer therapies. The surge of technological advancement in the field of personalized medicine promoted Clalit's long-term plan that was authorized in 2007 and was based on establishing a central diagnostic center for consolidation of the organizational theoretical and practical approaches, for performance of most available tests, for continued updating of methods, and for quality control and assurance, as well as for containment of costs and professional gate keeping. Alongside this centralized endeavor Clalit adopted and purchased other cutting edge, mostly patented, technologies from third parties thus presenting to its customers a wide spectrum of testing for disease prevention, determination of prognosis and selection of therapies, usually earlier than other leading medical organizations in the world. The advantages and disadvantages of centralized and de-centralized approaches in this field are currently under debate in Israel. All approaches should take into consideration the "rapidly moving target" nature of the field that requires extremely fast adoption of new technologies, availability of appropriate professionals alongside availability and capacities in evaluation of local phenotypic data for determination of organizational policies, as well as a dire need to contain costs and ensure quality. It seems that careful adoption of next generation sequencing, alongside continued collaboration for availability of other technologies as well as careful dynamic decentralization of some of the tests (based on volumes, quality assurance, price, and need) will provide the best updated service of a clinically relevant spectrum of personalized technologies to Clalit's customers.

Personalized medicine for the non-oncology patient: what should we do to ensure rational implementation?

Prof. Yossi Caraco

The response to many drugs in common use is characterized by a marked interindividual variability. Traditionally a major fraction of this variability has been ascribed to host factors such as age, weight, gender or the presence of liver and renal disease. Environmental influences like smoking and the interaction with other drugs were thought to be important determinants as well. With the advance made in molecular pharmacology it became apparent that genetic factors may also play a major role accounting according to some estimate for about 50% of this variability. In the ideal world the preemptive ability to predict patient's response to a given drug or class of drugs could potentially serve to enhance the efficacy and safety of drug therapy. Intense effort has been invested in the last two decades in an attempt to translate this information into clinical practice. Initial research focused on the development and validation of phenotypic measurements of polymorphic enzymes with bimodal distribution such as NAT2, CYP2D6 and CYP2C19. The theoretical advantage of these procedures was their ability to forecast the individual's enzyme activity which reflects the impact of all factors, genetic and non-genetic alike. Nevertheless the necessity to administer an exogenous compound on one hand and the rapid development of genetic methods has diverted the attention to genotyping. In the following years genetic markers that could explain at least some of the variability in the activity of drug metabolism enzymes were identified. The next stage was to apply similar methodology in order to detect genetic polymorphisms in drug's targets (i.e. receptors, VKORC1) and transporters. Despite this enormous amount of information the implementation into clinical medicine in the non-oncology patient was limited. During my presentation I will review the experience that has been gained in utilizing such data to optimize patient care and try to define the obstacles as well as the approach to ensure future implementation.

Barriers to Implementing Genomics into Clinical Practice

Dr. Geoffrey S Ginsburg

Although the potential for genomics to contribute to clinical care has long been anticipated, the pace of incorporating genomic findings into medical practice has been relatively slow.

In the United States and elsewhere, several institutions have begun “genomic medicine” programs, encountering many of the same obstacles and developing the same solutions, often independently.

Recently, NIH’s National Human Genome Research Institute brought together a number of these ‘genomic medicine early adopter’ groups to describe their ongoing projects and challenges, identify common infrastructure and research needs, and outline an implementation framework for introducing similar programs elsewhere.

Ongoing exemplar projects include screening for highly penetrant germline mutations (such as Lynch syndrome or hypertrophic cardiomyopathy) to identify genetically at-risk individuals; using web-based computerized tools to integrate patient-reported family history information into the electronic medical record (EMR) and provide appropriate clinical decision support (CDS); assaying pharmacogenetically important variants and integrating results into a decision support-enabled EMR for medication selection and dosing; and conducting genomic sequencing to solve diagnostic dilemmas and/or identify potential avenues for treatment.

Much of this work, supported largely by institutional rather than NIH funds, is being done in relative isolation and would benefit from more structured collaboration and sharing of approaches.

Chief among the challenges were lack of appreciation by clinicians, institutions, and payers of the potential for genomics to improve patient care; limited evidence and consensus on which genomic variants were medically relevant; and burden to patients and clinicians of assaying, reporting, intervening, and following up genomic findings.

Key infrastructure needs included an openly accessible knowledge base capturing sequence variants and their phenotypic associations and a framework for defining and cataloguing clinically actionable variants. Much of this work is being done in isolation and would benefit from more structured collaboration, nationally and internationally, and sharing of best practices.

In a World of Personalized Medicine, How (if at all) Can We Evaluate Doctors?

Prof. Jacob Glazer

An optimal reimbursement scheme is one that incentivizes the doctor to provide the most efficient (i.e., cost-beneficial) treatment to every patient. However, in a world of personalized medicine, the most efficient treatment will generally depend on many patient-specific factors that are observed only when the doctor begins diagnosing and treating the patient.

The efficient treatment will depend, for example, on the patient's medical history, on his comorbidities, on the other medications he is taking and the treatments he is receiving, on his mental and cognitive state, on his compliance history, on the support he receives at home, on his employment situation and the kind of job he does and so on.

In such a world, compensating the doctor for providing efficient care (and penalizing her if the care she provides is inefficient) becomes an extremely difficult task, as it requires the payer to evaluate and reimburse the doctor on the basis of very partial information that misses some of the most relevant data.

In this lecture we will discuss the difficulties of constructing an optimal incentive scheme in such a situation and the possible ways to address this problem.

Development and future of personalized medicine. Some challenges for health systems. Industry perspective.

Dr. Alicia Granados

During the past and current centuries, health care has experienced an explosion of innovations which have produced unprecedented contribution to human health.

However, successful major changes in health systems have been produced when the revolutionary findings from research and innovations were matched with the needed evolutionary actions in the processes of care.

Stratified Medicine/ Personalize Medicine is a medical model that proposes the customization of healthcare, with all decisions and practices being tailored to the individual patient by use of genetic or other information. Personalized medicine is about making the treatment as individualized as the disease. It involves identifying genetic, genomic, and clinical information that allows accurate predictions to be made about a person's susceptibility of developing disease, the course of disease, and its response to treatment.

Stratified Medicine/ Personalize Medicine is one of the current potential drivers of health systems evolution and is playing a growing role in biopharmaceutical development pipelines.

Nevertheless, the current adverse financial climate is becoming a source conflict. Departments of Finances are implementing unprecedented health care cost-saving measures while Departments of Health are wondering “how are we going to pay for all of the new when we have difficulties to sustain the current standard of care?”

A policy deliberation on alternatives to overcome the situation will be presented by outlining the role of Health Technology Assessment (HTA) best practices to inform decision making in health system to keep it sustainable and stressing the importance that appropriate HTA methodology is applied to answer the right research and fair policy questions.

Personalized Medicine in Practice

Prof. Raju Kucherlapati

The draft sequence of the human genome was published in 2001. At that time it was estimated that the public and private efforts spent more than 2 billion dollars to complete the draft sequence. Shortly after ten years of this remarkable achievement the cost of sequencing individual human genomes is approaching $10,000 and our understanding of the human genome has increased very significantly.

The use of genetic/genomic information for assessing risk, accurate diagnosis of certain diseases, determining the prognosis and finding the most appropriate drugs or treatment for many human diseases is called personalized medicine. Partial or whole genome sequencing is finding its place for many indications in health and disease.

Recent developments are promising to find non-invasive methods for obtaining fetal cells from maternal circulation opening the doors for safer prenatal diagnosis. Many childhood disorders with unknown etiology are becoming more amenable to accurate diagnosis that drives the management of the young patients.

In adult medicine, personalized medicine is finding considerable traction. Sequencing of tumor tissue is revealing many tumor specific genetic/genomic changes in that individual.

It is now possible to tailor treatment of these individuals with targeted therapies based on the specific vulnerabilities of the tumor.

All of these approaches are changing the health outcomes for many patients.

Applications of the principles of personalized medicine may also help in changing the rate of increase of the ever higher costs of healthcare.

Personalized Medicine: A Legal Perspective

Prof. Shai Lavi

Law and regulation are often seen as an obstacle to the advancement of scientific and medical progress. New technologies give rise to new public anxieties and often, so the argument goes, lead to over-regulation.

The lecture will discuss the legal challenges that have been associated with the development of PM.

Many of the issues are not unique to PM, but acquire a new urgency as PM develops. A partial list of the legal questions PM raises includes privacy and the protection of genetic information, gene based stratification during clinical trials, discrimination based on the use of PM results against patients, protecting innovation through patent law, regulating genetic testing and the interpretation of genetic information with the spread of direct to consumer genetic testing, and finally tort liability and no-fault insurance regimes.

Special attention will be given to what has been dubbed in recent years “soft law”, namely, voluntary unenforceable self-regulation of industry as an alternative approach to state-imposed “hard law”.

The other P's in Personalized Medicine – Permission and Provision of Genomic Information

Prof. Ephrat Levy-Lahad

Obtaining genomic information is the cornerstone of Personalized Medicine, and poses ethical challenges of both substance and scale. Because genomic testing is novel and utilizes evolving and often experimental technologies, the line between research and clinical genomic testing can become blurred, and it is crucial that care providers and researchers clearly differentiate between the two as much as possible. In the context of this workshop, discussion will focus on ethical aspects of *clinical* application. Within the process of genomic testing, permission, or consent (as a starting point) and provision of the resulting information (as an endpoint), are both critical steps.

Much of the *substance* of consent issues confronting genomic testing is no different from that of "traditional" genetic testing of a single or a few genes: e.g. consent for presymptomatic / predictive genetic testing of both treatable and untreatable conditions, familial implications of personal genetic information, potential discrimination by insurers or employers. The advent of Personalized Medicine has simply brought these issues to the general medical arena. However, the *scale* of genomic testing poses new questions – Can "large scale" consent be truly informed? Is general consent ethical or should consent be limited to a particular clinical question? Should testing be confined to what is interpretable? Should there be a distinction between consent to genomic testing of the person (i.e. germline DNA) vs. genomic testing of the disease (e.g. genomic testing of tumors)?

Ethical provision of genomic information can similarly be partly informed by lessons learned from provision of genetic information, e.g. provision of probabilistic results. However, a major challenge is keep evidence-based utility assessment abreast with rapidly amassed genomic information, so that Personalized Medicine will indeed be clinically useful to the Person.

Regulatory Aspects of Personalized Medicine

Dr. Osnat Luxenburg

Personalized medicine has been defined as the tailoring of medical treatments to the individual characteristics of each patient, and the ability to classify individuals into subpopulations based on their susceptibility to a particular disease or their responses to a specific treatment.

Personalized medicine (PM) is a complex issue that has broad implications and requires careful considerations of legal, ethical, social, economic as well as health issues.

While the advantages of PM medicine are obvious – on the one hand optimizing treatment while on the other minimizing exposure to unnecessary medications and adverse effects - tailored and personalized medicine requires regulatory authorities to evolve and create a mechanism and specialized infrastructure that address these issues within the existing regulatory system.

Moreover, the adoption and implementation of PM need to overcome economic barriers resulting from the rising cost of healthcare, especially that of medical technologies, which can limit access to medical treatment.

The transformation of the way we understand and practice medicine also necessitates coordination and collaboration among biomedical companies, medical research institutions, health care professionals and regulatory agencies.

This era of fast emerging and innovative medical technologies challenges regulatory authorities around the world. New approaches are needed to implement regulation that encompasses assessment of safety, efficacy and quality of biomedical technologies, clinical trial strategies as well as technology assessment tools, health insurance coverage and reimbursement policies.

The presentation will focus on the challenges facing the Israeli Ministry of Health, using relevant examples of approved pharmaceuticals and diagnostics in clinical practice, discuss approaches taken by other regulatory authorities, and will outline the needed steps to achieve the regulatory structure to support personalized medicine growth.

Personalized Diagnostics - a Paradigm Shift in the Treatment of Cancer Patients

Prof. Eli Pikarsky

The promise of personalized cancer treatment has been around for many years, but has yet to be implemented in routine clinical practice. The concept is to make use of the vast amount of information that can now be gained on a specific tumor, from its genomic, transcriptomic, and proteomic profiles to tailor a custom treatment plan. Molecular profiling approaches, including high-throughput sequencing, microarray analysis, array comparative genomic hybridization, and mass spectrometry, provide an enormous amount of information on the germline, the tumor tissue, and the complex traits of tumor metastases. There is now evidence showing that taking such data into account can have immediate implications for treatment which hopefully will dramatically improve patient care. Unlike most previous breakthroughs in clinical oncology, the current wave of change aims at the diagnostic stage, perhaps the least costly part of cancer patient management.

After the initial period of optimism for an imminent revolution in medical practice whereby the molecular “fingerprint” for each cancer patient would replace the clinicopathologic parameters, it has now become clear that the transition from the research bench to bedside is more challenging than was previously expected. The challenges we are facing are many and include choosing the most appropriate methodologies, data generation, data analysis, quality measures, clinical interpretation, tumor heterogeneity and complex ethical issues. Furthermore, the lack of evidence based studies for each person requires an alternative approach, based on professional skills of a multidisciplinary team including experts in oncology, pathology, molecular cancer biology, and bioinformatics.

Pharmacogenetics - Patient and Disease Stratification: Implications for Equity and (In)Equality

Dr. Efrat Ram-Tiktin

As research in the field of pharmacogenetics advances, we will witness the stratification of disease categories and patient populations. The stratification of diseases will create sub-categories of illness according to genetic criteria and enable improved diagnosis. Patient stratification will lead to the categorization of patients according to their genetic markers, correlating to either a beneficial response toward medication or the risk of an adverse reaction. The potential benefit of patient stratification is that it would aid physicians in prescribing the most suitable medication to their patients. However, because populations vary in their genetic makeup, this could lead to the creation of two kinds of orphan population.

1) Those who are “bad responders” to medications and for whom we cannot develop effective medications with the existing medical knowledge and technology (*orphan population type I*).

2) Those who have a rare genetic profile that makes them economically unattractive for pharmaceutical companies (*orphan population type II*).

Focusing on the relationship between justice and different principles of equality (formal and substantive principles), I will show that although this new technology could lead, in a certain sense, to an unequal distribution of health care, it is not necessarily unjust. According to Aristotle’s principle of proportionality, I will show that the application of unequal treatment to different patient groups (in a morally relevant sense) should not be regarded as an unjust distribution. In addition, I will claim that in designing a just distribution scheme, we act rationally and reasonably if we take consideration of efficacy into account.

Molecular Medicine - new promises, new problems

Prof. Gad Rennert

Personalized Medicine is the common (if not the most proper) term used to describe a new approach in medicine which relies on individual molecular/biological characteristics to make clinical decisions that are unique to each person. This field has developed tremendously in recent years following major technological advances in genetic analysis that have enabled deeper understanding of the molecular basis of causes and natural history of diseases and the development of many biologically targeted drugs.

Molecular information can serve to predict risk of disease (commonly done in the past only for rare syndromes, but now available for ever more common, multifactorial, diseases), to predict response to specific medications as well as the probability of side effects and to predict prognosis.

The biggest challenge of the health system is to extend high quality life expectancy. To respond to this challenge, our aim should be to prevent many diseases from occurring and to offer optimal treatment (effective and free of side effects) to existing diseases. This challenge, now supported by the modern approach of personalized medicine, will contribute not only to better health but also to economic efficiency.

Moving to individualization of medical care in a growing number of health and disease states requires proper organization of the health system at many levels, starting with education of the medical teams, most of whom are uneducated in the field of molecular medicine; investment in developing proper infrastructure which will enable equity in individual accessibility to the advanced technologies and knowledge; developing quality control programs and indicators to assure proper use of technologies and progress to an ever growing number of newer technologies, all while controlling the national expenditure on health.

The potential paradigm shift from the guidelines approach in which one size fits many to a much more delicate individual selection of intervention is very demanding, both for the providers as well as for the consumers (population). Socially this approach raises many issues, such as the legal definitions of “state of the art” in an era of moving targets and the loss of classical evidence based acquisition rules, ethical issues that stem from multiple genetic testing of individuals and populations which provides excess and sometimes unwanted information, and other educational challenges.

Personalized Medicine and Health Economy – Is small the new big?

Prof. Joshua Shemer

"There is going to be lots of economic incentive to do personalized medicine. When half of the drugs that people take don't work, there's a stake that the payer community has in getting it right the first time and not doing it by trial and error." Richard Hamermesh, Harvard Business School.

Personalized medicine (PM), incorporates the progress of genome-based knowledge into clinical practice and offers tremendous benefit opportunities for patients and our health care systems. PM can be defined as the tailoring of preventive, diagnostic, or therapeutic interventions to the genetic and molecular characteristics of an individual or population. This may involve genetic or laboratory biomarker information.

A 75% increase in PM investment by industry over the last 5 years deepened the attention towards personalized medicine interventions. This increased focus may create new challenges for those evaluating the impact of introducing personalized medicine interventions into clinical practice and the healthcare system. Currently, there are no clear guidelines for both industry and reimbursement regulators when creating coverage and payment for personalized medicine technologies.

Social, ethical, and regulatory issues need to be discussed and decisions should be taken to redesign the healthcare system in relation to personalized medicine. Obviously, this necessitates the adoption of changes in regulations and health policy, in order to achieve fair and equitable access to new promising personalized health technologies.

Many unanswered questions have been raised in the last decade regarding PM. A major issue concerns the shift from the one-size-fits-all concept, which is being replaced by targeted stratified medicine. In this document we shall address the impact of personalized medicine on the total national health expenditure including the public/private mix, future cost-containment measures, acceptable cost/QALY thresholds, clinical trials and regulatory and reimbursement mechanisms.

The Economic Challenges and Incentives Facing Stratified Medicine

Dr. Mark Trusheim

By actively exploiting variable patient responses to therapeutics by using companion diagnostics to target those most likely to benefit, stratified medicines are profoundly affecting decades old clinical development strategies, partnering business models, regulatory paradigms, clinical practices and innovator profitability. Examining all these key areas simultaneously, drawing on recently published quantitative analyses by a public/private consortium, a framework emerges that suggests stakeholder policy decisions in the next few years, not science alone, will create conditions for either continued Pharmaggedon or for a renewed virtuous cycle of clinical advances that benefit patients, payers and innovators.

Biographies:

Speakers & Chairpersons

Dr. Edward Abrahams, PhD

President of the Personalized Medicine Coalition (PMC), USA.

Representing scientists, patients, providers and payers, PMC promotes the understanding and adoption of personalized medicine concepts, services and products for the benefit of patients and the health system.

It has grown from its original 18 founding members in 2004 to over 200 today.

Previously Dr. Abrahams was Executive Director of the Pennsylvania Biotechnology Association, where he spearheaded the successful effort that led to the Commonwealth of Pennsylvania's investment of $200 million to commercialize biotechnology in the state. Earlier he had been Assistant Vice President for Federal Relations at the University of Pennsylvania and Director of Government Relations at Brown University.

Dr. Abrahams worked for seven years for the U.S. Congress, including as a legislative assistant to Senator Lloyd Bentsen, an economist for the Joint Economic Committee under the chairmanship of Representative Lee Hamilton, and as a AAAS Congressional Fellow for the House Committee on the Interior.

The author of numerous essays, Dr. Abrahams has also taught history and public policy at Brown University and the University of Pennsylvania.

Prof. Haim Bitterman, MD

Chief Physician, Clalit Health Services.

Professor of Medicine. The Ruth and Bruce Rappaport Faculty of Medicine, Technion – Israel Institute of Technology, Haifa, Israel.

Education and training:

2001: Visiting Professorship. Department of Cardiovascular Medicine. Stanford University, Palo Alto, CA, USA.

1985-1987: Research fellowship in Cardiovascular Physiology. Department of Physiology, Thomas Jefferson Medical College. Philadelphia, USA.1972: M.D. Hadassah and Hebrew University Medical School, Jerusalem.

1977-1982: Residency in Internal Medicine, Carmel Medical Center. Haifa, Israel.

1973: Internship: Soroka Medical Center.

Appointments:

2009-: Clalit Health Services, Israel – Chief Physician.

2005-2010: President of the Israel Association of Internal Medicine.

2003-2009: Chairman of Medicine, Carmel Medical Center, Haifa.

2000-2012: European Federation of Internal Medicine (EFIM) – member of the administrative council.

2009: Professor of Medicine. Faculty of Medicine, Technion, Haifa.

1999-2004: Vice Dean, Faculty of Medicine, Technion, Haifa.

1997: Associate Professor of Medicine. Faculty of Medicine, Technion, Haifa:

1990: Senior Lecturer of Medicine. Faculty of Medicine, Technion, Haifa.

1989: Director, Department of Internal Medicine, Carmel Medical Center, Haifa.

Prof. Yossi Caraco, MD

Head, Clinical Pharmacology Unit. Director, Hadassah Clinical Research Center, Division of Medicine, Hadassah University Hospital Jerusalem, Israel.

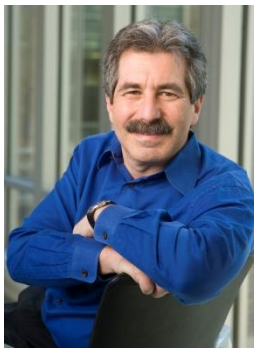
Graduated from The Hadassah Medical School of the Hebrew University in 1983.
Internship at the Hadassah University Hospital 1984-1985.
Internal Medicine Residency, Medicine B (Head, Prof. Yehezkel Stein) 1985-1989.
Board certified in Internal Medicine 1989.
Merck International Fellow in Clinical Pharmacology at Vanderbilt University School of Medicine, Nashville, TN (Mentor, Alastair J. Wood) 1991-1993.
Board certified in Clinical Pharmacology 1996.
Establishment of the Pharmacogenetic laboratory 1997.
Professor of Medicine and Clinical Pharmacology 2000.
Head of Department of Medicine C, 1999-2000.
Chairmen, the Israeli Society for Clinical Pharmacology, 2001-2005.
Appointed as the Head of The Clinical Pharmacology Unit, Division of Medicine, Hadassah University Hospital 2002.
Head of the Hadassah Hospitals Drug's Formulary Committee since 2004.
Establishment of The Hadassah Clinical Research Center 2008.
Establishment of the Drug Information Center for Elderly Patients 2008.
Main research area – Understanding genetic variability in response to drugs:
The pharmacogenetic of warfarin, from understanding to implementation.
The pharmacogenetic of adrenergic receptors.
The pharmacogenetics of immunosuppressant.
Recipient of the Binational Scientific Foundation grants in collaboration with Prof. Alastair J. Wood, Vanderbilt University School of Medicine 1998, 2004.
Recipient of the Israeli Science Foundation grant 2004.
Author of more than 75 publications in peered reviewed journals.

Prof. Roni Gamzu, MD, PhD, LLB, MBA

Prof. Gamzu has taken office as Director General of the Ministry of Health, Israel, since 2010, Israel.

From 2002 up to the end of 2007, Prof. Gamzu served as Associate Director General for health economics in the Tel-Aviv Medical Center, and from 2008 as the director-general of Ichilov Hospital of the Tel Aviv Sourasky Medical Center.

Prof. Gamzu, studied medicine at Ben-Gurion University of the Negev and at Tel Aviv University's Sackler Medical Faculty and also has a bachelor's degree in law, a master's degree in business administration and a doctorate in medical research. He holds diplomas in both gynecology and medical administration.



Dr. Geoffrey S Ginsburg, MD, PhD

Director, Genomic Medicine Duke Institute for Genome Sciences &Policy, Executive Director, Center for Personalized Medicine Duke Medicine, Professor of Medicine and Pathology Duke University Medical Center, USA.

Dr. Ginsburg is the founding director for Genomic Medicine at Duke and assumed his current position in the Duke Institute for Genome Sciences & Policy in 2004. He is also the founding executive director of the Center for Personalized Medicine established in the Duke University Health System in 2010.

While at Duke, Dr. Ginsburg has pioneered translational genomics, initiating programs in genome enabled biomarker discovery, longitudinal registries with linked molecular and clinical data, biomarker-informed clinical trials, and the development of novel practice models and implementation research for the integration of genomic tools in health care systems. With a strong commitment to interdisciplinary science he has led projects to develop predictive models for common complex diseases using high dimensional genomic data as well as collaborations with engineering groups to develop novel point of care sensors. His work spans oncology, infectious diseases, cardiovascular disease and metabolic disorders, and his research is addressing the challenges for translating genomic information into medical practice using new and innovative paradigms, and the integration of personalized medicine into health care. He is an internationally recognized expert in genomics and personalized medicine with over 200 published papers, and funding from NIH, DOD, Air Force, DARPA, the Gates Foundation, and industry.

In 1990, he joined the faculty of Harvard Medical School, where he was director of Preventive Cardiology at Beth Israel Hospital and led a laboratory in applied genetics of cardiovascular disease at Children’s Hospital. In 1997 he joined Millennium Pharmaceuticals Inc, as senior program director for cardiovascular diseases and was eventually appointed vice president of Molecular and Personalized Medicine, where he was responsible for developing pharmacogenomic strategies for therapeutics, as well as biomarkers for disease and their implementation in the drug development process.

He has received a number of awards for his research accomplishments, including the Innovator in Medicine Award from Millennium in 2004 and the Basic Research

Achievement Award in Cardiovascular Medicine from Duke in 2005. He is a founding member and former board member of the Personalized Medicine Coalition, a senior consulting editor for *The Journal of the American College of Cardiology, an editor for The HUGO Journal* and an editorial advisor for *Science Translational Medicine*. In addition he is the editor of *Genomic and Personalized Medicine* (Elsevier) whose first edition was published in 2009.

He has been a member of the Secretary of Veterans Affairs Advisory Council on Genomic Medicine and the National Advisory Council for Human Genome Research at NIH. He is currently an international expert panel member for Genome Canada, a member of the Board of External Experts for the National Heart, Lung and Blood Institute, the Institute of Medicine's Roundtable on Genome-Based Research to Human Health, and a member of the External Scientific Panel for the Pharmacogenomics Research Network. He has recently been appointed to the Advisory Council for the National Center for Advancing Translational Sciences at NIH and is the Vice Chair for the Cures Acceleration Network Board. He is also a member of the World Economics Forum's Global Agenda Council on Personalized and Precision Medicine.

He received his MD and PhD in biophysics from Boston University and completed an internal medicine residency at Beth Israel Hospital in Boston, MA. Subsequently, he pursued postdoctoral training in clinical cardiovascular medicine at Beth Israel Hospital and in molecular biology at Children's Hospital as a Bugher Foundation Fellow of the American Heart Association.

Prof. Jacob (Kobi) Glazer, PhD

Jacob Glazer received his Ph.D in Economics from the Kellogg School of Management at Northwestern University, in 1986.

He is currently a professor of economics at the Faculty of Management, Tel Aviv University, Israel and the Department of Economics, Boston University, USA. He is the Chair of the Master of Health Administration (MHA) program and the Academic Director of the Executive MBA programs at Tel Aviv University. In addition, he serves as the Head of the Kovens Institute for Health Systems' Management and is the incumbent of the Issachar Haimovich Chair for Strategic Management at Tel Aviv University.

Glazer's main areas of research are health economics, industrial organization and game theory. He has served as a consultant to many research projects funded, among others, by the NIH, NIA and the VA, in the US and to various organizations in Israel such as the Israeli Medical Association, the Israeli Ministry of Health and the Maccabi Healthcare Services.

He is currently an Associate Editor of the Journal of Health Economics.

Dr. Alicia Granados MD, PhD, PH

Dr. Alicia Granados serves as Senior Director of Global Evidence Definition/Health Technology Assessment (HTA). Global Medical Affaires at Genzyme a Sanofi Company, since January 2011, Spain.

Dr. Granados is a certified specialist in respiratory diseases. Who started her career in the medical profession in Hospital of Bellvitge, a teaching hospital in Barcelona (Spain) and later as associate professor of Medicine and Evidence Based Medicine at University of Barcelona. She was the European leader of Ulysses International HTA Master Program until 2007.

Dr. Granados has over 25 years of experience in HTA strategy development, assessment methods, practices and implementation. Her experience in the field started back in 1986 in relation to her clinical and research background and as advisor to the Catalan Department of Health (Government of Catalonia) in HTA and management. Later, in 1991, she was responsible for the creation and direction of Catalan Agency for Health Technology Assessment and Research (CAHTAR). Founder member of INAHTA, the first international HTA network. She was involved in several HTA European projects, such as EURASSESS, while being the General Director and CEO of CAHTAR until December 1999.

Former President of the international Society for Technology Assessment in Health Care (ISTAHC) and Chair of the Committee for the Creation of a New HTA Society: HTAi.

Dr. Granados has been Catalan Institute of Health' President and CEO, temporary advisor of several UN agencies on Evidence Based Health Care and Acting Regional Advisor of WHO European Office, leader of the Health Evidence Network.

She has more than 60 scientific articles published.

Member of several editorial boards in the field of evaluative research.

Currently Dr. Granados is also President of Autonomous University of Barcelona' Board of Trustees and member of the Advisory Council on Economic Affairs of Catalan Autonomous Government.

Prof. Eddy Karnieli, MD

Professor of Medicine, Director Institute of Endocrinology, Diabetes & Metabolism, Rambam medical Center and Director, Galil Center Medical Informatics, Telemedicine and Personalized Medicine, Rappaport Faculty of Medicine, Technion- Israel Institute of Technology, Israel.

2009: Professor of Medicine, Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel.

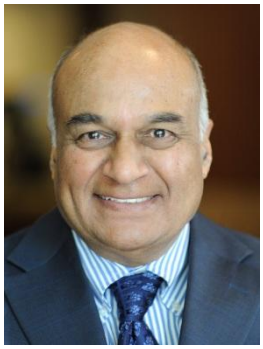
1992 - present: Director, Institute of Endocrinology, Diabetes & Metabolism, Rambam Medical Center and Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel.

2006 - present: Director, Galil Center for Tele-medicine, medical informatics and personalized medicine, Faculty of Medicine, Technion - Israel Institute of Technology, Haifa, Israel.

1991-1995: Acting Deputy - Director, Rambam Medical Center, Haifa, Israel.

1989-1991: Colonel, Commander of Northern Region Medical Corps, Israel Defense Forces.

1975: M.D. degree conferred by Technion - Israel Institute of Technology, Haifa, Israel.



Prof. Raju Kucherlapati, PhD

Dr. Raju Kucherlapati, Ph.D. is the Paul C.Cabot Professor in the Harvard Medical School Department of Genetics.

He is also a professor in the Department of Medicine at Brigham and Women's Hospital, USA.

Dr. Kucherlapati was the first Scientific Director of the Harvard Medical School-Partners Healthcare Center for Genetics and Genomics. His current research focuses on cancer genetics and genomics.

During 1989-2001, Dr. Kucherlapati was the Lola and Saul Kramer Professor of Molecular Genetics and Chairman of the Department of Molecular Genetics at the Albert Einstein College of Medicine in New York.

He was previously a professor in the Department of Genetics at the University of Illinois, College of Medicine.

He began his research as an assistant professor in the Department of Biochemical Sciences at Princeton University.

He has chaired numerous NIH committees and served on the National Advisory Council for Human Genome Research and the NCI Mouse Models for Human Cancer Consortium.

He is also a member of the Cancer Genome Atlas project of the National Institutes of Health.

He is a member of the Institute of Medicine of the National academy of sciences and a fellow of the American Association for the Advancement of Science.

He is a member of Presidential Commission for the Study of Bioethical Issues.

Dr. Kucherlapati received his B.S. and M.S. in Biology from universities in India, and he received his Ph.D. from the University of Illinois at Urbana, as well as conducting post-doctoral work at Yale University.

Prof. Shai Lavi, PhD

Shai Lavi is a Professor of Law, and the director of the newly founded Edmond J. Safra Center for Ethics and the co-director of the Minerva Center for the Interdisciplinary Study of End of Life both at Tel Aviv University, Israel.

He is an expert in sociology of law and the sociology of ethics, and has written among other topics on death and dying, reproductive technologies and animal rights.
In 2006, he was appointed as member of the National Helsinki Committee (IRB) for Medical Research.
Prof. Lavi received his PhD from the Jurisprudence and Social Policy Program at UC Berkeley (2001). His first book, "The Modern Art of Dying: A History of Euthanasia in the United States" (Princeton University Press, 2005) won the Book of the Year Prize from the American Sociology Association.
He received Fulbright Fellowship, Humboldt Fellowship and Townsend Fellowship. He is also the recipient of the Zeltner Prize awarded to an outstanding junior faculty in Law. He won prestigious grants, including most recently, a grant from the Max Planck Institute to cofound the Minerva Center for the Interdisciplinary Study of End of Life.

Prof. Ephrat Levy-Lahad, MD

Director of the Medical Genetics Insistute at Shaare Zedek Hospital in Jerusalem, and Associate Professor of Internal Medicine and Medical Genetics at the Hebrew University-Hadassah Medical School, Israel.

She received her MD degree from Hebrew University-Hadassah Medical School (1989; Jerusalem, Israel), and trained in Internal Medicine at Shaare Zedek Medical Center and in Medical Genetics at the University of Washington in Seattle. She is board certified in Internal Medicine (Israel) and in Clinical and Clinical Molecular Genetics (USA and Israel).

Dr. Levy-Lahad's clinical laboratory includes a large preimplantation diagnosis service, and cancer genetics diagnostics. Her research laboratory focuses on genetics of breast cancer, in particular the BRCA1 and BRCA2 genes, and on genetic and environmental factors that affect the risk associated with these mutations. During her fellowship Levy-Lahad discovered a gene for Alzheimer's disease gene (presenilin-2) and her laboratory is also involved in elucidating the genetic basis of rare diseases, including recent discoveries of novel genes for a rare congenital neurological disease in Ashkenazi Jews, and for defects in ovarian development.

Dr. Levy-Lahad is also active in bioethical aspects of genetic research, and is currently co-Chair of the Israel National Bioethics Council. She is currently a member of Israel's National IRB Committee for Genetics and Reproductive studies and the Israeli National Council for Women's Health and was a member the Israeli Ministry of Health's committee on regulation of fertility treatments and of a Ministry of Justice advisory committee on wrongful birth. Internationally, she was a member of UNESCO's IBC (International Bioethics Committee) (2006-2009), and is a member of the Clinical Trials Task Force of the International Society of Stem Cell Reseach (ISSCR).

Dr. Osnat Luxenburg, MD, MPH, MBA

The Director of the Medical Technology and Infrastructure Administration at the Israeli Ministry of Health, in this role since 2001, Israel.

She is responsible for the regulation and licensing of all medical technologies including - pharmaceuticals, biological products, medical devices, procedures etc.; decision-making on reimbursement at a national level; regulation of radiation protection in Israel and formulating national health policy.

Dr. Luxenburg graduated from the Technion, Israel Institute of Technology, Medical School in 1991, completing her Public Health specialization at the Sheba Medical Center in 1996. Dr. Luxenburg focused on medical management within the MPH degree from Hebrew University in Jerusalem and continued her studies to a MBA degree at Bar Ilan University.

Dr. Luxenburg is also a member of the management of ICTAHC - The Israeli Center for Technology Assessment in Health Care. She has authored various scientific publications in national and international journals and serves as lecturer at the - Graduate School of Business Administration at the Faculty of Management, Tel Aviv University.

Dr. Luxenburg has both executive national and international ties, working in cooperation with international bodies such as the FDA and EU organizations and International Atomic Energy Agency (IAEA) in promoting national policy.

Prof. Shlomo Mor-Yosef, MD

Prof. Shlomo Mor-Yosef is the Chairman of the Board of the Israel National Institute for Health Policy Research and the Director General of Bituach Leumi, National Insurance Institute of Israel.

Prof. Mor-Yosef recently completed his tenure as Director General of the Hadassah Medical Organization (HMO) in Jerusalem. His eleven years as Director General were the crowning glory of his 38 years at Hadassah, from his first year of medical school until 2011, with just a few brief exceptions.

Prof. Mor-Yosef graduated from the Hebrew University-Hadassah Medical School in 1980, completing his obstetrics and gynecology specialization at Hadassah. He served as a senior physician in the Department of Obstetrics and Gynecology at Hadassah with special focus on cervical cancer. From 1988-89 Prof. Mor-Yosef completed a subspecialty in Gynecological Oncology at Queen Elizabeth Hospital, Gateshead, England.

In 1990, Prof. Mor-Yosef assumed the position of Deputy Director of the Hadassah Ein Kerem Hospital, following which he studied at the Harvard University JFK School of Government where he received his Master's Degree in Public Administration. In 1994, he assumed the post of Deputy Director General of HMO and then served as Director of Hadassah Ein Kerem. Prior to assuming his post as Director General of HMO, Prof. Mor-Yosef served as Director General of the Soroka Medical Center of the Negev.

Prof. Mor-Yosef has authored more than 100 scientific publications and has served on the faculty of several universities and boards of various organizations and companies. From 2001 – 2012, Prof. Mor-Yosef served as Chairman of Hadasit, HMO's Technology Transfer Company. Among his present responsibilities, Prof. Mor-Yosef serves as Chairman of the Public Committee for Fertility and Birth appointed by the Director General of the Ministry of Health to recommend legislation in the field of fertility and birth in Israel; and Member of the Master Plan for Transportation Committee of the Association for Planning, Development & Urban Preservation – Jerusalem.

Prof. Yaakov Naparstek, MD

Dr. Yaakov Naparstek is the Chairman of Medicine at the Hadassah University Hospital, Israel.

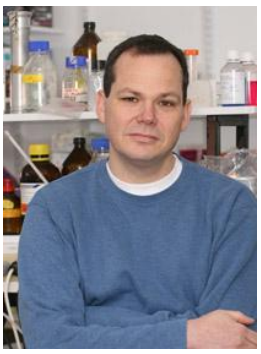
Dr. Naparstek is a graduate of the Hadassah-Hebrew University Medical School in Jerusalem, Israel. He is Boards certified in Internal Medicine, Rheumatology and Clinical Immunology and Allergy. Dr. Naparstek has been a research fellow and a visiting Professor at the Weizmann Institute of Science, Rehovot, Tuft's University, Boston, The National Institute of Health, Bethesda and Stanford University, Stanford.

Dr. Naparstek is currently a Professor of Medicine in the Hebrew University, Jerusalem. He is the Chairman of Medicine in the Hadassah University Hospital, as well as the Director of the Hadassah Clinical Immunology and Rheumatology Center.

Dr. Naparstek is the incumbent of the Leifferman Chair in Rheumatology.

His main research interests are in the field of autoimmunity, SLE, autoimmune arthritis and type 1 diabetes. In recent years his research group focused on the identification of the target antigens in SLE and in autoimmune arthritis and diabetes and in the attempts to develop antigen-specific therapeutic modalities to those diseases.

Dr. Naparstek is the Chairman of the Boards of the Israeli T-Cell Vaccination Center, The Head of the Israeli SLE Registry, the Head of the Israeli Cell therapy and Gene therapy Committees and a member in many other national and international committees. Dr. Naparstek is the founder and chief scientist of the Verto Medical and Protab Therapeutics biotechnological companies and a consultant and SAB member in other medical-biotechnoly companies. Dr. Naparstek is the recipient of national and international awards, including the 2011 Elkeles Prize in Medicine and the author of more than 100 publications and chapters in books as well as many patents in the field of autoimmune inflammatory diseases.



Prof. Eli Pikarsky, MD, PhD

Department of Pathology and the Lautenberg Center for Immunology and Cancer Research, The Hebrew University-Hadassah Medical School, Israel.

Trained surgical pathologist, actively engaged in clinical work and a trained molecular biologist. Runs a research lab at the medical school that focuses on studying tissue interactions that modulate cancer progression, combing various methodologies including mouse genetic manipulation, imaging and molecular biology. As a mentor encourages the students and staff to harness the power of tissue based analysis methods to reveal the underpinnings of disease processes and to look for specific points that are amenable for therapeutic manipulation.

2011 - Associate Professor, Hebrew University Hadassah Medical School.

2006 - Senior lecturer, Hebrew University Hadassah Medical School.

2005 - Lecturer, Hebrew University Hadassah Medical School.

2004 - Senior Staff Pathologist.

1999-2003 - Resident, Department of Pathology, Hadassah-Hebrew University Medical Center.

2000 - PhD, Molecular Biology, Hebrew University, Jerusalem.

1992 - MD, Medicine, Hebrew University, Jerusalem.

1987 - BSc, Medicine, Hebrew University, Jerusalem.

Dr. Efrat Ram-Tiktin, PhD

Department of Philosophy, Bar-Ilan University, Israel.

PhD. Philosophy (Bioethics, Ethics, Political Philo.), Bar Ilan University, Israel.

Work Experience

2009 - Instructor, Bar Ilan University (2009-) and The Hebrew University.

2010-2012: Asst. editor, *Blue and White Bioethics – Israel's perspective*, G. Siegal (Ed.).

2009-2011: Asst. editor, *Journal of Health Law and Bioethics*.

1997-2003: Vice President, Israel AIDS Task Force, Tel Aviv.

1993-1997: Education officer, Head, Research Unit, Israel Defense Force.

Publications

Ram-Tiktin, E. (2012). "The right to health care as a right to basic human functional capabilities", *Ethical Theory and Moral Practice*, 15(3):337-351.

Ram-Tiktin, E. (2011) "A decent minimum for everyone as a sufficiency of basic human functional capabilities", *American Journal of Bioethics,* 11(7):24-25.

Ram-Tiktin, E. (2011) Resource allocation under austere conditions – The IDF field hospital in Haiti. *Journal of Health Law and Bioethics*, 4:118-163. (Hebrew).

Prof. Avinoam Reches, MD

Department of Neurology at Hadassah Hospital, The Hebrew University in Jerusalem, Israel

2000-To Date	Chairman, Ethical Committee, Israel Medical Association.
2000-2005	Chairman, Curriculum Committee Hadassah - Hebrew University Medical School.
1999-2008	Chairman, Israel Neurological Association.
1985-2012	Tenured Senior Physician, Department of Neurology Hadassah University Hospital, Jerusalem Israel.
1995-2012	Professor of Neurology, Hadassah - Hebrew University Medical School, Jerusalem Israel.
1980-1983	Visiting Fellow, Neurological Institute, Columbia-Presbyterian College of Physicians and Surgeons, New-York, N.Y.
1980-1982	NIH Fogarty International Postdoctoral Research Fellowship.
1980-1982	United States – Israel Education Foundation Fulbright Fellowship.

Prof. Gad Rennert, MD, PhD

Prof. Rennert is the Director of the Clalit National Cancer Control Center and of the National Breast and Colorectal Cancer Detection Programs of Israel. He is Chairman, Department of Epidemiology and Community Medicine, Carmel Medical Center and Technion and the Clalit Department of Epidemiology and Disease Prevention, Israel.

He is also an expert molecular epidemiologist and is leading the Clalit national personalized medicine program. He received his MD degree from Ben-Gurion University in Israel and PhD from UNC School of Public Health, Chapel Hill. He published more than 200 articles in peer-reviewed journals and is on numerous journal editorial boards.

Prof. Joshua Shemer, MD

Chairman, Assuta Medical Centers, Deputy Chairman, Board of Directors, Maccabi Healthcare Services, Director, Israeli Center for Health Technology Assessment in Health Care (ICTAHC), The Gertner Institute for Epidemiology and Health Policy Research, Tel Hashomer, Full Professor, Internal Medicine, Sackler Faculty of Medicine, Tel Aviv University, Israel.

Leading Former Positions:

Director-General of the Ministry of Health (1999-2000)**;** Director-General, Maccabi Healthcare Services (2001-2007); Maccabi the second largest non-profit HMO in Israel with 1.8 million members, 9,000 employees, 3,500 physicians, more than 3,500 clinics and pharmacies and a budget of $1.8 billion; Head, School of Public Health, Tel Aviv University**;** Member and former Chairman of the National Public Committee for Updating the National List of Health Services in Israel; Member and former Chairman of the National Council for Trauma; Chairman and member, Supreme Health Authority for Emergency Situations, Ministry of Health, Israel (1989-2007); Founder & Chairman, National Council for Logistics in Health Services, Ministry of Health,Israel (1994-2000); Active membership on several National and International Committees and professional organizations; Alumnus, National Institutes of Health (N.I.H.), Bethesda, Maryland, U.S.A. (1984-1987, 1991-1992, 2001).

Professor Shemer has actively participated in over a hundred national and international scientific meetings abroad.

Prof. Shemer's academic activities incorporate over 250 publications in prominent professional peer reviewed publications including 6 books edited in the fields of trauma, health reforms, medical technology and management and over 20 chapters in several books.

Prof. Shemer is also Associate Editor of both the Israel Medical Association Journal (I.M.A.J.) (English) and Harefuah, Journal of the Israel Medical Association (Hebrew) and Member, Editorial Board of the International Journal of Technology Assessment in Health Care (I.J.T.A.H.C.)

Dr. Mark Trusheim

Mark Trusheim is a Visiting Scientist and Executive-In-Residence at the MIT Sloan School of Management, USA.

He has been a Special Government Employee for the FDA's Office of the Commissioner and is the Founder and President of Co-Bio Consulting, LLC. He holds degrees in Chemistry from Stanford University and Management from MIT. Mark's research focuses on the economics of stratified (personalized) medicines, particularly the integrated quantitative modeling of stratified medicine development and commercialization, to inform public policy, corporate strategy and individual product development programs.

He is a former Executive Committee Board Member and Interim President of the Massachusetts Biotechnology Council.

As an entrepreneur, Mark founded and was the first President and CEO of Cantata Laboratories which developed and marketed biochemical profiling clinical diagnostics and pharmaceutical biomarker services.

Prior to Cantata, Mark worked at Monsanto/Pharmacia, culminating his career there as Co-President and Chief Operating Officer of Cereon Genomics, LLC - a 5 year, $500M collaboration with Millennium Pharmaceuticals. Prior to his position at Cereon, Mark was responsible for Monsanto's external genomics relationships and held roles of Vice President in the Health & Wellness Sector, Marketing Director in Searle Pharmaceutical and Director in Agriculture Division Strategy.

Mark spent the first half of his career in the high tech industry working at both Wang Laboratories in computer hardware and the start-up Kenan Systems Corporation which focused on developing quantitative models and artificial intelligence based applications for large corporations and government agencies.

המכון הלאומי לחקר שרותי הבריאות ומדיניות הבריאות (ע"ר)
The Israel National Institute for Health Policy Research

טל': 03-5303516/7 פקס: 03-5303250
דוא"ל: nihp@israelhpr.health.gov.il

www.israelhpr.org.il