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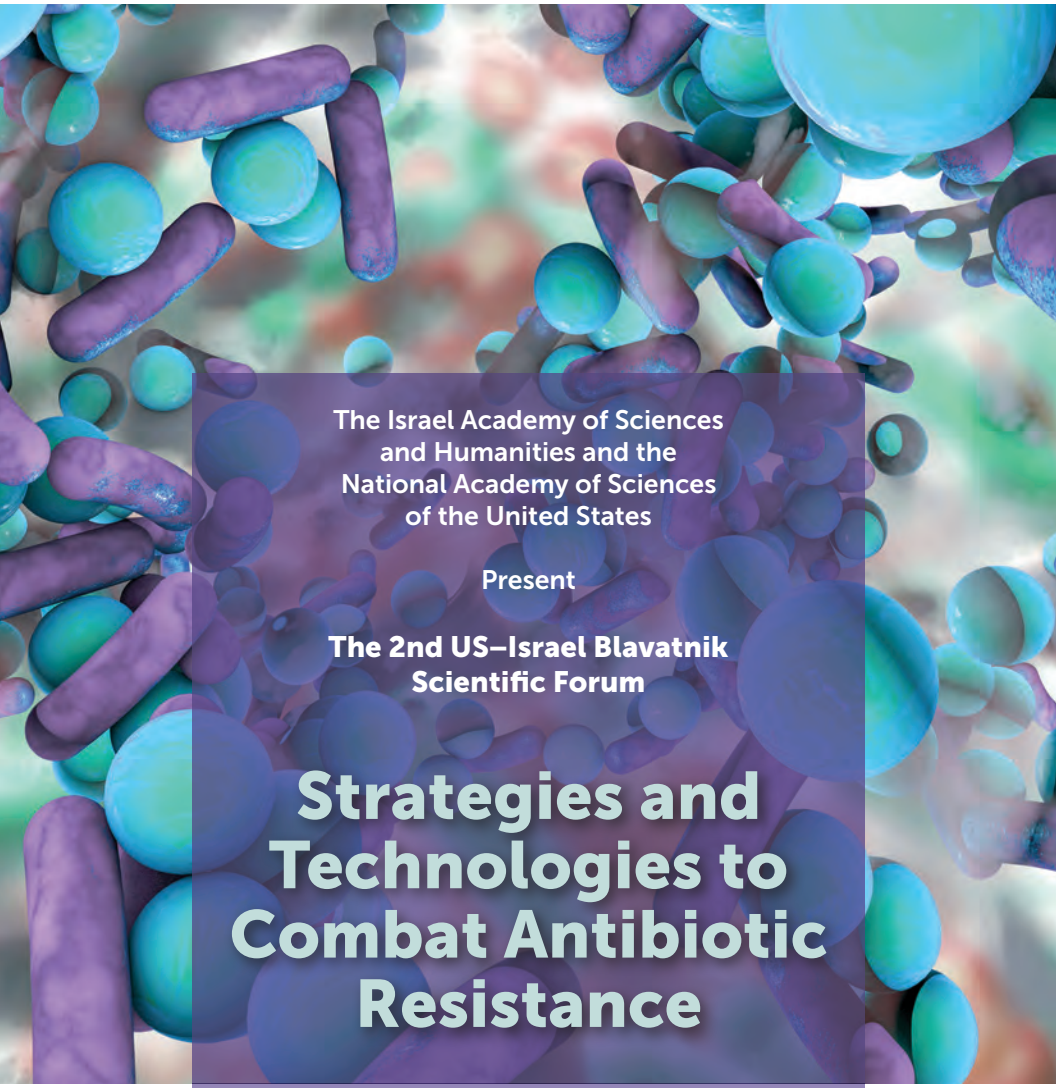

The Israel Academy of Sciences and Humanities and the National Academy of Sciences of the United States

Present

The 2nd US–Israel Blavatnik Scientific Forum

Strategies and Technologies to Combat Antibiotic Resistance

Program and Abstracts

Organizing Committee

Caroline Harwood (co-chair), Ada Yonath (co-chair), Timor Baasov, Richard Lenski, Carl Nathan, and Nathalie Questembert-Balaban

Washington, D. C. • April 6-7, 2022

The Israel Academy of Sciences and Humanities
2016 Udi Katzman

Left: The Albert Einstein Statue at the Israel Academy of Sciences and Humanities • 2016 Udi Katzman

The Israel Academy of Sciences and Humanities

The Israel Academy of Sciences and Humanities, established by law in 1961, is the preeminent scientific institution in Israel. It acts as a national focal point for Israeli scholarship in all branches of the sciences, social sciences, and humanities. The Academy comprises 135 of Israel's most distinguished scientists and scholars who operate in two divisions—the Sciences Division and the Humanities Division. It is tasked with promoting Israeli scientific excellence; advising the government on scientific matters of national interest; publishing scholarly research of lasting merit; and maintaining active contact with the broader international scientific and scholarly community.

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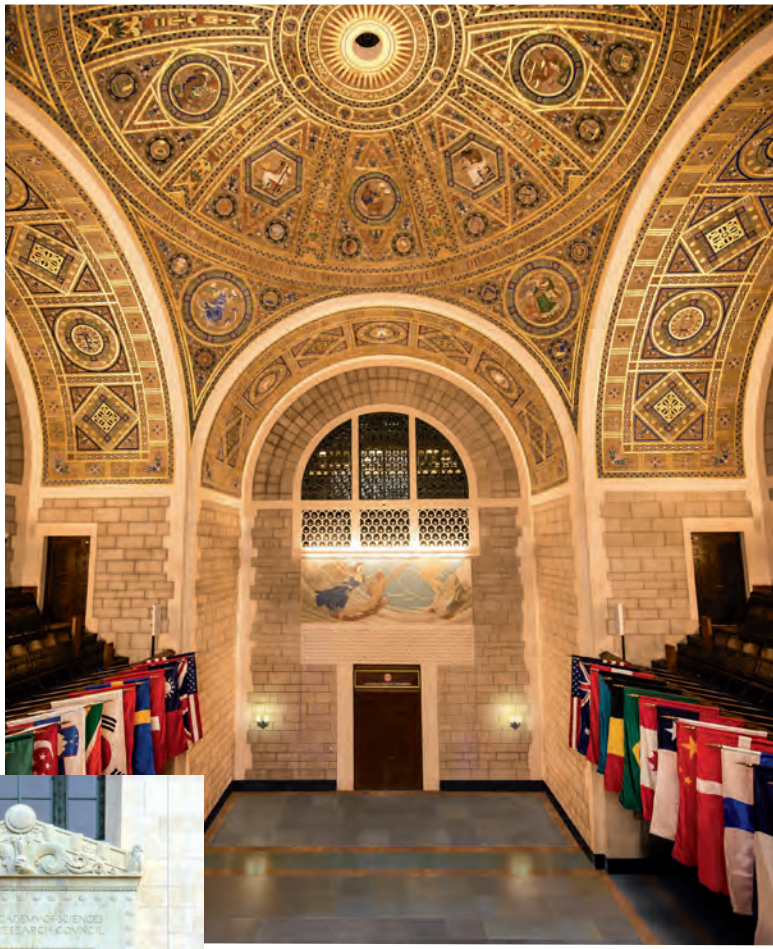

National Academy of Sciences • 2012 Maxwell MacKenzie

The National Academy of Sciences

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The National Academy of Engineering (NAE) and the National Academy of Medicine (NAM, formerly the Institute of Medicine) were founded under the NAS charter in 1964 and 1970, respectively. The three Academies work together as the National Academies of Sciences, Engineering, and Medicine to provide independent, objective analysis and advice to the nation and conduct other activities to solve complex problems and inform public policy decisions. The National Academies also encourage education and research, recognize outstanding contributions to knowledge, and increase public understanding in matters of science, engineering, and medicine. The National Academies' service to government has become so essential that Congress and the White House have issued legislation and executive orders over the years that reaffirm its unique role.

PROGRAM

Tuesday, April 5

6:00 pm **Welcome Reception** • Potomac Room, Fairmont Hotel

Day One • **Wednesday, April 6**

7:30 am **First Bus from Fairmont Hotel to NAS Building**

7:45 am **Breakfast**

8:00 am **Second Bus from Fairmont Hotel to NAS Building**

8:30 am **Welcome Remarks**
Carrie Harwood PhD. • University of Washington School of Medicine

8:45 am **Keynote Speaker**
Ada Yonath, PhD. • Weizmann Institute of Science
Next Generation Antibiotics

9:30 am **SESSION I** • **New Approaches to Diagnosis of AMR**
Speaker Presentations and Discussion

9:30 am **Deborah Hung, MD, PhD.** • Broad Institute and Harvard Medical School
Genomics, Antibiotic Resistance and Diagnostics

10:15 am **Morning Break**

10:45 am **Uri Gophna, PhD.** • Tel Aviv University
Antibiotic Resistance in the Gut - Lessons From Metagenomics

11:30 am **SESSION II** • **Phenotypic Resistance to Antibiotics**
Speaker Presentations and Discussion

11:30 am **Mark P. Brynildsen, PhD.** • Princeton University
Toward Knowing Thy Enemy: Investigations of Bacterial Persister Physiology

12:15 pm **Sophie Helaine, PhD.** • Harvard Medical School
Salmonella Persistence During Infection: Trade-off Between Mitigating DNA Damage and Ability to Relapse

1:00 pm **Lunch**

2:00 pm **Carl F. Nathan, MD.** • Weill Cornell Medicine
Cryptic Phenotypic Resistance: "Differentially Detectable" Bacteria

2:45 pm **Nathalie Balaban, PhD.** • The Hebrew Universityof Jerusalem
The Impact of the Disrupted Cellular State on Drug Response

3:30 pm **Afternoon Break**

4:00 pm **James J. Collins, PhD.** • Massachusetts Institute of Technology
Harnessing Deep Learning for Antibiotic Discovery

4:45 pm **Day 1 Roundup**

5:00 pm **Cocktail Hour and Dinner**

7:15 pm	**Keynote Speaker** **Martin J. Blaser, MD.** • Rutgers University **Antibiotic Resistance Is the Tip of the Iceberg of Ecological Change**
8:00 pm	**Bus from NAS Building to Fairmont Hotel**

Day Two • **Thursday, April 7**

7:30 am	**First Bus from Fairmont Hotel to NAS Building**
7:45 am	**Breakfast**
8:00 am	**Second Bus from Fairmont Hotel to NAS Building**
8:30 am	**SESSION III** • **Evolutionary Dynamics of AMR** Speaker Presentation and Discussion
8:30 am	**Michael Baym, PhD.** • Harvard Medical School **Non-anthropogenic Selective Pressures on Resistance Evolution**
9:15 am	**Jacob Scott, MD, PhD.** • Cleveland Clinic **Using Fitness Seascapes and Counterdiabatic Driving to Enable Control of Evolving Populations of Microbes**
10:00 am	**Morning Break**
10:30 am	**Roy Kishony, PhD.** • Technion–Israel Institute of Technology **Predicting Antibiotic Resistance and Treatment Failure**
11:15 am	**Avigdor Eldar, PhD.** • Tel Aviv University **Short-Range Bacterial Communication and Its Implications**
12:00 pm	**Lunch**
1:00 pm	**SESSION IV** • **Alternative Approaches to Therapy** Speaker Presentation and Discussion
1:00 pm	**Roi Avraham, PhD.** • Weizmann Institute of Science **Understanding Metabolic Preferences of Bacterial Pathogens as Novel Metabolotherapies to Infection**
1:45 pm	**Paul Turner, PhD.** • Yale University **Phage Therapy to Combat Infections by Antibiotic-Resistant Bacterial Pathogens**
2:30 pm	**Afternoon Break**
3:00 pm	**Ilan Rosenshine, PhD.** • The Hebrew University of Jerusalem **Life on the Surface of Intestinal Epithelium: The Enteropathogenic E. coli Paradigm**
3:45 pm	**Timor Baasov, PhD.** • Technion–Israel Institute of Technology **Towards Catalytic Antibiotics as a New Paradigm in Antibiotics Research**
4:30 pm	**Rotem Sorek, PhD.** • Weizmann Institute of Science **Phages, the Natural Killers of Bacteria**
5:15 pm	**Forum Conclusion and Adjourn**
5:30 pm	**Bus from NAS Building to Fairmont Hotel**

ABSTRACTS

(In order of presentation)

ABSTRACTS

Day One • Wednesday, April 6, 2022

SESSION I • New Approaches to Diagnosis of AMR

Next Generation Antibiotics

Ada Yonath • Weizmann Institute of Science

Ribosomes are the universal cellular multicomponent particles that translate the genetic code to proteins. Owing to their high significance they are targeted by many antibiotics. Structures of complexes of bacterial and eubacterial ribosomes with the commonly used antibiotics that paralyze them, illuminated common pathways in their inhibitory-actions, synergism, differentiation and resistance. Comparisons of structures of ribosomes from multi-resistant pathogens to those of harmless bacteria illuminated unique features that may become sites for the design of novel, next generation, species-specific antibiotics, thus microbiome preserving, and degradable, thus eco-friendly. The same method is being used for early detection of cancers linked to mutated ribosomes.

Genomics, Antibiotic Resistance and Diagnostics

Deborah Hung • Harvard Medical School, Massachusetts General Hospital, Broad Institute of MIT & Harvard

The post-genomic era has ushered in a period of tremendous activity to accelerate or improve infectious disease diagnostics, highlighted no less than by the current SARS-CoV-2 pandemic. Efforts to combine genomics with newer genomic technologies, such as CRISPR-Cas systems, will be discussed within the context of accelerating the ability to identify a culprit bacterial pathogen and identify antibiotic resistance, with an aspiration of achieving a rapid, deployable strategy applicable across all global, clinical settings.

Antibiotic Resistance in the Gut - Lessons From Metagenomics

Uri Gophna • Tel Aviv University

Traditionally antibiotic resistance has been studied in isolated bacteria, and for many pathogens this approach is sufficient. Nonetheless, there are some questions that are difficult to address without a comprehensive view of the microbial community that is currently available primarily through shotgun metagenomics. Here I will present evidence that different microbiomes within the human body respond differently to antibiotics and examine the various-sources of resistant bacteria in antibiotic-treated patients.

SESSION II • Phenotypic Resistance to Antibiotics

Toward Knowing Thy Enemy: Investigations of Bacterial Persister Physiology

Mark P. Brynildsen • Princeton University

Bacterial persisters are phenotypic variants with extraordinary tolerances toward antibiotics. Persister survival has largely been attributed to inhibition of essential cell processes, which prevents antibiotics from corrupting their primary targets, followed by reversion to normal physiology upon removal of the antibiotic. In recent years, exceptions to this one-size-fits-all model of persistence have been identified, with fluoroquinolone persisters constituting one of them. Increased understanding of fluoroquinolone persister survival has been enabled by examining the physiology of those survivors during and after treatment, which has led to the identification of fluoroquinolone persister sub-types and detection of accelerated resistance development from fluoroquinolone persisters compared to normal cells. In this talk, I will discuss my group's work studying fluoroquinolone persister physiology and how it has led to mechanistic understanding of how those bacteria survive in the face of certain death.

Salmonella Persistence During Infection: Trade-off Between Mitigating DNA Damage and Ability to Relapse

Sophie Helaine • Harvard Medical School

My lab studies the molecular mechanisms of bacterial persistence during infection. Bacterial persistence, characterized by chronic and relapsing infections, is a major threat to human health as these infections cause considerable morbidity and frequently require multiple courses of antibiotics. Such long-lasting infections are caused by a variety of bacterial pathogens including *Mycobacterium tuberculosis*, *Salmonella*, *Pseudomonas* and pathogenic Escherichia coli. We developed single cell reporters to track *Salmonella* growth history during macrophage and murine infections. It revealed the presence of non-growing bacteria in infected host cells, which had been hypothesized for decades but had remained elusive. Interaction between Salmonella and host macrophages has then proven to be a powerful and relevant model to study persister biology since we showed that the bacteria specifically respond to engulfment by the host defence cells by forming high proportions of persisters. I will present our characterization of how persisters survive antibiotics in this challenging environment.

Cryptic Phenotypic Resistance: "Differentially Detectable" Bacteria

Carl F. Nathan • Weill Cornell Medicine

Lysis of bacteria is the one certain way to define their death. The gold standard surrogate is inability to form a colony. *Mycobacterium tuberculosi*s (Mtb), the leading pre-COVID cause of death from infection, poses the clinical challenge of phenotypic resistance to antibiotics on the part of viable Mtb that are not colony-forming units and are therefore misconstrued as being absent or dead. Their viability is revealed in vivo by their ability to cause disease and in vitro by alternative methods of culture, such as limiting dilution, making them "differentially detectable" (DD). DD Mtb have undergone a degree of oxidative damage intermediate between what does not interfere with colony growth and what precludes recovery during replicative delay. DD Mtb are not "dormant", but they are profoundly resistant to antibiotics selected for their ability to kill replicating bacteria. We need antibiotics that can kill bacteria in DD states.

The Impact of the Disrupted Cellular State on Drug Response

Nathalie Balaban • The Hebrew University of Jerusalem

The evolution of antibiotic resistance in microorganisms is a major health issue. Understanding the factors affecting evolutionary trajectories from susceptibility to resistance is crucial. Quantitative experiments and mathematical modelling can shed light on the processes that speed up or delay the evolution of resistance. We previously showed that tolerance, a form of survival under antibiotics that is distinct from resistance, plays a major role in promoting the evolution of resistance *in vitro*. In order to determine the relevance of the *in vitro* experimental evolution results for the clinic, we followed the course of infection in patients with life threatening bloodstream infection. Further dissection of the response of the clinical strains to combinations of antibiotics reveals a new way by which resistance evolution is strongly promoted by the tolerance phenotype. Finally, we develop a global understanding of how stresses can push bacteria into a disrupted state which drives subsequent antibiotic tolerance.

Harnessing Deep Learning for Antibiotic Discovery

James J. Collins • Massachusetts Institute of Technology

In this talk, we highlight the Antibiotics-AI Project, which is a multi-disciplinary, innovative research program that is leveraging MITs world-leading strengths in artificial intelligence, bioengineering, and the life sciences to discover and design novel classes of antibiotics. The Antibiotics-AI Project is focused on developing, integrating and implementing deep learning models and chemogenomic screening approaches: (1) to predict novel antibiotics from expansive chemical libraries (1.5 billion molecules) with diverse properties, (2) to design de novo novel antibiotics based on learned structural and functional properties of existing and newly discovered antibiotics, and (3) to identify, using white-box machine learning models, the molecular mechanisms underlying the newly discovered and/or designed antibiotics. These deep learning approaches will utilize multi-scale computation to embrace and harness the complexity of biology and chemistry, so as to discover, design and develop new classes of antibiotics, up through preclinical studies. The platform has been designed so that it can be utilized and applied in a rapid fashion to emerging and re-emerging bacterial pathogens, including multidrug-resistant (MDR) bacteria and extensively drug-resistant (XDR) bacteria.

Antibiotic Resistance is the Tip of the Iceberg of Ecological Change

Martin J. Blaser • Rutgers University

Like that of all mammals, the human microbiome is ancient, diverse, numerous, niche-specific, and is comprised of both conserved and host-specific features. In early life, the microbiome develops in a choreographed manner, and is a part of the development of host metabolism, immunity and cognition. Antibiotic treatments, designed to suppress or eliminate pathogens, have substantial collateral effects on the microbiome, especially in early life. If the ill-effects of antibiotics on human biology were drawn as an iceberg, the tip would be the well-recognized selection for antibiotic resistance. But the body would represent the transient or long-term antibiotic-induced changes that affect developmental, situational, senescent, and generational phenomena, which themselves have metabolic, immunologic, neoplastic, or degenerative effects. There now is extensive evidence that correlates early life antibiotic exposures and subsequent disease risks. We have conducted experimental studies in animal models to determine the effects of such exposures. Multiple studies provide consistent evidence of causal roles, including those crossing host generations. The widespread use of antibiotics across several human generations now presents serious and increasing problems that require directed solutions. These include more restricted clinical use of antibiotics, narrow spectrum approaches to anti-bacterial activities, and strategies for the restoration of missing microbes and their host-signaling modalities and pathways.

Day Two • Thursday, April 7, 2022

SESSION III • Evolutionary Dynamics of AMR

Non-anthropogenic Selective Pressures on Resistance Evolution

Michael Baym • Harvard Medical School

While the human use of antibiotics does contribute to the evolution of resistance, the epidemiology of resistance we observe is inconsistent with it being the sole, or potentially even the primary, driver of resistance evolution. So what else is selecting on resistance? I will propose some possibilities, show how to discover phages that select against both resistance and the horizontal transmission of resistance, and show how evolutionary insight can teach us how to build better diagnostics.

Using Fitness Seascapes and Counterdiabatic Driving to Enable Control of Evolving Populations of Microbes

Jacob Scott • Cleveland Clinic

Antibiotic resistance represents a growing health crisis necessitating the immediate discovery of novel treatment strategies.

One treatment strategy involves probabilistically directing the evolution of bacterial populations toward increased drug-sensitive states.

This strategy however requires multiple rounds of prolonged drug exposure which select for resistant cells in a stochastic manner.

We will present results highlighting the stochasticity of these methods, in particular the possibility of evolutionary escape to genotypes which could access high fitness. We then present a solution to these limitations involving a quantum-inspired method to control the trajectory of evolving bacterial populations. This approach allows one to calculate a time-dependent drug dosage that will steer a bacterial population, in a finite time, toward a target genotype distribution. Finally, we will present novel data in the form of fitness seascapes for commonly used antibiotics — a sine qua non for these methods — and present a path toward validation of this control method.

Predicting Antibiotic Resistance and Treatment Failure

Roy Kishony • Technion–Israel Institute of Technology

Antibiotic resistance is growing as a major public health concern. Predicting antibiotic resistance and the evolutionary paths leading to resistance is key for our ability to control the spread of drug resistant pathogens. I will describe a series of experimental-computational methodologies for following and identifying recurrent patterns in the evolution of antibiotic resistance in the lab and in the clinic. Combined with machine-learning approaches applied to electronic patient records, these tools can lead to predictive diagnostics of antibiotic resistance and personalized treatments of microbial infections.

Short-Range Bacterial Communication and Its Implications

Avigdor Eldar • Tel Aviv University

Bacterial quorum sensing allows for coordinated cellular response through the secretion and detection of diffusible molecules. While many quorum-sensing bacteria grow in spatially structured and genetically heterogeneous communities, the principles that govern quorum-sensing under these conditions are largely unknown. Combining microfluidic experiments with mathematical modeling, we quantified signal propagation in synthetic bacterial communities at a single-cell resolution. We identify two generic quorum-sensing designs that profoundly differ in the spatial scale of their effect: one design allows for global communication among cell clusters in the community, whereas the other design allows localized communication with signaling length-scale of about 10 microns. We further show that phages and conjugative elements, employ short-range quorum to sense their frequency in a highly localized neighborhood and initiate horizontal gene transfer when this fraction is small. Finally, we constructed a synthetic gene network based on short range signaling which leads to pattern formation at the cellular scale.

SESSION IV • Alternative Approaches to Therapy

Understanding Metabolic Preferences of Bacterial Pathogens as Novel Metabolotherapies to Infection

Roi Avraham • Weizmann Institute of Science

Management of many bacterial infections is becoming increasingly difficult due to new, rapidly evolving pathogens with increased virulence and drug resistance. Promising alternatives to targeting pathogens, novel anti-infective approaches harness the host's own response to infection or target virulent processes of the pathogen. To realize the promise of these alternative therapeutic approaches, a comprehensive, systematic understanding of the complex dynamics between host and pathogen is required. Specifically, we believe that the early stages of infection, when bacterial numbers are relatively small, play a particularly critical role in determining infection outcome, and offers a unique opportunity to eradicate infection. Despite the huge medical importance and global health burden, our ability to assess the impact of host-pathogen interactions on infection outcome is limited, especially in the context of human infection. For this, one of the least-understood periods in the course of infectious disease lies between the initial inoculation with a dose of pathogens and the appearance of the first symptoms of disease, or the lack of appearance thereof. In my talk, I will present recent findings in our lab indicating that this can now be done by modelling the dynamics of metabolism, phenotype, and function of immune cells so as to identify cell type-specific states that represent their activation process during infection. I will present tools and approaches to study early infection dynamics and define two novel concepts of infection biology: 1) **Immune cell dynamic states (immDS)** – the range of metabolic and immunological changes of cells in response to pathogens, without losing their identity. 2) **Host-Patho-Cells**, cellular states determined by the immuno-metabolic-virulence crosstalk between infected host cells and intracellular bacteria. I will demonstrate how the landscape of immDS and Host-Patho-Cells at critical stages of early human infection can define the trajectory of infection outcome, and provide bona-fide targets to better treat infection.

Phage Therapy to Combat Infections by Antibiotic-Resistant Bacterial Pathogens

Paul Turner • Yale University

One possible strategy to combat the antibiotic resistance crisis is a renewed approach to 'phage therapy,' where these administered viruses not only kill the target bacteria, but also predictably select for phage resistance that reduces virulence and/or increases antibiotic sensitivity (evolutionary trade-offs). By utilizing virulence factors as receptor binding sites, the phages exert selection for bacteria to evolve phage resistance by modifying (or losing) the virulence factor, potentially reducing bacterial pathogenicity. We present examples of naturally-isolated phages that kill target bacteria while selecting for phage resistance that coincides with useful clinical traits, and compare in vitro data to phenotypic, genetic and metagenomics analyses of microbes isolated longitudinally from patient samples before, during and after emergency phage therapy treatments.

Life on the Surface of Intestinal Epithelium: The Enteropathogenic E. coli Paradigm

Ilan Rosenshine • The Hebrew University of Jerusalem

Enteropathogenic and enterohemorrhagic E. coli (EPEC and EHEC) are closely related human pathogens that target the intestine, causing conditions ranging from chronic asymptomatic colonization to an acute, life-threatening disease. These pathogens carry powerful virulence machinery termed type III secretion system (T3SS) that functions as a nano-syringe. Immediately upon host attachment, the pathogen utilizes its T3SS to inject the host cells with dozens of effector proteins that subvert host processes to promote bacteria colonization. A subgroup of these effectors (e.g., NleC, NleD, NleE) target and subvert specifically the MAP kinase and NF-κB pathways to intercept pathogen-detection signaling. Two additional processes contribute to successful colonization and are interlocked with T3SS activity. These include "host-contact sensing" by the pathogen, followed by massive gene expression and metabolic reprogramming, necessary for adapting to the host-adherent lifestyle. In parallel, the attached pathogens extend membranous nanotubes to enable nutrient extraction from the infected cells. These processes will be discussed.

Towards Catalytic Antibiotics as a New Paradigm in Antibiotics Research

Timor Baasov • Technion–Israel Institute of Technology

The appearance of bacterial strains resistant to multiple antibiotics has encouraged an extensive drive towards the goal of slowing down resistance development. One strategy is catalytic antibiotics, which seeks to mediate catalytic inactivation of the therapeutic target to form an inactive or dysfunctional entity. I will describe two parallel studies towards the development of catalytic antibiotics. One approach aims the development of catalytic aminoglycoside, and the second the development of catalytic fluroquinolone. Both studies considered the known structural and mechanistic data available on the aminoglycoside and fluoroquinolone families of antibiotics to rationally design new conjugates of these drugs with catalytic warheads so to cleave phosphodiester bond of ribosomal RNA (catalytic aminoglycoside) or bacterial DNA (catalytic fluoroquinolone), in such a manner as to cause bacterial ribosome or the bacterial DNA fragmentation in a catalytic fashion. The design principles along with the synthesis and biological evaluation of the target structures will discussed.

Phages, the Natural Killers of Bacteria

Rotem Sorek • Weizmann Institute of Science

Viruses that infect bacteria, or phages, are the most abundant viruses on Earth. To cope with frequent phage infection, bacteria have evolved a variety of defense systems that are collectively called the "immune system" of bacteria. The talk will present recent progress in the understanding of the bacterial immune system, and implications for the utilization of phages as an alternative to antibiotics.

BIOGRAPHIES

(In alphabetical order)

BIOGRAPHIES

Roi Avraham

Weizmann Institute of Science

Born in Jerusalem, Dr. Roi Avraham completed a BSc in computer science at Tel Aviv University in 2001 and earned his MSc magna cum laude in neuro- immunology there in 2006. He completed a PhD in biological regulation with Prof. Yosef Yarden at the Weizmann Institute of Science in 2011, followed by a postdoctoral fellowship at the Broad Institute of MIT and Harvard. He joined the Weizmann Institute's Department of Biological Regulation in May 2016 and is the incumbent of the Philip Harris and Gerald Ronson Career Development Chair.

Dr. Avraham's lab studies what happens in the body when invading pathogens, like the bacteria *Salmonella* or *Mycobacterium tuberculosis*, meet the body's immune cells. The lab uses cross-disciplinary, single-cell analysis platforms that enable them to extensively profile and precisely monitor host-pathogen interactions during infections in living tissues and look closely at the cellular interactions between cells of the immune system and the invading pathogens. Looking at this battleground allows the Avraham lab to analyze the very early events of infection. This unique opportunity allows him to develop new strategies predicting the outcome of infection and to suggest novel treatments addressing such attacks, especially in the face of widespread antibiotic resistance. For example, tagging bacterial cells with fluorescent dyes allows Dr. Avraham to see in vivo where the bacteria cell are and how they survive. Using advanced genomic labelling technology and cell sorting enables him to reveal functional determinants of host-pathogen encounters that can determine the different cellular outcomes. His gene expression analysis of the attacked cells showed that the bacteria that reside within specialized immune cells gives the cell protection from host immunity, and provide a niche from where the bacteria can then disseminate to cause systemic infection. Better understanding the complex dynamics of infection may help Dr. Avraham design new interventions which would center not on novel antibiotics, but on correcting the dysfunctional host-pathogen interaction as new strategies for fighting infection.

His academic and professional honors include an Israel Ministry of Science – Eshkol Fellowship from 2007 to 2010, an ERC starting grant (2017-2022), an ISF personal grant (2017-2022) and an NIH grant (2020-2022).

Roi is married, with 3 children and lives in Tel Aviv. His spouse, Shir, is a scientist at the Hebrew university.

Timor Baasov

Technion–Israel Institute of Technology

Prof. Baasov obtained his BSc and MSc from Tel Aviv University and PhD at the Weizmann Institute (1986) under the supervision of Mudi Sheves. Following postdoctoral research with J. R. Knowles at Harvard University, he joined Schulich Faculty of Chemistry at the Technion, Haifa, in 1988 and became Full Professor in 2004. His list of prizes and awards includes the Hershel Rich Innovation Award (2005, 2008, 2010), the Technion Excellence in Teaching Award (seven times: 2002-2015), the 2016 ICS-ICL Prize for Technological Innovation, and the 2020 NCK Prize for an Outstanding Medicinal Chemist in Israel. He holds the Irving and Jeanette Benveniste Chair in Life Sciences. Last two decades his lab has been involved in redesign of aminoglycoside antibiotics to treat genetic diseases like cystic fibroses, Usher's syndrome, Hurler syndrome, and more. One of the developed compounds, ELX-02, is currently in clinical phase 2 trials (USA and Israel) for the treatment of cystic fibrosis. Among his recent inventions are hybrid antibiotics and the innovative concept of catalytic antibiotics.

Nathalie Balaban

The Hebrew University of Jerusalem

Nathalie Q. Balaban's research interests focus on the development of experimental and theoretical approaches to the study of single-cell heterogeneity, and the determination of its role in disease and evolution. She has pioneered the use microfluidic devices and automated setups to study quantitatively the heterogeneous response of bacteria to antibiotics. Her work revealed the evolution of tolerance to antibiotics and the subsequent evolution of resistance, both in vitro and in patients. She has won the Krill prize from the Wolf foundation. She is an elected member of the European Academy of Microbiology, an EMBO member and a Fellow of the American Academy of Microbiology. Nathalie Q. Balaban has co-founded the Scholar-Teacher program, an initiative for improving science teaching in high schools.

Michael Baym

Harvard Medical School

My research is centers around the problem of antibiotic resistance, at the intersection of experimental, theoretical, and computational techniques. Our work on this problem ranges from understanding the basic mechanisms of evolution to the development of algorithms for computation on massive biological datasets. More recently, we have begun to focus on the role of phages and mobile genetic elements in the evolution of resistance. I am currently an Assistant Professor of Biomedical Informatics at Harvard Medical School. Before that I received his PhD in Mathematics from MIT and was a postdoctoral fellow at Harvard Medical School in Systems Biology. My lab has received several awards to support our work including a Packard Fellowship, a Pew Biomedical Scholarship, and a Sloan Research Fellowship.

Martin J. Blaser

Rutgers University

Martin J. Blaser holds the Henry Rutgers Chair of the Human Microbiome at Rutgers University, and serves as Director of the Center for Advanced Biotechnology and Medicine. Previously, he served as Chair of the Department of Medicine at New York University. A physician and microbiologist, Dr. Blaser has been studying the relationships we have with the human microbiome, the bacteria that live in us. Over the last 20 years, he has also been actively studying the relationship of the human microbiome with both health and important diseases including asthma, obesity, diabetes, and cancer. Dr. Blaser has been the advisor to many students, post-doctoral fellows, and faculty. He has served as President of the Infectious Diseases Society of America, Chair of the Board of Scientific Counselors of the National Cancer Institute, and Chair of the Advisory Board for Clinical Research of the NIH. He currently serves as Chair of the Presidential Advisory Council for Combatting Antibiotic Resistant Bacteria (PACCARB). He was elected to the National Academy of Medicine and the American Academy for Arts and Sciences. He has authored over 600 original scientific articles, holds 24 U.S. patents, and he also wrote Missing Microbes, a book targeted to general audiences, now translated into 20 languages.

Mark P. Brynildsen

Princeton University

Dr. Mark P. Brynildsen received his B.S. in Chemical Engineering from Rutgers University, New Brunswick in 2002 and earned his Ph.D. in Chemical Engineering from the University of California, Los Angeles (UCLA) in 2008, where he worked with Dr. James C. Liao. After working for 2 years as a Howard Hughes Medical Institute (HHMI) post-doctoral associate with James J. Collins within the Department of Biomedical Engineering at Boston University, Mark joined the faculty of the Department of Chemical and Biological Engineering at Princeton University in 2010. Currently, he holds the position of Associate Professor of Chemical and Biological Engineering at Princeton and was Director of Undergraduate Studies from 2019-2022. The overarching goal of his research group is to improve the performance of current antibiotics and identify targets for novel anti-infectives. To accomplish this, the Brynildsen group uses computational and experimental techniques to develop novel, fundamental understanding of the molecular mechanisms and networks pathogens use to thwart immune antimicrobials and antibiotics. Mark's research has been published in journals such as Nature, Nature Biotechnology, Nature Communications, PNAS, Molecular Cell, and Current Biology, and he has been the recipient of a Howard B. Wentz, Jr. Junior Faculty Award and an NSF CAREER Award.

James J. Collins

Massachusetts Institute of Technology

Jim Collins is the Termeer Professor of Medical Engineering & Science and Professor of Biological Engineering at MIT, as well as a Member of the Harvard-MIT Health Sciences & Technology Faculty. He is also a Core Founding Faculty member of the Wyss Institute for Biologically Inspired Engineering at Harvard University, and an Institute Member of the Broad Institute of MIT and Harvard. He is one of the founders of the field of synthetic biology, and his research group is currently focused on using synthetic biology to create next-generation diagnostics and therapeutics. Professor Collins' patented technologies have been licensed by over 25 biotech, pharma and medical devices companies, and he has co-founded a number of companies, including Synlogic, Senti Biosciences, Sherlock Biosciences and Cellarity, as well as Phare Bio, a non-profit focused on AI-driven antibiotic discovery. He has received numerous awards and honors, including a Rhodes Scholarship and a MacArthur "Genius" Award, and he is an elected member of all three national academies - the National Academy of Sciences, the National Academy of Engineering, and the National Academy of Medicine.

Avigdor Eldar

Tel Aviv University

Prof. Eldar did his undergraduate studies in mathematics and physics and a master degree in astrophysics. He then moved to do a PhD in systems biology of developmental systems at the Weizmann Institute. Following this he conducted his post-doctoral work at Caltech where he studied evolution and development of bacterial sporulation and their relation to noise in gene expression. Since 2010 he serves as a researcher at Tel-Aviv University. His lab focuses on the study of bacterial interactions and the use of bacterial cell-cell signaling. In recent years, his lab has also started to work on phages and additional mobile genetic elements, their interaction with each other and with their host.

Uri Gophna

Tel Aviv University

Uri Gophna obtained his PhD in microbiology with distinction from Tel Aviv University in 2003, where he studied molecular virulence factors of E. coli, under the supervision of Prof. Eliora Z. Ron. Following postdoctoral training in microbial ecology and evolution with Prof. W. Ford Doolittle at Dalhousie University, USA, Gophna returned to Tel Aviv University in 2005. After further postdoctoral training with Prof. Moshe Mevarech, Gohpna established an independent research group in 2006 at Tel Aviv University, where he is now a Professor.

Carrie Harwood

University of Washington School of Medicine

Caroline (Carrie) Harwood is the Gerald and Lyn Grinstein Endowed Professor in Microbiology and Associate Vice Provost for Research-External Relations at the University of Washington. Carrie earned her B.A. in Biology from Colby College and her Ph.D. in Microbiology from the University of Massachusetts. She completed postdoctoral work at Yale. She held academic appointments at Cornell University and the University of Iowa before moving to the University of Washington in 2005. She serves on the Scientific Advisory Board of the Howard Hughes Medical Institute and the Max Planck Institute for Terrestrial Microbiology. She is the recipient of the Proctor and Gamble Award in Applied and Environmental Microbiology and she is an elected member of the American Association for the Advancement of Sciences and the American Academy of Microbiology.

Sophie Helaine

Harvard Medical School

I graduated from Universite Paris 5, France and moved to London in 2007 at Imperial College London for my postdoc. I obtained an MRC Career Development Award in 2015 to launch my independent career. In August 2019, I moved my lab from Imperial College London, UK and I joined the Department of Microbiology in Harvard Medical School. My lab studies the molecular mechanisms of bacterial persistence during infection.

Deborah Hung

Harvard Medical School, Massachusetts
General Hospital, Broad Institute of MIT & Harvard

Dr. Deborah Hung is Professor of Genetics at Massachusetts General Hospital and Harvard Medical School, a Core Faculty Member, Co-Director of the Infectious Disease and Microbiome Program, and Director of the Center for Integrated Solutions to Infectious Disease at the Broad Institute of MIT & Harvard, and an attending physician in infectious diseases and pulmonary & critical care medicine at Brigham & Women's Hospital. She is also the director of the NIAID-funded Center of Excellence in Translational Research that is focused on innovative technologies for antibiotic discovery. She works at the interface of chemical biology, genomics, and bacterial pathogenesis to establish new paradigms for an antibiotic based on the essential biology required for a pathogen to cause disease within the host. Using her training as a synthetic chemist, bacterial geneticist, and clinical physician, she explores approaches to disrupting the pathogen-host interaction.

Dr. Hung received her BA and PhD from Harvard University and medical degree from Harvard Medical School. She completed a residency in internal medicine and fellowships in infectious disease and critical care medicine at Brigham and Women's Hospital and Massachusetts General Hospital.

Roy Kishony

Technion–Israel Institute of Technology

Prof. Kishony is the Marilyn and Henry Taub Professor of Life Sciences at the Faculty of Biology and Faculty of Computer Science (secondary) at the Technion-Israel Institute of Technology. Prof. Kishony received his B.A. in Physics and Mathematics from the Hebrew University and his Ph.D. in Physics from Tel-Aviv University (1999). He moved to Biology as a postdoc at Princeton and Rockefeller Universities and continued as a Bauer Fellow at Harvard University. In 2005 he joined the newly established Department of Systems Biology at

Harvard Medical School, where he was rapidly promoted to a Full Professor (2011). He joined the Technion in 2014 to lead interdisciplinary research at the interface of quantitative biology and biomedicine.Prof. Kishony is a world-renowned pioneer in developing and applying mathematical, computational, and experimental tools at the frontiers of biomedicine with a specific focus on antimicrobial multi-drug therapy. He uniquely bridges from elegant and daring experimental approaches, through bold new conceptual, theoretical, and computation ideas, to impactful bioinformatics research-to-bedside discoveries.

His lab has made a series of ground-breaking discoveries, showing how some drug interactions can select against resistance, unraveling mechanisms that keep resistance in check-in natural ecological environments, and pioneered unique experimental and theoretical methodologies for tracking the whole-genome evolution of pathogenic bacteria. The video of his experiment of evolving bacteria on a "MEGA-plate" was viewed more than 30 million times, making it one of if not the most viewed science videos in the world. These new approaches and discoveries inspire novel treatment paradigms for effective antimicrobial chemotherapy and genome-based diagnostics. Most recently, Kishony has contributed to the urgent understanding of COVID-19 and vaccine effectiveness, with his studies highlighted as part of key policymaking decisions by Dr. Walensky, Director of the USA Center for Disease Control, and by the Chief Medical advisor to the President, Dr. Fauci.

Carl F. Nathan

Weill Cornell Medicine

Carl Nathan studies host defense and pathogen resistance. He graduated from Harvard College and Harvard Medical School, trained in internal medicine and oncology at Massachusetts General Hospital and Yale and joined The Rockefeller University from 1977-1986. At Weill Cornell Medicine thereafter, he served as Stanton Griffis Distinguished Professor of Medicine, founding director of the Tri-Institutional MD-PhD Program, acting dean, and chair of the Department of Microbiology and Immunology. In the Weill Cornell Graduate School of Medical Sciences, he served as co-chair of the Program in Immunology and Microbial Pathogenesis and then dean. He served as a trustee of the Hospital for Special Surgery and on the SABs of the Global Alliance for TB Drug Development and the Cambridge Institute for Medical Research and is currently associate scientific director of the Cancer Research Institute, a governor and trustee of the Tres Cantos Open Lab Foundation and on the SAB of the Rita Allen Foundation. Nathan led the planning team for the Tri-Institutional Therapeutics Discovery Institute and serves on its board of directors. He helps edit the Journal of Experimental Medicine, Proceedings of the National Academy of Sciences and Science Translational Medicine. He was awarded the Robert Koch Prize and the Sanofi-Institut Pasteur Senior International Scientist Award and has been elected to the American Academy of Arts and Sciences, the National Academy of Medicine and the National Academy of Sciences.

Richard Lenski

Michigan State University

Richard Lenski is the John Hannah Distinguished Professor of Microbial Ecology at Michigan State University. His research examines the genetic mechanisms and ecological processes that are responsible for evolution. In an ongoing experiment that he started in 1988, he and his team have studied 12 populations of E. coli as they evolve in and adapt to a controlled environment for 75,000 generations. This work has generated insights into the dynamics of adaptation by natural selection and genome evolution during periods of both innovation and optimization. Samples are stored periodically in freezers, and the cells that lived in different generations can be revived and directly compared with their ancestors—in effect, allowing time travel. Lenski has served as President of the Society for the Study of Evolution, and he helped found the BEACON Center for the Study of Evolution in Action, which brings together biologists, computer scientists, and engineers to illuminate and harness the power of evolution. He is a member of the American Academy of Microbiology, the American Academy of Arts and Sciences, the American Philosophical Society, and the U.S. National Academy of Sciences, and he has had fellowships from the MacArthur and Guggenheim Foundations. Lenski has mentored dozens of graduate students and postdoctoral associates who are on the faculties of universities around the United States and the world.

Ilan Rosenshine

The Hebrew University of Jerusalem

Dr. Ilan Rosenshine obtained his Ph.D. from Tel Aviv University for his research in the biology of halophilic archaebacteria, followed by post-doctorate training at the University of British Columbia investigating host-pathogen interactions. In 1995 he received a position in the Department of Biotechnology and Molecular Genetics of the Hebrew University of Jerusalem (HUJI) and served in various academic and administrative functions. Currently, he is a professor in the Department of Microbiology and Molecular Genetics and Vice-dean for academic affairs in the Faculty of Medicine of the Hebrew University of Jerusalem.The Rosenshine research group studies the mechanism of bacterial virulence exploiting enteropathogenic *E. coli* (EPEC) and its interaction with epithelial cells as a primary model system. EPEC is a human pathogen that targets the intestine, causing conditions ranging from chronic asymptomatic colonization to acute life-threatening disease. This pathogen carries powerful virulence machinery termed type III secretion system (T3SS) that functions as a nano syringe utilized to inject proteins termed effectors into the host cells. The injected effectors subvert an array of host cell processes to benefit the pathogen. The Rosenshine group exploits this experimental system

to elucidate fundamental host-pathogen interactions and bacterial biology principles. They explore how the pathogen modulates the host immune response by an array of anti-immunity effectors; how the pathogen senses host attachment and in response rearranges its gene expression program to adapt itself to a host-attached lifestyle; and how the attached pathogen extracts nutrients from the injected cells using membranous nanotubes that bridge between the pathogen and host.

Jacob Scott
Cleveland Clinic

I am a veteran of the US Navy submarine force turned academic physician-scientist. Our lab pursues research decomposing the complexity of cancer and infections through mathematical and experimental modeling and the biological and clinical validation of these models. My educational background in physics, medicine, mathematics and engineering gives me a unique perspective on cancer, systems biology and infectious disease and provides a multi-fluency which allows me the opportunity to effectively communicate with professionals across many disciplines. I have worked extensively on mathematical modeling of disease evolution and treatment using a variety of models including evolutionary game theory, cellular automata, differential equations and Markov chains. My DPhil thesis focused on the role of heterogeneity, both genetic and microenvironmental, on cancer evolution and radiation response. Since starting my own laboratory, which we call Theory Division, we have begun to diversify, and the lab now has a significant experimental component, conducting experimental evolution in cancer cell lines as well as bacteria. Our laboratory holds dear the tenets of open science and inclusivity, and we are proud to host a diverse collection (intellectually, academically, socio-culturally and ethnically) of people working together in harmony. The combination of mathematics, experimental evolution and a clinical focus makes our laboratory stand out as one of the most interdisciplinary in the field of translational cancer evolution and evolutionary medicine, and our culture cements us a destination in which people of all walks of life can thrive in a welcoming environment. I am eager to use harness the distinct perspective that our diversity and curiosity provide to help advance the field of evolutionary therapy to help our patients and those around the world.

Rotem Sorek

Weizmann Institute of Science

Prof. Rotem Sorek received his PhD in Human Genetics from Tel Aviv University on 2006. Between the years 2006-2008 he conducted post-doctoral studies in Berkeley, CA, and on 2008 he joined the Weizmann Institute of Science.

The Sorek lab investigates phage biology and phage-bacteria interactions. Sorek is a co-inventor of 40 patents and patent applications and founded 3 biotech companies based on technologies developed in his lab. He has received numerous prestigious awards and is a fellow of the American Academy of Microbiology and EMBO.

Paul Turner

Yale University

Dr. Paul E. Turner is the Rachel Carson Professor of Ecology and Evolutionary Biology at Yale University, and Microbiology faculty member at Yale School of Medicine. He obtained a BA in Biology (1988) from University of Rochester, a PhD in Microbial Evolution (1995) from Michigan State University, and did postdocs at National Institutes of Health, University of Valencia in Spain, and University of Maryland-College Park. Dr. Turner joined Yale in 2001 and became Full Professor in 2011. He served 3 years as Director of Graduate Studies and 7 years as Department Chair. In addition, Turner served 1.5 years as Yale's Interim Dean of Science, and 5 years as Chair of the Biological Sciences Tenure & Promotion Committee, for Yale University and Yale School of Medicine. Dr. Turner is Director of the Center for Phage Biology & Therapy, as well as the Quantitative Biology Institute at Yale. Dr. Turner's current service includes the National Science Foundation's Bio Advisory Committee, the Health and Medicine Division Committee of the National Academies of Sciences, Engineering & Medicine, and editorships at several scientific journals. He is President-elect of the International Society for Evolution, Medicine and Public Health. Dr. Turner's honors include Fellowships in the National Academy of Sciences, American Academy of Arts & Sciences, and American Academy of Microbiology.

Dr. Turner examines the evolutionary genetics and genomics of microbes, especially virus ability to adapt (or not) to biotic/abiotic environmental changes at all levels of biological organization: molecules, proteins, cells, populations, communities and ecosystems. Turner's group studies a wide variety of RNA and DNA viruses, particularly phages that infect bacterial pathogens and RNA viruses transmitted by mosquitoes, and researches the use of phages to treat antibiotic-resistant bacterial diseases. He is very active in science-communication outreach to the general public, and is involved in programs where faculty collaborate with K-12 teachers to improve STEMM education in underserved public schools.

Ada Yonath

Weizmann Institute of Science

Ada Yonath is focusing on the translation of the genetic code to proteins by ribosomes, on antibiotics hampering this process, on human diseases associated with ribosomal mutations and on origin of life. She initiated these studies despite persistent global skepticism, and introduced forefront key scientific developments, which became common routines.

She is the director of the Kimmelman Center for Biomolecular Structures at Weizmann Institute (WIS), where she got her PhD and is currently a Professor. She postdoced at CMU, MIT and U. Chicago. In the seventies, she established at WIS a structural-biology lab, which was the only one in Israel for almost a decade. During 1986-2004, she headed Max-Planck-Research-Unit-for Ribosome-Structure in Hamburg, in parallel to her WIS activities.

Among others, she is a member of US-National Academy; British Royal Society; Israel Academy; German Leopoldina; Pontificia Accademia-delle-Scienze (Vatican); Japanese, Korean, Italian & European Academies, and holds honorary doctorates from over 45 Universities worldwide. Her awards include Louisa-Gross-Horwitz, Wolf, Harvey & Israel prizes; Linus-Pauling Gold Medal; UNESCO/L'Oreal Prize; Albert-Einstein Award for Excellence; and the 2009 Nobel Prize.

2nd Blavatnik US-Israel Scientific Forum

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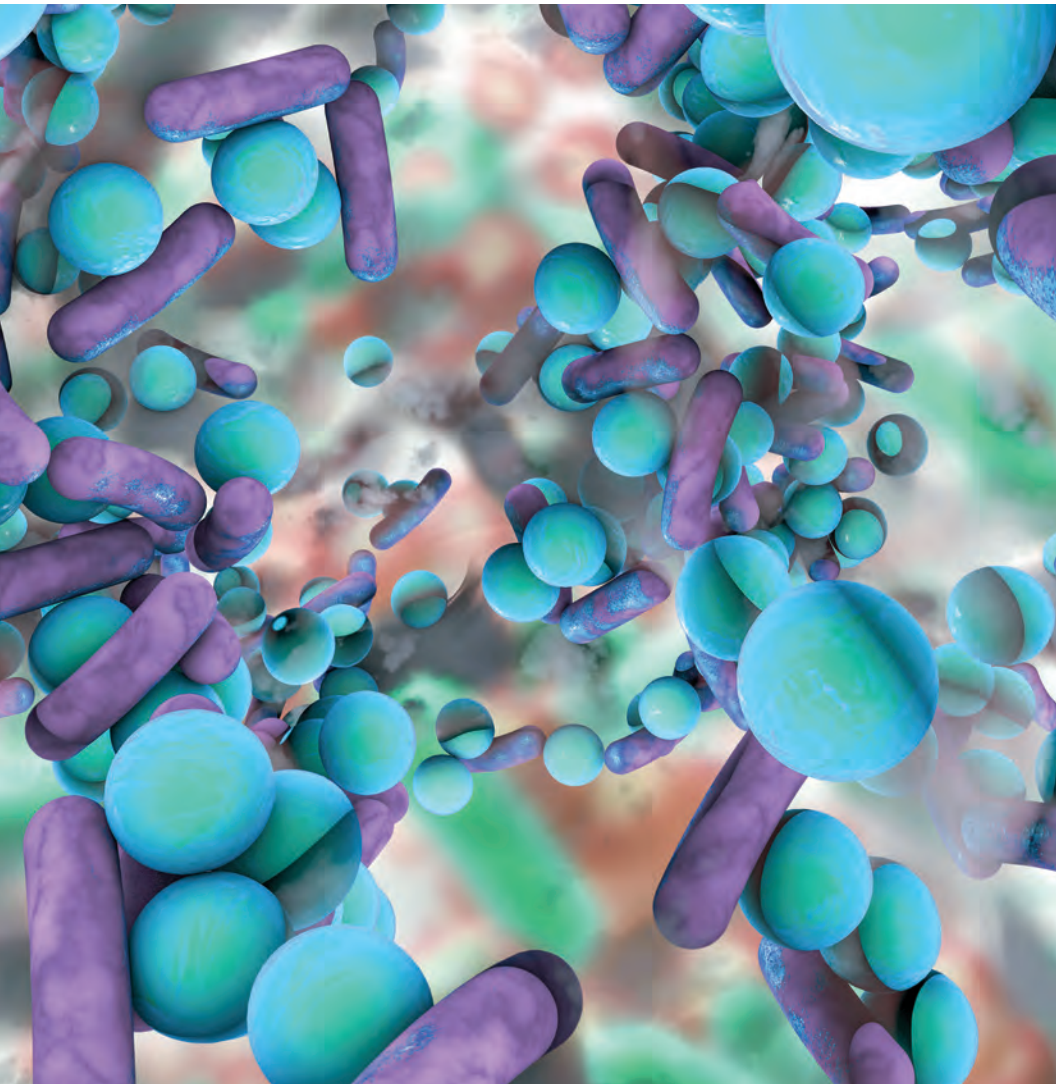

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